Chapter 13
Functional Food in Promoting Health: Global Perspective

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13.1 Introduction

Recent rechearch has shed light on how food ingredients impact our physiological functioning and overall health. A correlation between diet rich in nutritional value and the associated health benefits, is making functional foods (FF) an area of interest for both researchers ans well as consumers. The foods with great nutritional value, known as functional foods, exhibit immediate and long-term health benefits and lowering the risk of chronic diseases (Arshad et al. 2021). The origin of the term 'functional food' can be traced back to Japn in the early 1980s (Bellisle et al. 1998). While there is no universally accepted definition of functional foods, a common and straightforward explanation is that the processed foods that provide disease preventing and/or health-promoting benefits beyond their nutritional value. Functional foods often share similarities with different categories of foods such as nutraceuticals, medicinal food, pharmafoods, vitafoods, etc., to mention a few. However, the acceptance of functional foods by consumers depends on their interest in and confidence in these products. Therefore, accurate communication of the health benefits of these products and a supportive regulatory environment for their approval and associated health claims is essential (Spano 2010).

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The demand for beverages and foods that promote good health has risen over the last few decades due to increasing health care expenses, longer life expectancy, and a desire for an improved quality of life (Menrad 2003). Foods that seem to be functional in this context ensure certain health benefits as a result of specific food components present in them. Different countries have various interpretations of what constitutes functional foods. Functionalized meals are meals with components that help influence certain bodily processes in addition to being nourishing. The concept of functional foods dates back to ancient China (as early as 1000 BC), where medicinal and healing qualities were attributed to certain foods and herbs. Food items enhanced with unique ingredients that have beneficial physiological effects were originally referred to as functional foods in Japan (Hardy 2000). Some of the prominent ingredients of functional foods and functions have bben exhibited in Table 13.1. The requirement for these was acknowledged since several demographic surveys showed that the cost of medical care for the aging population is high. As mentioned earlier, in 1984, the concept of functional food was introduced by Japanese researchers who investigated the relationship among nutrient intake, olfactory pleasure, fortification, and the manipulation of physiological systems. In 1991, FOSHU or Food for Specified Health Uses standards were established by the Ministry of Health (Burdock et al. 2006).

Table 13.1 Types of functional food ingredients and their mechanism of action

Functional food ingredients	Dietary sources	Function	Mechanism of action
Carotenoids	Carrot, other vegetables	Anti-inflammatory activities	Autophagy activation and promotion of apoptosis.
Fibre	Fruits, vegetables	Prevents breast, colon, ovarian cancer	Reduces the amount of time that carcinogens are in contact with the intestinal lumen while fostering a healthy gut flora.
Lycopene	Tomato, watermelon, pink grapefruit	Antioxidants	Reduces cellular DNA deterioration by scavenging free radicals.
Alpha-linolenic acid	Flax seeds	Antioxidant properties	Controls cell proliferation and lowers the risk of colon cancer.
Omega-3 fatty acid	Sea fishes like mackerel, tuna salmon, sardines	Antineoplastic	Proinflammatory lipid byproducts and growth factor receptor signalling are decreased
Multivitamins	Meat, fish, poultry, carrots, beans, sweet spinach, potatoes,	Reduces cancer incidence	Improving cellular metabolism and serve as essential cofactors and enzymes
Probiotics	Yogurt, curd, other milk products	Maintains healthy gut microbiota	Controls immunological reactions and intestinal epithelial homeostasis
Calcium	Milk products, almonds, eggs, chia seeds, soybeans tofu	Antineoplastic	Delay the onset of colon cancer and calcium sensing receptor (CASR)-mediated antineoplastic action

The Japanese obsession and research with functional foods have raised awareness of the demand for such goods in regions like Europe and the US. Researchers in these nations realized that functional foods might provide the food sector with a commercial opportunity to improve the quality of life and reduce healthcare expenses. However, the nature of functional meals differs greatly between Eastern and Western cultures. The function is more important than taste in the case of such goods, which are frequently referred to as first-generation functional foods. A functional food product is expected to have certain positive effects on one or more body functions and they are expected to lowering health issues. The USA is the most significant and active market for functional foods and this is anticipated to increase in the coming days (Bech-Larsen and Scholderer 2007).

The global market for these types of functional foods is expected to be atleast 33 billion US Dollars based on their health promoting factors and the value-added product (Hilliam 2000). It is expected that the US will become a major player in the FF market, accounting for 50% of the total global share. Currently other prominent nations in the FF market are the United Kingdom, France, Germany, and the Netherlands. Sales of FF have significantly increased throughout Europe with rapid expansion in Spain and the Netherlands (Jago 2009). According to Euromonitor, sales of FF in the emerging markets of Hungary, Poland, and Russia are expected to grow moderately from 2005 to 2009 (Benkouider 2004).

13.2 Examples of Functional Foods in Our Daily Life

Initially, functional food discoveries focused on fortifying foods with essential vitamins and minerals. However, this approach evolved over time to include meals enriched with various micronutrients such as phytosterol, omega-3 fatty acids, and soluble fiber, to foster good health or reduce risk of chronic diseases. Over the yars, these foods have become increasingly popular and gained significance in our daily healthcare. Consequently, certain developed foods can be classified into functional foods, with their role in maintaining healthy lifestyles falling into three categories i.e. (i) mitigating the risk of Chronic lifestyle diseases (ii) enhancing the cognitive functions of the individuals and (iii) reducing the existing health risk problems (Sloan 2002). Common types of functional foods have been listed in Table 13.2.

Almost all food industries have developed functional foods categories and the functional property is important from a product's perspective. They can be a different variety of foods, such as probiotics, prebiotics, functional drinks, functional cereals etc.

13.2.1 Probiotics

Probiotics refer live microorganisms that are benficial for the digestive system, immune functions, and overall health when consumed in adequate amount. They are bacteria or yeasts that are similar to those naturally found in the gut. The most

Table 13.2 Types of functional food with examples

Type of functional food	Definition	Example
Fortified product	A portion of food fortified with additional nutrients	Fortified milk, juices with vitamins
Enriched product	Food with added new nutrients and components usually not present in that food.	Margarine with plant sterol esters. Vitamin D enriched low fat milk.
Altered product	A food product from which unwanted harmful component is removed and added with more beneficial components.	Genetically modified food products.
Enhanced commodities	By using special growing conditions the specified needful components have been enhanced and thereby increased their therapeutic efficacy.	Cereals and pulses with higher vitamin and mineral levels.

common lactic acid bacteria (LAB) and bifidobacteria (Charalampopoulos et al. 2002). Probiotics are commonly found in feremented foods like yougurt, kefir, sauerkraut, kimchi as well as in various formulated dietary supplements. In the probiotics industry, microorganisms have been extensively investigated and implemented. These microorganisms are natural components of the gut microbiota and have a long-standing record of safe utilization in the food industry (Salminen 2007).

13.2.2 Prebiotics

Prebiotics are indigestible food components like fibers or carbohydrates that serve as a food source for beneficial microorganisms in the gut, such as probiotics and therefore, in turn, have positive effect on human health (Stanton et al. 2005). Prebiotics are typically found in plant-based foods, such as fruits, vegetables, whole grains, and legumes. The global prebiotic demand is estimated to be approximately 167,000 tonnes. Fructo-oligosaccharides (FOS), polydextrose, lactulose, isomalto-oligosaccharides (IMO), and inulin and resistant starch are the primary components of prebiotics. The use of oligosaccharides, has been shown to aid in the control of obesity by reducing hunger and, therefore, food intake (Bosscher et al. 2006). Non-digestible fermented fructans like oligofructose and inulin are among the most researched and established prebiotics (Gibson 2004). These substances have also been found to enhance calcium absorption, increase the bone mineral density, and bone mineral content (BMD) (López-Molina et al. 2005). Furthermore, they have been shown to reduce serum glucose and cholesterol levels. When probiotics and prebiotics are combined, they are referred to as symbionts due to their potential to work together effectively (Gibson and Roberfroid 1995).

13.2.3 Functional Drinks

Fruit juice has been suggested as a novel product category that is rich in essential vitamins, such as vitamins C, A, and E, and is regularly consumed by a considerble portion of the consumers (Tuorila and Cardello 2002). However, there is a vast array of products available within this category, and the European market dominates the sector. Other functional beverages are designed to decrease cholesterol levels by incorporating soy and omega-3 fatty acids and improve eye and bone health (Keller 2006).

13.2.4 Functional Cereals

Oat and barley are two types of cereal that provide another option to create foods with useful properties. The numerous advantages of these grains can be utilized in a variety of ways, such as the creation of unique cereal products or cereal ingredients. Cereals are also beneficial as a substrate for fermentation for the development of probiotic bacteria. In addition to fostering a number of advantages and physiological benefits, cereals encourage the growth of lactobacilli and bifidobacterial and act as prebiotics, and are found in the colon. Components of cereals like starch can be utilized as a material for probiotic encapsulation to enhance their stability while being stored and increase their vitality while passing through unfavorable GIT disturbances (Brennan and Cleary 2005).

13.2.5 Bakery Products

While the popularity of functional foods is rising quickly in recent decades such as confectionery or dairy products (Menrad 2003). By creating a new type of white bread, Unilever revolutionized the bakery industry referred to as Blue Band Goede Start, the original white bread containing nutrients typically present in brown bread such as inulin, fibers, iron, zinc, vitamins B1, B3, and B6 and that product was made up of wheat. In creating functional baked goods (Benkouider 2005), such as bread, it is crucial to recognize that establishing functional food quality delivery of the active substance at the proper dosage for physiological efficiency while also providing a product that fits the demands of the customer in terms of look and flavor also texture (Alldrick 2010).

13.2.6 Spreads

Spreads that reduce cholesterol are likely to become more popular recently because of their therapeutic functionality. For example, butter with low cholesterol under Balade ™, a trading name has been created and marketed since 1992, in Belgium.

Other milk with low cholesterol cheese, milk, and even low-cholesterol eggs are examples of these items. Furthermore, meat and its by-products can also be categorized as functional foods, to the extent that they include a wide range of substances considered to be functional. The notion of consuming food depends on health reasons. In addition to customary displays, the meat business can investigate a number of options, such as controlling the formulation of the makeup of the raw and processed material dietary fiber, antioxidants, or fatty acid profiles.

13.2.7 Eggs

Eggs are especially interesting due to their relatively high fatty acid content and the corresponding solubility in fat substances. Fatty acid composition is an important factor in determining one's health. Recently, antioxidants and other vitamins have been employed to create fresh foods or VITA Eggs. According to them, their eggs were supplemented with selenium, vitamins D, E, B12, omega-3 fatty acids, and vitamin B12.

13.3 Global Perspective on Functional Foods

The concept of functional food is a crucial development in the field of nutrition, as it encompasses all the fundamental scientific knowledge that has been accumulated over the last few decades. The progree must be acknowledged and utilized for the betterment of public health. A comprehensive overview of functional food concepts from around the world was presented at the Functional Food Science in Europe (FUFOSE) project (Roberfroid 2002). This project featured an overview of dietary choices, functional foods, and remedies for health and disease, as well as cultural and religious differences in Asia, Europe, Latin America, and North America.

13.3.1 Asian Dietary Ingredients

Having a thorough understanding of functional foods will empower food scientists to utilize them more effectively for promoting health. Asian functional foods gain populairty worldwide. In various Asian nations, the term "functional foods"encompasses a range of interpretations including nutritional supplements, foods enriched with minerals and vitamins, health foods, and Indian traditional medicine as well as the Chinese traditional medicine system (Zawistowski 2017). Functional foods have been an integral part of Asian culture for centuries, with a belief that food and medicine share the same origins and functions. Traditionally, many foods were used as medicine to treat various ailments (Asian Functional Foods 2005). Use of traditional insect foods as medicine by different ethnic communities in Arunachal Pradesh, therapeutic uses of edible snail by tribal population in Madhya Pradesh, use of food to treat diseases etc. are a few among examples of use of trational foods as medicines. The success of food manufacturers lies in creating products that align with customers' existing perception and values of functional foods. Functional meals are believed to have a significant impact on all aspects of health, from maintaining health to preventing disease (Arai 2002). In the Asian countries, particularly in metropolitan areas, Over the last two decades, there has been a significant shift in dietary patterns and the incidences of chronic diseases such as diabetes and heart diseas are on the rise due to adoption of Western-style diets and lifestyles.. As a response to market trends, the industry has increased its efforts to produce functional foods with specific health benefits (Zawistowski 2008).

13.3.2 European Dietary Ingredients

In contrast to Asia, the idea of functional foods is very new in Europe. The first country in Europe to implement laws and regulations concerning food claims was Sweden, with the "Code of Practice in the Labelling of Food with Health Claims" (Asp and Bryngelsson 2007). The primary legislation concerning food and food supplements in the EU is Regulation (EC) 1924/2006, which was last amended in 2014. This regulation applies to "food," as defined in Article 2 of Regulation 178/2002, last amended in 2018, and "food supplements," mainly vitamins and minerals, as described in Regulation 2002/46/EC, last amendment in 2017 (*Regulation (EC) No. 178/2002 of the European Parliament and of the Council Laying down the General Principles and Requirements of Food Law, Establishing the European Food Safety Authority and Laying down Procedures in Matters of Food Safety | UNEP Law and Environment Assistance Platform*, 2002). However, there is no specific regulatory framework or statutory definition for functional foods and nutraceuticals in Europe. The regulatory requirements for these products depend on their composition and substances they contain, which are subject to specific regulations in the Europen market. Therefore, functional foods and nutraceuticals that contain claims related to nutrition and health must comply with the guidelines established Regulation (EC) 1924/2006 (Domínguez Díaz et al. 2020). There are several frameworks implemented in the EU are respectively

I. **In the year 2002 –** Regulation (EC) No. 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, concerned authority of European Food Safety Authority (EFSA) (*Regulation (EC) No. 178/2002 of the European Parliament and of the Council Laying down the General Principles and Requirements of Food Law, Establishing the European Food Safety*

Authority and Laying down Procedures in Matters of Food Safety | UNEP Law and Environment Assistance Platform, 2002)

II. **In the year 2002** – European Parliament and Council Directive 2002/46/EC of June 10, 2002, on Aligning the Laws of the Member States Relating to Food Supplements including bioactive products containing a higher quantity of vitamins and minerals (*EUR-Lex – 32002R0178 – EN – EUR-Lex*, 2002).

III. **In the year 2006 –** European Parliament and Council Regulation (EC) No. 1925/2006 of December 20, 2006, on the addition of vitamins, minerals, and certain other substances to foods (*EUR-Lex – 32006R1925 – EN – EUR-Lex*, 2006).

IV. **In the year 2013 –** European Parliament and Council Regulation (EC) No. 1925/2006 of December 20, 2006, on the addition of vitamins, minerals, and certain other substances to foods including taurine, inositol, amino acids, choline, carnitine, and nucleotides (*EUR-Lex – 32013R0609 – EN – EUR-Lex*, 2013).

V. **In the year of 2015 –** Legislation (EU) 2015/2283 of the European Parliament and the Council of November 25, 2015, on novel foods, amends Regulation (EU) No. 1169/2011 of the European Parliament and the Council, and repeals Regulation (EC) No 258/97 of the European Parliament and the Council, as well as Commission Regulation (EC) No. 1852/2001 excluding flavoring agents, enzymes, food additives (*EUR-Lex – 32015R2283 – EN – EUR-Lex*, 2015).

VI. **In the year 2017 –** According to Regulation (EU) 2015/2283 of the European Parliament and the Council on new foods, Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishes the Union list of novel foods (*EUR-Lex – 32017R2470 – EN – EUR-Lex*, 2017).

The European Commission's EU Framework Programs for the Research and Technology Development has been mentioned as the prioritized research on food and nutrition. Numerous EU initiatives from the 1990s focused on topics like fiber, probiotics, and prebiotics, but more current EU initiatives emphasize things like antioxidants, vitamins, and phytoestrogens as well as the socio-economic facets of diet and health.

13.3.3 American Dietary Ingredients

Food and drug standards in the United States are governed by the Food and Drug Administration (FDA) (Glasser et al. 2008). The regulatory framework in the US does not define functional foods and nutraceuticals. These goods are controlled as either foods or pharmaceuticals. The Dietary Supplements Health and Education Act (DSHEA) were passed by the US Congress in 1994. The DSHEA was created to control dietary supplement products. The US Food Drug and Cosmetic Act were modified by this act to include dietary supplements as a subcategory of food.

Therefore, items commonly regarded as functional foods and nutraceuticals are likely to be covered by American food legislation (*Office of Dietary Supplements – Dietary Supplement Health and Education Act of 1994*). The other exception, under which a product would not be regarded as a drug if it made a structure or function claim on the label or in labelling, applies to dietary supplement items. The Dietary Supplement Health and Education Act (DSHEA) of 1994 allows statements on supplement labels that describe the effects of a substance on the structure or function of the body, as long as they do not make any claim of curing or treating an illness (DSHEA which amended the FFDCA). However, if a product claims to diagnose, treat, mitigate, or prevent a condition, it would be classified as a drug (Young and Bass 1995).

13.3.4 Japanese Dietary Ingredients

Japanese people are recognized for their longevity and have a long history of eating foods that have health benefits. Foods for Specific Health Uses (FOSHU) are a functional food regulation that was adopted in Japan by the Ministry of Health, Labor, and Welfare in 1991. Following the development of the functional food system, several FOSHU products with positive health effects were created and released on the market. As a result, in 2007, FOSHU's net sales reached 6.2 billion dollars. The majority of health claims are related to probiotics to enhance digestive health. These claims are primarily associated with triglycerides, high blood pressure, high LDL-cholesterol, and high blood sugar (Iwatani and Yamamoto 2019) and are regulated by the Japanese Ministry of Health, Labour, and Welfare (MHLW) through "Foods for Specified Health Use" (FOSHU). Originally established in 1991, as we mentioned earlier, FOSHU's scope was expanded in 2001 to include capsule and tablet forms, and in 2003, around 330 items were recognized (Shimizu 2003). In April 2001, the MHLW implemented a new regulatory framework known as "Foods with Health Claims," which combined the FOSHU with "Foods with Nutrient Function Claims" (FNFC), covering twelve vitamins (A, B1, B2, B6, B12, C, E, and D) as well as two minerals (Ca and Fe) standardised under the FNFC (Warfel et al. 2007). These are some examples of statements made about these substances: "Calcium is a nutrient that is required to produce bones and teeth"; "Vitamin D is a nutrient that stimulates calcium absorption in the gut tract and aids in bone production." The maximum and minimum daily intakes of these nutrients are also established (Ohama et al. 2006). After 2007, the market for FOSHU goods was fully developed and generated $8 billion in sales in 2018 (Saito 2007; Iwatani and Yamamoto 2019).

13.4 Functional Food Marketing Development Considerations

Functional foods are becoming increasingly popular due to societal changes and trends in socio-demographics that them as a sustainable market for food (Bech-Larsen and Scholderer 2007). This is supported by the growing awareness among professionals and consumers of the tight relationship between diet and health status (Young 2000). A number of studies show that customers are also more thoughtful about health issues and willing to embrace dietary adjustments that are focused on health (Niva 2007). The benefits of functional food products cannot be overlooked to maintain general health to treat particular medical situations with a practical approach (Poulsen 1999). Furthermore, it goes beyond the economic and societal considerations (Jones and Jew 2007). This growing consumer consciousness together with improvements in numerous scientific fields provides businesses opportunity to create unlimited variety of new healthy food concepts (Biström and Nordström 2002).

While the benefits mentioned earlier are clear, the production and trade of these products can be complicated, and more expensive (Van Kleef et al. 2002). To successfully develop and market these products, significant research efforts are required to identify useful molecules, evaluate their physiological effects, creating an appropriate food matrix, and consider potential changes in bioavailability during food preparation and processing. Additionally, consumer education, and clinical trials to establish efficacy of the product and gain permission for marketing claims promoying health are necessary (Kotilainen et al. 2006). Table 13.3 represents the clinical studies of different functional foods. This process involves multiple stages and requires collaboration among business, academia, and regulatory bodies, with a focus on winning consumer trust and acceptance (Jones and Jew 2007). To ensure the successful development of functional foods, it is crucial to consider both consumer preferences and market opportunities from the outset, as well to take into account legislative rewuirements (Menrad 2003). Consumers' top health concerns include cardiovascular diseases, hypertension, stress, cancer, obesity, arthritis, and gastrointestinal conditions, according to research studies (Drbohlav et al. 2007). From the viewpoint of the consumer, the achievement of functional foods is dependent on several interrelated factors, such as considering the level of overall health concern and various medical conditions, and the idea that one's health may affect another's personal well-being. Qualitative studies has shown that consumers often lack the necessary background information to assess specific functional claims of a food products (Bech-Larsen and Scholderer 2007).

Table 13.3 Clinical trial with functional foods

SL No	Functional food	Disease	Population	Study design	Results	Reference
1.	Synthetic genistein	Prostate cancer	54 patients	For 3–6 weeks synthetic genistein (30 mg) daily	Decreases serum prostate specific antigen (PSA)	
2	Flaxseed	Prostate cancer	147 patients	Flaxseed (30 mg) 30 days	Important inverse association between enterolactone and total urinary enterolignans and Ki67 in the tumor tissue	
3	Curcumin and quercetin	Adenomatous polyposis	5 familial adenomatous polyposis	Quercetin (20 mg) and curcumin (480 mg) thrice daily for 6 months	Polyp number and size reduced from baseline without appreciable toxicity	
4	Curcumin	Colorectal cancer	126 patients	Curcumin (360 mg) thrice daily for 10–30 days	Increased expression of p53and body weight, serum level of TNF-α suppressed	
5	Fruit and vegetables	Colorectal cancer, colon cancer, and rectal cancers	61,463 women were recruited, 460 colorectal cancer 291 colon cancers, 159 rectal cancers, and 10 cancers at both sites)	Individuals who consumed less than 1.5 servings of fruit and vegetables per day	Relative risk for developing colorectal cancer of 1.65 (95% confidence interval¼1.23 to 2.20; Ptrend¼0.001)	
6		Metastatic melanoma Stage IV	112 patients with metastatic melanoma were recruited at MD Anderson cancer	Before and after treatment with PD-1 inhibitors were progression-free	Survival was significantly longer for patients with a high diversity in their gut	
7	Beta-carotene, alpha-tocopherol, selenium	Esophageal and gastric cancer	General population nutrition intervention trial, China healthy men and women at increased risk of developing cancer	30 mg alpha-tocopherol, 15milligrams (mg) beta-carotene and 50 micrograms (μg) selenium daily for 5 years in Linxian	Initial: No effect on risk of developing either cancer; decreased risk of dying from gastric cancer only later	

(continued)

Table 13.3 (continued)

SL No	Functional food	Disease	Population	Study design	Results	Reference
8	Pomegranate juice	Hypertension	Randomized hypertensive patients 10	Pomegranate juice consumption (50 mL, 1.5 mmol of total polyphenols per day, for 2 wk)	Reduction in serum ACE activity decrease SBP	Aviram and Dornfeld (2001)
9	Orange juice	Hypertension	Randomized, placebo-controlled 22 healthy volunteers	500 mL commercial and fresh orange juice, 4 weeks consumption of both juices	Decreased VCAM, hs-CRP, and selectin but increased Apo A-1. SBP and DBP were significantly decreased	Asgary and Keshvari (2013)
10	Omega-3 fatty acid	Cholesterol, blood sugar	Randomized, double-blind, placebo-controlled trial	48 coronary artery disease Omega-3 fatty acid supplement (720 mg eicosapentaenoic acid plus 480 mg docosahexaenoic acid) for 8 weeks	Increased serum irisin, decreased serum hs-CRP and LDL-C, not result in any significant changes in anthropometric measurements, blood pressure, serum lipids except for serum LDL, fasting blood glucose, body composition, or serum insulin level	Agh et al. (2017)
11	Garlic	Antiplatelet aggregation	Randomized, double-blind, crossover	Garlic 34 normal healthy adults' AGE/placebo, AGE: 2.4–7.2 g/day t.i.d., 44 weeks	Antiplatelet aggregation and adhesion	Steiner and Li (2001)
12	Garlic	CAC progression	Randomized	Garlic 65 asymptomatic patients with CAC >30%	AGE C vitamin B12 C folic acid C vitamin B6 C L-arginine/placebo, AGE: 250 mg, 1 year CAC progression: 65% reduction	Babu et al. (2013)
13	Nigella sativa oil	Cardiometabolic risk factors	Randomized controlled clinical trial 90 obese women	Nigella sativa oil 3 g per day for 8 weeks	Decline triglycerides and VLDL. NS oil concurrent with a low-calorie diet can reduce in obese women	Mahdavi et al. (2015)

14	Nuts	Cardiovascular risk factors	Randomized crossover	Nuts 72 participants 30 g/day of either raw or dry roasted, lightly salted hazelnuts for 28 days	Decreases LDL, TG; consuming both forms of hazelnuts significantly improved HDL-C and Apo A1, TC/HDL-C ratio, and SBP by consumption of dry form	Tey et al. (2017)
15	Legumes	CVR	Randomized controlled crossover trial	64 middle-aged men who had undergone colonoscopies-C/HDL-C	Legume enriched (1.5 servings/1000 kcal) for 4 weeks decreases TC, LDL, TC/HDL-C, and LDL	Zhang et al. (2010)
16	Coffee and tea	Atrial fibrillation and CVD	Cohort study	33,638 healthy women free of cardiovascular disease and atrial fibrillation at baseline	Elevated caffeine consumption was not associated with an increased risk of incident AF caffeine intakes across increasing quintiles of caffeine intake were 22, 135, 285, 402, and 656 mg/day	Conen et al. (2010)
17	Resveratrol	CVR	Randomized, placebo-controlled trial in postmenopausal women	Consumption of 150 mg of *trans*-resveratrol for 14 weeks	17% elevation in cerebrovascular responsiveness (CVR) and verbal memory as well as mood (cognition)	Evans et al. (2017)
18	Green tea catechin	Functional disability	Cohort study	13,988 Japanese individuals aged ≥65 y	3-y incidence of functional disability was 9.4% (1316 cases)	Tomata et al. (2012)
19	Dietary n-3 polyunsaturated fatty acids	Alzheimer disease	Prospective study	A total of 815 residents, aged 65–94 years, who were initially unaffected by Alzheimer disease	Participants who consumed fish once per week or more had 60% less risk of Alzheimer disease	Cardiology, JAMA Neurology, JAMA Network (2022)
20	Curcumin	Depression	A randomised, double-blind, placebo-controlled study	56 individuals with major depressive disorder were treated with curcumin (500 mg twice daily) or placebo for 8 weeks	Improving several mood-related symptoms, demonstrated by a significant group x time interaction	Lopresti et al. (2014)

13.5 Sources of Phytoconstituents with Therapeutic Activity

Plants contain a vast array of bioactive compounds (Fig. 13.1). They are secondary metabolites, essential for plants to protect them from pest and ensure plant health, are having significant functional properties when consumed as food (Oboh and Akindahunsi 2004). A low incidence of certain chronic diseases is connected with dietary intake of natural bioactive substances (Lima et al. 2014). According to epidemiological, clinical, and biochemical, these bioactive compounds have different activities in the body through different mechanisms, including antioxidant, antidiabetic, antihypertensive, and anti-Alchemic activities (Gupta and Prakash 2019). Antioxidants are essential in maintaining good health and preventing various diseases (Gupta and Prakash 2019). Free radicals, unstable molecules produced by metabolic processes, exposure to pollution, stress, and other factors, causesdamage to cells and tissues and antioxidants work by neutralizing free radicals and protecting the body from their hamful effects (Alía et al. 2003; Rakesh et al. 2010). Consuming a diet rich in antioxidants, which can be found in vegetables, fruits, nuts, whole grains, seeds, and, seasonings made from herbs, can help rejuvenate the body, delay the onset of age-related processes, and prevents degenerative illnesses (Adefegha et al. 2017). Additionally, functional foods, dietary supplements, and nutraceuticals in one's diet can provide antioxidant benefits and serve dietary remedies for a variety of illnesses (Olaiya et al. 2016). Flavonoids and phenols protect body cells from damage caused by oxygen, which is peoduced during energy production and can cause oxidative stress (Stratil et al. 2008). Natural polyphenols, mainly derived from plant sources, can neutralize free radicals, and activate antioxidant enzymes (Rakesh et al. 2010).

Phenolic Acids Phenolic acids are widely distributed in plants (Saxena et al. 2012) and are characterized by their hydroxycinnamic and hydroxybenzoic acid structures. The functions of these compounds in plants are still being studied. However,

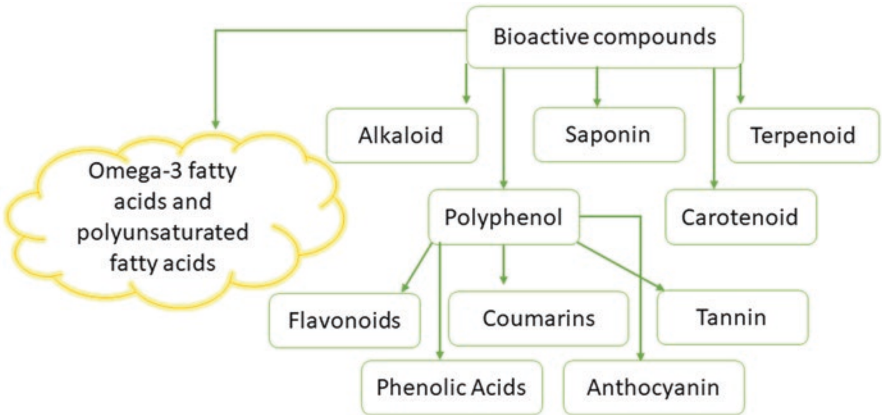

Fig. 13.1 Functional food bioactive components present in plants

phenolic acids have been found to play significant roles in enhancing the taste, appearance, nutritional and antioxidant properties of foods (El Gharras 2009). Gallic acid, caffeic acid, chlorogenic acid, p-coumaric acid, ferulic acid, vanillic acid, and protocatechuic acid are the most common types of phenolic acids (Robbins 2003). The concentrations of these compounds can be affected by environmental factors like temperature (Yousfi et al. 2006). The metabolic functions and bioavailability of these substances are nor fully understood, but the research has been conducted on the activity of ferulic, caffeic, and chlorogenic acids as they are involved in the management of certain disorders such as asthma, and allergic reactions (Yasuko et al. 1984).

Flavonoids Flavonoids are a major group of phenolic compounds that can be found in various plant-based diets. These secondary metabolites are synthesized through the phenylpropanoid pathway in plants (Liu 2002). Up to 6000 flavonoids have reportedly been discovered and isolated, with a majority being found in plants (Tolonen et al. 2002). Flavonoids can be classified into six main classes based on structure of their heterocyclic ring C (Temidayo 2013), which are flavonols (Eg: quercetin, myricetin, kaempferol, and galangin), flavones (Liu 2002) (apigenin, luteolin, and chrysin), flavanols (catechin, epigallocatechin, epicatechin, epicatechin gallate), anthocyanidins (peonidin, cyanidin, pelargonidin, malvidin, and delphinidin), isoflavonoids (daidzein, glycitein, genistein, and formononetin), and flavanones (naringenin, hesperetin, and erifoods. The primary flavonoids, such as quercetin, epicatechin, and cyanidin are found in apples, tomatoes, pineapples, guavas, and avocados contain a substantial quantity of rutin and quercetin. The free radical scavenging activity of flavonoids for preventing the generation of protein oxidation and lipid peroxidation products has been linked to their antioxidant capabilities (Kahali et al. 2014).

Alkaloids Alkaloids are secondary metabolites found in plants, fungi and animals and possess biological activity (Demirgan et al. 2016). These substances are composed of basic nitrogen with heterocyclic rings. These compounds are synthesized through the transamination reaction steps or the pathway for the biosynthesis of amino acids in plants. Alkaloids come from diverse range of botanical sources, and have various chemical compositions (Aniszewski 2007). Many of them exhibit pharmacological properties and are potential candidates for drug discovery.

Carotenoids Carotenoids are family of naturally occurring pigments that are lipid-soluble present in both animals and plants (Mortensen 2006). They are categorized based on specific traits and are considered part of the class of bioactive chemicals called isoprenoid polyenes. Due to their complicated structure, which includes several conjugated double bonds and cyclic end groups, carotenoids are among the most complex bioactive molecules. Over 700 carotenoids have been identified, however, only 50 are efficiently metabolized and digested (Grune et al. 2010). Some of the metabolizable carotenoids are lycopene beta-carotene, alpha-carotene, and xanthin those are frequently found in the blood. Epidemiological studies indicate that consuming large amounts of carotenoids provide numerous health benefits, as their antioxidant properties contribute to overall health (Miller et al. 1996).

13.6 Role of Functional Foods and Bioactive Compounds in Chronic Degenerative Diseases

The primary causes of morbidity and mortality worldwide are chronic lifestyle diseases, including cancer, cardiovascular diseases, arthritis, obesity, diabetes, and respiratory and neurological disorders. The influence of degenerative illnesses on quality of life, health, and life expectancy is enormous. These illnesses are spreading quickly over the world and are responsible for roughly half of the global burden of diseases and most of the documented global fatalities. Cardiovascular illnesses account for around half of all chronic disease-related deaths, and obesity and diabetes, which are now common in childhood, also play a significant role (Francesco et al. 2013). In many countries around the world, cancer and cardiovascular disease (CVD) are the two main causes of death. According to epidemiological and experimental research, consuming a lot of fruits, fish, spices, beverages, legumes, vegetables, whole grains, and other food-related products is strongly associated with a lower risk of developing chronic diseases (Hooper and Cassidy 2006).

13.6.1 Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder caused by inadequate or ineffective insulin secretion and changes to the metabolism of carbohydrate, protein, and lipid. The most prevalent form of this chronic condition is type 2 diabetes mellitus, which is not insulin-dependent (American Diabetes Association 2009). Extracellular hyperglycemia can induce tissue damage and diabetic consequences include heart disease, neurological illnesses, and diabetic retinopathy, etc. (Brownlee and Cerami 1981). Enzymes hydrolyze carbohydrates into glucose, which is then taken up by the intestinal epithelium and released into the blood circulation. Plant phenolics can inhibit these enzymes, delaying glucose absorption and reducing postprandial hyperglycemia. Studies have found that the phenol concentration and components of plant foods are responsible for their enzyme inhibitory actions (Nong and Hsu 2021). The antioxidant activity of phenolics may influence the five disulfide bridges on the outside of amylase, which could lead to inhibition via modulating changes in the enzyme's structure (Adefegha 2018). Flavonoids with more hydroxyl groups have stronger inhibitory effects on α-amylase activity, and green tea contains catechins and their derivatives, which may have anti-diabetic properties (Rasouli et al. 2017). Some flavonoids and flavones inhibit pancreatic α-amylase and it's interesting to note that intestine-glucosidase and pancreatic α-amylase activity can both be inhibited by cyanidin and its glycosides. In vitro and in vivo studies have demonstrated that phenolic acids with significant α -glucosidase inhibitory activity include gallic, caffeic, rosmarinic and chlorogenic acids (Ali et al. 2020). A significant α-glucosidase activity was also present in the sacrcoviolins and sarcoidosis that were isolated from the edible fungus Sarcodon leucopus (K. Ma et al. 2014). The presence of many hydroxyl groups on the structure was thought to be the cause of their inhibitory actions. It has been demonstrated that these hydroxyl groups play an important role in the inhibition of the enzyme (Ma et al. 2010).

Scientific evidence suggests certain alkaloids can act as enzyme inhibitors. Vasicinol and vasicine, for instance, have been found to exhibit high sucrase activity. Furthermore, the amount of caffeoyl groups in the structure of 3,4, 3,5, and 4,5-diccaffeoylquinicids can inhibit the maltase enzyme. Another example is berberine from *Tinospora cordifolia*, which has been shown to inhibit disaccharides and delay glucose absorption across the intestinal epithelium in Caco-2 cells (Singh et al. 2016). Similarly, 4-hydroxy isoleucine has been found to have hypoglycemic properties in alloxan-induced diabetic mice. These compounds were extracted from *Trigonella foenum graecum* seeds, having glucose-lowering impact when used in hyperglycemic conditions. In addition, 4-hydroxyisoleucine oral delivery to alloxan-induced diabetic rats resulted in beta cell regeneration as opposed to control animals that had damaged cells. The antihyperglycemic effect of β-carboline alkaloids has been demonstrated in prior research on natural antidiabetic drugs (Osigwe et al. 2015). Triterpenoids are well established to be effective hypoglycemic medications. Triterpenoids and their glycosides have been shown to have anti-diabetic properties in numerous investigations. Momordica charantia contains a steroidal saponin called charantin, which causes the release of insulin and prevents the bloodstream from absorbing glucose, causing it to have anti-diabetic properties. Aldose reductase hampering is yet another useful therapeutic strategy for the treatment of diabetes (Tang et al. 2012). By using the polyol pathway, aldoreductase catalyzes the conversion of glucose to sorbitol. High amounts of glucose may be influenced by hyperglycemia to enter the polyol pathway, which would result in an accumulation of sorbitol. Aldose reductase has been demonstrated to be effectively inhibited by a few natural bioactive substances.

Over time, there has been an increasing interest among researcher in exploring flavonoids and their derivatives as inhibitors of aldose reductase. Recent studies have suggested that hydroxylation, glycosylation, and hydrogenation of the double bond in flavonoids contribute to their inhibitory effect on aldose reductase activity. Polyphenolic components in green tea leaves have also been identified as potent aldose reductase inhibitors, with galloylated catechins exhibiting stronger inhibitory effects compared to nongalloylated catechins. The catechins' glycosylation was thought to be responsible for the stronger inhibitory effects (Plumb et al. 1998). Hispidin, inotilone, and hispolon are phenolic substances that were that were identified from an ethanol extract of Phellinus merrillii and found to be strong inhibitors of aldose reductase (Huang et al. 2011). Caffeic acid, gallic acid, caffeoylquinic acid, and p-coumaric acids, which have all been found in coffee beans, have been reported to be powerful inhibitors of aldose reductase (Xiao et al. 2015). These bioactive compounds' ability to inhibit aldose reductase has been associated with hydrogenation of the double bond and glycosylation of the stilbene structure's position.

13.6.2 Cardiovascular Diseases

Multiple elements make up the complicated and multifaceted condition known as cardiovascular disease (CVD). According to epidemiological research, the prevalence of CVD is rising. It is distinguished by various risk factors, including high blood pressure, poor diets, age, ethnicity, and family history increased serum lipids, obesity, type 2 diabetes, high blood pressure (cholesterol and triglycerides), enhanced platelet activation, elevated plasma fibrinogen and coagulation factors, and changes in oxidative stress, smoking, and glucose metabolism (WHO 2002).

Hypertension affects a significant pertange of people in several European countries, ranging from 30% to 45%, with its occurrence increasing gradually with age. The renin-angiotension system (RAS) is another critical enzyme that impacts blood pressure regulation, salt and water balance, as well as the development of cardiovascular and renal diseases (Maimaiti et al. 2019) (Fig. 13.2). RAAS dysregulation significantly influences the pathogenesis of these diseases. When stimulated, angiotensinogen release angiotensin I, which is then converted into angiotensin II by ACE, a potent vasoconstrictor. ACE inhibitors (ACEIs) reduce both local and

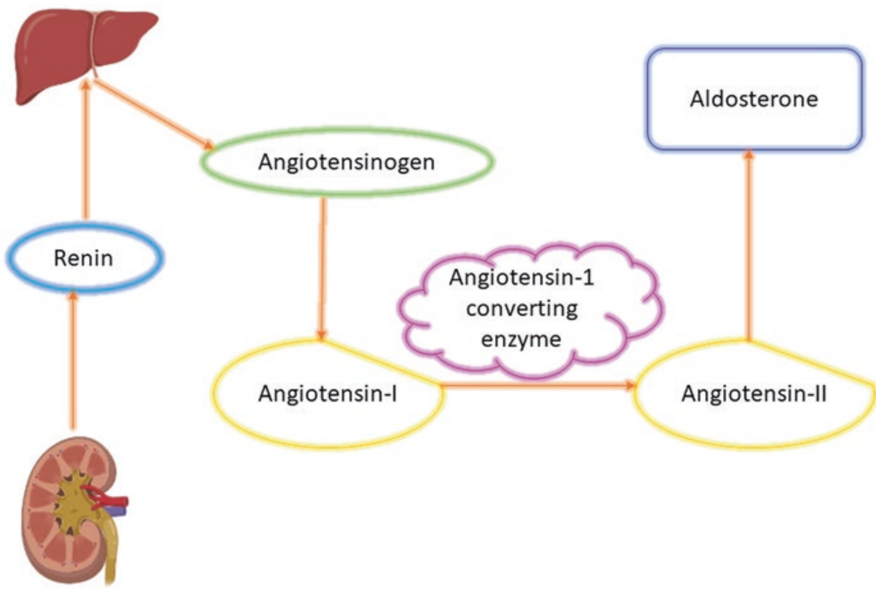

Fig. 13.2 Renin-Angiotensin mechanism

systemic levels of Angiotensin II (Ang II). Although the effectiveness of ACEIs in suppressing additional "tissue" functions of the RAAS is debatable, they also reduce sympathetic nerve activity and secretion of aldosterone and vasopressin secretion (Di Raimondo et al. 2012).

The prevention and treatment of hypertension and heart-related disorders are made easier by the use of functional foods and food items including cocoa, coffee, and condiments. The bioactive components of these functional meals are responsible for the therapeutic effects they produce. Recent studies have demonstrated the beneficial effects of these bioactive compounds by regulating abnormal lipids, lipoproteins, blood pressure, inhibiting platelet aggregation, and boosting antioxidant status.

13.6.3 Neurological Disorders

Dementia is a condition that occurs as a result from neurodegenerative illnesses, which involve gradual deterioration of neuronal integrity in the brain and spinal cord. The increase in neurodegeneration worldwide has been linked to the aging process which is often accelerated by excessive reactive oxygen species (ROS) production (Rohowetz et al. 2018). As oxidative stress accumulates, it can lead to mitochondrial dysfunction and oxidative damage, which in turn may result in neurodegenerative illnesses those are characterized by memory loss and cognitive dysfunction (Islam 2017). The brain is a crucial organ in the body that regulates both physiological and mental processes through the complex communication networks between its billions of neurons (Pushpalatha et al. 2013). To maintain optimal function, it is essential to manage oxidative stress and regulate neurotransmitters.

Cholinesterase inhibitors are the primary medications frequently prescribed for treating Alzheimer's disease (Haake et al. 2020). There has been a recent focus on tropical plant-based diets that are rich in antioxidants and phytochemicals to promote health as potential therapeutics. Epidemiological studies have shown that consuming fruits, vegetables, drinks, and spices, medicinal herbs may reduce the risk of developing neurodegenerative illnesses. The neurotransmitter acetylcholine (ACh) is hydrolyzed by the enzyme acetylcholinesterase (AChE), which is bound to the membrane. Low levels of ACh can be caused by hypoinsulinemia (low blood insulin levels) and insulin resistance, which may indicate a potential biochemical relationship between diabetes mellitus and Alzheimer's disease (Boccardi et al. 2019). Oxidative assaults can also affect Ach and contribute to the development of various diseases, such Alzheimer's disease, CVD, and diabetes mellitus (Mushtaq et al. 2015). The research on protocatechuic acid's potential effects showed that it changed the activity of the enzymes Na+/K + -ATPase, cholinergic, and antioxidant in rats (Adefegha et al. 2016). It has also been noted that in an in vitro model, alkaloid extracts from breadfruits and shea butter were able to prevent lipid peroxidation, monoamine oxidase, and cholinesterase (Adefegha et al. 2017).

13.6.4 Cancer

Epidemiological research conducted over the past three decades has found a direct link between the consumption of bioactive substances present in food and a lower the risk of cancer (Ruiz and Hernández 2014). Studies have shown that beta-carotene, lycopene, beta-cryptoxanthin, fibre and omega-3 fatty acids, when included in the diet, are useful in the managing cancer (Aghajanpour et al. 2017). Proteins present in unprocessed extracts and even whole meals are also believed to possess anti-tumor properties (Idowu et al. 2021). Functional foods contain bioactive substances that can have the potential to act as antimetastasis agents, reverse drug resistance in cancer cells and improve the sensitivity of cancer cells to treatment. To better understand how functional foods affect cancer, numerous significant randomized clinical trials currently underway (Russo et al. 2017).

Polyohenols present in food have been found to affect epigenetic changes through the expression of microRNAs associate with the fate of cancer cells and posttranslational modifications (Lall et al. 2015). Clinical investigations on polyphenolic phytochemicals have used tea polyphenols to treat and prevent cancer, while data ob cucurmin and soy isoflavones have shown mixed rsults (Yang et al. 2021). Dietary polyphenols can affect prostate cancer cells by controlling inflammatory genes and repairing oxidative DNA damage. Additionally, interactions between various dietary polyphenols may alter the risk of prostate cancer by activating both antioxidant and non-antioxidant pathways (Lall et al. 2015). Green tea's polyphenol content, including catechin, is primarily responsible for the beverage's health-promoting properties (Kazimierczak et al. 2015). Tea polyphenols were discovered to inhibit tumorigenesis in animal research in a number of organs, including the skin, oral cavity, lung, esophagus, stomach, colon, liver, small intestine, pancreas, and mammary gland (AL et al. 2020). Curcumin, a polyphenol produced from turmeric, has a variety of anti-inflammatory and anticarcinogenic properties. Research suggests that it can prevent tumor invasion and metastasis by modulating a number of signaling pathways in cells. Through the reduction of angiogenesis and metastasis, interference with cell cycle progression and apoptosis, and other mechanisms, curcumin may control the growth, development, and dissemination of cancer (KM et al. 2021). According to recent research, curcumin may improve the efficacy of chemotherapy and shield healthy cells from radiation damage (Hatcher et al. 2008).

One of the most prevalent acyclic carotenoids is lycopene, which can be found in watermelons, pink grapefruits, tomatoes, and tomato-based goods. Lycopene functions as a potent antioxidant that reduces the damage of DNA by disarming free radicals produced by both internal cellular processes and external factors like pollution and UV radiation (Bacanli et al. 2017). Additionally, it affects phase II detoxifying enzymes, antioxidant changes, growth factor signaling control, cell cycle arrest, anti-inflammatory conditions, and apoptosis (Holzapfel et al. 2013). Strong antioxidant and antiangiogenic properties are shown by the isoflavone and phytoestrogen genistein. Numerous studies have shown that genistein inhibits topoisomerase II, which causes fragmentation of DNA and cell death and which leads to cell differentiation. The levels of tumor biomarkers in several cancer cell lines can be reduced by genistein (Sarkar and Li 2003). Future research is required to determine the efficient therapeutic dose of genistein for the treatment of particular cancer types (e.g., microRNAs).

In addition to vitamins and minerals, mushrooms also provide high concentrations of uncommon antioxidants such as ergothioneine (Podkowa et al. 2021). By interacting with the gut microbiota, mushrooms and mushroom extracts strengthen the immune system and control inflammations, enhancing adaptive immunity and immune cell activity (Feeney et al. 2014). In Asia, more than 100 different varieties of mushrooms are utilized to treat cancer. In particular, numerous medicinal mushrooms appear to share specific polysaccharide-mediated anticancer immunomodulatory effects (Blagodatski et al. 2018). In Japan, a mushroom product called PSK is authorized for use in the treatment of patients with lung, colorectal, breast, and stomach cancer (PDQ Integrative 2019). According to preclinical and clinical research, mushrooms have complex anticancer properties that may manifest not only through the inhibition of specific cancer mechanisms but also through indirect processes including immunomodulation. Consuming grains, beans, and bean fiber has been found to reduce the risk of breast cancer (Vetvicka et al. 2021). Fiber can shorten the time that carcinogens come into contact with the intestine and support healthy microbiota, leading to changes in how the host's immune system is metabolically regulated, and this can prevent the growth of cancer cells and inducing apoptosis (Zeng et al. 2020). Flaxseed, which is high in lignin, fiber, and other phytochemicals, has been linked to decreased angiogenesis and cell proliferation, as well as increased apoptosis (De Silva and Alcorn 2019). Flaxseed is effective at halting the development of colon cancers in both human and animal models (Ganorkar and Jain 2013). Nuts are rich in fibre, vitamins, unsaturated fatty acids, carotenes, and phenolic compounds and their inclusion in the diet has been shown to reduce the risk of colorectal, stomach, esophageal, pancreatic, anal, and endometrial cancers (Rock et al. 2020).

Appropriate food and bacteria in the body can prevent the spread of cancer, increase the effectiveness of chemotherapy, and reduce the side effects caused by chemotherapeutic synthetic drugs. Certain probiotics can also trigger anticancer pathways by modulating gut epithelial homeostasis and immune responses. For example, *Lactobacillus acidophilus* and *Lactobacillus casei* have been shown to improve the ability of 5-fluorouracil to induce apoptosis in the colorectal cancer cell line LS513 and milk that has been fermented with probiotics may help prevent stomach cancer (Marinelli et al. 2017). *Lactobacillus reuteri* decreases the proteins that promote cell proliferation or block apoptosis and triggers TNF-induced apoptosis through the modulation of NF-B and MAPK signalling (Plaza-Diaz et al. 2012).

13.7 Future Prospect and Conclusion

More research in this area of functional foods is need of the hour. But clinical studies revealed that it is not predictable in global perspective. Few steps like regulations and implementation should be strictly followed while marketing a functional food. Functional food should be region specific as it will be more helpful in fulfilling its role and demand.

References

Adefegha SA (2018) Functional Foods and nutraceuticals as dietary intervention in chronic diseases; novel perspectives for health promotion and disease prevention. J Diet Suppl 15(6):977–1009. https://doi.org/10.1080/19390211.2017.1401573

Adefegha SA, Oboh G, Omojokun OS, Adefegha OM (2016) Alterations of Na+/K+-ATPase, cholinergic and antioxidant enzymes activity by protocatechuic acid in cadmium-induced neurotoxicity and oxidative stress in Wistar rats. Biomed Pharmacother 83:559–568. https://doi.org/10.1016/j.biopha.2016.07.017

Adefegha SA, Olasehinde TA, Oboh G (2017) Essential oil composition, antioxidant, antidiabetic and antihypertensive properties of two Afromomum species. J Oleo Sci 66(1):51–63

Agh F, Honarvar NM, Djalali M, Nematipour E, Gholamhoseini S, Zarei M, Ansari S, Javanbakht MH (2017) Omega-3 fatty acid could increase one of myokines in male patients with coronary artery disease: A randomized, double-blind, placebo-controlled trial. Arch Iran Med 20(1):28–33

Aghajanpour M, Nazer MR, Obeidavi Z, Akbari M, Ezati P, Kor NM (2017) Functional foods and their role in cancer prevention and health promotion: a comprehensive review. Am J Cancer Res 7(4):740–769

Al O, Ex F, Rimental P, Ical BME, Ien S (2020) Coffee, tea and cancer. J Exp Basic Med Sci 1(2):75–78

Ali SS, Ahmad WANW, Budin SB, Zainalabidin S (2020) Implication of dietary phenolic acids on inflammation in cardiovascular disease. Rev Cardiovasc Med 21(2):225–240

Alía M, Horcajo C, Bravo L, Goya L (2003) Effect of grape antioxidant dietary fiber on the total antioxidant capacity and the activity of liver antioxidant enzymes in rats. Nutr Res 23(9):1251–1267

Alldrick AJ (2010) The bakery: a potential leader in functional food applications. Functional Foods: Some Pointers for Success, p 220

Aniszewski T (2007) Alkaloids-secrets of life: Aklaloid chemistry, biological significance, applications and ecological role. Elsevier

Arai S (2002) Global view on functional foods: Asian perspectives. Br J Nutr 88(S2):S139–S143. https://doi.org/10.1079/BJN2002678

Arshad MS, Khalid W, Ahmad RS, Khan MK, Ahmad MH, Safdar S, Kousar S, Munir H, Shabbir U, Zafarullah M, Nadeem M, Asghar Z, Suleria HAR (2021) Functional Foods and human health: an overview. In: Functional foods – phytochemicals and health promoting potential. IntechOpen. https://doi.org/10.5772/intechopen.99000

Asgary S, Keshvari M (2013) Effects of citrus sinensis juice on blood pressure. ARYA Atheroscler 9(1):98

Asian Functional Foods (n.d.) Routledge & CRC Press. Retrieved 18 September 2022, from https://www.routledge.com/Asian-Functional-Foods/Shi-Shahidi-Ho/p/book/9780367393236

Asp N-G, Bryngelsson S (2007) Health claims in the labelling and marketing of food products. Scand J Food Nutr 51(3):107–126. https://doi.org/10.1080/17482970701652203

Aviram M, Dornfeld L (2001) Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. Atherosclerosis 158(1):195–198

Babu MS, Kaul S, Dadheech S, Rajeshwar K, Jyothy A, Munshi A (2013) Serum albumin levels in ischemic stroke and its subtypes: correlation with clinical outcome. Nutrition 29(6):872–875

Bacanli M, Başaran N, Başaran AA (2017) Lycopene: is it beneficial to human health as an antioxidant? Turkish J Pharm Sci 14(3):311–318

Bech-Larsen T, Scholderer J (2007) Functional foods in Europe: consumer research, market experiences and regulatory aspects. Trends Food Sci Technol 18(4):231–234

Bellisle F, Blundell J, Dye L, Fantino M, Fern E, Fletcher R, Lambed J, Roberfroid M, Specter S, Westenhöfer J, Westerterp-Plantenga M (1998) Functional food science and behaviour and psychological functions. Br J Nutr 80. https://doi.org/10.1079/BJN19980109

Benkouider C (2004) Functional foods: A global overview. Int Food Ingred 5:66–68

Benkouider C (2005) Dining with the Dutch. Functional Foods and Nutraceuticals

Biström M, Nordström K (2002) Identification of key success factors of functional dairy foods product development. Trends Food Sci Technol 13(11):372–379

Blagodatski A, Yatsunskaya M, Mikhailova V, Tiasto V, Kagansky A, Katanaev VL (2018) Medicinal mushrooms as an attractive new source of natural compounds for future cancer therapy. Oncotarget 9(49):29259–29274. https://doi.org/10.18632/oncotarget.25660

Boccardi V, Murasecco I, Mecocci P (2019) Diabetes drugs in the fight against Alzheimer's disease. Ageing Res Rev 54:100936

Bosscher D, Van Loo J, Franck A (2006) Inulin and oligofructose as functional ingredients to improve bone mineralization. Int Dairy J 16(9):1092–1097

Brennan CS, Cleary LJ (2005) The potential use of cereal (1→ 3, 1→ 4)-β-d-glucans as functional food ingredients. J Cereal Sci 42(1):1–13

Brownlee M, Cerami A (1981) The biochemistry of the complications of diabetes mellitus. Annu Rev Biochem 50(1):385–432

Burdock GA, Carabin IG, Griffiths JC (2006) The importance of GRAS to the functional food and nutraceutical industries. Toxicology 221(1):17–27

Charalampopoulos D, Wang R, Pandiella SS, Webb C (2002) Application of cereals and cereal components in functional foods: a review. Int J Food Microbiol 79(1–2):131–141

Conen D, Chiuve SE, Everett BM, Zhang SM, Buring JE, Albert CM (2010) Caffeine consumption and incident atrial fibrillation in women. Am J Clin Nutr 92(3):509–514

De Silva SF, Alcorn J (2019) Flaxseed lignans as important dietary polyphenols for cancer prevention and treatment: chemistry, pharmacokinetics, and molecular targets. Pharmaceuticals 12(2):68

Demirgan R, Karagöz A, Pekmez M, Önay-Uçar E, Artun FT, Gürer Ç, Mat A (2016) In vitro anticancer activity and cytotoxicity of some papaver alkaloids on cancer and normal cell lines. Afr J Tradit Complement Altern Med 13(3):22–26

Di Raimondo D, Tuttolomondo A, Buttà C, Miceli S, Licata G, Pinto A (2012) Effects of ACE-inhibitors and angiotensin receptor blockers on inflammation. Curr Pharm Des 18(28):4385–4413

Domínguez Díaz L, Fernández-Ruiz V, Cámara M (2020) The frontier between nutrition and pharma: the international regulatory framework of functional foods, food supplements and nutraceuticals. Crit Rev Food Sci Nutr 60(10):1738–1746. https://doi.org/10.1080/10408398.2019.1592107

Drbohlav J, Roubal P, Binder M, Šalaková A, Plechacová M (2007) Research and development of functional foods with special regard to dairy foods in The Czech Republic. Proceedings of the Fourth International FFNet Meeting on Functional Foods

El Gharras H (2009) Polyphenols: food sources, properties and applications – a review. Int J Food Sci Technol 44(12):2512–2518

EUR-Lex—32002R0178—EN – EUR-Lex (n.d.) Retrieved 19 September 2022, from https://eur-lex.europa.eu/eli/reg/2002/178/oj

EUR-Lex—32006R1925—EN – EUR-Lex (n.d.) Retrieved 19 September 2022, from https://eur-lex.europa.eu/eli/reg/2006/1925/oj
EUR-Lex—32013R0609—EN – EUR-Lex (n.d.) Retrieved 19 September 2022, from https://eur-lex.europa.eu/eli/reg/2013/609/oj
EUR-Lex—32015R2283—EN – EUR-Lex (n.d.) Retrieved 19 September 2022, from https://eur-lex.europa.eu/eli/reg/2015/2283/oj
EUR-Lex—32017R2470—EN – EUR-Lex (n.d.) Retrieved 19 September 2022, from https://eur-lex.europa.eu/eli/reg_impl/2017/2470/oj
Evans HM, Howe PR, Wong RH (2017) Effects of resveratrol on cognitive performance, mood and cerebrovascular function in post-menopausal women; a 14-week randomised placebo-controlled intervention trial. Nutrients 9(1):27
Feeney MJ, Dwyer J, Hasler-Lewis CM, Milner JA, Noakes M, Rowe S, Wach M, Beelman RB, Caldwell J, Cantorna MT (2014) Mushrooms and health summit proceedings. J Nutr 144(7):1128S–1136S
Francesco S, Rosanna A, Gian FG, Alessandro C (2013) Importance of diet on disease prevention. Int J Med Med Sci 5(2):55–59
Ganorkar PM, Jain RK (2013) Flaxseed–a nutritional punch. Int Food Res J 20(2)
Gibson GR (2004) From probiotics to prebiotics and a healthy digestive system. J Food Sci 69(5):M141–M143
Gibson GR, Roberfroid MB (1995) Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr 125(6):1401–1412
Glasser SP, Ashton CM, Wray NP (2008) The United States Federal Drug Administration (FDA) and clinical research. In: Glasser SP (ed) Essentials of clinical research. Springer, pp 93–110. https://doi.org/10.1007/978-1-4020-8486-7_6
Grune T, Lietz G, Palou A, Ross AC, Stahl W, Tang G, Thurnham D, Yin S, Biesalski HK (2010) β-Carotene is an important vitamin A source for humans. J Nutr 140(12):2268S–2285S
Gupta C, Prakash D (2019) Nutraceuticals from microbes of marine sources. Past, Present and Future 99:82369
Haake A, Nguyen K, Friedman L, Chakkamparambil B, Grossberg GT (2020) An update on the utility and safety of cholinesterase inhibitors for the treatment of Alzheimer's disease. Expert Opin Drug Saf 19(2):147–157
Hardy G (2000) Nutraceuticals and functional foods: introduction and meaning. Nutrition 16(7–8):688–689
Hatcher H, Planalp R, Cho J, Torti FM, Torti SV (2008) Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci 65(11):1631–1652
Hilliam M (2000) Functional food: how big is the market. World Food Ingred 12(50–52)
Holzapfel NP, Holzapfel BM, Champ S, Feldthusen J, Clements J, Hutmacher DW (2013) The potential role of lycopene for the prevention and therapy of prostate cancer: from molecular mechanisms to clinical evidence. Int J Mol Sci 14(7):7. https://doi.org/10.3390/ijms140714620
Hooper L, Cassidy A (2006) A review of the health care potential of bioactive compounds. J Sci Food Agric 86(12):1805–1813
Huang G-J, Hsieh W-T, Chang H-Y, Huang S-S, Lin Y-C, Kuo Y-H (2011) α-Glucosidase and aldose reductase inhibitory activities from the fruiting body of Phellinus merrillii. J Agric Food Chem 59(10):5702–5706
Idowu AT, Igiehon OO, Idowu S, Olatunde OO, Benjakul S (2021) Bioactivity potentials and general applications of fish protein hydrolysates. Int J Pept Res Ther 27:109–118
Islam MT (2017) Oxidative stress and mitochondrial dysfunction-linked neurodegenerative disorders. Neurol Res 39(1):73–82
Iwatani S, Yamamoto N (2019) Functional food products in Japan: a review. Food Sci Human Wellness 8(2):96–101. https://doi.org/10.1016/j.fshw.2019.03.011
Jago D (2009) Functional foods, market trends. Functional Foods Symposium
Jones PJ, Jew S (2007) Functional food development: concept to reality. Trends Food Sci Technol 18(7):387–390

Kahali B, Marquez SB, Thompson KW, Yu J, Gramling SJ, Lu L, Aponick A, Reisman D (2014) Flavonoids from each of the six structural groups reactivate BRM, a possible cofactor for the anticancer effects of flavonoids. Carcinogenesis 35(10):2183–2193

Kazimierczak R, Hallmann E, Rusaczonek A, Rembialkowska E (2015) Polyphenols, tannins and caffeine content and antioxidant activity of green teas coming from organic and non-organic production. Renewe Agric Food Syst 30(3):263–269

Keller C (2006) Trends in beverages and "Measurable Health". Proceedings of the Third Functional Food Net Meeting, pp 16–18

KM M, Palaniswamy DS, NP D, Jyothi Palati D (2021) Therapeutic importance of curcumin with a special emphasis on Mdr cancer cells and the factors influencing pharmacodynamics. Indo J Pharm:429–441

Kotilainen L, Rajalahti R, Ragasa C, Pehu E (2006) Health enhancing foods: opportunities for strengthening developing countries. Agric Rural Dev Dis 30:1–82

Lall RK, Syed DN, Adhami VM, Khan MI, Mukhtar H (2015) Dietary polyphenols in prevention and treatment of prostate cancer. Int J Mol Sci 16(2):2. https://doi.org/10.3390/ijms16023350

Lima GPP, Vianello F, Corrêa CR, Campos RADS, Borguini MG (2014) Polyphenols in fruits and vegetables and its effect on human health. Food Nutr Sci:1065–1082

Liu RH (2002) Health benefits of dietary flavonoids: flavonols and flavones. NY Fruit Quart 10(3):21–24

López-Molina D, Navarro-Martínez MD, Rojas-Melgarejo F, Hiner AN, Chazarra S, Rodríguez-López JN (2005) Molecular properties and prebiotic effect of inulin obtained from artichoke (Cynara scolymus L.). Phytochemistry 66(12):1476–1484

Lopresti AL, Maes M, Maker GL, Hood SD, Drummond PD (2014) Curcumin for the treatment of major depression: a randomised, double-blind, placebo controlled study. J Affect Disord 167:368–375. https://doi.org/10.1016/j.jad.2014.06.001

Ma TK, Kam KK, Yan BP, Lam Y-Y (2010) Renin–angiotensin–aldosterone system blockade for cardiovascular diseases: current status. Br J Pharmacol 160(6):1273–1292

Ma K, Han J, Bao L, Wei T, Liu H (2014) Two sarcoviolins with antioxidative and α-glucosidase inhibitory activity from the edible mushroom Sarcodon leucopus collected in Tibet. J Nat Prod 77(4):942–947

Mahdavi R, Namazi N, Alizadeh M, Farajnia S (2015) Effects of Nigella sativa oil with a low-calorie diet on cardiometabolic risk factors in obese women: A randomized controlled clinical trial. Food Funct 6(6):2041–2048

Maimaiti N, Wen L, Li X, Wang L, Abulimiti A, Tao W, Jiang W, Zhang D, Maimaiti N, Wen L (2019) Renal parenchymal hypertension. In: Secondary hypertension: screening, diagnosis and treatment. Springer, pp 125–185

Marinelli L, Tenore GC, Novellino E (2017) Probiotic species in the modulation of the anticancer immune response. Semin Cancer Biol 46:182–190

Menrad K (2003) Market and marketing of functional food in Europe. J Food Eng 56(2–3):181–188

Miller NJ, Sampson J, Candeias LP, Bramley PM, Rice-Evans CA (1996) Antioxidant activities of carotenes and xanthophylls. FEBS Lett 384(3):240–242

Mortensen A (2006) Carotenoids and other pigments as natural colorants. Pure Appl Chem 78(8):1477–1491

Mushtaq G, Khan JA, Kumosani TA, Kamal MA (2015) Alzheimer's disease and type 2 diabetes via chronic inflammatory mechanisms. Saudi J Biol Sci 22(1):4–13

Niva M (2007) 'All foods affect health': understandings of functional foods and healthy eating among health-oriented Finns. Appetite 48(3):384–393

Nong NTP, Hsu J-L (2021) Characteristics of food protein-derived antidiabetic bioactive peptides: a literature update. Int J Mol Sci 22(17):9508

Oboh G, Akindahunsi AA (2004) Change in the ascorbic acid, total phenol and antioxidant activity of sun-dried commonly consumed green leafy vegetables in Nigeria. Nutr Health 18(1):29–36

Office of Dietary Supplements—Dietary Supplement Health and Education Act of 1994 (n.d.) Retrieved 19 September 2022, from https://ods.od.nih.gov/About/DSHEA_Wording.aspx

Ohama H, Ikeda H, Moriyama H (2006) Health foods and foods with health claims in Japan. Toxicology 221(1):95–111. https://doi.org/10.1016/j.tox.2006.01.015
Olaiya CO, Soetan KO, Esan AM (2016) The role of nutraceuticals, functional foods and value added food products in the prevention and treatment of chronic diseases. Afr J Food Sci 10(10):185–193
Osigwe CC, Akah PA, Nworu CS, Okoye TC, Tchimene MK (2015) Antihyperglycemic studies on the leaf extract and active fractions of Newbouldia laevis (Bignoniaceae). Pharmacol Pharm 6(11):518
Plaza-Diaz J, Muñoz-Quezada S, Gomez-Llorente C, Gil A (2012) Probiotic mechanisms of action. Ann Nutr Metab 61:160–174
Plumb GW, De Pascual-Teresa S, Santos-Buelga C, Cheynier V, Williamson G (1998) Antioxidant properties of catechins and proanthocyanidins: effect of polymerisation, galloylation and glycosylation. Free Radic Res 29(4):351–358
Podkowa A, Kryczyk-Poprawa A, Opoka W, Muszyńska B (2021) Culinary–medicinal mushrooms: a review of organic compounds and bioelements with antioxidant activity. Eur Food Res Technol 247:513–533
Poulsen J (1999) Danish consumers' attitudes towards functional foods. University of Aarhus, Aarhus School of Business, The MAPP Centre
Pushpalatha B, Venumadhav N, Swathi M, Raju BA (2013) Neuroprotective effect of resveratrol against scopolamine-induced cognitive impairment and oxidative stress in rats. Archiv Biol Sci 65(4):1381–1386
Rakesh SU, Patil PR, Mane SR (2010) Use of natural antioxidants to scavenge free radicals: a major cause of diseases. Int J Pharm Tech Res 2(2):1074–1081
Rasouli H, Hosseini-Ghazvini SM-B, Adibi H, Khodarahmi R (2017) Differential α-amylase/α--glucosidase inhibitory activities of plant-derived phenolic compounds: a virtual screening perspective for the treatment of obesity and diabetes. Food Funct 8(5):1942–1954
Regulation (EC) No. 178/2002 of the European Parliament and of the Council laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety | UNEP Law and Environment Assistance Platform (n.d.) Retrieved 19 September 2022, from https://leap.unep.org/countries/eu/national-legislation/regulation-ec-no-1782002-european-parliament-and-council-laying
Robbins RJ (2003) Phenolic acids in foods: an overview of analytical methodology. J Agric Food Chem 51(10):2866–2887
Roberfroid MB (2002) Global view on functional foods: European perspectives. Br J Nutr 88(S2):S133–S138. https://doi.org/10.1079/BJN2002677
Rock CL, Thomson C, Gansler T, Gapstur SM, McCullough ML, Patel AV, Andrews KS, Bandera EV, Spees CK, Robien K (2020) American Cancer Society guideline for diet and physical activity for cancer prevention. CA Cancer J Clin 70(4):245–271
Rohowetz LJ, Kraus JG, Koulen P (2018) Reactive oxygen species-mediated damage of retinal neurons: drug development targets for therapies of chronic neurodegeneration of the retina. Int J Mol Sci 19(11):3362
Ruiz RB, Hernández PS (2014) Diet and cancer: risk factors and epidemiological evidence. Maturitas 77(3):202–208
Russo GL, Tedesco I, Spagnuolo C, Russo M (2017) Antioxidant polyphenols in cancer treatment: friend, foe or foil? Semin Cancer Biol 46:1–13. https://doi.org/10.1016/j.semcancer.2017.05.005
Saito M (2007) Role of FOSHU (food for specified health uses) for healthier life. Yakugaku Zasshi: J Pharm Soc Japan 127:407–416. https://doi.org/10.1248/yakushi.127.407
Salminen S (2007) Health claim opportunities within probiotics and prebiotics. Proceedings of the Fourth International FFNet Meeting on Functional Foods
Sarkar FH, Li Y (2003) Soy isoflavones and cancer prevention: clinical science review. Cancer Invest 21(5):744–757
Saxena M, Saxena J, Pradhan A (2012) Flavonoids and phenolic acids as antioxidants in plants and human health. Int J Pharm Sci Rev Res 16(2):130–134

Shimizu T (2003) Health claims on functional foods: the Japanese regulations and an international comparison. Nutr Res Rev 16(2):241–252. https://doi.org/10.1079/NRR200363

Singh B, Singh JP, Kaur A, Singh N (2016) Bioactive compounds in banana and their associated health benefits – a review. Food Chem 206:1–11

Sloan AE (2002) The top 10 functional food trends: the next generation. Food Technol (Chicago) 56(4):32–57

Spano M (2010) Functional Foods, beverages, and ingredients in athletics. Strength Cond J 32(1):79–86. https://doi.org/10.1519/SSC.0b013e3181c20d1c

Stanton C, Ross RP, Fitzgerald GF, Van Sinderen D (2005) Fermented functional foods based on probiotics and their biogenic metabolites. Curr Opin Biotechnol 16(2):198–203

Steiner M, Li W (2001) Aged garlic extract, a modulator of cardiovascular risk factors: a dose-finding study on the effects of AGE on platelet functions. J Nutr 131(3):980S–984S

Stratil P, Kuban V, Fojtova J (2008) Comparison of the phenolic content and total antioxidant activity in wines as determined by spectrophotometric methods. Czech J Food Sci 26(4):242–253

Tang WH, Martin KA, Hwa J (2012) Aldose reductase, oxidative stress, and diabetic mellitus. Front Pharmacol 3:87

Temidayo AR (2013) Extraction and isolation of flavonoids present in the methanolic extract of leaves of Acanthospermum hispidium Dc. Glob J Med Plant Res 1(1):111–123

Tey SL, Robinson T, Gray AR, Chisholm AW, Brown RC (2017) Do dry roasting, lightly salting nuts affect their cardioprotective properties and acceptability? Eur J Nutr 56(3):1025–1036

Tolonen M, Taipale M, Viander B, Pihlava J-M, Korhonen H, Ryhänen E-L (2002) Plant-derived biomolecules in fermented cabbage. J Agric Food Chem 50(23):6798–6803

Tomata Y, Kakizaki M, Nakaya N, Tsuboya T, Sone T, Kuriyama S, Hozawa A, Tsuji I (2012) Green tea consumption and the risk of incident functional disability in elderly Japanese: the Ohsaki cohort 2006 study. Am J Clin Nutr 95(3):732–739. https://doi.org/10.3945/ajcn.111.023200

Tuorila H, Cardello AV (2002) Consumer responses to an off-flavor in juice in the presence of specific health claims. Food Qual Prefer 13(7–8):561–569

Van Kleef E, Van Trijp HC, Luning P, Jongen WM (2002) Consumer-oriented functional food development: how well do functional disciplines reflect the 'voice of the consumer'? Trends Food Sci Technol 13(3):93–101

Vetvicka V, Teplyakova TV, Shintyapina AB, Korolenko TA (2021) Effects of medicinal fungi-derived β-glucan on tumor progression. J Fungi 7(4):250

Warfel K, Aso Y, Gee DL (2007) Regulation of functional foods in Japan: foods for specialized health uses (FOSHU). J Am Diet Assoc 107(8):A34. https://doi.org/10.1016/j.jada.2007.05.360

Xiao J, Ni X, Kai G, Chen X (2015) Advance in dietary polyphenols as aldose reductases inhibitors: structure-activity relationship aspect. Crit Rev Food Sci Nutr 55(1):16–31

Yang W, Cui K, Li X, Zhao J, Zeng Z, Song R, Qi X, Xu W (2021) Effect of polyphenols on cognitive function: evidence from population-based studies and clinical trials. J Nutr Health Aging 25:1–15

Yasuko K, Tomohiro N, Sei-Itsu M, Ai-Na L, Yasuo F, Takashi T (1984) Caffeic acid is a selective inhibitor for leukotriene biosynthesis. Biochim Biophys Acta Mol Cell Biol Lipids 792(1):92–97

Young J (2000) Functional foods and the European consumer, vol 248. Special Publication – Royal Society of Chemistry, pp 75–81

Young AL, Bass IS (1995) The dietary supplement health and education act. Food Drug Law J 50:285

Yousfi K, Cert RM, García JM (2006) Changes in quality and phenolic compounds of virgin olive oils during objectively described fruit maturation. Eur Food Res Technol 223(1):117–124

Zawistowski J (2008) Chapter 24 – regulation of functional foods in selected Asian countries in the Pacific rim. In: Bagchi D (ed) Nutraceutical and functional food regulations in the United States and around the world. Academic, pp 365–401. https://doi.org/10.1016/B978-012373901-8.00024-X

Zawistowski J (2017) Chapter 18 – health foods and foods with health claims in the Asian subcontinent: countries of the Association of Southeast Asian Nations. In: Bagchi D, Nair S (eds)

Developing new functional food and nutraceutical products. Academic, pp 323–367. https://doi.org/10.1016/B978-0-12-802780-6.00018-3

Zeng C, Fan D, Xu Y, Li X, Yuan J, Yang Q, Zhou X, Lu J, Zhang C, Han J, Gu J, Gao Y, Sun L, Wang S (2020) Curcumol enhances the sensitivity of doxorubicin in triple-negative breast cancer via regulating the miR-181b-2-3p-ABCC3 axis. Biochem Pharmacol 174:113795. https://doi.org/10.1016/j.bcp.2020.113795

Zhang Z, Lanza E, Kris-Etherton PM, Colburn NH, Bagshaw D, Rovine MJ, Ulbrecht JS, Bobe G, Chapkin RS, Hartman TJ (2010) A high legume low glycemic index diet improves serum lipid profiles in men. Lipids 45(9):765–775