Monika Thakur
Tarun Belwal *Editors*

Bioactive Components

A Sustainable System for Good Health and Well-Being

Springer

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Preface

The doctrine "*Let thy food be thy medicine and thy medicine be thy food*" espoused by Hippocrates nearly 2500 years ago is receiving renewed interest nowadays. In particular, there has been an explosion of consumer interest in the bioactive functional food components that have therapeutic and medicinal properties. The nutritional and bioactive components play a pivotal role to fight against many physiological disorders and sustain the health and well-being of an individual. The foods having both medicinal and nutritive value are of need in the current scenario. The massive abundance of studies relating to balanced nutritional approach and its effects on health has increased strikingly over the last few decades. The functional components are the ingredients that offer health benefits beyond their nutritional values; therefore, it is essential to have a comprehensive review and research on the sources and application of functional bioactive components.

First, it is necessary to understand the relationship between food and health outcomes, and then focus upon the sources of bioactive components and their role in health. Due to changing lifestyles and consumer awareness, there is a trend towards functional food. Therefore, scientists and technologists are focusing to develop functional foods, with knowledge of their extraction techniques and claims of health-promoting benefits. The bioactive components present in functional foods and nutraceuticals are sensitive to different processing technologies; therefore, researcher and scientists are always trying their best to adopt the processing technologies that minimally affect the bioactive components present in functional foods. Hence, this book will comprehensively discuss the bioactive components, their sources, extraction techniques, advancement in functional foods and nutraceuticals, and their role against various health-related issues.

A lot of research in the form of books, research publications, compendium and monographs is available, but no such complete information is available on the use of bioactive components with their sources, characterization, application, and finally their sustainability.

This book will be comprehensive and compendious approach as balanced and organized structure of "**Bioactive components: sources, applications & sustainability**". All chapters are contributed by academicians, food scientists, technologists and also medical practitioners with the interest of modern-day consumers in mind. The book addresses both the theoretical and applied aspects of bioactive components.

The book provides a very comprehensive outline on bioactive components and is divided into **four major parts** with **34 different chapters** in different areas of life sciences, food science and technology, functional foods and nutraceuticals, which balance perspectives and vision for new innovations, sources, applications and sustainability in bioactive components. All chapters in different sections have been written by key scientists with diverse backgrounds in industry/R&D/academia and will provide an update on emerging ideas and sustainable technologies as well as a vision for the future.

Part I deals with **Introduction to Bioactive Components** which has been covered in seven chapters as primarily focusing on bioactive components and their sources with respective health benefits.

Part II deals with **Bioactive Components: Technological Trends, Regulatory and Safety Aspects** elaborated in five chapters. This part deals with different technological trends, regulations, and safety aspects of bioactive components.

Part III deals with the **Role of Bioactive Components in Human Health** compiled in eight chapters that cover the role of functional foods in combating various health-related issues.

Part IV covers **Functional Foods: Emerging and Sustainable Innovative Trends** and consists of 14 different chapters. This part provides current knowledge and innovative developments related to the use of bioactive components in various food products.

There are many excellent books on Functional Foods and Nutraceuticals. This book is not designed to compete with these books. Rather, this book offers another option, both in approach and contents. Readers, technical institution, food technologists, technocrats, existing industries and new entrepreneurs will find valuable material in this book. This book gives a detailed introduction to bioactive components from different sources, technological trends, regulatory and safety aspects, and emerging and sustainable methods for their utilization. Comprehensive in scope, the book provides the knowledge and solutions specific to sustainable food systems for good health and well-being.

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Hangzhou, China Tarun Belwal

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Bioactive Components: A Sustainable System for Good Health and Well-Being provides a comprehensive review of food industry waste, standards, management, utilization of waste from food processing industries and emerging technologies on sustainable food waste management in the food sector. We are extremely indebted to Respected Founder President, **Dr. Ashok K Chauhan**, for the blessings and constant encouragement. We have great pleasure in acknowledging the whole-hearted support received from **Dr. Atul Chauhan**, Chancellor, Amity University Uttar Pradesh, and President RBEF; without their encouraging words, this endeavour is impossible. We are thankful to **Prof. Balvinder Shukla**, Vice Chancellor, Amity University Uttar Pradesh, for her constant motivation and support at all the stages of the progress.

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We are extremely indebted to all the authors who have contributed chapters and happily agreed to share their work on various aspects of bioactive components, their sources, potential applications and sustainability. Without their painstaking efforts, it would not have been possible for us to bring this volume. Our sincere thanks to Springer Publishing for their full support and cooperation during the publication of this volume. We are very thankful to the production team, Springer, for all their efforts in publishing the book.

At last, we want to acknowledge the gratitude of our family members for their astounding support and encouragement.

Contents

Part II Bioactive Components: Technological Trends, Regulatory and Safety Aspects

Part III Role of Bioactive Components in Human Health

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Monika Thakur works as an Associate Professor at the Amity Institute of Food Technology, Amity University, Uttar Pradesh, India. She is currently engaged in the development of functional foods, extraction of bioactive components, fungal functional potential, and bio-colorants. She was awarded a PhD in 2006 by Himachal Pradesh University. She is a double gold medalist (MSc and MPhil) and has received several prestigious awards such as Himalayan Research Scholar Association Award (2007); Young Scientist Award, IITT 2020; Best Speaker Award (2020, 2021); and Young Researcher Award (2021). Apart from her teaching assignments, she has been involved in various research and extension activities. So far, she has published more than 70 publications, holds patents and copyrights, and has 6 books to her credit. She has completed two industrial projects and is currently involved in a DST-sanctioned project.

Tarun Belwal working in the Department of Drug Science and Technology, University of Turin, Italy, is exploring food science, waste valorization, plant nutraceutical potential, and human health, including the effect of food bioprocess techniques on its quality and other functional attributes. He is currently engaged in the development and promotion of safer and greener food bioprocess techniques and valorization of food waste. Previously, Dr. Belwal worked at the College of Biosystems Engineering and Food Science, Zhejiang University, China. Dr. Belwal received his PhD (Plant Biotechnology) from Kumaun University, Uttarakhand, India, collaborating with G.B. Pant National Institute of Himalayan Environment (NIHE), Uttarakhand, India. So far he has edited 3 books, published more than 100 international peer-reviewed research articles, and authored 14 book chapters. His research work has been cited more than 2500 times.

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Abbreviations

%	Percent
&	And
/	Per
μg	Microgram
μl	Microlitre
μm	Micrometre
AAP	American Academy of Pediatrics
ACh	Acetylcholine
AHA	American Heart Association
AMD	Age-related macular degeneration
AP	Ascorbyl palmitate
ATPS	Aqueous two-phase systems
BCC	Business Communication Company
BHA	Butylated hydroxyanisole
BHT	Butylated hydroxytoluene
BMI	Body mass index
BRCGS	British Retail Consortium Global Standard
CFU/ml	Colony forming unit per ml
CLA	Conjugated linolenic acid
cm	Centimetre
conc.	Concentrated
DES	Deep eutectic solvents
DF	Dietary fibre
DHA	Docosahexaenoic acid
dil.	Dilute
DNA	Deoxy ribonucleic acid
e.g.	For example
EAE	Enzyme-assisted extraction
EAEP	Enzymes-assisted aqueous extraction processing
Ed.	Edition
ed.	Editor
eds.	Editors
EFSA	European Food Safety Authority

EMA	European Medicines Agency
et al.	Et alia; and others
etc.	et cetera
FAO	Food and Agriculture Organization
FBO	Food Business Operator
Fig.	Figure
FOSHU	Food for specified health use
FSSAI	Food Safety Standards Authority of India
FTIR	Fourier Transform Infrared Spectroscopy
g	Gram
GC	Gas chromatography
GERD	Gastroesophageal reflux disease
GIT	Gastrointestinal tract
GMP	Good manufacturing practices
GRAS	Generally recognized as safe
HACCP	Hazard analysis critical control point
HIV	Human immunodeficiency virus
HPLC	High-performance liquid chromatography
HPLC	High-pressure liquid chromatography
HPMCP	Hydroxypropyl methyl cellulose phthalate
HPP	High-pressure processing
HPTLC	High-performance thin layer chromatography
hrs.	Hours
HVEF	High voltage electric field
i.e.	That is
IAPB	International Agency for Prevention of Blindness
in vitro	Within glass
in vivo	Within the living
Kg	Kilogram
l	Litre
LD	Longissimus dorsi
LDL	Low-density lipoprotein
m	Metre
mAChR	Muscarinic metabotropic receptor
MAE	Microwave-assisted extraction
MEP	Non-mevalonate pathway
mg	Milligram
min	Minutes
miRNA	Micro-ribonucleic acid
ml	Millilitre
mln tons	Million tonnes
mm	Millimetre
MMT	Million metric tonnes
MoFPI	Ministry of Food Processing Industry
MS	Mass spectrometry

MUFA	Monounsaturated fatty acid
nAChR	Nicotinic ionotropic receptor
NADES	Natural deep eutectic solvents
NCED	Non-communicable eye diseases
NMR	Nuclear magnetic resonance
NTP	Non-thermal processing
°C	Degree Celsius
PA	Phytic acid
PACAP	Pituitary adenylate cyclase-activating polypeptide
PCOS	Polycystic ovarian syndrome
PEFAE	Pulsed electric field-assisted extraction
PG	Propyl gallate
PGC	Peroxisome proliferator-activated receptor gamma coactivator
PHWE	Pressurized hot water extraction
PLE	Pressurized liquid extraction
PLE	Pressurized liquid extraction
PPAR	Peroxisome proliferator activator receptor-α
PUFA	Polyunsaturated fatty acid
qRT PCR	Real-time quantitative reverse transcription
QS	Quorum sensing
RHT	Retinohypothalamic tract
RT	Room temperatures
RTE	Ready to eat
SCFE	Supercritical CO_2 fluid extraction
SDGs	Sustainable development goals
SE	Solvent extraction
SFC	Supercritical fluid extraction
SFQ	Safe quality food
Snc RNA	Small nuclear ribonucleic acid
sp.	Species (singular)
spp.	Species (plural)
sq. Km	Square kilometre
SSR	Sample solvent ratio
SubFE	Subcritical fluid extraction
TBHQ	Tert-butylhydroquinone
TLC	Thin layer chromatography
UAE	Ultrasound-assisted extraction
UCGE	Ultrasonic cell grinder extraction
U-NPCE	Ultrasound-negative pressure cavitation extraction
USDA	United States Department of Agriculture
UTI	Urinary tract infection
UV	Ultraviolet
var.	Variety
viz.	Videlicet; namely

vol. (s)	Volume(s)
w.r.t.	With respect to
WE	Water extraction
WHO	World Health Organization

List of Figures

List of Tables

Part I

Introduction to Bioactive Components

Introduction on Bioactive Compounds, Sources and their Potential Applications

1

Mrigya Bansal, Amrita Poonia, Sujohn R. Paulson Kolluri, and Vasundhara

Abstract

Bioactive components are active compounds present in small quantities in food having the ability to improve present or prevent any potential health condition. Compounds such as bioactive peptides, phytosterols, fibers, fatty acids, and vitamins have the ability to regulate various metabolic processes in human body such as free radical scavenging, inhibition or induction of gene expression, receptor activity, and enzymes. These compounds are becoming an essential ingredient for numerous food industries and food industry-based startups to come up with products that meet the increasing demand of consumer for natural, nutritious, and economical products. Natural and economical sources such as food industry waste, inedible portions of food (seeds, peels, fish head, etc.), aquacultural by-products, and secondary metabolites (microorganisms, plants, and animals) are being used for the extraction of these compounds. The exploitation of such sources contributes well to the economy and environment. Before the incorporation of these bioactive compounds into food application bioaccessibility (release of the compounds from the ingested food system into the gastrointestinal tract), bioavailability (quantity in the circulatory system after digestion and absorption) and bioactivity (physiological response of human on their reaction with other compounds) of these compounds should be taken into consideration.

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Encapsulation of bioactive compounds is a potential approach to stabilize their bioactivities, control their release, and increase their bioavailability. These are potential elements to replace numerous synthetic or artificial additives and dietary supplements. Still, a lot of detailed study and laboratory research need to be done to use these compounds to their full potential.

Keywords

Bioactive components · Waste · Encapsulation · Bioaccessibility · Bioavailability

1.1 Introduction

Bioactive compounds are naturally occurring biologically active extra nutritional compounds. Various food and food products of plant, animal, and aquatic origin contain these compounds in small quantities. Due to the presence of bioactive compounds, these foods are able to provide benefits beyond the delivery of the basic nutrients (Kris-Etherton et al. 2002). These compounds provide health benefits owing to their ability to regulate and modulate one or more essential metabolic processes and functions (Galanakis 2017; Kitts 1994). These biologically active compounds are generally produced as secondary metabolites by plants and microorganisms.

Increasing awareness about the effect of diet on the individual's health and well-being gives rise to consumers' concern about what they are being served in the name of RTE or processed foods (Day et al. 2009; Mollet and Rowland 2002). Numerous chronic diseases (obesity, diabetes, metabolic syndrome, cancers, etc.) are progressing as an effect of various environmental factors, specific type of eating (consumption of food high in fat, sugar, and salt), and lifestyle habits (lack of exercise, inactivity) (WHO 2003; Moebus and Stang 2007; Shahidi 2009). Foreseeing possibilities of chronic diseases, consumers demand for foods with health-promoting elements other than just containing basic nutrients and calories (Bech-Larsen and Scholderer 2007; Hasler 2002). As per the increasing demand of the consumer, now food industries also need to keep the focus on health-promoting element of the food and food ingredients other than just safety of these food and food ingredients (Day et al. 2009). In light of current scenario, the inclusion of natural bioactive compounds in processed food products is gaining more importance for food industries (Shahidi 2009). It will also aid in changing consumer perception that unprocessed or minimally processed foods hold more health benefits than their processed versions (Shahidi 2009). Therefore, more and more industries are engaged in the extraction of natural bioactive compounds so that these compounds can be used as additives in food processing where they will serve both the purposes of technological advancement in processing and health benefits to the consumers (Galanakis et al. 2013). Soluble dietary fibers are examples of one such bioactive compound. Food industries have initiated to incorporate these as fat substitutes and gelling agents, which lower the blood lipids level and stabilize emulsion,

Fig. 1.1 Source-based classification (Kumar et al. 2017*;* Zhao et al. 2015; Zhang et al. 2015; Tang et al. 2015)

respectively (Elleuch et al. 2011; Galanakis 2011, 2015; Galanakis et al. 2010; Patsioura et al. 2011; Rodríguez et al. 2006). Similarly, compounds such as ascorbic acid, polyphenols, tocopherols, and carotenoids can execute both preservation (vegetable oil and emulsions) and nutritional (reducing aging process, preventing cancer, etc.) functions by scavenging free radicals (Galanakis 2015; Galanakis et al. 2015; Moure et al. 2001) (Fig. 1.1).

1.2 Usual and Unusual Applications of Bioactive Compounds

Generally, these naturally ubiquitous bioactive compounds are added to the staple foods or food products to supply healthy calories and health-promoting nutrients to the consumer's daily diet. These compounds have the potential to synchronize essential metabolic processes in human body; a few to name are free radical scavenging, inhibition, or induction of gene expression, and receptor and enzymatic functioning (Correia et al. 2012). Biological activities such as antimicrobial, anticarcinogenic, antimutagenic, antiallergenic, antioxidant and antiinflammatory activities demonstrated by these compounds adds to their necessity for inclusion these compounds in the daily diet (Ham et al. 2009; Parvathy et al. 2009). Their addition to the food will contribute to treating and preventing various present and potent lifestyle diseases, respectively. After closely observing the current and near-future lifestyle and needs of the people, many commercial industries, such as pharmaceuticals, food, and chemicals, are setting foots into the business of bioactive compounds extraction. Other than the above described benefits, these compounds can also serve as food additive and processing aid of natural origin to food industries (Hamzalıoğlu and Gökmen 2016). Some of these could be as follows:

1. **Antioxidant**—Processing and prolonged storage conditions generate free radical in the food systems, which will affect the food quality. Bioactive compounds acting as antioxidant will resolve this problem by scavenging free radicals and single oxygen molecules, chelating metal ions (inducing agent), breaking chain reaction (autoxidation), reducing oxygen concentration in the storage or processing system, etc. (Frankel and Meyer 2000).
2. **Enzyme Inhibition or Induction**—These compounds will aid during the processing of the inhibition/induction of a particular type of reaction by controlling the activity of the enzyme (Correia et al. 2012).
3. **Coloring Agent**—Natural coloring agents such as anthocyanins, carotenoids, curcumin, and squid ink can replace all the synthetic colorants that are highly stable in the food systems but extremely toxic and non-nutritive at the same time to the masses.
4. **Flavoring Agents**—Various natural flavors such as **c**innamaldehyde and vanillin are used for flavoring sweet foods, chewing gums, and beverages (Hamzalıoğlu and Gökmen 2016).
5. **Antimicrobial Agents**—Food is the most suitable medium for the growth of millions of both food spoilers and foodborne pathogens. Food spoilers attack the organoleptic aspects of food by metabolizing various compounds in food to produce off-flavor, gases, slime, etc., and foodborne pathogens render the same unsafe for consumption. Antimicrobial agents such as phenolic compounds will enable us to get food, which is intact in quality and safe for consumption (Reineccius 1991; Bhattacharya et al. 2010).
6. **Texturizing Agents**—Various nutritive and non-nutritive gums, dietary fibers (soluble and insoluble), etc., can be used as texturizing agent. These compounds with their appreciable water- and oil-holding capacity enhance the solubility and

viscosity, which directly contribute to the textural element of the food products. Also, dietary fibers will maintain healthy gut and assist in body weight management (Elleuch et al. 2011).

7. **Fortifying Agent**—Bioactive compounds after extraction and purification can be used to fortify various staples (rice, salt, milk, oils, etc.) and vulnerable population targeted food products to provide them with deficient and essential components (functional and nutraceutical products).

1.3 Extraction Methods

Extraction involves combining a pretreated raw material with an appropriate solvent to ensure the complete dissolution of the bioactive compound of interest in the solvent, while the other components such as cells and tissues (other inert compounds) remain undissolved in the system (solvent + pretreated raw material). This process of extraction is dependent on numerous factors such as temperature, nature of the solvent, pressure, and type and portion of the raw material (plant, animal, microbes, etc.) (Khoddami et al. 2013; Smith 2003; Sasidharan et al. 2011; Baiano 2014). There are specific techniques for the extraction of each type of bioactive compound. These extraction techniques can be broadly classified into two major categories, i.e., conventional (maceration, hydrodistillation, and Soxhlet extraction) and nonconventional (pulse electric field, microwave-assisted, solvent extraction, subcritical water, supercritical fluid extraction, fermentation, controlled pressure drop, pressurized liquid, and ultrasound-assisted) techniques (Azeez et al. 2017) (Fig. 1.2).

1. **Maceration**—Within a closed vessel ground material (physically pretreated) is soaked in a suitable solvent for extraction of bioactive compound. Solution (containing bioactive compound and solvent) is separated while the remaining marc is pressed to extract the remaining solution (Azeez et al. 2017).
2. **Soxhlet Extraction**—Dried raw material along with a specific solvent is subjected to repeated heating and condensation in a distillation unit until exhaustive extraction of the bioactive compounds is achieved. It ensures the extraction of the targeted compound into the solvent, which is then collected in the distillation flask (Azeez et al. 2017).
3. **Hydrodistillation**—Either the targeted material is packed with boiling water or injected with steam so that water can be used as a solvent for the extraction of bioactive compounds. It involves diffusion, hydrolysis, and decomposition by heat using water (Silva et al. 2005).
4. **Pulse Electric Field**—Exposing raw material to moderate electric field (500 and 1000 V/cm) for 10–20 s enhances the permeability of the cells. Exposure to pulse electric field ruptures the membranes of the cells (raw material), which enhances the efficiency of extraction (Fincan and Dejmek 2002).
5. **Solvent Extraction**—Various solvents such as methanol, acetone, ether, ethanol, and hexane are used for selective extraction of the polar and nonpolar bioactive compounds (Plaza et al. 2010).

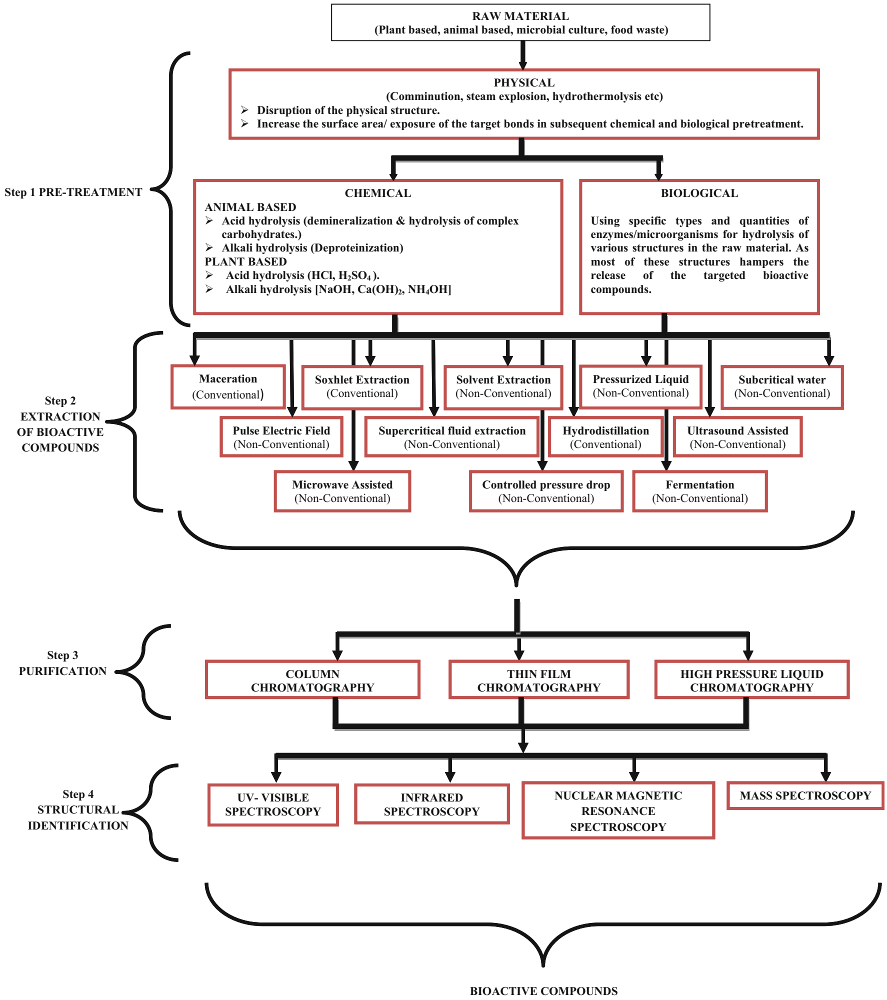

Fig. 1.2 Step of producing bioactive compounds (Azeez et al. 2017; Altemimi et al. 2017)

6. **Supercritical Fluid Extraction**—Targeted material is placed along with solvents such as methane, nitrogen, and ethylene in temperature-controlled and pressurized chambers for the extraction of bioactive compounds (Daintree et al. 2008; Cavero et al. 2006). Solvents under high temperature and pressure reach their supercritical state that has a better transportation property owing to their liquid-like density and gas-like viscosity (Herrero et al. 2006).
7. **Pressurized Liquid**—This type of extraction is performed at higher temperature (50–200 °C) and pressure (1450–2175 psi) to lower down the polarity of the solvents. Temperature can be utilized to match the polarity of solvent to that of

the targeted compounds. Pressure will push the solvent into the matrix of the raw material (Dunford et al. 2010; Miron et al. 2011).

8. **Subcritical Water**—Technique involves decreasing the dielectric constant of water to various values by using hot water (100–374 °C) at high pressure (10 to 60 bar) so as to replace normally used organic solvents with water for extraction of the bioactive compounds from the targeted raw material (Herrero et al. 2006).
9. **Fermentation**—Submerged (in liquid medium containing nutrients) or solid-state (on solid particles with the absence or presence of direct water) fermentation is practiced for the production of various bioactive compounds (Pandey 2003). These compounds are produced after the complete growth of specific microorganisms on the raw material as secondary metabolites (Nigam 2009). These compounds are also produced when one of the key nutrients is exhausted in the media for their growth (Barrios-González et al. 2005).
10. **Controlled Pressure Drop**—Material is exposed to saturated steam for a short duration followed by immediate pressure drop, which initiates auto-vaporization of volatile compounds (Ben Amor and Allaf 2009). Further instantaneous cooling due to pressure drop causes expansion of the material and hampers the thermal degradation (protect heat-sensitive compounds). This improves the mass transfer and recovery (Allaf et al. 2013).
11. **Microwave-Assisted**—Microwaves evaporate the moisture inside the cells by heating the water naturally present inside these cells. Pressure is built within these tissues when evaporation ruptures their cell wall and organelles, thereby enhancing the porosity of the biological matrix (Routray and Orsat 2012). This enhanced porosity of the raw material increases the solvent contact with the targeted compounds, which ultimately increases the yield of the same compound.
12. **Ultrasound-Assisted**—Acoustic cavitation is caused by the expanding cycles of the ultrasonic waves wherein bubbles/cavities are created in the liquid used for extraction. These bubbles after absorbing energy from the ultrasonic waves begin to collapse violently, which disintegrates the cells by hitting the surface of solid matrix of the raw material. This rupturing facilities the release of bioactive compounds (Leighton 2007; Soria and Villamiel 2010; Esclapez et al. 2011) (Table 1.1).

1.4 Bioaccessibility, Bioavailability, and Bioactivity

The three terms are interrelated to each other as a bioactive compound to perform its key activity on the living system, which needs to be available in the living system. For this compound to be available in the living system, it needs to be released out of the matrix along with which it was ingested. Bioaccessibility, bioavailability, and bioactivity decide the fate of the bioactive compounds in the living system. Hence, a detailed research is required about the compound’s bioaccessibility, bioavailability and bioactivity in human body and their respective food delivery systems, before their utilization in fortification and production of functional foods.

Table 1.1 Different bioactive compounds and their sources and mechanism/potential benefits

S. No.	Compounds	Sources	Mechanism/potential benefits	Reference
1.	**Bioactive peptides** (short-chain protein molecules usually less than 20 amino acids)	**Biologically active sources**—Fermented products **Biologically inactive sources**—Casein, whey proteins, lactoferrin, ovotransferrin, fish protein, wheat gluten, soy protein, chicken collagen, amaranth, maize, etc.	**Mechanism**—Presents in native proteins in functionally inactive form. Released after proteolysis (in vivo by digestive juices in human gastrointestinal tract and in vitro by enzymatic hydrolysis or bacterial fermentation) of these native proteins **Potential benefits**—Antihypertensive, hypocholesterolemic, antiobesity, opioid agonistic and antagonistic (pain reliever), antioxidant, anticancer, antidiabetic, immunomodulatory, antithrombotic, osteoprotective, hypolipidemic, increase absorption of minerals (chelating effect) and antimicrobials	Gibbs et al. (2004), Chakrabarti et al. (2014), Jakubczyk et al. (2020), Bhandari et al. (2020)
2.	**Dietary fibers** (edible residues of plants/plant cells that are resistant to hydrolysis/digestion by enzymes of human gastrointestinal tract and absorption in the small intestine, but completely or partially fermentable in the large intestine)	**Insoluble**—Cellulose, hemicellulose, lignin (cereals, legumes, bran portions, etc.) **Soluble**—Pectin, gum, mucilage, β-glucan, psyllium, etc. (seaweed extracts [carrageenan, alginates], fruits and vegetables, plant extracts [gum acacia, gum tragacanth], cereals [oats, barley, etc.], legumes,	**Insoluble**—Absorb water that causes fecal matter to be bulky, soft, and laxative (regulating the bowel movement), decreasing the time of intestinal transit (helps in weight loss), help in weight management (as it binds the bile acids) and glycemic levels (as nondigestible),	Galisteo et al. (2008), Wong et al. (2006), Heredia et al. (2002), Beecher (1999), Kris-Etherton et al. (2002), Sarker and Rahman (2017), Dhingra et al. (2012)

		leguminous seeds [guar, locust bean], microbial gums [xanthan, gellan])	sequester various harmful compounds (protect from colon cancers, etc.) **Soluble**—Act as prebiotic by stimulating growth of various beneficial intestinal microflora, upon colonic fermentation produce various short-chain fatty acids [SCFA] that have beneficial effects on lipid metabolism (prevent cardiovascular diseases [CVD], coronary heart diseases [CHD]). SFCA also has anticancer properties, facilitates extrusion processes, fat replacers (helps in reducing weight), holds moisture in bakery products, etc.	
3.	**Chitin** (polymer of β-(Agiba 2017; Al Khawli et al. 2020; Allaf et al. 2013; Altemimi et al. 2017) linked N-acetyl D-glucosamine) **and Chitosan** (copolymer consisting of β-[1–4]-2-acetamido-D-glucose and β-[1–4]-2-amino-D-glucose units obtained after deacetylation of chitin in alkaline conditions) **(amino polysaccharides)**	Shellfish waste mainly exoskeleton of crustaceans (oysters, shrimps, crabs, etc.), arthropods, mollusks, cell wall of fungi and algae	Antimicrobial activity, anti-inflammatory activity, antioxidant activity, anticarcinogenic activity, antiulcer activity, weight reduction, prevention of type II diabetes, reduce cholesterol level, prevents renal diseases, etc.	Jeon et al. (2000), Kumar (2000), Rinaudo (2006), Al Khawli et al. (2020)

(continued)

Table 1.1 (continued)

S. No.	Compounds	Sources	Mechanism/potential benefits	Reference
4.	**Glucosamine** (amino sugar)	Acid hydrolysis of shellfish by-product, fish, poultry, meat. Fungal biomass, fermentation of agricultural residues (corn cob, wheat bran, wheat straw, rice husk)	Antiviral activity, treatment of osteoarthritis (chondroprotective and anti-inflammatory effect), used in the treatment of migraine and inflammatory bowel disease (anti-inflammatory), precursor for hyaluronic acid, which helps in wound healing, skin hydration, anti-wrinkle treatment, and synovial fluid synthesis. Reduces facial pigmentation caused by melanin by inhibiting tyrosinase (key enzyme in the synthesis of melanin)	Agiba (2017), Lopes Junior and Inácio (2013), Pal et al. (2014), Sitanggang et al. (2012), Patil and Jadhav (2014), Anal (2018), Barrow and Shahidi (2007), Bissett (2006)
5.	**Omega-3 fatty acids** (unsaturated carboxylic acids with long aliphatic chains [even number of carbons] having either two or more double bonds [PUFA] or one double bond at the third carbon atom counting [MUFA] from the methyl end of the carbon chain)	**Monounsaturated fatty acid (MUFA)**—α-linolenic acid (ALA). Flaxseed, sesame seeds, walnuts, cereals, soybean, etc. **Polyunsaturated fatty acid (PUFA)**—Eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA). Fish and fish by-products, microalgae, shrimp, oysters, etc.	Brain development (protect from various cognitive disorders), anti-inflammatory properties (used in the treatment of inflammatory bowel disease, Crohn's disease, rheumatoid arthritis, etc.), reduce cholesterol levels, and treat type II diabetes, antitumor activity. Reduced risk of CVD, CHD, hyperlipidemia, atherosclerosis, colon cancer, pancreatic cancer, prostate cancer, etc. protect cardiac tissues from platelet aggregation. Essential for normal functioning of neurons	Cholewski et al. (2018), Schwalfenberg (2006), Zhang et al. (2015)

6.	**Conjugated linolenic acid (CLA)** (group of positional and geometric isomers of linoleic acid [18 carbons] having two double bonds that are separated by one single bond)	Isomerization and biohydrogenation of the dietary linoleic acid by bacteria in the rumen of ruminants result in the formation of natural CLA. Meat (beef, lamb), milk, dairy products (cheese). Industrial hydrogenation process produces small amount of CLA in partially hydrogenated fats, margarines, and cooking oils	Improves immunity, helps in weight loss and treating obesity (anti-adipogenic activity, i.e., inhibits triglyceride deposition in adipose tissues), antidiabetic (reduces hyperinsulinemia and improves glucose tolerance), anti-atherosclerotic (reduces plaque formation, serum triglycerides, total cholesterol and LDL levels), anticarcinogenic activity (inhibits tumor formation), promote bone development, and reduce resorption	Sehat et al. (1998), Yurawecz et al. (1998), Yurawecz et al. (1999), Zhang et al. (2015), Fernie (2003), Mcguire and Mcguire (2000)
7.	**Carotenoids** (yellow-orange compounds consisting of eight isoprenoid units joined together to form a conjugated double bond network)	**Carotenes** (pure hydrocarbons)—α-carotene, β-carotene (carrots, winter squash, red-orange sweet potato, saffron, dark green leafy vegetables, etc.), and lycopene (tomatoes, tomato products, saffron, etc.) **Xanthophylls** (containing oxygen as functional group)—β-cryptoxanthin (oranges, papaya, peaches, tangerines, yellow and orange maize, etc.), lutein (egg yolk, oil-based supplements, marigold flowers, corn, etc.), astaxanthin (by-products of crustaceans, etc.), and zeaxanthin (maize, green leafy vegetables, eggs, etc.)	Antioxidant activity (protects and prevents cancer, cardiovascular diseases, cataract, age-macular disease, skin cancer, lung cancer, etc.), anti-inflammatory (maintaining bone health and reducing risk of osteoporosis), boosting gap junction communication, immune enhancement, cell–cell signaling, etc.	Mattea et al. (2009), Zhao et al. (2015), Stahl and Sies (2005), Ozaki et al. (2015), Arab and Steck (2000)

(continued)

Table 1.1 (continued)

S. No.	Compounds	Sources	Mechanism/potential benefits	Reference
8.	**Prebiotic** (nondigestible carbohydrates or food ingredient that is neither digested nor absorbed in the small intestine but stimulates growth/activity of selective bacteria in the colon after fermentation by microbiota in large intestine)	Artichoke, banana, flaxseed, soybean, garlic, sugar beet, asparagus, tomato, rye, whole wheat grain, oats, mother's milk, unrefined barley, etc. (fructooligosaccharides, pectin Glucooligosaccharides, Glucooligosaccharides, isomaltooligosaccharides, soybean oligosaccharides, xylo-oligosaccharides, and maltitol)	**Mechanism:** Fermentation by gut microbiota results in the production of SCFA and promotes the growth of beneficial bacteria. Also, these acids change the pH of the gut, which alters the gut microbiota **Health benefits:** Effective in the treatment of obesity, irritable bowel syndrome, and Crohn's disease, protective effects against the risk of colorectal cancer and CVD, enhances the immune system by promoting the response of antibodies, etc., prevents diarrhea, increases the absorption of various minerals such as calcium (improves bone health), reduces risk or severity of skin allergies, etc.	Tang et al. 2015, Varzakas et al. (2018), Walker et al. (2005), Duncan et al. (2009), Davani-Davari et al. (2019)
9.	**Probiotic** (nonpathogenic microorganisms that exert several benefits on host health by stimulating the growth of other microbes after ingestion of an adequate amount of probiotic)	Fermented foods of both animal (yogurt, cheese, etc.) and plant origin (sauerkraut, sinki, miso, etc. (*Lactobacillus rhamnosus*, *Bifidobacteria*, the yeast *species Saccharomyces boulardii and* certain strains of *Lactobacillus casei*, *enterococci*, [*Enterococcus faecium SF68*], *Lactobacillus acidophilus*	**Mechanism:** Acts on various prebiotic to produce various antibiotic and health-promoting substances such as SCFA (organic acids), bacteriocins, hydrogen peroxide, etc. competing with pathogenic bacteria for nutrients and adhesion sites. Blocking binder	Tang et al. 2015, Khalighi et al. (2016), Pandey et al. (2015)

		group, *Escherichia coli* strain *Nissle 1917*, etc.)	site of toxins and degradation of toxins **Benefits:** Arrests all types of diarrhea, beneficial in the management of irritable bowel syndrome and inflammatory bowel disorder, aids in reducing lactose intolerance symptoms, modulates immune system, prevents or delays onset of various types of cancers, beneficial effects on aging, osteoporosis, obesity and type 2 diabetes, etc.	
10.	**Tannins** (water-soluble polyphenols also called as tannic acid)	**Hydrolyzable tannins**—Raspberries, strawberries, olives, mango, pomegranate, oak, meat, fish, wine, etc. **Condensed tannins**—Grapes, grapes skin, berries, apples, red wine, peanut inner skins, coffee beans, chocolates, pine bark, tea and cinnamon bark, etc.	Possess antitumor, anti-inflammatory, antioxidant, and antimicrobial activity. Acts as a cholesterol-lowering agent. Useful in the treatment of various infectious diseases and treatment of type II diabetes. Have the ability to prevent cardiovascular diseases	Zhao et al. (2015), Freile-Pelegrın and Robledo (2014), Chung et al. (1998), Arapitsas (2012)
11.	**Anthocyanins** (water-soluble phenolic compounds of pink, red, blue, and purple color consist of two benzene rings connected by linear three-carbon chain)	Cyanidin, delphinidin, pelargonidin, peonidin, petunidin, and malvidin (fruit and fruit derivatives [wines, juices, jams, strawberries, raspberries, blackberries, cherries, apples, plums, blueberries, cranberries], vegetables [eggplant, red onion, red cabbage], cereal [black rice], etc.)	Antioxidant, anti-angiogenic, anti-inflammatory, anticancer, antiobesity, antimicrobial, and antithrombotic activity helps to prevent neuronal diseases, CVD, illnesses, cancer, diabetes, inflammation and various other diseases, coloring agent, etc.	Krga and Milenkovic (2019), Zhao et al. (2015), Yousuf et al. (2016), Khoo et al. (2017)

(continued)

Table 1.1 (continued)

S. No.	Compounds	Sources		Mechanism/potential benefits	Reference
12.	**Phytoestrogens** (plant-based nonsteroidal compounds with structure and functions closely related to mammalian estrogens)	**Isoflavones (daidzein, genistein, Etc.)** —Clovers (red and white), soybeans, beans, split pea, etc.		Aid in reducing the risk of breast (estrogenic effect), prostate, colon, and other types of cancers based on its antioxidant. Protect people against CVD, menopausal symptoms in women, and osteoporosis	Mostrom and Evans (2011), Kris-Etherton et al. (2002)
		Flavanones (naringenins)—Hops (8-prenylnaringenin), apples, red onions, citrus peels, etc.			
		Flavonoids	**(Apigenin, Leteolin)**—Parsley, capsicum pepper**,** alfalfa, etc.		
			(Quercetin, Kaempferol)—Tomatoes, broccoli, onions, apples, etc.		
		Plant sterols (B-sitosterol)—Corn, soybeans, sugar beet forage, avocados, pistachios and almonds, etc.			
		Coumestans (Coumestrol)— Legumes (alfalfa, clover), spinach, lima beans, soybean sprouts, etc.			
		Stilbenes (resveratrol)—Grape skin (red wine), peanuts, etc.			
		Lignans (Secoisolariciresinol, Matairesinol)—Flaxseed (linseed), squash, pumpkin seeds, tea (black and green), sunflower seeds, strawberries, cranberries, etc.			

1. **Bioaccessibility**—It is about the amount of compound liberated from the food matrix along with which it was ingested in the gastrointestinal tract. It involves the action of gastric secretion on the food matrix for the digestive transformation so that bioactive compounds are ready for absorption/assimilation into the bloodstream via intestinal epithelium cells (Benito and Miller 1998; Heaney 2001).
2. **Bioavailability**—It is the quantity of the bioaccessible compounds that is absorbed by the intestinal epithelium cells and reached the circulatory system (blood or lymphatic circulation) to perform the desired physiological function (Schümann et al. 1997; Fairweather-Tait 1993). Not all the bioaccessible bioactive compounds are absorbed based on the presence or interaction with other compounds. For example, phytates decrease the absorption of proteins and minerals, whereas vitamin D and ascorbic acid increase the absorption of calcium and iron, respectively (Blenford 1995; Lesser et al. 2006).
3. **Bioactivity**—It is about the specific physiological function (e.g., antioxidant, anti-inflammatory, and antidiabetic) performed by the compound when in contact with targeted tissue. Bioactivity of the compound at the targeted site also signifies its level of interaction with other biomolecules during the absorption and circulation, influence of metabolism (gastric secretions), etc. (Fernández-García et al. 2009). In few cases, the bioactivity of the compounds is independent of digestibility and absorption of the compounds, for example, nondigestible polysaccharides, oligosaccharides, and dietary fiber (Roberfroid 2002).

Factors affecting bioavailability and bioactivity are as follows:

1. **Extraction Method**—It majorly affects the bioactivity of the compounds. Conditions such as temperature, pH, solvent used, and duration of extraction can have a major influence on functionality of these bioactive compounds. Therefore, the selection of an appropriate method for all compounds will not only maintain bioactivity but also optimize the quality and quantity (Pateiro et al. 2020).
2. **Food Matrix**—Bioactive compounds often interact with other components in the same food matrix, which can either reduce or increase the absorption (D'Archivio et al. 2010; Parada and Aguilera 2007).
3. **Chemical Structure**—Chemical structure is one of the main factors that influence the bioavailability of a target compound. In this way, the modification of the structure of the bioactive compound results in changes in the release, transformation, and absorption during the digestion process, decreasing its availability and/or its release into the bloodstream (Pateiro et al. 2020).
4. **Host-Related Factors**—Diffusion is a major mechanism for the absorption of the bioactive compounds from intestine to bloodstream and from bloodstream to targeted organ or tissue. Some of these are unable to pass through membranes via passive diffusion, and then, permeability, uptake, and efflux of these compounds are facilitated by (active diffusion) transmembrane transportation (Rein et al. 2013). During active diffusion, absorption of the targeted molecules is often

inhibited due to competition for binding sites on the membrane with other compounds, difference in affinity of the binding sites, etc. (Niot et al. 2009).

1.4.1 Method to Improve Bioaccessibility, Bioavailability, and Bioactivity

The inclusion of bioactive compounds in the food preparation and fortification possess a major challenge of maintaining the bioaccessibility, bioavailability, and bioactivity of these compounds until they reach the targeted site in human body (Mahfoudhi et al. 2016). Interaction with various compounds in the food matrix and exposure to varying conditions of pH, temperature, and oxygen during processing and storage adversely affect the functionality and biological activities of these compounds. Some of the bioactive compounds are either not released out of the food matrix or inefficiently absorbed in small intestine due to their reactions/bonding with other molecules (Mahfoudhi et al. 2016).

Encapsulation involves coating/trapping of the liquid, solid, or gaseous bioactive compounds (core material) into a thin film (coating material) as a potential to stabilize bioavailability and bioactivity of the bioactive compounds. Out of all three types of encapsulation (macro, micro, and nano), nanoemulsions, which are types of nanoencapsulation techniques, are the most efficient techniques to overcome the above problems (Mahfoudhi et al. 2016). Nanoemulsions are the dispersions of two immiscible liquids. This technique involves dispersion of nanometric droplets of one liquid phase into the continuous liquid phase of another liquid. Whole dispersion is stabilized via an interfacial film of emulsifier or surfactant molecules between the two phases (Mahfoudhi et al. 2016).

The continuous liquid phase (coating material) in the nanoemulsions acts as physical barrier. It protects the bioactivity, bioavailability of nanometric droplets of other phases from extreme conditions during processing and storage, acidic environment of stomach, digestive enzymes, and compounds that limit their release through bounding (Salvia-Trujillo et al. 2013). Several studies have proven that there is an inverse relationship between particle size and absorption through intestinal walls. Bioactive compounds having size below 500 nm are more readily bioavailable and absorbed (Acosta 2009). Nanosized particles of bioactive compounds achieved through nanoemulsions increase the surface that favors passive transportation/rapid penetration through intestinal walls (Hussain et al. 2001). Nanoemulsions have enhanced bioavailability of various lipophilic bioactive compounds such as omega-3 fatty acids, β-carotene, tocopherols, curcumin, and essential oils while protecting their bioactivity. For example, bioavailability of curcumin was enhanced five to six times after nanoencapsulation using poly-lactic-co-glycolic acid (European Food Safety Authority 2011). Similarly, bioavailability of fish oil was enhanced with decreased particle size after nanoencapsulation (Haug et al. 2011; Wakil et al. 2010).

1.5 Applications of Bioactive Compounds

The richest source of bioactive compounds is fruits and vegetables. They are naturally occurring biological compounds, which may or may not have nutritional attributes. They often play a very important role in the growth and development of humans and help in reducing the coronary diseases. Nowadays, the bioactive compounds have found different usage in industries such as food, medicine, and cosmetics. The extracts from the plants can be used as a functional component in the manufacturing of different food products and can also be incorporated into the cosmetics and pharma industry. About 30% of the bioactive compounds are now used in the food and cosmetic industry and 80% in the pharma. Bioactive compounds are generally extracted from the raw source and directly added to it. They have also been extracted from cyanobacterium and marine microalgae (de Jesus Raposo et al. 2013). They are generally extracted by the solvent extraction method. The encapsulation technique is often used in the food industry for maintaining the functionality of the bioactive compound. These compounds have various applications in different industries. The application of these compounds has been seen mainly in food industry, nutraceutical industry, and feed industry. Some of the applications of the compound have been discussed below.

1.5.1 Bioactive Compounds as DNA Damage-Protecting Agents

Edible resources available in the nature such as vegetables, plants, and cereals contain bioactive compounds in desirable amount. Diets enriched with these compounds often lay down the risk of certain diseases such as cardiovascular diseases, hypertension, cancer, and many more. These compounds have properties and functions as antimicrobial, anti-inflammatory, and anticancerous agents. It also acts as a DNA damage-protecting agent. Bioactive compounds present in the citrus fruits like lemon and oranges have been used for the treatment purpose of diseases like cancer. It also shows chemosensitive properties. Antioxidant-rich natural resources have proficient efficiency to inhibit DNA damage caused by radiation and other processes and reagents. Tough has not been used therapeutically yet because before using the compounds it should be checked for any toxicity (Kaur et al. 2019).

1.5.2 Bioactive Compound as Flavoring Agent and Sweetening Agent

Flavonoids are chiefly present in beverages like tea, wine, and beer. They are the chief sweeting constituents of these beverages. They play an important role in the flavor development and to some extent sweetness of tea, wine, and beer. In wine, there are mainly two types of flavonoids present namely anthocyanin, which constitutes the distinct color of the wine, and the pro-anthocyanin, which mainly constitutes the astringent property.

1.5.3 Bioactive Compounds as Natural Pigmentation Agent

Mainly carotenoids and the flavonoids are the compounds that are used as pigmentation agents. Other than these compounds, some other bioactive compounds are also used for food coloring and natural dyeing compounds. Anthocyanin is not only used in the food industry for imparting color, but also it has been seen to have benefits for therapeutic use as they have been used for the past several years for treating conditions such as hypertension, diarrhea, and dysentery. These are mainly used in the food industry for imparting color to the desired food products. Along with having distinct color imparting properties, they have great potential to be changed in nutraceutical and functional foods for commercial and domestic use. Lycopene, which is one of the major natural food colorant, is found in tomatoes, watermelon, etc. Due to its colorant properties, it is often used in human dietary products.

1.5.4 Bioactive Compound as Anti-Inflammatory and Anticancerous Agents

Flavonoids generally belong to large phenolic compound group. Further, it is subclassified into other six compounds namely flavones, isoflavones, anthocyanin, flavonols, flavanols, and flavanones. Among these, isoflavones are the most important group with anti-inflammatory effects. Isoflavones are abundantly found in soybeans and legumes. Along with anti-inflammatory effect, it also has anticancer and antimicrobial effects and acts as an antioxidant. The most common isoflavones are genistein and daidzein. They generally act as phytoestrogen. The general mechanism is that they bind to the site known as estrogen receptor in the mammals by employing pseudo-hormonal activities. Along with anti-inflammatory property, it also processes anticancerous property as it blocks the ways for any potent estrogen by binding to it. It plays a crucial role in fighting any hormone-related cancer such as prostate cancer and breast cancer (Choksi and Joshi 2007). Other bioactive compounds such as lycopene also possess anti-inflammatory and anticancerous property.

1.5.5 Bioactive Compound as Antioxidants

Phenolic compounds such as ascorbic acid and carotenoids are the most abundantly and commonly found bioactive compounds. Ascorbic acids are mainly found in citrus fruits, Brussel sprouts, tomatoes, etc. Carotenoids are usually found in papayas, sweet potatoes, carrots, etc. They are the richest source of antioxidants. The main role of these compounds is to protect cellular membrane and their components from damage, which is caused by free radicals. It has the capacity to retard microbial activity in some compounds (Martillanes et al. 2017). They have a wide application in food preservation.

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2 Plant-Based Bioactive Components: Phytochemicals: A Review

Fatma Tuğçe Gürağaç Dereli

Abstract

Therapeutic potential of medicinal plants goes back thousands of years, and they will continue to be significant in the discovery of novel drug lead molecules as main natural source. Phytochemicals, especially secondary metabolites, are responsible for the pharmacological effects of these plants. Classically, secondary metabolites are classified according to their chemical structure as terpenes, phenolics, and alkaloids. This review provides an overview of the plant-based bioactive components.

Keywords

Phytochemicals · Secondary metabolites · Natural sources · Plants · Pharmacological effects

2.1 Chemical Components in Plants: Phytochemicals

Medicinal plants have been the basis of several traditional medicine systems and still represent a significant resource pool for the discovery of novel drug lead molecules (Petrovska 2012). Biologically active compounds that naturally occur in the various parts of the plants are referred to as phytochemicals, and a vast range of pharmacological effects of the medicinal plants are attributed to these phytocompounds in them (Katz and Baltz 2016).

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Till date, thousands of phytochemicals have been evaluated for pharmacological activities, and some of them have opened a new horizon for the treatment of various diseases (Nyamai et al. 2016).

2.2 Classification of the Phytochemicals

Plants produce a broad range of organic compounds, which are traditionally classified as primary and secondary metabolites (Chinou 2008).

The primary metabolites are found in all plants and are produced by primary metabolic pathways. These phytochemicals are essential for the vital activities of plants and include proteins, carbohydrates, lipids, and nucleic acids. In contrast, secondary metabolites are produced from distinct pathways to perform specific tasks. Secondary metabolites accumulate in limited taxonomic groups in the plant kingdom and play a role in the adaptation of plants to changing environmental factors, enabling them to overcome biotic and abiotic stress factors. They are also primarily responsible for the pharmacological activity of the medicinal plants (Koche et al. 2016).

2.3 Classification of the Secondary Metabolites

Classically, the plant secondary metabolites have been classified as terpenes, phenolics, and alkaloids, depending on their chemical structure (Verpoorte 1998).

Terpenes or terpenoids are the main class of secondary metabolites with a wide range of pharmacological activities. They are made up of isoprene (2-methyl-1,3-butadiene, C_5H_8) (Fig. 2.1) units and classified depending on the number of these monomers (-mono,-di, -tri, etc.). In plants, terpenes are responsible for the fragrance and function as repellents/attractants. Furthermore, in high concentrations they can be toxic, and thus, they take role in the defense of the plants against pathogens and herbivores. Numerous in vivo and clinical studies have demonstrated that these compounds appear to have both preventive and treatment potential in combating several diseases and also to have antimicrobial, antiparasitic, antifungal, antiviral, antispasmodic, antiallergic, anti-inflammatory, immunomodulatory, and antihyperglycemic activities (Cho et al. 2017; Paduch et al. 2007; Silvestre and Gandini 2008).

Plant phenolics constitute a wide class of secondary plant substances, which are characterized by hydroxylated aromatic rings. They are classified into numerous categories including simple phenols, phenylpropanoids, flavonoids, tannins, and quinones. Phenolic metabolites have multiple functions in the plant, but the most

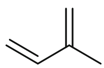

Fig. 2.1 Chemical structure of isoprene

important is to provide a defense against pathogens and predators. There is increasing evidence from pharmacological studies that phenolics may be useful in the prophylaxis and therapy of several disorders. These studies reveal the antioxidant, antiulcer, anticancer, antiaging, antidiabetic, antimicrobial, anti-inflammatory, cardioprotective, neuroprotective, and hepatoprotective properties of the phenolic compounds (Brodniewicz and Grynkiewicz 2012; Cosme et al. 2020; Pereira et al. 2009).

Alkaloids are defined as basic pharmacoactive organic compounds containing one or more nitrogen atoms. They can be classified according to their heterocyclic ring system or biosynthetic origin. In plants, alkaloids are associated with defense mechanisms. Most of them are highly toxic to other organisms even in small amounts, but some of them demonstrate several pharmacological effects. To give example, scopolamine is sedative, tubocurarine and papaverine are muscle relaxants, morphine is a narcotic analgesic, and vinblastine and vincristine are anticancer alkaloids (Cordell et al. 2001; Debnath et al. 2018; Qiu et al. 2014).

2.4 Importance of Phytochemicals in Drug Discovery

Medicinal plants have been used in several traditional healing systems from time immemorial. There are countless evidences for the usage of plants in folk medicine by Indians, Greeks, Egyptians, Chinese, etc. (Šantić et al. 2017).

Before it was realized that the pharmacological effects of medicinal plants were due to the phytochemicals in their contents, it was thought that their effects were due to their similarities with the organ they affected. As for instance, walnut looks like a brain and it affects brain function (Lev 2002; Rungsung et al. 2015). The isolation of morphine (Fig. 2.2a) from opium poppy by Serturner in the early nineteenth century showed the importance of phytochemicals responsible for the therapeutic activity of medicinal plants. Morphine is the first plant-derived drug, and it was commercialized by Merck in 1826. This event started medicine discovery from plants and led to the investigation of other medicinal herbs. In this way, many bioactive secondary metabolites have been obtained from nature and medicinal plants have formed the basis of many drugs used in the clinic today. In 1869, apomorphine (Fig. 2.2b) was derived from morphine and this drug molecule has been utilized for the treatment of Parkinson's disease as a nonselective dopamine agonist. A cardiotonic glycoside digitoxin (Fig. 2.2c) was obtained from *Digitalis purpurea* folium. Aspirin (Fig. 2.2d) is a semi-synthetic anti-inflammatory agent that was developed from the bark of *Salix alba*. Another famous drug molecule silymarin is a flavonolignan mixture extracted from the fructus of *Silybum marianum* and has been used to treat hepatic diseases worldwide (Fabricant and Farnsworth 2001; Rungsung et al. 2015).

Table 2.1 enlists more comprehensively some of the significant plant-based drug molecules used in modern therapy (Fabricant and Farnsworth 2001; Rungsung et al. 2015).

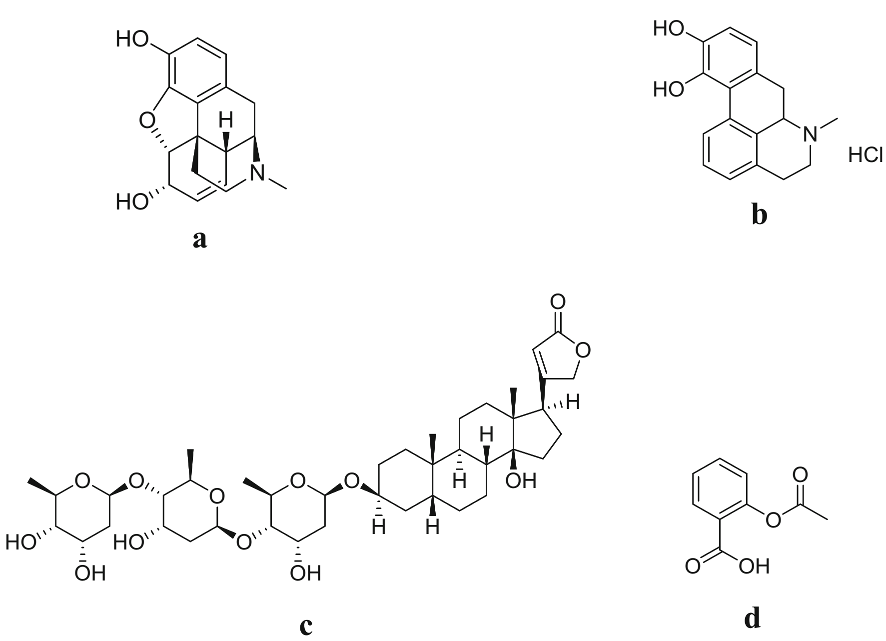

Fig. 2.2 Chemical structure of some historically significant plant-based drug molecules: (**a**) morphine; (**b**) apomorphine; (**c**) digitoxin; and (**d**) aspirin

2.5 Approaches to the Sustainable Bioproduction of Pharmacologically Active Phytochemicals

While phytochemicals are unique resources for new drug development, production of them by plants is not satisfactory. These metabolites are often synthesized only in trace quantities by certain species. Furthermore, the medicinal plant population is being depleted because of the anthropogenic factors and intense collection from the wild flora. All of these are limiting factors for continuity in the research and use of phytochemicals. Therefore, it is necessary to design new routes for sustainable supply of these substances. In this regard, biotechnological approaches become important to protect biological resources. In vitro production of functional phytochemicals in plant cell, tissue, and organ cultures is a biotechnological alternative to field cultivation. In addition, latest developments in this field have opened the doors for metabolic engineering that means the improvement of cellular activities by manipulation of metabolic pathways by recombinant DNA technology. This technique is expected to become much more important for the development of plant-based medicines in the near future (Atanasov et al. 2015; Bourgaud et al. 2001; Lee et al. 2009; Zhong 2001).

Table 2.1 Some of the bioactive phytocompounds used in modern therapy

Plant-derived drug molecules	Plant source	Indication
Acetyldigoxin	*Digitalis lanata* Ehrh.	Cardiotonic
Adonidin	*Adonis vernalis* L.	Cardiotonic
Aescin	*Aesculus hippocastanum* L.	Anti-inflammatory, vasoprotective
Aesculetin	*Fraxinus rhynchophylla* Hance	Antidysentery
Allicin	*Allium sativum* L.	Antimicrobial, anti-arteriosclerotic, hypocholesterolemic
Allyl isothiocyanate	*Brassica nigra* (L.) K. Koch	Rubefacient, fumigant
Arecoline	*Areca catechu* L.	Anthelmintic
Artemisinin	*Artemisia annua* L.	Antimalarial
Asiaticoside	*Centella asiatica* (L.) Urb.	Vulnerary
Atropine, hyoscyamine, scopolamine	*Atropa belladonna* L.	Anticholinergic
Berberine	*Berberis vulgaris* L.	Antimicrobial, antidysentery anti-inflammatory, antidiabetic, hypocholesterolemic
Bromelain	*Ananas comosus* (L.) Merr.	Anti-inflammatory, proteolytic
Caffeine	*Camellia sinensis* (L.) Kuntze	Central nervous system stimulatory
Camphor	*Cinnamomum camphora* (L.) J. Presl	Antitussive, antifungal
Camptothecin	*Camptotheca acuminata* Decne.	Anticancer
Capsaicin	*Capsicum annuum* L.	Analgesic
Codeine	*Papaver somniferum* L.	Analgesic, antitussive
Chymopapain	*Carica papaya* L.	Proteolytic, mucolytic
Colchicine	*Colchicum autumnale* L.	Antitumor, antigout
Convallatoxin	*Convallaria majalis* L.	Cardiotonic
Curcumin	*Curcuma longa* L.	Choleretic, anti-inflammatory, antioxidant, anti-Alzheimer, anti-arthritic
Cynarin	*Cynara scolymus* L.	Choleretic
Digitoxin, digoxin	*Digitalis purpurea* L.	Cardiotonic
Diosgenin	*Dioscorea* species	Anovulatory, contraceptive
Emetine	*Cephaelis ipecacuanha* (Brot.) A. Rich	Emetic, antiprotozoal
Ephedrine	*Ephedra sinica* Stapf	Sympathomimetic, hypotensive, decongestant
Etoposide	*Podophyllum peltatum* L.	Antitumor
Eucalyptol	*Eucalyptus globulus* L.	Expectorant

(continued)

Table 2.1 (continued)

Plant-derived drug molecules	Plant source	Indication
Galantamine	*Galanthus caucasicus* (Baker) Grossh.	Anti-Alzheimer
Ginkgolide	*Ginkgo biloba* L.	Antidementia
Ginsenoside (panaxoside)	*Panax* species	Aphrodisiac, antidiabetic
Glycyrrhizin	*Glycyrrhiza glabra* L.	Demulcent, expectorant
Harpagoside	*Harpagophytum procumbens* (Burch.) DC. ex Meisn.	Analgesic, antirheumatic
Khellin	*Ammi visnaga* (L.) Lam.	Bronchodilator
Lycopene	*Lycopersicon esculentum* Mill.	Cancer preventive, anti-arteriosclerotic
Menthol	*Mentha* species	Rubefacient
Morphine	*Papaver somniferum* L.	Analgesic
Papain	*Carica papaya* L.	Proteolytic; mucolytic
Papaverine	*Papaver somniferum* L.	Blood vessel relaxant
Parthenolide	*Tanacetum parthenium* (L.) Sch. Bip.	Analgesic
Physostigmine	*Physostigma venenosum* Balf.	Cholinesterase inhibitory
Pilocarpine	*Pilocarpus* species	Parasympathomimetic
Podophyllotoxin	*Podophyllum peltatum* L.	Anticancer, purgative
Pseudoephedrine	*Ephedra sinica* Stapf.	Sympathomimetic
Quinine, quinidine	*Cinchona* species	Antimalarial, antipyretic
Reserpine	*Rauwolfia serpentina* L. Benth. ex. Kurz.	Antihypertensive, tranquillizer
Ricinoleic acid	*Ricinus communis* L.	Purgative, anti-inflammatory
Salicin	*Salix alba* L.	Analgesic, antipyretic, anti-inflammatory
Scillaren A	*Urginea maritima* (L.) Baker	Cardiotonic
Sennosides A and B	*Cassia* spp.	Laxative
Silymarin	*Silybum marianum* (L.) Gaertn.	Antihepatotoxic
Taxol (paclitaxel)	*Taxus brevifolia* Nutt.	Antitumor/anticancer
Tetrahydrocannabinol (THC)	*Cannabis sativa* L.	Antiemetic, psychoactive
Theobromine	*Theobroma cacao* L.	Diuretic, myocardial stimulant, vasodilator
Thymol	*Thymus vulgaris* L.	Antiseptic
Vinblastine, vincristine	*Catharanthus roseus* (L.) G. Don	Anticancer, antileukemic

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3 Animal-Based Bioactive Components: Zoochemicals: A Comprehensive Review

Rohit G. Sindhav, Tanmay Hazra, and Deepak Mudgil

Abstract

Bioactive components can be defined as components in foods that have a physiological function. In this present era, bioactive substances originating from animal origin have been identified as potential and applied for designing functional foods with numerous health benefits. Most of the evidence for bioactive effects comes from in vitro studies, and there is a need for further research to fully evaluate the true potential of milk-derived bioactive factors. Animal genetics and animal nutrition play an important role in the relative proportions of milk proteins and could be used to manipulate the concentration of specific bioactive peptides in milk from ruminants. The knowledge described in the present chapter may set the basis for further research and for the development of new functional foods with healthy and beneficial properties for humans.

Keywords

Bioactive components · Zoochemicals · Animal nutrition

3.1 Introduction

Bioactive substances can be termed as those chemical molecules or substances that have specific biological effects like prevention of different diseases, antimicrobial properties, carrier of couple of enzymes or nutrients, and modification of bio-system

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function on living organisms. Apart from plant, animals are also an excellent source of bioactive components due to their wide biochemical natures (Colegate and Molyneux 2007). The integral relationship between human diet and bioactive compounds is well recognized since pre-historic age, and this well-being is not only restricted only in nutrition perspective but also actively engaged in immune-boosting activities. Therefore, in this current pandemic situation animal-originated bioactive components are used to design different types of functional foods by engaging different biotechnological and novel processing technologies approaches. However, a major challenge arises for extraction or purifications of bioactive components from animal origins. In pan world basis, in vitro, in vivo, or clinical trials are conducting sketch-out mechanisms for animal originated against different diseases.

3.1.1 Omega-3 Fatty Acids

Polyunsaturated fatty acids (PUFAs) having two or more unsaturated bonds where one of which is positioned at the third carbon atom from the methyl (CH_3) end of the carbon chain are termed as omega-3 fatty acids. Alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) are the most common omega-3 fatty acids found in diets. Apart from plant origin poultry, meats and seafood are the major sources of animal-originated omega-3 fatty acids in human diets. Fish oil is an attractive raw material source for fatty acid concentrate manufacture due to its high concentration of omega-3 fatty acids. Adsorption chromatography, fractional or molecular distillation, enzymatic splitting, low-temperature crystallization, supercritical fluid extraction, and urea complexation are all processes suited for large-scale manufacture of omega-3 fatty acid concentrate (Shahidi and Wanasundara 1998). Sea fishes like tuna, salmon, and sardines are the major source of EPA and DHA (Meyer et al. 2003; Covington 2004) in human diets.

The biological benefits of omega-3 fatty acids for the prevention and even therapy of a number of disorders have been extensively studied. Medical studies revealed a direct relationship between consumption of omega-3 fatty acids and cardio and the prevention of cardiovascular diseases (Ruxton et al. 2004). Research findings also concluded that this omega-3 fatty acid consumption dose, durations, and amounts directly reduce cardiac events and death.

Studies have revealed direct relation between consumption of omega-3 fatty acids with chronic diabetes problems like hypertension, hypertriglyceridemia, and hypercholesterolemia. Simopoulos (1991) reported that consumption of omega-3 fatty is able to reduce triglyceride levels in blood more over lower the mean albumin transcapillary escape rate that reducing blood pressure. Changes in vascular permeability are thought to be caused by a reduction in lipoprotein transport across the arterial wall. After taking fish oil, diabetic individuals had more biological effects, including a modest rise in plasma glucose, glycosylated hemoglobin, total cholesterol, and serum apoB (Simopoulos 1991).

Ruxton et al. (2004) reported that these types are able to create therapies for inflammatory illnesses like chronic inflammatory bowel disease and asthma. The consumption of omega-3 fatty acids in the diet may alter lipid metabolism. Modulation of prostaglandin synthesis, immunological function, free radical creation, membrane fluidity, intracellular transport systems, hormone secretion, calorie consumption, and gene expression are among the mechanisms under research for cancer prevention (Simopoulos 1991).

3.1.2 Conjugated Linoleic Acid

CLA stands for conjugated linoleic acid, which refers to a collection of geometric and positional isomers of linoleic acid (dienoic octadecadienoate, 18:2). Meat and dairy products originating from ruminants are two dietary groups that are high in CLA (Schmid et al. 2006). Lamb has the greatest CLA amounts, ranging from 4.3 to 19.0 mg/g lipid; beef has somewhat lower quantities, ranging from 1.2 to 10.0 mg/g lipid. CLA is also found in fish and meat from monogastric animals including turkey, pig, and chicken, although in considerably lesser amounts (Schmid et al. 2006). Pasture feeding and adding oilseeds, vegetable oil, or fish oil to the diet are two efficient ways to boost CLA content in ruminant meats (Raes et al. 2004; Schmid et al. 2006).

CLA has a wide range of bioactive qualities, including anti-adipogenic, antidiabetic, anti-atherosclerotic, and anticarcinogenic effects, all of which are detailed below.

Based on animal studies, few studies confirmed that regular CLA consumption is able to reduce adipose tissue mass; therefore, body weight is significantly reduced (Belury 2002; Salas-Salvado et al. 2006). Few studies linked direct relation between regular consumption of CLA and total removal of brown adipose tissue and decrease in leptin tissue (Belury 2002).

Dietary CLA treatment has been linked to elevated mRNA markers of adipose differentiation and glucose absorption in rat muscles in previous investigations. Long-term CLA feeding may cause insulin resistance and lipodystrophy, similar to what happens in anti-adipogenicity situations (Belury 2002). As a result, more research is needed to assess CLA's therapeutic potential in the treatment of type 2 diabetes.

Because obesity is one of the major risk factors for type 2 diabetes, it is fair to assume that CLA's antidiabetic activity will result in beneficial changes in metabolic parameters in type 2 diabetics. Rats in the experimental group showed lower fasting glucose, insulinemia, triglyceridemia, free fatty acid levels, and leptinemia in response to short-term CLA feeding than those in the control group (Belury 2002). Dietary CLA treatment has been linked to elevated mRNA markers of adipose differentiation and glucose absorption in rat muscles in previous investigations. Long-term CLA feeding may cause insulin resistance and lipodystrophy, similar to what happens in anti-adipogenicity situations (Belury 2002). As a result, more research is needed to assess CLA's therapeutic potential in the treatment of type 2 diabetes.

3.1.3 Chitin and Chitosan

After polymerization reaction β-(1-4)-*N*-acetyl-D-glucosamine is transferred into chitin; however in alkaline environmental condition chitosan is formed from chitin by deacetylation reaction. In this condition another copolymer consisting of β-(1-4)-2-acetamido-D-glucose and β-(1-4)-2-amino-D-glucose is formed. Jeon et al. (2000) reported that in this said polymer 80% β-(1-4)-2-amino-D-glucose is usually present.

Crab and shrimp shells are the most common commercial sources of chitin, particularly those collected as food manufacturing waste for economic reasons. Acid removal of calcium carbonate and later alkaline solubilization of proteins are used in the industrial extraction of chitin from crustaceans (Rinaudo 2006). The extracted chitin may be further decolorized and processed to eliminate colors and impurities due to the raw material sources and requirements for purity and color for later use. Chemical (acidic) hydrolysis and enzymatic hydrolysis are two ways of preparing chitin and chitosan oligomers with 10 units or less (Jeon et al. 2000). Chitin and chitosan can also be chemically and mechanically altered to increase their strength, solubility, and tractability in order to create new features, functions, and applications, particularly in the biomedical field (Pillai et al. 2009). Chitin and chitosan are biomaterials with a wide range of functions due to their multifunctional characteristics (Table 3.1).

Chitin and chitosan are constantly being discovered in new applications. Chitin and chitosan derivatives, for example, are used in water and wastewater treatment to remove metal ions, radionuclides, dyes, phenols, and other contaminants (Bhatnagar and Sillanpaa 2009).

Table 3.1 Applications of chitin and chitosan (Jeon et al. 2000)

Field	Application
Food	Antimicrobial and preservative agent; edible film
Nutritional	Dietary fiber; hypocholesterolemic or antihypertensive agent
Agricultural	Seed coating preparation; activator of plant cells
Pharmaceutical	Antibacterial, antitumor, or immunopotentiating agent; carrier for drug delivery
Medical	Accelerator for wound healing; artificial skin; fiber for absorbable structures
Biotechnological	Carrier for immobilized enzymes and cells; porous beads for bioreactors; resin for chromatography; membrane material

3.1.4 Milk Peptides

Milk proteins are the precursors and suppliers of a wide range of bioactive peptides, the majority of which are inert until they are liberated from the protein sequence by enzymatic proteolysis.

During the time of fermentation, cell-bound proteinase of lactic acid bacteria is able to fragment protein and generate bioactive peptides (Meisel and Bockelmann 1999).

Bioactive peptides can be identified and characterized using one of three approaches: They can be separated from in vitro enzymatic and in vivo gastrointestinal digested proteins, or they can be chemically generated. Table 3.2 shows the biochemical characteristics of 11 different kinds of bioactive milk protein-derived peptides. Some of them have the same protein precursor, such as casein, which is the most abundant protein in milk. Furthermore, certain peptides have been shown to be multifunctional because peptide sequences on the main protein structure that communicate various bioactivities often overlap in areas known as “strategic zones,” which are partially shielded from proteolytic breakdown (Meisel 2005).

Exogenous peptide ligands that interact with opioid receptors include casomorphins, α- and β-lactorphin, lactoferroxins, and casoxins. Depending on whether they have an agonistic or antagonistic effect, they are classified as opioid agonists or antagonists. Except for α-casein opioids, all opioid peptides have a tyrosine residue at the amino terminus and another aromatic residue in the third or fourth position (e.g., phenylalanine or tyrosine) (Meisel 2005). The structure is important not just for fitting into the binding region of the receptor, but also for expressing bioactivity. In both receptor studies and bioassays, the opioid peptides had naloxone-inhibitable opioid actions. When given to experimental animals, they can modify social behavior and generate analgesia (Meisel 2005). Prolonged gastrointestinal transit time, antidiarrheal activity, altered intestinal transport of amino acids, accelerated production of insulin and somatostatin, and therefore controlled postprandial metabolism are some of the other physiological effects documented (Meisel 2005).

In the renin–angiotensin system, angiotensin-converting enzyme (ACE) is a membrane-bound multifunctional carboxypeptidase. It is vital for controlling peripheral blood pressure and local levels of ACE inhibitors and competitive substrates,

Table 3.2 Bioactive peptides from milk proteins and their bioactivity (Meisel 2005)

Bioactive peptide	Bioactivity
Casomorphins, α-lactorphin, β-lactorphin	Opioid agonist
Lactoferroxins, casoxins	Opioid antagonist
Casokinin, lactokinins	ACE inhibitory
Immunopeptides	Immunomodulatory
Lactoferricin	Antimicrobial
Casoplatelins	Antithrombotic
Phosphopeptides	Mineral binding, anti-cariogenic

which are bioactive peptides produced by the body (Meisel 2005). Angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II, an octapeptide with significant vasoconstrictor properties (FitzGerald et al. 2004). To fit into the active site of ACE, most ACE inhibitory peptides are short-chain peptides with a tiny molecular size. The C-terminal tripeptide sequence plays a crucial role in ACE binding to hydrophobic and positively charged amino acid residues, according to structure–activity studies (Meisel 2005). The conformation, rather than the presence of specific amino acids, should contribute to the ACE inhibitory efficacy of longer chain peptides. Bioactive peptides like casokinin and lactokinins block ACE, preventing the synthesis of the vasoconstrictory (hypertensive) angiotensin II while potentiating the vasodilatory (hypotensive) characteristics of bradykinin, resulting in reduced blood pressure (Meisel 2005).

Immunopeptides, which may be made from α- and β-caseins, are used to boost immunological function. Immunostimulating effects have been reported in infants, as assessed by immune cell proliferation and antibody formation, and the peptides also aid adults' resistance to bacterial and viral illnesses (Meisel 2005). Although the chemical mechanism behind these immunomodulatory actions is unknown, the peptides are thought to bind to lymphocyte and macrophage receptors and promote their protective immune responses.

Lactoferrin is a peptide derived from whey protein that has antibacterial properties. Lactoferrin's antibacterial mechanism is comprised of both iron-binding sites and a common antimicrobial region at the *N*-terminus (Meisel 2005). Lactoferrin is cleaved by enzymes to produce lactoferricin, a peptide fragment containing the 17–41 lactoferrin residues. Lactoferricin has more strong antibacterial action than the original undigested lactoferrin because its smaller size allows it to reach target locations on the microbial surface, and the net positive charge of the peptide increases microbial membrane permeability (Meisel 2005).

Casoplatelins' antithrombotic properties are demonstrated by their ability to prevent platelet aggregation. Casoplatelins compete with human fibrinogen's γ-chain for binding to the platelet surface receptor due to their amino acid sequence similarity (Meisel 2005).

Phosphopeptides are the last type of bioactive peptides generated from milk protein, and they serve as transporters of several minerals, particularly calcium. The capacity to bind minerals is mostly due to negatively charged phosphate groups, but it is also regulated by surrounding amino acids around the binding site (Meisel 2005). Furthermore, phosphopeptides have an anticariogenic impact, as evidenced by their activities of recalcifying tooth enamel and competing for calcium with dental plaque-forming bacteria, preventing caries lesion development (Aimutis 2004; Meisel 2005).

Milk protein may be a valuable source of peptides with cytomodulating function, according to mounting data. Anti-proliferative and apoptosis-inducing peptides may be effective in cancer prevention, whereas cell growth-promoting peptides may aid in the development of neonates' digestive tracts. Finally, due to their superiority in ions and small molecule binding, surface and self-assembly, gelation and pH-responsive gel swelling, complex formation with macromolecules, shielding capabilities, biocompatibility, and biodegradability, milk proteins have recently been discovered to be natural vehicles for delivering bioactives (Livney 2010). Hydrophobic/heat-sensitive nutrition encapsulation and delivery, as well as medication delivery and targeting, are among the uses.

3.1.5 L-Carnitine

Free carnitine (3-hydroxy-4-*N*-trymethylaminobutyric acid) can be derived from cow muscles (Zhou et al. 2007). However, this amino acid derivative can be also isolated from milk and meat (Flanagan et al. 2010; Hurot et al. 2002). Table 3.3 represents carnitine content of animal and dairy foods.

The essential amino acids lysine and methionine serve as precursors, with ascorbate, niacin, pyridoxine, and Fe^{2+} serving as cofactors. Carnitine is mostly synthesized in the liver (Flanagan et al. 2010). Carnitine can also be made in the kidneys and the brain. The synthetic route in mammals begins with protein-bound lysine, which is converted to trimethyllysine by enzymatic methylation. To make carnitine, the trimethyllysine passes through four further enzyme steps (Flanagan et al. 2010). The largest amounts of carnitine are held in the cardiac and skeletal muscles, which cannot synthesize carnitine and must instead take it from the plasma (Flanagan et al. 2010; Hurot et al. 2002). Carnitine's L-isomer is the only one that is bioactive.

In humans, only 25% of L-carnitine is biosynthesized from scratch, with the remaining 75% coming from exogenous sources such as meat, poultry, and fish in the diet (Zhou et al. 2007). Circulating L-carnitine is made up of dietary L-carnitine absorbed via active and passive transport across enterocyte membranes, as well as free L-carnitine synthesized in the liver and kidney. It reaches cells in various tissues via the bloodstream and extracellular fluid and is metabolized for a variety of physiological purposes.

The reversible esterification of carnitine's 3-hydroxyl group by acyltransferase to generate acylcarnitines is the metabolic significance of L-carnitine in mammals. The mitochondrial oxidation of long-chain fatty acids, the export of acetyl and chain-shortened acyl products from peroxisomes, and the maintenance of cellular CoA homeostasis are only a few of the bioactive processes (Steiber et al. 2004).

Table 3.3 Carnitine content in animal and dairy foods (Steiber et al. 2004)

Food	Carnitine (μmol/100 g)
Prepared steak	525
Raw beef (tenderloin, shoulder, rump)	3691.4–4160.5
Prepared ground beef	300
Raw beef liver	160.4
Prepared chicken	60
Prepared chicken egg	5
Cow milk	16.4

Carnitine is essential for fatty acid oxidation because it is part of a transport system that includes three proteins: carnitine palmitoyltransferase I (CPT-I), acylcarnitine-carnitine translocase (CACT), and carnitine palmitoyltransferase II (CPT-II), all of which are found at different submitochondrial sites (Steiber et al. 2004). This transport pathway is required for the movement of activated long-chain fatty acids over the mitochondrial inner membrane and into the matrix, where they undergo β-oxidation (Flanagan et al. 2010; Steiber et al. 2004). As a result, active absorption of carnitine into the cytoplasm of cardiac and skeletal muscle cells is important for fatty acid oxidation energy metabolism in muscle.

Given the critical role of carnitine in fatty acid metabolism and energy generation, deficit in carnitine, whether caused by genetic mutations in carnitine transporters or liver or kidney disease, may impair cardiac/skeletal muscle and central nervous system function (Flanagan et al. 2010). L-carnitine supplementation is a relatively safe treatment method to alleviate the difficulties caused by carnitine deficiency due to its low toxicity and ease of excretion. L-carnitine may help with painful neuropathies, Alzheimer's disease, cardiovascular disease, and immunological function when used in the clinic. Furthermore, evidence of carnitine's advantages in treating obesity, reducing glucose intolerance, and raising total energy expenditure is growing (Flanagan et al. 2010).

3.1.6 Choline

Choline (trimethyl-hydroxyethylammonium) is a quaternary ammonium molecule identified in pig bile isolate for the first time. Choline is a component of the phospholipid "lecithin" (phosphatidylcholine), which is the form in which the majority of choline in the human diet is ingested. Choline concentrations are 5831, 75, 150, and 42 mol/kg in beef liver, beefsteak, bovine milk, and eggs, respectively (Zeisel and Blusztajn 1994). Although choline may be generated naturally, additional choline must be included in the diet to avoid liver and muscle problems. Sex, pregnancy and breastfeeding, clinical status, folate, vitamin B12, and methionine nutrition, as well as gene polymorphisms, all impact choline intake (Sanders and Zeisel 2007).

The upper small intestine absorbs the majority of free choline. Before choline may be absorbed, it is converted to betaine in around half of the cases. When substantial amounts of choline are consumed, intestinal bacteria are responsible for converting it to trimethylamine. Choline in the form of lecithin is first degraded by enzymes in pancreatic secretions and intestinal mucosal cells and then absorbed as lysolecithin, which is subsequently converted back to lecithin in the enterocyte. By enzymatically cleaving the lecithin transferred to the locations via systemic circulation, free choline will be freed at the tissues/organs. Other choline-containing molecules found in minute amounts in the food, such as glycerylphosphorylcholine, phosphorylcholine, and sphingomyelin, can all be cleaved to produce free choline in the enterocyte or tissues/organs (Zeisel 1981).

Table 3.4 Physiological importance of choline metabolites and choline-containing compounds (Zeisel and Blusztajn 1994)

Compound	Biological functions
Phosphocholine	Intracellular storage of choline
Phosphatidylcholine	Building block of biomembranes; VLDL component
Sphingomyelin	Building block of biomembranes
Betaine	Methyl group donor; renal osmolyte
Acetylcholine	Neurotransmitter
Lysophosphatidylcholine	Second messenger modulating protein kinase C (PKC) activity
Lysophingomyelin	Second messenger mediating growth factor actions, mitogen
Glycerophosphocholine	Renal osmolyte

Choline deficiency, as an important ingredient for human health, causes problems in a range of bodily systems and organs, and thus, choline has a long history as a therapeutic agent. In mammalian tissues, choline participates in four primary enzymatic reactions: phosphorylation, oxidation, acetylation, and base exchange (Zeisel 1981). Choline phosphotransferase catalyzes the transfer of phosphate from adenosine triphosphate to the hydroxyl group of choline, and the phosphorylated choline serves as the intracellular storage pool of choline. Phosphorylation of choline is also the initial step in the production of phosphatidylcholine. Choline's oxidation result is betaine aldehyde, which is then transformed to betaine by the choline oxidase enzyme system. Acetyl coenzyme A (acetyl-CoA) reacts with choline to create acetylcholine, which is catalyzed by choline acetyltransferase. The physiological significance of choline metabolites and choline-containing substances is summarized in Table 3.4.

Choline is a precursor for phosphatidylcholine production via the cytidine diphosphocholine route, and phosphatidylcholine accounts for 50% of phospholipids on cell membranes, as previously mentioned (Sanders and Zeisel 2007). As a result, adequate choline is required to maintain cell membrane structural integrity and transport activities. Phosphatidylcholine, a component of VLDL that is responsible for triglyceride excretion from the liver, is also an essential component. Choline shortage is therefore linked to the development of fatty liver and hepatocarcinoma in long-term deficit. Lack of choline may lead to a progressive increase in DNA synthesis and cell proliferation, making cells more sensitive to chemical carcinogens; the oxidized choline metabolite "betaine" is a major methyl donor, so choline deficiency is linked to undermethylation of DNA, resulting in chromosomal instabilities and abnormal expression of genetic information; increased lipid synthesis; and increased lipid synthesis (Zeisel and Blusztajn 1994).

Choline is a component of acetylcholine, a neurotransmitter that is widely used in the central nervous system. Because the availability of choline and acetyl-CoA influences the rate of acetylcholine production, a shortage of choline will impair the signaling function of cholinergic neurons. A choline-rich diet promotes the release of acetylcholine and has been used to treat diseases caused by neurotransmitter deficiencies (Zeisel 1981). Furthermore, the hypotensive effects of choline are mediated through its activation of the cholinergic vagus nerve (Zeisel 1981). Choline metabolism is intertwined with folate metabolism, and both are essential for early brain development. In animal studies, choline supplementation or shortage in the mother might result in irreversible changes in the brain development of the offspring (Sanders and Zeisel 2007). Choline supplementation may be used to improve elders' memory since the hippocampus is the brain region most responsive to choline availability (Zeisel 1981).

3.1.7 Coenzyme Q10

Coenzyme Q is a family of naturally occurring lipophilic molecules with a similar benzoquinone ring structure but varying isoprenoid side-chain lengths. Coenzyme Q10 (2, 3-dimethoxy-5-methyl-6-decaprenyl-1,4-benzoquinone) is a group member with ten repeating isoprene units on the side chain, as the name suggests (Bhagavan and Chopra 2006).

In humans and most animals, Q10 is the most common type of coenzyme. It can be biosynthesized from scratch in three processes (Overvad et al. 1999). The necessary amino acid tyrosine or phenylalanine is used to make the quinone ring, whereas acetyl-CoA residues are used to make the isoprenoid side chain. Under the catalytic activity of the enzyme polyprenyltransferase, the ring and side-chain structures are condensed together in the final phase.

Coenzyme Q10 is found in most tissues and can be found in two forms: oxidized (ubiquinone) and reduced (ubiquinol) (Overvad et al. 1999). In a healthy adult person, the overall quantity of coenzyme Q10 is roughly 0.5–1.5 g, with varying amounts in different organs. Coenzyme Q10 is found in the greatest quantities in tissues with high energy demands and lipid content, such as the heart, kidney, and liver, which have roughly 110, 70, and 60 g/g tissue, respectively (Bhagavan and Chopra 2006; Overvad et al. 1999). Lungs have the lowest content, with 8 g/g tissue. Except in the brain and lungs, coenzyme Q10 is mostly found in its reduced form (Overvad et al. 1999). In terms of subcellular distribution, 40–50% of coenzyme Q10 is found in the inner membrane of mitochondria (Bhagavan and Chopra 2006).

Human tissue Q10 is generated endogenously or acquired from meals and oral supplements. Table 3.5 contains a list of animal-origin food products and the quantity of coenzyme Q10 they contain. Meat, particularly the heart muscle, is said to be high in Q10. Q10 is also found in vegetables, fruits, and cereals, albeit in small amounts (10 g/g diet). Differences in animal species, seasonal fluctuations, and analytical methodologies all cause variances in the results (Overvad et al. 1999).

Coenzyme Q10 is now accessible as a nutritional supplement over the counter, and its popularity is growing as the public recognizes its relevance in supporting human health. Q10 has important functions in mitochondrial energy generation, antioxidation, cell signaling, and gene expression (Bhagavan and Chopra 2006). Heart disease, atherosclerosis, neurological disease, hypertension, male infertility, diabetes, and cancer have all been linked to Q10 supplementation (Bhagavan and Chopra 2006; Overvad et al. 1999).

Table 3.5 Coenzyme Q10 content in selected animal-origin food products (Overvad et al. 1999)

Food group	Food item	Cooking method	Q10 (μg/g food)
Meat and poultry	Pork heart	Fried	203 (151–282)
	Beef	Fried	31
	Chicken	Fried	17
	Pork chop	Fried	14 (9–17.8)
	Ham	Boiled	7.7 (5.4–9.4)
Fish	Herring	Marinated	27
	Rainbow trout	Steamed	11
	Salmon	Smoked	4.3
Dairy products	Yogurt	None	1.2
	Hard cheese	None	<0.2
	Cream cheese	None	<0.3
Egg	Hen's egg	None	1.5 (1–2.1)
	Hen's egg	Boiled	2.3 (1.7–2.9)

Q10 operates as a mobile redox agent shuttling electrons and protons in the respiratory chain as a cofactor in the mitochondrial electron transport chain and is thus required for the generation of adenosine triphosphate (ATP) (Bhagavan and Chopra 2006). The justification for using coenzyme Q10 as a cardiovascular disease therapy is based on the essential pathophysiological roles that mitochondrial dysfunction and energy deficiency are thought to play in heart failure. The amount of Q10 in plasma and cardiac tissue has been found to be inversely linked with the degree of cardiovascular symptoms and dysfunction. Supplementing with Q10 in addition to regular medical therapy has been linked to improvements in a few key clinical indicators in heart failure patients (Overvad et al. 1999; Sarter 2002; Singh et al. 2007).

Ubiquinol, a reduced form of coenzyme Q10, functions to eliminate free radicals, protecting membrane phospholipids, mitochondrial membrane proteins, and DNA from oxidative damage caused by free radicals. The ability of ubiquinol to convert tocopheryl radicals and semidehydroascorbate back to tocopherol and ascorbate, respectively, aids its antioxidative activity (Singh et al. 2007). Because ubiquinol and vitamin E are two endogenous antioxidants that protect LDL cholesterol from lipid peroxidation, coenzyme Q10 can help prevent atherosclerosis (Littarru and Tiano 2007; Sarter 2002).

Because Q10 levels fall with age (Overvad et al. 1999), elderly may benefit more from Q10 supplementation, especially given the potential usefulness of coenzyme Q10 in the treatment of degenerative neurological illnesses like Parkinson's and Alzheimer's diseases (Beal 2004; Shults et al. 2002). Significant evidence shows that mitochondrial malfunction and oxidative damage may play a role in neurodegenerative disease etiology. Significant evidence shows that mitochondrial malfunction and oxidative damage may play a role in neurodegenerative disease etiology. Q10 may have additive or synergistic positive effects on mitochondrial uncoupling proteins and oxidative species reduction when combined with other antioxidants (Beal 2004).

3.1.8 Glucosamine

Glucosamine (2-amino-2-deoxy-D-glucose) is an amino monosaccharide that is endogenously produced from glucose (Anderson et al. 2005; James and Uhl 2001). Meat, chicken, and fish are good sources of glucosamine, whereas glucosamine sulfate, a salt of D-glucosamine with sulfuric acid, is one of the most prevalent dietary supplements (James and Uhl 2001). Glucosamine nutritional supplements such as glucosamine hydrochloride and *N*-acetylglucosamine are also available, and all of these glucosamine compounds are made from the chitin discussed in "Chitin and Chitosan" (Anderson et al. 2005). Oral administration, intravenous injections, intramuscular injections, and intra-articular injections are all options for glucosamine supplementation. The absorption of dietary glucosamine sulfate into the circulation is rapid regardless of the mode of delivery. Orally given glucosamine may be absorbed in about 90% of cases, but only 26% of it is accessible for tissue utilization. Glucosamine is found in practically every human tissue, with particularly significant quantities in the liver, kidneys, and cartilage. Glucosamine is coupled with plasma proteins, reduced into smaller molecules, and utilized for various metabolic functions in the liver (James and Uhl 2001). The fact that glucosamine accumulates in cartilage implies that glucosamine plays a key role in cartilage formation and function. Glucosamine is a substrate for the manufacture of proteoglycans and glycosaminoglycans, which are components of cartilage's extracellular matrix. It is synthesized by chondrocytes from glucose.

Because of its relevance in cartilage health, glucosamine has been used to treat osteoarthritis, a progressive condition marked by changes in the subchondral bone as a result of continuous articular cartilage wear (James and Uhl 2001). Glucosamine supplements have been demonstrated to be effective in treating the symptoms of osteoarthritis in several trials over the last 40 years. Protection against joint space narrowing, improved mobility, a decrease in the Lequesne severity index, and a fall in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores are all prominent indicators of improved results (Vangsness et al. 2009). In addition to increasing proteoglycan and glycosaminoglycan production, glucosamine inhibits the tissue-damaging enzyme "hyaluronidase," repairs damaged articular cartilage, and improves the lubricating qualities of synovial fluid in the treatment of osteoarthritis (James and Uhl 2001).

The majority of scientific investigations show that glucosamine supplements are as safe as a placebo (Vangsness et al. 2009). Interference with glucose metabolism is one of the most well-known side effects of glucosamine administration. In vitro and animal studies have shown that glucosamine activates the hexosamine biosynthetic pathway, which reduces pancreatic insulin output and insulin resistance in the liver, muscle, and adipose tissue. However, under the glucosamine concentrations produced by standard oral dosages, these side effects are uncommon (Dostrovsky et al.

2011). To summarize, oral glucosamine appears to be moderately to extremely beneficial in reducing osteoarthritis symptoms and is well tolerated by people with relatively few side effects (Anderson et al. 2005).

3.1.9 Chondroitin

Chondroitin is a linear polysaccharide made up of alternating D-glucuronic acid and D-*N*-acetyl-galactosamine disaccharide units. Sulfate ester groups are mostly found at C-4 and/or C-6 of *N*-acetylgalactosamine and/or C-2 of glucuronic acid in naturally isolated chondroitin, whereas chondroitin sulfates have the same general structure but contain more sulfate ester groups, which are mostly found at C-4 and/or C-6 of *N*-acetylgalactosamine and/or C-2 of glucuronic acid (Pigman 2012). Chondroitin is a component of "proteoglycans," the structural macromolecules of extracellular matrix organization, and is attached to the serine residues of protein cores (Asimakopoulou et al. 2008). Chondroitin can be found in up to 35–40% in pig and ox cartilage. Shark, squid, and crab cartilage can also be used for isolation. Using 1 percent potassium carbonate and sodium chloride, pure chondroitin 4-sulfate may be recovered from cow nasal septa or trachea, and protein contaminants can be eliminated using precipitation, adsorption, or proteolytic degradation (Pigman 2012). However, separating chondroitin 4-sulfate from chondroitin 6-sulfate is difficult. One important medicinal application of chondroitin sulfate, like glucosamine, is the treatment of osteoarthritis. To lower chondrocyte catabolic activity, the mechanism may involve promotion of proteoglycan production and inhibition of proteolytic enzyme synthesis. Meanwhile, chondroitin reduces bone resorption and has anti-inflammatory properties through modulating the osteoprotegerin/receptor activator of NF-B ligand ratio (Martel-Pelletier et al. 2010). Chondroitin protects cartilage matrix and subchondral bone osteoblasts against cell death and injury in general. A sufficient amount of chondroitin sulfate is required to offer resistance and flexibility to the cartilage against tensile stresses (Martel-Pelletier et al. 2010). A series of recent clinical investigations have demonstrated the pharmacological efficacy of oral chondroitin sulfate supplementation in improving the algo-functional symptoms and joint structure of osteoarthritis of the knee, finger, and hip (Bruyere and Reginster 2007; Uebelhart 2008).

Scientific studies documented that oral administration of chondroitin sulfate is very promising for the treatment of osteoarthritis, without any adverse health effect (Uebelhart 2008). In addition to its involvement in cartilage function, chondroitin interacts with a range of molecules, including growth factors, cytokines, chemokines, adhesion molecules, and lipoproteins, to perform a variety of biological tasks (Asimakopoulou et al. 2008). Chemically modified or changed sulfation patterns of chondroitin sulfate have been created in response to the demand for novel medications or drug delivery methods that target tumor cells and their interactions with effective molecules in the extracellular matrix or on the cell surface (Asimakopoulou et al. 2008). As a result, chondroitin sulfate is a key precursor molecule for the production of anticancer drugs.

3.1.10 Melatonin

Melatonin (*N*-acetyl-5-methoxytryptamine) is a hormone produced and released mostly by animals' pineal gland (Carrillo-Vico et al. 2005). Tryptophan hydroxylase, aromatic amino acid decarboxylase, arylalkylamine-*N*-acetyltransferase, and hydroxyindole-*O*-methyltransferase catalyze four intracellular enzymatic processes catalyzed by tryptophan hydroxylase, aromatic amino acid decarboxylase, arylalkylamine-*N*-acetyltransferase, and hydroxyindole (Carrillo-Vico et al. 2005). Melatonin production and release have their own cycles, which are governed by a circadian clock in the hypothalamus (Pacchierotti et al. 2001). Because the production of this pineal hormone is hindered by light, the amount produced at night vastly outnumbers that produced during the day (Bubenik 2002). Extrapineal melatonin is abundant in animals' gastrointestinal tracts, and tissue and plasma melatonin concentrations are linked to food consumption (Bubenik 2002).

Melatonin is available without a prescription as "food supplement" in various nations' supermarkets. Limited use of melatonin for its therapeutic benefits is now thought to be safe (Bubenik 2002). Exogenous melatonin as a therapy for mental and sleep problems is based on the physiological significance of melatonin in regulating circadian and seasonal rhythms. Alteration or disruption of melatonin rhythm or pineal secretion has been described in several mental diseases, including seasonal affective disorder, unipolar depression, and bipolar disorder, resulting in lower melatonin levels in patients' serum than those in the control group (Pacchierotti et al. 2001). According to the "melatonin replacement" idea, replacing age-related melatonin loss with physiological dosages should help elderly insomniacs sleep better (Olde Rikkert and Rigaud 2001).

Melatonin appears to be effective in treating sleep problems in children with neurodevelopmental disorders, particularly in reducing the time it takes for them to fall asleep (Phillips and Appleton 2004). Melatonin also has the ability to modulate the immunological system. Exogenous melatonin may boost immune responses by enhancing lymphocyte proliferation, cell activity, and the generation of interleukin and interferon when it binds to receptors on diverse immunological organs and cells (Carrillo-Vico et al. 2005; Simonneaux and Ribelayga 2003). Melatonin has also been suggested as an antiaging and antioxidant agent that may protect cells against free radical cytotoxicity. Melatonin can not only eliminate harmful radicals (particularly the hydroxyl radical), but it can also increase antioxidant enzymes (such as superoxide dismutase and glutathione peroxidase) while suppressing pro-oxidant enzymes (such as nitric oxide synthetase) (Simonneaux and Ribelayga 2003).

Melatonin's anticarcinogenic effectiveness is thought to be linked to its effects on immunological responses and free radicals. Anti-mitosis may be used to decrease cancer development, as well as decrease tumor linoleic acid intake and metabolism (Mills et al. 2005). The role of maintaining a suitably high melatonin plasma level in reducing the evolution of estrogen-responsive breast cancers might be effectively characterized (Sanchez-Barcelo et al. 2003; Simonneaux and Ribelayga 2003). In cancer patients, the quantity of melatonin was found to be negatively associated with the number of estrogen receptors. Melatonin's influence on signal transduction pathways may potentially impact receptor transcriptional activity. Melatonin treatment caused uncoupled oxidative phosphorylation, morphological changes, and autophagocytosis in human breast carcinoma cells (MCF-7) in vitro (Simonneaux and Ribelayga 2003).

The findings support research on the therapeutic efficacy of melatonin in the treatment of breast cancer (Sanchez-Barcelo et al. 2003; Simonneaux and Ribelayga 2003). Other studies have found that melatonin can help with prostate, endometrial, lung, stomach, and colorectal cancers, with significant reductions in death risk, few side effects, and inexpensive expenses. Melatonin is also said to protect against chemotherapy-induced blood cell damage, asthenia, stomatitis, cardiotoxicity, and neurotoxicity, among other things (Mills et al. 2005).

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4 Marine Bioactive Components: A Sustainable System for Good Health and Well-Being

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Abstract

There is increasing demand from consumers for healthier and more sustainable foods. The significance of marine creatures as a source of unique bioactive compounds is expanding. Marine organisms constitute nearly half of the worldwide biodiversity; thus, oceans and sea present a vast resource for new substances and it is considered the largest remaining reservoir of beneficial natural molecules that might be used as functional constituents in the food sector and cosmetic and pharmaceutical industries. The algal bioactive compounds display numerous potential beneficial biological functions including antioxidant, antimicrobial, anticancer, tissue engineering, wound healing, and skin protection activities. Secondary metabolites in marine algae, bacteria, and viruses such as phenolic acids, flavonoids, and tannins could have great therapeutic implications due to their antifungal, antiviral, and antibiotic activities against several diseases. This review should provide academia and industry with new insights into the potential application of marine bioactives in products intended to improve human health and well-being.

Keywords

Bioactive · Food · Marine sources · Sustainable foods · Secondary metabolites

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4.1 Introduction

There are many sources from where bioactive compounds are derived, and among the sources, most available bioactive compounds are acquired from littoral microorganisms, albeit the earthbound environment is a bountiful source of bioactive producers, the revelation of novel metabolites is lessening (Jensen and Fenical 2000). As far as biodiversity, marine conditions are among the most complex and richest environments. Harsh environmental conditions (chemical and physical) have been significant drivers for the development of a variety of molecules with unique structural features. Microorganisms, including specific microorganisms (bacteria, fungi, and algae), produce secondary metabolites, which might have some level of bioactivity, either against one or more microorganisms or acting against certain physiological conditions of a diseased body. These metabolites, also called as bioactive substances, are significantly utilized as antibiotics and might be effective against illnesses such as HIV-1 (Newman and Hill 2006), different bacterial infections (penicillin, cephalosporins, streptomycin, and vancomycin), or neural tube defects and neuropsychiatric sequelae (Berdy 2005). Past examinations have shown that compounds derived from marine microorganism (fungi) such as alkaloids, terpenes, polyketones, peptides, sterols, and lactones may exhibit tremendous activities including antimicrobial, antioxidant, antitumor, anticoagulant, and enzyme inhibitory activities (Lombardi et al. 2019). Consequently, marine fungi involve significant hotspot for the development of novel drugs with low toxicity and high efficacy.

As per the Global Biodiversity Assessment by the United Nations Environment Program, there are 178,000 marine species, which belong to 34 phyla (Mitra and Zaman 2016). In this manner, ocean's biodiversity addresses half of the entire globe's biodiversity, making marine microorganisms a promising supportable wellspring of novel biologically active compounds (Jimeno et al. 2004; Vignesh et al. 2011).

4.2 Marine Microorganisms

The main species of microorganism (bacteria) found in seawater have a place with genera *Pseudomonas* sp., *Vibrio* sp., *Achromobacter* sp., *Flavobacterium* sp., and *Micrococcus* sp. (Baharum et al. 2010). However, the genus Streptomyces has been the fundamental supplier of new molecules so far (Blunt et al. 2018). Marine bacteria should have physiological, biochemical, and molecular properties that are not the same as their terrestrial counterparts and, in like manner, they may produce different compounds (Siddharth and Vittal 2018). So, marine bacteria are likely the most promising microorganisms for the detection of novel molecules with antibacterial properties, particularly, since the majority of natural antibacterial drugs come from one group of terrestrial bacteria, the actinomycetes (Butler et al. 2013).

A few myxomycetes were recuperated from freshwater conditions (Shearer and Crane 1986; Lindley et al. 2007), where they give off an impression relatively common. Dykova et al. (2007) detailed that they distinguished a possible myxomycetes living as an endocommensal of a sea urchin in the Adriatic Sea. It appears to be probable that any types of myxomycetes disengaged from marine habitats would incorporate uncommon taxa, perhaps including those new to researchers.

Marine fungi constitute the main degraders of lignocellulosic and sweet smelling (aromatic) materials in marine habitats (Ameen et al. 2014, 2015a, b, c, 2016; Hyde et al. 1998). As indicated by their capacity to grow in marine habitats, they are named as obligate or facultative marine fungi (Borse et al. 2012). The former grows quickly and sporulate only in a marine or estuarine environment, while the latter generally come from the terrestrial environment and are adjusted to the marine one. Marine fungi are connected to algae, corals, and detritus of marine macrophytes. About 1500 species of marine fungi, from which 530 relate to obligate marine fungi, are established. Incidentally, it is difficult to recognize the obligate or facultative character of the marine fungi, and henceforth, the broad term “marine-derived fungi” is used (Bugni and Ireland 2004). Almost all the marine fungi belong to the phylum Ascomycota (Jones et al. 2015), while the phylum Basidiomycota is under-addressed (Jones and Pang 2012; Jones et al. 2015; Raghukumar 2017).

Marine microalgae are minuscule unicellular plants, which form what is known as phytoplankton. They assume a significant role in oceans as primary producers of biomass and organic compounds, due to their photosynthetic process (Camacho et al. 2007; Kiuru et al. 2014). Also, marine microalgae produce around half of atmospheric oxygen (Singh et al. 2005). Marine microalgae are classified into three groups: blue-green algae (Cyanobacteria), diatoms (Bacillariophyta), and dinoflagellates (Dinophyceae). It is believed that there are around 50,000 species of microalgae, but not many of them have been described (Lee et al. 2013). The considerable biochemical differences found among marine microalgae make them an undiscovered hotspot for the biosynthesis of a huge diversity of bioactive molecules (Abida et al. 2013; Coêlho et al. 2019). Microalgae can be used for biomass creation, primary metabolite production (e.g., carotenoids, proteins, and lipids), as biosorbent for heavy metals (Al-Homaidan et al. 2018) and secondary metabolite production (generally compounds with pharmaceutical applications) (Khan et al. 2018).

4.3 Marine Environment as a Prolific Source of Bioactive Compounds

As life began in the universe, the Primordial Soup Theory suggested that when the chemicals from the atmosphere combined with some form of energy possibly a pond or ocean, there is evolution of life. The evolution of new species gave rise to the building blocks of proteins—the amino acids. Organic compounds are present in oceans and are considered to be favorable for the growth of life and evolution in general. Researchers emphasized oceans as a novel and unexplored source of potentially useful bioactive compounds in the early 1960s. The basis of this could be the fact that more than 95% of the earth’s biosphere is ocean (Davidson 1995) and

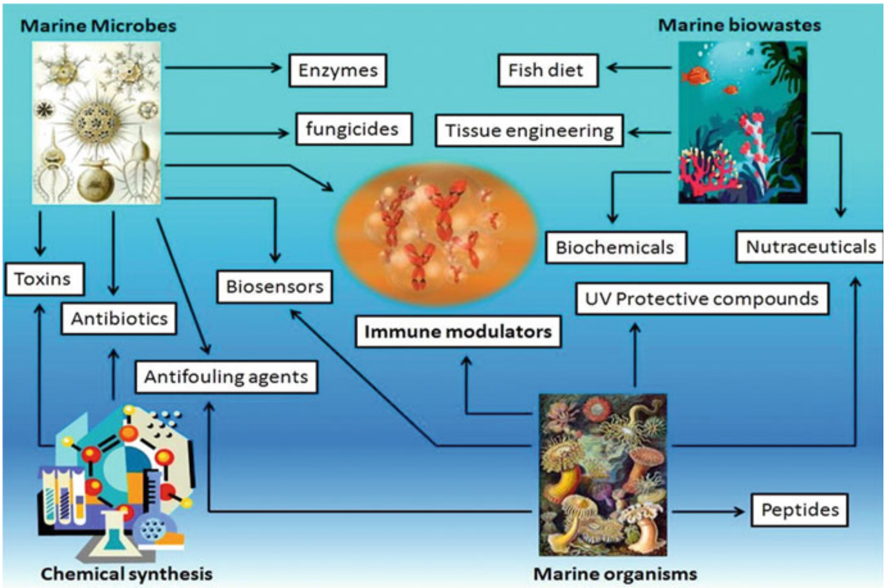

Fig. 4.1 Bioactive substances produced in the marine environment (source: Bhatnagar and Kim 2010)

scientists wish to unearth bioactive compounds in unexpected places as the antibiotic resistance increases and the production of novel bioactive compounds tapers down. Over the past five decades, more than 10,000 marine metabolites have been isolated and characterized (Fuesetani 2000).

An enormous number of bioactive substances are mostly found in the ocean (Fig. 4.1). The various inhabitants have tremendous potential to be utilized as cosmeceutical agents including bacteria, fish, algae, corals, crustaceans, and even sea mud (Kim et al. 2006). Demonstrated that methanol extracts of alga *Corallina pilulifera* possessed a high phenolic content, which reduced the expression of UV-induced MMP-2 and MMP-9, in human dermal fibroblast in a dose-dependent manner, thereby attaining the capability of inhibiting free radicals. There has been another study on the photoprotective effect of phlorotannins from *Ecklonia cava* against the photo-oxidative stress induced by UV-B irradiation (Heo et al. 2009).

4.4 Bioactive Compounds from Marine Microorganisms

4.4.1 Bioactive Compounds from Marine Bacteria

Marine bacteria are an increasingly studied source for novel metabolites including archaea and eubacteria (Blunt et al. 2014). Archaeabacteria are an interesting group as many of them are extremophiles, organisms that live in extreme conditions, e.g., deep sea, thermal vents, low temperature, or chemically challenging environment (salinity, pH, heavy metals). Archaean cell membranes consist of glycerol tetraethers and differ from those of eubacteria where the stabilizing element is a catenoid or hopanoid (Kornprobst 2010). Extremophiles have potential sources not only for stable enzymes for industrial purposes but also for pharmaceutical applications (Rothschild and Mancinelli 2001). Marine eubacteria consist of Gram-negative α-proteobacteria and γ-proteobacteria, Gram-positive actinomycetes and bacilli, and several anoxygenic anaerobes (Kornprobst 2010). Marine fungi, marine bacteria, some micro-algae cyanobacteria are living as symbionts in sediment, sponges, or with other invertebrates (Thomas et al. 2010). Only small amounts of sample are required to be grown in the laboratory for the cultivation of several marine bacteria or metagenomic approaches can be used to build libraries. Marine bacteria produce several classes of compounds. Salinosporamide A (marizomib) is isolated from sediment-based actinomycete *Salinospora* and is currently at phase II trials as proteasome inhibitor for multiple myeloma. Marine bacteria generate around 100 novel compounds per year (e.g., polyketides, alkaloids, fatty acids, peptides, and terpenes) (Kornprobst 2010). Bacterial metabolites are probably the most promising source for novel antibacterial compounds since most of the natural product-derived antibacterial drugs in the pipeline are from terrestrial actinomycetes (Butler et al. 2013). Antibiotic (Jang et al. 2013), isolated from Streptomyces species, is a potential antibiotic against *Bacillus anthracis* and methicillin-resistant *Staphylococcus aureus* (MRSA). Another potential antibiotic against MRSA and vancomycin-resistant *enterococci* is thiazolyl cyclic peptide PM181104, isolated from sponge-associated actinobacterium strain of the genus Kocuria (Mahajan et al. 2013).

Gram-negative gammaproteobacteria dwell on lithosphere and in a marine environment. The exploration of marine environment continues for isolation of more novel strains of *Pseudomonas,* which are probable sources of bioactive compounds. Romanenko et al. (2008) have isolated and taxonomically classified an aerobic, non-pigmented bacterium strain KMM 3042. It was found to cluster adjacent to *P. borbori* in the Pseudomonas genus, with 97% sequence homology. Although few, the chemical structures of these marine Pseudomonas-derived bioactive substances are diverse, including pyrroles, pseudo-peptide pyrrolidinedione, phloroglucinol, phenazine, benzaldehyde, quinoline, quinolone, phenanthrene, phthalate, andrimid, moiramides, zafrin, and bushrin (some of these bioactive compounds are antimicrobial agents, and dibutyl phthalate and di-(2-ethylhexyl) phthalate have been reported to be cathepsin B inhibitors) (Isnansetyo and Kamei 2009).

Galaviz-Silva et al. (2018) reported acute antimicrobial activity against the food-borne poisoning strains *Staphylococcus aureus* and *Vibrio parahaemolyticus* by the bacteria *Bacillus aerius*, *B. oryzicola*, *B. safensis*, *B. boroniphilus*, *B. altitudinis*, and *Virgibacillus senegalensis* isolated from marine habitats in Mexico. It would seem that these marine bacteria could serve as a potential alternative against other clinically important bacteria for the elaboration of new antimicrobials.

A newly discovered metabolite named dentigerumycin E by co-cultivation of the marine strains *Streptomyces* sp. and *Bacillus* sp., obtained from the shore of a muddy wetland, showed anti-proliferative and antimetastatic activities against human carcinoma. This indicated that co-cultivation of marine microorganisms could be a promising approach to find new bioactive microbial metabolites (Shin et al. 2018).

Shivale et al. (2018) isolated two novel antioxidant-producing bacteria from marine soil samples, which were identified as *Janibacter melonis* and *Pseudomonas stutzeri*. Nevertheless, more research is required to identify the antioxidant compounds produced and their possible industrial utilization.

Wang et al. (2018) isolated and purified an exopolysaccharide from the marine bacterium *Aerococcus uriaeequi* that exhibited antioxidant activities, which, according to its safety assessment on mice, were safe for both topical and oral application. Therefore, it could have potential applications in medicine.

Zhang et al. (2020) identified a new abyssomicin and six known abyssomicin and proximicin analogs from extracts of the cultures of a marine bacterium isolated from sea sediments and identified as *Verrucosispora* sp. MS100137. The new compound and two of the known ones exhibited considerable antiviral effects against the IAV.

4.4.2 Bioactive Compounds from Marine Fungi

Marine fungi belong to phyla Chytridiomycota, Oomycota, Ascomycota, Basidiomycota, Deuteromycota, and Zygomycota (Kornprobst 2010). Like marine bacteria, marine fungi often live as symbionts in algae or marine invertebrates, especially sponges. Collection of marine fungi usually requires the collection of the host or supporting material (e.g., algae, marine invertebrates, sediment, or water), which gives challenges to maintain the viability until extraction (Duarte et al. 2012). Most of the fungal species isolated from sponges belong to the genera *Aspergillus* and *Penicillium*. Around 150–200 new compounds are now isolated from marine fungi yearly (Blunt et al. 2014), and the number has been increasing. The compound classes include polyketides, sesquiterpenes, alkaloids, or aromatic compounds. Although no marine fungus-based drug is currently in the pipeline, promising cytotoxic, neuroactive, antibacterial, antiviral, and antifungal activities have been found from fungi metabolites.

A number of novel compounds and metabolites with bioactive potential continue to be isolated and characterized from marine-derived fungi, which are capable of producing not only antimicrobial but also antifouling compounds. In 2006, a bioassay-guided isolation and purification procedure were used to obtain a novel antifouling and antimicrobial compound from a marine-derived fungus

Ampelomyces sp. The isolate, 3-chloro-2,5-dihydroxybenzyl alcohol, effectively inhibited larval settlement of the tubeworm *Hydroides elegans* and of cyprids of the barnacle *Balanus amphitrite* and was nontoxic, suggestive of a potent antifoulant and/or antibiotic activity (Kwong et al. 2006). Another study from the same group concerned the antibiotic and antifouling compound production by the marine-derived fungus *Cladosporium* sp. F14. They reported that nutrient is enriched with cultivation media, and this strain produced antibiotic and antifouling compounds in the presence of glucose or xylose. In the search for novel antimitotic and antifungal substances from marine-derived fungi, Gai et al. (2007) reported that low concentration of the EtOH extracts of the culture broth of a *Fusarium* sp. (strain 05JANF165) was bioactive. Their search for the basis of this bioactivity led to the identification and purification of a new antifungal antibiotic, and the chemical structure was elucidated as fusarielin E (Gai et al. 2007).

Agrawal et al. (2018) isolated new marine fungal species identified as *Simplicillium lamellicola*, *Leptosphaerulina* sp., *Penicillium citrinum*, *P. chrysogenum,* and *Aspergillus sydowii* with high antimicrobial activity against the acne-inducing bacteria *Cutibacterium acnes* and *Staphylococcus epidermidis*.

Li et al. (2018) demonstrated the antitumoral effect on cervical cancer (HeLa cells) and breast cancer (MCF-7) human cells of a polysaccharide, containing mainly mannose, produced by cultivation of the marine fungus *Hansfordias sinuosae.* Chang et al. (2019) described the anti-quorum sensing (anti-QS) activity against *Chromobacterium violaceum* and *Pseudomonas aeruginosa* by ethyl acetate extracts of the marine fungus *Penicillium chrysogenum* DXY-1, isolated from sea sediments. One of the compounds showing anti-QS activity was identified as tyrosol. They observed that for the same concentration the anti-QS activity of the identified compound (i.e., tyrosol) was not higher than that of the whole extract. So, they concluded that other active compounds may exist in the crude fungal extracts.

4.4.3 Bioactive Compounds from Marine Microalgae

Cyanobacteria are a diverse group of Gram-negative bacteria, also known as blue-green algae that produce an array of secondary compounds with selective bioactivity against vertebrates, invertebrates, plants, microalgae, fungi, bacteria, viruses, and cell lines (Lopes et al. 2010). Some reviews in the past have proved that they produce a wide variety of secondary metabolites with antifungal, antiviral, antibiotic, and other activities, which make them an interesting candidate of potential pharmaceutical importance (Patterson et al. 1994). Certain anticancer compounds, which were initially thought to be obtained from marine sources, are now known to be produced by cyanobacteria (Luesch et al. 2002). Ulithiacyclamide and patellamide A belong to Cyanobactins, produced by *cyanobacteria*, which have potent antimalarial, antitumor, and multidrug-reversing activities (Sivonen et al. 2010).

De Vera et al. (2018) studied the bioactive potential of the extracts of thirty-three marine microalgae. They found that the dinoflagellates *Prorocentrum hoffmannianum*, *P. arenarium*, *P. reticulatum*, *Alexandrium tamarense,* and

Gambierdiscus carpenteri showed promising apoptotic activities. Also, the production of bioactive compounds by the marine microalga *Amphidinium carterae* was investigated. A new substance was identified that was linked to the amphidinol family, given the name amphidinol 22, with potent cytotoxicity activity and moderate antimicrobial activity against *C. albicans* (Martínez et al. 2019).

4.4.4 Bioactive Components from Marine Viruses

Viruses are typically viewed as pathogens that cause disease in animals and plants. In recent years, however, it has become increasingly clear that they play critical roles in the world oceans. Not much is known about the bioactive potential of marine viruses, but the focus is turning these days to discover newer marine viruses and to study their physiological processes and the secondary metabolites produced, if any (Bhatnagar and Kim 2010).

4.4.5 Bioactive Components from Marine Fishes

Fishes are a diverse group of living vertebrates with more than 27,000 species currently known, and over 16,000 of them are marine species (Nelson 2006). Fish-based omega-3 fatty acid ethyl esters are registered as a drug named Lovaza® in the USA or Omacor® in the EU; currently, it is the only fish-oil product approved as a drug. Oil from fresh livers of cod, *Gadus norhua*, and from halibut, *Hippoglossus*, is used in vitamin A and D therapy. Squalene, present in large quantities in shark liver oil and also in plant kingdom, e.g., in olives, is used as antimicrobial, immune system enhancer, and intermediate in the manufacture of pharmaceuticals and an adjuvant in the vaccines (Reddy and Couvreur 2009). Tetrodotoxin, one of the most toxic low molecular weight poisons, is produced by symbiotic bacteria and is found in certain puffers, ocean sunfishes, and porcupine fishes. Tetrodotoxin is also unique in preventing the usual increase in permeability to sodium ions without affecting the outward potassium flow, and it has potential for the treatment of neuropathic pain (Nieto et al. 2012).

4.5 Applications of Bioactive Components from Marine Sources

4.5.1 Pharmaceutical Industry

For a variety of biotechnological and medicinal applications, a varied spectrum of marine-derived bioactive chemicals is accessible. Natural materials can be converted into high-value-added goods of interest after careful consideration. Bio-products originating from the sea are regarded prospective options because they contain a large number of pharmacologically active ingredients with a wide range of chemical

Fig. 4.2 Marine-based potential sources and their various biomedical applications

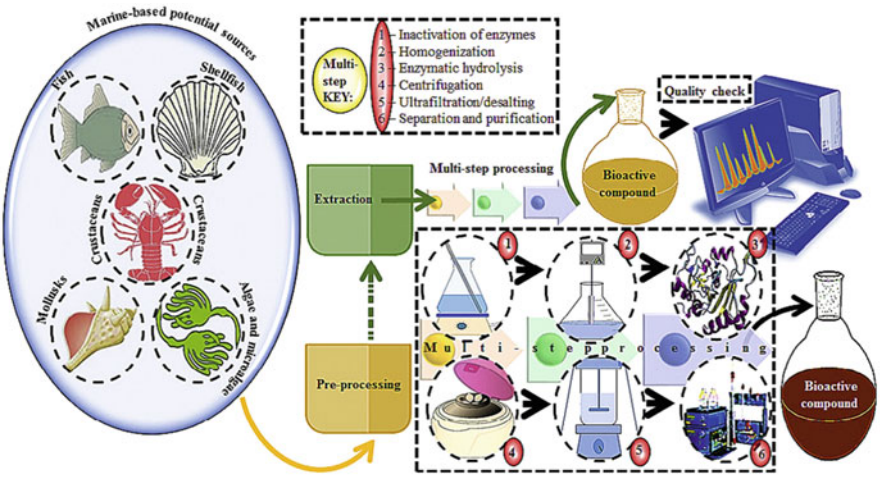

Fig. 4.3 A schematic illustration of bioactive compound purification process

and structural variety. As a result, they have a lot of potential to create high-value therapeutics. Various biotechnological and medicinal applications of marine-derived bioactive chemicals are depicted in Fig. 4.2. Step-by-step purification method for bioactive chemicals employing several marine-based potential sources is depicted in Fig. 4.3. Many additional fascinating traits, such as anticancer, antibacterial, cytotoxic, and ion channel blockers, have been investigated critically in addition to unique structural features. Fucoidan, a naturally occurring sulfated polysaccharide isolated from marine brown seaweeds, is a promising pharmaceutical medication candidate. This naturally occurring marine-based bioactive compound has been considered a potential alternative to commercially available steroidal drugs due to its many strong characteristics such as anticoagulant, antiviral, antiangiogenic, antitumor, anti-inflammatory, antioxidant, anti-proliferative, and immune-modulating properties.

4.5.2 Antimicrobial Potential

Microbial infections are one of the main factors that have an ongoing impact on human health. In light of this scenario, one of the major drawbacks of improved healthcare systems is the emergence of resistant strains to commercial products, such as antibiotics. This results in an increase in the flow of new medications into developed and developing countries. Researchers from all over the world are attempting to develop novel antimicrobial agents from a variety of sources, including natural elements produced from the sea. Laminarin is high in β-glucan, a polymeric chain containing a terminal glucose and another chain containing a terminal mannitol that has anticoagulant, anti-inflammatory, anticancer, and antioxidant properties. Pig growth performance was assessed using laminarin and fucoidan as a maternal food supplement from gestation to weaning. In comparison with pigs fed a diet lacking fucoidan, those fed a diet with it gained weight. Pigs were fed a laminarin and fucoidan-rich extract (L/F) for 21 days prior to slaughter, and lipid oxidation levels in the longissimus dorsi (LD) muscle were assessed. The addition of L/F had no antibacterial impact, but it did reduce lipid oxidation in the liver tissue, suggesting that L/F might be utilized as a natural antioxidant supplement for pig feed to replace synthetic antioxidants. It is well known that the piglet becomes sensitive to infections like *E. coli* and *Salmonella* shortly after weaning. Seaweeds have been investigated as a possible replacement to antibiotics in piglet feed. The effects of laminarin and fucoidan as additions in the post-weaning swine diet were studied separately and in combination. In comparison with the controls, pigs fed laminarin gained weight on a daily basis and had lower fecal *E. coli* counts. Overall, the best supplement for enhancing gut health in post-weaning pigs was laminarin. The effects of *Laminaria hyperborea* and *Laminaria digitata* extracts as feed supplements on gut architecture, intestinal microbiota populations, fatty acid concentrations, and immunological state in weaned pigs were investigated. The addition of seaweed extracts reduced the populations of *enterobacteriaceae, bifidobacteria*, and *lactobacilli*; however, there was no significant influence on the immunological response.

4.5.3 Anticancer Potential

Cancer is a huge health concern all around the world. In 2012, there were 8.2 million cancer deaths and 32.6 million cancer survivors globally. According to the American Cancer Society, 1.7 million people will be diagnosed with cancer in the United States in 2016. Apoptosis, angiogenesis suppression, and altering the tubulin–microtubule equilibrium are three methods that might cause cell death. Commercially accessible medications have primarily targeted at least one of the pathways outlined above. A number of anticancer bioactive chemicals derived from various marine resources have been studied. Fucoidans have been investigated *in vivo* and *in vitro* for a variety of physiological pathways, including oxidative stress, inflammation, and carcinogenesis. The connection between their structure and their activities is still a mystery. Though the exact mechanism is unknown, fucoidans are known to cause cytotoxicity and apoptosis in cancer cells. *In vitro*, a depolymerized fucoidan from *Saccharin cenchroides* showed almost the same anti-proliferative effect as the natural fucoidan against HT-29 cells. Figure 4.4 depicts the anticipated chemical pathway through which bioactive substances such as fucoidans promoted ROS-dependent apoptosis in a cancer cell. *In vivo*, the laminaran and the fucoidans containing galactose demonstrated no cytotoxicity. The active chemicals isolated from *A. angusta*, on the other hand, were found to be highly effective in inhibiting the proliferation of human colorectal (HT-29) cells. In breast cancer, colon cancer, and melanoma cell lines, fucoidans isolated from

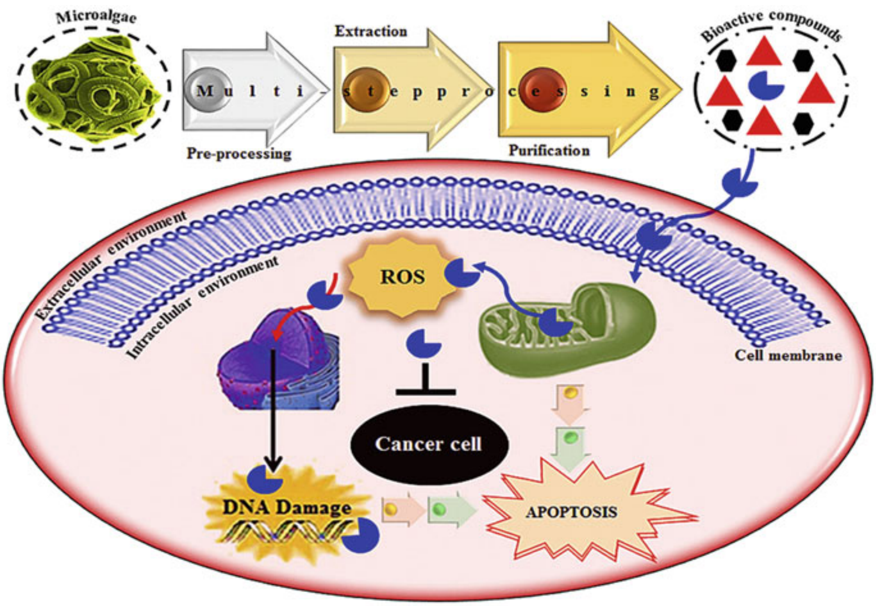

Fig. 4.4 Proposed molecular mechanism bioactive compounds, e.g. fucoidans induced ROS-dependent apoptosis in cancer cell

Saccharin cenchroides, *Fucus evanescens*, and *Undaria pinnatifida* were investigated for anticancer activity. When compared to fucoidan recovered from *F. evanescens* and *U. pinnatifida*, the highly sulfated fucoidan from *S. cichorioides* had stronger anticancer activity. By suppressing the phosphorylation of p65-NF-kB, the compound inhibited tumor cell migration and the chemokine CCL22, preventing lymphocyte recruitment, proving to be a potentially beneficial cancer treatment. Because of its low toxicity, fucoidan therapies are also reasonably safe. A phase 2 clinical research employing a food supplement containing 75 mg of fucoidan from seaweed extracts was shown to be safe after 4 weeks of oral use.

4.5.4 Tissue Engineering

Tissue engineering (TE) is a multidisciplinary field that combines engineering and biological (biomedical) sciences to create viable alternatives for maintaining, improving, or restoring the biological function of a tissue or an entire organ. Understanding the principles of tissue growth and applying them to create a functional replacement, repair, maintenance, and augmentation of tissue function for clinical use have also been classified. The National Science Foundation (NSF) produced a paper titled "The Emergence of Tissue Engineering as a Research Field" in 2003, which details the history of TE. Recent breakthroughs in biomimetic settings have opened up the possibility of fabricating tissues in the laboratory. Biodegradability of extracellular matrix is also acknowledged as a required quality for TE, in addition to biocompatibility and nontoxicity. The development of innovative materials for cell seeding, proliferation, and differentiation prior to the regeneration of biologically functioning tissues has piqued researchers' attention. The success of the final product is highly dependent on cellular adherence and development on the polymer surface. The chemical surface of a biopolymer can thereby influence cellular response by interfering with cellular adhesion, migration, and proliferation. To regenerate tissues, on the other hand, three specific variables are considered: culture, support, and growth factors. Cells provide a matrix for new tissues, while support holds and maintains a favorable environment for growth, and growth hormones aid and drive cell regeneration. New biomaterials and products can be easily generated now that the surface–cell interaction is thoroughly known at the cellular level.

4.5.5 Wound Healing

Wound healing is a complex process in which damaged skin must be healed either naturally or with the use of external intervention. Sophisticated wound care solutions are in high demand. The new method will significantly speed up the development of revolutionary wound-healing dressing materials. A superior dressing must provide a favorable environment for wound surfaces to heal at the fastest possible rate. Dressings are being created in practice to assist infection-free wound healing, in

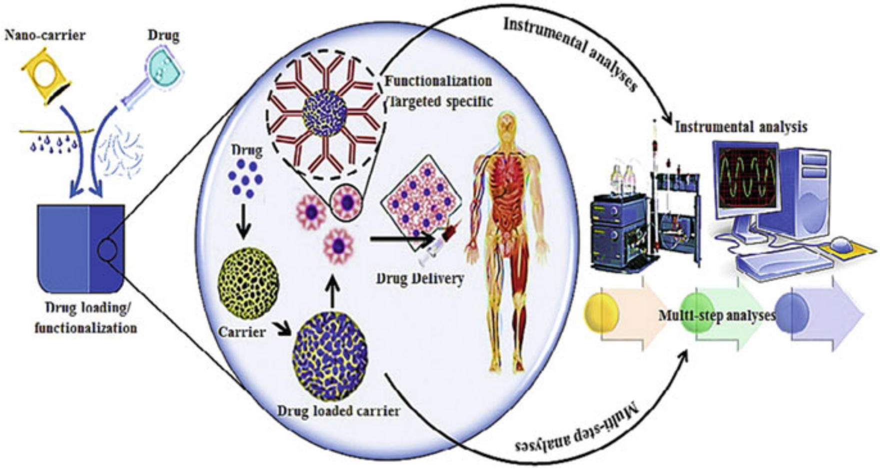

Fig. 4.5 A schematic representation of drug-loaded nanocarriers for the targeted delivery to deal with a diseased cell (Bedian et al. 2017)

addition to the fundamental covering role. The characteristics of (1) hemostatic, (2) exudate absorption, (3) provision and maintenance of a suitable environment (moisture, water, and adequate gaseous exchange), (4) functional adhesion, (5) painlessness, and (6) cost-effectiveness have been recognized and considered more critically with increasing awareness and demands of legislative authorities. Marine-derived bioactive chemicals have begun to be used in the treatment of skin wounds and skin tissue healing. All of the traits mentioned above have a lot of potential for promoting the use of marine-derived materials for wound healing. A large number of scientific investigations have been conducted with the goal of isolating, recognizing, and confining optimum candidate materials in order to provide an efficient environment for the regeneration of skin lost in wounds, such as skin burns and other healing applications. A variety of marine-derived polysaccharides, such as alginate, have attracted a lot of interest as a potential candidate material for skin tissue engineering. Figure 4.5 shows a schematic of drug-loaded nanocarriers for targeted delivery to treat a diseased cell for advanced therapies and notable applications.

4.5.6 Food Industry

A significant purity level, bioactivity, change in color and flavor, and enormous potential to develop various shapes and textures make marine-derived sources potential candidate in food industry. In comparison with the traditional dietary fibers along with many synthetic formulations, marine-derived materials offer a wider range of health benefits, thus has been classified as "generally recognized as safe" (GRAS). Antioxidative functional ingredients from marine-based resources have been represented as a potential alternative to many synthetic ingredients that can also additionally contribute to the consumer's well-being. These functional ingredients have demonstrated a vital role in human health and nutrition. In spite of the above discussed benefits, the development of marine-derived functional ingredients involves a range of biotransformation practices via synthetic (chemical) and biological (enzyme) catalyst-assisted hydrolyses. To obtain maximum yield, many other physiochemical reaction parameters in the reactant compartment, such as pH, temperature, and buffer solutions, must be optimized. Hydrolysis using enzymes allows for the creation of new physiologically active substances. In comparison with chemical-based catalysts, enzyme-assisted hydrolysis processes have a number of significant advantages, including (1) environmental friendliness, (2) mild reaction conditions, (3) energy savings, (4) ease of use, (5) no or fewer protection and de-protection steps, (6) no or reduced use of harsh chemicals, (7) high yield, (8) nontoxic in nature, (9) no or fewer by-products, and (10) follows the green agenda. The biological activity of these peptide molecules is significantly influenced by their composition and amino acid sequence, which typically ranges from 3 to 20 amino acid residues in length. Though short-chain amino acids are inactive within the original protein sequence, they have a high chance of being released during digestion, food processing, or fermentation. Antioxidant, antihypertensive, anticoagulant, anti-HBV, anti-inflammatory, antibacterial, and antifungal activity have been demonstrated in bioactive compounds produced through enzyme-assisted hydrolysis. Proteins, polysaccharides, vitamins, and a variety of other vital nutrients are abundant in marine-derived materials.

4.5.7 Biomedical and Food Applications of Fishbone

Fishbone has biomedical and culinary applications. Ca is mostly found in milk and other dairy products; however, lactose indigestion and intolerance prevent certain people from drinking milk. As a result, various studies have been conducted on calcium supplements as an alternative. Fishbone or skeleton is one of the most valuable sources for identifying health-promoting components and a potential source of minerals and calcium among fish processing by-products. Calcium phosphate bioceramics such as tetracalcium phosphate, amorphous calcium phosphate, tricalcium phosphate, and hydroxyl-apatite have been found as the best bone replacement materials in recent years. Because Ca is absorbed and transported as Ca^{++}, the uptake of Ca across the intestinal mucosa may be influenced by the ionization of Ca molecules prior to absorption. Ca is largely contained in the bones of tiny fish as the crystalline compound hydroxyapatite, which is insoluble at neutral pH. Nonetheless, the solubility of hydroxyapatite is increased by the stomach's gastric acid medium. Collagen makes up around 30% of the organic components of fishbones, whereas calcium phosphate and hydroxyapatite make up the majority of the inorganic compounds (60–70%). As a potential supply of calcium, fishbone is an important component of human health. Ca is essential for bone health and, when combined with vitamin D, helps to enhance cardiac health and a variety of ailments such as gastrointestinal disorders, diabetes, and hypertension. In rats, Patterson et al. (1994) found that eating tiny fish with bones increased Ca bioavailability. Fishbone peptides also improve Ca solubility and bioavailability in ovariectomized rats, according to Jung et al. (2006). Because fishbone contains hydroxyapatite, it can be used as a calcium supplement and as a substitute for manufactured hydroxyapatite; as a result, it can be ingested by persons who do not drink milk or dairy products. To include fishbone in cuisine, however, other processes such as hot water treatment and heat acetic acid solution need to be used to transform its structure into an edible form.

4.5.8 Cosmetics

"Any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips, and external genital organs) or with the teeth and mucous membranes of the oral cavity with the sole or primary purpose of cleaning, perfuming, changing their appearance, protecting them, keeping them in good condition, or correcting body odor," according to the European Commission. More lately, another category "cosmeceuticals" has piqued the industry's interest and piqued the curiosity of the most observant consumers. Despite the fact that it has no legal validity today, the industry continues to use this term to describe a product that falls between cosmetics and pharmaceuticals. Because of the benefits they provide and the absence of many dangerous chemicals found in conventional cosmetics, there is an increasing desire for more natural cosmetics, especially those manufactured with natural/organic ingredients. As a result, the cosmetics sector is rapidly expanding in order to meet these rising demands. Marine organisms, such as seaweeds, provide some of the primary active-based natural substances utilized in cosmetics. Vitamins, minerals, amino acids, antioxidants, and vital fatty acids can all be found in abundance in marine macroalgae. Seaweeds are unusual in that they contain bioavailable components, which mean that their active, nutrient-rich compounds can be absorbed more easily by the skin and body. Seaweeds provide a variety of advantages, including lowering the appearance of redness and blemishes, brightening, moisturizing, re-mineralizing, minimizing the look of sun damage, and firming skin, thanks to their bioavailable nature. Algae extracts of specific elements can be added into these products, or particles of dried seaweeds can be crushed and powdered and incorporated into skincare products such as exfoliating lotions, face masks, face washes, and soaps. On the labels of cosmetic products like creams and lotions, you could see words like "marine extract," "extract of alga," "seaweed extract," or something similar. This usually signifies that one of the seaweed hydrocolloids has been added to the product. Water-binding compounds, such as alginate or carrageenan, help hold water onto the skin and hair, improving the moisture balance. Both can be found in multiple products like lotions, creams, shampoos, conditioners, and toothpastes. Seaweeds can be used in two ways in cosmetics: They can either be a vehicle, serving as a stabilizing, emulsifying, or other types of agent necessary for product preparation; or as the active therapeutic ingredient in the product, for example, in antiaging skin treatments or after-sun skincare products. Saturated and unsaturated fatty acids, which are beneficial substances, are abundant in algae. Palmitic acid and other fatty acids, which are abundant in marine seaweeds, are used as emulsifiers in cosmetics, and ascorbyl palmitate, a derivative of palmitic acid, is an antioxidant with antiaging and anti-wrinkle properties. Purified phlorotannins isolated from brown seaweeds are used in cosmetics because they help to prevent and slow down the aging process of the skin, which is primarily caused by free radical damage and a decrease in hyaluronic acid content. Alginates, ulvans, laminarans, and fucoidans are some of the polysaccharides produced by marine algae. Large levels of L-fucose and sulfate are generally present, along with modest amounts of other sugars such xylose, galactose, mannose, and glucuronic acid. Polysaccharides' ability is influenced by their sulfated concentration, molecular weight (chain length), and the type of algae from which they are collected. CODIAVELANE®, a cosmetic made of propylene glycol, water, and *Codium tomentosum* extract, is an example. It has been demonstrated that adding oligoelements and increasing surface hydration normalize and regulate skin's moisture content. Mycosporine-like amino acids (MAAs), a collection of tiny water-soluble chemicals discovered in marine algae, is biologically significant due to its photoprotective properties. Furthermore, its antioxidant and skin-protective techniques pique attention for potential pharmacological and esthetic uses. Some lotions with antiaging benefits already contain an extract of *Asparagopsis armata* (ASPAR'AGETM) that contains these MAA molecules. Aside from the various existing and commercialized cosmetics and cosmeceuticals, several other seaweed extracts are being researched.

4.6 Sustainability

Seafood is a form of sea life regarded as food for humans, which includes fish and shellfish. Marine foods have been regarded as the rich protein source that contains all essential amino acids, polyunsaturated fatty acids (PUFAs), vitamins, and minerals like Ca, I, and other vital nutrients. Seafoods are available worldwide and are very tasty and nutritious. Marine bioactive constituents, obtained from various marine animals, plants, and lower organisms, have received greater attention due to their high level of diversity, thus making them a logical target for looking for natural products. Due to increasing need for novel bioactive components, for the treatment of human diseases like microbial infections, cancer and inflammatory processes, there is need to explore and extract new bioactive compounds from seafoods with beneficial effects. It has been also observed that the isolated isolated peptides from fish and algae that reported to have anticancer, anticoagulant, and anti hypercholesterolemic activities. Marine bacteria and fish oils contain omega-3 fatty acids, whereas seaweeds and shellfish contain phenolic compounds and carotenoids that have excellent antioxidant potential.

To raise the global standard of living without increasing the use of resources beyond globally sustainable levels has become the major aim of sustainability.

Search for successful bioactive compounds has a direct correlation with the number of the species being brought into culture. The controlled maintenance of marine organisms makes their sustainable exploitation for industrial use possible. Most organisms exhibit heterotrophic growth in the absence of light when nutrients are available. Bioactive compound profile produced is usually influenced by mode of nutrients also, and the biomass of the organisms of particular interest will be produced autotrophically, heterotrophically, and mixotrophically (growth in which nutrients are obtained both photosynthetically and heterotrophically) so that the product profiles can be determined under each condition. High-value bioactive compounds have been produced by heterotrophic cultures and hence offer the advantages of easier scale up and higher potential densities than photosynthetic cultures. It can be illustrated with the following example: Biomass densities by photosynthetic cultures are achieved in the range of 1–5 g L^{-1}, while heterotrophic cultures achieve biomass densities greater than 50 g L^{-1}. Microbial culture productivity got improved by culturing the organisms in the high cell density fed batch culture rather than batch culture; hence, high-density fed culture is relevant for heterotrophically produced compounds not practical for photosynthetic cultures. In the perspective of economic and environmental benefit, a quest for sustainable fuel has become an emergency to ensure the access of the biofuel from affordable, reliable, and sustainable bioresource.

Microalgae and macroalgae have been considered as a potential feedstock for biofuel and industrially important co-product extraction. These are untapped for production of bioenergy to assess the feasibility of future green fuel sustainability. Integrating bio-refined algal products would fetch good value in the market and also help in attaining sustainable goals for the betterment of life. About 221 species of microalgae have been exploited by humankind, of which 66% have been utilized for food production. Macroalgae-based biofuel has been considered as an alternative fuel for a fastest growing economy like India. Government has promoted small-scale industries for employment generation and economic development in such economies, and it has been growing with environmental problems.

Because of functional advantages, algal biodiesel production could become economical, but still needs research efforts to get sustainable productivity. The biofuel industry faces downfall as the cost is higher than crude oil price. In order to evade such shortcomings, the biofuel production coupled with a biorefinery needs to be practiced. Biorefinery produces bio-products by suitable processing methods with low environmental impact. Different types of co-products have been extracted from microalgae and macroalgae; however, proteins have been obtained as a by-product and can be utilized as an animal feed. Fuel production and products from algae avoid competition with food production and by cultivating microalgae on sites where no agriculture is practiced, food production might be diminished, further use of brackish water to mass cultivate algae. Hence, there is an absolute need to understand the bioenergy potential of micro- and macroalgae and also the classes of the industrially important high-value products extracted from those strains. Further, there is an unconditional necessity to analyze and interpret more on renewable energy from algae for a long-term vision for bioenergy production.

4.6.1 Bioenergy from Macroalgae

Seaweeds (macroalgae) are regarded as the richest source of phycocolloids like agar-agar, alginates, and carrageenan . These phycocolloids are utilized for various industrial applications and are edible. Pretreatment processes are required for biofuel production since phycocolloids are difficult to break. Such seaweeds can be used as an alternative source for biohydrogen, bioethanol, biogas, biobutanol, and biomethanol production. For biofuel production through aerobic and anaerobic fermentation process, sugars like glucose and cellulose could be effectively utilized. Galactose conversion to ethanol is a challenging task currently. Saccharomyces cerevisiae was found to be capable of galactose fermentation, but most of the bacteria and yeasts were found to be effective in glucose fermentation. The ethanol production using seaweeds is increasing tremendously globally. About 97% of ethanol production is by fermentation while catalytic hydration of ethylene contributes only 3%. Consider that feedstock price is US$ 100/MT, and then, the minimum ethanol selling price was observed to be in the range of US$ 3.6–8.5/gal and this will again reduce if the feedstock price reduced US$ 50/MT. The synthetic ethanol productions were economically less attractive than fermentation. Hence, bioethanol production by low-value by-product from waste seaweeds will pave ways toward the development of an economic biorefinery with zero-waste technology.

4.7 Conclusion

Awareness of functional food and the therapeutic properties of marine-purified products have been growing in recent years. Marine resources offer important bioactive molecules that have advantages on the human body and can be applied in many fields such as the food, cosmetic, and drug industries. From marine products, functional foods can easily be developed since they are widely available and they have the ability to cure some illnesses and prevent certain diseases. Various kinds of seafood are consumed as nutritionally beneficial food. These offer valuable source for finding novel compounds, and it is considered as the largest remaining reservoir of natural molecules that may be used as functional ingredients in the food industry. These marine bioactives from algae, bacteria, and viruses may be utilized as bioactive agents in nutraceuticals because of their beneficial functionalities including antioxidant, antimicrobial, anticancer, tissue engineering, wound healing, and skin protection activities. Consequently, efforts should be made to develop marine functional foods responsibly, since their consumption could result in the decrease in the occurrence of chronic diseases.

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5 Mushroom-Based Bioactive Components: Sources, Applications, and Sustainability

Himanshi Rathore and Satyawati Sharma

Abstract

Mushroom fruit bodies are extensively used for treating, curing, and preventing various degenerative diseases like cancer and diabetes. They are powerhouse of proteins and other nutrients like good carbohydrates, essential fatty acids, and vitamin D (ergosterol) and important minerals like selenium, zinc, and calcium. Their bioactive compounds like polysaccharides, secondary metabolites (phenols, flavonoids, terpenes, etc.), and antioxidants make mushrooms a perfect and cheapest source for developing nutraceuticals and health supplements for humans. Clinical studies indicate the roles of bioactive components in curing and treating life-threatening disease like cancer. Unfortunately, their usage in India is limited to only as food that too in few regions due to the lack of knowledge. This chapter focuses on the role of bioactive molecules present in mushrooms and their role in curing cancer and its possible mechanism. A light on commercial usage and availability of mushroom-based nutraceutical products have also been highlighted so that these can be better utilized for the mankind.

Keywords

Mushroom · Vitamin D · Minerals · Cancer · Nutraceuticals

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5.1 Introduction

Edible fungi, i.e., mushrooms, are not only consumed as food these days, but also their usage has been expanded to wider extents in the domains of pharmaceuticals, cosmeceuticals, and nutraceuticals too for the mankind (Rathore et al. 2020). There are thousands of mushroom species grown all over the world depending on the environmental conditions. As per the current estimates, 200 mushroom species are being used as nutraceuticals around the world; about 35 mushroom species are commercially cultivated, whereas ten species are grown at the industrial level in several countries (Rathore et al., 2017). In India, only five mushroom species viz. button mushroom (*Agaricus bisporus*), oyster (*Pleurotus* spp.), paddy straw (*Volvariella volvacea*), milky (*Calocybe indica*), and shiitake (*Lentinula edodes*) are in commercial cultivation (Sharma et al. 2017).

Mushrooms are also known as superfoods because they are highly nutritious and contain quality proteins, notable fibers, antioxidants, and good contents of vitamins and minerals. Along with that, they exhibit activities against cancer (Lakhanpal and Rana 2005; Thakur 2012; Djibril et al. 2021), hyperlipidemic activity (Kała et al. 2020), hypocholesterolemic activity (Kała et al. 2020), antidiabetic activities (Stojkovic et al. 2019), immunomodulatory effects (Zhao et al. 2020a, b), and antioxidation (Kozarski et al. 2015). These therapeutic implications of mushrooms are reportedly due to the presence of certain nutraceutical compounds like polysaccharides, terpenoids, triterpene sterols, biologically active proteins, alkaloids, vitamins, and antioxidants (Rathore et al. 2017).

Due to the increasing population and economic slowdown, there is a continuous crisis of quality food in our country. Mushroom containing quality protein and other nutrients can be proved to be a great alternative source for combating widespread protein malnutrition. National nutritional program *Poshan Abhiyaan* and the Sustainable Development Goals (SDGs) of the United Nations collectively aim to end hunger, attain food security, and upgrade nutrition by 2030, particularly for the poor and vulnerable parts of society including infants. Mushroom technology fits in the picture of today's scenario. It is a complete technology starting from the utilization or conversion of organic wastes into consumable protein-rich food addressing vast problem of malnutrition, employment generation, and waste utilization. This chapter is focused on the nutritional and therapeutic implications of the edible mushrooms.

5.2 Nutritional and Nutraceutical Potential of Mushrooms

The mushroom fruiting bodies approximately contain 65–95% moisture, 50–65% carbohydrates and good quality proteins around 19–35%, and fat content of 2–6% (Rathore et al. 2017). Apart from these, they also exhibit bioactive agents such as polysaccharides, some biologically active proteins (enzymes, lectins, and ergothioneine), essential fatty acids like linolenic, oleic, and linoleic acids, and various secondary metabolites like phenolic compounds, terpenoids, vitamin D (ergosterol), and antioxidants, which are responsible for curing various degenerative diseases (Lakhanpal et al. 2016).

Ergosterol found in mushrooms is of great value as they are the precursors of vitamin D and help in formation of this wonder vitamin in humans. Hence, apart from the sunlight we can fulfil our the recommended dietary allowances of vitamin D by simply including the mushrooms in our daily diets. Moreover, research on the therapeutic importance of ergosterol has also been explored by various authors. Chen et al. (2017) concluded that the derivatives of ergosterol isolated and purified from the lipid-enriched fraction of species *Ganoderma lucidum* possess anti-proliferative effects on human tumor cells and hence can be used as a natural nutraceuticals and functional food ingredients for treating such ailments. Also, a derivative of ergosterol extracted from species *A. blazei* has been found to positively induce apoptosis in human carcinoma cells and hence indicated its potential usage as an anticancer agent (Shimizu et al. 2016). A clinical study conducted on mice claimed that oral administration of ergosterol extract of species *A. blazei* continuously for 20 days to sarcoma 180-bearing mice significantly reduced the growth of the tumor (Takaku et al. 2001). Hence, the ergosterol mushroom extracts could be potentially utilized to develop anticarcinogenic drugs.

Extracts from different species of mushrooms containing phenolics, vitamin E, vitamin C, and carotenoids have also been reported to boost the immune system, have anticancerous, antihypercholesterolemic activity, and antiviral activity (Rathore et al. 2017). Moreover, according to Watanabe et al. (2014) almost all species of mushrooms are rich source of vitamin B_{12} and he concluded that the consumption of approximately 50 g *of L. edodes* dried fruiting bodies can meet the daily recommended dietary allowances of an adult, which is 2.4 μg/day. Moreover, they also contain L-ergothioneine, which is an unusual amino acid that possesses high antioxidant properties, and hence works as a free radical blocker with an ability to protect cells from oxidative stress (Figueiredo and Regis 2017). Fruiting bodies of mushrooms are also found to be rich in soluble and non-soluble fibers. These fibers are known to help in lowering the total cholesterol levels and therefore can be used to treat cardiovascular diseases (Cheung 2013).

Polysaccharides extracted from mushroom species also possess many therapeutic properties. Along with the nutrients like proteins and nucleotides, they play important roles in various activities of the biological system such as cell–cell communication, adhesion, and molecular recognition in the immune system (Mohammed et al., 2021). Polysaccharides derived from edible fungi, specifically β-glucans, are responsible for many physiological activities like antitumor, immunomodulatory, antioxidant, antiviral, anti-inflammatory, anticarcinogenic, and neuroprotective activities (Rathore et al. 2017).

5.3 Anticancer Property of Mushroom and Its Mechanism

Mushroom extracts are known for their potent activity against cancerous cells. Polysaccharides including glycans and homopolymers to highly complex heteropolymers all exhibit anticancerous activities (Niego et al., 2021). As shown in Fig. 5.1, the mechanism behind the destruction of cancer cells involves the activation of cytotoxic macrophage, natural killer cells, and dendritic cells, which triggers the responses toward killing the unwanted cells (Rathore et al., 2020).

According to Blagodatski et al. (2018), mushroom fruit bodies contain compounds that intervene in the signals to the tumor-specific proliferation pathways, regulation of apoptosis, angiogenesis, metastasis, and regulation of immune system. Several extracts from medicinal mushrooms have been studied for their anticancerous properties. In a study conducted by Joseph et al. (2018) concluded that the ß-glucans, which are a polysaccharide, have potent action in curing lung cancer in humans, whereas Pires et al. (2017) revealed that mannogalactoglucan again a polysaccharide extracted from mushroom species *A. bisporus* exhibited

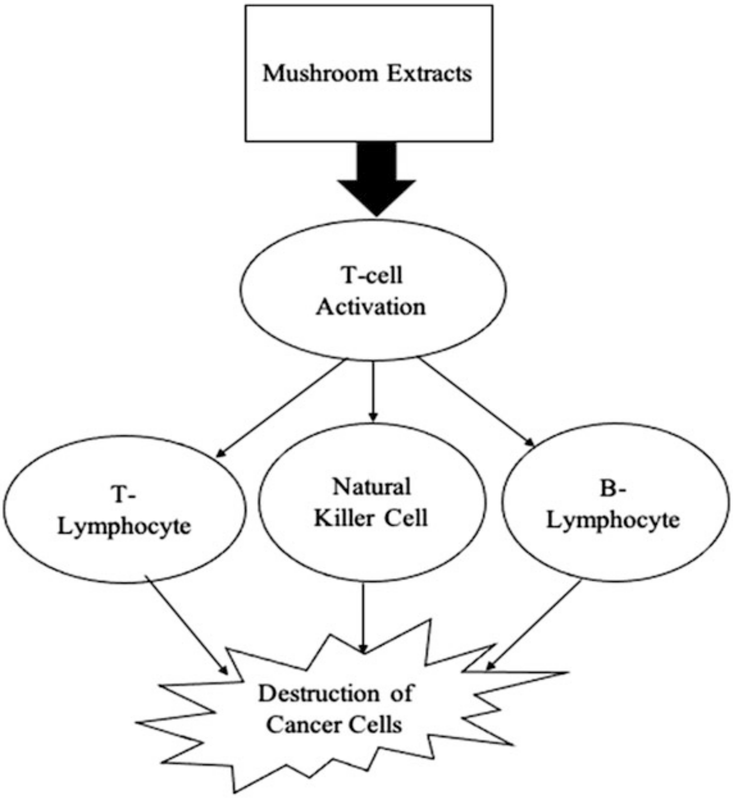

Fig. 5.1 Mechanism behind destruction of cancerous cells by mushroom extracts

antitumoral activities against human hepatocarcinoma cells. Similar results have been published by Zhao et al. (2020a, b) indicating the role of glucogalactomanan polysaccharide extracted from *A. bisporus* as a potent immune modulator, which significantly inhibited the proliferation of RAW 264.7 cells. Role of medicinal mushroom *L. edodes* polysaccharides has also been investigated against antitumor activity in cervical carcinoma cells and found effective in inhibiting the proliferation and apoptotic death of tumor cells (Ya 2017). Lentinan, which is again a polysaccharide found in *L. edodes,* possesses antitumoral activities. Liu et al. (2019) concluded that lentinan exhibited the inhibitory effects against human ovarian cancer when tested in mice models. Similarly, Alonso et al. (2018) revealed that a proteoglucan extracted from the mushroom species *Grifola frondosa* has also been found to exert both antitumoral effects on various types of cancers. A detailed list of some edible mushroom species indicating the activity against cancerous cell growth is highlighted in Table 5.1.

5.4 Commercial Mushroom-Based Nutraceuticals

Mushroom usage is not limited only as an food ingredient, and their fruiting bodies or extracts are also being successfully utilized for making various dietary supplements and nutraceuticals to improve the quality of human life. In vitro and in vivo studies have indicated that mushrooms exhibit great potential in treating and curing various life-threatening diseases such as cancer, diabetes, and heart stroke. Various brands are selling variety of mushroom and their extract-based health supplements and drugs in the form of capsules, powders, and fluids (Rathore et al. 2017). Some commercial products like 'four Sigmatic 10 Mushroom Blend supplement' which is mixture of ten different mushroom species offer ample number of health benefits to the consumer. Moreover, mushroom-based coffee creamer, named "The Laird Superfood Liquid Creamer," has also been launched, which is of great importance to the consumer to enhance the nutritional importance of their cup of coffee. Table 5.2 comprises a list of such latest mushroom-based nutraceuticals commercially available in the market.

5.5 Conclusion

High protein value, good amount of fiber, vitamins, and mineral makes mushroom a superfood that can be consumed at any stage of life. They are powerhouse of various ranges of bioactive compounds like polysaccharides, antioxidants, and vitamins. Inclusion of mushroom-based products in the daily diets may help in improving the health and found to meet the nutritional requirements of the human beings. The therapeutic and nutraceutical exploration of mushrooms gives the impression that they are the next-generation food, not only in providing quality protein but also in curing deadly diseases like cancers, tumors, and nervous disorders.

Table 5.1 Recent (2017–2021) in vitro and in vivo studies of anticancerous properties of some edible mushroom species

Species name	Responsible compound	Activity	Target cell	Reference
Agaricus bisporus	Mannogalactoglucan polysaccharide	Antitumor activity (lung cancer)	Human hepatocarcinoma cells (HepG2)	Pires et al. (2017)
	Glucogalactomanan polysaccharide	Antitumor activity	RAW 264.7 cells.	Zhao et al. (2020a, b)
Ganoderma lucidum	*Ethanolic extract*	Antitumor activity (prostate cancer)	Prostate cancer PC-3 cells	Wang et al. (2020)
	Polysaccharide	Anticancer (gastric cancer)	Gastric cancer cell lines BGC823 and SGC7901	Yang et al. (2019)
	Polysaccharides	Antitumor activity (colorectal cancer)	Colorectal cancer HT29 (p53R273H) and SW480 cells	Jiang et al. (2017)
	Polysaccharides	Anticancer activity (prostate cancer)	Human prostate cancer cells LNCaP	Zhao et al. (2017)
Grifola frondosa	A proteoglucan (D-fraction)	Anticancer activity	Human breast cancer	Alonso et al. (2018)
	A *α-glucan YM-2A*	Antitumor activity	Colon-26 carcinoma and B16 melanoma	Masuda et al. (2017)
	Polysaccharides	Anticancer activity (breast cancer)	MCF-7 and MDA-MB-231 cells, as well as in nude mice bearing MCF-7 tumor xenografts	Zhang et al. (2017)
Lentinus edodes	Water-extracted polysaccharide	Anti-proliferation activity and antitumor activity	H22 cells in mice	Zhang et al. (2020a, b)
	Lentinan-polysaccharide	Anticancer activity	Human ovarian cancer	Liu et al. (2019)
	Lentinan-polysaccharide	Anticancer activity	Lung cancer	Zhao et al. (2021)
	Polysaccharides	Anticancer (colon cancer)	HT-29 colon cancer cells	Wang et al. (2017)
Pleurotus eryngii	β-glucan	Antitumor activity	MCF-7 and HepG2 cell lines	Al-Saffar et al. (2020)

(continued)

Table 5.1 (continued)

Species name	Responsible compound	Activity	Target cell	Reference
	Polysaccharides PEP-1 and PEP-2	Antitumor activity	Human hepatoblastoma HepG-2 cells	Ren et al. (2016)
Pleurotus ostreatus	Selenium polysaccharide fraction	Anticancer activity	Human cancer cell lines HepG2, MCF-7, SKOV3, HeLa, and PC-3	Zhang et al. (2020a, b)
	Polysaccharides	Antitumor activity	Ehrlich Ascites Tumor cell line in animal mice	Hereher et al. (2018)
	Polysaccharides	Anticancer activity	Sarcoma 180 tumor cells	Wisbeck et al. (2017)

Table 5.2 Commercial mushroom-based products available in the market

Mushroom species	Brand name	Form	Health benefits clammed
G. lucidum	Nature Sure Ganoderma Capsule 60s	Capsules	Improves immunity
	REISHIMAX—Red Reishi mushroom	Capsules	Immunity support, supports relaxation, and total body detox
G. lucidum, *L. edodes*, Cordyceps and Chaga	Avocare Biotech 4 Mushroom Complex	Capsules	To boost immune system, stamina, and stress relief
L. edodes	Rooted active naturals (Shiitake Mushroom Extract)	Capsules	Immunity, cholesterol and BP support, supports skin and hair health, powerful antioxidant
A. blazei	Superfood Science Agaricus Bio	Capsules	Immune system booster
G. lucidum, *L. edodes*, Cordyceps	Doctor's Best, Three Defenders Mushroom Complex	Capsules	Helps optimize the immune system
Cordyceps, *G. frondosa*, and *Hericium erinaceus*	The Laird Superfood Liquid Creamer	Liquid	Boost energy
P. ostreatus	IMMUNITY BOOSTER—Mushroom Powder by Golden Crops	Powder	Immunity booster
Cordyceps, *G. lucidum*, *L. edodes*, *Turkey Tail,* and *P. ostreatus*	Rooted 5 in 1 Super Defence Mushroom Blend	Powder	Cardio health, blood sugar, cholesterol, gut, and liver health. Also strong adaptogen (anti-stress) and antioxidant

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Algal Bioactive Components: Sources, Health Benefits, and Sustainability

6

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Abstract

Algae are gaining popularity as a source to be used for nutraceuticals and health therapies. They are an abundant source of an array of bioactive molecules such as polysaccharides, steroids, lipids, polyphenols, and pigments with potential usage in cosmetics, agribusiness, food supplements, and pharmaceuticals. These bioactive molecules are reported to have antitumor, antimicrobial, antioxidant, anti-ulcerogenic, and pro-healing properties. Thus, they have the potential to offer significant health benefits to humans. The ability of algae to grow rapidly on large scale along with efficient extraction procedures is making them the next-generation sustainable resource for various valuable metabolites. Technological advances in algal biotechnology are further strengthening their role as bio-factories for such products. In this chapter, we discuss the various types of algal bioactive components, their sources, extraction, role in health, and emerging technologies in their sustainable utilization.

Keywords

Algae · bio-factories · Chlorophyceae · Phaeophyceae · Rhodophyceae

6.1 Introduction

In recent times, there has been a rapid growth in the mortality and morbidity of the metabolic diseases arising due to changes in our lifestyle. A switch toward healthier lifestyle is the need of the hour. Due to advances in research and growing awareness

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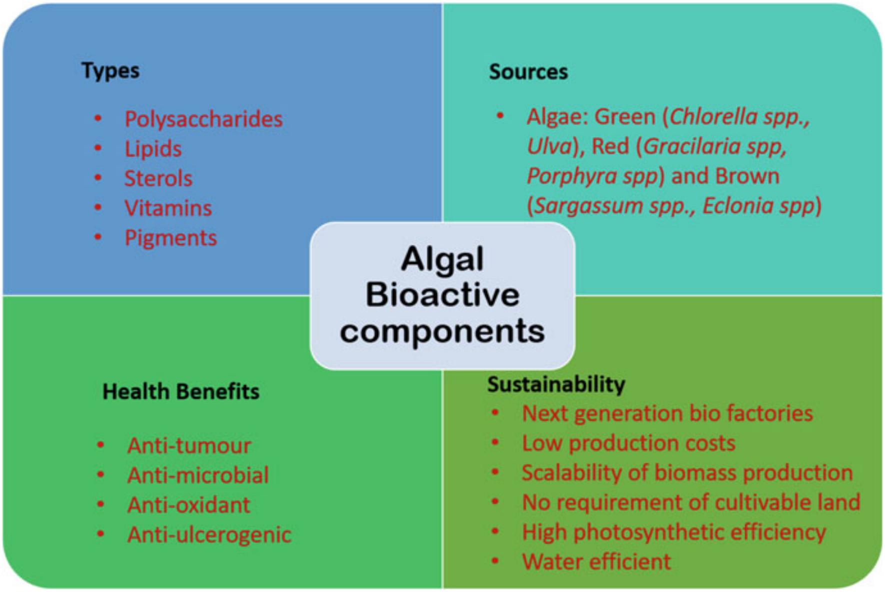

Fig. 6.1 Types, sources, health benefits, and sustainability of algal bioactive components

among the masses, it is becoming a trend now to consume food, which is organic, natural, and beneficial for the consumer. Traditional food is now being supplemented and replaced with more varieties and components, which aid in increasing their nutritional and nutraceutical content. In this regard, algae are playing a pivotal role. Algae are the diverse group of photosynthetic eukaryotic microorganisms that are ubiquitous in nature, colonizing both fresh and seawater habitats. This heterogeneous division includes macroalgae and microalgae. Macroalgae or seaweeds are multicellular organisms reaching sizes of up to 60 m in length and microalgae are unicellular organisms, measuring from 1 mm to several cm. Broadly, algae can be classified on the basis of the pigment they produce, for example, green algae or Chlorophyceae, brown algae or Phaeophyceae, and red algae or Rhodophyceae. There has been tremendous increase in demand for algae as they are potential source of novel bioactive compounds and are also being marked as nutraceuticals or functional foods. This chapter highlights the various algal bioactive components, their sources, extraction procedures, and potential as sustainable sources to supplement human health needs (Fig. 6.1).

6.2 Algal Bioactive Molecules

Algal extracts have been found to possess a variety of bioactive substances, which confer immense health benefits. Table 6.1 enlists the various bioactive molecules along with their sources, cellular effects, and applications.

Table 6.1 Bioactive molecules from different algae

Bioactive molecules	Types	Algal sources	Cellular effect	Application	Reference
Polysaccharides	Agar	*Gelidium amansii*, *Gracilaria*, *hydropuntia*, *Pterocladia*, *Agarophyton tenuistipitatum*	Antiviral properties, antitumor activities in vitro, protects against microcystin oxidative stress	Cosmetic, pharmaceutical, food supplements, manure and food industry	Aziz et al. (2020), García-Poza et al. (2020)
	Alginate	*Laminaria hyperborean*, *Laminaria digitata*, *Macrocystis pyrifera*, *Lessonia* sp., *Treptacantha barbata*, *Sargassum vulgare*, *Ascophyllum*, *Alaria*, *Ecklonia*, *Lessonia*, *Durvillaea potatorum*			Singh et al. (2021), Yarkent et al. (n.d.)
	Agarans	*Gracilaria*			Macchiavello et al. (1999)
	Carrageenan (high molecular weight sulfated galactans)	*Hypnea*, *Furcellaria*, *Iridaea*, *Gigartina*, *Eucheuma denticulatum*, *Chondrus crispus*, *Betapphycus gelatinum*, *Kappaphycus alvarezii*			García-Poza et al. (2020)
	Laminaran (sulfated polysaccharides)	*Laminaria hyperborean*, *Laminaria digitata*, *Fucus vesiculosus*, *Undaria pinnatifida*, *Ascophyllum nodosum*			García-Poza et al. (2020)
	Fucans—fucoxanthins, fucoidan (sulfated polysaccharides)	*Sargassum aquifolium*, *Fucus Vesiculosus*,			García-Poza et al. (2020)

(continued)

Table 6.1 (continued)

Bioactive molecules	Types	Algal sources	Cellular effect	Application	Reference
		Saccharina japonica, *Undaria pinnatifida*			
	Porphyran (complex sulfated galactan)	*Porphyra*, *Bangia*			García-Poza et al. (2020)
	Xylomanan sulfate	*Sebdenia polydactyla*, *Scinaia hatei*			Ghosh et al. (2009), Ray et al. (2015)
	Ulvan (sulfated polysaccharides)	*Monostroma*, *Gayralia*, *Ulva*			Hans et al. (2021)
Pigments	Carotenoids—Alloxanthin, astaxanthin, fucoxanthin, zeaxanthin, siphonaxanthin, lutein	*Haematococcus*, *Dunaliella*, *chlorella*, *Chlamydomonas*, *Scenedesmus*	Antioxidants, antitumor properties, scavenger of peroxyl radical, anti-inflammatory and antioxidant properties, and anti-obesity		Takaichi (2011)
	Chlorophyll	*Dunaliella*, *Chlorella*, *Tetraselmis,Isochrysis*, *Skeletonema*			Hosikian et al. (2010)
	Phycobilins—phycocyanin and phycoerythrin	*Porphyridium cruentum*, *Rhodella*			PaggiMatos (2019), Aziz et al. (2020)
Dietary fibers		*Neopyropia yezoensis*, *N. tenera*, *N. haitanensis*, *Phcocalidia suborbiculata*	Laxative and purgative properties		García-Poza et al. (2020)
Phenolic substances meroditerpenoids (chromanols,		*Sargassum fallax*, *Sargassum*	Antidiabetic, anti-HIV, antiadipogenic, anticancer, bactericidal,		Reddy and Urban (2009), García-

plastoquinones, and chromenes), phlorotannins, flavons-3-ols		*Micracanthum*, *Ecklonia kurome*	antioxidant, and neuroprotective antiallergic effects and also inhibits telomerase		Poza et al. (2020), Menaa et al. (2021)
Fatty acid derivatives—PUFA, EPA	PUFA	*Phorphyra*, *C. crispus*, *Ulva fasciata*, *Isochrysis galbana*, *Gracilaria salicornia*, *Laurencia papillosa*, *Taonia atomaria*, *Dictyota fasciola*, *Chaetoceros*, *Tetraselmis*, *Thalassiosira*, Undaria pinnatifida, *Nannochloropsis*	Regulate blood pressure, membrane fluidity, anti-coagulating properties		García-Poza et al. (2020), Aziz et al. (2020), Menaa et al. (2021)
Sterols		*Ulva*, *Codium*, *Chaetomorpha* spp., *Phorphyra, C. crispus*, *Agarum cribrosum*, *Laminaria japonica*, *Undaria pinnatifida*, *Sargassum horneri*	Antidepressants		García-Poza et al. (2020), Menaa et al. (2021)
Lectins		*Amansia multifida*, *Eucheuma serra*, *Bryotham nion seaforthii*, *B. triquetrum*, *Acrocystis nana*, *Solieria filiformis*	Analgesic, antitumor, and anti-inflammatory		Aziz et al. (2020), Singh and Walia (2018)

6.2.1 Polysaccharides

Algae are a rich source of various polysaccharides such as agar, alginate, agarans, carrageenan, laminaran, and fucans under natural conditions (Table 6.1). The carbohydrate content in edible seaweeds ranges from 4.1/100 g wet weight in *Ulva* to 13.1/100 g wet weight in *Ascophyllum nodosum* (Biris-Dorhoi et al. 2020). In general, polysaccharides account for approximately 76% of the dry weight of algae (Saadaoui et al. 2020). Polysaccharides exhibit a wide spectrum of biological activities such as antioxidant, anti-inflammatory, and antiviral (Biris-Dorhoi et al. 2020). They are also of a great interest to pharmaceutical industry to develop new drug combinations as they possess the potential to activate macrophages through reactive oxygen species, chemokines, cytokines, and nitric oxides that influence the immune response of the organism (Xiong et al. 2006). In addition to polysaccharides, the non-digestible oligosaccharides can be used as prebiotics by gut flora.

6.2.2 Lipids

Lipids that are secondary metabolites of algae include eicosapentaenoic acid (EPA), stearidonic acid, docosahexaenoic acid (DHA), polyunsaturated fatty acids (PUFA), polysterols, and arachidonic acid. Lipids account for 1–5% of the dry weight of algae. Essential fatty acids and functional lipids including PUFAs, fat-soluble vitamins, glycol, and phospholipids make up to 25% and 60%, respectively, of the total algal lipid content. Brown algae including *Laminaria japonica* and *Agarum cribrosum* have the substantial amount of fucosterols, a phytosterol derivative (Yan et al. 1999; Cunha and Grenha 2016; Jia et al. 2014). Algal sterol and lipid moieties have been reported to have positive effects in diseases like atherosclerosis heart and decreasing the total cholesterol, especially low-density lipoprotein (Francavilla et al. 2010; Kini et al. 2020). *Chaetoceros*, *Nannochloropsis*, *Ulva fasciata*, *Thalassiosira*, *Laurencia papillosa*, *Tetraselmis*, *Dictyota*, and *Gracilaria salicornia* are examples of marine alga rich in PUFAs (Saadaoui et al. 2020; Hamid et al. 2015). Food-containing PUFA omega-3 components, according to Food and Drug Administration (FDA), are pharmacologically crucial, offering numerous health benefits by regulating cell membrane fluidity, blood clotting, and pressure, lowering the risk of cardiovascular diseases and diabetes, and improving the brain nervous system coordination. *Chaetoceros*, *Nannochloropsis*, *Ulva fasciata*, *Thalassiosira*, *Laurencia papillosa*, *Tetraselmis*, *Dictyota*, and *Gracilaria salicornia* are examples of marine alga rich in PUFAs.

6.2.3 Amino Acids

Algae are typically considered a suitable source for proteins since their essential amino acid composition meets the Food and Agriculture Organization criteria and is comparable to other sources including egg and soybean. Algae such as *Fucus* and *Ulva* are reported to have high amounts of aspartic acid and glutamic acid and can account for 22–44% of the total amino acids. Most algal species have tryptophan and lysine as limiting amino acids. Likewise, red and brown algae are found to have low amounts of leucine, isoleucine and methionine, cysteine, and lysine, respectively (Bleakley and Hayes 2017).

Algal species can be employed as components in variety of dishes as they are loaded with proteins. *Porphyra* species have long been utilized in traditional sushi recipes. *Ulva pertusa, Monostroma species*, and *Enteromorpha* sp. are blended to make aonori, a protein-rich foodstuff popular in Japan. In Canada and Europe, *Palmaria palmata* is commonly used in food (Biris-Dorhoi et al. 2020).

6.2.4 Vitamins

Vitamins are required for critical metabolic activities and serve as precursors of crucial enzyme cofactors. *Dunaliella tertiolecta* contains vitamins B12, B2, and E, and provitamin A. *Tetraselmis suecica* is also a viable source of vitamins B1, B3, B5, B6, and C. Vitamin B7 has been found in significant proportions in *Chlorella* species, and roughly 9–18% of *Chlorella* isolates have been shown to contain vitamin B12 (Abidizadegan et al. 2021).

Vitamin B9 (folic acid), a key vitamin for cell differentiation and formation of bone and tooth, is abundant in *Chlorella*. It also helps to maintain proper metabolism and the integrity of epidermal membranes. The vitamin C content found in algae varies; however, one study found a significant amount of vitamin C in the *Cryptomonas maculata*. The *Rhodomonas salina* has a substantial thiamine (B1) content (Abidizadegan et al. 2021).

6.2.5 Pigments

Algae produce a variety of pigments such as chlorophyll, carotenoids, carotene, xanthophyll, and phycobilins pigments. Green algae have beta carotenes, carotenoids, and astaxanthin in abundance. Up till now, 23 carotenoid types including all-trans lutein, all-trans beta carotene, and all-trans echinenone have been characterized (Kini et al. 2020). *Dunaliella salina* produces beta carotenes at approximately 14% of its dry weight. Astaxanthin is mostly used as food color and feed supplement in poultry and aquaculture industries. It is also known to be one of the most powerful antioxidant xanthophyll carotenoids. *Haematococcus pluvialis* produces astaxanthin (1–8% of its dry weight) and is used as a supplement in diet.

6.3 Extraction of Bioactive Molecules from Algae

Conventional, traditional, and modern technologies can be used to extract bioactive substances such as pigments, polysaccharides, and fatty acids. Table 6.2 summarizes the extraction procedure for various bioactive compounds from algae. Liquid–liquid and solid–liquid extraction method involves a lot of energy, organic solvents, money, and time. To address these issues, improved innovative sustainable extraction methods including green technologies are required. These methods have various advantages over traditional and conventional methods including decreased solvent usage and shorter extraction time and efficiency at lower temperatures (Kini et al. 2020). These approaches provide higher selectivity for isolating desirable chemicals

Table 6.2 Extraction methods used for bioactive substances

Bioactive compound	Detection method	Extraction method	Reference
Flavonoids, saponins, steroids, glycosides, coumarins	NaOH test, foam test, Shinoda test, Liebermann–Burchard test	Crushing the biomass and methanol extraction using Soxhlet apparatus	Baviskar and Khand (2015), Menaa et al. (2021)
Alkaloids	Mayer's test	Maceration, percolation, Soxhlet extraction, digestion, microwave-assisted extraction (MWE), superfluid extraction (SFE), sonication (USE)	Madhumitha and Fosiya (2015), Menaa et al. (2021)
Tannins	$FeCl_3$ test in methanolic extracts	Ultrasonic-assisted maceration	Cuong et al. (2019)
Phycoerythrin and cyanin	TLC, HPLC, GC, HPAEC-PAD	Ultrasound-assisted extraction	Mittal et al. (2017)
Polysaccharides	Differential scanning calorimetry, thermogravimetric analysis, dynamic mechanical analysis	Subcritical water extraction Microwave-assisted extraction	Otero et al., 2021
Carotenoids	UV-visible spectrophotometric method, enzymatic assays, HPLC-photodiode array, LC-MS	Ultrasound and microwave-assisted, pressurized liquid extraction, supercritical CO2, and ethane extraction	Menaa et al. (2021), Mäki-Arvela et al. (2014), Cuellar-Bermudez et al. (2015)
Lipids	FAME, gravimetric measurements, dye partition assay, NMR, GC/MS, RP-HPLC	Folch/Bligh method, organic solvent extraction, Dyer method	Menaa et al. (2021), Ranjith Kumar et al. (2015)
	Glycoprotein-infrared spectrometry, Kjeldahl analysis		

and the ability to minimize undesired reactions during harvesting and large-scale recoveries. As bioactive substances have different physiochemical properties, a size-dependent extraction approach is adopted. Finding an appropriate method for extraction of the desired product and its optimization is critical to the whole process.

Ultrasonication, homogenization, freeze–thawing, and maceration with liquid nitrogen were conventionally used to harvest phycobiliproteins from rhodophytes. Carotenoids and proteins are typically harvested using solvent extraction (Soxhlet extraction) process that employs a variety of solvents and that too in considerable amounts, thus making the process quite expensive and nonviable and not environment-friendly.

There are many innovative techniques for extracting bioactive substances including PLE, UAE, SWE, MAE, and SFE. The SFE methodology for green extraction is primarily utilized to extract high-value bioactive chemicals such as fatty acids and pigments. SFE employs supercritical fluids and has a fast-processing duration, low degradation of the recovered products, and uses minimum solvents. During the procedures like SFE, carbon dioxide is commonly used to improve extraction efficiency (Duarte et al. 2014). The UAE approach was used to extract the bioactive component taurine from *Porphyra yezoensis*, which resulted in enhanced yields. Based on the extracted material, UAE may use low- or high-frequency ultrasound waves to resolve separation. During extraction of temperature labile products such as carotenoid temperature can be maintained via heat exchanger. Super-heated and pressurized water is employed as a polar solvent for harvesting oxygen and light-sensitive molecules like carotenoids in the PLE and SWE process. Further in MAE, microwave radiation is used to provide heat to the medium and aids in dissolution. The efficiency of MAE is affected by conditions used for extraction, microwave treatment, and algal cell composition.

6.4 Importance and Role of Algal Bioactive Compounds in Human Health

The bioactive components like beta carotene, astaxanthin, lutein, phycobilins, sulfated polysaccharides (SPs), and zeaxanthin have been found to positively impact the cellular metabolism and physiology (Table 6.1). There are enormous reports documenting the anti-inflammatory, antimicrobial, and antioxidant effects of these algal products. These bioactive molecules can definitely aid in mitigation of our lifestyle diseases including metabolic disorders.

6.4.1 Antioxidant Properties

Many species from algae are reported to be used in culinary practices including *Laminaria digitata*, *L. saccharina*, *Palmaria palmate*, and *Himanthalia elongata* as they have substantial amounts of flavonoids, phenolic substances, and tannins. These antioxidant molecules from *H. elongate* have considerable DPPH (1,1-diphenyl-2-

picrylhydrazyl) scavenging activity and therefore can be used as alternative strategy for food preservation. It has been documented that methanolic extracts of *H. elongate* prevented the growth of food spoilage microbes such as *P. aeruginosa* and *E. faecalis* and pathogenic microbes such as *Listeria monocytogenes* and *Salmonella abony* (Biris-Dorhoi et al. 2020).

Chlorella species have also been reported to decrease the free radicals and total cholesterol. Phlorotannins and SPs from these algal extracts have been documented to have anticoagulant and antiplatelet properties as well. They are also associated with fibrinolytic enzyme production (Matsubara 2005). Brown algae belonging to genus *Ecklonia* species (*E. cava*, *E. kurome*, *E. stolonifera*), *Ishige okamurae*, and *Eisenia bicyclis* are well reported for phlorotannins (Kim and Wijesekara 2011). Fucoidans derived from *Sargassum fluitans*, *Pudina sanctaecrucis*, and *Dictyota ciliolate* also possess significant antioxidant activity (Biris-Dorhoi et al. 2020).

6.4.2 Antitumor Properties

Over centuries, algae have been touted as having the ability to inhibit tumor and its growth. It is claimed to promote health recovery following cancer treatment therapies. Omega-3 fatty acids including hexadecatetraenoic acid and stearidonic acid from algae such as *Ulva* and *Undaria* are reported to have apoptotic effects in cancer cells. These fatty acids make up 40% of the total fatty acids of the cell (Biris-Dorhoi et al. 2020). Many kelps such as *Palmaria*, *Ascophyllum*, *Ulva*, and *Porphyra* contain large quantity of polysaccharides such as fucoidan, laminarin, and alginate, which have also been shown to have anticancer properties. These polysaccharides enhance the gut environment and have been shown to trigger apoptosis, thus lowering the cancer risk (Biris-Dorhoi et al. 2020). In cell line studies done with human breast cell line MCF7 and melanoma cells, fucoidan extracted from *Sargassum polycystum* and *Fucus evanescens* was reported to have strong anti-proliferative, antioxidant, and anticancer properties (Biris-Dorhoi et al. 2020). Algal carotenoids and terpenoids are also known for scavenging free reactive oxygen species and radicals, thereby exhibiting the strong inhibitory effects in cancer proliferation.

6.4.3 Antihypertensive Properties

Astaxanthin, an important bioactive molecule from algae, has been reported to have hypertensive effects and therefore can affect blood pressure and reduce heart strokes in mouse models. Beta carotene may inhibit the transcription factor activation and their nuclear translocation (Abidizadegan et al. 2021).

6.4.4 Anti-ulcerogenic Properties

Specific bioactive molecules from algae have also been reported to have anti-ulcerogenic properties. Lectins harvested from red algae including *Gracilaria changii* and *Bryothamnion seaforthii* have anti-ulcerogenic and healing properties as demonstrated in mouse models (Gonzaga do Nascimento-Neto et al. 2012).

6.4.5 Anti-inflammatory Properties

Inflammation is one of the most easily encountered medical conditions arising due to several reasons including infection, pollution, and allergy. It causes significant harm and eventually leads to an exacerbated situation causing death. Chronic inflammation is responsible for roughly 20% of the reported malignancies. Algal extracts from *Dictyopteris prolifera*, *Grateloupia filicina*, *G. lanceolata*, *Porphyra dentata*, *Caulerpa mexicana*, and *Ulva reticulate* have been shown to have anti-inflammatory properties. Sulfated polysaccharides from *Laminaria saccharina* and *Caulerpa cupressoides* have been shown to prevent the recruitment of leukocytes in mouse models. Carrageenan, Chondroitin, and Fucoidan from red algae were reported to inhibit pro-inflammatory cytokine and COX pathway (Biris-Dorhoi et al. 2020).

6.4.6 Antimicrobial Properties

6.4.6.1 Antibacterial Properties

Extracts from various algae have been reported to possess antibacterial properties. Algal extracts from *C. mediterranea*, *E. linza*, *E. siliculosus*, *U. rigida*, and *G. gracilis* in diethyl ether had significant antimicrobial activity against variety of bacteria particularly *E. coli*, *Pseudomonas aeruginosa*, *S. aureus*, and *Enterococcus faecalis*. Similarly, the toluene–methanol mixtures (1:3 v/v) with fresh algal biomass from numerous algal species such as *Bryopsis plumosa*, *Ulva fasciata*, *Acrosiphonia orientalis*, *Chaetomorpha antennina*, *Sargassum wightii*, *Hypnea pannosa*, *Grateloupia filicina*, *Portieria hornemannii*, *Gracilaria corticated*, *Centroceras clavulatum*, *Cheilosporum spectabile*, *Padina tetrastromatica*, and *Chnoospora bicanaliculata* were reported to have a significant amount of antimicrobial activity (Biris-Dorhoi et al. 2020).

Escherichia coli have all been found to be susceptible to organic acids such as butanoic and propanoic acids isolated from *Haematococcus pluvialis*. Laminarins derived from *Ascophyllum nodosum*, and *Laminaria hyperborean* has been found to suppress the growth of *Listeria monocytogenes*, *Escherichia coli*, *Salmonella typhimurium*, and *S. aureus*. *Bacillus cereus* growth was reported to be inhibited by ethanolic extracts of *Kappaphycus alvarezii.* Similarly, extract from another red algae, *Symphyocladia lastiuscula*, was reported to have high antimicrobial action, especially against *Vibrio* species including *V. mimicus* and *V. vulnificus* (Biris-Dorhoi et al. 2020). Antibacterial action was also found in algal fucoidan and laminarin polysaccharides against *S. aureus* and *E. coli*. It has the ability to prevent the formation of biofilm within mucosal membranes of stomach by *Helicobacter pylori* (Besednova et al. 2015; Hernández et al. 2016; Yu et al. 2015).

Due to the widespread of antimicrobial drug resistance, new therapeutic drug combinations are the need of the century. Bromophycolides P and Q from *Callophycus serratus* were found to have antibacterial action against methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE). *Bacillus weihenstephanensis*, *B. cereus*, *Staphylococcus aureus*, *S. epidermidis*, and MRSA were reported to be inhibited by eicosapentaenoic acid and hexadecatrienoic and palmitoleic acids from *Phaeodactylum tricornutum*. Neurymenolides A and B, two alpha macrolides from *Neurymenia fraxinifolia*, also had action against MRSA and VRE (Lane et al. 2009; Desbois et al. 2008, 2009).

6.4.6.2 Antiviral Properties

Numerous polysaccharides derived from algae as mentioned in Table 6.1 have been evaluated and found to have interesting antiviral properties. *Gigartina skottsbergii*'s carrageenan has been discovered to attach to enveloped and non-enveloped viruses. The SPs hinder the attachment of viruses like dengue, human papilloma, and human immunodeficiency virus to the host receptor and prevent internalization. Galactans, alginate, fucan, and laminarin have also been reported to have remarkable antiviral properties against herpes simplex virus, human papillomavirus, human immunodeficiency virus, and dengue. (Buck et al. 2006; Carlucci et al. 2004; Witvrouw et al. 1994).

6.4.6.3 Antifungal Properties

The antifungal effect of *Laurencia paniculata*'s ethanolic fraction bearing sesquiterpene aristolene, particularly in bronchial asthma cases has been reported. Pigments and organic solvent extract consisting of carotene and chlorophyll a/b from *Chlorococcum humicola* may prevent the growth of *Candida albicans*, *Aspergillus niger*, and *A. flavus*. *Haematococcus pluvialis* short-chain fatty acids were also found to have antifungal action against *C. albicans*, *A. niger*, *C. albicans*, *Staphylococcus* aureus (Mickymaray and Alturaiki 2018; Bhagavathy et al. 2011; Santoyo et al. 2009; Mendiola et al. 2007).

6.4.6.4 Antiprotozoal Properties

Antiprotozoal activity of *Lobophora variegata* extracts was found against *Trypanosoma cruzi*, *Leishmania mexicana*, *Trichomonas vaginalis*, *Giardia intestinalis*, and *Entamoeba histolytica*. (Vieira et al. 2017). *Cladophora crispata* alkaloids and ethyl acetate were found to have action against protoscolices of *Echinococcus granulosus*. Extract from number of algae including *Dictyota pfaffii*, *Ochtodes secundiramea*, *Padina*, *Caulerpa cupressoides*, *Canistrocarpus*, and *Anadyomene saldanhae* has been reported to possess anti-leishmanial activity (*L. braziliensis*) (Bianco et al. 2013). Fucoidan produced by brown alga also exhibited anti-leishmanial activity. Dolabelladienetriol extracted from *D. pfaffii* is even effective against intracellular amastigote form of the parasite (Soares et al.

2012). Elatol, another extract from red algae *Laurencia dendroidea*, has inhibitory effects against amastigote as well promastigote form of the *L. amazonensis*. It is also active against other trypanosomatids including *T. cruzi.* Organic extract of *Udotea flabellum* and *U. conglutinate* were also found to be effective in inhibiting the *T. cruzi* (Veiga-Santos et al. 2010; León-Deniz et al. 2009).

6.5 Algae as a Sustainable Source for Bioactive Compounds

With the ever-increasing challenges of population growth, climate change, and scarcity of cultivable land, the need for sustainability has become inevitable. In this regard, algae are emerging as next-generation bio-factories for sustainable production of valuable bioactive compounds. The extensive diversity of algae offers a huge pool of potential metabolites that can be exploited for human health benefits. Presently, only a small fraction of algal species is being utilized for bioactive molecule production. They have an immense potential if biochemical profiling of untapped algae is also done. Algal cultivation possesses an array of advantages such as low production costs, large scalability of biomass, and no requirement for cultivable land, which make them a sustainable resource. In future, algae are expected to surpass the plant-based bioactive molecule production as they have the ability to grow rapidly generating large amounts of biomass compared to plants. They have the capacity to grow on large-scale outdoor systems and in enclosed photobioreactors. They even have an edge over other microbial-based products as they mostly are photosynthetic and thus are less dependent on sugars in the media or environment for growth. Some algae also have higher photosynthetic efficiency than plants (Bhola et al. 2014). Microalgae are also water-efficient compared to plants as they can grow rapidly in lesser amounts of freshwater. They can even grow in seawater or wastewater (Demirbas 2009). Thus, nonagricultural wasteland and minimal water can be utilized for large-scale production of algae.

Along with scaling up the production, efficient downstream processing adds on to the sustainability of a process. To attain this, modern extraction procedures described above are being employed. They provide higher selectivity, minimize undesired reactions, and result in large-scale recoveries. Thus, overall algal biorefineries prove to be a less expensive, eco-friendly, and sustainable platform for the production of high-value bioactive compounds.

6.6 Emerging Technologies for Sustainability

Technology and innovation are being employed to widen the horizons of algal bioproduct formation. Microalgae that naturally produce numerous bioactive metabolites are now being genetically engineered to express plant-based metabolites such as terpenoids. Terpenoids are an important class of bioactive molecules with immense nutraceutical and pharmaceutical applications. They are produced in trace amounts in plants so large-scale production is not feasible economically and environmentally. Microalgae are being used to produce them in higher concentration (Lauersen 2019). Likewise, other molecules like antibodies, vaccines, immunotoxins, and enzymes can also be expressed using microalgae (Dixon and Wilken 2018; Fabris et al. 2020). Further, the combined approach of phenomics, genetic engineering, and synthetic biology is being employed to increase the yield of the bioactive products from algae (Fabris et al. 2020).

Technological advances are also being applied for automating extraction procedures to achieve maximum bioproduct yields. Advanced approaches based on machine-to-machine communication technologies, involving automation, sensors, and machine learning can be extrapolated to create microalgal biorefineries where algal cultivation, product formation, and harvesting can be monitored in real time and adjusted to achieve maximum yield (Fabris et al. 2020).

Another recently emerging field is the biological biosynthesis of nanoparticles using microbes. In this regard, algal species such as *Gelidium amansii*, *Corallina elongate*, *Portieria hornemannii*, and *Lemanea fluviatilis* have been used to synthesize nanoparticles for application in specific delivery of the drugs (Castro et al. 2013; Li et al. 2014).

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7 Microbial Bioactive Components: Sources, Applications, and Sustainability

Vandana Singh

Abstract

Microbial-based bioactive metabolic compounds are a pool of metabolites that have confident positive effects on environment, humans, plants, and animals that ingest them. As bioactive compounds originated from microbial origin are valuable to the human health, researchers are enticing attention in modern life, besides that their increasing consumption is stimulating the continuous development of new products and synthesis modes that are eco-friendly, cost-effective, sustainable, and more efficient than their chemical version. Among all the emerging synthesis techniques, microbial biotechnology-based cohort by genetically engineered microbes demonstrates great potential to be explored as an alternative to chemical version. These microbial metabolites basic chemistry belongs to polysaccharides, lipids, ethanol, lactic acid, amino acids, etc. and can be utilized in numerous of applications. This chapter is mainly emphasized on the microbial-based bioactive sources and type of bioactive compounds, including polyphenols, polysaccharides, amino acids, and vitamins, along with that application.

Keywords

Bioactive metabolites · Microbial metabolites · Bioactive microbial components · Microbe-based bioactive compounds

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7.1 Introduction

Microbes, in the form of bioactive substances, are widely known for their therapeutic properties. The bioactive chemicals produced by microorganisms play a critical function in the human host's metabolic activity. Microorganisms are found across all environments and have varying degrees of ability to interact with various beings. They can also be divided into two categories: pathogenic (also described as harmful) and non-pathogenic (which means helpful). Non-pathogenic microorganisms are abundant in the environment and can create a wide range of bioactive metabolites that are physiologically active and have a wide range of applications in a variety of sectors (Fig. 7.1; Ziemer and Gibson 1998).

Bioactive microbial chemicals or metabolites are the naturally active components produced by many bacteria. These bioactive metabolites are produced in trace amounts by microbiota but have high-grade applications such as antibiotics, antibacterial, antitumor, antifungal, and so on; therefore, these bioactive compounds are quite well known to be applicable in disciplines such as medicine science, biochemistry, and food and agriculture industries. Newly found bioactive microbial metabolites comprise avermectin, nanaomycin, rokitamycin, tilmicosin, and many others. These microbial bioactive metabolites are indeed getting lots of attention due to potential long-lasting and incredibly powerful chemotherapeutic properties. To put it another way, microbial bioactive components are biochemical compounds

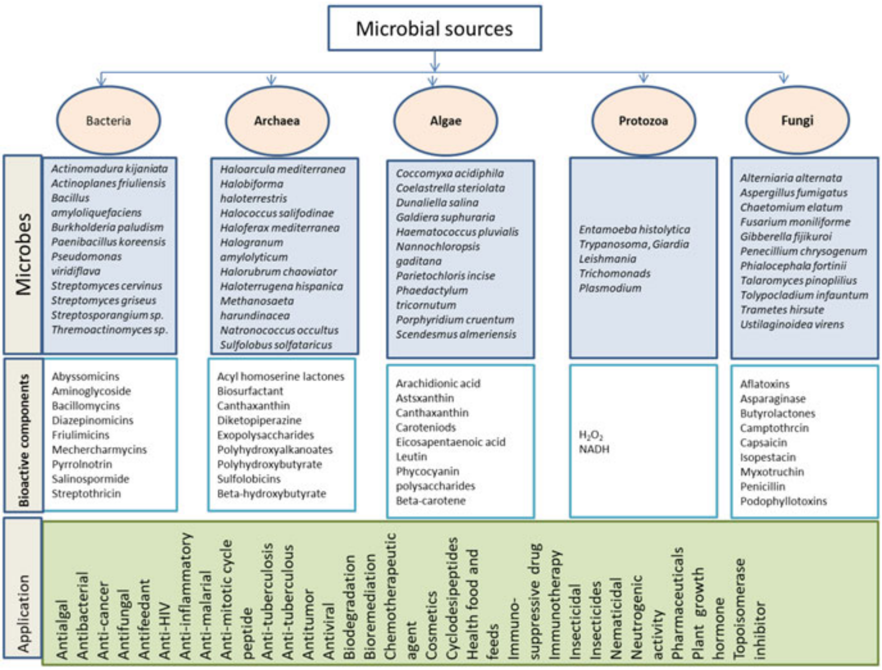

Fig. 7.1 Comprehensive view of microbial bioactive components and their applications

discovered or synthesized in minute amounts by microorganisms. Bioactive chemicals have health-promoting properties too (Sanders and Huis In't Veld 1999).

Microorganisms, such as bacteria, yeast, Actinomycetes, fungi, and algae, produce secondary metabolites which may have some degree of bioactivity against other microorganism. Metabolism is a process that includes catabolism and anabolism, which is the requirement of life-sustaining chemical transformations in any organism, and the metabolic intermediates are termed as metabolites (small molecules). Amid the metabolites, the microbial primary metabolite such as ethanol, lactic acid, and amino acids are necessary for their growth, multiplication, reproduction, and development, whereas secondary microbial metabolites such as pigments and antibiotics are useful for other living organisms for their improved metabolic processes (Gobbetti et al. 2010).

Eukaryotes, archaea, and bacteria are the three primary types of microorganisms that have been studied for the creation of bioactive, low molecular weight natural compounds and their applications in medicines, food, agrochemicals, and industries. Based on various studies of microbial bioactive compounds and secondary metabolites, it can be concluded that these microbes belong to *Rhodophyta* sp., *Mucoromycota* sp., *Firmicutes* sp., *Eustigmatophyceae* sp., *Haptophyta* sp., *Proteobacteria* sp., *Euryarchaeota* sp., *Cyanobacteria* sp., *Basidiomycota* sp., *Crenarchaeota* sp., *Dinoflagellata* sp., *Chlorophyta* sp., *Ascomycota* sp., *Bacillariophyta* sp., *Actinobacteria* sp., *Bacteroidetes* sp., *Streptomyces* sp., *Halococcus* sp., *Aspergillus* sp., *Acremonium* sp., *Bacillus* sp., *Halobacterium* sp., *Pestalotiopsis* sp., *Pseudomonas* sp., *Penicillium* sp., *Fusarium* sp., etc. (Singh et al. 2005; Yadav and Negi 2021).

Some soil bacteria like *Serratia* species have antagonistic effect on worms and their virulent factor. Similarly, Zeamine produced by same microbe can act against yeast and other living pathogens. On the same pace, the bacterium *Vibrio ruber* produces pigment called Prodigosin which has antibacterial effect. Some researcher also stated that Gram-positive bacteria produce antibiotic as their cellular component, which is more stable and also protease resistant. For the sustainability, all these bioactive molecules synthesized from microbial origin can be processed and engineered to provide antibiotic therapy which may overcome antibiotic resistance caused by multiple organisms (Rani et al. 2021). Superbugs, also called the multi-resistant bacterial strains, can be also killed, and its pathogenicity can be overcome by potential bioactive molecules; researchers are still exploring its (bioactive metabolites) potential, which is underway in discoveries. These microbial metabolites were also explored for *Cytomegalovirus*-infected cells that produce certain molecules that can help virus to dissemination persistence and pathogenesis by host immune response. Ascertain of bioactive molecules which counteract this mechanism will prove the effectiveness against cytomegalovirus infection.

Many normal florae of animal and human gut produce bioactive molecules that help in the health of the host; for example, these organisms produce bioactive chemicals that include short-chain fatty acid, vitamins, and aromatic compounds which are proven to be useful for controlling cholesterol synthesis, obesity, cardiovascular diseases, metabolic syndrome, etc. Similarly, lactic acid-producing bacteria present in food can produce bioactive peptides or amino acids which are antioxidant in nature, having metal chelating and immunomodulatory properties; along with that, it is also a controller of hyperglycemia, hypercholesterolemia, hypertension, cell cycle, apoptosis, and refolding action on damaged proteins (Ziemer and Gibson 1998).

The most known Gram-positive strain *Streptococcus* species and Gram-negative rod *Fusobacterium* species can also produce gallic acid and pyrogallol which have anticarcinogenic properties. Amines derived from these microbes have positive effect on allergy, smooth muscle relaxation, anxiety, appetite, and depression. Gamma aminobutyric acid produced by lactic acid-producing bacteria of gut can help brain in signaling. Researchers also explored *Saccharomyces cerevisiae* which can convert tryptophan to serotonin and melatonin that helps in cardio rhythm and also active component in prevention of neurodegenerative diseases. This chapter mainly emphasizes on different types of microbial strains producing biologically active metabolites and its application along with sustainability.

7.2 Microbial Sources of Bioactive Metabolites

7.2.1 Algae

The algae are one of the important examples of seaweed which comes in the category of microorganisms. Among all known functional foods, seaweeds play an important role as it produces bioactive compounds which have human health benefits (Holdt and Kraan 2011). The species of seaweed usually taken for scientific consideration for synthesis studies are *Laminaria* sp., *Fucus* sp., *Ascophyllum* sp., *Chondrus crispus*, *Porphyra* sp., *Ulva* sp., *Sargassum* sp., *Gracilaria* sp., and *Palmaria palmate*. These organisms are not only known for their rich nutritional content but also contain bioactive substances like polysaccharides, proteins, peptides and amino acids, lipids, minerals, vitamins, fatty acid, and polyphenols which have antiviral, antibacterial antioxidants, and antifungal properties (Yadav 2021). Physiologically, algae are classified into two types based on the difference in mechanism, that is, non-absorbed high molecular materials (dietary fibers) and low molecular materials which are absorbed and affect the maintenance of human homeostasis directly. Further, based on morphology, these algae are classified into two types, i.e., macro- and microalgae. These algae possess many functional benefits associated with dietary fibers, cholesterol, maintaining diabetes, antioxidants, etc. Generally, two groups of bioactive proteins are present in these algae, i.e., lectins and Phycobiliproteins. Lectins are a group of carbohydrate-binding proteins that display antibacterial, anticancer, anti-HIV, and anti-inflammatory biological activity (Rani et al. 2021). A well-known seaweed called *Palmaria palmate*, generates phycobiliproteins, which are bioactive compounds with antiviral, anti-inflammatory, cholesterol lowering and antioxidant characteristics. Along with these proteins, they also have bioactive amino acids (taurine, laminine, kainoids, and microsporine), polysaccharides (Laminarin (kelp and fucoids), Fucoidan-sulfated polysaccharides (fucans), mannitol, alginates, ulvan (rhamnose)), polyphenols (phlorotannins, flavonoids, carotenoids fucoxanthin, B-carotene, violaxanthin), fatty acids (eicosapentaenoic and docosahexoic acids, called oxylipins), and iodine (Okami 1986). Microalgae have been claimed to have approximately 28,000 possible compounds, with hundreds of new compounds being identified every year. The majority of them have been identified in *Chordata* (including ascidians) and *Porifera* (sponges) (Nataraj et al. 2020). Microalgae's biotechnological potential has gotten a lot of attention recently since they have a quick generation time, are easy to culture, and represent an environmentally benign method to drug development (Rani et al. 2021). Microalgae are photosynthetic eukaryotes that are important members of both freshwater and marine phytoplankton. They are excellent cradles for pigments, carotenoids, omega-3 fatty acids, lipids, sterols, and other biomolecules. Green microalgae include about 7000 species that develop in a variety of environments. *Haematococcus pluvialis* is the most important commercial microalgae among them, as well as the greatest source of natural astaxanthin, a "super antioxidant." Apart from carotene, astaxanthin has recently gained a lot of attention. Astaxanthin (3,3′-dihydroxy-,′-carotene-4,4′-dione), a marine xanthophyll pigment, from a lobster, was first employed as a colorant in aquaculture and has been approved as a food supplement coloring ingredient since 1991 (Seghiri et al. 2019).

7.2.2 Bacteria

Bacteria exhibit a great numbers of diverse and versatile biological effects and are well known for their antimicrobial activities. Both Gram-positive and Gram-negative bacteria are associated with production of biologically active compounds. The most frequent test organisms were *Bacillus subtilis*, *Micrococcus luteus*, *Staphylococcus aureus*, *Escherichia coli*, *Saccharomyces cerevisiae, Pseudomonas aeruginosa*, *etc.* Scleric acid ((2-(benzoyloxy) acetyl)-L-proline from *Mycobacterium tuberculosis*), enterocin (from *Streptomyces avermitilis*) alterochromide (from *Pseudoalteromonas piscicida*), taromycin A (*Saccharomonospora sp.*), streptoseomycin (from *Streptomyces seoulensis*), syringolin (from *Pseudomonas syringae*), amicoumacin (from *Bacillus subtilis*), gacamide A (lipopeptide from *Pseudomonas fluorescens*), etc., are some examples of these bioactive metabolites which are very useful for the humans as they have ability as antimicrobial, antiviral, anti-inflammatory, and so on (Rani et al. 2021). Probiotics and prebiotics are other examples which confer the health beneficial effects by diverse mechanism such as preventing pathogen adhesion and colonization to gut, along with that production of important metabolites, and also enhancing immune system by the production of antibodies (Ig) (Sanders and Huis In't Veld 1999). The most commonly used probiotics are from the bacterial genera *Bifidobacterium* and *Lactobacillus*. The probiotic microbial strains generally produce therapeutic molecular compounds such as protein, amino acids, bacteriocins, vitamins, enzymes, short-chain fatty acids, and immunomodulatory compounds (Roberfroid 2002). Cyanobacteria is another example of aerobic bacteria and has been identified as one of the most promising groups of organisms from which novel and biologically active natural products have been isolated. Cyanobacteria such as *Microcystis*, *Anabaena*, *Nostoc*, and *Oscillatoria* produce a variety of secondary metabolites such as lipopeptides, amino acids, fatty acids, macrolides, and amides. Furthermore, organisms and their bioactive components are summarized in Table 7.1.

7.2.3 Archaea

Archaea thrive in extreme environments, such as those with drastically higher or lower temperatures, pH, and salinity. Because halophilic archaea are a better choice for generating carotenoids, their colonies are red and orange in hue. Carotenoids have a common purpose; that is, their antioxidant action protects cells from oxidative stress, which is beneficial to human health. The presence of BR gene (bacteriorhodopsin) in the cell membrane aids haloarchaeal cells in acclimating to hypersaline environments, resulting in cell membrane stabilization under such conditions. Researchers also examined and characterized haloarchaea for biomedical implications (Rani et al. 2021). Researchers also explored the production of BR and its derivatives at a mid-scale and large scale, as well as its contemporary biotechnology and biomedicine applications. Haloarchaea is resistant to UV irradiation, radiography, and H_2O_2 exposure, as well as irradiation, bright light, and DNA damage. When compared to ascorbic acid, carotenoids from Halorubrum sp. were found better antioxidant (Wu et al. 2020).

7.2.4 Fungi

The tale of penicillin has been repeated many times whenever there is a debate concerning fungal metabolites. In 1929, Alexander Fleming found that *Penicillium notatum* a mold juice possessed antibacterial properties and termed this biological activity “penicillin.” Researchers have been looking for a fungus strain that can grow swiftly and generate bioactive compounds in submerged culture for a few years. *Penicillium chrysogenum* was later chosen for large-scale penicillium manufacturing. Flavonoids, phenols, steroids, alkaloids, xanthones, and other primary and secondary metabolites generated by the most varied group of fungus have antioxidant properties and are heavily used by the therapeutically, pharmacological, and medical sectors (Venegas-Ortega et al. 2019). The majority of therapeutically and pharmacological research has been concentrated on *Ascomycota* and *Basidiomycota* species, which comprise endophytic fungi with increased antioxidant capacity. Endophytic fungi have been shown to produce a wide range of natural chemicals, including antioxidants, anticancer, antiviral, anti-insecticidal, immune-suppressant, antimycobacterial, antimicrobial, and antimalarial compounds. Bioactive components present in the fungi generally range from polysaccharide, peptides, proteins, proteoglycans, phenolic compounds, terpenes, lectins, etc. Amid the eukaryotes microscopic organisms, fungi are the one producing capability of

Table 7.1 Examples of microbial-based bioactive metabolites

Bioactive components	Applications	Microbes	Reference
Acetic acid	Used for the production of adenosine-5′-triphosphate by metabolization of acetate in the muscle	*Bifidobacterium sps*	Fukuda et al. (2012)
Butyric acid	Contains antitumor and anti-inflammatory properties and used as source of energy for colonocytes	*Butyricicoccus pullicaeorum*, *Roseburia* spp. *F. prausnitzii*	Geirnaert et al. (2017)
Enterocins	Used as antimicrobial agent for Pseudomonas aeruginosa	*Enterococcus casseliflavus MI001*	Indira et al. (2019)
Bacteriocins	Works like signaling molecules and destroys multiple intestinal pathogens. Aids in the bacterial survival in gastrointestinal tract	*Lactococcus lactis*	Sankar et al. (2012)
Arginine	Works on both male and female reproductive system	*Fusobacterium varium*	Dai et al. (2015)
Amino acids (lysine)	It is the requisite amino acid for the host	*Clostridium sps*	Dai et al. (2015)
Propionic acid	Takes part in gluconeogenesis	*P. freudenreichii*	Vorobjeva et al. (2008)
Lactic acid	Reduces viginal pH and works as substrate for metabolism of lipids, cholesterol and glucose	*Lactobacillus sps*	Tachedjian et al. (2017)
Amino acids (metabolites)	Necessary growth nutrients	*Enterobacteriaceae*	Dai et al. (2015)
Riboflavin	ATP production for nutrients	*Lactococcus lactis*, *L. fermentum CECT 5716*	Cardenas et al. (2015)
Thiamin	Plays a part in amino acid precursors, steroids fatty acids, and nucleic acid synthesis. These substances are important for proper functioning of the brain.	*Lactobacillus sps*	Gu and Li (2016)
Vitamin B9	ATP production from the nutrients	*L. fermentum CECT 5716*	Cardenas et al. (2015)
Pyridoxine	Metabolism of amino acid	*Bifidobacterium sps*	Patel et al. (2013)
Folate	Nucleic acids synthesis ATP production from nutrients	*B. pseudocatenulatum*, *B. adolescentis DSM 18350*	Strozzi and Mogna (2008), Asrar and O'Connor (2005), Rossi et al. (2011)

(continued)

Table 7.1 (continued)

Bioactive components	Applications	Microbes	Reference
Vitamin B12	Aids in DNA and red blood cell formation	*Lactobacillus reuteri JCM1112*	Santos et al. (2008)
Levans	Lowers the absorption of cholesterol	20,077 and 20,604	Anwar et al. (2010)
Catalase, super oxide dismutase	Functions as antioxidant	*Lactobacillus casei BL23*, *Lactobacillus fermentum E-18* and *Lactobacillus fermentum E-3*	Wang et al. (2017)
Insulin	Lowers the absorption of fat	*L. gasseri strains DSM*	Anwar et al. (2010)
Beta-galactosidase	Helps is beta-galactoside hydrolysis	*P. freudenreichii*	Vorobjeva et al. (2008)
Tyrosine and tryptophan	Works in the reproductive system of male	*Bacillus sps*, *streptococcus sps*, *Enterococcus sps*	Dai et al. (2015)
Amylase	Starch hydrolysis	*Lactobacillus sp G3_4_1TO2*	Padmavathi et al. (2018)

metabolites. In the same concern, (Rani et al. 2021) *Ascomycetes* are one of the filamentous and endophytic fungi species studied most significantly for the production and application of bioactive metabolites. The *basidiomycetes* are another example of frequently reported producers, whereas yeasts, for example, phycomycetes and slime molds, are also known for rarely producing bioactive metabolites. Similarly, *Candida albicans* and *Aspergillus* are also pathogenic fungi known for the production of phytochemical such as phenolic, flavonoid, and triterpenoid, which have therapeutic applications. These bioactive natural–chemical compounds have properties like anticancer, antifungal, antibacterial, antiviral, antioxidant, and anti-inflammatory and may also work as antibiotic (Chandra et al. 2020) (Yadav and Negi 2021).

7.2.5 Protozoa

Protozoa are the first and simplest organisms discovered by Anton van Leeuwenhoek in the animal kingdom. The majority of protozoan species are unicellular, free-living, motile, and tiny; however, others are parasitic and mutualistic. *Entamoeba histolytica*, *Trypanosoma*, *Giardia*, *Leishmania*, *Trichomonads*, and *Plasmodium* are normally anaerobic; however, they can also be microaerophilic and create H_2O_2 as a metabolic product. The harmful oxygen metabolites created by the host's effector immune cells make some intracellular protozoans visible. Antioxidant enzyme systems including CAT, GSH, and SOD, which are required for the detoxification of H_2O_2, are either absent or inadequate in protozoa. They do, however, have different detoxifying systems. This goal was thought to be accomplished by having a larger concentration of NADH-dependent oxidase and a lower concentration of NADH-dependent peroxidase activities. NADH oxidase activity has been found in *Entamoeba histolytica*, *Trichomonas vaginalis*, and *Tritrichomonas foetus*. Because protozoa are parasitic, there are limited findings on their antioxidant function. Study also stated that Giardia intestinalis has well-organized antioxidant defence systems despite lacking normal antioxidant enzymes. This allows it to endure nitrosative and oxidative stress. Some researchers also addressed about the treatment of filariasis, helminths, and other parasitic illnesses using the parasite thiol-based enzymatic antioxidant thioredoxin reductase (TrxR) (Rani et al. 2021).

7.3 Applications and Sustainable Approach

As we know, microorganism living in an environment produces numerous metabolites/compounds which are biologically active and have various applications (Fig. 7.1). Such biologically active compounds produced by microorganisms which have biological application are called bioactive molecules. These compounds have antibacterial, antimicrobial, antitumor and anti-inflammatory and other similar properties. Bioactive molecules are generally used in medicine, biochemistry, agriculture, therapeutics, and many more. Newly discovered antibiotic which is a major bioactive molecule includes monobactam, compactin, bialaphos, Fk sob, staurosporine, tunicamycin, and ivermectin. Most of the bioactive compounds act as immune modulates, effectors of neurotransmitters, enzyme inhibitor, antagonistic to receptor binding, and many more (Rani et al. 2021). The applications of biologically produced bioactive component from microbial strains are listed below.

7.3.1 Insecticidal Activity of Bioactive Compounds

Bioactive molecules may not be used directly as insecticides, but they can be used as insect repellant. Entomopathogenic fungi can be an effective pest control method. The insecticidal activity of bioactive chemicals from *B. bassiana* against salina was used as a model organism to examine insecticidal activity. The entomopathogenic fungus, for example, might proliferate in insect bodies and spread widely due to insect movement, rather than being treated directly as a commercial insecticidal treatment. Even if just a little number of entomopathogenic fungus spores are applied, the entomopathogenic fungus would provide effective pest control (Wu et al. 2020).

7.3.2 Antitumor Activity of Bioactive Compounds

Beauvericin is used as antitumor agent for leukemia cells in human (Bilharz et al. 2019).

7.3.3 Antibacterial Activity

Most of the bioactive molecules function as antibacterial agent for pathogenic organism in human. They are found to be effective against Gram-positive and Gram-negative bacteria. Bioactive compounds with antibacterial activity obtained from fungi can be used for treatment of other plant and animal bacterial disease. A bioactive chemical exhibits potent antibacterial action against bacteria that cause disease in humans, animals, and plants, with no preference for Gram-positive or Gram-negative one. It is possible that bioactive substances target other cell organelles or enzyme systems. Bioactive substances can be utilised as a single agent for both action (antibacterial and antifungal), which is an unique combination. They exhibit broad-spectrum antibacterial action as well as fungal activity. As a result, bioactive chemicals have diverse targets in bacterial and fungal spp., which might include the lysis of ribosome or the disruption of cell nucleus. The activity of bioactive substances against drug-resistant microorganisms should be explored. Bioactive chemicals with antibacterial action against plant pathogens might be used to combat non-food crop illnesses, as well as to combat medicine resistance and lethal bacterial infections (Abdel-Wareth et al. 2019).

7.3.4 Antifungal Activity of Bioactive Molecules

There are very limited functions of bioactive molecules as antifungal because most of the bioactive compounds are derived from fungal sp. When bioactive compounds are combined with antifungal agent like miconazole or ketoconazole, their efficiency is highly increased and it proves effective against pathogenic flora such as *Candida parapsilosis*. Because many bioactive chemicals are fungal products, their antifungal effectiveness as a single agent is limited. Bioactive substances combined with ketoconazole or miconazole have antifungal action in better way. The combination of bioactive substances with ketoconazole demonstrated significant antifungal action against *Candida parapsilosis*, which can cause high death rates, especially in newborns (Aboody and Mickymaray 2020). On *C. parapsilosis,* both bioactive substances and ketoconazole had little to no impact. If bioactive chemicals' antifungal function is comparable to the cytotoxic process in leukemia cells, this suggests that the fungus can suppress the "unknown signal system" until another molecule, such as ketoconazole, is given to unlock it. The process of mixing bioactive compounds with another substance provides a novel way to produce and use bioactive compounds which is biological activity (Omura 1992).

7.3.5 Antiviral Activity of Bioactive Compounds

Some bioactive molecules are focused to be effective inhibitor of cyclic beta-depsipeptide that can inhibit the enzyme HIV integrase. Antibiotic called erythromycin, extracted from *Saccharopolyspora erythraea*, is used as chemotherapeutic agent. It is used as protective measure from bacterial infection caused by mycoplasma species and beta-lactamase releasing bacteria. Fatty acid inhibitors like triacsin, and 1233A, have been found effective in balancing lipid level and metabolism and present from hypercholesterolemia, hypertension, diabetes, etc. Triacsin is bioactive inhibitor obtained from *Streptomyces aureofaciens* and it inhibit the enzyme acyl Co-A. Another inhibitor called 1233A inhibits the activity of HMG-Co synthase and may work as hypocholesterolemic agents (Wu et al. 2020). Purpactin inhibits acyl Co-A cholesterol transferase; as a result, accumulation of cholesterol is prevented which can prevent disease like hypertension and atherogenesis. Bioactive chemicals are the most potent inhibitors of the cyclic hexadepsipeptides that block HIV-1 integrase. Despite having a similar structure, enniatins have a low activity, suggesting that the activity of bioactive compounds might be attributable to the fundamental structural variation, N-methylation. Infections with viruses can lead to deadly and pandemic illnesses. As a result, bioactive substances' antiviral activity should be explored for possible therapeutic impacts and action against other severe viruses as HBV, SARS, H1N1, and AIV (Wu et al. 2020).

7.3.6 Bioactive Compound Against Protein Phosphorylation

Protein kinase and phosphatase can cause phosphorylation of proteins and cause severe health impact such as metabolism, cell growth and its motility, differentiation, and neurological function. Bioactive compound like staurosporine extracted from *Saccharothrix* species acts as inhibitor for protein phosphorylase and prevents diseases like asthma, blood coagulation, and hypertension (Reddivari et al. 2010).

7.3.7 Bioactive Compounds Against Cancer

Pradimicins and benanomicins are two important bioactive molecules extensively used for cancer treatment. Some strains of actinomycetes are used to extract molecules like calicheamicins which are capable to be used for cancer treatment. Kazusamycin is a bioactive molecule extracted from *Streptomycin species* and is also newly isolated for cancer treatment like leukemia. Another molecule extracted for cancer treatment is pentazocine from *Streptomyces species*. This molecule is used for treatment of HeLa-S3 cells. Furaquinocin A and Furaquinocin B are extracted from Streptomyces species and are proved to be effective against cancer (Wu et al. 2020).

The methods for the discovery of drugs are constantly developing. It has become necessary to explain the structure of chemical compounds, genomics, phylogenetic studies, proteomics, etc. One of the key components that need to develop is the culture media, as it plays an essential role in the proper growth of all strains of potential microbes required for bioactive compounds production. Diets and functional foods have emerged as feasible choices for preventing and treating a variety of disorders in the recent decade (Joana Gil-Chávez et al. 2013; Tripathi and Giri 2014). Bioactive peptides are being studied as a health-promoting functional meal. Food proteins have been found to provide health benefits in addition to addressing the body's nutritional demands (Chakrabarti et al. 2018). Because patients' acceptance of chronic drug prescriptions is generally very low, reducing doses of drugs or improving the response of patients to care is one option for early prevention. Food bioactive components have been demonstrated to have an impact on immune system parameters. Cancer, hypertension, diabetes, cardiovascular disease, osteoporosis, obesity, and stress are all lifestyle-related disorders that can be avoided or controlled using antihypertensive, antimicrobial, and immunomodulatory actions. Both stable and allergic persons who are impacted can benefit from this type of nutritional therapy (Mondal et al. 2021). Antioxidants are important chemicals that can break-down oxidants, guard against free radicals, and scavenge those (Nimse and Pal 2015). As a result, there is a growing global demand for promising and stable antioxidants, making it critical to investigate natural antioxidants from a variety of sources. Microorganisms that produce bioactive molecules are quite widespread in nature and are thought to be a significant source of medicinal bioactive compounds that could help improve the development of new medications. Phenolic and flavonoids are microbial bioactive chemicals that have a favorable effect on human health. Approximately 60% of medications on the market today are derived from natural sources. Nearly 23,000 secondary metabolites have been identified in microorganisms (Sinha et al. 2014). Although the medical value of microbial antioxidants has been extensively documented, antioxidant research remains a serious and significant problem for this century. Microorganisms are now thought to be a substantial source of medicinal bioactive chemicals that could lead to the development of new drugs. Aside from the strong demand, getting a novel antioxidant to market is a lengthy and complex process for companies of pharmaceuticals. The full course takes more than a decade to finish, with a maximum rate of failure. Antioxidants must first pass clinical trials before being licensed for use in the public sector by national regulatory agencies. Another key challenge is elucidating the structural properties of microbial antioxidants to proceed with the expulsion of critical materials and negative factors, respectively, to enable the development of novel antioxidants. Understanding antioxidant performance at the molecular and cellular levels would require detailed structural knowledge. As a result, future research should concentrate on elucidating physicochemical properties, antioxidant structure, and effects in vitro and in vivo models, allowing for the disclosure of new tactics in present industrial sectors. The use of bioactive compounds in conjunction with pharmaceuticals is a safe and effective method of preventing cardiovascular disease (Rangel-Huerta et al. 2015). However, information on the bioavailability of bioactive dietary components and the optimal amount required in humans is required to maximize health benefits. To translate the significant functional qualities of food into therapeutic applications, these peptides must be isolated and identified, as well as their pharmacodynamic factors. To investigate further, novel facilities such as revolutionary proteomics techniques, microbial fermentation, and recombinant enzyme technologies must be used.

7.4 Conclusion

Bioactive compounds from microbes have lots of applications in the field of health, and agriculture, and environment sciences. These metabolites can be synthesized from various microbial sources such as protozoa, actinomycetes, cyanobacteria, bacteria, fungi, and archaea species. These organisms are not producing rich nutritional content but also contain bioactive substances like polysaccharides, proteins, peptides and amino acids, lipids, minerals, vitamins, fatty acid, and polyphenols which have antiviral, antibacterial antioxidants, and antifungal properties. There is still essential to explore the novel and advanced biological approaches for medical, health, and sustainable agriculture industries. These bioactive microbial components have also applications in the field of environment science to protect it from environmental pollution, global warming, and moreover controls the health of humans from the side effects of several chemical-based pharmaceuticals products.

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Part II

Bioactive Components: Technological Trends, Regulatory and Safety Aspects

8 Extraction and Characterization of Bioactive Compounds from Different Sources

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Abstract

Natural bioactive compounds are molecules' treasure trove for nutraceuticals, food additives, and functional foods, as they exhibit several structures and activities. Some of these chemicals, such as polyphenols, can be found in high concentrations in nature. However, others are present in such low concentrations that significant harvesting is vital to achieving sufficient quantities, and chemical synthesis is unprofitable due to their structural diversity and complexity. Because screening and synthesizing these compounds are complex, new technologies have been created. The most common approach is traditional liquid or solid–liquid extraction also termed solvent extraction, although modern approaches comprise supercritical and subcritical extractions, pressured liquid extraction, along with microwave and ultrasound-assisted extractions. Such technologies could give a novel technique for increasing the construction of bioactive and usage of such particular compounds as nutraceuticals or as ingredients in functional foods.

Keywords

Pressured liquid extraction · Bioactive components · Solid–liquid extraction · Functional potential

8.1 Introduction

The term "bioactive" is a combination of two words: "bio" along with "active". Bio is derived from the Greek word "bios", which means "life", while active word is derivative from the Latin word "activus", which means "dynamic, full of energy"

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(Ballard et al. 2010; Alain 1994). All phenomena that result in the manifestation of a form of life, a function, or a process are included in activity (Anonymous 1994). “Bioactive” is a synonym for “biologically active” (Cammack et al. 2006).

Bioactive components are also called nutraceuticals, a word originated by Stephan and DE Felice in 1979 to highlight their ubiquity in the diet consumed by humans and their biological activity. These components, which are found in food as natural constituents, have health benefits in addition to the product’s primary nutritional value that included everything from isolated nutrients, nutritional supplements, along with diets to genetically modified “designer” foods, as well as processed meals including soups, cereals, along with drinks designated as bioactive compounds or nutraceuticals. Consumer interest in nutraceuticals is being driven by epidemiologic research. A portion of a particular food or component of a diet, for example, is connected with a low chronic illness risk, which is communicated to consumer through media. Vitamins and other micronutrients have recently been proposed to minimize deficient symptoms. Long-term low micronutrient consumption can lead to scientific deficient symptoms. Inadequate micronutrient delivery to the target tissue, on the other hand, creates changes that can contribute to the development of chronic illness before symptoms appear.

The most researched component is antioxidants, which have been reported to minimize the risk of chronic ailments like cardiovascular and cancer when taken in larger doses. Even with adequate micronutrient intake (as defined by recommended daily consumption), some people are at a high risk of long-term diseases like coronary heart illness or cancer. A polymorphism is a change in one or more enzymes included in micronutrients distribution or metabolism. This polymorphism results in abnormal micronutrient function or tissue concentration, which are detrimental to human health (Boushey et al. 1995; Kong et al. 2002; Morita et al. 1997). In the case of increased homocysteine, consuming more folate than recommended in those with the mutation may help protect against coronary heart disease.

Over the last decade, phytochemicals such as polyphenols have been studied in the context of various disorders at a rapid pace. Numerous phytochemical classes (e.g., phytoestrogens) have been found. At the very early phases of illness development, these phytochemicals have a preventive effect against several diseases, particularly cancer. These components are typically found in vegetables, and a high vegetable intake has been related to a lower risk of some cancers.

Because of this, it is necessary to investigate the health effects of phytochemicals utilizing isolated compounds, well-characterized composites, or extracts in well chosen as well as validated in vitro–vivo settings. There are several instances of this: bioavailability, dose–effect levels in target tissues, and the creation of biological markers (biomarkers), which enable the research or analysis of a phytochemical’s effects at an early stage in disease development.

8.2 Sources of Natural Bioactive Compounds

Natural bioactive components including fungi, cyanobacteria, microalgae, algae, plants, exotic fruits, olive oil, and tea have mainly been studied in their biological matrices. A rising number of scientific experiments on these compounds and their sources have been done in this area.

8.2.1 Plant Tissues

Plants produce two natural compounds: primary and secondary metabolites (Wu and Chappell 2008). Nucleic acids, fatty acids, amino acids, and sugars are primary metabolites, as are compounds used by all plants for development and growth, such as cell wall components and growth regulators. Secondary metabolites are vital in the plant's life cycle for various reasons (Balandrin et al. 1985). These functions include pollination, attracting, and mediating plant–environment interactions like plant–plant interactions, plant–microorganism, along with plant–insect. Consequently, these secondary metabolites have a wide range of functions and are of great interest to researchers interested in studying their bioactivity for practical applications.

The plant's developmental and physiology stages influence the natural synthesis of these metabolites. Plants' secondary metabolites are classified as polyketides, isoprenoids, alkaloids, phenylpropanoids, and flavonoids, relying on their metabolic origin (Oksman-Caldentey and Inzé 2004). Such compounds are only produced in specific cell types and throughout specific development phases or environmental/ seasonal circumstances, making isolation and characterization extremely difficult (Verpoorte and Memelink 2002). Plant secondary metabolites include phenylpropanoids, alkaloids, terpenoids, carotenoids, and more selective molecules like vincristine, vinblastine, ellagic acid, and corilagin (Szőke et al. 2004; Nobili et al. 2009; Yang et al. 2010). Such compounds are used to produce pharmaceuticals and can also be used as food additives to boost food output (Shahidi 2009; Ayala-Zavala et al. 2010).

Natural bioactive chemicals found in plant tissues are vital since they contain a wide range of biological activities and bioactive features, and they must play a vital role in developing new products (Wu and Chappell 2008). Natural bioactive compounds were the source of 60 to 70% of therapeutic development for cancer and infectious disorders from the previous 25 years (Newman and Cragg 2007). It has been noticed that more than two-thirds of the population in the world still get their primary pharmacological care from medicinal plants (McChesney et al. 2007). However, while these substances have been empirically tested by the ordinary person and have positive impacts on human health, additional scientific suggestion is required to back up their efficacy and ensure their safety.

8.2.2 Microorganisms

Microorganisms are essential because they produce vital biomolecules using their biological system (Demain 2000; Donnez et al. 2009). Approximately 23,000 natural bioactive compounds of microbial origin have been found, with the majority of these compounds being derived from a small number of bacteria (Olano et al. 2008).

Fungal microbes appear to exist in almost every nonliving as well as living niche on the planet, comprising those occurring in deep rock strata, deserts, along with aqueous surroundings (Strobel 2003). Prokaryotes along with plants and fungi synthesize bioactive components that serve an ecological purpose. Diverse compounds have different activities, ranging from photooxidation prevention to environmental stress protection (Mapari et al. 2005). Bioactive substances are made by fungi such as Aspergillus, Penicillium, along with Streptomyces that are also utilized for making bioactive molecules, including enzymes, antibiotics, and 3 organic acids (Liu et al. 2004; Silveira et al. 2008).

Microorganisms produce natural bioactive substances that can be used as nutritional supplements, surfactants, acidulants, emulsifiers, preservatives, texturizers, flavour enhancers, or thickeners in food. Isoprenoids such as carotenoids (e.g., lycopene and beta-carotene) and phenylpropanoids such as stilbene derivatives (resveratrol and others) are the beneficial compounds isolated from bacteria (Chang and Keasling 2006; Klein-Marcuschamer et al. 2007; Ajikumar et al. 2008; Donnez et al. 2009). However, only 1% of bacteria are cultured in vitro, meaning that microorganisms have a broad range of biodiversity and many natural chemicals that have yet to be discovered (Van Lanen and Shen 2006). The fundamental reason for employing microorganisms (rather than microbes) to manufacture compounds from animals and plants is the relative ease with which high yields may be obtained, as well as the potential for genetic manipulation and environmental (Demain 2000). Additionally, microbes are good at producing a variety of essential compounds that are often produced in modest quantities for their benefit (Demain 2000). However, the deficient level of bioactive compounds produced limits their potential application in this area.

8.2.3 Algae and Microalgae

Algae play a vital role in ecosystems ranging from the ocean to freshwater to dry sands (Guschina and Harwood 2006; El Gamal 2010). There are about 30,000 microalga species on the planet, and over 15,000 new compounds were extracted chemically from them (Metting john 1986; Cardozo et al. 2007; Rodríguez-Meizoso et al. 2010). Their prominence as new compounds source is quickly expanding, whereas researchers have discovered that such compounds have a wide variety of biological actions (Wijesekara et al. 2010).

Algal bioactive compounds are abundant, where several of them have antioxidant, antibacterial, and antiviral properties (Onofrejová et al. 2010; Plaza et al.

2010a; Rodríguez-Meizoso et al. 2010). Such organisms must be able to adapt fast and efficiently to their environment since they exist in extreme settings. This results in the production of physiologically active secondary metabolites, which contribute to the body's natural defence systems (Rodríguez-Meizoso et al. 2010). Such defence measures can lead to high structural diversity among molecules derived from various metabolic processes.

Microalgae produce polyphenols, carotenoids, along with other antioxidant pigments, as well as flavonoids including dipeptides, acid derivatives, tiliroside, catechin, and quercetin (Lam 2007). Algae are essential not only because of their bioactive compounds but also because of their enormous diversity and the ability to harvest and grow them under a variety of conditions, resulting in the production and enrichment of bioactive compounds that can be utilized in the pharmaceutical as well as food industries as part of new supplements or drugs (El Gamal 2010).

Even though natural bioactive compounds can be extracted from several sources, the limiting aspects of their production are at low concentration where they can be found. Again, developing novel tactics and methods to maximize the recovery and manufacture of natural bioactive compounds is a critical strategy that many laboratories worldwide are pursuing right now.

8.3 Classification and Synthesis of Bioactive Compounds

The bioactive components' classification into multiple groups is inconclusive, depending on the classification's purpose. Biosynthetic classifications, for example, serve to simplify the biosynthetic pathways' description, which do not correspond to scope of the pharmacological classification. Plant bioactive chemicals are grouped into three categories, according to Croteau et al. (2000): (a) terpenoids and terpenes (around 8000 types). Phenolic compounds (about 12,000 types) along with alkaloids (roughly 12,000 types). Figure 8.1 depicts the general structure of many bioactive chemical types.

Most bioactive compounds are divided into various families, each with its own set of structural characteristics based on how they originate in nature (biosynthesis). In order to produce secondary metabolites or bioactive chemicals, four key steps must take place (Tiaz and Zeiger 2006):

These are as follows:

1. MEP (nonmevalonate) pathway,
2. mevalonic acid pathway,
3. malonic acid pathway, and,
4. shikimic acid pathway.

Aromatic amino acids are converted into alkaloids (through the shikimic pathway), while aliphatic amino acids are converted into fatty acids (tricarboxylic acid cycle). The malonic acid and shikimic acid pathways are used to make phenolic compounds. Terpenes are made using the mevalonic acid pathway and MEP.

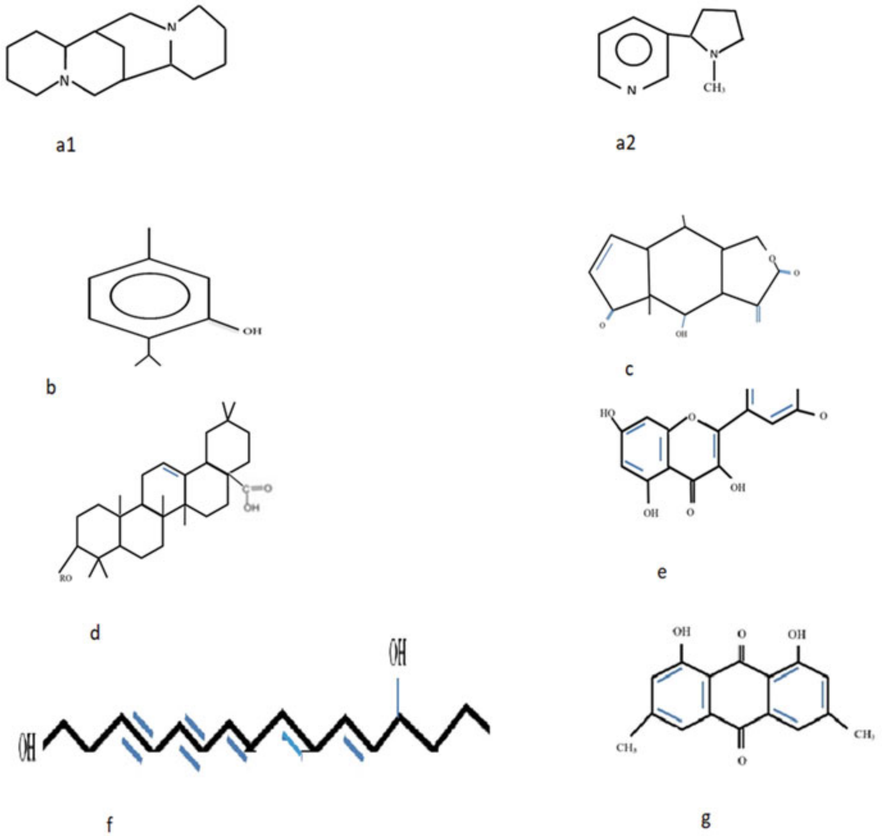

Fig. 8.1 General structure of different plant bioactive compounds: alkaloids (**a1** and **a2**), monoterpenes (**b**), sesquiterpenes (**c**), triterpenes, saponins, steroid (**d**), flavonoids (**e**), polyacetylenes (**f**), and polyketides (**g**) (Wink 2003)

Figure 8.2 shows simplified schematics of three essential plant bioactive compound families and their production routes.

8.4 Technological Methods for Optimizing Bioactive Compound Production

Several approaches, including various extraction techniques and ME, were established for increasing the recovery and synthesis of natural bioactive compounds. Within the following sections, we will discuss the most often utilized extraction processes as well as the key chemicals that have been recovered based on current reported literature.

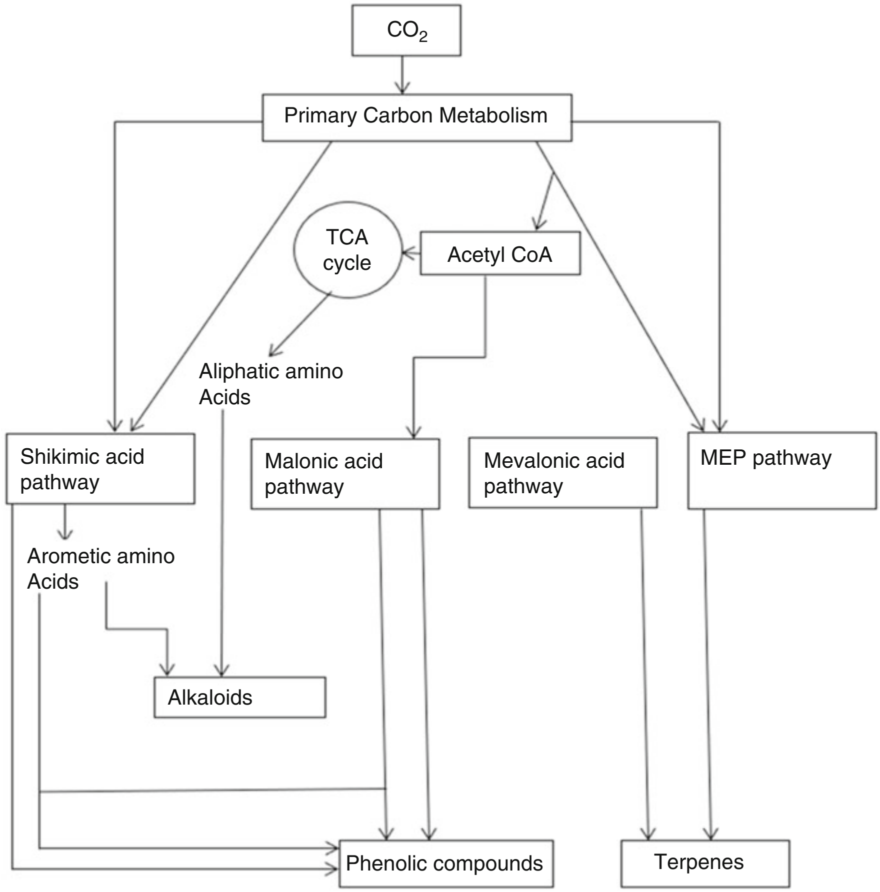

Fig. 8.2 A simplified description of the pathways for the synthesis of three major groups of plant bioactive chemicals (Adapted from Tiaz and Zeiger 2006)

8.4.1 Solvent Extraction

Solvent extraction is a method of extracting specific components from a wide range of materials, for example, microalgae, algae, fungi, bacteria, polymers, soil, sediments, and, more often, plants (Hattab et al. 2007; Plaza et al. 2010c). Several solvents are used to remove compounds of interest and additional agents (flavours along with colours) from pretreated source materials (Starmans and Nijhuis 1996). To remove solid residue, samples are centrifuged and filtered, and extract can be utilized as food additive, supplement, or for production of food items (Starmans and Nijhuis 1996).

Several natural bioactive compounds were extracted traditionally utilizing organic solvents (provided in Table 8.1), marking the critical stage in optimizing solvent extraction technique recovery of desirable components (Li et al. 2006;

Table 8.1 Studies published on the use of solvent extraction and pressurized liquid solvent extraction for the recovery of natural bioactive compounds

Condition used	Raw material	Compound extracted	Response variable	Applications	Reference
PLE hexane, ethanol, and water at 25–200 °C for (20 min)	Algae: *Himanthalia elongate and Synechocystis* sp.	Carotenoids, volatiles, and fatty acids	7.59% yield with hexane, 36.91 ethanol % and 46.43% water	Ingredients that are antimicrobial, antioxidant, or useful in food	Plaza et al. (2010c)
PLE n-hexane, chloroform, petroleum ether, ethanol, 80–125 °C,1500 psi, 3 × 15 min	Wheat straw, germ, and bran	Policosanols	1026 ± 18,27.6 ± 0.04 and 43.2 ± 3.7 mg/100 g	LDL cholesterol is being reduced, while HDL cholesterol is being raised. Supplements for cardiovascular health in the diet	Dunford et al. (2010)
SE (methanol)	Five varieties of eggplant	Flavonoids and phenolics	739.36–1116.13 mg GAE/100 g and 19 91.29–3954.20 mg CE/100 g, respectively	Ingredients with antioxidant and hepatoprotective/nutraceutical properties	Akanitapichat et al. (2010)
SE acetone 50%, solvent-to-solid ratio 20 ml/g, 35–36 °C and 100–102 min	*Parkia speciosa and pod agro-waste*	Flavonoids and total phenolics	668 mg GAE/100 g and 49.6 mg pyrocatechol E / 100 g	Antioxidant/nutraceutical agent for human health protection	Gan and Latiff (2010)
PLE ethanol and water 25/75–50/50–75/25,1500 psi, 20 min, 50–200 °C	Oregano, tarragon, and wild thyme	Phenolics	184.9 mg GAE/g in oregano	Functional/antioxidant compounds for the food industry	Miron et al. (2010)

Dunford et al. 2010). In varying proportions with water, ethanol, benzene, acetonitrile, chloroform, ether, and hexane are often employed solvents in this extraction process (Starmans and Nijhuis 1996; Vatai et al. 2009; Plaza et al. 2010a, b, c). These organic solvents can extract polar and nonpolar organic compounds, for example, oils, fatty acids, aromatic hydrocarbons, phenols, organochlorine insecticides, and alkaloids (Szentmihályi et al. 2002; Li et al. 2006; Hattab et al. 2007; Villa-Rodriguez et al. 2010; Plaza et al. 2010c). Though some solvents are dangerous to humans and environmentally harmful, they must be handled with caution; also, extraction conditions can be time-consuming (Li et al. 2006; Miron et al. 2010). The solvent should be extracted from final extract, which is particularly critical when the product is utilized in functional foods (Starmans and Nijhuis 1996).

Compared to other methodologies, the solvent extraction technique is beneficial because of its low processing cost along with operation ease. Instead, this approach involves toxic solvents, necessitates concentration/evaporation stage for recovery, as well as necessitates typically an enormous amount of solvent and a long time taken to complete. Furthermore, due to the high temperature of the solvent throughout extended periods of extraction, natural bioactive compounds may be thermally degraded. In general, separation technology is enhancing, with new techniques along with procedures being created rapidly. Solvent extraction has improved in recent years due to the use of Soxhlet, ultrasonic, or microwave extraction, as well as SFE (Szentmihályi et al. 2002).

8.4.2 Pressurized Liquid Extraction

New extraction technologies were developed for replacing the solvent extraction method. Presently, pressurized liquid extraction (PLE) is gaining popularity and is widely utilized to extract natural bioactive compounds from natural sources (Plaza et al. 2010a; Miron et al. 2010).

PLE is also defined as pressurized SE or accelerated SE since it utilizes organic liquid solvents at high temperatures (50–200 °C) along with pressure (1450–2175 psi) for facilitating quick compound extraction (Dunford et al. 2010). The solvent's dielectric constant falls as temperature rises, reducing the solvent's polarity (Abboud and Notario 1999). As a result, temperature control might be utilized for matching the solvent's polarity to the substance's polarity (Dunford et al. 2010; Miron et al. 2010). The extraction cells are filled faster due to higher pressure, which drives liquid into the solid matrix. Compared to conventional SE, PLE allows for faster extraction while using fewer solvents and yielding higher yields. Only water or other GRAS solvents, for example, ethanol, are utilized in PLE to produce food-grade extracts (Plaza et al. 2010b).

PLE's ability to extract natural bioactive compounds has been demonstrated in several studies that have given many methodologies for optimizing extraction conditions or assessing their efficacy to other approaches (Sporring et al. 2005; Mustafa and Turner 2011; Santos et al. 2012). Table 8.1 summarizes recent investigations on the natural bioactive compounds' recovery utilizing PLE in various matrices. Despite its benefits over traditional methods, this technique is not suited for thermolabile compounds since high temperatures may disrupt their function and structure (Ajila et al. 2011).

8.4.3 Subcritical Fluid Extraction

Extraction activities involving high pressures and temperatures below supercritical levels are denoted as subcritical water extraction. Subcritical fluid extraction was developed to replace existing extraction procedures. SWE has significant advantages over previous methods: This is faster, achieves higher yields, as well as uses fewer solvents (Plaza et al. 2010a). This is also more ecologically acceptable than current organic liquid SE approaches.

SWE uses hot water (between 100 °C and 374 °C, with latter being an essential water temperature) at high pressure (typically between 10 and 60 bar) for keeping water in a liquid form (Herrero et al. 2006). When a liquid is sustained in a liquid state, it influences solvent characteristics like dielectric constant and solubility and temperature. As a result, while the water's dielectric constant is about 80 °F at room temperature, it can be minimized to roughly 30 °F at 250 °F. Under these conditions, a value similar to various organic solvents, for example, methanol or ethanol, is produced. The solubility parameter declines simultaneously, reaching the value found for less polar substances (Adil et al. 2007). As a result, the SWE approach can be utilized to extract nonpolar natural bioactive compounds without using organic solvents. However, the variety in dielectric constants for different compounds must be taken into account.

SWE was utilized for extracting various natural bioactive compounds (primarily antioxidants, as shown in Table 8.2) from various plants along with other matrices. Hot water, subcritical water, and ethanolic water were used to extract antioxidant components from canola seed meals in a study conducted by Hassas-Roudsari et al. 2009. Eventually, they discovered that SWE cooked at 160 °C had the most overall phenolic content as well as the highest antioxidant capacity per gramme of food. Similarly, according to García-Marino et al. (2006), the catechins and proanthocyanidins' recovery from wine-related products was examined in consecutive extractions at a variety of temperatures over a period of time. When three sequential extractions of samples at 50, 100, and 150 °C were carried out, the maximum yield was obtained. However, a one-step extraction at various temperatures can precisely extract molecules with varying degrees of polymerization. Bioactive compounds such as citrus pomace (Kim et al. 2009), oregano (Rodriguez-Meizoso et al. 2006), and rosemary (Plaza et al. 2010c), along with few microalgae (Herrero et al. 2006), have been extracted using SWE. However, multiple components may be transformed in their matrix during the extraction procedure, influencing their functionality (Plaza et al. 2010a). The matrices' cellular structure comprising natural bioactive compounds may be disrupted under SWE circumstances, releasing them into the extracellular environment, where they dissolve in hot liquid water. During the extraction, these compounds may interact,

Table 8.2 Studies on the recovery of natural bioactive compounds using subcritical fluids

Extraction condition	Raw material used	Extracted compound	Research	Result	Reference
"Subcritical water 100, 150, 200, and 250 °C 30 and 300 min"	Basil and oregano	Terpenes: Carvacrol, citronellol, camphor, limonene, and α-pinene	Terpene recovery and quantitation using GC-FID at various temperatures and heating intervals. Molecule stability under extraction conditions	Antioxidant and anti-inflammatory characteristics	
"Subcritical water 50–200 °C 5 min 20–260 °C, 5 min and 200 and 260 °C 5–120 min"	Rice bran biomass (by-product)	Phenolic compounds	The temperature effect and time of exposure on phenolic compounds, electrical conductivity, PH, total soluble sugar, antioxidant activity, and total phenolic content were explored	It has anticancer and antidiabetic properties. Benefits in the food industry, as well as the health and cosmetics industries	Pourali et al. (2010)
"Subcritical water 275 °C 1 h"	Bovine bones (bio-waste)	Hydroxyapatite	Alkaline hydrothermal and thermal decomposition process are compared	It has a medical application. Because of their biocompatibility and strong osteoconductive, osteoinductive, and nontoxic qualities, they are used as bioceramics	Barakat et al. (2009)
"Subcritical water 50,100 and 150 °C 1500 psi"	Winery grape seeds (by-product)	Catechins along with proanthocyanidins	Impact of temperature on the extraction process. HPLC-DAD-MS was used to analyse the extract composition. Solid–liquid extraction is compared	Pharmaceutical and food sectors applications	García-Marino et al. (2006)

generating new compounds with different structures and properties than the initial target. Maillard reaction or caramelization is example of similar interactions, which may be favoured in SWE extractions (Plaza et al. 2010a).

Plaza et al. (2010a) investigated the antioxidants' neoformation during SWE extraction of microalgae (*Chlorella Vulgaris*), algae (*Halopitys incurvus*, *Undaria pinnatifida*, *Cystoseira abies-marina*, *Porphyra* spp., *Sargassum muticum*, and *Sargassum Vulgare*), and plants (thyme—*Thymus vulgaris*; rosemary—*Rosmarinus officinalis* L; as well as verbena—*Verbena officinalis*). They postulated that depending on the nature of the sample, neoformed molecules obtained from Maillard, caramelization, and thermoxidation processes during the extraction process alter the water subcritical extracts' total antioxidant capacity. As a result, to better understand the possible applications of these extracts, bioactive characteristics of an individual compounds produced by SWE should be examined.

SWE has numerous advantages over traditional extraction procedures, including shorter extraction times, higher quality extracts, less extraction agent costs, and environmental compatibility. Interactions and modifications among extracted components, similar to SWE, can aid future research in understanding the newly generated antioxidants' structure along with their specific contributions to the extract's total antioxidant potential. This method is applicable to health-promoting nutraceuticals.

8.4.4 Supercritical Extraction

Since the substances are usually taken from natural sources, supercritical extraction was regarded as an environmentally friendly technology (Herrero et al. 2006). Microalgae, algae, food by-products, and plants are examples of natural sources. Furthermore, SFE aspires for excellent selectivity, quick extraction times, reduced pollution, as well as utilization of nontoxic organic solvents (Wang and Weller 2006).

To achieve a supercritical fluid (SF), SFE is based on many fluid parameters, for example, viscosity, dielectric constant, diffusivity, and density, and generally varies from some circumstances, for example, temperature and pressure (Sihvonen et al. 1999; Herrero et al. 2006). SFs have densities similar to liquids and viscosities similar to gases, which makes them an excellent choice for many applications. It is categorized as fluid between gas and liquid under these conditions (Sihvonen et al. 1999; Wang et al. 2008).

A contractor's vessel is used to move raw materials in order to get the required outcomes. The temperature and pressure of the vessel are kept constant. After that, the fluid is pumped into the extractor vessel by means of a pump. A tap is positioned in the lower section of a separator, and it is used to collect the products after the fluid and dissolved chemicals have been transported to the separator. Then, the fluid is regenerated along with released back into the environment (Sihvonen et al. 1999).

The choices of supercritical fluids are essential in SFE, and as a solvent in this method, a broad variety of compounds can be utilized. (Sihvonen et al. 1999).

Ethylene, methane, nitrogen, xenon, and fluorocarbons are among the many hydrocarbons that can be employed as solvents; nevertheless, most separation systems rely on carbon dioxide because of their low cost and safety (Daintree et al. 2008). Carbon dioxide is thought to cause only minor changes in bioactive substances, preserving their therapeutic or functional characteristics (Cavero et al. 2006). Supercritical carbon dioxide (SC-CO_2) is an excellent replacement to organic solvents since this is nontoxic, nonexplosive, and affordable and has the potential to solubilize lipophilic compounds (Wang and Weller 2006; Wang et al. 2008; Sahena et al. 2009). CO_2 is also gaseous at standard temperature along with pressure, making compound recovery straightforward and allowing for solvent-free extracts. The carbon dioxide molecule is also eco-friendly and has been designated as "generally recognized as safe" (GRAS) by FDA along with EFSA "European Food Safety Authority". CO_2, on the other hand, is less efficient at isolating highly polar molecules from their matrices due to its low polarity (Herrero et al. 2006) (Table 8.3).

SFE is now widely employed in various industrial purposes, for example, extracting essential oils, fatty acid purification, coffee decaffeination, and flavours from natural sources, with applications in functional along with nutraceuticals foods (Wang and Weller 2006; Daintree et al. 2008). This approach is a credible alternative to traditional organic solvent extraction methods for obtaining bioactive molecules chemicals (Wang and Weller 2006). However, various aspects must be considered to build a successful SFE, including co-solvents, raw materials, supercritical fluids, along with extraction situations for the extraction of a specific molecule to maximize the extraction. SFE was utilized to obtain active compounds in microparticles in dry powder form that retain their activity and stability. This research paves the way for novel applications of such compounds in pharmaceutical along with food businesses. The applicability of different supercritical approaches to fabrication of active powders along with particles, as well as the potential issues, was recently examined by Cape et al. (2008).

8.4.5 Microwave-Assisted Extraction

When extracting unstable compounds like carotenoids, UAE should be used safely because it has been shown to degrade compared to other technologies (Zhao et al. 2006). It makes the basis for MAE (microwave-assisted extraction) that operates by heating and evaporating the moisture inside the cells, putting tremendous pressure on cell wall. Because of the increased pressure in biomaterial, the physical characteristics of biological tissues (cell walls and organelles are broken) are altered, and biological matrix (porosity) is increased. The extracting solvent would penetrate deeper into the matrices, yielding larger yields of the required compounds. NBCs may be extracted rapidly and safely by solvent and less energy when utilizing MAE rather than traditional SE since it warms the matrix inside out without producing a thermal gradient. MAE has since become the most innovative approaches for

Table 8.3 Studies on the recovery of natural bioactive compounds using supercritical fluids

Extraction conditions	Raw material used	Extracted compound	Research	Result	Reference
Supercritical fluids $C0_2$ 40–60 °C 150–360 bar 0–7% EtOH	Oregano leaves (plant herb)	Flavonols, flavanone, and flavone	HPLC has been utilized for identifying extracted compounds, as well as DPPH and b-carotene bleaching for determining antioxidant activity	Sausages, beef, along with salads are examples of food components used to flavour food. Antioxidant activity and its advantages to one's health	Cavero et al. (2006)
Supercritical fluids CO_2 45,55,and 65 °C 15,25, and 35 MPa	*Patrinia villosa juss*	Volatiles	Extracts' antioxidant activity (ABTS and DPPH) along with chemical content	Antibacterial and antiviral properties	Xie et al. (2008)
Supercritical fluids CO_2 50 °C, 25 MPa, 60 min	Cherry	Phenols and perillyl alcohol	A high-performance liquid chromatography (HPLC) analysis was used to determine the amount of extract present and its characteristics (HPLC). Antioxidant potential (ORAC and TEAC). The cytotoxicity and antiproliferative properties of the compound are tested	Give protection against skin, colon, as well as lung cancer as an anticancer and antioxidant agent	Serra et al. (2010)
Supercritical fluids CO_2 40,60, and 80 °C 200,275, and 350 bar	Tomato juice	Lycopene	It is possible to increase extraction efficiency by adjusting the pressure and temperature. The yield, active fractions, along with antioxidant activity of lycopene have been quantified and identified	Food colourant	Egydio et al. (2010)
Supercritical fluids CO_2 323 K 350 bar 10,20 ml/min	*Nannochloropsis oculate*	Carotenoids and lipids	Comparison with soxhlet (hexane, CH_2Cl_2, along with EtOH) and triglycerides, ultrasonic extraction (HPLC), and total yield of the extraction. Utilization of co-solvents (dichloromethane and EtOH)	Food supplements and functional foods	Liau et al. (2010)

Table 8.4 Studies on the use of microwave and ultrasonic-assisted extraction from different natural matrices

Method and condition	Materials	Bioactive compounds	Applications	Reference
MAE EtOH 47.2%, at 150 W, for 4.6 min, 60 °C	Grape seeds of cultivars cabernet sauvignon, Shiraz, sauvignon Blanc and chardonnay by-product	Polyphenols	Food, cosmetics, and pharmaceutical industry	Li et al. (2011)
MAE EtOH 30% 1.5 g skins, tat 855 W, for 30s	Peanut skin by-products	Phenolics	Prevention of cancer	Ballard et al. (2010)
UAE n-heptane, 167 W/cm^2, 30 °C	*Spirulina platensis*	Beta-carotene	Pharmaceuticals industry. Diabetes, cancer, along with other chronic disorders can all be prevented with the use of this supplement	Dey and Rathod (2012)
UAE MetOH 20%, 60 min, 60 °C	*Forsythia suspense*	Phillyrin	Having antiviral, antioxidant, and anti-inflammatory properties, this is utilized as a medicine	
UAE MetOH, 60 kHz, 40 °C	Penggan peel by-product	Hesperidin	Pharmaceuticals along with food industry. Having allergy-fighting, anti-inflammatory, along with antioxidant properties	Ma et al. (2008)
UAE EtOH 41%, for 30.5 min, 79 °C	Prunella vulgaris L. plant	Flavonoids	Medical applications as well as utilized for alleviating sore throat, accelerating wound healing, and reducing fever	Zhang et al. (2011)

extracting natural bioactive compounds from various matrices due to these characteristics (Table 8.4).

MAE was utilized for retrieving several natural bioactive compounds, but it has primarily been used to recover natural bioactive compounds with antioxidant potentials, for example, phenolic compounds (Simsek et al. 2012; Li et al. 2011; Moreira et al. 2012) and carotenoids (Zhao et al. 2006; Choi et al. 2007; Pasquet et al. 2011). MAE was also utilized for recovering natural bioactive compounds including saponins, alkaloids, along with terpenoids (Zhang et al. 2011). MAE uses less solvent and takes less time to extract, and it has a more potent antioxidant capacity and extraction yields than other procedures.

Natural bioactive compounds' MAE is impacted by numerous factors, for example, number of extraction cycles, extraction pressure, solid–liquid ratio, solvent concentration and type, extraction temperature, particle size and moisture content of sample matrix, time, frequency, and microwave power (Mandal et al. 2007). However, an essential component is solvent selection, influenced by three factors: dissipation, dielectric constant, along with solubility. Polar solvents and water with a high dielectric constant that can absorb a lot of microwave radiation are generally better solvents as compared to nonpolar solvents (Wang and Weller 2006). Furthermore, the dissipation factor (efficiency where various solvents heat up under microwave) is crucial. For example, when phenolic compounds are retrieved utilizing solvents, for example, methanol or ethanol rather than water that has a higher dissipation factor, this was discovered that phenolic compounds' recovery is also higher (Ajila et al. 2011).

MAE has several benefits over traditional extraction approaches such as reduced pollutants, increased extraction efficiency, and reduced extraction time. The nonpolar molecules' recovery and changing of the chemical structure of target compounds, both having the potential to impact their bioactivity and limit their usage, must be solved before the technology may be considered for commercial applications.

8.4.6 Ultrasonic-Assisted Extraction

Although ultrasonic technology is not new, the most recent advancements in its use have focused on the natural bioactive substances' recovery from a several natural sources, for example, plants.

Ultrasound-assisted extraction (UAE) was promoted as safer alternative to traditional SE, claiming to deliver improved compound recovery with less solvent usage and speedier analysis and bioactivity features. Acoustic cavitations, a mechanism that increases extraction efficiency, are responsible. A high enough level of ultrasonic intensity might cause holes or microbubbles to form in the liquid, which can be dangerous. Sound waves cause bubbles to absorb energy and expand during expansion cycle before contracting throughout compression cycle. Bubbles can also start a new scattering cycle or collapse, resulting in extreme temperature and pressure (a few 100 atmospheres and over 5000 °C) (Leighton 2007; Soria and Villamiel 2010; Esclapez et al. 2011). Consequently, in some cases, cavitation bubbles may contact with solid matrix's surface, causing the cells to dissolve and release the substances that were originally contained inside them.

The UAE has traditionally been a desirable area for extracting valuable substances. It has been used to extract proteins, oil, sugars, polysaccharides–protein complexes, (Qu et al. 2012; Karki et al. 2010; Adam et al. 2012). The antioxidants' extraction, for example, phenolic compounds, was explicitly addressed using experimental design to optimize their recovery based on antioxidant potential and yield (some examples are presented in Table 8.4). When extracting unstable compounds like carotenoids, however, UAE should be used with care because it has been shown to degrade significantly compared to other technologies (Zhao et al. 2006).

8.5 Conclusion

The many approaches for isolating and synthesizing bioactive compounds from natural sources are discussed in this paper. People are becoming more conscious of components that are used in food, and they prefer those that come from natural sources, owing to the assumption that some chemically synthesized compounds are harmful. Functional foods and nutraceuticals that include natural bioactive ingredients are the wave of the future in both the functional food and nutraceutical industries. Shortly, additional research is needed to demonstrate efficacy with more in vivo trials so that innovative functional foods and nutraceuticals may be produced faster. This will make complying with WHO clearance regulations and expanding the use of these products much more accessible.

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9 Bioavailability of Bioactive Components and Safety Aspects

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Abstract

Plants provide vital nutrient sources throughout the planet. Plant portions that are edible and high in micro- and macronutrients are consumed as food. Aside from providing necessary nutrients for metabolic needs, it can also be used as a magical therapy for a variety of health benefits. Polyphenols, phytosterols, carotenoids, vitamins, and monoterpenes are all bioactive chemicals found in plant-based foods, each with its own chemical and biological capabilities. These are both essential and nonessential chemicals that are found in small amounts in plant products. Plant-derived compounds with protective and therapeutic qualities are also exploited in the development of medications for the treatment of chronic diseases such as cardiovascular disease, diabetes, and cancer. The effectiveness of a bioactive chemical is determined by its bioavailability, bioactivity, and stability. Many processes are addressed by bioavailability of bioactive compounds, including liberation from a dietary matrix, absorption, distribution, metabolism, and elimination phases. Various factors, such as food composition and absorption method, have a direct impact on the bioavailability of active substances during intake. The estimated initial value when they arrived in the circulatory system may differ. As a result, determining the presence of bioactive compounds in food

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is insufficient for determining their impact on human health. The goal of these studies is to look at various approaches for assessing bioavailability of bioactive compounds, including in vivo and in vitro models.

Keywords

Bioactive compound · Bioavailability · In vivo model · In vitro model

9.1 Introduction

Food is essential for our survival and to quench our appetite. Aside from that, an increasing number of people are interested in learning more about the components of food that, in addition to nutrition, can help with health promotion, disease prevention, and performance enhancement (Kussmann et al. 2007). All of these traits can be found in bioactive components, which are found mostly in plants. Several studies have found that fruits and vegetables high in non-nutrient components aid in enhancing our health and lowering the risk of chronic and degenerative diseases (Arts and Hollman 2005). People's interest in meals that bring strength to health beyond basic nutritional requirements has risen dramatically in recent years. There are bioactive components that are both hydrophilic and lipophilic in nature. Many studies have found that fruits and vegetables are the primary sources of bioactive compounds with antioxidant properties (vitamin C, carotenoids, phenolic compounds, vitamin E, glucosinolates, daidzein, resveratrol, 3-deoxyanthocyanidins, tannins, and policosanols) (Nehir and Simsek, 2012; Barba et al. 2013; Carbonell-Capella et al. 2013; de Morais Cardoso et al. 2017; González, 2020). These substances aid in the prevention of cardiovascular and neurological disorders (Den Hartogh and Tsiani 2019; Mayo et al. 2019). Researchers claimed that phenolic substances (phenolic acids, flavonoids, anthocyanin, and resveratrol) have favorable biological effects on human health, such as lowering lipid peroxidation, inflammation, and oxidative stress (Den Hartogh and Tsiani 2019; González 2020). Milk, on the other hand, is a product of animal origin that contains anticarcinogenic bioactive compounds such as carotenoids, peptides, lactoferrin, lactoglobulin, vitamins A and B, and fatty acids (Özer and Kirmaci 2010).

To obtain the health benefits of bioactive components, the food must remain unaltered after processing, and it must be liberated from the food matrix, changed in the gastrointestinal (GI) tract, and delivered to the target location after ingestion (Espin et al. 2007). In regard to health claims of bioactive and food components, bioavailability is a key stage, followed by knowledge of the metabolites system, which leads to an understanding of the mechanisms of action with regard to benefit. Bioavailability of dietary components is a critical stage in making health claims, followed by an understanding of the process of circulating metabolites, and finally, providing information about the health benefits of the product. The effectiveness of functional products in avoiding diseases, according to Fang and Bhandari (2010), is dependent on the active components' stability, bioactivity, and bioavailability. The complexity of food matrices, the process of absorption of lipid and water-soluble molecules, and the interaction with the gut bacteria are all variables that influence the transfer of bioactive compounds from food during digestion.

Diet, genetic background, gut microbiota makeup, and activity are all factors that influence bioavailability (Ferreira et al. 2017). Bioavailability can be improved simply by understanding the mechanisms of food ingredient absorption, resulting in the greatest possible health advantages. As a result, the scientific community created a variety of digestive models that accurately imitate the physiological and physicochemical conditions of the gastrointestinal environment.

9.2 Different Kinds of Bioactive Compounds in Food

Compounds are produced by all biological systems in order to survive and thrive. These are usually separated into two categories:

1. Primary metabolites—chemical substances required for cell maintenance, growth, and development (e.g., carbohydrates, amino acids, proteins, and lipids).
2. Low-molecular-weight molecules such as phenolic acids, alkaloids, and terpenes are examples of secondary metabolites. These compounds are important for improving general survival and defense abilities (Azmir et al., 2013).

Secondary metabolites extracted from plants are known as bioactive compounds. They categorized them into two groups based on extraction: Phenolic acids, flavonoids, organic acids, and sugars are examples of hydrophilic or polar substances. Carotenoids, alkaloids, terpenoids, fatty acids, tocopherols, and steroids are examples of lipophilic or nonpolar substances. Table 9.1 shows some bioactive compounds isolated from various food sources, as well as evaluation methodologies for bioavailability and bioaccessibility.

9.3 Overview of Bioavailability, Bioaccessibility, and Bioactivity of Bioactive Compounds

Bioavailability is defined as the proportion of an ingested component that is available at the site of action for use in normal physiological functions, and it is measured using in vivo and in vitro experiments (Carbonell-Capella et al. 2014; Brodkorb et al. 2019). The bioavailability of an element is determined by three factors: the element's digestibility and solubility in the gastrointestinal tract; the element's absorption by intestinal cells and transport into the circulation; and the element's incorporation from the circulation to the functional entity or target (Etcheverry et al. 2012; Carbonell-Capella et al. 2014; Brodkorb et al. 2019). Bioavailability also encompasses two other concepts: bioaccessibility and bioactivity. The fraction of a molecule that is liberated from its food matrix within the gastrointestinal tract and so

Table 9.1 Bioactive compounds present in many foods, as well as bioavailability and bioaccessibility estimate techniques

Food sample and bioactive compounds	Methods of estimation of Bioavailability and bioaccessibility	References
Tomato pulp: Lycopene	Simulated gastric and small intestinal digestion	Colle et al. 2012
Carrot juice: Lutein α-carotene and β-carotene		Courraud et al. 2013
Soy milk fruit beverage: Neoxanthin + 9-cis-violaxanthin, zeaxanthin, lutein		Cilla et al. 2012
Coffee: Chlorogenic acid, benzoic acid	In vivo rat models	Dupas et al. 2006
Orange juice: Carotenoid	In vitro static digestion methods	Stinco et al. 2012
Cassava: Phenolic compound		de Lima et al. 2017
Fresh carrots: β-carotene		Knockaert et al. 2012
Cookies with malted oat flours: Avenanthramides	In vitro bioaccessibility methods	Ninfali et al. 2019
Chlorogenic acid, epicatechin gallate, and quercetin	Caco-2/HT29-MTX cell model (mucus-secreting goblet cells)	Volstatova et al. 2019
Green tea polyphenols	Caco-2 cell models	Van Buiten et al. 2018
Sardinian wine extracts (red cannonau and white vermentino)	Caco-2 cell models	Biasi et al., 2013
Fuzhuan brick tea extract	Caco-2 cell models	Song and Gao 2014
Flavan-4-ols enriched maize	In vivo mice models	Wu et al. 2020a
Flavan-4-ols- and anthocyanin-enriched maize		Wu et al. 2020b
Rice bran phenolic extract		Xiao et al. 2020

becomes available for intestinal absorption is known as bioaccessibility. It covers the sequence of activities that occur during food digestion in order to turn food into potentially bioaccessible material, but it does not include absorption/assimilation through epithelial tissue or pre-systemic metabolism (both intestinal and hepatic). The events related to how the nutrition or bioactive substance is transported and reaches the target tissue, how it interacts with biomolecules, the metabolism or biotransformation it may undergo, the development of biomarkers, and the physiological responses generated are all part of bioactivity. Although the terms bioavailability and bioaccessibility are frequently interchanged, it is important to note that bioavailability includes bioactivity (Etcheverry et al. 2012; Carbonell-Capella et al.

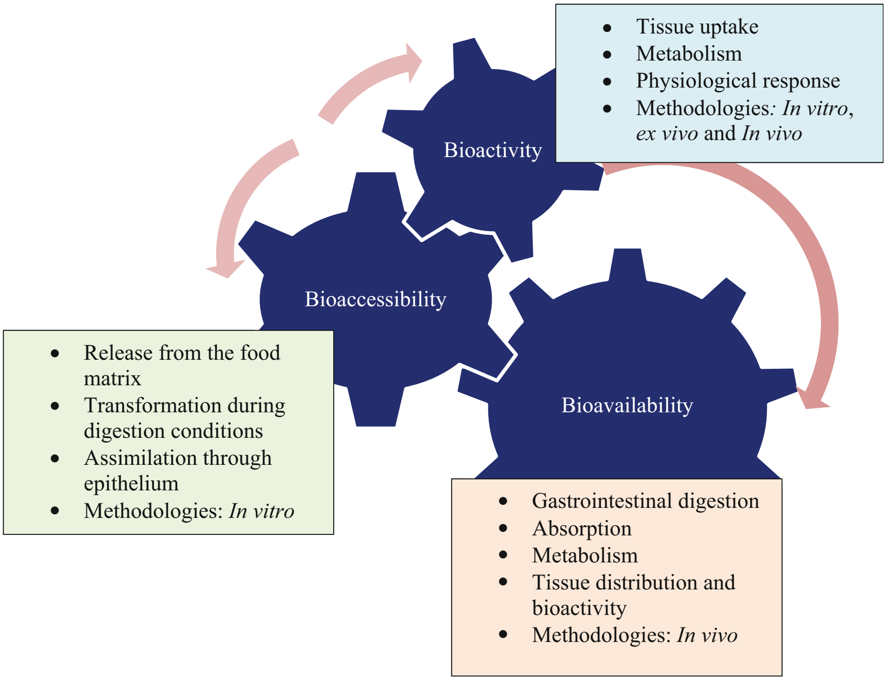

Fig. 9.1 Diagrammatic presentation of bioaccessibility, bioavailability, and bioactivity, as well as their potential assessment procedures

2014; Brodkorb et al. 2019). Figure 9.1 depicts the relationship between bioaccessibility, bioavailability, and bioactivity, as well as alternative approaches.

9.4 Factors Affecting the Bioavailability and Bioaccessibility of Bioactive Compounds

Bioactive chemicals' bioavailability and health-promoting effectiveness are influenced by their molecular mass, chemical structures, and concentration in food, as well as food matrix interaction and digestion routes. The site where these bioactive substances are digested and absorbed from the alimentary tract, as well as the pathway by which they are metabolized, is determined by the aforementioned parameters. These parameters also influence the kind of transport through the gut barrier (passive, requiring specific enzymes, or facilitated by specific transporters), as well as the metabolic course and profile of the substances (Ferreira et al., 2017; Oracz et al., 2020). Bio-efficacy, on the other hand, can be improved by increasing bioavailability. Because the compounds reaching the circulatory system are the product of a complex digestion process, determining bioactive substances directly in food is insufficient to evaluate their bioavailability and bioaccessibility, and thus their effects in vivo. In vivo methods such as gastrointestinal digestion, absorption, metabolism, tissue distribution, and bioactivity are used to determine bioavailability. Bioaccessibility of bioactive chemicals and nutrients can be determined in vitro by separating them from the food matrix, simulating gastrointestinal digestion, and assimilation by the intestinal epithelium (Santos et al. 2019; Bao et al. 2021). Nanoencapsulation of bioactive chemicals improves a variety of properties, including degradation resistance, stability, solubility, and bioavailability (Bazana et al. 2019; Bao et al. 2021; Dima et al. 2021).

9.5 Methodologies Used for Assessment of Bioactive Compounds

Bioavailability and bioaccessibility of bioactive chemicals in food are evaluated utilizing a variety of techniques, including in vivo, in vitro, ex vivo, and in situ testing (Table 9.1 and Fig. 9.1). Each method has its own set of benefits and drawbacks.

9.5.1 In Vitro Model

Researchers in the fields of food and pharmacy have recently increased their focus on determining the bioavailability of bioactive components by creating novel in vitro inquiry methodologies. The human gastrointestinal tract model is exceedingly simple, inexpensive, and repeatable. Gastrointestinal models are static or dynamic models that simulate gastrointestinal digestion in a laboratory setting. In vitro gastrointestinal digestion mimics physiological processes in the gastrointestinal tract of the human digestive system, such as transit duration, enzymatic conditions, and pH (Buniowska et al. 2017). Bioaccessibility is usually assessed using in vitro digestive techniques. In vitro procedures can mainly be divided into two categories:

- In vitro static digestive models.
- In vitro models of dynamic digestion.

9.5.1.1 In Vitro Static Digestion Models

Static digestion models are straightforward to design and use. The model contains immobilized digestive products and is unable to replicate physical processes such as shearing, mixing, and hydration. The digestive conditions in a single digestion stage (small intestine) or multiple digestion stages (mouth, stomach, small intestine) of a GIT model that passes sample sequentially may be mimicked in an in vitro static model. Because the small intestine digests the most nutrients, some studies emulated single small intestinal digestion. However, many additional studies have discovered that when food moves from the mouth to the stomach and then to the small intestine, various changes in the bioavailability of bioactive compounds in the food occur, which differ from when food digestion occurs directly in the intestine (Ozturk et al. 2015; Winuprasith et al. 2018; Dima et al. 2021).

Static digestive models have the following advantages:

- Reproducibility: control condition.
- Rapid and easy.
- Cost-effective.

Static digestion models have the following drawbacks:

- Other bioavailability parameters (age, physiological status, illnesses, etc.) were not investigated.
- The dynamic environment of the intestine was not replicated.

9.5.1.2 In Vitro Dynamic Digestion Models

In order to better simulate the human GIT, a dynamic in vitro model has been built (Minekus 2015). This model is based on in vivo digestive mechanisms, such as the steady acidification of gastric contents by adding HCl, pepsin flow rate, and gastric discharge (Hoebler et al. 2002). A computerized instrument regulates the physiological and biomechanical parameters of each compartment of the simulated GIT. Dynamic in vitro approaches allow for the computerized regulation of the physiological and biomechanical circumstances corresponding to each GIT compartment, obtaining samples from various compartments and simulating the digestive conditions specific to various human age groups (Havenaar et al. 2013; Passannanti et al. 2017).

Dynamic digestion models include the following advantages:

- Use of complicated food matrices (any masticated food/ drink matrix).
- Providing a realistic tool for simulated human stomach digestion.
- In vivo correlation: using the same meal that was used in a clinical trial.

Dynamic digestion models include the following drawbacks:

- There are no in vivo satiety cues that affect digesting rate.

9.5.2 In Vivo Methods

In vivo investigations are frequently used in conjunction with in vitro research because they are more representational of the complexity of organisms. Clinical and animal research provides more detailed information and direct results on bioactive component bioavailability. Table 9.1 summarizes the research on the effects of in vivo digestion on bioavailability and bioaccessibility of bioactive compounds.

9.6 Safety Aspects of Bioactive Compounds

Bioactive chemicals' efficacy and safety are determined by a number of known and unknown characteristics. What is a physiologic dose, and how can it be established in the case of bioactive chemicals whose supply and distribution are unknown? What safety equipment is required? How can individual factors like polymorphisms or absorption discrepancies be taken into account? (Biesalski et al. 2009). The European Food Safety Authority (EFSA) conducts scientific reviews to determine the dangers of bioactive chemicals found in foods to human health. Food-related bioactive component toxicity testing is divided into four areas: (a) toxicokinetics; (b) genotoxicity; (c) subchronic and chronic toxicity and carcinogenicity; and (d) reproductive and developmental toxicity (Vettorazzi et al. 2020). Vilas-Boase and colleagues reviewed the literature on natural bioactive compounds from food waste: toxicity and safety concerns, and summarized the valorization path that a bioactive compound recovered from agro-food waste can face from the moment its potentialities are displayed until it reaches the final consumer, as well as the safety and toxicity challenges that they may overcome (Vilas-Boase et al. 2021). HACCP is a successful technique for preventing, controlling, and monitoring hazards at all stages of the food supply chain, from farm to fork (Cinar and Onbaşı 2020).

9.7 Conclusions

Bioactive compounds are a type of healthcare molecule that can be employed in a wide range of food categories, including food additives, dietary supplements, functional foods, and nutraceuticals, and providing customers with a natural and sustainable option to synthetic alternatives. Plant-derived compounds with preventive and therapeutic properties are also being used in the creation of nutraceuticals and nutritional supplements to treat chronic diseases like diabetes, heart disease, and cancer. The bioavailability, bioactivity, and stability of a bioactive molecule determine its effectiveness. The absorption of bioactive chemicals from food products is being studied using both in vitro and in vivo methods. The food industry's awareness of the importance of safety aspects must adhere to varying regulatory standards depending on the country in which they are implemented.

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10 Regulatory Aspects of Nutraceuticals and Functional Foods in India

Vineet Shyam and Deepshikha Thakur

Abstract

The food and beverage industry of India has seen an escalating growth in the last few years. Nutraceuticals and functional food sector are evolving as a popular segment owing to the increasing awareness of the people towards good health. Another driver for its growth is the factors like unhealthy lifestyle, less exercise, and workouts, which make the dependence on nutraceuticals and functional foods inevitable. It is claimed by many that the Indian nutraceuticals and functional food market are yet to experience the exponential growth. This exaggerates the need and importance of the regulations specific to the nutraceuticals and functional foods. Historically, in India, the food laws were highly ambiguous and the regulations related to this segment were at the back seat, but with the introduction of Food Safety Standards (FSS) Act, 2006, a special emphasis is being given to the regulations of nutraceuticals and functional foods. The nutraceuticals and functional foods that are imported into India also need compliance with the Food Safety Standards (FSS) Act and its rules and regulations. Although the FSS Act 2006 is reforming in terms of compliance and ease to the operators, there still is the need of significant expansion of this act, in order to increase the impact of this law in the whole functional food and nutraceutical industry of India.

Keywords

Food Safety Standards · Functional food sector · Regulations · Standards

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10.1 Introduction

Nutraceuticals and functional foods are gaining constantly escalating attention among people due to their potential role in betterment of the health and reducing the health risks. This recent popularity is expanding the market of these products justifying the need of proper regulations. The nutraceuticals are described as the foods or its components that have the potential to cure specific health conditions (Kalra 2003; Hardy 2000). Nutraceutical is the combination of the words "nutrition" and "pharmaceutical," and another definition by Keservani et al. (2014) defines it as a food or food product that reportedly prevents and treats the specific diseases owing to the reported health and medical benefits through its usage. Stephen DeFelice, founder and chairman of the Foundation for Innovation in Medicine, was the first person to use the term nutraceuticals (Biesalski 2001). Nutraceuticals can be classified on the basis of treatment or prevention of disease, based on chemical constituents, traditional or non-traditional (Jain et al. 2018). Some of the functional food components are carotenoids, dietary fibres, fatty acids, phenolics, plant sterols, prebiotics, probiotics, and soy phytoestrogens (International Food Information Council 1999).

On the other hand, functional food is the broad and a non-specific term used for food that is associated with various health benefits. Functional foods are more of a concept than a well-defined group of food products (Diplock et al. 1999). A food or a part of food that provides medical and health benefits such as prevention and treatment of disease can be classified as functional foods and dietary supplements. According to an article of Health Canada (1998), when a new ingredient or ingredients is added to the food that is responsible for providing an additional function to the new food product, such as health promotion or disease prevention, the food can be categorized as functional food. The regulatory facets of such health-benefiting products are imperative and were in a stage of evolution in twentieth century. Even till date, the regulations around the globe are not in synchrony and vary from country to country. But the importance of the regulations for nutraceuticals and functional foods has now been acknowledged around the world and thus leading to more efficient market of these products.

10.2 Indian History of Food Regulations

India despite huge efficiency and opportunities in food sector holds backseat in the food barriers, due to various barriers in the food sector such as poor infrastructure, logistics, and tight food regulations. Previously, India had multiple laws and regulations regarding various food commodities such as food, food additives, contaminants, food colours, preservatives, and labelling which lead to non-clarity in the compliance of those regulations (FICCI 2009). The following food processing sector laws were framed for the regulations in food industry: (a) Export (Quality Control and Inspection) Act 1963, (b) Solvent Extracted Oil Control Order 1967, (c) The Insecticide Act 1968, (d) Meat Food Products Order 1973, (e) Prevention of

Food Adulteration Act (PFA) 1954 rules, (f) BIS Act 1986, (g) Environmental Protection Act 1986, (h) Pollution Control Act 1986, (i) Milk and Milk Products Order 1992, (j) The Infant Milk Substitutes Feeding Bottles and Infant Food (Regulation of Production, Supply) Act 1992 and Rules 1993, (k) Food Product Order 1995, (l) Agriculture Produce Act, (m) Essential Commodities Act 1995 (Ministry of Food and Consumers Affairs), (n) Industrial license, and (o) Vegetable Oil Product Control order 1998.

This multiplicity of food regulations, their policy makers, and enforcement agencies in various sectors of the food industry was causing lead confusion among the consumers, producers, and retailers. This situation was proving to be detrimental to the functional food and nutraceutical industry's growth and development (Hardy 2000). For addressing this issue, the Prime Minister's council on trade and industry appointed a committee on food and agriculture industries in the year 1998. This committee recommended an establishment the formation of a single food regulatory authority for the unified legislation for all regulations of food industry. In the year 2005, various committees were also established emphasizing the need for a sole regulatory body and integrated food law (Keservani et al. 2014). The convergence of existing food laws with single regulatory authority was also supported by public experts and members of the Standing Committee of Parliament. In the year 2006, India passed the Food Safety and Standard Act 2006, merging the food processing sector laws and forming one integrated food law that serves as a single reference point for regulation of all food commodities including nutraceutical, dietary supplements, and functional food. The Indian Food Safety and Standard Act was established with two main objectives, i.e., introduction of a single statute relating to food and contributing to the scientific development of the food processing industry. The section of nutraceutical and functional foods was at the backseat in previous food regulatory laws. In the newly formed Food Safety and Standard Act 2006, a nutraceutical and functional foods were provided with a special emphasis.

Genesis of this new integrated act was a very significant progress for the food industry of India, yet there is much more that needs to be done in order to establish clarity about the current food laws and eliminate the confusions caused by the previous food laws and regulations. Also, there is a need of significant expansion of the FSS Act 2006, to increase the impact of this law in the whole Indian functional food and nutraceutical industry. Currently, in India the segregation of functional foods/nutraceuticals is not very refined if compared to other progressive countries such as USA, Japan, and Europe. The term functional food is variedly administered in different countries. The Japanese regulations of functional foods define them on the basis of their use of natural ingredients. On the other hand, regulations of functional foods in USA allow the inclusion of ingredients that are products of biotechnology (source: New food words). Indian regulations recognize fruits, extracts of herbs, spices, foods with improved nutritional properties, and food products with added functional ingredients as functional foods.

10.3 Indian Market in Relation to Nutraceuticals and Functional Foods

India is one of the fastest growing economies in the world and holds a lot of opportunities for the investors in the food industry. Strong macro-economic indicators, strategic location availability, and overall infrastructure are the major supply drivers for the Indian food market. Recently, India has focussed on the policy reforms that will hasten and escalate the foreign investments in the Indian food industry establishing many multinational and national food companies, further contributing to the growth of Indian economy. Nutraceuticals and functional foods are an important segment of food and are gaining escalating popularity due to their beneficial effects on human health. The Indian nutraceuticals and functional foods market are not very prominent and still hold a lot of potential for growth (Fig. 10.1). Entering the Indian market is a multistep process which is a little complex. India is among the rapidly growing functional food markets, along with China and Southeast Asia. All these food markets are experiencing escalating growth. The social factors that contribute to the growth of the nutraceuticals and functional foods are awareness among the young population, dual-income households, rising incomes, and growing awareness of healthier eating (https://www.figlobal.com/).

In the pool of global nutraceutical market, India accounts for the total of 2 per cent and India's nutraceutical market has experienced a significant 21 per cent annual increase according to a report by FnBnews.com (2021). According to a report by Yadav and Mehta (2020), the Indian nutraceuticals market in 2017 was $ 4 billion, which is expected to see escalation to $ 18 billion in 2025 owing to the increasing demand for dietary supplements in upper and middle class of the country. The Indian nutraceutical market is sectioned into two major categories, i.e., functional foods and

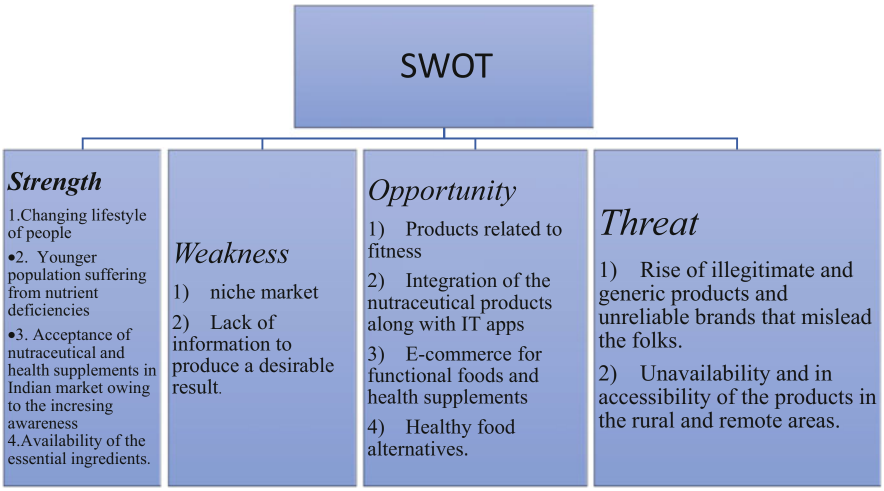

Fig. 10.1 SWOT analysis on the Indian nutraceutical and health supplement market's growth and development (source: FnBnews.com)

beverages, and other is dietary supplements (Ganesh et al. 2015). Dietary supplements (macronutrients, and herbal and non-herbal extracts), constitute over 65% of the Indian nutraceutical market. The major players of this segment are Amway, Himalaya, Dabur, and Emami. This sector is growing at a rate of 17 per cent and, hence, will drive the growth of the market (Yadav and Mehta, 2020). According to a report by FnBnews.com, (2021), one of the leading nutraceutical products in India is probiotic yoghurt, which contributes with 24 per cent increase in its sales. The same report also recognizes Britannia, Cargill, Nestle, PepsiCo, GlaxoSmithKline, Patanjali, and Ruchi Soya as the key players in the Indian functional food sector and Dabur, Herbalife International, Danone, and Amway as the leading companies in health supplement sector.

10.4 Regulations of Functional Foods and Nutraceuticals in India

The regulatory framework of India that governs the major jurisdictions of foods industry is growing and getting more organized eventually. The compliance of food regulations by the FBOs is also increasing significantly owing to the research advancements in the food research leading to process and product innovations and change in consumer behaviour. In addition, the contribution can also be majorly credited to the proven therapeutic reports in some specific diseases and providing good health. Food laws in every country are the basis of regulations of all kinds of food including health food, dietary supplements, functional food, and nutraceuticals as specific guidelines/regulations are framed to regulate health food.

The Food Safety and Standards Authority of India (FSSAI) published regulations for functional foods in India's official gazette with the title "Food Safety and Standards (Health Supplements, Nutraceuticals, Food for Special dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016." Products affected by the new regulations include nutritional supplements, nutraceuticals, special dietary foods, and medical or therapeutic food products.

10.4.1 General Requirements

1. The food articles sold in capsule format, hard or soft or vegetarian, shall comply with the specific general monograph and quality requirements mentioned for them in Indian Pharmacopoeia.
   Provided that the food business operator (FBO) may use the approved colours and additives permitted in **Schedule VF** and provided further that the FBO may use the natural flavours or nature identical flavours or synthetic flavours in accordance with the provisions of regulation 3.3.1 of Food Safety and Standards (Food Product Standards and Food Additives) Regulations, 2011.

2. For the purposes of sub-regulation (1), the FBO may declare the addition of flavour on labels of such products in accordance with the FSS (Labelling and Packaging) Regulations, 2011.
3. The tablets, capsules, and syrups shall fulfil the general quality standards and requirements as mentioned in Indian, British, or United States Pharmacopoeia.
4. The nutrient quantity of added to the articles of food should not exceed the recommended daily allowance as specified by the ICMR, and in case such standards are not specified, the standards laid down by international food standards body, namely Codex Alimentarius Commission, shall apply.
5. For the food products categorized as health supplement, the individual nutrient content shall not be less than 15% of the recommended daily allowance where a nutrient content claim is being made: Provided that, if claim of higher nutrient content is made, the nutrient content should exceed the recommended 30% of daily allowance.
6. For the food articles specified in these regulations, the Food Authority may permit the food business operator to add food colours subject to the level restrictions as mentioned in FSS (Food Product Standards and Food Additives) Regulations, 2011.
7. The articles of food with standard nutrient shall consist of ingredients that deliver the protein, energy, vitamins, minerals, and other essential nutrients required for respective age, gender, and physiological stage in accordance with the guidelines made by the ICMR.
8. The official gazette of the Food Authority shall notify the criteria for the purity of ingredients used in the categories of food articles covered under these regulations, from time to time.
9. In case of non-specified standards, the criteria of purity that is generally accepted by pharmacopoeias, namely Indian Pharmacopoeia, Ayurvedic Pharmacopoeia of India, relevant Bureau of Indian Standards Specifications, Quality Standards of Indian Medicinal Plants, Indian Council of Medical Research, British Pharmacopoeia, United States Pharmacopoeia, Food Chemical Codex, Joint Food and Agriculture Organization or World Health Organisation Expert Committee on Food Additives or CODEX Alimentarius, may be adopted by food business operators.
10. The food business operator shall communicate to the Food Authority, the criteria of purity that has been adopted for ingredients and if any changes when adopted.
11. During the sample analysis of finished products of the food articles covered in these regulations, the tolerance limit for variation shall not be more than (−) 10% from the declared value of the nutrients or nutritional ingredients on the label.
12. The manufacturing of ingredients and products covered under these regulations shall be carried out in compliance with the established good manufacturing practices.
13. For purposes of these regulations, any of the ingredients specified in **Schedule I, Schedule** II, Schedule III, Schedule IV, Schedule VI, Schedule VII, and

Schedule VIII may be used in food in accordance with the provisions of these regulations and, for the said purpose, may use additives as applicable to categories specified in Schedule VA to Schedule VF.

14. The formulation of articles of food shall be based on the principles of sound medicine or nutrition and supported by validated scientific data, wherever required.
15. No hormones or steroids or psychotropic ingredients shall be added to any of the articles of food specified in these regulations.
16. The label on articles of food shall specify the purpose, the target consumer group, and the physiological or disease conditions which they address, recommended duration of use, and the specific labelling requirements as mentioned against each type of article of food.
17. The label, accompanying leaflet or other labelling and advertisement of each type of article of food, referred to in these regulations shall provide sufficient information on the nature and purpose of the article of food and detailed instructions and precautions for its use, and the format of information given shall be appropriate for the intended consumer.
18. An article of food which has not been particularly modified in any way but is suitable for use in a particular dietary regimen because of its natural composition shall not be designated as "health supplement" or "special dietary" or "special dietetic" or by any other equivalent term, and such food may bear a statement on the label that "this food is by its nature X" ("X" refers to the essential distinguishing characteristic as demonstrated by the generally accepted scientific data), provided that the statement does not mislead the consumer.
19. The Food Authority may suspend or restrict sale of such articles of food as have been placed in the market that are not clearly distinguishable from articles of food for normal consumption and are not suitable for their claimed nutritional purpose or may endanger human health, in accordance with the provisions of the Act.
20. The Food Authority may, at any time, direct a food business operator manufacturing and selling such special type of article of food, to furnish details regarding the history of use of the novel or modified ingredients added and their safety evaluation.
21. The mere combination of vitamins and minerals formulated in tablets, capsules, and syrup formats shall not be covered in any of the categories of these regulations except when vitamins and minerals are added to an article of food or in a food format.
22. The labelling on the article of food shall be in accordance with the Food Safety and Standards (Packaging and Labelling) Regulations, 2011, and the specific labelling requirements provided in these regulations.
23. The articles of food shall conform to the Food Safety and Standards (Contaminants, Toxins and Residues) Regulations, 2011.
24. No person shall manufacture, pack, sell, offer for sale, market or otherwise distribute or import any food products referred to in these regulations unless they comply with the requirements laid down in these regulations.

25. Whoever contravenes the provisions of these regulations shall be liable for punishment provided under Chap. 9 of the Act.

10.5 Regulations of Nutraceuticals in India

- In the FSSAI act, 2006 various rules and regulations associated with nutraceuticals have been framed.
- Food products obtained from processing of organic sources, which are not only safe but also not mentioned in the act are also included rather than the food ingredients obtained through modern biotechnology like, genetically modified or engineered organisms which may also contain the same has also been included in the act.
- Of the twenty-one chapters contained in FSSAI act, the fourth article, i.e., 22 of the act, mentions nutraceuticals, dietary supplements, and various functional foods. It also mentions that these products may include nutraceuticals, dietary supplements, functional food, organic food, unprocessed food, can food, novel foods, and irradiated foods and can be produced/manufactured and marketed/imported by any company.
- Article 23 and 24 of FSSAI act, addresses the packaging and labelling of nutraceutical and their also the claims including restrictions in their advertisements.
- The nutraceuticals, those do not claim to cure or mitigate any specific disease, disorder, or condition, can be permitted by the regulations made under this Act.
- The substances listed in Schedules E and EI of the D&C Rules, 1945, do not include a narcotic drug or a psychotropic substance as defined in the Schedule of the Narcotic Drugs and Psychotropic Substances Act, 1985.
- The FSSAI authority would also have to put in place the various minimum levels of compliance of food laws.
- Rules and regulations formed for controlling the claims and the quality of nutraceuticals by the food safety commissioner of each state need their implementations to be expedited.
- In the act, the food either composed of or containing ingredients derived from modern biotechnology such as genetically modified or engineered organisms may also be included.
- The provisions of various testing and tracing the origin of the food products right back up to farm level are done with the help of drafted guidelines (FSSAI 2011).

Nutraceuticals shall contain any of the ingredients specified in Food Act Schedule. Schedule I: vitamins and minerals, Schedule II: essential amino acids and other nutrients, Schedule IV: list of plants and botanical ingredients, Schedule VI: list of ingredients as nutraceuticals, Schedule VII: list of strains as probiotics, and Schedule VIII: list of prebiotic compounds.

In 2018, FSSAI issued a notice banning the usage of numerous ingredients in nutraceutical foods, viz. silica, raspberry ketone, *Paullinia cupana, Angelica* *sinensis*, notoginsing, chaga extract, saw palmetto, tea tree oil, chlorella growth factor, vitamin D3 veg, pine bark extracted to *Pinus radiate*, pine bark extracted from *Pinus pinaster*, oxalobacter formigenes, and phytavail iron. Some of the other ingredients such as artichoke, kale powder, salvia hispanica, and cashew fruit are under assessment and approval by the FSSAI authority, and till then, the FBOs are restricted to claim the products made from these ingredients as supplements or nutraceuticals (Putta 2020).

10.6 Licensing and Registration Requirements for Nutraceuticals and Functional Foods

In order to market the nutraceutical or a functional food in the Indian market, the food business operator is obligated to register and procure the license in compliance with the process mentioned in FSSAI (licensing and registration of food business) regulation 2011 (www.granthornton.in). Without a valid FSSAI license, a manufacturer cannot instigate a business unless his product is either registered or has a valid FSSAI license.

- The FBOs and food manufacturers having an annual turnover of less than Rs.12 lacs are liable to register with the commissioner, whereas the manufacturers and FBOs with the turnover of more than 12 lacs are bound to obtain a food license from the central or regional FSSAI office.
- An applicant shall file an application in the form B of schedule 2 to the concerned licensing authority which will be followed by the issue of an application ID number. Further, the license shall be issued within 60 days.
- Once the application ID number is issued by the licensing authority, it may direct the food safety officer for premises inspection according to FSSAI rules and regulations.
- Followed by the successful inspection and reporting, the license is issued by the licensing authority in format C under schedule 2 of these regulations.
- The license or registration granted under these regulations shall be valid and subsisting, for a period of 15 years, unless otherwise specified.

10.7 Regulatory Requirements for Entry in Indian Market

In order to sell and market the nutraceutical or functional food in Indian market, a multistep procedure needs to be followed that starts with product evaluation followed by actual product analysis, applying and obtaining the food licenses. Developing health and label claims that are specific to India food regulations are very important and playing a pivotal role in the society. The first and foremost step is to evaluate the product to be marketed in terms of regulatory definition by Indian standards, defining the active ingredient and additive in the context to the level of permissibility, standards, and dosage of vitamins/minerals allowed as per the therapeutic, prophylactic, or RDA for Indians. It is also imperative to analyse the product's ingredients and combination of ingredients. Based on this, the products are classified as food or food supplement or drug in the context of the Prevention of Food Adulteration Act 1954 and Rules 1955, Food Safety and Standards Act 2006, and Drugs and Cosmetics Act 1940 and Rules 1945.

Product analysis is a multistep procedure that includes developing and validating the extracts of documents followed by sample collection in witnesses' presence and sample dispatch to concerned authority. For dispatch, different processes are followed for single packages and bulk packages. Food analysis is the next important step that has to be completed within stipulated period of time. After food analysis, adjudication proceedings such as holding enquiries, appeal procedures, and hearing are held. Food Safety and Standards Rules (2011) mentions the hierarchy of the officials involved in the process of product analysis at subsequent stages. The described hierarchy descends from commissioner to food safety officers and other number of officers involved in the process.

For the licensing and registration of nutraceuticals and functional foods in India being imported, approximately 4 to 5 licenses are required depending upon factors such as whether the intended product to be marketed is to be sold as a finished formulation or just as a bulk drug; the finished product is being imported or a bulk ingredient; the product to be imported is with or without an India-specific label; the claims will be developed in India; the product to be imported is with or without an India-specific label; the company has a packaging license; and the company needs manufacturing or marketing license. For filing the license, the registration application dossiers have to be submitted by the FBO to the FSSAI authority. Before launching the imported nutraceuticals or functional food products in India, few other licenses should be procured: import licensing, manufacturing licensing, marketing licensing, and some other state and national level clearances/licenses are also required from the regulatory side.

Another major component to be considered for introduction into the Indian market is the claims pertaining to health and label. These claims are required to be specific to Indian regulatory guidelines. In addition, a number of other concerns also need to be addressed such as Indian labelling and packaging requirements, packing of consignment, composition of consignment, and sample material. Declaration for registration, label content, and structure function claim and label claim also needs to be addressed. After all this, the label content and claims specific to Indian regulations are developed.

10.8 Conclusion

Nutraceuticals and functional foods hold a big opportunity in Indian market, as India has a huge population which is becoming increasingly aware towards the health benefits of these products. In India, the regulations related to nutraceuticals and functional foods have always been ambiguous, which makes it difficult for the manufactures and FBOs to comply with the food laws in a proper way. As these nutraceuticals and functional food market are growing, the development of these products and the claim enhancement also need to be refined. The FSS Act 2006 has been created to consolidate the various rules and regulations related to the food and make the compliance clear and simple for the food manufactures and FBOs. More ammendments in the rules and regulations of nutraceuticals and functional food are still required for the easy amenability of the food laws. This will create a strong impact on the Indian nutraceutical and functional food market.

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Good Manufacturing Practices and Safety Issues in Functional Foods and Nutraceuticals

11

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Abstract

Good manufacturing practices are the fundamental operating and environmental conditions that must be met to produce safe foods. GMP coordinates all sections of the facility to ensure food safety. The safety of the products being manufactured is critical at every stage of production including manufacturers, product processing, packaging, storage, and allocation. Food safety is continually related to every activity before during and after processing. The food processing industry bears primary responsibility for food safety by ensuring that the products and materials supplied to them along with their own processes and products are safe for consumption. This chapter discussed the fundamental GMP and food safety regulations for manufacturers of functional foods and nutraceuticals. Good manufacturing practices are essential to produce safe food for the public, increasing the chances of customer satisfaction, regulatory approval, and business survival.

Keywords

Food safety · Good manufacturing practices · Functional foods and nutraceuticals

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11.1 Introduction

Food safety and food security are indispensable but are different concepts. Moreover, food safety, food security, and nutritional value of a food item are highly interlinked. Food safety is a multidisciplinary scientific approach applicable to all the stages from food preparation, handling, and storage till consumption that ensures that food is fit for consumption. During this journey of "farm to fork," food item encounters numerous health risks associated with processing procedures, and each of these operations is likely to contribute hazardous elements that eventually make the food unhealthy (Sattigere et al. 2020). For that reason, food safety management practices are now being implemented at each step from farm to fork. Food items are the most trafficked merchandise across the globe. Each country has its regulatory food standards, and the food product must meet those minimum standards for smooth trading between the national boundaries (Mtewa et al. 2020).

Food safety, food security, and nutrition are closely linked. The consumption of unsafe food can pose an adverse impact on consumers' health. As per the World Health Organization (WHO), unsafe food may contain harmful biological or chemical agents that can cause <200 different ailments ranging from dysentery to cancer (Fung et al. 2018). The bacteria (*Escherichia coli*, *Listeria*, *Enterohamorrhagic E. coli*, *Vibrio cholerae*, and *Campylobacter*), viruses (Norovirus, hepatitis A), parasites (*Echinococcus* spp, *Ascaris*, *Entamoeba histolytica*, *Cryptosporidium*), prions, and chemicals (heavy metals, toxins, persistent, and organic pollutants) are found in unsafe/contaminated foods. An estimated six hundred million, almost 1 in 10 people, fall sick after the consumption of unsafe food per year, which means 420, 000 demise (Fung et al. 2018).

The hazard analysis critical control points "HACCP" and good manufacturing practices "GMP" played an imperative role in ensuring food safety and quality, beverages, pharmaceuticals, and other food supplements during food processing, packaging, and supply chain management (Blanchfield 2005; Wallace and Mortimore 2016). The HACCP is an organized approach to avert the physical, chemical, and biological hazards that may gain entry at any level during production to distribution, where GMP confirms the applicability of quality assurance that ensures the safety of food products and creates confidence that the product is as per legal standards (Srivastava and Bhargava 2012). GMP is a standard for all practices related to food processing, manufacturing, and dispensation of foods. GMP is defined as "a component of quality assurance that assures that goods are consistently manufactured and regulated to the quality standards relevant to their intended use and as required by marketing authorization and product specifications" (Jarvis 2014). Besides these, some other internationally recognized food safety organizations, viz. ISO22000, Safe Quality Food (SFQ), British Retail Consortium Global Standard (BRCGS), and Global Food Safety Initiative, play a key role as a protective management, to provide certification and auditing for the food manufacturers worldwide.

Nowadays, consumers are more health conscious, and their understanding of food beyond the nutritional aspects has elevated the demand for functional foods and nutraceuticals. The pressure on manufactures has increased to maintain the availability, economic, safety, effectiveness, no-side effects, and adequate nutritional value of the products and also must offer numerous therapeutic applications toward lifestyle disorders (Dudeja and Gupta 2017; Singh et al. 2018; Lagouri 2019). Functional/nutraceuticals foods have more potential than synthetic drugs in the pre-treatment of numerous chronic diseases (Ray et al. 2016). The market of these "designer food" is rapidly spread worldwide. As per the report of the "Business Communication Company (BCC)," the nutraceutical global market may reach $336.1 billion by 2023 at the compound annual growth rate of 7.8%. Considering the market potential and demand of functional foods and nutraceuticals, this chapter provides an insight into the good manufacturing methods and concerns about safety in functional foods and nutraceuticals.

11.2 Good Manufacturing Practice Principles

Good manufacturing practice (GMP) guidelines are designed to ensure that the results are secured for human utilization as illustrated in Fig. 11.1. All defined GMP standards follow a series of comparable basic principles. WHO-GMP regulations have taken into account altogether the criteria of various GMP manuals as well as obligations, particularly in the international commerce arena in emerging nations.

11.2.1 The Principles of GMP Compliance Include the Following

(1) Design and build facilities and equipment correctly and clarify responsibilities; (2) follow written procedures and instructions; (3) preparation of documents; (4) verify the process and carry out the evaluation; personnel performance: (5) regular monitoring and inspection of accident prevention amenities and types of equipment; (6) compilation of stepwise operational instructions and procedures; (7) strategy, development, and validate job skills; (8) prevent pollution and improve the quality and safety of work; (9) control the parts and processes related to the product to ensure the quality of the material; (10) develop plans and review lists regularly to help identify errors immediately and improve the non-compliance process (Blanchfield 2005; Sheikh-Hosseini et al. 2020).

11.3 Good Manufacturing Practice Regulations and Guidelines

GMP regulations and guidelines include all manufacturing sectors, including material inspection, raw equipment, production control, laboratory control, defense product, and the stability of products and sterility. Each stage in the production process should have specific written guidelines that describe methods in larger depths. In addition, a broad framework is essential to ensure that the ideals that

Fig. 11.1 An overview of good manufacturing practice

will be discontinued shortly in each phase will be followed continuously. GMP guidelines are a collection of the number of basic rules that apply to all aspects of production and quality control. They are not a complete process guide, as each system is responsible for implementing its programs following the approved recommendations on the implementation of both business obligations and regulations simultaneously.

11.4 Safety Considerations of Functional Foods and Nutraceuticals

Both nutraceuticals and functional foods are rapidly growing categories of the food market. Nowadays, consumers are more conscious about their vigor and shifting toward foods that offer a variety of health benefits beyond basic nutrition under a single entity. For that reason, food manufactures and researchers are continuously working to design novel foods containing dietary ingredients or bioactive components/phyto-constituents which have positive health outcomes toward human health. Further, these formulated food supplements with bioactive ingredients are labeled/ marketed as "functional foods" or "nutraceuticals" foods. Functional foods can be referred to as the nutrients that positively affect physiological processes in addition to establishing nutritional functions. The functional foods are located at the boundaries of foods and medicines, so when taken as part of a balanced diet, they offer great nutritional and therapeutic applications as comparing other conventional foods (McElhatton and Sobral 2012; Singh et al. 2018).

11.4.1 Safety Considerations for Functional Foods and Nutraceuticals Are as Follows

- Develop and disseminate rules or other recommendations related to the safety of industries.
- Labeling necessity for the food supplements.
- Formulate and publish evidence-related laws or other industry recommendations to substantiate the safety of new-fangled ingredients incorporated in food supplements.
- Developing successful methods for reporting, recording, and analyzing health issues related to functional foods and nutritional supplements.

11.5 Safety of Functional and Nutraceuticals Foods

Both functional and nutraceutical foods played an imperative role in modern nutrition, the risk of low health, and the low risk of chronic disease (Dudeja and Gupta 2017). All food safety assessment requirements must be fulfilled by functional foods. However, in this type of food, the concept of profits for the risks of long-term consumption should be investigated, developed, and verified. Along with the interaction between the food ingredients and the biological processes, it is necessary to define low level or high-level nutrients and a large amount of non-benign safety associated with the long-term use of functional foods. Nutrition research is required before marketing functional foods and marketing monitoring protocols (Hasler 2005; Coppens et al. 2006), considering the safety considerations, such as the likelihood of increased contamination, unfavorable metabolic consequences, overstimulating immune systems, and possible gene transfer (McElhatton and Sobral 2012).

The FAO/WHO Functional Food Safety Standard gives producers responsibility for conducting placebo-controlled clinical studies and assessing the results on a four-point scale.

- 1. Safety.
- 2. Efficiency.
- 3. Efficiency.
- 4. Monitoring.

The sustainability of dietary supplements needs to be thoroughly investigated. The ingredients used the novelty of the procedures, and the possibility of their use in food remains to be investigated. The adoption of different laws that restrict any innovation in food components and the associated production procedures ensures safety. The test scheme used to assess safety will be determined by the category of food innovation and whether or whether it is regarded functional; The legislation that governs certain materials will control the assessment of its safety (McElhatton and Sobral 2012).

11.6 Hazard Analysis Critical Control Point "HACCP"

HACCP is a globally recognized science-based systematic management approach for identifying and controlling physical, chemical, and biological risks in raw materials, manufacturing, handling, distribution, and consumption of final products. This systematic approach of HACCP is based on seven concise principles as illustrated in Fig. 11.2. HACCP is a scientific methodology-based system that food additive companies must adopt to ensure that their products are always safe. The more cost-effective and secure method is to focus on hazard mitigation throughout the whole production process rather than simply final product testing (FAO 2003).

HACCP is the following structural approach.

- Identify the main hazard areas of your work.
- Adopt appropriate control measures.
- Ensure that these controls are carried out correctly.

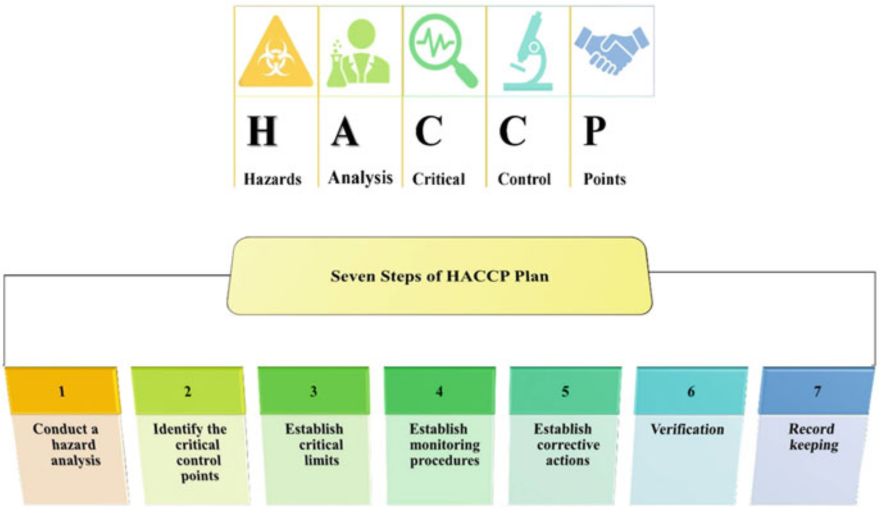

Fig. 11.2 HACCP seven principles

The HACCP system is intended to acclimate to changes in raw materials, equipment, processing conditions, and technology. HACCP should be considered as an integrated element of GMP and not as a distinct legal entity (Hermans et al. 2004).

11.6.1 Requirement of HACCP

According to food hygiene regulations, all food manufactures must have to implement a HACCP plan, regardless of the scale of their operations. Within the food supplement sector, HACCP is recognized as an essential component of GMP (Pal et al. 2016).

11.6.2 Implementing a HACCP System

HACCP can be applied successfully only by complying with all corporate hygiene and GMP regulations; that is, all controls, schemes, and procedures are in place.

11.6.2.1 Assemble HACCP Team

A small interdisciplinary team, such as a quality assurance manager, food technologist, engineer, production manager, and microbiologists, should conduct the HACCP research. Other professionals, such as those from the purchasing department, may be called in as required. The HACCP team should have a coordinator who has received adequate training in HACCP concepts and their operation and execution.

11.6.2.2 Responsibilities

The HACCP team is in charge of the continuing assessment and administration of the HACCP plan. The food supplement manufacturers are responsible for managing the HACCP system as well as developing and implementing the food supplement safety control system.

11.6.2.3 Describe the Possibility of Study

- Limit the investigation to a single process and product.
- Define the category of risk it contains (physical, microbial, and chemical).
- Define the section of the food chain that is being studied (e.g., from production to consumption).

11.6.2.4 Identify the Hazards

- The HACCP team should identify and list any dangers connected with each stage.
- The hazards must be identified in terms of physical, chemical, microbiological, and foreign materials. The possible introduction, growth, or survival of the hazard should be assessed at each point.

11.6.2.5 Determine the Critical Control Point

The critical control point (CCP) determination is an important component of the HACCP procedure. This objective aim is to determine/regulate the key points, steps, or methods that can be applied to control and can avoid, eliminate, or reduce security threats to an acceptable level.

11.6.2.6 Establish the Target Level and Tolerances for Each CCP

It is of utmost important to establish target levels and critical limits for each CCP. The critical limit is a value that distinguishes between acceptable and unacceptable. For each CCP, significant limits should be established for at least one observable or measurable parameter. The criterion for each preventive action or process step is an easy indication that the CCP is being managed. Critical limits are based on subjective data, such as tests, which should be reinforced by unambiguous descriptions of what is accepted and what is not.

11.6.2.7 Establish Monitoring Scheme for Individual CCP

Monitoring is a planned observation or measurement of the CCP against a set threshold limit. Follow-up measures should be utilized to detect any loss of CCP control. Surveillance must ideally be able to provide the essential information in time to make necessary changes to ensure process control and avoid divergence from critical limits. When divergence is detected, the process should be adjusted. Monitoring must be performed or reviewed at defined frequencies by a recognized and trained person.

11.6.2.8 Establish Corrective Actions

It is decisive to explain what action to take when the critical limit is exceeded. The corrective action plans must include taking specified action, responsibilities, authorizations, and management system for faulty materials or goods arising from deviations. Deviations and product disposal measures must be recorded in the HACCP credentials.

11.6.2.9 Verification of HACCP System

Verification is required to confirm that HACCP system complies with the HACCP strategy and has been created according to the current process or product. The person in charge of monitoring and remedial measures should not be in charge of HACCP system verification.

11.6.2.10 Build a Documentation System

A defined scheme is required for operative HACCP deployment and control. This involves predefined methods and record-keeping for the type and size of work, and HACCP work is kept in sync with proposed changes such as formulating, modifying, supplier changes, process equipment changes, and others.

11.6.2.11 Evaluation of HACCP System

The HACCP plan must be reviewed if processes and formulations are changed or if a need is recognized during validation. HACCP protocol should be reviewed at least once a year. HACCP plans should be reviewed regularly to ensure flexibility and adaptability to changes such as advances in technology, changes in formulation, and advances in device design. It also provides a way to eliminate errors in risk management that could endanger the safety of customers and the company (European Medicines Agency (EMA) 2014).

11.7 Establishment Design and Facilities

Healthcare and nutrition facilities should be kept away from ecologically contaminated areas, such as open sewers, drains, public restrooms, or anything that emits foul odours in order to prevent contamination of the surrounding environment. Plant layout should be developed, built, and maintained to enable proper manufacturing and sanitation practices (Soares et al. 2013).

The facility must provide a suitable working space, which should have a reasonable flow of materials, products, and workers, as well as physical separation of raw and processed areas to the greatest degree practical to avoid cross-contamination. Manufacturers must indicate appropriate controls (for local segregation) where items such as prebiotics and probiotics are produced. Walls and partitions must be made of strong and durable materials, clean, impervious to food, oil, and water and have no hazardous effects when used as intended. Ceilings must be made of materials that keep them in good shape and are durable, can be cleaned, do not penetrate food, oil, or water, and do not adversely affect when used as intended. The floor must be non-slip and properly sloped. Therefore, proper drainage is possible. Drainage must flow in the opposite direction to the flow of the manufacturing process. Smooth, non-absorbent surfaces are required for doors. Wooden doors are not advised since they foster mold development and termites as they age. Doors must be close-fitting and have appropriate safeguards to prevent insect invasion (CFDA 2011; Soares et al. 2013).

11.7.1 Facilities/Utilities

The facilities provide key services that are critical to the industry. High-quality public facilities and services, such as water, lighting, and sanitation facilities, are required to achieve optimal food safety. Backup and parallel infrastructure systems can be planned to achieve continuous and uninterrupted supply. Personnel sanitation facilities must be accessible to certify that an acceptable level of personal hygiene is maintained to minimize cross-contamination. These facilities need to be placed and labeled in the right place. Hand washing, toilets, changing rooms, and refreshment rooms are required. These facilities must be appropriately placed and recognized (CFDA 2011).

11.8 Maintenance and Sanitization

11.8.1 Cleaning and Sanitization

The facility must carry out cleaning and maintain clean food processing facilities and surroundings to prevent food contamination from metal shards, flaking plaster, and food waste. Cleaning must remove food particles and debris and can be achieved using separate or combination physical procedures such as heating, scraping, flow regimes, and vacuum cleansing, or other techniques that do not involve the use of water and chemical treatment utilizing appropriate cleaning agents. Wherever possible and applicable, a CIP technique for cleaning equipment should be specified (Cramer 2006).

11.8.2 Maintenance

Maintenance workshops must be kept isolated from manufacturing areas. Spares changed parts and instruments must be kept in designated rooms or lockers. Tools and replacement parts used in manufacturing that are susceptible to microbial contamination must be disinfected before being transferred within the processing areas. Buildings must be maintained in good condition to reduce insect activity and avoid possible breeding grounds. Drains holes and other areas where rodents are probable to enter must be sealed (Cramer 2006). All health supplement/nutraceuticals waste and other types of waste products must be removed from areas where health supplements/nutraceuticals are stored, refined, or packaged regularly. The treatment of waste, viz. solid, liquid, gas, and effluents, shall be in accordance with the provisions of the Plant/Environmental Pollution Control Board.

11.9 Training and Management

The staff handling food must receive appropriate training to ensure that they have the necessary expertise and skills in GHP and GMP for particular duties and also personal cleanliness requirements consistent with their professional habits, food supplement quality, handling, manufacturing, planning, packing, transportation, operation, and distribution. Food process managers and supervisors must have the necessary competence and abilities in food hygiene (GHP and GMP) standards and practices to assess possible risks and take corrective steps. Periodic evaluations of the quality of training and guidance programs, as well as regular monitoring and inspections, should be carried out to verify that all personnel implement food cleanliness and food safety practices correctly and effectively (Singh et al. 2018).

11.10 Audit Documentation and Record-Keeping

Good and effective documentation is an integral part of Good Manufacturing Practices (GMP), which forms the basis of an effective HACCP strategy. The document system can be set up to check the product history of each lot to ensure traceability. The user handbook, as well as the disposal of raw materials, intermediates, bulk goods, or completed products, must be included in the paperwork.

The purpose of the documentation is as follows:

- To identify the components, processes, procedures, control measures, and products.
- To records and transfer the required information before, during, or after manufacturing.
- To minimize the risk of errors due to verbal communication.
- To allow defective items to be investigated (Singh et al. 2018).

A health supplement/nutraceutical organization must conduct routine self-inspections at least once a year to ensure the execution and conformity with GMP standards and to recommend any necessary corrective measures (Coppens et al. 2006).

Here, it includes the following:

- Establishment.
- Equipment.
- Manufacturing.
- Quality control.
- Stock allocation.
- Documentation.
- The systematic system deals with complaints, withdrawals, and recalls of defective products.

Relevant personnel must be provided with adequate instruction on how to complete the records, and the quality of this training should be evaluated on daily basis. A handbook that explains the overall quality assurance (QA) system, methods, and documentation utilized might be valuable. The manual must be completely integrated with HACCP documents (European Commission 2019).

11.11 Complaint's Procedure and Product Withdrawal Recall

General food law puts absolute liability on food business owners to ensure that the food items they put on the market are safe for consumers. If a food corporation believes or has a reason to suspect that a food product purchased, manufactured, packaged, or sold does not comply with food safety standards, it may need to expedite the process to remove the substance from the market. Food production companies are also required to inform the relevant competent authorities of the countries in which their products are sold and work with them on measures they have taken to prevent or mitigate the risks their products face. Adequate documents must be kept ensuring product traceability, allowing for quick and reliable removal or recall.

11.11.1 Complaints

Procedures for collecting, reviewing, and handling all customer grievances received by the firm should be created. They can provide procedures to troubleshoot production issues related to slight potential health impacts and methodology to deal with complaints about dangerous accidents or safety issues that could lead to potential health effects. The protocol should specify the appropriate responsible person for which the complaint is intended. Employees of both companies must be sufficiently qualified to ensure proper identification, mediation, and documentation of complaints (European Medicines Agency (EMA) 2014).

11.11.2 Product Withdrawal and Recall

A product withdrawal is a decision made by the customer/retailer to return the goods to the seller, not the final customer. The recall of products must be a voluntary action taken by the manufacturer in response to dissatisfaction with the superiority of the product, but it is not necessarily the safety of the product.

Product withdrawals or recalls may occur for several reasons; generally, they can be divided into three basic categories:

(a) When national or regional authorities become aware of a hazard or suspect hazard and require explanation and assistance from the manufacturer or supplier.
(b) When a manufacturer, importer, seller, or supplier becomes aware of or suspects the presence of a threat.
(c) Where there is no risk or suspected hazard, but a scenario (e.g., low quality, incorrectly labeled) has arisen, causing the manufacturer, importer, or distributor to withdraw or recalled the affected goods (CFDA 2011).

11.12 Self-Inspection

Food companies should conduct regular self-inspections, especially in departments with work related to quality and safety, to ensure that GMP principles are being followed and to recommend any necessary corrective measures.

- Personnel matters.
- Establishment.
- Equipment.
- Manufacturing.
- Quality control.
- Stock allocation.
- Documentation.
- Complaints and recalls are handled in a systematic manner.

Self-inspection must be performed on a regular basis, or yearly, depending on the scope and importance of excellence and safety-related tasks performed in specific units. Self-inspection procedures should adhere to a predetermined schedule to ensure compliance with quality assurance standards. At the stage of analysis, recommendations, and steps taken during the inspections, it is necessary to record an opinion on the appropriate completion period and actions taken. This report can be retained for a while and can be reviewed regularly by senior management in the company (Hermans et al. 2004).

11.13 Laboratory Testing

The quality control (QC) laboratory must have sufficient space, services, supplies, and personnel, as well as be organized in such a way that it can fulfill good laboratory practice and good manufacturing specifications. Personnel in the laboratory should be well educated. High standards should be established and sustained by strict adherence to accepted and agreed-upon procedures and process reviews. The quality control laboratories should be constructed and outfitted to accommodate the activities that will be carried out. Space should be made available for writing and storing papers and archives, as well as for certain specific arrangements such as storing samples, etc., at the proper temperature. Sufficient facilities must be provided before disposal to dispose of laboratory waste. Procedures should be to ensure that any such waste is disposed of safely and responsibly (European Medicines Agency (EMA) 2014).

11.13.1 Sampling

Regardless of whether you need an official sampling method, you must define a written sampling protocol and specify:

- The sampling process and frequency.
- Type of sampling device and sample container used.
- Special actions to be taken.
- The amount of sample required.
- Sample segmentation instructions.

- Sample handling and storage requirements.
- Cleaning and storage of sampling or reusable equipment.

The contents, product ID number, lot number, and date sampled should all be clearly labeled on sample containers. Validation should be performed on all tables or notes used to calculate sample criteria (European Medicines Agency (EMA) 2014).

11.13.2 Analysis

Written protocols for preparing the reagents to be used in the tests should be established. Reagents must be specified with the manufacture and receipt date, concentration normalization factor, storage conditions, and shelf life as required. The reference standard and auxiliary standards derived therefrom must be processed, processed, and used following the manufacturer's instructions. The date of receipt or preparation of the reference standard and the secondary standard, concentration normalization factors, storage conditions, and shelf life should all be specifically indicated. Samples should be analyzed under written protocols, using either legally mandated or internationally approved test methods for the appropriate sample matrix.

The following parameters are commonly used for validation:

- Specificity/selectivity.
- Accuracy.
- Recovery.
- Linearity and range.
- Precision.
- Detection limit (LOD)/quantitative limit (LOQ).

Verification details need to be recorded and saved. The results of the study of all samples are within the validated range of the method (European Medicines Agency (EMA) 2014).

11.14 Benefits and Drawbacks of Using GMP in Organizations

11.14.1 Benefits

Proper GMP implementation in businesses provides numerous benefits, both in terms of the manufacturing process and, as a result, refinement of the manufactured product. It also opens up opportunities for professional effectiveness by increasing the organization's competitiveness (Mtewa et al. 2020). GMP makes it less expensive and safer by preventing quality discrepancies rather than investigating their root causes after the fact. GMP focuses on error correction. It necessitates an internal audit, which identifies flaws in an organization and provides recommendations for future action. As a result, the GMP is consistent with the overall concept of the quality management system. It allocates employees established responsibilities in a specific organization, and as a result, people follow certain procedures and instructions. It reduces the possibility of errors and ensures improved safety during production, particularly when using raw materials that are lethal in high concentrations (Sikora 2015).

11.14.2 Drawbacks

When considering the numerous benefits of GMP implementation, it is also necessary to consider its drawbacks. One of them is the dearth of a comparable manufacturing plant, equipment, technology, or documentation models (Mtewa et al. 2020). All GMP elements are interconnected, and any error in any of them has an impact on the entire system. Any action in one component of the system causes a reaction in another. The GMP system is analogous to a chain with many links, and one broken link destroys the entire chain. All the connections are equally important (Sikora 2015).

11.15 Future Prospects in Functional/Nutraceutical Food Manufacturing

Change in the lifestyle, consumption of junk food results in numerous health diseases, for that reason the nutraceuticals and functional food supplements can be consumed for prophylactic uses. The rapid expansion of global nutraceutical and functional industries has further emphasized the need for progress of regulatory bodies (Coppens et al. 2006). Good manufacturing practices (GMP) lay the foundation to ensure that the food supplements are being processed/manufactured endlessly to improve the quality and safety. This involves executive management, cleaning, engineering, and the supply chain for all commodities utilized in the processing plant. Companies now have a better understanding of how nutrients affect people's health. Investment in new technologies and the usage of genetically modified technology in the food industry owing to therapeutic advantages are likely to fuel further expansion in the health functional and nutraceuticals food market. More investment will be facilitated for technology and application areas that will increase the amount of systematic scientific study to verify the effectiveness and security of these new products. Food technology advancements can also lead to new developments in the production of food items that support optimal health. Increased consumer knowledge of functional foods and nutraceuticals, on the other hand, will fuel additional worldwide sales growth. The industry's international expansion is projected to continue as emerging countries boost their consumption of functional foods (Coppens et al. 2006; Daliri and Lee 2015; Mtewa et al. 2020).

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Effect of Processing on the Functional Potential of Bioactive Components

12

Suka Thangaraju, Monica Shankar, Malini Buvaneshwaran, and Venkatachalapathy Natarajan

Abstract

Bioactive compounds are secondary metabolites produced during the growth and development of plants, animals, and marine organisms. Bioactive compounds are categorized into three categories, namely phenolic compounds, terpenoids and terpenes, and alkaloids. Bioactive compounds have various health benefits with functional properties like anti-inflammatory, antibacterial, anticancer, antidiabetic, antibiotic, etc. Any food being cooked or processed (canning, pasteurization, baking, roasting, steaming, freezing, drying) to reduce the post-harvest loss and to improve the quality and shelf life changes availability, accessibility, and nature of bioactive compounds because of the change in food matrix and structure. Many researchers have studied the effect of bioactive compounds on health and processing on the functional properties of bioactive compounds. This chapter comprises the sources (plant, animal, marine), health benefits, and the effect of processing on the functional properties of bioactive compounds.

Keywords

Bioactive compounds · Post-harvest loss · Functional properties

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12.1 Introduction

During the growth and development of plants, secondary metabolites are produced as a result of the primary metabolic and biosynthetic pathway, and this secondary metabolite is called "bioactive compounds." These bioactive compounds are also considered the outgrowth of cell metabolism. The word "bioactive" is derived from two words of different origins, "*bios*" a Greek word with the meaning "life," which gives the word "bio," and "*activus*" a Latin word with the meaning "energetic" which gives the word "active" (Shrinet et al. 2021). Foods or dietary supplements containing bioactive substances are intended to provide the basic nutritional requirements for good health and disease-free human life. They promote pharmacological and toxicological effects in humans and animals. As a result of the concentration of the bioactive components, they can have either positive or negative effects, or both, depending on the type of component or substance, their reaction with biological substances, dosage, exposure route, and bioavailability of the compounds. The application of bioactive compounds is wide in every field of biologies such as biochemistry, agrochemistry, biotechnology, pharmaceutical industry, plant and animal science, and the food industry. The increase in interest in bioactive compounds has also increased the curiosity of researchers on bioactive compounds in foods like spices, condiments, herbs, fruits, and vegetables that are used in day-to-day life. All parts of plants contain bioactive compounds in small to very small amounts in products like fruits/vegetables, nuts, and oils (Segura Campos 2018).

The natural resources of bioactive compounds have good physiological and immunological effects on the body to maintain and support good health. However, these nutrients are not taken as the term "plant bioactive components." Generally, secondary metabolites, which are not required for the survival of the plants, but are needed for defense, competition, attraction, and signaling, are termed bioactive compounds. Several properties of bioactive chemicals can be used to explain the definitions like immune boosters, antiaging, anticancerous, antipyretic, healing properties, and antioxidant. They may also have adverse health effects after a certain dose. Phytochemicals contained in foods that can alter metabolic processes to enhance human health are examples of bioactive molecules. According to the literature, the known beneficial effects are based on trials of antioxidant activity, inhibition or induction of enzymes, inhibition of receptor functions, induction, and inhibition of gene expression (Correia et al. 2012).

12.2 Sources of Bioactive Compounds

Bioactive compounds are derived from different sources, including plant, animal, and marine sources, which are secondary metabolites (Magnúsdóttir 2002). Different macromolecules like proteins, lipids, and carbohydrates are commonly mixed with fruit antioxidants (Galanakis 2017). Bioactive compounds are classified into three groups: phenolic compounds, about 8000 types, terpenoids, terpenes which include 25,000 types, and alkaloids, with 12,000 types. These compounds are present in vegetables, fruits, and whole grains (Carbonell-Capella et al. 2014).

12.2.1 Phenolic Compounds

Mostly distributed all over the plant, secondary metabolites are phenolic compounds absent in algae, fungi, and bacteria. Widely phenol is a word that mentions the chemical structure of a phenyl ring consisting of one or more of the hydroxyl side chains. About 4000 flavonoids and 8000 different other compounds are differentiated. Hence, polyphenol refers to the chemical structure with multiple phenol rings with two or more hydroxyl side chains (Vuong 2017). Generally, phenolic compounds are used against ultraviolet radiation as it has a protection mechanism for a broad range of the spectrum, which also changes the gene expression with biochemical activities related to anticarcinogenic, antioxidant, and antimutagenic effects and also destroys predators, pathogens, and parasites (Shrinet et al. 2021).

Carrageenans, ulvan, and fucoidan are sulfated polysaccharides with antioxidant and antiviral properties used as food additives. In contrast, ulvan has anticarcinogenic properties used for food and pharmaceutical applications, and fucoidan is used to develop functional foods (da Silva Vaz et al. 2016). Quinones and orcinols are prepared by the polyketide pathway, where phenolic compounds are synthesized through the shikimate pathway (Ben-Amotz 2019). The categorization of phenolic compounds which are not linked to the hydroxyl group is used indistinctly but comprises their functional groups like glycosides. Mostly, all plant polyphenols contain glycosides with various sugar groups and acylated sugars present in polyphenolic structure at a different position. Compounds like gossypol and estrogen are also known as polyphenols. The classification includes lignans, flavonoids, phenolic acids, and stilbenes based on the structural elements bound to the phenol rings and on the different groups with different numbers of phenol rings with a functional group, and the classification includes lignans, flavonoids, phenolic acids, and stilbenes (Vuong 2017).

1. *Flavonoids:* Flavonoids are secondary metabolites and very important polyphenols which contain 4500 variety of compounds. The majority of the flavonoid structures consisting of 2 phenolic rings, A and B, are linked with 3 carbon atoms, which finally form an oxygenated heterocycle ring C (Câmara et al. 2020). The differentiation of flavonoids into their subgroups is based on their heterocyclic ring, a key functional group. The subgroups of flavonoids include flavonols, anthocyanidins, and flavanones (Carbonell-Capella et al. 2014). The main principles in red pepper and lime juice fractions are hesperidin, and eriocitrine (Patil et al. 2009). Flavonoids maintain the quality of the food source by preventing the deterioration of vitamins and enzymes in food and fat oxidation. The most important flavanol in a huge amount in broccoli, apple, and onion is quercetin, whereas green tea contains catechin, and berries contain

anthocyanin cyanidin glycoside. Grapefruit contains naringenin (Shrinet et al. 2021). Compound with phenol group has anticancer, anti-inflammation, and antioxidant properties (Ben-Amotz 2019).

2. *Flavones:* Fruits and vegetable skins and savory herbs contain mainly flavones consisting of luteolin and apigenin. The luteolin is present in large amounts in apple skin, carrots, celery, cabbages, and broccoli. In contrast, apigenin is predominately found in savory herbs like dried marjoram, fresh sage, onion, and celery.
3. *Flavonols:* Another term for flavanols is flavan-3-ols or catechins, present in apples, red wine, and tea (Jawad et al. 2013). Flavonols are the very important flavonoids present as glycosides with sugar units linked to the C-3 position and found in different food sources like fruits and vegetables including apples, grapes, and onions and also found in tea, ciders, and wine, where they are commonly present in outer parts, roots of plants, and plant leaves (Shrinet et al. 2021). Myricetin, quercetin, and kaempferol are the important compounds that present higher levels in apple kale, tea, and onions (Jawad et al. 2013). Apigenin and luteolin are the main components (Câmara et al. 2020). Normally, foods contain not above 30 mg/kg of the flavonol. However, foods like onion and cranberries contain a high amount of quercetin 15 mg/100 g, kale with 25 mg/100 g myricetin, and the ripening stage of fruits contains a high level of myricetin. Galactose, xylose, arabinose, glucuronic acid, glucose, and rhamnose are glycosidic sugars (Shrinet et al. 2021).
4. *Flavanones:* Flavanones are especially phenolic compounds in citrus foods, tomatoes, and aromatic plants (Câmara et al. 2020). The structure of flavanones contains a chiral center in a three-ring structure of flavonoids at the second position, and between the second and third positions, a double bond is absent. Naturally, different types of about 100 aglycones, glycosides, and flavanones are identified (Shrinet et al. 2021). From the food manufacturing point of view, the most common food containing a high amount of about 90% hesperidin and 10% of narirutin is orange juice. Flavanones are also present in herbs, spices and legumes, fruits, vegetables, and tea. Furthermore, many catechins are recently interested due to their health effects and proanthocyanidins forms. Fruits such as apricots and red wine contain catechins (Vuong 2017).
5. *Isoflavones:* As in the other flavonoids, the B ring is integrated into the central ring C third position instead of the second position. Naturally, about 900 isoflavonoids are present as aglycones. Based on their modifications in the carbon chain, they can be divided into 14 classes and 23 subclasses (Shrinet et al. 2021). Isoflavones are present in black gram and soybeans, which are diphenolic compounds. Daidzein and genistein are the isoflavones present in soy (Câmara et al. 2020). These compounds have the same structure as mammalian estrogen and have estrogenic and non-estrogenic effects. Genistein and daidzein are the two important isoflavones in soybeans with 3 mg/g. Another name for isoflavones is phytoestrogens. The main source of isoflavones is the bean family Fabaceae (Ben-Amotz 2019). Phytoestrogens are present in fruits, vegetables, soy, whole

grains, and flaxseed oil which have antioxidant properties and have the same molecular level as estrogen (Hamzalioğlu and Gökmen 2016).

6. *Catechins:* Strawberries, broad beans, apricots, and black grapes have a high catechin concentration. Catechin, gallocatechin, and epicatechin are the main flavanols. Green tea contains gallocatechin. The flavanols present with gallic acid in the ester form called epigallocatechin gallate and epicatechin gallate are high in chocolate, apples, pears, and blackberries. Oligomeric catechins are bonded covalently known as procyanidins. Epigallocatechin is found in grape seeds and leguminous plants (Câmara et al. 2020). Plums, grapes, apples, cocoa, blackberries, and wine contain high procyanidins levels. Researchers have identified the procyanidins effects such as reducing lipid peroxide, low-density lipoprotein levels, and platelet aggregation and curing vascular-related problems (Jawad et al. 2013).
7. *Anthocyanidins:* Anthocyanins have been identified in over 27 families of food plants, and in the USA, the consumption has been estimated at 215 mg during summer and 180 mg during winter (Jawad et al. 2013). Anthocyanidins are compounds linked to the sugar units and derivatives of the flavium salt like glycosylated, polymethoxy, and polyhydroxy. These compounds are mostly related to the various types of vibrant colors like red, purple, and blue in many flowers, fruits, and vegetables. Black rice is rich in anthocyanins (Câmara et al. 2020). About six types of anthocyanidins such as delphinidin, peonidin, cyaniding, malvidin, petunidin, and pelargonidin were discovered in food sources from 90 percent anthocyanidins. Black currants (86.68 mg/100 g) and black grapes (39.23 mg/100 g) have a high amount of anthocyanidins and provide resistance against biotic stress to plants by phytoalexins, antibacterial, and anti-oxidant agents (Shrinet et al. 2021).
8. *Stilbenes*: Stilbenes are polyphenols derived from the phenylpropanoid pathway present naturally in less amount in foods and also fewer concentrations in the human diet (Câmara et al. 2020). Stilbenes are present in many plants and are synthesized from cinnamic acid derivatives (Jawad et al. 2013). Resveratrol is stilbenes and one of the polyphenols present in little amounts in edible plants like grapes, including the seed and skin of grapes. It has many useful health benefits like anti-inflammatory properties. It is examined to be present in wine; a large amount of resveratrol is present in red wine, where rose and white wine contain less resveratrol. Grapes, soy, peanuts, peanut products, and wine are the main sources of stilbenes (Shrinet et al. 2021). The extrinsic factors include environmental aspects, climatic conditions, and the variety of the grapes that decide the amount of resveratrol present in red wine. Also, red currants and strawberries contain resveratrol.
9. *Carotenoids:* Fruits like mangoes, apricots, and vegetables like pumpkin, carrots, and tomatoes contain carotenoids and have antioxidant properties (Hamzalioğlu and Gökmen 2016).

12.2.2 Salicylates

The potential medicinal effect of salicylates includes aspirin tablets and acetylsalicylic acid used to treat many diseases. Many studies have identified that many types of fruits, spices, vegetables, and herbs contain salicylic acid, and food sources rich in salicylic acid can prevent chronic diseases. Plant stanols and sterols have the same chemical structure as cholesterol (Jawad et al. 2013).

12.2.3 Polyphenols

Most plants contain phenolic compounds and are present broadly in olive oil, tea, vegetables, cereals, nuts, legumes and fruits like grapes, strawberries, plums, raspberries, that have antioxidant properties and protective effects on heart-related cardiovascular diseases (Hamzalioğlu and Gökmen 2016). Several thousand polyphenols exist and are subdivided into different subclasses (Jawad et al. 2013). Polyphenols vary from simple compounds like phenolic acids and highly polymerized tannins (Câmara et al. 2020). Polyphenols are also rich in spices and herbs, like eriocitrin, eugenol, pinocembrin, rosmarinic acid, and anethole (Michalak et al. 2021). The total phenolic compounds of the sesame seeds and seed milk have antioxidant properties (Aydar et al. 2020).

12.2.4 Glucosinolates

All pungent plants like cabbage, horseradish, and mustard naturally contain glucosinolates that hinder enzyme activation, produce Phase I and Phase II enzymes, and are under examination to reduce cancer (Hamzalioğlu and Gökmen 2016). A wide group of sulfur-containing compounds known as glucosinolates is found in watercress, cabbage, broccoli, cauliflower, and Brussels sprouts. In the human body, by the enzymatic action of intestinal flora, glucosinolates are broken down into isothiocyanates that have anticarcinogenic properties that got limelight recently. Based on climate, growing, and species conditions, the glucosinolates composition will vary in the food sources (Jawad et al. 2013).

12.2.5 Alkaloids

Alkaloids are secondary metabolites in higher plants biosynthesized from transamination, amination reactions, and amino acids, such as tyrosine which are organic compounds with nitrogen with abundant beneficial properties. They are important for fruit and vegetable quality, taste, and flavor. The border between the other natural compounds with nitrogen and alkaloids needs to be explained (Vuong 2017). Fungi and ergot alkaloids contain some of these compounds such as Apocynaceae, Papaveraceae, Fabaceae, Ranunculaceae, Rutaceae, Solanaceae, and Rubiaceae, which are alkaloids (Ben-Amotz 2019).

Hydrogen, nitrogen, and carbon alkaloids consist of sulfur, phosphorus, bromine, chlorine, and oxygen. Natural alkaloids are present in bacteria like Streptomyces and fungi like Penicillium, Aspergillus, Rhizopus, and Claviceps. A variety of natural compounds nearly 12,000 compounds and their derivatives are found as alkaloids. Based on the chemical structure, biosynthetic pathway, ecological, and biological activity, alkaloids can be differentiated, and also based on the carbon skeleton and natural sources, alkaloids can be classified. The nitrogen atom alkaloids are classified into spermine, spermidine, storied, terpene, heterocyclic, putrescence, and peptide alkaloids. All parts of plants such as seeds, bark, leaves, roots, and fruits contain huge alkaloids in non-homogeneous form. Natural alkaloids in herbs show many medicinal and pharmacological functional properties. They have been used in ancient times for treating antiviral, anti-inflammatory, adrenergic, antibacterial, anticancer, hypoglycemic, central nervous system, and antimalarial problems. From by-products of tomato and potato wastes two alkaloids' chemical structures can be regained, but there are no standard methods for extraction of alkaloids. Other methods include microwave-assisted extraction, ultrasound-assisted extraction, pressurized liquid extraction, Soxhlet extraction, solid-liquid extraction, and enzyme-assisted extraction since alkaloids are lightly water-soluble and ether, chloroform, benzene, and ethanol-soluble (Vuong 2017).

12.2.6 Glycosides

Glycosides are commonly present in plants which are organic compounds and in their structure contain alcohol or sulfur compounds and phenol compounds. The glycosides are defined as prodrugs mostly diverse. They are present in the inactive form in the large intestine until they are activated by hydrolysis, which shows the aglycone that the non-sugar part is released (Vuong 2017). Oligo-saccharide, or uronic acid, and monosaccharide are linked with secondary metabolites to form glycosides. Glycosides are found as flavonoids (Ben-Amotz 2019). These compounds are distinguished by sugar part or linked mostly with one or non-sugar compounds by a glycosidic bond. The chemicals stored by most plants are activated by removing the sugar portion known as hydrolysis, which is originally in the idle form of glycosides to make them beneficial. Different molecular ranges like quinines, phenols, steroids, and terpenes are heterogeneous structures based on glycoside. Based on their medicinal properties, glycosides can be differentiated into various types like flavonoid, saponin, cardiac/steroidal, coumarin, anthraquinone, isothiocyanate, chromone, cyanophore, alcohol, phenolic, and lactone glycosides. Depending on the glycosidic bond type or atoms used for the glycosidic bonding, glycosides are classified into four groups such as sulfur glycoside (*S*-glycoside), carbon atom glycoside (*C*-glycoside), oxygen glycoside (*O*-glycoside), and nitrogen glycoside (*N*-glycoside) (Vuong 2017).

Glycosides are responsible for the color, taste, and flavor of plant food. Likewise, most food color is due to anthocyanin, which is cyanidin-3-glucoside. Furthermore, includes some medicinal properties like sedative effects, anticancer effects, anticonvulsant activities, central nervous system, and antidepressants (World Health Organization 2014). Solvent extraction method like ethanol or methanol is used to regain glycosides.

12.2.7 Phenolic Acids

Phenolic acids are present in conjugated and free forms in various food sources and classified as benzoic acid derivatives and cinnamic acid derivatives, mostly ferulic acid and caffeic acid. Naturally, phenolic acids are present in derivatives of glycosylated esters of shikimic, tartaric acids, and quinic, whereas, in processed food, it undergoes fermentation, freezing, and sterilization. The acid that shows higher antioxidant activity is hydroxycinnamic acids, followed by hydroxybenzoic acids, as it consists of a carboxyl group in resonance with the benzene group (CH=CH–COOH). When compared with hydroxybenzoic acid, hydroxycinnamic acids show the higher donation of proton and radical stabilization skill (Shrinet et al. 2021). Ferulic acid comprises about 90 percent of overall polyphenolic content and is most importantly found in cereal grains and seeds. Ferulic acid, also present in the wheat endosperm's outer side, includes aleurone and pericarp layer, same as caffeic acid. The reduction or phenolic acid losses happens during flour production. Fruits and vegetables contain a much less quantity of benzoic acid than food sources like red-colored fruits and onions and tea found to have gallic acid.

Caffeic acid comprises 75% of most fruits acid content, where mainly higher levels are present in the fruits skin or outer layer and one of the abundant phenolic acids. Generally, the caffeic acid increases with the enlargement of the size of the fruit, and while the ripening of fruits, it gets decreases (Vuong 2017).

12.2.8 Lignans

Lignans are commonly found in all food materials with a remarkable amount of fiber like wholegrain foods and where other food sources like cereals, oilseeds, nuts, and in some kinds of fruits with different levels of concentration and a nearly small quantity is present in the resin and wood of plants as dimers like glycosides which are very complex in structure (Vuong 2017). Lignans form an 18-carbon skeleton with two phenylpropanoid units and have lipophilic properties. Higher levels of lignans are found in oilseeds which shows cathartic, or antineoplastic, and phytoestrogenic effects (Ben-Amotz 2019). Lignans belong to the pharmacologically active compounds. Their structure consists of two cinnamic residues classified into five first groups: lignans, oligomeric lignans, norlignans, neolignans, and hybrid lignans. Although they are present in high concentrations in linseed (flaxseed), they are also present in measurable amounts in many kinds of cereal, pulses, fruits, and vegetables commonly consumed in the Western world (Jawad et al. 2013). Matairesinol, lariciresinol, syringaresinol, pinoresinol, and medioresinol are the important dietary lignans (Câmara et al. 2020). Almost trimers and tetramers have low molecular weight found in plant structure. Lignans are present in vegetables like cabbage, Brussel sprouts, and fruits like banana and apricot. Lignan is present in cashew nuts, sunflower seeds, sesame, and flaxseeds at low to high levels. Cereals like rye, wheat, and oat have a high amount of lignan.

12.2.9 Triterpenoids and Terpenes

Triterpenoids are found in the form of glycosides naturally in plants. The triterpenoids have complex structure that consists of cycloartanes, lanostanes, euphanes, tetranortriterpenoids, tirucallanes, dammaranes, oleananes, hopanes, lupanes, dammaranes, quassinoids, serratanes, ursanes, and friedelanes. The chemical structure obtained from isoprene is terpenes, which are hydrocarbon-based compounds with medicinal effects like antineoplastic, antibacterial, and antiviral effects (Ben-Amotz 2019). Different types of triterpenoids are present in medicinal and edible plants. An esterified and free form of triterpenoids has a low polarity present in plant stem and surface cuticle waxes. Hence, the source of bioactive compounds includes fruit peels which is the most available source. There is very little information about triterpenoid content for the other vegetative parts of plants like fruit cuticular waxes compared to the fruit peels.

The structure of triterpenic gives new derivatives with the chemical modifications that give pharmacological property. Oleane, lupine, and ursane are the important three triterpene groups. In the lupine group, lupeol, betulinic acid, and betulin are present in the lupine family, which is present in grape berries and mango cuticle where uvaol and ursolic acid are found in ursane group which is present in apple cuticle. Erythrodiol, β-amyrin, and oleanolic acid are the main triterpene present in oleane. Grapes, tomatoes, and olive skin contain maslinic acid, β-amyrin, and oleanolic acid. Fruit peels are available from the juice, and the canned foods manufacturing industry produces a huge quantity of waste where disposal is the main problem that causes severe environmental pollution. Hence, this can be converted into value-added food ingredient that is advantageous economically. Fruit wastes from grape, apple, tomato, orange, and olive are generated in million tonnes during industrial processing, can be used in nutraceutical and pharmaceutical applications. Both nature and a synthetically modified form of triterpenoids are used in the industry (Vuong 2017).

12.2.10 Tannins

Based on their structural complexity, tannins are in condensed ellagitannins, phlorotannins, complex tannins, gallotannins, and hydrolyzable forms (Câmara et al. 2020). Tannins are composited with proteins, alkaloids, polysaccharides, and these are almost high-molecular-weight compounds (Shrinet et al. 2021). Tannins showed antinutritional effects when binding with protein and minerals (Ben-Amotz 2019).

12.2.11 Other Bioactive Compounds

Bioactive compounds from seaweeds such as proteins, polysaccharides, polyphenols, and lipids have functional properties like antiviral, antifungal, and antibacterial properties, rich in minerals, vitamins, and polysaccharides. These properties of seaweeds make them a functional food for extraction purposes (Holdt and Kraan 2011). Aromatic plants include herbs and spices, which have been used in ancient days as medicine and preservative in foods. The major aromatic plants include rosemary, oregano, basil, sage, and anise. These bioactive compounds include antibacterial, antifungal, anti-inflammatory, antiparasitic, antioxidant, and antiprotozoal properties (Christaki et al. 2012). Several functional properties of microalgae bioactive compounds include anti-inflammatory, antiangiogenic, antiobesity, neuroprotective, antioxidant, and antitumor. Phycobiliproteins and carotenoid pigments in microalgae are used in food dyes, fortified foods, dietary supplements, pharmaceutical products, cosmetic products, and animal feed. Bioactive peptides are present in food proteins. Bioactive compounds from a marine source have a functional property like antihypertensive property (Hernández-Ledesma and Herrero 2013). Bioactive compounds also present in microalgae have a beneficial effect on treating chronic diseases. Microalgae source of bioactive compounds includes Botryococcus, Dunaliella, Haematococcus, Spirulina, Nostoc, and Chlorella. Carrageenans, ulvan, and fucoidan are sulfated polysaccharides with antioxidant and antiviral properties used as food additives. Ulvan has anticarcinogenic properties used for food and pharmaceutical applications, and fucoidan is used to develop functional foods (da Silva Vaz et al. 2016). Cyanobacteria contain low bioactive compounds when compared to other microorganisms. The cryptophycins, dolastatin 10, and dolastatin 15 are cyanobacterial origin with anticancer properties (Shiono and Kimura 2011). Bioactive compounds from natural sources include algae, microorganisms, and plant tissue. About 60–70% of approved drugs for treating cancer and infectious diseases are derived from the bioactive compounds from the plant tissues. Streptomyces, aspergillus, and penicillium are fungi that produce organic acids, antibiotics, and enzymes (Joana Gil-Chávez and Villa-Rodriguez 2013).

12.3 Health Benefits of Bioactive Compounds

Bioactive compounds include vitamins, minerals, polyphenols, choline, phytosterols, phytoestrogens, taurine, glucosinolates, carnitine, and flavonoids. Each has different functional properties like anti-inflammatory, antioxidant, antimicrobial, and antitumor properties (Hamzalioğlu and Gökmen 2016). As vitamins are essential nutrients, much less is required for the organism. Vitamins are taken through diet since the human body cannot produce them. They have various functions, and health effects like Vitamin C and E have antioxidant properties. The World Cancer Research Fund concludes that the consumption of cruciferous vegetables in human diet reduces the cancer risks in the rectum, thyroid, and colon (Jawad et al. 2013). Vitamins present in vegetables, meats, nuts, bananas, and wholegrain products are pyridoxal, which helps treat the risk of cardiovascular disease and its antitumor properties. Niacin is found in tomatoes, chicken, sweet potatoes, liver, beef, avocados, cereal, peanuts, legumes, leaf vegetables, fish, and carrots, reducing cardiovascular disease risk (Hamzalioğlu and Gökmen 2016). Different alkaloid groups have different health benefits. For example, in the Solanaceae family, like *Hyoscyamus niger*, tropane alkaloids are found, and these have an anticholinergic effect that helps relieve pain (Ben-Amotz 2019). From the plant species *Stevia rebaudiana*, Stevia is extracted, a bioactive compound with antibacterial and antifungal properties that helps to reduce Type 2 diabetes and arterial hypertension (Stachnik 2017). Some other bioactive compounds and their health effects are shown in Table 12.1.

12.4 Effect of Processing on Bioactive Compounds

To improve the shelf life, the quality is maintained and the post-harvest losses are minimized, food materials undergo various process conditions such as canning, drying, freezing, pasteurization, fermentation, smoking, packaging, and storage. In each process condition, the availability and the nature of bioactive compounds get changed by modifying the food matrix and microstructure. Numerous researchers focused on the changes in bioactive compounds during the processing techniques. The process parameters can control these changes, including process time, temperature, condition, and working medium.

12.4.1 Minimal Processing

During the minimal processing (washing, peeling, cutting, and slicing), disruption of cell walls leads to an increase in enzymatic reactions, which breaks down the anthocyanin pigments in fruits and vegetables. The research identified that rutin content in the asparagus gets reduced during primary processing steps like cutting and chopping. The same operation does not affect quercetin present in the onion. Flavanone in citrus fruits is hydrolyzed to corresponding aglycons during slicing and cutting. For example, in orange, narirutin and hesperidin are hydrolyzed to naringenin and hesperetin. Soaking legumes and cereals results increase in digestibility of starch, protein, mineral bioavailability, a decrease in trypsin inhibitor (17–19.9%), decrease in phytic acid (40–48% in peas), loss of total saponins (1–8% in chickpea seeds), and loss of mineral (Fe and Zn) in the water (Boye and Ma 2015; Pasha et al. 2014).

Table 12.1 Bioactive compounds and their health effects

Bioactive compounds	Source	Functional property	Health benefits	References
Quercetin	Fruits, vegetables, and grains	Anti-inflammatory, antiallergic, and antitumor properties	Prevent blood clots	(Stachnik 2017)
Luteolin and apigenin	Pigeon pea leaves	Anti-inflammatory, antiallergic	Osteoporosis, hypoglycemic effect	(Joana Gil-Chávez and Villa-Rodriguez 2013)
Anthocyanins	Blackberry	Antidiabetic potential	Cholesterol lowering	(Misra et al. 2021)
Ajoene	Garlic	Antibiotic, antitumor properties	Reduces bad cholesterol, heals pseudomonas aeruginosa infections.	(Stachnik 2017)
Resveratrol	Grapes, blackberries, tomatoes, blackcurrant, blue berries	Anti-inflammatory, and antiaging property	Reduces the risk of platelet aggregation, atherosclerosis, and myocardial fibrosis	(Sharifi-Rad et al. 2020)
Xylitol	Fruits and vegetables	Antibacterial property	Boost immune system, fight against tooth decay	(Stachnik 2017)
Proanthocyanidin	Red and purple color rice	Antioxidant and antidiabetic	Reduces the risk of cancer	(Verma and Srivastav 2020)
Lycopene	Tomatoes, red-colored fruits, and vegetables	Antitumor property	Treats cataracts and asthma	(Ali et al. 2021)
Catechin	Gooseberries, black grapes, and cherries	Anticancer activity	Reducing coronary heart diseases	(Dhalaria et al. 2020)
Hydroxytyrosol	Olive oil	The antioxidant, anti-inflammatory property	Protects nerve cells	(Grodzicki and Dziendzikowska 2020)
Beta carotene	Spirulina platensis algae	Anticancer property	Diabetic and chronic disease	(Joana Gil-Chávez and Villa-Rodriguez 2013)
Ellagic acid		Antioxidant, anti-	Prevents skin wrinkling	(Stachnik 2017)

(continued)

Table 12.1 (continued)

Bioactive compounds	Source	Functional property	Health benefits	References
	Strawberries, grapes, pomegranate	inflammatory, and anticancer properties		
Curcumin	Turmeric	Antioxidant property, antiarthritic	Wound healing and improving memory	(González 2020)
Nicotinamide, ascorbic acid, riboflavin	Mushrooms, fish, meat, tomatoes, citrus fruits, liver, milk	Anti-inflammatory, antioxidant property, anticancer property	Reduces cardiovascular risk, migraine protection	(Hamzalioğlu and Gökmen 2016)
Isoquinoline alkaloids	Berberidaceae, papaveraceae	Anticancer, antibacterial property	Increases myocardial contractility and the bone marrow leucocytes	(Ben-Amotz 2019)
Glycoside niazirin	Moringa leaves	Antidiabetic and antibacterial activity	Used for treating ulcer, fever, hypertension	(Chhikara et al. 2021)

12.4.2 Thermal Processing

Most agricultural and animal products contain high moisture content, which is prone to microbial and enzymatic degradation. Food products undergo several thermal processing like blanching, cooking, pasteurization, sterilization, canning, drying, baking, roasting, and frying to reduce the moisture or destroy microbes or inactivate the enzymes. Here, canning and pasteurization are considered mild heat processes, and baking, roasting, and frying are severe.

12.4.2.1 Blanching, Boiling, and Cooking

Blanching at a low temperature helps inactivate enzymes and improves the stability and retention of anthocyanins during processing (Ifie and Marshall 2018). Based on the process temperature, the anthocyanin is degraded into different forms, resulting in the degradation of color in the heating process. The final form is phenolic acids and phloroglucinaldehyde. Because of this, phenolic acid content in the dried and concentrated products is always higher than the fresh ones (e.g., garlic, ginger, orange). The antioxidant (free radical scavenging) activity in potatoes is reduced by 26% by boiling due to the increase in extractability of antioxidants by structural changes in starch during cooking. During microwave and backing, the reduction was identified as 32% and 38%, respectively (Narwojsz et al. 2020). Losses of phenolic compounds during boiling were higher than others, which may be occurred by the diffusion of phenolic compounds to the wet medium. Complete inactivation of polyphenol oxidase during blanching at 60-80 °C helps to get the higher antioxidant activity (Ghafoor et al. 2020). Boiling helps to reduce the phytic acids up to 51–58%. Pressure cooking reduced the phenolic contents by 89% in field peas (Boye and Ma 2015).

Cooking is an important processing technique, which improves the palatability of the food material. Rather than that, it also reduces the antinutrient phytochemicals and improves the bioavailability of active compounds. Different cooking methods available include toasting, boiling, autoclaving, and steaming. During this process, thermolabile antinutrient factors are removed completely/partially, and phenolic compounds are reduced. For example, phytic acid (PA) in raw lupin flour, total phenolic compound, flavonoid compounds, and antioxidant activity in faba beans are reduced to 19.78%, 50%, 40%, and 10–40% by toasting. It may be because of the formation of insoluble complexes from PA or soluble of PA in the cooking medium. However, steaming and boiling reduce the phenolic content in faba seeds to 25.9% and 41.38%, respectively. Trypsin inhibitors and lectins are inactivated during cooking. In contrast, tannins are unaffected by cooking. A 60–65% of flavonoids and quercetin are degraded by boiling process, but kaempferol derivatives in beans are increased to 5.82% (Lopez-martinez et al. 2017). Cell distribution induced by high-temperature microwave heating increases the release of the active compound during digestion. Mainly, tubers like potatoes retain high vitamin C content of 90.1% during microwave heating and exhibit the highest DPPH radical activity by the grilled ones (Narwojsz et al. 2020).

12.4.2.2 Pasteurization and Sterilization

The thermal process destroys or softens the cell wall and membranes that entrapped the bioactive compounds, so the carotenoid contends increase during destruction. In nature, most bioactive compounds are vulnerable to heat, light, pH, and oxygen levels. Heating is the type of physical factor which involves high temperature. It leads to the loss of heat-sensitive compounds (e.g., vitamin C and β-carotene). These vitamin losses can be minimized by changing the heating medium, process condition, and equipment. Compared to bottle sterilization, ultra-high temperature (UHT) can retain the vitamin C content up to 65% (Sommano 2013). Steaming is mostly recommended for leafy vegetables (e.g., cabbage, spinach, broccoli) to preserve vitamin content, quercetin derivatives, and flavonol because it needs less cooking time.

Most of the fruits and vegetables contain a *trans*-isomer form of lycopene in their fresh state, which is an inactive configuration. The inactive configurations are converted to active cis-isomer lycopene during the heating process. The absorption of thermal energy induced these configuration changes. For example, the heating of tomatoes increases the cis-isomer concentration and improves the overall bioavailability of lycopene in the presence of lipid. In terms of vitamin C, the hydrothermal process such as cooking and blanching reduce the vitamin C content by increasing the ascorbic acid oxidation action, which depends on the process temperature and duration. The losses are higher when the tomato is heated in the concentrated form than the non-concentrated ones.

On the other hand, tocopherol is stable in various heat ranges. Homogenization of the food matrix before heat treatment increases the surface area for digestion, which favors the carotenoid releasing mechanism. The presence of oil during heating creates a hydrophobic environment for carotenoids. Protease inhibitors present in cereals are heat liable. Their activity can be reduced by wet and dry thermal processing. A significant amount of trypsin inhibitor and phytic acids are reduced during the thermal processing in pulses, cereals, and field peas.

12.4.2.3 Extrusion

A hydrothermal process like extrusion induces to release of the phenolic compounds from the cell wall of wheat, barley, and other cereals. Hence, this releasing mechanism increases the free form of phenolic acids. In cereal grains, ferulic acids are released by extrusion. Higher processing temperature range (145–160 °C) during the extraction process improves the extractability of phenolic compounds and antioxidant activity by Maillard products. Nearly 98–100% of hemagglutinating activity, 83.6% of tannins in field peas, and monomeric and condensed tannins and polyphenols in faba beans and lentils are reduced during extrusion was found out (Boye and Ma 2015; Lopez-martinez et al. 2017).

12.4.2.4 Roasting

Compared to the “wet” methods (blanching and steaming), “dry” methods (roasting and grilling) help to retain the phenolic compounds. The catechin content in cocoa beans increases by epicatechin’s epimerization at the higher roasting temperature ($>$70 °C). In cocoa beans, roasting reduced the phenolic and antioxidant activity. In opposite, grinding improve phenolic compounds by cell wall breakdown. Roasting of poppy seeds is carried out by oven and microwave roasting by Ghafoor et al. (2018). Results showed that the increase in acidity and peroxide value of oil is due to hydrolytic degradation. Denature of phenolic compounds and heat liable antioxidants are identified at 130 °C oven roasting. Compared to the oven, loss of flavonoid and anthocyanins in microwave roasting is higher. Between the oven and microwave roasting, microwave roasting gives higher individual phenolic contents. During roasting, major fatty acids in poppy seeds, such as palmitic, linoleic, and oleic acids, are unchanged. However, stearic acid contents, tocopherols, and linolenic acids are reduced in the range of 10–12%, 2.53%, and 54%, respectively.

12.4.2.5 Baking

Baking improves the total phenolics and antioxidants in the fresh product. Lutein content in wheat flours is reduced during the baking of bread, muffin, and cookies, so this needed additional fortification of lutein. Higher fat content in cookies improved the bioavailability of lutein. On the other hand, lutein degradation is higher in high-fat foods because of oxidation and isomerization. Degradation of conjugated phenolic compounds during baking increased free phenolic compounds. The baked products contain higher free phenolic acids including ferulic acid (32%), but bound ferulic acids are decreased by 38%. This will help to improve the bioavailability of the free compounds. The anthocyanins and zeaxanthins are unaffected in this process. Sinapinic and β-cryptoxanthin are affected by baking (Rabalski 2013). Before baking, dough fermentation help improve the bioavailability of bioactive components (Saa et al. 2017).

Overall thermal processing has a diverse effect on phenolic compounds. This is not always on the negative side. By damaging the food matrix's cell wall, the accessibility and extractability of active compounds after thermal processing get increased.

12.4.3 Nonthermal Processing

Quality changes during processing conditions and demerits of thermal processing lead to the innovation of several nonthermal processing in food industries. While considering bioactive compounds' bioavailability, carotenoid content has deteriorated during thermal processing. High-pressure homogenization, high-pressure processing, pulsed electric field, and ultrasound are promising nonthermal processing techniques in the food industry. In general, nonthermal processes disrupt the cell wall based on their phenomena. It helps to (1) facilitate the release of carotenoid, anthocyanins, and phenolic compounds, (2) increase in accessibility of compounds, and (3) improve extractability of the compounds. Because of this, the overall bioaccessibility of bioactive compounds gets increased, but this can be differed by the nature of the food matrix, process parameters, types and conditions, targeted compounds, and pre-treatment conditions.

12.4.3.1 High-Pressure Processing (HPP)

During high-pressure processing, the changes acquired in the cell wall and cell membrane alter the location of active components. Mainly, disruption of the cell wall during high pressure increases the accessibility and availability of the active compounds (especially carotenoids and lipophilic compounds). The high-pressure processing of fruits and vegetables and juices have higher bioavailability of carotenoids, phenolic compounds, and vitamin C than thermal processing. In contrast, specific groups of tocopherols (γ, δ) is reduced during high-pressure processing, with no changes in remaining forms (α). Some food materials such as apples, grapes, and orange juices do not have any impact during HPP on bioactive compounds bioaccessibility. It is because of the process condition such as pressure, temperature, and duration. High-pressure conditions did not affect the bioaccessibility of lycopene contents in food materials, but its activity increased during the enzymatic digestion and fermentation process (Barba et al. 2017).

12.4.3.2 Pulsed Electric Field

Permeabilization phenomena disrupt the cell walls during the pulsed electric field (PEF) process. This phenomenon facilitates the releasing mechanism of carotenoids and phenolic compounds accessibility, and the solubility of carotenoids in different food processing includes milk, soy milk, and fruit juice processing. Bioaccessibility of carotenoids is doubled in papaya and mango juice mixture by PEF process (de Guine and Barroca 2016).

12.4.3.3 Ultrasound

Ultrasound processing produces the free radicals during the cavitation process and induces the reaction between radicals and antioxidants, reducing the compounds' antioxidant activity. It is considered a major disadvantage in the ultrasound (US) process. The US-treated cashew apples and orange juices have higher vitamin C than thermal processing (Barba et al. 2017). Very few products like tomato, olive leaf, and cashew apple products are subjected to the US to study bioactive compounds like lycopene, polyphenols, phenolic compounds, respectively.

12.4.4 Freezing and Freeze-Drying

Both in freezing and freeze-drying inactivation of microorganisms is carried out by a reduction in water activity of the food matrix. Cell wall and structural disruption happen during ice crystals formation. It facilitates the increase in phenolic activity of the food. Changes in active compounds mainly occur during the storage of frozen and freeze-dried products. During storage of frozen (−18 °C) fruits and vegetables, average deterioration in vitamin C, B1, B2, niacin, and carotene content is identified as 18%, 29%, 17%, 16%, and 37%, respectively. Vitamin B6 and pantothenic acid are unchanged during storage (Sommano 2013).

Ghafoor et al. (2020) conducted a study on bioactive compounds in ginger during freeze-drying. Results prove that freeze-dried products contain the maximum bioactive compounds compared to other drying methods because of the release of cellular components by cell wall destruction during the formation of ice crystals pre-freezing. Fresh to freeze-dried ginger slices contain the total phenolic content and antioxidant activity, and carotenoid contents are 43.75 to 931.94 mg GAE/100 g, 12.05–82%, and 2.27–6.61 μg/g, respectively. Inactivation of polyphenol enzymes helps to get higher antioxidant contents. Ascorbic acid in green peas and peas is 60% and 30% during freeze-drying. Vitamin content, color, and flavor characteristics of a matrix are retained in freeze-drying. The percentage of bioactive compound losses during green leafy vegetables is varied based on different treatment conditions (Table 12.2).

12.4.5 Fermentation

During the fermentation, structural changes of phenolic compounds result in a change in bioavailability, color, taste, and aroma. For example, in black tea processing, the astringent flavor is obtained by theaflavins and thearubigins, which are produced from the catechins by oxidative enzymes such as polyphenol oxidase and polyepoxides. In the case of cocoa beans, fermentation catechins and epicatechins are converted to insoluble tannins. Fermentation of wheat grains

Table 12.2 Percentage of loss in chlorophyll and ascorbic acid during boiling, freezing, and storage of leafy vegetables compared to the raw products

Bioactive compound	Food matrix	Process Condition		
		Boiling	Freezing	Storage
Chlorophyll a	Asparagus	1.09	29.32	13.58
	Green beans	23.25	76.27	23.25
	Zucchini	3.89	37.27	3.88
Chlorophyll b	Asparagus	4.44	38.06	1.48
	Green beans	20.75	73.09	37.75
	Zucchini	2.72	6.46	9.41
Ascorbic acid	Asparagus	28	16	80
	Green beans	4.8	2	60
	Zucchini	15.7	6.5	65

(Mazzeo et al. 2015)

using enzymes includes amylase and xylanase which improve the bioavailability and generation of 3-phenyl propionic acid. Fermentation reduces the phytic acid and trypsin inhibitor to 70% and 41% in field peas; also, it increases the mineral bioavailability by stimulating the degradation of phytate and polyphenol (Boye and Ma 2015).

12.4.6 Germination

Germination is a hydrothermal process commonly used in cereals and pulse processing. Germination reduces the polyphenolic (21–62%) content, phytic acid in the field, and vegetable peas. The reduction percentage directly impacts the germination period (Boye and Ma 2015). On the other hand, it increases the thiamine and riboflavin content in the food matrix. Bioactive compounds in rice, especially gamma-aminobutyric acid (GABA) and antioxidants, are retained or increased by increasing the activity of glutamate decarboxylase (GAD) when cereals such as rice are subjected to germination. Germination does not significantly affect the ferulic acid content in rice and aglycone in black beans and increases the saponin content in sprouts of black beans. Pigment losses in seed coats are identified during germination (Lopez-martinez et al. 2017).

12.4.7 Parboiling and Polishing

Parboiling and polishing are the most important unit operations in cereal processing (e.g., rice). Kongkachuichai et al. (2020) conducted the study to find out the changes in bioactive compounds regarding the various rice processing. Generally, brown rice contains higher phenolics than parboiled brown, germinated parboiled brown, and polished rice. Nearly 57–73% phenolic compounds, 65–73% of ferulic acids, and

29–92% of GABA content are lost during the polishing and milling by the removal of rice outer protective layers such as pericarp, bran, and embryo, which are a rich source of phenolics. Parboiling at high temperatures decomposes the phenolic compounds in rice, reducing the total phenolic contents much lower than polishing loss.

12.4.8 Storage

The storage temperature, duration, packaging type, and prior processing types highly affect the food matrix's bioactive components. Refrigerated storage of minimally processed orange and mango reported the increase in β-carotene content, loss in orange, mango, pineapple, and kiwi to the percentage of 13–25%, 5%, 10%, and 12%, respectively. Ascorbic acid degradation by light, heat, oxygen, and enzymes reduces vitamin C during storage (Pasha et al. 2014). In contrast, there is no change in vitamin C content while storing strawberry in 5 °C. Several studies have shown the accumulation of phenolic compounds during refrigerated storage. During the storage of high sugar products (e.g., jam and jelly), flavylium cations are secured from the carbinol base, resulting in the preservation of phenolic compounds. In long-term storage, the Millard reaction produces the furfural that stimulates the degradation of anthocyanins. On the other hand, the presence of pectin in jam and jelly reduces the degree of esterification favors the anthocyanins and procyanidins retention (Shinwari and Rao 2018). Losses of bioactive compounds during storage of strawberry, blackberry, bilberry, and red raspberry are estimated as 70–75%, 2–3%, 41–57%, and 7–13%, respectively. The major principle involved in changes of bioactive components during different processing of food matrix is listed in Table 12.3.

12.5 Change in Bioavailability of the Compounds During Processing

The major key terms of bioactive compounds are bioavailability, which refers to the quantity of digested phytochemicals absorbed and metabolized by a normal pathway. On the other hand, bioaccessibility of active compounds is defined as the number of active components released in the gastrointestinal tract and available for absorption. Rather than calculating the number of active compounds, quantifying the bioavailability of active compounds can be helpful to estimate the enhanced health benefits of active components by different processing methods (Kongkachuichai et al. 2020). Bioaccessibility and bioavailability of active compounds are affected by chemical characteristics such as solubility, hydrophobicity, molecular weight, and isomer configuration. For example, 95% of lycopene in fresh tomatoes is in trans-isomers, but in tissues, nearly 50% of cis-isomers are found. It may be due to isomerization during digestion and absorption *cis*-forms during intake (Sommano 2013).

Table 12.3 Mechanism of deterioration of bioactive compounds during different processing

Process condition	Bioactive components	Changes in active compounds	Reference
Minimal processing	Vitamins, phenolic compounds	Rupture in the cell wall during cutting, slicing	Pasha et al. (2014)
	Flavanone	Hydrolyzed to corresponding aglycones	
Blanching	Carotene	Formation pheophytin reduces the chlorophyll contents by pheophytinization Destruction of peroxidizing and lipoxygenase facilitates carotenoid retention	Mazzeo et al. (2015)
	Lutein	Softening of the vegetable matrix improves the lutein content	
	Phenolic compounds	Cell wall softening and partial hydrolysis of ester bonds	
	Ascorbic acid	Leaching from cells, enzymatic degradation, destruction by heat. The stability of ascorbic acid increased by the inactivation of ascorbate oxidase	
Boiling	Ascorbic acid and polyphenol	Loss of thermal unstabled ascorbic acid and polyphenols due to wet heating	Narwojsz et al. (2020)
Cooking	Phytochemical	Destruction or rearrangement of phenolic compounds with other substances	Lopez-martinez et al. (2017)
Germination	GABA	The hydrothermal process stimulates the gad, which converts glutamate to GABA	Kongkachuichai et al. (2020); Narwojsz et al. (2020)
	Total phenolics	Accumulation of soluble phenolic in seeds and sprouts	
Parboiling	Phenolic content	Decomposition of phenolic compounds at high temperature	
Polishing	Polyphenols	Removal of pericarp, aleurone, and embryo of the grains during polishing and milling	
Roasting	Phenols	Denature of phenols at high temperature Hydrolytic degradation increases the free fatty acid content	Ghafoor et al. (2018)
Baking	Phenolics	Degradation of conjugated compounds	Rabalski (2013)
Freezing/ freeze-drying	Phenolic compounds	Destruction of the cell wall during the ice crystals formation	Ghafoor et al. (2020)
Storage of frozen foods	Pigments	Degradation of chlorophyll to pheophytin	Sommano (2013)

(continued)

Table 12.3 (continued)

Process condition	Bioactive components	Changes in active compounds	Reference
		Precipitation of anthocyanins changes the color	
	Vitamin	Vitamin losses by drip loss	
Oil storage	Antioxidant	Reduction of α-tocopherols in the presence of light	Ghafoor et al. (2018)
	Phenols	Degradation of phenolic compounds	
Storage of tomato pulp	Carotene	Maximum losses of lycopene in the presence of light	Sommano (2013)
Storage of jam and jelly	Bioactive compounds	Preservation of changes in bioactive compounds by restricting the esterified reaction by producing hydrogen or hydrophobic bonds in the presence of sugar and pectin	Shinwari and Rao (2018)
Storage of citrus fruit juice	Ascorbic acid	50% losses	Plaza et al. (2011)
	Total flavone	Significant rise in their contents	

Thermal processing reduces the concentration of lipophilic compounds such as carotenoids. Still, they improve the bioaccessibility of the compounds by structural changes in the food matrix, which help the carotenoid releasing mechanism and its solubilization. At a temperature range of 130–140 °C significant improvement in the bioaccessibility of the compounds was observed during thermal processing. No significant changes were observed in flavanone-7-O-glycoside compounds during low-temperature pasteurization and pulsed electric field treatment in orange juice, likewise, no carotenoid changes were observed in thermal and microwave treatment of kiwi puree (Plaza et al. 2011; Barba et al. 2017). In the case of milk processing at 90 °C, it harms the bioavailability of β-carotene, β-cryptoxanthin, lutein, and zeaxanthin (Sommano 2013). By altering the structural composition, the fermentation process helps to improve the bioavailability and bio efficiency of the active compounds. Based on the binding nature of the bioactive compounds to the other food matrix, cell wall structure, and concentration, the molecular structure of active compounds is considered a determining factor to calculate the bioavailability. Normally presented glycosylated polyphenols in food have low bioavailability, by hydrolysis and extraction (tomato puree), extrusion (cereal grains), and fermentation (soybean), and the bioavailability of the compounds can be increased to the desired level (Barba et al. 2017).

The different processing has both positive and negative effects on bioactive compounds, and it mainly depends on the nature of the plant matrix, processing methods, and conditions. The positive and negative impacts on specific bioactive compounds during processing are listed in Table 12.4. Optimizing the processing conditions based on the process's quality helps reduce the adverse effect on the end product.

Table 12.4 Changes in bioactive compounds during the different processing techniques in a food matrix

Process condition	Food matrix	Bioactive compound	Effect of active compounds	Reference
Minimal processing	Orange	Total carotenoid Vitamin A Vitamin C Antioxidant	Increase Increase Decrease No change	Pasha et al. (2014)
Cooking/ boiling	Green vegetables	Phenols Chlorogenic acid	Increase Increase	Boye and Ma (2015); Lopez-martinez et al. (2017)
	Cereals	Antinutritional compounds Polyphenols	Decrease Decrease	
Drying	Fruits and vegetables	Phenolic compounds Antioxidants	Increase Increase	Nunes et al. (2016)
Freeze-drying	Ginger	Phenolic compound Antioxidant activity	Increase Increase	Buvaneswaran et al. (2021)
Germination Parboiling Polishing	Rice	GABA Phenolic content Phenolic, ferulic acid, and GABA	Increase Increase Decrease	Kongkachuichai et al. (2020)
Roasting	Poppy seeds	Phenolic content Antioxidant	Decrease Decrease	Ghafoor et al. (2018)
Baking	Wheat flour	Free phenolics Bound phenolics	Increase Decrease	Saa et al. (2017)
Storage 4 °C for 12 days	Orange	Flavanone	Increase	Plaza et al. (2011)
Frozen storage	Green vegetables	Pigments Flavonols Phenolic compounds	More stable Positive effect Increase	Mazzeo et al. (2015)
	Cauliflower, cabbage, and spinach	Flavonols	Decrease	

12.6 Sustainable Approach

Food and agricultural wastes like skin or peel, pomace, seeds, leaves, and stems can be the most sustainable and valuable sources of bioactive components. They have a good amount of proteins, fiber, minerals, vitamins, and phenolic compounds. Thermal processing methods reduce the concentration and yield of the bioactive components, but they increase the bioaccessibility of the compounds. Nonthermal processing methods like the PEF and HPP increase both the availability and accessibility of the bioactive compounds because they disrupt the cell wall. Ultrasound technology may reduce the antioxidant activity but increase the yield of other components like lycopene, polyphenols, vitamin C, etc. Hence, the sustainable approach to increasing bioactive compounds' bioavailability and bioaccessibility is nonthermal processing methods.

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Part III

Role of Bioactive Components in Human Health

Role of Bioactive Components in Psychosomatic Disorders

13

Bushra Shaida and Shaista Arzoo

Abstract

The World Health Organization defines psychosomatic medicine as "the study of biological, psychological and social variables in health and disease". It is widespread across the globe, and it has a significant effect on the quality of life. Bioactive compounds exist in little quantities in foods and many medicinal and non-medicinal plants and show therapeutic potential by reducing oxidative stress, pro-inflammatory effects and various metabolic disorders. These compounds work in different ways; studies suggest that fruit and vegetable consumption can counteract the progression of numerous diseases because of the presence of bioactive molecules in these foods. Several studies have given a relationship between mental stress and somatic disorders which can lead to serious consequences. Standard treatment of psychosomatic disorder includes mostly psychopharmacological and psychotherapeutic interventions. This chapter will examine the role of bioactive components in psychosomatic disorders such as stress and depression.

Keywords

Psychosomatic disorder · Bioactive compounds · Stress · Depression · Therapeutic

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13.1 Introduction

13.1.1 Psychosomatic Disorder

In psychosomatic disorder physiological functioning is adversely affected by psychological stresses to the point of distress (Nisar and Srivastava 2017). The psychosomatic symptom also makes physiological connection with emotional state and can be explained such as elevation in blood pressure and increase in pulse and respiratory rate of stressed person. Psychosomatic disorder is defined as a condition where unsettling of mental or enthusiastic influence by bodily aliment and antagonistically physiological (somatic) working to the point of distress is being affected by psychological stress (World Health Organization 2001). In ancient times, "psyche" meant "soul or mind," and recently, it has been referred to as behaviour. Soma implies the body of organism. Different body parts get affected by mental stress which is connected by hormonal, neural, and immunological components. Both, mind and body are involved in this disorder (Rafanelli and Ruini 2011). Although sometime there is absence of any physical disease, mental factors cause physical symptoms in psychosomatic disorder; the symptoms vary from person to person (Thayer and Brosschot 2005).

Psychosomatic disorders include diseases like eczema, stomach ulcer, hypertension, psoriasis and heart disease. Study shows that the disease like myocardial infarction is also caused due to anxiety and stress (Littman 1993). Body organs via amalgamation of three interrelated component hormonal, neural and immunologic affected by mental states. Voluntary movement is controlled by motor neurons from conscious command of brain while in stress; it may or may not act likely as a voluntary and conscious by same motor neuron (Nisar and Srivastava 2017). Any part of body which is not in voluntary control mainly affected by psychosomatic disorders or we can say improper activation of the involuntary nervous system and glands of internal secretion in body organs can cause damage to structures, and dysfunction also occurs in psychosomatic disorder (Culpepper et al. 2015).

According to Franz Alexander and group in 1934, only autonomic nervous system innervated organs show psychosomatic symptoms and physiological accompaniments of such particular unconscious repressed conflicts have no psychic meaning but are prolonged physiological states end results (Eidelberg 1949). Psychic factors and some constitutional organic predisposing factors responsible for repressing psychic energy resulted in physiologically discharge (Bransfield 2019). Herbert Weiner's in 1957 favours Alexander's studies and proposed pepsinogen hyper-secretion (Ortonne et al. 1983).

It is important for everyone to maintain balance in nutrition for proper growth and development of body. Basically, a proper, balanced nutrition decreases the risk of developing various prevalent chronic diseases and infections (Thakur et al. 2012). A psychosomatic illness originates from or is aggravated by emotional stress and manifests in the body as physical pain and other symptoms (Bohra et al. 2015). Depression can also contribute to psychosomatic illness, especially when the body's immune system has been weakened by severe and/or chronic stress (Salleh 2008).

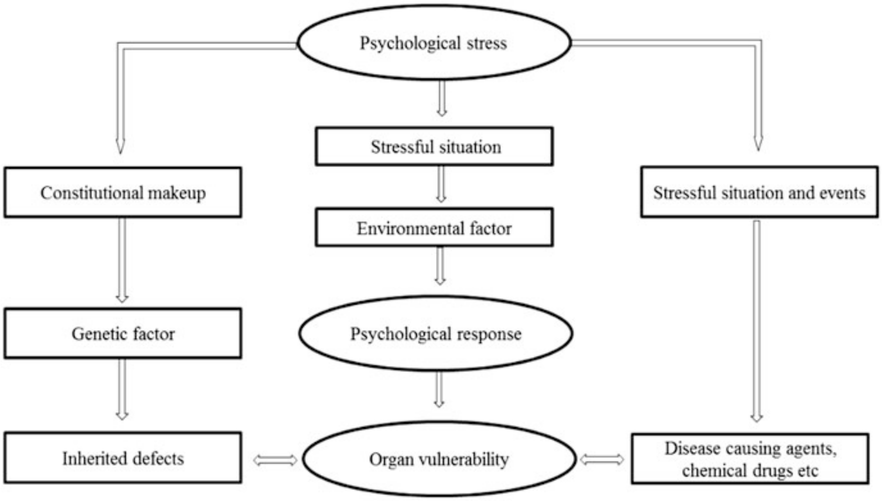

Fig. 13.1 Stress-related disease and psychological disorders

Anxiety is a normal human emotion. Instead, it is considered as pathological once it results from stressful situations and it leads to psychological, social, occupational, biological, and alternative impairment (Bystritsky et al. 2013; Fig. 13.1).

13.2 Theories for Relationship Between "Psyche" and "Soma"

Generally, it is very difficult to explain the relationship between "psyche" and "soma" but Patricia Coughlin Della Selva proposed two hypotheses which explain their relationship.

13.2.1 Specific Hypothesis

Specific hypothesis relates to the psychological stress which leads to developing specific cell or tissue damage. That effect leads to damage to any body part or organ and thus affects the functioning of the body. Pressure is stifled through the ANS; anyway, the thoughtful reactions may stay alert for elevated animosity or flight or parasympathetic sensory system reactions might be adjusted for increment vegetative action (Singh 2016). Such delayed readiness and strain can create physiological issues and in the long run pathology of organs or viscera, e.g. peptic ulcer (Culpepper et al. 2015).

13.2.2 Non-Specific Hypothesis

This hypothesis states that stress can lead to number of predetermined diseases. These hypotheses state four types of reactions that occur because of stress. They are as follows:

(a) The neurotic: anxiety signals are big enough that defence not able to work.
(b) The psychotic: alarms were not taken seriously or misperceived.
(c) Healthy normal: when defence work with the action of alertness.
(d) The Psychosomatic: mental defence is not effective and leads to somatic damages in body tissues thus causing psychosomatic disorders.

13.3 Classification of Psychosomatic Disorders

On the basis of International Classification of Diseases, the psychosomatic disorders can be classified as follows:

(a) Psychological malfunction arising from mental factors: It happens when autonomous nervous system (ANS) meditates psychological functions leading to malfunction of physical manifestations involving tissue damage. Example of this category is respiratory dysfunctions like hyperventilation and cardiovascular disturbances like cardiac neurosis.
(b) When disease conditions are persistent in the patients, then psychological stress leads to its severity and involves more damage of tissues. Example of such condition is asthma, dermatitis, eczema, colitis, etc.

The classification of the psychosomatic disorders is presented in Table 13.1 as below:

Table 13.1 Classification of psychosomatic disorders

S. No.	Type of psychosomatic disorder	Characteristics	Symptoms
1	Psychoneurotic	Feeling of anxiety	Phobic, depressive, conversion, obsessive
2	Psychophysiological	Mental disfunction leads to physical distress	Psychotic distress, neurotic defence
3	Personality	Physical actions effects mental disorders	Here somatic disorders lead to psychological stress
4	Psychotic	Personality distress leads to failure in ability to evaluate, perceive and test reality	Physical symptoms were seen with mental disorders

Table 13.2 Magnitude of mental health

S. No	Magnitude of mental health
1	Self-acknowledgement (an optimistic point of view towards self)
2	Constructive bonds with people (friendly, fulfilling, confiding connections)
3	Self-governance (self-assurance and liberty)
4	Ecological authority (feeling of dominance and capability in dealing with nature)
5	Goals in life (objectives and a feeling of certainty)
6	Self-improvement (sentiments proceeded with advancement)
7	Self-acceptance (a positive attitude towards self)
8	Positive relations with others (warm, satisfying, trusting relationships)
9	Autonomy (self-determination and independence)
10	Environmental mastery (sense of mastery and competence in managing the environment)
11	Purpose in life (goals and a sense of directedness)
12	Personal growth (feeling of continued development)

As per international classification, in psychosomatic disorders, only tissue damage or physical manifestations is not involved, instead mental originated psychological malfunctioning mediated via autonomic nervous system is also involved.

Ryff and Singer stated that generally psychological analysis is significantly weighted on the side of mental impairment and well-being is compared with the nonattendance of ailment instead of the presence of health (Ryff 2015). Exploration on mental health has shown that it gets from the association of a few interrelating magnitude (Table 13.2). There is generous proof that mental health assumes a buffering function in adapting to pressure, favourably affects sickness course, and has significant immunological and endocrine undertones (Rathod et al. 2017).

Information on the anatomical and physiological premise of enthusiastic experience and conduct and their impact on instinctive capacity is presently adequate far cutting edge to give at any rate the start of a comprehension of the manner by which passionate pressure might be identified with the improvement of physical and mental ailment. A large number of psychosomatic indications are created as a result of stress. Nutrition and food have significant role in diminishing these pressure-related indications.

13.4 Epidemiological Evidence for an Association Between Food and Diseases

"*Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems*" (Porta 2006). Nutritional sciences are becoming increasingly concerned with the role diet plays in chronic, degenerative diseases, and epidemiology is becoming a key component of the discipline. In the past, epidemiology was exclusively concerned with the epidemiology of communicable diseases

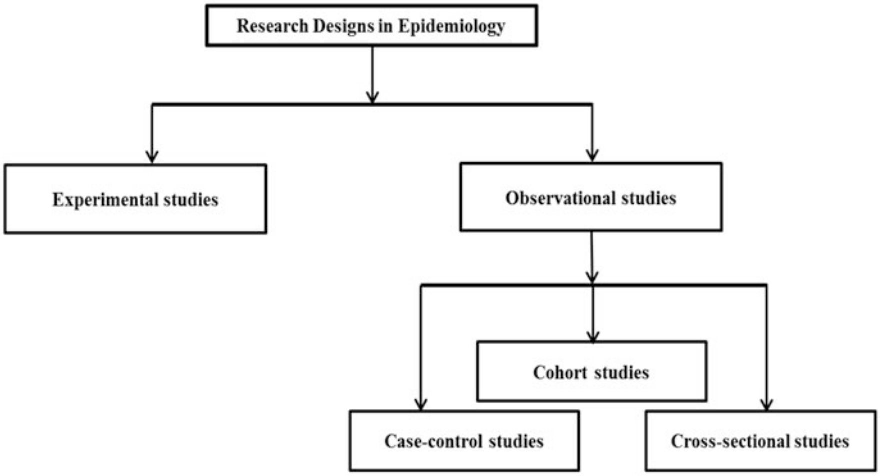

Fig. 13.2 Research design for epidemiological research

(Bracken 2003), but it was subsequently expanded to encompass endemic communicable diseases and non-communicable infectious diseases as well. Epidemiology and the information provided by epidemiologic methods have been used in the assessment of the community's health as public health officials responsible for policy development, implementation, and evaluation use epidemiologic information as a factual framework for decision-making, and consciously or unconsciously, the epidemiologic information is also used by individuals in making individual decisions to make daily decisions affecting their health (Fig. 13.2). Some basic research designs in epidemiology are mentioned in the flow chart.

Experimental studies or experimental epidemiology employs classic experimental techniques to test hypotheses about the links between diet and specific diseases. Experimental studies involve a controlled process that determines the exposure for each participant (clinical trial) or community (community trial), and once these exposures are determined, the investigator tracks the signs of health or disease status in individuals or communities after a certain period of time to determine the effects of the treatment on disease outcome. Randomized control trial (RCT) is the primary study design in the area of nutritional epidemiology. But the experimental epidemiology is limited in its application to nutrition questions because of the difficulty in conducting controlled interventions involving dietary variables and by the high costs associated with population-based studies designed to reduce chronic disease risk (Tarasuk and Brooker 1997). Contrary to this, the study of diet and disease outcomes usually involve observational studies to describe the distribution and determinants of specific dietary intake patterns, and in an observational study, the epidemiologist simply observes the exposure and disease status of each study participant (CDC) (Centers for Disease Control and Prevention 2013). In a Cohort study, the epidemiologist registers the participants on the basis of exposure and follows over some predefined time period to observe the status of health and disease. It is quite similar to the experimental study with a difference that in the cohort study instead of determining the researcher or the epidemiologist observes the participants' exposure status. Cohort studies provide significant insight into causal relationships between diet and disease outcomes because dietary patterns are assessed before the onset of disease. In a Case-control study, the epidemiologists enrol a group of participants with disease (case) and another group of participants without disease (controls) and then compare the previous exposures between the two groups and if the extent of exposure among the case group is considerably greater than the expected amount than disease is said to be related with that exposure. Hennekens and Buring (1987) reported that the results from case–control studies are usually presented as "odd ratios" or the odds of developing disease with no or very low level of dietary factors. In a cross-sectional study, a sample of participants from a population is enrolled and their exposures and health outcomes are measured simultaneously, and in this study, data on dietary patterns and disease incidence or prevalence rates are compared across countries in these studies.

For centuries, the epidemiological approaches have been used widely to analyse the relationship between diet and disease, originally to identify nutritional deficiencies and target foods to ameliorate them (Cervantes-Laurean et al. 1999). A significant amount of evidence from nutritional epidemiology is used to guide dietary recommendations for prevention of diseases such as cancer. Public health nutrition transforms the data provided by epidemiologist about diet–disease relationships into practice of prevention. In the year 1747, Captain James Lind on the HMS Salisbury starts losing his sailors due to some mysterious disease. He divided his sailors into 6 groups (2 in each group) decided to give some addition food the same basic diet. The group which received citrus fruits quickly recovered from the mysterious disease later identified as scurvy Stewart and Guthrie (1953). Peto et al. (1981) assessed the input of various elements responsible for development of cancer in the USA (Peto et al. 1981), and they reported that between 10% and 70% of cancers might be accredited to factors related to diet and adiposity. Efforts had also been undertaken during the last years to extend existing nutrient databases towards bioactive compounds in addition to nutrients and to apply this knowledge in studies assessing the intakes. Thus, it is now possible to determine intake of carotenoids, flavonoids, phenols, and phytoestrogens using integrated food code systems and nutrient databases (Zamora-Ros et al. 2012). As new high-throughput technologies of mass spectrometry are applied to the investigation of bioactive substances as potential biomarkers of nutritional intake and status, concentration measurements in body fluids will be possible (Boeing 2013).

13.5 Psychosomatic Symptoms and Treatment

The psychosomatic disorders as name suggested are characterized by physical symptoms like pain and fatigue which are caused because of stress or any other mental distress. It is quite difficult to diagnose it, as it is just the reaction of mental stress(Groër et al. 2010). Explicit sensations, for example, pain or breathlessness, or general symptoms include fatigue or weakness in muscles. Irrelevant to any clinical reason that can be recognized, or identified with an ailment, for example, malignant growth or coronary illness, yet more noteworthy than what's typically anticipated solitary manifestation, numerous indications or changing side effects mild, moderate or serious (Al-Harbi 2012). It is quite difficult to treat psychosomatic patients as maximum of them take the treatment of physician rather that psychiatrist.

While treating the psychosomatic patients, consideration must be done on following points: age of patients, illness duration, stress of environment, and personality of the individual (Schneiderman et al. 2005).

Various psychiatric measures which have been employed include electroconvulsive treatment, psychotropic medications, spellbinding, drug abreaction, bunch treatment, strong psychotherapy, and analysis (Mitchell 2000). Therapy gives the best comprehension of the psychodynamics of psychosomatic ailment yet is, for an assortment of reasons, material just too few patients. Variations and evacuation of upsetting manifestations can be cultivated by the other remedial methods.

13.6 Role of Bioactive Compounds in Prevention of Psychosomatic Disorder

Nutrition is an important part of living a healthy lifestyle. It appears to enact in the prevention of neurodegenerative disorders like psychosomatic diseases (Trojanowski and Hampel 2011). Disease risk can be reduced by eating a well-balanced diet rich in bioactive substances. Given the paucity of human interventional studies, it is uncertain regardless if these compounds have the same neuroprotective benefits as in different studies like in vitro and in vivo and humans under medical conditions. There is also no way of knowing whether the quantity and chemical types of nutrients in meals are sufficient for bioavailability. This review describes the promising therapeutic benefits of a number of bioactive substances. Many of these substances are phenolic compounds, fat-soluble vitamins and important omega-3 fatty acids, isothiocyanates, or carotenoids, among other chemical families.

Key studies examining the effects of bioactive compounds on psychobiological responses in human subjects:

	Bioactive components	Mechanism of action	Effect on human subjects	References
Phenolic compounds	Oleuropein	Acts as an antioxidant who saves nerve cells from neurotoxin-producing apoptosis. Also, it benefits a lot because it has	Preventing neurotoxic effects will reduce psychosomatic response	(Nediani et al. 2019)

(continued)

	Bioactive components	Mechanism of action	Effect on human subjects	References
		glycosylated secoiridoid		
	Hydroxytyrosol	Phase II detoxification enzymes can be activated from it. It is a strong antioxidant and free radical scavenger	Some neurotoxic reactions caused by amyloid plaques which are the resultants of nuclear factor-kappa B(NF-B) can be controlled by it. And also, it is an anti-inflammatory agent	(Yu et al. 2016)
	Anthocyanin	It is a flavonoid group member and supports red, blue, and violet colours of many vegetables and fruits	On reducing lipid peroxidation and free radical production anthocyanins ameliorate oxidative stress. By inhibiting COX, they also lower prostaglandin synthesis. Neuroprotective effects of anthocyanins were analysed in vitro	(Khoo et al. 2017)
	Curcumin	Works as a strong antioxidant which helps in reduction of protein oxidation products; by inhibiting COX and lipoxygenase enzymes, it weakened the inflammation and lowers microglia activity	Empiric studies show that curry which has large quantity of curcumin can encourage the support of mental functions	(Grodzicki and Dziendzikowska 2020)
	Genistein	It is another compound which is	Neuronal damage can be lessened and	(Pizzino et al. 2017)

(continued)

	Bioactive components	Mechanism of action	Effect on human subjects	References
		possibly effective in preventing stress. And an isoflavone which one can get from mainly soy products. By hindering the synthesis of oxygen-reactive species, oxidative stress can be lessened	phosphorylated tau levels are reduced in the hippocampus. This isoflavone has neuroprotective properties which are helped by watching Asian population data, whose convectional diets have huge quantities of soy products. Foregoing studies show that large intake of these foods can save one from dementia	
Omega-3 fatty acid	Docosahexaenoic acid (DHA)	DHA is the most favourable omega-3 fatty acid in the conditions related to age CNS diseases because of Δ4 desaturase activity; this enzyme which is involved in DHA synthesis decreases with age, in resultant with decrease in DHA synthesis in the elderly	Brain inflammation can be reduced by lowering the synthesis of these eicosanoids. It acts as essential structural membrane phospholipid components of the brain cells; DHA is available in the synaptic membrane regions and cerebral cortex	(Bradbury 2011)
	Vitamin D	Vitamin D has anti-inflammatory and anti-amyloid properties which can prevent dementia. It is another neuroprotective compound. Despite the fact	It remarkably affects neurogenesis by promoting neuronal growth in the hippocampus. Also, it affects calcium homeostasis, which is frequently disturbed in	(Sultan et al. 2020)

(continued)

	Bioactive components	Mechanism of action	Effect on human subjects	References
		that its synthesis is restorative essentially by ultraviolet radiation, one can also obtain it from eating food like fish	neurodegenerative diseases	

Even though more experimental human inquisitions are required to properly understand the exact association between nutrition and the development of psychosomatic diseases, epidemiological data have shown promising results. Both the MD and DASH diets have been demonstrated to improve mental health, but it will be more effective when we combine their selected neuroprotective components (Omar 2019). Morris et al. described a dietary regimen called the MIND diet, which is centred on whole foods high in bioactive compounds (Morris et al. 2015) "Whole grains (at least 3 servings/day), green leafy vegetables (at least 6 servings/week), other vegetables (at least 1 serving/day), berries (at least 2 servings/week), fish (at least 1 serving/week), poultry (at least 2 servings/week), legumes (at least 3 servings/week), nuts (at least 5 servings/week), olive oil as the main added fat source, and wine (1 serving/day) are among its primary components"(Morris et al. 2015). It was proven in a 4.5-year observational research of 923 people in the age group of 58 and 98 years, which found that individuals who followed this nutritional plan had a 53% lower risk of psychosomatic disease (Dominguez et al. 2021). And it makes a MIND diet a success despite the fact that more clinical trials are needed, for understanding more about the relation of diet with the disease condition.

13.7 Conclusion

Dietary therapies have the potential to be a novel intervention for lowering depression symptoms in the general population. Future study is needed to identify the specific components of dietary interventions that promote mental health, investigate underlying mechanisms, and develop successful delivery schemes in clinical and public health contexts. Finally, more research should be focused on establishing cost-effective and long-term techniques for delivering lifestyle modification within mental health services, as well as developing and accessing public health plans to promote dietary habits across the population.

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Role of Functional Foods in Human Health and Disease Prevention

14

Luxita Sharma and Akanksha Yadav

Abstract

The functional foods cover a variety of food components such as class of bioactive compounds and substances. The functional foods are present in both plant and animal sources. The evidence-based science shows the beneficial effects of functional foods on human health and reduction in development of chronic disorders. The functional foods are present in large amounts in the animal foods such as dairy products (probiotics and prebiotics), fish (omega-3 and DHA) and meat products (peptides), and B group of vitamins and minerals. The functional foods in form of bioactive compounds can be induced in the diet in form of palaeolithic diet, Atkins diet or ketogenic diet (not in extreme phases) for short duration of time. Various researches demonstrate the benefit of the bioactive compounds present in functional foods in improving human health; for example, probiotics and fibres are important for maintaining gut health, antioxidants and polyphenols remove free radicals and reduce oxidative stress, and flavonoids have anti-carcinogenic properties and many more. The functional foods have numerous benefits for the disease prevention and maintaining human health which is evidence based and will be elaborated in the chapter.

Keywords

Functional foods · Antioxidants · Phytochemicals · Flavonoids · Prebiotics · Health · Disease prevention

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14.1 Introduction to Functional Foods

Before discussing about the main topic which is functional foods, firstly let's make ourselves acquainted with the word "food". Food, what is it? or why is it so important for us or in fact for all the other species living on this earth. Why do we have to consume it for our survival? Or how will it benefit us? And many other such type of questions come to our mind when we start thinking about this word. "Food", one word many meanings. "Food" as the heading indicates one word with many meanings. Nutrition or rather nutrients, energy, growth, or some other words like happiness or a way to experience pleasure, or enjoy life and many more. Now, everybody must be thinking how do these words relate to food. Food if I say in normal scientific or medical language will be described as something which can provide all human beings and other species as said earlier nutrition for proper growth of the body and all the different changes that take place inside it, and energy for leading a healthy life. Now interestingly, food can be related to the other words used above like happiness, pleasure, way of enjoying life and acts as a token of love or reward. Yes, food can be given a proper definition in relation to these words. Many scientific researches have proved that food has a very strong relationship with happiness, and in fact, it is also found that whenever we eat good food, we start feeling good as dopamine a hormone is released in our body especially brain part which creates a positive feeling or rather sensation of thoughts in our body (Singh 2014).

Food is something that also acts as a token of reward as whenever somebody does good thing or for example a child does something good or behaved in a proper manner then we reward him or her with their favourite food right! and it brings smile on their face. So, yes food has one word many meanings. "Food and Life" works simultaneously why food is so important for us for our survival. Earlier, we all have heard from the other people especially from our elder generation that we can survive without food for few days only. But why? Have you thought of it earlier. Let's discuss it. Food is very important for our survival because our body needs nutrients (proteins, carbohydrates, fats), vitamins and minerals as it gets energy in order to stay strong and healthy just like a car needs fuel to work or a plant is linked with water and sunlight for its survival. So this was the scientific or biological reason for eating food to survive. Interestingly, there are many other reason people eat food to live their life like for comfort, to strongly connect with others, etc. As these things are equally important for all of us to survive, food can prevent different types of diseases whether acute or chronic as eating good food and in proper proportion can provide good nutrition to the body and keep it healthy. Functional foods a "Boon" to all contemporarily or at present what people are doing is that they are basically moving towards the natural or rather more to be precise towards the "Organic" food products which do not contain any chemical and are good for the well-being of an individual (Vella et al. 2014). So, various nutraceuticals companies or the industries have started making different types of food products which contain the natural ingredients (bioactive compounds, certain phytochemicals, etc.) in one food item proving to be beneficial in improving the health of the general public not only by reducing or by minimizing the risk of certain diseases but also in controlling them to some extent (Cencic and Chingwaru 2010). Let me be more clear that these food products are created by crossbreeding, certain traits or characterizes of the plant biased crops to make a new edible plant having high nutrient content besides providing basic nourishment to the body. Everyone must have heard that famous proverb which says "Let Food be your medicine, and not medicine be your food"; these functional foods or rather functional food products resemble the exact meaning of this proverb. Nowadays, we all hear about nutritional foods, superfoods but what are functional foods or what does the term functional food means. Basically, the term functional food does not contain a specific definition. Functional foods are known to be the new trendsetters in the world of food nutrition and medicine as they are considered to be those nutraceutical products or food substances which not only contain the main and essential nutrients to meet the requirements of the human body but also provide some of the profitable results towards minimizing the risk of various chronic diseases in people (Banerjee 2019). These food products are known to be the ones in which there are certain ingredients which are natural or herbal or certain ingredients which are high in these food products as compared to others and have a major role in enhancing the function of various target functions of the body. So, the question arises that modified food products can also be called as functional food product as they also have certain qualities from the above definition. But all-modified food products cannot be called as functional food products because these functional food products are those food products which have the presence of certain bioactive factors, phytochemical components which are good for the proper and in fact improved working of the physiological functions of the body. So, this was all about functional foods and what are its functions in our body. But still there is a question knocking around the corner of my mind and I am sure it must be in everybody's mind that how does it (functional foods) do that? Some of the functional food products present in the market are a great source of antioxidants because of which they help in neutralizing certain harmful compounds such as free radicals in our body thus protecting the individual from various chronic diseases like diabetes, heart diseases, etc. (Lobo et al. 2010). Division of functional foods: In today's market, there are broad or varied ranges of functional foods items because of high competition between various food and nutraceuticals industries. They are in forms of prebiotics, probiotics, stanols and sterols. Prebiotics are known to be those functional food items which are referred to those living microorganisms (basically bacteria) infused food products which when eaten in adequate amounts then are beneficial for maintaining good health of an individual (Peng et al. 2020).

Now, everybody must be knowing that these probiotics are consumed or rather taken as a part of daily dietary intake. Since prebiotics are considered as one of the functional foods these are referred to be providing positive outcomes for curing health-related problems. These probiotics have a very tangled process in our body and help in making our digestive system strong. Now, if these are consumed on a regular basis in the diet, what effects will they provide to our body. Let's see what happens when we take it on a regular basis. It has been seen that consuming these prebiotics on a regular basis have led to a positive increase in the level of mineral absorption in the body, even helped in prevention of cancer, relieved constipation, etc. (Whisner and Castillo 2018). Probiotics are known to be those food products which comprise of microorganism which provide positive results in order to maintain the gut health and even prevent the growth of harmful microorganism in the gut or to be more clear in the intestine (Hemarajata and Versalovis 2013). During the childhood, yes those golden days! In school, everybody must have learned in their biology classes about bacteria present in yoghurt; they have certifiably proven to be providing good effects for improving gut health of an individual. Trust me guys, these probiotic functional foods are really beneficial for health and it does not stop here let me tell you several researches have shown that these probiotics when consumed can show positive results for the patients suffering from chronic diarrhoea and have also caused lowering the symptoms of these irritable bowel syndromes including enhancement of immune system. Stanols and sterols are considered to be some essential compounds which are present in plants in very limited amounts and are considered to be good for controlling cholesterol levels in the body (Jones et al. 2018).

The above definition has given us a little bit idea about what really are stanols and sterols. Now, while understanding about them in detail, they can be understood as those membrane permeability and fluidity controlling components present in plants which when consumed can help in lowering the bad or low-density lipids (LDL) cholesterols in the body. Everybody must be very curious to know their exact reason behind functioning in this way in our bodies. Let's see what it says according to several researches it has been seen or rather to be more precise it is observed that these plant sterols and stanols have very similar chemical structures to that of the cholesterols present in our body because of which they have the power to compete with these LDL cholesterols leading to reduction of this cholesterols from the body and are excreted out as waste (Ras et al. 2014). In fact, because of this property, they are really good for various cardiovascular diseases. As after several experiments which were carried on rats and mice, it has been seen that normally the percentage of cholesterol absorption in the body is approximately 60%, and when these functional foods (sterols and stanols) are taken, it is lowered to 15% which is just two times half of the original (Plat et al. 2014). Functional foods have a very huge market so; surprisingly, they are even bifurcated into conventional food ingredients and modified food ingredients. So, conventional food ingredients can be introduced as those natural or nature-related products which are a good or high source of important nutrients like vitamins, minerals and certain kind of antioxidants. Modified food ingredients are those ingredients that are added with extra nutrients in order to enhance the nutritional quality of the food product. Certain functional foods have certain benefits which are provided to our body and mantains health. But in order to make our concept clear about them, let's look at certain examples of these food products, e.g. probiotic ingredient-containing food products such as a probiotic yoghurt blended with cereals and fruits (Yahyaoui et al. 2017) and certain protein bars or snacks provided with increased nutritional value that is with additional amount of fibre and other essential vitamins and minerals (Voss et al. 2021). There are many other innovative products launched by different companies like a combination of soy and oats products and many more. Now, surprisingly besides just being limited to the solid food products, these functional foods have also increased their market in drinks and beverages also. There are several functional drinks being commercialized in the market and have proven to be favourable for certain health conditions (Allgeyer et al. 2010). In fact, let me make it more clear, in order to make it more feasible for the general public, companies have manufactured specific drinks for specific health issues. So, let's have a look at these "Health friendly, Tasty drinks". There are certain drinks which are good for heart and lowering the cholesterol as they are made by combining omega-3 and some amount of soy products. Where some of them are good for "eye vision", some are good for "health of bones" (as they are manufactured by combining calcium- and insulin-rich ingredients) and many more. There are many other food products which are categorized under functional foods like spreads which contain camelina oil being a good source for omega 3 content, cheese, cholesterol lowering eggs, cereals, and low fat dairy products. Now, let's have a look in detail about how functional foods help in management and prevention of various types of ailments. Functional foods and diabetes mellitus: Till now we have discussed about the functional foods and their benefits to our body and life. Diabetes or diabetes mellitus everyone must have heard about this ailment or rather illness which basically a disorder or imbalance of sugar or insulin in the blood of an individual. In today's time, this chronic disease has shown very alarmed increasing rate in the population. But, due to advancement in the field of medicine and food industry, people who are at a risk or those who are suffering from this chronic disease do not have to worry about it. Coming to the point, there are certain functional foods which when consumed on a regular basis in diet can help in preventing as well as controlling or managing this disease and the individual can live a healthy life. Several researches have found out that consumption of natural and plant-based products like high amount of vegetables, fruits, legumes and lower amount of animal-based products like red meat which have higher amount of polyphenols, flavonoids, alkaloids has shown certain meaningful results in controlling and management of this disease. Certain examples of functional foods for diabetes like starchy foods with low glycaemic index like whole grains are considered to be beneficial as they improve the insulin sensitivity and even reduce its resistance in the body (Mirmiran et al. 2014). Foods like flaxseeds, olive oil, nuts which are a good or rich source of polyphenols have proven be good for management and prevention of type 2 diabetes ((Tharwat et al. 2017), Schwingshackl et al. 2017), Hernández-Alonso et al. 2017)). Functional foods a therapy for preventing and treating inflammatory bowel syndrome: it is categorized as a type of gastrointestinal disorder (Salminen et al. 1998a, b). This type of illness is related to gastrointestinal tract and is characterized by symptoms such as severe damage to the mucus lining of the intestine and relapsing inflammation. This type of chronic disease has really become a matter of concern because of severe rise of its cases in several countries such as Australia and China). But why is it so, it is basically because of the Western-eating habits adapted by the individuals. Surprisingly, by various researches it has been found out that consumption of derivatives of certain fruits and vegetables which are a rich source of dietary fibres, probiotic components and certain amounts of fat soluble vitamins (vitamin A, D, E and K) is preferred to be very beneficial in reducing or lowering the symptoms of this disease in people. As it has been seen that foods which have the presence of these components (probiotic components, antioxidants, phytochemicals, dietary fibres, polyunsaturated fatty acids) are very beneficial because of their anti-inflammatory effects on the people leading to the lowering of their symptoms (Slavin and Lloyd 2012). Now, everybody must be thinking that how foods rich in probiotics or bioactive compounds can help in treating this disease. So, earlier we made ourselves acquainted with the fact that these probiotic and bioactive compounds help in elimination of harmful microorganisms from the gut. But besides this function, they even help in lowering the pH level of the gut which further helps in reducing inflammation and enhances absorption of the nutrients (Shi et al. 2016). For example, everybody must have heard of soy milk which is said to be composed of Lactococcus lactis bacteria which help in reducing spleen enlargement and also have a great role in repairing the tissues of the gut. Let me tell you that it is said that products which contain soy protein have also shown promising and meaningful results in the treatment of this disease because of its cytoprotective and antioxidant properties (Niyibituronsa et al. 2019). Further, it is said that foods which are non-starchy (insulin, pectin, oligosaccharides) can also be consumed by these patients because they also contain anti-inflammatory components (Kumar et al. 2012). So, according to me people suffering from these ailments should really consider functional foods which are rich in omega 3 fatty acids, dietary fibres and all the other stuff discussed above in their daily diet routine instead of taking too much medicines. Conclusion—According to me, these functional foods are really a boon to mankind as they really have beneficial effects in preventing and managing various chronic diseases like heart diseases, diabetes which is a blood glucose imbalance and GI disorders. So, I am not saying that people should completely stop their medications but at some or the other point everybody knows deep in their heart that eating too much medicines can provide harm to the body. Besides, these are all natural products or some are made from natural components whose consumption will not lead to any harmful effects. In fact there are chances that people who are at high dosage of medicines their dosages can be reduced. And believe me that in "Future doctors won't treat their patients with medicines, but will prevent and even cure diseases with healthy Nutrition"!!

Functional foods are the dietary items which include whole foods, fortified foods, enriched foods which not only provide energy and nutrients but also beneficially affect one or more target functions of the body, beyond the adequate nutritional effects. They reduce the risk of acquiring disease as they enhance the physiological responses in the body. They are also known as nutraceuticals as they are highly nutritious and have powerful benefits for health. They are considered to be a part of the normal diet pattern (Hasler 2002). Functional foods help in proper growth and development of the body. They also help in providing the body with adequate amounts of vitamins, fats, proteins and carbohydrates which are necessary for the healthy survival of a person. They contain various supplements and ingredients which are mainly intended to improve the health of an individual. The term "functional" basically the foods that are enriched with the nutrition that directly have the potential to influence the health over and above the basic nutritional value. Functional foods contain biologically active compounds which are beneficial for the health and mainly include processed foods or fortified foods. The bioactive compounds are naturally found chemical compounds which are present in plants, animals, marine sources (Teodoro 2019). They are also known as phytochemicals which are mainly present in cereals, fruits, vegetables, legumes, herbs, oilseeds and spices (Kaur et al. 2020). In the food industry, they are growing very rapidly. Health Canada defines them as the foods which have similar appearance as conventional foods which can be consumed in basic diet as they reduce risk of chronic diseases. Functional foods present either inherently in food or via fortification.

The idea of functional foods was first described in ancient Vedic texts from India as well as in the Chinese traditional medicine as the vision of these foods mainly reflected the oriental philosophy that the medicine and foods both have a common origin (Chen 2000). Japan was the first country that recognized functional foods as a distinct category in 1980s. In 1991, the Japanese law entered the work definition of "Foods For Special Health Use" (FOSHU) which mainly gave the permission of first health claims on the labelling of the food and stated that these foods exhibit positive health effects, improve state of mind and are in the form of foods in the diet and not as supplements (Ono and Ono 2015). After Japan, the functional foods spread to North Europe and North America. The second definition of functional foods was developed by the "Functional Food Science in Europe" (FUFOSE) which stated that these foods have beneficial effects on the target functions of the body which improves health status of the body thus reducing risk of diseases and they can be taken as a part of normal diet and they are not at all used in the form of any type of pills. Functional Food Centre (FFC) stated a new definition that they are processed or natural foods that possess biologically active compounds which in effective non-toxic amounts provide clinically proven and documented health benefits and also aid in preventing chronic diseases (Martirosyan and Singh 2015).

14.2 Classification of Functional Foods

14.2.1 Probiotics

Probiotics are the live microorganisms mainly bacteria which provide various benefits when consumed in an adequate amount. Probiotics help to prevent diarrhoea. It helps in reducing chronic constipation. Probiotics involve consumption of bacterial cells mainly lactic acid-producing bacteria, lactobacillus or Bifidobacterium genera (Amara and Shibl 2013).

14.2.2 Prebiotics

The prebiotic was first used in 1985 and is defined as the non-digestible food ingredient that helps in stimulating growth and promotes healthy bacteria in the colon. Its daily consumption helps in aiding mineral absorption, reducing blood cholesterol levels and improving immune function (Thammarutwasik et al. 2009).

14.2.3 Synbiotics

The synbiotics are important functional food compounds. They are synergistic combinations of pro and prebiotics. Synbiotic targets towards two different areas of the gut, both the small and large intestinal tracts. Probiotic bacteria are stimulated by prebiotic oligosaccharides in the colon as well as probiotic microorganisms use prebiotic carbohydrates for its growth and replication in gut. Synbiotics have systemic effects on the host's health metabolism and immune system (Anandharaj et al. 2014).

14.2.4 Phytochemicals

These are plant chemicals which contain particular nutrients. They contain essential nutrients like vitamins, fats, proteins and minerals. They are only found in plants. The main phytochemicals are flavonoids which have hormonal and antioxidant properties. Carotenoids are group of pigments which act as pigments giving plants bright colours. Beta carotene reduces risk of prostate cancer (Zhang et al. 2015). Antioxidants act as defence against free radical damage and help in maintaining optimum health (conventional foods are the basic functional foods as they cannot be modified by enrichment of fortification while the modified foods are enriched, fortified and enhanced with beneficial nutrients.

14.3 Importance of Functional Foods

Functional foods prevent the body from deficiency of the nutrients. Functional foods are high in important nutrients like vitamins, minerals, fibre and the healthy fats. Adding conventional and fortified foods to the diet help to provide the body with proper nutrients which further give protection against the nutrient deficiencies. Disease caused due to nutrient deficiency like rickets, goitre and birth defects can be prevented by eating functional foods.

- Functional foods protect against diseases. Functional foods give the body with proper nutrients which helps to protect against disease. These foods are rich in antioxidants which neutralize the harmful compounds called free radicals, thereby preventing the cell form being damaged and various chronic diseases like heart disease, cancer and diabetes (Miano, 2016).
- Functional foods are also high in omega-3 fatty acids which reduce the inflammation in the body and also promote heart health as well as boost the functioning of the brain (Kaur et al. 2014).

- Functional foods rich in fibre promote the better control of blood sugar and also give protection from diabetes, obesity, stroke and heart diseases. Digestive disorders, haemorrhoids, stomach ulcers, diverticulitis and acid reflux can also be prevented (Dhingra et al. 2012).
- Functional foods also help in proper growth and development of the body. Functional foods ensure that the nutritional needs of the body are met properly. The body gets proper amount of folic acid which decreases the risk of neural tube defects which can affect the brain, spinal cord or spine (Greenberg et al. 2011).

14.4 Nutraceuticals

Nutraceuticals is a combination of hybrid of nutrition and pharmaceuticals. This term was coined by Stephen De Felice in the year 1989 (Kalra 2003). According to the Health Canada, nutraceutical is defined as a product which is isolated or is purified from foods and mainly sold in the medicinal forms not usually associated with the food and are demonstrated to have a physiological benefit or provide protection against a chronic disease (Das et al. 2012a, b). These are generally extracted from the plant, animal or marine source or produced from dried powder or pressed plant material. They help in increasing awareness about public health consciousness.

14.5 List of Functional Foods

- Cereals as functional foods: Cereals provide dietary fibre, proteins, energy, vitamins and minerals to the body. The outer layer of the brain is rich in B vitamins and phytonutrients like flavonoids, indoles and also some amount of protein. It prevents cancer, CVDs, and reduces blood pressure, tumours and fat absorption rate. Buckwheat possesses cholesterol reducing effects, improves constipation and has inflammatory properties (Das et al. 2012a, b).
- Legumes as functional foods: Pulses are rich source of vitamins, minerals, dietary fibre and omega-3 fatty acids. Soyabean has phytoestrogens called isoflavones (Angeles et al. 2021).
- Vegetables as functional foods: Vegetables are rich source of fibre, vitamins, carotene, pigments and flavonoids. Lycopene pigment is present in the tomato which decreases risk of chronic diseases like cancer and cardiovascular diseases (Neira et al. 2017).
- Fruits as functional foods: Fruits contain vitamins, minerals, phytonutrients and many antioxidants like polyphenolic flavonoids, vitamin C and anthocyanin which protect from infections, colon cancers, Alzheimer's disease. Apples with skin help in boosting immunity and endurance (Neira et al. 2017).
- Dairy products as functional foods: Yoghurt is nutrient-dense food which contains good source of calcium, protein, vitamin B12. It is the healthiest dairy product which reduces risk of osteoporosis (Bhat and Bhat, 2011).

- Beverages as functional foods: Green tea helps in boosting the metabolism (Adak and Gabbar, 2011).
- Herbs and spices as functional foods: Turmeric helps to reduce inflammation and cancer risks. Ginger helps in reducing digestive tract issues (Sharma et al. 2017).

14.6 Health Benefits of Functional Foods

- Functional foods reduce the inflammation.
- Reduces the pathogenic bacteria as well as the microbes.
- They provide the body with prebiotics that help feed the probiotics.
- Functional foods also support the gut health thereby enhancing the immune system of the body.
- Provide the body with the live microbial cultures also known as probiotic bacteria.
- Providing antioxidants like carotenoids, flavonoids, lycopene, anthocyanin, and polyphenols which fight free radical damage.
- Functional foods aid in disease prevention like reducing the risk for cardiovascular diseases, neurological conditions, depression and cancer.
- Help to prevent obesity and also aid in weight management of the body.
- They help in managing the levels of blood sugar by providing the body with fibre and anti-inflammatory compounds.
- Balances the cholesterol levels and levels of blood pressure as well as regulates the heartbeat.
- They help in building as well as maintaining the bone mass by lowering acidity and helping in alkalizing the body.
- Aid in nutrient absorption.
- Supports the detoxification and digestive health.
- Protect the brain from free radical damage and supports the mental health.
- Supresses the negative effects of stress by providing the body with B vitamins, magnesium, omega-3 fatty acids.

14.7 Best Functional Foods for Better Health

- Turmeric: Turmeric is the champion of all the functional foods. It carries anti-inflammatory properties. It helps in alleviating joint pains and arthritis. It also has the ability to stop the growth and spread of cancer. It reduces inflammation in the body and it also contains antioxidants (Nasri et al. 2014).
- Cinnamon: Cinnamon has been used as a spice in daily life by people all over the globe. The properties of cinnamon in the forms of bark, essential oils, bark powder, phenolic compounds, flavonoids and isolated components. It contains vital oils and other derivatives, such as cinnamaldehyde, cinnamic acid, cinnamate and sources of biologically active ingredients with specific functional effects for human health (Rao et al. 2014). A multitude of beneficial

pharmacological properties have been granted to the *cinnamon,* including an antioxidant, anti-inflammatory, antidiabetic, antitumor, anticancer and anti-hypertriglyceridemia agent mainly due to its phytochemical constituents such as phenolic and volatile compounds.

- Garlic: The main bioactive compound of garlic such as allicin together with other organosulfur compounds has been credited to confer manifold healthy properties (Bayan et al. 2014). Garlic has been evidenced to impart relief from obesity, diabetes, liver, stomach, microbial infection, as well as their successful prevention of cardiovascular diseases, high blood cholesterol (LDL, triglycerides, VLDL) levels, skin problems and various infectious diseases.
- Blue berries: These were popularized as a "superfruit" due mainly to the high vitamins and minerals' antioxidant capacity of their abundant polyphenolic compounds. Blueberries are available in fresh form for consumption and are a key ingredient of several thermally processed foods and beverages (e.g. jams, jellies, juices) and being available in preserved forms (e.g. canned, frozen, dried). Blueberry fruits have radioprotective and cardioprotective effects, reduce the risk of chronic and degenerative diseases such as atherosclerosis neurodegeneration, cognitive defects, microcirculation diseases, coronary heart diseases, and inhibit tumorigenesis (Kalt et al. 2020).
- Pumpkin seeds: Pumpkin seeds are highly nutritious and have therapeutic potential as well as rich source of energy and various nutrients like protein, dietary fibre, vitamins, minerals and polyunsaturated fatty acids, etc. Pumpkin seeds recognized as a functional food and also helpful in preventing the risk of osteoporosis hypertension, high cholesterol, arthritis, diabetes mellitus, obesity, cardiovascular diseases and various type of cancer due to its antioxidant properties. They can be consumed in roasted form or grind as flour and various nutritious healthy recipes can be prepared by supplementing it with other ingredients like cakes, biscuits, muffins, sprinkled on desserts, salads, smoothies, etc. (Dotto and Chacha, 2020).
- Soya bean: Soy and soy foods are common nutritional solutions for vegetarians, due to their high protein content and versatility in the production of meat analogues and milk substitutes. Soya beans have numerous nutritional quality as well as its inherent health promoting compounds like omega-3-fatty acids, peptides, saponins, phytates, phytosterols, and isoflavones particularly genistein, daidzein, and glycitein. Because of this, soya bean could serve as a therapeutic effect in combating various lifestyle diseases like diabetes, obesity, osteoporosis, and cardiovascular diseases (Messina 2016).
- Apple cider vinegar: Apple cider vinegar helps to burn fat and reduce the harmful blood lipid levels which can lead to cardiovascular diseases. It is made up of acetic acid that delays the gastric emptying and slows down the release of sugar into the bloodstream by keeping the person full for a longer duration of time. It aids in weight as well as fat loss (Singh and Mishra 2017).
- Ginger: Ginger is mainly useful in dealing with the issues related to the digestive tracts. It is full of nutrients which boost weight loss and banish the bloat. It helps to relive gassiness from the stomach (Anh et al. 2020).

- Fatty fish: Fatty fish is the best source of omega-3 fatty acids as they contain active forms of EPA and DHA. It helps in strengthening the heart, flattening the belly and also sharpening the mind of an individual. These healthy fats have anti-inflammatory properties which fight against mental health, depression, arthritis and osteoporosis (Hosomi et al. 2012).
- Bone broth: The gelatine present in the bone broth acts as intestinal band-aid and heals the lining of the digestive tract by absorbing more nutrients. It helps in healing the gut and also in diminishing the joint pains (Hsu et al. 2017).
- Eggs: It is considered as complete food containing high-quality protein as well as rich source of natural antioxidants like vitamin E, selenium, carotenoid pigments, flavonoid compounds, lecithin and phosvitin. It acts as anti-inflammation, anti-microbial and anti-viral activities. Eggs boost immunity and aids in weight loss. It helps in immunity boosting and strengthens the bones of the body (Ruxton et al. 2010). It provides numerous health benefits with respect to cardiovascular diseases, metabolic syndrome, mental development, eye, muscle and ageing health.
- Walnuts: They are biggest pack of omega-3 fatty acids which are also high in disease fighting antioxidants (Gammone et al. 2018). They contain PUFA and MUFA which improve the functioning of immune system, lower risk of heart disease, bad cholesterol levels and inflammation.
- Red peppers: Chilli peppers are rich in many minerals, vitamins and amino acids essential for human health and growth. Peppers contain wide array of phytochemicals such as vitamins, phenolics and flavonoids that are important antioxidants which may reduce degenerative diseases. Peppers are rich in vitamin C, vitamin A, vitamin E and most B vitamins and in particular vitamin B5. They also are very high in potassium, magnesium, iron and rich in calcium and phosphorus. Red pepper helps in minimizing stress and boosting the immunity as it has high amount of vitamin C (Singletary 2011).
- Coconut oil: Coconut oil has an anti-microbial known as caprylic acid which destroys the bad bacteria of the body and helps in improving the gut health. Candida is also present in this oil which is a fungus that breakdown intestinal walls and decreases stomach acid and also reduces inflammation. It improves poor digestion (Boemeke et al. 2015).
- Olive oil: Olive oil is considered to be very healthy as it improves the health of the heart. Those who consume it have lower risk of getting heart attack and strokes. It also lowers blood pressure and also boosts the levels of adiponectin hormone that breaks down fat (Gaforio et al. 2019).

14.8 Effects of Functional Foods on Health

- **Antioxidant Effect**: Functional foods have high amount of antioxidants which help to neutralize and counteract free radicals. Foods are rich in antioxidant are garlic, onion, ginger, oats, sweet potato, turmeric, soyabean and tea (Wilson et al. 2017).

- **Detoxifying Effect**: Foods like cabbage, tomato, strawberries, green peppers, pineapples, green tea and black tea contain detoxifying chemicals. The limonene present in the citrus fruit peels protects against cancer. The cruciferous vegetables like garlic, onion, cabbage and turnip help to activate the detoxification activity of the liver enzymes and reduce the incidence of the tumours (Hodges and Minich, 2015).
- **Supressing Effect**: Garlic contains allelic sulphides which prevent the potential toxic agents and carcinogens from reaching the target tissues by supressing their action. Allelic sulphides help to protect against tumours and give cardiovascular protection as they are anti-mutagenic and anti-carcinogenic. Flavonoids are the phytochemicals which enhance the effectiveness of vit C in the body and protect against allergies, ulcers, tumours and platelet aggregation. They help in reducing the risk of oestrogen-induced cancer and also control high blood pressure (Tiwary and Hussain 2021).
- **Hypoglycaemic Effect**: The hypoglycaemic effects are seen in soluble dietary fibre fraction of the fenugreek seeds. It impairs the mixing of intestinal contents and digestion as the access of the food to the enzymes is limited. Consuming legumes like beans and whole grams positively affect the blood glucose management and insulin sensitivity (Alkhatib et al. 2017).
- **Antibacterial Effect**: Probiotics which are the live microbial food supplements which in a good way affect the host by improving its microbial balance in the intestine. Probiotics act on the prebiotics that are non-digestible carbohydrates. The pH of the gut is modified by the probiotics and the pathogens are antagonized. They compete for the pathogen building and receptor sites. The probiotic bacteria also somehow inhibit the gastric colonization and the activity of the Helicobacter pylori. In the spices, antibacterial factors are found (Gobbetti et al. 2010). The germicidal spices include cinnamon and cloves. Cloves contain eugenol while the cinnamon contains cinnamic aldehyde. Garlic has antibacterial properties against the gram-positive and gram-negative bacteria.
- **Digestive and Related Effect**: Spices stimulate acid secretion, salivation and the enzymes of the digestive tract. The best remedy for indigestion is omum which is also known as ajwain. It has various effects like antispasmodic and carminative. Aniseed or the fennel seeds, and ginger help in counteracting the flatulence and are also used in colic pain. Capsaicin increases the gastric secretion. It is a substance which is mainly present in the chillies (Salminen et al. 1998a, b). It stimulates the digestive system. Cloves have anti-flatulent and anti-helminthic properties. In the treatment of dysentery, fenugreek seeds are used with buttermilk**.**
- **Hypercholesteraemic Effect**: The concentration of the plasma cholesterol is reduced by the soya protein as it contains isoflavones, daidzein and genistein. Garlic helps in reducing the levels of plasma LDL cholesterol and triglyceride concentration. Milk and yoghurt reduce the synthesis of cholesterol. Diet rich in high fibre also reduces the cholesterol by enhancing the faecal steroids excretion. The viscosity of the intestinal contents is increased due to presence of soluble dietary fibre while on the other hand it decreases the peristaltic movements of the

gut (Al-Muzafar and Amin 2017). The hypercholesteraemic effect is present in guavas, beta-glucan and pectin of the apples.

- **Immuno-Potentiating Effect**: Probiotics help in enhancing the immune responses of the body, both specific and non-specific. The effect on the immune response is mediated through the activating macrophages, increasing the levels of cytokines, natural killer cell activity and levels of immunoglobulins. When the probiotics like lactobacillus and bifidobacteria are consumed together, then the immune system gets enhanced (Lopez-Varela et al. 2002). The immune-potentiating effect is exerted by the garlic by stimulating the natural killer cell activity. Beetroot juice helps in boosting the immunity building function of the person.
- **Anti-Inflammatory Effect**: Omega-3 fatty acid reduces the inflammation of mucous membrane of the uterus and reduces abdominal pain before and after menstrual periods. They increase the cell membrane of eicosapentaenoic acid and docosahexaenoic acid which further increases the production of anti-inflammatory group, eicosanoid. They also decrease the production of interleukin 1 and tumour necrosis factor (Lu and Yen 2015). The ginger contains monoterpenes, sesquiterpenes and gingerols which possess anti-inflammatory action by exerting modulation of eicosanoid synthesis. Cinnamon also has the anti-inflammatory activities (Fig. 14.1).

14.9 Role of Functional Foods in Prevention from Diseases

- **Diabetes**: Functional foods like whole grains, phytochemical rich fruits and vegetables, legumes, nuts and cinnamon are very beneficial for diabetic patients. Whole grains are cereal-based products that provide the body with carbohydrates and fats and it plays an important role in glycaemic as well as insulin secretory response. Fruits and vegetables are rich sources of soluble and insoluble dietary fibre and they help in prevention of chronic disease by enhancing antioxidant defence system, reducing triglyceride levels (Pathak 2014). Legumes contain alpha-amylase inhibitory peptides which is a bioactive compound which help in improving digestion. Cinnamon extracts have polyphenol which has insulin-mimetic properties.
- **Cardiovascular Diseases**: Functional foods for CVDs include fruits, fish, whole grains, legumes, vegetables and nuts which are high source of antioxidants (Johnston 2009).
- **Obesity**: Functional foods for obesity mainly include fruits like berries, vegetables, fibre-enriched grains and beverages like tea and coffee (Myrie and Jones 2011).
- **Cancer**: Consumption of functional foods like whole grains including barley, brown rice, buckwheat and vegetables like bitter melon, spinach, garlic, onions, mushrooms, broccoli, cabbage give protection from cancer. They all possess anticancer properties (Aghajanpour et al. 2017).

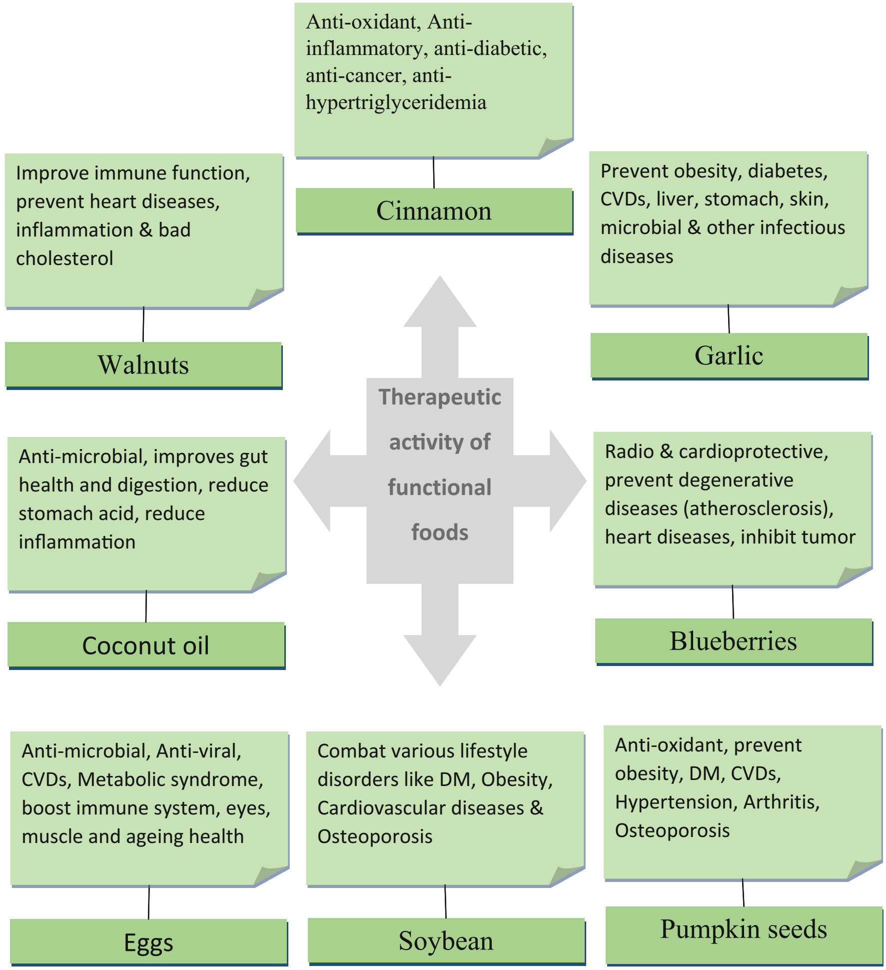

Fig. 14.1 Therapeutic activity of functional foods

- **Renal Diseases**: Functional foods which are beneficial for renal diseases include blueberries, cauliflower, red grapes, garlic, buckwheat, olive oil, bell peppers, pineapples (Rysz et al. 2021).
- **Liver Diseases**: Functional foods for liver disorders include oatmeal, green tea, berries, grapes, garlic, fatty fish, nuts and olive oil (Abdelgayed et al. 2018).
- **Gastrointestinal Diseases**: Probiotics help in improving the intestinal microbial balance (Saunier and Dore 2002).

14.10 Conclusion

Functional foods are those foods which are rich in a particular ingredient which makes it useful for curing various diseases by maintaining good health. It helps in proper growth and development of the body. They are mainly classified into probiotics, prebiotics, synbiotics and phytochemicals. They prevent the body from various deficiencies. The list of functional foods mainly includes cereals, legumes, dairy products, fruits, vegetables, beverages, herbs and spices. They have various health benefits on the health of a person, both mentally and physically. They possess various effects on the body of an individual which improve their health. They are very unique and part of the normal diet and are totally natural. Various diseases can be prevented by consuming functional foods. The demand of functional foods is increasing in the market and consumers are more people are coming to know about their health benefits for the human mankind.

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Functional Foods and Nutraceuticals for Maternal Health

15

Karuna Singh and Geetanjali Tahilramani

Abstract

Maternal nutrition is very vital for both newborn and mother well-being and overall health. Due to fundamental physiological differences, females have their own set of health-associated issues and face different challenges at different stages of life cycle. For centuries, various nutraceuticals because of their therapeutic values were consumed for varied health-promoting roles like immunity booster; antidiabetic, anticancer, antimicrobial, and gastroprotective agents; and what not. The biodiversity of India is one of the primary reasons for the enriched traditional medicine system, and at various life stage, functional food and nutraceuticals become a part of our daily diet and were consumed as food, spice, and medicine. Throughout the lifecycle due to various reasons, a female's body undergoes a lot of changes. Various types of nutraceuticals and functional food play a very important, protective role and definitely aid in reducing the stress faced at each stage and alleviating the pains and various physiological symptoms faced during different stages. As women age, various botanicals and functional food can be used for various problems faced like UT infections, nausea associated with pregnancy, lactation issues and also for menopausal symptoms, osteoporosis, anaemia, or just to boost immunity. Women must be encouraged to discuss their use of these natural products with their health care providers for assistance in managing all aspects of their health throughout their lives.

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15.1 Introduction

As far as the history of mankind goes, food has been an indispensable part for human existence. From hunter-gatherer stage of human history till now, food (searching/making/collecting) is the driving force. It is equally important across all stages of human life cycle. Along with providing energy and required nutrients, food products nowadays are being used for another function, which is nothing less than pharmaceutical task.

Stephen L. Defelice in 1989 coined the word "Nutraceutical" which is a portmanteau of the words "nutrition" and "pharmaceutical" (Singh and Sinha 2012). Nutraceuticals are the components present in edible food along with basic nutrition providing additional health benefits like delaying of ageing, chronic disease prevention, and maintaining overall health and structural integrity and functional capacity of the body (Chaudhari 2017).

An optimal status of maternal nutrition is a very vital contributor to the survival of both that is the newborn and mother. Simultaneously, it is associated with promotion of women's overall health, productivity, and well-being. As per the data available, the two most vital pathways through which a woman's nutritional status is impacted are iron and calcium intakes and absorptions. The deficiency of these 2 can lead to negative pregnancy outcomes.

Both the genders that is male and female have similar health issues but due to fundamental physiological differences females have their own set of health-associated issues. A female's life cycle can be classified as follows (Fig. 15.1):

15.1.1 Birth

Birth of a female as any other male's birth is also dependent on the mother's health. Maternal nutritional status has a direct impact on the child's well-being. Foetal health is directly proportional to maternal health.

Fig. 15.1 Different stages of a female's life cycle

15.1.2 Adolescence

Adolescence is time period of shift from childhood to adulthood. It is the phase that comes around 10–13 years of age and is associated with onset of puberty. Optimum nutritional status during this phase plays a pivotal role in optimum physical growth and reproductive maturation. An adequate diet leads to optimum and well-regulated growth and development. Both macronutrients and micronutrients are equally important during this stage of life cycle.

During this phase, menstrual cycle begins. Around menarche, many females experience what is commonly referred to as premenstrual syndrome. The most common ailment is the menstrual cramps. Due to various changes in hormones and due to their imbalances, cramps can worsen in females with age and various other conditions like uterine fibroids / PCOS many times resulted. Nutraceuticals have various effects like anti-inflammatory which can smooth muscle relaxing and help in reducing cramps in the body. Owing to the ability to relax muscles, Dong Quai, Chasteberry, ginger, evening primrose, valerian, and Black Haware commonly used to treat common menstrual disorders.

15.1.3 Young Adults

During young age because of various deriving forces like friend circle, eating outs, sedentary lifestyles, many teenagers started compromising with macro- and micronutrients especially calcium, zinc, and iron. Their deficiencies are very common during teenagers. This may also lead to low body mass index (BMI), and weak and fragile bony structures and can even result in infertility. Along with micronutrient deficiencies, urinary tract infections (UTIs) are one of the most common bacterial infections affecting females. As compared to males, chances of women developing UTIs are 30 times higher. Various nutraceuticals can play an important role against various infections and most common nutraceuticals used to treat UTIs are cranberry and bearberry. These berries contain proanthocyanins which have antibacterial effect and that prevent bacteria from adhering to the walls of the urinary tract, subsequently blocking the further steps of uropathogenesis (Fuller 1991).

15.1.4 Child-Bearing Age

Endometriosis often results in pain in pelvic region, irregular menstrual cycles, and even infertility in severe cases. Common spices /food items such as garlic, curcumin, and aloe vera are storehouses for antioxidants along with Resveratrol, Inositol, genistein, and danshen.

Hormonal imbalance during the reproductive age is a leading cause of polycystic ovarian syndrome (PCOS). This may manifest as irregular periods, excessive facial hairs, acne, weight gain, mood swings, and most important infertility. Nutraceuticals are being tested for beneficial effects in PCOS and alleviating symptoms especially in improving fertility levels.

15.1.5 Pregnancy

Pregnancy is a phase of huge physiological turmoil for expecting female. The requirements of both macro- and micronutrients are elevated. Most vital nutrients are iron, calcium, folic acid, iodine, Vitamin A, B6, B12, C, D, and the DHA. Thus, a healthy eating plan can be of immense help in fulfilling the gaps and providing all the requisite nutrients. Nausea and vomiting are quite common in pregnancy and can impact the quality of life of expecting female. For few females, it can even lead to significant health risks. For ages, ginger a common kitchen ingredient has been used to overcome common ailments such as nausea and morning sickness during pregnancy.

15.1.6 Menopause

Hot flashes that can even be life threatening for some and very mild for few are very common symptoms of menopause. Adequate intake of calcium during this phase reduces bone mineral losses and simultaneously increases the risks of fracture. Women are recommended to consume calcium supplements, folic acid, vitamin D, B group vitamins, folic acid, fish oil, CoQ-10. Osteoporosis is a common occurrence in postmenopausal women. As a result of low oestrogen levels, bone density is lost at rapid rates. Nutraceuticals that might have protective effects against osteoporosis are vitamin D, red clover, soy, genistein, calcium, and liquorice. Symptoms of menopause are easily managed by regular consumption of pycnogenol, melatonin, vitamin E, Black cohosh, valerian, red clover, soy, liquorice, flax seeds, rhubarb, chasteberry.

Breast cancers are the most common cancers occurring in postmenopausal women and risks increase with age. Antioxidant consumption is very important for all especially the postmenopausal women. Nutraceuticals have been used traditionally for women's health. Various botanicals showing properties like anti-inflammatory, antimicrobial, anticancer, and chemopreventive activities can be used to enhance maternal health. Soy, Red clover, milk thistle, *Humulus lupulus* (Hops), and *Angelica sinensis* (Dong Quai) are being explored and tested globally for use in preventing breast cancer.

15.2 Health Issues During Different Stage of Life of a Female

Females belonging to different age groups have their own sets of problems (Table 15.1) which can be enumerated as:

Table 15.1 Health issues during different stages of life of a female

Gynaecological issues	Disorders associated with infertility	Oncological issues
• Menstrual irregularities • UTI • Fibroids • Bacterial vaginosis • Viginitis/vulvo-vaginitis	• Uterine fibroids • PCOS • Endomitrosis	• Uterine cancers • Ovarian cancers • Cervical cancer • Breast cancer

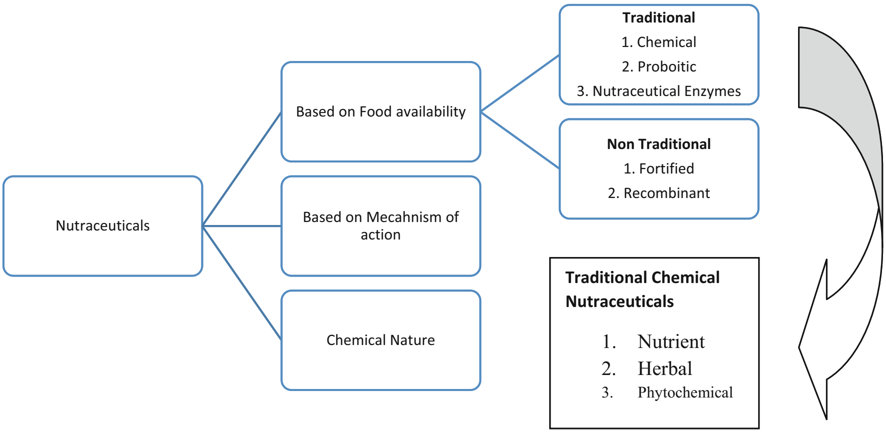

Fig. 15.2 Classification of nutraceuticals

For centuries, nutraceuticals have been used for their therapeutic values. In the current scenario, these items of consumption have found varied uses in the forms of immunity booster; antidiabetic, anticancer, antimicrobial, and gastroprotective agents; and what not. Various herbs have been used as a better option to be formulated as nutraceuticals. India per se is a blessed land, as majority of the above-mentioned herbs/medicinal plants are available across various regions. The biodiversity of India is one of the primary reasons for the enriched traditional medicine system. India has close to 2.45% of the world's area and is blessed with 8.10% of the world's total biodiversity. In terms of flora as well, the country is expected to have 45,944 species, which accounts for 10.75% of the known world plants (Chandrakar 2012). Owing to medicinal properties, more than 8000 plants are of regular consumption especially in rural India.

As per the traditional system of Ayurveda medicine, ginger, garlic, and onion are basics for all healing food recipes. Garlic is one of the most widely used natural health products. They are part of our daily diet. These are considered as food, spice, and medicine. Thus, these are the most common nutraceutical of mass consumption. It is clearly evident from Fig. 15.2; nutraceutical is a very broad term and can include components from all classes of edible food items (Chanda et al. 2019).

15.2.1 Nutraceuticals Based on Food Availability

15.2.1.1 Traditional Nutraceuticals

These products are derived directly and naturally. This class includes constituents as saponins, lycopene, omega3 fatty acids, etc., derived from soy, tomato, salmon, respectively (Fig. 15.3). These constituents are the part of food and are used for varied health benefits.

Probiotic Microorganisms

Metchnikoff had coined the term "Probiotic". These are intestine-friendly microorganisms and aid in processes like absorption and metabolism. Recently, they have found utilization in modern medicine as well. They work by maintaining a friendly environment in gut by removing toxins.

Nutraceutical Enzymes

Proteins are the basic structural components of enzymes. Cells produce enzymes which also act as a biological accelerator. Enzymes ease the metabolic rates and the life processes are fastened. Health issues involving GIT like GERD, constipation, diarrhoea, or ulcerative colitis can be treated with supplements having enzymes.

15.2.1.2 Non-traditional Nutraceutical

These are food products enriched with biotechnologically designed crops or supplements to boost the nutrients that are inherently available (Fig. 15.4). For example, broccoli and rice are rich in vitamins and β-carotenes, respectively.

As can be interpreted from Table 15.2, that nutraceuticals are of use at practically every stage of a female's life especially after conception and during lactation. As a matter of fact, the initial 2 years of a child's life are the most crucial ones for the wholesome growth and development (Ayana et al. 2017). According to the statistics, there is a global trend of improved nutritional status among children. Data suggest that close to 28% of children under the age of 5 years are still stunted in low- and

Traditional Nutraceuticals		
Nutrients	Herbals	Phytochemicals
Various vitamins Amino acids, and fatty acids are primary metabolites & thus have definitive roles in various systemic bodily processes. Products from plant & animal origin along with multi vitamins have myriad health benefits including anemia, providing bone strength, building muscle mass.	Herbal nutraceuticals have a wonderful effect on preventing different chronic diseases. They have clinically proven effects that can be classified into differen catagories like anti-inflammatory, analgesic, antipyretic, astringent & anti arthritic	Phytochemicals have been known for preventing diseases. Various phytochemicals enhance immune system like carotenoids. Anthocynins, polyphenols also help in reducing the growth rate of malignant cells etc.

Fig. 15.3 Traditional nutraceuticals

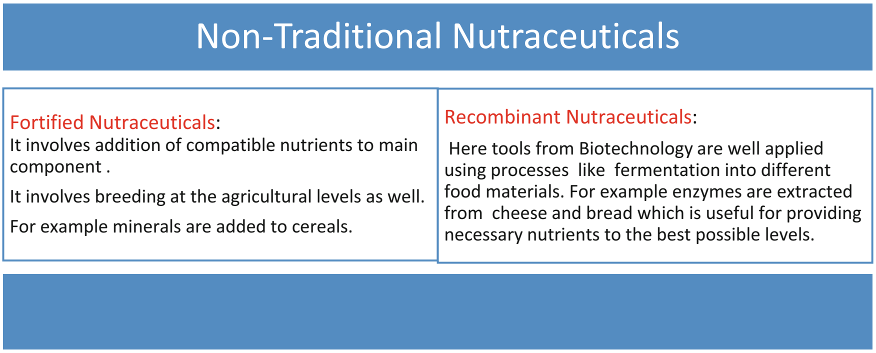

Fig. 15.4 Classification of non-traditional nutraceuticals

middle-income countries (Black et al. 2013). Thus, maternal nutritional status and the IYCF practices have a direct bearing on child's health. Along with these, successful breastfeeding practices are important for the baby's attaining optimum growth potential.

Nowadays research on the therapeutic aspects of food and medicinal plants based on traditional systems of medicines is playing important role in providing health care (Danditiya et al. 2013) as enlisted in Table 15.2.

15.3 Physiology of Lactation

Stem cells along with highly differentiated alveolar cells with terminal ducts are present in mammary gland. An entire mammary epithelial outgrowth, capable of full secretory differentiation. These are stimulated by insulin and HGH synergized by hormone prolactin. These cells are highly active in synthesizing milk and secreting it.

The best stimulus for milk production is suckling on breasts by newborn infant. Due to suckling by an infant, a neuroendocrine reflex begins, the sensory nerve fibres in the areola are triggered, and this results in milk secretion from lactocytes into the alveoli. Oxytocin hormone is released by the posterior pituitary gland. Oxytocin helps in Let-down reflex, where myoepithelial cells are stimulated to squeeze milk from the alveoli which is drained into lactiferous ducts, collected in lactiferous sinuses, and finally discharged through the nipple pores.

In general, there is a probability that the breastmilk production is not impacted highly by moderate maternal under-nutrition. But severe malnutrition which comes along with ill health or other negative situations can reduce the milk output and production. The most common reasons for not enough milk have been enumerated in Table 15.3 below:

Table 15.2 Commonly used herbs during various gynaecological health conditions

Physiologic condition/health indications	Recommended herbs and nutraceuticals	Scientific name	References
Morning sickness, Nausea, Vomiting	Ginger	*Zingiber officinale*	Lete and Allué 2016; Viljoen et al. 2014, Gibson et al. 2001; Tomuno et al. 2011
	Peppermint	*Mentha piperita*	
	Raspberry	*Rubus idaeus*	
	Bishop's weed	*Aegopodium podagraria*	
	Garlic	*Allium sativum*	
	Anise	*Pimpinella anisum*	
Anxiety and Stress	Anise	*Pimpinella anisum*	Khadivzadeh and Ghabel 2012; Ernst 2002; Illamola et al. 2020; Coussons-Read 2013
	Peppermint	*Mentha piperita*	
	Chamomile	*Matricaria chamomilla*	
	Thyme	*Thymus vulgaris*	
	Rosemary	*Rosmarinus officinalis*	
	Valerian	*Valeriana officinalis*	
Gestational Diabetes (Obese Females)	Myo-inositol supplementation		NFHS-4 2015
Urinary Tract Infection	Cranberry	*Vaccinium macrocarpon*	Kennedy et al. 2013; Daniela et al. 2021
	Bearberry	*Arctostaphylos uva-ursi*	
	Parsley	*Petroselinum crispum*	
	Fenugreek	*Trigonella foenum-graecum*	
	Rosemary	*Rosmarinus officinalis*	
	Peppermint	*Mentha piperita*	
	Sage	*Salvia officinalis*	
Labour preparation, facilitation, and induction	Rooibos tea	*Aspalathus linearis*	Zamawe et al. 2018; WHO 2014; Frawley et al. 2015
	Coconut oil	*Coco nucifera*	
	Date palm		

(continued)

Table 15.2 (continued)

Physiologic condition/health indications	Recommended herbs and nutraceuticals	Scientific name	References
		Phoenix dactylifera	
	Golden buttons	*Matricaria aurea*	
	Watercress	*Nasturtium officinale*	
	Cinnamon	*Cinnamomum verum*	
	Fenugreek	*Trigonella foenum-graecum*	
	Rosemary	*Rosmarinus officinalis*	
	Raspberry	*Rubus idaeus*	
	Cannabis	*Cannabis sativa*	
	Evening primrose	*Oenothera biennis*	
Anaemia	Spinach	*Spinacia oleracea*	Owusu-Sarpong and Tetteh 2017; Saha et al. 2018
	Fenugreek	*Foeniculum vulgare*	
	Cinnamon	*Cinnamomum verum*	
	Rosehip	*Rosa spp*	
Cancers (Breast Cancer)	Omega-3 fatty acids		Fabian et al. 2015
Postmenopausal vascular disease	Omega-3 polyunsaturated fatty acid supplementation		Losurdo et al. 2015

Delayed initiation is on the top of the list. As per the recommendations by WHO and UNICEF, the mother should initiate breastfeeding the newborn within the first hour of birth. Prolonged separation between mother and child due to any reason may lead to further reduction in milk output. Apart from that involvement of feeding bottles/pacifiers or not giving the night feeds can be the other major contributors to reduced milk output. Once the mother's confidence levels are reduced it leads to anxious and stressed situation and this will acts like a vicious circle difficult to breakthrough. Stress and anxiety have a major negative impact on breastfeed production.

Table 15.3 Reasons for low production of milk during lactation

Reasons Why A Baby May Not Get Enough Breast Milk			
Breastfeeding factors	Mother: psychological factors	Mother: physical condition	Baby's condition
Delayed start Feeding at fixed times Infrequent feeds No night feeds Short feeds Poor attachment Bottles, pacifiers Other foods Other fluids (water, teas)	Lack of confidence Worry, stress Dislike of breastfeeding Rejection of baby Tiredness	Contraceptive pill, diuretics Pregnancy Severe malnutrition Alcohol Smoking Retained piece of placenta (rare) Poor breast development (very rare)	Illness Abnormality
These are common		These are not common	

Inadequate breast milk production is primary reported reason for stopping breastfeeding and shifting to top feeding, thus resorting to mix feeding or starting galactogogues. Again, a point of emphasis is that breastmilk output is directly proportional to suckling by infant, which has to be emphasized repeatedly during antenatal period and immediately after birth. During postpartum contacts with the physician and paediatrician, the positioning attachment and suckling have to be emphasized & re-emphasised.

For mother's facing issues with breastfeeding the baby, galactogogues are of immense help. By definition, a galactagogue is a food derivative that aids in process of lactation, in humans and other mammals. It can be a synthetic item, a plant-based derivative, or having an endogenous (Danditiya et al. 2013). Galactogogues do come to immediate rescue of mothers who go through these phases of reduced milk production. Various herbs and plant derivatives act like as milk production stimulant which have been tabulated in Table 15.4.

Thus, the growth of foetus, foetal well-being, and the birth outcome are largely impacted by maternal nutrition status. The low-income countries and developing countries have a huge burden of adverse foetal outcome, and thus, it has immense public health importance. The statistics from developing countries are not very encouraging. In India, as per NFHS 4, only 21% mothers had full antenatal check-ups. Apart from that only, 30.3% females consumed iron folic acid supplementations as per the recommendations (National Family Health Survey-4 2015).

Well-being of mother is of vital importance for positive pregnancy outcomes. Thus, during all stages of life cycle, the nutritional status of a female cannot be ignored. All females should be advised and supported to consume a diet which is healthy and balanced. A diet that consists of a balanced proportion of macronutrients and micronutrients. Postpartum mothers are very fragile especially in terms of psychological well-being. If need of galactogogues is there, the consumption of nutraceuticals should not be restricted so that both mother and child can benefit. Apart from that, even in non-pregnant non-lactating females, there can be certain

Table 15.4 Some traditional Indian galactagogues

Sr No	Galactagogues	Scientific name	Formulations
1	Shatavari	*Asparagus racemosus*	Dried root (2–5 g) powder to be consumed with milk
2	Dudhai	*Euphorbia hirta*	10–15 ml fresh juice to be given with honey
3	Kenchua	*Pheretima posthuman*	Dried earthworm powder or decoction quite effective in lactation induction
4	Anddi, Arand	*Ricinus communis*	Fresh leave's decoction and seed oil for breast massage
5	Madder	*Rubia tinctorum*	
6	Caraway	*Carum carvi*	Dry powder (2–5 g) to be consumed with milk or a decoction
7	Fenugreek	*Trigonella foenum-graecum*	Dry powder (2–5 g) to be consumed with milk or a decoctio
8	Cinnamon	*Cinnamomum verum*	Dry powder (2–5 g) to be consumed with milk or a decoction
9	Cumin	*Cuminum cyminum*	Dry powder (2–5 g) to be consumed with milk or a decoction
10	Fennel	*Foeniculum vulgare*	Dry powder (2–5 g) to be consumed with milk

Table 15.5 Nutraceuticals for common health issues

Physiologic condition/health indications	Recommended herbs	Scientific name
Pain (gastralgia and other types of pain)	Lemon verbena	*Aloysia citriodora*
	Anise	*Pimpinella anisum*
	Cumin	*Cuminum cyminum*
	Fennel	*Foeniculum vulgare*
	Golden buttons	*Matricaria aurea*
	Sage	*Salvia officinalis*
Cold and Flu	Madder	*Rubia tinctorum*
	Anise	*Pimpinella anisum*
	Golden buttons	*Matricaria aurea*
	Liquorice	*Glycyrrhiza glabra*
	Borage	*Borago officinalis*
	Echinacea	*Echinacea purpurea*
	Wild thyme	*Origanum syriacum*
Anxiety and stress	Anise	*Pimpinella anisum*
	Peppermint	*Mentha piperita*
	Chamomile	*Matricaria chamomilla*
	Thyme	*Thymus vulgaris*
	Rosemary	*Rosmarinus officinalis*
	Valerian	*Valeriana officinalis*
Oedema	Turmeric	*Curcuma longa*
	Fennel	*Foeniculum vulgare*

health issues which need attention and can be cured with help of traditional herbs and nutraceuticals (Table 15.5).

Maternal health and her nutritional status are directly related to foetal growth and birth outcomes. Optimum nutritional status of mother is like a strong backbone. To ensure mother's well-being and favourable pregnancy outcomes, consumption of a healthy and balanced diet is genuine necessity. Specific micronutrient consumption during both the phases, i.e., pregnancy and lactation are on lower sides even in most developed nations. Situation in developing nations is also not very optimistic. Thus, pregnant ladies should be counselled to consume a diet that is balanced in nature comprising of fats that are high quality, proteins and carbohydrates, along with vitamins and other food groups. (Sadia et al. 2020).

It is very important to approach "health" as a whole (combination of multiple factors) instead of considering as a series of separate/individual factors. It is an amalgamation but not a separate entity. All dimensions of health as mentioned above are inter-linked. Thus, people should target overall well-being and balance as the keys leading to good health. Thus, a holistic and well-co-ordinated approach is the most apt and vital one. During various phases of life, owing to ageing and other factors, our body undergoes lots of internal stress. Due to seasonal changes and temperature fluctuations, we face pain, cold cough, etc. Due to limited/no side effects, nutraceuticals have found immense acceptance among masses.

Few of the common health conditions and associated herbs of common use are tabulated below.

Anaemia is a very common observation in a female's life cycle. Herbs and food items are available in plenty to lend support as has been mentioned in Table 15.3. Apart from that we have a food item or other mentioned in our ancient scriptures mentioning about protection from one disease or another.

Alzheimer's disease is a form of dementia that is a general term for memory loss and other cognitive abilities serious enough to interfere with daily life. Till date, there is no set cure for this disease. It is most found in people age > 65 years (Nasri et al. 2014a; b). As per the literature available, women are affected more practically 2:1 is the ratio. Evidence available correlated oxidative stress with onset of Alzheimer's.

Antioxidants present in curcumin, lutein, and lycopene are also used as commonly used nutraceuticals exerting positive effects on various targeted diseases by lowering the oxidative stress. Researchers are supporting consumption of different plants such as *Ziziphus jujuba* and *Lavandula officinalis* as nutraceuticals on AD, memory, and learning (Rabiei et al. 2014a, b).

Cancer It has recently gained prominence as a public health problem effecting masses all across**.** A healthy diet along with an active lifestyle can help in protecting one from cancer. (Nasri et al. 2013). High cancer risk is also associated with chronic inflammations and suppression of immune system. This also acts as cancer risk factor. It is reported that Ginseng has an anti-inflammatory action. Carotenoids and lycopene present in vegetables and fruits of mass consumption show cancer-protective effect. This is due to capacity to lower oxidative stress and reduced DNA damage (Shirzad et al. 2013)· Soybean has been reported to offer protection against uterine, breast, colorectal, lung cancers. β-Carotenes are present abundantly in yellow, orange, and green leafy vegetables like spinach, lettuce, tomatoes, sweet potatoes, broccoli, winter squash, carrots and fruits such as oranges, cantaloupe, etc. These β-carotenes also offer anticancer activity (Thomasset et al. 2007).

Cardiovascular Disease is an amalgamation term for diseases of heart, arteries/blood vessels. A consumption of diet low in fibre/fruits and vegetables is associated with elevated risks for CVD. Flavonoids—commonly distributed in vegetables and fruits of common and mass consumption like onions, endives, cruciferous vegetables, apples, pomegranate, berries, cherries, black grapes, grapefruits, and red wine, are available as flavones, flavanones, and flavonols (Asgary et al. 2014; Gharipour et al. 2013).· These nutrient components have a prominent role in prevention and protecting the consumers from CVD. Ginger has active antioxidants and many anti-inflammatory activities. It is being commonly recommended for various diseases like palpitations and hypertension (Ghayur et al. 2005). Phytosterols are present in buckwheat seeds. Buckwheat proteins are equally helpful in lowering blood cholesterol and helping in hypertension. Fatty acids of the omega3 series ($n - 3$ fatty acids) available in abundance in fishes are dietary components that have strong effects on plasma lipids and protective effects against CVD. Whole grains, fruits, and leaves of many plants have octacosanol, which has lipid-lowering actions, with no reported negative impact. (Sidhu 2003).

Diabetes: During recent times, a wide range of herbal products including dietary supplements have been specifically proven to aid people suffering from type 2 diabetes mellitus. For reduction of glucose levels, compounds containing omega 3 fatty acids have always come to rescue. Dietary fibres especially from psyllium husk have dual roles in controlling obesity and reducing blood sugar levels. It also aids in controlling lipid levels. Antioxidants in form of lipoic acid are being utilized in treating diabetic neuropathy for many years and are perceived to be effective as a long-term dietary supplement for protection of diabetics from complications arising due to elevated blood sugar levels. (Coleman et al. 2001; D'Anna et al. 2015). Plants extracts such as extracts from cinnamon, *Teucrium polium*, and bitter melon have been used in treating diabetes (Nasri and Rafieian-Kopaei 2013).

Immune System: Lots of nutraceuticals have shown promising roles in maintaining immune system at crucial times. The immune boosters include extracts from herbs from genus Echinacea—coneflower. Herbs available from genus Astragalus are also amazing immune boosters. These stimulate development of vital stem cells in marrow.

Garlic is a very common condiment which aids in stimulating the nervous system (Limer and Speirs 2004) while morphine is another example that suppresses the immune response (Gupta et al. 2000). Probiotics also help in management of immune system as they can manipulate gut microflora so as to differentiate and maintain balance between bacteria that are pathogenic and nonpathogenic. Most used probiotic preparations are from lactobacillus, Bifidobacterium, and streptococcus species (Fuller 1991).

15.4 Toxicity

The nutraceuticals are in general considered as safe, but they are definitely not without any associated side effects. Just like the common medicines, there can be some supplements that have active ingredients which provide pharmacological or physiological effects. Due to which there is a likelihood of having adverse effects in individuals with susceptibility. To avoid serious medical outcomes, more diligent attention to adverse effects and potential interactions is needed (Martin et al. 2018).

Thousands of species of plants and other nutraceuticals are consumed by a lot of females globally so as to meet the basic nutritional needs. But the scientific studies are largely limited.

These vital plant by-products require scientific validations in combination with the conventional medicine systems so as to know and understand the relationship between the disease and dose better in order to avoid any form of toxic effects (Nasri et al. 2014a; b).

15.5 Conclusion

Nutraceuticals have been known to aid in body's defence mechanisms against different types of common illness including cold, cough, fever, etc. They might help in improving physical health, mental health along with delaying the ageing process leading to increased quality of life, and an elevated life expectancy. Due to advances in field of science and technology, advanced research is taking place and more and more promising results can be seen. The nutraceuticals of common use, under investigation, are persistently changing reflecting upon the ongoing market developments, research, and consumer interest. Substantial researches are very important and need of the hour so as to warrant for the safety and effectiveness of nutraceuticals. Nutraceuticals are socially acceptable and cost-effective simultaneously leading to an easy acceptance. Throughout the lifecycle due to various reasons, a female's body undergoes a lot of changes. The nutraceuticals definitely aid in reducing the stress and alleviating the pains. Only one word of caution here that consumption should be under prescription.

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Importance of Functional Foods in Child Development: A Review

16

Sunayan Sharma

Abstract

Functional foods are those wholesome, fortified, and enriched foods which help to provide better health conditions beyond the optimum levels of vital micronutrients (e.g. vitamins and minerals), when such food is taken at efficient amounts as part of a varied diet on a consistent basis. They are formulated by manipulating the preparations or engineered genetically or by other conventional means to provide the desired function. If functional food is recommended to children, its safety and efficacy must be established. The gut microbiota is implicated in gastrointestinal health, nutrient metabolism, and benefits such as prevention of infection. Dietary fibre, including prebiotics, escapes digestion in the small intestine and reaches the colon intact, where they are partially or completely fermented by the gut microbiota. Breastfeeding is the good example for useful nutrition during the first year of life. Probiotics health-promoting bacteria added to infant formula is one of the successful ways in the preventive measure and treatment of diarrhoea. Prebiotics promote growth of gut health by adding in infant formula which are helpful in lowering the frequent occurrence of high temperature, cold, and severity of diarrhoea. When prebiotics are consumed before, during, and after measles, vaccination helps in lowering the incidence of infection.

Keywords

Probiotics · Prebiotics · Children immunity · Functional foods

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16.1 Introduction

Certain factors in supply of food and breakdown and absorption food are of great biologic importance in comparison of pregnant women and lactating mothers, and their infants and young children. Nutritional and dietary factors in children during their early development do not only impose temporarily effects on growth and development, composition of body and bodily functions but then it also wields in long-term impact on health, disease, and mortality risks during adulthood. Such food offers therapeutic benefits which are becoming a new concept. The viewpoint that food has achieved significant acceptance in recent years and disease-inhibiting outcomes of nutrition has preceded the new science of functional foods. Foods that produce beneficial effect on specific functions of the body, beyond nutritional effects that are sufficient to well-being, health, and decline in disease rate all gain respect as a form of medicine. Nutritional foods can be consumed by improving their concentrations of by adding or enhancing the bioavailability of certain components of these foods. Many of them of the biological-active substances contains that have been discovered and exemplified in not long past years. Certain fruits and vegetables which are rich in micronutrient like fruits, vegetables, nuts, seeds, and grains are often considered functional foods as well benefits health long term. Oats are one of such food items that include a type of fibre called β-glucan, which helps to reduce inflammation, enhance immune function, and improve heart health (Bashir and Choi 2017). Functional foods are generally characterized into two: conventional foods *and Modified Foods*. Food that are natural, whole-food ingredients that are rich in essential nutrients like vitamins, minerals, antioxidants, and heart-healthy fats is called conventional food, whereas food that have been fortified with other ingredients, such as vitamins, minerals, probiotics, or fibre, to increase a food's health benefits is called modified food (Table 16.1). Some of them are as follows:

The functional food cannot be a single well-described entity. The term 'functional food' was derived in Japan. In 1980s, Japanese government initiated large-scale research programmes on systematic analyses and development of food functions, analysis of physiological management of functions by food, and analysis of

Table 16.1 Conventional food and their sources

Conventional/functional food	Sources
Fruits	Berries, pears, peaches, apples, oranges
Vegetables	Broccoli, cauliflower, kale, spinach, zucchini
Nuts	Almonds, cashews, macadamia nuts
Seeds	Chia seeds, flax seeds, hemp seeds, pumpkin seed
Legumes	Black beans, chickpeas, lentils
Whole grains	Oats, barley, buckwheat, brown rice
Seafood	Salmon, sardines, anchovies, mackerel
Fermented foods	Tempeh, kombucha, kimchi, kefir, sauerkraut
Herbs and spices	Turmeric, cinnamon, ginger, cayenne pepper
Beverages	Coffee, green tea, black tea

Table 16.2 Proposed definition of terms related to functional foods

Term	Definition	References
Nutraceuticals	Any ingredient of food or any part of a food item that provides medicinal and/or health betterment which includes the preventive measures and treatment to disease Food products that are produced from foods item but sold in powders, pills associated, and other medicinal forms not generally associated with food and demonstrated to have physiological benefits	
Dietary supplements	Produced intended to supplement the diet that contains one or more of the following dietary ingredients: Vitamins, minerals, essential amino acids, dietary substance that are used by humans in order to complement the diet by increasing the total nutritional intake	
Fortified food	These are the normal food products enriched with specific nutrients, with energy and/or proteins, minerals, vitamins, trace elements, etc.	
Functional foods	Food that helps to provide health benefits beyond basic nutrition Foods or food product marketed with the message of the benefits to health Everyday food transformed into a potential lifesaver by the addition of a magical ingredient Food that encompasses potentially helpful products including any modified food or food component that may contribute to health benefit which is beyond that of the traditional nutrient in contains	Hasler (2002)

functional foods. These group of foods intends to facilitate health benefits and certain health claims that were included as one of the important food categories in Nutrition Improvement Law for special dietary use. Table 16.2 depicts the proposed definition of terms related to functional foods indicated by FOSHU (Food for Specified Health Use), Japan 1991.

It is also a concept that clearly belongs to food and not to pharmacology. The above-mentioned definition is substitute, which refers to the fortified food or supplemented with macro- or micronutrients that are already present in them or other complementary nutrients. Such can be made by manipulating through the formulation or genetically engineered method to provide specific functions. Functional foods usually have an effect of decreasing the risk of disease somewhat than inhibiting it. In last few decades, emphasis has been given to the functional food to suggest the ways to decrease the rising cost on the health care system by a constant prophylactic mechanism. The International Life Science Institute defined it 'as food, by virtue of presence of biological-active components, in providing health benefits which are beyond the functions of essential nutrition'. The functional food market of India is estimated to be around four billion dollars in 2017 and it is anticipated to gain a hike at a significant 21 per cent CAGR to 10 billion dollars in 2022 (Fig. 16.1). A food is said to be functional if it contains components which may or may not be a nutrient affective in one or more limited number of functions in body

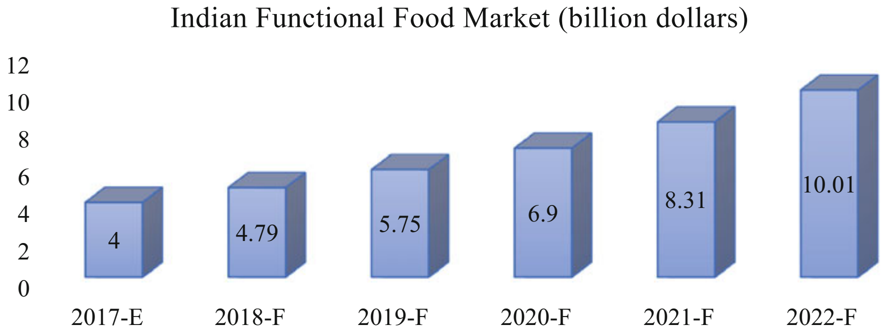

Fig. 16.1 Indian functional food market

targeted way, leading to beneficial effects that might justify the functional or other health assertions (Roberfroid 2000).

Some instances of functional foods are omega-3-enriched eggs, oats, fortified margarines, iodized salts, probiotic yoghurt, nuts (walnuts, cashews, etc.) are certain examples of functional foods. As per the perspective, the American Heart Association (AHA) stated that 27 million children almost 19 years and under have high cholesterol levels. Million of children are either overweight or obese which in turn increasing in the rapid rise of type II diabetes. Centres of Disease Control and Prevention (CDC) assessed that between 8 and 43 per cent of children are being detected as having type II diabetes. Increasing children's diet with functional foods with added superfoods not only preventing health diseases but naturally lowering down the percentage of behaviour and emotional problems. Research shows that lot of childhood behavioural problems are curtailing from added artificial ingredients in processed/packaged foods. With the help of natural functional foods, primary caregivers or parents can reduce the amount of toxins that are being added to children's diet. Incorporating superfoods and functional foods daily will provide increased energy and vitality and strengthened the immune system. The American Academy of Paediatrics (AAP) recently reviewed the medical uses of probiotics and prebiotics to help guide physicians in counselling parents about the use of these products as dietary supplements added to foods for children, including infant formula.

Functional foods consumed for the prevention of cancer, heart disease, and osteoporosis as well as for the improvement and maintenance of bone health, digestive health, immunity, and cognitive function (Hasler 2002). In recent years, this has become very difficult to feed the child with healthy plate of food. Over the years, overweight and obesity among children have grown significantly in the past thirty years. In 2012, more than one third of children has quadrupled (National Center for Health Statistics 2011).

16.2 Functional Foods for Infants and Supplementary Purpose

India is among many other nations that have higher prevalent rate of child malnutrition and deficiency disorders. According to an estimated data, more than 50% of infants are born with low birthweight resultant in underdeveloped growth. The absence of vital nutrients and bio-preventive elements during infancy stage leads to higher incidence of anaemia and contagious disease in early and middle childhood years. Breastmilk has always been regarded as an indispensable food item, but many instances of maternal nursing are not possible, and many neonates are being fed with infant formula. Infant formula has been considered as one of the best examples of functional food. Majority of infant formula are manufactured from cow's milk, but in turn it demands considerable modifications to correspond to the composition of breastmilk. Such modifications involve reducing protein and mineral content; there is an increase in carbohydrates and the slight addition of vitamins and trace elements. Recent studies indicated that infants might develop less ability to synthesize substances like taurine and carnitine, and therefore, such dietary sources become indispensable. Carnitine is also important for the transportation of long-chain fatty acids into cell for the beta-oxidation and more energy production. Fatty acid profile from different fat sources which may not be able to meet the complexity of breastmilk; hence, the mixture from different fat sources are chosen. The fat source may also provide the essential fatty acid which may include linoleic acid (C18:2, ω-6) and α-linolenic acid (C18:3, ω-3). The ratio of linoleic acid in breastmilk is 5:1 that is, ω-6: ω-3. Linoleic acid and α-linolenic acid are the precursors of the very-long-chain (C20-C22), polyunsaturated fatty acids (LCPUFA): arachidonic and docosahexaenoic acid (DHA). LCPUFA are generally involved in the neural and vascular development of the foetus and neonates and are present in breastmilk Many manufacturing producers incorporate the mixture of vegetable oils (Simmer 2000).

Nucleotides, a compound of non-protein nitrogen in breast milk, is important for normal functioning of immune system. Supplementation of infant formula with nucleotides has proven to be very beneficial in many scientific trials, although future research is needed that would consider the same results. Featuring in, special formulas incorporate certain clinical situations, for premature neonates or for infants and toddlers with specific inborn deficiencies of metabolism may provide with special dietary foods. The GI tract of infant is dominated by bifidobacterial which delivers health-promoting properties like activation of immune system by inhibiting the pathogens which in turn secretes a substance which acts as direct inhibitors towards certain bacterial growth. It also helpful in lowering the pH by producing acids such as acetate and lactic acids, leading to production of digestive enzymes such as casein phosphatase and lysozyme and production of vitamins. With the administration of prebiotics like oligosaccharides and probiotics, supplements appear to be most effective way to increase the number of bifidobacteria in the intestine. Breastmilk containing oligosaccharides are mainly responsible for bifidogenic effects. However, the addition of unconventional ingredients in the manufacturing of infant formula needs long-term research that needs to be approved.

Dietary recommendation is being formulated with respect to micronutrients and macronutrients. However, infants and children do not eat as per micro- and macronutrients. The consumption is majorly from miscellaneous food products that are composed with variety of mixtures containing several complex chemical entities. Probiotics can be defined as live microbial supplements, which majorly impact the host by improving its microbial balance (Roberfroid 2000). With inadequte intake of nutritional components during the first 2–3 years of life span, it often leads to the various health complications which are associated with malnutrition among the several developing nations in the world. Complimentary nutrition becomes important in maintaining the normal and healthy growth of a child after the age of six months, owing to increase the requirement of nutrition which can be provided by breastmilk. Furthermore, the food items which are produced and consumed as weaning foods do not contain such sufficient nutrients as per the recommended dietary intake children. Conventional infant-feeding practice, adopted in countries like India, is usually cereal based. In the preparation of such food items, grains are often germinated, fermented, processed, and cooked in various ways in order to enhance digestibility and to improve the nutritional profile. Cereals in combination with milk solids are commonly used for the formulation of weaning foods. Milk–cereal–millet-based complimentary food found to be distinctive in the sense that they can provide variety of nutrients to children and complement each other as well.

16.3 Paediatric Probiotics and Prebiotics

16.3.1 Probiotics

Infants have sterile gastrointestinal tracts at birth, but bacterial colonization happens quickly. Gestational age, mode of delivery, and diet seem to have significant effects on this process. In recent years, there has been enhanced concern in adding probiotics and prebiotics to nutritional products to optimize intestinal microflora. However, as with antibiotics, the purpose of these supplements must be supported by evidence-based medicine. Probiotics are live microbial feed supplements that constructively influence the host by enhancing the intestinal microbial balance. Probiotic bacteria also reinforce the intestinal walls by crowding out pathogenic organisms, thereby helping to prevent their attachment to where they can cause disease. Probiotic bacteria also stimulate antigen-specific and nonspecific immune responses (Thakur 2016). Prebiotics are non-digestible food elements that beneficially impact the host by selectively promoting the growth or an activity of one or a limited number of bacteria in the colon and having an intent of improving host health. Based on the concept that a breastfed decal flora protects the neonate from infectious disease and certain allergies, pre- and probiotics have been introduced to infant formula. With an increase in allergy during the first year of human life span, these attempts to modulate the bottle-fed neonate flora. So far, the bifidogenic effect of certain prebiotics has been demonstrated in preterm infants and toddlers. Such of these prebiotics in infant formula soften stools but other putative effects remain to be demonstrated (Boehm et al. 2002). Many studies on probiotics revealed that bifidobacterial in infant formula provide protection against the gastrointestinal infections and helpful in modulating the immune response (Saavedra 2000). Lactobacilli have been significantly studied with respect to various food allergy and as gut barrier and emerges as protective when it is administered on infants or even to the mother prepartum (Kalliomaki et al. 2003). Pre- and probiotics have been linked with few paediatric diseases. The severity of necrotizing enterocolitis (NEC), diarrhoea, irritable bowel syndrome, and lactose tolerance may be reduced by incorporating functional food. Probiotics help in treating inflammatory bowel disease. They also reduce the duration of diarrhoea caused by gastroenteritis. During pregnancy and lactating mothers, probiotics help to reduce the development of eczema and allergies in their infants (Armstrong 2011).

As of December 2010, at least two infant formulas that include probiotics were being advertised in the United States. One contained *Bifidobacterium Lactis*, and the other contained *Lactobacillus rhamnosus* GG (LGG). The addition of probiotics to powered infant formula has not been proven harmful to healthy term infants. However, there is no evidence of clinical efficacy, and the usual use of these formula is not mentioned. No studies have evaluated the health benefits of using these formulas versus breastfeeding. Probiotics should not be offered to children who are seriously or chronically ill until the safety of these products has been established. The ideal duration of probiotics supplement is not known, nor is the optimal dosage or species. The long-term effects on intestinal microflora in children also are not known.

16.3.1.1 Acute Infectious Diarrhoea

Intake of probiotics at the initial course of diarrhoea from acute viral gastroenteritis might delimit the duration by one day in otherwise healthy infants and young children. The benefit of this is strain dependent; LGG is the most effective probiotic reported. Though the data do not encourage the regular use of probiotics to counteract infectious diarrhoea unless there are special circumstances (e.g. in childcare centres), there has been little evidence that supports the use of probiotics to avoid antibiotics-associated diarrhoea, but there is no evidence that it is effective for treatment. *LGG, B. lactis Streptococcus thermophilus,* and *Saccharomyces boulardii* were the most common probiotics used in randomized controlled trials (RCTs). There have been no RCTs examining the effects of probiotics use in children with clostridium difficile antibiotic-associated diarrhoea.

16.3.1.2 Chronic Inflammatory Bowel Disease

This has been assessed that almost 70% of children with chronic inflammatory bowel disease (i.e. Crohn disease of chronic ulcerative colitis) regularly use of complementary and alternative medicine, including probiotics as replacement therapy for prescribed medications. Hypothetically, probiotics may be beneficial in the treatment of such conditions (Gupta et al. 2000).

16.3.1.3 Other Conditions

The persistent or long-term benefit of employing probiotics to treat disorders such as irritable bowel syndrome, constipation, and extraintestinal infections requires further study; currently; use is not recommended in children. Probiotics have not been proven beneficial in treating or preventing cancer. There are safety concerns with the use of probiotics among infants and children who are immunocompromised, chronically incapacitated, or seriously ill and who have indwelling medical devices.

16.3.2 Prebiotics

Human milk contains considerable magnitudes of prebiotics and is preferred for infants up to six months of age. The addition of oligosaccharides as prebiotics to infant formula is not reasonable but lacks evidence showing clinical effectiveness. It is not known whether their use is cost-effective. The ingestion of prebiotics in inhibiting or treating diseases in children has not been tested extensively in RCTs, but the available evidence shows that there may be some long-term benefits for the prevention of atopic eczema and common infections in healthy infants. However, confirmatory studies, especially in children who are given formula that is not partially hydrolysed, are needed before recommendations can be made (Wauters 2004).

The mechanism of, prebiotics seem to be very engaging in inhibiting and management of many clinical conditions in contrast to probiotics that might have considerable amount of control on the bacterial growth in the gut, both in terms of their structure and performance. The strongest evidence on beneficial effects of prebiotics in children exists in relation to fight against constipation, poor weight gain in preterm infants, and eczema in atopic children. The reasonableness of using prebiotics in some other diseases, including infantile colic, absorption of minerals, and infectious diseases is still under investigation (Orel and Rebersak 2016).

16.4 Conclusion

The usage of probiotics among very low birthweight infants is frequently increasing, as probiotics are believed to reduce the prevalence of acute disease, such as necrotizing enterocolitis (NEC) and late-onset sepsis and to enhance feeding tolerance. According to feeding type, the favourable effect of probiotics was approved only in exclusively human milk-fed preterm infants. The exploration of foods as medicines, beyond their normal nutritional benefits, is providing interesting clinical results, with great promise for possibly preventing and treating certain diseases, some with well-established genetic origins. Administration of probiotics during pregnancy and breastfeeding appears to be a prudent and effective way to provide protection against atopic disease early in life. Prebiotics are given, during the prenatal period, to pregnant mothers who have at least one first-degree relative with atopic disease and to infants post-naturally for six months.

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Bioactive Components Having Antimicrobial and Anticancerous Properties: A Review

17

Anuradha Singh, Anupam Prakash, and Richa Choudhary

Abstract

Bioactive compounds isolated from plant sources are the secondary metabolites that have toxicological or pharmacological properties depending upon their structure. Recently, these compounds have received more attention due to their diverse role in providing protection against various types of pathogenic and non-pathogenic diseases. These miraculous bioactive compounds also pursue pharmacological activities against several microbial pathogens and are also known to exhibit antidiabetic, antipyretic, anticancerous, antidiuretic, and antioxidant properties. Some bioactive compounds extracted from plants such as phenolic compounds, anthocyanidins, flavonoids, tannins, and flavones are found in significantly high concentration in the biosphere, and certain others are present in less amount but their pharmacological as well as commercial importance cannot be denied. The activities of bioactive compounds like flavonoids, polyphenols, not only functions to inhibit microbial growth but also they act synergistically with other drugs which make them ideal for alternative cancer remedies. This chapter provides a general insight into secondary metabolites having antimicrobial and anticancerous properties, their plant source, and their mode of actions.

Keywords

Bioactive compounds · Antimicrobial · Anticancerous · Human health

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17.1 Introduction

Fruits and vegetables are rich sources of micronutrients (magnesium, calcium, and potassium) and fair amount of macronutrient (protein, carbohydrate) and bioactive components (including non-nutrients) consisting of various phytochemicals like polyphenols, dietary fibers, carotenoids, and vitamins. Natural occurring bioactive compounds originating from metabolism found in plants are secondary metabolites that are well known for their crucial role in maintaining general plant health and are readily available in plant parts in small quantities. Bioactive compounds have an impact on living organisms, tissues, or cells and contribute to many physiological properties These compounds are present in small quantities in foods and their outcome on health is being continuously investigated. More recently, bioactive compounds isolated from plant sources are grasping more attention because of their curative as well as preventive role in several chronic disorders. Emerging infectious diseases, caused by numerous pathogens including bacteria, viruses, fungi, and parasites, have always been a matter of concern since the past and also in the present time. Interestingly, the uses of various natural bioactive compounds like curcumin, myricetin, geraniin, and tocotrienols are gaining popularity in treating a variety of deadly diseases. The growing bodies of evidence suggest that they can enhance the efficacy of chemotherapy and also exhibit the ability to modulate the expression of various gene expressions which are responsible for cancerous growth. Most of them have medicinal properties that have been exploited by the human race since ages.

These compounds are categorized under an extremely heterogeneous class of compounds (carotenoids, polyphenolic compounds, alkaloids, terpenoids, phytosterols, and organosulfur compounds) having diverse chemical structure and biological activities. Figure 17.1 shows a brief overview of bioactive components from vegetables and plants.

Several bioactive phytochemicals are known to exhibit antioxidant activity, anticancerous, antimicrobial, antipyretic, and antidiuretics traits. Like fresh and

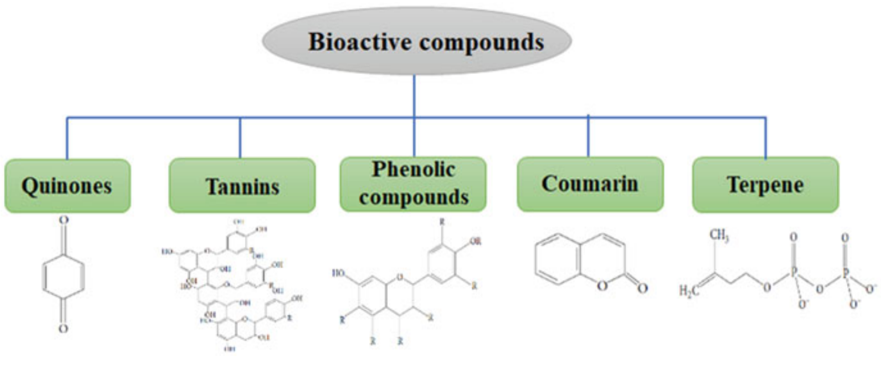

Fig. 17.1 Major class of bioactive compounds

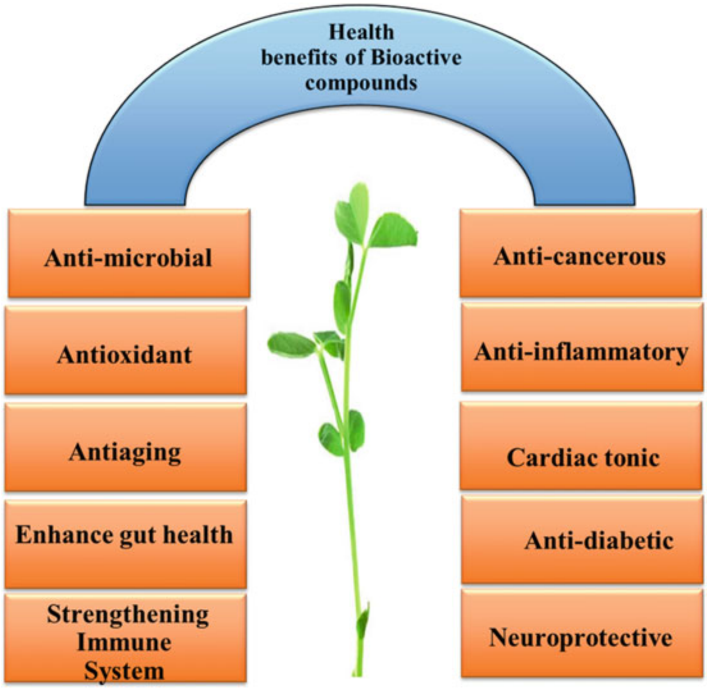

Fig. 17.2 Various health benefits of Bioactive compounds

dry garlic (*Allium sativum* L.) contain plentiful sulfur composite like alliin (*S*-allyl-L-cysteine sulfoxide), alliin can rapidly change into allicin (diallyl thiosulfinate) which has been described as (a major organosulfur compound) and have health benefits like antiviral activity, immunomodulatory, anti-inflammatory effect (Lawson and Bauer 1998; Borlinghaus et al. 2014; Arreola et al. 2015), antioxidant effect, and other pharmacological properties (Prasad et al. 1995; Lawson and Bauer 1998).

Numerous health benefits for example antibacterial, antifungal, antiviral, anti-allergenic, antiparasitic, anticancer, antioxidant, anti-inflammatory, antitumorigenic, antihyperglycemic, immunomodulatory, and neuroprotective effects on human health and well-being have been credited to the terpenoids (Shah et al. 2009). Leafy vegetables, such as amaranthus and spinach, contains carotene, lutein, zea-xanthin which have antioxidants and anti-aging effects, prevent osteoporosis and iron-deficiency anemia (Prakash and Pal 1991; Venskutonis and Kraujalis 2013), and prevent cardiovascular diseases, and colon and prostate cancer (Johnson 2014). Numerous health benefits of bioactive compounds are shown in Fig. 17.2.

The pharmacological activities of bioactive phytochemicals like steroids, alkaloids, terpenes, polyphenols, and essential oils from different plant species have played a substantial role as therapeutic agents against many microbial pathogens. Certain secondary metabolites extracted from different plant sources like *Aloe barbadensis*, *Withania somniferum*, *Ocimum basilicum* have been used traditionally in ethnomedicine to fight against several chronic microbial diseases.

However, the unlimited benefits of bioactive compounds cannot subside, but in this chapter, we are exploring antimicrobial as well as anticancer properties of plant-derived bioactive compounds. These phytochemicals that include polyphenols, terpenoids, carotenoids, and alkaloids also have the ability to modulate the metabolism process which is beneficial for human health in many aspects.

17.2 Plant-Based Secondary Compounds with Antimicrobial Properties

Due to growing concerns about the sustainability of humans, the control of the damaging effects of microorganisms is becoming very important. In this context, the study on plants is becoming important that possess multifunctional qualities in common with any other living organism. Besides serving as food sources, they are known for their medical uses as well (Bitchagno et al. 2015, 2019). Plants have always been linked to human history. Reports indicate that human beings have been using plants for their primary health since the dawn of time (Nganou et al. 2019; Mbaveng et al. 2019; Sonfack et al. 2021). Plants remain widespread and safe for health issues, despite the development of technology that allows for the creation of synthetic medications that are sometimes more efficient. The literature regarding plant chemistry and biology is currently flooded with research. The focus of the work is the experimental validation of ethnopharmacological uses of some plants and formulation of plant extracts for long-term health care (Bitchagno et al. 2019; Bitchagno et al. 2015; Nganou et al. 2019; Mbaveng et al. 2019; Sonfack et al. 2021). As a consequence, plants are ground and processed for testing on various biological properties including their ability to inhibit microbial growth. The main benefit of employing plant-derived antimicrobials for medicinal reasons is that they do not have the negative side effects that synthetic drugs have (van Wyk and Gericke 2000). As far as we are aware, these phytochemicals have not been associated with antimicrobial resistance most likely due to their various modes of action, which might limit the selection of resistant bacterial strains. In the livestock and poultry industries, these compounds are widely used as growth promoters due to their notable antimicrobial action, non-toxic nature, and affordability. As antimicrobial and disinfectant agents in the food industry, components of herbal medicine in veterinary medicine, and sources of novel antibiotics in pharmaceutical research and development.

Microbial infections are the second leading cause of death worldwide, according to the WHO, in developing nations bearing the brunt of the load. As well as bacteria or fungi, these diseases can also originate from viruses and protozoa (https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance). It is thought that their origin predates that of human life on earth (Hartman and Matsuno 1996). As a matter of fact, humans developed through bacterial evolution and mutation in the course of time (Hartman and Matsuno 1996). They are considered as the part of microflora of the human body (Rosner 2014; Abbott 2016). Some of them have proven to be beneficial in human existence, where they play an important part in metabolism. Since the dawn of time, there has been a concentrated endeavor to understand the biology of infectious diseases and how to manage them. It has been successful in some ways, although it is still necessary to conduct more research in this area. We develop “new organisms” by using a large quantity of chemicals, including a variety of drugs, together with our constant manipulation of these pathogens. As a result, we end up developing characteristics that differ from our natural counterparts. The pathogens begin to develop resistance to the drugs previously used to eradicate them, which makes the problem more severe (Abreu et al. 2012; Kuete 2010; Kuete and Efferth 2015; Cowan 1999). The environment in which these microorganisms live is critical to determining how resistant they are to commercialized drugs. Several misconceptions about bacteria have led to the belief that they are individually living things (Watnick and Kolter 2000). Things, on the other hand, are not the same. A colony of bacteria lives. Bacteria gathered in colonies to survive. They usually attach to a surface and congregate in order to live (Watnick and Kolter 2000; O'Toole and Kolter 1998). Biofilm is a type of biofilm that is made up of bacteria that have been enveloped with a peculiar liquid (extracellular matrix). For bacteria, the whole constitution serves as a protective barrier. In this situation, the cellular make-up of this living organism constitutes the primary barrier against bacteria and consequently the initial stage of resistance (Briandet et al. 2001; Takahashi et al. 2010). Biofilms are more prevalent in nursing homes and hospitals. They are found in industrial pipes and home, biomaterials like medical devices like urinary catheters and implants, contact lenses, and plant and animal tissues, etc.

Despite the fact that synthetic antimicrobial agents have already been approved in many countries, researchers are seeking natural antimicrobial agents because they are derived from microbial, animal, and plant sources (Gyawali and Ibrahim 2014; Moloney 2016). There has been promising success in reducing the emergence of antibiotic resistance in bacterial pathogens using these compounds (Rossiter et al. 2017). The compounds derived from plants have shown to be the most promising option in the fight against bacterial infections. The mode of action of various plant-based bioactive compounds against microorganisms is shown in Fig. 17.3.

There is abundant evidence that these compounds have beneficial effects that work against bacteria and fungi and also have antioxidant properties. By increasing the potency of older antibiotics, they can restore the clinical application of these drugs and prevent resistance from developing (Barbieri et al. 2017). Plant-derived compounds based on their chemical structure can be categorized into various classes including alkaloids, polyphenols, sulfur-containing compounds, and terpenoids.

17.2.1 Alkaloids

The chemical structure of alkaloids is extremely diverse because they are heterocyclic nitrogen compounds. A number of studies have proven that alkaloids can be

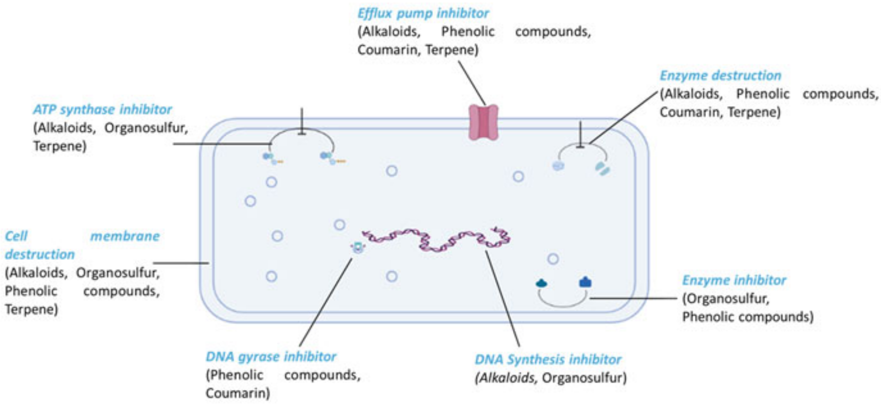

Fig. 17.3 Mode of action of various plant bioactive compounds as antimicrobial agents

used to treat infectious diseases, and their antibacterial properties have been well established (Cushnie et al. 2014). EPI activity makes up the most important mechanism of action for alkaloids as antibacterial agents. Table 17.1 shows important alkaloids and their mode of action.

17.2.2 Organosulfur Compounds

Studies that have been done on sulfur-containing compounds that originate from plants have found that they have antibacterial and antifungal properties (Kim et al. 2006; Iranshahi et al. 2008). A wide range of sulfur-containing compounds have been discovered to display antibacterial properties, including allicin, ajoene, dialkenyl, and dialkyl sulfides, *S*-allyl cysteine, *S*-ally-mercapto cysteine, and isothiocyanates (Barbieri et al. 2017; Sobolewska et al. 2015). Based on the investigations conducted, it has been found that plants with high organosulfur compound concentrations can exhibit a broad spectrum of antimicrobial properties (Asili et al. 2019; Boghrati and Iranshahi 2018); details are listed in Table 17.1.

17.2.3 Phenolic Compounds

There are many bioactive compounds in phenolic compounds that have been used to treat a variety of medical conditions. Various mechanisms are involved in the modulation of antibiotic activity by these molecules as bioactive molecules (Farhadi et al. 2019a; b; Ramezani et al. 2004; Górniak et al. 2019). Majority of phenolic compounds show one of the most significant mechanisms for antimicrobial activity, i.e., by reducing the efflux pump activity. Table 17.1 lists important phenolic compounds and their mode of action.

Table 17.1 Different classes of bioactive compounds with antimicrobial activity and mechanism of action (adapted from Khameneh et al. 2019)

Class of compound	Name of compound	Source of compound	Mechanism of action	Activity on microorganism	References
Alkaloids	Piperine	*Piper nigrum* and *Piper longum*	Efflux pump inhibitor	Methicillin resistant *Staphylococcus aureus* (MRSA) And *Staphylococcus aureus*	Khameneh et al. 2015
	Berberine	Berberis species *Rhizoma coptidis* and *cortex phellodendri*	Cell division inhibitor, protein, and DNA synthesis inhibitor	*Escherichia coli Candida albicans*	Boberek et al. 2010; Zoric et al. 2017
	Ungeremine	*Pancratium illyricum L*	DNA cleavage, inhibiting the bacterial topoisomerase IA	*Flavobacterium columnare*	Casu et al. 2011; Schrader et al. 2013
	Quinoline	*Teclea afzelii*	Inhibit type II topoisomerase enzymes and inhibit the DNA replication	*Escherichia coli, Bacillus subtilis, Microsporum audorium*	Lin et al. 2000; Kuete et al. 2008; Heeb et al. 2011
	Reserpine	*Rauwolfia serpentina*	Efflux pump inhibitor	*Staphylococcus sp., streptococcus sp., Micrococcus sp., A. baumannii*	Sridevi et al. 2017
	Sanguinarine	*Chelidonium majus, Sanguinaria canadensis, macleaya cordata*	DNA intercalator, transcription inhibitors	MRSA	Obiang-Obounou et al. 2011; Al-Ani et al. 2015
	Tomatidine	*Solanum lycopersicum, S. tuberosum, S. melongena L.*	ATP synthase inhibitor	*Listeria, Bacillus* and *Staphylococcus spp*	Lamontagne Boulet et al. 2018; Guay et al. 2018

(continued)

Table 17.1 (continued)

Class of compound	Name of compound	Source of compound	Mechanism of action	Activity on microorganism	References
	Chanoclavine	*Ipomoea muricata*	Efflux pump inhibitor	*E. coli*	Dwivedi et al. 2019
	Solasodine	*Solanum nigrum L*	Destruction of bacterial membrane	*C. albicans*	Chang et al. 2017
	Conessine	*Holarrhena antidysenterica*	Efflux pump inhibitor	*Pseudomonas aeruginosa*	Siriyong et al. 2017
	Lysergol	*Rivea corymbosa, Ipomoea violacea, and Ipomoea muricata*	Efflux pump inhibitor	*E. coli*	Maurya et al. 2013; Khanuja et al. 2006
Organosulfur compounds	Allicin	*Allium sativum*	Sulfhydryl-dependent enzyme inhibitor, DNA, and protein synthesis inhibitor	*Staphylococcus epidermidis, P. aeruginosa, Streptococcus agalactiae*	Reiter et al. 2017
	Ajoene	*Allium sativum*	Sulfhydryl-dependent enzyme inhibitor	*Campylobacter jejuni*, *Streproproteus*, *Staphylococcus, and E. coli*	Rehman and Mairaj 2013
	Isothiocyanates (ITCs)	Brassicaceae family *Brassica oleracea var. botrytis* *B. oleracea var. capitata, B. juncea* *Armoracia rusticana*	Inhibit ATP binding sites	*Helicobacter pylori*	Park et al. 2013
	Sulforaphane	*Diplotaxis harra*	Destruction of bacterial membrane, ATP synthase inhibitor, DNA, and protein synthesis inhibitor	*E. coli*	Wu et al. 2012

	Allyl ITCs	*Armoracia Rusticana and Eutrema japonicum*	Leakage of cellular metabolites	*E. coli*, *S. aureus*	Lu et al. 2016; Luciano and Holley 2009
	Benzyl ITCs	*Alliaria petiolata*	Disturb the membrane integrity	MRSA	Dias et al. 2014; Sofrata et al. 2011
	Phenethyl ITCs	*Brassica campestris* and *Brassica rapa*	Intracellular accumulation of reactive Oxygen species, depolarization of mitochondrial membrane	*E. coli*, *MRSA*, *Alternaria brassicicola*	Aires et al. 2009; Drobnica et al. 1968; Calmes et al. 2015
	Berteroin	*Brassica oleracea L*		*Helicobacter pylori*	Haristoy et al. 2005
Phenolic compounds	Resveratrol	*Vitis vinifera, Rubus idaeus, Morus alba, Vaccinium subg. Oxycoccus, Vaccinium sect. Cyanococcus*	Efflux pump inhibitor	*Campylobacter jejuni*, *Mycobacterium smegmatis*	Klancnik et al. 2017; Lechner et al. 2008
	Baicalein	*Thymus vulgaris, Scutellaria baicalensis,* and *Scutellaria lateriflora*	Efflux pump inhibitor	*C. albicans, M. smegmatis, MRSA*	Lechner et al. 2008; Chan et al. 2011; Huang et al. 2008
	Biochanin A	*Cicer arietinum*	Efflux pump inhibitor	*Chlamydia spp., M. smegmatis, MRSA*	Lechner et al. 2008; Zou et al. 2014; Hanski et al. 2014
	Chrysosplenol-D	*Artemisia annua*	Efflux pump inhibitor	*S. aureus*	Stermitz et al. 2003
	Chrysoplenetin	*Artemisia annua*	Efflux pump inhibitor	*S. aureus*	Stermitz et al. 2003
	Silybin	*Silybum marianum*	Efflux pump inhibitor	*S. aureus*	Stermitz et al. 2001
	Quercetin		Efflux pump inhibitor	*S. aureus*	Brown et al. 2015
	Chalcones (4′,6′-Dihydroxy-3′,5′-dimethyl-2′-methoxychalcone;	*Dalea versicolor*	Efflux pump inhibitor	*S. aureus*	Belofsky et al. 2004; Holler et al. 2012a, b

(continued)

Table 17.1 (continued)

Class of compound	Name of compound	Source of compound	Mechanism of action	Activity on microorganism	References
	4-phenoxy-4′-dimethylamino Ethoxychalcone; 4-dimethylamino-4′-dimethylamino Ethoxychalcone)				
	Epigallocatechin gallate		DNA gyrase, Beta-ketoacyl-[acyl carrier protein] reductase (FabG) Inhibition of dihydrofolate reductase	*E. coli, Stenotrophomonas maltophilia*	Gradisar et al. 2007
	Chebulinic acid	*Terminalia chebula*	DNA gyrase	*M. tuberculosis*	Patel et al. 2015
	Eriodictyol	*Eriodictyon californicum*	Beta-ketoacyl acyl carrier Protein synthase (KAS) III	*E. faecalis*	Jeong et al. 2009; Deng et al. 2020
	Rhamnetin		Efflux pump inhibitor	*S. aureus*	129 Brown et al. 2015
	3-*p*-trans-coumaroyl-2-hydroxyquinic acid	*Cedrus deodara*	Damage to the cytoplasmic membrane	*S. aureus*	Wu et al. 2016
	Naringenin	*Ficus carica*	Beta-Ketoacyl acyl carrier protein synthase (KAS) III	*E. faecalis*	Jeong et al. 2009; Salehi et al. 2019
	Myricetin	*Vaccinium subg. Oxycoccus*	Efflux pump inhibitor	*M. smegmatis*	Lechner et al. 2008
	Kaempferol	*Alpinia calcarata*	Efflux pump inhibitor	*C. albicans* and MRSA	Randhawa et al. 2016; Shao et al. 2016

	Kaempferol rhamnoside	*Persea lingue*	Efflux pump inhibitor	*S. aureus*	Holler et al. 2012a, b
	Luteolin	*Daucus carota* subsp. *sativus, Piper nigrum, Brassica oleracea* var. *capitata*	Efflux pump inhibitor	*Mycobacteria spp*	Lechner et al. 2008; Rodrigues et al. 2011
	Formononetin		Efflux pump inhibitor	M. smegmatis	Lechner et al. 2008
	Genistein	*Lupinus argenteus*	Efflux pump inhibitor	*S. aureus*	Belofsky et al. 2004
	Orobol	*Lupinus argenteus*	Efflux pump inhibitor	*S. aureus*	Belofsky et al. 2004
	Bergamottin epoxide	*Citrus paradisi*	Efflux pump inhibitor	*MRSA*	Abulrob et al. 2004
	Apigenin	*Matricaria chamomilla, Hypericum perforatum*	d-Alanine, d-alanine ligase	*H. pylori* and *E. coli*	Wu et al. 2008; Shankar et al. 2017
	Sophoraflavanone B	*Desmodium caudatum*	Inhibit cell wall biosynthesis	*MRSA*	Mun et al. 2013; 2014
	Sakuranetin	*Polymnia fruticose*	Inhibited FabZ	*H. pylori*	Zhang et al. 2008
	Taxifolin	*Allium cepa, tamarind seeds, Pinus pinaster*	Beta-Ketoacyl acyl carrier protein synthase (KAS) III	*E. faecalis*	Jeong et al. 2009
	3,6-Dihydroxyflavone		Beta-Ketoacyl acyl carrier protein synthase (KAS) III and I	*E. coli*	Farhadi et al. 2019a, b
	Curcumi	*Curcuma longa*	Sortase A	*S. aureus* and *E. coli*	Tyagi et al. 2015
	Morin	*Rhus verniciflua*	Sortase A and B	*S. aureus*	Kang et al. 2006
	4′,7,8-trihydroxyl-2-isoflavene		Urease inhibitor	*H. pylori*	Xiao et al. 2013
Coumarin	Aegelinol	*Ferulago campestris*	DNA gyrase inhibitor	*Salmonella enterica serovar Typhi, Enterobacter aerogenes,*	Basile et al. 2009

(continued)

Table 17.1 (continued)

Class of compound	Name of compound	Source of compound	Mechanism of action	Activity on microorganism	References
				Enterobacter cloacae, S. aureus, H. pylori	
	Agasyllin	*Ferulago campestris*	DNA gyrase inhibitor	*S. enterica serovar Typhi, E. aerogenes, E. cloacae, S. aureus, H. pylori*	Basile et al. 2009
	4′-senecioiloxyosthol		DNA gyrase inhibitor	*B. subtilis*	Tan et al. 2017
	Osthole	*Cnidium monnieri* and *Angelica pubescens*	DNA gyrase inhibitor	*B. subtilis, S. aureus, K. pneumoniae, MSSA*	Tan et al. 2017
	Asphodelin A 4′-*O*-β-D-glucoside	*Asphodelus microcarpus*	DNA gyrase inhibitor	*S. aureus, E. coli, P. aeruginosa, C. albicans, Botrytis cinerea*	El-Seedi 2007
	Asphodelin A	*Asphodelus microcarpus*	DNA gyrase inhibitor	*S. aureus, E. coli, P. aeruginosa, C. albicans, B. cinerea*	El-Seedi 2007
	Bergamottin epoxide	*Citrus paradisi*	Efflux pump inhibitor	*MSRA*	Roy et al. 2013
	6-Geranyl coumarin		Efflux pump inhibitor	*S. aureus*	de Araujo et al. 2016
	Galbanic acid	*F. galbaniflua* Boiss. & Buhse, *F. szowitsiana* DC., and *F. Assa-foetida* Boiss. & Buhse	Efflux pump inhibitor	*S. aureus*	Bazzaz et al. 2010; Kasaian et al. 2013
Terpene	α-Amyrin	*Licania pyrifolia* Grisebach, *Centella asiatica*	Cell membrane disturbance	*E. coli*	Broniatowski et al. 2015
	Carvacrol	*Thymus capitatus*	Cell membrane disturbance, efflux pump inhibition	*A. niger, A. fumigatus, A. flavus, A. ochraceus, Alternaria alternata,*	Abbaszadeh et al. 2014; Althunibat et al. 2016

				Botrytis cinerea, Cladosporium spp., Penicillium citrinum, P. chrysogenum, Fusarium oxysporum, Rhizopus oryzae, E. coli, E. aerogenes, S. aureus, P. aeruginosa	
	Cinnamaldehyde	*Cinnamon trees*	Cell membrane disturbance	*H. pylori, E coli, S. aureus*	Zhang et al. 2015; Ali et al. 2005
	Dehydroabietic acid	*Pinus* sp.	Cell membrane disturbance	*S. aureus*	Söderberg et al. 1996; Helfenstein et al. 2017
	Eugenol	*Syzygium aromaticum, Ocimum tenuiflorum, Curcuma longa, Laurus nobilis*	Cell membrane disturbance	*A. niger*, *A. fumigatus*, *A. flavus*, *A. ochraceus*, *Alternaria alternata*, *Botrytis cinerea*, *Cladosporium spp.*, *Penicillium citrinum*, *P. Chrysogenum*, *Fusarium oxysporum*, and *Rhizopus oryzae*, *H. pylori*, *MRSA, MSSA*, *P. aeruginosa*	Abbaszadeh et al. 2014; Ali et al. 2005; Yadav et al. 2015; Rathinam et al. 2017; Khalil et al. 2017
	Farnesol	*Cymbopogon nardus*, *C. citratus, Polianthes tuberosa L.*, *Cyclamen persicum*, *Rosa hybrida*, *Citrus aurantium subsp. Amara*, *Abelmoschus moschatus*	Cell membrane disturbance	*S. aureus*	Togashi et al. 2010a, b; Jung et al. 2018

(continued)

Table 17.1 (continued)

Class of compound	Name of compound	Source of compound	Mechanism of action	Activity on microorganism	References
	(4R)-(−)-carvone		Cell membrane disturbance, inhibits the transformation of cellular yeast form to the filamentous form	*C. jejuni*, *Enterococcus faecium*, *E. coli*, *C. albicans*	De Carvalho and Da Fonseca 2006; Paduch et al. 2007a, b
	(4S)-(+)-carvone		Cell membrane disturbance	*L. monocytogenes*	De Carvalho and Da Fonseca 2006
	Nerolidol	*Piper claussenianum, Zanthoxylum hyemale* A. St.-Hil, *Zornia brasiliensis* Voge, *Swinglea glutinosa* (Blanco) Merr.	Cell membrane disturbance	*S. aureus*	Togashi et al. 2010a, b; Chan et al. 2016
	Menthol	*Mentha canadensis*	Cell membrane disturbance	*A. niger, A. fumigatus*, *A. flavus*, *A. ochraceus*, *Alternaria alternata*, *Botrytis cinerea*, *Cladosporium spp.*, *Penicillium citrinum*, *P. Chrysogenum*, *Fusarium oxysporum*, *Rhizopus oryzae*	Abbaszadeh et al. 2014; Kamatou et al. 2013
	Thymol	*Thymus capitatus*	Inhibits H(+)-ATPase in the cytoplasmic membrane, cell membrane disturbance, efflux pump inhibition	*C. albicans*, *C. glabrata*, *C. krusei*, *A. niger*, *A. fumigatus*, *A. flavus*, *A. ochraceus*, *Alternaria alternata*, *Botrytis cinerea*, *Cladosporium*	Sharifzadeh et al. 2018; Abbaszadeh et al. 2014; Althunibat et al. 2016

				spp., *Penicillium citrinum*, *P. chrysogenum*, *Fusarium oxysporum, Rhizopus oryzae, E. coli*, *E. aerogenes*, *S. aureus*, *P. aeruginosa*, *Salmonella typhimurium*, *S. enteritidis*, *S. saintpaul*	
	Ursolic acid	*Vaccinium* subg. *Oxycoccus*, *Ocimum basilicum*, *rosemary*, *Lavandula*	Cell membrane disturbance	*E. coli*	Broniatowski et al. 2015

17.2.4 Coumarins

Plants and microorganisms both produce coumarins in nature (Smyth et al. 2009). Coumarins have been reported to possess a variety of physiological roles, including analgesic, anticoagulant, anti-inflammatory, estrogenic, sedative and hypnotic, hypothermic, anti-helminthic, anticancer, antioxidant, and dermal photosensitizer vasodilator (Kayser and Kolodziej 1999; Kostova 2005; Wu et al. 2009; Al-Majedy et al. 2017). Table 17.1 lists important coumarins and their mode of action.

17.2.5 Terpenes

Terpenoids can be divided into two categories: isoprenoids and terpenes. In nature, cholesterol, steroids, and quinones are ubiquitous and play numerous roles from forming the primary structural material of cells (cholesterol) to participating in the cellular functions (Paduch et al. 2007a; b; Oldfield and Lin 2012). Additionally, they are plentiful in flowers, fruits, and vegetables. In particular, they can be observed abundant in foliage of plants and the reproductive structures. Herbal resins are primarily composed of terpenes, which are also responsible for the characteristic aroma of the resin (Paduch et al. 2007a; b). The defense against herbivores and pathogens provided by various terpenes and derivatives has been demonstrated (Paduch et al. 2007a; b; Togashi et al. 2010a; b; Lee and Ho 2008; Catteau et al. 2018; Shakeri et al. 2017). Various plant terpenes with potential antibacterial properties are discussed in Table 17.1.

17.3 Plant-Based Compounds with Anticancer Features

Cancer is a devastating disease that causes an increase in health and economic burden worldwide. Cancers could result from inflammatory processes and dysfunction in cell cycle regulation that leads to the rapid growth of cells. This type of uncontrolled cell growth shows certain characteristics (i) inhibition of apoptosis process, (ii) rapid induction of angiogenesis, (iii) potent ability of replication, (iv) compromised immunity, and (v) lastly invasion and metastasis (Fig. 17.4). Many medical interventions and approaches like chemotherapy and radiotherapy are used to provide treatment to the disease but many of these remedies have certain side effects that result in compromised quality of patient life and recurrence of disease is one of the major concerns. The plant-based secondary metabolites are popularly used in the last decade to effectively treat not only disease but also reduce the chances of its reoccurrence and also increase the effectiveness of chemotherapy in combination.

Bioactive compounds derived from various plant parts have been extensively studied and reported to be successful in effective management of a variety of cancer. Several anticancer agents have the ability to inhibit cell cycle in breast cancer cells (Kolodziej et al. 2015) and L1210 leukemia cells (Yamasaki et al. 2007). Some

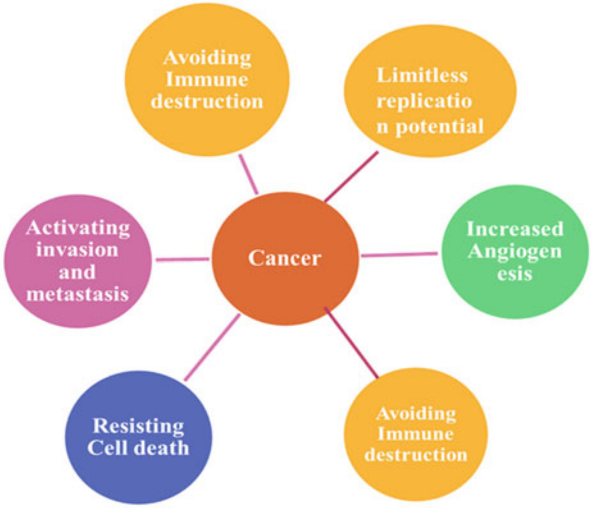

Fig. 17.4 General characteristics of Cancerous cell

phytobioactive compounds like colchicine are widely used as anticancerous agents as they destabilize the formation of microtubules; therefore, it ceases cell division process in A549 (human non-small cell lung cancer cell line) and MDA-MB231 (human breast cell lines). Growing bodies of evidence also suggest that bioactive compounds like curcumol, dinoxin B, etc. possess anti-apoptosis properties to control unlimited cell division. They induce apoptosis via alternating proapoptosis and anti-apoptosis protein expression (Chinnasamy et al. 2010; Vermillion et al. 2011; Shankara et al. 2016). Limonoids isolated from *Azadirachta indica* trigger apoptosis in HL60 leukemia cells by activating caspase 3, 8, and 9 (Kikuchi et al. 2011; Sophia et al. 2018). Moreover, polyphenol cynidine isolated from *Glycine max* exhibits potent anti-inflammatory effects via suppressing COX-2 (cyclooxgenase-2) and iNOS (inducible nitric oxide synthase) expression (Wang et al. 2010). In the past decade, a number of plant-based bioactive compounds having anticancer activities have been identified. Their detailed molecular mechanisms of action against various cancers are summarized in Table 17.2 and Fig. 17.5.

17.4 Conclusions and the Future Scope

The present chapter deals with evaluation of various bioactive compounds for their antimicrobial and anti-carcinogenic protective effects in human health. These compounds are mainly found in fruits and vegetables; and their consumption in diets with appropriate valuable health effects makes them a suitable candidate for development of new functional food with potential protective properties. Recently, the idea that natural remedies are more secure for use in comparison with prescription medications has gained traction and contributed to an enormous growth in

Table 17.2 Bioactive compounds with anticancer properties and their mode of action

Tested Cell line/organ	Plant source	Compound name	Dose/ concentration	Mode of action	References
MDA-MB-435 (Breast cancer cell line)	*Bellevalia eigii*	Isoflavanone	1.0–1.1 μM	Induce apoptosis	Alali et al. 2015; El-elimat et al. 2018
Jurkat T cells	*Inula japonica*	Sesquiterpene	5.9 μM	Trigger apoptosis	Xu et al. 2015
HSC-T6 (hepatic stellate cells)	*Curcuma longa*	Curcumol	30 μM	Induce apoptosis through PI3K/NF-κB pathway	Chen et al. 2014
Multiple myeloma cell lines	*Allium sativum*	Alliin	3 mg/ml	Trigger apoptosis through PI3K pathway	Petrovic et al. 2018, Li et al. 2018
MCF-7 cells (human breast adenocarcinoma cell line)	*Hypericum calycinum*	Hypericin	0.5 μg/ml	Induce apoptosis	Mirmalek et al. 2016
Human colon adenocarcinoma (HCT 15) and human larynx cancer cell lines (Hep-2)	Datura innoxia	Dinoxin B	300 μg/ml	Trigger apoptosis: by decreasing expression of antiapoptotic Bcl-2 protein	Chinnasamy et al. 2010, Vermillion et al. 2011
MCF-7 (Human mammary gland adenocarcinoma) and A549 (Human lung cancer cell line)	Terminalia chebula	Phenolics/ flavanoi ds	643.13 μg/ml	Induce apoptosis by regulating the Bcl-2 family protein expression	Shankara et al. 2016
Human gastric cancer SGC-7901 cells	Cannabis sativa	Cannabidiol	23.4 μg/ml	Cell cycle inhibition at the G0–G1 stage, induce apoptosis by downregulating the Bcl-2 expression levels	Zhang et al. 2019; Daris et al. 2019
Breast cancer cells MDAMB231	Raphanus sativus	Roscovitine	10 μg/ml	Cell cycle inhibition	Kolodziej et al. 2015
BALB/c mouse-tumor model	Gingiber officinale	Zingerone	2 mM	Cell cycle inhibition	Choi et al. 2018; Bae et al. 2019
HL60 leukemia cells	Azadirachta indica	Limonoids	2.7–3.1 μM	Induce apoptosis by activation of activated caspases 3, 8, and 9	Kikuchi et al. 2011; Sophia et al. 2018

A549 lung cancer cells	Murraya koenigii	Girinimbine	19.01 μM	Induce apoptosis by activating caspase 9 and 8	Mohan et al. 2013; Bhoj et al. 2019
A549 cell line	Ipomoea carnea	Leaves extract	40.0 μg/ml	Show cytotoxic effects	Rane and Patel 2015; Marilena et al. 2012
Cervical OV2008 and breast MCF-7 cancer cells	Ziziphus mauritiana	Coumaroyl alphitolic	0–3 mg/ml	Induce apoptosis by modulating BAX/Bcl-2 ratio	Abedini et al. 2016; Minna et al. 2018
A549 (human non-small cell lung cancer cell line) and MDA-MB231 (human breast cell lines)	*Gloriosa superba*	Colchicine	60 nM	Microtubule destabilization	Balkrishna et al. 2019; Kumar et al. 2016
Jurkat leukemic T cells	*Catharanthus roseus*	Vinblastine	10, 500 and 1000 μg/ml	Apoptosis induces the DNA-binding activities of the transcription factor NFκB	Ahmad et al. 2010; Selimovic et al. 2013
451Lu melanoma cells	*Acacia greggii*	Fisetin	40–80 μM	Cell cycle arrest	Syed et al. 2011
Mammalian lung adenocarcinoma	*Brassica vegetables*	Indole-3-carbinol (I3C)		Modulation of PI3K/Akt signaling pathway	Wang et al. 2012a, b
HT-29 human colon adenocarcinoma cells	*Glycine max*	Cyanidin	1 microM	Suppression of iNOS and COX-2 gene expression	Kim et al. 2008
L1210 leukemia cells	*Flemingia vestita*	Genistein	3.5 to 6.2 mg/ml	Cell cycle inhibition	Yamasaki et al. 2007
MCF-7 and MDA-MB-231 breast cancer cells	*Crocus sativus L.*	Crocetin	400 μg/ml	Induce apoptosis	Chryssanthi et al. 2007; Gutheil et al. 2012
Vascular smooth muscle cell	*T. Asthmatica (syn. T. indica)*	Tylophorine	0.13 μmol/l (IC50)	Cell cycle arrest	Joa et al. (2019)

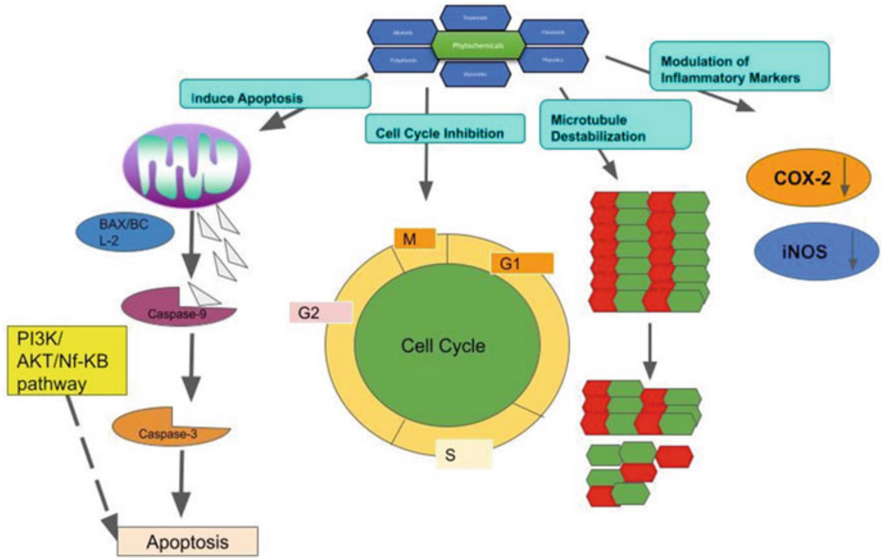

Fig. 17.5 Overview of the molecular actions of bioactive compounds leading to anticancer effect

phytopharmaceutical applications. Therefore, future research can focus on the characterization of new natural compounds using plants as a safe source and the effect of different herb combinations, like therapeutic cocktails for future beneficial progressions. These studies will address the development of new natural antibiotics and better pharmaceutical products to resolve the problem of adverse effects associated with most synthetic drugs and to help to battle the threat of cancer and bacterial infections which are life-threatening diseases that have affected and killed large numbers of people. The use of emerging technologies, such as nanotechnology, bio-adhesive technology and materials, edible packaging materials in combination with plant bioactive components, should be considered in order to improve the efficiency of plant antimicrobial components. Studies are needed for exploring ways to use natural plant products with anticancer effects along with standard chemotherapy treatments to increase potency while reducing side effects of actual drugs.

There are minimal data and research on plant extract application in food systems as antimicrobials, and significant knowledge gap between traditional utilities and scientific evidence for their health attributes; therefore, continued research is essential to understand the exact mechanisms of their biological actions. Popularizing fruits and vegetable-eating habits and their health resources to consumers will benefit from their positive health effects. The present review can also help investigators in developing countries working on plants, to re-focus their research works.

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Role of Functional Foods in Cardiovascular Disease Prevention

18

Luxita Sharma

Abstract

Functional foods are a class of bioactive compounds that have proven benefits on the human health, especially the prevention of cardiovascular diseases. The foods having these benefits are components of our daily diets. Functions foods have the capability of lowering the blood lipid levels, reducing the low-density lipoproteins, prevention plaque deposition and also platelet aggregation. Nutrition composition of the foods matters because of their phytoprotective substances and bioactive compounds which reduce the cardiovascular risk. The functional foods such as flavonoids, phytochemicals and antioxidants present in plant and animal sources act as cardio-protective agents. The legumes, peas and lentils are rich in iron, antioxidants and healthy proteins which are helpful in maintaining heart health and reducing the blood levels of atherosclerotic LDL cholesterol. The interaction of functional food bioactive compounds such as phenolic acids, hydroxybenzoic acids, omega-3 fatty acids and PUFA is linked to prevention of degeneration of heart muscles and arteries. One of the animal sources that rich in functional foods is the Fish. It has Omega-3 fatty acids and the intake of fish twice a day strengthens the heart muscles. As concluded in many researches, the fish is a functional food source that has high levels of good fats and high proteins which are recommended for heart. Therefore, this area has many science-based evidences which would be elaborated to enlighten the subject further.

Keywords

Cardiovascular disease · Functional foods · Nutrition · Antioxidants · Phytochemicals

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18.1 Introduction

Functional foods have active compounds present in all food groups such as cereals and its products, pulses, milk and milk products, fruits and vegetables. The functional foods provide the nutritional benefits that are beyond meeting just the nutritional needs. The naturally occurring compounds in the foods are antioxidants, flavonoids and pigments that act as functional foods. An example of a naturally occurring functional food would be the probiotics in fermented foods, while an example of an added functional nutrient would be folic acid baked into cereal (Hasler et al. 2000).

There is no defined definition for functional foods, but the term functional foods exists in the world of nutrition. And it is high time that the people and our students should learn the 39 benefits of functional foods. The ingestion of funtional foods can stop the development of diseases in the body. The concept of the antioxidants and polyphenols is important for health and well-being of general population. The food industry knows the usage of functional foods in developing the food products. The functional foods are the natural ingredients present in the foods.

Functional foods are referred to those types of food products which not only fulfil the basic nutritional needs of the body but also provide certain beneficial effects to the health and help in managing and preventing different chronic diseases.

18.2 Cardiovascular Diseases

18.2.1 Introduction

Cardiovascular disease is a collective term used for different types of heart-related diseases (like coronary heart disease, heart failure, rheumatic heart disease and many more). Coronary artery disease has grown to be one of the major topics of concern in the medical world because of the increase in its cases. Coronary artery disease as the name suggests is related to the main artery of the heart which is coronary artery. This type of ailment or rather illness occurs when there is blockage of the artery by the accumulation of plaque in it (Pekka and Norrving 2011). An important phrase says that "Heart Known as The Bank of The Body" as heart supplies blood and oxygen to all the parts of the body. Most people are unaware of the causes of the disease.

18.2.2 Rheumatic Heart Disease

Another type of cardiovascular disease is the rheumatic heart disease. In other words, if streptococcal infection like scarlet fever or strep throat is not treated properly, then it can lead to the damage of the heart valves resulting in this type of heart condition. The other cardiac problems related to the diseases of heart or to be more precise, it is the other rheumatic heart conditions. The other conditions are the damage caused to the valves of heart are pericarditis, endocarditis and blockage caused in the heart

(Nkomo et al. 2006). Certain types of symptoms indicate the rheumatic heart disease such as painful joints with redness, swelling and warm on touching. Chest pain, heart murmur and jerky movements are other symptoms of the rheumatic heart disease. There are many other causes which can lead to the development of the illness as stress, unhealthy eating habits, increased weight, alcohol drinking, smoking and lack of physical exercise (Kumar et al. 2017).

18.2.3 Congenital Heart Disease

Congenital heart disease is termed as an abnormality or irregular defect in the heart which is developed or rather present at birth and is basically divided into three types which include problem in heart walls, blood vessels and the valves of the heart (National Heart, Lung, and Blood Institute 2015). It has been found out that it may be because of the genetic reasons or family history of the family or may be the result of some of the medications taken by the women during the term of pregnancy or even consumption of too much alcohol during pregnancy (National Heart, Lung and Blood Institute 2011). As far as the symptoms are concerned for congenital heart disease, at birth of the baby there are no such symptoms found except some of them which may include exercise problems, shortness in breathing, poor feeding, infection in lungs, poor gain in weight or slightly bluish tint on the skin (Hoffman 2005).

18.3 Functional Foods and Cardiovascular Diseases

"Functional foods are known to be those types of food substances which may or may not be fortified and provide various health-related benefits other than providing the basic nutritional need of the human body. Functional foods act as a weapon against cardiovascular diseases. In today's time, several doctors, especially dieticians, are recommending functional foods to their patients for the management of this disorder (Fig. 18.1). There are various types of functional foods which are effective in preventing and managing the cardiovascular diseases. There are certain food substances which can be functional and can be enjoyably eaten by the people suffering from cardiovascular disorders. This type of foods includes spreads which are low in cholesterol and are a rich source of these plant sterols and stanols, fruits and vegetables (Hasler et al. 2000).

After research, it has been found out that foods or rather functional foods contain high amounts of antioxidants, phytochemicals, flavonoids and high amounts of fibre. These compounds are known to control and manage cardiovascular disorders. The foods which we eat on a daily basis like tomatoes, onion, cabbage and certain types of fruits like the class of berries which may include cranberries, raspberries and cherries are considered to be good sources of the above-mentioned nutrients and play an important role in managing these cardiovascular disorders. It has been found out that these above-mentioned nutrients help in reducing or rather lowering the

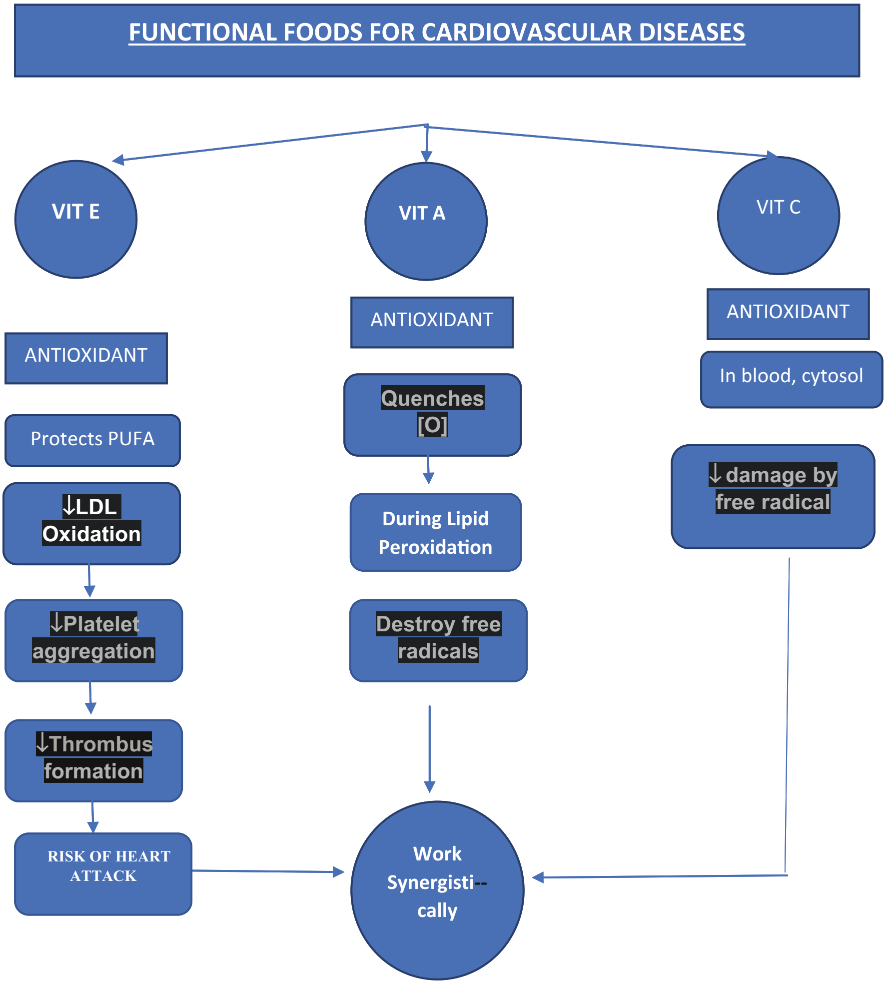

Fig. 18.1 Role of Vitamin E, A and C in protecting cardiac health

inflammation caused in the heart and blood vessels and enhance the endothelial function of the heart (Hasler et al. 2000).

In several research it has been found out that foods rich in omega 3 fatty acids, high in protein, and are low in saturated fats are considered to be good for cardiovascular disorders and also prepare the healthy cardiac organ. Omega-3 fatty acids help in lowering or reducing cholesterol (Chaddha and Eagle 2015).

The concept of Functional foods originated from Japan in 1980 because they wanted to find the food products which would be beneficial for the general population to help in curing ailments. The diet should contain foods from all the food groups which must include a source carbohydrate, a source of protein, a source of fat and sources of all the essential minerals and vitamins. This requirement can also be met by certain food products and nutritional supplement (Bjelakovic and Gluud 2007). The foods can be eaten naturally in form of salads, curries and pancakes. These food groups can be used to develop food products in a successful manner.

Then, these food products can be marketed and sold in the market as well. The food industry is fortifying the nutrients in the food products to make them nutritionally adequate for the general population. So, in order to keep your Heart, Kidneys, Liver, Brain and all other systems of the body then the functional foods is the answer.

In this chapter, we have elaborated the most common functional foods that we use daily in our diets. There are some of the non-vegetarian foods which are superfoods such as salmon and sea food. So, they can also be included in one's diet. The major functional foods which are helpful in managing cardiovascular diseases are discussed.

18.3.1 Cereal and Cereal Products

Whole grains are the staple part of Indian diets. The research is being explored, and the findings are given. Whole grains serve as class of superfoods. They have many benefits as explained as follows:

- **Lower the Risk of Heart Disease**: One of the greatest medical advantages of entire grains is that they bring down your danger of coronary illness, which is the main source of death worldwide, while most investigations bump together and a wide range of entire grains class is produced. The entire grain breads and oats, just as included wheat, have been explicitly connected to a lower danger of coronary illness (Nettleton et al. 2008).
- **Lower the Risk of Stroke**: Whole grains may likewise help bring down your danger of stroke. Those eating the most entire grains had a 14% lower danger of stroke than those eating the least. Besides, three mixes in entire grains—fibre, nutrient K and cell reinforcements—can decrease the danger of stroke. Whole grains are likewise prescribed in the DASH diet and Mediterranean eating regimen, the two of which may help bring down the danger of stroke (Mellen et al. 2008).
- **Reduce Chronic Inflammation**: Irritation is at the foundation of numerous perpetual diseases. Fortunately, some proof proposes whole grains can help reduce stress. Whole grains are important to reduce cell inflammation and injury. This makes the cells of the body healthy (Katcher et al. 2008).

18.3.2 Role of Pearl Millet in Managing Cardiovascular Diseases

Lack of physical activity, obesity, improper dietary habits and smoking can lead to increase in the incidence of heart attacks (NHLBI 2016). Many countries in the world are facing high rate of heart diseases. It has been found that when food rich in dietary fibres is consumed, it lessens the total serum cholesterol level and low-density lipoproteins. Atherosclerosis is often characterized by the oxidation of low-density lipoproteins which can be prevented by the phenolic extracts of the pearl millet as they hinder this oxidation reaction which is copper catalysed by approximately 30% at a concentration of 50 μl/ml. These millet phenolics inhibit this reaction possibly by chelating cupric ions and scavenging of peroxyl radicals (Klevay 1975).

A positive relation is found between total phenolic content and antioxidant activity. The flavonoid content is important because of its health benefits. These benefits include mainly antioxidant activity and work synergistically with other antioxidants. The flavonoid content in pearl millet differs from 1721 to 2484 μg catechin equivalent per gram. Wheat flour also found to have the same range of flavonoid content (Emiola and De la Rosa 1981). The presence of transition metals functions as catalyst in the free radical's generation. The metal chelators can lead to the stabilization of the metal ions in vivo and hinder the radical production which in turn lessens the damage caused by free radicals. But the metal chelating activity was observed to be more in chapatti. The decrease in phenolic content can be due to the heat effect as heat-sensitive phenolic compound can be destroyed because of reduction and degradation. The increase in metal chelating activity can be attributed to formation of Maillard reaction in products (Jayalaxmi et al. 2018). In research, it was found that total phenolic compounds in the pearl millet are higher than the African locust bean. This suggests that the daily consumption of pearl millet can serve as a good source of dietary antioxidants.

18.3.3 Oats and Heart Health

The American Diabetes Association to optimize aldohexose utilization and enhance internal secretion sensitivity recommends a diet low in saturated fat, cholesterol, with 20–35 g/day of fibre (USDA 2015). Oats are significantly hypocholesterolemic and decrease total and LDL steroid alcohol by 2–23%. Oats improves supermolecule profile by considerably enhancing the blood concentrations of HDL cholesterol in conjunction with apolipoprotein A-1, a serious part of lipoprotein. As oats are loaded with β-glucan, they are thought about to be sensible choice as β-glucan possess potential to regulate blood sugar level and reduces all the danger factors to learn the treatment of polygenic disorder and associated complications. β-glucan in oats is conjointly known with the wound-healing properties (Richardson and Peltola 2004) (Fig. 18.2).

Oats are systematically hypocholesterolemic, no matter whether they are incorporated into energy- and fat-restricted diet. Oats were shown to cut back

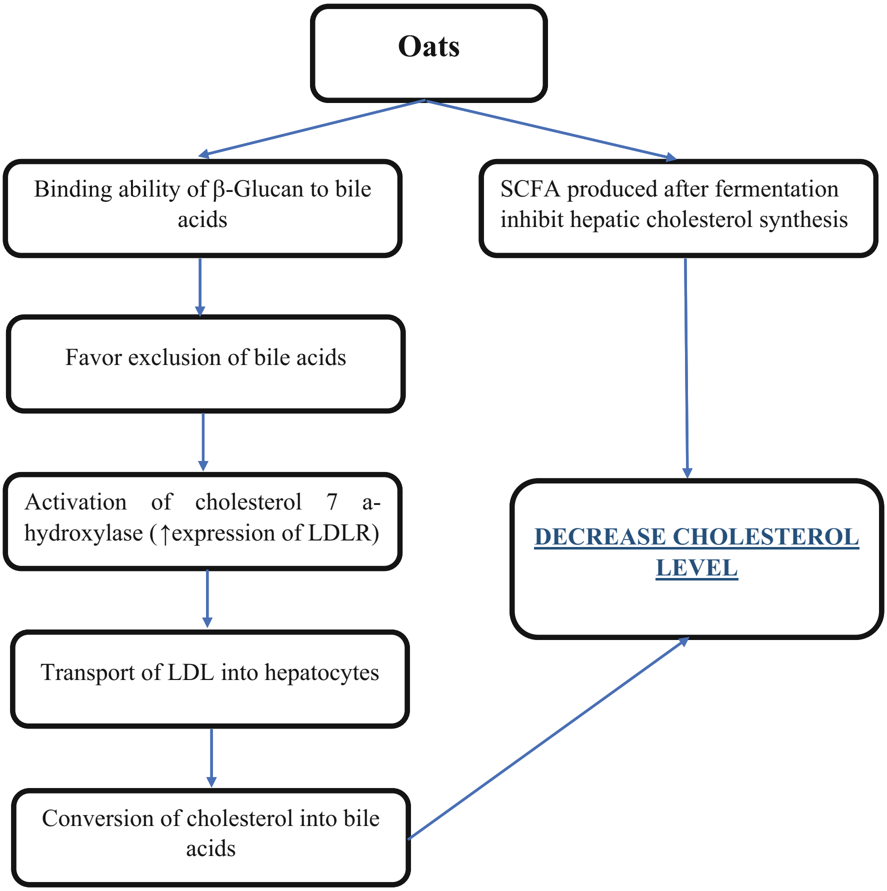

Fig. 18.2 Cholesterol-lowering action of oats

blood steroid alcohol levels even once a baseline diet low in fat is consumed. In most of the studies given, oats reduced LDL cholesterol levels. In many studies, however, oats improved blood concentrations of HDL cholesterol in addition to apolipoprotein A-I, a part of lipoprotein.

Several studies claim that β-glucan (beta-glucan) is that the major active cholesterol-reducing part of oats. Oat's soluble fibre forms a viscous gel. This gel then binds gall acids and will increase their excretion through faecal matter. The ingestion of oats showed the hypocholesterolemic effectiveness in subjects with higher blood cholesterol levels (Richardson and Peltola 2004).

Oats will lower cholesterol levels with fermentation of beta-glucan which will increase the release of short-chain fatty acids, which can inhibit cholesterol synthesis. Soluble fibres of oats could reduce the enteral absorption of cholesterol (Queenan et al. 2007).

It has been suggested that Oats with DASH (dietary approaches to prevent high blood pressure) diet could be beneficial in maintaining blood pressure which is due to its high fibre content. Alternative medicine, clinical, and animal studies proven the reduced high blood pressure with fibre sources, together with oats ingestion (JCHI 2004).

A pilot run study for the comparison of oats and wheat was conducted on thirty-six subjects, and the antihypertensive properties of oats were examined. It was found that majority of the patients eliminated or reduced their requirements for hypertensive medications. The antihypertensive effects, of oats are due to viscous soluble fibre that yields positive impact by mantaining the glycemic and insulinemic profiles.

In an ongoing trial, it has been hypothesized the potential of oat consumption and therefore the B-glucans, phytoestrogens, and fat-soluble inhibitor contents in oats play vital roles in mediating epithelium responses to foods, which can be a vital determinant in CHD (coronary heart disease) risk and also reduce the risk of hypertension. Oats have multipurpose functions, and they help to maintain a healthy body (Singh et al. 2013).

18.3.4 Serum Lipid Reduction with Quinoa

18.3.4.1 Nutritional Profile of Quinoa

Quinoa is a rich bouquet of health benefits, majorly all because of its great nutrient composition. Different varieties of it have different nutrient content, but almost all the varieties have their protein content in the range of 13.81 to 21.9%. It is also considered as the only plant with all the essential amino acids present in it (Longvah et al. 2017).

The nutritional varieties and benefits of quinoa have made it popular worldwide. It is being widely recognized for it being a great source of protein and especially because of its high biological value and presence of essential amino acids, along with it is also a rich source of carbohydrate, mineral and vitamin and dietary fibre content (Vidueiros et al. 2015). Quinoa is also rich in bioactive compounds—polyphenols and triterpenoids (Filho et al. 2017). Apart from its vast nutritional background, quinoa is also becoming popular due to possession of many pharmacological properties and health benefits such as its hypocholesterolemic activity, antioxidant and anti-inflammatory properties and anticancer effects; also, not only it is safe and tolerated well by the patients of celiac disease, but also it helps in its treatment. Still a lot of research and human trials are needed to explore the untouched benefits of quinoa (Yao et al. 2015).

In a study conducted, twenty-four Wister rats were divided into four groups and were fed on quinoa seeds (310 g/kg), corn starch (control group), fructose (control group with 31% of fructose) and quinoa seeds (310 g/kg) with 31% fructose. It was found that the group that were fed upon quinoa seeds showed to have decreased levels of low-density lipoproteins by 57%, serum total cholesterol by 26%, triglycerides by 11per cent and glucose by 10%. In a double-blinded study, the effect of consumption of 24 g of quinoa flakes in comparison to 24 g of corn flakes for 4 weeks on the lipid profile was seen in 37 postmenopausal women who were overweight, and it was reported that the women who fed on quinoa flakes showed reduced levels of triglycerides, total cholesterol and LDL with increase in glutathione levels (De Carvalho et al. 2014).

18.3.5 Lipid Level Reduction Through Almonds

Almonds generally contain around 575 kcal per a hundred grams. However, the carboxylic acid composition of almonds is helpful, because monounsaturated fatty acids (MUFA) predominate and the saturated fat content (3.7 g per a hundred grams of almonds) is lowest. The fatty acids from almonds are important contributors to the useful health effects specifically reduced risk of vessel damage and abrupt internal organ death, lowering of blood cholesterol or improvement of lipoprotein (LDL) levels (Berryman et al. 2011). The entire macromolecule content of almonds is twenty-one per cent, creating them a decent supply of plant macromolecule, and also the proteins in almonds are high in essential amino acids. Almonds additionally contain five grams sugars per a hundred grams; they will be represented as “naturally low in sugars” below the new European regulation on nutrition 1924/2006 on nutrition and health claims.

18.3.5.1 Beneficial Fibre Content in Almonds

Whole natural almonds contain around twelve grams of dietary fibre per a hundred gram that is ample to assert “naturally high in fibre”. These embrace reduction within the risk of developing CHD and polygenic disease and positive effects on the system, e.g. prebiotic effects. Plant cell walls are supramolecular networks of polyose, hemicelluloses, cellulose substances and non-carbohydrate parts (e.g. phenoplast compounds) and that they are the foremost supply of dietary fibre. Different kinds of dietary fibre will attenuate the increase in postprandial glycaemia and lower plasma concentrations of cholesterol. Increasing the intake of dietary fibre can even increase satiety and reduce weight gain over time. The addition of round almonds to low-calorie diets for weight loss might increase satiation and lead to incomplete internal organ absorption of fat. These latter two effects are also due mostly to the high fibre and macromolecule contents of the nut. The structural characteristics of almond cell walls (dietary fibre) play a very important role. A typical serving of almonds (28–30 g) provides a substantial amount of the daily fibre demand (Lamarche et al. 2004).

In a study conducted on metallic element by Berryman et al. (2015), it was absolutely reported that almonds have a homogenous LDL cholesterol result in healthy subjects and in subjects with high cholesterol and polygenic disorder, within the management and independent settings. Almonds being low in saturated fatty acids and wealthy in unsaturated fatty acids, fibres, phytosterols, plant supermolecule, α-tocopherols, arginine, magnesium, copper, manganese, Ca and metallic element play a big role in cholesterol lowering. The mechanism of LDL

Cholesterol reduction is attributed to the nutrients present in the almonds. There is reduction in the cholesterol absorption in the body. Further , Almonds ingestion aids in the excretion of the extra cholesterol from the body. The enzymes that are concerned within the cholesterol synthesis and steroid production are regulated by the nutrients that are provided by the almonds.

18.3.6 Chia Seeds and Cardiovascular Disorders

Fibre is gift in considerable quantity in chia seeds that may absorb up to fifteen times water the load of seed. Chia seeds being high in fibre help in polygenic disorder by fastness down the digestion method and unleash of aldohexose; it conjointly facilitates peristaltic movement of intestine and decreases plasma steroid alcohol. The chia seeds lack protein that adds another positive purpose towards its consumption as can even be consumed by celiac patients. The nine essential amino acids are gift in considerable quantity in chia seeds (Ullah et al. 2015).

A study was conducted on twenty subjects with kind to controlled polygenic disorders (with medication). The themes were chosen indiscriminately. All subjects consumed 37 g of chia seeds (added in white bread) daily. The results showed that symptom and pulsation force per 58 unit area were controlled attributable to high fibre content of chia seeds. Chia seeds consumption on day after day resulted into magnified levels of ALA. Strokes and incidence of heart attacks could also be prevented attributable to the anticoagulant and anti-inflammatory impact of chia seeds (Vuksan et al. 2007).

The seeds vary in their super-molecule content from twenty five to forty percent. Their 60% content of lipids is ALA (n-3) and 20% is polyunsaturated fatty acids (n-6) (Álvarez-Chávez et al. 2008). Once chia seed oil is extracted, the remnants left are (33.9 g/100 g) of dietary fibre and (17 g/100 g) of macromolecule. Of the whole dietary fibre, the best fraction includes insoluble fibres (53 .45 g/100 g) that play an important role in fullness and correct bowel movements (Porras-Loaiza et al. 2014). Chia seed being rich in metallic element and phenolic compounds (majorly quercetin and kaempferol) provides important inhibitor activity, on the opposite hand, its Ca and mineral content suggest that it is going to be useful in CVD and high blood pressure (HBP) (Ulbricht et al. 2009).

18.3.7 Garden Cress Seeds and Heart Health

18.3.7.1 Lowers the Cholesterol Levels

The protective effect of garden cress seed extract and garden cress seed powder on hypercholesterolemic rats was reported. Hypercholesterolemic rat showed a significant lower value of weight gain, serum cholesterol, feed efficiency ratio, LDL-c (low-density lipoprotein cholesterol) level, triglycerides, VLDL-c (very low-density lipoprotein cholesterol), cholesterol/HDL-c (high-density lipoprotein cholesterol levels), LDL-c/HDL-c, liver cholesterol, serum creatinine, urea and total lipids with a significant increase in both liver 64 triglycerides and serum globulin when orally administered with garden cress seeds extract and powder, in comparison to positive control group (Al Hamedan 2010).

Experiments on alloxan induced diabetic male Wistar rats reported the hypoglycemic and hypolipidemic effects of Garden Cress seed powder. Diabetic and hyperlipidemic rats showed a significant decrease ($p \leq 0.05$) in fasting blood glucose levels, total cholesterol, lipid profile, glycosylated haemoglobin, triglycerides and lipoprotein fractions (LDL-c and VLDL-c) with a significant increase in HDL-c levels when administered with garden cress seeds (3 g/kg body weight). Garden Cress Seeds fed diabetic and hyperlipidemic rats had restored reduced glutathione and antioxidant enzyme activity in diabetic control and high fat & high cholesterol diet fed experimental rats and increased thiobarbituric acid reactive substances levels were also neutralized (Prajapati and Dave 2018).

A study was conducted on rats to evaluate the effects of garden cress (Lepidium sativum) on serum biochemistry and liver histopathology. Test rats were fed a high cholesterol diet. Activity of serum triacylglycerol, total cholesterol and alanine transaminase (ALT) were significantly increased in the test group in comparison to the control group. Total cholesterol and ALT were reduced by *Lepidium sativum* extract. Hepatoprotective action of *Lepidium sativum* extract was seen. It was concluded that hypocholesterolemic and hypolipidemic activities were shown by garden cress seeds in rats (Shukla et al. 2015).

18.3.8 Role of Sesame Seeds—*Sesamum Indicum* L.—On Cardiovascular Disorders

The genus *S. indicum* L. is the dominant cultivated species. Distribution of maximum of the species takes place in three areas, viz., Africa, India and the Far East and Africa, is known for wide variety of wild species of sesame, and some genetically modified species are also available.

18.3.8.1 Regulating LDL Cholesterol and Maintaining Heart Health

Dietary sesame reduces the level of cholesterol in blood serum and increasing the free radical scavenging capacity in people with high levels of cholesterol. Twenty-one people with high level of lipid profile were taken as subjects, who were instructed to continue their usual diets for at least two weeks of initiating the experiment. The experiment was to incorporate 40 g of roasted till in usual diets of all subjects for a span of 28 days and then removing the sesame from diet for another 28 days. It was observed that cholesterol levels were reduced during the span of consuming sesame in diets; there was a reduction in the levels of LDL as well.

The low-density lipoproteins are responsible for causing the heart disease, arthrosclerosis, which in simple terms is known by the blockage of the arterial walls, but the presence of freeradical eating antioxidants like sesaminol, sesamin and sesamolinol in the sesame helps to keep fat in balance. Vitamin E can provide immunity against oxidizing compounds which are thus present in sesame oils. Lignan, an important agent present in seeds of sesame, is responsible in reducing the cholesterol. Studies carried out show that sesamin, a compound found in these seeds, reduces the cholesterol of patients. These studies were proved by patients who consumed sesame seeds in their daily diets. Sesamin was combined with vitamin E and was used as epimers of sesamin and episesamin in equal ratios and was fed to rats, who later showed lower cholesterol.

Experiment carried out for sixty days on patients having high levels of cholesterol, were supposed to take forty grams of sesame seed on daily basis and the amount of calories taken by these seeds were removed from their daily diets, along with all measurements of height, weight, and BMI along with their lipid profile at the start of their experiment, after 60 days there was no change in the anthropometric measurements, but a significant reduction was observed in LDL and total cholesterol in serum and increase in antioxidant inherent (Alipoor et al. 2012).

18.3.9 Effect of Flaxseeds—*Linum Usitissimum*—On Cardiovascular Disorders

The scientific name for flax is *L. usitissimum* which also reveals a lot about our human relationship to the plant. Flax seed is known as “linseed” in many parts of the world.

As a functional food as said prior, flaxseed is additionally a great source of dietary fibre in soaked fat and tall in omega-3 fats. The functional properties of full roasted and non-roasted flax seed have no significant difference between them. Full roasted and non-roasted had bulk density of 0.83 and 0.78 g/ml, water absorption capacity of 1.83 and 1.48 g/g and fat absorption capacity of 1.31 and1.20 g/g, respectively. This study showed the higher fat absorption in flax flour of full fat roasted (1.31 g/g). Flaxseed of Janaki variety has the critical sum of impartial cleanser fibre (57.2%) and hemicelluloses (31.7%), cleanser fibre (31.2%) and lignin (17.2%). Flaxseed supper is high in fibre, a lot of which is dissolvable (20%), as gums and adhesives (Morris 2001).

Flax Seeds Role in Cardiovascular Disorder/Cardiovascular ailment, specifically coronary illness is brought about by the atherosclerosis, which is the narrowing of the courses because of greasy develop of plaque. There are two sorts of lipoproteins, low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Flaxseed contains alpha-linolenic acid (ALA) and lignans which have been appeared to help decrease the dangers of cardiovascular sickness and disease (Lanzmann-Petithory et al. 2002). In one examination, 10 youthful people devoured flaxseed muffins that gave 50 g flaxseed/day for about a month. The outcomes from this investigation demonstrated that plasma cholesterol was decreased by 6%; LDL cholesterol was diminished by 8%, and plasma HDL and triglycerides did not change (Hutchins et al. 2001).

ALA lessens the danger of cardiovascular sicknesses in two different ways: by altering layer phospholipids and by increasing eicosanoid generation (Fig. 18.3). An

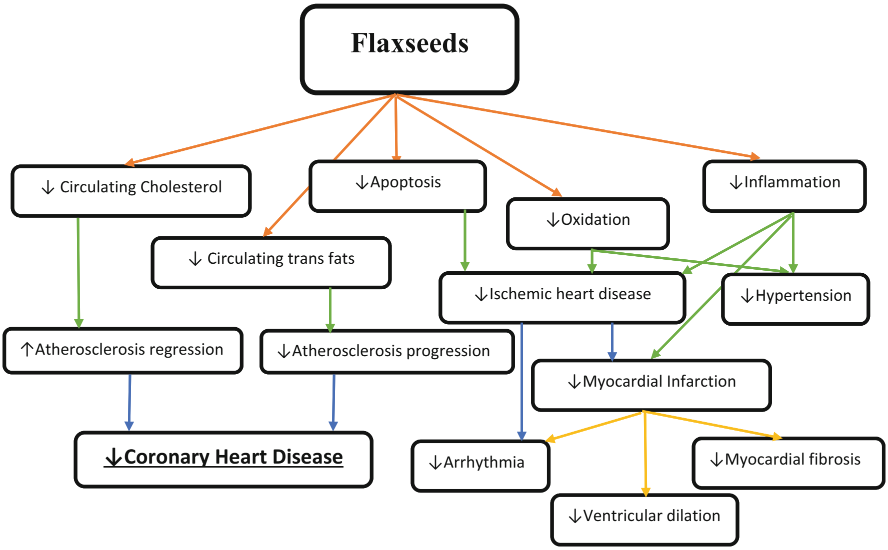

Fig. 18.3 Cardiac health benefits of flaxseeds

eating routine that contains flaxseed has been appeared to help increment the ALA substance of blood phospholipids, triglycerides or potentially cholesterol esters. This expansion in the omega-3-unsaturated fat substance of layer phospholipids will, thusly, help increment film smoothness and modify layer work. Because of these changes, the hazard for cardiovascular illnesses is decreased. ALA likewise interferes with the response that produces arachidonic acid, which is the antecedent of eicosanoids. Eicosanoids help advance platelet accumulation and vasoconstriction. In this manner, lessening the generation of eicosanoids may help decline the dangers for cardiovascular infection (Kinsella et al. 1990).

A study was conducted to survey serum lipid changes by a phytoestrogen dietary supplement made from flax seeds compared with oral oestrogen–progesterone substitution in hypercholesterolemic menopausal ladies. It was found that hormonal substitution treatment and flaxseed separately for decreasing of low-density lipoprotein and increment of high-density lipoprotein, cholesterol and increment of apolipoprotein. Both medications delivered comparable diminishes menopausal side effects and in glucose levels (Hutchins et al. 2001).

18.3.10 Dates as a Functional Food and its Effect on Cardiovascular Disorders

Dates are loaded with nutrients. The biological process composition of dates: contains (70–80%) carbohydrates, (0.20–0.50%) fat, (2.30–5.60%) macromolecule, (6.40–11.50%) dietary fibres, (0.10–916 mg/100 g dry weight), and conjointly contain bound vitamins (C, B1, B2, B3, and A). and has very little or no starch (Longvah et al. 2017).

Date fruit functions as an honest supply of vital phytochemicals, carotenoids, phenolics and flavonoids. Date serves as inhibitor, antimutagenic and immunomodulatory to health. Dates even have another extra various medicative benefits together with antihyperlipidemic, anticancer, gastroprotective, hepatoprotective and nephroprotective. There are varied health benefits of feeding dates together with relief from constipation, heart issues, enteral issues, sexual dysfunctions, anaemia, abdominal cancer and plenty of additional conditions (Rahmani et al. 2014).

18.3.10.1 Anti-Inflammatory Impact

A study conducted on animal model rumoured that dates palm has important potential protecting impact by modulation of cytokines expressions. Another study showed that the methanolic extract of edible portion of the date fruit plays a major role in reducing foot swelling and plasma clotting factor. A vital study within the support of dates showed that leaves of dates are thought about as an honest supply of natural inhibitor and anti-inflammatory medicine (Al-Yahya et al. 2016).

Dates have very good nutritional value; it contains the good amount of dietary fibre, vitamins and total phenolics, and this confirms that dates are a richest source of antioxidants mostly seed by-products and can be considered as functional foods or used as one of the important ingredients in functional foods (Al-Dashti et al. 2021).

18.3.11 Therapeutic Uses of Beet on Heart Health

18.3.11.1 Effect on Decreasing Blood Pressure and Cardiovascular Disease: Beetroot

Beetroot prevents the high risk of cardiovascular disease. Consumption of beetroot shows positive effect on systolic blood pressure of older and obese person (Jakubcik et al. 2021). Consumption of beetroot juice increases cyclic guanosine monophosphate and thus possesses antihypertensive activities. Beetroot juice also reduces cardiac ischemia–reperfusion injury in patients (Salloum et al. 2015).

Dietary intake of nitrate supplement helps reduce blood pressure in hypertensive people. The abundant nitric oxide present in beets is highly bioavailable; it aids in vasodilation along with reducing the central sympathetic outflow (Notay et al. 2017).

Beetroot has role as functional food with numerous functions to manage diseases in human body. Consumption of beetroot as salad or in form of juice is being recommended (Kim et al. 2003).

18.3.12 Role of Pomegranate—Punica Granatum—In Managing Cardiovascular Disorders

Pomegranate peels are a good source of fibre and antioxidants. Pomegranate peel has shown to have the highest antioxidant activity, due to the presence of large amounts of phenolics as shown by many of the researches carried out. According to the researchers conducted, out of 28 different fruits, pomegranate peel showed the highest antioxidant activity among them (Zarfeshany et al. 2014).

18.3.12.1 Pomegranate Peel Helps to Lower Cholesterol Levels

But this definitely plays an important role in reducing the cholesterol levels of the blood, that is, the LDL cholesterol and the total cholesterol. Pomegranate has shown to have the ability to prevent the formation of fatty plaques in the arteries; that is, it can prevent atherogenesis and the inflammatory disorders, both of which are associated with the obesity that is mainly induced by diets (Davidson et al. 2009). It is very much clear that pomegranate fruits are very much rich in the phenolic compounds, but the maximum amount of these phenolic compounds is mainly concentrated in the peels of this fruit. Out of these phenolic compounds, many of them reported were flavonoids, which included anthocyanins such as cyanidins, delphinidins, pelargonidins and also some of their derivatives were found also some of the anthoxanthins such as quercetin, catechin and epicatechin. Tannins were also found to be present in these peels which included ellagitannins and derivatives of the ellagic acids such as punicalagin, punicalin and pedunculagin. The presence of phenolic acids was also found such as the gallic, ellagic, p-coumaric, ferulic, chlorogenic, caffeic, syringic, sinapic and cinnamic acids. It is found that, by increasing the efficiency of the extraction from the peels, the phenolic compounds can be more easily recovered from the peels. But till now since all these experiments were conducted in vitro, by which the relevance of these compounds for their curing properties was analysed, the correct validation of their health benefits cannot be confirmed without any proper clinical trial (Jurenka 2008).

Although the fresh pomegranate peel powder was observed to have a good amount of nutritional content in it, the de-tanninated peel powder was found to have even more better levels of nutritional qualities compared to the fresh pomegranate peel powder. The de-tanninated peel powder and the separated hydrolysable tannins were found to have good amount of nutritional content within them. It also had appropriate amount of tannins in it (Lansky and Newman 2007).

18.3.13 Kiwi—Actinidia Deliciosa—and Cardiovascular Disorders

Kiwi fruit, known as Chinese gooseberry, has become terribly popular in last few years due to its various medicinal properties. From the Land of New Zealand, kiwi got its name. The flowers of kiwi are fragrant with 5 to 6 petalled, 2.5–5 cm broad (Beutel James 1990).

18.3.13.1 Kiwi Role in Maintenance of Cardiovascular Health

The fibre and potassium that is present in kiwi support heart health. Increasing potassium intake and decreasing sodium may help in the reducing the risk of cardiovascular disorders. Kiwi fruit can assist in reducing high blood pressure because of its high potassium content (Rust and Ekmekcioglu 2016). Some evidences are there that show that Kiwi fruit may have the ability to affect various risk factors for cardiovascular disease, such as blood pressure, plasma triglycerides and platelet aggregation. Studies showed that eating two to three Kiwi fruits per day helps in reducing triglyceride levels by 15% and reduces platelet aggregation response by 18% compared to control. Many more studies have shown that daily kiwi consumption helps in improving not only triglyceride levels, but also the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol (Chang and Liu 2009). One clinical trial was studied on 148 male smokers, and were given three kiwis to eat per day for eight weeks. It was found that the patients had significantly reduced blood pressure and angiotensin-converting enzyme (ACE) activity (a component of the blood pressure-regulation process), especially with people having hypertension (Karlsen et al. 2013).

Kiwi fruit is a bit costly to be afforded by poor man, but nowadays, all the fruits are costly. The Kiwi fruit has numerous benefits for health, and daily one kiwi can improve health to great extent. So, it is a functional food indeed.

18.3.14 Prebiotics

The prebiotic was first used in 1985 and is defined as the non-digestible food ingredient that helps in stimulating growth and promotes healthy bacteria in the colon (Hutkins et al. 2016). Its daily consumption helps in aiding mineral absorption, reducing blood cholesterol levels and improving immune function (Carlson et al. 2018).

Table 18.1 describes the complete list of functional foods for cardiovascular diseases.

18.4 Conclusion

Functional foods are the dietary items which include whole foods, fortified foods and enriched foods which not only provide energy and nutrients but also beneficially affect one or more target functions of the body, beyond the adequate nutritional effects. They reduce the risk of acquiring disease as they enhance the physiological responses in the body. They are also known as nutraceuticals as they are highly nutritious and have powerful benefits for health. They also help in providing the body with the adequate amounts of vitamins, fats, proteins and carbohydrates which are necessary for the healthy survival of a person. They contain various supplements and ingredients which are mainly intended to improve the health of an individual. The term "functional" means basically the foods that are enriched with the nutrition, which directly have the potential to influence the health over and above the basic nutritional value. Functional foods contain biologically active compounds which are beneficial for the health and mainly include processed foods or fortified foods. The bioactive compounds are naturally found chemical compounds which are present in

Table 18.1 List of functional foods for cardiovascular diseases Srilakshmi (2018)

Functional foods	Effect	Foods
Soya protein	• ↓ Plasma total cholesterol • Isoflavones, genistein and daidzein prevent transition of fatty streaks to lesions	Soya milk, tofu, soy sauce and soya supplements
Beans	Soluble fibre binds bile acids ↓ ↓ **cholesterol**	Pinto beans
Garlic	1. Sulphur compounds such as Allicin, allyl mercaptan, diallyl disulphides ↓ Block cholesterol biosynthesis 2. Allyl Sulphur compounds alter cellular thiols. 3. Nicotinic acid, adenosine + other compounds ↓ ↓ **HMG- CoA reductase** (it is an enzyme in cholesterol biosynthesis)	
Nuts	High amount of MUFAs (oleic acid) Mg and cu in nuts also protect from CHD Nuts reduce SFA content of diet by replacing SFA energy by UFA energy ↓ ↓ **LDL and total cholesterol**	Almonds, walnuts, pecans
Fruits and vegetables	Flavonols present in them protect against heart disease by scavenging free radicals	
Tea	Polyphenols present in tea helps by ↓ Prevent oxidation of LDL ↓ **Inhibits formation of atherosclerotic plaques**	
High fibre foods	Pectin ↓ ↓ **serum cholesterol** ↓ Enhances excretion of faecal steroids	Guar gum (cluster beans) reduces cholesterol Psyllium has soluble fibre which helps in lowering serum LDL cholesterol
Vitamin A rich foods	Mechanism in flow chart	Green leafy vegetables, yellow-, orange- and red-coloured fruits and vegetables

(continued)

Table 18.1 (continued)

Functional foods	Effect	Foods
Vitamin E rich foods	Mechanism in flow chart	Vegetable oils, nuts, whole grains
Vitamin C rich foods	Mechanism in flow chart	All citrus fruits, lemons, oranges, sweet limes, lime, amla and guava

plants, animals and marine sources. They are also known as phytochemicals which are mainly present in cereals, fruits, vegetables, legumes, herbs, oilseeds and spices.

Health Canada defines them as the foods which have similar appearance as conventional foods which can be consumed in basic diet as they reduce risk of chronic diseases. Functional foods present either inherently in food or via fortification. Functional Food Centre (FFC) stated a new definition that they are processed or natural foods that possess biologically active compounds which in effective non-toxic amounts provide clinically proven and documented health benefits and also aid in preventing chronic diseases.

Functional foods protect against diseases. Functional foods give the body with proper nutrients which help to protect against disease. These foods are rich in antioxidants which neutralize the harmful compounds called free radicals, thereby preventing the cell form being damaged and various chronic diseases like heart disease, cancer and diabetes. Functional foods are also high in omega-3 fatty acids which reduce the inflammation in the body and also promote heart health and boost the functioning of the brain. Functional foods rich in fibre promote the better control of blood sugar and also give protection from diabetes, obesity, stroke and heart diseases. Digestive disorders, hemorrhoids, stomach ulcers, diverticulitis, acid reflux can also be prevented.

Functional foods are those foods which are rich in a particular ingredient which makes it useful for curing various diseases by maintaining good health. They are mainly classified into probiotics, prebiotics, symbiotic and phytochemicals. They prevent the body from various deficiencies. The list of functional foods mainly includes cereals, legumes, dairy products, fruits, vegetables, beverages, herbs and spices. They have various health benefits on the health of a person, both mentally and physically. They possess various effects on the body of an individual which improve their health. Various diseases can be prevented by consuming functional foods. The demand of functional foods is increasing in the market, and consumers are more people are coming to know about their health benefits for the human mankind.

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Role of Bioactive Compounds in Hormonal Bioregulation

19

Manjari Chandra

Abstract

Bioactive compounds possess the ability to interact with living tissues and impact cellular activities. Concerning human beings, these bioactive components exhibit a wide range of health benefits upon interacting with different physiological systems. Flavonoids, tannins, anthocyanins, carotenoids, betalains, plant sterols, and glucosinolates are few examples of bioactive compounds. They are found primarily in fruits and vegetables. Multiple research studies are being conducted to verify their role in the prevention and possible reversal of cancer and cardiometabolic disorders, such as diabetes, hypertension, and hypothyroidism. Available data and research indicate their role as anti-inflammatory and antioxidant components, facilitating hormonal regulation, immune system modulation, and anticarcinogenic activities. This chapter discusses the impact of bioactive compounds on hormonal regulation in humans. For instance, flavonoids mediate antidiabetic activity by modulating carbohydrate metabolism and insulin sensitivity. Some bioactive compounds have been reported to exhibit neuroprotective effects. Omega-3 fatty acids, phenolics (lignin and tannins), and plant sterol esters can alleviate the risk of cardiovascular disorders and atherosclerosis by reducing inflammation, LDL cholesterol level, and oxidative stress. The chapter also discusses the latest sustainable methods developed to extract and produce bioactive compounds via different kinds of green technologies like microwave-assisted extraction and ultrasound-assisted extraction.

Keywords

Bioactive components · Green technologies · Hormonal regulation · Immune system modulation

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19.1 Introduction to Bioactive Compounds

The term, bioactive compound, does not have a universal definition in the scientific community but is widely defined as the compounds, which have the capability to interact with one or more component(s) of living tissue by presenting a wide range of probable effects (González 2020). The Office of Dietary Supplements at the NIH defines bioactive compounds as constituents in foods or dietary supplements responsible for changes in health status (Weaver 2014). We require these compounds in addition to those needed to meet our basic nutritional requirements. Bioactive compounds are found in plants and plant- and animal-based products, including milk, eggs, fruits, vegetables, herbs, oils, and whole grains. They interact with our physiological system in a manner that promotes overall health. They are being studied in the prevention of cancer, cardiac diseases, and other metabolic disorders (Walia et al. 2019). Bioactive compounds comprise a broad range, including vitamins, minerals, and certain fatty acids to phenolic compounds (flavonoids, lignin, and tannins), lycopene, carotenoids, glucosinolates, etc.

19.1.1 Bioactive Food Components from Plant Sources

In plants, phytochemicals are the naturally occurring bioactive constituents that have also been found to exhibit therapeutic benefits to humans. These compounds serve as antioxidants and anti-inflammatory components possessing anticancerous properties and helping in antimicrobial activities, hormonal regulation, and immune system modulation (Saxena et al. 2013).

The most widely distributed category of phytochemicals comprises polyphenols. Polyphenols are a category of plant compounds that consists of one or more benzene rings and hydroxyl (OH), carbonyl (CO), and carboxylic acid (COOH) groups in different numbers (Soumya et al. 2021). Many plant polyphenols primarily occur in conjugated forms with one or multiple sugar residues attached to the hydroxyl groups (Pandey and Rizvi 2009) (Fig. 19.1).

Flavonoids are the most common class of polyphenols. Other subclasses of polyphenols include isoflavones, catechins, and theaflavins. One can consume

Fig. 19.1 Ellagic acid, a polyphenol

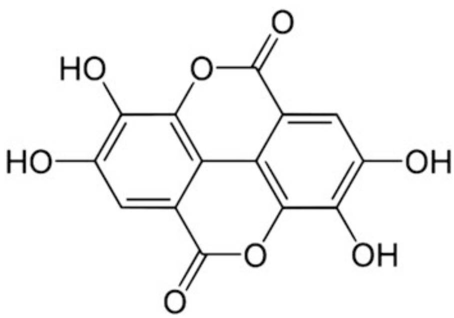

Table 19.1 Common plant-based food sources with their bioactive components and biological functions (source: Soumya et al. 2021)

Food item	Bioactive compound	Biological function
Broccoli, cauliflower, Brussels sprouts, garlic, onions	Glucosinolates, diallylsulfides, isothiocyanates	Antimicrobial, immunomodulator, anticancer, detoxification
Grapes, red wine, tea, fresh fruits, and vegetables	Isoflavonoids and polyphenols	Antioxidant, lipid-lowering, immunomodulator, anticancerous
Carrots, corn, squash, greenleafy vegetables, oranges,papaya, red palm oil	Carotenoids	Antioxidant, immunomodulators
Navra rice	Phenolic compounds, monounsaturated fatty acid omega-9	Hepatoprotective, antispasmodic, antirheumatic, anti-inflammatory, hypocholesterolemic, cancerpreventive, antihistaminic
Turmeric	Curcuminoids	Anti-inflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antidiabetic, antibacterial, antifungal
Ginger	Gingerols and shogaols	Antioxidant, anti-inflammatory, antimicrobial, anticancer, neuroprotective, cardiovascular protective, respiratory protective, antidiabetic
Lemon and citrate fruits	Flavonoids, vitamin C	Antibacterial, antifungal, anti-inflammatory, anticancerous, cardioprotective
Flaxseeds, chia seeds, tofu, walnuts, fatty fish	Polyunsaturated fatty acids, omega-3	Cardioprotective, antioxidant
Vegetable oil, nuts, seeds	Vitamin E (tocopherols)	Antioxidant, immunomodulator, lipid-lowering
Tomatoes	Lycopene	Anti-proliferative, anticancer
Legumes, onion, garlic, asparagus, spinach	Saponins	Antidiabetic, lipid-lowering, anticancer

polyphenols and flavonoids in the diet via fruits, vegetables, cereals, legumes, and nuts (Soumya et al. 2021). Polyphenols, along with other bioactive compounds like omega-3 fatty acids (n-3 FA) and plant sterol esters (PSE), have exceptional capabilities to potentially reduce the atherosclerosis burden by alleviating oxidative stress, inflammation, and LDL cholesterol (LDL-C) levels (Scolaro et al. 2018). Table 19.1 mentions foods carrying multiple bioactive compounds exhibiting health benefits as their biological function.

19.1.2 Bioactive Food Components from Animal Sources

Animals, similar to plants, serve as abundant reservoirs of bioactive components playing various biological roles for human health, promoting various activities, such

Table 19.2 Common animal-based food sources with their bioactive components and biological functions

Food item	Bioactive compound	Biological function
Milk-based products	Whey protein and probiotics	Antimicrobial, immunomodulation, anticancer, detoxification, antioxidation, GI modulation
Meat	Vitamins, minerals, peptides, fatty acids, ACE inhibitory peptides	Antioxidant, antihypertensive activities
Egg	Phospholipids, ovalbumin, ovotransferrin, ovomucin,lysozyme, and avidin	Antimicrobial, immunomodulatory, anticancer, antihypertensive activities
Fish	Fatty acids, polysaccharides,polyether, peptides, proteins,enzymes, and lectins	Antihypertension, immunomodulatory, antithrombotic, antioxidant, anticancer, andantimicrobial activities

as lowering inflammation and cholesterol levels and modulating immune response (Table 19.2; Soumya et al. 2021).

One major category of bioactive compounds derived from animal sources is bioactive peptides. These peptides are generated through microbial fermentation, enzyme digestion, or enzyme proteolysis in vitro. They support various physiological activities, including controlling blood pressure, blood sugar levels, and fighting microbes (Hartmann and Meisel 2007).

19.1.3 Role of Bioactive Components in Therapeutics

Isoflavones can bind to cholesterol molecules in the intestinal tract and helps in eliminating oxidized low-density plasma lipoproteins (LDL cholesterol) (Potter et al. 1998). Further, they facilitate bile excretion and modulate arterial elasticity, thereby improving blood vessel dilation and constriction responses and controlling high blood pressure (Setchell and Cassidy 1999).

Multiple epidemiological studies have revealed that functional foods and herbs and spices containing bioactive compounds can prevent inflammation, which is the leading cause of carcinogenesis or cardiovascular diseases (Teodoro 2019).

Bioactive compounds like polyphenols, carotenoids, and isothiocyanates carry antioxidant potentials that help them eliminate reactive oxygen species, free radicals, and other potential carcinogenesis initiators, which might contribute to premature immune cell death (Fig. 19.2) (Brennan et al. 2000). They can stimulate the proliferation of B- and T-lymphocytes and enhance the activity of macrophages and cytotoxic T-cells, thus boosting immune response. Further, carotenoids like β-carotene, lycopene, lutein, and zeaxanthin have the ability to potentially reduce the risk of cardiovascular disorders (CVDs) via lowering blood pressure and reducing pro-inflammatory cytokines (Milani et al. 2017).

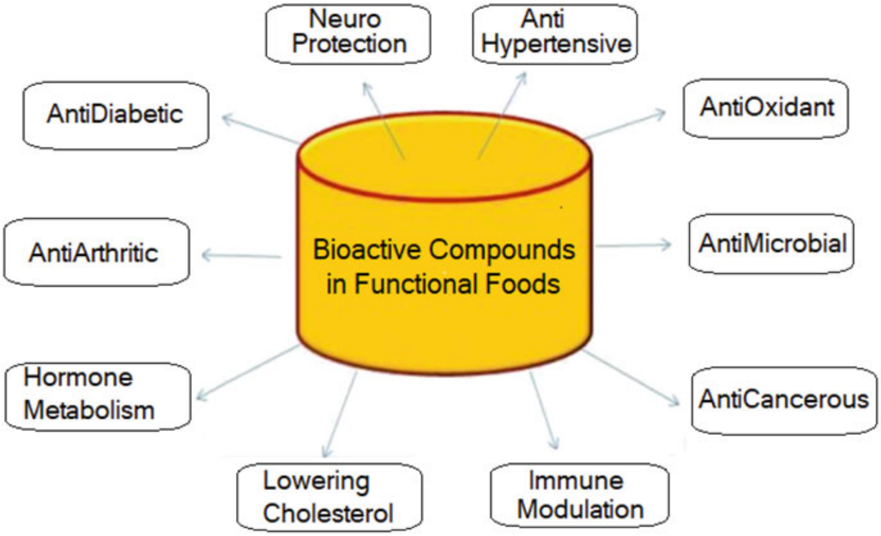

Fig. 19.2 Therapeutic properties of bioactive compounds (Soumya et al. 2021)

Mammalian milk also contains a range of potent immunomodulatory peptides, influencing immune function by stimulating certain immune factors. These bioactive peptides exhibit antioxidant, enzyme inhibitory, antithrombotic, and antagonistic activities against a range of toxic agents (Mohanty et al. 2016), thereby assisting in controlling diet-related metabolic disorders, such as obesity, hypertension, and diabetes.

19.2 Hormonal Bioregulation by Bioactive Compounds in Humans

19.2.1 Regulation of Neurotransmitters

Neurohormones are the hormones produced by neurosecretory cells and secreted by nerve impulses. These include dopamine, serotonin, norepinephrine, oxytocin, vasopressin, and adrenaline (Peres and ValenÇa 2010). Neurohormones are released similar to hormones for systemic effect, but they also serve the role of neurotransmitters when needed.

Balance in neurotransmission is essential for the proper functioning of the nervous system and even a small, but prolonged disturbance can induce the negative feedback mechanisms leading to various neuro-pathologies (Rebas et al. 2020).

Phytochemicals can be classified into several groups, and most of them possess anticancer, antioxidative, anti-inflammatory, and neuroprotective properties. They can also modulate the metabolism or action of some neurotransmitters and/or their receptors. Among many functions, biologically active plant compounds have been shown to exert a positive impact on the function of the central nervous system, including modulation of metabolism and action of some neurotransmitters (Bhullar and Rupasinghe 2013).

19.2.1.1 Effect of Polyphenols on ACh Receptor

Acetylcholine (ACh) is an abundant neurotransmitter found in both central (CNS) and the peripheral (PNS) nervous systems. It stimulates all motor neurons and is responsible for body movements. In the brain, ACh plays roles in learning, memory and improves cognitive functions (Fig. 19.3) (Rebas et al. 2020).

ACh has two types of receptors through which it interacts with other components. These are nicotinic ionotropic receptor (nAChR) and muscarinic metabotropic receptor (mAChR). Curcumin, a polyphenol, can activate one of the subtypes of nAChR receptor, known as α7-nicotinic acetylcholine receptor. The α7nAChR subtype, unlike other neuronal nicotinic receptors, exhibits a relatively high permeability to calcium ions (Zhang et al. 2014). Hence, curcumin can show significant potentiation of choline-induced Ca^{2+} transients.

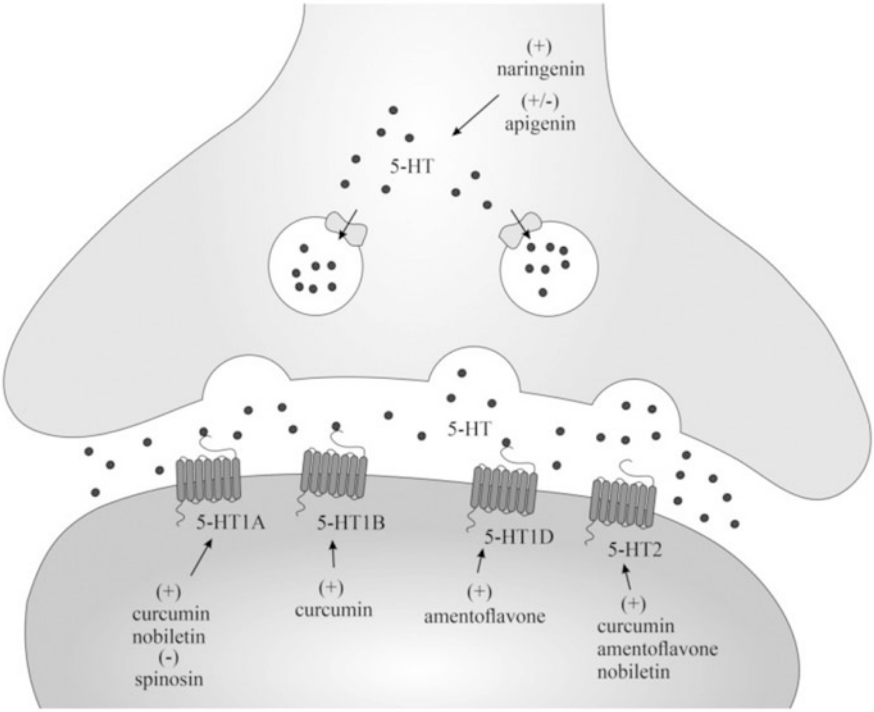

Fig. 19.3 Effect of polyphenols on serotonergic signaling components. 5-HT: serotonin, 5-HT1A, 5-HT1B, 5-HT1D, 5-HT2: serotonin receptors, (+) enhancement or activation of signaling component, (−) inhibition or blocking of signaling component

Similarly, other polyphenols can interact with α7nAChR or increase the expression and surface density of mAChR (Rebas et al. 2020). As ACh plays roles in learning and memory and improves cognitive functions, polyphenols can serve as drugs in the treatment of neurodegenerative diseases.

19.2.1.2 Polyphenols and GABA-Ergic Signaling

GABA is a primary inhibitory neurotransmitter in the mammalians' central nervous system (CNS) that plays a crucial role in maintaining balance in the nervous system. Abnormalities in the GABA expression or modulation can lead to schizophrenia, Alzheimer's disease, and anxiety. Benzodiazepine derivatives, such as diazepam, have been used as drugs to modulate GABA-ergic signaling and treat cognitive decline and mood issues (Uzun et al. 2010).

Many of the flavonoids modulate GABAA receptors by two separate approaches (as shown in Fig. 19.4). The difference between the two mechanisms is that one uses a flumazenil-sensitive high-affinity benzodiazepine binding site, and the other uses a flumazenil-insensitive low-affinity benzodiazepine site (Rebas et al. 2020). Of note, flumazenil serves as a selective benzodiazepine GABAAR antagonist acting through competitive inhibition. Several lipophilic flavonoids have been shown to induce sedative and anxiolytic effects via interaction with the benzodiazepine binding site (Wasowski and Marder 2012). Apigenin, a flavonoid found in chamomile tea, is widely regarded for its anti-anxiety properties due to agonistic action on GABAA-R.

In most cases, flavonoids directly act on the benzodiazepine site, exhibiting anxiolytic effects and reducing anxiety in humans. These effects have been reported for the naringenin-dihydroderivative of apigenin, found in many citrus products. Epigallocatechin gallate, a flavanol found in green tea, exhibits neuroprotective, anxiolytic, sedative–hypnotic, and amnesic properties.

19.2.1.3 Regulation of Dopaminergic Signaling by Carotenoids

The transcription factor NF-κB is responsible for the production of a spectrum of pro-inflammatory molecules. Carotenoids, on the other hand, exhibit strong antioxidant properties, regulating ROS production that in turn inhibits the activity of NF-κB. It is due to this inhibition of NF-κB activity and related expression of pro-inflammatory cytokines in the brain that carotenoids help boosting the production of dopamine and improving cognitive performance and memory retention (Cho et al. 2018).

19.2.1.4 Regulating Serotonergic Signaling

Current research correlates depression with disturbances in serotonergic and dopaminergic signaling. Polyphenols can lower depression symptoms via the activation of monoamine synthesis or the serotonin (5-HT) receptors. For example, curcumin can positively modulate the serotonergic system by interacting with three subtypes of serotonergic receptors: 5-HT1A, 5-HT1B, and 5-HT2C (Rebas et al. 2020). Long-term consumption of curcumin can significantly boost the serotonin level in the

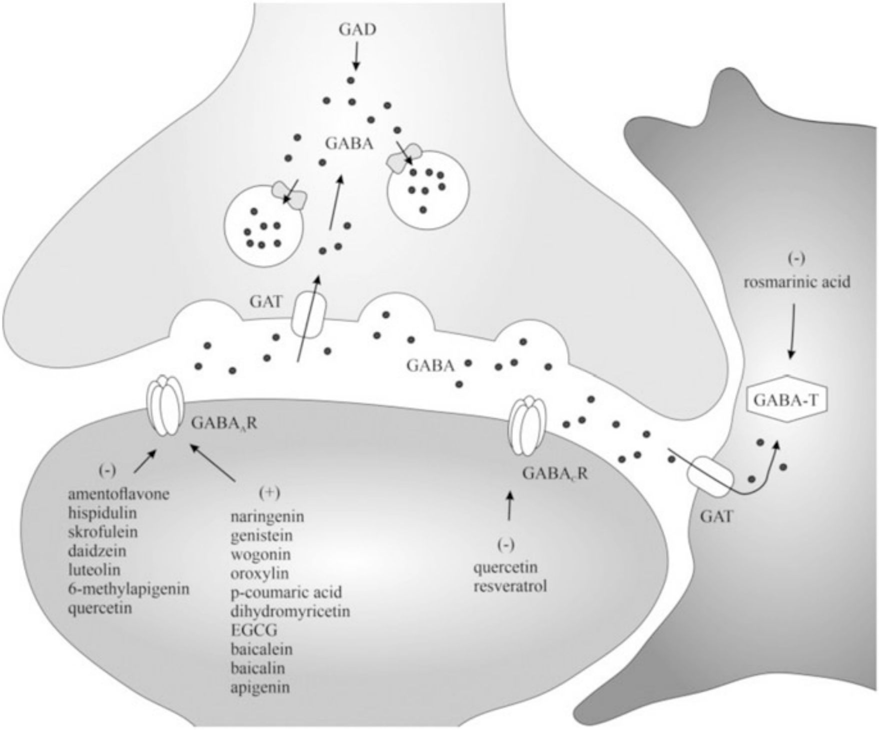

Fig. 19.4 Effect of polyphenols on GABA-ergic signaling components. (From Rebas et al. 2020). GABA-γ: aminobutyric acid, $GABA_AR$: $GABA_A$ receptor, $GABA_CR$: $GABA_C$ receptor, GABA-T: GABA transaminase, GAD: glutamate decarboxylase, GAT: glutamate transporter, (+) enhancement or activation of signaling component, (−) inhibition or blocking of signaling component

frontal cortex and hippocampus, as shown by Chang et al. (2016) with their experiments on rats. Additionally, amentoflavone, a bi-flavonoid found in 100+ plants, has been shown to exhibit agonistic activity to 5-HT1Dα and 5-HT2C receptor subtypes (Ishola et al. 2012).

Research done by Yi et al. (2011) has highlighted antidepressant action exhibited by nobiletin, an O-methylated flavone obtained from citrus peels, via the mechanism involving the participation of 5-HT1A and 5-HT2 receptors. Additionally, α1-adrenoceptor and DA receptors (D1 and D2) are suspected to be the targets for nobiletin, indicating its strong therapeutic potential for the treatment of depression (Rebas et al. 2020).

Jung et al. (2014), in their research, showed the ameliorating effect of spinosin, a C-glycoside flavonoid, on scopolamine-induced cognitive impairment in mice. The research indicated the potential use of spinosin to treat cognitive dysfunction disorders, such as Alzheimer’s disease.

19.2.2 Impact of Bioactive Compounds on Appetite-Regulatory Hormones

Two primary hormones linked to regulating appetite in humans are ghrelin and leptin. Ghrelin is an orexigenic neuropeptide secreted in the stomach (Date et al. 2000) and stimulates appetite. It is also known as the physiological hunger hormone. Ghrelin expression is inversely proportional to the amount of food intake. It implies that ghrelin production increases during fasting and decreases following the consumption of food.

Leptin is an endocrine hormone, which is secreted predominantly by adipocytes. Leptin interacts with the hypothalamus to control food consumption, suppress appetite, and increase energy metabolism and expenditure (Schwartz et al. 1999).

19.2.2.1 Appetite Suppression Via Regulation of Ghrelin and Leptin

Polyphenols can suppress appetite using 3 major mechanisms (Geoffroy et al. 2011):

- Slowing down secretion of appetite-stimulating hormones, such as ghrelin.
- Modulating melanin concentration hormone (MCH) receptors as MCH is also an appetite-stimulating hormone.
- Inactivating appetite sensors.

Bioactive compounds like polyphenols can regulate food intake by modulating adipohormones and the expression of gut peptides (Singh et al. 2020). Polyphenols alleviate insulin resistance and regulate the expression and production of leptin, ghrelin, and glucagon-like peptide 1. Boix-Castejon et al. (2018) administered an isocaloric diet, which included plant-based polyphenol-rich extract, to obese individuals. Results showed a significant reduction in body weight up to 3.48 kg when compared to the placebo group. The study also showed a reduction in hunger and appetite suppression after two months of intervention.

19.2.2.2 Significance in Obesity Management

Obesity management via controlling appetite involves both neurological and hormonal processes (Singh et al. 2020). Evidence from research studies on rats and mouse indicates that polyphenols cross the blood–brain barrier (BBB) (Panickar 2013). Experiments confirm the neural effects of polyphenols as they have been found in the brain of animal subjects in significant concentration. Various studies on human subjects and animals indicate the potential role of polyphenols on neurohormones that modulate food intake and energy regulation in obesity (Table 19.3).

19.2.3 Bioregulation of Metabolically Active Hormones

Metabolic syndrome encompasses various conditions of metabolic dysfunction and is characterized by obesity, insulin resistance, dyslipidemia, and hypertension (Kirk

Table 19.3 Role of polyphenols in the bioregulation of neuropeptides/neurohormones affecting central nervous system in managing obesity. Adapted from Panickar (2013)

Polyphenol	Neuropeptide	Observed bioregulatory effects (from research studies)
Resveratrol	Insulin	• Improved insulin resistance in fructose-fed insulin-resistant animal subjects • Attenuated abnormal insulin secretion from islets of high-fat-fed mice • Improved insulin sensitivity in normal lemurs without affecting insulin secretion
Cinnamon polyphenol	Insulin	• Improved insulin sensitivity in human subjects with type 2 diabetes, metabolic syndrome, and women with PCOS • Boosted antioxidant effects in obese subjects • Improved insulin sensitivity in an animal model of metabolic syndrome
Adlay seed water extract	Leptin	• Upregulated leptin mRNA, exhibiting antiobesity effects
Carob pulp polyphenol	Ghrelin	• Decreased acylated ghrelin in healthy subjects and enhanced lipid oxidation
Green tea polyphenol	Ghrelin	• Lowered ghrelin prepropeptide mRNA levels in the liver in rats fed with a high-fat diet
	Leptin	• Served as appetite suppressor by boosting leptin levels in obese rats

and Klein 2009). Every phenomenon of chronic inflammation includes deregulation of the MAPK/EKR/JNK, Nrf2, and NF-κB signaling pathways (Esteve 2020). Where the Nrf2 pathway is a protective mechanism against oxidative stress, the NF-κB signaling pathway correlates with inflammation.

The NF-κB pathway is activated in obesity, resulting in the elevated production of pro-inflammatory cytokines such as TNF-α that induce insulin resistance. Further, insulin resistance is promoted through white adipose tissue (WAT) inflammation generated in obesity via lipid accumulation in the liver. On the other hand, the transcription factor Nrf2 orchestrates the cellular mechanisms of defense against oxidative stress (Esteve 2020).

19.2.3.1 Regulating Insulin Production—Improving Insulin Sensitivity

Glucosinolates

Glucosinolate (GLS) and its derivatives, such as isothiocyanates (ITCs) and indoles, activate the Nrf2 pathway and inhibit the NF-κB signaling pathway to improve glucose tolerance and insulin sensitivity. GLS derivatives reduce fat deposition in WAT and liver and alleviate proliferation and differentiation of adipocytes. Additionally, they promote the "browning" of white adipose tissues, which boosts energy metabolism and enhances energy expenditure, resulting in improved insulin sensitivity with reduced inflammation and decreased craving for food intake (Esteve 2020).

Polyphenols

Gingerol, shogaol, and flavonoids can regulate the production of insulin in multiple ways. They exhibit restorative effects on pancreatic β-cells, increasing insulin sensitivity (Otunola and Afolayan 2019). Gingerol and shogaol can also enhance glucose uptake via increased expression and translocation of GLUT-4 (a glucose transporter) to the plasma membrane of the cells, thus clearing excess glucose from the serum (Otunola and Afolayan 2019) (Fig. 19.5). Other mechanisms include the following:

- Enhanced hepatic glycogen synthesis via enhancement of glycogen regulatory enzyme expression in the liver,
- Inhibition of carbohydrate metabolizing enzymes,
- Stimulation of pancreatic insulin release, and
- Inhibition of hepatic glucose production.

Epicatechin and quercetin are some of the few polyphenols extensively studied on humans to assess their effect on insulin resistance. Polyphenols can affect glucose uptake pathways in response to insulin in multiple ways (Yellow arrows in Fig. 19.5). Consumption of carbohydrates (starch and/or sugar) will increase blood glucose levels. This will release insulin from β-cells to allow glucose uptake into tissues via GLUT4 activation by translocation. Certain polyphenols can inhibit α-amylases and α-glucosidases, slowing down the rate of digestion and avoiding glucose spikes (Williamson and Sheedy 2020). Slowing down the rate of digestion is

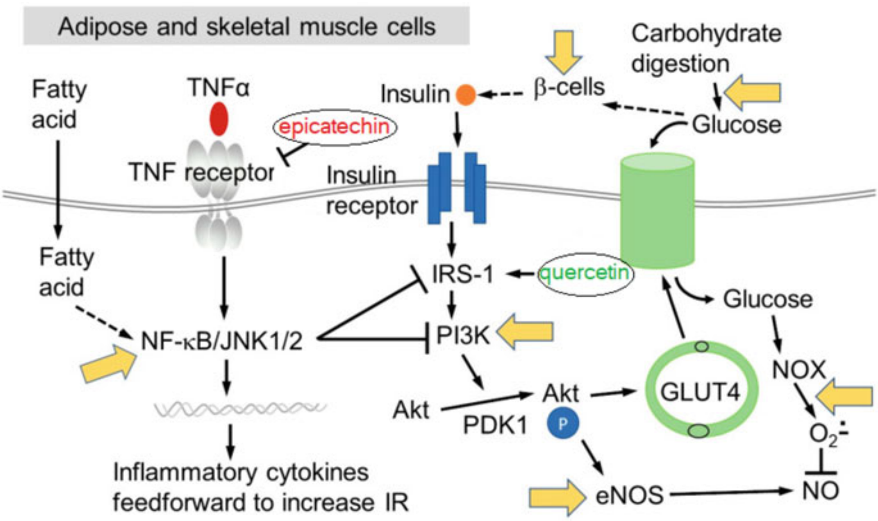

Fig. 19.5 Simplified mechanism of glucose uptake by adipose or muscle tissue. (Adapted from Williamson and Sheedy (2020)). JNK1/2: c-Jun N-terminal kinase 1/2; PDK1: pyruvate dehydrogenase kinase 1; IRS-1: insulin receptor substrate 1; TNF: tumor necrosis factor; PI3K: phosphoinositide 3-kinase; eNOS: endothelial nitric oxide synthase

beneficial since rapidly elevated glucose can result in the formation of reactive oxygen species (ROS) in endothelial cells via NADPH oxidase 4 (NOX4), causing oxidative stress.

Epicatechin can inhibit the TNF receptor from inducing NF-kB/JNK 1/2 pathway, thereby activating IRS-1 and P13K pathways for effective glucose utilization and controlling insulin resistivity (Fig. 19.5). On the other hand, quercetin can restore GLUT4 translocation by upregulating IRS-1 expression and improving insulin sensitivity (Williamson and Sheedy 2020).

Saponins

Saponins and terpenoids enhance insulin secretion by the islets of Langerhans. It controls and reduces glycogenesis in liver tissue, thus enhancing peripheral glucose utilization and elevating serum protein levels (Pehlivan 2021a; b).

Polyunsaturated Fatty Acids

Polyunsaturated fatty acids, such as omega-3, increase absorption of other polyunsaturated fatty acids into β-cells of the pancreas, activating insulin secretion. Omega-3 also induces changes in the phospholipid membrane composition of peripheral cells, enhancing insulin receptor binding affinity, thus improving insulin sensitivity (Lardinois 1987). The combined effect of omega-3 on β-cells and peripheral cells increases plasma insulin concentration and reduces insulin resistance. Free fatty acids have also been found to inhibit glucagon release (Bhathena 2006).

Carotenoids

Oxidative stress causes impairment of insulin secretion from β-cells, playing a critical role in the progression of type 2 diabetes via increasing insulin resistance. Hence, bioactive compounds like vitamins or carotenoids exhibiting antioxidant properties can protect against the development of diabetes mellitus.

Carotenoids like β-carotene and lutein also block the activation of transcription factor NF-kB, resulting in inhibition of the production of pro-inflammatory cytokines and improvement of insulin sensitivity in muscle, liver, and adipose tissues. Additionally, carotenoids can also have an impact on C-reactive protein (CRP), which is an inflammatory marker, further improving insulin sensitivity (Gammone et al. 2015).

19.2.3.2 Polyphenols at Large Amounts Can Interfere with Thyroid Hormone

Hypothalamus–pituitary–thyroid axis and few other factors regulate the secretion and the mechanism of action of thyroid hormones (THs). Endocrine disruptors of THs can act at any level of this regulatory mechanism (Oliveira et al. 2019). Thiocyanate and thioamides found in cabbage, broccoli, and cassava have been well-characterized as goitrogens and are considered antithyroid compounds. Also, some studies have indicated a risk of hypothyroidism with the consumption of flavonoids in high quantities. It is because they may interfere with thyroid function by inhibiting thyroid peroxidase (TPO), the essential enzyme for TH synthesis

(Oliveira et al. 2019). The flavonoids include isoflavones from soy protein and apigenin, chrysin, vitexin, and baicalein from parsley, thyme, olives, tea, and broccoli. When TPO activity is inhibited by phenolic compounds, reducing thyroid hormone synthesis, a compensatory increase in TSH may be observed; this may lead to goiter, especially when these compounds are consumed in high quantities (Oliveira et al. 2019; Paunkova et al. 2019).

Isoflavones can interact with thyroid hormone transport proteins and interfere in their functioning. Also, isoflavones can inhibit the enzyme 5′-deiodinase type I (5DI) in peripheral tissues, leading to changes in thyroid hormone activity at the cellular level (Paunkova et al. 2019). The enzyme 5DI catalyzes the conversion of T4 to T3, the biologically active hormone. A study by Sosić-Jurjević et al. (2010) showed a significant reduction in total serum T4 and T3 levels in middle-aged rats after treatment with daidzein and genistein. Flavonoids like baicalein, quercetin, kaempferol, and rutin can also affect 5DI enzyme activity negatively.

19.2.4 Regulation of Androgenic Hormones

19.2.4.1 Polyphenols Serve as Ligands of ERs (Estrogen Receptors)

Polyphenols can bind to estrogen receptor α (ERα) and β (ERβ) with their characteristic phenolic ring. As they bind, polyphenols induce biological effects in human cells through mimicking or inhibiting the action of endogenous estrogens (Cipolletti et al. 2018).

Competition-binding studies validate that different polyphenol have differing affinities for the two ERs. For instance, genistein, daidzein, and coumestan coumestrol exhibit a greater affinity for ERβ than ERα. On the other hand, 8-prenylnaringenin is an ERα agonist, showing a 100-fold more potent affinity toward the sub-receptor.

19.2.4.2 Vitamin E for Boosting Fertility Via Gonadotropin Hormones

Oxidative stress causes adverse effects on reproductive function in both women and men. Antioxidants (such as vitamins C and E) and antioxidant cofactors (such as selenium, zinc, and copper) have the potential to dispose of, scavenge, and suppress the formation of ROS (Ruder et al. 2008). Animal models have suggested that vitamin E can upregulate the expression of genes that produce FSH and LH (Huang et al. 2019; Zhang et al. 2021). Also, it antagonizes the decline of these hormones in case of any toxicity.

Gonadotropin hormones like luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are responsible for sexual function in both men and women. LH boosts testosterone production by signaling the testes to produce the hormone. FSH stimulates follicular growth and regulates ovulation in females. In males, FSH stimulates spermatogenesis.

As vitamin E induces FSH activity, it stimulates follicular growth. And when the follicle matures, it begins to secrete estradiol (E2) in significant quantities. The combined effect of alleviating oxidative stress and stimulating FSH growth results in regular menstrual cycles and improved ovulatory functions in women. The critical role that vitamin E plays for fertility in rodents prompted scientists to name its dietary compounds “tocopherol,” a combination of Greek words for “childbirth” (tocos) and “to bring forth” (pheros) (Evans 1963; Ruder et al. 2008).

Nitric oxide (NO) plays an essential role in activating the release of luteinizing hormone-releasing hormone (LHRH) in the hypothalamus, which helps in the secretion of LH. Both vitamins E and C can scavenge NO free radicals and improve NO production in the brain, which ultimately leads to regulated production of LH, improving sexual function (Karanth et al. 2003). It is also why nutritionists and dieticians recommend vitamin E and C supplements or functional foods rich in these antioxidants to treat erectile dysfunction in males.

19.2.4.3 Saponins Improve Sexual Function in Males

Saponins like furostenol and protodioscin can increase testosterone production by regulating NF-κB and Nrf2/HO–1 pathways in males, thereby improving sexual function (Zhu et al. 2017). They have also been found moderately helpful in treating disorders like erectile dysfunction (ED). Saponins can also boost the levels of dehydroepiandrosterone (DHEA), which is a precursor molecule for testosterone. Saponins like ginsenoside-RB1 from ginseng can promote the release of luteinizing hormone, thereby resulting in increased testosterone levels (Zhu et al. 2017).

19.2.4.4 Hormonal Regulation in Preventing/Reversal of Cancer

Polyphenols can induce estrogenic or antiestrogenic responses in the target cells by blocking or altering the effects of the endogenous hormone (i.e., 17β-estradiol and E2). It makes polyphenol potential therapeutic agents that can affect cancer cells. ERα and ERβ are ligand-activated transcription factors that mediate the cellular effect of E2 (Cipolletti et al. 2018).

Since different polyphenols have differing affinity toward the estrogen receptors, their modulatory effect is mainly dependent on the type of target tissues/cell and their contrasting patterns of ERα/ERβ expression. Polyphenols’ differing bioavailability, metabolism, and their effects on enzyme and receptors can impact cancerous cells and their progression.

19.2.5 Hormonal Regulation by Bioactive Compounds in Prevention of Cancer

19.2.5.1 Impact on Breast/Ovarian/Prostate/Colon Cancer

Epidemiological studies show an inverse correlation between a traditional soy-rich diet and breast and prostate cancer risk (Pehlivan 2021a; b). Soy isoflavones and phytoestrogens bind to the estrogen receptor and modulate ER signaling. For instance, genistein can act to eliminate oxidative stress and modulate cell-cycle regulation that inhibits the activity of carcinogens and promote apoptosis, reducing inflammation (Pehlivan 2021a, b).

Research studies have found ERα to be overexpressed by 75% in invasive breast cancer, whereas ERβ expression decreases in the presence of usual conditions (Herynk and Fuqua 2004). Soy isoflavones (genistein, daidzein, glycitein) have been shown to upregulate ERβ expression, which helps them to suppress colon carcinoma cell growth by inhibiting the mitogenic signaling pathways (ERK1/2 and PI3K/Akt) and reducing the expression of proliferating cell nuclear antigen (PCNA) and NF-κB. They have also been able to restore ERβ expression in ovarian cancer cells and breast cancer cells, resulting in increased apoptosis and robust inhibition of cancerous cell proliferation (Cipolletti et al. 2018).

19.2.5.2 Impact on Thyroid Cancer

In addition to inducing changes in thyroid function upon excessive intake, flavonoids also play a critical role in regulating events associated with carcinogenesis, including invasion, apoptosis induction, and cell-cycle regulation. Given the way flavonoids interfere with thyroid hormone, it should not come as a surprise that they can also inhibit the proliferation of thyroid cancer cells by interfering with enzymes in cell signaling and proliferation pathways. Flavonoids like apigenin, chrysin, and genistein can interact with enzymes like protein tyrosine kinase (PTK), protein kinase C (PKC), and DNA topoisomerases I and II to effectively inhibit thyroid carcinoma cell proliferation (Paunkova et al. 2019).

Recent work has shown that Nrf2 protects the thyroid from oxidative damage induced by iodide overload and coordinates antioxidant defense in the thyroid gland. Curcumin, luteolin, and apigenin can stimulate Nrf2 transcriptional activity and induce heme oxygenase 1 (HO-1) protein (Paunkova et al. 2019). HO-1 exhibits antioxidative and anti-inflammatory functions via catalyzing oxidative degradation of cellular heme to carbon monoxide, biliverdin, and a free ion (Chao 2015). Also, HO-1 prevents vascular formation, not allowing tumorous cells to go malignant. Isothiocyanates can induce cytoprotective proteins via upregulating the Nrf2 pathway, thereby exhibiting antioxidative activities. It allows them to exert potential therapeutic actions against various diseases (Paunkova et al. 2019).

19.3 Sustainable Methods for the Production of Bioactive Compounds

The agri-food industry generates up to 140 billion tons per year of organic wastes as byproducts in the form of biomasses (Zuin and Ramin 2018). Disposing of these byproducts impacts the environment negatively. Further, these biomasses can serve as a low-cost energy source for biofuel production and an excellent resource for producing value-added compounds like bioactive components (Ayala-Zavala et al. 2018). Their large availability as byproducts makes them a perfect choice for the production of bioactive components.

As discussed previously in the chapter, naturally occurring phenolic compounds and other phytochemicals are well known for their beneficial effects on human health, such as preventing cancer and cardiometabolic disorders. These therapeutic properties have prompted using bioactive compounds as food supplements and biomedicine (Panzella et al. 2020). Therefore, it becomes more important to extract and produce these bioactive compounds sustainably and cost-effectively. It implies using eco-friendly measures and complying with the principles of the green economy to recover bioactive compounds from agri-food wastes (Panzella et al. 2020).

19.3.1 Green Technologies

Green technology is an umbrella term that indicates the environmental-friendly application of science and technology to create products via sustainable methods. Earlier, scientists have developed extraction methodologies requiring excessive use of organic solvents, such as methanol, ethanol, or acetone. However, there is an increasing need for a paradigm shift toward green and sustainable approaches for producing phenolic-rich extracts with low environmental impact (Panzella et al. 2020). A couple of such technologies are microwave-assisted extraction (MAE) and ultrasound-assisted extraction (UAE), which reduce the extraction time and limit the use of solvents.

19.3.2 Microwave-Assisted Extraction

Microwave-assisted extraction (MAE) is based on dielectric heating, wherein a microwave electromagnetic radiation heats a dielectric material by molecular dipole rotation of the polar components present in the matrix (Ran et al. 2019) (Fig. 19.6).

The MAE method involves the following:

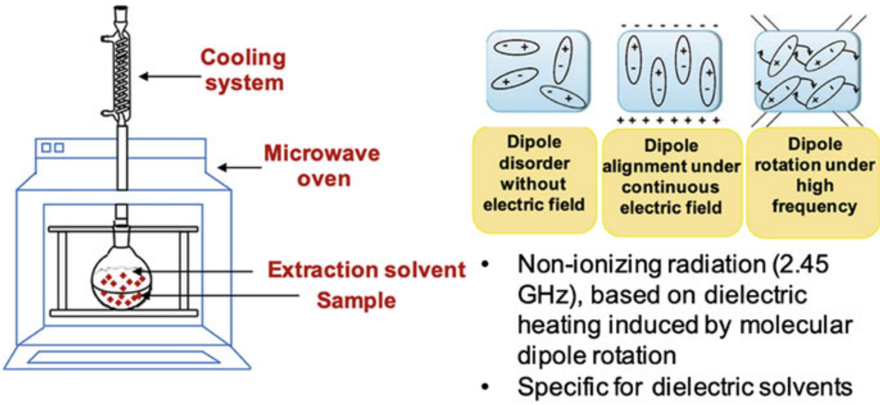

Fig. 19.6 Schematic representation of MAE equipment and characteristics. (From Panzella et al. 2020)

1. Penetration of the solvent into the matrix;
2. Solubilization and breakdown of components;
3. Transportation of the solubilized compounds from the insoluble matrix to the bulk solution; and
4. Separation of the liquid and residual solid phase.

A review study by Panzella et al. (2020) highlights that the microwave-assisted extraction technique is applicable to extract bioactive compounds from grape, wine, vegetable oil, potato, tomato, and citrus byproducts.

19.3.3 Ultrasound-Assisted Extraction

Ultrasound-assisted extraction (UAE) is one of the simplest extraction procedures requiring the use of an ultrasonic bath. It is based on the cavitation process induced by compression and expansion cycles associated with the passage of ultrasounds (20 kHz to 100 MHz frequency) through the sample. Therefore, the effectiveness of UAE depends upon the sample characteristics, such as consistency, rheology, and particle mobility, as these qualities affect the ultrasound energy dispersion (Panzella et al. 2020).

The UAE method involves the following:

1. The implosion of the cavitation bubbles inducing inter-particle collisions.
2. Particle disruption and enhanced diffusion of the extractable compounds into the solvent (Fig. 19.7).

Apparently, UAE seems to be the only effective green extraction methodology applied to pomegranate wastes. Further, UAE can also be used to extract bioactive compounds from citrus, apple, onion, potato, and carrot byproducts (Panzella et al. 2020).

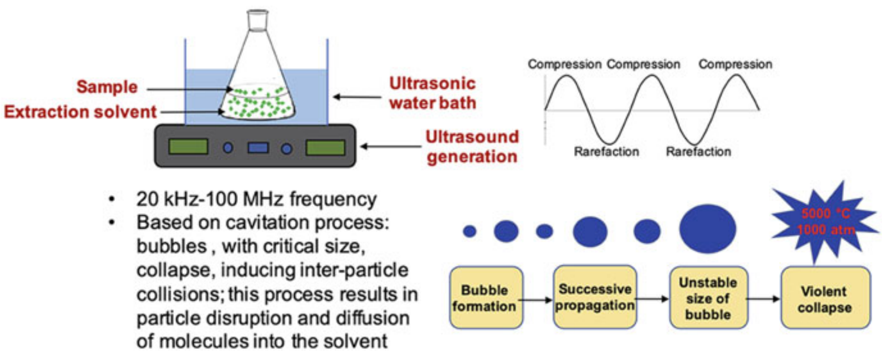

Fig. 19.7 Schematic representation of UAE equipment and characteristics (Source: Panzella et al. 2020)

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Bioactive Components for Ocular Health

20

Anmol Kumar

Abstract

Vision impairment significantly affects the quality of life. It is related to several diseases such as age-related macular degeneration (AMD), diabetic retinopathy, cataract, and glaucoma. According to World Health Organization (WHO), globally at least 2.2 billion people have a distance or near vision impairment. Almost in half of these cases, vision impairment has yet to be addressed or it could have been prevented. It includes people with moderate or severe distance vision impairment or blindness due to cataract (94 million), diabetic retinopathy (3.9 million), glaucoma (7.7 million), corneal opacities (4.2 million), trachoma (two million), or unaddressed refractive error (88.4 million) and near vision impairment due to unaddressed presbyopia (826 million). Ocular health has become a major concern lately due to a significant increase in screen time due to the pandemic which has restricted almost everyone to technological devices for their work, education, and all other basic activities. Blue light emitting from the screen can cause damage to the retina if exposed at high intensity in the visible range (390–600 nm). The damage to the eyes can be controlled or minimized by reducing the oxidative stress on the retinal cells. Several bioactive components and functional foods can help minimize the effect of blue light on the eyes and also reduce the risk or severity of several eye-related disorders.

Keywords

Ocular health · Oxidative stress · Functional components

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20.1 Introduction

The basic function of the eye is to collect light from the visible surroundings around us, converting it into a nerve impulse and helping us see the world around us. The cornea, pupil, iris, and lens play a pivotal role in transmitting and focusing the light on a light-sensitive tissue layer at the back of the eye, retina. The photoreceptors then turn the light into electrical signals which travel to the brain via the optic nerve. Then, the brain turns the signals into the images which we see.

A significant variation is observed in the causes within the countries as per the availability of eye care services, age, economic status, and eye care literacy among the population. The reason behind the degrading global eye health is due to the vertical running of health programs, focusing on a specific disease and not addressing the holistic health of a person. It can be corrected by providing comprehensive eye care which not only involves the treatment of ocular diseases but also involves the promotion, prevention, and vision rehabilitation of the incurable blindness caused due to non-communicable eye diseases (NCEDs) such as age-related macular degeneration (AMD), cataract, diabetic retinopathy, and more.

Vision 2020: Right to Sight, a global initiative, was launched by International Agency for Prevention of Blindness (IAPB) and WHO in 1999 to arrest and reverse the problem of blindness. The collaboration of both organizations has led to the elimination and prevention of avoidable blindness and considerably reduced the burden of cataracts in India (Deshpande 2008).

20.2 Concerns

20.2.1 Vision Impairment

Vision impairment impacts the quality of life drastically, as it reduces social participation and productivity and increases the risk of anxiety and depression. As per WHO, it also leads to an increase in global financial burden as the global annual cost of productivity losses due to uncorrected myopia was estimated to be US $244 billion, and for presbyopia, it was US $25.4 billion.

It is well-known that increased oxidative stress leads to or increases the severity of retinal degenerative disorders such as age-related macular degeneration, diabetic retinopathy, and glaucoma.

20.2.2 Diabetic Retinopathy

Diabetes mellitus is a major public health condition in developing and developed nations. Four hundred and twenty-two million people across the globe are affected by diabetes mellitus.

Urbanization and sedentary lifestyle have increased the incidence of diabetes mellitus in developing countries. It is a metabolic disorder, reflected by high blood glucose levels (hyperglycemia).

The lifestyle transformation and changes in dietary preferences of the urbanized generation including high glycemic index foods lead to obesity and diabetes mellitus, therefore increasing the risk of diabetic retinopathy. The retina of the eye is affected by this disease. It is caused due to high amounts of glucose levels in blood vessels of the retina blocking them and causing bleeding.

Hypertension or hypocholesterolemia along with diabetes mellitus increases the risk of diabetic retinopathy.

Diabetes mellitus can be treated or controlled with adequate physical activity, appropriate diet, medication, and regular screening. Keeping blood sugar levels in control will reduce the risk of accumulation of blood glucose in the retina's blood vessels and will reduce the risk of diabetic retinopathy.

20.2.3 Age-Related Macular Degeneration (AMD)

It is one of the most common NCED, leading to vision impairment in the elderly population. It is a disease in which the central vision gets blurred when the macula (which controls straight and sharp vision) starts getting damaged progressively due to the aging process.

It can be of two types: dry AMD (slow, gradual onset) and wet AMD (fast onset).

20.2.4 Cataract

A cataract is a condition when the protein in the lens breakdown and causes blurred, hazy, and cloudy vision.

Aging, heredity, diabetes mellitus, smoking, and exposure to ultraviolet (UV) rays can lead to the formation of cataracts.

20.2.5 Glaucoma

It is a disease in which the eye's optic nerve gets damaged due to the extra aqueous humor fluid buildup in the front part of the eye and therefore increasing the pressure in the eye.

20.3 Blue Light

Light acts on the body by two pathways: The primary optic tract governs visual perception and responses, whereas the retino-hypothalamic tract governs circadian, endocrine, and neurobehavioral functions. The retinohypothalamic tract is most sensitive to blue light stimulation—energy in the wavelength of roughly 459–485 nm (Holzman 2010).

The largest source of blue light is sunlight. The spectrum of the light has been exaplained in (Fig. 20.1):

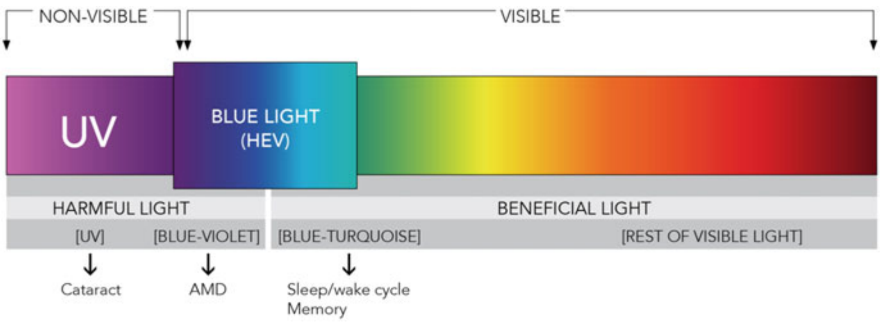

Fig. 20.1 Spectrum of light

- Fluorescent light
- CFL (compact fluorescent light) bulbs
- LED light
- Flat screen LED televisions
- Computer monitors, smartphones, and tablet screens (preventblindness.org).

Blue light exposure you receive from screens is small compared to the amount of exposure from the sun. And yet, there is concern over the long-term effects of screen exposure because of the proximity of the screens and the length of time spent looking at them. According to a recent NEI-funded study, children's eyes absorb more blue light than adults from digital device screens (preventblindness.org).

Blue light has a significant impact on mood, memory, and alertness. Exposure to blue light increases alertness, but it also tends to lower active memory and reaction time. Exposure to blue light for 8–9 h straight can cause phase shifts, depression, memory dysfunction, and sleep deprivation (Tosini et al. 2016).

Sleep is an integrated part of human health and life and is crucial for learning, performance, and physical and mental health. Increased duration of media exposure and the presence of a television, computer, or mobile device in the bedroom in early childhood have been associated with fewer minutes of sleep per night. Even infants exposed to screen media in the evening hours show significantly shorter nighttime sleep duration than those with no evening screen exposure. Mechanisms underlying this association include arousing content and suppression of endogenous melatonin by blue light emitted from screens (American Academy of Pediatrics).

Light-induced damage occurs to the retina when eyes are exposed to light of high intensity in the visible range (390–600 nm). Blue light can induce photoreceptor damage. Studies have shown that melanopsin-based photoreception is involved in the modulation of sleep, mood, and learning. Melanopsin plays an important role in mediating human circadian rhythms. Studies also suggest that it is a key player in the photic regulation of melatonin levels. Intrinsically photosensitive retinal ganglion cells (ipRGCs) play a major role in non-image forming photoreception, i.e., a photoreceptive system that regulates circadian photic entrainment, pupillary light response, and other important biological functions. They express pituitary adenylate cyclase-activating polypeptide (PACAP) and form the retinohypothalamic tract (RHT). The RHT is responsible for conveying the light information from RGCs to the part of the brain that controls circadian rhythms within the whole body (Tosini et al. 2016).

Various carotenoids are present in human plasma, but only the xanthophylls, lutein, and zeaxanthin are found in the retina in considerable amounts with particularly high levels in the macula lutea, the yellow spot in the center of the fovea. Carotenoids can quench singlet oxygen and scavenge reactive oxygen species (ROS), thus protecting biologically relevant molecules from oxidative modification. Junghans et al. investigated the blue light filter efficacy of carotenoids in unilamellar liposomes loaded in the hydrophilic core space with a fluorescent dye, Lucifer yellow excitable by blue light. Carotenoids were incorporated into lipophilic membranes. Fluorescence emission in carotenoid-containing liposomes was lower than in carotenoid-free control when exposed to blue light, indicating a filter effect. Filter efficacy was in the order lutein > zeaxanthin > beta-carotene > lycopene (Junghans et al. 2001).

Light-emitting diodes (LEDs) have been used to provide illumination in commercial and household environments. LEDs are used in televisions, computers, tablets, and smartphones. Although the light emitting through these gadgets seems to be white, LEDs have peak emission in the blue light range (400–490 nm). These days, people have become addicted to these devices and are also incorporating this habit in the younger generation. For example, mothers these days feed their children by switching on their child’s favorite TV show or YouTube channel. And thus, not only the adult population but also the young population is being affected by the tech devices and the light emitted by these devices in several ways.

Blue light at night can cause indirect disruption of homeostatic processes, like circadian clock, neurotransmission, melatonin secretion, and neuroplasticity involved in mood, and ultimately causes depressed mood and deficits in learning, memory, and cognition. Nighttime light can also affect mood through aberrant signals transmitted from ipRGCs in the retina to brain regions involved in emotional regulation and, thus, also cause depression and cognitive dysfunctions.

20.4 Bioactive Components and Functional Foods

A bioactive component is a compound that has the capability and the ability to interact with one or more components of the living tissue by resenting a wide range of probable effects, whereas a functional food consists of bioactive components that are extra-nutritional constituents that occur in small quantities and are said to be beneficial for the health.

Functional foods usually act as antioxidants that help scavenge the free radicals, reducing the severity of the disease in the body.

- *Marigold Flower*
  Peng et al. (2016) concluded that daily supplementation with lutein complex (12 mg lutein + 2 mg zeaxanthin) can remarkably ameliorate the antioxidant enzyme activity and plasma total antioxidant capacity. A preliminary HPLC test analysis of the lutein complex showed two distinctive peaks after extraction which represent lutein and zeaxanthin; therefore, it was speculated that the

retino-protective property of lutein complex would be due to lutein and zeaxanthin in marigold flowers. It is one of the richest sources of lutein and zeaxanthin. They constitute the main pigments found in the human retina's yellow spot, which protects the macula from damage by blue light, improves visual acuity, and scavenge harmful reactive oxygen species. They have also been linked with a reduced risk of age-related macular degeneration (AMD) and cataracts.

- *Kale Extract*
  Arnold et al. (2013) demonstrated the treatment of AMD patients with Kale extract for 4 weeks. It shows the increase in serum lutein and zeaxanthin levels and plasma xanthophyll levels improving the visual functioning in AMD patients.
- *Chlorella Powder*
  Jung et al. (2016) did a comparison with marigold petal extract to check the bioavailability of carotenoids from chlorella in healthy subjects. It was concluded that chlorella can be used as a carotenoid source (lutein) which is equivalent to marigold extract but with greater diversity and reliable mass production.
- *Einkorn Wheat*
  Antognoni et al. (2017) did an integrated evaluation of the potential health benefits of the einkorn-based bread. It was found that carotenoid levels are higher in einkorn bread than in the modern wheat species.
- *Bilberry Extract*
  Ozawa et al. (2015) examined the effect of bilberry extract supplementation on eye fatigue induced by acute video display terminal loads (VDT). It was observed that bilberry extract mitigated the VDT load-induced ocular fatigue sensation, pain, heaviness, uncomfortable sensation, and Week 8 and also protects against blue LED light-induced retinal cell damage (Ogawa et al. 2014).
- *Lingonberry Extract*
  Ogawa et al. (2014) conducted an in vitro study to understand the protective effect of lingonberry extract against blue LEDs. It was concluded that lingonberry containing high amounts of polyphenols (resveratrol, anthocyanin) exerts a protective effect against blue LED light-induced retinal photoreceptor cell damage by inhibition of reactive oxygen species and production and activation of pro-apoptotic proteins.
- *Taurine*
  Castelli et al. (2021) explained the relationship between taurine and oxidative stress in retinal health and disease. Taurine is one of the most abundant non-essential amino acids present in the anterior part of the eye.

  Taurine acts upon reducing the oxidative stress on the retinal cells and thus helps in treating most of the non-communicable eye diseases such as AMD, glaucoma, and diabetic retinopathy.
- *Cranberry Juice*
  Chang et al. (2017) conducted a study to understand the photoreceptive effects of cranberry juice and its various fractions against blue light-induced impairment in human retinal pigment epithelial cells. The study proved that condensed tannin-containing fraction of cranberry juice probably exhibits better free radicals scavenging activity and thereby effectively protected the human retinal pigment epithelial cells and thus hampers the progress of AMD.

20.5 Market Survey: Products Related to Ocular Health

Functional product name	Format type	Manufactured by/marketed by	Country	Target group	Recommended dosage	Nutrition	Claims for	Source
Bausch + Lomb Lutein Detskiy Kompleks	Chew	Valeant	Russia	Children (5–12)	–	Per 1 unit serving: energy 10 kJ/2.4 kcal, carbohydrate 0.6 g, vitamin A 250 μg, vitamin E 4 mg, vitamin C 30 mg, zinc 3 mg, taurine 50 mg, lutein 1 mg, lycopene 700 μg, zeaxanthin 250 μg, anthocyanins 4 mg	Eye health	GNPD
Bioglan Healthy Kids (blueberry-flavored eyegaurd chewable tablets)	Tablet	Natural bio	Australia	Children (5–12)	1 tablet/day	Per 1 unit serving: lutein 5 mg, D-alpha-tocopheryl acid succinate 4.5 IU/UI (of which vitamin E 5.45 IU/UI), beta-carotene 500 μg	Antioxidant, eye health	GNPD
Green Health Augen-Gold Kapseln (eye health supplement capsules)	Capsules	Panaceo International Active Mineral Production	Austria	–	–	Per 1 unit serving: vitamin C 80 mg (100% RDA), zinc 12 mg (120% RDA), vitamin E 12.5 mg-alpha-TE (104% RDA), copper 1 μg (100% RDA), vitamin B2 1.75 mg (125% RDA), beta-carotene 6 mg	Other (functional), gluten-free, cardiovascular (functional), low/no/reduced allergen, vegan, no animal ingredients, low/no/reduced lactose, eye health, dairy-free	GNPD
Twenty-first Century Mimi Bears (children's omega + DHA supplement)	Chew	DSM Nutritional Products	UAE	Children (5–12)	2–4 years: 1 gummy/day 4 and above: 2 gummies/day with any meal	Per 1 unit serving: calories 11.7 kcal, sodium 8 mg, total carbohydrates 3 g (1% RDA) (of which sugars 1.7 g), vitamin C 6.7 mg (11% RDA), total omega oil 62.7 mg (of which omega-3 44.7 mg, omega-6 14 mg, omega-9 4.3 mg), DHA 16.7 mg	Vegetarian, botanical/herbal, gluten-free, cardiovascular (functional), brain and Nervous System (functional), low/no/reduced allergen, eye health	GNPD
Bedeco Csokis Varázs (banana miracle chocolate drink)	–	Bedeco	Hungary	–	–	Per 100 mL: energy 328 kJ/ 78 kcal, fat 1.7 g (of which saturated fatty acids 1.1 g), carbohydrate 12.2 g (of which	Other (functional), vitamin/ mineral fortified, cardiovascular (functional), bone health, brain, and	GNPD

(continued)

Functional product name	Format type	Manufactured by/marketed by	Country	Target group	Recommended dosage	Nutrition	Claims for	Source
						sugars 11.7 g), protein 3.4 g, salt 0.12 g, vitamin C 15 mg, vitamin D 3.6 μg, thiamin 0.12 mg, calcium 86 mg, magnesium 28.5 mg, iron 1.6 mg, zinc 1.1 mg	nervous system (functional), immune system (functional), time/speed	
Dr. Loges Omega-3 Loges (dietary supplement with omega-3 fatty acid from microalgae)	Capsule	Dr. Loges	Germany	–	2 capsules/day	Per 2 unit: DHA and EPA 500 mg	Botanical/herbal, gluten-free, brain and nervous system (functional), low/no/reduced allergen, vegan, no animal ingredients, low/no/reduced lactose, eye health	GNPD
A. Menarini Sustenium i 5 Colori Della Salute Mix 5 Junior (red fruit-flavored multivitamin and multimineral food supplement)	Powder	A. Menarini Industrie Farmaceutiche Riunite	Italy	Children (5–12)	–	Per 1 unit serving: vitamin A 369 μg (46% RDA), beta-carotene 4.143 mg, vitamin A total 1060 μg (132% RDA), vitamin B1 0.305 mg (28% RDA), vitamin B2 0.225 mg (16% RDA), vitamin PP 3.25 mg (20% RDA), pantothenic acid 2.056 mg (34% RDA), vitamin B6 0.479 mg (34% RDA), folic acid 112.5 μg (56% RDA), vitamin C 36 mg (45% RDA), vitamin E 3.2 mg (27% RDA), vitamin K 28.95 μg (39% RDA), manganese 0.392 mg (20% RDA), potassium 534.5 mg (27% RDA), phosphorus 125.5 mg (18% RDA), magnesium 140 mg (37% RDA), calcium 121 mg (15% RDA), iron 3.3 mg (24% RDA), copper 0.27 mg (27% RDA), zinc 3.495 mg (35% RDA), selenium 15.5 μg (28% RDA), fructooligosaccharides 300 mg, lycopene 2.767 mg,	Botanical/herbal, gluten-free, antioxidant, cardiovascular (functional), digestive (functional), bone health, brain, and nervous system (functional), immune system (functional), low/no/reduced allergen, energy (functional), eye health, skin, nails, and hair (functional)	GNPD

						cranberry, e.g., 15 mg (of which anthocyanins 5.4 mg)		
GSK Scott's DHA gummies	Chew	GlaxoSmithKline	Philippines	Children (5–12)	3 gummies	Per 9 g serving: energy 138 kJ/33 kcal, protein 0.8 g, DHA 40 g, vitamin D 1.5 μg	Other (functional), bone health, brain and nervous system (functional), and eye health	GNPD
Haliborange Mr. Men Little Miss	Chew	Seven seas	UK	Children (5–12)	1–2 fruit softies daily	Per 1 unit: flaxseed oil 220 mg (of which omega 3 ALA 100 mg), vitamin A 400 μg-RE (50% RDA), vitamin D 2.5 μg (50% RDA), vitamin E 6 mg-alpha-TE (50% RDA), vitamin C 60 mg (75% RDA), niacin 8 mg-NE (50% RDA), vitamin B6 1.4 mg (100% RDA), vitamin B12 2.5 μg (100% RDA), pantothenic acid 6 mg (100% RDA)	Brain and nervous system (functional), immune system (functional), eye health	GNPD
Happi Kidz (multivitamin + mineral gummies)	Chew	British Life Sciences	India	Children (5–12)	4 gummies/day	Per 4 unit serving (15 servings per pack): calories 44.64 kcal, total carbohydrates 11.16 g, protein 0 g, fat 0 g, vitamin A 1000 IU/UI (20% RDA), vitamin D 220 IU/UI (55% RDA), vitamin E 6 IU/UI (20% RDA), vitamin C 20 mg (33% RDA), vitamin B1 0.3 mg (20% RDA), vitamin B2 0.3 mg (18% RDA), vitamin B6 0.4 mg (20% RDA), vitamin B3 4 mg (20% RDA), vitamin B12 1.2 μg (20% RDA), biotin 60 μg (20% RDA), choline 44 mg (8% RDA), folic acid 80 μg (20% RDA), calcium D pantothenate 2 mg (20% RDA), iodine 25 μg (17% RDA), selenium 20 μg (67%	No additives/preservatives, other (functional), vegetarian, gluten-free, antioxidant, brain and nervous system (functional), immune system (functional), low/no/reduced allergen, GMO-free, eye health, social media	GNPD

(continued)

Functional product name	Format type	Manufactured by/marketed by	Country	Target group	Recommended dosage	Nutrition	Claims for	Source
						RDA), zinc 0.75 mg (5% RDA)		
Nutrizeit Nutri Gummi	Chew	Nutrizeit	India	Children (0–12)	Below 4: 1 gummy/day 4 and above: 2 gummies/day	Per 1 unit serving: energy 7.5 kcal, docosahexaenoic acid 6.6 mg, eicosapentaenoic acid 10 g, vitamin A 1200 IU/UI, vitamin B6 0.5 mg, vitamin B12 2 μg, vitamin C 10 mg, vitamin E 5 IU/UI, zinc 1 mg, sodium 1 mg, total fat 0 g, total carbohydrates 2 g (of which sugars 1.5 g)	No additives/preservatives, all-natural product, other (functional), gluten-free, cardiovascular (functional), digestive (functional), bone health, brain, and nervous system (functional), immune system (functional), low/no/reduced allergen, ethical-environmentally friendly package, eye health, skin, nails, and hair (functional)	GNPD
Nutrizeit Nutri Gummi	Chew	Nutrizeit	India	Children (0–12)	Below 4: 1 gummy/day 4 and above: 2 gummies/day	Per 1 unit: energy 7.5 kcal, vitamin A 1250 IU/UI, vitamin B5 2.5 mg, vitamin B6 0.5 mg, vitamin B7 30 μg, vitamin B9 120 μg, vitamin B12 2 μg, vitamin C 10 mg, vitamin D 100 IU/UI, vitamin E 7.5 IU/UI, iodine 20 μg, zinc 1.1 mg, choline 15 μg, inositol 15 μg, total fat 0 g, total carbohydrates 2 g (of which sugar 1.5 g)	No additives/preservatives, all-natural product, other (functional), vegetarian, gluten-free, cardiovascular (functional), digestive (functional), bone health, brain, and nervous system (functional), immune system (functional), low/no/reduced allergen, ethical-environmentally friendly package, no animal ingredients, eye health, skin, nails and hair (functional)	GNPD
Bilberry Capsules	Capsule	Vitawin	India	Teenagers, adults	1 capsule/serving (twice a day)	Bilberry (*Vaccinium myrtillus*) 500 mg, excipients q.s.	Healthy eyesight, better blood flow, supports connective tissue health	Amazon
Eyevitan	Tablet	Healthvit	India	–	1–2 tablet/day	Bilberry, lutein and zeaxanthin, vitamin A, D, E, C, B1, B2, B3, B6, 12, folic acid, magnesium, iron, zinc, copper, selenium, chromium, iodine. Others—Dibasic calcium phosphate, maize starch,	Supports vision health powerful antioxidant general wellness	Healthvit.com

						povidone. Colloidal silicon dioxide. Magnesium stearate, purified talc, croscarmellose sodium, anhydrous lactose.		
Ocuvite Blue Light	Soft Gel	Bausch & Lomb	US	–	1 soft gel/day	Lutein (marigold flower extract) 25 mg, zeaxanthin (marigold flower extract) 5 mg.	Shields eye and filters blue light	Ocuvite.com
						Other ingredients—soybean oil, gelatin, glycerin, sunflower oil, yellow beeswax, soy lecithin, natural tocopherols, titanium dioxide, FD&C red 40, FD&C blue 1.		
Ocuvite Adult 50+	Soft Gel (Mini Gel)	Bausch & Lomb	US	Adults above 50	1 soft gel/day	Total fat <0.5 g	Protect eye health by replenishing the important nutrients	Ocuvite.com
						polyunsaturated fat <0.5 g		
						cholesterol 0 mg		
						Vitamin C (ascorbic acid) 150 mg		
						Vitamin E (D-alpha tocopherol) 20 mg		
						Zinc (zinc oxide) 9 mg		
						Copper (copper oxide) 1 mg		
						Omega-3 fatty acids (160 mg EPA, 90 mg DHA) 250 mg		
						Lutein (marigold flower extract) 5 mg		
						Zeaxanthin (marigold flower extract) 1 mg		
						Other ingredients—fish oil (from anchovies, sardines), gelatin, glycerin, yellow beeswax, silicon dioxide, carmine, caramel, natural flavor, soy lecithin, titanium dioxide.		

20.6 Conclusion

A review of the concerns related to ocular health in the current scenario and the various bioactive components and functional foods was conducted. It has been observed that along with the number of major ocular diseases such as AMD, glaucoma, diabetic retinopathy, and cataract, exposure to blue light has been increased lately, which has been affecting the ocular health of all age groups significantly. There are few functional foods such as marigold flower, kale, and bioactive components such as lutein, zeaxanthin, and taurine that have been effective in reducing the damage from blue light or severity from the disease. A total of 16 products related to ocular health were surveyed on online portals such as GNPD, Amazon, and brand websites. It was concluded that lutein, zeaxanthin, taurine, lycopene, zeaxanthin, anthocyanins, D-alpha tocopheryl acid succinate, beta-carotene, vitamin E, C, B2, zinc, copper, omega-3, and bilberry were some of the common bioactive components which were used in the products.

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Part IV

Functional Foods: Emerging and Sustainable Innovative Trends

21 Nutrigenomics Research: A Review

Swarnima Dey and Yogesh Kumar

Abstract

In past 20 years, it has been told us to take nutrient-rich food for maintaining good health. Recently, it is studied that nutrient is responsible for the modification of gene and protein expression and at last influences cellular and organismal metabolism. Nutritional genomics, i.e., nutrigenomics, is behind the alteration of gene–diet interaction. The diverse tissue and organ-specific results of bioactive dietary components consist of gene expression patterns (transcriptome), enterprise of the chromatin (epigenome), protein expression patterns, inclusive of post-translational modifications (proteome), as nicely as metabolite profiles (metabolome). Nutrigenomics goes deeper, using molecular tools to become aware of how vitamins and bioactive meal compounds alter the DNA transcription and translation process, affecting the expression of genes that alter essential metabolic pathways, which may also finally affect health results. Ultimately, nutrigenomics will give the gene-nutrient information for restoring health and preventing nutrient-related disease. In this chapter, we provide an overview of nutrigenomics, gene–nutrient interactions, role on human health, and future opportunities.

Keywords

Nutrigenomics · Transcriptome · Epigenome · Proteome · Metabolome

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21.1 Introduction

The Nutritional Genomics has immense potential and has affected the future for different dietary guidelines & personalized recommendations for the health seeking communities. It covers two main areas: Nutrigenetics and Nutrigenomics. Nutrigenetics is defined as the scientific study that analyses the effects of certain allelic variations of genes associated in nutrition metabolism on human health. Nutrigenomics, on the other hand, is a modern -omic science that studies the impact of food molecules on gene expression. The most modern conceptions of "environment-DNA" and/or "nutrient-DNA" epigenetic relationships are encapsulated in a single title and package. These associations, in most situations, do not influence or affect the DNA sequence, but rather operate on its own chemistry and alter gene expression, often in a genetically determined manner. The nutrient-DNA interactions involve a number of players, and understanding all of their components is made to explain how food and lifestyle might affect human health (Bordoni and Capozzi 2014). Nutrigenetics and Nutrigenomics, as separate disciplines, can provide future food science operators with specialised integrated training and a cross-disciplinary approach. According to the research, the World Health Organization believes that main risk factors like lifestyle, eating choices, physical inactivity, smoking and alcohol consumption are responsible for roughly 30% of cancer fatalities (Gavrilas et al. 2016). DNA and chromatin serve as metabolic sensors at the "cell" level (Gut and Verdin 2013) while dietary chemicals, including alcohol, work as epigenetic modulators of I DNA methylation, histone acetylation/deacetylation, and the action of short non-coding RNAs. The long-term effects of moderate alcohol use, as contrast to excessive consumption, are inconsistent since there is no universal agreement on what constitutes "light" or "moderate" drinking. DNA and chromatin serve as metabolic sensors at the "cell" level (Topiwala and Ebmeier 2018).

A nutrigenetic/nutrigenomic paradigm can aid in the clarification of the debate. In reality, allele variants for several alcohol metabolism-related genes (e.g., ADH, ALDH, CYP2A6) can help address some of the variation in consumption of alcohol and can be utilized to investigate some of the relationships between consumption of alcohol and major disorders, including cancer. Similarly, it may be feasible to help understand the mechanisms involved by which, for example, the antioxidant effect of polyphenols found in wine and other alcoholic beverages decreases the risk of neoplastic and non-neoplastic disorders through in vitro or in vivo nutrigenomic investigations. Collecting information on such topics is extremely important in today's society because the idea that every dose of "natural alcohol" like wine, beer, and other crop-derived alcoholic drinks can be healthy could be diffuse, especially among those individuals who are very responsive to the so-called natural or bio. As can be seen, the natural origin of any bioactive chemical does not guarantee its low degree of toxicity or absence of toxicity (Caradonna et al. 2022).

The goal of nutrigenomics is to characterize, analyse, and reconcile the interactions among food components and gene expression across the genome. Genomic loci associated with metabolic and/or regulatory channels may provide a biological explanation for how a food chemical mediates its impacts and increases the risk of diet-related disorders. Epigenomics is a branch of biology that explores the impact of environmental factors on gene expression. Diet is the human body's primary environmental exposure and the most important daily lifestyle choices that each person makes. As a result, one of the main goals of epigenomics is to figure out how food chemicals alter the epigenome and, as a result, gene expression. As a result, nutrigenomics and epigenomics are linked. Both fields' information may be used to construct methods that allow for optimal lifestyle decisions that lead to healthy, disease-free ageing (Carlberg 2019).

RNA sequencing, chromatin immunoprecipitation accompanied by sequencing (ChIP-seq), and formaldehyde-assisted identification of regulatory elements guided by sequencing (FAIRE-seq) are examples of next-generation sequencing technologies that allow unbiased evaluation of genome-wide mRNA expression, transcriptionally binding, histone modifications, and chromatin accessibility. Large research consortia like ENCODE (www.encodeproject.org) and Roadmap Epigenomics (www.roadmapepigenomics.org) amassed massive volumes of data on the baseline state of over a century human cell lines, as well as roughly the very same number of important human tissues and cell types (Carlberg 2019).

21.2 Nutrient-Sensing Mechanism

The metabolic enzymes, regulatory kinases, membrane receptors, and transcription factors focus on sensing the quantity of fatty and amino acids along with glucose. Glucose plays an important role as a member of the nuclear receptor superfamily in the nutrient-sensing pathways. Macronutrients and micronutrients are bound to nuclear receptors with their metabolites like fatty acids to PPARs, oxysterols to liver X receptors, and vitamin D to vitamin D receptors, allowing nutritional variations to be translated into genomic responses. Nuclear receptors in metabolic organs response to nutrients changes by activating the numerous target genes. Furthermore, nuclear receptors and their ligands activate the immune system's inflammatory and antigen responses. Additionally, nuclear receptors are transcription factors that come into play a key role in the management of the circadian system in both the CNS and peripheral organs.

Essentially, all of our body's tissues and cell types have a functional molecular base, whose coordination is critical for optimal physiological metabolism. The selection of robust nutrition sensing mechanisms was influenced by periodic scarcity of nutrients. The direct binding of the macronutrient or micronutrient to its sensor and an indirect method based on the identification of a metabolite that indicates the nutrient's availability are both possibilities for this sensing process. The relevant sensor is a protein which binds nutrients with the affinity for variations in physiological concentrations. The release of hormones or other signalling molecules into the circulation may be triggered by the detection of nutrients, resulting in a coordinated response of the entire organism. Lipids are rarely encountered free in soluble form due to its non-polar behaviour, i.e., its insolubility in aqueous phase. They are either carried in lipoproteins and chylomicrons or coupled by albumin in serum.

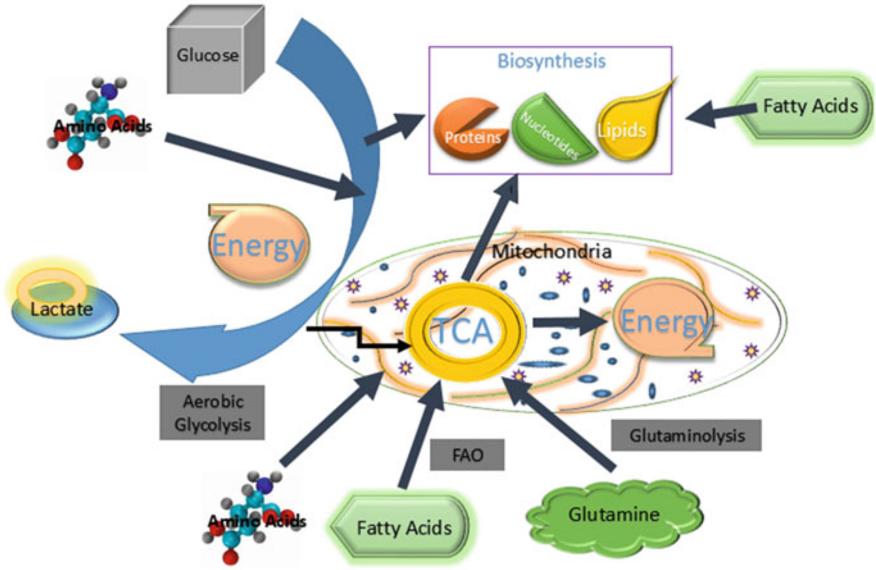

Fig. 21.1 Nutrient-sensing mechanism

GPRs (G protein-coupled receptors) engaged with long unsaturated fatty acid chains, like those found in the membrane of pancreatic cells, and boost glucose-triggered insulin release in these cells. The binding of lipids to GPRs in enteroendocrine cells of the intestine results in the production of incretins (i.e., gastrointestinal hormones that amplify insulin secretion). The scavenger receptor binds fatty acids in the intestinal lumen and begins their absorption (Carlberg 2019). Figure 21.1 shows the nutrient-sensing mechanism in brief.

Internal cholesterol levels must be accurately sensed in order to avoid activation of the energetically difficult cholesterol synthesis pathway and hazardous levels of free cholesterol in the cell in the event of plentiful external supply. SCAP is a protein that binds cholesterol. SCAP enhances its affinity for the INSIG1 (insulin-induced gene 1) protein, which anchors SCAP and the transcription factor SREBF1 (sterol regulatory element-binding transcription factor 1) within the ER membrane, when intracellular cholesterol levels are high. SCAP-SREBF dissociates from INSIG and shuttles to the Golgi apparatus, where SREBF is liberated, translocates to the nucleus, and activates genes involved in lipid anabolism, such as cholesterol production and lipogenesis. Further, the enzyme HMGCR (HMG-CoA reductase), that is also found in the ER membrane, catalyses a rate-limiting phase of cholesterol de novo synthesis at low cholesterol levels. High quantities of substrates in the cholesterol production pathway, such as lanosterol, on the other hand, cause HMGCR to bind to INSIG, resulting in the enzyme's ubiquitin-mediated destruction. High cholesterol levels activate LXRs, implying that the SREBF and LXR pathways function in concert to sustain cellular and overall cholesterol homeostasis. When amino acids are in insufficient supply, cellular proteins are employed as a reserve and destroyed by the proteasome or autophagy. Therefore, by maintaining cellular energy levels, this mechanism aids survival during hunger. In contrast, amino acids can be catabolized for the generation of glucose and ketone bodies during periods of protracted hunger and hypoglycaemia; i.e., they supply important energy sources for the brain. Hepatic gluconeogenesis elevates glucose levels within liver cells during hypoglycaemia, and plasma membrane protein exports glucose to the circulation. The enzyme glucokinase, which catalyses the initial phases in the storage and consumption of glucose, i.e. glycogen formation and glycolysis, is involved in intracellular glucose sensing. The glucokinase has a low insulin affinity than the other hexokinases; hence, it is only active at high sugar levels. As a glucose sensor, glucokinase works similarly to plasma membrane protein. This characteristic permits glucokinase to transport non-phosphorylated glucose from the liver towards the brain and skeletal muscles under lower glucose levels. The comprehensive research towards nutrient-sensing systems, particularly those mediated by nuclear receptors, would enable a more holistic understanding of our body's biochemical reactions to food components. This will include not just the cross-regulation of distinct nutrient-sensing pathways, but also other signalling pathways including those that control cellular development or mediate chronic inflammation (Carlberg 2019).

Many extracellular growth factors and cytokines (signalling molecules) all seem to be hydrophilic and therefore cannot pass through cellular membranes, requiring interaction with membrane receptors to activate a signal transduction pathway that ultimately leads to changes in gene expression via the activation of a transcription factor. As a result, transcription factors act as sensors for a wide range of cellular changes. The signal transduction process is simpler in the case of lipophilic signalling molecules, like steroid hormones, because these molecules can pass through cellular membranes where it binds straightforwardly to the nuclear receptors which are the ligand-sensitive transcription factors. Nuclear receptors are a group of transcription factors that can bind to and be activated by small lipophilic molecules termed ligands. There are 48 nuclear receptors in humans. Micro- and macronutrients, as well as their metabolites, make up a large portion of these nuclear receptor ligands. It thus involves retinoic acid (vitamin A derivate), fatty acids, lipids, bile acids, oxysterols, and other hydrophobic food ingredients. The specificity of such nuclear receptors towards specific distinct ligands varies from 0.1 nM to greater than 1 mM and reflects normal molecular concentrations. As a result, few nuclear receptors act as real micronutrients and macronutrient sensors. Other nuclear receptors, such as the hepatocyte nuclear factor liver receptor and steroidogenic factors, bind nutritional derivatives like sterols, phospholipids, fatty acids, and haem, and the interaction does not fall under sensing. The sensor's heterodimers' correct and precise detecting nuclear receptors attach to certain nucleotide sequences. Other nuclear receptors, on the other hand, form homodimers or even touch DNA as monomers. Heterodimer complexes are found in the nucleus, where they do not disintegrate from the chaperone proteins to diffuse back into nucleus. This shows that the nucleus is where macro- and micronutrient sensing occurs through nuclear receptors. Nutrients can thus operate as gene switches by causing a structural shift in the ligand-binding regions of certain nuclear receptors (Carlberg 2019).

The immune system is made up of a variety of highly specialized cells which are all produced through a process known as haematopoiesis, which involves the differentiation of blood cells. Epigenetic pathways regulate cellular differentiation, and a number of developmental transcription factors play a critical role. Immune system cells have a high turnover rate, allowing them to respond to environmental changes as quickly as possible. The differentiation and subtype specification of immune cells such as T cells, macrophages, and dendritic cells is aided by lipid sensing and signalling via nuclear receptors. Notably, such cells seem to be mobile and can be found in various different subtypes almost anywhere in human bodies, including metabolic tissues and disease scenarios like obesity. Thus, alterations in the transcriptome profile and subtype specification of macrophages and dendritic cells, as well as their precursors, monocytes, coordinate metabolic, inflammatory, and general stress-response pathways show maximal adaptive environmental changes. Nuclear receptors play a crucial role in perceiving these endogenous and external stimuli, as well as modifying the immune cells' gene expression profiles (Carlberg 2019).

21.3 Interference of Human Genome and Nutrients

Nutrigenomics is a new field that has been used to investigate the effects of specific foods on gene expression, metabolic processes, and epigenetic variables in cells (Gilani et al. 2021). It serves as a tool for assessing the impact of enhanced nutrient digestion and absorption on health and productivity (Nowacka-Woszuk 2020). Nutrients have various biological functions, including radical scavenging (antioxidants) and powerful signalling molecules, in addition to their role as building blocks and energy sources (nutritional hormones). As a result, in livestock systems, a modified diet is utilized to infer the function of nutrients in the host on gene expression, protein levels, and metabolite synthesis (Vilar da Silva et al. 2020).

The intricate relationship between our environment, diet, and genome is discussed in this section. Genes determine how we respond to food, and nutrients, or a lack thereof, can influence gene expression. More than 90% of our genes have remained unchanged since the stone ages, when existence depended on food availability. The molecular basis for our genome's latest adaptation to environmental changes, such as less UV-B exposure after migrating north, and nutritional options, such as lactose tolerance, will be described in this paper. The majority of our genome's trait-associated variations are found outside of protein-coding areas, such as regulatory SNPs near transcription factor binding sites. Nutrigenomics has combined components of molecular biology and next-generation sequencing technologies to investigate how food affects our epigenome, genome, transcriptome, proteome, and metabolome. These approaches can be used to examine persons holistically, such as in iPOP (integrated personal omics profile) assessments. The corresponding datasets serve as the foundation for optimising individualized nutrition and protecting health by preventing nutrition-related disorders. Selected stresses in local habitats, along with random genetic drifts, result in population-specific genetic adaptations during the last 50,000 years of migration. Variations in pigmentation genes are a prime example of environmental adaptation in Europe and Asia. The amino acids phenylalanine, tyrosine, and cysteine are transformed to melanin during the process of melanogenesis. Light hair, light skin, and blue eyes can be caused by variations in genes encoding for enzymes in this pathway, as well as ion channels in melanocytes and transport molecules involved in melanosome maturation and export. After being transported from melanocytes to keratinocytes or hair shafts, the amount of eumelanin (black-brown) and pheomelanin (yellowish-reddish) produced within melanosome granules impacts skin and hair colour (Carlberg 2019).

Our diet is primarily made up of starches such as grain flour, rice, and potatoes. The carbohydrate starch is broken down into glucose by enzymes from the amylase gene family, which are found in saliva and the pancreas of some species, including humans. Individuals in agricultural civilizations with starch-rich diets have more copies of the amylase genes than hunters and gatherers who eat less starch. Humans, unlike archaic homini, have up to 20 copies of the gene, which results in higher levels of salivary protein expression. This improves the digestion of starchy foods and gives the mouth a pleasant taste. The amplification of the gene is an example of positive evolutionary selection, emphasising the importance of these staples in our diet for a long time. The ADH (alcohol dehydrogenase) gene cluster encodes for ethanol metabolising enzymes and is another example of a gene locus that was positively selected when agriculture made fermented alcoholic beverage manufacture simple. These examples imply that the switch to new diet sources following the introduction of agriculture, as well as the colonization of new environments, played a significant role in human gene selection (Carlberg 2019).

The consumption of fresh milk from infancy through adulthood, referred to as lactase persistence, is probably the most well-known example of our genome adapting to dietary changes. Lactose, a disaccharide, is the primary carbohydrate in milk and a major source of energy for most baby animals. Lactose is converted into glucose and galactose by the intestinal enzyme lactase non-persistence, commonly known as lactose intolerance, which is an autosomal recessive trait marked by decreased expression of the lactose gene after weaning, i.e. older children and adults no longer express the enzyme. Lactose intolerance was presumably the default genetic configuration of early humans (and most other mammals) to minimize competing for breast milk between infants and older children or even adults. In addition to not receiving direct energetic benefits from lactose digestion, lactose-intolerant persons who consume lactose may have digestive symptoms such as bloating, flatulence, cramps, nausea, and diarrhoea, which may result in nutritional loss. Lactase persistence mutations are among the most strongly chosen genetic variants in all human positive selection episodes (Carlberg 2019).

According to a GWAS research, 88% of trait-associated variations are found outside of the human genome's protein-coding regions. The detection of transcription factor binding to the variable genomic region, for example, can offer possible therapeutic approaches when the associated transcription factor is "druggable." Gene regulatory events involving regulatory SNPs are influenced not only by the sequence of the genomic region, but also by its accessibility within chromatin. This stresses epigenomics' impact on regulatory variation. Unlike the genome, which is the same in all 400 tissues and cell types of an individual, the epigenome, and hence gene expression, is dependent on the specific tissue and the signals it is exposed to; i.e. it represents the cell's dynamic state. The expression quantitative trait locus mapping is based on the next-generation sequencing method RNA-seq in combination with SNP information. This method allows for the functional evaluation of a genetic variation at the transcriptome level. In general, functional genetic variations can influence several steps in the gene expression pathway, from genes to mRNAs to active proteins which are as follows:

- An alteration in transcription factors' preference for its genomic binding locations in promoters and enhancers.
- The interactions between chromatin are disrupted.
- The modification of ncRNA functioning.
- Alternative splicing is induced.
- A change in the pattern of protein post-translational modifications.

The effect size of functional SNPs is difficult to anticipate because it is dependent on the affected regulatory pathway and its epigenomic environment. Changes in transcription factor association caused by variations in their specific binding locations are now the best-understood types of regulatory SNPs. Epigenomics has developed a unique genome-wide asset that aids in the identification of regulatory SNPs at the level of post-translational histone modifications, such as methylations and acetylations at various positions of histones that indicates active and repressed enhancer and promoter regions; chromatin accessibility; genomic association of more than 100 transcription factors; DNA methylation indicating inactive genomic binding profiles; and the non-coding transcriptome. The database contains data on chromatin state, transcriptional regulator binding, and eQTLs, making it possible to identify and analyse functional DNA elements at regulatory variant sites (Carlberg 2019).

21.4 Nutritional Epigenetics and Signalling

Numerous studies in humans, animals, and cell cultures have validated that macronutrients (e.g., fatty acids and proteins), micronutrients (e.g., vitamins), and naturally occurring bioreactive chemicals (e.g., phytochemicals such as flavonoids, carotenoids, coumarins, and phytosterols, and zoochemicals such as eicosapentaenoic acid and docosahexaenoic acid) regulate gene expression in various methods. The essential agents through which vitamins affect gene expression are transcription factors. Among the most vital team of nutrient sensors is the nuclear receptor superfamily of transcription factors, with 48 contributors in the human genome. Numerous receptors in this superfamily bind vitamins and their metabolites (Müller and Kersten 2003). For example, nuclear receptors, such as peroxisome proliferator activator receptor-α (PPAR α) (binding fatty acids) or liver X receptor α (binding cholesterol metabolites), bind as heterodimers collectively with retinoid X receptor to unique nucleotide sequences (response elements) in the promoter regions of a giant wide variety of genes. During ligand binding, nuclear receptors endure a conformational exchange that outcomes in coordinated dissociation of corepressors and recruitment of coactivator proteins to allow transcriptional activation. In metabolically energetic organs, such as the liver, intestine, and adipose tissue, these transcription factors act as nutrient sensors with the aid of altering the stage of DNA transcription of specific genes in response to nutrient changes. Nuclear receptors have necessary roles in rules of numerous processes, including nutrient metabolism, embryonic development, and cell differentiation. Not surprisingly, nutrients, by way of activating these receptors, are able to have an impact on a broad array of cell functions. As an example, the PPAR team of nuclear receptors acts as nutrient sensors for fatty acids and influences expression of particular genes. One of the three PPAR isoforms, PPAR α is current chiefly in the liver (Mandard et al. 2004). The more than 3000–4000 target genes of PPAR α are concerned in several metabolic processes in the liver, which includes fatty acid oxidation, ketogenesis, gluconeogenesis, amino acid metabolism, cellular proliferation, and the acute-phase response (Mandard et al. 2004). Hepatic PPAR α is mainly important throughout fasting, when free fatty acids are launched from adipose tissue. These fatty acids then journey to the liver, where they undergo partial or entire oxidation. However, these fatty acids additionally bind PPAR α, which then increases expression of a suite of genes via binding to precise sequences in their promote regions. Fasted PPAR α null mice (mice that lack functional PPAR α) suffer from a range of metabolic defects, which include hypoketonaemia, hypothermia, multiplied plasma-free fatty acid levels, and hypoglycaemia (Mandard et al. 2004; Kersten et al. 1999). Recently, it has been verified that PPAR α directly regulates expression of genes involved in hepatic gluconeogenesis and glycerol metabolism (Mandard et al. 2004; Afman and Müller 2006). Because fatty acids are ligands for PPAR α, the latter mechanism may want to provide an explanation for the stimulatory effect of improved plasma-free fatty acids on hepatic gluconeogenesis and glucose output. In addition to its important feature in the physiological response to food deprivation or starvation, the role of PPAR α in obesity is much less clear, however most likely relevant to our perception of the obesity-linked pathophysiology of kind 2 diabetes (Patsouris et al. 2004; Afman and Müller 2006). Visceral weight problems are linked to increased free fatty acid degrees and, interestingly, these molecules might also be recognized by means of the liver as "hunger" or "in want of glucose" signals, ensuing in improved gluconeogenesis in a PPAR α-dependent manner, especially beneath prerequisites of hepatic insulin resistance (Moller and Kaufman 2005).

In addition to the group of sensing transcription factors that without delay have interaction with DNA by using binding to unique response elements, the importance of corepressor and coactivator proteins became extra evident because a tremendous issue of gene manipulate is directed at the expression of coactivators. Coactivators exist in multiprotein complexes that dock on transcription elements and regulate chromatin, permitting transcription to take place. Recent facts on two coactivators of PPARγ, known as peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1α and PGC-1β), are fascinating (Afman and Müller 2006). PGC-1 α has been related with electricity homeostasis, diabetes, and lifespan legislation. Polymorphisms in the genes encoding PGC-1α and PGC-1β have been related with development of kind 2 diabetes. Recently, high-fat feeding in a mouse mannequin has been shown to set off hyperlipidaemia and atherogenesis and to stimulate expression of PGC-1β in liver. Through molecular studies, the authors linked this mechanism to accelerated lipogenesis and very low-density lipoprotein excretion because of enhancer outcomes of PGC-1β on gene transcription ruled by using the transcription elements sterol regulatory issue binding protein 1 and liver X receptor α (Ling et al. 2004; Patti et al. 2003). From these results, a mechanism has been proposed by using which dietary saturated and transfatty acids can stimulate hyperlipidaemia and atherogenesis (Lin et al. 2005). This find out about demonstrates sensitivity of contemporary microarray evaluation and is an instance of nutrigenomics lookup due to the fact it permits simple detection of profound adjustments in hepatic gene expression patterns because of an adaptive response by the organism to modifications in dietary macronutrient composition (Afman and Müller 2006).

The 3-dimensional complex of genomic DNA and nucleosome-forming histone proteins is known as chromatin (Carlberg and Molnár 2014). It is classified into much less densely packed euchromatin, which without difficulty on hand to transcription elements and other nuclear proteins, and compact heterochromatin, which is a functionally repressed country (Beisel and Paro 2011) (Fig. 21.2). Post-translational histone modifications and DNA methylations as nicely as modifications of the third-dimensional structure signify functionally relevant chromatin levels. Euchromatin is placed closer to the centre of the nucleus, and in this open form of chromatin, histone proteins are frequently acetylated and genomic DNA is unmethylated. In contrast, heterochromatin is determined closer to the nuclear membrane, and in this closed chromatin form, both nucleosomes and genomic DNA are methylated. Epigenomics studies chromatin differences that do not contain adjustments to the genome (Carlberg 2019). Epigenome changes, additionally referred to as epigenomic programing, are very outstanding during embryogenesis, the place totipotent stem cells beget a number pluripotent traces of the embryo, which in turn act as precursors of terminally differentiated cells (Perino and Veenstra 2016). This differentiation manner restricts the access to an increasing quantity of genomic regions and genes that they are controlling, so that terminally differentiated cells are capable to focal point on their specialized functions. Thus, chromatin accessibility performs a necessary function in regulating gene expression. There is dynamic competition between nucleosomes and transcription factors for crucial binding regions within genomic DNA, such as enhancers and promoters. Chromatin dynamics are influenced by using a large set of chromatin modifying and redesigning enzymes, which interpret ("read"), add ("write"), or put off ("erase") post-translational histone modifications or DNA methylation (Carlberg and Molnár

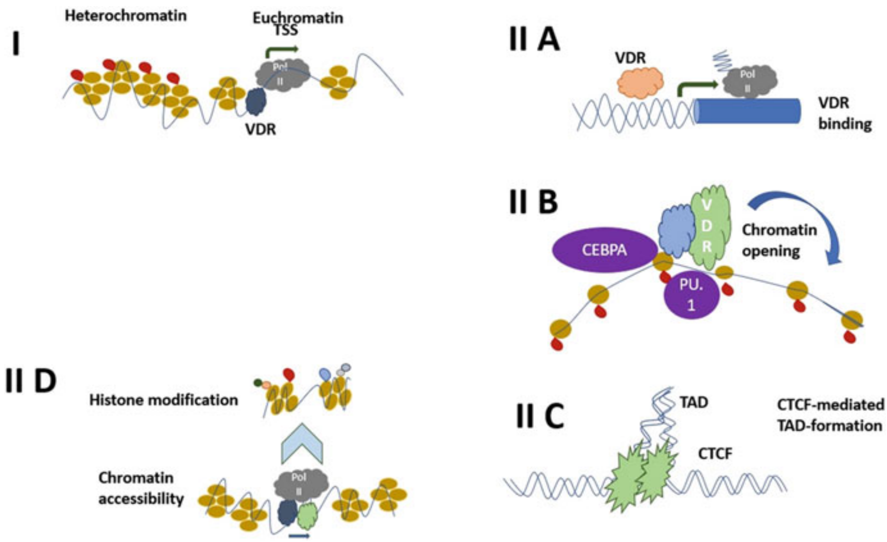

Fig. 21.2 Vitamin D and the epigenome. Chromatin is segregated into non-accessible heterochromatin and euchromatin, where VDR can find its genomic binding sites. (I) Vitamin D can influence the epigenome in multiple ways. (II) Such as increasing genomic VDR binding (A) affecting the binding of pioneer transcription factor (B) influencing CCCTC binding factor (CTCF) binding and the formation of topologically associated domains (TADs) (C) and changing histone modification and chromatin accessibility (D)

2014). Interestingly, the pastime of many of these chromatin modifiers significantly relies upon on intracellular ranges of key middleman metabolites, such as NAD+, acetyl-CoA, and α-ketoglutarate (Gut and Verdin 2013). In this way, environmental inputs, such as the availability of power substrates, have direct effects on the epigenome and, via this, on gene expression. This implies that chromatin modifiers act as sensors of metabolic information, such as cells being in a fasting or feeding state. The subject of dietary epigenomics describes numerous connections between diet-derived metabolites and the epigenome. For example, a wide variety of secondary metabolites from fruits, vegetables, spices, teas, and medicinal herbs, such as resveratrol, genistein, curcumin, and polyphenols, affect the endeavour of chromatin modifiers and transcription factors. Vitamin D and different micro- and macronutrients have an effect on by means of their nuclear receptor sensors of chromatin accessibility; i.e., they belong to area of dietary epigenomics (Carlberg 2017). Importantly, in distinction to epigenomic programing for cell fate selections during cellular differentiation, which is largely irreversible, diet-induced epigenomic changes are dynamic; i.e., they are frequently transient and reversible (Carlberg 2019).

21.5 Role of Nutrigenomics on Human Health

Ben van Ommen, director of the European Nutrigenomics Organization, and colleagues hypothesize that all illnesses can be reduced to imbalances in four overarching processes: inflammatory, metabolic, oxidative, and psychological stress. Diseases arise because of genetic predispositions to one or greater of these stressors. Nutrigenomics represents a major effort to improve our appreciation of the position of vitamin and genomic interactions in at least the first three of these areas, says Kaput (Table 21.1). Also, the nutrigenomics help in the prevention of many ailments inclusive of obesity, diabetes, cardiovascular disease, cancer, inflammatory disorders, age-related cognitive disorders, visual function, and of route many vitamin deficiency problems. From an evolutionary perspective, food regimen is a limiting factor that imposes selective pressures on a population, tons like other environmental factors. Some genotypes inside a populace are associated with greater nutrient needs, and when these desires are not met, there will be selection towards these specific genotypes. From the nutrigenomic perspective, diabetes and weight problems are each the end result of an imbalanced food regimen interacting with genes that were as soon as functional and adaptive in an earlier phase of human evolution, when meals were less abundant. In the current context, these same genes are regarded to code for hormonal or metabolic inclinations that have become maladaptive and pathological in the modern environment. Risk of developing these illnesses is idea to be modulated by genetic susceptibility differences among ancestral corporations to the effect of the Western diet in precipitating insulin resistance.

Table 21.1 Gene alteration due to nutrient deficiency

Nutrients	Gene alteration	Disease
Vitamin A	Repression of PEPCK gene	Abortion in pregnant female night blindness, drying of skin, eye, and foetal death
Vitamin D	Prevent gene variation	Fatigue, breast and prostate cancer and bone pain
Vitamin E	Mimics radiation damage	Colon cancer, nerve and muscle damage and CVD
Vitamin B3	Hampers DNA repair	Nerve problems, dermatitis, dementia, and loss of memory
Vitamin B6	DNA methylation	Cancer, microcytic anaemia, and CVD
Vitamin B9	Chromosome break, disturbance in DNA repair	Brain dysfunction, anaemia, male infertility, cancer, CVD, and leukaemia
Vitamin B12	Chromosome break, DNA methylation	Memory loss, cancer, CVD, anaemia, and brain dysfunction
Fatty acids	Change in gene expression	Diabetes, scaly dermatitis, obesity, and heart disease
Proteins	Change in gene expression	Kwashiorkor and marasmus
Flavonoids	Change in gene expression	Cancer
Zinc	Breakdown of chromosome	Brain dysfunction, growth retardation, and weakness

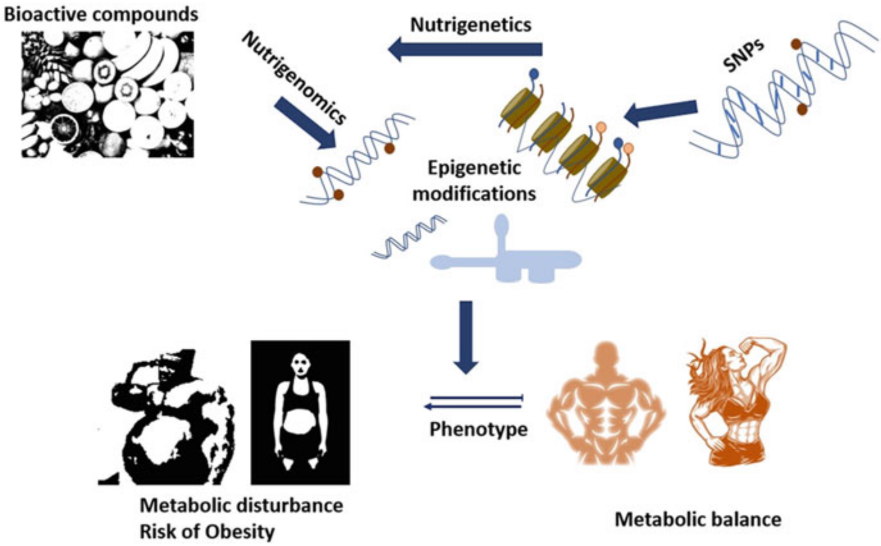

Fig. 21.3 Interactions among gene, diet, and human health

Nutrigenetics can be described as the field of dietary genomics, which studies (1) the role of specific genetic variants, in the structure of single-nucleotide polymorphisms (SNPs), in the modulation of the response to dietary components, and (2) the implications of such interaction, such as the influence on fitness status and predisposition to nutrition-related illnesses (Simopoulos 2010; Ferguson et al. 2016) (Fig. 21.3). Thus, the fundamental purpose of nutrigenetics is to format effective, personalized nutritional techniques that now not only result in body weight loss but also stop metabolic disturbances such as Type 2 diabetes (T2DM), hypertension, dyslipidaemias, and cardiovascular disorder (CVD). Several genes inside our genome are recognized to have an effect on the metabolism of vitamins (Goni et al. 2015). The main genes, whose editions are associated with physique weight loss in response to hypocaloric diets and/or bodily recreation applications in adults, are worried in the law of lipid metabolism and adipogenesis; others are associated with carbohydrate metabolism, strength intake and expenditure, and the circadian machine (Goni et al. 2015; Franzago et al. 2020).

The significant nutrigenetic interactions were reported as follows:

- Saturated fats intake, APOA2 2265T>C variant and BMI (Grimaldi 2014)
- Coffee intake, gene variants mostly involving adrenergic receptors, and hypertensive response (De Caterina and El-Sohemy 2016)
- Folic acid supplementation, MTHFR gene variants, homocysteine levels, and CVD risk (Grimaldi 2014).

Among genetic versions related to nutrition, a key position is played by using SNPs in the FTO gene affecting body weight and physique composition. In fact, carriers of the FTO rs9939609 AA genotype are likely to be extra overweight than non-carriers of the A danger allele (Frayling et al. 2007). This variant is viewed one of the strongest threat elements for polygenetic obesity. Nevertheless, it has been tested that the increased susceptibility to obesity brought on via the A danger allele can be modified with the aid of both bodily endeavour and reduction in strength intake.

Accordingly, based totally on the specific genotype, different folks metabolize lipids, carbohydrates, and folates in different ways and have a unique response to same diets. Nutrigenetic assessments are currently used in particular situations for deciding on an excellent weight-reduction plan in patients at risk of different conditions. For example, our group, through the use of a simple panel of nine nutrigenetic variants, demonstrated a multiplied chance of gestational diabetes mellitus (GDM) in ladies carriers of the TT genotype of the TCF7L2 gene (OR 2.5). Moreover, an association between variants in PPARG2, APOA5, MC4R, LDLR, and FTO genes and lipid parameters has been detected. The diagnosis of GDM approves the identification of a population that is highly vulnerability to T2DM and metabolic syndrome, providing a handy and perfect device that suits activities anthropometric and biochemical factors, dietary assessments and genetic make-up in clinical exercise (Franzago et al. 2018, 2020).

21.6 Future of Nutrigenomics: Transcriptomics, Proteomics, and Metabolomics?

Different genomic technologies, particularly transcriptomics, proteomics, and metabolomics, are complementary in the types of information they generate, however are at distinctive factors in their improvement at this time. Ultimately, parallel use of these techniques will enable us to describe the phenotype of an organic system, such as a human being, in all its complexity, which is the important purpose of dietary structures biology (Van Ommen 2004; Afman and Müller 2006). Without a doubt, there is no "one and only" technological know-how to solve all our lookup questions, so one has to be very clear about the aim of a study and its possible limitations. Given the many complex things to do of the human liver, transcriptome and proteome analysis would be desirable, but tissue samples of human liver from healthful people are not with no trouble available. Alternatively, researchers can also be capable to use plasma profiling of metabolites that might specially serve as biomarkers for liver health or dysfunction. Transcriptomics is an incredibly mature technology compared with other "-omics" technologies. At this point, it is viable to get an overview of the expression of without a doubt all genes in a single microarray experiment; however, it is now not but possible to measure the total proteome or metabolome. However, research in proteomics is progressing rapidly (Davis and Milner 2004). Studies of protein structure, expression level, mobile localization, biochemical activity, protein–protein interactions, and cellular roles are underway, and widespread growth in novel instrumentation, experimental strategies, and bioinformatic techniques has been achieved. Research growth in plasma proteomics is of specific hobby to diet and nutrigenomics research because, if successful, a wealth of information could be generated about important proteins, such as a number of cytokines or hormone levels, from a small plasma sample. In order to acquire this, the primary plasma proteins have to be separated and ultimate plasma proteins must be recovered in a quantitative way for in addition analysis. Recent growth in this location is promising (Okerberg et al. 2005) and suggests that proteome-derived biomarkers useful in figuring out nutrition fame might also be recognized earlier than too long. Metabolomics is additionally in the early degrees of development. It is not regarded how many endogenous metabolites exist or how many exogenous food-derived metabolites can be measured in human samples (urine, plasma). Scientists ought to first overcome a wide variety of hurdles, such as full healing of all metabolites from body fluids or tissue samples and the need to advance large databases with the required facts about the nutritionally relevant metabolome. Metabolomics produces big quantities of records that require state-of-the-art instrumentation and software to permit researchers to extract significant records from the data. Existing instrumentation is quite sophisticated; the current limitations appear to be with the software program needed to deal with metabolomic data. The plausible for dietary functions of metabolomics is considerable, and a variety of research teams are addressing these barriers (Afman and Müller 2006).

Will nutrigenomics continue to be interesting sufficient over the subsequent quite a few years to sustain improvement of a big research foundation? We are certain this will be the case because it is extensively appreciated that further tendencies in nutrition and meal improvement are impossible besides exploring the mechanisms underlying nutrition. Will it then be feasible from nutrigenomics research to strengthen food and beverage merchandize that can assist prevent or minimize onset and impact of complex diseases, such as type two diabetes, cardiovascular disease, and some varieties of cancers? Can meal products be tailored to promote the health and well-being of organizations in the populace recognized on the basis of their person genomes? However, it is essential to re-examine expectations on an everyday basis. What can we acquire within the scope of the knowledge and strategies we have reachable now and in the close to future? In the coming years, we have to put all our efforts into gaining a thorough understanding of how vitamins interact with the human genome at a molecular level. To be in a position to use genetic blueprints or genotypes in dietary prevention of disease, we must first pick out the mechanisms driving the connection between eating regimen and the outward manifestation of our genes, our phenotype (Afman and Müller 2006).

Nutrigenomics studies how food can modulate gene expression (Bordoni and Gabbianelli 2021). This self-discipline focuses on the function of macro- and micronutrients, bioactive compounds and dietary regimens in regulating gene expression and consequentially affecting the health status. In particular, nutriepigenomics investigates the role of epigenetics in mediating the outcomes of food on gene expression. The term nutrimiromics has been coined to outline the find out about of how vitamins and bioactive molecules (e.g., selenium, zinc, resveratrol, curcumin, and quercetin) can modulate miRNA concentrations in the human body (Quintanilha et al. 2017). While the capacity of food to modulate endogenous sncRNA production has been significantly shown, the existence of food-derived sncRNA, that continue to be secure and can probably be absorbed, used to be proven by means of Yang et al. (2015) and it is nevertheless a mentioned topic. Exogenous sncRNA has been observed in each plant- and animal-derived foods. The mobility of sncRNA from one species to every other is regarded one of the primary mechanisms which vary in organisms, even between species from one-of-a-kind kingdoms and help in transcriptional and translational process (Zeng et al. 2019). While the sequence of some miRNA is specific to a few flowers or animal lineages, others are conserved in animals and flora. Since ingredients contain sncRNA that ought to probably target human genes, it has been speculated whether or not an inter-species genomic legislation with the aid of sncRNA should exist and have a precise position in ailment pathogenesis (Bordoni and Gabbianelli 2021). However, although sequence conservation of miRNA and goal genes may also recommend conservation of expression patterns and functions, various questions continue to be to be addressed: the stability and bioavailability of sncRNA as a function of the food matrix, the efficiency of their uptake in the intestine gadget, and the amount of xeno-microRNA wanted for organic actions. Major worries about the possibility that sncRNA could have giant organic results in mammals have been raised. On the different hand, some authors have described an enormous bioavailability of both plants and animal-derived sncRNA (Benmoussa et al. 2020; Bordoni and Gabbianelli 2021), suggesting that they may be absorbed in the gut and transferred into the blood circulation (Bordoni and Gabbianelli 2021). Izumi et al. (2015) confirmed that miRNA from milk may be taken up via human intestinal cells and macrophages. This counselled that positive sorts of food, past being a source of macro- or micronutrients, bioactive molecules and energy, might also furnish biologically lively sncRNA. Although the possibility of systemic results is nonetheless open, the exposure to exogenous sncRNA coming from meals has been stated, and the possibility that they may exert vast biological effects in mammals needs in addition find out about (Nguyen 2020). Bacteria should also produce miRNA-like molecules that may want to modulate the host's gene expression, as in the past proven for sncRNA produced by using viruses (Bordoni and Gabbianelli 2021). However, solely restrained statistics are accessible on their capability to goal human gene expression (Lee 2019). On the other hand, bacteria manipulate the expression of quite a number miRNA in the host to modulate mobile methods that desire their survival and proliferation (Duval et al. 2017). Moreover, it has been shown that faecal miRNA (including these deriving from food) can shape the gut microbiota, as a consequence representing a workable future method for manipulating the human microbiome (Liu et al. 2016).

Transcriptomics approaches are used for the evaluation of genomic information generated related to nutrients and consist of standardized protocols for coding and noncoding (miRNAs, lncRNA, UCG) genes (Braicu et al. 2014). The most frequently exploited technologies for the contrast of the transcriptomics signature consist of gene expression analysis, splicing genetic versions study, mainly SNPs with the aid of microarray and gene expression, single-nucleotide variants profiling, post-transcriptional single-nucleotide versions, and fusion gene deletions by next technology sequencing (RNA-seq) (Irimie et al. 2015). Some of the microarray machineries enable now not only the comparison of transcriptomics pattern, however additionally highlight distinctive splicing or different genetic variants, especially SNP. Recently, nanostring technological know-how permits evaluation of a custom panel of coding or non-coding transcripts, targeted on a particular mechanism. Other options are represented with the aid of PCR-array cards, which have a spotted panel of goal molecules for a mechanism of action study, or easy variant is by way of the usage of qRTPCR (Irimie et al. 2015). Valid data and terrific conclusions are obtained by way of bioinformatics tools (Grant 2012). The remarkable data generated by using transcriptomics approaches need to be validated. Different tools like proteomics and metabolomics analysis can be beneficial in this regard. Proteomics and metabolomics processes have as an essential purpose to consider the protein composition or abundance and metabolic pattern in normal state and physiological repute as related to xenobiotic exposure. Proteomics and metabolomics techniques mean the utilization of throughput techniques based totally on mass spectrometry (MS) and nuclear magnetic resonance (NMR) (Wang and Chen 2013). These strategies make sure excessive sensitivity, accuracy, and rapidity to determine lots of proteins or metabolic merchandise in a single experiment (Braicu et al. 2017). Proteomics identifies the expression level of proteins of interest, post-transcriptional alteration, or unique protein–protein interaction, at a unique and precise moment in a biological system. Metabolomics profiles metabolites and can be used to tune the biochemical adjustments in special most cancers types. Metabolomics evaluates a range of small molecules, like sugars and amino acids constituting the substrates or intermediates for a multitude of mobile processes. Proteomics and metabolomics adjustments are interconnected. They determine the position of one of the kind protein interactions accountable for physiological and pathological processes. These two strategies are used for the contrast of the phytochemical's metabolism (quinones or semiquinones) (Muzolf-Panek et al. 2008), however additionally for the evaluation of the entire proteomic mobile phone pattern, especially at the stage of the tissue or the complete body (Grant 2012). They are very beneficial for the identification of metabolic alterations, specially the Warburg effect retrieved in the case of most cancers cells, characterized by means of a high glycolysis price followed by means of lactic acid fermentation, requiring a high amount of glucose. The use of "omics" allows to enforce advanced protocols for the investigation of molecular differences and to deliver dependable connection between medicinal drug and nutrition. Natural compounds affect coding and non-coding genes and proteins, and their therapeutic role nonetheless need to be elucidated. Currently, preclinical tests are available, but these statistics still want to be analysed and integrated (Pavlidis et al. 2015).

21.7 Future Prospects

Study of biomarkers would be carried out to identify the mechanisms behind the early stages of disease development. Nutrigenomic techniques are properly setup to detect and validate such biomarkers. Currently, the nutrigenomics field lacks, to some extent, the standardized approaches which can act as a pleasant control when designing and implementing nutrigenomics studies. However, some examples exist where recent growth has been made, such as the improvement of a set of criteria for validation of food intake biomarkers within the food ball consortium (Brennan and de Roos 2021). Some researches endorse that modifications in the transcriptome, proteome, metabolome, or gut microbiome, in particular when measured on the mobile level, may signify a extra sensitive and early-stage marker of efficacy in contrast with systemic modifications in metabolism, which are measured extra automatically in scientific studies. In particular, metabolomics presents an effective device for the development of objective markers of food intake. However, in addition, lookup is warranted in the improvement of approaches that display the utility of such biomarkers for assessments of food consumption. Epigenetic research will increasingly more be of interest, as this technique is a key to gene expression and therefore telephone function, especially in relation to getting older and chronic disorder development. However, strong evidence about the effects of dietary factors other than folic acid on DNA methylation patterns in humans is limited, and there seems to be splendid heterogeneity in the methods used for assessing DNA methylation and in the genomic loci investigated. On a molecular level, vitamins transmit indicators that can be translated into adjustments in gene, protein, and metabolite expression. Applying nutrigenomics to daily existence as the future of diet science presents new tools for dietitians to format and prescribe diets for persons based on their genome and their genetic versions. El-Sohemy, who's founder, president, and chief scientific officer of Nutrigenomix, a biotechnology business enterprise that works with dietitians to provide testing for nutrition-related genetic variants, says nutrigenomics is about customer genetic testing for customized nutrition. "What does it mean to your affected person on a day-to-day basis? Do we have scientific evidence that can tell us, based totally on your genes, how you need to eat?"

21.8 Conclusion

Plant- and animal-derived foods consist of carbohydrates, protein, lipids, and bioactive compounds that are responsible for the final effect on gene expression regulation. The chemical structure of these constituents contributes to produce secondary metabolites with several impacts on molecular responses. Alterations at molecular level can be study using nutrigenomics tools, i.e. transcriptomics, proteomics, metabolomics, and epigenetics research. These tools help in diagnose of specific gene which is responsible for causing any chronic disease during gene-diet interactions. By studying the effect of diet on gene, we can prevent the harmful effect of food constituents that causing chronic diseases. Therefore, nutrigenomics may additionally have the doable to stop and deal with diet-related persistent disease. Nutrigenomics goes deeper, the use of molecular tools to discover how nutrients and bioactive meal compounds alter the DNA transcription and translation process, affecting the expression of genes that modify fundamental metabolic pathways, which might also subsequently affect fitness outcomes.

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Fortification of Bioactive Components for the Development of Functional Foods

22

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Abstract

One of the most critical uses in the food business is the encapsulation of food components. Bioactive components are being used in food applications due to growing consumer interest in natural ingredients. Encapsulation is a promising method for improving the stability of bioactive components while allowing for regulated release. This chapter presents an overview of various encapsulation procedures, viz. spray drying, freeze-drying, extrusion, emulsification, coacervation, cocrystallisation, supercritical fluid method, and different encapsulated bioactive compounds, which have been used to fortify food components and deliver them into various functional foods.

Keywords

Encapsulation · Spray drying · Freeze-drying · Extrusion · Emulsification · Coacervation · Cocrystallisation

22.1 Introduction

Nutraceuticals, a term devised by Stephan DE Felice in 1979 to express their presence in the human diet and biological activity, are also termed bioactive components. In addition to the fundamental nutritional value, bioactive components found in food as natural ingredients give health beneficial properties. "Bioactive compounds" are extra nutritional components that characteristically occur in minor quantities in foods. They are being thoroughly examined to see how they influence the public's health. They contain compounds present in small amounts of vegetation

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and particular foods like fruits, vegetables, nuts, oils, and grains. The overview of some of the essential potential health benefits of bioactive compounds is as follows:

- Improved brain health and reduced oxidative stress
- Lowering of blood pressure and cardiovascular disease
- Anticancer
- Antidiabetic
- Better intestinal health
- A better lipid profile

22.2 Sources of Natural Bioactive Compounds

Tropical plants, aquatic cyanobacteria, microalgae, and filamentous fungi have bioactive compounds explored in their biological matrices. As a result, current studies into these compounds and their sources are becoming more common.

22.2.1 Plant Tissues

Plants manufacture two types of bioactive, viz. primary and secondary metabolites (Wu and Chappell 2008). Primary metabolites encompass sugars, amino acids, fatty acids, and nucleic acids, and all plants are used for growth and development, such as growth factors and cell wall components. Secondary metabolites play a set of functions within the plant's existence cycle and modulate plant–environment interactions like plant–microbe, plant–insect, and plant–plant interactions, and pollinating and attracting pollinators (Balandrin et al. 1985). As a result, these secondary metabolites are helpful for a wide range of actions, and scientists investigating their bioactivity for practical applications are of particular interest. The plant's physiology and biological process stage impact the natural synthesis of these metabolites (Table 22.1).

Plant secondary metabolites can be categorised into five groups depending on their metabolic origin: Polyketides include isoprenoids, alkaloids, phenylpropanoids, and flavonoids (Oksman-Caldentey and Inzé 2004). Plant secondary metabolites can be categorised into five groups depending on their metabolic origin: Polyketides include isoprenoids, alkaloids, phenylpropanoids, and flavonoids (Oksman-Caldentey and Inzé 2004). These compounds are only produced in specific cell types and at specified stages of growth or during particular periods, making their isolation and purification extremely tough (Verpoorte et al. 2002). Carotenoids, terpenoids, alkaloids, phenylpropanoids, and some specialised compounds such as corilagin, ellagic acid, vinblastine, and vincristine are commercially used secondary plant metabolites (Sőzke et al. 2004; Nobili et al. 2009; Yang et al. 2010) and are used in the production of pharmaceuticals and also can be employed as a food additive to improve food functioning (Shahidi 2009; Ayala-Zavala et al. 2010).

Table 22.1 List of bioactive components from plant sources

Plant source	Bioactive components	Health benefits	References
Buckwheat	Bioactive peptides (DVWY, FDART, FQ, VAE, VVG, and WTFR)	Lowering of blood pressure	Koyama et al. (2013)
Chia seeds	Bioactive peptides (ACE inhibitory)	Lowering of blood pressure	Campos et al. (2013)
Maize seed	Anthocyanins (cyanidin–glucoside, cyanidin–malonylglucoside, pelargonidin–malonylglucoside, cyanidin–dimalonylglucoside)	Prevention of cardiovascular diseases	Toufektsian et al. (2008)
Olive oil	Polyphenols (hydroxytyrosol)	Prevention of cardiovascular diseases	Tejada et al. (2017)
Eggplant	Eggplant peel extract	Poisonous effect on cancer cells	Afshari et al. (2017)
Eggplant	Glycoalkaloids (solasodine and solamargine)	Anticancer activity	Shen et al. (2017)
Soy	Isoflavone genistein	Anticancer activity	Montales et al. (2012)
Maclura Pomifera	Pomiferin (inhibitor of glioma)	Therapeutic agent/anticancer activity	Zhao et al. (2013)
Blueberries	Polyphenolic acids (pterostilbene)	Anticancer activity	Mak et al. (2013)
Quinoa	Chenopodium peptides	Antidiabetic effects	Vilcacundo et al. (2018)

Natural bioactive compounds found in plant tissues are essential because they have an extensive range of biological activities and bioactive properties. They must play a vital part in the evolution of new commodities (Wu and Chappell 2008). Natural bioactive has been the source of 60–70% of healthy development for cancer and infectious diseases over the last two decades (Newman and Cragg 2007). It has been reported that more than two-thirds of the world's population still gets primary medicinal care from medicinal plants (McChesney et al. 2007). Additionally, the human population has carefully investigated these compounds and proved to have beneficial health effects on humans; furthermore, research data are required to ensure their safety and efficacy.

22.2.2 Microorganisms

Microorganisms are vital because they employ their biological system to manufacture essential biomolecules (Demain 2000; Donnez et al. 2009). An average of almost 23,000 natural bioactives of microbial origin have been discovered, most of

Table 22.2 List of bioactive components from microorganisms

Microorganisms	Health benefits	References
Cyanobacteria		
Dolastatin 10	Antitumor	
Dolastatin 15	Antitumor	
Curacin A	Antimicrotubule	
Toyocamycin	Antifungal	Burja et al. (2001)
Actinomycetes		
Resistoflavine	Anticancerous	Gorajana et al. (2007)
Marinomycin A	Antibiotic	Kwon et al. (2006)
Daryamide C	Antitumor	Asolkar et al. (2006)
Violacein	Antiprotozoal	Matz et al. (2008)
Bacteria		
Macrolactin S	Antibacterial	Lu et al. (2010)
Pyrones I and II	Antibacterial	Maya et al. (2003)
MC21-B	Antibacterial	Isnansetyo and Kamei (2009)
Fungi		
Meleagrin	Antitumor	Du et al. (2010)
Oxaline	Antitumor	Koizumi et al. (2004)
Alternaramide	Antibacterial	Kim et al. (2009)

which are produced from a limited number of microorganisms (Olano et al. 2008). Fungal organisms have been found in practically every living and non-living habitat on the planet, including deep rock deposits, deserts, and aquatic environments (Strobel 2003). Plants and prokaryotes of fungal origin generate bioactive compounds beneficial to the environment (Table 22.2). These compounds can perform various functions, including preventing photooxidation, protecting against environmental stress, and being used as cofactors in enzymatic reactions (Mapari et al. 2005). Fungal species such as *Penicillium*, *Aspergillus*, and *Streptomyces* produce bioactive antibiotics, enzymes, and organic acids, having beneficial effects (Liu et al. 2004; Silveira et al. 2008).

Natural bioactive substances manufactured by microorganisms can be employed as nutritional supplements, flavour-inducing agents, texturisers, preservatives, emulsifiers, acidulants, surfactants, or thickeners in food. Bioactive compounds extracted from bacteria include isoprenoids such as carotenoids (beta-carotene and lycopene), and phenylpropanoids such as stilbene derivatives (resveratrol and others) have beneficial properties (Chang and Keasling 2006; Klein-Marcuschamer et al. 2007; Ajikumar et al. 2008; Donnez et al. 2009). However, only 1% of bacteria are cultivated in vitro, implying that microorganisms have diverse biodiversity, and many natural bioactivities are still being investigated. The main reason behind using microorganisms (rather than microbes) to generate compounds from plants and animals is the high efficiency with which high yields can be developed and the possibility of environmental and genetic modification (Demain 2000). Additionally, bacteria can create several vital compounds in small quantities for their advantage

(Demain 2000). Nevertheless, because the number of bioactive compounds produced is minimal, their application in this field is limited.

22.2.3 Algae and Microalgae

Algae can be found in various surroundings, including the ocean, freshwater, and deserts (Guschina and Harwood 2006). Over 30,000 genera of microalgae are present globally, and over 15,000 novel compounds have been chemically isolated from them (Metting John 1986; Cardozo et al. 2007; Rodríguez-Meizoso et al. 2010).

Researchers have revealed that these compounds exhibit a wide range of biological effects, and their importance as a source of novel compounds is proliferating (Wijesekara et al. 2010).

Many bioactive compounds are present in algae possessing antioxidant, antibacterial, and antiviral properties (Onofrejová et al. 2010; Plaza et al. 2010; Rodríguez-Meizoso et al. 2010). These organisms adapt rapidly and successfully since they live in a hostile atmosphere, producing many physiologically active secondary metabolites that boost natural defence mechanisms (Rodríguez-Meizoso et al. 2010). These defence mechanisms can result in mutations in molecules hailing from different metabolic pathways (Table 22.3).

Carotenoids, polyphenols, and other antioxidant pigments, as well as polyphenols, notably quercetin, catechin, and tiliroside, acid derivatives, and dipeptides, are produced by microalgae (Lam 2007). Algae have not only bioactive compounds but also possess extraordinary diversity and ability to harvest and grow under a variety of conditions making them significant, thereby resulting in the economic gain and production of a variety of bioactive compounds that can be used in the pharmaceutical and food industries as part of new stimulants or supplements (El Gamal 2010).

Although natural bioactive substances can be derived from various sources, one of the inhibiting variables in their synthesis is the low concentration they can generate. Many scientists worldwide are presently exploring novel techniques to optimise the recovery and synthesis of natural bioactive compounds.

Table 22.3 List of bioactive components from an algal source

Algae	Health benefit	References
Norharman	Enzyme inhibitor	Volk (2008)
Calothrixin	Antimalarial and anticancerous	Rickards et al. (1999)
Eicosapentanoic acid (EPA)	Prevents cardiovascular diseases, anti-inflammatory	Singh et al. (2005)

22.3 Fortification of Bioactive Components by Encapsulation Techniques

There has been a significant emphasis on human well-being in recent years, mainly through nutritional approaches. The nutraceuticals and functional foods industries have witnessed many innovations to accomplish customers' requirements. People are looking for novel and safer dietary elements that will supply nutrition and boost their health and well-being. As a result, consumers' attention has been drawn to food bioactive molecules, nutraceuticals, and functional foods. Many diets contain bioactive molecules such as vitamins, pigments, enzymes, flavours, and vital fatty acids. However, these bioactive molecules are susceptible to destruction due to heat, light, oxygen, and other stressors (Assadpour and Jafari 2019).

Because many bioactive compounds are poorly solvable, micro/nanoencapsulation simplifies the transfer of poorly soluble bioactive molecules into functional food components (Bazana et al. 2019). It promotes bioactivity and the physical stability of bioactive in produced foods and during processing. Bioactive compounds are better absorbed in the gastrointestinal tract when encapsulated (Zanetti et al. 2018). Encapsulation is often used to prevent bioactive compounds from reacting with other degrading elements like oxygen and light (Suganya and Anuradha 2017; Nedovic et al. 2011).

On a nanoscale, micrometre, and millimetre scale, encapsulation is the process of embedding one material into another and preparing particles (Burgain et al. 2011). Encapsulation is being used in several industries, and its rapid growth has influenced many sections of the food business, including processing, packaging, and storage. There are multiple methodologies for encapsulating bioactive components, but none of them can be referred to as a universal medium. Encapsulation enhances the transfer of bioactive substances and allows for a controlled drug release over time. This methodology helps to ensure the compound's security, efficacy, and stability (Zanetti et al. 2018). The product size in microencapsulation ranges from 1 to 1000 μm. However, the size and shape of the substance in nanoencapsulation should be smaller than 1 μm (1000 nm), as this encourages more accessible active sites on the surface of these delivery systems, facilitating absorption in the digestive system (Suganya and Anuradha 2017). The encapsulation efficiency is determined by the encapsulation technology used, the wall material used, and the process variables used (Kavitakea et al. 2018).

The various factors affecting the microencapsulation efficiency include the following:

1. Capsule characteristics concerning the environment
2. Polymer concentration and bead diameter
3. Capsule material, coatings, and processes
4. Initial concentration of microbial cell
5. Environmental conditions
6. Modification of capsule material

7. Effect of the bacterial cell on capsule
8. Condition of processing factors

22.4 Encapsulation Techniques

22.4.1 Spray Drying

For many years, spray drying has been employed to produce powders. Spray drying converts a liquid feed into a dried particulate form by spraying it into a hot air drying medium. It generates fine particles in a shorter timeframe and at a lesser cost per operation unit (Masters 1991). It is often commonly used in industrial processes due to its continuous production of powders with a low water activity (Anandharamakrishnan et al. 2008; Kuriakose and Anandharamakrishnan 2010). Moreover, this technology over decades has been frequently used for encapsulation in the food industry. Spray drying has also been used to encapsulate a wide variety of food ingredients, including flavours, vitamins, minerals, colours, fats, and oils, to protect them from the harsh conditions of the environment and thereby preserve the food (Pillai et al. 2012). As a result, it fits the definition of being a good microencapsulation technique (Table 22.4).

Spray drying of nanoparticles has been proposed as a promising method for producing macroscopic compact structures and submicron spherical powders having nanometre-scale properties (Okuyama and Lenggoro 2003).

It was reported by Jafari et al. (2007, 2008) that Hi-Cap modified starch was found superior to whey protein isolates due to having less interface oil in the encapsulated powders. The nanosize of the emulsion droplets was reported to be 200–800 nm, but during spray drying, they were altered to a micron size of above 20 μm. To encapsulate catechin in a carbohydrate matrix, Ferreira et al. (2007) employed homogenisation proceeded by spray drying at a temperature of 150–190 °C and manufactured spherical-shaped particles with smooth surfaces having a diameter in the range of 80 nm. Encapsulating catechins also lowered oxidation while increasing bioavailability.

De Paz et al. (2012) reported nanosuspensions synthesising by encapsulating beta-carotene with modified octenyl succinate starch and spray drying them. The nanosuspensions were synthesised under different experimental operating conditions with high antioxidant activity and enhanced encapsulation effectiveness of 65–90% and a particulate size ranging from 300 to 600 nm. However, after spray drying, the particles collected were around 12 μm in diameter.

In the dairy industry, the utilisation of nonfat milk, whey protein, and casein powders has been widely used to enhance milk and milk-related products (Schuck et al. 2016). Spray drying is generally accomplished by atomising the feed solution and injecting and circulating hot air into a drying compartment with a predefined inflow temperature. The input solvent is then evaporated at an exact moment by the hot air. The hot air then evaporates the input solvent in an instant. A cyclone collects

Table 22.4 Encapsulation techniques of various bioactive compounds

Nanoencapsulation technique used	Raw material used	Bioactive compound	Important inference	Reference
Spray drying	Wall material used: carbohydrate matrix and maltodextrin	Catechin (H)	Increasing the stability of the product, protecting it from oxidation, and incorporating it into beverages	Ferreira et al. (2007)
Coacervation	Wall material used: tannins, gelatine, and maltodextrin	Capsaicin (L)	Biocompatibility and biodegradability are provided by masking the punitive odour	
	The emulsifier used: Tween-60			
Freeze-drying	Wall material used: polycaprolactone, β-cyclodextrin	Fish oil (L)	Defending against oxidation and concealing the odour	Choi et al. (2010)
	Emulsifier used: Pluronic F68			
Emulsification	Wall material used: maltodextrin; emulsifier used: modified starch (Hi-Cap 100)	D-limonene (L)	Preventing recoalescence of the droplets	Jafari et al. (2007)
Supercritical fluid technique	Wall material used: hydroxypropyl methylcellulose phthalate	Lutein (L)	Bioactivity, food industry promotion, and protection from thermal and light degradation	Heyang et al. (2009)

the produced particles (the exit temperature is specified to be lower than the entrance temperature in this section) (Deshmukh et al. 2016).

Spray drying nanocapsules is a great idea to maintain their shelf stability. It continuously produces spherical particles that protect the core material enclosed in them. Drying nanoemulsions and nanosuspensions results in the formation of micron-sized particles. The core material inside the micron-sized particle matrix had been in the nanosize range (nanosuspension and nanoemulsion), which Jafari et al. (2007) demonstrated as nanoparticle encapsulation. In particular, spray drying nanoencapsulation is interdependent on other nanoencapsulation techniques (such as emulsification) before spray drying. As a result, conventional spray drying may not be considered an independent nanoencapsulation method. On the other end, spray drying permits particle size and morphology to be controlled by modifying process parameters and formulations (Anandharamakrishnan et al. 2008). As a result, spray drying must be adjusted appropriately to preserve the nanoscale size of nanoemulsions and suspensions. The schematic presentation of the spray drying procedure is shown in Fig. 22.1.

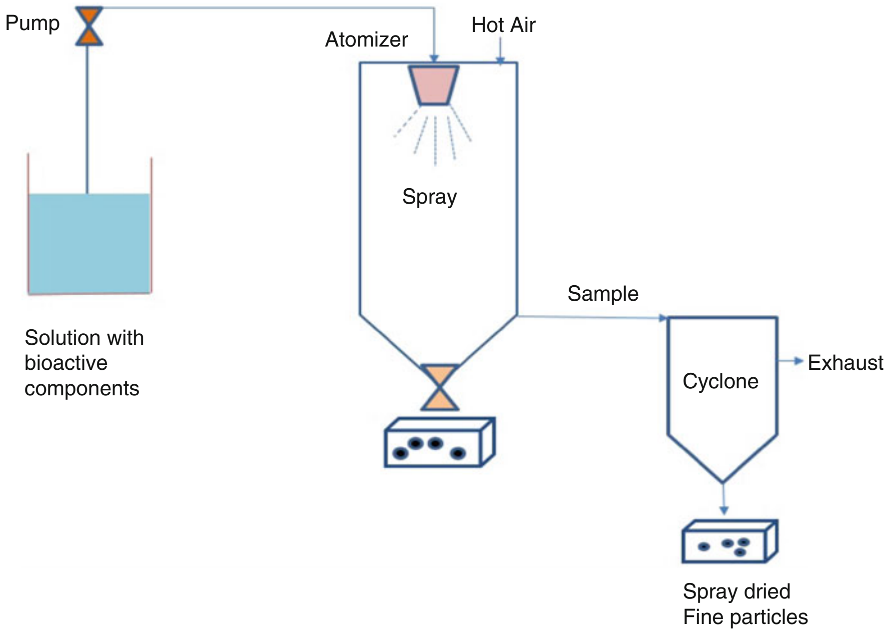

Fig. 22.1 Spray drying procedure

22.4.2 Coacervation

Coacervation is the method for separating a single or a mixture of polyelectrolytes from a solution and distributing the newly formed coacervate phase around the active constituent. By crosslinking hydrocolloid shells with a suitable chemical or enzymatic crosslinker such as glutaraldehyde or transglutaminase, the durability of coacervate can be increased (Zuidam and Shimoni 2010). Coacervation can be categorised into simple coacervation (using only one kind of polymer) and complex coacervation (using multiple polymer types). The several factors that regulate the strength of interactions between the biopolymers and the nature of the complex formed include the type of biopolymer, pH, ionic strength, concentration, and biopolymer ratio (Tolstoguzov 2003; De Kruif et al. 2004; Turgeon et al. 2007). Hydrophobic contacts and hydrogen bonding can play an essential role in forming complexes, despite ionic interactions between biopolymers with opposing charges. According to Gouin (2004), coacervation is a unique and effective encapsulation method because of the high payloads (up to 99%) and controlled release options based on mechanical stress, temperature, or sustained release. To encapsulate capsaicin, Wang et al. (2008) accomplished a simple coacervation technique by using gelatine, crosslinked with glutaraldehyde, and dehydrated in a vacuum oven. The nanocapsules produced were 100 nm in diameter. Due to the crosslinking of gelatine over the surface of capsaicin, the melting and thermal temperature of the nanocapsules were improved. Xing et al. (2004) performed a complex coacervation methodology to encapsulate capsaicin in gelatine and acacia. The nanocapsules were manufactured by freezing encapsulated capsaicin after treating it with hydrolysable tannins and crosslinking it with glutaraldehyde. Nanocapsules have spherical shapes with a mean diameter of 300–600 nm. The overall encapsulation efficiency in this analysis was 81%, with good dispersion characteristics. Due to the synergistic effects of hydrogen bonding and hydrophobic effects, adding hydrolysable tannins to the mixture considerably impacted the nanocapsules' shape and particle size distribution, used a similar complex coacervation technique with a vacuum oven to encapsulate capsaicin. Having stronger shearing force (15,000 rpm agitation rate), reduced gelatine viscosity (15–20 cPs), suitable crosslinking length (40–80 min), use of tannin, and other required experimental parameters all improved nanocapsule production as investigated by researchers. The nanocapsules produced exhibit specific properties like having spherical morphology, an average diameter of about 100 nm, a higher melting point (75–85 °C), and higher breakdown properties. Gan and Wang (2007) encapsulate bovine serum albumin (BSA) in chitosan by using polyanion tripolyphosphate (TPP) as crosslinking agent. BSA-loaded chitosan-TPP nanoparticles successfully synthesised under varying conditions had diameters ranging from 200 to 580 nm. A quantitative sequential time frame transmission electronic microscope (TEM) imaging displayed a swelling and particle breakdown process, revealing the morphological alteration of BSA-loaded particles. According to their conclusions, the polyionic coacervation process may be controlled to modify protein encapsulation efficiency and release profile.

The coacervation method produced 100–600 nm nanocapsules. This method used gelatine, acacia gum, and chitosan as wall components. The morphology (outstanding dispersion and shape) and particle distribution of nanocapsules were also impacted by tannin treatment. After crosslinking with glutaraldehyde for a specific period, the nanoencapsulation's melting point and thermal stability were increased. The biggest challenge with this procedure is actively promoting the coacervated foodstuffs due to the usage of glutaraldehyde for crosslinking, which must be used cautiously according to the country's legislation. Despite this, many crosslinking enzymes are currently being created (Gouin 2004).

22.4.3 Freeze-Drying

Freeze-drying, also described as lyophilisation, is a technique for dehydrating practically all heat-sensitive materials and aromas (Anandharamakrishnan et al. 2010). *Freeze-drying* is a multistage procedure encompassing freezing, sublimation (primary drying), desorption (secondary drying), and, subsequently, storage. Freeze-drying produces commodities that are greater in durability, easier to reassemble, and have a longer shelf life. According to Singh and Heldman 2009; freeze-drying's main disadvantages were its high-energy consumption, long processing time (over 20 h), and open porous structure. On the other hand, freeze-drying is often used to separate nanoparticles manufactured by other nanoencapsulation methods (i.e. removing water from the compounds). During the freeze-drying process, pores develop due to the ice sublimation process. As a result, this technology is not strictly encapsulated because active food elements are exposed to the atmosphere due to porosity on the particle surface. As a result, any release mechanism, such as diffusion or erosion, is challenging to develop. The freeze-drying technology is now the most widely used method for evaporating water from nanocapsules without causing structural or form changes.

As a substitute for spray drying, freeze-drying of heat-sensitive bacteria combined with matrix molecules has been proposed (Augustin and Hemar 2009). Choi et al. (2010) utilised cyclodextrin (-CD) and PCL (Food and Drug Administration (FDA)-approved edible drug delivery material) to encapsulate fish oil using a self-aggregation approach and an emulsion diffusion method with freeze-drying. With a mean particle size of 250–700 nm, PCL/fish oil (99%) has higher fish oil loading and encapsulation efficiency and much less fish oil leakage than -CD fish oil (84–87%). Bejrapha et al. (2010) assessed the stability of fish oil-filled nanocapsules encapsulated in PCL when they used vacuum freeze-drying (vacuum-pressured freezing and drying) vs. standard freeze-drying (atmospheric pressurised freezing and drying). In their study, the particle size of fish oil nanocapsules was revealed to be below 360 nm, and they were discovered to be aggregated. Vacuum freeze-drying demonstrated a higher encapsulation performance than traditional freeze-drying except at a freezing temperature of -30 °C. Furthermore, the researchers noted that the vacuum freezing approach might damage the PCL membrane due to poor encapsulation performance and particle aggregation.

Ionic gelation, sonication, and freeze-drying were adopted by Dube et al. (2010) to encapsulate (+) catechin and (−) epigallocatechin gallate (EGCG) in chitosan-tripolyphosphate. Nanoencapsulation's potential to inhibit catechin and EGCG degradation was compared to the addition of reducing agents, including ascorbic acid, dithiothreitol, and (tris 2-carboxyethyl) phosphine (TCEP). Nanocapsules have an average particle size of fewer than 200 nm. The reducing agents TCEP and ascorbic acid conferred lesser protection than catechin and EGCG nanoencapsulation. Surassamo et al. (2010) encapsulated capsicum oleoresin in PCL through using the emulsion diffusion method (the method involves forming an emulsion between a water-miscible solvent containing drug and the aqueous polymer phase; adding water to the system causes the solvent to diffuse to the external degree, leading to the formation of nanospheres). The process conditions were optimised by varying the concentration of the surfactant, Pluronic F68 (PF68). Nanoemulsions with a diameter of 320–460 nm were generated—the size of the nanocapsule particles reduced as the emulsifier concentration was raised. As the surfactant concentration was increased, the particle size contracted. Using an emulsion–diffusion method followed by freeze-drying, Nakagawa et al. (2011) analysed the dispersibility of capsicum oleoresin encapsulated in PCL and stabilised with gelatine. The nanocapsules have a diameter of fewer than 200 nm on average. The dried bulk sample also revealed that the created freeze-dried capsules had variable dispersion characteristics in different regions. The diversity was influenced by the cooling programme utilised during the processing. They indicated that forming a gel network in nanocapsule gelatine will assist in the development of better nanocapsule dispersion characteristics after drying.

To make capsicum oleoresin-loaded nanocapsules with PCL, Bejrapha et al. (2011) applied a modified emulsion–diffusion process combined with freeze-drying. The consequences of freezing temperatures on the characteristics of capsicum oleoresin-loaded nanocapsules were studied at −40, −20, and −15 °C. The effects of active ingredients such as gelatine and κ-Carrageenan on the stability of capsicum-loaded nanocapsules during freeze-thawing and freeze-drying methodologies were evaluated. According to their observations, the size of nanocapsules after freeze-thawing and freeze-drying was significantly influenced by a relatively high temperature (−15 °C). Abdelwahed et al. (2006) investigated the freeze-drying of PCL nanocapsules encapsulating MIGLYOL 829 oil produced by emulsion–diffusion and stabilised by polyvinyl alcohol. During the freeze-thawing study, PVA and PCL concentrations, cooling rate, cryoprotectant concentrations (sucrose and polyvinyl pyrrolidone), type of encapsulated oil, and nanocapsule purity were all studied. The outcome of annealing on nanocapsule stability and sublimation rate has also been explored. They demonstrated that if the PVA stabiliser concentration is high enough (5%), PCL nanocapsules can be freeze-dried without the need for a cryoprotectant. The size and rehydration of freeze-dried nanocapsules were almost unaffected by the kind of cryoprotectant used, and the annealing method expedited sublimation while keeping the nanocapsule size constant. Tiyaboonchai et al. (2007) encapsulated curcuminoids into solid lipid nanoparticles using the microemulsion method and freeze-drying. Under optimum process conditions, lyophilised curcuminoid-loaded nanoparticles revealed spherical particles with a mean particle size of 450 nm and incorporation efficacy of up to 70%. According to the findings, the proportion of components such as fat and emulsifier substantially impacted the curcuminoid loading capacity and size distribution. Curcuminoids were formed slowly (up to 12 h) and retained their physical and chemical stability over a 6-month storage period, according to in vitro release experiments.

Zhang et al. (2009) exploited the freeze-drying method to encapsulate trehalose in a thermally responsive pluronic nanocapsule. The nanocapsule may physically contain trehalose for cellular ingestion at 37 °C with only minimal release in hours, and its cytotoxicity is low. To encapsulate tocopherol in zein and zein/chitosan complexes, used a freeze-drying approach. The particle size of the compound ranged from 200 to 800 nm, and the efficacy of encapsulation ranged from 77% to 87%. The kinetic release profile of tocopherol showed a burst effect followed by progressive release. The zein/chitosan complex produced more tocopherol release against acute gastroenteritis than zein alone due to the chitosan coatings. To synthesise standard liposomes and polyethylene glycol (PEG)-coated vitamin E lyophilised proliposomes, Zhao et al. (2011) used thin-film ultrasonic dispersion and lyophilisation (PLP). Proliposomes are coated with PEG and lyophilised with a mean diameter of 164 nm and encapsulation efficiency of 84%. Vitamin E contained in PLP presented more excellent stability than standard liposomes, with a retention percentage of 90% at 4 °C after 15 days of storage.

For nanocapsule stabilisation, freeze-drying proves to be an effective drying process. Even after drying, it retained particle sizes in the nanometric range (below 400 nm and a few near 800 nm), improving core component stability against degradation and reaching a 70% encapsulation efficiency. It also appears to be an excellent drying process for heat-sensitive foods and bioactive components. The attributes of the final freeze-dried nanoparticles, on the other hand, are dependent on the use of a suitable high-energy emulsification procedure and other encapsulating techniques for breaking down the droplets into nanoform. Cryoprotectants such as sucrose, trehalose, and mannitol are also necessary to maintain particle size and reduce aggregation during freeze-drying. The size of nanocapsules has been affected by varied freezing temperatures. Polymers such as PCL and chitosan were used as a wall material in the majority of the researches.

22.4.4 Extrusion

Extrusion technologies are affordable and straightforward but take a long time to complete. The process of propelling a solution through nozzles or small apertures in droplet-generating equipment to produce a tiny droplet of an encapsulating substance is known as extrusion—the smaller the inner diameter of the nozzle or opening, the small the capsules. Industry-focused groups typically argue that this approach is only appropriate for laboratory processes and does not allow large-scale production. Extrusion-based upscaling of encapsulating technologies, on the other hand, has made enormous progress. Multiple nozzle systems, spinning disc atomisers, and jet-cutter techniques can all be used (De Vos et al. 1997; Kailasapathy 2002).

In most cases, extrusion technology has the advantage of being an accurate encapsulation method rather than an immobilisation technique. Swelling can be decreased during the encapsulation technique by selecting materials with low or negligible swelling kinetics and an appropriate quantity of cells per millimetre of encapsulating substance (De Vos et al. 1996a, b). When it comes to encapsulating bacteria, extrusion technologies offer a variety of benefits. It is low impact, chemical-free, and can be done in aerobic and anaerobic situations. When anaerobic microbes are used in food items, this is exceptionally advantageous. The modifications required to accomplish this are relatively simple. The extrusion device must be warehoused in a sterile cabinet with oxygen replacing nitrogen. Extrusion technology is used to make flavours, enzymes, and proteins.

22.4.5 Emulsification

Emulsification refers to dispersing one liquid into a second immiscible liquid. The bioactive component can be encapsulated by immersing the core material in the first liquid. In most instances, researchers and industry use electrostatic interactions, hydrophobic interactions, or hydrogen bonding between the bioactive molecule

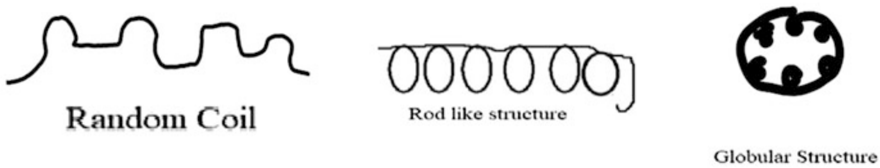

Fig. 22.2 Transition in molecular conformation by emulsification technique

and the encapsulating molecule to encapsulate bioactive components in food-grade (GRAS)-derived molecules. The encapsulating agent is usually a chemical found in food (Augustin and Hemar 2009). Surfactants that assist encapsulation by forming micelles, vesicles, bilayers, and reverse micelles around bioactive substances are also commonly prescribed as a remedy (Augustin and Hemar 2009; McClements et al. 2009a, b). When lipase is secreted, it safeguards the bioactive molecules in the products and allows them to pass through the duodenum. Biopolymers, such as proteins and polysaccharides, can also be used to encapsulate sensitive bioactive compounds by constructing random coil, sheet, or rod-like structures around them (Fig. 22.2). The biopolymer's type and digestibility impact how quickly it is absorbed in the gut (Champagne and Fustier 2007; McClements et al. 2009a, b). The biopolymer used is determined by the product's content. Bulk emulsification techniques are used in some situations to improve packing efficacy. The bioactive compounds are often encased in fat droplets or water–oil–water emulsions (Augustin and Hemar 2009; McClements et al. 2009a, b). Bulk emulsification is more commonly thought of as a technique for finely controlling the release of molecules rather than a natural encapsulating system. A large number of dietary components can be used as emulsion building blocks. The options are vast and have been thoroughly examined (Augustin and Hemar 2009). The use of monoglycerides can briefly explain the emulsification principle. Monoglycerides can self-assemble into a range of forms in water. With minimal and non-laborious modification, micelles, hexagonal, cubic, or even lamellar geometries of glycerides that enclose one or more bioactive chemicals can be developed. It is a simple technology that is already being used to control the release of odours and flavours (Augustin and Hemar 2009).

A modified version of the solvent evaporation process is the emulsification solvent evaporation technique, whose schematic representation is shown in Fig. 22.3.

22.4.6 Co-crystallisation

Co-crystallisation is a technique that requires immersing active composites in a high-carbohydrate solution. Over-saturation causes carbohydrate crystallisation, which begins with a decline in temperature. The compound to be enclosed becomes imprisoned as the crystal form (Champagne and Fustier 2007). Because of its simplicity and improved stability, co-crystallisation is cost-effective and adaptable.

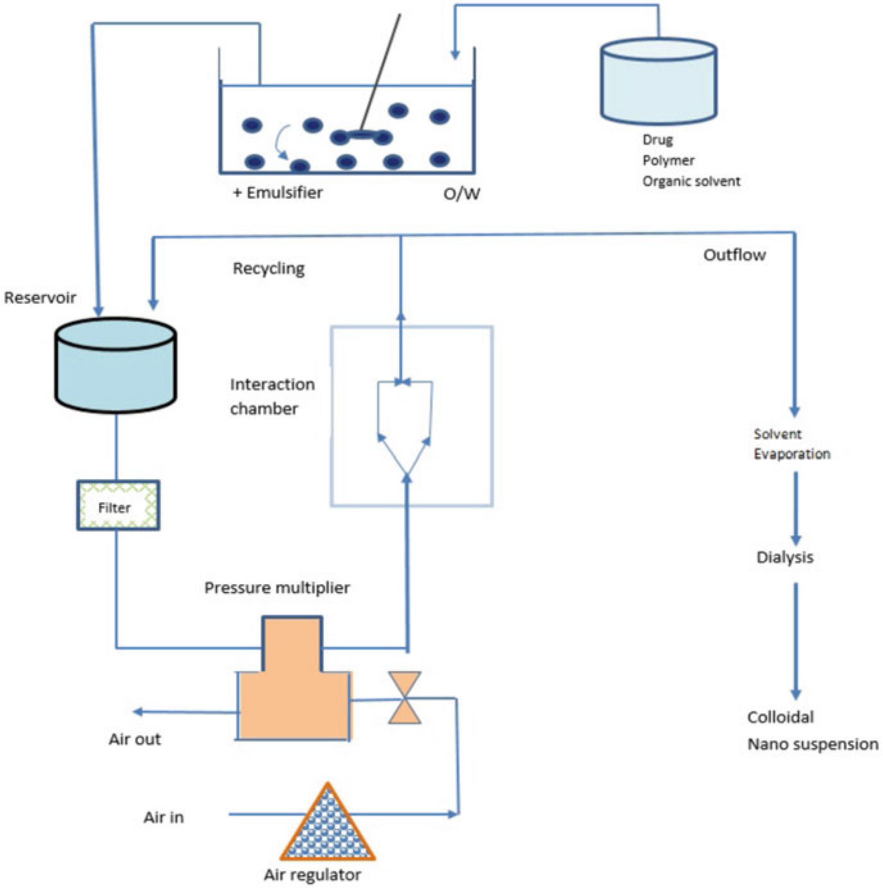

Fig. 22.3 Nanoparticle preparation by emulsification solvent evaporation (Kwon et al. 2006)

The disadvantage of this approach is that it produces low hygroscopic granular products, and the heat-labile core bioactive substance may be degraded (Pegg and Shahidi 2007).

22.4.7 Supercritical Fluid Technique

A supercritical fluid is a liquid or gas used at temperatures and pressures higher than its thermodynamic critical point (Jung and Perrut 2001). Supercritical fluids, intermediate between liquids and gases, have low viscosity, low density, solvating solid power, high diffusivities, and high mass transfer rates above the critical points. Supercritical conditions can be achieved with carbon dioxide, water, propane, nitrogen, and other substances (Gouin 2004). Some of the technologies utilised in supercritical fluid technology include rapid expansion from supercritical solution, gas antisolvent, supercritical antisolvent precipitation, aerosol solvent extraction, and precipitation with a compressed fluid antisolvent (Kikic et al. 1997).

Supercritical fluids encapsulate thermally sensitive compounds in a process similar to spray drying. In this method, the bioactive component and polymer were dissolved in a supercritical fluid before inflating through a nozzle. During the spraying operation, the supercritical liquid was evaporated, resulting in the precipitation of solute particles (Reis et al. 2006). This approach is widely used due to its low critical temperature and limited use of organic solvent.

Heyang et al. (2009) used supercritical antisolvent precipitation to encapsulate lutein in hydroxypropyl methyl cellulose phthalate (HPMCP) to retain its bioactivity and avoid thermal/light degradation. A variety of parameters, including lutein loading efficiency, particle size, and nanocapsule distribution, influenced the yield.

22.5 Conclusion

Nanoencapsulation techniques have been shown to have a higher possibility of increasing the efficacy of bioactive component delivery in humans. Various nanoencapsulation techniques evolve, each with its advantages and disadvantages. Lowering the risk of specific diseases in a population is predicted to be met by a nano-approach in distributing bioactive food components with documented health benefits.

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Biotechnological Tools for Extraction, Identification, and Detection of Bioactive Compounds

23

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Abstract

Plants are used as medicinal agents due to their wide range of structural diversity and pharmacological activities. The biologically active compounds that are present in plants are referred to as phytochemicals. These phytochemicals are derived from different parts of plants such as leaves, barks, seed, seed coat, flowers, roots, and pulps. The plants are the natural reservoirs of structurally diverse secondary metabolites. The extraction of bioactive compounds from the plants and their quantitative and qualitative estimation is important for the exploration of new biomolecules, which can be used in various industrial applications directly or can be used as a lead molecule to synthesize more potent compounds. This chapter highlights various methodologies used for the analysis of bioactive compounds present in the plant extracts involving the applications of chromatographic techniques such as high-performance liquid chromatography (HPLC), thin-layer chromatography (TLC), gas chromatography (GC), and high-performance thin-layer chromatography (HPTLC) and its detection through Fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR), and mass spectrometry (MS). The chapter also covers the conventional techniques (Soxhlet method, cold maceration method, hydro-distillation method) for extraction of phytochemicals that generally require large amounts of organic solvents, are high energy expenditure, and are time-consuming. Hence, the new technologies of extraction viz. supercritical fluid extraction (SFC), pressurized liquid extraction (PLE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE) that are referred to as clean or green technologies are also discussed here. These recent techniques used to extract bioactive compounds

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from natural sources can reduce or eliminate the use of toxic solvents and thus preserve the natural environment and its resources.

Keywords

Phytochemicals · Green technologies · Organic solvents · Industrial applications

23.1 Introduction

The extraction of new bioactive components from natural plants has now become an important aspect for the use in traditional medicines (Yuan et al. 2016). Traditional medicine and medicinal plants are widely used as a fundamental framework for maintaining good health in most developing countries, with around 80% of the world's population relying on herbal remedies (Ekor 2013). Plants possess a variety of chemical components that are utilized for the treatments of both chronic and infectious disorders (Sofowora et al. 2013). Microbial resistance to chemical compounds has special importance, which leads us toward the study of ethnopharmacognosy. Thousands of phytochemicals were discovered to be useful and possess biological activity including anticancer, antibacterial, antioxidant, antidiarrheal, analgesic, and wound healing (Sasidharan et al. 2011). Plant components, particularly phenolic compounds, carotenoids, and vitamins, which are results of plant secondary metabolism, provide resistance against several diseases (Sricharoen et al. 2016). Approximately 20% of known plant species have been used in pharmacological investigations, having a favorable impact on the healthcare system by treating cancer and other disorders (Atanasov et al. 2015). Bioactive chemicals originated from both natural and synthetic have unique metabolic or physiological effects, if their safety have been investigated. Generally, the number of bioactive compounds present in plants is affected by various factors such as the plant variety used, growing conditions, storage, and transport conditions and many more such factors.

Plants that contain important phytochemicals may act as natural antioxidants, supplementing the human body's demands (Zhang et al. 2015). Several studies have shown that antioxidants are abundant in many plants. For example, vitamins A, C, and E, as well as phenolic chemicals found in plants contain mainly flavonoids, tannins, and lignins, all behave as antioxidants (Salehi et al. 2020). Beta carotene, ascorbic acid, and various phenolic compounds play important roles in antiaging, anti-inflammation, and cancer prevention (Zhang et al. 2015). Many institutions and healthcare systems have advocated increasing the consumption of herbal/medicinal plants all around the world (Altemimi et al. 2017). Bioactive compounds have also been utilized in food additives due to their strong antioxidant properties. Antioxidants are compounds that prevent oxidation and minimize oxidative damage in plants by delaying or suppressing oxidation caused by reactive oxygen species (ROS), extending their shelf life, and improving their quality (Tan et al. 2018). Synthetic antioxidants are widely employed due to their stability and widespread availability, but they have been linked to the consequences of mutagenesis and carcinogenesis, prompting researchers to look for antioxidants isolated from natural plant species (Soquetta et al. 2018).

The extraction of bioactive substances is influenced by several parameters, including the extraction process, raw materials, and extraction solvent (Tiwari 2015). There are two types of techniques: conventional and nonconventional. Organic solvents, heating, and agitation are all required in traditional techniques. Examples of this type of technique include Soxhlet, maceration, and hydro-distillation. Modern techniques, also known as non-conventional techniques, are green or clean procedures since they require less energy and employ organic solvents, both of which are good for the environment (Chel and Kaushik 2018). Because of the variation in the polarity of compounds, it is difficult to come up with a single strategy for extracting all of them efficiently. Generally, a good solvent possesses low toxicity, low boiling point, efficient mass transfer, preservation action, and difficulty dissociating the complex extract. The extract yield obtained also depends upon additional factors including the type of extract being used, the temperature, and the time of extraction (Silva et al. 2016). Many researchers have already looked into the use of green technology in the processing of food (Barba et al. 2016; Boussetta and Vorobiev 2014; Chemat et al. 2017; Mustafa and Turner 2011). This chapter examines the extraction of bioactive chemicals from natural plant species utilizing conventional and nonconventional energy sources because different polarity solvents are required for the identification and isolation of individual compounds. However, the focus of this chapter was on analytical procedures, which included extraction methods and the analysis and identification of bioactive chemicals present in plant extracts using a variety of techniques that included chromatographic techniques and several detection methods.

23.2 Extraction Methods of Phytochemicals

Bioactive compound extraction from plants is a realistic technique since various solvents are utilized at varying temperate conditions. Different bioactive compounds present in plants can dissolve in a particular solvent. Not all compounds can dissolve in a single solvent. Therefore, for the extraction, various solvents are required for the appropriate isolation of all active compounds. A bioactive compound extracted from plants needs further separation from its co-extractive components. Therefore, different solvents are used based on their acidity, polarity, and molecular size.

There are two types of extraction procedures used to separate distinct bioactive chemicals from plant parts:

- conventional and
- nonconventional techniques.

Conventional techniques (Soxhlet extraction, maceration method, and hydro-distillation) use organic solvents in large volumes for extraction and require

Table 23.1 Comparison of different extraction methods

Method	Solvent used	Organic solvent required	Running time	Temperature used
Conventional techniques				
Cold maceration	Aqueous and nonaqueous solvents	Large volume	Lengthy	Room temperature
Soxhlet extraction	Organic solvents	Moderate volume	Lengthy	High temperature
Hydro-distillation	Water	None	Lengthy	High temperature
Percolation	Aqueous and nonaqueous solvents	Large volume	Lengthy	Room temperature but sometimes required high heat
Decoction	Water	None	Moderate	High temperature
Non-conventional techniques				
Pressurized liquid extraction	Aqueous and nonaqueous solvents	Small volume	Short	High temperature
Supercritical fluid extraction	Supercritical solvent (mainly S-CO_2), sometimes with modifier	Very little or none	Short	Room temperature
Ultrasound-assisted extraction	Aqueous and nonaqueous solvents	Very little or none	Short	Room and sometimes high temperature
Microwave-assisted extraction	Aqueous and nonaqueous solvents	Moderate or none	Short	Room temperature

additional time for the process to run, whereas non-conventional extraction techniques (supercritical fluid extraction, extraction with pressurized liquid, ultrasound-assisted extraction, and microwave-assisted extraction) offer some advantages in the practice of less organic solvent, shorter duration of extraction time, and higher selectivity. A summary of the various extraction method used for natural bioactive compounds is listed in Table 23.1.

23.2.1 Conventional Extraction Techniques

23.2.1.1 Soxhlet Extraction

The word Soxhlet was named after "Franz Ritter von Soxhlet," a German agricultural chemist. This is the most suitable method for the continuous extraction of solid–liquid solvent by using high temperatures (Rasul 2018). Soxhlet apparatus is a specific glass-designed refluxing unit, particularly used for the extraction of organic solvents. In the Soxhlet apparatus, the dried and powdered plant material is placed in a thimble constructed of filter paper. The Soxhlet apparatus was fitted into a round bottom flask containing some extract volume and a reflux condenser.

The solvent in the round bottom flask was heated and boiled upon requirement, and the vapors flow up through the side of the tubes, then condense by the condenser, and finally drop into the thimble containing plant material. When the solvent reaches the highest of the tube, it drains out into the flask, thus taking away the portion of the compounds that have been extracted. This whole process is repeated for around 10 cycles for each solvent until the plant material becomes colorless. The resulting solvent extract is filtered, concentrated in a vacuum evaporator, and preserved in vials at 4 °C for further experimentation (Ingle et al. 2017). This technique is a well-established, continuous, highly efficient extraction process that requires less time and solvent than other conventional techniques. The high temperature and longer time duration in Soxhlet extraction will increase the chance of chemical decomposition (Zhang et al. 2018).

23.2.1.2 Cold Maceration Method

Maceration is the process of grinding a sample to improve its surface area for optimum solvent mixing. It is one of the ancient and extensively used techniques used for herbal preparation. Maceration involves solid–liquid extraction of plant material. This method is used to extract essential oils and bioactive substances from various plant sections (Azmir et al. 2013). In this method, the powdered plant material is placed in a closed flask containing solvent. The flask is allowed to stand for 2–3 days with periodic shaking in an incubator shaker. The solvent is diffused into the cell wall to dissolve the chemical components present in plant material during this time. This process is called molecular diffusion. After a few days, the liquid is filtered and evaporated to get the solid residue from the solvent. If water is taken as a solvent for extraction, a slight amount of alcohol needs to be added to prevent the growth of the microorganisms (Pandey and Tripathi 2014). The maceration process involves three basic principles:

1. Plant material was initially powdered with the help of a grinder
2. This increases the surface area of the plant material to allow proper contact between the solvent and the plant material
3. Further, the liquid is drained off but the solid residue was concentrated and collected as an extract.

During the maceration process, occasional shaking is an important step as it facilitates proper extraction by increasing diffusion of the powdered material with the solvent to remove chemical components from the surface for more extraction yield (Devgun et al. 2010).

23.2.1.3 Hydro-Distillation

Hydro-distillation is the most common and old conventional technique that does not require organic solvents to extract plant materials. In this technique, plant material is seal packed in a steel compartment containing water in significant volume and then allowed to boil. On the other hand, fumes are directly injected into the plant samples. Hot water and fumes are significant contributors to the isolation of free bioactive components from plant tissue. The vapor mixture of water and oil is condensed by indirect cooling through the water. It is considered the most effective method to extract the essential oil from different parts of the medicinal and aromatic plants. The yield of the extract through this method usually relies upon the weight, size, and nature of raw material and volume of water (Parikh and Desai 2011). This process involves three chief physicochemical characteristics: hydro-diffusion, hydrolysis, and heat decomposition. Due to high temperature during extraction, some volatile compounds may vanish, restricting their use for the extraction of thermolabile compounds. The principle behind this technique involves isotropic distillation at atmospheric pressure and heating of water, oil molecules, and other solvents during the extraction process. The advantages and disadvantages of conventional techniques are presented in Table 23.2.

Table 23.2 Advantages and disadvantages of conventional techniques

Extraction method	Advantages	Disadvantages
Soxhlet extraction	• At a time, a large quantity of plant material can be extracted	• Samples were continuously exposed to high temperature for a longer time; hence, the risk of thermal destruction of certain compounds cannot be counterbalanced
	• Solvent can be reused again for the extraction	• It takes a longer time for the extraction process
	• Sometimes, it does not require filtration after the extraction process	• Labor-intensive
	• Does not rely upon the matrix type	• It allows manipulations of restricted variables
	• Simple technique	
Cold maceration	• Simple technique	• Long extraction time usually takes up to 2 weeks
	• No utensils or equipment required	• Pure extraction is not possible
	• No need for a skilled operator	• Very slow and time-consuming process
	• Energy-saving process	• Large volume of solvent is required for extraction
	• Suitable for less potent and inexpensive drugs	
Hydro-distillation	• Higher yield of oil content	• Complete extraction is not done
	• Volatile oil compounds are less prone to hydrolysis and polymerization	• Impart an unpleasant odor to the essential oil
	• Loss of polar compounds can be minimized if refluxing can be controlled	• The continuous exposure to high temperatures can cause hydrolysis of some important components of the essential oil, for example, esters.
	• Oil quality can be improved by steam and water distillation	• Temperature control is problematic as it causes variation in the rates of distillation
	• Cheap and environment-friendly technique	• More space and more fuel are required
	• No organic solvent is required	• Uneconomical process

23.2.2 Nonconventional Extraction Techniques

23.2.2.1 Supercritical Fluid Extraction (SFC)

Supercritical fluid extraction is categorized by the transformation of gas in the supercritical fluid by the change in temperature and pressure. The critical temperature is the highest temperature at which a gas can be converted to a liquid by raising the pressure, while the critical pressure is the highest pressure at which a liquid can be converted to a gas by increasing the temperature (Soquetta et al. 2018). The main transport mechanism in the supercritical solvent phase is convection as a mass transfer operation (Silva et al. 2016). This extraction is generally used to isolate nonpolar bioactive constituents including carotenoids and lipids. This process of extraction is fast, selective, and can be utilized for a small number of samples (Oroian and Escriche 2015). With the use of analytical chromatographic techniques such as gas chromatography (GC) and supercritical fluid chromatography, the main benefit of this extraction process is the ability to detect unknown components contained in the sample (SFC) (Silva et al. 2016). This technique involves two important steps:

- Chemical components first solubilize in the solid matrix and then separate in the supercritical solvent.
- The solvent penetrates through the packed bed and dissolves the solid matrix's components.

The solvent then exits the extractor with a decrease in pressure and increase in temperature, and extracted compound becomes solvent-free (Silva et al. 2016). Supercritical fluids possess low surface tension, low viscosity, disperse easily within the solid matrix, and increased extraction efficiency compared to the liquid solvent used in conventional extraction processes (Pouliot et al. 2014).

23.2.2.2 Extraction with Pressurized Liquid

This method includes transferring solutes from a solid matrix through a separation technique. Liquid solvents are utilized at high pressure and temperature, resulting in a lowering in the solvent's surface tension. As a result, the solvent is capable of penetrating deeper into the cell. Matrix pores are indeed a type of pore found in the matrix. The process causes the matrix to be disrupted. As a result, the mass transfer of the analyte from the sample including solvent rises (Garcia-Castello et al. 2015). The solvents are chosen based on the solubility characteristics of the necessary solute. The physicochemical features of pressurized solvents, such as density, diffusivity, viscosity, and dielectric constant, which may be changed by adjusting the temperature and pressure of the extraction system, make them extremely versatile (Pronyk and Mazza 2009). Extraction using pressurized liquid is appealing because it provides quick extraction with less solvent usage. This method has been used to extract anthocyanins from a variety of plants with great success (Santos et al. 2012).

23.2.2.3 Ultrasound-Assisted Extraction (UAE)

Ultrasound is a type of sound wave that has a frequency range of 20 kHz to 100 MHz. Cavitation is a phenomenon caused by ultrasound-assisted extraction, which requires generation, bubbles' expansion, and deflation (Azmir et al. 2013). UAE is a versatile extraction method that has been used for a long time and may be used on a variety of materials and analytes derived from different forms of samples. Ultrasounds can speed up heat and mass transfer by disrupting plant cell walls, resulting in a better release of target substances from a variety of natural sources (Roselló-Soto et al. 2015).

Ultrasound extraction involves two primary physical phenomena:

1. Diffusion through the cell wall
2. Rinsing the cell content after the walls have been disrupted.

The activity of ultrasound is regulated by temperature, pressure, frequency, and sonication time (Rajha et al. 2015).

Ultrasound is a relatively simple extraction procedure when compared to other extraction techniques; it is versatile, flexible, and requires a low initial investment. Among other molecules and biomaterials, ultrasound has been used to extract polysaccharides, essential oils, proteins, peptides, dyes, pigments, and bioactive substances (Briones-Labarca et al. 2015; Tiwari 2015). This phenomenon can occur in two ways: indirectly or directly. When ultrasound is delivered directly to the medium without the use of a barrier, such as a probe device, the intensity increases 100-fold. The waves must travel through the water until they reach the sample when using an ultrasonic water bath for indirect sonication (Kek et al. 2013). The use of ultrasonic energy has been contemplated to be a promising method for extracting bioactive components from plant samples. It boosts the mass transfer coefficient, speeds the kinetics, and raises the final concentration of bioactive compounds (Zhang 2014).

23.2.2.4 Microwave-Assisted Extraction

Microwave-assisted extraction is a term that encompasses both microwave and classical solvent extraction. It increases the kinetics of extraction by boiling the solvents and plant tissue with a microwave (Delazar et al. 2012). The minute microscopic residues of moisture that occurs in plant cells are the focus for heating in dried plant material. Evaporation occurs as a result of the microwave effect heating the moisture inside the plant cell, putting great pressure on the cell wall. Due to the pressure, the cell wall is forced from within, and the cell wall ruptures. Exudation of active ingredients from burst cells happens as a result of enhancing phytoconstituent production.

MAE has grabbed researchers' interest as a method for extracting bioactive chemicals from a wide range of plants and natural remnants (Anokwuru et al. 2011). Microwaves emit electromagnetic radiation with frequencies ranging from 300 MHz to 300 GHz and wavelengths ranging from 1 cm to 1 m. An electric field and a magnetic field are both present in electromagnetic waves. These are referred to as two fields that are perpendicular to each other. Microwaves were first used to heat items that could absorb heat transform a portion of the electromagnetic energy into heat. Commercial microwaves generally use 2450 MHz frequency, which equates to an energy output of 600–700 W (Ballard et al. 2010).

Advanced approaches have recently become popular to limit bioactive compound loss without increasing extraction time. As a result, microwave-assisted extraction is a useful technology in a variety of sectors, particularly in the medicinal plant field. Furthermore, this method reduced the number of biological components lost during extraction (Suzara et al. 2013). Because of its potential to minimize both time and extraction solvent volume, microwave-assisted extraction (MAE) has been employed as an alternative to traditional procedures for the extraction of antioxidants (Suzara et al. 2013). The primary goal of MAE is to heat the solvent and extract antioxidants from plants using a smaller amount of these solvents (Altemimi et al. 2017).

23.3 Identification Tools for Phytochemicals

Identification of bioactive compounds and their characterization from plant extracts are still challenging as plant extracts contain a mixture of compounds possessing different polarities. These compounds are isolated using different chromatographic techniques including TLC, HPTLC, paper chromatography, column chromatography, gas chromatography, and HPLC. Chromatographic techniques help in obtaining pure compounds and thus are among the various identification tools for the phytochemical analysis. Chromatography occupies a leading position as it contributes to the highly accurate analysis of organic compounds. It is majorly based on the interaction between the mobile phase, stationary phases, and the mixture components (Sasidharan et al. 2011). The mixture components are separated in the two different phases in chromatography. The pure compound isolated is further utilized for the analysis of the structure and its biological activities. In chromatography, the molecules are separated based on size, shape, and charge (Heftmann 1992).

23.3.1 Thin-Layer Chromatography (TLC)

TLC is considered to be the latest version of paper chromatography and is a widely used laboratory technique. TLC includes adsorbent materials such as alumina, silica, and cellulose on inert materials like glass, plastic, or aluminum foil (Kumar et al. 2013). In TLC, a small amount of sample is applied to a starting point on the chromatography plate, which is allowed to dry. Further, the prepared plate is placed in the developing chamber with a small amount of solvent. The level of solvent should be such that it is not touching the level at which the sample was applied. Along with the solvents, the sample components will move at different speeds on the plate, and thus, the mixture is separated. Highly soluble components will travel farthest on the plate when compared to the less soluble ones (Singhal et al. 2009). R_f (retention factor) can be analyzed by dividing the distance traveled by an individual compound from its original position by the overall distance traveled by the solvent. TLC is mainly employed for the separation of various components such as amino acids, alkaloids, phenols, steroids, and proteins, utilizing different solvent systems and adsorbents. Adsorbents like silica gel are mainly utilized for the separation of amino acids, alkaloids, sugars, lipids, etc. Adsorbents such as cellulose powder, starch, and Sephadex are used for the separation of mainly amino acids and proteins. Similarly, alkaloids, steroids, phenols, vitamins, and carotenoids are separated using adsorbents aluminum and celite. Once the components are separated, the chromatographic plate is sprayed using different spray reagents like iodine vapors and potassium dichromate, which will confirm the compounds present based on the color development after the spray reagent (Chauhan and Dahiya 2016).

TLC also serves as a tool for screening antimicrobial agents via bioautography. Bioautographic techniques include contact bioautography, agar overlay bioautography, and direct TLC bioautographic detection (Wagman and Bailey 1969).

23.3.2 Contact Bioautography

Agar diffusion or contact bioautography includes the diffusion of antimicrobial agents (Sherman 2008). Developed chromatogram on TLC plate is then placed face down on agar for a certain duration to have proper diffusion. Further, the agar layer is incubated and checked for zones of clearance corresponding to the color spots on the chromatographic plates. The time of incubation for the growth is in between 16 and 24 h, and it can be reduced to approximately 5 h by spraying it with reagent 3,5-tetrazolium chloride. Contact bioautography is a familiar technique for the microbiologist to screen the antimicrobial agents. Diffusion of individual components from chromatogram to agar plate and establishing a closed contact in between the plate and the agar are some of the disadvantages associated with the technique. Various polyether antibiotics, bromoditerpene antibiotic, and several antifungal agents were isolated using contact bioautography (Jayasinghe et al. 2003). The disadvantages such as sensitivity and low resolution can be overcome by using advanced chromatographic tools like HPTLC (high-performance thin-layer chromatography). HPTLC use also reduces the time required and solvent used. Ramirez et al. (2003) observed multiple antibiotic residues in cow's milk by HPTLC contact bioautography.

23.3.3 Direct TLC Bioautography

Direct TLC bioautography includes the spraying/dipping of the bacterial or fungal suspension on the developed TLC plate at a specific concentration (10^6 CFU/mL). The prepared bioautogram is further incubated in a dark and humid chamber for 24–48 h at room temperature. The bioautogram was further sprayed with 2,3,5-triphenyl tetrazolium chloride (TTC) and incubated at room temperature for 4 h. Microbial growth inhibition appeared in the form of the zone of clearance against a pink backdrop. The R_f values corresponding to the spots possessing clearance zone were determined (Dahiya and Manglik 2013). Direct bioautography is found suitable for both spores forming fungal cultures like *Aspergillus* and *Penicillium* sp. and for bacteria such as *Bacillus* sp., *Staphylococcus* sp., and *E. coli*. TLC bioautography suggests that aloe vera extracts possess anti-MRSA potential, which is maybe because of the presence of tannins in the extracts (Dahiya and Purkayastha 2012a). The bioactive components of juniper essential oil were evaluated against potential inhibitors, *E. coli* and *Staphylococcus aureus* 2, via TLC bioautography, which confirmed the bioactive compound tannin responsible for the antibacterial activity when sprayed with 10% $FeCl_3$ spray reagent (Purkayastha et al. 2012). Similar results were reported by Dahiya and Purkayastha (2012b) for *Psoralea corylifolia* essential oil tested against Enterococcus sp. and Klebsiella pneumonia. TLC bioautography revealed the presence of more than one bioactive component at different R_f values (0.10–0.15 and 0.70–0.83) on plate B against *Enterococcus* sp. and R_f value (0.12–0.15) against *Klebsiella pneumonia*. The significant antimicrobial activity was found to be due to tannins when sprayed with 2% $FeCl_3$ spray solution.

23.3.4 Agar Overlay Bioautography

This technique combines the features of direct and contact bioautography. This technique involves the covering of chromatogram with molten, seeded agar medium. Once the agar solidifies, the bioautogram is sprayed with tetrazolium dye and incubated, which will allow the visualization of inhibition/growth bands. The microorganism acts on the tetrazolium salt and converts it to intensely colored formazan (Saxena et al. 1995). This technique is widely used for bacterial (*E. coli*, *Pseudomonas aeruginosa*, *S. aureus*, etc.) and yeast cultures like *Candida albicans*. Using this technique, the antibacterial activity of isoflavonoid, carotenoids, alkaloids, and several antimicrobial compounds was isolated and characterized (Dewanjee et al. 2015; Zaidi and Dahiya 2015). Manhas and Dahiya (2017) reported hexane extract of *Michelia champaca* leaf, which showed significant antibacterial activity against *S. aureus* 1. Bioautography confirmed three active compounds at different Rf values. The observed inhibition was possibly due to more than one active compound, which is overlapping possibly due to the solvent system used.

23.3.5 High-Performance Liquid Chromatography (HPLC)

HPLC is an analytical technique that is highly flexible as the mobile and stationary phase, and the elution technique can be modified depending on the analysis. It is also known as high-pressure liquid chromatography and can separate the compounds based on their interaction with the column and the solvent phase. There are two types of HPLC that are normal and reverse-phase types. In the normal phase, the solid phase is more polar when compared with the mobile phase, whereas the reverse phase typically includes a more polar mobile phase compared to the stationary phase.

HPLC helps identify and separate organic/inorganic solutes from the sample and phytochemical analysis of plant extracts. Quantification of berberine, an alkaloid obtained from *Tinospora cordifolia*, was studied by HPLC using acetonitrile and water in the ratio of 60:40. Comparative studies related to berberine content obtained from the wild type and micropropagation were studied by Sivakumar et al. (2014) and observed that methanolic extract of micropropagated one gave a higher quantity of berberine (1.2%) as compared to only 0.2% in the wild type.

23.3.6 Gas Chromatography (GC)

Gas chromatography (GC), commonly known as gas–liquid chromatography (GLC), is a technique for separating mixtures into components based on component redistribution over a stationary phase or support material in the form of a liquid, solid, or a combination of both, and a gaseous mobile phase. Many pharmacologically active ingredients of herbal remedies are known to be volatile chemical molecules. As a result, the examination of volatile chemicals in gas chromatography is critical in the analysis of herbal medicines. Because measurements of the area under the peaks revealed on the GC trace are directly related to the quantities of the individual components of the original mixture, GC offers both qualitative and quantitative data on plant compounds. The GC equipment can be set up so that the separated components are subjected to spectral or other analysis after separation. GC is routinely connected to mass spectrometry (MS), and the combined GC-MS equipment has emerged as one of the most important techniques for phytochemical analysis in recent years (Garud et al. 2017). Not only is a chromatographic fingerprint available with the GC-MS, but also information about qualitative and quantitative compositions. This will be very helpful in determining the link between various elements and their pharmacology. As a result, GC-MS is the preferred method for analyzing volatile chemical components in herbal medicines nowadays (Revathy et al. 2011).

23.3.7 High-Pressure Liquid Chromatography (HPLC)

Liquid chromatography is chromatography that uses a liquid as the mobile phase. The “eluent” is the liquid employed as the mobile phase, and the stationary phase is usually a solid or a liquid. The sample solution is supplied to a porous stationary phase, and the mobile phase is delivered at a greater pressure via the column, causing separation depending on the solute’s affinity for the stationary phase. The development of HPLC is aided by the need for a higher degree of separation and faster analysis, which is met by refining the stationary phase packing material to a size of 3–10 m and eluent delivery via a high-pressure pump. HPLC instruments comprise mobile phase reservoir, a pump, an injector, a separation column, and a detector as defined by Gupta and Shanker (2008).

The mobile solvent is delivered by the solvent delivery pump, and it is introduced into the mobile phase or onto the chromatographic bed by the injector. The column is the most significant part of the HPLC system because it separates the sample components as it goes through them. The column is a stainless-steel tube with a diameter of 3–5 mm that is filled with silica gel and measures 10–30 cm in length. The separated components in the column will be quantified and recorded in the computer system using a detector. The phytochemical components will be provided as a fingerprint with peaks by the system.

HPLC is the newest chromatographic technology to join the repertoire of phytochemists. This method is mostly utilized for nonvolatile chemicals, such as higher terpenoids, phenolics of all types, alkaloids, lipids, and sugars. It is best for substances that can be identified in the ultraviolet or visible spectrum. It is best for substances that can be identified in the ultraviolet or visible spectrum. As a result, HPLC has seen the most widespread use in the analysis of herbal medicines in recent decades. The most common column used in the analytical separation of herbal medicine is reversed-phase (RP) columns.

HPLC is a very adaptable technology since its mobile phase, stationary phase, and elution process may all be changed to satisfy a variety of analysis needs (IUPAC 2006). The two forms of HPLC are the normal phase and reverse phase, which are distinguished by the stationary phase being more polar than the mobile phase in the normal phase and vice versa in the reverse phase. Normal phase chromatography is used to separate lipophilic compounds such as oils, fats, and lipids. Reverse-phase chromatography is extensively used for phytochemical fingerprinting of medicinal plants since most plant extracts are polar compounds.

23.3.8 High-Performance Thin-Layer Chromatography (HPTLC)

HPTLC is planar chromatography, which is highly sophisticated with advanced features of detection and separation. In this technique, the separation is because of partition/adsorption or both and majorly depends on the solvent and adsorbents used. Using a sample applicator, a sample (0.1–0.5 μL) is applied on a TLC plate designed for HPTLC on the silica gel for the normal phase and C8 and C18 for the reverse phase. The chromatogram is developed, which can be viewed at different wavelengths. In HPTLC, the analysis time is greatly reduced, and efficiency is high due to the smaller particle size generated. It is controlled by software that can develop a peak corresponding to the active compound, and the result can be analyzed (Ingle et al. 2017). Various advancements like the use of densitometers, high-resolution sorbents, UV/Visible/fluorescence scanners, and the use of new software with advanced features make the analysis and detection process more efficient and sensitive resulting in the replacement of HPLC and GC by HPTLC technique. This tool is mainly utilized for the separation and detection of bioactive compounds from medicinal plants and the standardization of herbal drugs. The bulky size, large space needs, technical operator requirement, cost factor, etc., are some of the disadvantages associated with its use.

23.4 Detection of Bioactive Compounds-Fourier Transform Infrared Spectroscopy (FTIR)

Infrared spectroscopy using Fourier transforms is a useful method for identifying functional groups in plant extracts. It aids in molecular identification and structural determination (Ingle et al. 2017). FTIR samples can be made in a variety of ways. Placing one drop of the sample between two plates of sodium chloride is the simplest method for liquid samples. Between the plates, the drop produces a thin film. Solid materials can be milled with potassium bromide (KBr) to form a thin pellet that can be examined. Solid samples can also be dissolved in a solvent such as methylene chloride, and then, a few drops of the solution are dropped onto a single high attenuated total reflectance (HATR) plate and the spectra are recorded in percentage transmittance.

23.4.1 Nuclear Magnetic Resonance (NMR) Spectroscopy

Physical, chemical, and biological aspects of the matter are determined via nuclear magnetic resonance spectroscopy. The one-dimensional approach is commonly employed; however two-dimensional NMR techniques could be applied to achieve the intricate structure of the molecules. The state of being solid, the molecular structure of solids is determined via NMR spectroscopy. Radiolabelled C NMR is used to determine which carbon types are present in a compound. H-NMR is utilized to determine the types of hydrogen contained in a compound and the connections between the hydrogen atoms (Ingle et al. 2017).

The magnetic properties of particular atomic nuclei, such as the nucleus of the hydrogen atom, the proton, carbon, and a carbon isotope, are the focus of NMR. Many researchers have been able to examine molecules using NMR spectroscopy, which records the differences between the various magnetic nuclei and so provides a clear picture of where these nuclei are in the molecule. Furthermore, it will show which atoms are present in adjacent groups. It will eventually be able to determine how many atoms are present in each of these situations. Several attempts have been undertaken in the past to isolate individual phenols using preparative or semi-preparative thin-layer chromatography, liquid chromatography, and column chromatography, with the structures identified afterward by NMR offline (Kemp 1991).

23.4.2 Mass Spectrometry (MS)

In mass spectrometry, organic molecules are bombarded with electrons or lasers and transformed to charged ions, which are highly energetic. The relative abundance of a fragmented ion is plotted against the mass/charge ratio of these ions in a mass spectrum. Relative molecular mass (molecular weight) may be estimated with high accuracy using mass spectrometry, and an exact molecular formula can be derived by knowing where the molecule has been fragmented (Christophoridou et al. 2005).

Mass spectrometry is a strong analytical technique for determining the structure and chemical characteristics of molecules, as well as identifying novel chemicals and quantifying known substances. The molecular weight of a sample can be determined using the MS spectrum.

This method is commonly used for structural elucidation of organic compounds, peptide, or oligonucleotide sequencing and monitoring the presence of previously identified compounds in complex mixtures with high specificity by simultaneously defining the molecular weight and a diagnostic fragment of the molecule.

23.5 Conclusion

The increasing demand for the extraction of plant bioactive components involves a never-ending search for efficient extraction methods. Since bioactive chemicals found in plant material are multi-component combinations, their extraction, identification, and determination still remain a challenge. The extraction of bioactive components is a difficult process that can be achieved using a variety of methods. The traditional approaches are based on the solubility of the solute in the solvent from plant materials. As a result, it frequently uses a substantial amount of solvent to extract the target chemical, even though sometimes aided with increased temperature and mechanical stirring or shaking. It has been proved that replacing traditional procedures with green technology can improve extraction yields, minimize processing time, and prevent the environmental damage caused by toxic solvents. Various studies suggested that a mixture of strategies might help in the optimization of these processes. Bioactive substances such as phenolics, flavonoids, lignins, and anthocyanins are implicated in the protection of various diseases such as cancer, neurological problems, cardiovascular disease, and hypertension. Extracting and optimizing these chemical compounds from plant material are critical. The traditional or conventional method involves hazardous organic solvents that cause a threat to the environment. Each process has its own advantages and disadvantages, and extraction technique selection might be depending on the plant sample employed as a source of bioactive compound. It may be concluded that no single extraction method is appropriate, and each extraction approach is specific to the plants. The measurement of extraction efficiency is also influenced by the use of standard procedures. On the other hand, the growing economic importance of bioactive compounds and bioactive compound-rich commodities may lead to the development of more complex extraction technologies in the future.

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Strategy and Approaches of Extraction of Natural Bioactive Compounds and Secondary Metabolites from Plant Sources

24

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Abstract

This chapter covers primary and secondary information on bioactive compounds with their extraction techniques. This covers all classical and advanced extraction techniques of bioactive compounds from natural sources like herbs, shrubs, fruits, vegetables, biological sources, and secondary metabolites as it is a sustainable approach to preserve bioactive compound for the development of nutraceuticals and drugs. All new composition in drug industries is mixed with natural bioactive substance to balance the loss of human immunity after disease. Bioactive substance is classified into phenolic, alkaloids, flavonoid, carotenoids, and others. There are a lot of health benefits of polyphenols, which can be utilized by nutraceutical and pharmaceutical drugs. The purification and extraction techniques are very difficult to meet consumer demand, but many classical and advanced techniques are working on it. This review covers a brief introduction and classification of bioactive substance with the type of extraction method and their effect.

Keywords

Bioactive compounds · Natural metabolites · Extraction techniques · Anthocyanin · Polyphenols · Terpenoids

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24.1 Introduction

Nature is blessed with numerous bioactive compounds for the treatment of chemo and other therapeutic multiple diseases (Mukheriee and Wahile 2006). All natural sources from plants like fruit, vegetable, leaves, pomace, stem, and bark are rich in various medicinal qualities with diversified structural and chemical properties. Many food plants have been (Kohli et al. 2019) used in food industries for natural compound as an alternative option of health supplement to fight chronic degenerative diseases and increased quality of life (Zhou et al. 2016). Wrong eating habits and food approaches increased the chances of chronic disease. The advancement of natural compound with different extraction methods again improves the utility of drug discovery process (Vats 2017). Awareness of bioactive components is essential in a diet plan (Weber 2001). Quality delivery of natural bioactive substance with nominal making process is the priority of drug industries in present and future scenarios. There are few nutritional and antinutritional substances, which are categorized in bioactive compounds that are available in environment, are part of the food system, and are well known for their good effect in human health (Biesalski et al. 2009).

The molecular weight of bioactive substances is very low so that derivatives are easily separated from plant, animal, and other microbes (Nicoletti and Fiorentino 2015). Vegetables and fruit (Upadhyay et al. 2017a, b) food groups are classified by plant sources. These plant sources are rich sources in minerals, vitamins, and nonnutritive bioactive chemicals, which are also known as phytochemicals (Upadhyay et al. 2017a, b). All types of flavonoids, alkaloids, carotenoids, phenolics (Anand et al. 2020), and other phytochemicals come in bioactive substance. The famous Poem "An Apple a day keeps doctor away" fulfills the requirement of bioactive in daily life in scientifically and medical point of view. This quote stated that there is an inactive free radical cell proliferation and low level of bad cholesterol and oxidation of fat, by daily intake of bioactive foods in terms of fruits, vegetables, and plant sources.

There are numerous important compounds that are available in plant and animal sources, and one of the important compounds is secondary metabolites, which are fabricated by plants and animals to protect itself against various infection and diseases. Many pathogens, pest, and infection can be controlled in human body by suitable use of secondary metabolites. Secondary metabolites are not affected by growth and reproduction of plants. Phenolic compounds like lignin, saponins, glycosides, tannins, and terpenoids are major sources of secondary metabolites. These are popular for an integral part of plant–microbe interactions and adapting properties toward environmental changes. The overall regulation and synergy are high in bioactive compound. Bioactive compounds are involved in germination and propagation, which is useful in medicinal and herbal treatment.

The role of diet and nutrition is always an important area for knowledge of molecular and genetic regulation of diet (Patil et al. 2009) and nutrient. The role of the bioactive compound as a secondary metabolite accelerates the pace because of its medicinal importance. Many bioactive compounds as a phytochemical for specific role have been identified as an option of preventive medicine of secondary lifestyle disease.

Mostly bioactive substances are available natural in wild and rural areas (NPs), and they can be used as a holistic food or medicine with low molecular weight compounds. Derivatives of bioactive are separated from different plants, animals, and microbes (Nicoletti and Fiorentino 2015). Research and review showed that 400,000 plants are available in form of endophytes, which reside in plants. Bioactive compounds are useful in antimicrobial, cytotoxic, anticancer, antiparasitic, and insecticidal activities (Singh et al. 2017). This review chapter covers the use of conventional and nonconventional technologies for the separation and extraction of bioactive compounds with the addition of extraction efficiency and their health benefit.

Bioactive compounds are mostly available in plants and their parts, which can identify and be utilized by researcher thousand years before. Many food substances not only provide adequate essential compound but only meet metabolic requirement of human body (Nicoletti and Fiorentino 2015). Bioactive substances contribute maximum effort for the improvement of physical and mental levels of human health. Fruit and vegetable extracts are popular for nutritional values and bioactive substance in terms of phytochemicals, which are healthy to fight with antioxidant (Branca et al. 2001). Identification of accurate bioactive substance from any plant is the main work of researcher for the development of drugs or food supplement for human welfare and development of society.

24.2 Properties of Bioactive Compounds

All traditional food patterns are rich in vital nutrient and bioactive substances, and identification and separation are important and possible by scientific and technical method of determination. Modification of traditional food increases the bioactive substances in food (Ziegler and Facchini 2008). All discipline of science and technology is able to identify and apply bioactive molecules in food and health supplement for welfare of society. Therefore, it is important to identify and develop bioactive product from natural source, which is safe and inexpensive antioxidant product. Phenolic bioactive is widely used in pharma and food industry for the treatment of carcinogenic problem in human health (Fig. 24.1).

Phenolic substance-rich compounds are widely used in daily household cooking in terms of boiled rice, cereals, legumes, etc. All nuts, green tea red wine, green vegetable, and fresh fruits are rich in phenolic substances. Many fruits and flowers contain flavonoids, which are important for antidiabetic and anticancerous properties. Bioactive substance is useful in cardiovascular treatment as it is rich in antioxidant properties. It reduces risk factors. There are many free radical scavengers, which are useful and are the most potent antioxidant compounds. There are a lot of fruits and vegetables like pumpkins, apricots, mangoes, mustard seeds, tomatoes, and carrots. They are rich in carotenoids and phenolic substances. There are many pungent plants such as mustard seeds and leaves, cabbage, and

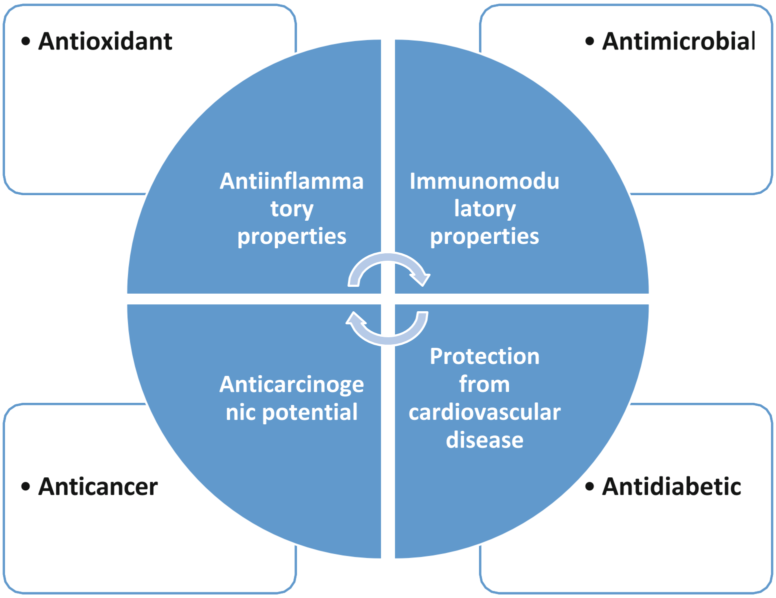

Fig. 24.1 Biological properties of bioactive compounds

pomegranate. These are rich in antioxidant with phase I and phase II enzymes. It increases the activity of enzymes. That is why it can be useful for good immunity. All natural fruit and vegetable easily contain bioactive substance, but variation of amount has been seen in natural foods. There are few food substances treated for flavor and additive in food products for the enhancement of taste, color, and flavor. These flavor substances also carry lots of important micronutrient and bioactive substance with health-promoting properties. They are being used as processing agents and additives. Many carotenoids, curcumin, and anthocyanin are widely used as coloring and taste enhancer in processed food, which increases carotenoid and antioxidant levels in processed food products like instant soup and instant curry masala. These flavoring agents reduced oxidation tendency in food product and maintained ascorbic acid level in prepared food (Aniszewski 2015). There are many active substances like cinnamaldehyde and vanillin, which increase natural sweetness and flavor in food. It is widely used in chewing gums, and beverages are used for flavor enhancement. It is very clear that bioactive substances are available naturally in various fruits, vegetable, herbs, and plants. In food process industry, bioactive substances are added in food product to increase nutritional properties. There are few coloring substances, which also come in category of bioactive substances that are carotenoids, anthocyanins, and curcumin.

New innovative endophyte-derived metabolites are alkaloids, terpenoids, aliphatic compounds, polyketides, phenylpropanoids, and peptides (Kumar et al. 2021).

24.3 Classification of Bioactive Compound

Bioactive substances are rich in nutritional and non-nutritional constituents that are found in very little but important quantities in fresh and processed foods (Fig. 24.2). They are providing numerous benefits in human health beyond the nutritional value of the food product (Kitts 1994).

24.3.1 Bioactive Phenolic Compounds

Phenolic bioactive compounds are one of the important bioactive substances available in cereal and raw plant-based products. Phenolic bioactive compounds have the ability to decrease the efficacy of many harmful substances like artificial antioxidant compounds, butylated hydroxytoluene (BHT), tert-butylhydroquinone (TBHQ), butylated hydroxyanisole (BHA), propyl gallate (PG), and ascorbyl palmitate (PA). These are commonly available in the food process industries to control the rancidity, oxidation, spoilage, and deterioration in the prepared food products

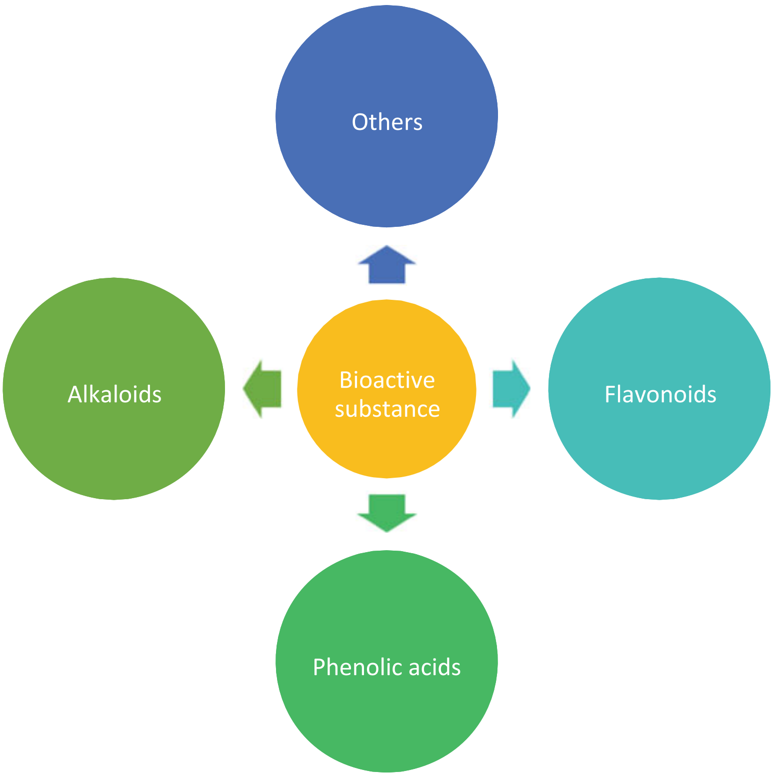

Fig. 24.2 Classification of bioactive substance

(Wong-Paz et al. 2017) although it is well defined that these synthetic compounds are life-threatening chemical, harmful, and can enhance chronic diseases and degenerative disease, particularly many types of cancerous tumors. Therefore, natural sources of bioactive compound are safe and reliable and healthy antioxidant and phenolic compounds, which can use in food process and pharmaceutical industry. Conventional practice of primary health care gives support to understand the value of natural compound; bioactive substance is well known due to gradual increase in chronic health issues, such as type 2 diabetes, cancer, cardiovascular diseases, and obesity (He et al. 2016). Phenolic compounds are rich in bioactive compound and have been reported as antimicrobial agent. There are numerous mechanisms of action to identify phenolic compounds in different food products; for example, phenolic content is available in beetroot and green tea. These compounds give safety and protection against oxidizing agents, reactions, and reactive agents (Lorenzo and Munekata 2016).

For improving shelf life of foods, there is major scope of antimicrobial phenolic compounds and antioxidants activities. Thus, they act as a protective layer to resist microbial attacks on food.

24.3.2 Alkaloids

All plants, flowers, and seafoods sources have alkaloids as natural compound in them. One-quarter of plants contain alkaloids, whose thousands of verities are being identified. The concentration of alkaloids is high just before seed formation and then decreases at the ripening of seed. Alkaloids may be useful in protecting plants from some harmful insects. Alkaloids are large group of secondary metabolites. They contain nitrogen in a heterocycle, which has a variety of chemical structures and pharmacological actions (Evans 1996). Each alkaloid carries one nitrogen atom and one amine-type structure. This alkaloid is derived from ammonia; it is the replacement of hydrogen and carbon atoms called hydrocarbons.

24.3.3 Flavonoids

Flavonoids are polyphenolic compounds, which occur naturally available in flowers. For their compositions, they have two rings of benzene; it is linked and attached. It has a heterocyclic pyrone ring. Plant sources constitute flavonoids, which are well known and are one of the major constituents, which are used in daily consumption in human diet in different forms. Flavonoids are involved in many biological activities like enzyme inhibitors and antioxidants. Another benefit is reported as anti-inflammatory properties of flavonoids (Hamalainen et al. 2007). Flavonoids are rich in biochemical and antioxidant effects (Kumar et al. 2020). It is important in disease control and prevention like cancer, Alzheimer's disease (AD), atherosclerosis, etc. (Panche et al. 2016). Flavonoids are good for vegetables growth and their protection from plaques. Flavonoids with a ketone group are called flavonols, which are building blocks of proanthocyanins. Flavonols are present in fruits and vegetables. Kaempferol, quercetin, myricetin, and fisetin (Pathania et al. 2020) are mostly researched flavonols.

24.3.4 Other Bioactive Compounds

Numerous bioactivities such as antihypertensive, antithrombotic, immunomodulatory, and antioxidative activities are present in fish and marine food. These are known as bioactive substance. B-carotene, lycopene, ascorbic acid, curcumin, ellagic acid, omega-3 and omega-6 fatty acids, and quercetin are also bioactive compound with numerous health benefits (Patil et al. 2009).

24.4 Secondary Metabolites

Secondary metabolites are abundant in plants and environment. Secondary metabolites are important for pharmaceutical and nutraceutical industries (Rao and Ravishankar 2002). Secondary metabolites have been seen in plant cell and tissue culture, which are good for controlled production of myriad (DiCosmo and Misawa 1995). Advances in plant cell cultures can offer reasonable and commercial production of new plant-based products, their cells, and their chemicals (Thengane et al. 2003).

24.5 Type of Extraction Methods and Their Impact on Bioactive Compounds

Extraction is a process of separation of solvents out of a mixture of substances. There are many conventional methods that exist in the literature for the extraction techniques and the recovery of major compounds mentioned in Tables 24.1 and 24.2.

Emerging and recent techniques are more convenient methods of extraction of bioactive compounds due to the latest technology and suitable solvents in minor proportions. Due to such changes, extraction times are reduced *w.r.t.* conventional techniques, while suitable conditions during extractions can make efficient extractions and vice versa. Inefficient extractions may provide in reduced amount of the bioactive compound and their biological activities.

Classification of conventional techniques of bioactive compounds.

24.5.1 Folch Method of Extraction

In lipid biochemistry, Folch's method is major contribution. In this technique, lipid is extracted from plant's biological substance using solvent extraction method. In

Table 24.1 Different extraction techniques and their bioactive compound

Bioactive compound	Plant sources	Extraction and analytical technique	References
Luteolin	Broccoli, green pepper, parsley, oregano, carrots, and rosemary	Conventional extraction method	Lama-Muñoz et al. (2019)
Phenolic compound	Cereals	Enzymatic digestion	Saura-Calixto et al. (2007)
Carotenoids	Cabbage	Colonic fermentation	Kaulmann et al. (2016)
Anthocyanins	Grape peel and pulp	Ultrasound-assisted extraction	Corrales et al. (2008)
Phenolic acids and antioxidants	Wheat	Solvent extraction method	Rudjito et al. (2019)
Apigenin	Many fruits and vegetables, parsley, celery, celeriac, and chamomile tea	Conventional method	Osada et al. (2004)
Naringenin	Oranges and tomatoes	Solvent extraction method	Hamalainen et al. (2007)
Curcumin	Turmeric	Solvent extraction method	Toda et al. (2003)
Silymarin	Milk sources	Lipid extraction method	Sharma et al. (2003)

Table 24.2 Impact of bioactive compound on human health

Bioactive compounds	Health benefits	References
β-carotene and lycopene	Prevention from prostate cancer	Kucuk et al. (2001)
Ellagic acid	Prostate cancer	Malik et al. (2011)
Curcumin	Anti-inflammatory and anticancer	Dcodhar et al. (2013)
Tea phenolics	Antioxidant effects	Rietveld and Wiseman (2003)
Green tea	Anticancer antiangiogenesis	Marwick (2001)
Luteolin	Anticarcinogenic activity	Lin et al. (2008)
Apigenin	Anticarcinogenic activity	Patel et al. (2007)
Naringenin	Antioxidant and anti-inflammatory activity	Cavia-Saiz et al. (2010)
Curcumin	Antibacterial and antibacterial activity	Negi et al. (1999)
Silymarin	Anticarcinogenic activity	Saller et al. (2008)

this technique, chloroform and methanol are mixed to prepare a monophasic solvent system (Kumar et al. 2021). Chloroform and methanol are used in ratio of 2:1 to homogenize a tissue sample.

The primary method of extraction step gives non-resultant residual and biomolecules. Methanol is widely used as medium for extraction. It is polar component for extraction of any compound in the mixture; it increases the solubility of lipid mixed molecules from cell membranes and compartments. This method applies the ratio of 2:1 mixture. This mixture is prepared with chloroform or methanol with the crude extract of NaCl/KCl/$MgCl_2$. These are mixed with salt solutions, and this retains the acidic lipids in mixture. This is a time-consuming process and thus not useful for bioactive substances.

24.5.2 Bligh and Dyer Method of Extraction

This is an advanced method of Folch procedure. The Bligh and Dyer method is developed by extraction of fatty cells and tissues. The volume of solvent is the main method of changes in the protocols of Folch and Bligh method. The sample size of Folch et al. is usually used volume of sample. It is 2:1 (v/v) with mixture of chloroform and methanol. This method is used for the extraction of chloroform–methanol with a concentration volume of 1:2. This makes a perfect solution for extraction.

24.5.3 Soxhlet Methods of Extraction

In Soxhlet's extraction method, lipids are extracted by frequent filter material with a fresh organic solvent. This is percolation method for the extraction of lipid. Generally, petroleum ether or hexane is used. The triacylglycerol extraction is coved by hexane, which is the mostly used hydrocarbon solvent. Dried and powdered samples are used in extraction method. This type of extraction is performed in cellulose thimble (Kulma and Szopa 2007). The solubility of lipids depends on affinity between the solvents. They are either hydrophobic or the hydrophilic in nature. In hexane, chloroform, ethers, and similar solvent are easily soluble in lipid such as triacylglycerides or sterol esters. Polar lipids like phospholipids are lesser soluble in hydrocarbon solvents, while their dissolution becomes easier with the presence of other lipids (Eguchi et al. 2019). Although it dissolves easily in a few other solvents like methanol and chloroform due to their high polarity, lipid extraction is closely from biological tissues; the focus is on dissolution of lipids.

There are following advance techniques of extraction of bioactive compounds are.

24.5.4 Gas Chromatography Analysis of Extraction

This is useful for fatty acids identification and quantitates trans-esterified from saponified different lipid varieties like cholesteryl esters, phospholipids, triglycerides, and FFA. The lipid extract should be in volatilized form before gas chromatography. The process called methanolysis gives polar to less polar methyl esters derivatives. Extract from lipid compound is volatized before this separation Thus, in this gas chromatography, the polar FA is converted into their low or non-polar substance like methyl ester derivatives (FAMEs). This process is known as methanolysis.

There are many methods and chemicals available for the transesterification of fatty acids. Moreover, many chemicals are well known and categorized as either alkaline or acid-catalyzed reaction. GCMS has been used for determination of mass spectrum as per reference spectrum. This is approved by commercial database and dataset library.

24.5.5 HPTLC High-Performance Thin-Layer Chromatography

HPTLC is one of the advanced techniques of analysis of microorganism. There are various methods of separation of lipid from microorganism, but this technique is conceptualized on thin-layer chromatography. There are improvements required for accurate quantitative analysis and better resolution of compounds in this HPTLC method. Numerous separation of a biomolecule from aquatic and natural plant sources, are performed by HPTLC. It has been reported for all qualitative and quantitative tests. The quantitative analysis needs fine particle information and detail, which is done by HPTLC plate in a very fine way than TLC plates. Thus, it is better suited for quantitative analysis and information collection. Other techniques are time-consuming and energy-consuming and cost-intensive. These techniques are very cost-effective for several testing and analysis; there are three common steps for typical chromatogram evaluation; they are sample application, chromatogram development, and chromatogram evaluation.

24.5.6 Ultrasound-Assisted Extraction Technique

This is one of the mechanical vibration machines depending on their frequency known as ultrasound-assisted extraction machine. It is identified by its frequency range (from 20 kHz to 10 MHz). There are mainly two types of ultrasound-assisted extraction techniques; they are diagnostic and power ultrasound.

- **Diagnostic Ultrasound-Assisted:** In this ultrasound extraction technique, the frequency range is between 1 and 10 MHz. The ultrasonic intensity is also below 1 W/cm^2. It is useful in medical, therapeutic, and diagnostic area.
- **Power Ultrasound-Assisted:** It is well known for low frequency with high-power work. The density of repetition of power ultrasound-assisted ranges from 20 kHz to 1 MHz. The intensity of ultrasonic-assisted is above 1 W/cm^2, which is usually used to build chemical or physical outcome reaction into the medium. It is useful for batch sonication. There are mainly two types of ultrasound instruments for high-power reaction. These are used for separation and extraction purposes: (1) ultrasonic baths and (2) ultrasound probes. The first extraction machine is an

ultrasonic bath, it is more advance and, has been applied in sonochemistry. The given mentioned frequencies of this instrument range from 25 to 50 kHz. The intensity of ultrasonic-assisted range between 1 and 5 W/cm^2. There are many benefits, but the main feature of this instrument is its reasonable and economical price and its cost-effectiveness effect in the extraction process. There are many applications of ultrasonic bath, which can be used in medical and pharmaceutical industries like solid dispersion preparation, cleaning, sample homogenization, and degassing.

24.5.7 Microwave-Assisted Extraction

This extraction technique was first reported (Ganzler et al. 1986) firstly in the extraction process of edible compound and products like citrus plant, fruit, aromatic plants, cereal, and legumes. This process is composed of heat with microwave matrix; it is mixed with good absorbing solvent like methanol. This is useful for the extraction of polar compound. This microwave extraction process combination of microwave matrix and high heat and merged into a highly soluble solvent like methanol. This methanol is important for the extraction of many compounds which are based on polar compound or which are useful for low soluble compound. There are non-polar compounds for extraction from *n*-hexane. This solution is not able to achieve boiling point because it was heated for short period of time followed by quick cooling step. The oil containing plants are pressed by localized high pressure and thermal stress. In microwave heating, the force exceeds its capacity for expansion. It is higher than conventional extraction techniques. This technique is well known for its effectiveness of extraction and is approved for many bioactive extraction examples such as fat, organic solvent, essential oils, antioxidants, and oils in terms of production. These extraction techniques are classified into open and closed vessel systems. The open vessel is known for system operating method. It is based on atmospheric pressure; the closed vessel is also known for controlled temperature and pressure.

24.5.8 Supercritical Fluid Extraction

When temperature and pressure are above than the usual critical point, then fluid and liquid are categorized in supercritical point. There is no comparison between gas and fluid phase in this extraction. This was known as alternative process to plant distillation. In this method, the technique of extraction is somewhere similar to conventional method of solid–fluid extraction. The product specialty depends on alternate method of determination of physical properties in supercritical fluids. This process can be controlled by pressure and temperature modification above their critical values. The supercritical fluid is manufactured by two important steps. The extraction step is started after separation method of solute from the solvent. The method comprises first by successive pressure and heat on fluid to reach their severe state. After the successive pressure on resulted supercritical fluid, the flux of ascending or descending manner is applied on critical and supercritical feeds for fluid. The expected solute of supercritical fluid is received in the form of matrix after the treatment of supercritical fluid, and it will come in gaseous form inside the chamber of separator and the solute will be in gaseous form, so it will no longer be solvable, so it will separate by gravity after the processing the extract of the sample is collected in the separator. It is separated at the bottom of the separator. The recycling or reinjected process of gas is depending on the equipment. It may be released in atmosphere, which is purely based on equipment and instrument.

24.5.9 Pulse Electric Field Extraction

Pulse electric field extraction is widely used in genetic processing. It is used for intermixed DNA molecules. This is useful for large molecules and electrofusion of DNA. This technique has been used in food engineering, food processing, preservation extraction, and transformation. The short pulse of high electric field is applied during short time. The approximate time is around micro- to milliseconds. It is the main principle of pulse electric extraction technology. The processing time of pulse extraction is monitored and calculated by pulse time multiplication. It is effective with pulse duration. This technique is formulated by pores inside cell membrane method. This is due to the use of high-power electric field. This technique is responsible for the penetration of plant cell, which increases the embellishment of solute diffusion in cell membrane.

24.5.10 Mechanical Pressing Extraction

The pressing method for extraction of lipid is well-known and ancient technique for isolation of bioactive substances. Pressing is very simple technique for the extraction of fluid from oily seeds. Pressing is possible by the excretion of a fluid filled in a penetrable seed material. It can retrieve by force or condense forces. It is also useful for increasing extraction product. This mechanical pressing method is generally followed by a many pre-treatment such as cleaning, drying, and dehusking for algal biomass, which is energy-consuming process. Pressure is applied in a particular range to improve the oil extraction in expeller press or screw press. The efficiency of extraction in this method is increased, but too much pressure will generate heat and a loss of lipids; therefore, this technique is progressively used in oil mills. As the success rate screw pressing is high, it replaces the hydraulic presses. A helical screw is used during expeller pressing.

24.5.11 Bio-Based or Agrosolvent Extraction

This is widely used extraction process where extraction of oil from biowaste and microorganisms such as fungi, yeast, bacteria, or microalgae. It is method of solvent extraction, where mixtures of petroleum ether solvents or else such as chloroform/methanol or hexane can be used for extraction. It is environmental safe in terms of safety and protection for biowaste. It enhances the growth of green chemistry. In future, petroleum solvent will be replaced by all bio-based or agrosolvent. Cereal and sugar wastes are a source of agrosolvent production by natural fermenting process. It is derived from carbohydrate, especially fruit sugar, sugar beet, sugarcane, wheat, and corn. Ethanol production from vegetable, also called bio-ethanol, is manufactured about 60% from sugarcane and 40% from other crops.

24.5.12 Enzyme-Assisted Extraction

Enzyme-assisted extraction is also known as enzyme-assisted aqueous extraction processing (EAEP). It had past historical importance from last several years for bifurcation of biological material. It is useful for the extraction of biomolecules in an effective and precautionary manner (Martins et al. 2010). Metabolic reaction of living organism is increased by enzymes that speed up the performance. Enzymes are protein in nature, except ribozymes (RNA). They offer a catalytic activity, and they do not involve in the reaction process, which help only in the occurrence of reaction. They remain stable until the end of reaction. They change only kinetic of reaction up to 1012 times, without changing any of the reaction mechanism or constants. Enzymes are biological catalysts. They are different from chemical catalysts.

The application of enzymes increases the extraction of lipid from microorganisms due to the excretion of oil from the plant tissue breakdown such as proteases and hydrolase polysaccharides. Enzyme-assisted extraction (EAE) is very successful method to increase lipid extraction (Khan and Giridhar 2015).

It is applicable for different types of extraction from cereal, pulses, vegetables and fruits, and microalgae. Living organism also involves enzyme extraction from bacteria to fungi and plant to animals. Maximum enzymes are used for industrial purpose.

24.6 Conclusion

Extraction techniques are based on the requirement of bioactive compound and secondary metabolites. All old traditional techniques are bound with the diffusion of solvent into biomass. There is no best technique of extraction for all compounds. The variation of compound decides the type of extraction. The nature of bioactive compound determined the extraction method. Many technologies enhance the diffusion quality of solvent for the disruption of cell wall. The electric pulse field extraction and ultrasound techniques are known for high disarranging of cell. This cell allows increasing the displacement. Thus the collection of lipids through this extraction is completed in a short time. There are numerous innovative extraction techniques, which are known for their unique work process. The uniqueness of work and principle of each innovative extraction techniques are based on work requirement. The use of innovative extraction techniques is a sustainable approach to preserve nutrient based on their unique work processes such as ultrasound, instant controlled pressure drop, microwave, supercritical fluid, pulsed electric fields, mechanical pressing, agrosolvent, and enzyme-assisted extraction. All extraction of bioactive compound is classified as per substances like alkaloids, and the alkaloid is categorized as per requirement of their biosynthetic pathways, such as the amino acids that provide nitrogen atoms and part of their skeleton including terpenoids and purines. Mainly, all classification of extraction techniques is grouped into two parts: conventional extraction technologies of bioactive substance from plants, fruits, and their by-products. It is accomplished by means of agitation, heating, boiling, or refluxing extraction, which result in several disadvantages, such as high impurity contents and long extraction time. The main emerging technologies are microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), and ultrasound-assisted extraction (UAE); therefore, there is no best way of extraction techniques, and the method is based on scientifically and economically selected techniques, which are suitable for extraction.

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Microencapsulation of Bioactive Components for Applications in Food Industry

25

Prity Pant

Abstract

The phytochemicals present in foods which can transform metabolism and support good health are known as bioactive compounds. Various types of bioactive compounds are phenolic compounds, flavonoids, phytoestrogens, carotenoids, glucosinolates, vitamins, anthocyanins, tannins, betalains, plant sterols, etc. These compounds have exceptional antioxidant, anti-inflammatory, and anticarcinogenic properties. These impart physiological and cellular effects on us so that they can give protection against many chronic diseases and metabolic disorders like diabetes, CVD, cancer, etc. These are mainly found in fruits and vegetables. Consumption of these bioactive compounds having relevant valuable health effects are the criteria to develop novel functional food with potential protective and preservative properties.

Keywords

Microencapsulation · Bioactive compounds · Metabolic disorders · Food industry

25.1 Introduction

The compounds which express biological activity on living matters and activate a response in them are known as bioactive compounds. In Greek, "bios" stands for life and in Latin "actives" implies dynamic or full of energy. So as the name states, these compounds are present in living organisms and stimulate or generate biological activities.

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We also can say that phytochemicals present in foods which can transform metabolism and support good health are known as bioactive compounds. A bioactive compound implies its direct physiological or cellular effects on a living organism. These effects may be positive or negative as according to the characteristics, dose, and bioavailability of these compounds. These are components in foods other than those required to give the elementary nutrition.

Bioactive compounds are generally only related with positive effects on an organism. These are present in both plant and animal products or can be synthetically produced. These compounds contain chemicals that are present in small quantity in fruits, vegetables, nuts, oils, and whole grains. They are also present in a varied variety of living organisms and microorganisms, such as bacteria, fungi, cyanobacteria, bryophytes, lichens, higher plants, and some groups of animals. Some examples of plant bioactive compounds are carotenoids and polyphenols found in fruits and vegetables or phytosterols in oils. These compounds found in animal products are fatty acids in milk and fish. Some examples of bioactive compounds are flavonoids, caffeine, carotenoids, carnitine, choline, coenzyme Q, creatine, dithiolthiones, phytosterols, polysaccharides (Srivastava and Kulshreshtha 1989), phytoestrogens, glucosinolates, polyphenols, anthocyanins (Golmohamadi et al. 2013), prebiotics, and taurine (Voedingscentrum 2014).

They have antioxidant, antineoplastic, anticancer, and anti-inflammatory effects so are able to prevent and treat some diseases. The role of these compounds are prominently in the area of geo-medicine, plant science, modern pharmacology, agrochemicals, cosmetics, food industry, nano-bio-science, etc.

25.2 Various Types of Bioactive Compounds

Bioactive compounds are present naturally in several foods. These are extra-nutritional ingredients present in minor amounts in foods. These can deliver health benefits over the elementary nutrition of the product.

Various types of bioactive compounds are phenolic compounds, flavonoids, phytoestrogens, carotenoids, glucosinolates, vitamins, anthocyanins, tannins, betalains, plant sterols, etc. (Fig. 25.1).

Phenolic Compounds and Flavonoids These are found in nearly all plants. These are found widely in cereals, legumes, nuts, olive oil, tea, red wine, vegetables, and fruits. These compounds generally have antioxidant properties and provide health benefits on cardiovascular diseases.

Flavonoids Six classes of flavonoids are found such as flavonols, anthocyanidins, proanthocyanidins, flavones, flavanones, and flavan-3-ols. Intake of these compounds considerably reduces the risk of CVD, mainly by employing their advantageous effects on LDL cholesterol, endothelial function, and insulin sensitivity.

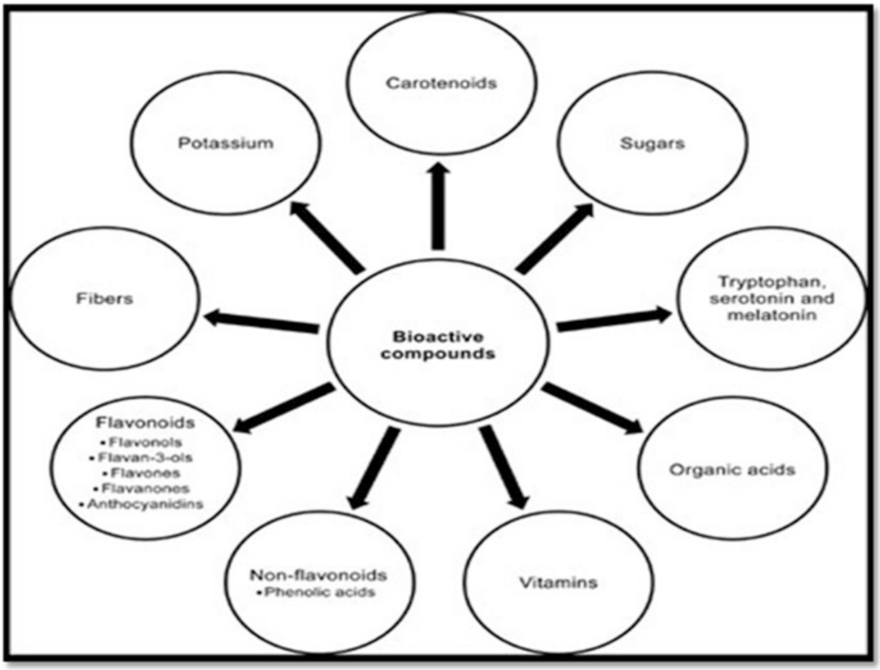

Fig. 25.1 Types of bioactive compounds

Phytoestrogens Several phytoestrogens are found in soy, flaxseed oil, whole grains, fruits, and vegetables. These have antioxidant properties.

Carotenoids These are found in nearly all plants. These are found widely in cereals, legumes, nuts, olive oil, tea, red wine, vegetables, and fruits. These compounds generally have antioxidant properties and provide health benefits on cardiovascular diseases (Schrooyen et al. 2001).

These are present in green leaves, in the majority of yellow and red fruits, and in various roots. They also impart color to egg yolk and a number of fish. Carotenoids are richly found in carrots, plums, apricots, mangoes, sweet potatoes, spinach, coriander, turnip greens, and winter squash. Carotenoids are good to improve eye and skin health, as well as prevent against a number of cancers, such as lung cancer, prostate cancer, breast cancer, and head and neck cancers. β-Carotene is a precursor of vitamin A, required for immunity, healthy skin, mucous membranes, and eyes. Foods rich in carotenoid decrease the symptoms of eyestrain as dry eye, headaches, and blurred vision and improve night vision (Zhongxiang and Bhesh 2010).

Glucosinolates These compounds are present in some sharp-flavored plants such as mustard, cabbage, and horseradish. These are also present in their secondary metabolites, which comprise sulfur and nitrogen. On masticating, cutting, and denting of these plants, glucosinolates yield mustard oils which are responsible for the particular sharp flavor of these plants and products. These compounds stimulate Phase I and Phase II enzymes, hinder the enzyme activation, so are under research for lessening the cancer (Desai and Park 2005). It is said that these compounds are effective to kill several cancer cells without giving harm to normal cells. They lower the risk of dementia and slow down the rate of cognitive decline in elders.

Anthocyanins and Anthocyanidins Color of fruits, vegetables, and flowers are due to these compounds, many of which are used in the human diets. These compounds stimulate insulin secretion and have protective effects on β-cells of the pancreas.

Berries (Anthocyanins) Berries are good source of anthocyanins. We also get micronutrients and fiber from these. In several studies, it has been shown that berries are associated with improving heart health. Intake of chokeberries, cranberries, blueberries, and strawberries (either fresh, or as juice, or freeze-dried) is helpful to recover LDL oxidation, lipid peroxidation, total plasma antioxidant capacity, dyslipidemia, and glucose metabolism.

Vitamins These are fundamental nutrients which we need in trace quantity. We get the vitamins through our diet. These are fat soluble and water soluble. Fat-soluble vitamins are A, D, E, and K and water-soluble B and C. These vitamins have various functions and biological effects on our body. These vitamins are required for our metabolic activities. They act as catalyst in the body. Vitamin E and vitamin C also act as antioxidants (Boh and Kardos 2003).

Tannins Tannins are polyphenolic biomolecules that bind to and precipitate proteins and various other organic compounds and macromolecules. There are two groups of tannins: condensed tannins and hydrolyzable tannins. Tannins may be found in various colors. The range of color of tannins may be from colorless to yellow or brown. It is responsible for astringency of foods and enzymatic browning reactions. Sources of tannins are tea, coffee, pomegranate, persimmon, most berries (cranberries, strawberries, blueberries), grapes, red wine, chocolate (with cocoa content 70% and higher), and spices (cinnamon, vanilla, cloves, thyme) (Gibbs et al. 1999). In diet, tannins are nontoxic and therefore can be used in functional foods. They can be used to cure oxidative stress, inflammation, and dyslipidemia-related diseases such as stenosis of the arteries, atherosclerosis, hypertension, and cancer.

Betalains Betalains are pigments, derived from indole. They are of two types: red-violet betacyanins and the yellow betaxanthins. They are soluble in water and therefore can be combined into aqueous food (Jeyakumari et al. 2015; Pratibha et al. 2014). Sources of betalains are red and yellow beetroot, colored Swiss chard, leafy or grainy amaranth, prickly pear, red pitahaya, and several cacti. They have antioxidant, anticancer, anti-lipidemic, and antimicrobial properties. Therefore, betalains have progressive health effects.

Bioactive Carbonyls These are also known as bioactive compounds. They have a carbonyl group. Some of the bioactive carbonyl compounds, their occurrence in food, and health supporting characteristics are given in Table 25.1.

25.3 Sources of Bioactive Compounds

Bioactive compounds are present in little amount in food, chiefly in fruits, vegetables, and whole grains. These compounds promote health more than providing the fundamental nutrients. These compounds consist of flavonoids, carotenoids, anthocyanins, tannins, betalains, plant sterols, and glucosinolates. A variety of fruits and vegetables have various nutrients and bioactive compounds including phytochemicals, for example, phenolics, flavonoids, and carotenoids. Actinobacteria found in sea produce various types of different bioactive compounds. Fruits, vegetables, and grains contain various advantageous compounds, such as antioxidants. They protect cells from injury or else may cause disease. Diet rich in polyphenol antioxidants helps to maintain lower rate of depression, diabetes, dementia, and heart disease (Table 25.2).

25.4 Extraction of Bioactive Compounds

Various methods to extract bioactive compounds from the plant materials are solvent extraction, supercritical extraction, ultrasound-assisted extraction, pressurized liquid extraction, and microwave extraction methods (Fig. 25.2).

25.4.1 Techniques Used for Phtyo-Extraction

1. Selection of plant species
2. Assessment of toxicity
3. Preparation of plant sample and the elemental analysis
4. Biological resting
5. Separation of active compounds
6. Lab studies
7. Marketing

These methods are according to the raw materials as well as the chemical composition of compounds to be extracted.

Solvent system is used according to the particular characteristics of the bioactive compound. Polar solvents such as methanol, ethanol, or ethyl-acetate are used for hydrophilic compounds. Dichloromethane or a mixture of dichloromethane/

Table 25.1 Bioactive carbonyl compounds, their occurrence in food, and health supporting characteristics

Bioactive carbonyls	Occurrence in food	Health supporting characteristics
Flavonoids		
Flavones		
Luteolin	Broccoli, green pepper, parsley, oregano, carrots, and rosemary	Anticarcinogenic activity
Apigenin	Many fruits and vegetables, parsley, celery, celeriac, and chamomile tea	Anticarcinogenic activity
Tangeritin	Citrus peels	Antihypercholesterolemia effect, antioxidant activity, and anticarcinogenic activity
Flavonol		
Quercetin	Fruits and vegetables, especially onions, citrus, apples, dark berries, grapes, olive oil, green tea, and red wine	Encouraging blood flow and promoting cardiovascular health properties
Kaempferol	Apples, grapes, tomatoes, green tea, potatoes, onions, broccoli, Brussels sprouts, squash, cucumbers, lettuce, green beans, peaches, blackberries, raspberries, and spinach	Anticarcinogenic activity and antioxidant activity
Myricetin	Vegetables, fruits, nuts, berries, tea, and red wine	Anti-inflammatory activity, anti-nonenzymatic glycation, and antihyperlipidemia
Galangin	Propolis	Antimicrobial activity, antioxidant activity, anticarcinogenic activity, and anti-inflammatory activity
Flavanone		
Hesperitin	Citrus fruits	Antioxidant activity, anticarcinogenic activity, hypolipidemic activity, and vasoprotective activity
Naringenin	Grapefruits, oranges, and tomatoes	Antioxidant activity, anti-inflammatory activity, and immune system modulator
Isoflavones		
Genistein	Soybeans, legumes, and chickpeas	Antioxidant activity and estrogen mimicking property
Daidzein	Soybeans and soy products like tofu	Antioxidant activity and estrogen mimicking property
Glycitein	Soy products	Antioxidant activity and estrogen mimicking property
Vitamins		
Pyridoxal	Meats, whole grain products, vegetables, nuts, and bananas	Reducing cardiovascular disease risk property and anticarcinogenic activity
Niacin		

(continued)

Table 25.1 (continued)

Bioactive carbonyls	Occurrence in food	Health supporting characteristics
	Liver, chicken, beef, fish, cereal, peanuts, legumes, avocados, tomatoes, leaf vegetables, carrots, sweet potatoes, asparagus, nuts, whole grain products, and legumes	Reducing cardiovascular disease risk property
Riboflavin	Milk, cheese, leafy vegetables, liver, kidneys, legumes, yeast, mushrooms, and almonds	Antioxidant property and protection from migraine
Nicotinamide	Meat, fish, nuts, mushrooms, and some vegetables	Anti-inflammatory activity and antianxiety activity
Ascorbic acid	Citrus fruits, tomatoes, tomato juice, potatoes, red and green peppers, kiwifruit, broccoli, strawberries, Brussels sprouts, and cantaloupe	Antioxidant activity, anticarcinogenic activity, and reducing cardiovascular disease risk property
Others		
Silymarin	Milk thistle	Anticarcinogenic activity, preventing liver from alcoholic cirrhosis
Vanillin	Vanilla, Paraguay orchid, and Chinese red pine	Antimicrobial activity and antioxidant activity
Cinnamaldehyde	Cinnamon bark	Antimicrobial activity and anticarcinogenic activity
Punicalagin	Pomegranates	Antioxidant activity
Curcumin	Turmeric	Antibacterial activity, anti-inflammatory activity, and antioxidant activity

Table 25.2 Food stuffs, active ingredients, and beneficial effects

Food products	Active ingredients	Beneficial effects
Turmeric	Curcumin	Anti-inflammatory, anti-coagulant, in dental use
Garlic	Allicin, diallyl disulphide (DADS), Diallyl tri sulphide (DATS)	Anti-bacterial. Antiviral, anti-fungal, anti-ulcerogenic, anti-carcinogenic
Ginger	Gingerol, paradol, zingerone	Anti-inflammatory, anti-ulcerogenic, antifungal, antiviral, anticlotting, helpful in toothache
Honey	Polyphenol	Anti-microbial, antifungal, antiviral, wound repair, stomatitis, anticarcinogenic
Anise	1-methoxy-4-1(1-propenyl) benzene	Anti-microbial, anti-oxidant, anti-inflammatory
Lycopene	Beta-carotene	Modulation of immune function, suppressions of inflammation

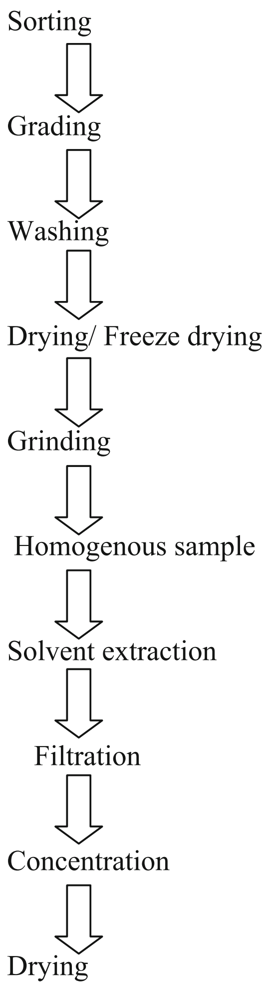

Fig. 25.2 Flow diagram of the extraction of compound from plant sample

methanol in a ratio of 1:1 is used for lipophilic compound extraction. In some cases, extraction with hexane is used to eradicate chlorophyll (Cosa et al. 2006).

25.4.2 Benefits of Bioactive Compound Extraction Method

- These are mostly used for digestion studies on simple foods.
- Separated food components are assessed for their impact on human health.
- Improved method for isolation.
- Option solvents can be attained for every method.
- Little effect of environmental conditions.
- Upgrading of nutritional or sensory characteristics of food.

- Extract is pure and harmless.
- Capability to provide high returns of capital investment after the extracted pure bioactive Compound.
- The extracted bioactive compounds have nutritional, toxicological, pharmaceutical, and microbiological importance.

25.4.3 Drawbacks of Bioactive Compound Extraction Procedure

- It confines in designing the experiments.
- Complications to explain statistical analysis.
- Expensive equipment and labor.
- Ethical restrictions.
- Inaccessibility of proficient references.
- Expert person is required for conducting the experiments.

Bioactive compounds have exceptional antioxidant, antimicrobial, anti-inflammatory, and anticarcinogenic properties. They have effects at physical and cellular level. They can be used to fight against different chronic diseases and metabolic disorders like diabetes, cancer, etc.

25.5 Microencapsulation

Microencapsulation is a method by which distinct particles of an active agent can be stored within a shell, enclosed, or covered with a constant film of polymer to form the particles of the size of micrometer to millimeter. It is done to guard the particles and/or to release in the future.

As we have studied above, various bioactive compounds are present in food. These are carotenoids, essential oils, antioxidants, flavors, etc. These compounds increase the sensory characteristics, as well as extend nutritional and health properties of food products. These compounds are less soluble in aqueous phases. These are highly instable in food products throughout the processing and preparation. They have lesser bioavailability, so that sometimes the utilization of these substances is inadequate.

Encapsulation is a method through which these compounds can be stabilized to organize their release and enhance their bioavailability. Microencapsulation of bioactive compounds is defined as a procedure through which particles or droplets are bounded by a coating or embedded in a homogeneous or heterogeneous matrix to provide minute capsules with vigorous properties (Fig. 25.3).

The expansion of microencapsulated products came in progress in the 1950s. It was done to explore the pressure-sensitive coatings to produce carbonless copying paper (Green and Scheicher 1955). After that, this technology was developed in the pharmaceutical, cosmetic, chemical, and food industries. Microencapsulated

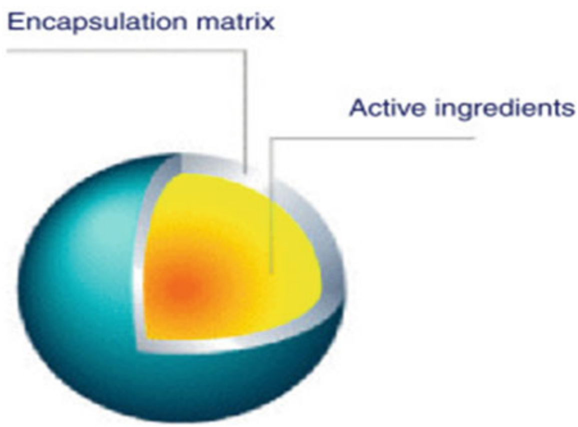

Fig. 25.3 Encapsulation

bioactive molecules are also known as core materials or active ingredients or encapsulated agents.

The microcapsules are prepared by various procedures. These procedures can be of two types, physical and chemical method. Physical method comprises spray drying, spray chilling, rotary disk atomization, fluid bed coating, coextrusion, and pan coating. The chemical method comprises simple and complex coacervation, interfacial polymerization, and phase separation (Table 25.3). The methods of microencapsulation and major steps of process are given below in the table (Jeyakumari et al. 2016).

25.6 Microencapsulation of Various Bioactive Compounds

There are various techniques for microencapsulation of bioactive compounds. These techniques are given below:

25.6.1 Encapsulation of Omega-3 Fatty Acids

Omega-3 fatty acids are essential (polyunsaturated) fatty acids. The most essential omega-3 fatty acids are alpha linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid. These fatty acids are prone to oxidation and also generate hydro peroxides and off-flavors. These are not acceptable by customers. To conquer these problems, microencapsulation can be done of these fatty acids (Jeyakumari et al. 2014, 2015; Pratibha et al. 2014). Various processes of microencapsulation of omega-3 fatty acids are explained in Table 25.4.

Table 25.3 The methods of microencapsulation and major steps of process

Methods	Major steps in process
Spray drying	• Dissolve active in aqueous coating solution
	• Homogenization of the dispersion
	• Atomization
	• Dehydration of the atomized particles
Spray cooling or spray chilling	• Disperse active in heated lipid solution
	• Homogenization of the dispersion
	• Atomization
	• Cool
Fluid bed coating	• Preparation of coating solution
	• Fluidization of core particles.
	• Coating of core particles
	• +Dehydrate or cool
Spinning disk and centrifugal coextrusion	• Preparation of core and coating solution
	• Coextrusion of core and coat solution through nozzles
Extrusion	• Preparation of molten coating solution
	• Dispersion of core into molten polymer
	• Cooling or passing of core-coat mixture through dehydrating liquid
Freeze-drying/lyophilization	• Mixing of core in coating solution
	• Freeze-drying of the mixture
	• Grinding (option)
Coacervation	• Formation of a three-immiscible chemical phases
	• Deposition of the coating
	• Solidification of the coating
Supercritical fluids technology	• Create a dispersion of active agent in supercritical fluid
	• Release the fluid to precipitate the shell on to the active
Liposome entrapment	• Microfluidization
	• Ultrasonication
	• Reverse-phase evaporation
Co-crystallization	• Preparation of supersaturated sucrose solution
	• Adding of core into supersaturated solution
	• Emission of substantial heat after solution reaches the sucrose crystallization temperature
Inclusion complexation	• Preparation of complexes by mixing or grinding
	• Incubate and dry if necessary

25.6.2 Encapsulation of Polyphenols/Flavors

Flavors extracted from fruits and spices are very delicate and volatile, as well as very costly also (Atmane et al. 2006). It is not easy to add in-liquid flavors into foods. Various flavors are extremely susceptible to oxygen, light, and heat also. These problems can be solved by encapsulation. So, by encapsulation flavors can be protected from degradation, oxidation, and moved out from food.

Table 25.4 Various processes of microencapsulation of omega-3 fatty acids

Methods	Wall material
Spray drying (fish oil)	Gelatin, maltodextrin, casein, lactose, sodium caseinate, dextrose equivalence, highly branched cyclic dextrin, methylcellulose, hydroxypropyl methylcellulose, *n*-octenylsuccinate, derivatized starch/glucose syrup or trehalose, sugar beet pectin, gum arabic, corn syrup solids, egg white powder
Spray drying (flaxseed oil)	Whey protein isolate, gum arabic and lecithin, maltodextrin, whey protein concentrate, gum arabic and two chemically modified starches, tapioca starch and waxy maize
Freeze-drying (fish oil)	Sodium caseinate, carbohydrate, egg white powder, gum arabic, lactose and maltodextrin
Freeze-drying (flaxseed oil)	Gelatin
Simple coacervation	Hydroxypropyl methylcellulose
Complex coacervation	Gelatin-gum arabic with transglutaminase (TG) as cross-linking agent
Electrostatic layer by layer (multilayer) deposition and spray drying (fish oil)	Lecithin and chitosan
Double emulsification and subsequent enzymatic gelation (fish oil)	Soy protein, whey protein, wheat protein sodium caseinate, transglutaminase
Ultrasonic atomization and freeze-drying (fish oil)	Chitosan
Electrospraying (fish oil)	Zein prolamine (corn protein)
Spray granulation and fluid bed film coating (fish oil)	Soybean soluble polysaccharide (SSPS) and maltodextrin, hydroxypropyl beta cyclodextrin (HPBCD)

Essential oils can be extracted from aromatic plants. They are volatile and have strong odor. Various essential oils can be gotten from ginger, garlic, cinnamon, coriander, clove, peppermint, citrus peel, oregano, thyme, rosemary basil, and eucalyptus Bennick (2002); Quideau and Feldman (1996). Volatility and unlikable taste of polyphenols are controlled by encapsulation before assimilation into foods (Manach et al. 2004). Various techniques of encapsulation of polyphenols are mentioned below (Table 25.5; Zhongxiang and Bhesh 2010; Amr et al. 2015).

25.6.3 Encapsulation of Vitamins and Minerals

Various vitamins and minerals can be encapsulated and used for the fortification of foods (Wilson and Shah 2007). Various techniques for it are mentioned in Table 25.6.

Table 25.5 Various techniques of encapsulation of polyphenols

Methods	Wall material	Polyphenols
Spray drying	Maltodextrin, gum arabic, chitosan, citrus fruit fiber, colloidal silicon dioxide, maltodextrin and starch, sodium caseinate-soy lecithin, skimmed milk powder, whey protein concentrate, gelatin	Black carrot extracts (anthocyanins), procyanidins, olive leaf extract, *Hibiscus sabdariffa* L. extract (anthocyanins), soybean extract, grape seed extract, apple polyphenol extract and olive leaf extract, oregano essential oil, mint oil, cardamom oleoresin, black pepper oleo resin, cumin oleo resin, turmeric oleo resin
Coacervation	Calcium alginate, chitosan, gelatin (type A), glucan, chitosan, and κ-carrageenan	Yerba mate extract, EGCG, black currant extract, pimento oil
Co-crystallization	Sucrose syrup	Orange peel oil
Freeze-drying	Maltodextrin DE20, maltodextrins DE5-8 and DE18.5, pullulan	Anthocyanin, cloudberry extract, Hibiscus anthocyanin, orange oil
Molecular encapsulation	HP-β-CD, β-CD and maltosyl-β-CDs, α-CDs, hydrophobically modified starch	3-Hydroxyflavone, morin and quercetin, ferulic acid, rutin, curcumin, citrus oils, cinnamon leaf and garlic oil, citrus oil
Extrusion	Corn syrup solids, glycerine, sodium alginate	Citrus oil, clove oil, thyme oil, cinnamon oil
Electrostatic extrusion	Calcium alginate gels	Ethyl vanillin (3-ethoxy-4-hydroxybenzaldehyde)

Table 25.6 Techniques for encapsulation of vitamins and minerals

Method	Wall material	Active agents
Spray drying	Tripolyphosphate, cross-linked chitosan, starch, β-cyclodextrin, malto dextrin, gum arabic	Vitamin C, vitamin A
Spray cooling and spray chilling	Waxes, fatty acids, water-soluble polymers and water-insoluble monomers, soy lecithin	Ferrous sulfate, vitamins, minerals, acidulants
Liposome entrapment	Egg phosphatidylcholine, cholesterol, DL-α-tocopherol	Vitamin C, Iron
Extrusion	Maltodextrin (DE7-10), lactose, fructo-oligosaccharide	Vitamin C
Fluidized bed coating	Polymethacrylate, ethylcellulose, waxes, hydrogenated vegetable oil, stearin, fatty acids, emulsifiers, gums and maltodextrins	Vitamin C
Coacervation	Gelatin and acacia	Vitamin A
Molecular inclusion	β-Cyclodextrin, maltodextrin	Vitamin A
Liposome entrapment	Hormones, enzymes, and vitamins	Liposome entrapment

25.6.4 Encapsulation of Enzymes

The methods of encapsulation for various enzymes and wall material used are explained in Table 25.7 (Cisem 2011).

25.6.5 Encapsulation of Microorganism

The methods of encapsulation for various microorganisms and wall material used are given in Table 25.8. Among various methods, spray-coating and gel-particle technologies are most frequently used for microencapsulation of probiotics (Champagne and Patrick 2007).

25.6.6 Encapsulation of Protein Hydrolysate and Peptide

Bitter taste and hygroscopic nature of protein hydrolysates and peptides can be controlled by encapsulation (Erdmann et al. 2008). The encapsulation of protein hydrolysate and peptide is discussed in Table 25.9.

Table 25.7 Methods of encapsulation of enzymes

Method	Wall material	Enzymes
Liposome	Alginate	Proteolytic enzyme
Complex coacervation	Chitosan/$CaCl_2$ polyelectrolyte beads, sodium alginate and starch	Protease enzyme, Flavourzyme®
Spray drying	Chitosan, modified chitosan (water soluble), alginate, calcium alginate and arabic gum, α-amalase	β-Galactosidase, lipase from *Y. lipolytica*
Liposome entrapment	Alginate, carrageenan	Mixture of proteolytic and lipolytic enzyme

Table 25.8 Methods of encapsulation of microorganisms

Wall material	Microorganisms
Alginate and its combinations	Lactic acid and probiotic bacteria
High-amylose cornstarch	Probiotic bacteria
Mixture of xanthan-gellan	Probiotic bacteria
Carrageenan and its mixtures	Lactic acid bacteria such as *Streptococcus salivarius* sp. *thermophiles* and *Lactobacillus delbrueckii* (traditional yogurt bacteria), *Bifidobacterium* sp.
Gelatin or gelatin and gum	*Lactobacillus lactis*
Cellulose acetate phethalate	*Bifidobacterium pseudolongum*
Mixture of chitosan and hexamethylene diisocyanate	Probiotic bacteria

Table 25.9 Encapsulation of protein hydrolysate and peptide

Method	Wall material	Hydrolysates and peptide
Spray drying	Soy protein isolate, gelatin, whey protein concentrate, alginate, maltodextrin, gum arabic, carboxymethylated gum	Casein hydrolysate, whey protein hydrolysate, rapeseed peptide, chicken hydrolysate
Coacervation	Soy protein isolate and pectin	Casein hydrolysate
Liposome entrapment	Phosphatidylcholine, phosphatidyl glycine, lecithin, stearic acid, and cupuacu butter	Fish hydrolysate, sea bream collagen peptide fraction, casein hydrolysate

25.7 Microencapsulation Techniques Used in Food Industry

As we know, bioactive compounds are naturally found in several foods. These are also used as an additive in the processed food products. These are added to increase their nutritional qualities, so that these products become more useful to improve our health.

Carotenoids, anthocyanins, and curcumin are acknowledged as coloring agents in food. Ascorbic acid is commonly used to prevent oxidation. Cinnamaldehyde and vanillin are used as flavoring agent in sweet foods, chewing gums, and beverages.

25.7.1 Controlled Release System

In this system, one or more active agents are present at the target site and active components are released at the required pace and time (Pothakamury and Barbosa Canovas 1995). The active components are released at controlled rate (Brannon 1993). Thermal and moisture release methods are used most frequently (Risch 1995).

The main mechanisms implicated are pH, temperature, use of solvent, diffusion, degradation, and swelling or osmotic pressure activated release. Usually, a grouping of more than one method is used (Desai and Park 2005).

25.7.2 Diffusion Controlled Release System

In this method, active components are released by diffusion through the polymer or pores presented in the polymer (Table 25.10). Essential techniques used for encapsulation of bioactive compounds for food industry are given below (Nesrine et al. 2016).

In food industry, microencapsulation method has many advantages, such as the following:

Table 25.10 Essential techniques used for encapsulation of bioactive compounds for food industry

Techniques	Encapsulated bioactive	Encapsulation matrices
Spray drying	Fish oil, flavors, lycopene, β-carotene	Starch, chitosan, modified starch, proteins, natural gums
Coacervation	Polyunsaturated fatty acids, essential oils, flavors, enzymes	Gums, proteins, starch, maltodextrin, xanthan gum, pectin
Extrusion	Flavor, carotenoids, probiotic bacteria, oils	Sodium alginate, maltodextrin, modified starch, pectin
Fluid bed coating	Probiotic bacteria, vitamins, lactic acid carotenoids	Cellulose, maltodextrin gums, proteins
Nanoemulsions	β-Carotene, aroma, curcumin, oils	Chitosan, gums, carbohydrates

- To guard the core material from ruin and to decrease the rate of evaporation of core material to the outside environment
- To change the nature of the original material for easier handling
- To release the core material gradually over time persistently
- To prevent undesirable flavor or taste of the core material
- To separate the components of the mixture that can react one another

25.7.3 Application of Microencapsulated Bioactive Compounds in Food Industry

There are various benefits of the microencapsulation in food industry explained in Table 25.11.

25.7.4 Fortification of Dairy Products by Encapsulated Bioactive Compounds

Yogurt can be fortified by pure carotenoids or with the fruit and vegetable extracts. Palm oil has good quantity of carotenoids. These can be entrapped into yogurt after encapsulation. They give more constant color to yogurt due to the higher carotenoid withholding as judge against the free form. It increases the antioxidant activity of yogurt (Horuz 2019). Astaxanthin can be used to enrich dairy products, which is obtained from shrimp waste.

Different encapsulation systems may be emulsion-based, including solid lipid nanoparticles; biopolymer-based, including molecular inclusion complexes; surfactant-based (liposomes); and freeze- and spray drying (Šeregelj et al. 2019; Gomes et al. 2014; De Oliveira et al. 2019; Coronel-Aquilera and Martin-Gonzalez 2015; Toniazzo 2014; Molina et al. 2019; Donhowe et al. 2014; De Campo 2019; Taksima et al. 2015; Gomez-Estaca et al. 2016; Rutz et al. 2016, 2017).

Tomato peel extract can be encapsulated to enrich yogurt by its nanofibers which are prepared by electro-spinning technique Horuz (2019). Yogurt can be fortified by

Table 25.11 Benefits of the microencapsulation in food industry

Type of encapsulated food ingredients with examples	Aim
Lipids	
Fish oil, linolenic acid, rice bran oil, sardine oil, palmitic acid, seal blubber oil	To prevent oxidative degradation during processing and storage
Flavoring agents: citrus oil, mint oils, onion oils, garlic oils, spice oleoresins	To transform liquid flavorings into stable and free flowing powders which are easier to handle
Vitamins	
Fat soluble: vitamins A, D, E, and K	Reduce off-flavors, permit time-release of nutrients, enhance the stability to extremes in temperature and moisture, reduce each nutrient interaction of other ingredients
Water soluble: vitamin C, vitamin B1, vitamin B2, vitamin B6, vitamin B12, niacin, folic acid	
Enzymes and microorganisms	
Lipase, invertase	Improve stability during storage in dried form, reduces the ripening time; Improve the stability of starter cultures; Improved retention in finished products
Brevibacterium linens	
Penicillium roqueforti, *lactic acid bacteria*	
Acidulants	
Lactic acid, glucono-d-lactone, vitamin C, acetic acid, potassium sorbate, sorbic acid, calcium propionate, and sodium chloride	Used to assist in the development of color and flavor. Baking industry uses stable acids and baking soda in wet and dry mixes to control the release of carbon dioxide during processing and subsequent baking
Sweeteners	
Sugars, nutritive or artificial sugars; aspartame	To reduce the hygroscopicity, improve flowability, and prolong sweetness perception
Colorants	
Annatto, β-carotene, turmeric	Encapsulated colors are easier to handle and offer improved solubility, stability to oxidation, and control over stratification from dry blends

phenolics also. They have antioxidant, antimicrobial, and anti-inflammatory properties and anticarcinogenic effect (Esfanjani et al. 2018; De Araujo et al. 2021; Shahidi and Ambigaipalan 2015). However, their use is limited due to instability in food, bitter taste, and low bioavailability.

Yogurt can be fortified with vitamin D_3 to increase its nutritional value (Markman and Livney 2012; Semo et al. 2007; DeRitter 1982). This vitamin can be distributed in the form of spray-dried nanoliposomes (Jafari et al. 2019), nanocapsules based on the lipid carrier Precirol (Sharifan et al. 2020), oil-in-water emulsion stabilized by whey protein or by whey protein + carboxymethylcellulose (Leskauskaite et al. 2016), or encapsulated in re-assembled casein micelles.

The essential oil obtained from garlic has antibacterial activity against both Gram-positive and Gram-negative bacteria, due to the presence of organo sulfur compounds. Allicin is the main constituent of garlic essential oil, which is very susceptible to high temperature and high pH. Its stability and solubility in water-based foods can be enhanced and unpleasant smell controlled by encapsulation.

Fortification of kefir can be done by encapsulated structured lipids, prepared by the process of coacervation to use gelatin and gum arabic as wall materials (Yuksel-Bilsel and Sahin-Yesilcubuk 2019). Microcapsules were prepared by the process of coacervation using gelatin and gum arabic as wall materials. The enzyme, transglutaminase, was used as a traverseconnecting agent.

Soft and hard cheese is fortified with encapsulated bacteria from the *Lactobacillus* and *Bifidobacterium* genera. Extrusion and emulsification are two of the most accepted processes in which alginate is used as a wall material. The fortification of cheese with free phenolics can influence the cheese texture, color, and taste during its storage. The extracts of rosemary, fennel, and chamomile can be encapsulated by atomization or coagulation method to use sodium alginate as a covering matter (Ribeiro et al. 2016; Caleja et al. 2016). Cottage cheese enriched with these microcapsules does not change the nutrition and color but, furthermore, sustain the antioxidant property.

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Innovative and Sustainable Techniques for the Development of Functional Foods

26

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Abstract

This chapter provides insights on the sustainable development of functional foods from various sources such as plants, seaweeds, microbes, encapsulated functional compounds, and edible packaging films. The chapter deals with the basic understanding of functional foods and the impact of their consumption in the human system. It provides a detailed description of the recent innovations in functional foods developed from various sources and the effect it renders on human health. The sustainable development of foods with a great impact on identifying indigenous and tropical region-specific crops is also discussed. The bioavailability of consumed functional molecules is evaluated based on in vivo and in vitro studies. The market of such novel food products mainly depends on consumer purchase behavior as consumers' presumption about the sensory and price of such commodities results in market drive of a particular product. The packaging and labeling of such products should be carefully designed to avoid false claims and increase consumer understanding of the health benefit it provides.

Keywords

Functional foods · Bioavailability · Sustainable development · Health benefits

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26.1 Introduction

The word functional food was first used in Japan which has a great impact on individual and public health when consumed (Astrini et al. 2020). Functional foods are those foods that are consumed like daily meal but provides health benefit and retards chronic illness on regular consumption. It provides functional nutrition such as anti-cancer and reduces cardiovascular ailments apart from providing basic nutrition. It improves the health and well-being of the consumer. It alters the organoleptic property of foods, nevertheless, its health-boosting activity is also enhanced (German et al. 1999). Functional foods are regarded as a particular food commodity that gives nutrition beyond basic requirement (Sibbel 2007).

Functional foods changed the perspective of consumers from "adequate nutrition" to "optimum nutrition." The present population requires products with less or no inclusion of chemical additives (Karelakis et al. 2020). The packaging of foods loaded with functional property must provide the consumer with the health benefits it provides to avoid unwanted false claims.

Functional foods protect the consumer from various cardiovascular and neurodegenerative diseases which are otherwise treated with synthetic medicines. Functional foods help to reduce or prevent various illnesses and inflammations in the human body with compounds of natural origin. Some cancers are also cured by mere consumption of functional foods in the diet (Aghajanpour et al. 2017). It was also suggested by them that food products rich in antioxidant activity have anticancer effects on consumption.

Various plants are identified in our country from ancient times that possess nutraceutical properties. But a very few of them are added to our regular diets. Thus, compounds from various sources are extracted and incorporated in regular use foods to enhance their consumption by the population (Radrigán et al. 2017).

26.2 Development of Functional Foods

This section deals with the development of functional foods from various sources and their effect on consumption. It also provides details about the nutraceutical property acquired on consuming functional activity-loaded food products, its development, and utilization.

26.2.1 Plant-Based Functional Foods

This section provides information regarding the development of functional foods from plant-based materials such as fruits, vegetables, and cereal grains. Gong et al. (2020) reviewed the effects of functional compounds from plant-based origin in the treatment of hyperlipidemia which induces several chronic ailments such as obesity, diabetes, cardiovascular, and cerebrovascular illness. The presence of protein and dietary fiber in functional foods induces a satiating feel on consumption (Munekata et al. 2021b).

26.2.1.1 Fruits

Rosa roxburghii Tratt fruit is a rich source of plant polysaccharides and exhibits antioxidant properties due to the presence of phenolic acids such as hydroxybenzoic acids and ellagic acid. The fruit is also a rich source of flavonols such as quercetin, kaempferol, and myricetin which imparts therapeutic action on consumption against Alzheimer's, rheumatoid arthritis, cancer, diabetes, and various other illness (Wang et al. 2021). The sustainable cultivation of old apple cultivars in the Croatian region results in the production of bioactive compound-rich fruits that have inbuilt functional value. Duralija et al. (2021) investigated the old apple varieties of the region and concluded the presence of catechins, epicatechins, phloridzin, quercetin, and hydroxycinnamic acids that impart antioxidant properties.

Pacheco et al. (2020) studied the functional properties of freeze-dried orange pulp powder with the incorporation of gum arabic and bamboo fiber. Polyphenol content increased on freeze-drying exhibiting antiradical and antioxidant properties. John et al. (2019) investigated the functional property of Australian fruit, Davidson's plum (*Davidsonia pruriens*), a native fruit that is used as traditional medicine. The intake of this particular fruit aids in reducing fat in the abdomen and visceral region, lowers blood pressure, reduces inflammation near the left ventricle and the liver, minimizes fat vacuoles present in the liver, and reduces knee cartilage degradation due to obesity.

Grape pomace is a by-product obtained from the wine industry. The utilization of pomace as a feed to animals results in nutrient-rich availability of meat and milk, thus providing a product of high biological value to the consumers (Kandylis 2021). The antioxidant property and presence of fructose-oligosaccharides make it compatible as an active ingredient in functional yogurt preparation.

Pessoa et al. (2020) studied the effect of foliar spray of calcium chloride at 8 kg/ha on the increase in calcium content of Rocha pears. There was no difference in morphological and colorimetric parameters suggesting that foliar spray can be used as an agronomic biofortification technique to increase Ca levels. Melon peels and seeds are a major by-products with nutritional and bioactive components (Silva et al. 2020). The sustainable use of valorized melon by-products on incorporation into functional foods imparts a beneficial effect on consumption.

Fuentes et al. (2019) reviewed the functional effects of Patagonian berries and concluded that the presence of high flavonol and anthocyanin content aids in the treatment of inflammation and several other cardiovascular illnesses. Limareva et al. (2019) investigated the effects of grape pomace ensuring the sustainability of pectin production for beverage and fruit juice industry. The polysaccharide extracted from mulberry leaf shows immunity improving effects by increasing the thymus index with cytokines and splenic lymphocytes transformation. Khalifa et al. (2018) investigated the effects of polyphenols of mulberry fruit which aids in reducing blood glucose levels and inflammations of various kinds and offers neuroprotective effects. Consumption of mulberry can be increased by incorporating it into different fruit juices, spray-drying the polyphenols using various wall mixtures, and shelf-life extension using various packaging techniques. Jiang et al. (2021) reviewed the bioactive compounds present in plant-based materials carrying immune-boosting effects.

26.2.1.2 Vegetables

The vegetable by-products are known for the presence of unidentified functional compounds which require extensive research. The peel of most fruits and vegetables contains certain compounds that aid in the betterment of human health. The bioactive compounds present in the by-products of fruits and vegetables contain certain phytochemicals and nutrients that can be extracted and further processed before discarding (Coman et al. 2020). Leidi et al. (2018) reviewed the functional components of root and tuber crops that are cultivated in the Andean region. The species *ahipa*, *arracacha*, *mashua*, and *yacon* are popularly known in that region for their functional properties such as phytoestrogens, low GI, natural antioxidants, and anti-diabetic properties, respectively. Muchiri and Mccartney (2017) studied the prebiotic effect of orange flesh sweet potato rich in nutrition such as provitamin A, natural sugar, and dietary fibers. The prebiotic activity resulted in maintaining the gut microbiota and aiding in the growth of beneficial microorganisms. The banana inflorescence is one of the widely consumed food crops due to its effect on cardiovascular health (Lau et al. 2020). It displays antidiabetic, anti-inflammatory, anticancer, and antioxidant properties. The chemical fractionation of banana inflorescence shows high phenolic (gallic acid and epicatechin) and flavonoid content resulting in high antioxidant capacity.

Edible colorants are recently making their way in the food industry. Betalain is the most widely used food colorant used for bright red color and is known for its antioxidant and anticancer properties. Gengatharan et al. (2015) reviewed the biological activity of the use of betalain extracted from red beetroot, prickly pear, amaranth, and red pitahaya in the food industry as alternative colorants. Owing to the water-soluble nature of betalains, they can be included in liquid food products. Oral consumption of quercetin included in foods impart functional property and provides therapeutic effect against various health ailments such as hyperuricemia, PCOS, obesity, rheumatoid arthritis, cardiovascular illness, and inflammatory conditions (Lai and Wong 2021). Pandya et al. (2019) examined the effects of tocotrienol incorporation in various food matrices such as margarine, milk, granola bars, dry mix lemonade, yogurt, and bread to check its stability over storage. Colantuono et al. (2017) investigated the effects of dietary fiber content in pomegranate, artichoke, and olive by-products for its inclusion in the development of functional foods. Moringa incorporation in bakery products results in high bioactivity of the product due to excellent source of phytochemicals. Milla et al. (2021) concluded that with the increase in the concentration of moringa, the nutritional value increases with a decline in the organoleptic property. Saucedo-Pompa et al. (2018) and Coello et al. (2020) conducted a detailed review on moringa incorporation in food products. Gutiérrez (2018) studied the effects of functional properties of plantain flour. It was concluded that phosphated plantain flour increases the resistant starch content and lowers the rate of in vitro digestibility paving way for its inclusion in the preparation of bread and cookies, thus enabling its consumption by diabetes and celiac patients.

The consumption of various parts of moringa can be enhanced by including powder of the same in soups, cakes, biscuits, herbal concoctions, etc. to acquire therapeutic and nutritional benefits (Sahay et al. 2017). This could lead to increased fortified food product development to combat malnutrition among the population.

26.2.1.3 Grains and Legumes

Buckwheat seeds flour can be used as a substitute for gluten-based flour as it contains a well-balanced amino acid profile and can be consumed by individuals suffering from celiac disease (Li and Zhang 2001). Holasova et al. (2002) compared the antioxidant property of buckwheat with oats and barley. It was concluded that buckwheat seeds and leaves displayed better antioxidant properties with the presence of methanol soluble substances for their incorporation into functional foods. The by-products of cereal grain processing such as cereal bran are rich in non-starch carbohydrates such as arabinoxylan and beta-glucan, phenolic acid (ferulic acid), oil component (γ-oryzanol), flavonoids such as anthocyanin, and vitamins such as carotenoids and tocols. The presence of such properties makes it desirable for its inclusion in the development of functional foods (Patel 2015). The inclusion of bran provides a feeling of satiety on consumption. Functional foods from cereal by-products exhibit antiatherogenic, antihypertensive, hypoglycemic, and antilipemic properties. Pea is a legume crop that serves as a storehouse of protein, namely, globulin, albumin, prolamin, and glutelin. Globulin is a salt-soluble part that consists of legumin and vicilin, while albumin is a water-soluble part consisting of metabolic and enzymatic proteins. Pea protein displays a well-balanced amino acid profile with a peak of lysine. Thus, pea protein can be incorporated in food products demanding a high protein content in place of animal protein (Lu et al. 2020).

Kairam et al. (2021) investigated the effects of incorporation of flaxseed oil and garlic oil in the development of functional bread. A high degree of color change was observed in the bread prepared from flaxseed oil compared to garlic oil or hybrid oil incorporation. The bread was sensorially accepted with various functional compound incorporation through its storage life. Vladimir et al. (2018) studied the effects of incorporation of functional flour in bread production to increase the intake of nutrients with minimal cost.

Sorghum-based cookies were developed (Infante et al. 2017) with biofortification of carotenoids from sweet potato. The results concluded that the inclusion of sorghum and sweet potato carotenoid was highly accepted on sensory analysis and cookies exhibited increased iron bioavailability, thus being a substitute for wheat-based cookies for anemic patients. Čukelj et al. (2017) studied the effect of 10% flaxseed flour incorporation with wheat, rye, oat, and barley to reduce the lipid oxidation on storage and increase consumer acceptability. Oat and flaxseed flour was sensorially accepted by the consumers but a decline in acceptance was observed due to the initiation of lipid oxidation on storage.

Plant-based non-dairy milk beverages also impart potential health benefits such as imparting essential nutrients and minerals, unsaturated fatty acids, etc. from various sources like soybean, almonds, oat, cocoa, rice, kidney bean, peanut, coconut, and hemp (Paul et al. 2020). The main disadvantage observed is its physical instability and off-flavor development which can be minimized upon thermal and ultrasound treatments.

26.2.1.4 Spices

The antioxidant, antimicrobial, and DNA protecting properties of various spices were studied (Bhattacharya et al. 2021), where clove, ginger, and java long pepper exhibited high DNA damage protecting ability and antimicrobial activity was displayed by clove, ginger, and chili. Owing to their respective antioxidant and DNA protecting abilities, clove and ginger are regarded as suitable spices for their incorporation in functional foods and nutraceuticals. Munekata et al. (2021a) investigated the effects of different treatments on the extraction of curcuminoids from turmeric. Turmeric is a spice that is used traditionally in the treatment of wounds and health ailments owing to its anti-inflammatory activity.

26.2.2 Marine Based

This section provides details about the utilization of the marine ecosystem in the development of functional products. Marine microalgae possess a rich source of polyphenols offering bioactive components as sources of functional food development to reduce blood glucose and insulin level in animals (Murray et al. 2018).

Sea cucumber species such as *Stichopus herrmanni*, *Thelenota ananas*, *Thelenota anax*, *Holothuria fuscogilva*, and *Actinopyga mauritiana* contain a low level of lipids and is a rich source of amino acids, PUFA, carotenoids, vitamins, triterpene glycosides, collagen, gelatin, and bioactive peptides. The dried form of sea cucumber is included in soups and various other poached or stir-fried products owing to its antimicrobial, neuroprotective, and anti-inflammatory properties (Pangestuti and Arifin 2018). Microalgae are a rich source of vitamin B_{12} which is deficient in fruits and vegetables. Astaxanthin from freshwater microalgae plays the role of a strong antioxidant compared to carotenoids, vitamin C, and zeaxanthin (Koyande et al. 2019).

Peptides extracted from marine biosystems provide therapeutic effect in the treatment of several cardiovascular and non-communicable diseases. Hypertension-controlling functional foods and nutraceuticals are prepared from marine-derived renin and angiotensin-converting enzyme inhibitory peptides. Discodermins, halicylindramides A–C, jaspamide, and Geodiomolides A, B, H, and I are some of the marine sponge-derived peptides that aid in the treatment of cancer in patients. Similarly, various peptides such as Neovastat, pardaxin, PAB 1 and 2, PG155, Syngnathusin, Epinecidin-1, etc. are extracted from fish species having functional compounds that help in cancer treatment (Pangestuti and Kim 2017). Seaweed peptides have a bioactive potential that prevents diabetes. The method of production involves grinding and milling of protein sources into fine seaweed powder. The cell wall is disrupted by enzymatic or mechanical methods to obtain the protein. The intact protein is converted to protein hydrolysates by the process of protein hydrolysis, and the hydrolysates are filtered to fractionate bioactive peptides that are isolated by gel filtration and reverse-phase chromatography (Admassu et al. 2018).

Microalgae are another class of marine biological systems that possess functional values for their inclusion in various bioactive functional foods such as pasta, noodles, soups, etc. The presence of PUFA, polysaccharides, vitamins, sterols, and cholesterol reducers enable its usage in products such as nutraceutical tablets, soup powders, pasta, noodles, beverages, and chips (Andrade et al. 2018). Galasso et al. (2019) reviewed the nutraceutical effect of functional compounds derived from microalgae.

Berberine, garlic, guggulsterone, resveratrol, probiotics, seaweeds, green tea, hawthorn, and soy protein are effective in reducing the LDL levels in blood cholesterol. Marine-derived omega-3-fatty acids prove to be effective in controlling blood lipid levels and are a major source for the development of functional foods to treat patients suffering from dyslipidemia (Hunter and Hegele 2017). Isoelectric solubilization/precipitation (ISP) is followed to recover proteins from fish by-products. The inclusion of ISP-derived fish protein isolate in the production of low sodium foods to reduce salt intake in the diets of patients with cardiovascular illness (Tahergorabi et al. 2015). Fucoidan is a bioactive substance that is extracted from brown seaweeds having anticancer, antioxidant, and anticoagulative properties. It can be included in the manufacture of cookies, beverages, noodles, tea, and restructured meat (Zhao et al. 2018).

26.2.3 Microbe Based

This section provides details about the incorporation of microbial strains in the development of functional food products. Microbial strains are used in the preparation of probiotic functional foods. Beneficial microbes such as *Bifidobacterium* during break preparation helps in increasing the bioavailability of iron and zinc by the process of phytate degradation. Similarly, *Lactobacillus* species exert probiotic effects by pH modification and pathogen neutralization by exerting their antimicrobial property to maintain the gut microbiota. The consumption of probiotics reduces gastrointestinal issues and enhances the mood of an individual (Yadav et al. 2017).

Pleurotus species is a sustainable functional food source microorganism that is grown on by-products of industrial wastes such as wheat straw, wheat stalk, and spent beer grains. It is developed into a functional compound owing to its high protein content and various micronutrients. *Pleurotus* species is used as a fortifying agent in bread (5–25% as flour), biscuits (4–12% as flour), pasta (2–6% as flour), chips (5–20% as flour), instant beverage mix (as broth), chicken and beef patties (25–50% as powder), RTE products (4–20% as powder), etc. to increase the nutritional and functional profiles (Lavelli et al. 2018). It is also used as an expensive protein replacer with the incorporation of low-cost *P. sajor-caju* in place of mushroom and coconut milk powder. It can also contribute to the growth of gut microorganisms by acting as a prebiotic.

Iraporda et al. (2019) studied the effects of fermentation of inulin extracted from artichoke using *Lactobacillus* strains. The inulin compounds from Jerusalem artichoke extract improved the survival of the strains in the gastrointestinal tract on consumption as a probiotic supplement. Functional yogurt is one of the common food products and the inclusion of Jerusalem artichoke powder as a prebiotic agent in its preparation provides a bifidogenic function (Ribeiro et al. 2019). The resistant starch content of functional foods with prebiotic effect can be increased by the addition of 3% green banana flour where the inclusion of banana flour was found to enhance the firmness, PUFA profile, aroma, and flavor profiles of fermented milk samples (Batista et al. 2017). Fermented foods are prepared from various substrates such as roots, tubers, and cereals. Fermented functional yam food prepared from *Lactobacillus lactis*, *Lactobacillus plantarum*, and *Lactobacillus fermentum* strains was evaluated, and it was concluded that cell viability above 8 log CFU/mL was maintained by *L. lactis* (Batista et al. 2019).

Apart from functional benefits, prebiotic and probiotics are also consumed by the population who are obese as a healthy alternative to high-calorie foods consumed otherwise (Green et al. 2020). Functional food consumption increases insulin sensitivity and adaptive immunity while it reduces inflammation and CVD. Siciliano et al. (2021) reviewed the effects of para-probiotics in the production of functional foods. The intake of foods with such microorganisms has a profound effect in regulating the health of intestinal microbiota. Fermented milk beverage, yogurt, a sports drink, is some of the examples of para-probiotics in use. Vegan-based probiotic products have an impact in reducing LDL profile and enhancing the immune system. The stability of microbial strains on vegan foods relies on the steps of processing, vegan food matrix, probiotic strain under study, and its method of incorporation, storage condition, and enrichment of prebiotic compounds (Pimentel et al. 2021).

26.2.4 Encapsulated Functional Foods

This section provides details about the encapsulation of functional foods to maintain their characteristic functionality during processing conditions and to provide targeted release of such compounds. The sustainable means of utilizing the bioactives present in food industry by-products is a means to provide functional food to the growing population such as orange pulp industrial by-products in spray-drying, apple pomace as a prebiotic source and as a stabilizing agent in Pickering-type emulsions, and *Saccharomyces cerevisiae* as an encapsulating agent while its extract as a sensory enhancer in cooked ham products (Comunian et al. 2021). Valorization of by-products is a new industry that helps to meet the sustainable food supply demands in the market.

Microencapsulation is regarded as a technique to preserve the molecular nature of the bioactive compounds from oxidization or hydrolysis and maintain its properties till it reaches a specific site, such as the stomach or intestine to release its specific nutraceutical property (Betoret et al. 2011). The developed microencapsulated compounds are checked for their efficacy of release mechanisms during in vitro and in vivo studies to predict the effect of temperature, pH, and enzyme on release (Ye et al. 2018).

Nano-based encapsulated delivery systems for functional compounds identified in marine biological systems prove to be advantageous in effective retaining of the bioactives through various processing conditions, reduce the off odor observed in marine functional compounds, cause the effective release of functional ingredients at specific sites in the body, and improve the stability of the same through its passage in the gastrointestinal duct to improve its bioavailability (McClements 2015). The growing demand in the production and consumption of functional foods among consumers requires a highly stable and sensorially acceptable product. The main drawback of functional foods is their instability and sensory changes at various environmental conditions and storage time. The need to retain the functional compounds is of prime concern. One way of preserving and maintaining the functionality of the compounds is through encapsulation technique using various wall matrix solutions, the most common being protein and carbohydrate solutions (Dias et al. 2017). The final probiotic concentration should be maintained to provide the desired effects when the functional food reaches the intestine. The main disadvantage of processing is a decrease in the viability which can be reduced on encapsulation with matrix material made of polysaccharides from various gums, such as xanthan gum and gellan gum, chitosan from crustacean shell, carrageenan from red algae, starch from maize, milk protein, etc. (Chew et al. 2019).

Green tea catechins express a variety of health benefits such as antidiabetic, anti-inflammatory, and anticancer on consumption. Nanoencapsulation of GTC can help in protection against oxidation when included in bakery, beverage, and dairy products like cheese, yogurt, ice cream, etc. (Rashidinejad et al. 2021). In a study conducted by Costamagna et al. (2017), *Geoffroea decorticans* extract was encapsulated with zein matrix to protect its antioxidant ability and polyphenols and inhibit pro-inflammatory enzymes. The matrix effectively protected the bioactive compound and releases it at specific pH during digestion for effective absorption. Similarly, β-carotene and eugenol co-encapsulated flaxseed oil powder components were maintained intact with OSA starch as wall material for 28 days at 40 °C (Sharif et al. 2017).

26.2.5 Dairy-Based

This section provides details about the functional ability of dairy-based products from various animal milk sources. Dairy products such as curd and yogurt are proven to be prebiotic sources for a long time. Apart from cow-based dairy products, functional foods produced from other animal milk such as camel milk, sheep milk, and goat milk also enhance the bioactivity and prove to be functional sources in recent food manufacture.

Sustainable use of fruit waste and its incorporation into dairy products like cheese and yogurt have gained importance lately. The inclusion of fruit peels increases bioactivity and serves as a source of prebiotics in yogurt manufacturing (Fazilah et al. 2018). Pomegranate peel extract increases antioxidant activity of yoghurt, while pineapple waste increases the antioxidant, antimutagenic, and prebiotic potential. Yogurt with fortified grape skin exhibits greater phenolic content. Prebiotic sheep functional ice cream reduced calorific intake due to the replacement of fat with prebiotic fibers inulin and fructo-oligosaccharides (Balthazar et al. 2017). Similarly, in a study conducted by Al-shamsi et al. (2018), protein hydrolysates from camel milk increased the antioxidant potential. It was included in minced fish and grape seed o/w emulsion to inhibit lipid peroxidation. Microencapsulated yogurt produced from co-encapsulation of echium oil, phytosterols, and sinapic acid with gelatin-arabica gum and gelatin-cashew gum combinations as wall matrix material aided in enhancing oxidative stability (Comunian et al. 2017). Goat milk is regarded as a main probiotic carrier in the non-bovine milk category as viability is maintained for a long time compared to sheep, camel, and donkey milk (Ranadheera et al. 2018). Goat milk contains bioactive peptides that induce anti-inflammatory, antioxidative, anti-platelet, antiatherogenic, and anti-allergic properties, improve calcium uptake, modify gut microbiota, and improve digestibility because the presence of lower fat globules and conjugated linoleic acids provide anti-carcinogenic property. Thus, product development like prebiotic and probiotic goat milk, kefir, cheese, ice cream, and yogurt from goat milk imparts a variety of health benefitting activities. An increase in total intestinal feruloyl esterase activity and protection against stress disorders such as cancer, diabetes, various cardiovascular diseases, and neurodegenerative disorders were observed on consuming goat-based products (Verruck et al. 2019). Carotenoid fortified dairy products improves cognitive function, eye health and increase provitamin A, lutein, and zeaxanthin activity (Stephenson et al. 2021).

LAB and bifidobacteria present in dairy milk show potential biofunctional effects in antioxidative, anti-hypertensive, anti-inflammatory, and cholesterol-lowering ability. Thiamine, riboflavin, biotin, cobalamin, folic acid, GABA, conjugated linoleic acids, and exopolysaccharides are some of the bioactive nutrients obtained on consumption (Linares et al. 2017). Whey protein is a by-product obtained during cheese processing that is rich in bioactive peptides to impart functional properties whose hydrolysates are utilized on a large-scale manufacture of functional foods (Dullius et al. 2018).

26.2.6 Edible Functional Packaging System

This section deals with the incorporation of functional microbial strains onto food packaging films to maintain the product quality characteristics and to maintain the viability of microbial strains. Probiotic strains are entrapped onto edible packaging films which are in direct or indirect contact with the food material and can be consumed with the food article.

The benefits of probiotic consumption include the following:

1. Sustain intestinal health
2. Ameliorate irritable bowel syndrome
3. Protection against pathogens
4. Sustains nutrient absorption
5. Initiates micronutrient production
6. Enhances immunity
7. Retards inflammation

The edible coating of packaging material suspension is done by the process of dipping, spraying, coating, or wrapping around the food material. The edible package protects the food material, acts as a carrier of a functional compound, and modifies the sensory aspects of the food material. The probiotic strains are entrapped into films made from hydrocolloids, lipids, and composites (Zoghi et al. 2020). Edible films are regarded as green technology and provide good water and oxygen barrier properties. They are known to be a sustainable trend in the case of food packaging systems.

Direct application of edible film suspensions is carried out in eat-based foods and minimally processed fruits and vegetables. Sodium-alginate edible films were prepared to provide a probiotic effect by including various microbial strains onto ham slices pretreated with high-pressure processing. These films increase the shelf-life by retarding the growth of pathogenic microorganisms by the functional compound present in them (Pavli et al. 2017). Beef meat was packed in edible films containing zein starch and monolaurin with *Zataria multiflora* essential oil as an antimicrobial agent (Moradi et al. 2016). The growth of pathogenic organisms was inhibited for 3 days at 4 °C under this environment. Alginate and gellan based edible films with ascorbic and citric acid incorporation were used to pack high moisture fresh-cut fruits like papaya and apples (Tapia et al. 2007). Gellan coating proved to be more water-resistant than alginate coating. Gelatin, wheat dextrin, inulin, glucofiber, and polydextrose-based films with glycerol as a plasticizer were used in the entrapment of *Lactobacillus rhamnosus GG* (Soukoulis et al. 2014). Wheat dextrin- and inulin-based film maintained high stability and viable microbial counts than gelatin-based films.

Sodium alginate-based films are also used in the edible coating of minimally processed carrots with *Lactobacillus acidophilus* strains. It was observed that moisture loss and color change during storage was minimized with such barrier coatings (Shigematsu et al. 2018). The shelf-life was increased by 19 days using the edible coating technique. Functional bread coated with starch-based *Lactobacillus acidophilus* strain showed an increase in the water activity content of the crust layer after baking (Altamirano-fortoul et al. 2012). Linseed mucilage incorporated alginate-based edible film with *Lactobacillus casei* resulted in increasing the shelf-life of yacon cubes and reduced weight loss and color degradation during storage (Rodrigues et al. 2018). Similar studies were carried out by Alvarez et al. (2021) where fresh-cut apples were coated with alginate films incorporated with prebiotics (inulin and oligofructose) and probiotics (*Lactobacillus* spp. and *Bifidobacterium* spp.) maintained viability above 9 log CFU/g after 8 days of storage.

Gelatin and low methoxy pectin (LMP) films were studied to evaluate the viability of probiotic strains (Khodaei et al. 2020). It was concluded that gelatin and LMP-based films maintained the viability for 42 days and 21 days at 4 °C and 25 °C, respectively. The edible films prepared from whey protein isolate and lactic acid bacteria were maintained in refrigerated conditions to maintain viable counts for 60 days (Pereira et al. 2016). It was further concluded that refrigerated storage of probiotic edible film maintains viability for a greater period than at ambient conditions. Cellulose films with citric acid cross-linking aided in better entrapment of *Lactobacillus rhamnosus GG* for sustainable and environmentally friendly packaging substitutes for food applications (Singh et al. 2019).

26.3 Methods to Measure the Biological Activity of Functional Foods

Various methods help in identifying the bioaccessibility of functional foods such as in vitro, in vivo, and ex vivo metabolism methods. Nutraceuticals developed with targeted drug delivery systems are bio-assessed with such metabolisms to ensure proper release of target functional compound at the required site (oral/stomach/GIT/intestine/colon) in the animal body. The common in vivo delivery systems include (a) phospholipid-based delivery systems, (b) emulsion-based delivery systems, (c) chemical modification methods, (d) chitosan-based delivery systems, and (e) nanodispersions (Ting et al. 2014).

In vivo method of metabolism is monitored when the particular functional food is consumed by the animal body and the whole system is tested. Ex vivo studies involve studies outside the human or animal system. In vitro studies are performed outside the human system, such as in test tubes or artificial environment that mimics the environment of an animal system. The static method of in vitro study is a convenient and cheap technique where physiological parameters such as the ratio of meal to digestive fluids, the concentration of enzyme, and pH are constant throughout digestion process and digesta discharge is not mimicked (Wu and Chen 2021). Pellegrini et al. (2017) studied the in vitro GIT digestion of quinoa seeds.

In recent times, digestion experiments using artificial stomach and buccal systems are carried out to study the effects of the release mechanism. In vivo studies are carried out to predict the release of sodium from functional foods to provide a feeling of satiety (Munekata et al. 2021b). Similarly, anti-diabetic effects of seaweeds were studied using in vivo mechanisms with clinical trials and daily supplementation (Shannon and Abu-ghannam 2019). Digestion metabolism and colon fermentation effects of consuming *Myrciaria trunciflora* fruit peel during in vitro gastrointestinal tract digestion were studied by Quatrin et al. (2020).

Several microencapsulated nano-delivery systems use in vivo and in vitro release mechanisms to study the bioavailability and targeted release of functional compounds (Costamagna et al. 2017). Hosseini et al. (2021) reviewed the bioavailability of nano-fortified functional foods.

26.4 Sustainable Development of Functional Foods

Sustainability is the ability to meet the needs of the present without compromising from the future requirements. The major rules of sustainability are reduce, reuse, and recycle. It should be taken into consideration that reduced carbon emissions are taken into account while developing new technology. Sustainable food production can be maintained through the process of valorization and utilization of local varieties of commodities that are available in surplus in a particular area (Betoret et al. 2022). The manufacturers and stakeholders should depend on low emission systems that reduce carbon footprint while formulating or developing a new product.

With the prevailing climate change conditions, sustainable means of food production are necessary to meet the most basic human demand. Complex functional food formulation consists of both risk and benefit. The perception of the commodity by the consumer results in economic risk while the benefit relies on healthy diet substitutes to maintain well-balanced nutrition (Sibbel 2007). Traditional Ayurvedic medicines used to treat a variety of illness are developed from roots, stem, leaves, and fruits of herbal plants with a functional element. John et al. (2020) reviewed the tropical foods having a metabolic effect on functional foods. The use of tropical and region-specific plant variety can lead to an increase in cost-effective, sustainable economic growth and availability of such products.

The identification of foods that possess more than one functional ability is also important in developing novel functional foods. The basidiomycetes fungi *Pleurotus* spp. possess high protein content, unique dietary profile, valuable amino acid profile, essential mineral, and vitamin which result in circular reuse of such bio-resources (Lavelli et al. 2018). The consumption of sustainable functional foods helps in reducing the risk of diseases with a healthy nutrition supply. It also reduces the impact of degradation of natural bioavailability in the environment by ensuring a safe food supply for future generations (Castillo et al. 2018). The use of indigenous food items which are poorly utilized and obtaining their functional profile is important to process a variety of novel foods that attract consumers across the globe (Granato et al. 2020).

26.5 Challenges in Testing the Efficacy of Functional Compound Incorporation in Foods Among Consumers and Consumer Purchase Behavior

The market of food products increases based on consumers' trust. The growth of a particular food industry relies on the purchase attitude of that particular product by the consumer (Huang et al. 2019). Consumer is heterogeneous in food and consumer behavior domains and careful generalizations lead to market attention of novel foods. There is a recent increase in the market value of foods incorporated with functional benefits by the consumers with an increase in awareness about the health benefits of functional food consumption. The present population tends to experiment with novel foods available on the market shelves. Thus, foods suitable for all ages of consumers have a high chance of a market score. The optimization of new product development is based on intrinsic (sensory) and extrinsic (market) factors (Bogue et al. 2017). Lifestyle attitude resulted in the purchase of products, whereas healthy lifestyle attitude had a negative effect in a study conducted to experiment the market behavior of consumers toward functional foods in Spain using general contrast model (Küster-boluda and Vidal-capilla 2017). It was concluded in that study that the women population tend to purchase healthier products available in the market than men.

In a study conducted to assess Vietnamese behavior toward functional yogurt launched in the market, multivariate data analysis was performed that revealed health-conscious attitude of consumers increased purchase of yogurt while the perceived price of the same by them resulted in a negative attitude toward the purchase (Nguyen et al. 2020).

The process of production of functional foods depends on the development of a suitable food component and testing the efficacy of the same using clinical trials. The clinical trials using medical reports and scans provide an idea about the pattern of functional compound incorporation in the human body. The health claims of developed product are based on in vivo testing (Granato et al. 2020). Brown et al. (2018) conducted a study on the challenges of testing the efficacy of functional foods on the human population. While conducting clinical trials, safety should be maintained and tests should be carried out with control individuals with their consent and cooperation.

26.6 Conclusion and Future Perspectives

Functional foods are at a steady increase in the market due to raising awareness among consumers. Sustainable production of functional foods from industrial waste and by-products is increasing. Manufacturers opt for valorization techniques to obtain specific compounds from waste materials and utilize such compounds in the large-scale development of functional foods. Functional foods provide basic nutrients with additional nutraceutical properties on long-time consumption. They are advantageous compared to synthetic or chemical-based drugs to treat various ailments. The future study in this area includes opting for various processing aids to maintain the bioactivity of the compounds through high-temperature processing and storage. Research can also be focused on indigenous or region-specific traditional functional foods to the market through various products by industrial scale-up. Procedures for standard testing methods of the efficacy of bioactivity should be formulated in future studies.

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Novel Bioactive Compounds for Enhancing Micronutrient Bioavailability 27

Akanksha Singh, H. K. Dikshit, Naleeni Ramawat, and Shiv Kumar

Abstract

Micronutrients are required for normal growth and development of human beings. More than two billion people suffer from micronutrient deficiency. Micronutrient deficiency affects around half of the population. The most widely spread deficiency is of iron and zinc, and it affects population majorly residing in developing countries. Phytic acid is the primary form in which phosphorus can be stored in legumes, nuts, cereals, legumes, and oil seeds. It has a property of chelating micronutrient and hence makes them unavailable for monogastric animals, including humans. The unavailability of phytic acid is due to the lack of phytase enzyme present in the digestive tract. In this review, we have discussed about sources, variation, and digestibility of phytic acid and diverse approaches for reducing phytic acid in food crops. Different approaches like soaking, fermentation, transgenics, and marker-assisted selection have been discussed. But development through marker-assisted selection is the most sustainable approach and can be utilized for the development of low phytic acid genotypes.

Keywords

Phytic acid · Micronutrient bioavailability · Transgenic approach · Marker-assisted selection

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27.1 Introduction

Phytic acid (PA) is generally referred to as *Myo*-inositol 1,2,3,4,5,6-hexa*kis*phosphate (InsP6). It is the primary form in which phosphorus can be stored and have approximately 65 to 85% of the total phosphorus composition of seed (Raboy et al. 2000). The remaining phosphorus is present in the cellular form of total seed phosphorus (10 to 20%) and soluble inorganic phosphate (about 5%) (Larson et al. 2000). The phytic acid content in seed and grain is extremely variable, and different researchers analyzed the level of phytic acid by differential experimental conditions (age of the sample, growth conditions, harvesting and processing methods, and testing methods). During the process of ripening in seeds, phytate accumulation takes place in seeds. In cereals like rice, wheat it is present in bran (pericarp and aleurone layer), and in maize, it is present in endosperm (O'Dell et al. 1972). In oilseeds and leguminous seeds, it is found in the globoid crystal within the protein bodies (Erdman 1979). Due to lack of phytate-degrading enzymes in the digestive tract of monogastric animals (such as humans and poultry), they are not able to metabolize phytic acid in the body (Wodzinski and Ullah 1996; Singh et al. 2011). Therefore, inorganic phosphate needs to be supplemented to maintain the phosphorus requirement (Vats et al., 2004). Inability to uptake phosphorus in monogastric animals leads to loss of approximately 70% of the total phosphorus that is mainly released in excreta (Milko et al. 2008). It is negatively charged and present in the form of mixed salts known as phytate (Raboy 2003), and it leads to chelation of cations of minerals such as iron, zinc, magnesium, potassium, and calcium. The insoluble nature of PA leads to the poor absorption of vital nutrients and cause deficiency of micronutrients in human body (Mitchikpe et al. 2008). The requirement of phytic acid is variable and depends upon several factors such as the age and physiological stage of a person (Amirabdollahian and Ash 2010; Niknamian and Niknamian 2016). The intake of phytic acid is more prevalent in developing countries in contrast to developed countries where the huge cluster of population predominantly depends on non-vegetarian diet leading to lower level of phytic acid ingestion (Amirabdollahian and Ash 2010).

27.2 Global Micronutrient Malnutrition and Requirement for Enhancing Bioavailability of Micronutrients

Micronutrient malnutrition is a global health problem, and it occurs due to inadequate intake of essential nutrients in daily diet. Globally, it affects approximately two billion people; however it is more widespread in developing countries, where the vegetarian diets were consumed on daily basis (Ranganathan et al., 2016). Due to the micronutrient malnutrition, around 155 million children suffer from stunting, and it is the primary cause of death (45%) in children under 5 years (WHO 2017). Deficiency of minerals such as iron and zinc affects the immune system and cognitive abilities and also leads to retarded growth (Osendarp et al. 2007; Kambe et al. 2014). Despite the inflation in the food crop production, there is a prevalence of micronutrient malnutrition (Gould 2017). The human health is the extremely neglected area of agricultural research. The foremost emphasis of agricultural research is improving and enhancing the food grain production and productivity of crop. This approach has led to expeditiously rise in micronutrient deficiency in food grains and therefore demand of nutrient rich food by consumers. The entire agriculture now bent toward producing more quality food in sufficient quantity. This whole approach assists in eradication of micronutrient deficiency, with prime focus on poor and developing countries (Khush et al. 2012). Therefore, improving crops with essential micronutrients specifically iron and zinc by biofortification is identified as strategy for solving this major problem (Bouis and Saltzman 2017).

Anti-nutrients are also one of the components of plants. These anti-nutrients restrain the bioavailability of nutrient in the plants. Reduction of these anti-nutrients by alleviating enhancers which promote absorption of iron in potato (Bonierbale et al. 2010) or by reducing the inhibitors such as phytic acids in legumes and cereals (Raboy et al. 2000) led to increase in the micronutrient bioavailability in food crops. To address these bioavailability issues, it is required to change the physiology of plants or develop genotypes having mechanism of accumulating low anti-nutrient in plants. Phytic acid reduces the bioavailability of minerals and is also crucial for the storage of phosphorus. But phytic acid cannot be eliminated from crops completely as it will hamper the viability of plant (Zhao and Shewry 2011).

27.3 The Sources of Phytic Acid in Food and Digestibility

Phytic acid can be obtained from legumes, nuts, oilseed, and cereals. These sources contribute to the 40 to 60% of the total calories consumed by human population (Schlemmer et al. 2009). Cereals are rich in phytate, and cereal food products show higher phytic acid content (Wise 1983). Other food crops such as vegetables, tubers, and roots also have extremely low amount of phytic acid. It is mainly in the aleurone layer of grains except in legumes, where phytic acid is present in cotyledon. There are several studies on molecular, genetics, and physiological aspects to develop biofortified genotypes. But information on lowering phytic acid content in food crops and their mineral bioavailability is very confined.

The digestibility of micronutrient is directly proportional to the amount of phytic acid. In non-ruminant animals, there is absence of enzyme phytase. Phytase enzyme hydrolyses the phosphorus from the phytic acid molecule and results in non-availability of phytic acid (Marounek et al. 2010). But ruminants have the ability to digest phytic acid due to the presence of phytase enzyme. This major hurdle can be resolved by feeding non-ruminants with phytase (Pontoppidan et al. 2007). But it results in generation of another challenge, which is eutrophication. It results in environmental pollution due to excess excretion of phosphorus. Low phytic acid grains are of greater relevance for non-ruminants. There is now urgent need for incorporating the objective of developing lower phytic acid grain in breeding program. The physiological and biochemical mechanism of phytic acid accumulation to enhance the micronutrient bioavailability by developing low phytic acid crops still need to be explored.

27.4 Variation for Phytic Acid in Food Crops

The concentration of phytic acid in rice bran is approximately 8.7% (Lehrfeld 1994) whereas in wheat bran, it ranges from 2.0–5.3%, respectively (Kasim and Edwards 1998). In leguminous crops, the phytic acid is present in endosperm of grains. The concentration ranges from 0.2 to 2.9% in whole grain to more than 3.7% in cotyledons (Lestienne et al. 2005). The wild species (0.98–3.14 g/100 g) of legumes have higher concentration of phytic acid in comparison to cultivated species. Soaking reduces the concentration (Vellingiri and Hans 2010). The range of phytic acid in nuts varies from 0.1 to 9.4% (Schlemmer et al. 2009). The phytic acid content ranges from 1.0 to 5.4% (dw) in oilseeds, for example, sesame seeds, rape seeds, sunflower kernels, soybeans, and linseeds (Lolas et al. 1976). In soybean, highest amount of phytic acid (10.7%) is reported by Lehrfeld (1994).

27.5 Approaches for Developing Low Phytic Acid Food Crops with Enhanced Micronutrient Concentration

Reduction in the phytic acid content is the major challenge for developing genotypes comprising bioavailable micronutrients, due to their ability to inhibit the absorption of micronutrients.in food crops. Mitigation of phytic acid results in improving the absorption of iron (Hurrell et al. 2003) and zinc (Egli et al. 2004). There are various approaches—physical as well as biological methods—and biotechnological approaches for reducing the phytic acid content and therefore enhancing the bioavailability of micronutrients (Ertas and Turker 2014). One of the strategies for lowering phytic acid is soaking of seeds. Soaking assists in activation of phytase enzyme which helps in hydrolyzing phytic acid grain (Mahesh et al. 2015). Although soaking results in hydrolyzing the phytic acid, if there is limitation of time, then a combination of cooking and soaking is more effective (Huma et al. 2008). Fermentation is the other approach of reducing the content of phytic acid. It is one of the most economic and effective measures. Several studies exhibited that fermentation with starter culture as well as spontaneous fermentation significantly results in decreasing the phytic acid content (Murali and Kapoor 2003). Different processing methods like milling helps in solving this issue by removing phytic acid but major minerals get removed from the grain and therefore this process is not suitable for removal of phytic acid (Liang et al. 2008). Biotechnological methods, for example, genetic engineering, are also one of the approaches for reducing phytic acid. Transgenic cereals have been developed with better accumulation of phytase enzymes in seed and grain. The drawback of this approach is its complex mechanism and expensive and laborious process (Brinch-Pedersen et al. 2003). Hence it is the future thrust to develop a methodology which is simpler, easy to adapt, sustainable, and cost-effective (Kuwano et al. 2009).

27.6 Transgenic Approaches

Utilization of transgenic approach is a better way to develop genotypes, lacking the genotypic variation for the trait of interest. Development of transgenic rice with decreased phytic acid content by the gene expression of RINO1 gene resulted in availability of Pi, but there was no reduction in the total P level in seed and grain (Feng and Yoshida 2004). They had observed that various promoters CaMV35S and RINO1 are present in developing seeds and also in active stages in the vegetative part of the plant. Therefore seed-specific promoters from storage proteins 18-kDa Oleosin 18 and GlutelinB-1 were used to suppress RINO1 gene expression in rice seeds (Kuwano et al. 2009). This results in development of low phytic acid rice with approximately 68% reduction in the phytic acid content, and the results were inversely proportional to the germination, grain weight, and growth of the plant (Kuwano et al. 2009). IPK1 gene was silenced with the assistance of promoter Ole 18 to develop rice with reduced phytic acid content by using RNAi approach. The developed transgenic rice variety exhibits significant reduction in the phytic acid content without impeding the germination, growth, and development of seed (Ali et al. 2013).

27.7 Marker-Assisted Selection in Development of Low Phytic Acid Genotypes

Marker-assisted breeding helps in the development of genotypes with improved traits. Utilizing molecular marker can speed the process of developing improved genotypes and enhances the efficiency of breeding programs designed for specific trait of interest. In case of recessive traits, marker-assisted backcross breeding provides immense possibility for transfer of desirable trait of interest into the genetic background of a recipient genotype by recurrent backcrossing. Along with transfer of trait, recovering of the recurrent parent genome is also completed with the help of marker-assisted selection. Utilizing the molecular markers QTLs have been identified in many crops. Two quantitative trait loci for phytic acid content were identified in biparental mapping population of ‘IR64’ X ‘Azucena’. These QTL regions were present on chromosomes 5 and 12, explaining phenotypic variation of 24% and 15%, respectively (Stangoulis et al. 2007). In mungbean, six QTLs were identified for phosphorus compound in the seedlings of mungbean. Three QTLs were identified for PAP, two for TP, and one for IP (Sompong et al. 2012). In maize, two mutant lines were crossed and developed UMI395 (low phytic acid and agronomically superior lines). The low phytic acid trait was transferred from donor parent (EC 659418). SSR marker “u mc2230’ was identified linked with the low phytic acid trait (Kumar et al. 2014).

27.8 Conclusions

Micronutrient malnutrition remained a widespread global health problem in developing countries. Increasing micronutrient intake in food through food-based approaches is a sustainable method of prevention of micronutrient malnutrition which should be achieved through food diversification and biofortification. Micronutrient malnutrition eradication and sustainable solutions for improvement of mineral bioavailability can be attained by several independent methods like presoaking, fermentation, conventional breeding, and modern biotechnological tools. Presoaking and fermentation methods are short-term methods but development of low phytic acid genotypes through conventional breeding methods and transgenic approaches. Characterization of genotypes for low phytic acid content and identification of low phytic acid genotypes assist in biofortification program of food crop. The knowledge of absorption, translocation, and accumulation of phosphorus in grain need further research for manipulation phytic acid content in grain. Future research is also required to identify new phytase enzymes responsible for phytic acid in plants to engineer them to develop desired characteristic and to determine the optimal dose and appropriate delivery of phytase to human foods.

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Microgreens: An Emerging and Sustainable Innovative Approach for Functional Properties

28

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Abstract

Microgreens are new specialty crops gaining popularity and increased attention nowadays. These are the juvenile and tender cotyledonary leafy greens having catchy appearance, tender texture, and strong flavor and provide full pack of healthful nutrients. They range in size from 1″ to 1 1/2″ including stem and leaves. Microgreens are considered to be beneficial for health and provide necessary nutrients to human body. Microgreens represent a new group of vegetables considered to be "functional foods" as they possess disease-preventing properties, in addition to their nutritional value. Microgreens have a short life cycle of 5–10 days which may go to few days more if they have not attained the desired height. Common examples of microgreens include red amaranth, green basil, cabbage, broccoli, cilantro, etc. Despite small size, microgreens have strong flavors including higher amounts of vitamins and minerals. Microgreens are rich in various phytochemicals as carotenoids, tocopherols, ascorbic acid, and phylloquinones. Microgreens are perishable and the problem results in case of their post-harvest storage and shelf life. The problems including rotting, foul odor, and premature degradation leads to shorter shelf life and hence, the spoilage of the product.

Keywords

Microgreens · Functional foods · Post-harvest storage

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28.1 Introduction

Microgreens are the latest rising food products, which are juvenile seedlings of vegetables and herbs, having two grown up cotyledons with the first duo of true leaves upcoming and uprising or moderately extended and up to inches tall. They range in size from 1″ to 1 1/2″ including the stem and leaves (Poorva and Aggarwal 2013). When the greens grow ahead of this size, it should no more be taken into account as a microgreen. The life cycle of microgreen takes only 14 days from seed to harvest. Some of the common microgreens that we have in our daily life includes basil, celery, broccoli, cabbage, mustard and cress, fennel, mint, etc. Microgreens need about 4 h every day of direct sunlight to bloom. Now, the growers after knowing the importance need vegetables that are even more babyish than babies—seedlings so small, and so young, are called microgreens; examples include baby-fication of our vegetables—baby spinach, baby lettuce, and baby squash valued for their tenderness and appealing size have attracted everyone.

In winter months, the microgreen production needs even more time. Depending upon the type of seed preferred, it will take about 2–3 weeks to harvest microgreens after planting. They are harvested at the first true leaf stage and sold with the stem, cotyledons, and first true leaves attached, though the post-harvest storage problems add in early dreadful conditions of the crops which results in little shelf life, tainted odor, and rotting. The commercial marketing of microgreens is principally under fire toward restaurant chefs or upscale grocery store. The product is packed in plastic clamshell containers or is sold in bunches.

Microgreens are well thought of as *functional foods* which are actually food product that possess specific health-promoting or disease-preventing properties that are additional to their normally nutritional value (Xiao et al. 2012). The epidemiological studies show that the everyday intake of microgreens especially broccoli and other cruciferous vegetables results in decreased cancer risk. Epidemiological studies on *Brassica* vegetables summarized the protective effect of *Brassica* against cancer due to hydrolysis product of glucosinolates (Verhoeven et al. 1996).

Verhoeven et al. (1996) conducted studies on consumption of cabbage, broccoli, cauliflower, and Brussels sprout (Table 28.1). They showed percentages of opposite involvement with cancer and were 70, 56, 67, and 29%, respectively. Verhoeven et al. (1997) certified the carcinogenic properties of cruciferous vegetables to their relatively high content of glucosinolates (Fig. 28.1).

Currently, the demand for these food products has been growing briskly, and consumption is increasing given their particular characteristics: exclusive color, prosper flavor, and considerable content of bioactive substances.

28.2 Nutritional Value

Microgreens are gaining fame as a fresh culinary ingredient, giving intense flavors, bright colors, and crisp texture when supplemented to salads and other food preparations. Even though microgreens would intrinsically be regarded as a healthy

Table 28.1 Twenty-three commercially grown microgreens assayed in the nutrient study

S. no	Commercial name	Family	Scientific name	Plant color
1	Arugula	Brassicaceae	*Eruca sativa Mil*	Green
2	Celery	Apiaceae	*Apium graveolens* L.	Green
3	China rose radish	Brassicaceae	*Raphanus sativus* L	Purplish-green
4	Cilantro	Apiaceae	*Coriandrum sativum* L.	Green
5	Garnet amaranth	Amaranthaceae	*Amaranthus hypochondriacus* L.	Red
6	Golden pea tendrils	Fabaceae	*Pisum sativum* L.	Yellow
7	Green basil	Lamiaceae	*Ocimum basilicum* L.	Green
8	Green daikon radish	Brassicaceae	*Raphanus sativus* L. var. *longipinnatus*	Green
9	Magenta spinach	Chenopodiaceae	*Spinacia oleracea* L.	Red
10	Mizuna	Brassicaceae	*Brassica rapa* L. spp. *Nipposinica*	Green
11	Opal basil	Lamiaceae	*Ocimum basilicum* L.	Greenish-purple
12	Opal radish	Brassicaceae	*Raphanus sativus* L.	Greenish-purple
13	Pea tendrils	Fabaceae	*Pisum sativum* L.	Green
14	Peppercress	Brassicaceae	*Lepidium bonariense* L.	Green
15	Popcorn shoots	Poaceae	*Zea mays* L.	Yellow
16	Nutrient purple kohlrabi	Brassicaceae	*Brassica oleracea* L. var. *gongylodes*	Purplish-green
17	Purple mustard	Brassicaceae	*Brassica juncea* (L.) Czern.	Purplish-green
18	Red beet	Chenopodiaceae	*Beta vulgaris* L.	Reddish-green
19	Red cabbage	Brassicaceae	*Brassica oleracea* L. var. *capitata*	Purplish-green
20	Red mustard	Brassicaceae	*Brassica juncea* (L.) Czern.	Purplish-green
21	Red orach	Chenopodiaceae	*Atriplex hortensis* L.	Red
22	Red sorrel	Polygonaceae	*Rumex acetosa* L.	Reddish-green
23	Sorrel	Polygonaceae	*Rumex acetosa* L.	Green

addition to the diet, no information is accessible on their nutritional content. The present study conducted by Xiao et al. (2012) in the Department of Nutrition and Food Science, University of Maryland, USA, found out the concentrations of carotenoids, tocopherols, ascorbic acid, and phylloquinones in 25 commercially obtainable microgreens. Outcomes show that different microgreens supply tremendously varying amounts of vitamins and carotenoids. Total ascorbic acid ranged from 20.4 to 147.0 mg/100 g fresh weight, while beta carotene, lutein/

Fig. 28.1 Images of microgreens

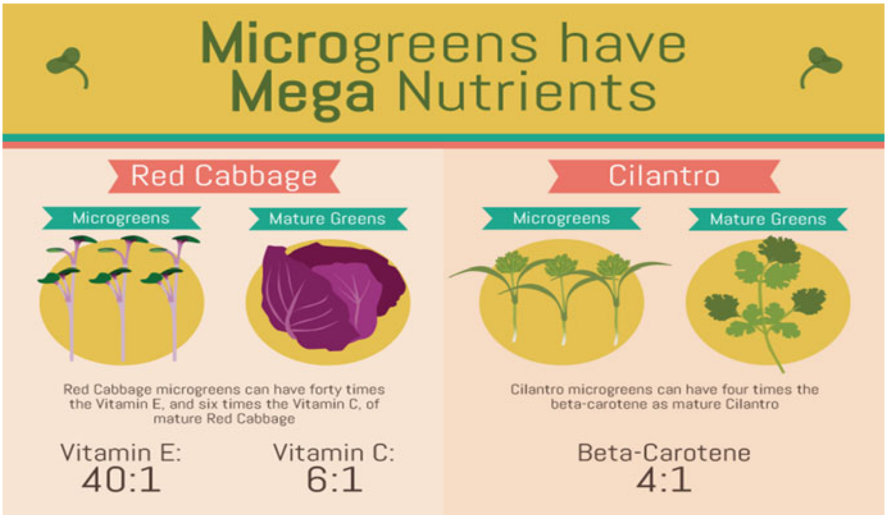

Fig. 28.2 Comparison of microgreen with mature green

zeaxanthin, and violaxanthin concentrations ranged from 0.6 to 12.1 μg/100 g, fresh weight, meanwhile α tocopherol and β tocopherol ranged from 4.9 to 87.4 and 3.0 to 39.4 mg/100 g fresh weight, respectively. Also, amid these micrograms, red cabbage, cilantro, garnet amaranth, and green daikon radish had the maximum concentration of ascorbic acids, carotenoids, phylloquinones, and tocopherols, respectively (Fig. 28.2). It was observed that in contrast with mature leaves, microgreen cotyledon leaves possessed higher nutrition densities (Tables 28.2 and 28.3).

Table 28.2 Comparison of major nutrients in the following greens with their mature plants as per USDA National Nutrient Database

	Green daikon radish 		Red cabbage 		Garnet amaranth 		Cilantro 	
	Micro green	Mature	Micro green	Mature	Micro green	Mature	Micro green	Mature
Total ascorbic acid (mg/100 g)	70	14.8	130	43.3	40	27	140	57
Phylloquinone (μg/g)	1.75	1.3	4	1140	2.5	310	2.75	38.2
α-Tocopherol (mg/100)	90	0.0	15	–	50	2.5	25	0.11

Table 28.3 List of soil pathogens found on plant

S. no.	Pathogen	Plant
1	*Clostridium botulinum*	Cabbage
2	*Listeria monocytogenes*	Cabbage
3	*Shigella flexneri*	Scallions
4	*Campylobacter jejuni*	Lettuce, peppers, and spinach
5	*Salmonella* spp.	Cantaloupe, strawberries
6	*Escherichia coli*	Apple cider, lettuce, radish, alfalfa sprouts, and other mixed salads

28.3 Bioactive Components and Health Benefits of Microgreens

Due to changed lifestyle and increased health consciousness among people, the microgreen consumption has increased to a great extent. Microgreens contain more concentrated functional components than the mature leafy greens (Chandra et al. 2012; Xiao et al. 2012; Kou et al. 2013). There is an increase in demand for these products as people are paying more attention toward functional foods. Since microgreens are rich in amino acids, vitamins, antioxidants, and trace elements, therefore they are greatly valued for their health benefits (Finley et al. 2001; Han et al. 2006). Sun et al. (2003) used ultrahigh-performance chromatography photodiode array high-resolution multistage mass spectrometry to profile the five *Brassica* species microgreens. There were 164 polyphenols found in all, including 30 anthocyanins, 105 flavonol glycosides, and 29 hydroxycinnamic and hydroxybenzoic acids. When compared to mature plant equivalents, *Brassica* species microgreens had more complex polyphenol profiles and included more kinds of polyphenols, according to the findings.

28.3.1 Phytonutrients

1. Microgreens are the juvenile seedlings that contain large concentration of vitamins, minerals, and other health-giving phytonutrients than the mature leaves (Janovská et al. 2010).
2. The younger leaves of baby spinach (*Spinacia oleracea* L.) usually contain large amount of phytonutrients, vitamin C, Ba, and K1 and the carotenoids (lutein, violaxanthin, zeaxanthin, and β-carotene), than the mature leaves (Lester et al. 2010).
3. Oh et al. (2010) found that young lettuce (*Lactuca sativa*) seedlings, after 7 days of germination, contain the highest total phenolic concentration and antioxidant capacity in comparison to older leaves.

4. The red cabbage, garnet amaranth, and green daikon radish microgreens contain highest concentration of vitamin E, vitamin C, and vitamin K (Poorva and Aggarwal 2013).

28.3.2 Anticancerous

1. All the nutrients that are packed in microgreens are essential for the skin and eyes and also help fighting cancer. The number of studies has been done on cancer prevention by these microgreens (all *Brassica*: broccoli, cabbage, etc.).Various studies conducted on microgreens show that there have been a great reduction in the cases of lung, breast, colon, ovarian, and bladder cancer in people who eat diets high in these vegetables (Franks and Richardson 2009).
2. The balance that's being created by this compound results in better resistance to cancer plus the encouragement of overall hormone balance.
3. These microgreens contain crystalline compounds (indoles) having a wide range of health benefits. These contain an estrogen stabilizer, DIM (diindolylmethane), and are necessary for both men and women. DIM acts as an inhibitor of growth.

28.3.3 Prevention of Inflammation

C-reactive protein (CRP) and tumor necrosis factor alpha (TNF-α) levels in the liver were reduced by eating red cabbage microgreens. This impact could be owing to the microgreen's capacity to reduce liver lipids, which have been linked to inflammatory reactions in the past (Huang et al. 2016). Other potential effects generated by microgreens can also be deduced by looking at some of the most well-known inflammation-related pathways.

28.4 Pathogen Risk

Pathogens may be defined as the organisms flourishing on plants and causing disease in their host. Since microgreens are lucky plants that are harvested at early stages of their growth, therefore pathogen risk is low (Table 28.3). However, if not handled properly may get prone to occurrence of soilborne pathogens resulting in health hazards.

28.5 Marketing

The interest toward microgreens has expanded. Since their introduction in high-end culinary establishments (Kaiser and Ernst 2012) in the late 1990s, the main market continues to be restaurant chefs. Further direct market opportunity may include upscale or gourmet grocery stores, as well as health food stores (Table 28.4).

Table 28.4 Few functional microgreens with their flavors and food uses

S. no.	Microgreens	Flavor	Food use
1	*Arugula*	Rich peppery taste with strong distinct flavor	Use it in foods with olives, garlic, tomatoes, peppers
2	*Red amaranth*	Mild beet root	Fries, salads, egg dishes, garnish
3	*Green basil*	Spicy, peppery	Tomatoes, soft cheeses, salads, pasta, pizza
4	*Lemon balm*	Lemon sherbet	Fish, chicken, leafy salad, fruit salad, iced tea
5	*Broccoli*	Mild broccoli	Eggs, sandwiches, cheeses, smoked fish
6	*Celery leaf*	Celery, lemony	Salads, soups, garnish
7	*Coriander*	Aromatic	Curries, salads, soups, salsa
8	*Pea shoots*	Freshly podded peas	Seafoods, salads, stir fries, sandwiches, cheeses
9	*Thyme*	Spicy	Chicken, meat, fish, vegetables, pizza
10	*Garlic chive*	Mild onion garlic	Seafood, eggs, sour cream, cheese, garnish
11	*Purple shiso*	Cumin, cinnamon, anise	East Asian cuisine, sushi, salads, soups
12	*Wasabi*	Spicy	Japanese cuisines
13	*Mizuna*	Mild peppery, slightly spicy	Stir fries, soups, nabemono
14	*Opal basil*	Slightly stronger anise flavor, mild ginger tinge	Garnish for desserts, salads, pizza, and pastas

Microgreens are the food commodities requiring very little initial investment with more varieties in less amount of space. Once sown, they start generating income in just 2 to 3 weeks.

28.5.1 Market Outlet

Microgreens one of the most recent cooking trends are gaining popularity. Microgreens are being promoted as an extremely nutritious food product. The demand for these juvenile plants has increased since being recognized as a national trend in haute cuisine around 2006. Microgreens are added as garnishes or flavoring substances by many white tablecloth restaurants. Microgreens have gained attention particularly among health-conscious consumers; the primary market is still fine dining establishments. Some specialty grocers and health food stores are interested in supplying microgreens to consumers, but the highly perishable nature of the crop can create substantial marketing challenges, particularly for inexperienced growers. The most excepted flourishing marketing strategy for the producers who are interested in growing microgreens is to work directly with a restaurant or chef, growing and delivering microgreens at the requests and preferences of the restaurateur. The rapid growing and harvest time of microgreens make it most interesting crop for small growers paying attention in developing nearby, high-end specialty markets for fresh produce.

28.5.2 Microgreen Production

Microgreens may be developed by persons for home use. Growing miniature amount at home is comparatively simple; however, growing and marketing high-quality microgreens commercially is much hard. Having the right blend at the perfect stage for harvest is one of the most decisive production tactics for success. The time from seeding to harvest fluctuates significantly from crop to crop. When seeding a blend of crops in a single planting flat, growers should choose crops that have a comparable growth rate so the whole flat can be harvested at once. On the other hand, growers can seed the various crops singularly and blend them after harvest.

Microgreens can be grown up in a normal, disinfected, slack, soilless germinating media. Many blends have been used effectively with peat, vermiculite, perlite, coconut fiber, and others. Moderately fill up tray with the media selected to a depth of 1/2 in. to 1 or 2 in., depending on irrigation programs. Overhead mist irrigation is normally used only through the germination period in these media systems. After germination, trays should be subirrigated to shun excess moisture in the plant canopy.

A substitute production system uses one of several materials as a mat or lining to be placed in the bottom of a tray or longer trough. These materials are normally fiber-like and give a brilliant seeding bed. Materials may consist of burlap or a food-grade plastic particularly designed for microgreens. These mat systems are frequently used in a commercially available production system using wide NFT-type troughs. The burlap mat may be enough alone for certain crops or may necessitate a light topping with a media after seeding. Seeding may be ended as a broadcast or in rows. Seeding density is complicated to suggest. The majority of the growers state that they want to seed as densely as possible to maximize production, but not too densely because crowding encourages elongated stems and increases the risk of disease. Most crops necessitate slight or no fertilizer, as the seed provides adequate nutrition for the young crop. Long growing microgreens, such as micro carrot, celery, and dill, may perhaps benefit from a light fertilization applied to the tray bottom. Some of the rapid growing greens, the same as mustard cress and chard, may also benefit from a light fertilization because they germinate quickly and exhaust their self-contained nutrient supply speedily. Light fertilization is mostly achieved by allowing each tray of microgreens to float for 30 s in a prepared nutrient solution of approximately 80 ppm nitrogen.

Microgreens are ready for harvest when they attain the first true leaf stage, usually at about 2 in. tall. Seeding to harvest time vary greatly by crop from 7 to 21 days. Production in small trays will likely require harvesting with cutters. This is a very time-consuming part of the production cycle and is frequently mentioned by growers as a major disadvantage. The seeding mat type of production system has gained fame with many growers because it facilitates faster harvesting. The mats are usually picked up by the hands and are held vertically. An electric knife or trimmer may be used for harvesting and permitting cut microgreens to drop from the mat into a clean harvest container. Harvested microgreens are highly perishable and should be washed and cooled as quickly as possible. Some chefs request growers to deliver microgreens in the trays or mats as such so that they will incise these as needed to improve quality. Microgreens are washed using good handling practices for food safety reasons. Microgreens are mostly packed in a small, plastic clamshell packages and are then cooled to recommended temperatures for the crops in the mix. Growers must be aware that marketing agreement such as the National Leafy Green Marketing Agreement (NLGMA) has been proposed so as to reduce the risk of microbial contamination of mature and immature leafy greens.

28.6 Microgreen Vs. Sprouts

When anyone says the word "Microgreen," the things that strike our mind are:

1. It's the kid version of the mature vegetables.
2. It's a sprout.
3. It's an appealing and decorative plant.

But among the three, only first the option is the most accurate. Microgreens, divergent to accepted belief, are not the same things as sprouts. Indeed, not only they appear and taste poles apart, but even the way in which they are grown is different. One more difference between the two is that both are technically different at different parts of the cycle (Fig. 28.3).

Fig. 28.3 Sprouts vs. microgreens

Table 28.5 Various dissimilarities between microgreens and sprouts

S. no.	Microgreens	Sprouts
1	Microgreens are grown in soil	Sprouts grow in water
2	Leaves and stems of microgreens are eaten	Seeds of sprouts are eaten as such
3	It takes 1 to 3 weeks for microgreens to grow	Sprouts grow in a week
4	Microgreens are filled with flavor and are frequently used as garnishes	Sprouts are frequently great for crunch

Since all plants begin their journey as a seed. Seeds are embryos that come with a defensive shell particularly termed as the seed coat and inside it are present all essential nutrients and vitamins that are required by plant to burst out of that coating.

Sandwiched between the protective coating and the embryo is that endosperm, which hushes up the embryo and gives the baby nutrition. Now comes sprouts which are germinated seeds. By utilizing the nutrients present in the seed, the embryo develops its stem. Most of the times, people germinate sprouts in water. To make sure that they do not mold, the seeds are bathed once or twice a day. Sprouts grow fast and are harvested just in 4 to 6 days. Since only little amount of light and nutrition is need by sprouts to grow. In addition, they are embedded in fiber, protein, essential nutrients, and enzymes. A considerable amount of humidity is required so that a condition is created in which bacteria thrive in.

According to Foodsafety.gov, there have been at least 30 reported outbreaks of foodborne illness allied with sprouts since 1996 caused by *Salmonella* and *E. coli* (https://www.foodsafety.gov/keep/types/fruits/sprouts.html). The best and simple way to lessen the risk of illness is to cook the sprouts, which, optimistically, will kill all of the bacteria.

Sprouts are nutritional powerhouses that hold a high concentrate of antioxidant nutrients. Microgreens are the outcome of the cotyledon growth stage, becoming the plant's initial set of leaves. These are shaped in the seed and function in similar way as leaves do when it comes to photosynthesis—both change light energy into chemical energy that the plant uses to grow. The leaves and stem can usually be eaten, and the seeds are started in soils or peat moss, as opposed to in water like sprouts.

Microgreens take around 1 to 3 weeks, depending on the plant. They require a plenty of light and good air ventilation. Many studies have also shown that, depending on the variety, microgreens are more concentrated in nutritional value than their mature counter parts (Table 28.5).

28.7 Post-Harvest Storage of Microgreens

Microgreens senesce fast after harvest and have usually a very small shelf life (1–2 days) at ambient temperature, due to the abrupt disruption of plant growth at a very early stage (Guo and Gan 2012; Xiao et al. 2015).

Microgreens that are produced conventionally are highly perishable and are fragile having shelf life of only about 5 to 10 days. This short shelf life of these microgreens is considered to be a major limitation and detriment in the use and marketing of microgreens. So these should be consumed within few days after receiving or have to be discarded resulting in more waste because of loss in color and flavor and begin to rot. On the other hand, regular sized greens such as lettuce have a shelf life of about 14 days. Currently, the blends of microgreens such as beets, broccoli, kale, and radish are sold and used and the most common mixture is known as "Micro Rainbow Mix," and it consists of four to six varieties. The shelf life of the blend depends on the components of blend; in simple words, the component that will rot first will cause whole blend to be unusable even if other components are not rotted. By knowing the shelf life of specific varieties, it is easy to make the blend of these microgreens resulting in longer shelf life and hence profit to the growers, distributors, retailers, and consumers.

28.8 Conclusion

The study done on new specialty crops: Microgreens show that they are juvenile version of green leafy vegetables ranging in size from 1″ to 1 1/2″ including stem and leaves. Microgreens can be eaten as whole and waste is very minute. They have catchy appearance, tender texture, and strong flavor and provide full pack of healthful nutrients. Microgreens are usually more nutrient-dense than their mature counterparts, compared with the records in the USDA National Nutrient Database. They have good consumer acceptability correlated with flavor acceptability. These are perishable and the problem results in case of their post-harvest storage and shelf life. The problems including rotting, foul odor, and premature degradation leads to shorter shelf life and hence, the spoilage of the product. The quality can be maintained by exposing them to low temperature with modified atmosphere packaging. Compared to sprouts, microgreens bear relatively low safety risk.

28.9 Future Work

As the conservative produce lacks the trace minerals our body needs to function, people will start to make links between poor health and lack of nutrient-based foods in their diet. Microgreens are in demand not because of appealing appearance but they have appealing taste as well as have complete pack of nutrients embedded in them. Yet, there is no ready-to-eat microgreens available in the market, therefore it's necessary to develop the ready-to-eat microgreens with best quality, long shelf stability, and ensured safety. Based on the research results on the comparison of *E. coli* growth on sprouts and microgreens, it can be seen that microgreens seem to present a lower food safety risk. As a result, the mechanism of bacterial distribution, attachment, and interaction with the microgreen plants could be further investigated.

Moreover, there will be great demand in the coming years for establishment of such techniques that will keep these products shelf stable. The microgreens need more attention as various physiological and biochemical changes occur during storage. Post-harvest processing and packaging technology advancements will help to keep quality for extended periods of time and improve shelf life. In addition to quality parameters, functional information about microgreens will aid in the selection of the right crop and harvesting at the right time.

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Traditional Food Adjuncts: Sustainable and Healthy Option for Functional Foods

29

Renu Khedkar

Abstract

Food adjuncts include an assortment of items that are consumed as an accompaniment to the staple food and add variety, spice, and crunch to the common menu with standard items. Indian traditional food adjuncts include pickle, chutney (wet and dry), preserves, *wadis*, papad, salads, sauces, etc. Different ingredients such as fruits, vegetables, pulses, oilseeds, spices, and condiments in various types of adjuncts make it difficult to generalize the nutritional importance. Although consumed in small portions, adjuncts play an important role in nutrition and health. The food adjuncts are good sources of functional components, e.g., proteins, vitamins, minerals, and phytochemicals. The ingredients like curry leaves, coriander leaves, mint leaves, green chilies, tomatoes, Bengal gram, black gram, sesame seeds, flax seeds, etc. are rich in bioactive compounds. Bioactive compounds play an important role in human health as antioxidant; they act as antibacterial, antifungal, anti-inflammatory, antiallergic, antidiabetic, anticancer, etc. In the era of functional foods, the knowledge of the medicinal benefits of the food adjuncts can encourage the entrepreneurs to position the products in the global market with their functional benefits.

Keywords

Food adjuncts · Nutritional importance · Functional properties · Bioactive compounds

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29.1 Introduction

Indian cuisine is a varietal spectrum of food cultures having distinctive regional differences and preferences and includes thousands of regional cuisines evolved over thousands of years. All the different Indian regional cooking styles make liberal use of spices, condiments, herbs, vegetables, fruits, cereals, and pulses that result in fascinating, delicious dishes. All families of Indian cuisine are characterized by a wide assortment of dishes and cooking techniques. The extensive movement of population, communication facilities, and impact of media in the last two decades have paved the path toward global food culture, which is a blend of ethnic traditional taste, combined with variety and convenience, resulting in innovative fusion foods.

29.2 Food Adjuncts

Food adjuncts include an assortment of items that are consumed as an accompaniment to the staple food and add variety, spice, and crunch to the common menu with standard items (Khedkar et al. 2016b). Permutations and combinations of the ingredients available in different parts of the country and the cultural traditions are expressed as a group of items, covering a variety of tastes, textures, and consistencies. The traditional food adjuncts are those which have been a part of the cuisine for many generations, the production process for which has been transmitted from generation to generation through oral means or other.

29.3 Global Scenario of Food Adjuncts

The global cuisine includes different cuisines from various regions of the world. These cuisines are characterized by their particular style of cooking practices and traditions associated with the specific region, country, or culture. It includes Japanese cuisine, Chinese cuisine, Thai cuisine, Indian cuisine, French cuisine, Greek cuisine, Italian cuisine, North American cuisine, Mexican cuisine, etc. All of these cuisines relish the adjuncts or accompaniments with the main dish. Some of the examples include salads, sauces, ketchup, dips, gravies, pickles, and condiments.

29.4 Classification of Indian Traditional Food Adjuncts

The classification of Indian traditional food adjuncts is shown in Table 29.1.

Table 29.1 Classification of Indian traditional food adjuncts (Source: Shastri 2006)

Type	Product	Example
Fruit and vegetable products	Pickle	Mango pickle, lime pickle, green chilies pickle, mix pickle (carrot, cauliflower etc.), karaunda pickle, amla pickle, etc.
	Wet chutneys	Coriander chutney, mint chutney, tomato chutney, coconut chutney, curry leaves chutney
	Preserves	Mango preserve, amla preserve
	Dried vegetable products	Stuffed green chilies (*bharwa mirch*), *sandge*, etc.
Products from starchy material	Papad from cooked slurry	Sago papad, potato papad, etc.
	Wadi from fermented and cooked slurry	
	Papad from fermented and cooked slurry	*Sandaya* made from wheat, *jowar* papad and *poha* papad from Maharashtra, papad from South India
	Extruded products from cooked slurry	*Kurdai* from Maharashtra
Legume-based semi-processed products	Rolled papad	Made from black gram or green gram
	Wadi	*Wadi* made from black gram from Punjab and West Bengal, *Wari* made from black gram and soybean from Uttar Pradesh, *Masyaura* from Darjeeling and Sikkim
	Dry chutney powders	Peanut chutney, sesame chutney, flaxseed chutney, curry leaves chutney, *metkut* from Maharashtra

29.5 Nutritional Importance of Food Adjuncts

A wide range of the ingredients such as fruits, vegetables, pulses, oilseeds, spices, and condiments in various types of adjuncts makes it difficult to generalize the nutritional importance. The formulations of the adjuncts also vary according to the region. Locally available ingredients are preferred in the products. Although consumed in small portions, adjuncts play an important role in nutrition and health.

- The pickles and chutneys are very good source of vitamin C and other valuable nutrients such as minerals, carotenoids, isoflavones, and antioxidants.
- The essential oils from spices and condiments enhance the salivation, add pungency, and facilitate the digestion process.
- Powdered chutneys contain pulses and oilseeds, e.g., black gram, Bengal gram, sesame seeds, groundnut, coconut, etc., and are an excellent supplement to the cereal-based vegetarian staple diet for improving the protein quality.

- Legume-based *papad*, *wadis*, etc. add to the protein value of staple diet and can act as a replacement of vegetables/dal in lean season. Fermentation in some *papads* and *wadis* improves the digestibility and reduces anti-nutritional factors. Ingredients like garlic, ginger, spices, turmeric, fenugreek seeds, etc. are known to contain functional constituents like curcumin, isoflavones, and essential oils.

29.6 Functional Properties of Food Adjuncts

29.6.1 Coconut

Coconut (*Cocos nucifera*) belongs to the family of Palmae and plays an important role in the human diet due to the presence of physiologically important functional components. The Philippines is the leading producer of coconut followed by Indonesia and India (Gupta et al. 2008).

The fatty acids present in coconut have health benefits. Natural coconut fat in the diet helps in improving anti-inflammatory response of the immune system. It also normalizes body lipids and protects the liver against alcohol damage. It is a rich source of edible oil and is used as a frying medium. Coconut is also used in the preparations of chutney and curries and is used as shredded coconut, coconut milk, coconut honey, sweetened condensed coconut milk, coconut syrup, etc. Coconut chutney is an essential accompaniment to the traditional South Indian dishes such as *idli*, *dosa*, and *utappam.* It is made by finely grinding the fresh coconut white meat with green chilies, coriander leaves, spices such as cumin seeds, and salt added to it (Amit 2021b).

Mature (190 days) wet coconut meat contains around 67% moisture content, 3% crude protein, 10.2% crude fat, 1.2% crude fiber, 2% ash, and 16.2% carbohydrates. The total phenolic content was reported as 9.84 mg GAE/100 g FW, whereas the % DPPH radical scavenging activity was 77.54%. The main phenolic compounds found in coconut meat are gallic, caffeic, salicylic, and *p*-coumaric acids. The medium-chain fatty acids (MCFA) in coconut meat are caprylic, capric, lauric, and myristic acid (Mahayothee et al. 2016). Ninety percent of the fat in coconut meat is saturated fatty acids. Saturated fatty acids mainly contain up to 60% MCFA and 32% LCSFA. Lauric acid (C12:0) is the most prominent fatty acid in coconut meat. Lauric acid offers more health benefits as it increases more HDL cholesterol and reduces the ratio TC/HDL cholesterol (Ngampeerapong and Chavasit 2019).

29.6.2 Coriander

Coriander chutney is a relished chutney in Indian cuisine and is used as a dipping sauce with Indian snacks. The making of chutney includes grinding of fresh coriander leaves with ginger/garlic and green chilies with salt added to it (Amit 2021a).

Coriander (*Coriandrum sativum*) belongs to the family Apiaceae and is an annual plant. India is the largest producer, consumer, and exporter of coriander with annual production of over 822 thousand metric tons (Statista 2021a). All parts of the plant are used as flavoring and in traditional remedies for treatment of various diseases (Chawla and Thakur 2013). This plant has played a critical role in maintaining human health for thousands of years. It is used to cure digestive tract disorders, respiratory problems, and urinary tract infections. It possesses antioxidant, antidiabetic, antimutagenic, and antispasmodic activities. Its leaves are rich sources of vitamins, e.g., vitamins A (12 mg/100 g) and C (160 mg/100 g), minerals (iron, zinc), and fiber (Sharma et al. 2014).

29.6.3 Mint Leaves

Mint or *Mentha* belonging to the Lamiaceae family is a perennial, popular aromatic herb. It has high economic value and is used in pharmaceutical, food, beverage, confectionery, perfume, cosmetic, and tobacco industries. It is traditionally used as flavoring, fresh vegetable, infusion, decoction, and distillate. Mint chutney is a popular adjunct savored with snacks such as *samosas*, *pakora*, etc. It is prepared by grinding mint leaves, green chilies, ginger, cumin seeds, lime juice, and salt (Amit 2019).

It is also used as breath freshener, carminative, choleretic, anti-infective, anti-inflammatory, antiemetic, diaphoretic, antispasmodic, analgesic, stimulant, emmenagogue, anticatarrhal, diuretic, antiallergic, stomach tonic, and insecticidal agents (Chawla and Thakur 2013b). Mints are used in herbal medicine for treatment of several health problems and discomforts like gastric acidities, aerophagia, nausea, flatulence, vomiting, ulcerative colitis, stomach aches, dyspepsia, diarrhea, jaundice, liver complaints, anorexia, cramps, bronchitis, throat infections, and viral hepatitis. Several bioactivities such as antibacterial, antifungal, antioxidant, anticandidal, pesticidal, insecticidal, antimutagenic, anticancer, calcium channel blocking, cyclooxygenase, and HIV 1 inhibitory properties have been reported for this species. Also, some remedial effects, namely, sedative, spasmolytic, diaphoretic, antipruritic, carminative, antiseptic, choleretic, central nervous system stimulant, antihistamine, diuretic, and hepatoprotective traits, of *M. longifolia* have been verified (Bahadori et al. 2018).

29.6.4 Sesame Seeds

Sesame seeds chutney is a favorite adjunct in the Indian cuisine. It is made by roasting and grinding white sesame seeds, desiccated coconut, red chilies, cumin seeds, and salt (Ramakrishnan 2021).

Sesame (*Sesamum indicum* L.) belonging to the order tubiflorae, family Pedaliaceae, is a herbaceous annual plant cultivated for its edible seed, oil, and flavorsome value. It is also known as gingelly, til, benne seed, and popularly as "Queen of Oilseeds" due to its high degree of resistance to oxidation and rancidity. Sesame seed contains 50–60% of high-quality oil which is rich in polyunsaturated fatty acids (PUFA) and natural antioxidants, sesamin, sesamolin, and tocopherol homologues. These bioactive components enhance the stability and keeping quality of sesame oil along with numerous health benefits. Sesame seeds are considered as valuable foods as they enhance the diet with the pleasing aroma and flavor and offer nutritional and physiological benefits. Recent studies on the antioxidant and anti-carcinogenic activities of sesame seed have greatly increased its applications in health food products that assert for liver and heart protection and tumor prevention. Sesame seed is high in protein, vitamin B1, and dietary fiber as well is an excellent source of phosphorous, iron, magnesium calcium, manganese, copper, and zinc. In addition to these important nutrients, sesame seeds contain two unique substances, sesamin and sesamolin. Both of these substances belong to a group of special beneficial fibers called lignans and have a cholesterol lowering effect in humans and prevent high blood pressure and increase vitamin E supplies in animals.

Sesame seeds possess many health-promoting effects, some of which have been attributed to a group of compounds called lignans (sesamin, sesamolin, sesaminol, and sesamolinol). Sesame seed also contains lignan aglycones in oil and lignan glucosides. Sesame seed is rich in oil and contains high amounts of (83–90%) unsaturated fatty acids, mainly linoleic acid (37–47%), oleic acid (35–43%), palmitic (9–11%), and stearic acid (5–10%) with trace amount of linolenic acid. The seeds are a rich source of antioxidants and bioactive compounds including phenolics, phytosterols, phytates, PUFA, and short-chain peptides. Sesame cake is a rich source of protein, carbohydrate, and mineral nutrients. Sesame seeds have special significance for human nutrition on account of its high content of sulfur amino acids and phytosterols. The antioxidative agents (sesamin, sesamolin, sesamol), their glycosylated forms sesaminol glucosides, and tocopherol make the oil very stable and therefore it has a long shelf life.

Sesame lignans have various pharmacological properties, e.g., antioxidant activity and antiproliferative activity, and are responsible for enhancing antioxidant activity of vitamin E in lipid peroxidation systems, lowering cholesterol levels, increasing hepatic fatty acid oxidation enzymes, and showing antihypertensive effects. Apart from sesame lignans, sesame seed and oil also contain other important biologically active compounds such as vitamin E (Rai et al. 2014).

29.6.5 Flaxseeds

Flaxseeds chutney is a healthy way to introduce omega-3 fatty acids in the vegan diet. It is traditionally prepared by dry roasting flaxseeds and grinding with garlic, cumin seeds, red chilies, and salt (Madhura 2015).

Flaxseeds have been consumed by humans since ancient times. It is known for its medicinal properties. In India, flaxseed is used as food as well as for its health benefits. It has exceptionally high content of ALA, dietary fiber, proteins, and phytoestrogens. The biologically active components, ALA, dietary fiber, and lignan-secoisolariciresinol diglycoside (SDG) are responsible for the potential health benefits (Toure and Xueming 2010). Flaxseeds are a good source of phenolic compounds – flavonoids and phenolic acids—and the richest source of lignans (phytoestrogens). Flaxseeds possess antioxidant, antitumor, and hepatoprotective properties. The phytoestrogens reduce the risk of heart diseases, hormone-dependent cancers, and osteoporosis. Flaxseeds serve as a good source of both soluble and insoluble dietary fiber. It contains 35–45% of fiber and two-third is insoluble and one-third is soluble fiber. Insoluble fiber content of flaxseeds is useful in treatment of constipation and irritable bowel syndrome (Sharma et al. 2015).

29.6.6 Curry Leaves

Khedkar et al. (2019) studied the standardization of curry leaf chutney. The chutney was prepared by using grinding roasted Bengal gram, black gram, dried curry leaves, and spice mix.

Curry leaves (*Murraya koenigii* Spreng) are popular due to its large spectrum of medicinal properties and also because of the use of its leaves for centuries as a natural flavoring agent in various curries and food items. Curry leaves (*Murraya koenigii*) or “Kadipatta” are widely used as a culinary spice in Indian cookery in curries, pickles, and chutneys. The leaves are slightly bitter, cooling, and weakly acidic in taste. The tree is found in tropical and subtropical regions from Sri Lanka, India, China, Malaysia, Australia, and in the Pacific from the Mariana Islands to Vanuatu and New Caledonia. The tree is native to India, Bangladesh, Sri Lanka, and the Andaman Islands which later spread to other parts of the world with Indian immigrants. Curry leaves are known worldwide for their excellent antibacterial, antifungal, antioxidant properties, pesticidal, and nutraceutical potential. Curry leaves are rich in fibers, minerals, and vitamins such as calcium, iron, phosphorus and carotene, niacin, vitamin B_2, and vitamin C. They are a good source of β-carotene. Various bioactive compounds of curry leaves are proven to have many functional properties, e.g., antioxidant, antimicrobial, antitumor, antidiabetic, and hypercholesteremic. The functional compounds of curry leaves include oxalic acid, vitamin A, koenigin, bicyclomahanimbicine, cyclomahanimbine, murrayastine, coumarine, koenidine, and pypayafolinecarbazole imparting nutraceutical potential to the leaves. Bioactive compounds of curry leaves like carbazole alkaloids and essential oils are proven to have many functional properties like antioxidant, antimicrobial, antitumor, antidiabetic, hypercholesteremic, and many more (Khedkar 2015).

29.6.7 Peanut

Peanut chutney is prepared by using roasted Bengal gram, peanuts, curry leaves, garlic, cumin seeds, green chilies, salt, and tamarind or lemon juice (Swasthi 2020).

Ground nut or peanuts are rich in proteins, fat, and fiber. India is the largest producer of peanuts having estimated production of more than nine million metric tons in the year 2021 (Statista 2021c). They are good sources of proteins composed of essential amino acids, resveratrol, vitamin E, B complex, and minerals. Peanuts contain good amount of monounsaturated fatty acids and polyphenol content (Chandrasekhar et al. 2015). Because of the high nutritive value, they are used for the elimination of malnutrition in many African countries (Guimon and Guimon 2012).

29.6.8 Cumin Seeds

The seed of *Cuminum cyminum* is native to the Mediterranean region and is mentioned in Indian literature after about 300 BC (Achaya 1998). Cumin (*Cuminum cyminum* L.) belongs to the family Apiaceae. It is the dried, white fruit with grayish brown color of a small slender annual herb. Cumin seeds have an aroma and bitter taste. It is used as a condiment and is an ingredient in curry powders like garam masala, sambhar masala, chat masala, etc. It is also used in meat products, condiments and relishes, processed vegetables, soups, gravies, snack foods, seasonings of breads, cakes, and cheese. It is employed in native dishes of Central and South America. In Mexican cooking, cumin seed or oil is mixed with chili and added to chili powders and pepper sauces. Cumin seed is used as stimulant, antispasmodic, carminative, and antimicrobial agent. It is widely used in traditional medicine to treat flatulence, digestive disorders, and diarrhea and for treating the wounds. In India, it is used to relieve mental stress and lower blood pressure. It relieves menstrual cramps, promote breast milk secretion, and stimulate circulation. It is a diuretic and is used as immunostimulant against viruses harming the spleen and liver (Charles 2013). It is shown to have antidiabetic and anticancer activity (Nalini et al. 1998; Jagtap and Patil 2010). Cumin extract and essential oil has been shown to possess antioxidant activity (El-Ghorab et al. 2010; Thippeswamy and Naidu 2005).

29.6.9 Bengal Gram

Bengal gram is known in this country since ancient times. It is said to be one of the oldest pulses known and cultivated in Asia and Europe. Bengal gram (*Cicer arietinum* L.), also called chickpea, gram, or chana dal in Hindi, is a major pulse crop in India. It accounts for nearly 49% of the pulse production in India. India is the largest producer of this crop. It is widely used as a health food supplementing protein to the cereal-based diet in India. It helps in reducing bad cholesterol in the blood, improves immunity, and helps in preventing stroke, dementia, and depression. It is an important ingredient in wet or dry chutneys, *papad* (flat, thin rolls), *wadis* (dried balls), and *pakoras* (fried snack). Khedkar et al. (2016a) standardized the process of preparation of *Metkut*, a popular chutney powder of Maharashtra region of India. It is prepared by grinding roasted Bengal gram, black gram, rice, and spices.

29.6.10 Black Gram

Black gram or *Urad* bean (*Vigna mungo* (L.) Hepper) is one of the most important cultivated pulse crops of the "Vigna" group. It is cultivated since prehistoric period in India and considered to be originated from *Vigna silvestris*. Archeological studies have shown that black bean was cultivated in the country as far back as 2200 BC. Major portion of black gram is utilized in making dal, for curries, soup, sweets, and snacks. *Papad* made from black gram is a popular adjunct all across India. In South India, the most popular idli and dosa are prepared using mixed proportions of rice and black gram. The food values of black bean lie in its high and easily digestible protein. Used extensively in South Indian cuisine, black gram is a rich source of protein, potassium, vitamin B, calcium, iron, niacin, thiamine, and riboflavin. It is useful for improving reproductive health and gut health, healing swollen tissues, has antidiabetic and antihypertensive properties, is diuretic, and helps in maintaining heart and bone health (https://www.netmeds.com/health-library/post/black-gram-nutrition-therapeutic-benefits-uses-for-skin-and-hair).

29.6.11 Green Chili

Chili (*Capsicum* sp.) is a dicotyledonous flowering plant and belongs to the Solanaceae family. It is used in human diet all over the world as a spice, condiment, and vegetable since ages. India is the largest producer of chilies. Green chilies are used in pickle, chutney, stuffed dried chili, etc. Capsaicin, which is responsible for the pungency of chilies, is the main bioactive compound present in it. Chilies are used in the management of arthritis pain, herpes zoster-related pain, diabetic neuropathy, mastectomy pain, and headaches and lower blood sugar levels, heal intestinal problems such as ulcers, boost immunity, improve heart health, and protect against stroke. It also has anticancer properties and has been shown to kill prostate cancer cells in human studies.

Fresh green and red chilies are great source of vitamin C. Chili contains good amount of other antioxidants such as vitamin A, B complex group of vitamins such as niacin, pyridoxine (vitamin B6), riboflavin, and thiamin (vitamin B1) and flavonoids like β-carotene, α-carotene, lutein, zeaxanthin, and cryptoxanthin. Chili also contains minerals like potassium, manganese, iron, and magnesium (Chakrabarty et al. 2017).

29.6.12 Tomatoes

Tomato (*Solanum lycopersicum* L.) fruit is an integral part of cuisines all across the world and also serves as a staple food for many nations. The cultivated world area and the total production of tomato during 2018 were 4.76 M ha and 182.25 Mt., respectively. Tomatoes are used in chutney and sauces. Tomato ketchup is a very widely used adjunct in different cuisines. Being a rich source of vitamins, minerals, phenolic content, flavonoid groups, dietary fibers, proteins, and a large number of antioxidant compounds, tomato helps us effectively in fighting against many types of cancer and reduces the risk of developing hypertension and other cardiovascular diseases. Tomato is one of the rich sources of natural antioxidants. Therefore, the beneficial properties of tomatoes are mainly attributed to a diverse range of antioxidative, chemopreventive, and antiproliferative activities of its dietary antioxidants. Tomatoes also contain valuable phytochemicals, including carotenoids and polyphenols. For instance, carotenoids, such as the red pigmented lycopene; β-carotene, a provitamin A compound; phytoene; and phytofluene are all found in abundance in raw tomatoes and tomato products. Flavonol content of tomatoes is also high, with up to 98% of the total flavonols contained in the skin as the conjugated forms of quercetin and kaempferol (Erdman et al. 2005).

29.6.13 Amla

Amla (*Phyllanthus emblica*) or Indian gooseberry is a wonder fruit for mankind. It contains protein, carbohydrate, minerals, fiber, and vitamin C. It is the most concentrated form of vitamin C in all the plants and the fruit is easily assimilated by the human body (Nisha et al. 2004; Gopalan et al. 1991). In India, the plant is considered medicinal and sacred and is used extensively in Ayurveda for preparation of medicines. It has high tannin content, which is responsible for its antioxidative property. *Amla* also contains gallic acid, a potent polyphenol, and has been found to improve immunity. It is also a rich source of pectin, an important form of dietary fiber. *Amla* helps in digestion, absorption, and assimilation of food; strengthens the liver, heart, and lung function; nurtures the reproductive system; and is good for the skin, hair, and eyes. Amla fruit is a powerful antioxidant and antidiabetic and has anti-inflammatory, anti-pyretic, anticancer, and anti-ulcer properties (Sharma et al. 2011). Amla is used in pickle, chutney, juice, candy, powder, and *murabba* (preserve).

29.6.14 Mango

Mango (*Mangifera indica* L.) is a king of tropical fruits and is known for its exotic flavor, succulence, and delicious taste. It is a good source of vitamin A, B, and C and is rich in bioactive compounds responsible for its health-promoting properties. Mango has its origin in India and its annual production in 2021 is estimated to be 20.9 million metric tons (Statista 2021b). Polyphenols present in the fruit provide the protective effects in the human body. The main phenolics present in mango are catechin, epicatechin, quercitrin, quercetin, gallic acid, mangiferin, and others. The mango fruit extract has shown to have antitumor activities in various cancer cell lines, including leukemia, breast, cervical, colon, lung, and prostate cells, among others (Ali et al. 2012). It has also shown to possess anti-hyperlipidemic, antidiabetic, and anti-inflammatory activity. In India, green mangoes are used as pickles and chutneys. They are made from peeled or unpeeled fruit with or without stones and with different proportions of spices (Ravani and Joshi 2013).

29.7 Market Potential of Traditional Food Adjuncts

Indian food processing industry is one of the largest in the world and its turnover is expected to reach USD 535 billion by 2025–2026 (IBEF 2020). Although the volume is difficult to assess, the traditional food processing industry is very widely spread in the urban as well semiurban areas in India. The industry works mainly in the unorganized sector. Multinational companies like Nestle, Haldiram's and Bikano have made entry in the sector. The sector is seeing exponential growth due to the changing lifestyle and entry of bigger players. The easy availability of labor and the growing demand for the products have proved to be a boon for the traditional food processing industry. Changing consumer choices and developments in packaging have made the local entrepreneurs brace new technology and compete with the established players in the sector.

29.8 Future Scope

Traditional food adjuncts are highly nutritious and well accepted to the people as generations have relished it. Growing urbanization, rise in the income levels, and increasing women workforce have been the reasons behind the high growth of the Indian food processing sector. The sector is still poised for high growth due to various initiatives like foreign investments, joint ventures, subsidy, skill enhancement, technology upgradation, and export promotion.

Increasing demand for nutritional packaged food and fortifying it with essential nutrients will drive the growth of the industry in future.

29.9 Conclusion

Food-based approach to combat and deal with health problems is a sustainable and practical approach. The traditional Indian diet is rich in functional components. The food adjuncts like pickles, chutney, papad, sauces, *wadis* spices, and condiments are an integral part of the food culture. The adjuncts prepared with fruits, vegetables, oilseeds, cereals, pulses, and spices are rich in functional components, e.g., proteins, vitamins, minerals, and phytochemicals. The ingredients like curry leaves, coriander leaves, mint leaves, green chilies, tomatoes, Bengal gram, black gram, sesame seeds, flax seeds, etc. are rich in bioactive compounds. Bioactive compounds play an important role in human health as antioxidant; they act as antibacterial, antifungal, anti-inflammatory, antiallergic, antidiabetic, anti-cancer, etc.

With the upsurge in the use of natural products since the past years, there is a need for scientific data supporting nutritional and medicinal benefits of the food adjuncts prepared in different parts of the country with various formulations. These products having health benefits will generate opportunities for export in the international market. Also, the traditional food processing industry has provided livelihood to the local population. Rise in the growth of this industry will generate more revenue and employment opportunities for the people.

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Functional Fermented Foods

30

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Abstract

In the last few years, functional foods have been in the limelight especially among the healthiness and wellness groups. They are also referred to as nutraceuticals and remain extremely nutritious. They are associated with many significant health benefits. For instance, they help in preventing nutritional deficiencies and diseases and also promote adequate growth and development. Fermented foods are foods that are made by the help of microbes under controlled growth. These foods also undergo change of certain components by enzymatic action. In the last few years, fermented foods have encountered a high in their popularity, majorly due to their well-being benefits. When considered alongside, an increase in the amount of evidence expresses the potential of inclusion of fermentation with functional foods, for the benefit of consumers, like promotion of cognitive health development. The chapter contains an in-depth knowledge about fermented functional foods.

Keywords

Fermentation · Nutritional deficiencies · Microorganisms · Probiotics

30.1 Functional Foods

In addition to their nutritional value, the ingredients in functional foods have health benefits. Supplements and other health-promoting components are included in some varieties. Fortification with vitamins, minerals, probiotics, or fibre comes under this

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category. Oats, for example, comprise a kind of fibre called beta glucan, which reduces inflammation, enhances immune system, and makes healthy heart. Likewise, fruits and vegetables filled by antioxidants, which are helpful compounds that defend against disease, also find their way into this category of foods (Bagchi 2008; Ohama et al. 2006).

Functional foods are divided into two groups: conventional and modified.

30.1.1 Conventional Functional Foods

Ingredients of natural and whole foods are rich in key elements including vitamins, minerals, antioxidants, and healthy fats especially with respect to heart. Such foods make up conventional functional foods.

They include the following:

- Fruits like apples and berries.
- Vegetables like broccoli, kale, and zucchini.
- Nuts like almonds and pistachios.
- Seeds of hemp, pumpkin, chia, and flax.
- Legumes like black beans and navy beans.
- Whole grains including oats, brown rice, and buckwheat.
- Seafood especially salmon, sardines, and anchovies.
- Traditional fermented foods like tempeh, kefir, etc.
- Herbs, spices, and condiments like cayenne pepper.
- Beverages like green tea.

30.1.2 Modified Functional Foods

Modified functional foods, on the other hand, are foods fortified using additional supplements like vitamins, probiotics, minerals and/or fibre to boost the health benefits of the food.

They include:

- Fortified juices.
- Fortified dairy products, like milk.
- Fortified milk alternatives, including almond, rice, coconut, and cashew milk.
- Fortified grains like bread and pasta.
- Fortified cereals and granola.
- Fortified eggs.

Consuming them (both conventional and fortified functional foods) abundantly in your diet helps in fulfilling the nutritional requirements and protecting against nutrient deficiencies (Cencic and Chingwaru 2010; Mazza 1998). Many functional foods tend to be high in antioxidants, which neutralise dangerous components called free radicals, preventing cell damage and chronic ailments like heart disease. Omega-3 fatty acids, a fat which is healthy and has been demonstrated to lower inflammation, improve brain function, and support heart health, are found in some functional foods. Other varieties are high in fibre, which helps to control blood sugar levels and protects against diabetes, obesity, and stroke. Fibre may also help prevent digestive disorders like diverticulitis, haemorrhoids, and acid reflux (Lobo et al. 2010).

30.2 Fermentation

Fermentation is among the oldest biotechnologies, being used for improving shelf life and producing food products with desirable properties such as good organoleptic properties to make foods both useful and therapeutic. Final product acquired post fermentation usually have a better stability and safety with respect to microbes, increased nutritional value, better digestibility, and enhanced palatability for consumers (Dimidi et al. 2019)

Fermentation is thought to play a number of important roles, including:

1. Forming of inhibitory metabolites like organic acid.
2. Reduction in the water activity.
3. Improvement of safety of food through inhibition of pathogens.
4. Removal of compounds that are toxic.
5. Enhancing the nutritional value.
6. Increasing organoleptic quality of the food.

Fermentation, using a biological standpoint, is a *metabolic process* for obtaining energy derived from organic substances without the use of an exogenous oxidising agent. Fermentation serves a variety of purposes in the food industry.

The everyday groups of microbes associated with food fermentation are bacteria, yeasts, and moulds. Lactobacillaceae (LAB) are the most significant bacteria in food fermentation because they can create lactic acid from carbohydrates (Kim et al. 2016). Other important bacteria include the acetic acid producing *Acetobacte*r and *Bacillus* species.

In terms of favourable food fermentation, yeasts from the *Saccharomyces* family, particularly *S. cerevisiae*, are advantageous. Yeasts are important in the food industry because they produce enzymes that aid in the formation of beneficial biochemical processes such as wine, beer, and ethanol, as well as bread leavening. However, lactic acid bacteria (LAB) are the most widespread microbes found in fermented foods (Maicas 2020).

Their vital importance is related with their physiological characteristics such as substrate utilisation, metabolic capabilities, and probiotic properties. Their acceptance as GRAS (generally recognized as safe) for human consumption is aided by the fact that they have a long history of use and occur frequently and abundantly today as well.

Fermentation of foods has been pursued since many decades all around the world, owing to their commercial relevance in terms of flavour and nutrition. Recent evidence of fermented foods' health advantages, which go beyond their historically acknowledged effects on the digestive system, has spurred their increased use.

30.3 Fermented Functional Foods

One of the oldest traditional processes involved in conserving food is fermentation. In the evolving realm, the significance of fermented foods cannot be overestimated (Blandino et al. 2003; Nyanzi and Jooste 2012).

Fermentation has long been used to extract various products from various cereals in various parts of the world. Fermentation of food has a number of advantages, including energy savings during matrix processing, desirable biochemical changes for nutritional enhancement, food safety, product shelf life, and increased sensory qualities (Guyot 2012).

There are fermented foods with the use of different bacteria that have been developed all around the world depending on regions and culture. Table 30.1 represents examples of such foods.

30.3.1 Tempeh

Tempeh is a conventional food from Indonesia, gotten from two progressive fermentations involving soybeans as a substrate. Fermentation using bacteria during soaking of cooked shelled soybeans is followed by solid-state fermentation of the seed mass by the mould *Rhizopus oligosporus*. Tempeh has been effectively delivered from *L. albus*, *L. angustifolius*, and combinations of both with soybeans. Indonesian buyers love the flavour of lupine-based tempeh yet frequently notice that the surface is excessively firm. Freshly made tempeh is a cake-like item, totally engulfed and pervaded with white mycelium, and has a clean yeasty smell. When cut and seared, it tastes really nutty, it has a charming smell, and the surface is crunchy, filling in as a fundamental course or as a meat substitute. Tempeh is observed as a rich source of vitamins, protein, antioxidants, and other gainful bioactive substances. There are numerous components of tempeh fermentation, including pH, temperature, and chemical composition of the soybean substrate. All of those are added by growth of microbe and enzymatic actions. All through the preliminary level of fermentation, the mould spores are allowed to germinate, and the temperature of the mass increases step by step. Later, the mould growth reaches at the top rapidly and afterwards starts to reduce step by step. Temperatures as high as 45–46 °C have been recorded at the top. At this time, the soya beans are now joined right into a solid mass with the aid of using mould mycelia, and the tempeh is prepared to be reaped. Further than this level, the mould sporulates and NH_3 is formed because of protein breakdown. Microorganisms produce various enzymes that break down soybean components as they grow. There is an improvement in free amino acid stages, a slight decrease in

Table 30.1 Common fermented functional foods worldwide and their fermentative bacterial species

Name	Origin	Microorganism involved	Fermentation base
Acidophiline	Russia, Ukraine	*Lactobacillus acidophilus*	Milk
Appam	India	*LAB*	Rice
Angkak	Philippines	*Monascus purpureus*	Rice
Beer	Semi nomadic times	*Yeast*	Grains and hops
Blaand	Scotland	*Bacillus*	Whey
Bread	Europe	*S. cerevisiae*	Wheat
Brem	Indonesia	*Rhizopus oligosporus*	Rice
Buttermilk/ Lassi/Chaas	India	*LAB*	Milk
Calpis	Japan	*LAB*	Yoghurt
Cheese	Kuyavia, Poland	*Mucor miehei* and *Cynara thistle* family	Milk
Cheonggukjang	Korea	*Bacillus subtilis*	Soya bean
Chicha	Latin America	*S. cerevisiae*	Maize
Cincalok	Malaysia	*LAB*	Shrimp
Curtido	Central America	*Lactobacillus*	Cabbage
Dayok	Philippines	*B. licheniformis*	Tuna
Dhokla	Gujarat, India	*Lactobacillus*	Rice and chickpea splits
Doenjang	Korea	*Aspergillus oryzae*	Soya bean
Doogh	Iran	*Lactobacillus*	Yoghurt
Dosa	India	*Lactobacillus*	Rice and black lentils
Fermented bean curd	China	*LAB*	Tofu
Fish sauce	East Asia	*Halanaerobium*, *Bacillus*, and *Tetragenococcus*	Fish
Ganjang	Korea	*Debaryomyces*, *Tetragenococcus*, and *Staphylococcus*	Soya bean
Garri	West African	*LAB*	Cassava tubers
Gundruk	Nepal	*Lactobacillus plantarum*	Brassica family
Idli	India	*L. mesenteroides*	Rice
Kefir	Russia	*Lactobacillus kefiranofaciens* and *Saccharomyces turicensis*	Milk
Kenkey	Ghana	*Lactobacillus fermentum* and *S. cerevisiae*	Maize
Khanom chin	Thailand	*Bacillus subtilis*	Rice

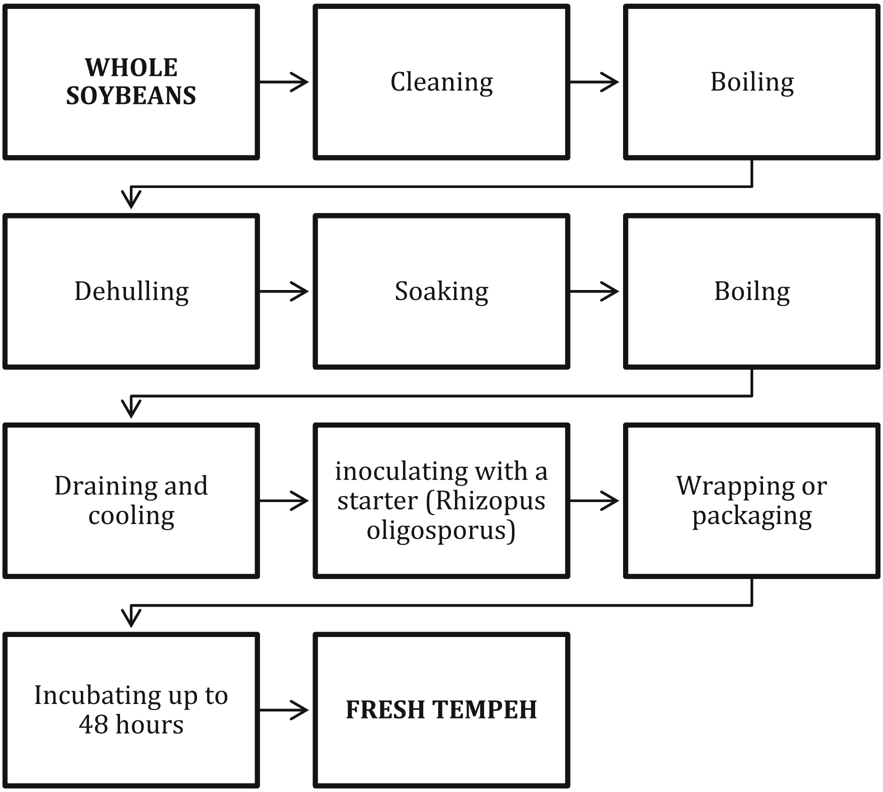
(continued)

Table 30.1 (continued)

Name	Origin	Microorganism involved	Fermentation base
Kimchi	Korea	*Leuconostoc*	Cabbage or radish
Kombucha	China	*Acetic acid bacteria*	Tea
Kvass	Russia	*Saccharomyces cerevisiae* and *Leuconostoc mesentericus*	Rye bread
Lufu	China	*Aspergillus oryzae*	Bean curd
Mageu	Southern Africa	*LAB*	Maize
Meigan cai	China	*Lactobacillus*	*Brassica* family
Miso	Japan	*Aspergillus oryzae*	Soya bean
Nata de piña	Philippines	*Komagataeibacter xylinus*	Pineapple juice
Nattō	Japan	*Bacillus subtilis* var. *natto*	Soya bean
Salami	Italy	*Staphylococcus xylosus* or *Micrococcus*	Pork
Sauerkraut	German	*Leuconostoc*, *Lactobacillus*, and *Pediococcus*	Cabbage
Sour cabbage	Germany	*Leuconostoc mesenteroides Brassica oleracea* var. *capitata*	Whole cabbage
Soy sauce	Korea, Japan, China, Taiwan, Philippines, Indonesia	*Aspergillus sojae*, *Saccharomyces rouxii*, and *Pediococcus halophilus*	Soya bean
Stinky tofu	China, Hong Kong, Taiwan	*Lactobacillus*	Tofu
Tempeh	Indonesia	*Rhizopus oligosporus*	Soya bean
Vinegar	Greek, Rome	*Acetobacter*, *Gluconacetobacter*, *Gluconobacter*	Fruits/malts/ alcohol
Wine	china	*Saccharomyces cerevisiae*	Grapes
Yakult	Japan	*Lactobacillus paracasei*	Milk
Yoghourt	Turkish	*Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus*	Milk
Chakuli pitha	India	*Enterococcus and Lactobacillus*	Rice and black gram

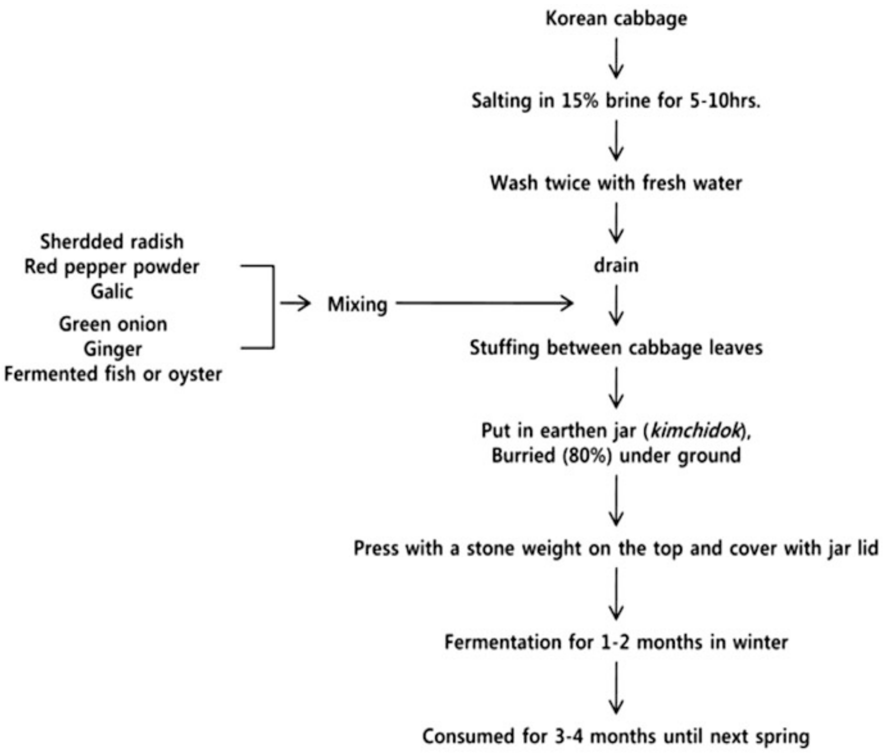
Sources: Bourdichon et al. (2012), Farnworth (2008), Marsh et al. (2014) and Macori and Cotter (2018)

oil content, and no change in protein and ash levels. Furthermore, the content of various vitamins, such as riboflavin, nutrition B6, pantothenic acid, nicotinic acid, biotin, and folacin, has increased significantly (Nout and Kiers 2005; Shurtleff and Aoyagi 2001).



30.3.2 Kimchi

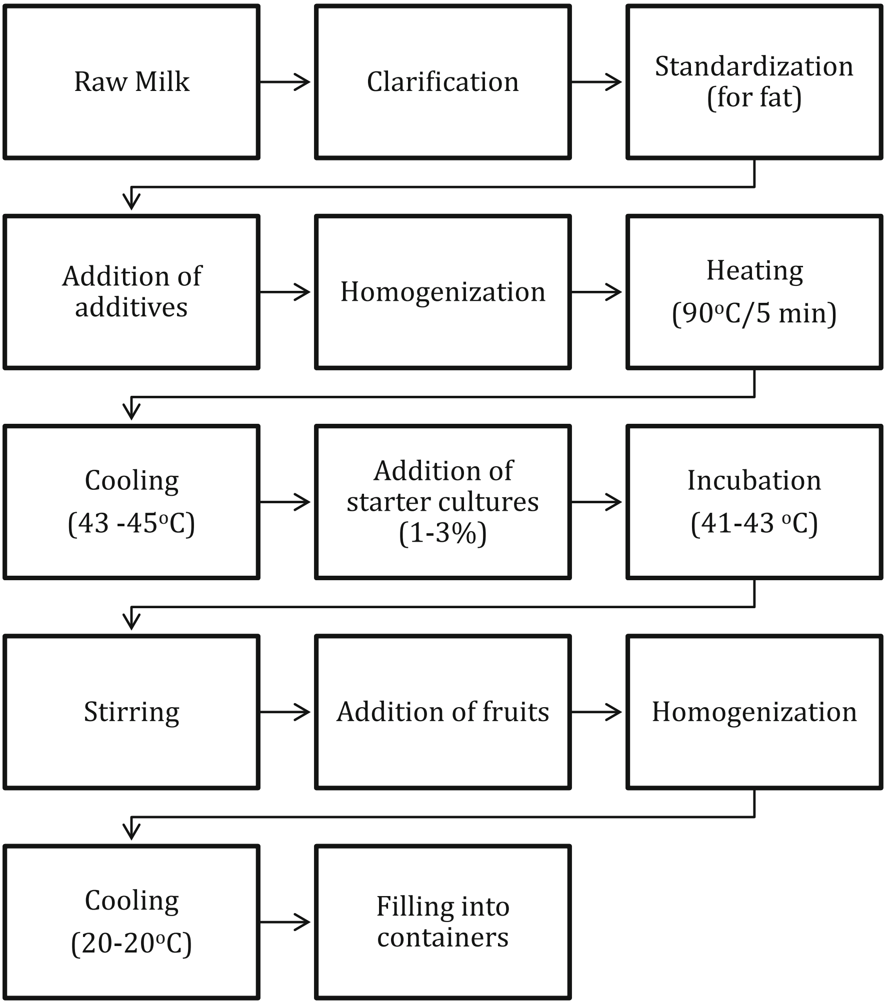
Kimchi is a customary Korean fermented vegetable. The main ingredient is Chinese cabbage. Ginger, radish, and garlic are used as side dishes. Add salt and red pepper powder and ferment the pulp for 40–60 days, typically in cold weather. Many LABs were isolated from kimchi and contained *Leuconostoc citreum*, *Weissella confusa*, and *Lactobacillus* spp. Many biochemical changes occur during the fermentation of kimchi, producing flavoured composites and altering the feel of vegetables. A firm and chewy texture is extremely desirable for the vegetable ingredients of kimchi. As evidenced by the many components of kimchi, kimchi is a significant source of vitamins such as vitamin B group, beta-carotene, ascorbic acid, and their precursors. Kimchi is also a worthy source of dietary fibre. Ingestion of kimchi looks to have a lipid-lowering effect on humans as well. Certain of the raw vegetables utilised in kimchi, like cabbage, perilla leaves, parsley, pepper leaves, red pepper, and garlic, are tested in an in vitro test system and have been shown to be antimutagenic. Kimchi extract has shown anti-carcinogenic effects in animal experiments. This may be due to the strengthening of the host's immune system or the ability of kimchi to influence the metabolism of mutagens. Furthermore, LAB produced from kimchi was found to block the attachment of *Helicobacter pylori* to human gastric epithelial cell lines and prevent the development of *H. pylori* in vitro (Jung et al. 2014)



30.3.3 Yoghurt

Yoghurt is a popular fermented dairy product that contains both *Lactobacillus bulgaricus* and *Streptococcus thermophilus* cultures. Yoghurt contains probiotics, which are live bacteria that can help keep the intestines healthy. It is usually created from milk that has undergone spontaneous or induced lactic acid fermentation. Calcium, vitamins B6 and B12, riboflavin, potassium, and magnesium are all found in yoghurt. The amounts vary according to the category. Basically, yoghurt can be divided into two groups called standard cultured yoghurt and organic yoghurt, or functional or probiotic yoghurt (Kok and Hutkins 2018; Stanton et al. 2005; Yildiz 2016).

Standard yoghurt is usually made from the traditional starter culture strain, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. On the other hand, organic yoghurt, which is a functional or probiotic yoghurt, is complemented by probiotic bacteria like *bifidobacteria* and *Lactobacillus acidophilus*. These are considered to provide numerous health benefits and must survive after ingesting sufficient amounts (Tamime and Deeth 1980).



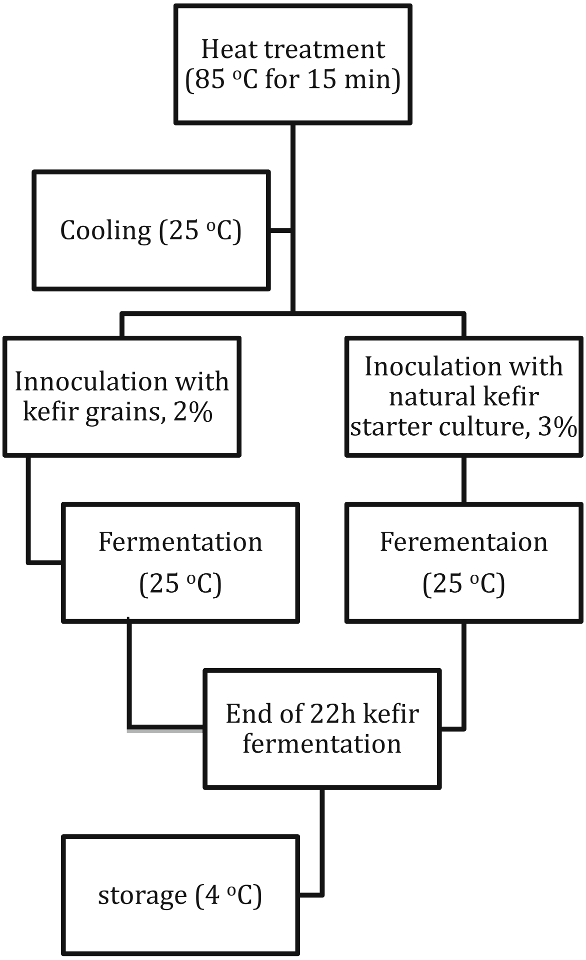
30.3.4 Kefir

Kefir is a fermented milk beverage made by bacteria and yeasts living in a symbiotic relationship in kefir grains. Acid, ethanol, and CO_2 are the major results of kefir fermentation, giving this beverage its viscosity, acidity, and low alcohol level. Minor components such as diacetyl, acetaldehyde, ethyl, and amino acids can also be present, contributing to the flavour composition. This drink is distinct from other fermented dairy products in that it is not the consequence of one or a few bacteria species' metabolic activities. The abundance of probiotic bacteria in kefir consumers' guts has been linked to improved health; as a result, it has been proven that the cell-free fraction of kefir improves the ability to digest lactose, alleviating symptoms (Istrati et al. 2018).

Another explanation for the growing interest in kefir-derived probiotic strains is that it lowers cholesterol levels.

There are alternative ways during which bacteria can adjust serum cholesterol:

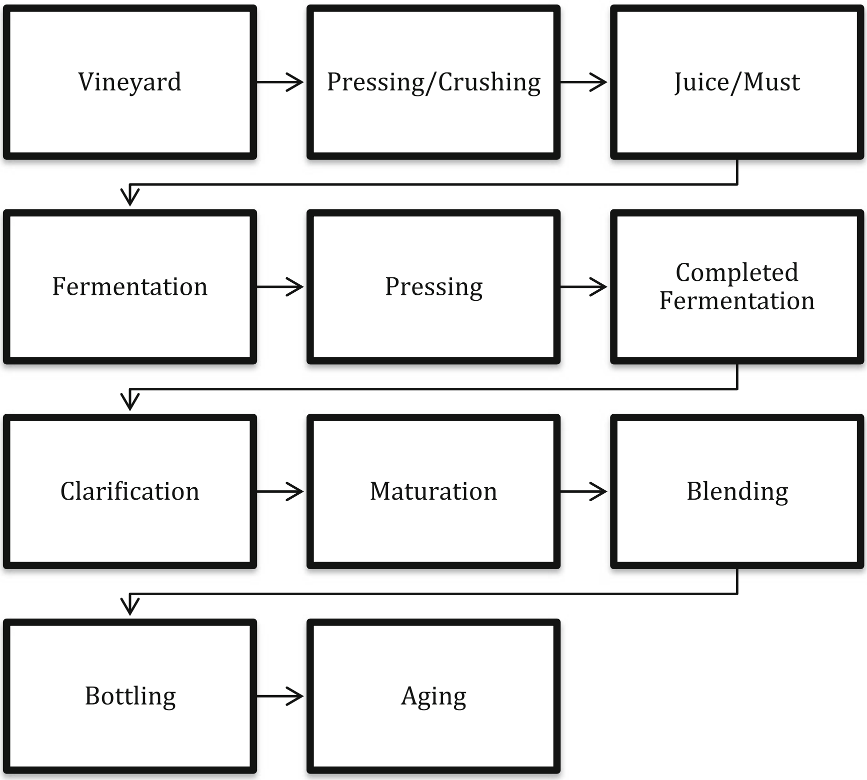
1. Through the binding to and absorption into the cell before it are often absorbed into the body.
2. Producing free and conjugated bile acids.
3. Inhibiting the enzyme HMG-CoA reductase (Leite et al. 2013).



30.3.5 Wine

Wine is an alcoholic beverage prepared from grape juice that has been fermented. Other fruits, berries, and vegetables can also be fermented to produce wine. Wines come in a variety of colours (red, white, and rose) and styles, including dry and sweet, still and effervescent, and grape spirit-fortified wines (brandy). Wine coolers, as well as peach, kiwi, and strawberry wines, are among the wine-based beverages available. There are far too many different types of wine to fulfil a wide range of individual tastes, and wine can be paired with a wide range of foods based on personal preferences and circumstances. The majority of table wines are dry in the technical sense, meaning that all of the sugar has been fermented off. Because of its fruit flavours, wine can be sweet in the tongue, and many kinds, such as chardonnay, shiraz, and zinfandel, have a sweet fruit dimension. Yeasts, particularly *S. cerevisiae*, have been utilised to make alcoholic beverages.

Pre-fermentation, fermentation, and post-fermentation operations are the three basic processes in winemaking. When grapes are used to make wine, pre-fermentation entails smashing the fruit and releasing the liquid. The juice is separated from the skin in white wine, while the skins are not separated from the juice in red wine. Sedimentation or centrifugation is commonly used to clarify white wine juice. The clarified juice is then inoculated with yeast to begin the fermentation process. The pulp, skins, and seeds of grapes are retained together after crushing and throughout the fermentation process in red winemaking. This is done to extract the flavour and colour of the food. In the production of red wine, yeast is added to the mashed pulp (must) (Zoecklein et al. 2013).

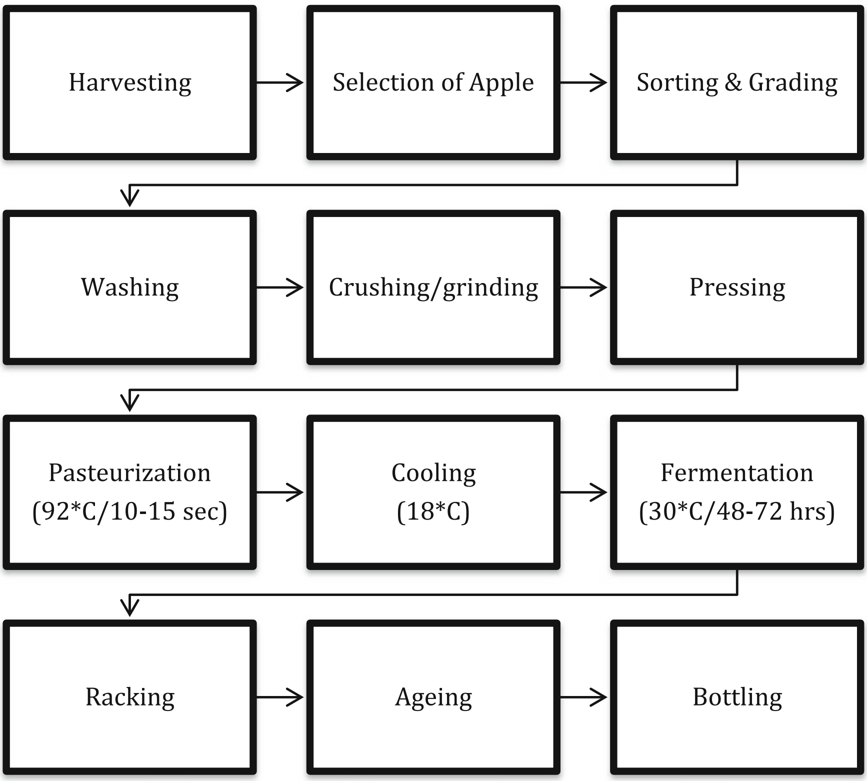


30.3.6 Cider

Cider may be a low alcohol made up of apple juice by alcoholic fermentation. Cider is a substitute term for cyder, while both words have been in use since at least 1631, including in Australia. However, in certain locations, the terms cyder and cider are used interchangeably: cyder is often apple juice or a non-alcoholic beverage, whereas cider is an alcoholic beverage (apple juice). In England, the fermented juice is known as cider, but in the United States, it is known as cider. Fermented apple juice is known in Europe as cider (France), sidre (Italy), sidra (Spain), or applewein (Germany and Switzerland), while the similar unfermented product is known as apple juice. Cider can be either a soft (1–5% alcohol) or a harsh cider, depending on the alcohol content (6–7%).

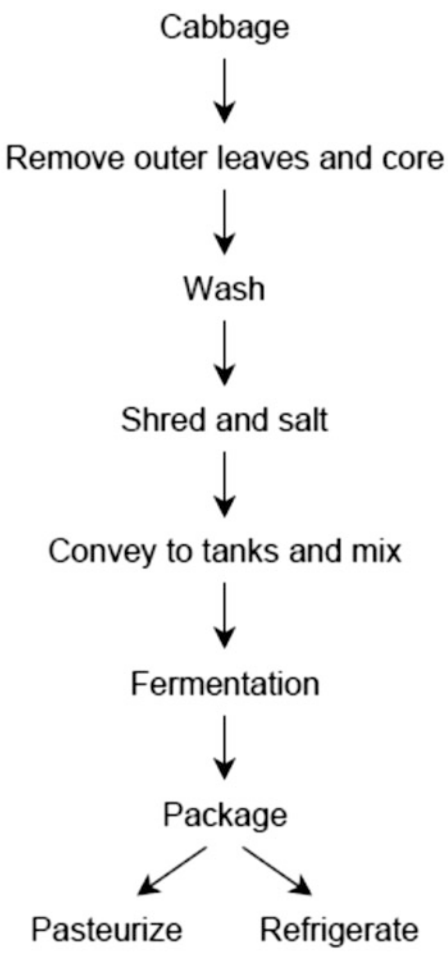
30.3.6.1 Cider Making Methods

The flowchart depicts a general procedure for manufacturing cider. It's a posh process that combines two biological fermentations: the first is the traditional alcoholic fermentation of sugar into alcohol carried out by yeast strains such as *S. cerevisiae*, and the second is the malolactic fermentation carried out by lactic acid bacteria during the maturation process. The latter is an important manufacturing process that reduces the acidity of the cider while also stabilising it against microbial spoilage thanks to the bacteriostatic impact of the lactic acid produced. At laboratory and consumer survey scales, cider with 5% alcohol and a TSS/acid ratio of 25 was shown to be the most popular (Vidrih and Hribar 1999).



30.3.7 Sauerkraut

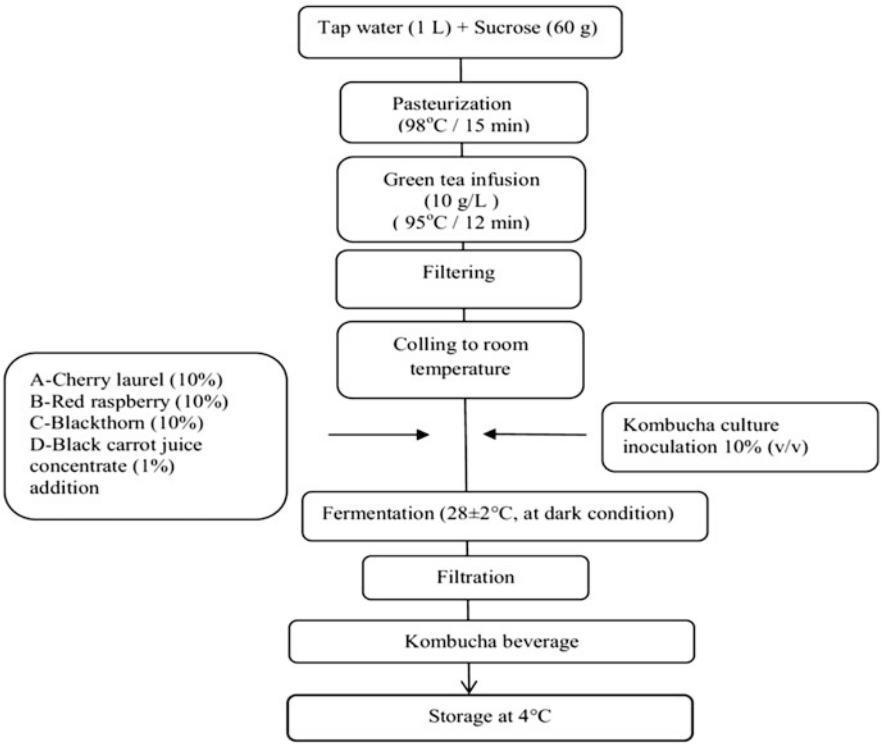
Sauerkraut presently is a product of lactic acid fermentation of shredded, salted white cabbage (*Brassica oleracea* var. *capitata* f. *alba* L.). Sauerkraut is one of the few fermented foods that appear to be made in such a straightforward manner. Only two ingredients are required: cabbage and salt, and if they are properly combined, the producer has little to do until the fermentation is complete. The US Standards reflect the method's simplicity, stating that sauerkraut is a "product of characteristic acid flavour, formed by the entire fermentation of shredded cabbage in the presence of not less than 2% nor more than 3% of salt". Sauerkraut should have no more than 1.5% acid after fermentation (expressed as lactic acid). The selection of the raw substrate material is the first step in the production of sauerkraut. Although there are many different cabbage cultivars, white cabbage is most commonly utilised since it has a mild, somewhat sweet flavour and contains at least 5% fermentable sugars (mostly equimolar amounts of glucose and fructose, with a little amount of sucrose). Cabbage that will be used to create sauerkraut should be fully ripe with few outside leaves. For a day or two, some manufacturers allow the cabbage heads to wilt (Holzapfel et al. 2003; Zakhia-Rozis 2014)



30.3.8 Kombucha

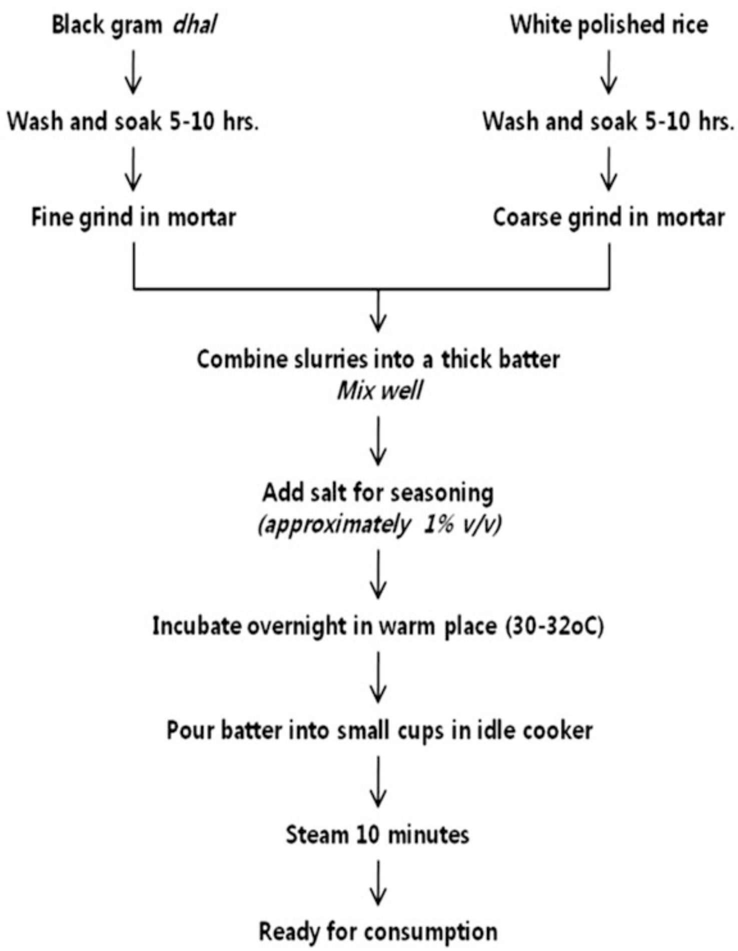
Originally, the traditional drink was produced by fermenting sweetened black tea (*Camellia sinensis*). Other teas, on the other hand, can be used to make it. A symbiotic colony of bacteria and yeasts established during the cellulose film fermentation produces tea. SCOBY is the name of this cellulose film (Symbiotic Colony of Bacteria and Yeasts). Tea fungus or kombucha mother are two more names for it. Bacteria oxidise alcohol and produce ethanoic acid, whereas osmophilic yeasts consume sugar in tea and produce ethanol. Other organic acids, including as gluconic, lactic, malic, citric, and tartaric, are generated in addition to ethanoic acid and have antibacterial properties, preventing kombucha infection by harmful microorganisms.

The inclusion of probiotic microbes (acetic and lactic bacteria), antibiotics, amino acids, and polyphenols from tea, sugars, organic acids, ethanol, water-soluble vitamins, and a range of micronutrients created during fermentation is credited with kombucha's therapeutic effects. Kombucha's flavour is somewhat acidic and mildly carbonated, which makes it more appealing to customers. Because of its high carbonation level, it can be used as a low-alcohol substitute for sparkling wines or soft drinks, making it a healthier option. On the market, kombucha is available in non-alcoholic and low-alcohol variants (less than 0.5% alcohol by volume), as well as perhaps alcoholic versions (Sreeramulu et al. 2000).



30.3.9 Idli

Idli is a fermented meal consisting primarily of rice and black gram that is popular throughout the Indian subcontinent. When idli batter is fermented overnight, naturally occurring bacteria in grains, legumes, and utensils, such as *Leuconostoc mesenteroides* and *Streptococcus thermophilus*, overwhelm the initial pollutants and take control of the fermentation. These microorganisms create lactic acid (1.0%) and carbon dioxide, rendering the batter anaerobic and causing it to separate from the product. Raw material effects, fermentation or processing temperature effects, and microorganisms involved in biochemical and nutritive changes are all factors to consider. It has also been claimed that during fermentation, vitamin B and C levels rise and phytate is nearly 50% hydrolysed. At the soaking stage, *L. mesenteroides* (leavening) and *S. faecalis* (acid production) develop together and continue to multiply after grinding (Ghosh and Chattopadhyay 2011).



30.4 Health Benefits of Functional Fermented Foods

Ethnic foods have built-in systems that serve as both food and medicine to satisfy hunger while also being restorative. Traditional and cultural foods such as natto, miso, tofu, shoyu, fermented vegetables, cholesterol-free, low-fat, and high bioactive-compound foods, as well as active physical activity, a healthy environment, happiness, and other factors, contribute to the best longevity observed among the people of Okinawa Prefecture in Japan. Korean kimchi is said to have health-promoting properties. Kimchi contains anti-ageing properties as well. Dahi, a famous fermented milk drink popular in India, has anti-carcinogenic properties. Carboxylic acid found in kimchi has been shown to reduce fat accumulation and improve obesity-related cardiac disease. Kimchi has been shown to have anti-obesity properties. Because of the presence of melatonin, which regulates the body clock, wine offers anti-ageing properties.

Ethnic people have long believed in the medicinal properties of a variety of ethnic cuisines, including fermented foods and beverages; however, scientific trials and validation of the health benefits claims of nearly all naturally fermented foods and beverages around the world must be investigated (Rezac et al. 2018).

30.5 Conclusion

Functional foods are foods which are related to a category of various potent health benefits, like they can prevent nutrient deficiencies and diseases. They also stimulate proper growth and development.

With a thorough examination of fermented foods and their possible cognitive benefits, their effect on cognitive enhancement and neuroprotective can be of great benefit if utilised globally. Fermented functional foods have been present in local diets since the prehistoric period, and studies have time and again proved their importance, both medically and economically.

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31 Extraction and Use of Bioactive Components from Underutilized Horticultural Crops

Uma Prajapati, Vikono Ksh, and Alka Joshi

Abstract

Various bioactive compounds such as phenolics, flavonoids, saponins, carotenoids, etc. are found in fruits and vegetables. Although literature is available on the use and importance of commercial fruits and vegetables, little information is known about the underutilized horticultural commodities. Underutilized horticultural crops, such as drumstick, red cabbage, turmeric, beetroot, avocado, passion fruit, jamun, bael, etc. can be utilized as an important source of health-promoting bioactive compounds. Various methods of extraction of bioactive compounds are ultrasound-assisted extraction (UAE), supercritical fluid extraction (SFE), liquid-liquid extraction (LLE), enzyme-assisted extraction (EAE), pressurized liquid extraction (PLE), microwave-assisted extraction (MAE), and high-voltage electrical discharge (HVED). The bioactive compounds extracted from underutilized horticultural crops find a number of uses in pharmaceuticals and food industries as antioxidant, preservatives, antimicrobial, prebiotic, anticancer, food colorant, food packaging, cosmetics, insecticide, etc.

Keywords

Bioactive compounds · Underutilized horticultural crops · Extraction techniques

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31.1 Introduction

Fruits and vegetables are rich sources of various bioactive compounds such as phenolics, flavonoids, saponins, tannins, terpenoids, glycosides, carotenoids, betalains, etc. These bioactives are not only found in the flesh or pulp of fruit or vegetables but also present in peel, seeds, and other parts which are not generally consumed (Rudra et al. 2015). Change in lifestyle of consumer due to higher income and advanced knowledge lead to shifting of preference from casual diet to a healthy diet rich in specific nutrients and bioactives. The recent scenario of food demand is not only based on hunger satisfaction but also on the food which prevents nutrient-related disorders or mental health. This all leads to the higher demand of consumers toward plant food with higher nutraceutical as well as pharmaceutical potential. Due to the rigorous use of commercial fruits and vegetables, ample literature is available on their use and importance but less is known about the underutilized horticultural commodities.

Nowadays, due to agrobiodiversity exploitation by continuously growing crops, there is a need to concentrate more on the underutilized crops for their extraordinary potentialities toward nutrition and health. Underutilized horticultural crops such as vegetables (*basella*, drumstick, gac, red cabbage, turmeric, and beetroot) and fruits (avocado, passion fruit, mangosteen, jamun, baobab, jujube, garcinia, datepalm, soh-shang, God's crown, bael, wood apple, anatto, Indian gooseberry, blackberry, blueberry and lollipop climber) could serve as an important source of health-promoting compounds which could be attained by identification and quantification of bioactive components present in these crops. Moreover, the evaluation studies of their biological activity will be an important factor to assess their food efficacy as a functional food and that these can also be served as ingredients of various food supplements.

Extraction is the most important step in the quantification of bioactive compounds from fruits and vegetables, and it varies with the type of plant part (stem, flower, leaves, and fruits) used for extraction (Sasidharan et al. 2011). Methods of extraction also depend on temperature, pressure, and type of solvent used (Hernández et al. 2009). Several extraction techniques such as ultrasound-assisted extraction (UAE), supercritical fluid extraction (SFE), Soxhlet extraction (SE), hydrodistillation, liquid-liquid extraction (LLE), solid-phase extraction (SPE), enzyme-assisted extraction (EAE), pressurized liquid extraction (PLE), pulsed electric field (PEF), microwave-assisted extraction (MAE), and high-voltage electrical discharge (HVED) have been utilized so far for the extraction of bioactive compounds from underutilized horticultural crops.

Scientific studies carried out on underutilized horticultural crops revealed that bioactive compounds extracted from these possess nutrigenomic properties and may prevent several degenerative diseases also. In addition, the phytochemicals extracted from these fruits and vegetables have excellent uses in the food industry and have the potential to improve the shelf life and stability of products. Several strategies need to be used in the study such as (1) toxicological properties of bioactive extracts, (2) metabolism of bioactive compounds (including their bioavailability), and

(3) sensory and nutritional properties of foods containing biological active molecules from underutilized horticultural crops.

31.2 Bioactive Compounds Found in Underutilized Horticultural Crops

31.2.1 Drumstick

Moringa oleifera L. belongs to the family Moringaceae widely grown in North India. It is vernacularly known as drumstick tree, white lily, horseradish tree, and *Sehjan*. All the plant parts of moringa possess immense pharmacological benefits such as leaves extract showing hypocholesterolemic, antiulcerative, bradycardic, and hypotensive properties, while seeds possess antimicrobial, anti-inflammatory, antitumor, antispasmodic, and diuretic activity (Ferreira et al. 2008). *M. oleifera* is a rich source of various bioactive compounds such as kaempferol, alkaloids, and quercetin, where quercetin and kaempferol are flavonoids with potential therapeutic use (Siddhuraju and Becker 2003). The whole plant of *M. oleifera* contains a high amount of γ-tocopherol which ranges from 5.7 μg/g (in adult leaves) to 27.8 μg/g (in 6-month-old leaves) on a dry weight basis. Traces of some carotenoids such as ß-carotene (401 mg/kg dw) and xanthins (neoxanthin 219 mg/kg dw, violaxanthin 76.5 mg/kg dw, zeaxanthin 19.4 mg/kg dw) were also found (Foidl et al. 2001). In other study, seven bioactive compounds were identified as 3,4-methyleneazelaic acid, (2S)-2-phenylmethoxybutane-1,4-diol, (2R)-2-phenyl methoxy butane-1,4-diol, γ-diosphenol, 2,2,4,4-tetramethyl-6-(1-oxobutyl)-1,3,5 cyclohexanetrione, 3-hydroxy-β-ionone, and tuberonic acid from the MO leaves extract. Further, it has also been found that these bioactive compounds possess strong antioxidant and anti-inflammatory activity (Luetragoon et al. 2020).

31.2.2 Gac Fruit

Momordica cochinchinensis (Lour.) commonly known as gac fruit, spiny bitter-cucumber, and Chinese bitter gourd belongs to Cucurbitaceae family with similar characteristics as that of bitter gourd. Gac fruit is sensitive to frost, and its cultivation is restricted to the tropical and subtropical climates of the world. Leaf extract of gac fruit contains β-carotene, triterpenoid ester, phenols, and flavonols which possess antioxidant, antimicrobial, and nutritional properties, respectively (Nantachit and Tuchinda 2009; Lim 2012; Mukherjee et al. 2017). Fruit aril and fruit peel of gac were found to contain several bioactive compounds such as β-carotene, lycopene, phenolics, flavonoids, retinol, and zeaxanthin which act as a potential antioxidant and anticancerous agents. Different types of carotenoids were found effective in maintaining health and reducing anemia while phenolics and flavonoids were found to maintain reproductive health (Huynh and Nguyen 2019). The fruit pulp of gac fruit contains apigenin which possesses antioxidant properties (Kubola and

Siriamornpun 2011). Gac fruit seeds were found to contain cochinin B, saponins I and II, momorcochin-S, and triterpenoid ester which acts as potential anticancerous agent (Chuethong et al. 2007; Bolognesi et al. 1989). Moreover, saponin affects glucose uptake activity and acts as anti-inflammatory agent. The whole fruit of gac contains carotenoids, flavonoids, phenolics, phytosterols, and saponins which possess analgesic properties. Its root contains oleanolic acid glycosides, which act as abortifacient and glycosides which possess antipruritic properties (Huynh and Nguyen 2019).

31.2.3 Avocado

Avocado (*Persea americana* Mill.) belongs to Lauraceae family widely grown in subtropical and tropical parts of the world. Avocado is consumed fresh or can be processed to extract oil (Salazar-López et al. 2020). Fresh avocado and its by-products are rich sources of carbohydrates, protein, dietary fiber, vitamins, minerals, and various bioactive compounds such as hydroxycinnamic acids, phenolic-alcohol derivatives, hydroxybenzoic acids, flavonoids, proanthocyanidins, terpenoids, saponins, alkaloids, phytosterols, and acetogenins (Dalle Mulle Santos et al. 2016; Araújo et al. 2018). There are several health benefits of these compounds as they induce neuroprotection, maintain brain and memory health, prevent cancer, and regulate lipid as well as carbohydrate metabolism. Bioactive compounds such as alkaloids, glycosides, triterpenoids, saponins, and phenolic compounds present in avocado seeds were found effective in reducing breast cancer and were associated with anti-inflammatory and anti-proliferative effects (Abubakar et al. 2017).

31.2.4 *Phaleria macrocarpa*

Phaleria macrocarpa (Scheff.) Boerl commonly known as God's crown fruit belongs to the family Thymelaceae and is widely used as a medicinal plant to control cancer, hemorrhoids, diabetes, impotency, allergies, blood-related diseases, kidney disorders, acne, stroke, liver and heart diseases, migraine, and various skin ailments (Easmin et al. 2015). Every part of this plant is used for disease prevention and the herb can be used both in processed and unprocessed form. A plethora of bioactive compounds has been reported in God's crown fruit such as dodecanoic acid, palmitic acid, flavicordin-A glucoside, and mahkoside-A (Hendra et al. 2009). From bark and stem, phytochemicals such as alkaloids, phenols, polyphenols, saponins, flavonoids, tannins, and lignans were reported (Hendra et al. 2011). From fruit, pericarp kaempferol, naringin, myricetin, phalerin, and rutin were obtained. Leaves of *P. macrocarpa* contain polyphenols, mangiferin, and saponin. The stem contains phenolics, flavonoids, tannins, and alkaloids (Easmin et al. 2015).

31.2.5 Passion Flower/Fruit

Passion flower/fruit (*Passiflora* spp.) also known as the apricot vine, passion vine, maypop, and granadilla belong to the family Passifloraceae. There are several species of *Passiflora* such as *P. quadrangularis* used for the treatment of snake bites, *P. alata* used for the treatment of occupational allergic diseases, *P. incarnata* used for the treatment of neural disorders, and *P. edulis* possess anti-inflammatory properties (Ingale and Hivrale 2010). Bioactive components such as phenols, alkaloids, glycosyl flavonoids, and cyanogenic compounds were reported in *P. incarnata* and *P. edulis* (Dhawan et al. 2004). Chrysin was found in *P. edulis*, and harman alkaloids, flavonoids, maltol, and ethyl maltol were reported in *P. incarnata*. *P. incarnata* possess aromatic properties due to the presence of chrysin and benzoflavone moiety (Dhawan et al. 2002; Ingale and Hivrale 2010).

31.2.6 *Syzygium cumini*

Syzygium cumini Skeels (Syn. *Eugenia jambolana* Lam.) also known as *jamun*, Indian blackberry, black plum, Java plum, and Portuguese plum. This evergreen tree belongs to family Myrtaceae and is widely grown in South America, Eastern Africa, India, and Madagascar (Ramya et al. 2012). Different plant parts of jamun such as leaves, bark, fruits, and seeds have been utilized as a traditional medicine to cure stomachache, fever, constipation, and dermopathy and are also known to possess astringent, diuretic, antidiabetic, antidiarrheal, stomachic, and antibacterial properties (Warrier et al. 1996; Migliato 2005). Several bioactive components such as betulinic acid, caffeic acid, bergenins, ellagic acid, ferulic acid, eugenol, citronellol, gallic acid, kaempferol, isoquercetin, petunidin, and quercetin have been reported in jamun tree (Ramya et al. 2012).

31.2.7 Mangosteen

Mangosteen (*Garcinia mangostana* L.) is a tropical evergreen tree species grown widely in Thailand, Malaysia, and Indonesia belonging to the family Guttiferae. It is also termed as “Queen of Fruits” due to its sweet-sour taste (Aizat et al. 2019a). Its fruit is a rich source of bioactive compounds such as xanthones and anthocyanins extracted from fruit pericarp. Mangosteen fruit extract is used to treat several disease ailments including diabetes, tumors, hypertension, arthritis, and bacterial infections. In addition to this, it also possesses anti-inflammatory and antioxidative properties (Aizat et al. 2019b). Among all bioactives, xanthones are the main metabolites and range at least 70 in the mangosteen extract. Xanthone particularly α-mangostin, β-mangostin, γ-mangostin, 8-deoxygartanin, garcinone E, and gartanin were found and constituted the medicinal properties such as antioxidant, anticarcinogenic, antiperiodontitic, antibiofilm, and antiperiodontitic activity. Anthocyanin particularly cyanidin-3-sophoroside and cyanidin-3-glucoside were also reported in mangosteen fruit pericarp (Aizat et al. 2019b). Other than this, major benzophenones such as garcimangosone D, chrysanthemin, and kolanone were also reported in the extracts of mangosteen fruits (Murthy et al. 2019).

31.2.8 Opuntia

Opuntia ficus-indica commonly known as prickly pear or nopal cactus belongs to the family Cactaceae and is widely grown in arid and semiarid parts of the world particularly in Mexico, South Africa, Latin America, and Mediterranean countries (Butera et al. 2002). Its fruit pulp and peel act as a major source of bioactive compounds and are utilized for nutrition, health, and cosmetic purpose in the form of juice, jam, tea, and oil (from seeds). The flowers and fruits of cactus possess antiulcerogenic, anti-hemorrhoidal, and antidiarrheal properties. Several bioactive compounds such as alkaloids, indicaxanthin, neobetanin, and various flavonoids were reported in *Opuntia* fruits (Valente et al. 2007). The flower of *Opuntia* contain gallic acid, quercetin 3-*O*-rutinoside, 4 kaempferol 3-*O*-rutinoside, and 8 isorhamnetin 3-O-glucoside; fruit pulp contains phenolic acid, quercetin, isorhamnetin, kaempferol, and luteolin; seed contains flavonoids, tannins, and sinapoyl-diglucoside; fruit skin contains kaempferol, quercetin, and isorhamnetin; while cladode contains gallic acid, coumaric acid, ferulic acid, isoquercetin, nicotiflorin, rutin, and narcissin (El-Mostafa et al. 2014).

31.2.9 Baobab Fruit

Baobab (*Adansonia digitata* L.) also known as monkey bread or pharmacist tree belongs to the family Malvaceae and is cultivated in tropical parts of the world mainly in African countries (Savić et al. 2021). Usually, all the plant parts such as leaves, bark fibers, fruit pulp, and seed are traditionally used for medicinal and nutritional purposes (Selvarani 2009). It is used for the treatment of skin and intestinal problems and also possesses antipyretic, anti-inflammatory, immunostimulant, analgesic, anti-dysenteric, and diaphoretic properties. Baobab fruit pulp and leaves are rich sources of phenolic compounds such as catechin, epicatechin, apigenin O-pentoside quercetin glycoside, vitexin/isovitexin, kaempferol glycoside, rutin, quercetin 3-O-glucoside, procyanidins, and flavonol glycosides. The presence of these potential nutraceutical and pharmaceutical agents will be promising to develop safe food products and additives to fight malnutrition and disease ailments (Braca et al. 2018).

31.2.10 Jujube

Zizyphus lotus (*Z. lotus*), commonly known as jujube, belongs to family Rhamnaceae and is grown in arid and semiarid countries particularly in China, Africa, South Korea, Spain, Greece, and Iran (Maraghni et al. 2010). Jujube is consumed in several forms such as tea, jam, honey, juice, oil, and cake. It is also employed for health, nutrition, and cosmetic purpose. Apart from this, jujube also possesses antidiabetic, hypoglycemic, antifever, and antidiarrheal properties (Abdoul-Azize 2016). Whole plant parts of jujube are enriched with several bioactive compounds such as fruit contain phenolic acid, flavonoids, and tannins; leaves contain phenolics, flavonoids, tannins, saponin, jujuboside B, and rutin. Its seeds contain polyphenols; root bark contains polyphenols, proanthocyanidins, flavonoids, saponins, jujubosides A and C, and lotosides A, B, C, D, and E; fruit pulp contains tannins and phenols (Maciuk et al. 2004; Ghazghazi et al. 2014; Abdoul-Azize 2016).

31.2.11 *Basella*

Basella alba L. (green stem) and *B. rubra* L. (red stem) belong to the family Basellaceae. Bioactive compounds found in *Basella* are anthocyanins, proanthocyanidins, β-carotene, α-carotene, polyphenols, flavonoids, and xanthophylls (violaxanthin, lutein, zeaxanthin, and neoxanthin). Phenolic acid particularly gallic acid, ferulic acid, and salicylic acid were found in *B. alba* and caffeic acid, 4-hydroxy benzaldehyde, p-coumaric acid, galloylshikimic acid, and trans-cinnamic acid were found in *B. rubra* leaves (Kumar et al. 2018, 2021). These bioactive compounds possess antidiabetic, anti-mutagenic, anticancerous, anti-inflammatory, and anti-hyperlipidemic properties (Phadungkit et al. 2012). Isovitexin is a glycosyl isoflavone found in *Basella* and acts against cancer cells in a dose-dependent manner (Kilari et al. 2018). Fruits of *Basella* plant are deep red with violet flesh containing bioactive pigment betalains which range from 22.32 to 143.76 mg 100/g fw (Kumar et al. 2015).

31.2.12 Bael

Bael (*Aegle marmelos*) is an underutilized fruit of a subtropical area belonging to the family Rutaceae. It possesses several biological properties such as anticancerous, anti-inflammatory, antihistaminic, antimicrobial, antihistaminic, and anti-amoebic activity. Phytochemical compounds such as flavonoids, phenolics, alkaloids, terpenoids, tannins, carotenoids, and saponins were found in the leaves and fruits of bael (Venthodika et al. 2021). Benzopyrones are another class of bioactive compound, constitutes coumarin that possesses aroma-enhancing, antifungal, bacteriostatic, and antitumor properties. Fruit of bael contains marmelosin which possesses antibacterial and antihelminthic properties, marmelide (antiviral), luvangetin (antiulcer), and psoralen (cytotoxic, antispasmodic, artemicide properties), and leaves of bael are a rich source of eugenol, citral, cuminaldehyde, and cineol which acts as antioxidant, antiulcer, antiallergic, anticeptic, and antibacterial agent, respectively (Maity et al. 2009; Arumugam et al. 2008;

Manandhar et al. 2018). Hence, bael fruit has a great scope to be utilized as functional food or other value-added products with several health advantages.

31.2.13 Wood Apple

Wood apple (*Feronia limonia* Swingle) is an underutilized fruit crop of Indian origin also known as kaitha, elephant apple, monkey fruit, or curd fruit. There are several ethnopharmacological benefits of wood apple from its different plant parts (Srivastava et al. 2019). Bioactive compounds extracted from leaves are polyphenols, flavonoids (such as bergapten, xanthotoxin, and imperatorin), and alkaloids which possess antimicrobial, diuretic, analgesic, and anti-inflammatory properties. Seeds of wood apple constitute psoralen, orientin, vitexin, bergapten, and saponarin which are used for the treatment of urinary disorders, piles/hemorrhoids, diarrhea, acidity, and ulcer (Intekhab and Aslam 2009). The bark of this fruit contains phenols which have antimicrobial, diuretics, antiasthmatic, and anti-inflammatory potential, while the stem contains coumarin, alkaloid, and flavanone, which have cytotoxic and antioxidant activity (Muthulakshmi and Mohan 2012). Thus, wood apple can be potentially utilized to cure a variety of disease ailments and could be used for the development of a wide range of food products.

31.2.14 Garcinias Fruit

Garcinias are tropical fruits broadly cultivated in Asian, American, and African countries for their high nutritional and medicinal value. Garcinias are brindle berry (*Garcinia gummi-gutta*) and kokum fruits (*Garcinia indica*) belong to the family Guttiferae (Murthy et al. 2019). Important bioactive compounds found in the brindle berry are xanthones (particularly oxy-guttiferone I, oxy-guttiferone K, oxy-guttiferone K2, and oxy-guttiferone M) and benzophenones (particularly guttiferone I, guttiferone N, guttiferone J, guttiferone K, and guttiferone M) which were isolated from its fruit (Masullo et al. 2010). Major bioactive compounds such as benzophenone derivatives (garcinol, isogarcinol, isoxanthochymol, and xanthochymol) and anthocyanin derivatives (cyanidin-3-sambubioside and cyanidin-3-glucoside) were reported in kokum fruits (Jayaprakasha and Sakariah 2002; Murthy et al. 2019). Bioactives extracted from garcinias owned antiulcer, anticancer, anti-inflammatory, antiparasitic, antiallergy, and antihelminthic properties. Thus, these can be safely utilized by consumers as a natural compound (Murthy et al. 2019).

31.2.15 Date Fruit

Date palm (*Phoenix dactylifera*) is grown widely in arid and semiarid parts of the world and belongs to the family Palmaceae. Date fruit has four botanical developmental stages Kimri, Khalaal, Rutab, and Tamr. The main bioactive compound found in date fruit is phenolic (particularly quercetin, apigenin, chrysoeriol, kaempferol, 3-methyl-isorhamnetin, and luteolin) (Al-Farsi et al. 2005). The ripe date fruits contain 1.5% of proanthocyanidins, 3% of condensed tannins, and 95% of total polyphenols. Other than these bioactives, rutin, catechin, and caffeic acid are also present. These bioactives possess antifungal, antibacterial, anticancerous, antioxidant, and antidiabetic properties (Maqsood et al. 2020). The presence of various nutraceutical and pharmaceutical properties in date fruit has led to its utilization in functional food and processed food preparation such as *idli* and baked food (Gad et al. 2010).

31.2.16 *Bryonopsis laciniosa*

Bryonopsis laciniosa also known as shivlingi belonging to the family Cucurbitaceae is an annual climber with bright red fruits occurring widely in India. Its whole plant is ethnobotanically important with several pharmacological properties (Kumar et al. 2018). There are valuable medicinal properties present in its fruit due to bioactive components such as alkaloids, tannins, saponins, flavonoids, alkenyl phenols, terpene lactones, and glycol-alkaloids (Manjamalai et al. 2010). Leaves and seeds of *B. laciniosa* are used to treat fever, inflammation, and flatulence and also possess antibacterial and antifungal properties. Other bioactives present in shivlingi fruits are hexanoic acid, caproic acid, and 2(3H)-furanone used as herbal medicine for treating various disease ailments (Ramya et al. 2015).

31.2.17 *Elaeagnus latifolia*

Elaeagnus latifolia Linn. belongs to Elaeagnaceae family popularly known as bastard oleaster, musleri, and sohsang in different parts of India. Its fruits are eaten both in raw and processed forms. Polyphenols such as ferulic acid, gallic acid, catechin, and p-coumaric were detected in the fruit extract of musleri (Dasila and Singh 2021). Its nutraceutical properties are mainly due to hydroxybenzoic acid particularly gallic acid and also possess high antioxidant potential due to hydroxycinnamic acid. Coumarin present in its fruit has cytotoxic properties and plays important role in reducing neurodegenerative diseases such as diabetes, cancer, and cardiovascular diseases (Miri et al. 2016). Catechins present in this played an important role as reactive oxygen species and for the production of detoxification enzymes (Bernatoniene and Kopustinskiene 2018).

31.2.18 Beetroot

Beetroot (*Beta vulgaris* L.) is a root crop belonging to the Chenopodiaceae family. It is native to Asia and Europe and can be successfully cultivated in cool areas.

Beetroot is a rich source of various phytochemicals and contains several nutritional and health benefits. Bioactive compounds such as betalains, carotenoids, polyphenols, flavonoids, and saponins were found at high levels, while folate and glycine betaine were found in low quantities (Chhikara et al. 2019). Betalains are further divided into red-purple and violet betacyanins (particularly probetanin, isobetanin, betanin, and neobetanin) and yellow betaxanthins (miraxanthin, vulgaxanthin, portulaxanthin, and indicaxanthin) which have been recognized to possess antioxidant, anticarcinogenic, anti-inflammatory, and hepatoprotective activities and also help in preventing hypertension, diabetes, and cardiovascular disease (Nowacka et al. 2019). Between these two, betacyanins exhibit antioxidant and free radical-scavenging activities (Escribano et al. 1998), and betaxanthins are used as a food supplement to fortify processed food products with essential amino acids. Therefore, betalains have also been recognized as “essential dietary colourants” (Leathers et al. 1992).

31.2.19 Red Cabbage

Red cabbage (*Brassica oleracea* var. *capitata* F. rubra) belongs to the family Brassicaceae and is widely grown as an annual vegetable. It is a rich source of anthocyanins that possess health-promoting properties and has wide applications as a natural food colorant. Anthocyanins mainly cyanidin 3,5-diglucoside, cyanidin 3-sophoroside-glucoside, and cyanidin 3-sophoroside-5-glucoside were found in red cabbage heads (Kannan 2011). The color of red cabbage could be used for the preparation of fruit sauces, wines, beverages, cakes, and candies. Apart from its use as food colorant, anthocyanins also possess several health benefits such as anticarcinogenic activity which includes colon, pancreatic, lung, and skin cancer. It also possesses antidiabetic and anti-inflammatory properties (Kataya and Hamza 2008).

31.2.20 Turmeric

Curcuma longa is vernacularly known as turmeric and belongs to the family Zingiberaceae. Since ancient times, it is used for condiments, flavoring, coloring, and preservative purposes. Turmeric is cultivated in warm areas particularly in India which is the largest exporter in the world and is commercially available as the powdered form of rhizome (Osorio-Tobón et al. 2016). Turmeric is a rich source of bioactive compounds particularly phenolic compounds where curcumin is only present in the highest quantity (70–75%) followed by demethoxycurcumin and bisdemetoxicurcumin whose value ranges from 25 to 30%. These bioactives are responsible for the yellow color of the turmeric and possess a wide range of pharmacological benefits such as anti-inflammatory, antioxidant, antibacterial, anti-fungal, antidiabetic, larvicidal, and insecticidal activities (de Oliveira Filho et al. 2021). Other bioactive compounds present in turmeric are aromatic-turmerone, phellandrene, terpinolene, zingiberene, and curzerenone which have antioxidant, antifungal, antimicrotoxigenic, and antimicrobial properties (Singh et al. 2010; de Oliveira Filho et al. 2021).

31.2.21 Indian Gooseberry

Indian gooseberry (*Emblica officinalis*) is a valuable fruit crop commonly known as asamla or amla and belongs to the family Phyllanthaceae. It is a rich source of several bioactive compounds such as polyphenols, tannins, emblicanins A and B, gallic acids, and ellagic acid which possess antioxidative properties. Amla fruit can be eaten raw or can be processed to make candies, juice, powder, jam, pickle, sauce, etc. (Chakraborty et al. 2020). The bioactive present in its fruit possesses antipyretic antimicrobial, anti-inflammatory, and analgesic activities (Mayachiew and Devahastin 2008). Other bioactive compounds present in amla are myricetin, quercetin, kaempferol, and chlorogenic acid which also possess antioxidative properties (Bansal et al. 2014).

31.2.22 Annatto

Annatto (*Bixa orellana* L.) belongs to the Bixaceae family and is widely grown for its fruits. Its seed aril has a thin layer of reddish pigment which is used for medicinal application, painting of skin, or for insect protection (Hojo et al. 2014). Anatto contains bioactive compounds mainly polyphenols (caffeic acid and hypolatin) and carotenoids such as bixin which possess antioxidative properties (Quintero Quiroz et al. 2019). Bioactive compounds such as vitamin E and geranylgeraniol have also been found in the oily extract of anatto seeds. Geranylgeraniol has several medicinal properties such as it helps in testosterone production, acting against leishmaniasis, and showing anti-inflammatory and anticancerous activity (Vardanega et al. 2019).

31.2.23 Blackberry

Blackberries (*Rubus* spp.) belong to the family Rosaceae and are utilized in raw as well as a processed form for the preparation of juices, ice creams, jellies, and dietary supplements. It is not only known for its good taste but also for its high nutritional value and several health benefits. It is also an important source of various bioactive compounds such as phenolic acids, flavonoids, anthocyanins, tannins, and ellagitannins. Polyphenols present in this prevent degenerative diseases and act as a potent antioxidant. Anthocyanins are used as natural dyes and also plays important role in human nutrition (Machado et al. 2015). Apart from this, tocopherols and β-carotene were also reported in blueberry which has a higher antioxidant capacity (Hassimotto et al. 2008). Polyphenolic compounds such as cinnamic acids, catechins, rutin, quercetin, hyperoside, and isoquercitrin and benzoic acids such as ellagic acid and gallic acid were also reported in blackberry fruits (Donno et al. 2016).

31.2.24 Blueberry

Blueberry (*Vaccinium corymbosum* spp.) belongs to the family Ericaceae and is cultivated largely in North America, Australia, New Zealand, and European countries. Blueberry is a rich source of several bioactive compounds such as flavonols (particularly quercetin, kaempferol, and myricetin), hydroxybenzoic acids (procatchuic and gallic acids), hydroxycinnamic acids (ferulic acids, caffeic acids, and coumaric acids), tannins such as gallotannins and ellagitannins, and resveratrol and pterostilbene (Miller et al. 2019). Other than this, it is also a rich source of anthocyanins particularly pelargonidins, peonidins, malvidins, cyanidins, petunidins, and delphinidins which possess antioxidant, anti-inflammatory, and anticancerous activities (Shi et al. 2017). Chlorogenic acid acts as copigment which enhances the intensity of color intensity of anthocyanins (Michalska and Łysiak 2015).

31.3 Extraction Methods of Bioactive Compounds

Extraction of bioactives from plant tissues has gained popularity due to its many benefits such as antioxidant activity, antidiabetic, antiaging, anticancer, etc. Extraction, in a nutshell, is simply the process by which biomolecules of interest are transferred from the plant tissues (solid matrix) to the solvent used for extraction (i.e., mass transfer). Mass transfer occurs in three stages: firstly, the solvent enters the solid matrix and solubilizes the biomolecule; secondly, the solution so formed migrates to the surface of the solid matrix; finally, the solution dissolves into the solution bulk surrounding the solid matrix (Table 31.1).

Solvents are selected such that they can selectively solubilize the required biomolecule from the solid matrix. Increasing the surface area of the solid matrix is known to increase the extraction efficiency as it directly increases the mass transfer. Hence, the solid matrix is usually crushed or powdered before actual extraction. Temperature also plays a direct role in increasing the extraction efficiency up to a certain limit. However, the temperature is self-limiting as usually most of the bioactive compounds are heat sensitive. The pressure of the system can also be altered to increase the extraction efficiency, but this adds to the extraction cost. Another parameter that influences the extraction yield is the solvent-to-solid ratio; usually the higher its value, the higher will be the extraction efficiency. However, too high a value will add to the cost as well as create problems in disposing of the used solvent.

Extraction can be broadly classified into conventional extraction methods (maceration, solvent extraction, water extraction, etc.) and modern or greener extraction methods (supercritical fluid extraction, natural deep eutectic solvents (NADES)

Table 31.1 Summary of extraction of bioactive compounds from some underutilized crops

Crop	Solid matrix	Bioactive compound	Method	Reference
Aloe vera	Leaves	Polyphenols, uronic acid, malic acid, lignin	Mechanical pressing for gel and liquid SE for bagasse	Flores-López et al. (2016)
	Gel	Acemannan	WE	Chokboribal et al. (2015)
	Gel	Acemannan	WE	Kumar and Kumar (2019)
Achiote	Seed	Bixin	SE, MAE, UAE	Bachtler and Bart (2021)
	Seed	Polyphenols, bixin	MAE	Quintero Quiroz et al. (2019)
	Seed	Polyphenols, bixin	UAE	Quintero Quiroz et al. (2019)
	Seed	Geranylgeraniol, tocotrienols	SCFE	Vardanega et al. (2019)
Avocado	Seed	Polyphenols	UAE	Segovia et al. (2016)
	Seed	Polyphenols	MAE	Araújo et al. (2020)
	Peel	Polyphenols	MAE	Araujo et al. (2021)
	Peel	Phenolic compounds	PLE	Figueroa et al. (2018)
	Peel	Phenolic compounds	ATPS	Jiménez-Velázquez et al. (2020)
Bael	Pulp	Carotenoids, soluble dietary fiber, volatile compounds	EAE	Charoensiddhi and Anprung (2010)
	Pulp waste	Carotenoids, polyphenols, flavonoids	UAE	Sonawane et al. (2020)
Baobob	Pulp	Phenolic compounds	Maceration, decoction, MAE	Hussain et al. (2019)
	Seeds	Flavonoids	UAE	Ismail et al. (2019)
Beetroot	Pulp waste	Betalains, polyphenols	UAE	Fernando et al. (2021)
	Leaves	Polyphenols	SCFE	Goyeneche et al. (2020)
	Root	Betanin, phenolic compounds	UAE	Tutunchi et al. (2019)
	Root	Betalains	PEFAE	Nowacka et al. (2019)

(continued)

Table 31.1 (continued)

Crop	Solid matrix	Bioactive compound	Method	Reference
Blackberry	Pulp waste, bagasse	Anthocyanins, phenolic compounds	PLE	Machado et al. (2015)
	Pulp	Anthocyanins, phenolic compounds	UAE, MAE	Espada-Bellido et al. (2019)
	Bagasse	Anthocyanins, phenolic compounds	SE, maceration, SCFE assisted by ultrasound	Reátegui et al. (2014)
Blueberry	Pulp	Anthocyanins	UCGE	Jiang et al. (2017)
	Pulp	Anthocyanins	MEA	Yu et al. (2016)
	Pomace	Anthocyanins, phenolic compounds	SE, UAE	He et al. (2016)
	Leaves	Anthocyanins, flavonoids, phenolic compounds	U-NPCE	Wang et al. (2018)
	Pomace	Anthocyanins, flavonoids, phenolic compounds	UAE	Bamba et al. (2018)
Bryonopsis laciniosa	Fruit	Steroids, saponins, alkaloids, flavonoids, phenolic compounds, tannins, steroids terpenoids	SE	Sanjeevkumar et al. (2016)
Date palm	Fruit	Anthocyanins, flavonoids, carotenoids	PEFAE	Siddeeg et al. (2019)
Bastard oleaster	Pulp	Phenolic compounds, carotenoids	SE, UAE, hydro-distillation	Magnusson et al. (2021)
Gac	Peel	Carotenoids	SE	Chuyen et al. (2017)
	Peel	Carotenoids	MAE, UAE	Chuyen et al. (2018)
	Peel	Carotenoids	UAE	Chuyen et al. (2020)
	Leaves	Flavonoids, phenolic compounds, chlorophyll	UAE, HVEF, HPP, HVEF +UAE, HPP + UAE	Nguyen et al. (2021)
	Defatted seeds	Trypsin inhibitors, saponins, phenolics	WE, SE, MAE, UAE	Le et al. (2018)
Garcinia cowa	Fruit	Hydroxycitric acid	MAE	Parthasarathi et al. (2013)
Garcinia mangostana	Pericarp	Alpha-mangostin, phenolics	SCFE + hydrothermal	Chhouk et al. (2016)
Garcinia indica	Fruit		ATPS	Nainegali et al. (2019)

(continued)

Table 31.1 (continued)

Crop	Solid matrix	Bioactive compound	Method	Reference
		Anthocyanin, garcinol, isogarcinol, hydroxycitric acid		
Indian gooseberry	Seed coat, embryo	Polyphenols	SE	Jaiboonma et al. (2018)
	Fruit	Flavonoids	SE	Verma et al. (2018)
Jujube	Seeds	Total phenolics, flavonoids	UAE	Berkani et al. (2020)
	Seeds	Total phenolics, flavonoids, peptides	MAE	Berkani et al. (2021)
	Pulp, seed	Total phenolics, flavonoids	SE	Han et al. (2015)
	Leaves	Flavonoids	SE, UAE, SCFE	Song et al. (2019)
	Peel, seed	Total phenolics, flavonoids	SE	Wang et al. (2019)
Moringa oleifera	Leaves	Glucosinolates, chlorogenic acids, flavonoids	SE, NADES extraction, APTS, PHWE	Djande et al. (2018)
	Seed	Kernel oil	SE	Mani et al. (2007)
	Leaves	Phenolics	UAE	Pollini et al. (2020)
	Leaves	Phenolic acid derivatives, flavonoids	SE, UAE	Rodríguez-Pérez et al. (2015)
	Leaves	Phenolic acid derivatives, flavonoids	WE, SE	Siddhuraju and Becker (2003)
	Bark, leaves, flowers	Phenolics, anthocyanin, ascorbic acid	SE	Vats and Gupta (2017)
Moringa peregrina	Seed	Kernel oil	SE, UAE	Mohammadpour et al. (2019)
Opuntia joconostle	Endocarp	Phenolics, flavonoid, betalains, ascorbic acid	MEA	Dávila-Hernández et al. (2019)
Opuntia ficus-indica Opuntia engelmannii	Peel	Phenolics, betalains	SE	Melgar et al. (2017)
Opuntia ficus-indica	Fruit	Polyphenols	PEFAE	Surano et al. (2021)
Passion fruit	Epicarp	Anthocyanins	SE	Ghada et al. (2020)

(continued)

Table 31.1 (continued)

Crop	Solid matrix	Bioactive compound	Method	Reference
	Seed	Fatty acids, tocopherol, phenolics	SubFE, SE, UAE	Pereira et al. (2019)
	Seed	Phenolics, flavonoid	SE	de Santana et al. (2017)
	Epicarp	Phenolics	SE, maceration, PLE	Viganó et al. (2016)
	Defatted bagasse	Phenolics, piceatannol	PLE assisted by ultrasound	Viganó et al. (2020)
Phaleria macrocarpa	Fruit	Mangiferin	UAE	Lim et al. (2019)
Red cabbage	Leaves	Phenolics, anthocyanin	MEA	Nguyen et al. (2020)
	Leaves	Anthocyanin	UEA	Ravanfar et al. (2015)
Syzygium cumini	Leaves	Flavonoids, saponins, phenols	WE, SE	Ramos and Bandiola (2017)
	Pulp	Phenolics, anthocyanin	SCFE	Maran et al. (2014)
Turmeric	Rhizomes	Cucurminiods	PLE, SCFE	Osorio-Tobón et al. (2014)
Wood apple	Pulp	Polyphenols	SE	Ilaiyaraja et al. (2015)
	Pulp	Polyphenols, flavonoids	SE, UAE	Karunanithi and Venkatachalam (2019)

WE water extraction, *SE* solvent extraction, *MAE* microwave-assisted extraction, *UAE* ultrasound-assisted extraction, *SCFE* supercritical CO_2 fluid extraction, *PLE* pressurized liquid extraction, *ATPS* aqueous two-phase systems, *EAE* enzyme-assisted extraction, *PEFAE* pulsed electric field-assisted extraction, *UCGE* ultrasonic cell grinder extraction, *U-NPCE* ultrasound-negative pressure cavitation extraction, *HVEF* high-voltage electric field, *HPP* high pressure processing, *NADES* natural deep eutectic solvents, *PHWE* pressurized hot water extraction, *SubFE* subcritical fluid extraction, *DES* deep eutectic solvents

extraction, ultrasound-assisted extraction (UAE), microwaved-assisted extraction (MAE), etc.). The conventional extraction methods usually employ organic solvents, requiring a large solvent volume and longer extraction time, while modern methods consume lesser organic solvents, shorter extraction time, and better selectivity (Zhang et al. 2018).

31.3.1 Maceration

Maceration is one of the most common conventional techniques used for the extraction of juices and active biomolecules from plant tissues. It involves the mixing of a whole or comminuted solid matrix with solvents in a closed vessel with or without agitation. It is usually performed at room temperature and atmospheric pressure by using water, aqueous or non-aqueous solvents.

Hussain et al. (2019) reported that maceration was the recommended extraction method and ethanol was desirable solvent for the extraction of phenolic-rich crude extracts with the highest antioxidant activities (based on ABTS assay) from baobab when comparing maceration, decoction, and MAE using water, ethanol, and 50% ethanol, respectively. Viganó et al. (2016) observed that the global yield, phenolic content, and antioxidant activity of extract from passion fruit rinds were lower in maceration than those of pressurized liquid extraction (PLE) for the same extraction condition (temperature: 30–60 °C; ethanol concentration: 70–100% (v/v); pressure 10 MPa for PLE and atmospheric pressure for maceration). Maceration greatly increases the amount of betacyanin for both the fractions, i.e., peel and the flesh of the beetroot fruit. A novel method of beetroot juice extraction was developed by Pothula et al. (2014). They found hammer mill pulverization followed by basket pressing extracted the beetroot juice very efficiently. Through hammer mill, frozen beetroots could also directly be used for juice extraction with higher sugar content than the unfrozen ones.

31.3.2 Solvent Extraction (SE)

SE involves the use of different solvents such as hexane, methanol, ethyl acetate, etc. for extraction by stirring, agitation, Soxhlet percolation, or grinding. Depending on the relative solubility of the compounds, the target bioactives are separated out from the solid matrix as it solubilizes into the surrounding solvent. It is usually carried out at a low temperature and atmospheric pressure. Magnusson et al. (2021) compared different extraction techniques and concluded that solvent extract from Soxhlet (using ethanol as a solvent; 120 min of extraction) had the highest extract yield (63.5 g/100 g of raw material), total phenolic compounds (3.3 mg gallic acid equivalent/g extract), and carotenoids (176.6 mg β-carotene equivalent/kg raw material). When different organic solvents, viz., acetone, ethanol, ethyl acetate, and hexane were explored for extraction of carotenoids from gac peel, the highest carotenoid yield (271 mg/100 g dry weight) was reported for ethyl acetate. A solvent-solid ratio of 80 mL/g and extraction temperature of 40.7 °C with agitation for 150 min were concluded as the optimum extraction condition (Chuyen et al. 2017). Although solvent extraction gives higher yields, it is not sustainable or environment friendly as it usually involves the use of toxic solvents. Therefore, it is advisable to use safe solvents for extraction such as water, so that extractants can be used in food preparations. According to Castellar et al. (2006), water extracted more pigments from *Opuntia* fruits than the ethanolic aqueous solution. Barrera et al. (1998) found that acidic ethanol (99% by volume) extracted more betalains than aqueous media. However, improved pigment stability was reported in aqueous extract.

31.3.3 Extraction Using Natural Deep Eutectic Solvents (NADES)

Deep eutectic solvents (DES) are derived from natural and renewable compounds. They are advantageous as they can be developed without involving purification steps. They are inexpensive, noninflammable, sustainable, and biodegradable and can be recycled to naturally derived compounds. DES comprises quaternary ammonium salts (e.g., choline chloride) and hydrogen bond donors such as carboxylic acid (e.g., citric acid). When they are derived from primary metabolites of living cells, they are referred to as natural deep eutectic solvents (NADES). NADES are a promising replacement for toxic organic solvents. In addition to their nontoxic and sustainable nature, their viscosity is easily adjustable which makes it very effective for extraction (Wei et al. 2015; Mulia et al. 2015; Matong et al. 2017; Tang et al. 2016).

Wang et al. (2017) concluded that DES extraction is suitable for the extraction of oxygen-sensitive and heat-sensitive bioactive compounds such as catechins, flavonoids, and alkaloid from tea leaves. In another study, Djande et al. (2018) put together a NADES system comprising choline chloride and citric acid and heated to 70 °C till a homogenous solution was obtained. To this, deionized water was added to decrease the solvent viscosity. The final NADES (final concentration of 40%) was added to comminuted *Moringa oleifera* leaves at a ratio of 1:10 (m/v) and homogenized at 50 °C for 1 h in a sonicator bath after which the mixture was filtered. Analysis of the filtered extract confirmed the presence of glucosinolates, chlorogenic acids, and flavonoids which established the effectiveness of NADES-assisted extraction of pharmacologically relevant bioactive compounds from plant tissues.

31.3.4 Microwave-Assisted Extraction (MAE)

In microwave-assisted extraction, high-energy electromagnetic waves ranging from 300 MHz to 30 GHz frequency, 3×10^{-9} s to 33×10^{-12} s oscillation period, and wavelength ranging from 1 to 10 mm are employed. This modifies the molecular rotation and ionic mobility of the sample which in turn generates adsorption and dissipation of energy causing generalized heating and migration of the active compounds from the sample to the solvent surrounding the sample (Quintero Quiroz et al. 2019).

Quintero Quiroz et al. (2019) employed a microwave unit operating at 2450 MHz and 700 W power. At the optimum extraction condition (treatment time = 5 min; pH = 7; ethanol concentration = 96%; ethanol to seed ratio = 5.95), the extract had a total polyphenol concentration of 3.08 mg gallic acid/g seed and 0.58% bixin. The extract was observed to exhibit antimicrobial activity against *B. cereus* and *S. aureus*. An increase in the polyphenols and bixin content along with the antioxidant activity was observed for the optimal MAE extract in comparison to the leaching extract (extracted at optimal concentration, pH, and seeds-to-solvent ratio as MAE, with continuous agitation for 48 h). However, no significant improvement in antimicrobial activity was observed. In another study, a microwave system (220–240 V, 50/60 Hz, up to 800 W) with a thermometer and magnetic stirrer (800–1000 rpm) was employed. A 95% recovery of bixin was observed as compared to 85% in sonification (Bachtler and Bart 2021). Araújo et al. (2020) optimized MAE of avocado seeds using 70% acetone and ethanol. Both extracts indicated high polyphenolic content (307.09 ± 14.16 and 254.40 ± 16.36 mg GAE/g extract) and high antioxidant activity. For avocado peels, the highest antioxidant capacity using 70% acetone was reported at 74.48 °C for an extraction period of 14.32 min, and for ethanol, it was observed at 66.37 °C for an extraction period of 0.97 min at 42.58% of ethanol concentration (Araujo et al. 2021).

31.3.5 Pressurized Liquid Extraction (PLE)

In PLE, extraction is achieved by employing liquid solvents at elevated temperature and pressure, which results in superior extraction efficiencies in comparison to those extraction methods carried out at near room temperature and atmospheric pressure. At the elevated extraction condition, the solubility as well as the mass transfer increases (Mustafa and Turner 2011). PLE provides better extraction efficiencies, lesser solvent consumption, and quicker extraction and permits the extraction of compounds with a wide polarity range by simply altering the temperature and extracting fluid composition (Herrero et al. 2013). However, the higher extraction temperatures restrict its applicability to the extraction of bioactive compounds which are comparatively less heat sensitive.

Figueroa et al. (2018), extracted bioactives from avocado peels in a pressurized liquid extractor with 1:1 (v/v) ethanol:water as solvent at 200 °C. A total of 47 phenolic compounds were quantified in the extracts. Bioactives from blackberries pulp waste and bagasse were also extracted by PLE. Solvent combination of ethanol and water (1:1) at 100 °C was found to be the best extraction condition (compared to conventional methods) and yielded total phenolic content of 7.36 mgGAE/g fresh residue and monomeric anthocyanins of 1.02 mg C3GE/g fresh residue (C3GE—cyanidin-3-glucoside equivalent) (Machado et al. 2015).

31.3.6 Aqueous Two-Phase Systems (ATPS)

ATPS is a separation technique which consists of a mixture of two polymers (polyethylene glycol and polyvinylpyrrolidone), or a polymer and a salt, or an organic solvent and a salt. The components form a true solution in one phase, but in others, the mixture forms two immiscible phases, and thus the compounds separate. Its operation is based on a "salting-out" phenomenon which determines the techniques' capacity to separate out or to extract the desired compound. Hydrophobic and hydrogen bonds and ionic interactions are the driving forces responsible for aqueous two-phase formation in ATPS. Physicochemical factors like hydrophobicity, pH, and the affinity of the biomolecule for the phases will decide the partition activity of biomolecules. All these make APTS ideal for extraction of soluble and insoluble compounds and also advantages of being economic compared to conventional extraction techniques (Sadeghi and Maali 2016; Djande et al. 2018; Domínguez-Puerto et al. 2018; Patel et al. 2018; Nainegali et al. 2019).

Jiménez-Velázquez et al. (2020) extracted phenolic compounds from avocado peels using ATPS comprising polyethylene glycol 4000 (PEG4000) with sodium citrate (Na3Cit) or magnesium sulfate ($MgSO_4$). Recovery of more than 82% of soluble phenols, flavonoids, and tannins was reported with high antioxidant activity for ATPS with 24.9–14.5% Na3Cit–PEG4000 and 12.2–15.5% MgSO4–PEG4000. For *Garcinia indica* fruits, an ATPS system containing ethanol and ammonium sulfate system was found to be most suitable for extracting bioactives like anthocyanin, garcinol, isogarcinol, and hydroxycitric acid (Nainegali et al. 2019).

31.3.7 Enzyme-Assisted Extraction (EAE)

This technique utilizes enzymes such as cellulose, α-amylase, pectinase, etc. for the extraction of biomolecules. The basic principle of EAE is the disintegration of the cell wall of plant tissues by the hydrolytic action of the enzymes under optimal extraction conditions. The cell walls disrupt releasing the intercellular components, thereby aiding in mass transfer between the solid matrix and the solvent. It is a promising green alternative to their conventional counterparts as it has a short extraction time, is efficient and sustainable, does not require hazardous solvents, and is suitable for heat-sensitive biomolecules (Nadar et al. 2018).

Homogenized bael fruit pulp was treated with pectinase at a varying concentration (1.0–3.0%, v/w) and hydrolysis time (0–6 h) with the temperature maintained at 30 °C. After the treatment, samples were heated at 100 °C for 5 min to inactivate the enzyme. Enzyme-treated hydrolysate showed increased antioxidant activities, total carotenoids, soluble dietary fiber, and volatile compounds (Charoensiddhi and Anprung 2010). EAE was ineffective in extracting betalains from wet beetroot pulp waste (Fernando et al. 2021).

31.3.8 Ultrasound-Assisted Extraction (UAE)

In ultrasound-assisted extraction, the ultrasound waves create cavitation of small bubbles in the solvent allowing for a greater penetration of the solvent within the material, thereby increasing the surface area and hence, the mass transfer rate. Additionally, the waves also cause cavitation of the cell walls of the solid matrix which allows the bioactives to interact more conveniently with the solvent which contributes to the mass transfer (Righi Pessoa da Silva et al. 2018).

Quintero Quiroz et al. (2019) employed an ultrasound system (37 KHz frequency and 320 W power) for extraction from annatto seeds. The process was optimized at 7.0 pH, 1:7 seed-to-solvent ratio, and treatment time of 20 min. The optimal extract was found to contain 0.62% of bixin and 3.81 mg gallic acid/mg equivalent of polyphenol compounds and exhibited antimicrobial activity against *B. cereus* and *S. aureus* at a concentration of 32 and 16 mg/L, respectively (Sonawane et al. 2020). A probe-type ultra-sonicator (power rating of 700 Watt and 20 kHz frequency) was employed for the extraction of bioactives from bael pulp obtained after juice extraction. Using response surface methodology, extraction was optimized at ethanol concentration of 51.22%, ultrasound amplitude of 51.45%, and ultrasound treatment time of 6.11 min. Ultrasound treatment time had the least influence on the extraction of bioactive compounds than ethanol concentration and ultrasound amplitude. Total carotenoids which were the major targeted compounds ranged from 7.09 to 4.92 μg β-carotene equivalents per 100 mL of extract. Ismail et al. (2019) documented that the recovery of total flavonoid content, total phenolic content, and antioxidant activity (DPPH and FRAP) was significantly greater in UAE with a shorter extraction time than that of maceration and heat-assisted extraction techniques.

An ultrasonic cell grinder extractor which consists of ultrasonic generator and ultrasonic transducer (converts the electrical energy of ultrasound into mechanical energy) was reported to extract higher anthocyanins (2.89 mg/g higher) than that of conventional UAE. The optimized conditions were as follows: 25:1 (mL/g) solution-to-solid ratio, the extraction power of 1500 w, 3 s buffer time, and extraction time of 40 min (Jiang et al. 2017). Fernando et al. (2021) observed that UAE using 30% ethanol was more effective for the extraction of betalains and polyphenols from dried pulp waste of beetroot obtained after juice extraction. Betalains were found to be more stable in the dried pulp.

31.3.9 Supercritical Fluid Extraction (SFE)

It is considered as a "green" technology that utilizes a solvent in its critical state for extraction. Carbon dioxide is the most commonly employed solvent as it is nontoxic, cheap, non-inflammable, and a "green" solvent, allows easily removable from the product, and has moderate critical temperature and pressure (31.1 °C, 73.8 bar). SFE has high extraction efficiencies because the solvent in its critical state will easily diffuse into the solid matrix like a gas while solubilizing the target biomolecule like a liquid solvent. It is also flexible and versatile in the sense that the solvent power/selectivity can be changed by simple manipulation of process parameters (pressure and temperature) of supercritical fluid which can obtain different extract compositions (Goyeneche et al. 2020). In cases when co-solvents are not employed, the extract obtained from SFE can be used directly without involving procedures for solvent removal. However, the high cost of the set-up often limits its applicability.

Vardanega et al. (2019) used a two-step SFE with CO_2 at 60 °C, 10 MPa, and CO_2 density of 290 kg/m^3 in the first step for geranylgeraniol-rich fraction recovery and at 40 °C, 20 MPa, and CO_2 density of 840 kg/m^3 in the second step for tocotrienol-rich fraction recovery. Reátegui et al. (2014) reported that when ultrasound is coupled with SFE processes, the extraction efficiency is increased at beginning of the process as observed for the lowest pressure applied (15 MPa), shortening the extraction time and thereby the operational cost.

31.3.10 Pulsed Electric Field-Assisted Extraction (PEFAE)

When a moderate-intensity electric field (0.5–10 kV/cm) and relatively low energy (1–10 kJ/kg) are applied to plant tissues in short pulses (few μs up to 1 ms), electroporation occurs, i.e., there is the formation of pores or enlargement of the existing pores. This increases the permeability of cell membranes and facilitates the release of bioactive compounds from the plant tissues (Grimi et al. 2011; Praporscic et al. 2007).

Nowacka et al. (2019) observed that the highest yield of betalain compounds in beet extract (betanin by 329%, vulgaxanthin by 244%, in comparison to the control sample) was obtained at 20 pulses of the electric field at 4.38 kV/cm of strength when using a PEF generator. Siddeeg et al. (2019) treated date palm fruit with PEF (frequency: 10 Hz, time: 100 μs, 30 pulses, electric field strength: 1, 2, and 3 kV/cm) and observed that by increasing the electric field strength (up to 3 kV/cm), the extract yielded higher carotenoids, anthocyanins, flavonoids, and phenolics content. It was suggested that PEF can be employed as a suitable technique for enhancing solvent extraction on an industrial basis.

31.3.11 Combined Methods

Extracts derived from combined extraction technologies are reported to be more superior than those extracts which are derived from single technologies. Nguyen et al. (2021) assessed different extraction techniques such as UAE, high voltage electric field (HVEF), high pressure processing (HPP), and two innovative combined methods (HVEF+UAE and HPP + UAE) for extracting bioactives from gac leaves. The highest values of total phenol content (5200 mg GAE/100 g DW) and total flavonoid content (620 mg QE/100 g DW) were obtained from the combined method (HVU + HPU) extract. In another study, blueberry leaves extract obtained from an ultrasound-negative pressure cavitation extraction (U-NPCE) reported a stronger DPPH radical scavenging activity and higher anthocyanins, flavonoids, and phenolic content than the extracts obtained from UAE and negative pressure cavitation extraction separately (Wang et al. 2018).

31.4 Utilization of Bioactive Components from Horticultural Crops

Extracts obtained from different extraction techniques are rich in bioactive compounds such as anthocyanins, carotenoids, flavonoids, catechins, bixin, etc. which promotes health. Isolated bioactive compounds or extracts hence find a number of uses in pharmaceuticals and food industries. Some of the existing applications along with some potential applications have been listed below.

1. *Antioxidant*
   The presence of bioactives such as bixin, catechin, chlorogenic acid, chrysin, butein, hypolaetin, licochalcone A, and xanthohumol in annatto extract makes it a rich source of antioxidants (Quintero Quiroz et al. 2019). Polyphenols from jujube extracts have antioxidant activity (Berkani et al. 2020). Prickly pear extracts (rich in phenols, flavonoids, betaxanthins, and betacyanins) and jambolan extract (rich in catechin, gallic acid, and epicatechin) are both hailed for their antioxidant property.
2. *Preservative*
   Annato extract can be used as a preservative due to its antioxidant and antimicrobial activity (Viuda-Martos et al. 2012). The use of grape seed extract is reported to prevent fruit decay and ensure longer storage of grilled chicken (Chen et al. 2020). For raw meat packaged in a modified atmosphere package, phenolic compounds from *Moringa oleifera* leaf extract were found to ameliorate the functional properties of muscle proteins and check lipid oxidation. *Moringa peregrine* extract has been identified as a source of new antibiotic compounds making it suitable as a microbial preservative (Saucedo-Pompa et al. 2018). *Phaleria macrocarpa* extract is also reported as a potential natural food preservative (Andrean et al. 2014).
3. *Antimicrobial and antifungal*
   Annatto seed extract doses of 1.024 mg/mL, 256 mg/mL, 512 mg/mL, and 256 mg/mL were found to be effective against *P. aeruginosa*, *B. cereus*, *L. innocua*, and *A. hydrophila*, respectively. Thus, it is an excellent candidate as an alternative to artificial antimicrobials (Viuda-Martos et al. 2012). Betalain pigments exhibit antimicrobial activity (Gengatharan et al. 2015). *Moringa oleifera* seeds are known to possess antifungal and antibacterial properties (Ferreira et al. 2008).
4. *Prebiotic activity*
   Bael extract can be used as prebiotics (Charoensiddhi and Anprung 2010). Foam mat bael powder hence is being used in so many formulations for its prebiotics activity.
5. *Anticancer*
   A 35 kD protein found in gac aril along with other smaller molecules from the aril, peel, and seeds have been documented to reduce oxidative stress and destruction of cancer cells (Huynh and Nguyen 2019). Grape extract which is rich in polyphenols possess anticancer properties (Pintać et al. 2018).
6. *Prevention of cardiovascular disease or hypertension, diabetes, and other diseases*
   Acemannan from *Aloe vera* is documented for treating oral disease, cardiovascular disease, metabolic disease, tumor disease, and wound healing (Chokboribal et al. 2015). Polyphenols, carotenoids, and vitamin-rich extract of beetroot contribute to its antioxidant, anti-inflammatory, anticarcinogenic,

and hepatoprotective activities which can deter the occurrence of cardiovascular disease or hypertension and diabetes (Slavov et al. 2013). Polyphenols and ursolic acid from grape extract are known to be cardioprotective, hepatoprotective, and antidiabetic in addition to being anti-inflammatory, immunomodulatory, and gastroprotective (Pintać et al. 2018). Bioactive compounds, such as phenolic contents, carbohydrate, ascorbic acid, thiamine, and riboflavin from jujube extract, exhibit antihepatic property (Han et al. 2015). Jujube leaves can be employed as an antipyretic and to deter hemorrhage and diarrhoea (Song et al. 2019). Jujube leaf extract is used to nourish the heart, soothe the nerves, and for better sleep (Zhang et al. 2014). Prickly pears are used traditionally for the treatment of burns, wounds, edema, hyperlipidemia, obesity, and catarrhal gastritis (El-Mostafa et al. 2014).

7. *Food colorants*
   Beetroot extract is non-precarious, nontoxic, non-carcinogenic, and non-poisonous and are hence used as food dyes (Chhikara et al. 2019). Red gac arils are a suitable substitute for artificial red and orange color with added nutritional benefits (Huynh and Nguyen 2019). *Opuntia* spp. extract can be explored as a natural colorant with inherent antimicrobial and antioxidant properties (Melgar et al. 2017). Anthocyanin extract from passion fruit epicarp is suggested as a potential bio-based colorant (Ghada et al. 2020). Jambolan extract which is rich in anthocyanins (3,5-diglucoside, petunidin, malvidin, and delphinidin) is also an alternative to artificial colorants (Koop et al. 2021). Black carrot anthocyanin-rich aonla candy and betalains enriched papaya candy are developed by ICAR-IARI, Pusa, New Delhi, in which anthocyanins and betalains extracted by low-value crops are used as a replacement for artificial colorant. Such enrichment enhances the antioxidant potential of the matrix also by the non-biotechnological approach.
8. *Analgesics*
   Ingestion of gac fruit extracts has been documented to give responses like that of synthetic pain reliever (Huynh and Nguyen 2019). *Moringa oleifera* root extract is used to depress the central nervous system causing analgesia and potentiating a similar analgesic effect as that of morphine (Ferreira et al. 2008).
9. *pH indicator*
   Red cabbage anthocyanins are pink at pH 3, violet at pH 5, and blue at neutral pH and are hence employed as a broad natural pH indicator (Ghareaghajlou et al. 2021). *Garcinia indica* pigments also change their color from red to blue/violet at pH beyond 5.0 (Nayak et al. 2010).
10. *Bakery industries*
    Kokum butter manufactured from the edible oil extracted from *Garcinia indica* seeds is employed as a healthier substitute to shortening in chocolates and confectionary preparations (Nayak et al. 2010). In margarine and other foodstuffs containing solid and semi-solid fat, hydrogenation processes can be eliminated by using *M. oleifera* seed oil as a solidifying agent (Ferreira et al. 2008). Moringa powder and extracts which are packed with bioactives have

been incorporated in bakery products such as cookies, crackers, bread, etc., to name a few, to enhance its nutrient content (Saucedo-Pompa et al. 2018).

11. *Food packaging*
    Grape seed extract-based packaging film which is food grade and environmentally friendly along with edible packaging film has been documented by Chen et al. (2020).
12. *Cosmetics*
    Pigments extracted from *Garcinia indica* have the potential for UV light absorption which may be utilized for the production of sunscreen lotions and pastes in cosmetic industries (Nayak et al. 2010). The grape seed extract is used in cosmetics to delay skin aging and prevent UV damage due to its antioxidant properties (Chen et al. 2020). Polyphenols from grapes and Indian gooseberry (seed coat and embryo extract) are known to be antiaging (Pintać et al. 2018; Jaiboonma et al. 2018).
13. *Nutraceuticals application*
    Jujube seed extract and *Opuntia* spp. extract (rich in ascorbic acid, vitamin E, carotenoids, fibers, amino acids) have potential as sources for nutraceutical development (El-Mostafa et al. 2014; Berkani et al. 2020; Fernández-Luqueño et al. 2021).
14. *Insecticide*
    Moringa oleifera seed extract has been reported to exhibit larvicidal activity against mosquitos capable of transmitting dengue and yellow fever (Ferreira et al. 2008). Ethanolic extracts of leaves and ripe fruit of bastard oleaster (*Elaeagnus latifolia*) are documented to possess insecticidal properties. When employed at 5% concentration, adult mortality of 67–87% was observed for diamondback moth (Pumnuan et al. 2018).

31.5 Safety and Toxicity Issues Related to Overdose of Bioactive Compounds

The increasing presence of items on the market with health benefits necessitates their regulation and harmonization in key areas such as safety. The toxicology applied to bioactive chemicals should demonstrate the absence of harmful effects at acceptable levels, as well as assess the possible chronic effects if the goods are utilized in quantities greater than those suggested. The specific strategy should be determined on a case-by-case basis; so, prior to any toxicological development, it is critical to review all existing data including traditional art on bioactive compound characterization, nutridynamics, and nutrikinetics. This guideline proposes a broad strategy to be used in the development of bioactive compounds. It contains a first in vitro phase to rule out genotoxicity and endocrine effects, as well as a second in vivo phase with several options for study duration and extension.

The increased availability of functional foods and nutraceuticals on the market necessitates more safety studies and validation of their health claims. Because the food sector must meet the primary criterion of commercializing safe products and providing information in accordance with existing regulatory standards, its safety evaluation is a top priority. While utilizing the bioactive extracted from underutilized fruits and vegetables, there is a standard question always whether the bioactive compounds we are consuming possess risk with respect to food safety perspective.

Studies conducted on some polyphenols found that they may exert genotoxic or carcinogenic effects when consumed at higher concentrations. For example, caffeic acid at 2% level in the diet may induce kidney tumors and forestomach in rats and mice (Mennen et al. 2005). Thyroid peroxidase is inhibited by flavonoids, which interfere with thyroid hormone production (free radical iodination). Proanthocyanidins and ellagitannins have also been found to exert an antinutritional effect on animal nutrition by interacting with proteins and inhibiting several enzymes. 10 g/kg consumption of these bioactives has affected the growth and digestibility of rates. Proanthocyanidin-rich diet has reduced the net protein utilization in Egyptian boys. Chronic nephropathy has been observed in rats when higher doses (2–4%) of quercetin were taken (Santos-Buelga and Scalbert 2000). Acetogenins extracted from avocado seeds have shown toxic effects at 60–100 mg/kg bw, in mice. Studies on safety evaluation of Avosafe® have indicated that it has non-mutagenic effect on rats with lethal oral dose (LD50) of >2000 mg/kg and does not show any signs of abnormalities of organs when administered for the same dose for 14 days (Rodríguez-Sánchez et al. 2019).

Consumption of *Moringa* has not shown any toxic effects on humans, but there is a limit of its intake beyond which it may cause toxicity. Thus, to minimize the cumulative toxicity of the vital elements over time, a maximum of 70 g/day of *Moringa oleifera* leaves should be consumed. While its aqueous seed extract (400 mg/kg/day) has not shown any adverse effects so can be utilized as a nutraceutical alternative for functional food development (Chhikara et al. 2020). Studies conducted on the consumption of bael fruit extract showed that its administration up to a maximum concentration of 250 mg/kg body weight up to 30 days have not shown any significant effect in rats (Baliga et al. 2011). The toxicological database has suggested that acceptable daily intake (ADI) of bixin extracted from annatto seeds is 6 mg bixin/kg body weight (bw) per day while norbixin is 0.3 mg/kg bw per day (EFSA Panel 2019). Betanin is the major pigment of beetroot poorly absorbed in the human body also it was found to increase the blood pressure and heart rate if its dose is not administered properly. Recently, no genotoxicity and mutagenicity have been reported in betanin. One major concern related to its use is beeturia which means excretion of colored urine after consumption of red beetroot. As mentioned in several studies about the biological activity and bioavailability of betalains, its concentration in food should not exceed 100 mg per day in its pure form (preferably encapsulated). More studies involving health professionals are needed to reach a conclusion regarding its dose (Khan 2016). Saponins, phytates, and glycoalkaloids are examples of controversial bioactives in terms of their beneficial and harmful effect, their effective doses, limits, effects of processing, etc. (Thakur et al. 2011; Singh et al. 2016). Therefore, the safety of such bioactives must be fully ensured before consumption. Molecular characterization of bioactives should be done after extraction as well as in the final product to ensure whether any unknown interaction/

modification has happened or not during extraction and processing, storage, etc. One more important concern is mere traditional art should not be treated as full proof of safety since the toxic effect, though it may be mild, maybe neutralized by any other compounds/art which is consumed/practiced by a particular population group but that was not even known by other targeted population. Therefore, the next-generation research pertaining to bioactives would not be limited to extraction, stabilization, and utilization but it would be extended up to characterization, interactions, metabolite products, and their safety concerns.

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Sustainable Functional Food System: Key to Achieve Sustainable Development Goal 3

32

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Abstract

The world has been dealing with an epidemic of undernutrition as a result of population growth, necessitating an increased food supply. The goal of food security is to increase food availability for the population, resulting in a healthier and more favourable imbalance between food demand and supply. Recent advances in food technology, plant breeding, and genetic engineering have enabled places around the world to have enough food, resulting in a reduction in undernutrition and the growth of obesity and non-communicable diseases. Because functional foods can help to alleviate these issues, there is a need to produce more of them in order to ensure that they are used more efficiently and equitably as part of a complex and integrated worldwide plan for global functional food security. Thus all national as well as international agencies should collaborate to educate the global food business and governments about the importance of increasing the production of functional foods. Such attempts to buy or produce have not been made in middle-income countries, resulting in an obesity epidemic, which must be addressed across Africa to prevent obesity. Functional Food Security appears to be sufficient to treat all aspects of global malnutrition, including undernutrition, micronutrient deficiencies, overweight, obesity, and diet-related National Sustainable Development Strategies (NSDS). This chapter contains a comprehensive view of the kinds of functional foods, their utility as a tool to mitigate nutritional deficiencies and achieve the SDG3 of good health and well-being, their use from a global perspective, and their role in the alleviation of food insecurity.

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32.1 Introduction

A food, when ingested, has three functions, i.e. providing nourishment through carbohydrates, proteins, fats etc., aesthetic and gustatory satisfaction, and providing overall health benefits to the body. A functional food is a food that provides energy and is taken as a normal diet food but it also provides with some added benefits and reduces the risk of diseases in body. It is also termed as nutraceuticals, medical foods, etc. (Guo 2013). These functional foods become beneficial because of bioactive compounds present in them. These are some small quantity parts in foods that provide the extra nutrition and health benefits to our body. With these bioactive components and functional foods, we can have definite positive health effects that can help in sustainable development and also, help in inching closer to its mentioned goal 3, i.e. good health and well-being. People can incorporate some foods in their diet and make use of them for leading a better life. These extra benefits can include anti-carcinogenic properties, antioxidants, polyphenols, phytosterols, carotenoids, fibre, etc.

Fruits like pears, berries, kiwi, and vegetables like broccoli, spinach, with other legumes, nuts, and seeds fall in the category of functional foods. Also, fortified foods are functional foods because of the added vitamin or mineral.

The sustainable development goals that need to be completed till 2030 include SDG3, i.e. good health and well-being. And here, functional food system can be used to make it happen. With added benefits of functional food, people would get both nutrition and added antioxidant, anti-carcinogenic, and other properties.

32.2 Different Types of Functional Foods and Their Bioactive Compounds

Functional foods not only have benefits of nutritional aspect, it also protects against disease and support better health and development. They can be classified on the basis of its origin like plant, animal, microbial, and miscellaneous (Vattem and Maitin 2015).

32.2.1 Plant-Derived Functional Foods

They are separated as primary (important for growth) and secondary metabolites (not essential for growth, but important for plant survival mechanisms).

Primary metabolites include plant proteins, beta-glucans, and omega-3-fatty acids. Here, plant proteins decrease consumption of fat and cholesterol, for example, soy protein isolates, texturised vegetable proteins, etc. Beta-glucans also lower cholesterol absorption in the body. Omega-3-fatty acids reduce platelet aggregation (Vattem and Maitin 2015).

Secondary metabolites can include steroids, antioxidants, vitamins, phytoestrogens, etc. Here, phytoestrogens are oestrogen-like compounds that decrease post-menopausal cancer development in body. Antioxidants lower oxidation and vitamins prevent deficiencies. Steroids present in oilseeds compete for cholesterol absorption and lowers its content. There are many examples of utilising waste materials also from plant that can be utilised for extracting many different bioactive components having functional potential (Thakur et al. 2021).

32.2.2 Animal-Derived Functional Foods

These are zoochemicals, including omega-3 and omega-6 fatty acids, small peptides, whey protein, casein protein, etc. Here, omega 3 and omega 6 fatty acids are anti-inflammatory, enhance immunity, and protect against neurodegenerative diseases (Vattem and Maitin 2015). Omega-3 fatty acids are present in soy oil, canola oil, and walnut, salmon. And omega-6 is present in vegetable oil, whole grains, nuts, etc. Whey, casein, and small peptides get digested and absorbed easily and help in building muscle mass.

32.2.3 Microbial Functional Foods

These include probiotics, prebiotics, symbiotics, etc. Probiotics are natural gut microflora, and prebiotics are included in the diet so as to promote growth of gut microflora. Symbiotics are those which contain both pro- and prebiotics in a random fashion. These help as functional foods by promoting growth of gut microflora so as to reduce the growth of pathogens (Vattem and Maitin 2015).

32.2.4 Miscellaneous Functional Foods

Mushroom and algae come under this category. Mushrooms have antibacterial, antiviral, and anti-inflammatory properties. Algae provide omega-3 fatty acids, thus enhancing immunity, protecting against neurodegenerative diseases, and having anti-inflammatory properties (Vattem and Maitin 2015).

There are many functional foods in our diet, and they are gaining importance because of their additional benefits. Some functional foods are discussed below:

Berries—Different types of berries (cranberry, blueberry, strawberry, gooseberry, raspberry, etc.) have flavonoids and other phenolic compounds that help in promoting health development. These phytochemicals possess some good properties for the body.

For example, cranberry is a good source of anthocyanin, vitamins, minerals, fibre, etc. It helps in preventing urinal tract infections and influenza. It has high vitamin C content and thus, can be used to prevent scurvy too.

Cranberry also has anthocyanin, flavanol glycosides, and phenolic acids and has good antioxidant properties (Guo 2013).

Grapes—Grapes have phenolic compounds present in them. Red grapes have anthocyanins and white grapes have flavanols as the main phenolics. These provide with the antioxidant properties in the diet. Grape seeds, skin, and stem have flavanols and proanthocyanins as flavonoids.

Also, grapes have phytoalexins like resveratrol which have anti-infective, anti-inflammatory, and antioxidant properties in the human body. This compound also helps in lowering of LDL cholesterol and reducing risk of CVDs (cardiovascular disease) (Guo 2013). Grapes have these therapeutic effects leading to high immunity and inhibiting allergies.

Tomato—Tomatoes are used widely and are a rich source of antioxidants. They have vitamin C and lycopene. This lycopene has the most effective antioxidant property and also helps in preventing cancer of gastrointestinal tract and also reduces risk of cardiovascular disease. These are included in therapeutic effect of tomato.

Prebiotics—Prebiotics are some non-digestible food ingredients that stimulate activity of microbes in the gut and improve health of a person. It also shows other benefits on lipid metabolism, enhancing immunity of the gut, glycaemic control, maintaining gut hormones, providing satiety, etc. Trans-galacto-oligosaccharides and inulin are two prebiotics that have been validated (Saarela 2011).

Apart from them, many other prebiotics are also coming up for the industries. Like soybean, gluconic acid, polydextrose, etc.

Garlic—Garlic has a lot of sulphur-containing compounds that have antioxidant properties. Apart from it, there are many therapeutic effects of garlic. It reduces harmful LDL cholesterol, prevents blood clots, has the ability to block chemical carcinogens, and protects oxidation of cells. It can all be grouped together as antimicrobial, cardiovascular effects, anti-carcinogenic, and other related benefits (Guo 2013).

It strengthens the heart and keeps human well-being. It reduces lipid content in arterial cells and prevents intracellular lipid accumulation. Also, it has the ability to activate gastric secretions leading to prevent gastrointestinal cancers.

And garlic is truly having many benefits including those of enhancing immunity, thiamine absorption, and treating stomach problems and respiratory problems and also shows hypoglycaemic effects.

Tea—Consumed worldwide, tea consists of many kinds of polyphenols and catechins.

Tea is related with having anti-carcinogenic properties. It prevents cancers related to bladder, stomach, colon, breast, etc. In green tea, this cancer prevention is mediated by epigallocatechin-3-gallate, a polyphenolic group in green tea (Guo 2013).

It has antibacterial effects, and also, because of the antioxidants in tea, LDL build up in blood is prevented, leading to less risk of heart disease. Apart from this, tea also protects liver from alcohol and has some anti-inflammatory effects too.

Mushrooms—Edible mushrooms have a lot of bioactive compounds that help in reducing risk and treating some diseases. It has antitumour, antimicrobial, hypoglycaemic, enhancing immune system, and health-promoting effects on the body. Thus, it is emerging as a functional food in the industry.

This is because of the presence of structural polysaccharide, beta-glucans, which may form complex with proteins (Vattem and Maitin 2015). The most active form of these beta-glucans in mushroom was isolated from different mushrooms. Also, due to triterpenes and alkaloid eritadenine in shiitake mushroom, it has properties in lowering of cholesterol. Terpenes not only have low cholesterol properties but also show anti-inflammatory, hypotensive, and antiplatelet activity too.

Mushrooms have polyphenols and ergosterol acting as antioxidant compounds. Some mushroom polysaccharides boost immunity against tumours and viral and bacterial diseases. They also have properties to protect and treat against CVD. Not only this, it is effective against diabetes and also rich in dietary fibre reducing blood glucose levels (Vattem and Maitin 2015).

Whey protein—Whey protein are one important protein that possesses many health benefits like improved physical performance, faster recovery after exercise, weight management, reducing blood pressure, anti-carcinogenic effects, anti-stress effects, prevention of mucosal inflammation, etc.

32.3 Sustainable Development Goal (SDG)

Sustainable development is the process of meeting human development goals with also, sustaining the ability to get all natural systems for its resources for further use. Sustainable Development Goals (SDGs) which are also called Global Goals were taken up by United Nations in 2015 for eradicating poverty, better health, no discrimination against girls, and improving a sustainable life with peace. They are formed to get fulfilled by 2030 and are a total of 17 goals for ensuring the same (WHO 2019).

32.3.1 The Third SDG Mentioned Is Good Health and Well-Being

A healthy individual is very important in maintaining a sustainable life. With healthy individuals, the world will see decrease in diseases and death, and people will work with their utmost performance and help in building a better environment. Some goals for this third goal are as follows (WHO 2019):

- To reduce global maternal mortality rate.
- To end preventable deaths of children and newborn under 5 year age.

- To end epidemics of AIDS, malaria, tuberculosis, and other waterborne diseases.
- To prevent drug abuse and implementing tobacco control.
- To achieve universal health betterment, including financial protection, good health care services, quality medicines at affordable prices, etc.
- Focusing on mental health issues.

Poor health leads to sufferings and diseases. With SDG3, this wants to be ensured that there is increase in life expectancy, providing healthcare systems and reducing diseases (WHO 2019). Or else, people would be burdened with these losses and problems. Thus, the health of people at all ages is required to be a goal for sustainable development of the world. People after being healthy become an asset for strengthening economic growth of country too. Thus, SDG3 is equally important as other goals.

32.4 Functional Food System: Key to Achieve Sustainable Development Goal 3

When we talk about a balanced diet, it includes all the nutrients and essential compounds that our body needs to function properly. It lowers the risk of nutritional deficiencies and heart disease by lowering the levels of cholesterol and blood pressure. Nowadays, with increase in junk food, there are a huge number of cases of obesity, some nutritional deficiencies, and also, cardiovascular diseases.

With nutrients and compounds like carbohydrates, proteins, fats, vitamins, and minerals, the body functions properly, and including functional foods in diet enhances this nutrition giving part with some additional benefits. Eating functional foods would reduce the risk of heart disease, cancer, and other health problems. This in turn would help in coming closer to the main Sustainable Development Goal 3 of good health.

As we now know that functional foods are whole, enriched, and fortified. They are beneficial for our health not only with nutrients in them but also with some extra add-ons (Vattem and Maitin 2015). Hence, by using functional food system as a new approach can be a good option to inch closer towards SDG3. Consumers are now trying to move to a better diet and include nutrition and other benefits in their plate. So, applying our knowledge and research to use it for a further goal is important.

Food is the one thing that is needed by the body to sustain life. And for a healthy living, functional foods having bioactive compounds like flavonoids, polyphenols, vitamins, and pigments are important in our diet. They protect our body from diseases and enhance growth and development. They reduce cholesterol, blood pressure, and risk of cardiovascular disease and have antioxidant and anti-carcinogenic properties which, in turn, would help in maintaining good health and well-being of people for a sustainable life.

By vision of this goal, by 2030, this is to be completed, and we should try to make that happen. SDG3 can be effective if we include some more functional foods in diet, so as to retard some processes, prevent some diseases, and make our body healthier.

They are easily available and would help in making people work to their best level and eventually come in economic growth of country.

32.5 The Role of Food Industry in the Processing of Functional Foods

The potential health impacts of food processing are receiving more attention in terms of health promotion and illness prevention. Almost all foods must be processed in some way before they can be consumed. Cooking, smoking, drying, salting, fermenting, preserving, heating, milling, and refining are all examples of food processing. Foods become more appetising after processing due to improvements in nutrient bioavailability, diversity, time span, and convenience, as well as a lower risk of food-borne diseases. Loss of nutrients, vitamins, minerals, omega-3 fatty acids, fibre, phenolics, and other bioactive substances are all possible side effects of food processing. There could also be increased dosages and introduction of hazardous components including trans-fat, advanced glycation end products, peroxidised nutrients, salt, and other preservatives, heterocyclic amines, and other chemicals due to the quick digestion of starch and sugar (Doyon and Labrecque 2008).

There's a belief that frying foods increases the risk of cardiovascular disease, but this isn't supported by the research. An outsized randomised study that included as part of the intervention the advice to use high amounts of virgin vegetable oil, including for frying foods, was supported by the results of a meta-analysis of 23 studies that found virgin vegetable oil significantly reduced the risk of CVDs. Increased consumption of fried foods may be linked to a higher risk of weight gain, while the type of oil used may alter this link. Some more natural foods, such as eggs, butter, and unprocessed red meats, have been related to better cardiometabolic results. Other packaged or processed foods, such as nut- and fruit-rich snacks, phenolic- and omega-3-rich vegetable oils, and margarines, have been shown to improve cardiovascular and metabolic health (Saarela 2011; Shetty 2015).

Similarly, certain beneficial foods, such as fruits, nuts, and seafood, are little processed, whereas cereals, refined grains, preserved meats, and other high-sodium foods, as well as dishes cooked with hydrogenated oils, are hazardous. These viewpoints can give the impression that you should always choose "natural" foods and avoid processed or ultra-processed foods, which is incorrect. Many less processed foods appear to be healthy, whereas many more highly processed foods appear to be unhealthy, which may serve as a good general rule, albeit it is not absolute. It's likely that both the type of food and how it's processed play a role. By focusing solely on natural versus processed foods, the healthcare professional, consumer, significant other, and food producer can find items that are both healthy and little processed.

Avoid foods high in refined grains and carbs, as well as those with added sugars and hazardous additives such as salt, saturated fat, and trans-fat. As the world's food production shifts towards increasingly processed foods, more research is needed to identify and spread methods for effective processing, rather than an unfeasible specialisation in food processing inhibitors.

Dietary supplements are commonly consumed by the general people, often in high or pharmaceutical amounts, despite the lack of clear evidence for their therapeutic effects. Observational studies and controlled trials do not support the use of several vitamins as prospective therapeutics to prevent CVD or other illnesses; however, the majority of trials have ruled out the function of vitamins, minerals, and antioxidants in NCD prevention (Hill 2009).

32.6 Overview of Global Developments in Functional Foods

ILSI organised the second Asian Regional Workshop on Functional Foods in Bangkok in October 2004. The symposium, which brought a total of 30 regulators and experts from numerous Asian countries, focused on advancing harmonisation efforts, notably in the areas of scientific substantiation and safety evaluation. Participants in the event felt that the region had a lot of potential for developing functional meals. A diverse range of products and physiologically active compounds can be found in the region. Progress in this sector has been hampered by misunderstandings and misuses of the term "functional foods." A well-coordinated plan was deemed to be advantageous to regional growth. Let's take a look at the global evolution of functional meals (FAO 1983).

32.6.1 Bangladesh

The majority of Bangladeshis, including food and nutrition professionals and policymakers, are unfamiliar with the term "functional food." Some foods, on the other hand, are categorised as "health" or "healthful" foods, as well as functional foods, since they are known to provide health benefits.

Plant items account for about 90% of total food mass and 96% of total dietary energy in Bangladeshi cuisine. Plants have been shown to contain thousands of bioactive compounds, pigments, and natural antioxidants, many of which have been related to health advantages such as protection against heart disease, hypertension, cancer, diabetes, and other illnesses. As a result, phytoprotectants have been coined. These include (a) organosulphur compounds present in *Allium* (garlic, onions) and *Brassica* species (cauliflower, cabbage) as well as (b) isoprenoid pathway products found in all vascular plants (e.g. coloured vegetables) (Kris-Etherton et al. 2002).

32.6.2 India

India has a long history of producing a diverse range of traditional and ethnic foods with beneficial properties. Various condiments, spices, herbs, whole meals, seasonal fruits, and vegetables have been chronicled in the literature and even in India's ancient scriptures for their health benefits. Functional foods in India encompass everything from herbal extracts to functional components, as well as nutritionally enhanced conventional foods and unusual ingredients added to them.

Turmeric, black pepper, cloves, cinnamon, asafoetida, cumin seeds, omum, mint, tulsi (holy basil) leaves, various green leafy vegetables, other vegetables and fruits, whole wheat, and millets are some of the functional foods used in India's everyday diet. These foods are used in everyday culinary preparations as well as in special cuisines. Each of these foods offers unique health benefits that are well-known. Those useful meals are used to treat a variety of diseases (Guo 2013).

Food to food fortification, sprouting, malting, and fermentation are all techniques that improve the functional characteristics of food and are common in Indian cuisine. Nutrient fortification of foods has also been attempted. These include hydrogenated fats fortified with vitamins A and D, iodised salt, vitamin A-fortified milk, flour fortified with iron and vitamin B, and iron-, vitamin B-, and vitamin A-fortified chocolates.

Research and development in the field of functional foods, which includes nutraceuticals, pre- and probiotics, and novel additives, has grown increasingly important in recent years, with a focus on prevention. R&D institutes like as the Central Food Technological Research Institute in Mysore and others are leading the way (FAO Regional Office for Asia and the Pacific 1998).

Various traditional foods containing bioactive compounds that give extra health advantages beyond the physiological role of nutrients found in such foods must be scientifically supported. Because of its health-based approach and claims of illness prevention, research on functional foods claims has gained traction in recent years. The regulatory issue of functional foods demands specific attention and will not only be supported by a rustic approach but will also occupy a key position in Codex, which will be driven by the region. The discovery that a particular component is beneficial to one's health is only the beginning of the event of marketable functional foods. By confirming the proven with enough scientific basis, this has a huge reassuring effect on the buyer. The biotechnology and nutrigenomics facilities have a significant impact on functional foods. The growing field of nutrigenomics, as well as existing initiatives and network projects within it, are extremely important (Asgary et al. 2018).

The overall perspective for food safety and functional foods is critical, not only for the health claims made by such foods but also to reassure customers about their safety. In terms of convenience and nutritional benefits, functional foods are projected to play a significant role. At the same time, both rural and urban communities should have access to these at reasonable pricing.

Recognising that the practice of consuming traditional foods and using special processes like sprouting, fermentation, malting, supplementation, and others for food preparation is on the decline as a result of increasing urbanisation and globalisation, it's critical to strengthen sound nutritional practices that enhance functional components in food through extensive awareness generation about functional foods with the goal of improving people's nutrition and health.

32.6.3 Indonesia

The demand for healthy food and functional foods has increased as a result of consumer knowledge and interest in the relationship between diet or diet components and health. In urban Indonesia, using functional foods and supplements to prevent sickness and preserve health has become fashionable. As a result, the availability and demand for commercial functional food products has skyrocketed. The Indonesian government is making progress in the legal elements of functional foods in line with these advancements in the country. The National Agency for Food and Drug Control is now reviewing a draught regulation on functional food control and a draught functional food guide. An expert group and stakeholders drafted the draughts, which are likely to become legal documents in the near future. Functional food is defined as natural or processed food that contains one or more components that have been scientifically demonstrated to have health benefits.

Definitions, coverage, criteria, standards, production, labelling and advertising, restriction, supervision, inspection, and sanctions are all included in the upcoming rule on functional food control. The majority of functional foods on the market are aimed at children and young men and women. Essential fatty acids such as omega-3 (eicosapentaenoic acid and docosahexaenoic acid) and omega-6 fatty acids, as well as calcium, are the most common components of functional foods advocated by food manufacturers for young children's foods. Curcuma, a herbal component, is also added to several drinks for children. The addition of iron, calcium, and traditional herbal components like ginseng, ginger, and yohimbine to functional diets for young women and men is meant to promote stamina. A herbal component of *saoropus androgynus* leaves, a green leafy plant (Katuk) has been shown to increase nursing women's breast milk production, has been put to a particular milk for lactating mothers. Research and laws are being strengthened, and information is being shared (Nakai 2018).

32.7 Functional Food Security

Functional food security can also be described as a state of food availability in a country where functional foods are available to all or any sectors of society at a reasonable price. Food is termed "functional" if, in addition to providing basic nourishment, it benefits at least one or more target functions in the body when ingested as part of a regular diet. In Japan, where a food category called FOSHU (Foods for Specific Health Use) was formed in 1991 to reduce rising healthcare expenses, the first functional food products were introduced (Shaw and Clay 1998). Vitamins, as well as nonvitamin components like polyphenols, are required for antioxidant and redox systems. Antioxidant and redox activities are critical for all cells and tissues, but their benefits have only been established when ingested as part of a diet rich in fresh fruits and vegetables. The balance of colonic microbiota and other gastrointestinal functions is also maintained by antioxidants (Rao et al. 2019).

The food components found in functional foods may have an impact on moods, behaviour, as well as cognitive and physical abilities. There's the regulation of macronutrient metabolism (carbohydrates, amino acids, and fatty acids) as well as hormonal regulation (e.g. insulin/glucagon balance). Consuming functional dairy products with specific therapeutic effects to inhibit TAMO is often a delectable reward for living a healthy life free of CVDs and malignancies (Maxwell 1996; Maxwell and Smith 1992; Mozaffarian et al. 2021).

The Seven Countries Study was the first large study to suggest that dietary fat could be a risk factor for cardiovascular disease (CVD), coronary artery disease (CAD), and stroke. However, it is the standard of fat, not the number that is linked to CVDs and other chronic diseases.

Further research revealed that flavonoids and omega-3 carboxylic acid content of foods can explain variation in CAD and cancer risk across the seven countries: lower risk in Japan and Mediterranean countries; higher risk in northern European countries and thus the United States, where diets are high in fast foods and the majority of the population has food security (Vattem and Maitin 2015; Roger et al. 2012).

Between 1972 and 1992, heart disease mortality in Finland decreased by 55% in men and 68% in women, according to the North Karelia Project's 20-year results and experiences. The total fat composition of the Finnish diet reduced from 38% to 34%, saturated fat from 21% to 16%, and fat from 3% to 5%, resulting in a 16% reduction in cholesterol intake. A switch from boiled to filtered coffee could have resulted in an additional 0.3 mmol/L (11 mg/dL) drop in blood cholesterol (Takahashi et al. 2019).

As a result, these alterations could explain the entire change in serum cholesterol, which has been 1.0 mmol/L (38 mg/dL) on average. During this time, fruit and vegetable intake climbed by two to triple. Dietary changes appear to explain the drop in blood cholesterol and inflammation that has led to the remarkable fall in coronary heart disease mortality in Finland. Six randomised, controlled trials with sufficient sample sizes have been published, all of which suggest that diet can reduce the risk of CVDs. These groundbreaking clinical trials were released following the Seven Countries Study, and therefore the North Karelia Project proved that dietary modification can result in significant reductions in CVDs (Rao et al. 2019). Effects of dietary modifications in fat, fish, and fibre on death and myocardial infarction in the Diet and Reinfarction Trial (DART), and show the effect of Mediterranean-style diets in the Lyon Trial. The Indian Experiment and therefore the Indo-Mediterranean Diet Heart Study reported that that diets rich in vegetables, fruits, nuts, and whole-grain legumes in conjunction with mustard oil (rapeseed) can cause a big decline in CVDs in patients to post arteria coronaria disease. The beneficial effects of those diets could also be thanks to the decline in inflammation and increased content of omega-3 fatty acids and flavonoids within the diet (Singh et al. 2019).

The PREDIMED trial might be a large primary prevention trial in which Mediterranean-style diets with nuts or vegetable oil were utilised to show that both diets resulted in a significant reduction in CVDs when compared to a control group. Further cohort studies with a large number of patients revealed that Mediterranean-style diets can lower mortality and improve survival. Consumption of those diets may also be linked to higher intakes of antioxidant polyphenolics and flavonoids, omega-2 fatty acids, fibre, and vitamins, all of which have been shown to reduce oxidative stress and inflammation, as well as antiplatelet effects (Tsao and Akhtar 2005).

Functional food security appears to address undernutrition and micronutrient deficiencies, as well as overweight, obesity, and diet-related NCDs. More explicit targets across all of these challenges are needed to urge donors, countries, and others to address these fundamental difficulties (Watson et al. 2018).

32.8 Conclusion

From production to consumption, food systems may be improved more nutritious and environmentally sustainable as a whole. Malnutrition and micronutrient deficiencies, as well as the rise of overweight and obesity, are still prevalent in many parts of the world, according to the United Nations Food and Agriculture Organization (FAO). Multiple forms of malnutrition can coexist in the same country, household, and individual. Millets, in particular, can help food systems become more sustainable and supportive of excellent nutritional outcomes by increasing their production and consumption. It can also serve to raise awareness about the need for a multi-sectoral approach that includes agriculture and food systems, health, sanitation, social protection, employment, and education, all of which contribute to enhanced economic security (World Bank 1986).

To close the gaps in core data on diets and nutritional status, all major stakeholders, including healthcare providers and food and agricultural experts, must collaborate. Promotion of management approaches and technology to improve sustainability and nutrition, as well as assessing the effects of markets, commerce, and market structure on environmental sustainability need to be worked upon. The importance of human nutrition cannot be overstated. Finally, efforts need to be made in the sphere of television commercials and awareness of the importance of client choice. The food sector is critical for widespread health and long-term human advancement in order to meet nutritional and sustainability goals (Dixon et al. 2009).

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Non-thermal Processing Techniques for the Extraction of Bioactive Components of Food

33

Kanishka Singh and Vatsala Sharma

Abstract

In today's era, the consumers are getting more aware and concerned about food quality. Hence, there is demand of high-quality, minimally processed, and nutritionally healthier food. The focus of food scientists and engineers have been driven from traditional food processing and has moved toward minimal food processing and preservation technologies that are environment-friendly, sustainable, low cost, and able to preserve quality attributes of the food. This has led to the non-thermal technologies which basically are processing methods that allows enhancing mass transfer rates, increasing cell permeability as well as increasing secondary metabolite diffusion, leading to higher extraction yields, fewer impurities on the final extract, extractions at room temperature with thermo-sensitive structures preservation, use of different non-organic solvents, low energy consumption, short operation time, and have no significant or lower effect on the structure of bioactive compounds. It consists of Pulse Electric field (PEF) and High-Pressure Processing (HPP). This paper aims to review the effect of the main emergent extraction technologies (high hydrostatic pressure, pulsed electric fields) on the individual profile of bioactive compounds from plant material.

Keywords

Nonthermal food processing · Bioactive components · Sustainable · Nutrition

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33.1 Introduction

Food preservation has become the most important need and challenge for food industry. There is an endless conflict between the microorganism and food either spoiling it or making it unsafe to consume. Contemporarily, food industry is investigating on the replacement of traditional food preservation techniques like heating, salting, drying, etc. with new innovative techniques. The consumer is also becoming more aware about their health and therefore demands minimum processed food which have least loss of nutritional properties. Nowadays, easy-to-handle, less processed, high-quality, tasty food is demanded. The most investigated new preservation technology is nonthermal processing (NTP). The main task for nonthermal processing is food safety, microbial inactivation, and preservation while retaining all the nutrients and quality of product. Apart from providing safe food, this technology has to be low in cost, consume less energy, and shorten treatment time, lowering carbon footprint (Djekic et al. 2018).

Many researchers have worked on several nonthermal technologies such as pulse electrified field (PEF) and high-pressure processing (HPP) that can ensure sensory quality and nutrient values of food with less processing time and low temperature and still ensure food safety and long shelf life. Efforts are made to develop nonthermal processing with no harmful side effects to ensure the delivery of safe food. NTP application has huge advantage for foods which have strong flavor, aroma, and stronger taste comparatively toward food which does not acquire strong flavor and taste. Beverages, sauces, seasonings, meat products, seafoods, starch, cereal, grains, and more also created potential for nonthermal processing. Table 33.1 illustrates the types of NTP and what is their mechanism of activation and its application. Different NTP are used depending on the profile of the food products, whether it is highly perishable or non-perishable. NTP can operate at refrigerated or room temperatures (RT), ensuring that compound denaturation is avoided or at least decreased, since they do not use high temperatures, easing the extraction of such compounds, particularly the volatile oils. For so, in this review, the authors aim to analyze the effect of such technologies (high hydrostatic pressure, pulsed electric fields) on the bioactive individual compounds profile from herbal materials.

The sterilization mechanism of nonthermal processing mainly depends on few salient features listed below:

1. Attack on cell membrane and changing the regulatory functions of microorganism.
2. Changes the genetic materials to cause metabolic disorders in microbes.

Considering the organoleptic changes, NTP techniques (like UV radiation, irradiation, HPP, PEF, irradiation) have been develop with the ability to inactivate pathogenic and spoilage microorganism. The objective of this review is to highlight its technology, implementation application in food industry, and their effect on quality attributes of food.

Table 33.1 Different types of NTP, their mechanism, and application

Process	Mechanism of inactivation	Application
UV light	UV exposure helps in mutation of DNA	Control fungal decay in fruits and vegetables, food packaging, and also on surface of food
Pulse electric field (PEF)	Helps in the destruction of cell wall of the microorganism	Extend shelf life of milk and juices. Mainly used in liquid food
Ozone processing	It affects the unsaturated lipids in cell membrane causing leakage of cellular components which lead to death of the microorganism	To enhance the shelf life of meat and poultry products, used in sanitization of vegetables
Irradiation	Its ionizing radiation sends energy into bacterial or mold cells and help in breaking their chemical bonds	To extend shelf life of fruits and vegetables, controls sprouting of onions and potatoes, also helps in killing bacteria in meat, seafood, poultry, and spices
Cold plasma	It alters the lipid, protein, and nuclide acid of microorganism or making it harmless	It helps in inactivating microbes on meats, poultry, fruits, and vegetables
High-pressure processing	Permeabilization of cell membrane	Used in packaged foods or bulk food

33.2 Nonthermal Processing Techniques

33.2.1 PEF (Pulse Electric Field)

Pulse electric field is nonthermal technology that is used to inactive bacterial cell at ambient temperature. It is potentially seen as an alternative technique to thermal pasteurization because it reduces detrimental changes in sensory and physical properties of food (Kumar et al. 2016). This technology has been found better comparatively to other instant heat technology because it kills the microorganism without destroying the important qualities like flavor, color, texture, taste, and nutritional value of processed food. During PEF process, energy is stored in the capacitor retrieved from high-voltage power and discharge through food which is stored in treatment chamber. The basic diagram of PEF treatment is mentioned below (Fig. 33.1). It contains high-voltage power source, an energy storage capacitor bank, and treatment chamber.

In the process of PEF, it involves the application of high-voltage pulses 12–80 kV/cm for short time period on fluids between two electrodes (Senorans et al. 2003). High-voltage impulse break the cell membrane making it permeable into small molecules which causes it to get broken (Zimmermann 1986). Time of exposure depends on several things like design of the chamber.

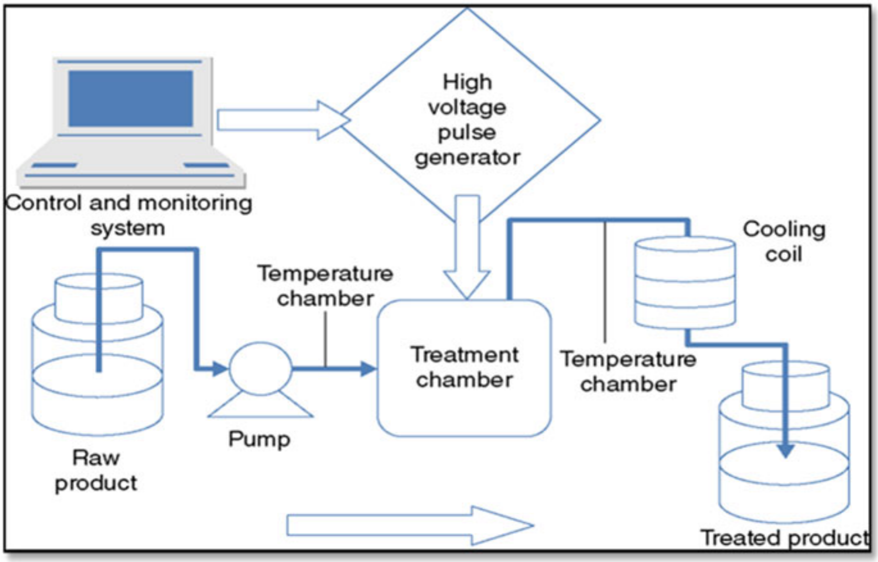

Fig. 33.1 Schematic diagram of PEF process. (Gamli 2014)

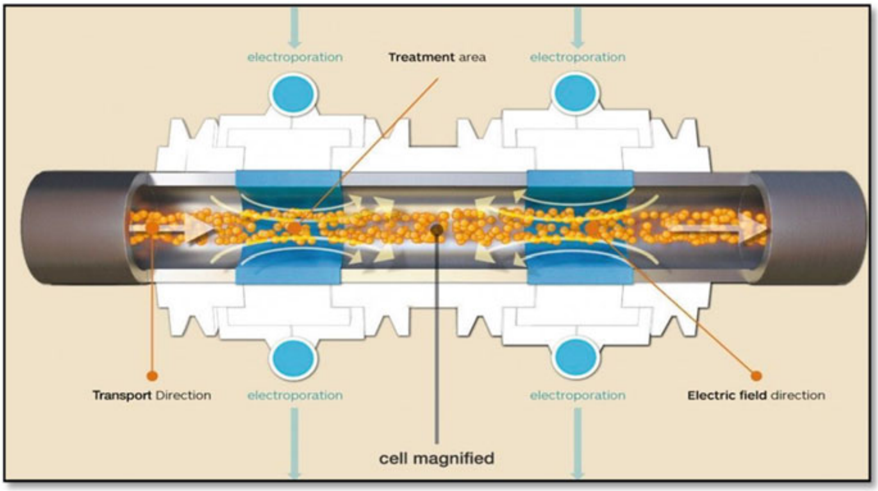

Fig. 33.2 Pulsed electric field preservation. (From i3 Food: New Treatments for Better Food 2022)

Among all the emerging nonthermal technology, PEF is considered to be more effective and appealing technology due to its short treatment time and reducing heating treatment effect with respect to other technologies (Fig. 33.2). The application of electric field results in cellular death in the bacterial cell due to generation of pores without affecting protein and nutrition of food.

33.2.2 Application of PEF

The advantages of PEF exhibits the extraction of high-added value compounds from a large number of fruits and vegetables (apple, carrot, table beet, etc.), food wastes and by-products, leaves (tea, spinach), herbs, mushrooms, and suspensions of cells (yeasts, microalgae, etc.). This distillation method is apt for the discerning recovery and extraction of sugar, inulin, starch, proteins, polysaccharides, polyphenols, pigments, flavor compounds, phytochemicals, and other high-esteemed components (Novosad et al. 2021).

The effect of PEF on bioactive components, color, and flavor of green tea (GT) infusions were analyzed by Zhao et al. (2009). These authors came to the results that PEF is a propitious nonthermal pasteurization technology which efficiently retains polyphenols, catechins, and original color of GT infusions using an electric field strength from 20 to 40 kV/cm for 200 μs. Additionally, PEF causes an increase of 7.5 % in the total free amino acids at 40 kV/cm. The most recent published works are presented in Table 33.2.

33.3 High Hydrostatic Pressure Processing

High hydrostatic pressure (HPP) processing is a novel thermal method which has potential in producing safer products while maintaining characteristic of food products. HPP uses water as a medium for pressure transfer to the product to inactivate pathogenic and spoilage organisms like molds, yeast, and gram-positive and gram-negative bacteria. This NTP has a minimal effect on flavor, taste, texture, appearance, and nutritional value of food. HPP pressure ranges between 100 and 800 MPa. This technology is mostly recognized by the USFDA as ready-to-eat foods. The processing is conducted at refrigerated temperature eliminating all the loss caused by thermal effects and that's why highly beneficial for heat-sensitive products.

The basic principle in which HPP affects different food products are:

1. Pascal's isostatic principle.
2. Le Chatelier's principle.

Shown in Fig. 33.3 is a schematic layout for high hydrostatic pressure treatment plant. The HPP requires pressure vessel, heat/cold system, pressure transmitting system, and maintaining it and control process.

The main function of HPP is sterilization which is irreversible destruction of cellular structure which results in disruption of cell after undergoing HPP processing. Moreover, every complex structure present in the cell such as ribosomes and proteins are changed by HPP treatment that causes death of the cell by affecting its metabolism (Zhang et al. 2018).

Post HPE, some variations were found, in different types of studies of herbal materials, such as the extraction of ginsenosides from ginseng, salidroside from

Table 33.2 Optimized extraction conditions for extraction of bioactive components using PEF

Optimized extraction conditions											
Plant material	Compounds (yield, %)	Frequency (Hz)	Electric field intensity (kV/cm)	Pulse duration (us)	Number of pulses	Pulse intervals (ms)	Specific energy input (kJ/kg)	Ratio (g/mL)	Solvent	Number of compounds	Biological activities
Green tea (*Camellia sinensis*)	Total phenolics; free amino acids; volatile compounds; tea catechins (gallocatechin, epigallocatechin, epigallocatechin gallate, epicatechin, epicatechin gallate)	–	20–40	2	100	–	–	1/100	Water	*n*	1
Mandrake (*Podophyllum peltatum*)	Podophyllotoxin	840	19.4	2	302–400	1.188	–	60/90	Water	1	X
Sesame (*Sesamum indicum* L.)	Total polyphenols; lignan glucosides	–	13.3	10	0–700	2000	0–291	35/350	Water	*n*	–
Borage (*Borago officinalis* L.)	Total phenolics	300	1–7	3	5–50	15–150	0.04–0.61.1	10/100	Acidic water	–	Antioxidant
Stevia (*Stevia rebaudiana* Bertoni)	Chlorophyll a; chlorophyll b; total carotenoids; total phenolics; chlorogenic acid; caffeic acid;	–	13.3	10	0–300	–	24–141	20/320	Water	6	Antioxidant

	ferulic acid; protocatechuic acid; gallic acid; catechin										
Spearmin (*Mentha spicata* L.)	Total phenolics	–	4.5	10	99	100	4.10	0.2/0.8	Mannitol	–	Antioxidant
Ginseng (*Panax ginseng*)	Total saponin; ginsenosides (Rb1, Rc, Rb2, Rd., Rg1, and re)	1000–3000	15	2	10	–	–	1/50	Water	5	–

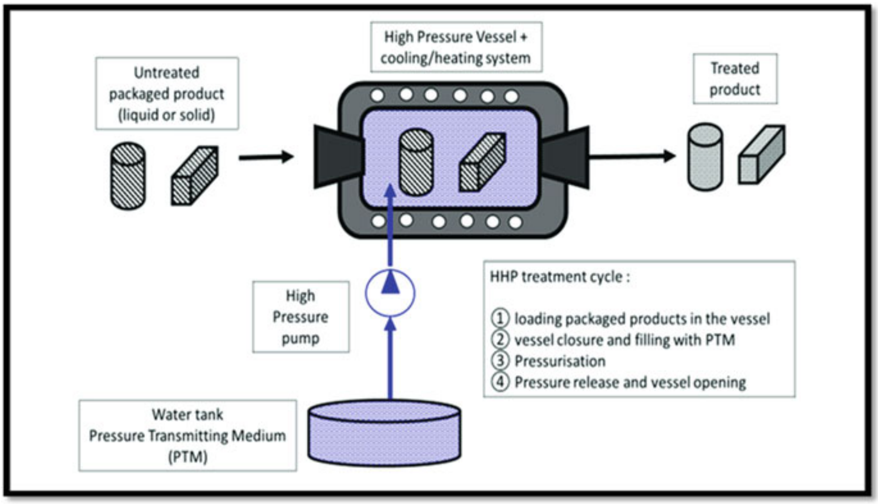

Fig. 33.3 Schematic layout of HPP. (Picart-Palmade et al. 2019)

rhodiola, *p*-coumaric acid from pinyin, catechins and caffeine from GT, deoxyschisandrin and y-schisandrin from magnolia berry, podophyllotoxin and 4′-demethylpodophyllotoxin from Hance, and total phenolic compounds and flavonoids from Korean barberry and deodeok. Substantial amount of phenolic compounds in GT were reported, such as caffeine and catechins, with proven biological activity. Xi (2009) studied the effect of caffeine extraction by HPE from GT leaves and compared the results with conventional extraction methods. This work establishes that HPE for only 1 min, at 500 MPa, and RT gave similar extraction yields of caffeine (4.0 %) as extraction at RT for 20 h (4.2 %), ultrasonic extraction for 90 min (4.1 %), and heat reflux for 45 min (3.9 %); therefore HPE was considered as the most efficient method. The same authors extracted phenolic compounds from dried GT leaves using HPE and major components like caffeine, epigallocatechin gallate, epicatechin gallate, epigallo catechin, epicatechin, and gallic acid were quantified using HPLC (Jun et al. 2010). The authors studied that the concentrations present in the final extract were majorly manipulated by the level of pressure, as pressure increased, the concentration of phenolic compounds increased as well and vice versa. Moreover, the extraction yields achieved with HPE (at 400 MPa of pressure) for only 15 min at RT were similar to those of organic solvent extraction for over 2 h (Jun et al. 2010). The results showed that HPE independently obtains higher total phenolic yields than the conventional extraction technique or the combination of other techniques (Lee et al. 2010).

33.4 Conclusion

Novel non-thermal technologies have the capability to increase shelf life while maintaining its texture, taste, appearances, and nutritional value with minimal processing. It has potential to improve food chain security and add value to food products. As heating production is not important in NTP, that's why it is economical. When compared with thermal technologies like drying, evaporation, pasteurization, blanching, etc., these NTP have more advantage over it because of higher energy efficiency, shorter time, and prolonged shelf life. However, with these advantages, there are certain limitations in ensuring food quality in terms of sensory properties as they are deteriorated because of high pressure, temperature, and treatment time. In order to obtain safer food and health food, both technologies can be combined. Moreover, nonthermal technology is riskier to the people who are working with those technology, for instance, ozone processing. Once these issues can be solved, nonthermal technologies will be accepted in a larger scale. They present many advantages, such as being rapid, convenient, and safe, operate at low or room temperatures, allowing heat-sensitive compound extraction, and allow the use of different solvents (and solvent ratios).

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34 Physicochemical Properties and Antioxidant Potential of Curry Leaf Chutney Powder: A Traditional Functional Food Adjunct

Renu Khedkar, Karuna Singh, Vatsala Sharma, and Monika Thakur

Abstract

Curry leaf (*Murraya koenigii*) or "kadipatta" is an important natural flavoring leaf spice used in pickles, curries, and chutneys. The standardized formulation of curry leaf chutney (CLC) powder was analyzed for its physicochemical properties and found to be rich in protein, vitamins, and minerals such as calcium and iron and can be used as a traditional functional food adjunct. The product had a low moisture content of 5.39% and is rich in protein (20.01%) and carbohydrates (54.18%). The CLC was rich in calcium 2.59 g/100 g and iron 42.45 mg/100 g. The fatty acid composition was analyzed as saturated fat (13.36 g/100 g), PUFA (55.74 g/100 g), and MUFA (30.90 g/100 g). The net dietary protein calorie percent (NDPCal %) was found to be 5.97%. The investigations designed to screen the phytochemicals in ethanolic extracts of CLC powder showed the presence of proteins, amino acids, carbohydrates, phenols, terpenoids, flavonoids, alkaloids, glycosides, and saponins. The TPC in ethanolic extracts, estimated by Folin-Ciocalteu reagent, was 120.56 mg/g GAE. The in vitro free radical scavenging activity determined by DPPH method and hydrogen peroxide method was 87.5 ± 0.179% and 88.8 ± 0.024% at 500 μg/mL concentration, respectively, comparable to that of ascorbic acid. Thus, CLC powder is an excellent food adjunct and has immense functional potential.

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Keywords

Curry leaves chutney (CLC) powder · Food adjunct · Functional potential · Phytochemicals

34.1 Introduction

Globally, the increase in urbanization and industrialization has led to a change in lifestyles and eating habits of masses. Accordingly, there has been a tremendous rise in lifestyle-related diseases like diabetes, obesity, cardiovascular disease, hypertension, cancer, etc. At the same time, life expectancy is also on the rise. Day by day, the consumers are increasingly becoming aware of quality life by paying more attention to lifestyle, health, and healthy food (Szakaly et al. 2012). The current trend of rapid growth of functional foods market clearly indicates the upsurge of wellness through "food as medicine."

Traditional Indian foods prepared by established indigenous processing and preservation techniques and their proven therapeutic benefits have been widely used since ages. They are also recognized as functional foods because of the presence of functional components such as antioxidants, dietary fiber, probiotics, vitamins, etc. (Sarkar et al. 2015; Thakur et al. 2020; Thakur and Modi 2020). People are becoming more aware nowadays for their health concerns in developing countries, and this triggers the development of new innovations in the traditional food sector (Khedkar et al. 2016a).

Food adjuncts add variety and spice to the common menu. Pickles, wet and dry chutneys, preserves, and *papad* are some of the traditional food adjuncts in Indian diet (Khedkar et al. 2016a). Various types of chutneys are consumed in India as adjunct along with chapattis, paratha, idli, dosa wada, etc. Generally, chutneys are classified into two categories: freshly made for immediate consumption and cooked chutneys for longer shelf life (Achaya 1998). Many studies have been reported on the development and standardization of chutneys and chutney powders based on fruits, vegetables, or pulses, e.g., mango, jackfruit, tamarind, peanut, flaxseed, etc. (Sagar and Khurdiya 1998; Satyanarayana et al. 2013; Chandrasekar et al. 2015; Jyothirmayi et al. 2006; Rao et al. 2008; Khedkar et al. 2016b, 2019). Curry leaves are the flavoring culinary spice used widely in Indian cuisine in the formation of curries, pickles, and chutneys. Because of its peculiar fragrant aroma, it is also used to temper recipes like rassam, sambar, dal, and dhokla (Khedkar 2015). The health benefits of curry leaves (*Murraya koenigii*) are recognized since times immemorial. They are known as tonic, analgesic, anti-helminthic, digestive, and appetizing and to possess excellent antimicrobial and antioxidant properties with immense nutraceutical potential (Parrota 2001). Traditionally curry leaves have been recommended in the treatment of diseases such as diabetes mellitus, body pain, inflammation, vomiting, kidney pain, blood disorders, and piles (Jayaprakash and Ebenezer 2012). These leaves are also used for the treatment of poisonous animal bite (Gupta and Nigam 1970). Curry leaves are rich source of vitamins and minerals (calcium, iron, phosphorus and carotene, niacin, vitamin B_2 and vitamin C) and fibers (Ganesan et al. 2013). Chutney powder made from curry leaves is an excellent way of consumption of this highly nutritious functional vegetable for incorporation in the diet.

Nutraceutical properties of curry leaves are well known, but the nutritional properties of the product made from curry leaves and other functional ingredients and the curry leaf chutney are not standardized and documented. Therefore, the aim of the present research is to determine the nutritional properties (including the fatty acid profile and trans-fat content) and the functional potential (total phenolic content and antioxidant properties) of the CLC powder.

34.2 Materials and Methods

34.2.1 Materials

The main ingredients used for the preparation of CLC were fresh leaves (*Murraya koenigii*), dehulled-split bengal gram (*Cicer arietinum*), and dehulled-split black gram (*Phaseolus mungo* Roxb.). The other minor ingredients used were sesame seeds (*Sesamum indicum*), sugar, salt, dry mango powder (*Mangifera indica*), cumin seeds (*Cuminum cyminum*), and red chili powder (*Capsicum annum*). All ingredients were procured from the local market at Noida, Uttar Pradesh, and were cleaned of any dirt or impurities.

34.2.2 Preparation of CLC Powder

Fresh curry leaves were dried in a tray dryer (45 ± 2 °C) till constant weight achieved. The Bengal and black gram, sesame, and cumin seeds were measured and roasted in an open pan till they turn brown. The dried curry leaves were measured and roasted in 10% (of the total quantity of chutney) in refined oil till become crisp. The roasting temperature was kept constant at 150 °C. The spice mix has been prepared mixing salt, sugar, roasted sesame and roasted cumin seeds, red chili, and dry mango powder. The mix has been grinded in a mixer grinder (Inalsa, India). CLC powder was prepared by mixing the dried and oil roasted curry leaves, roasted Bengal gram, black gram, and spice mix in the proportion (10:40:20:30) and grinding it to a fine powder with a mixer (Inalsa, India) (Table 34.1). The chutney was sieved though BS: 30 (500 μ) and packaged in PET/metallized polyester/ polyethylene pouches (Khedkar et al. 2019).

Table 34.1 Composition of spice mix in CLC powder

Ingredients	Composition (% by weight)
Sesame seeds	40
Sugar	20
Cumin seeds	13.33
Dry mango powder	10
Salt	13.33
Red chili powder	3.34

34.3 Physicochemical Evaluation of CLC Powder

34.3.1 Proximate Composition

The standardized samples of CLC powder were analyzed in triplicate for proximate composition. Standard methodology was followed for the estimation of moisture, crude fat, total protein, crude fiber, ash, and salt content (Ranganna 2001). Carbohydrates were estimated by the difference method, calcium by gravimetry, while carotene and iron by spectroscopy (Systronics model 2202 UV-visible double beam spectrophotometer). Energy values were calculated by the standard method of summing up the values obtained and multiplying the quantity of carbohydrate and protein per 100 g by 4 kcal and that of fat per 100 g by 9 kcal, respectively. The protein value of curry leaf chutney expressed as net dietary protein calorie percent (NDPCal%) was determined (Platt et al. 1961). Bulk density measurement in the samples was determined by the standard procedure (Narayana and Rao 1984).

34.3.2 Fatty Acid Profile

The fatty acid profile was determined by the procedure given by AOAC: 996.06 (AOAC 2012). The GC-FID analysis was performed with Agilent HP GC 6890 series gas chromatograph equipped with a flame ionization detector (FID). For FAME, a capillary column 30 m, 0.25 mm i.d. was used. The column temperature was initially maintained at 100 °C for 4 min, increased to 180 °C at 3 °C/min, maintained for 2 min at 180 °C, then further increased to 230 °C at 4 °C/min, and finally maintained for 10 min at 230 °C. The carrier gas was nitrogen at a flow rate of 2 mL/min. The injector and detector temperatures were maintained at 225 °C and 285 °C, respectively, and the split ratio was 50:1. The peaks obtained were recorded and compared with the standard.

34.3.3 Trans-Fat Content

For the trans-fat estimation, AOAC: 985.21 (AOAC 2012) was adopted. The methyl esters separated as mentioned in the above procedure were made to run through the

Agilent HP GC 6890 series gas chromatograph equipped with a flame ionization detector (FID). A capillary column of 30 m, 0.25 mm i.d. was used. The carrier gas was nitrogen at a flow rate of 2 mL/min. The injector and detector temperatures were maintained at 225 °C and 285 °C, respectively. The peaks obtained were recorded and compared with the standard.

34.3.4 Antioxidant Potential of CLC Powder

34.3.4.1 Preparation of Extract

The curry leaves were collected from the local market. The fresh leaves were thoroughly cleaned of extraneous matter and then shade dried completely. The CLC extract was prepared by mixing 10 g of sample with 60 mL of ethanol. This process was repeated thrice, and filtrates were collected until the extraction solvents become colorless. The extract was filtered by Whatman filter paper no. 1 paper and was concentrated under vacuum on a rotary evaporator (Buchi Rotary Evaporator, Model R-124) and stored at 4 °C for further use to prevent oxidative damage until analysis.

34.3.4.2 Phytochemical Screening

Ethanolic extracts of CLC were used for qualitative screening of various phytochemicals such as alkaloids, anthocyanins, anthraquinones, carbohydrates, flavonoids, glycosides, proteins and amino acids, phenols, saponins, steroids, terpenoids, and tannins (Amin and Thakur 2014).

34.3.4.3 Total Phenolic Content

The total phenolic content in ethanolic extracts of grounded sample was estimated by Folin-Ciocalteu reagent, as described by Singleton and Rossi (1965). 100 mg of gallic acid was dissolved in 100 mL ethanol to prepare gallic acid stock solution (1000 μg/mL). Various dilutions of standard gallic acid were prepared from this stock solution. 1 mL aliquots of 1.0, 2.5, 5.0, 10, 25, 50, and 100 μg/mL of gallic acid solution were mixed with 5.0 mL of Folin-Ciocalteu reagent (diluted tenfold) and 4.0 mL of sodium carbonate solution (75 g/L) and calibration curve was plotted. The absorbance was measured after 30 min at 20 °C at 765 nm. 1 mL extract was mixed separately with the same reagents and absorbance was measured at 765 nm after 1 h. The total phenolic compound in the extract was determined using the formula:

$$C = C_1 \times \frac{V}{m}$$

C = total content of phenolic compounds in mg/g in GAE (gallic acid equivalent); C_1 = the concentration of gallic acid established from the standard curve in mg/mL; V = the volume of extract in mL; and M = weight of extract in grams.

34.3.4.4 In Vitro Antioxidant Activity of the CLC Powder Extracts

In vitro antioxidant activity of the extract of the chutney was determined by using two different methods: Free radical scavenging activity using DPPH method and hydrogen peroxide.

Free Radical Scavenging Activity Using DPPH Method

The free radical scavenging activities of sample extract was measured by 1,1-diphenyl-2-picrylhydrazyl (DPPH) (Sayeed and Thakur 2019). Briefly, 0.1 mM solution of DPPH in ethanol and 1.5 mL of this solution was added to 0.5 mL of extract solution in ethanol at different concentrations (50–300 μL/mL). The mixture was shaken and allowed to stand at room temperature for 30 min. The absorbance was then measured at 517 nm using a spectrophotometer. A blank without DPPH was used to remove the influence of the color of the extracts, and the methanolic solution of DPPH was used as a negative control. Ascorbic acid was used as a reference. All of the measures were carried out in triplicates. The DPPH radical scavenging activity was calculated using the following equation:

$$\%\text{Scavenging effect} = \frac{A_0 - A_s}{A_0} \times 100$$

where A_o is the absorbance of negative control and A_s is the absorbance of the sample. Tests were carried out in triplicate.

Free Radical Scavenging Activity Using Hydrogen Peroxide

The free radical scavenging activity of sample extract was determined by using hydrogen peroxide (Ebrahimzadeh et al. 2010; Thakur and Sayeed 2014; Sayeed and Thakur 2019; Sayeed et al. 2020). An aliquot of 0.6 mL of hydrogen peroxide (43 m) and 1.0 mL of various concentrations of the extract prepared using phosphate buffer (200–400 μg/mL) were mixed followed by 2.4 mL of 0.1 M phosphate buffer (pH 7.4). The resulting solution was kept for 10 min and the absorbance was recorded at 230 nm. All measures were repeated triplicate. For each concentration, mixture without sample was taken as a control and a mixture without hydrogen peroxide was taken as a blank. Ascorbic acid was used as a standard compound. The percentage scavenging activity of hydrogen peroxide was calculated as:

$$\text{Scavenging effect}\,(\%) = \frac{A_0 - A_s}{A_s} \times 100$$

where A_o is the absorbance of negative control and A_s is the absorbance of the sample. Tests were carried out in triplicate.

34.4 Results and Discussion

The final compositions of standardized CLC powder were taken as per the standardized recipe of dried curry leaves (Fig. 34.1 and Table 34.2). The standardized process for preparation of CLC powder was adopted from the standardized recipe given by Khedkar et al. (2019).

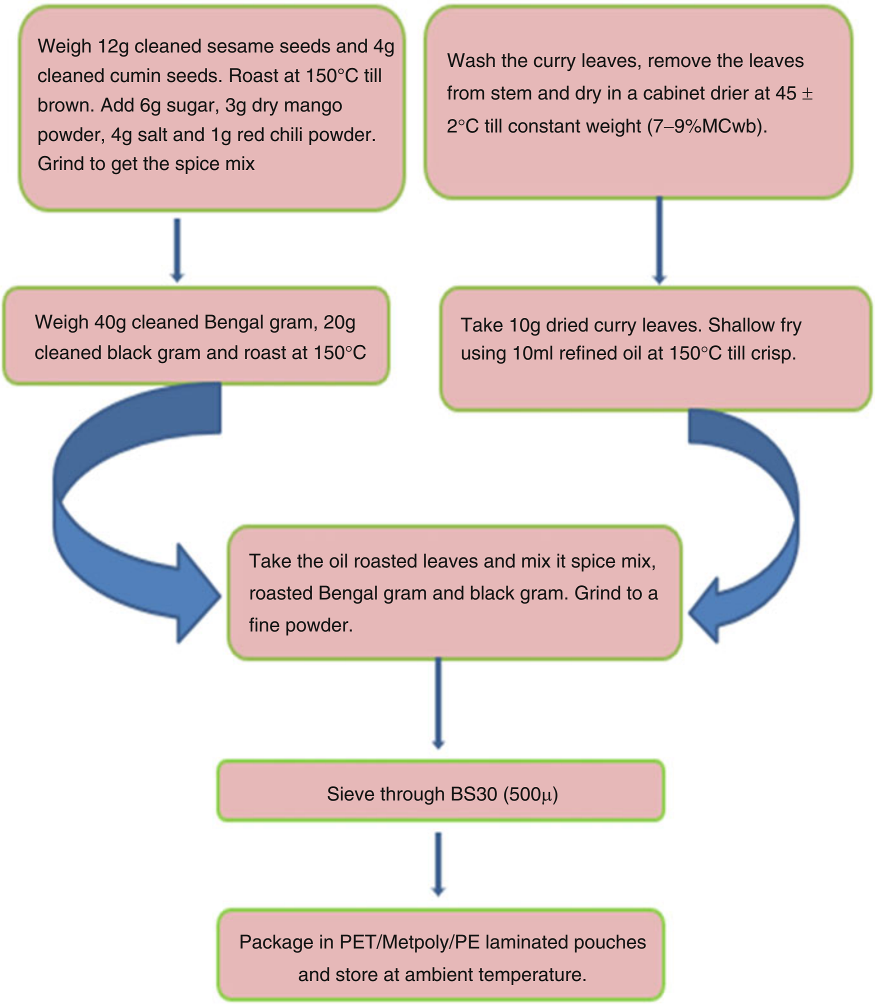

Fig. 34.1 Process standardization for preparation of CLC powder

Table 34.2 Composition of CLC powder (per 100 g)

Ingredients	Composition (g)
Curry leaves (dried)	10
Bengal gram	40
Black gram	20
Spice mix	30

Table 34.3 Chemical and nutritional composition of CLC powder

S. no.	Parameter (g)	Curry leaf chutney (per 100 g)
1.	Moisture	2.57 ± 0.18
2.	Protein	20.01 ± 0.07
3.	Fat (crude) Saturated fat % PUFA % MUFA%	14.81 ± 0.15 13.36 55.74 30.90
4.	Total ash	5.61 ± 0.21
5.	Salt (NaCl)	1.25 ± 0.06
6.	Carbohydrates	56.99 ± 0.23
7.	Crude fiber	1.99 ± 0.19
8.	Energy value (kcal)	441.29
9.	Calcium	2.59 ± 0.06
10.	Iron (mg)	42.45 ± 0.29
11.	Vitamin C (mg)	8.03 ± 0.08
12.	Carotene (mg)	0.06 ± 0.02
13.	NDPCal %	5.97

(Values are average ± S.D. and are expressed on sample basis)

34.5 Physicochemical and Nutritional Composition of CLC Powder

In Table 34.3, the mentioned product had a low moisture content of 2.57% and was rich in protein (20.01%) and carbohydrates (56.99%). The crude fat content was found to be 14.81%, crude fiber 1.99%, total ash 5.61%, and energy value 441.29 kcal. Gopalan et al. (2014) reported that sesame seeds and cumin seeds are a good source of protein (18.3% and 18.7%, respectively) and fat (43.3% and 15%, respectively). The high protein and fat content can be attributed to the presence of the seeds in the curry leaf chutney. The curry leaf chutney was rich in calcium 2.59 g/100 g and iron 42.45 mg/100 g. The curry leaf chutney had a balanced composition of mono-unsaturated, poly-unsaturated, and saturated fatty acids. The fatty acid composition of curry leaf chutney was found to be saturated fat (13.36 g/100 g), PUFA (55.74 g/100 g), and MUFA (30.90 g/100 g). No trans-fat was detected in the sample. The protein value of curry leaf chutney expressed as net dietary protein calorie percent (NDPCal%) was found to be 5.97%, where chemical score (CS) was 32.11 with methionine and cysteine as the limiting protein. Balaswamy et al. (2004) reported moisture content (5%), crude protein (16.4%), crude fat (14.2%), total ash

(4.0%), crude fiber (7.0%), carbohydrates (57%), and salt (9.1%) in curry leaf chutney powder prepared from fresh curry leaves fried in 10% oil, Bengal gram, black gram, green gram, coriander seeds, cumin seeds, red chili powder, and tamarind pulp. Purohit and Rajyalakshmi (2011) also reported the bulk density of chutney powder incorporated with defatted groundnut cake flour to be 550 kg/m^3, while the bulk density of CLC powder was found to be 642 kg/m^3.

Very limited studies have been conducted on curry leaves use as traditional adjunct. Therefore, the study results indicated that the curry leaf chutney had a good nutritional profile and could be used as an economical source of nutritional supplement for the masses.

34.6 Phytochemical Screening of the Ethanolic Extract of CLC Powder

Phytochemicals are widely available in fruits, vegetables, whole grains, legumes, nuts, seeds, spices, and fungi. They are accumulated in the plants in the roots, stem, leaves, flowers, fruits, or seeds. Phytochemicals protect the plants from disease and contribute to the color, flavor, and aroma. They are classified as primary and secondary compounds. The primary constituents include proteins, amino acids, common sugars, chlorophyll, etc., whereas the secondary constituents are the alkaloids, flavonoids, lignans, terpenes, saponins, phenolics, and glucosides (Ranganna 2001).

The results of the phytochemical screening are presented in Table 34.4. The results indicate that proteins, amino acids, and carbohydrates are present in the ethanolic extract of the chutney. The extract also contains phenols, terpenoids, flavonoids, alkaloids, glycosides, and saponins. Terpenoids show various pharmacological activities, e.g., anti-inflammatory, anticancer, antimalarial, antiviral, antibacterial, and for inhibition of cholesterol synthesis (Mahato and Sen 1997).

Table 34.4 Qualitative phytochemical screening of chutney extracts

S. no.	Phytochemicals	*Curry leaf chutney*
1	Alkaloids	+
3	Anthocyanins	–
4	Proteins and amino acids	+
5	Carbohydrates	+
6	Phenols	+
7	Terpenoids	+
8	Sterols	–
9	Saponins	+
10	Glycosides	+
11	Flavonoids	+
12	Tannins	–

Note: (+): Shows that phytochemicals are present and (−): shows that phytochemicals are absent

Alkaloids are natural compounds containing heterocyclic nitrogen atoms and are basic in nature (Mueller-Harvey and McAllan 1992). Alkaloids are significant for the protection and survival of plants because of antibacterial and antifungal activities. They are also said to possess other pharmacological activities including antihypertensive effect, antimalarial effect, antiarrhythmic effect, and anticancer action (Wink et al. 1998). Curry leaves are the richest source of carbazole alkaloids. Carbazole alkaloids exhibit antitumor, antioxidative, anti-mutagenic, antimicrobial, and anti-inflammatory properties (Mackeen et al. 1997; Kusuma et al. 2011; Khedkar 2015). Flavonoids are reported to exert various biological activities including antimicrobial, cytotoxicity, antitumor, anti-inflammatory, antioxidant, and enzyme inhibition, estrogenic, and anti-allergic activities (Tapas et al. 2008). Glycosides exhibit anti-inflammatory properties, protect against endotoxemia and are used for cardiac treatment for congestive heart failure (Sood et al. 2012).

34.7 Total Phenolic Content

Phenols are the secondary plant metabolites which function as the defense compounds. They exhibit several properties beneficial to humans and are especially known for their antioxidant properties protecting against the free radical-mediated diseases. The ethanolic extract of curry leaf chutney powder showed the concentration of TPC of 120.56 mg/g GAE (Table 34.5). Many researchers have studied the antioxidant potential and phenolic content of curry leaves. Aradhana et al. (2009) reported high concentration of total phenolic compounds (290 μg/mg GAE) in the methanolic extract of dried curry leaves. Selamat et al. (2018) studied the efficacy of different organic solvents for extraction of antioxidant phenolic compounds of curry leaves and found that the polyphenols present in curry leaves are more soluble in alcoholic solvent. Gitanjali and Shivaprakash (2004) observed reduction in TPC after shallow frying of spinach, amaranth, and potato. Jaganathan and Jaganathan (2013) reported the total phenols as 102.62 mg/100 g GAE in roasted Bengal gram. Zhou et al. (2017) reported the total phenolic content of white sesame seeds of different varieties to be in the range 370.5–786.8 mg GAE/100 g. The high amount of free phenolics in the sesame seeds is responsible for their antioxidant, and antiproliferative activities make them potential source of functional food.

Table 34.5 Total phenolic content of the ethanolic extract of CLC powder

S. no.	Sample	Absorbance at 765 nm (mean ± standard error)	Total phenolic content (mg gallic acid equivalents per gram weight)
1	CLC powder	0.813 ± 0.00057	120.56 ± 0.1321

34.8 Antioxidant Potential

The antioxidant and free radical scavenging properties of plants are associated with their medicinal benefits. Antioxidant activity of ethanolic extracts of CLC powder was determined by DPPH method and hydrogen peroxide method. The results obtained for the antioxidant assay using both the methods are shown in Tables 34.6 and 34.7, respectively.

DPPH accepts an electron and forms a stable molecule. It is unaffected by side reactions such as metal chelation and enzyme inhibition (Amarowicz et al. 2004) The color of DPPH radical changes from purple to colorless on acceptance of electrons or the presence of hydrogen. The percent radical scavenging activity of different concentrations of the CLC powder extract ranged from 31.6 to 87.5. Sasidharan and Menon (2011) also reported highest DPPH activity in the aqueous ethanolic extract of curry leaves.

The free radical scavenging activity of the curry leaf chutney powder at different concentrations was also investigated using hydrogen peroxide, and it ranged from 31.9 to 88.8%. The scavenging activities of the extract were concentration dependent. It was found that the antioxidant activity of the ethanolic extract of CLC powder increased with increase in concentration of extracts.

The antioxidant activities of the legumes are very well established (Takahata et al. 2001; Amarowicz et al. 2004). Shahidi et al. (2006) reported that the free radical scavenging activity of white sesame seeds using DPPH radical at 40 μg/mL was 2.5 ± 0.4. The antioxidant activities contribute to the beneficial health effects of phenolic compounds (Fang et al. 2002).

Table 34.6 Percentage scavenging activity of the chutney extract at different concentrations at 765 nm using DPPH method

Concentration (μg/mL)	Absorbance of the sample	Percent scavenging activity
100	0.561	31.6 ± 0.31428
200	0.443	46.0 ± 0.43074
300	0.325	60.4 ± 0.31421
400	0.254	69.0 ± 0.43071
500	0.102	87.5 ± 0.17950

(Values are the average of triplicate experiments and represent as mean ± S.E.M.)

Table 34.7 Percentage scavenging activity of the chutney extract at different concentrations using hydrogen peroxide (230 nm)

Concentration (μg/mL)	Absorbance of the sample	Percent scavenging activity
100	0.545	31.9 ± 0.02331
200	0.438	45.3 ± 0.07261
300	0.312	61.0 ± 0.01760
400	0.235	70.6 ± 0.02402
500	0.089	88.8 ± 0.02403

(Values are the average of triplicate experiments and represent as mean ± S.E.M.)

34.9 Conclusion

In the recent times, people have realized the importance of consumption of traditional foods. Although raw foods are healthier, still processing before consumption is a common practice. CLC powder is a widely used traditional food adjunct in Indian cuisine. This study evaluated the nutritional composition, phytochemicals, total phenolic content, and antioxidant activity of the food adjunct and revealed that the CLC is rich in macro- as well as micronutrients. Thus, the knowledge of the traditional foods, rich in essential nutrients and bioactive compounds, can open a new market avenue for processed functional food products. The present research on CLC has summarized the functional importance of untapped traditional food adjuncts and also has plethora of functional potential (Fig. 34.2).

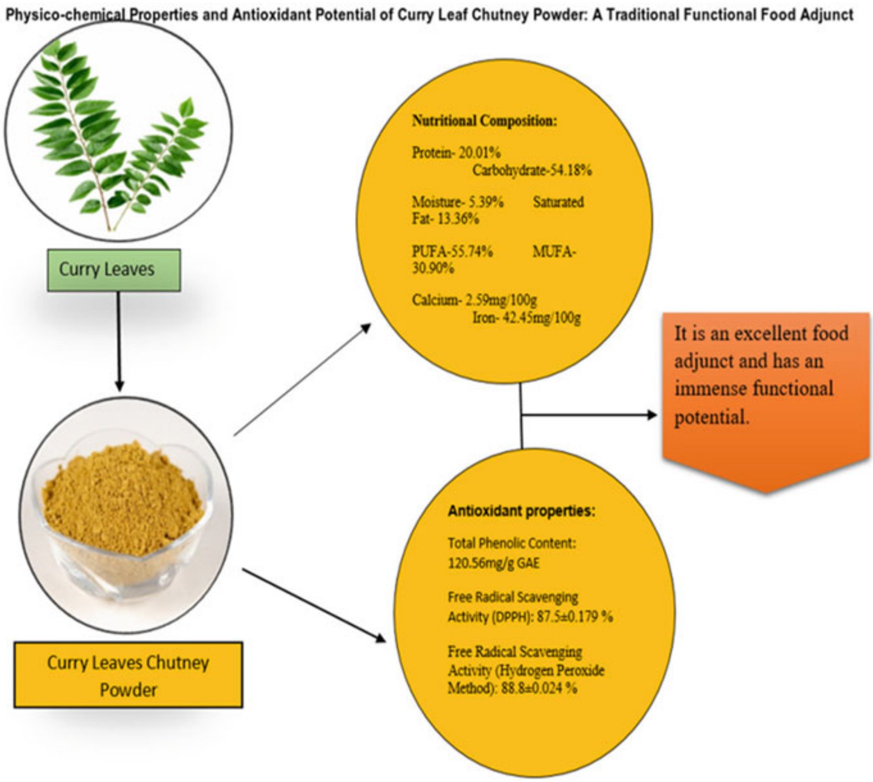

Fig. 34.2 Curry leaf chutney powder: a traditional functional food adjunct

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