Chapter 12
Nutraceuticals and Functional Foods in Aging and Aging-Associated Diseases

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Abstract Aging results in a gradual decline in the physiological functions of the body and is often accompanied by aging-associated diseases, which may have a great impact on the quality of life. Allopathic medicines are prescribed to alleviate the symptoms, but their use is associated with plenty of side effects and high cost. Recently, nutraceuticals and functional foods market has boomed and caught attention of the general public owing to their medicinal properties and health benefits, especially in safeguarding and treating chronic diseases. Nutraceuticals can be classified into phenolic compounds, carotenoids, organosulfur compounds, polyunsaturated fatty acids, minerals and vitamins that are useful in decelerating aging process and preventing aging-associated diseases. Nutraceuticals act mainly by boosting the immune system against cellular oxidation, improving the balance of gut flora and lowering blood cholesterol levels. Moreover, they may enhance health span by preventing/slowing down age-associated diseases such as Parkinson's disease, Alzheimer's disease, cardiovascular diseases, type 2 diabetes mellitus, osteoarthritis and cancer.

Keywords Nutraceuticals · Functional foods · Aging · Phenolic compounds · Carotenoids · Polyunsaturated fatty acids · Aging · Parkinsons disease · Alzheimers disease · Cardiovascular disease · Type 2 diabetes · Osteoarthritis · Cancer

12.1 Introduction

Nutraceuticals can be defined as foods or any of their part which can supply medicinal or health benefits, mostly safeguarding and treating diseases (Chiu et al. 2018; Vaclavik et al. 2021), so this term incorporates fortified/functional foods and their

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nutrients (Ghosh et al. 2012). Nutraceuticals include a range of products from isolated nutrients (such as ω-3 fatty acids, β-carotene, gingerol, glucosamine, curcumin, ginseng, lycopene and folic acid), health supplements, herbal products or natural bioactive foods (such as garlic/green tea/soybeans) (Dominguez Diaz et al. 2020). Functional foods maybe described as a category of nutraceuticals as they also provide health benefits apart from nutrition. These foods are categorized as fortified, enriched, altered and enhanced products. Popular functional foods include margarine with incorporated phytosterols, yoghurt containing beneficial bacteria, fortified vitamins, mineral and fiber rich fruit juices (Longoria-García et al. 2018). Nutraceuticals and functional foods may be used to tackle the growing prevalence of chronic diseases, especially aging-associated diseases worldwide (Tang 2020).

Aging can be defined as a natural biological process that is associated with a gradual decline in the physiological functions and an increased vulnerability to diseases and mortality. The major aging-associated diseases include neurological disorders such as Parkinson's and Alzheimer's disease, cardiovascular disease such as atherosclerosis, type 2 diabetes, osteoarthritis and cancer. The conventional therapies for aging-associated diseases usually have many side effects and are costly as well. Since these diseases have been associated with unhealthy dietary habits, foods which impart positive health benefits besides their nutritional values may be an answer to prevent the onset of these diseases.

The rising interest in healthy diets has significantly impacted the direction of research for product development in the areas of nutraceuticals, functional foods and nanotechnology. Therefore, many pharmaceutical and nutritional products-based corporations have brought nutraceuticals and functional foods into the market owing to their property of not only having a nutritional value but also their therapeutic potential (Vaclavik et al. 2021). The health promoting effects of nutraceuticals and functional foods have been comprehensively described by many recent studies in literature (Grumezescu 2016; McWilliams 2017; Rajasekaran 2017; Pandareesh et al. 2018). Taking leads from the aforementioned knowledge, the purpose of this review article is to emphasize the role of nutraceuticals and functional foods in decelerating the aging process and preventing the incidence of aging-associated diseases.

12.2 Classes of Nutraceuticals/Functional Foods, Extraction and Their Delivery

Nutraceuticals and functional foods are categorized according to their chemical constituents into phenolic compounds, carotenoids, organosulfur compounds, polyunsaturated fatty acids, minerals and vitamins that are useful in preventing and alleviating aging-associated diseases. The major nutraceuticals, their sources and health promoting as well as anti-aging effects have been presented in Table 12.1. Phenolic compounds, carotenoids and organosulfur compounds are also termed as phytochemicals/phytonutrients because they are primarily synthesized in plants.

Phenolic compounds are the nutraceuticals and bioactive components of the diet which play an important role in good health and are further categorized as phenolic acids, flavonoids, tannins and lignins (Singh et al. 2016). The important phenolic compounds that act as nutraceuticals are presented in Fig. 12.1. Quercetin, naringenin, apigenin, kaempferol, genistein, cyanidin, epigallocatechin-3-gallate and

Table 12.1 Major nutraceuticals, their sources, and health-promoting as well as anti-aging activities

Category of Nutraceutical	Individual Nutraceutical	Health-promoting and anti-aging functions	Primary sources
Phenolic compounds	Curcumin	Reduces the incidence of neuroinflammation; lowers the levels of C-reactive protein; functions as an antioxidant, chemopreventive, chemosensitizer chondroprotective and anti-inflammatory agent	Turmeric rhizome and curry
	Epigallocatechin gallate	Mimics the anti-aging properties of metformin and rapamycin; has a neuroprotective role; reduces UVR-induced DNA damage and lowers ROS as well as free radical production.	Green tea, white, oolong, and black teas, blackberries
	Resveratrol	Restricts mitochondrial dysfunction and apoptosis; increases the intracellular free-radical scavenger glutathione amounts	Peanuts, pistachios, and grapes
	Genistein	Cardioprotective effects; protects from diabetes and cancer	Soybean and soy-based foods
	Lycopene	Relieves oxidative stress, increases NADH dehydrogenase and superoxide dismutase activity; lowers the number of low-density lipoproteins as well as pro-inflammatory cytokines	Tomatoes, watermelon and grapefruits
Carotenoids	β-Carotene	Lowers free radicals and singlet oxygen-induced lipid peroxidation; scavenges ROS to protect against oxidative stress and decreases UV exposures	Leafy vegetables, carrots, and sweet potatoes.
	Lutein and zeaxanthin	Reduces free radical damage and decreases exposure to UV damage	Green leafy vegetables and egg yolks

(continued)

Table 12.1 (continued)

Category of Nutraceutical	Individual Nutraceutical	Health-promoting and anti-aging functions	Primary sources
Polyunsaturated fatty acids	Eicosapentaenoic acid, α-Linolenic acid and docosahexaenoic acid	Reduce the amounts of triglycerides in the body; anti-inflammatory effects; enhance mitochondrial membrane lipids; lower calcium release and pyruvate dehydrogenase enzyme activity	Salmon and trout fish, flaxseed oil, canola oil and nuts
Minerals	Copper, manganese, and iron	Enzyme co-factors for antioxidant enzymes such as catalase and superoxide dismutase	Nuts, beans and leafy vegetables, red meat
	Zinc	Decreases oxidative damage and inflammation	Lean meat, poultry; eggs, beans, and nuts
	Selenium	Removes lipid hydroperoxides; supports DNA synthesis as well as repair	Meat and Seafood
Vitamins	Vitamin C	Free radical scavenger; stimulates the metabolism of chondrocytes, collagen, and proteoglycan synthesis	Citrus fruits, peppers, and broccoli
	Vitamin E	Has free radical scavenging properties; stabilizes cell membranes, reduces the number of apoptotic cells	Wheat germ oil, sunflower seeds, almonds, and peanuts

catechin are flavonoids (the largest class of phenolic compounds), while caffeic acid, curcumin and resveratrol are non-flavonoid phenolic compounds. Phenolic compounds can regulate the activity of many enzymes and cell receptors, such as in case of cancer they may inhibit enzymes which promote cell division or upregulate enzymes causing cell apoptosis (Rajasekaran 2017). Functional foods such as fruits, vegetables, herbs, nuts, tea and coffee contain adequate levels of these compounds (Singh et al. 2020).

Carotenoids are a vast group of hydrophobic pigments that are naturally produced inplants, algae, bacteria, and fungi. These compounds are carotenes or xanthophylls depending on their chemical structures (Rodriguez-Amaya 2015). The structures of major carotenoids acting as nutraceuticals is illustrated in Fig. 12.2. Lycopene, α-carotene and β-carotene are carotenes, while lutein, zeaxanthin, β-cryptoxanthin, astaxanthin and fucoxanthin are xanthophylls. One of the most important carotenoid pigments is lycopene (red in color) and has been recognized to have potent activities against aging-associated diseases (Chaudhary et al. 2018).

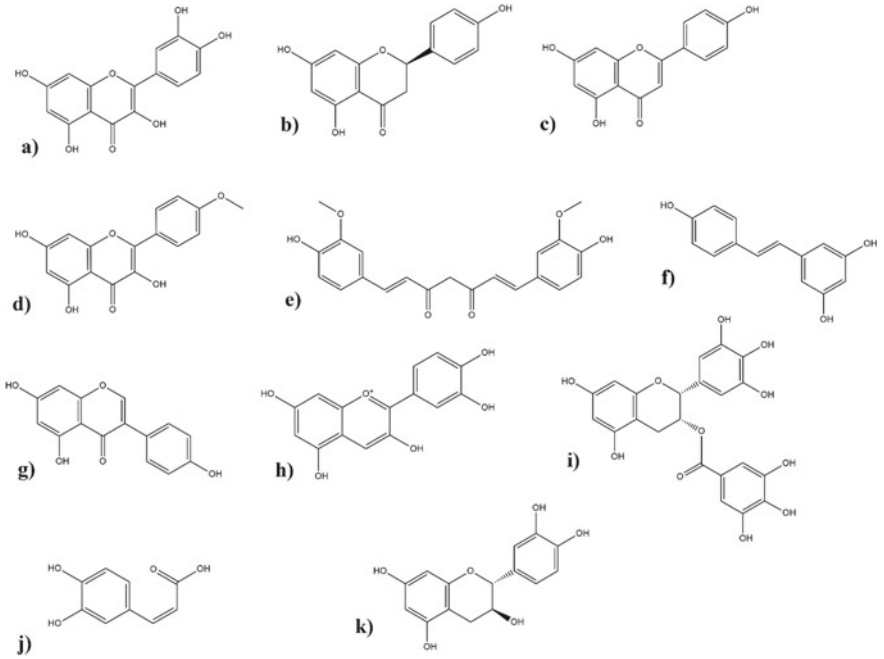

Fig. 12.1 Chemical structures of phenolic compounds having nutraceutical properties. The compounds shown are quercetin (a); naringenin (b); apigenin (c); kaempferol (d); curcumin (e); resveratrol (f); genistein (g); cyanidin (h); epigallocatechin-3-gallate (i); caffeic acid (j) and catechin (k)

Polyunsaturated fatty acids (ω-3 and ω-6 fatty acids) are an essential class of nutraceuticals important for human beings (Falinska et al. 2012). The structures of main polyunsaturated fatty acids are depicted in Fig. 12.3. Among these, linoleic acid, γ-linolenic acid, dihomo γ-linolenic acid, arachidonic acid are ω-6 fatty acids, while α-linolenic acid, eicosapentaenoic acid, docosapentaenoic acid and docosahexaenoic acid are ω-3 fatty acids. ω-3 and ω-6 fatty acids are processed by the identical enzymes and compete with each other for the enzyme active sites. Both ω-3 and ω-6 fatty acids produce compounds called eicosanoids during metabolism. Eicosanoids have been known to have anti-inflammatory roles (Saini and Keum 2018).

Organosulfur compounds are organic compounds containing sulfur in their chemical structures. These compounds are primarily present in cruciferous vegetables (especially broccoli, cauliflower, garlic, and onion). They can be further classified asallylic sulfur compoundssuch as aliin and allicin (present in garlic and onions), glucosinolates, isothiocyanates and indoles (Dwivedi et al. 2020).

Minerals can also act as nutraceuticals and are classified as macrominerals and trace minerals. Macrominerals are required in larger amounts than trace minerals and include calcium, phosphorus, magnesium, sodium, potassium, chloride and sulfur. On the other hand, trace minerals include iron, manganese, copper, iodine, zinc,

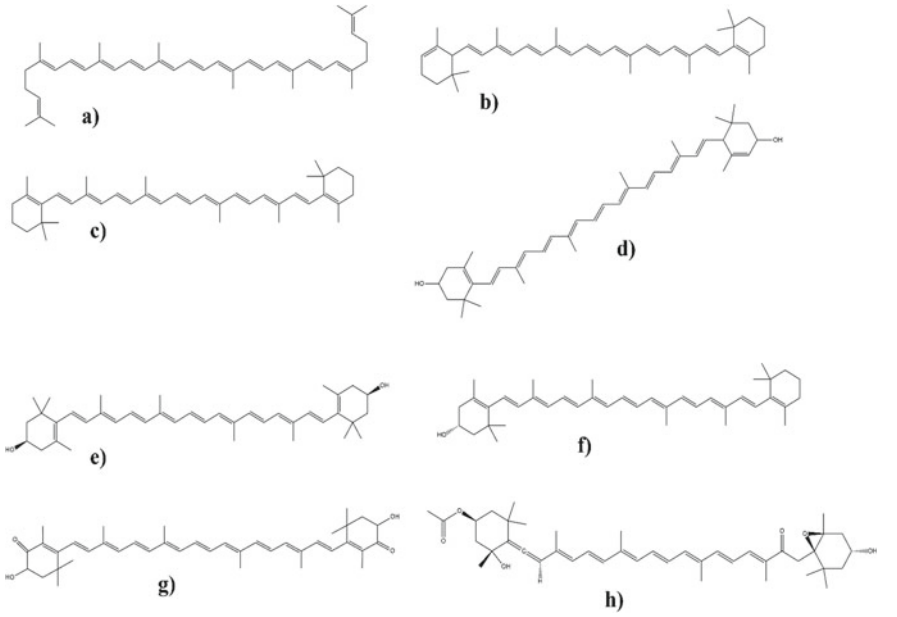

Fig. 12.2 Chemical structures of carotenoids having nutraceutical properties. The compounds shown are lycopene (a); α-carotene (b); β-carotene (c); lutein (d); zeaxanthin (e); β-cryptoxanthin (f); astaxanthin (g) and fucoxanthin (h)

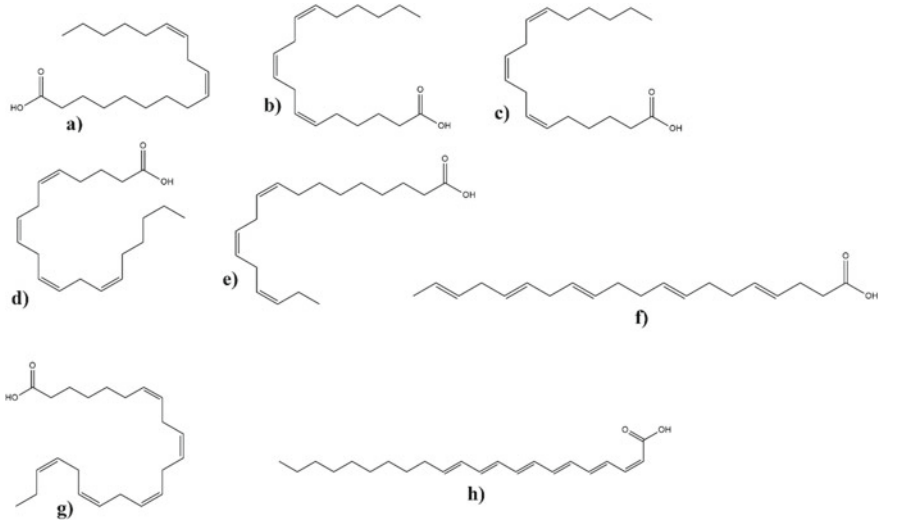

Fig. 12.3 Chemical structures of polyunsaturated fatty acids, linoleic acid (a); γ-linolenic acid (b); dihomo γ-linolenic acid (c); arachidonic acid (d); α-linolenic acid (e); eicosapentaenoic acid (f); docosapentaenoic acid (g) and docosahexaenoic acid (h)

cobalt, fluoride and selenium. Vitaminsare another class of nutraceuticals that have a complex organic structure and are required in small levels for a good human health. Fat soluble vitamins (A, D, E, and K) and water-soluble vitamins are the two different classes of vitamins. Water soluble vitamins include vitamin B and C having very important roles in the human body.

Apart from the aforementioned classes of nutraceuticals and functional foods, probiotics and prebiotics can be recognized as functional foods. Probiotics are health-promoting bacteria present in dairy products such as yogurt. *Lactobacillus acidophilus*, *L. bulgaricus, Bifidobacteriumlactis,* and *B. subtilis* are common examples of probiotic bacteria (Parker and Pace 2016). On the other hand, prebiotics (such as fructooligosaccharide, inulin, and honey) are ingredients that increase the growth of health-promoting bacteria.

Nutraceuticals are extracted from living sources by various methods and techniques. These include Soxhlet extraction (traditional method requiring good amounts of solvent and is time consuming), sonication assisted extraction (use of ultrasound extractor), supercritical fluid extraction and microwave assisted extraction (Grumezescu 2016). After extraction, nutraceuticals are characterized by different analytical techniques such as high-performance liquid chromatography, mass spectrometry, nuclear magnetic resonance and atomic spectroscopy.

Nutraceuticals often have low dispersibility in water and bioavailability (amount of nutraceutical that reaches the systemic circulation after consumption) (Singh et al. 2018; Tang 2020). Therefore, to reduce these limitation various delivery methods have been used recently. These include phospholipid-based delivery vehicles, liposome-based carrier system, and emulsion-based delivery system (such as microemulsions, nano emulsions, and double emulsions) (Grumezescu 2016). Nanoencapsulation is an emerging technique for not only improving the water dispersibility of nutraceuticals but also their bioavailability (Acevedo-Fani et al. 2017). Nano complexation (complexation of a nutraceutical with proteins at nanoscale) can be helpful for poorly soluble compounds such as curcumin (Singh 2007), while nano emulsions can also play an important role for improving solubility (Zhang et al. 2020). Apart from these, other latest developments for better delivery and bioavailability of nutraceuticals involve electrospinning and electro spraying techniques (do Evangelho et al. 2019; Coelho et al. 2020).

12.3 Current State of Knowledge About Nutraceuticals/Functional Foods

Nutraceuticals and functional foods can have a plant or animal origin, and the current research is primarily focused on understanding the mechanism of action, safety concerns and efficacy. Interestingly, nutraceuticals can be a boon for the treatment of long-term diseases in patients which do not qualify for a treatment by pharmaceuticals. Moreover, these substances may impact the health in a complicated

and interactive manner. The current research on nutraceuticals has highlighted the need of newer processing methods and techniques (such as high-pressure processing and pulsed electric field processing) for nutraceuticals, so that they can not only have good microstructures but also acceptable sensory characteristics. Apart from this, newer packaging methods for nutraceuticals include the use of nanomaterials that can enhance their safety and efficacy without compromising bioavailability. Nutraceuticals and functional foods are suitable candidates for personalized nutrition which aims to provide health benefitting diets to people according to their genetic traits (especially for the prevention of aging-associated diseases) (Corzo et al. 2020). However, it must be realized that only nutrition without regular physical exercise cannot guarantee a long and robust life. Additionally, it needs to emphasized that nutraceuticals and functional foods are not substitutes for a healthy diet. With their increased advertising, many elderly people have started using health supplements which have nutraceutical claims but sometimes these supplements are deficient in what the labels claim. A healthy diet itself contains these nutraceuticals in balanced amounts, so the idea of healthy nutrition should never be neglected.

12.4 Role of Nutraceuticals/Functional Foods in Delaying the Aging Process

At present, the major goal of gerontology research is to discover natural chemicals that can modulate aging process. These compounds can be helpful either in suppression of senescent cells or their clearance. Among these, molecules having antioxidant or anti-inflammatory activities have received considerable interest in the recent years (Gurău et al. 2018). The use of nutraceuticals and functional foods in the diet has been considered as a promising approach against the aging process, especially in alleviating the impairment of body functions (Singh et al. 2021). However, as of now nutraceutical supplementation to reverse the aging process is very challenging, owing to the dosage as well as timing optimization and different individual responses. It has been widely recognized that a diet rich in fruits and vegetables, and whole grains can be effective because of the presence of adequate amounts of nutraceuticals.

Ferrari (2004) has comprehensively highlighted the roles of nutraceuticals and functional foods in delaying the progression of aging. He reported that these compounds can act as mitochondrial membrane stabilizers and enhancers, have metal chelating and antioxidant properties, and induce apoptosis of senescent cells. Apart from these, some nutraceuticals such as epigallocatechin gallate, allantoin and ginsenoside can mimic the anti-aging properties of metformin and rapamycin (anti-aging drugs) (Aliper et al. 2017). Moreover, nutraceuticals can decelerate aging process by improving the balance of gut flora and lowering blood cholesterol levels. The molecular mechanisms of their action have been reported to be by modulating the gene expression, modifying patterns of DNA methylation and acting as epigenetic modifiers (Lee et al. 2014). It has been validated that free radical clearance can

be effectively enhanced by using nutraceuticals at adequate levels (Pisoschi and Pop 2015).

There have been many reports of nutraceuticals and functional foods in delaying the process of aging. Phytochemicals, probiotic bacteria and ω-3 fatty acids have been reported to have anti-cellular senescence capacity in the immune cells which affect aging (O'Shea et al. 2009). Flavonoids, along with other phenolic compounds, can protect against oxidation of polyunsaturated fatty acids present in the membranes and circumvent mitochondrial membrane disruptions (Pisoschi and Pop 2015). In terms of molecular events, foods rich in phenolic compounds can effectively modulate the activity of some enzymes such as DNA methyltransferase and histone deacetylases, which may be responsible for delaying the aging process (Gurău et al. 2018). ω-3 fatty acids have been documented to enhance mitochondrial membrane lipids, lower calcium release and pyruvate dehydrogenase enzyme activity (O'Shea et al, 2009). Nutraceuticals that function as antioxidants can regulate the mitochondrial functioning and lower the release of cytochrome c for apoptosis (Adachi and Ishii 2002). Nutraceutical microelements such as copper, manganese, and iron function as enzyme co-factors for antioxidant enzymes such as catalase and superoxide dismutase. This activity is responsible for clearance of free radicals responsible for early aging.

12.5 Nutraceuticals and Functional Foods Role in Reducing Aging-Associated Diseases

It is well established that aging is responsible for the start and progression of several diseases, that mainly include neurological disorders such as Parkinson's and Alzheimer's disease, cardiovascular disease such as atherosclerosis, type 2 diabetes mellitus diabetes, osteoarthritis and cancer (Hou et al. 2019; Yang et al. 2020). Aging progresses with malfunctioning in nutrient signaling, protein machinery and mitochondria and leads to cell senescence (Saraswat and Rizvi 2017). Neurological disorders in the elderly people cause changes in both the structural and biochemical functions of the brain. Owing to these changes, patients demonstrate many symptoms such as paralysis, muscle weakness, improper coordination, seizures, pain and loss of consciousness (Fonseca-Santos and Chorilli 2020). Other diseases such as atherosclerosis, type 2 diabetes mellitus diabetes, osteoarthritis and cancer also result from the physiological changes during aging. The roles of nutraceuticals and functional foods in reducing the incidence of aging-associated diseases is as follows:

12.5.1 Parkinson's Disease

Parkinson's disease is a neurodegenerative disease that affects around 1–2% of the world population (Khan et al. 2019). The usual treatment of Parkinson's disease involves providing dopamine replacement therapy. The combination medication of levodopa and carbidopa is generally used for the patients suffering from this disease. Nutraceuticals have recently gained a lot of attention because of their therapeutic properties, so an integrative use of nutraceuticals and functional foods along with the standard therapy of medication has been proven to be effective in many cases of Parkinson's disease (Lama et al. 2020). This addition can have an important role in improving the quality of life of the suffering patients. Nutraceuticals and functional foods generally are helpful in this disease by targeting and weakening various pathogenic events which include neuroinflammation, mitochondrial dysfunction, apoptosis and oxidative stress. Oxidative stress in Parkinson's disease manifests by forming α-synuclein aggregates and lowering amounts of neuromelanin (Knörle2018; Ludtmann et al. 2018). The biggest role played by nutraceuticals is to restore mitochondrial homeostasis by reducing oxidative stress and correct faulty electron transport chain as well as mitochondrial dynamics.

Many nutraceuticals have been investigated to alleviate the symptoms of Parkinson's disease. Among phenolic compounds, epigallocatechin-3-gallate (a major phenolic compound in tea plant) has shown a neuroprotective role because of its ability to cross the blood–brain barrier. Based on having a catechol-like structure, it has been described as a good radical scavenger and chelator of iron ions (Morgan and Grundmann 2017). Moreover, it also encourages the proper folding of α-synuclein monomers into stable oligomers in a concentration-dependent manner (Šneideris et al. 2015). Another phenolic compounds under investigation include curcumin and resveratrol. Curcumin reduces the incidence of nuclear factor κ-B (a family of inducible transcription factors) mediated neuroinflammation and targets Toll-like receptor-4 (known to modulate immune responses as well as stimulate synthesis of inflammatory chemokines and cytokines) (Zhu et al. 2014). Resveratrol has been reported to restrict mitochondrial dysfunction and apoptosis in nigrostriatal cells by acting through the protein kinase B/glycogen synthase kinase-3β pathway (Zeng et al. 2017). In a study by Ho and Pasinetti (2010), grape seed polyphenol extract was reported to be helpful in the reducing the incidence of Parkinson's disease that involve misfolded proteins. This was due to its ability to interfere with the development of misfolded-protein aggregates generated from Aβ peptides.

Lycopene has been documented to relieve oxidative stress, increase NADH dehydrogenase and superoxide dismutase activity in the corpus striatum and lower malondialdehyde levels (Prema et al. 2015). In addition, it also enhances the amounts of other antioxidant enzymes, such as catalase and glutathione peroxidase in animal as well as cellular models of Parkinson's disease (Kaur et al. 2011; Paul et al. 2020). Coenzyme Q10 prevents1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neurotoxicity and blocks the electron transfer between complex 1 and other complexes of the electron transport chain (Cleren et al. 2008). Niacin

(vitamin B3) is a precursor of NAD–NADH and is needed for producing dopamine and may be helpful for managing Parkinson's disease. Its effects include reduction in inflammation through NIARC1-associated mechanisms, enhancing the ratio of NAD/NADH, reestablishing complex 1 functioning and boosting dopamine synthesis in the striatum via the supply of NADPH to mitochondria (Bjørklund et al. 2020). Ginsenosides restrict astrogliosis as well as microgliosis and reduce the synthesis of proinflammatory cytokines in substantia nigra pars compacta (Fu et al. 2015). Probiotics can be helpful in restoring gut dysbiosis taking place during Parkinson's disease, improving gastrointestinal functioning, decreasing the enteric nervous system neuroinflammation and gut leakiness (Castelli et al.2020). In a recent study by Ma et al. (2020), peptides present in sesame cake reduced α-synuclein aggregation and reduced MPP+ -induced dopaminergic neuron degeneration.

12.5.2 Alzheimer's Disease

Alzheimer's disease is a neurological disorder which leads to loss of hippocampal and cortical neurons and clinically exhibits impairment of the cognitive capabilities along with aphasia, disorientation, and disinhibition (Scheltens et al. 2016). Nutraceuticals and functional foods have a role to play in reducing the risk of Alzheimer's disease. Phenolic compounds have been reported to be effective against this disease and act as antioxidants (Singh et al. 2016). Curcumin has been reported to lessen the assemblage of Aβpeptides in the neural tissue and its associated inflammation. He et al. (2016) reported that oral in take of curcumin can reduce the deposition and oligomerization of Aβ peptide, together with phosphorylation of the tau protein. In addition, curcumin can bind with metal ions, primarily Cu (II) and Zn (II), that are common in the central nervous system (especially in the synapse regions), adding to its neuroprotective activity (Sadhukhan et al. 2018). Genistein has the potential to reduce the activity of DNA topoisomerase as well as tyrosine protein kinase (Sadhukhan et al. 2018). Moreover, it has specificity for epidermal growth factor receptor, which is a growth regulatory transmembrane protein binding certain protein such as epidermal growth factor and transforming growth factor-β. Many phenolic moieties in the molecular structure of genistein leads to its good antioxidant activity. Resveratrol activates reactive protein kinase C that might stimulate α-secretase and result in lowering of Aβ synthesis, thereby increasing the intracellular free-radical scavenger glutathione amounts and lowering malondialdehyde and acetylcholinesterase levels (Han et al. 2004; Fonseca-Santos and Chorilli 2020). Carotenoids such as lycopene can stop the activities of the secretases (responsible for the processing of amyloid precursor protein) and glycogen synthase kinase 3β, which leads to neuroprotection in Alzheimer's disease (Paul et al. 2020). Fatty acids such as docosahexaenoic acid intake enhances the cognitive function and reduces the incidence of dementia (Cunnane et al. 2009). Additionally, eicosapentaenoic acid also has been reported to have a good role in the normal brain development (Cunnane et al. 2009).

12.5.3 Cardiovascular Disease

Cardiovascular disease is one major cause of death worldwide, becoming a significant healthcare problem in the developed countries (Sacks et al. 2017). The underlying cause of cardiovascular disease is atherosclerosis (a long-term inflammatory ailment of medium and large arteries). Taking this into consideration, prevention of atherosclerosis is the key target for lessening the risk of developing cardiovascular diseases. Nutraceuticals and functional foods can have a significant role in controlling atherosclerosis, especially during the promotion stage when circulating monocytes penetrate vascular endothelial cells and later differentiate into macrophages and foam cells. Among these compounds, catechin class of flavanols present in cocoa as well as green tea have been well researched and are well known for their antioxidant activities along with capacity to reduce inflammation by reducing release of cytokines and chemokines from the activated endothelial cells (Mangels and Mohler 2017). Curcumin has been reported to lower the levels of C-reactive protein (produced by the liver during inflammation and is the indicator of atherosclerosis) not only in animal models but also in humans (Sahebkar 2014). Carotenoid pigment lycopene has been documented to lower the amounts of low-density lipoproteins as well as pro-inflammatory cytokines in humans (Cheng et al. 2017; Chaudhary et al. 2018). Apart from these, phytosterols have also been reported to reduce atherosclerosisin mouse models and humans by lowering blood plasma low-density lipoprotein levels (Rocha et al. 2016). Fatty acid eicosapentaenoic acid is known to reduce the amounts of serum triglycerides without enhancing the amounts of low-density lipoproteins in the body (Ballantyne et al. 2012). Yan et al. (2020) have reported that the nutraceutical Coenzyme Q10 decreased atherosclerosis in apolipoprotein E-deficient mice and enhanced the efflux of cholesterol in humans.

12.5.4 Type 2 Diabetes

The conventional treatment of type 2 diabetes often involves many strategies which can be diet control, exercise, administration of insulin and drugs. Apart from these strategies, nutraceuticals and functional foods are generally utilized as an adjuvant/alternative therapy, in combination with relevant changes in the lifestyle. Many nutraceuticals and functional foods are known to ameliorate the symptoms of diabetes. Epigallocatechin-3-gallate (a catechin present in good levels in green tea) has significant antioxidant and anti-inflammatory activities (Singh et al. 2018). The administration of epigallocatechin-3-gallate on streptozotocin-induced diabetic rats has been reported to reduce glucose as well as lipid amounts, along with enhancement in insulin concentration. Epigallocatechin-3-gallate has also been reported to reduce troponin T level, lactate dehydrogenase, and aspartate aminotransferase enzyme activities in the serum (Othman et al. 2017). Monounsaturated fatty acids and polyunsaturated fatty acids (as components of olive oil and nuts) have been

documented to improve glucose metabolism, insulin sensitivity and blood lipids in patients suffering from this disease (Mirabelli et al. 2020). The supplementation of chromium (as chromium histidinate) in the diet lowered the amounts of glucose, glycosylated hemoglobin, and total cholesterolin streptozotocin-induced diabetic rats (Ulas et al. 2015). Similarly, administration with zinc (a constituent of insulin and insulin receptors), decreased oxidative damage and inflammation in the kidneys of streptozotocin-induced diabetic rats (Tang et al. 2010). Garg (2016) reported that cinnamonas a supplement had a good role to play in managing type 2 diabetes.

12.5.5 Osteoarthritis

Osteoarthritis is the most prevalent form of arthritis that accounts for about half of the total cases, with other ones being rheumatoid arthritis, gout, and lupus (Wang et al. 2018). The conventional medical therapy includes oral and topical non-steroidal anti-inflammatory drugs but these can be toxic to the body producing rashes, increasing bleeding risk and can affect kidney functioning. Nutraceuticals and functional foods can be effective in reducing osteoarthritis pain. Epigallocatechin gallate has an anti-inflammatory activity on osteoarthritis chondrocytes by lowering the synthesis of important inflammatory mediators such as inducible nitric oxide synthase and prostaglandin-endoperoxide synthase 2 (Henrotin et al. 2011). Curcumin has been reported to play the role of an antioxidant, chondroprotective and anti-inflammatory agent (Kuptniratsaikul et al. 2009). Within a month of trials, the patients who were administered turmeric extracts (at 2 g per day dose) had a significant reduction in pain in comparison to those who took ibuprofen. In addition, their pain on level walking as well on stairs decreased over time. Procyanidins, particularly Procyanidin B2, have exhibited suppression of articular cartilage vascular endothelial growth factor (a signaling protein which induces new blood vessel growth), a key mediator of osteoarthritis pathogenesis as well as pain (Wang et al. 2018). Fatty acids such aseicosapentaenoic acid and docosahexaenoic acid have demonstrated anti-inflammatory effects (Henrotin et al. 2011). In case of animal models, vitamin C stimulated the metabolism of chondrocytes, collagen, and proteoglycan synthesis, while vitamin E was reported to have free radical scavenging properties (Lopez 2012). Functional foods such as green tea and fish oil have been conventionally recognized for their pain management activities in osteoarthritis patients (Schell et al. 2017). Moreover, functional foods are often enriched with natural active ingredients that can reduce pain and inflammation.

12.5.6 Cancer

Chemotherapy although is mainstream therapy for cancer but its usage has failed to achieve its maximum therapeutic potency. Because of the presence of acquired

and intrinsic chemoresistance. There are many side effects of chemotherapy such as reduced immunity, loss of digestive tract lining along with hair loss (Nair et al. 2020). Nutraceuticals and functional foods can be helpful for the cancer patients especially for the management of adverse effects of chemotherapy.

Phenolic compounds such as curcumin has been reported as a potential chemo preventive and chemosensitizer agent among nutraceutical compounds because of its high efficacy (Mao et al. 2018). Puliyappadamba et al. (2015) have comprehensively reported the antiproliferative and pro-apoptotic activity of curcumin in lung cancer. Resveratrol has been reported to reduce inflammation, oxidative stress and multi-step tumorigenesis. It has been documented to be a chemo preventive and chemo sensitizing agent against breast cancer (Nair et al. 2020). Genistein has the property of being effective in lowering the growth of cancer cells without any side effects. Quercetin has been reported to enhance immune system response against tumor growth by increasing mitochondrial membrane permeabilization. Another nutraceutical named Polyphenon E (a green tea catechin mixture) has been successful in clinical trials against cancer cells proliferation (Zhang et al. 2004). Apart from phenolic compounds, lycopene has been effective against cancer by suppressing the phosphorylation of tumor suppressor p53 and stopping tumor cell division (Nair et al. 2020).

12.6 Conclusion

There is a conclusive evidence that the consumption of nutraceuticals and functional foods have health benefits and might keep aging-associated diseases at bay. However, more extensive research needs to be done in order to comprehensively demonstrate whether nutraceuticals and functional foods can successfully delay aging in humans. Moreover, the present limitations of nutraceuticals such as slow metabolism, poor solubility and reduced bioavailability needs more consideration. Despite of the present limitations, the future of nutraceuticals of both plant and animal origin holds exciting opportunities for the food and pharmaceutical industry to create novel products. There is a need to establish efficacy and safety parameters which comply with the regulatory requirements for maintaining consumer confidence.

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Compliance with Ethical Standards

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Conflict of Interest All authors declare they have no conflict of interest.

References

Acevedo-Fani A, Soliva-Fortuny R, Martín-Belloso O (2017) Nanostructured emulsions and nanolaminates for delivery of active ingredients: improving food safety and functionality. Trends Food Sci Technol 60:12–22

Adachi M, Ishii H (2002) Role of mitochondria in alcoholic liver injury. Free Radical Biol Med 32(6):487–491

Aliper A, Jellen L, Cortese F, Artemov A, Karpinsky-Semper D, Moskalev A, Zhavoronkov A (2017) Towards natural mimetics of metformin and rapamycin. Aging (albany NY) 9(11):2245

Ballantyne CM, Bays HE, Kastelein JJ, Stein E, Isaacsohn JL, Braeckman RA, Soni PN (2012) Efficacy and safety of eicosapentaenoic acid ethyl ester (AMR101) therapy in statin-treated patients with persistent high triglycerides (from the ANCHOR study). Am J Cardiol 110(7):984–992

Bjørklund G, Dadar M, Anderson G, Chirumbolo S, Maes M (2020) Preventive treatments to slow substantia nigra damage and Parkinson's disease progression: a critical perspective review. Pharmacol Res 105065

Castelli V, d'Angelo M, Quintiliani M, Benedetti E, Cifone MG, Cimini A (2020) The emerging role of probiotics in neurodegenerative diseases: new hope for Parkinson's disease? Neural Regeneration Res 16(4):628

Chaudhary P, Sharma A, Singh B, Nagpal AK (2018) Bioactivities of phytochemicals present in tomato. J Food Sci Technol 55(8):2833–2849

Cheng HM, Koutsidis G, Lodge JK, Ashor A, Siervo M, Lara J (2017) Tomato and lycopene supplementation and cardiovascular risk factors: a systematic review and meta-analysis. Atherosclerosis 257:100–108

Chiu HF, Shen YC, Venkatakrishnan K, Wang CK (2018) Popular functional foods and nutraceuticals with lipid lowering activity and in relation to cardiovascular disease, dyslipidemia, and related complications: an overview. J Food Bioactives 2:16–27

Cleren C, Yang L, Lorenzo B, Calingasan NY, Schomer A, Sireci A, Beal MF (2008) Therapeutic effects of coenzyme Q10 (CoQ10) and reduced CoQ10 in the MPTP model of Parkinsonism. J Neurochem 104(6):1613–1621

Coelho SC, Estevinho BN, Rocha F (2020) Encapsulation in food industry with emerging electrohydrodynamic techniques: electrospinning and Electrospraying-a review. Food Chem 127850

Corzo L, Fernández-Novoa L, Carrera I, Martínez O, Rodríguez S, Alejo R, Cacabelos R (2020) Nutrition, health, and disease: role of selected marine and vegetal nutraceuticals. Nutrients 12(3):747

Cunnane SC, Plourde M, Pifferi F, Bégin M, Féart C, Barberger-Gateau P (2009) Fish, docosahexaenoic acid and Alzheimer's disease. Prog Lipid Res 48(5):239–256

do Evangelho JA et al (2019) Thermal and irradiation resistance of folic acid encapsulated in zein ultrafine fibers or nanocapsules produced by electrospinning and electrospraying. Food Res Int 124:137–146

Dominguez Diaz 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

Durazzo A, Lucarini M, Santini A (2020) Nutraceuticals in human health. Foods 9:370

Dwivedi A, Singh S, Kumar S, Mittal PC (2020) Organosulfur phytochemicals against metabolic and neurodegenerative diseases: benefits and risks. In: Phytochemicals as Lead Compounds for New Drug Discovery, pp 179–194. Elsevier

Falinska AM, Bascoul-Colombo C, Guschina IA, Good M, Harwood JL (2012) The role of n-3 dietary polyunsaturated fatty acids in brain function and ameliorating Alzheimer's disease: opportunities for biotechnology in the development of nutraceuticals. Biocatal Agric Biotechnol 1(2):159–166

Ferrari CK (2004) Functional foods, herbs and nutraceuticals: towards biochemical mechanisms of healthy aging. Biogerontology 5(5):275–289
Fonseca-Santos B, Chorilli M (2020) The uses of resveratrol for neurological diseases treatment and insights for nanotechnology based-drug delivery systems. Int J Pharmaceutics 119832
Fu W, Zhuang W, Zhou S, Wang X (2015) Plant-derived neuroprotective agents in Parkinson's disease. Am J Transl Res 7(7):1189
Garg RC (2016) Nutraceuticals in Glucose Balance and Diabetes. In: Nutraceuticals, pp 145–160. Academic Press
Ghosh D, Das S, Bagchi D, Smarta RB (eds) (2012) Innovation in Healthy and Functional Foods. CRC press, Boca Raton
Grumezescu A (2016) Nutraceuticals. Academic Press
Guru F, Baldoni S, Prattichizzo F, Espinosa E, Amenta F, Procopio AD, Olivieri F (2018) Anti-senescence compounds: a potential nutraceutical approach to healthy aging. Ageing Res Rev 46:14–31
Han YS, Zheng WH, Bastianetto S, Chabot JG, Quirion R (2004) Neuroprotective effects of resveratrol against β-amyloid-induced neurotoxicity in rat hippocampal neurons: involvement of protein kinase C. Br J Pharmacol 141(6):997
He GL, Luo Z, Yang J, Shen TT, Chen Y, Yang XS (2016) Curcumin ameliorates the reduction effect of PGE2 on fibrillar β-amyloid peptide (1–42)-induced microglial phagocytosis through the inhibition of EP2-PKA signaling in N9 microglial cells. PLoS One 11(1):e0147721
Henrotin Y, Lambert C, Couchourel D, Ripoll C, Chiotelli E (2011) Nutraceuticals: do they represent a new era in the management of osteoarthritis? –A narrative review from the lessons taken with five products. Osteoarthritis Cartilage 19(1):1–21
Ho L, Pasinetti GM (2010) Polyphenolic compounds for treating neurodegenerative disorders involving protein misfolding. Expert Rev Proteomics 7(4):579–589
Hou Y, Dan X, Babbar M, Wei Y, Hasselbalch SG, Croteau DL, Bohr VA (2019) Ageing as a risk factor for neurodegenerative disease. Nat Rev Neurol 15(10):565–581
Kaur H, Chauhan S, Sandhir R (2011) Protective effect of lycopene on oxidative stress and cognitive decline in rotenone induced model of Parkinson's disease. Neurochem Res 36(8):1435–1443
Khan AU, Akram M, Daniyal M, Zainab R (2019) Awareness and current knowledge of Parkinson's disease: a neurodegenerative disorder. Int J Neurosci 129(1):55–93
Knörle R (2018) Neuromelanin in Parkinson's disease: from Fenton reaction to calcium signaling. Neurotox Res 33(2):515–522
Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V (2009) Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. J Alternative Complementary Med 15(8):891–897
Lama A et al (2020) Nutraceuticals: an integrative approach to starve Parkinson's disease. Brain, Behavior, Immunity-Health 2:100037
Lee JH, Lim H, Shehzad O, Kim YS, Kim HP (2014) Ginsenosides from Korean red ginseng inhibit matrix metalloproteinase-13 expression in articular chondrocytes and prevent cartilage degradation. Eur J Pharmacol 724:145–151
Longoria-García S, Cruz-Hernández MA, Flores-Verástegui MIM, Contreras-Esquivel JC, Montañez-Sáenz JC, Belmares-Cerda RE (2018) Potential functional bakery products as delivery systems for prebiotics and probiotics health enhancers. J Food Sci Technol 55(3):833–845
Lopez HL (2012) Nutritional interventions to prevent and treat osteoarthritis. Part II: focus on micronutrients and supportive nutraceuticals. PM&R 4(5):S155–S168
Ludtmann MH, Angelova PR, Horrocks MH, Choi ML, Rodrigues M, Baev AY, Al-Menhali AS (2018) α-synuclein oligomers interact with ATP synthase and open the permeability transition pore in Parkinson's disease. Nat Commun 9(1):1–16
Ma X, Li J, Cui X, Li C, Wang Z (2020) Dietary supplementation with peptides from sesame cake alleviates Parkinson's associated pathologies in Caenorhabditis elegans. J Functional Foods 65:103737

Mangels DR, Mohler ER III (2017) Catechins as potential mediators of cardiovascular health. Arterioscler Thromb Vasc Biol 37(5):757–763

Mao XY, Jin MZ, Chen JF, Zhou HH, Jin WL (2018) Live or let die: neuroprotective and anti-cancer effects of nutraceutical antioxidants. Pharmacol Ther 183:137–151

McWilliams M (2017) Foods: Experimental Perspectives. Pearson Education, Inc., London

Mirabelli M, Chiefari E, Arcidiacono B, Corigliano DM, Brunetti FS, Maggisano V, Brunetti A (2020) Mediterranean diet nutrients to turn the tide against insulin resistance and related diseases. Nutrients 12(4):1066

Morgan LA, Grundmann O (2017) Preclinical and potential applications of common western herbal supplements as complementary treatment in Parkinson's disease. J Dietary Suppl 14(4):453–466

Nair HH, Alex VV, Anto RJ (2020). Significance of nutraceuticals in cancer therapy. In: Evolutionary Diversity as a Source for Anticancer Molecules, pp 309–321. Academic Press

O'Shea KM, Khairallah RJ, Sparagna GC, Xu W, Hecker PA, Robillard-Frayne I, Stanley WC (2009) Dietary ω-3 fatty acids alter cardiac mitochondrial phospholipid composition and delay Ca2+-induced permeability transition. J Mol Cell Cardiol 47(6):819–827

Othman AI, El-Sawi MR, El-Missiry MA, Abukhalil MH (2017) Epigallocatechin-3-gallate protects against diabetic cardiomyopathy through modulating the cardiometabolic risk factors, oxidative stress, inflammation, cell death and fibrosis in streptozotocin-nicotinamide-induced diabetic rats. Biomed Pharmacother 94:362–373

Pandareesh MD et al (2018) Nutrition and nutraceuticals in neuroinflammatory and brain metabolic stress: implications for neurodegenerative disorders. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders) 17(9):680–688

Parker R, Pace M (2016) Introduction to Food Science and Food Systems. Cengage Learning, Inc.

Paul R et al (2020) Lycopene-a pleiotropic neuroprotective nutraceutical: deciphering its therapeutic potentials in broad spectrum neurological disorders. Neurochemistry Int 140:104823

Pisoschi AM, Pop A (2015) The role of antioxidants in the chemistry of oxidative stress: a review. Eur J Med Chem 97:55–74

Prema A, Janakiraman U, Manivasagam T, Thenmozhi AJ (2015) Neuroprotective effect of lycopene against MPTP induced experimental Parkinson's disease in mice. Neurosci Lett 599:12–19

Puliyappadamba VT, Thulasidasan AKT, Vijayakurup V, Antony J, Bava SV, Anwar S, Anto RJ (2015) Curcumin inhibits B [a] PDE-induced procarcinogenic signals in lung cancer cells, and curbs B [a] P-induced mutagenesis and lung carcinogenesis. BioFactors 41(6):431–442

Rajasekaran A (2017) Nutraceuticals. Comprehensive Med Chem III(1):107–134

Rocha VZ, Ras RT, Gagliardi AC, Mangili LC, Trautwein EA, Santos RD (2016) Effects of phytosterols on markers of inflammation: a systematic review and meta-analysis. Atherosclerosis 248:76–83

Rodriguez-Amaya DB (2015). Food Carotenoids: Chemistry, Biology and Technology. John Wiley & Sons, Hoboken

Sacks FM, et al (2017) Dietary fats and cardiovascular disease: a presidential advisory from the American heart association. Circulation 136(3):e1–e23

Sadhukhan P, Saha S, Dutta S, Mahalanobish S, Sil PC (2018) Nutraceuticals: an emerging therapeutic approach against the pathogenesis of Alzheimer's disease. Pharmacol Res 129:100–114

Sahebkar A (2014) A systematic review and meta-analysis of randomized controlled trials investigating the effects of curcumin on blood lipid levels. Clin Nutr 33(3):406–414

Saini RK, Keum YS (2018) Omega-3 and omega-6 polyunsaturated fatty acids: dietary sources, metabolism, and significance—a review. Life Sci 203:255–267

Saraswat K, Rizvi SI (2017) Novel strategies for anti-aging drug discovery. Expert Opin Drug Discov 12(9):955–966

Schell J, Scofield RH, Barrett JR, Kurien BT, Betts N, Lyons TJ, Basu A (2017) Strawberries improve pain and inflammation in obese adults with radiographic evidence of knee osteoarthritis. Nutrients 9(9):949

Scheltens P, Blennow K, Breteler MM, de Strooper B, Frisoni GB, Salloway S, Van der Flier WM (2016) Alzheimer's disease. Lancet 388:505–517

Serviddio G, Davide Romano A, Cassano T, Bellanti F, Altomare E, Vendemiale G (2011) Principles and therapeutic relevance for targeting mitochondria in aging and neurodegenerative diseases. Curr Pharm Des 17(20):2036–2055

Singh S (2007) From exotic spice to modern drug? Cell 130(5):765–768

Singh JP, Kaur A, Singh N, Nim L, Shevkani K, Kaur H, Arora DS (2016) In vitro antioxidant and antimicrobial properties of jambolan (Syzygiumcumini) fruit polyphenols. LWT-Food Sci Technol 65:1025–1030

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

Singh B, Singh JP, Kaur A, Singh N (2018) Phenolic compounds as beneficial phytochemicals in pomegranate (Punica granatum L.) peel: a review. Food Chem 261:75–86

Singh B, Singh JP, Kaur A, Singh N (2020) Phenolic composition, antioxidant potential and health benefits of citrus peel. Food Res Int 109114

Singh P, Sivanandam TM, Konar A, Thakur MK (2021) Role of nutraceuticals in cognition during aging and related disorders. Neurochem Int 143:104928

Šneideris T, Baranauskienė L, Cannon JG, Rutkienė R, Meškys R, Smirnovas V (2015) Looking for a generic inhibitor of amyloid-like fibril formation among flavone derivatives. Peer J 3:e1271

Tang CH (2020) Nanocomplexation of proteins with curcumin: from interaction to nanoencapsulation (a review). Food Hydrocolloids 106106

Tang Y, Yang Q, Lu J, Zhang X, Suen D, Tan Y, Li X (2010) Zinc supplementation partially prevents renal pathological changes in diabetic rats. J Nutritional Biochem 21(3):237–246

Ulas M, Orhan C, Tuzcu M, Ozercan IH, Sahin N, Gencoglu H, Sahin K (2015) Anti-diabetic potential of chromium histidinate in diabetic retinopathy rats. BMC Complementary Alternative Med 15(1):16

Vaclavik VA, Christian EW, Campbell T (2021) Essentials of Food Science. Springer, Cham, pp 137–175

Wang A, Leong DJ, Cardoso L, Sun HB (2018) Nutraceuticals and osteoarthritis pain. Pharmacol Ther 187:167–179

Yang C et al (2020) A natural product solution to aging and aging-associated diseases. Pharmacol Therapeutics 107673

Zeng W, Zhang W, Lu F, Gao L, Gao G (2017) Resveratrol attenuates MPP+-induced mitochondrial dysfunction and cell apoptosis via AKT/GSK-3β pathway in SN4741 cells. Neurosci Lett 637:50–56

Zhang Q, Wei D, Liu J (2004) In vivo reversal of doxorubicin resistance by (–)-epigallocatechin gallate in a solid human carcinoma xenograft. Cancer Lett 208(2):179–186

Zhang R, Zhang Z, McClements DJ (2020) Nanoemulsions: an emerging platform for increasing the efficacy of nutraceuticals in foods. Colloids Surfaces B: Biointerfaces 194:111202

Zhu HT, Bian C, Yuan JC, Chu WH, Xiang X, Chen F, Lin JK (2014) Curcumin attenuates acute inflammatory injury by inhibiting the TLR4/MyD88/NF-κB signaling pathway in experimental traumatic brain injury. J Neuroinflammation 11(1):59