

# Cannabis as a Unique and Valuable Nutraceutical Formulation for the Current and Future Global Wellbeing



Suhrud Pathak, Rishi Nadar, Jack Deruiter, Sindhu Ramesh, Jayachandra Babu Ramapuram, Manoj Govidarajulu, Timothy Moore, Dinesh Chandra Agrawal , and Muralikrishnan Dhanasekaran

**Abstract** Nutraceuticals are a type of nutritional supplement used for healthcare in addition to nourishment. They can be used to maintain the body's structure and function to promote health, slow down the aging process, prevent chronic diseases, and extend life. Echinacea, ginseng, green tea, glucosamine, omega-3, lutein, folic acid, and cod liver oil have been popular global nutraceuticals in the past few decades. The majority of nutraceutical products are regulated like pharmaceuticals, food additives, and dietary supplements. Nutraceuticals can be classified based on the source, methods of action, chemical structure, composition, etc.

In addition to the recreational and medicinal value, Cannabis has been widely established globally as a primordial source of fiber, protein, and fat with great nutritional value. Cannabis has been legally utilized as human food in the United States for the past 10 years. The hemp seed oil is an excellent prophylactic and therapeutic potential to prevent and treat various human-related health ailments. Cannabis contains active bioactive ingredients and oils with polyunsaturated fatty acids, which can be a potent nutraceutical for the current and future generations. Cannabis alone or in combination with the other existing nutraceutical (s) can provide additive or synergistic protective effects to improve human healthcare. It is estimated that by 2028, the worldwide cannabis nutraceuticals market is projected to be worth 19.25 billion USD. The present chapter dwells on the concept of nutraceuticals, the classification of nutraceuticals, their health benefits, and the potential of cannabis as a nutraceutical source.

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S. Pathak · R. Nadar · J. Deruiter · S. Ramesh · J. B. Ramapuram · M. Govidarajulu · T. Moore · M. Dhanasekaran (✉)

Department of Drug Discovery and Development, Harrison School of Pharmacy, Auburn University, Auburn, AL, USA

e-mail: [dhanamu@auburn.edu](mailto:dhanamu@auburn.edu)

D. C. Agrawal (✉)

Department of Environmental Engineering and Management, Chaoyang University of Technology, Wufeng, Taichung, Taiwan

Department of Applied Chemistry, Chaoyang University of Technology, Taichung, Taiwan

e-mail: [dcagrawal@gm.cyut.edu.tw](mailto:dcagrawal@gm.cyut.edu.tw)

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## Abbreviations

ALA	$\alpha$ -Linolenic acid
CBD	Cannabidiol
CNS	Central nervous system
CVDs	Cardiovascular diseases
DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid
FAO	Food and Agriculture Organization
IBD	Inflammatory bowel disease
ISO	International Standards Organization
NSP	Non-starch polysaccharides
PUFA	Polyunsaturated fatty acids
THC	Delta-9-tetrahydrocannabinol
USA	United States of America
US-FDA	United States of America Food and Drug Administration
WHO	World Health Organization

## 1 Introduction

The word “nutraceuticals” was initially coined in 1989 by Dr. Stephen DeFelice, a physician, and founder and chairman of the Foundation for Innovation in Medicine. The term “nutraceutical” originates from the word “nutrition” and “pharmaceutics.” Nutraceuticals are commonly used to describe natural and/or synthetic substances or products made from herbal extracts, dietary supplements (nutrients, particular diets), and processed foods, including cereals, soups, and beverages utilized for not only nourishment but also for the wellness of animals and humans (Nasri et al. 2014). Ginseng, Echinacea, green tea, glucosamine, omega-3, lutein, folic acid, and cod liver oil are the popular nutraceuticals (Zeisel 1999) currently in use throughout the globe. Nutraceuticals are currently deemed as a reliable alternative to modern-day science-validated drugs or allopathic medicine. They can be viewed as a dietary supplement that aims to boost the health of animals and humans by supplementing the diet with one or more of the following dietary ingredients: a vitamin, mineral, amino acid, herb, or other botanical. Furthermore, it is a dietary substance intended for ingestion (oral route of administration) in the form of a capsule, granules, soft gel, or gel-cap, to supplement the diet by increasing total dietary intake and is not represented as a conventional food or as a sole item of a meal or the diet. For example, withal nutraceuticals are extensively used for wound healing effects as a

dermal preparation and part of antiaging cosmetics in different dosage forms (ointments, drops).

Nutritional/dietary supplements, nutraceuticals, and functional foods (foods that have a potentially positive effect, promote optimal health, reduce the risk of disease) provide an essential supplementary complement to the human diet by increasing the intake of bioactive chemicals to improve health and fitness. Individuals have always been interested in the healing effects of foods, regardless of their social or economic status. Herbs and spices have a long history of use in this context, both for their flavor-enhancing and prophylactic properties (Kaefer and Milner 2008). Nutraceutical products are not strictly regulated like pharmaceuticals but are handled similarly to food additives and dietary supplements in the United States of America (USA). Perspective, the term “nutraceutical” isn’t always defined or viewed the same way globally. However, it is frequently characterized as a food-derived product with beneficial or curative effects and possesses healing properties. Currently, a substance with health benefits or protection against acute and chronic diseases in animals and humans can be considered a nutraceutical product. Nutraceuticals at present are in heavy demand throughout the world because they maintain the body’s structure and function, promote health and wellbeing, slow down the aging process, prevent acute & chronic diseases, and extend life (Kalra 2003). Although pharmaceuticals and nutraceuticals may be used to prevent or treat illness, each country’s government or regulating agency approves only pharmaceutical compounds (Baby et al. 2013) for therapeutic applications. Contrary to pharmaceutical drugs, nutraceuticals are not generally protected by patents.

Most nutraceuticals have a variety of medicinal uses. Recent research has demonstrated that nutraceuticals have promising health outcomes in reducing the risk or treating various pathological consequences. Nutraceuticals can reduce the risk of diseases associated with the central nervous system (CNS), eye, gastrointestinal tract, cardiovascular system, lungs, hormones (endocrine), integumentary system (skin), kidney, skeletal (bone), and muscles. Therefore, nutraceuticals are considered a safe drug alternative with prophylactic and/or therapeutic effects (Crescente et al. 2018).

Cannabis is being consumed or used in numerous cultures and different religions for the past thousands of years. One of the reasons for its continuous use throughout the centuries may not be attributed only to its healing, beneficial or commercial properties, but mainly due to the lack of significant toxic effects. Like the nutraceuticals, Cannabis (synonym = dope, grass marijuana, pot, weed,) a natural botanical, is currently used as a prophylactic/therapeutic medication and a recreational substance throughout the world. Like the nutraceuticals, Cannabis (because of its potent bioactivity) can also exert multi-pharmacodynamic effects. The healthcare and food industries are currently looking for novel, safe, and affordable natural/synthetic products to prevent health defects and improve animal/human acute and chronic health conditions. Thus, Cannabis may be a promising nutraceutical product for the present and future generations.




## 2 Beneficial Effects of Nutraceuticals

Nutraceuticals have been shown to exert central and peripheral neuroprotection by decreasing the rate of neuronal death, increasing the level of cellular energy, decreasing hyperarousal (stress and anxiety), and counteracting depression (Williams et al. 2015; Dhanasekaran et al. 2007, 2008; Tharakan et al. 2006; Pondugula et al. 2021). In the eye, nutraceuticals have been shown to prevent glaucoma (increased intraocular pressure), macular degeneration, retinopathy, xerophthalmia, and inflammation (Morrone et al. 2018; Stice and Kolanos 2021). Nutraceuticals can significantly affect gastrointestinal motility and acid secretion in the gastrointestinal tract. They have been shown to exhibit hepatoprotective and gastrointestinal protective effects and decrease and/or prevent the risk of several gastrointestinal-related diseases and disorders (Romano et al. 2012; Gao et al. 2020). Similarly, in the respiratory tract, nutraceuticals have been associated with a decreased risk for cancer, pulmonary fibrosis, asthma, and chronic obstructive pulmonary disorder (Gulati et al. 2021; Hwang and Ho 2018; Allam et al. 2021; Ciprandi et al. 2019). In the cardiovascular system, nutraceuticals significantly reduce the risk of heart disease and prevent hypertension (Sosnowska et al. 2017). Nutraceuticals possess nephron-protective and diuretic effects in the renal system and reduce renal dysfunction (Gwaltney-Brant 2016; Cosola et al. 2018). Endocannabinoids are present in both the male and female gonads, and they help signal fertility in the cycle of reproduction, regulate gonadic hormones, and aid in the function of spermatozoa. Thus, they can significantly increase the reproductive functions in males and females and reduce reproductive dysfunction (Zhao et al. 2021). In the skeletal system, nutraceuticals and thus prevents sarcopenia and skeletal muscle wasting (Rao et al. 2021; Gras et al. 2021; Pandey et al. 2018). Skin being the largest organ of the human body needs more care and protection. Several nutraceuticals can prevent skin-related diseases and have been used as cosmeceuticals (Lu et al. 2021; Geng et al. 2021; Michalak et al. 2021). Nutraceuticals possess significant immunomodulatory and endocrinological effects. Thus, the nutraceuticals can reduce the risk of several immunological and endocrinological disorders (Hepler and Bass 2021; Miao et al. 2021; Goyal et al. 2021; Upton 2021; Berberich and Hegele 2018) (Table 1).

## 3 Classification of Nutraceuticals and Their Healthcare Benefits: Inclusion of Cannabis



Nutraceuticals can be classified in various ways to make them easier to understand and apply, such as academic, clinical trial design, functional food production, or dietary advice. Nutraceuticals can be classified by food sources, methods of action, chemical composition, and so on. All of the food sources used as nutraceuticals are natural and fall into the following categories (Kalia 2005; Kokate et al. 2002):

**Table 1** Beneficial effects of nutraceuticals

Organ system	List of nutraceuticals	Beneficial effect
Nervous (Central and Peripheral)  “Brain” by Rev314159 is licensed under CC BY-ND 2.0	<ul style="list-style-type: none"> <li>• Antioxidants (vitamin-E, vitamin-C)</li> <li>• Polyphenols</li> <li>• Vitamin-B (folate, pyridoxine, cobalamin)</li> <li>• Plant sterols</li> <li>• Caffeic acid</li> <li>• Allicin</li> <li>• Melatonin</li> <li>• Coenzyme-Q10</li> <li>• Traditional/tribal medicines (Trichopus, Bacopa, Centella, Oroxyllum, Mucuna, turmeric)</li> </ul>	<ul style="list-style-type: none"> <li>• Retard the rate of neuro-degenerative diseases (Alzheimer’s disease, Parkinson’s disease)</li> <li>• Anti-fatigue action</li> <li>• Anti-stress effects</li> <li>• Reduce anxiety</li> <li>• Mood elevators (decrease depression)</li> <li>• Increase mitochondrial function</li> <li>• Decrease oxidative stress</li> <li>• Combat apoptosis</li> <li>• Reduce inflammation</li> </ul>
Ophthalmic “Sleepy eye” by emrank is licensed under CC BY 2.0 	<ul style="list-style-type: none"> <li>• Alpha-lipoic acid</li> <li>• Citicoline</li> <li>• Coenzyme-Q10</li> <li>• Curcumin</li> <li>• Flavonoids (kaempferol 3-O-rutinoside, quercetin, rutin)</li> <li>• Forskolin</li> <li>• Lutein</li> <li>• Lycopene</li> <li>• Polyunsaturated fatty acids (PUFA)</li> <li>• Resveratrol</li> <li>• Taurine</li> <li>• Traditional/tribal botanicals (<i>Ginkgo biloba</i>)</li> <li>• Vitamins (A, C, D, E, folic acid, thiamine, pyridoxine, cobalamin)</li> <li>• Zeaxanthin</li> <li>• Zinc</li> </ul>	<ul style="list-style-type: none"> <li>• Prevents macular degeneration</li> <li>• Anti-glaucoma effect</li> <li>• Prevents cataract</li> <li>• Decrease retinopathy</li> <li>• Prevents retinitis pigmentosa</li> <li>• Reduce the risk of diabetic retinopathy</li> <li>• Decrease age-related ophthalmic degeneration</li> <li>• Decrease xerophthalmia (dry eye)</li> <li>• Decrease glutamate induce excitotoxicity</li> <li>• Provides antioxidant effect</li> <li>• Promote cell survival signaling pathways</li> <li>• Anti-inflammatory effect</li> </ul>
Gastrointestinal (GIT)  “Stomach pic for food poisoning thingy” by danxoneil is licensed under CC BY 2.0	<ul style="list-style-type: none"> <li>• Allicin</li> <li>• Anthraquinone</li> <li>• Curcuminoids</li> <li>• Fiber (soluble and insoluble)</li> <li>• Flavonoids/isoflavones</li> <li>• Pentacyclic triterpene</li> <li>• Polyphenols</li> <li>• Prebiotics and probiotics</li> <li>• Psyllium</li> <li>• Resveratrol</li> <li>• Traditional/tribal medicines (<i>Aloe vera</i>, <i>Curcuma longa</i>, <i>Aegle marmelos</i>, garlic, croton species, natural honey, <i>Nigella sativa</i>, apple, <i>Cordyceps Sinensis</i>, Senna, cascara,</li> </ul>	<ul style="list-style-type: none"> <li>• Reduce constipation</li> <li>• Treat diarrhea</li> <li>• Decrease the risk of chronic gastritis-<i>H. pylori</i></li> <li>• Decrease the risk of proctitis</li> <li>• Decrease the risk of Crohn’s disease</li> <li>• Decrease the risk of adenomatous polyps</li> <li>• Hepato-protective effect</li> <li>• Decrease the risk of various types of GIT cancer/ polyps/neoplasia (colorectal, colon)</li> <li>• Reduce the risk of</li> </ul>

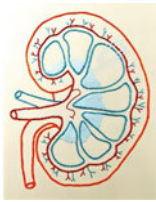
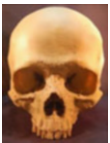
(continued)

**Table 1** (continued)

Organ system	List of nutraceuticals	Beneficial effect
	<p><i>Saccharomyces cerevisiae</i>, <i>Andrographis paniculate</i>, <i>Curcuma longa</i>, ginger, purple potato, green tea)</p>	<p>inflammatory bowel disease (irritable bowel syndrome)</p> <ul style="list-style-type: none"> <li>• Possess antibacterial effects</li> <li>• Possess wound healing properties</li> <li>• Reduce ulcer</li> <li>• Ability to stimulate</li> <li>• Increase collagen synthesis and fibroblast activity</li> <li>• Decrease diverticular disease</li> <li>• Reduce the risk of increased gastric acid associated or reflux diseases (dyspepsia, gastroesophageal reflux disease, ulcerative colitis)</li> </ul>
<p>Respiratory</p>  <p>“[H] Ma Han—Breathing Systems—Lungs (2008)” by Cea. is licensed under CC BY 2.0</p>	<ul style="list-style-type: none"> <li>• Calcium</li> <li>• Flavonoids</li> <li>• Natural products from animals (fish oil- omega-3 fatty acids, docosahexaenoic acid-DHA/eicosatetraenoic acid-EPA, heparin)</li> <li>• Traditional/tribal medicines (green tea- epigallocatechin gallate)</li> </ul>	<ul style="list-style-type: none"> <li>• Reduce the risk for cancer</li> <li>• Decrease pulmonary fibrosis</li> <li>• Decrease the risk of chronic obstructive pulmonary disease</li> <li>• Decrease bronchoconstriction</li> <li>• Induce bronchodilation</li> <li>• Decrease the risk for asthma</li> <li>• Decreases the production of pro-inflammatory cytokines (IL-8, TNF-<math>\alpha</math>)</li> <li>• Decrease necrosis</li> </ul>
<p>Cardiovascular</p>  <p>“Human heart W/color” by brick red is licensed under CC BY-ND 2.0</p>	<ul style="list-style-type: none"> <li>• Antioxidant (vitamin-E, vitamin-C)</li> <li>• Polyphenols</li> <li>• Potassium</li> <li>• Omega-3 fatty acids (DHA, EPA)</li> <li>• Coenzyme-Q10</li> <li>• Spirulina (<i>Cyanobacterium</i>)</li> <li>• Sterols/stanols</li> <li>• Traditional/tribal medicines (green tea- epigallocatechin gallate)</li> </ul>	<ul style="list-style-type: none"> <li>• Reduce the risk of heart disease</li> <li>• Decrease hypertension</li> <li>• Reduce endothelial dysfunction</li> <li>• Decrease hypercholesteremia</li> <li>• Reduce obesity</li> <li>• Reduce coronary heart disease</li> <li>• Fight against cardiometabolic risk factors</li> </ul>
	<ul style="list-style-type: none"> <li>• Catechins</li> <li>• Curcumin</li> <li>• Curcumin</li> <li>• Dietary protein</li> </ul>	<ul style="list-style-type: none"> <li>• Possess diuretic effect</li> <li>• Reduce renal dysfunction</li> <li>• Decreases chronic kidney disease</li> </ul>

(continued)

**Table 1** (continued)

Organ system	List of nutraceuticals	Beneficial effect
<p>Renal</p>  <p>“Framed embroidery kidney anatomy art. Hand embroidered.” by hey Paul studios is licensed under CC BY 2.0</p>	<ul style="list-style-type: none"> <li>• Fatty acids</li> <li>• Fiber</li> <li>• Resveratrol</li> <li>• Traditional/tribal medicines (<i>Stevia rebaudiana</i>, green tea, coffee)</li> </ul>	<ul style="list-style-type: none"> <li>• Exhibit antioxidant action</li> <li>• Exhibit anti-inflammatory effect</li> <li>• Possess antifibrotic activities</li> <li>• Protects against infectious</li> <li>• Reduce inflammatory conditions</li> <li>• Protects against hypoxia or ischemia</li> <li>• Blocks nephrotoxicity</li> <li>• Protects against metabolic derangements,</li> <li>• Prevents neoplastic conditions</li> <li>• Decrease the production of uremic toxin</li> <li>• Decrease ammonia production</li> <li>• Protects against glomerulonephritis</li> <li>• Protects against hypertension-related nephrosclerosis</li> </ul>
<p>Reproductive</p>	<ul style="list-style-type: none"> <li>• Acetyl L-carnitine</li> <li>• Coenzyme Q10</li> <li>• Fertility vitamins</li> <li>• Ferulic acid</li> <li>• Onion</li> <li>• Quercetin</li> <li>• Quercetin glucoside</li> <li>• Red-fleshed apple anthocyanin extracts</li> <li>• Traditional/tribal medicines: (fennel, berberine, dietary soluble flaxseed oil, palm dates, <i>Trigonella foenum-graecum</i> L., <i>Coleus Amboinicus</i>)</li> </ul>	<ul style="list-style-type: none"> <li>• Menopausal symptoms (hot flushes)</li> <li>• Increases sperm count</li> <li>• Reproductive protective</li> <li>• Increase breast milk production</li> <li>• Attenuate male reproductive system dysfunction</li> <li>• Fertility booster</li> <li>• Increase the possibility to conceive (give birth)</li> <li>• Erectogenic properties</li> </ul>
<p>Skeletal (bones)</p>  <p>“Object 3” by bansidhe is licensed under CC BY 2.0</p>	<ul style="list-style-type: none"> <li>• Calcium</li> <li>• Chondroitin</li> <li>• Cocoa flavanols</li> <li>• Collagen</li> <li>• Copper</li> <li>• Creatinine</li> <li>• Ferulic acid</li> <li>• Glucosamine</li> <li>• Green tea catechins</li> <li>• Raspberry ketone</li> <li>• Vitamin-D</li> <li>• Whey protein</li> </ul>	<ul style="list-style-type: none"> <li>• Decrease osteoporosis</li> <li>• Reduces osteoarthritis</li> <li>• Decrease sarcopenia</li> <li>• Blocks bone degradation</li> <li>• Prevents sarcopenia and skeletal muscle wasting</li> </ul>

(continued)

**Table 1** (continued)

Organ system	List of nutraceuticals	Beneficial effect
Integumentary (dermal)	<ul style="list-style-type: none"> <li>• Allicin</li> <li>• Carotenoids</li> <li>• Curcumin</li> <li>• Fatty acids</li> <li>• Green tea catechins</li> <li>• Minerals</li> <li>• Polyphenols</li> <li>• Probiotics</li> <li>• Sesame oil</li> <li>• Vitamins</li> </ul>	<ul style="list-style-type: none"> <li>• Skin softener</li> <li>• Decrease the risk of melanoma</li> <li>• Treat fungal infection</li> <li>• Possess antibacterial effect</li> <li>• Prevents psoriasis</li> <li>• Prevents erythema</li> <li>• Possess wound healing effect</li> <li>• Prevents skin photoaging induced by ultraviolet (UV) irradiation</li> </ul>
Immune	<ul style="list-style-type: none"> <li>• Omega-3 fatty acids (DHA, EPA)</li> <li>• Zinc</li> <li>• Coenzyme-Q10</li> </ul>	<ul style="list-style-type: none"> <li>• Possess immunomodulatory action</li> </ul>
Endocrine	<ul style="list-style-type: none"> <li>• Calcium</li> <li>• Vitamin D</li> <li>• Plant sterols</li> <li>• Fiber (soluble and insoluble)</li> <li>• Garlic</li> <li>• Probiotics</li> <li>• Synbiotics</li> <li>• Phytoestrogens</li> </ul>	<ul style="list-style-type: none"> <li>• Reduces the risk of diabetes mellitus</li> <li>• Decrease the cholesterol (hypercholesterolemia)</li> <li>• Prevents insulin resistance</li> <li>• Prevents polycystic ovary syndrome</li> <li>• Decrease thyroid dysfunction</li> <li>• Neuroprotective role in Parkinson's disease</li> <li>• Decrease obesity</li> <li>• Decreases the risk of metabolic syndrome</li> </ul>

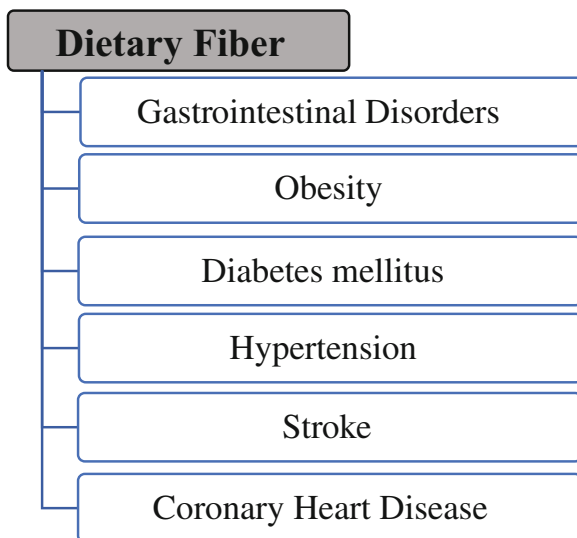
(1) Dietary Fiber (2) Probiotics, Prebiotics, and Synbiotics (3) Polyunsaturated fatty acids (4) Vitamins; (5) Polyphenols (6) Spices.

### 3.1 Dietary Fiber

Dietary fiber refers to botanical-based carbohydrates, significantly distinct from other carbohydrates such as monosaccharides, disaccharides, and starch. Dietary fibers are not digested in the small intestine and reach the large intestine or colon to exert pharmacological effects. The primary fiber-rich foods are wholegrain/wheat (cereals, pasta, bread, oats, barley, rye), fruit (berries, pears, melon, oranges), vegetables (beans, broccoli, carrots, peas, pulses, sweetcorn), nuts and seeds, potatoes with skin. The dietary fibers are classified as water-insoluble/less fermented, water-soluble/well fermented or soluble fiber, and insoluble fiber. Soluble fiber



**Fig. 1** Potential protective effects of dietary fiber in healthcare



dissolves in water and lowers glucose and cholesterol content in humans and animals. Nutrients and diets with soluble fiber include oatmeal, nuts, beans, lentils, apples, and blueberries. Insoluble fiber typically does not dissolve in water but accelerates the bowel movement of food in the digestive system, fosters bowel movement consistency, and avoids constipation. Foods with insoluble fibers include wheat, whole wheat bread, whole grain couscous, brown rice, legumes, carrots, cucumbers, and tomatoes.

Based on the above observation, there are several dietary fiber products containing cannabis/hemp. Cannabis/hemp seed (*Cannabis sativa*), like other botanicals such as faba bean (*Vicia faba*), lupin (*Lupinus angustifolius*), rapeseed press cake (*Brassica rapa/napus*), flaxseed (*Linum usitatissimum*), buckwheat (*Fagopyrum esculentum*), and quinoa (*Chenopodium quinoa*), is an excellent resource of dietary fiber, essential amino acids, and minerals (Dhingra et al. 2012; Mattila et al. 2018; Farinon et al. 2020). Cannabis/hemp oil is used as dressing in salads, sprinkled on yogurt, cereals, oatmeal, baked in muffins, cookies, bread, granola, and meal bars.

Dietary fiber is a type of food, specifically a type of plant material, that is not hydrolyzed by digestive enzymes and is instead digested by gut bacteria. Non-starch polysaccharides (NSP) such as celluloses, hemicelluloses, gums and pectin, lignin, resistant dextrin, and resistant starches make up the majority of dietary fibers (Das et al. 2012). The potential protective effects of dietary fiber in healthcare are depicted in Fig. 1.

### 3.2 *Probiotics, Prebiotics and Synbiotics*

Probiotics and prebiotics assist the beneficial bacteria and yeasts in the body to thrive, resulting in healthy living. The terminology of probiotics has undergone many modifications (Fuller 1989). Currently, the probiotics must be viable microorganisms that positively impact their host to emphasize their microbial origin, and one or more microbial strains may be present in probiotic supplements. *Lactobacillus*, *Bifidobacterium*, *Lactococcus*, *Streptococcus*, and *Enterococcus* are the most commonly found bacteria in human probiotics. Additionally, gram-positive bacteria strains from the genus *Bacillus* and certain yeast strains from the family *Saccharomyces* are often utilized in probiotic products (Fuller 1989).

Prebiotics are specified by the Food and Agriculture Organization (FAO) and World Health Preorganization (WHO) as a non-viable dietary component that provides health benefits to the host by modulating the body's microbiota. Prebiotics are a varied collection of carbohydrate components whose origins, fermentation characteristics, and doses needed for health benefits are not well understood. Breast milk, soybeans, inulin sources (Jerusalem artichoke, chicory roots, and others), raw oats, unprocessed wheat, unrefined barley, yacon, and non-digestible carbohydrates, particularly non-digestible oligosaccharides, are all excellent sources of prebiotics.

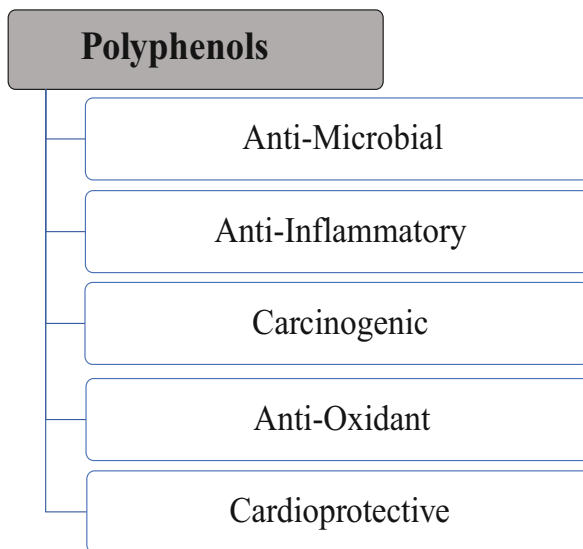
Since the term "synbiotics" implies synergism, it should only be used for the products in which the prebiotic compound(s) benefit the probiotic organism preferentially (s) (Pandey et al. 2015). By selectively boosting the development and/or activating the metabolism of one or a restricted number of health-promoting bacteria, a synbiotic product aids the host in enhancing the survival and implantation of live microbial dietary supplements in the gastrointestinal system. Synbiotics have been reported to combat inflammatory bowel disease (IBD), reduce diarrhea, decrease lactose intolerance, and the combination of prebiotics and probiotics that may boost the host immune system, decrease obesity and hyperglycemia (Benisek 2021).

Cannabis oil is a potentially beneficial probiotic for human use. Recent research has shown CBD probiotics to have the ability to protect joints, support the immune system, strengthen bones, relax emotions, enhance prostate, and vaginal health, protect neurons and increase neuronal function, increase sleep quality, as well as help with pain relief. Additionally, researchers have found that CBD oil can treat skin problems (acne, dark spots, and xeroderma). Currently, Cannabis-based nutraceuticals are available as topical creams and ointments and can be ingested orally as gummies, soft gels, and pills (WebMD 2020).

### 3.3 *Polyunsaturated Fatty Acids (PUFA)*

Polyunsaturated fatty acids (PUFAs) are also referred to as "essential fatty acids" because they are required for the body's normal physiological function and are obtained through the diet (Mahan and Escott-Stump 2004). PUFA's provide

**Fig. 2** Major health benefits of polyphenols



essential structural and functional components of the plasma membrane. PUFA's are designated by the number of unsaturated bonds in their structure by the letter "n" (Fig. 2). PUFA's with either n-3 or n-6 ( $\omega$ -3 or  $\omega$ -6) are beneficial in the ideal ratio of n-3 to n-6 is 1:5. The amount of n-3 or n-6 PUFAs in food has a direct impact on their bioavailability. PUFA's accumulate into the neuronal phospholipids mostly during brain development. PUFA's also influence synaptic function by changing the neuronal membranes' dynamic and enhancing the functionality of membrane-associated proteins. Additionally, PUFA's can aid in neurogenesis and neuroprotection. Interestingly, PUFA's are also precursors are endocannabinoids (Al-Khalifa et al. 2007; Layé 2016).

Endocannabinoid neurotransmission is a newly studied and researched transmitter system compared to the cholinergic, serotonergic, GABAergic, and glutamatergic neurotransmitter systems. This transmitter system significantly regulates the central and peripheral signaling mechanisms associated with food intake, lipids synthesis and turnover in the liver and adipose tissue, and glucose metabolism in muscle cells. This system significantly influences the central nervous system, peripheral nervous system, immune systems, and hormones. The endocannabinoids regulate the secretion of hormones related to reproductive functions and stress response. Furthermore, endocannabinoids control energy homeostasis and significantly affect food intake centers/regions of the brain/central nervous system and gastrointestinal tract activity.

Cannabis-based nutraceuticals have been reported to improve gonadotrophin pulsatility, fertilization ability and decrease the risk of various neurodegenerative (Alzheimer's, Parkinson's, and Huntington's diseases) and neurological disorders (epilepsy, anxiety, and stroke). Thus, a new or an existing cannabis-based nutraceutical selectively act on central and peripheral cannabinoid-1 receptor (CB1) receptor and reduce body weight, improve metabolic syndrome (decrease hyperglycemia and

hypercholesteremia), decrease cardiovascular diseases in obese patients by increasing blood HDL-cholesterol, adiponectin, and lowering LDL-cholesterol, leptin, and C-reactive protein (a pro-inflammatory protein). Furthermore, linoleic acid, alpha-linolenic acid, and gamma-linolenic acid are three polyunsaturated fatty acids in hemp seed oil. The fatty acid ratio of hempseed omega-6 (linoleic acid) to omega-3 (alpha-linolenic acid) is 3:1. According to the current literature, the 3:1 fatty acid ratio is beneficial for human health.

### 3.4 Vitamins

Vitamins are synthetic or natural substances essential for physiologic function, can help prevent or delay certain types of cell damage, and prevent the initiation and progression of a disease. Casimir Funk, the Polish-born biochemist, coined the term “*vitamine*” in 1912. Vitamins are organic molecules with a wide variety of functions within the body. They act as coenzymes/cofactors for enzymatic reactions. Generally, vitamins cannot be synthesized by mammalian cells and therefore must be supplied in the diet. Vitamins are classified mainly based on their solubility (water-soluble and fat-soluble vitamins) (Table 2). Important features of fat-soluble vitamins (A, D, E, K) are given in Table 3.

In general, deficiency of Vitamin-B leads to various types of anemia, such as pernicious anemia (B<sub>12</sub> deficient), folic acid deficient anemia, riboflavin deficient anemia, pyridoxine deficient anemia, and sideroblastic anemia.

#### 3.4.1 Thiamine (Vitamin B<sub>1</sub>)

The dietary requirement for thiamine is 1–1.5 mg/day. It is mainly present in lentils and whole grains. The primary functions are that it acts as a cofactor for pyruvate and alpha- $\alpha$ -ketoglutarate dehydrogenase and helps in forming acetyl-CoA. The major symptoms of thiamine deficiency are constipation, appetite suppression, nausea, mental depression, peripheral neuropathy, fatigue, ataxia, loss of eye coordination,

**Table 2** Water-soluble and fat-soluble vitamins

The water-soluble vitamins	The fat-soluble vitamins
<ul style="list-style-type: none"> <li>• Thiamin (B<sub>1</sub>)</li> <li>• Riboflavin (B<sub>2</sub>)</li> <li>• Niacin (B<sub>3</sub>)</li> <li>• Pantothenic acid (B<sub>5</sub>)</li> <li>• Pyridoxamine (B<sub>6</sub>)</li> <li>• Biotin (B<sub>7</sub>)</li> <li>• Cobalamin (B<sub>12</sub>)</li> <li>• Folic acid</li> <li>• Ascorbic acid (vitamin C)</li> </ul>	<ul style="list-style-type: none"> <li>• Retinol, retinal, retinoic acid (vitamin A)</li> <li>• Calcitriol (vitamin D)</li> <li>• <math>\alpha</math> Tocopherol (vitamin E)</li> <li>• Phylloquinone (vitamin K)</li> </ul>

**Table 3** Important features of fat-soluble vitamins (A, D, E, and K)

Vitamin	Structure/chemical name	Precursor	Function	Storage	Deficiency symptoms	Toxicity
<b>A</b>	Retinol, retinal, retinoic acid	Beta-carotene	<ul style="list-style-type: none"> <li>• Photoreception: Opsin bound to vitamin A</li> <li>• Retinol helps in mucous production &amp; normal growth regulation</li> </ul>	Liver	<ul style="list-style-type: none"> <li>• Night blindness</li> <li>• Xerophthalmia</li> <li>• Cancer</li> <li>• Infection</li> </ul>	<ul style="list-style-type: none"> <li>• Liver toxicity</li> <li>• Bone pain</li> <li>• Nausea</li> <li>• Diarrhea</li> <li>• Hepato-splenomegaly</li> <li>• Headache</li> <li>• Acne, skin disorder</li> </ul>
<b>C</b>	Ascorbic acid	Glucose L-gulonolactone oxidase absent in primates	<ul style="list-style-type: none"> <li>• Reduce cytochrome a, c, and oxygen of the respiratory chain</li> <li>• Cofactor for hydroxylation of proline in collagen</li> <li>• Catabolism of tyrosine</li> <li>• Synthesis of bile acids, steroid</li> <li>• Enhances the absorption of iron</li> </ul>	Adrenal cortex	<ul style="list-style-type: none"> <li>• Wound healing (proline-collagen)</li> <li>• Scurvy</li> </ul>	<ul style="list-style-type: none"> <li>• Indigestion</li> <li>• Diarrhea</li> </ul>
<b>D</b>	Steroid hormone, biologically active = Calcitriol-1,25-(OH) <sub>2</sub> -D <sub>3</sub>	Ergosterol, 7-dehydro-cholesterol	<ul style="list-style-type: none"> <li>• With parathyroid hormone regulates calcium and phosphorus level</li> <li>• Promotes bone formation</li> <li>• Stimulates immunogenic and antitumor activity</li> <li>• Decreases risk of autoimmune disorders</li> </ul>	Adipose tissue	<ul style="list-style-type: none"> <li>• Children: Rickets</li> <li>• Adults: Osteomalacia</li> </ul>	<ul style="list-style-type: none"> <li>• Hypercalcaemia</li> </ul>

(continued)

**Table 3** (continued)

Vitamin	Structure/chemical name	Precursor	Function	Storage	Deficiency symptoms	Toxicity
<b>E</b>	$\alpha$ -Tocopherol, $\beta$ , $\gamma$ , $\delta$ -tocopherols, 4-tocotrienols		<ul style="list-style-type: none"> <li>Free radical scavenger</li> <li>Prevents peroxidation of polyunsaturated membrane fatty acids</li> </ul>	<p>Absorbed in the intestine and packed in chylomicrons and transported to the liver</p> <p>Stored in adipose tissue, cellular membrane, circulating lipoproteins</p>	<ul style="list-style-type: none"> <li>Increase in red cell fragility</li> <li>Neurological disorders</li> </ul>	<ul style="list-style-type: none"> <li>Increased risk for cancer</li> </ul>
<b>K</b>	Phylloquinone (K1 green vegetables) Menaquinone (K2 intestine) Menadione (K3 synthetic)		<ul style="list-style-type: none"> <li>Blood clotting</li> <li>Conversion of inactive enzymes to the active form (carboxylation)</li> </ul>	<p>Absorbed in the intestine in the presence of lipids and bile salt</p>	<ul style="list-style-type: none"> <li>Hemorrhage syndrome</li> </ul>	<ul style="list-style-type: none"> <li>Increases the risk for coagulation</li> </ul>

cardiovascular problems, and musculature defects. The deficiency diseases are Beriberi, Wernicke-korsakoff syndrome, and dementia. It is prophylactically used to reduce the risk of cataracts, Alzheimer's disease, congestive heart failure, and various cancers. The significant adverse effect or toxicity associated with the use of thiamine is anaphylactic shock.

Thiamine has several drug and herbal interactions, and they are listed below:

Interaction with therapeutic drugs:

- Phenytoin (anticonvulsants) reduces thiamine levels in the blood and cerebrospinal fluid
- Antacids may lower thiamine levels in the body by decreasing absorption and increasing excretion or metabolism.
- Barbiturates may lower thiamine levels in the body by decreasing absorption and increasing excretion or metabolism.
- Loop diuretics (furosemide, Lasix®) have decreased thiamine levels by increasing urinary excretion (and also possibly by reducing absorption)
- Tobacco use decreases thiamine absorption and may lead to decreased levels
- Oral contraceptives (birth control pills)
- Chemotherapy Patient receiving fluorouracil-containing drug therapy
- Antibiotics destroy gastrointestinal flora (normal bacteria in the gut). It may decrease thiamine (slight depletion because thiamine is obtained through the diet and not via bacterial production).

Interactions with Herbs and Dietary Supplements:

- Consumption of betel nuts (*Areca catechu* L.) may reduce thiamine due to chemical inactivation
- Horsetail (*Equisetum arvense* L.) is used as a diuretic for the treatment of edema. It contains a thiaminase-like compound that can destroy thiamine in the GI tract. The Canadian government requires that horsetail products should be certified free of thiaminase activity.

### 3.4.2 Riboflavin (Vitamin B<sub>2</sub>)

Important features of vitamin B<sub>2</sub> like functions, use, deficiency symptoms, deficiency disorders, adverse effects, and drug interactions are given in Table 4.

### 3.4.3 Niacin (Vitamin B<sub>3</sub>, Pyridine-3-Carboxylic Acid, Nicotinic Acid)

The dietary requirement of niacin is 13–19 niacin equivalents. This water-soluble vitamin is required to synthesize NAD<sup>+</sup> and NADP<sup>+</sup>, which functions as a cofactor for various dehydrogenase enzymes (lactate, malate dehydrogenase). Niacin deficiency can result in reduced capacity to generate energy (ATP). The symptoms of niacin deficiency are glossitis, dermatitis, diarrhea, depression, dementia, and weight

**Table 4** Important features of riboflavin

Functions	Deficiency symptoms	Deficiency disorder	Uses	Adverse effects	Drug-interaction
Precursor for FMN & FAD	Glossitis, seborrhea, angular stomatitis, cheilosis, photophobia	Skin problems	Cosmetic use: Maintains the health of hair, nails, and skin	Urine coloration	The dose must be increased while consuming alcohol, antibiotics, and birth control pills or during a restricted diet

loss. The primary disease that occurs due to niacin deficiency is Pellagra. Prophylactically niacin is used in the treatment of hypercholesterolemia. The other clinical benefits of niacin are to control atherosclerosis and osteoarthritis. The primary adverse effects associated with elevated niacin levels include increased uric acid and glucose production. Hence, niacin should be used carefully in diabetes mellitus patients and patients suffering from gout. Niacin has a significant drug-interaction when used with the antitubercular drug isoniazid.

#### 3.4.4 Pantothenic Acid (B<sub>5</sub>)

Williams and his coworkers in 1933 isolated the crystalline product from yeast and named it pantothenic acid (Williams et al. 1933). Chemically, pantothenic acid (vitamin B<sub>5</sub>) is 3-[(2,4-dihydroxy-3,3-dimethyl-butanoyl)amino] propanoic acid. It is synthesized from beta-alanine and pantoic acid. Vitamin B<sub>5</sub> is necessary for synthesizing acetyl-CoA (acetyl coenzyme A) and is required for the metabolism of carbohydrates via the tricarboxylic acid cycle (TCA). Furthermore, acetyl-CoA is also involved in other biochemical reactions associated with protein and lipid metabolism. Acetyl-CoA is also required for the biosynthesis of the neurotransmitter acetylcholine, a reaction catalyzed by the enzyme acetyltransferase. The primary source of pantothenic acid is whole grain cereals, legumes, meat, and the dietary requirement is 5 mg/day adult. Deficiency of this vitamin can lead to fatigue (reduced capacity to generate energy), glossitis, dermatitis, diarrhea, depression, dementia, weight loss. The diseases due to the deficiency include adrenal insufficiency, hepatic encephalopathy, Hartnup disease, and malignant carcinoid syndrome. Vitamin B<sub>5</sub> is prophylactically used for hair care and to reduce acne and diabetic peripheral polyneuropathy. The major adverse effects are an upsurge in alanine transaminase (ALT) and creatine phosphokinase (CPK) content, pain (abdominal, joint, and muscle), constipation, dizziness, flu-like symptoms, headache, infection (urinary tract), nausea, pancreatitis, and sore throat. Furthermore, several Type-I hypersensitivity reactions such as hives, itching, rash, and swelling have been reported with Vitamin B<sub>5</sub> ingestion. Vitamin B<sub>5</sub> has very minimal pharmacodynamic drug interactions with other drugs. However, moderate drug interactions have been reported with some antibiotics (azithromycin, clarithromycin, erythromycin, and roxithromycin).



### 3.4.5 Pyridoxine (Vitamin B<sub>6</sub>)

Vitamin B<sub>6</sub> possesses a pyridine ring with hydroxyl, methyl, and hydroxymethyl substituents. It is mainly found in adults, whole grain cereals, legumes, meat, and the dietary requirements are 1.4–2.0 mg/day. The three major forms of vitamin B-6 are pyridoxine, pyridoxal, and pyridoxamine. Three forms of vitamin B-6 are precursors of an activated compound known as pyridoxal 5'-phosphate (PLP), which plays a vital role as the cofactor of many essential enzymes, including neurotransmitter decarboxylases used in the biosynthesis of dopamine, norepinephrine, and serotonin. Vitamin B<sub>6</sub> is generally indicated for pathological conditions that occur due to Vitamin B<sub>6</sub> deficiency. These include alcoholism, malabsorption, congestive heart failure, severe diarrhea, congenital metabolic dysfunction, hyperthyroidism, renal and hepatic disease, drug-induced conditions, and during pregnancy and lactation. It is also used to treat pyridoxine-dependent syndromes (pyridoxine-dependent seizures in infants, homocystinuria, pyridoxine-responsive anemia, and hyperoxaluria). Pyridoxine is also an antidote for isoniazid, hydrazine, and ethylene glycol-induced toxicities. Vitamin B<sub>6</sub> deficiency symptoms are anxiety, depression, loss of libido, insomnia, fluid retention, inability to process glucose (weight loss/gain). Adverse effects of Vitamin B<sub>6</sub> overuse include a feeling of disembodiment common with the loss of proprioception and increased dream vividness. The primary drug interactions are with isoniazid and oral contraceptives.

### 3.4.6 Biotin (Vitamin B<sub>7</sub>)

The chemical structure of biotin consists of an ureido (tetrahydroimidizalone) ring fused with a tetrahydrothiophene ring. It includes a valeric acid substituent is attached to one of the carbon atoms of the tetrahydrothiophene ring. Intestinal bacteria mainly synthesize it. Physiologically, it is essential in the catalysis of essential metabolic reactions to synthesize fatty acids, gluconeogenesis, and metabolize leucine. It is also a cofactor required for enzymes involved in carboxylation reactions (acetyl-CoA carboxylase). Since biotin is found in numerous foods, deficiency syndromes and symptoms are very rare and mild. It is prophylactically used to prevent Cradle cap (seborrheic dermatitis), diabetes mellitus, hair, and skin problems. It is reported to have significant drug interactions with antibiotics, anti-epileptics (carbamazepine, phenobarbital, phenytoin), and various herbal products.

### 3.4.7 Cobalamin (Vitamin B<sub>12</sub>)

The vitamin cobalamin contains a corrin ring with cobalt in the center, like the porphyrin ring found in heme, chlorophyll, and cytochrome. It is mainly found in foods of animal origin. Cobalamin is required for the physiological functioning of the TCA cycle (methylmalonyl mutase requires vitamin B<sub>12</sub>), in converting

homocysteine to methionine, and folate generation. It can be stored in the liver for 6 years; hence deficiency is rare (however, vegetarians can develop deficiency). The deficiency symptoms are neurological syndromes (cognitive impairment, movement impairment), anemia, and impaired DNA synthesis. Pernicious anemia occurs due to cobalamin deficiency. An intrinsic factor in the stomach is required for its physiological action, which helps in its absorption. It is prophylactically used to treat anemia, cyanide poisoning, and various types of dementia. The adverse effects associated with cobalamin overuse include allergy, diarrhea, and thrombosis. The major drug interactions are with alcohol, antibiotics, birth control pills, histamine (H<sub>2</sub>) antagonist, metformin, and nicotine.

### 3.4.8 Folic Acid

Folic acid is found in leafy plants, yeast, and the liver. Normally body stores 10–20 mg; hence it takes 3–4 months for the deficiency to occur when the diet is deficient in this vitamin. Folic acid is required for DNA, RNA, and protein synthesis as well as normal cell division. Impaired cell division (mainly in the rapidly proliferating cells) occurs due to increased folic acid requirement (pregnancy), decreased folic acid intake, impaired folic acid absorption, Crohn's disease, chronic use of anticonvulsants, and the use of dihydrofolate reductase inhibitors (methotrexate, trimethoprim). Poor absorption of folic acid can result in disorders of the small intestinal and alcoholism. Folic acid deficiency leads to megaloblastic anemia. The major symptoms are fatigue, dizziness, increased cardiac output leading to heart failure, gastrointestinal symptoms (diarrhea), glossitis (tongue beefy and red), and muscle wasting. Neurological symptoms are rare, with folic acid deficiency and usually not present.

### 3.4.9 Ascorbic Acid (Vitamin C)

Important features of vitamin C such as precursor, functions, storage in the organ, deficiency symptoms, and toxicity are given in Table 5.

## 3.5 Polyphenols

Polyphenols are naturally occurring compounds present in certain beverages (tea, coffee, and red wine), cereals, fruits, and vegetables (legumes). In food, polyphenols may contribute to bitterness, color, flavor, and odor. Polyphenols are plant metabolites and are generally involved in defense against ultraviolet radiation or harmful pathogens. Polyphenols are grouped into two major classes, flavonoids and phenolic acids. Flavonoids are further subclassified into flavones, flavanones, flavonols, flavonols, isoflavones, and phenolic acids are subclassified into hydroxybenzoic

**Table 5** Important features of ascorbic acid (Vitamin C)

Chemical name	Precursor	Functions	Storage	Deficiency symptoms	Toxicity
Ascorbic acid	Glucose L-gulonolactone oxidase absent in primates	<ul style="list-style-type: none"> <li>• Reduce cytochrome a, c, and oxygen of the respiratory chain</li> <li>• Cofactor for hydroxylation of proline in collagen</li> <li>• Catabolism of tyrosine</li> <li>• Synthesis of bile acids, steroid</li> <li>• Enhances the absorption of iron</li> </ul>	Adrenal cortex	<ul style="list-style-type: none"> <li>• Wound healing (proline-collagen)</li> <li>• Scurvy</li> </ul>	<ul style="list-style-type: none"> <li>• Indigestion</li> <li>• Diarrhea</li> </ul>

and hydroxycinnamic acids. The most common explanation for the beneficial effects of polyphenols is the “biochemical scavenger theory.” This theory proposes that polyphenolic substances neutralize free radicals by creating stable chemical complexes, limiting further reactions that can lead to pathology at the cellular and tissue levels. Another method by which polyphenols protect against oxidative stress is via the production of hydrogen peroxide, which may subsequently assist in controlling immune response activities such as cellular development (Cory et al. 2018).

Polyphenols’ beneficial effects are either as protective/prophylactic chemicals or as therapeutic molecules, may be obtained by consuming a naturally polyphenol-rich diet, ingesting dietary supplements, or using pharmaceutical drugs/nutraceuticals formulations (Silva and Pogačnik 2020). Polyphenols offer the benefit of providing a sufficiently active dosage, but they also have a range of adverse effects. Polyphenols invariably interact with other nutrients; in meals may slow down the rate of carbohydrate digestion, reducing postprandial glucose rises. A supplement would have no impact on this parameter if taken without food; therefore, the optimum scenario would be to ingest the polyphenol with foods. Similarly, polyphenol supplements may alter bioavailability, discouraging people from eating a ‘healthy diet’ instead of augmenting poor food (Williamson 2017).

Industrial hemp (*Cannabis sativa* L.) belongs to the family Cannabaceae. The plant contains many bioactive compounds, mostly polyphenols, including flavonoids, phenolic acids, phenol amides, and lignanamides, which are well known for their therapeutic properties. The phytochemical characterization of Cannabis highlights various non-cannabinoid components, including various phenolic compounds, steroids, and alkaloids. Many polyphenols-related products consisting of herbal extracts are marketed and benefit health (Smeriglio et al. 2016; Pandey and Rizvi 2009; Pollastro et al. 2018). Based on the above scientific fact, the phenolic compounds within industrial hemp inflorescence showcase an innovational source of bioactive compounds to be used in nutraceutical formulations and can commonly be observed in products such as cold-pressed seed oil (containing the Finola cultivar of industrial hemp). Significant in vitro evidence suggests that dietary polyphenols

may influence various cellular processes, including gene expression, apoptosis, platelet aggregation, and intercellular communication, which may have anti-carcinogenic and anti-atherogenic effects (Duthie et al. 2003). Major health benefits of polyphenols are depicted in Fig. 2.

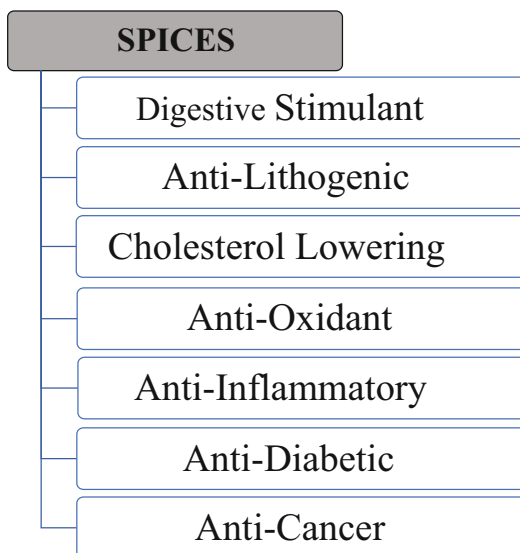
### 3.6 Spices

Spices are abstruse food additives that have been used to improve the overall aesthetic quality of foods for thousands of years. They are natural substances that primarily consist of substances obtained from the bark, fruit, root seed, and other botanicals. According to the United States of America Food and Drug Administration (US-FDA), spices are “aromatic vegetable compounds, in whole, broken, or crushed form, whose main role in food is flavoring rather than nutrition.” According to the above FDA’s description, onions, garlic, celery, and seeds like poppy and sesame are generally considered food and not spices. Various spices are used predominantly internationally for flavoring or coloring food, where a minimal quantity can considerably enhance the aesthetic property, quality, and taste (deliver a unique flavor). Many foods without spice (s) are usually flavorless, bland, and odorless. Some spices like paprika, turmeric, and saffron are used in cuisine to improve color and taste. Thus, these spices are categorized as “flavoring and coloring” agents when used or added to a cuisine. The majority of spices come from bark (cinnamon), fruit (red and black pepper), and seed (cumin and nutmeg). Interestingly, spices are generally distinguished from herbs, leaves, flowers, or stalks/stems of plants used as a garnish. Herbs used in cooking are usually made up of leaves and stems.

Similar to FDA, The Geneva-based International Standards Organization (ISO) defines spices and condiments as “Vegetable products or mixtures thereof, free from extraneous matter, used for flavoring, seasoning and imparting aroma in foods.” Furthermore, any aromatic botanical/vegetable (cinnamon, cloves, mace, nutmeg, pepper, ginger) used to season and flavor sauces, pickles, or other food/drink, usually in the form of a powder; collectively are also considered spices. A standard and traditional classification of spices are based on the degree of taste and flavor. The spices are classified as mild (paprika, coriander), aromatic (pimento, cardamom, cassia, cinnamon, clove, cumin), and hot (Capsicum/chilies, Cayenne pepper, black and white peppers) spices.

According to recent research studies, dietary spices may considerably benefit human health due to diverse pharmacological profiles. The multiple actions reported for spices include antioxidant, chemopreventive, antimutagenic, anti-inflammatory, and immunomodulatory effects. Due to the above multi-potent pharmacological actions, spices exhibit many positive, beneficial effects on human health. Spices can significantly affect the human body’s neurological, ophthalmic, gastrointestinal, cardiovascular, respiratory, metabolic, reproductive, renal, skeletal, and other physiological functions.

**Fig. 3** Major health benefits of spices



Several flavorful cannabis-infused seasonings are currently available (<https://www.keithlorren.com/shop/keith-lorren-canna-spice>, <https://emilykylenutrition.com/cannabis-taco-seasoning/>, <https://www.evolvecannabiscompany.com/product/cured-cbd-infused-spices/>, <https://nevadawellnesscenters.com/?product=edible-soul-dlicious-vegetable-infused-seasoning-thc-100-69mg>).

Hemp/Cannabis extracts (organic cold-pressed) are commonly added to omega 3,6,9 essential fatty acids, garlic, trace minerals, and other substances. These Cannabis-based spice combinations are usually added at the end of the cooking process to conserve the beneficial effects of Cannabis. The Cannabis-infused spices can be added to burgers, burritos, baked potatoes, pasta, roasted vegetables, sliced fruit, and steak. Moreover, Cannabis-infused spice combinations can also be added to any drink (Elliott 1999; Lampe 2003). The major health benefits of spices are depicted in Fig. 3.

Moreover, in general, nutraceuticals can be divided into two categories:

1. Nutraceuticals with potential
2. Nutraceuticals that are well-established

Only after reliable clinical data on a potential nutraceutical's health and medical advantages is collected can it become a well-established product. It's worth noting that many nutraceutical products are still classified as "potential" (Pandey et al. 2010).

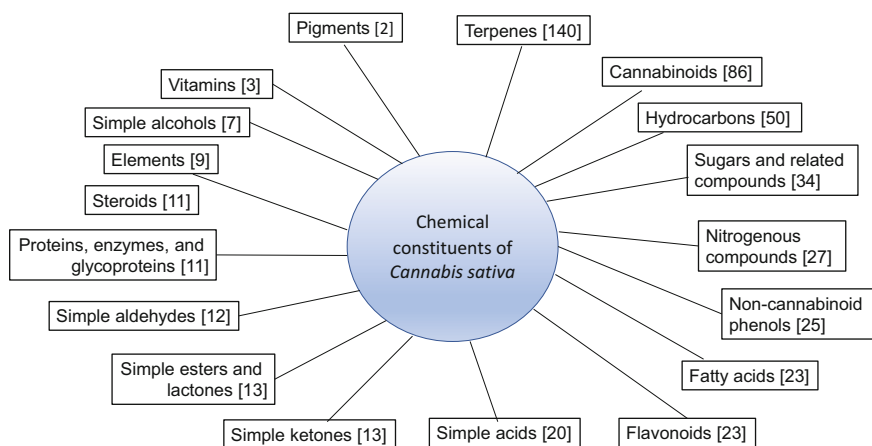
## 4 Cannabis as a Nutraceutical

Cannabis has been widely established as a primordial source of fiber, protein, and fat with great nutritional value, whether raw, boiled, or squeezed into the oil. In addition, Cannabis has been employed in traditional oriental medicine for thousands of years to treat and prevent diseases. Cannabis has been utilized as a food or medicine source in China for at least 3000 years, whether raw, baked, or roasted. Traditional Asiatic diets and treatments continue to use the seed, both crushed and whole. Cannabis has been legally utilized as human food in the United States for the past 10 years. Cannabis is primarily used for animal feed, but their products (oil, meal, flour, protein powder) are gaining popularity in human nutrition as a source of nutrients (Andre et al. 2016).

### 4.1 Chemical Constituents

Cannabis products comprise all essential amino acids and fatty acids in significant quantities and proportions to meet human dietary requirements. They include 25%–35% lipids, 20%–25% proteins, 20%–30% carbs, 10%–15% insoluble fibers, and a wide range of minerals, including phosphorus, potassium, salt, magnesium, sulfur, calcium, iron, and zinc. Protein (25%) and vitamin E (90 mg/100 g). Concerning the chemistry of *Cannabis sativa*, more than 750 natural compounds of different chemical classes have been reported (Upton 2021). Major chemical classes reported in *C Sativa* are depicted in Fig. 4.

Additionally, Cannabis comprises more than 30% oil, with polyunsaturated fatty acids accounting for more than 80% of the total, mainly linoleic  $\omega$ -6 and -linolenic



**Fig. 4** Major chemical classes of compounds reported in *Cannabis sativa*. The numbers in parentheses are the number of compounds identified under each class

$\omega$ -3 acids. Anti-cancer, anti-inflammatory, and anti-thrombotic effects and an increase of general metabolism and fat burning have all been linked to  $\omega$ -3 (Callaway 2004). The hemp seed oil has a  $\omega$ -6/ $\omega$ -3 ratio of roughly 3:1, which is excellent for human health. Recent research has found that these fatty acids and dietary hemp seeds have favorable impacts on platelet aggregation, ischemic heart disease, and other aspects of cardiovascular health. Furthermore, hemp seeds and derivatives have been discovered as a valuable antioxidant diet for the favorable effects of hemp bioactive molecules; further research and clinical studies for any potential adverse effects of hemp products in the diet have been advised. Several researchers have found that dietary hempseed has modestly positive effects on contractile dysfunction associated with atherosclerotic arteries in the cholesterol-fed rabbit (Frassinetti et al. 2018; Gavel et al. 2011).

Hemp seeds also contain minerals and nutrients such as Vitamin C, Calcium, Iron, Omega-3 fatty acids, Magnesium, and B vitamins, many of which are antioxidants. Many of these nutrients provide the body with necessary minerals and also contribute to overall health. Hemp seeds additionally contain a significant amount of iron, which can help prevent iron deficiency or anemia. Furthermore, Hemp seed oil is used as a remedy for a range of conditions (Atalay et al. 2019; Koekkoek and van Zanten 2016).

Based on the previous information, hemp seed oil and other hemp-based products contain minerals and antioxidant vitamins that can work individually and in combination to prevent oxidative processes that contribute to cancer, cardiovascular disease, cataracts, protect the body by scavenging free radicals and other degenerative disorders, and reduced bodily inflammation (Elliott 1999). While there are several research publications on the health advantages of hemp seeds, oils, and meals, there are few references on hemp sprouts' biological activities and possible health benefits. One study indicated that hemp sprouts might be used as a new anti-inflammatory hemp food product. Thus, Cannabis, due to its bioactive contents and its action, can be a valuable nutraceutical in the future.

## **4.2 Products and Their Uses**

Cannabis is now used by nearly 147 million people globally, mainly due to its recreational and medicinal properties. The vast majority of individuals who only know Cannabis as a recreational substance are unaware of its immense social, industrial, and economic benefits (Cerino et al. 2020). According to the FDA (<https://www.fda.gov/media/131878/download>), THC and CBD products are exempt from the dietary supplement classification under section 201(ff)(3)(B) of the FD&C Act [21 U.S.C. § 321(ff)(3)(B)]. Based on the FDA's current requirements, if a substance (such as THC or CBD) is an active ingredient in a drug product approved under section 505 of the FD&C Act [21 U.S.C. § 355], or has been authorized for investigation as a new drug for which substantial clinical investigations and the existence of such investigations has been made public, then products

containing that substance are prohibited. The demand for cannabidiol-based products has increased tremendously (by 500% since 2017). Several nutraceutical companies market cannabis nutraceutical products like CBD capsules, CBD tinctures, water soluble cannabinoids and dietary supplements to reduce stress boost immunity, maintain muscle and bone structure pain relief, insomnia, muscle spasms, nervous system degradation, and anxiety.

Cannabinoid extracts have been added to a wide range of foods, including beverages (both dairy and non-dairy), breakfast cereals, cookies, brownies, ice cream, snacks, bread, pizza, vegan burgers and sausages, and, more recently, beer, wine, hemp-infused milk, barley-based sodas, health beneficial honey, and fortified sports products. In the USDA's Food Data Central database, 680 branded food items containing hemp seed derivatives in the form of oil, extract, flour, or powder have been registered till now. To be legal in the United States, any of these items must have less than 0.3% THC (King 2019; Martínez et al. 2020). Additionally, hemp seeds, which are often used to enhance the flavor of healthful salads, can also be ground into a multipurpose flour that can be used to create a variety of meals. Hemp flour has 21% fewer calories than "00-flour" produced from conventional cereals and has a bitter, rustic taste similar to the whole meal. It is also gluten-free, making it a perfect option for celiac disease patients. An additional advantage of Cannabis is that it is vegan-friendly and contains plant-based protein. Hemp may be utilized instead of pea protein or rice protein, which are the most common plant-based proteins currently in the market. Hemp oil is a good source of fatty acids (EFAs) and is generally allergy-friendly and gluten-free. Aside from celiac disease, other diseases benefit from gluten-free diets, such as Hashimoto's thyroiditis, and hemp may be included in protein powders. It's a good option for individuals who are allergic to dairy or soy in other foods. Hemp is a plant source of Vitamin D. It has been observed that an increased requirement for Vitamin D is required to prevent or protect against COVID-19 induced pathological effects (Grant et al. 2020). Hemp flour is a byproduct of the hemp oil manufacturing process and is contains high fiber, microelements, and phytosterols. The above bioactives help to maintain normal cholesterol and decrease the risk of hypercholesteremia and cholesterol-mediated adverse effects in the body (Sorrentino 2021). CBD has been demonstrated in various pre-clinical models to have anticonvulsant, anxiolytic, anti-inflammatory, immune-modulating, and antineoplastic action (Cerino et al. 2020).

### ***4.3 Health Benefits***

Similarly, hemp seed also has been linked to a variety of health benefits and possible treatments. As hemp seed has a healthy omega-6 to omega-3 PUFA ratio, which might have the following nutraceutical values to exhibit the following pharmacological and therapeutic benefits: antitumor, anti-inflammatory, analgesic, antidepressant, antispasmodic and anticonvulsant, diuretic, antiemetic, appetite enhancer, anticancer, antibacterial, virucidal, sleep aid, cardiovascular aid, neuroprotective



and Neurorestorative to combat various neurological disorders (Alzheimer's disease, Parkinson's disease, brain trauma, and stroke) (Rupasinghe et al. 2020). Moreover, CBD contains immunomodulatory properties, such as reducing inflammatory responses, suppressing cellular and humoral immunity, and inducing the death of specific lymphocytes. Therefore, these properties are helpful in the treatment of inflammatory disorders (Booz 2011). Diabetes mellitus is primarily an endocrine disorder. However, inflammation may also play an essential aspect in the pathology of this devastating chronic illness. This hyperglycemic disorder may significantly benefit from preventive CBD therapy. Furthermore, non-obese hyperglycemic mammals administered with CBD exhibited a delayed onset of diabetes mellitus and substantially reduced leukocyte activation (Lehmann et al. 2016).

#### ***4.4 Future Prospects***

Due to the rising obesity and related endocrine and neurological diseases, rising health consciousness, and increased scientific knowledge about the advantages of cannabidiol nutraceuticals, demand for CBD nutraceuticals is projected to rise substantially in the future. Interestingly, CBD has been reported to exert several physiological, biochemical, and psychological effects that can benefit adults of all ages, individuals with anxiety disorders and have the potential to benefit performance athletes. Early pre-clinical and clinical data suggest that CBD has anti-inflammatory, neuroprotective, analgesic, and anxiolytic properties and the potential to protect against GI damage caused by inflammation and aid the repair of severe skeletal injuries (McCartney et al. 2020). The legalization of hemp-derived goods in late 2018, along with rising consumer disposable income and a growing trend toward health and wellness products, has resulted in a substantial rise in demand for cannabidiol nutraceuticals. The market is divided into various CBD products and formulations (capsules, tinctures, candies, bubble gum, chocolates) and other products based on the kind of product. Cannabidiol tinctures are rapidly being utilized for various ailments, including pain alleviation, sleeplessness, muscular spasms, nervous system degeneration, and anxiety. Governments all around the world are progressively enacting legislation to encourage the development of cannabidiol nutraceuticals. Therefore, by 2028, the worldwide CBD nutraceuticals market is projected to be worth 19.25 billion USD.

## **5 Conclusion**

Due to various health benefits, Cannabis-based products are attracting much worldwide attention in addition to the existing sources of nutraceuticals. Though all parts of a Cannabis plant have significant values, seed and oil are mainly used in food preparations. Every year market size is increasing, and governments worldwide are

progressively enacting legislation to encourage the development of cannabidiol nutraceuticals. It is estimated that by 2028, the worldwide CBD nutraceuticals market is projected to be worth 19.25 billion USD. Therefore, it is important to carry out intensive, evidence-based research in this promising area.

## References

- Al-Khalifa A, Maddaford TG, Chahine MN et al (2007) Effect of dietary hempseed intake on cardiac ischemia-reperfusion injury. *Am J Physiol Regul Integr Comp Physiol* 292(3):R1198–R1203. <https://doi.org/10.1152/ajpregu.00661.2006>
- Allam V, Chellappan DK, Jha NK et al (2021) Treatment of chronic airway diseases using nutraceuticals: mechanistic insight. *Crit Rev Food Sci Nutr* 2021:1–15. <https://doi.org/10.1080/10408398.2021.1915744>
- Andre CM, Hausman J-F, Guerriero G (2016) *Cannabis sativa*: the plant of the thousand and one molecules. *Front Plant Sci* 7:19
- Atalay S, Jarocka-Karpowicz I, Skrzydlewska E (2019) Antioxidative and anti-inflammatory properties of cannabidiol. *Antioxidants (Basel)* 9(1):21. <https://doi.org/10.3390/antiox9010021>
- Baby C, Gopal K, Nazia K, Shahid HA (2013) Current concepts and prospects of herbal nutraceutical: a review. *J Adv Pharm Technol Res* 4(1):4–8. <https://doi.org/10.4103/2231-4040.107494>
- Benisek A (2021) Synbiotics: what to know. WebMD. <https://www.webmd.com/digestive-disorders/synbiotics-what-to-know>. Accessed 21 Apr 2021
- Berberich AJ, Hegele RA (2018) Nutraceuticals in 2017: nutraceuticals in endocrine disorders. *Nat Rev Endocrinol* 14(2):68–70. <https://doi.org/10.1038/nrendo.2017.169>
- Booz GW (2011) Cannabidiol as an emergent therapeutic strategy for lessening the impact of inflammation on oxidative stress. *Free Radic Biol Med* 51(5):1054–1061. <https://doi.org/10.1016/j.freeradbiomed.2011.01.007>
- Callaway JC (2004) Hempseed as a nutritional resource: an overview. *Euphytica* 140(1):65–72. <https://doi.org/10.1007/s10681-004-4811-6>
- Cerino P, Buonerba C, Cannazza G et al (2020) A review of hemp as food and nutritional supplement. *Cannabis Cannabinoid Res* 6(1):19–27. <https://doi.org/10.1089/can.2020.0001>
- Ciprandi G, Aragona SE, Drago L, La Mantia I (2019) The nutraceuticals: a new therapeutic strategy in the management of digestive and respiratory disorders. *Acta Biomed Ateneo Parmense* 90(7-S):5–7. <https://doi.org/10.23750/abm.v90i7-S.8648>
- Cory H, Passarelli S, Szeto J, Tamez M, Mattei J (2018) The role of polyphenols in human health and food systems: a mini-review. *Front Nutr* 5:87–87. <https://doi.org/10.3389/fnut.2018.00087>
- Cosola C, Sabatino A, di Bari I, Fiaccadori E, Gesualdo L (2018) Nutrients, nutraceuticals, and xenobiotics affecting renal health. *Nutrients* 10(7):808. <https://doi.org/10.3390/nu10070808>
- Crescente G, Piccolella S, Esposito A et al (2018) Chemical composition and nutraceutical properties of hempseed: an ancient food with actual functional value. *Phytochem Rev* 17(4):733–749
- Das L, Bhaumik E, Raychaudhuri U, Chakraborty R (2012) Role of nutraceuticals in human health. *J Food Sci Technol* 49(2):173–183. <https://doi.org/10.1007/s13197-011-0269-4>
- Dhanasekaran M, Tharakan B, Holcomb LA et al (2007) Neuroprotective mechanisms of ayurvedic antidementia botanical *Bacopa monniera*. *Phytother Res* 21(10):965–969. <https://doi.org/10.1002/ptr.12195>
- Dhanasekaran M, Tharakan B, Manyam BV (2008) Antiparkinson drug-*Mucuna pruriens* shows antioxidant and metal chelating activity. *Phytother Res* 22(1):6–11. <https://doi.org/10.1002/ptr.2109>
- Dhingra D, Michael M, Rajput H, Patil RT (2012) Dietary fibre in foods: a review. *J Food Sci Technol* 49(3):255–266

- Duthie GG, Gardner PT, Kyle JAM (2003) Plant polyphenols: are they the new magic bullet? *Proc Nutr Soc* 62(3):599–603. <https://doi.org/10.1079/PNS2003275>
- Elliott JG (1999) Application of antioxidant vitamins in foods and beverages: developing nutraceuticals for the new millennium. *Food Technol* 53(2):46–48
- Farinon B, Molinari R, Costantini L et al (2020) The seed of industrial hemp (*Cannabis sativa* L.): nutritional quality and potential functionality for human health and nutrition. *Nutrients* 12(7):1935
- Frassinetti S, Moccia E, Caltavuturo L et al (2018) Nutraceutical potential of hemp (*Cannabis sativa* L.) seeds and sprouts. *Food Chem* 262:56–66. <https://doi.org/10.1016/j.foodchem.2018.04.078>
- Fuller R (1989) Probiotics in man and animals. *J Appl Bacteriol* 66(5):365–378
- Gao X, Liu J, Li L, Liu W, Sun M (2020) A brief review of nutraceutical ingredients in gastrointestinal disorders: evidence and suggestions. *Int J Mol Sci* 21(5). <https://doi.org/10.3390/ijms21051822>
- Gavel NT, Edel AL, Bassett CMC et al (2011) The effect of dietary hempseed on atherogenesis and contractile function in aortae from hypercholesterolemic rabbits. *Acta Physiol Hung* 98(3): 273–283. <https://doi.org/10.1556/APhysiol.98.2011.3.4>
- Geng R, Kang SG, Huang K, Tong T (2021) Boosting the photoaged skin: the potential role of dietary components. *Nutrients* 13(5):1691. <https://doi.org/10.3390/nu13051691>
- Goyal A, Verma A, Agrawal N (2021) Dietary phytoestrogens: neuroprotective role in Parkinson's disease. *Curr Neurovasc Res* 18:254–267. <https://doi.org/10.2174/1567202618666210604121233>
- Grant WB, Lahore H, McDonnell SL et al (2020) Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients* 12(4):988
- Gras S, Blasco A, Mòdol-Caballero G et al (2021) Beneficial effects of dietary supplementation with green tea catechins and cocoa flavanols on aging-related regressive changes in the mouse neuromuscular system. *Aging* 13(14):18051–18093. <https://doi.org/10.18632/aging.203336>
- Gulati K, Verma P, Rai N, Ray A (2021) Role of nutraceuticals in respiratory and allied diseases. In: Gupta RC, Lall R, Srivastava A (eds) *Nutraceuticals*, 2nd edn. Academic Press, Boston, pp 101–115. <https://doi.org/10.1016/B978-0-12-821038-3.00007-0>
- Gwaltney-Brant SM (2016) Nutraceuticals in renal diseases. In: Gupta RC (ed) *Nutraceuticals*. Academic Press, Boston, pp 101–108. <https://doi.org/10.1016/B978-0-12-802147-7.00008-5>
- Hepler C, Bass J (2021) Supplements to treat prediabetes. *Science* 372(6547):1147–1148. <https://doi.org/10.1126/science.abj0764>
- Hwang Y-Y, Ho Y-S (2018) Nutraceutical support for respiratory diseases. *Food Sci Human Wellness* 7(3):205–208. <https://doi.org/10.1016/j.fshw.2018.09.001>
- Kaefer CM, Milner JA (2008) The role of herbs and spices in cancer prevention. *J Nutr Biochem* 19(6):347–361. <https://doi.org/10.1016/j.jnutbio.2007.11.003>
- Kalia AN (2005) *Textbook of industrial pharmacognosy*. CBS publisher and distributor, New Delhi
- Kalra E (2003) Nutraceutical-definition and introduction. *AAPS J* 5(3):27–28
- King JW (2019) The relationship between cannabis/hemp use in foods and processing methodology. *Curr Opin Food Sci* 28:32–40. <https://doi.org/10.1016/j.cofs.2019.04.007>
- Koekkoek WA, van Zanten AR (2016) Antioxidant vitamins and trace elements in critical illness. *Nutr Clin Pract* 31(4):457–474. <https://doi.org/10.1177/0884533616653832>
- Kokate CK, Purohit AP, Gokhale SB (2002) *Nutraceutical and Cosmeceutical*. In: *Pharmacognosy*, 21st edn. Nirali Prakashan, Pune
- Lampe JW (2003) Spicing up a vegetarian diet: chemopreventive effects of phytochemicals. *Am J Clin Nutr* 78(3):579S–583S. <https://doi.org/10.1093/ajcn/78.3.579S>
- Layé CB-BS (2016) In: Meccariello R, Chianese R (eds) *Dietary Omega-6/Omega-3 and endocannabinoids: implications for brain health and diseases*. IntechOpen, London. <https://doi.org/10.5772/62498>
- Lehmann C, Fisher NB, Tugwell B et al (2016) Experimental cannabidiol treatment reduces early pancreatic inflammation in type 1 diabetes. *Clin Hemorheol Microcirc* 64(4):655–662. <https://doi.org/10.3233/ch-168021>

- Lu W, Deng Y, Fang Z et al (2021) Potential role of probiotics in ameliorating psoriasis by modulating gut microbiota in imiquimod-induced psoriasis-like mice. *Nutrients* 13(6). <https://doi.org/10.3390/nu13062010>
- Mahan LK, Escott-Stump S (2004) Krause's food, nutrition, & diet therapy, vol 11. Saunders, Philadelphia
- Martínez V, Iriondo De-Hond A, Borrelli F et al (2020) Cannabidiol and other non-psychoactive cannabinoids for prevention and treatment of gastrointestinal disorders: useful nutraceuticals? *Int J Mol Sci* 21(9):3067. <https://doi.org/10.3390/ijms21093067>
- Mattila P, Mäkinen S, Euroala M et al (2018) Nutritional value of commercial protein-rich plant products. *Plant Foods Hum Nutr* 73(2):108–115
- McCartney D, Benson MJ, Desbrow B et al (2020) Cannabidiol and sports performance: a narrative review of relevant evidence and recommendations for future research. *Sports Med Open* 6(1): 27. <https://doi.org/10.1186/s40798-020-00251-0>
- Miao C, Guo Q, Fang X et al (2021) Effects of probiotic and synbiotic supplementation on insulin resistance in women with polycystic ovary syndrome: a meta-analysis. *J Int Med Res* 49(7): 3000605211031758. <https://doi.org/10.1177/03000605211031758>
- Michalak M, Pierzak M, Kręcis B, Suliga E (2021) Bioactive compounds for skin health: a review. *Nutrients* 13(1):203. <https://doi.org/10.3390/nu13010203>
- Morrone LA, Rombola L, Adornetto A et al (2018) Rational basis for nutraceuticals in the treatment of glaucoma. *Curr Neuropharmacol* 16(7):1004–1017. <https://doi.org/10.2174/1570159X15666171109124520>
- Nasri H, Baradaran A, Shirzad H, Rafeian-Kopaei M (2014) New concepts in nutraceuticals as alternative for pharmaceuticals. *Int J Prev Med* 5(12):1487–1499
- Pandey KB, Rizvi SI (2009) Plant polyphenols as dietary antioxidants in human health and disease. *Oxid Med Cell Longev* 2(5):270–278. <https://doi.org/10.4161/oxim.2.5.9498>
- Pandey M, Verma RK, Saraf SA (2010) Nutraceuticals: new era of medicine and health. *Asian J Pharm Clin Res* 3(1):11–15
- Pandey KR, Naik SR, Vakil BV (2015) Probiotics, prebiotics and synbiotics—a review. *J Food Sci Technol* 52(12):7577–7587. <https://doi.org/10.1007/s13197-015-1921-1>
- Pandey MK, Gupta SC, Karelia D et al (2018) Dietary nutraceuticals as backbone for bone health. *Biotechnol Adv* 36(6):1633–1648. <https://doi.org/10.1016/j.biotechadv.2018.03.014>
- Pollastro F, Minassi A, Fresu LG (2018) Cannabis phenolics and their bioactivities. *Curr Med Chem* 25(10):1160–1185. <https://doi.org/10.2174/0929867324666170810164636>
- Pondugula SR, Majrashi M, Almaghrabi M et al (2021) *Oroxylum indicum* ameliorates chemotherapy induced cognitive impairment. *PLoS One* 16(6):e0252522. <https://doi.org/10.1371/journal.pone.0252522>
- Rao S, Kurakula M, Mamidipalli N et al (2021) Pharmacological exploration of phenolic compound: raspberry ketone-update 2020. *Plants (Basel)* 10(7):1323. <https://doi.org/10.3390/plants10071323>
- Romano M, Vitaglione P, Sellitto S, D'Argenio G (2012) Nutraceuticals for protection and healing of gastrointestinal mucosa. *Curr Med Chem* 19(1):109–117. <https://doi.org/10.2174/092986712803414042>
- Rupasinghe HPV, Davis A, Kumar SK et al (2020) Industrial hemp (*Cannabis sativa* subsp. *sativa*) as an emerging source for value-added functional food ingredients and nutraceuticals. *Molecules* 25(18):4078. <https://doi.org/10.3390/molecules25184078>
- Silva RFM, Pogačnik L (2020) Polyphenols from food and natural products: neuroprotection and safety. *Antioxidants* 9(1):61
- Smeriglio A, Galati EM, Monforte MT et al (2016) Polyphenolic compounds and antioxidant activity of cold-pressed seed oil from finola cultivar of *Cannabis sativa* L. *Phytother Res* 30(8): 1298–1307. <https://doi.org/10.1002/ptr.5623>
- Sorrentino G (2021) Introduction to emerging industrial applications of cannabis (*Cannabis sativa* L.). *Rend Lincei Sci Fis Nat*:1–11. <https://doi.org/10.1007/s12210-021-00979-1>

- Sosnowska B, Penson P, Banach M (2017) The role of nutraceuticals in the prevention of cardiovascular disease. *Cardiovasc Diagn Ther* 7(Suppl 1):S21–S31. <https://doi.org/10.21037/cdt.2017.03.20>
- Stice SA, Kolanos R (2021) Nutraceuticals in ophthalmic diseases. In: Gupta RC, Lall R, Srivastava A (eds) *Nutraceuticals*, 2nd edn. Academic Press, Boston, pp 167–180. <https://doi.org/10.1016/B978-0-12-821038-3.00012-4>
- Tharakan B, Dhanasekaran M, Brown-Borg HM, Manyam BV (2006) *Trichopus zeylanicus* combats fatigue without amphetamine-mimetic activity. *Phytother Res* 20(3):165–168. <https://doi.org/10.1002/ptr.1773>
- Upton N (2021) Developing our understanding of nutrition in depression. *Br J Nutr*:1–25. <https://doi.org/10.1017/s0007114521001744>
- WebMD (2020) What are probiotics? <https://www.webmd.com/digestive-disorders/what-are-probiotics>. Accessed 30 Jul 2020
- Williams RJ, Lyman CM, Goodyear GH et al (1933) "Pantothenic acid," a growth determinant of universal biological occurrence. *J Am Chem Soc* 55(7):2912–2927. <https://doi.org/10.1021/ja01334a049>
- Williams RJ, Mohanakumar KP, Beart PM (2015) Neuro-nutraceuticals: the path to brain health via nourishment is not so distant. *Neurochem Int* 89:1–6. <https://doi.org/10.1016/j.neuint.2015.08.012>
- Williamson G (2017) The role of polyphenols in modern nutrition. *Nutr Bull* 42(3):226–235. <https://doi.org/10.1111/nbu.12278>
- Zeisel SH (1999) Regulation of "nutraceuticals". *Science* 285(5435):1853–1855. <https://doi.org/10.1126/science.285.5435.1853>
- Zhao XX, Lin FJ, Li H et al (2021) Recent advances in bioactive compounds, health functions, and safety concerns of onion (*Allium cepa* L.). *Front Nutr* 8:669805. <https://doi.org/10.3389/fnut.2021.669805>