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Natural nutraceuticals, especially functional foods, their major bioactive components, formulation, and health benefits for disease prevention: an overview

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Abstract

Nutraceuticals play wide range of important roles, from health promotion, increasing life expectancy, maintaining body cell integrity, to reducing the risks of many diseases. As consumers continue to be attracted to nutraceuticals, such as superfoods, vegetables, fruits, high-protein foods, eating healthy intertwines with finding the right balance. Nowadays, the nutraceutical industries are among the many that target to meet the dynamically growing consumers' expectations. Moreover, foods and agricultural commodities contain bioactive constituents, which are mostly responsible for their nutraceutical functions. How nutraceuticals, especially functional foods, etc., help in tackling health challenges increase the interest among several researchers in this subject area, and given the ever-growing need across communities around the globe for healthy living, strengthens the need for continued synthesis of published information to supplement existing knowledge. This overview, therefore, discusses natural nutraceuticals, especially functional foods, their major bioactive components, formulation, health benefits for disease prevention.

Keywords: Nutraceuticals; Functional foods; Dietary supplements; Bioactive compounds; Consumer health; Disease prevention.

1. Introduction

Nowadays, foods and dietary solutions that meet consumers unique personal health are highly sought after (Sloan, 2020). Nutraceuticals (also known as bioceuticals) are food products considered as pharmaceutical alternatives with physiological or medicinal benefits (Sarris et al., 2016; Banach et al., 2018; Shahidi, 2012), which help improve body functions, prevent various health conditions, increase life expectancy, maintain body cell integrity, as well as support body structure (Meštrović, 2021; Shahidi, 2012; Yeh et al., 2022). On the other hand, functional foods (and dietary supplements) are among the four major classes of nutraceuticals that provide added value especially towards health promotion and/or disease prevention, mostly formulated by the addition of new components or improving the existing ingredients (Shahidi 2009 and 2012; Ellis, 2021; Xu et al., 2022). In fact, the term "functional food" was first used in Japan in the 1980s, where a government approval process exists for functional foods known as Foods for Specified Health Use (FOSHU) (Alongi and Anese, 2021). More so, nutraceutical industries are among the many that target to meet the growing and dynamic consumers' expectations (Shahidi, 2012; Sloan, 2020). Nutraceuticals in human nutrition provide wide implications for consumers, food producers, regulators, distributors, nutritionists, as well as healthcare providers (Meštrović, 2021).

Consumers continue to be attracted to nutraceuticals, together with superfoods, vegetables, fruits, high-protein foods, etc. (Kalra,

2003; Nishizawa et al., 2019; Sloan, 2020). In February 2020, for instance, the global sales of functional/fortified food was estimated at □ $267 billion, whereas the (global) sales of natural healthy food was estimated at □$259 billion (Euromonitor, 2020). Asia Pacific region continues to lead in the global quest for health/wellness in foods/nutrition (Mascaraque 2018; Barbalova, 2019). Indeed, the benefits of nutraceuticals, especially their nutritional and therapeutic effects, which are very key in many physiological processes, vary from antioxidant processes, gene expression, cell proliferation, mitochondrial integrity, to cardiovascular functions, immune boosting, etc. (Nystrand and Olsen, 2021; Meštrović, 2021; Singh et al., 2021). Concurrently, eating healthy intertwines with finding the right balance—reducing personally perceived "bad" nutrients (such as sugar, carbohydrates, sodium), and same time, increasing personally perceived "good" nutrients (such as protein, fiber, vitamins, minerals) (Sloan, 2020). Nonetheless, given the ever-growing need across communities around the globe for healthy living, how nutraceuticals, such as functional foods and dietary supplements, help in tackling health challenges strengthens the need for continued synthesis of published information to supplement existing knowledge. This overview, therefore, discusses natural nutraceuticals, especially functional foods, their major bioactive components, formulation, health benefits for disease prevention. This overview is constructed as follows: a) Brief differentiation between nutraceuticals, dietary supplements, and functional foods; b) Common functional foods from the nutraceutical context, and their biological strengths; c) Major bioactive components of nutraceuticals, especially functional foods; d) Formulation of functional foods; and e) Health benefits for disease prevention by nutraceuticals, especially functional foods.

2. Brief differentiation among different nutraceuticals

Dietary supplements—nutrients derived from foods or other safe sources, are usually concentrated in form of a pill, powder, liquid, capsule, gel caps, or soft gels, taken orally to supplement the diet (Liao et al., 2017; Hofmeyr et al., 2019). Dietary ingredients/supplements in the form of concentrates or extracts might include minerals, vitamins, amino acids, herbs (botanicals), and other constituents, e.g., secondary metabolites, enzymes, glandulars, and organ tissues (Nicolson et al., 2014; Shahidi, 2012; National Institute on Aging, 2021). Dietary supplements are manufactured products aimed at supplementing one's diet and can be taken in various forms, and are not necessarily food-derived (National Institute on Aging, 2021). Differently, formulation of medical foods and their administration/consumption has to be supervised by a qualified and trained physician. Medical food is precise dietary management of a known or suspected disease/condition with scientifically established distinctive nutritional requirements (Bass, 2021). Medical foods particularly their formulation focus on dietary therapy, which usually aim to tackle specific disease conditions given that the normal diet alone cannot meet. As components of medical value, farmaceuticals have been coined by combining the words "farm" and "pharmaceuticals", which are produced from the modification of animal products or agricultural crops (Sheridan, 2016).

Functional foods are usually consumed as part of diets, and have scientifically proven extra benefits to human health apart from the basic benefits of consuming foods. The role of functional foods to either exert physiological benefits beyond the basic functions of nutrition, include their ability to reduce the risks of chronic diseases (Shahidi, 2009; Arshad et al., 2021; Nystrand and Olsen, 2021). Health Canada considers functional foods as products that liken to traditional foods, yet able to provide physiological merits. Functional foods, dietary supplements, etc., are considered as the major classes of nutraceuticals. Functional foods and dietary supplements, in many general classifications, have oftentimes been included as nutraceuticals. Nutraceuticals have also been described as commodities derived from foods, which have medicinal properties, and can exist in form of foods, capsules, pills, and potions, and are able to exert physiological benefits (Shahidi, 2009). Nutraceuticals' description, efficacy and products largely depend on their sources and components, with their classification largely associated with their pharmacological properties, sources, and/or composition (Meštrović, 2021). To throw more light on this, the classification of nutraceuticals is shown in Figure 1. Nutraceuticals derived mostly from foods believed to have additional health benefits, along with the normal food nutritional values (Lim et al., 2021) may be marketed as preventive and treatment alternatives for many health conditions, despite being interchangeably used sometimes with functional foods and dietary supplements (Heinrich, 2019).

3. Common functional foods from the nutraceutical context, and their biological strengths

Table 1 shows the major classes of functional foods, from the nutraceutical context, and their associated bioactive components/effects. The functional food classification would include beverages (Nutraceutical beverages) (Saeed et al., 2019; Díaz et al., 2020; Bulman et al., 2021), fermented foods (Islam et al., 2019; Vasilean et al., 2021; Yun et al., 2021), fruits (Ellis, 2021; Lim et al., 2021), herbs and spices (Ahmad et al., 2020; Pandey et al., 2022; Chopra et al., 2022), honey (Anfang et al., 2018; Grüter, 2020; Berenbaum and Calla, 2021; Martinez-Armenta et al., 2021), legumes (Barman et al., 2018; Carrera et al., 2021), nuts (Del Gobbo et al., 2015; ARS, 2019; Ros et al., 2021), seafood (fishes) (Telessy, 2019; Ashraf et al., 2020; Ellis, 2021), seeds (Kawakami et al., 2015; Khosravi-Boroujeni et al., 2017; Robertson, 2017; Suryapal et al., 2021), vegetables (Saiwal et al., 2019; Arya et al., 2019), as well as whole grains (Priebe and McMonagle, 2016; Kelly et al., 2017; Zabolotneva et al., 2022), which will be further discussed in this section. Further illustrating the above-mentioned, some vegetables with their associated nutraceutical potentials are presented in Table 2, in terms of plant species, image display, common cultivars and parts commonly used.

3.1. Beverages

Many beverages have known and/or promising nutraceutical properties/potentials. Some common nutraceutical beverages include tea/coffee, enhanced/mineral water, plant milks, fortified fruit drinks/juices, smart drinks, ready-to-drink teas, performance/sports drinks, dairy beverages, etc. (Corbo et al., 2014; Díaz et al., 2020; Bulman et al., 2021). Some beverages produced from nuts, herbs (medicinal plants), grains, seeds, etc. are also considered nutraceutical beverages. Nutraceutical beverages improve digestion, overall health, immunity, heart health, energy boost, etc. (Corbo et al., 2014; Díaz et al., 2020). Coffee and tea are among the most common beverages globally, which are briefly expatiated below.

Coffee is an important nutraceutical beverage, with anti-obesity, antidiabetic, antimicrobial, cardioprotective, prebiotic, antioxidant, antidyslipidemic, lipid peroxidation inhibitory, and antiinflammatory properties, which are important for preventing and treating

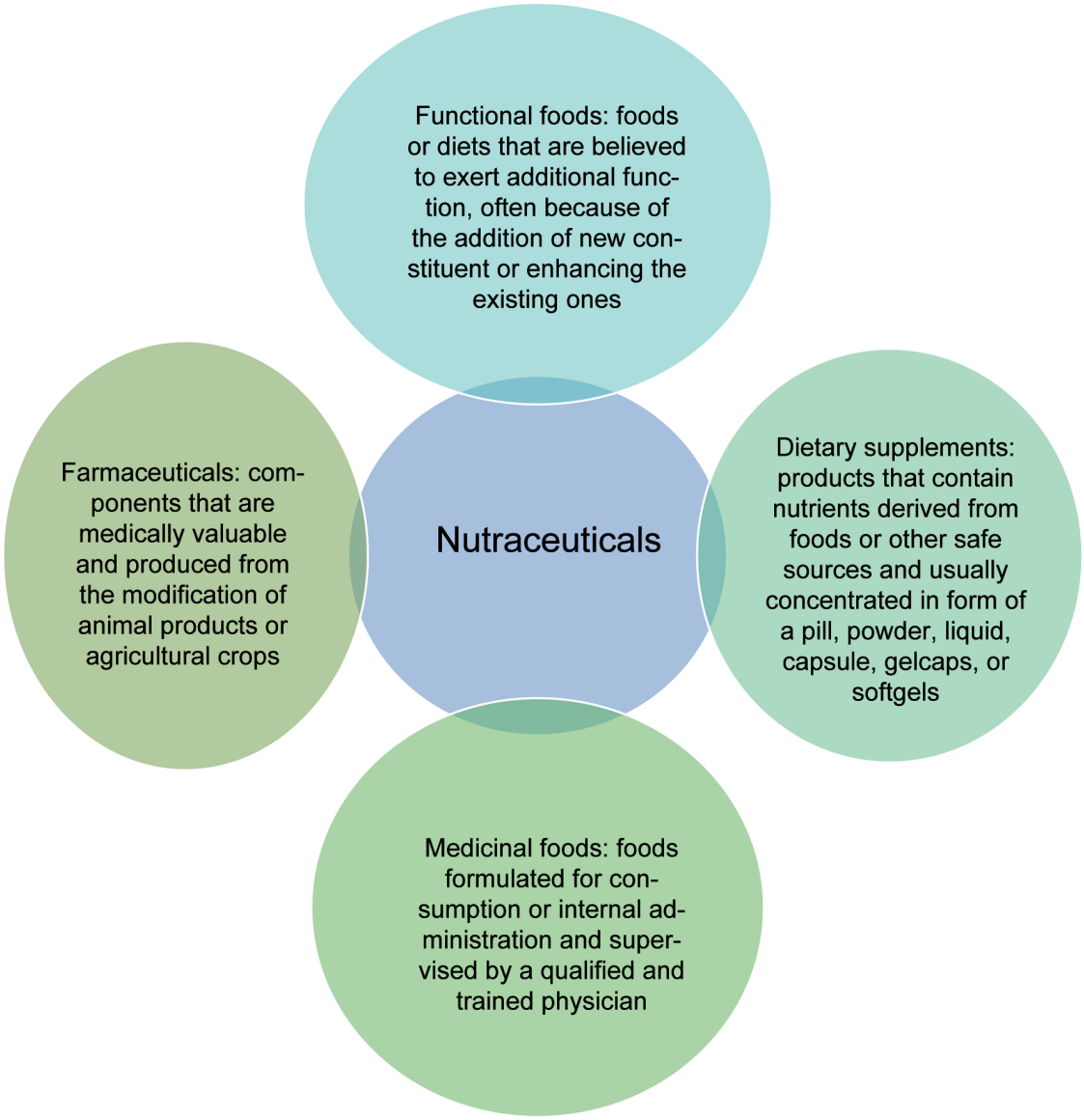

Figure 1. Classification of nutraceuticals.

diseases (Saeed et al., 2019). There is growing evidence that coffee consumption might reduce the incidence of many chronic conditions, such as mental health, liver disease, suicidal risks, all-cause mortality, etc. Conversely, Saeed et al. (2019) and Quarta et al. (2021) associated excessive coffee intake with increased risk factors of CVD, including blood pressure, plasma homocysteine, and cholesterol (e.g., LDL cholesterol). Pregnant women are advised not to take coffee partly to avoid miscarriages and/or impaired growth and development of fetus (Saeed et al., 2019; Al-Bari et al., 2021).

Tea is a popular nutraceutical beverage that have important bioactive compounds and nutrients with strong antioxidant, anticancer, antiinflammatory, immunomodulator, antihistamine, antimicrobial, antidepressant, cardioprotective, blood pressure lowering, nervous system protective, and health promoting properties. Bioactive compounds in tea, such as green tea, black tea, herbal tea, oolong tea, etc., can prevent many diseases, including CVDs, cancers, etc. Tea contains stimulants, e.g., caffeine, and catechins, which act as chemopreventive and anticarcinogenic agents. The astringency of tea is attributed to polyphenols presence, which are abundant in tea leaves, constituting about 30 to 40% of the total composition (Ferruzzi, 2010; Williamson et al., 2011).

3.2. Fruits

Fruit are important source of essential nutrients, such as vitamins, minerals, phytochemicals, etc., with ample amounts of fiber. They also provide several health-boosting antioxidant, anti-inflammatory, anticancer, immunomodulatory, and antidiabetic compounds, other bioactive compounds (phytochemicals) including polyphenols (e.g., flavonoids) (Donno et al., 2018; Yip et al., 2019; Sarvarian et al., 2022). Regular fruit consumption in diets can improve overall health and reduce disease risks, from cardiovascular dis-

Table 1. Major classes of functional foods, from the nutraceutical context, and their associated bioactive components/effects

Functional food classification	Examples	Major bioactive components	Nutraceutical/functional effects	References
Beverages (Nutraceutical beverages)	Tea, coffee, enhanced/ mineral water, plant milks, fortified fruit drinks/juices, smart drinks, ready-to-drink teas, performance/ sports drinks, dairy beverages, etc. Nutraceutical beverages are mostly obtained from fruits, vegetables, coffee, tea, soybean, milk, dairy products, etc.	Epigallocatechin-3-gallate, epicatechin gallate, caffeine, etc.	Nutraceutical beverages improve digestion, overall health, immunity, heart health, energy boost, etc. Tea is a popular nutraceutical beverage that have important bioactive compounds and nutrients with strong antioxidant, anticancer, antiinflammatory, immunomodulator, antihistamine, antimicrobial, antidepressant, cardioprotective, blood pressure lowering, nervous system protective, and health promoting properties. Several studies have shown that the consumption of coffee might reduce incidence of many chronic conditions, such as mental health, liver disease, suicidal risks, all-cause mortality, etc.	Saeed et al., 2019; Díaz et al., 2020; Bulman et al., 2021
Fermented foods	Yoghurt, sauerkraut, soy products, tempeh, kefir, barley, kimchi, rice bran, kombucha, etc.	Polyphenols, dietary fiber, probiotics, prebiotics, conjugated linoleic acid, calcium, cobalamin, magnesium, fatty acids, etc.	Fermented foods have immune-modulatory, antioxidant, chemoprotective, anti-inflammatory, cardioprotective, immune boosting, and anticancer, and antidiabetic properties. The microorganisms mostly used for fermentation are yeasts and lactic acid bacteria, which can improve nutrients bioavailability and increase the bioactive compounds in the foods. fermentation favour *in vitro* antioxidant activities of fermented products. Citrus blended vinegars can be used as functional foods due to their anti-obesity, anti-aging, and antioxidant properties. Yogurt helps benefit digestive health, strengthen immune system, protect against osteoporosis, benefit heart health, promote weight management, etc.	Islam et al., 2019; Vasilean et al., 2021; Yun et al., 2021
Fruits	Limes, strawberries, blackberries, blueberries, bananas, oranges, apples, peaches, pears, kiwi, avocado, bananas, pineapple, pomegranate, apples, grapefruit, oranges, lemons, etc.	Polyphenols (e.g., flavonoids), vitamins, minerals, dietary fiber, ellagitannins, prodelphinidins, gallocatechins, catechins, alkaloids, cardiac glycosides, pelargonidin glycosides, cyanidin, delphinidin, etc.	They have health-boosting antioxidant, cardioprotective, anti-inflammatory, antimicrobial, anti-depression, anticancer, immunomodulatory, nervous system enhancement, and antidiabetic properties, among others. Regular consumption of diets high in fruits can improve overall health and reduce one's risk of developing diseases, such as cardiovascular diseases, inflammation, cancer, diabetes mellitus, obesity, etc.	Ellis, 2021; Lim et al., 2021
Herbs and spices	Ginger, cinnamon, cayenne pepper, fenugreek, garlic, turmeric, red pepper, etc.	Curcumin, gingerol saponin, fiber, capsaicin, allicin, shogaols, piperine, etc.	The nutraceutical, anti-oxidant, anti-diabetic, nutritional, anti-hypercholesterolemic, cardioprotective, anti-microbial, anti-inflammatory, anticancer, and anti-carcinogenic activities of spices have significant importance as nutraceuticals. Curcumin in turmeric, [6]-gingerol in ginger, saponin and fiber in fenugreek, capsaicin in red pepper, allicin in garlic have important nutraceutical properties due to their several physiological and medicinal effects. Spices and herbs have been shown to have the nutraceutical properties, including antioxidant, antimicrobial, antidiabetic, immune promoting, antihistamine, immunomodulatory, anticancer, cardioprotective, and blood pressure lowering properties, among others.	Ahmad et al., 2020; Pandey et al., 2022; Chopra et al., 2022

Table 1. Major classes of functional foods, from the nutraceutical context, and their associated bioactive components/effects *- (continued)*

Functional food classification	Examples	Major bioactive components	Nutraceutical/functional effects	References
Honey	Mostly honey bees and other bees	Organic acids (gluconic, succinic, palmitic, formic, capronic, valeric, propionic, acetic, pyroglutamic, malic, lactic, citric, and butyric acids, among others), royalisin (defensin-1), hydrogen peroxide, methylglyoxal, sugar, eugenol, naringin, luteolin, syringic acid, p-coumaric acid, kaempferol, galangin, apigenin, quercetin, chrysin, gallic acid, isorhamnetin, pinocembrin, pinobanksin, caffeic acid, ferulic acid, etc.	Bioactive compounds in honey help resist infections, tolerate cold, possibly live longer, heal wounds, and prevent some diseases. They also have antioxidant, anticancer, antidiabetic, anti-inflammatory, immune boosting, blood pressure lowering, antihistamine, antimicrobial, cognitive, cardioprotective, and nervous improving properties. Honey is topically used as antibiotic in herbal and traditional medicine. It is used for treating burns and skin injuries in traditional medicine. Honey usage is recommended as provisional intervention for suspected or known ingestions of button cell battery to decrease the severity and/or risk of esophagus injury induced by the battery before its removal. Honey might be beneficial for the control of side effects of chemotherapy or radiation therapy used in cancer treatment.	Anfang et al., 2018; Grüter, 2020; Berenbaum and Calla, 2021; Martinez-Armenta et al., 2021
Legumes	Beans, lupins, peas, peanuts (groundnut), black beans, chickpeas, navy beans, lentils, soybean, etc.	Dietary fiber, protein, dietary minerals, isoflavones (genistein, daidzein, glycitein), phytosterols, peptides, saponins, resveratrol, etc.	Due to their nutritional and phytochemical compositions, legumes generally help to prevent or treat diseases, including cancer, obesity, cardiovascular diseases, overweight, diabetes mellitus, digestive diseases, nervous system disorders, etc. Regular consumption of soybean can ameliorate the menopause symptoms and reduce the risk of cancers, including breast and prostate cancers. Peanuts have been used to fight malnutrition for decades.	Barman et al., 2018; Carrera et al., 2021
Nuts	Tree nuts, peanuts, almonds, macadamia nuts, cashews, pistachios, Brazil nuts, macadamias, pecans, cashews, walnuts, hazelnuts, pine nuts, etc.	α-linolenic acid, minerals, polyunsaturated fatty acids, L-arginine, dietary fiber, antioxidants (polyphenols, tocopherols, etc.), folate, etc.	The components in nuts synergistically and favorably influence vascular and metabolic physiology pathways, improve cardiovascular prognosis, and reduce the risk of cardiovascular diseases. The consumption of nuts within a given population is associated with lower incidence of cancer and cancer related mortality, and decrease in all-cause mortality. The consumption of nuts also has moderate improvements on inflammation, endothelial function, blood pressure (BP), and glycaemic control. Nuts generally have preventive, protective, and ameliorative effects on cardiovascular diseases, hypertension, diabetes, cancer, brain health, overall mortality, lowering blood pressure, improving lipid profile, improving epithelial functions, antiinflammatory actions, obesity/overweight, etc.	Del Gobbo et al., 2015; ARS, 2019; Ros et al., 2021
Seafood (fishes)	Salmon, trout, herring, sardines, anchovies, cod, mackerel, lobster, tilapia, perch, mollusks, sea slugs, bryozoans, shrimp, tunicates, tuna, sponges, etc.	Polyunsaturated fatty acids, linoleic acid, arachidonic acid precursor, thromboxanes, leukotrienes, α-linolenic acid, highly unsaturated fatty acids (HUFA) >C20, docosahexaenic acid (DHA), docosapentaenic acid (DPA), eicosapentaenic acid (EPA), gelatin, collagen, myosin, peptides, copper, zinc, calcium, essential amino acids, vitamin B_{12}, sodium, iodine, selenium, potassium, β-carotene, astaxanthin, glycosaminoglycans, glucosamine, chitosan, chitin, etc.	Seafood generally have high levels of essential fatty acids, including omega-3 fatty acids, that reduce the risks of cardiovascular diseases (heart diseases) and can improve the health of infants when consumed by pregnant or breastfeeding women. The bioactive compounds in seafood exert several physiological functions, such as antioxidant, antimicrobial, anticoagulant, anti-obesity, antitumor, anti-allergic, neuroprotective, anti-atherosclerotic, antihypertensive, antioxidant, anticancer, anticoagulant, anti-inflammatory, anti-obesity, appetite-suppressing, muscle relaxant, cardioactive, antidiabetic, hypotensive, analgesic, antibiotic, and immunomodulatory properties, among other nutraceutical properties	Telessy, 2019; Ashraf et al., 2020; Ellis, 2021

Table 1. Major classes of functional foods, from the nutraceutical context, and their associated bioactive components/effects *- (continued)*

Functional food classification	Examples	Major bioactive components	Nutraceutical/functional effects	References
Seeds	Flaxseeds, chai seeds, Sesame seeds, avocado seeds, Black seeds, pumpkin seeds, hemp seeds, sunflower seeds, etc.	Fiber, essential oils, omega-3 fats, antioxidants, polyunsaturated and monounsaturated fats, vitamins, minerals, lignans, caffeic acid, triterpenes, campesterol, ferulic acid, p-coumaric acid, neolinustatin, lariciresinol, pinoresinol, sesamin, sesamolin, linystatin, secoisolariciresinol diglucoside (SDG), sitosterol, stigmasterol, catechins, triterpenoid glycosides, ferulic acid, coumaric acid, etc.	The inclusion of seeds in regular diets can reduce blood pressure, control blood sugar, lower LDL cholesterol, reduce risk of cancer, reduce the risk cardiovascular diseases, fight microbial infections, etc. reduce the risk of heart disease and cholesterol levels. In addition to reducing the risk of heart disease and cancer, flaxseeds can reduce blood sugar level and risk of diabetes mellitus. Seeds contain many important polyphenols that have antioxidant, antiinflammatory, anticancer, immune promoting, and cardioprotective properties, among other health and medicinal benefits.	Kawakami et al., 2015; Khosravi-Boroujeni et al., 2017; Robertson, 2017; Suryapal et al., 2021
Vegetables	Broccoli, cauliflower, zucchini, pumpkin, kale, spinach, scent leaves, carrot, tea leaves, etc.,	Omega-3 fatty acids, dietary fiber, cryptoxanthin, vitamins, zinc, β-carotene, selenium, lycopene, isoflavones, flavonoids, carotenoids (carotenes and xantophylls), epigallocatechin-3-gallate, epicatechin, epigallocatechin, epicatechin-3-gallate, glucosinolates, phytosterols, thiols, etc.	Vegetables play an important role in human health, including the prevention and treatment of many diseases such as diabetes, cardiovascular diseases, infections, etc. Regular inclusion of vegetables in the diets leads to a decrease in incidence of cardiovascular diseases, stroke, cancer, and other diseases. Carotenoids in vegetables such as the carotenes, e.g., beta carotene, and the xanthophylls, e.g., astazanthin, zeaxanthin, canthaxantin, cryotpxanthin, etc., have a wide range of nutraceutical and health benefits	Saiwal et al., 2019; Arya et al., 2019
Whole grains	Wheat, barley, rice, rye, oats, corn/ maize, millets, job's tears, canary grass, fonio, sorghum, wild rice, triticale, teff, buckwheat, amaranth, quinoa, Tartary buckwheat	Dietary fiber, minerals, vitamins, polyphenols, inulin, β-glucan, carotenoids (lutein, zeaxanthin, β-cryptoxanthin, β-carotene), lignans, vitamin E compounds, folate, betaine, phytosterols, tocols, etc.	The inclusion of whole grains in breakfast cereals is associated with improvement in the intake of micronutrient and reduced risk of diseases such as gastrointestinal conditions, poor cognition, obesity, CVDs, type 2 diabetes mellitus, coronary heart disease, cancer, all-cause mortality, stroke, diverticulosis, etc.	Priebe and

Table 2. Some vegetables with their associated nutraceutical potentials

Plant species	Image display	Common cultivars	Parts commonly used
Beta vulgaris		Swiss chard, beetroot, sugar beet, sea beet	Leaves, roots
Vicia faba		Broad bean	Seeds, pods
Brassica oleracea		Broccoli, cabbage, collard greens, Savoy cabbage, red cabbage, kohlrabi, cauliflower, kale, Brussels sprouts, etc.	Flower heads, axillary buds, leaves, stems
Daucus carota		Carrot	Root, stems, leaves
Cucumis sativus		Cucumber	Fruits
Solanum melongena		Eggplant (aubergine)	Fruits
Allium ampeloprasum		Elephant garlic, leek	Leaf sheaths
Lactuca sativa		Celtuce, lettuce	Leaves, seed oil, stems

Table 2. Some vegetables with their associated nutraceutical potentials - *(continued)*

Plant species	Image display	Common cultivars	Parts commonly used
Brassica rapa		Napa cabbage, turnip, bok choy	Root, leaves
Allium cepa		Onion, shallot, scallion, spring onion	Bulbs, leaves
Cucurbita spp.		Pumpkin, gourd, zucchini (courgette), marrow, squash	Leaves, flowers, fruits
Raphanus sativus		Daikon, radish, seedpod varieties	Leaves, root, sprouting, seed oil, seed pods
Spinacia oleracea		Spinach	Leaves
Ipomoea batatas		sweet potato	Leaves, shoots, tubers
Solanum lycopersicum		Tomato	Fruits

eases, inflammation, cancer, diabetes mellitus, to obesity (Butler, 2019; Davidson, 2021). Dietary fiber from fruits when consumed promotes satiety, increases intestinal transit, and helpful in controlling body weight and reducing blood cholesterol (Salas-Salvadó et al., 2008). Besides being equipped with excellent nutraceutical properties, fruits such as pomegranates contain ellagitannins, prodelphinidins, gallocatechins, catechins, alkaloids, cardiac glycosides, pelargonidin glycosides, cyanidin, delphinidin, etc., which provide antiinflammatory, antioxidant, anticancer, immune boosting, antimicrobial enhancement properties, among other medici-

nal and health benefits (Lim et al., 2021; Ellis, 2021; Yip et al., 2019). Some underutilized fruits, such as *Amelanchier canadensis, Morus nigra*, *Lycium barbarum*, *Crataegus azarolus*, *Asimina triloba*, etc., have promising potentials to serve as nutraceuticals and sources of health-promoting compounds (Donno et al., 2018).

3.3. Herbs and spices

In traditional medicine, herbs and spices have been used for centuries, with much information currently growing regards their-beneficial properties, largely immune-enhancing and anti-inflammatory aspects that show promising results. In a recent review that spices and herbs as immune enhancers and anti-inflammatory agents, Garnier and Shahidi (2021) in addition to providing a historical, traditional function, biological relevance, and associated background, identified widely researched examples, namely turmeric (*Curcuma longa*), chili powders (*Capsicum* species), South African geranium (*Pelargonium sidoides*), Devil's claw (*Harpagophytem procumbens*), Africanpotato (*Hypoxis hemerocallidea*), saffron (*Crocus sativus*), allspice (*Pimenta dioica*), basil (*Ocimum basilicum*), rosemary/sage (*Salvia rosmarinus/officinalis*), lavender (*Lavandula angustifolia*), black pepper (*Piper nigrum*),clove (*Syzygium aromaticum*), fenu-greek (*Trigonella foenum-graecum*), rooibos (*Aspalathus linearis*), ginger (*Zingiber officinale*), as well as oregano (*Origa-num vulgare*). Further reading at Garnier and Shahidi (2021) is encouraged because this review discussedexamples exhaustively the above-named herbs /spices based on current uses, bioactive compounds, immune enhancing /antiinflammatory aspects, as well as recent advancements, where applicable.

Generally, spices from seeds, barks, roots, fruit, and/or other plant materials (Ahmad et al., 2020) provide nutraceutical, antioxidant, anti-diabetic, nutritional, anti-hypercholesterolemic, cardioprotective, anti-microbial, anti-inflammatory, anticancer, and anti-carcinogenic activities with significant importance for health maintenance and disease prevention (Shylaja and Peter, 2007; Pandey et al., 2022). For instance, curcumin in turmeric, [6]-gingerol in ginger, saponin and fiber in fenugreek, capsaicin in red pepper, allicin in garlic have nutraceutical properties given by several physiological and medicinal effects. Spices and herbs such as ginger, cinnamon, cayenne pepper, fenugreek, garlic, turmeric, red pepper, etc., have nutraceutical properties, including antioxidant, antimicrobial, antidiabetic, immune promoting, antihistamine, immunomodulatory, anticancer, cardioprotective, and blood pressure lowering properties, among others (Chauhan et al., 2013; Garnier and Shahidi, 2021; Chopra et al., 2022).

3.4. Legumes

Legumes are plants that belong to the Fabaceae (or Leguminosae) family, or the seed or fruit of such plants. Legume seeds, also called pulses when used as dry grains, are promising nutraceuticals with beneficial and therapeutic effects (Barman et al., 2018). Legumes are cultivated due to their seeds for consumption by humans and animal, as well as for oil production. Common legumes include beans, lupins, peas, peanuts (groundnut), black beans, chickpeas, navy beans, lentils, soybean, etc. (Barman et al., 2018; Nicholas, 2020).

Groundnut (peanut) is a rich source of potassium, B vitamins, phosphorus, calcium, resveratrol, protein, essential fats, and many other essential nutrients, and bioactive compounds, all of which have several health and medicinal benefits. Besides comprising mix of protein, healthy fats, and fibre which regulate glucose levels in the blood, maintain appetite, reduce risk of heart disease, maintain healthy digestive tract, etc, peanuts have long been used to fight malnutrition for decades (Udeh et al., 2020). Peanut skins are rich in resveratrol associated with many medicinal and therapeutic effects, including anticancer, antiviral, antidiabetic, antiinflammatory, antioxidant, and immunomodulatory effects (Sales and Resurreccion, 2014). Peanut oil is a common salad and cooking oil, and contains monounsaturated fats (mostly oleic acid), polyunsaturated fats (mainly linoleic acid), and saturated fats (mostly palmitic acid) at 46%, 32%, and 17% respectively (Ozcan, 2010; Nayak et al., 2020). Regular daily peanut consumption can reduce LDL cholesterol and improve heart health and entire cardiovascular health (Times of India, 2021).

Soybean is among nutritional crops, increasingly popular due to its nutraceutical properties, given by the ample presence of protein, essential amino acids, dietary fiber, vitamins and minerals, and important bioactive compounds such as isoflavones, phytosterols, peptides, saponins, etc. (Tidke et al., 2015; Carrera et al., 2021). Containing antinutrients, such as phytic acids and trypsin inhibitors managed by adequate processing, the phytochemicals in soybean serve as functional components, able to reduce cholesterol levels and help prevent such disease conditions like diabetes, cardiovascular diseases, cancer, etc. (Tidke et al., 2015). Regular consumption of soybean can ameliorate the menopause symptoms and reduce the risk of cancers, including breast and prostate cancers (Arnarson, 2019). Major soybean isoflavones include genistein, daidzein, and glycitein, and constitute 50%, 40%, and 10% of the total soybean isoflavones, respectively (Arnarson, 2019).

3.5. Seeds

Broadly, seeds are important for healthy diets with many health promoting, protective, and therapeutic properties. Many seeds have excellent nutraceutical properties, and can form the basis and/or part of nutraceutical formulations and development (Suryapal et al., 2021). As rich sources of fiber, essential oils, omega-3 fats, antioxidants, polyunsaturated and monounsaturated fats, vitamins, minerals, and many important other phytochemicals, seeds when included in regular diets can help reduce disease conditions, from blood pressure, control blood sugar, lower LDL cholesterol, cancer, to cardiovascular risks (Robertson, 2017). Some examples of well-known seeds include chia, flaxseeds, hemp, pumpkin, sesame, etc., which would be expatiated briefly below.

Chia seeds are rich in essential and therapeutic nutrients, such as fiber, omega-3 fats, etc. Chia seeds contain many important polyphenols that have antioxidant, anti-inflammatory, anticancer, immune promoting, and cardioprotective properties. Studies showed that chia seeds consumption can increase blood levels of ALA, which helps reduce inflammation (Nieman et al., 2012). In the body, ALA can be converted to other omega-3 fats, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), having important health and therapeutic properties, like reducing blood sugar and appetite (Vuksan et al., 2017).

Flaxseeds, also called linseeds, are rich in fiber, important phytochemicals, and omega-3 fats (especially alpha-linolenic acid [ALA]). Omega-3 fats in flaxseeds are usually within the fibrous outer shell cannot be easily digested by humans (Patenaude et al., 2009). Flaxseeds contain many compounds, including lignans, which play antioxidant roles in human body. In addition to omega-3 fats and ligand, the flaxseeds also contain phytochemicals that help reduce heart disease risks, and cholesterol levels (Kawakami et al., 2015). A 28 g of flaxseeds contains many nutrients, such as fiber

(7.8 g), protein (5.2 g), omega-3 fats (6.5 g), omega-6 fats (1.7), minerals, vitamins, etc. (Robertson, 2017). Flaxseeds consumption may decrease tumor growth markers in breast cancer, and can reduce blood sugar level and risk of diabetes mellitus (DM) (Vuksan et al., 2017).

Hemp seeds contain high amount of healthy fats, such as omega-3 and omega-6 fats, which help to reduce blood pressure, cholesterol, and triglycerides, and also improve heart health (Christiansen, 2021). The inclusion of hemp seed oil to regular diets can reduce the risk of heart diseases (Farinon et al., 2020; Christiansen, 2021). Besides the many associated nutraceutical benefits, sunflower seeds are of three varieties, which include linoleic, high oleic, and sunflower oil seeds, with linoleic being the most common (Petraru et al., 2021). A 100 g of sunflower seed is 50% mostly of polyunsaturated and monounsaturated fats, especially linoleic acid. The seeds have phytosterols that when consumed contribute to low cholesterol levels in the blood (Ciarka et al., 2009).

Sesame seeds are among valuable as nutraceuticals. A 100 g dried whole sesame seeds contain 18% protein, 50% fat, 12% dietary fiber, etc. Whole sesame seeds contain ≥20% Daily Value of many B vitamins and minerals, including iron, folate, zinc, thiamine, phosphorus, niacin, calcium, magnesium, etc. A meta-analysis study reported sesame seeds consumption would decrease blood pressure (both systolic and diastolic) (Khosravi-Boroujeni et al., 2017). Given the presence of lignans lariciresinol, pinoresinol, sesamin, sesamolin, etc, sesame oil could decrease in lipid peroxidation and oxidative stress markers (Gouveia et al., 2016; Kuo et al., 2011). Able to trigger allergic reactions in humans, including anaphylaxis, sesame oil are believed to be a source of allergen for the allergy-triggering proteins (Adatia et al., 2017).

Pumpkin seeds contain essential fats (especially oleic acid, linoleic acid), dietary fiber, protein, and many micronutrients. Rich in vitamin K, zinc, phosphorus and manganese, pumpkin seeds help in wound healing, and can boost the immune system to fight viruses and bacteria. Many studies have reported pumpkin seeds' usefulness in managing urinary tract infection, bladder infections, high blood pressure, and high blood sugar level (Zhang et al., 2019; WebMD, 2020). Consumption of pumpkin seeds have associated benefits to bone health, management of diabetes mellitus, weight loss, immune functions, skin and eye health, etc. Pumpkin seeds anti-inflammatory and anticancer properties (WebMD, 2020). Pumpkin seeds contain carotenoids (lutein, zeaxanthin, β-carotene), flavonols, tyrosol, caffeic acid, vanillin, phenolic acids, pyrazine, p-hydroxybenzoic acid, saponins, flavonoids, squalene, unsaturated fatty acids, coumarins, triterpenoids, phytosterols, etc (Kulczyński et al., 2020; Dotto and Chacha, 2020; Cvetković et al., 2021).

Other seeds like those from avocado contain phytochemicals like flavonoids, alkaloids, saponins, tannins, etc. (Setyawan et al., 2021), which have antioxidant and anti-inflammatory properties. Phenols in avocado seeds mainly include catechins, ferulic acid, coumaric acid, chlorogenic acid, caffeic acid, hydroxybenzoic acid, etc., with therapeutic and medicinal benefits (Setyawan et al., 2021). Black seeds (*Nigella sativa* seeds) are also among excellent source of nutraceuticals (Kalonji, 2021), given the presence of *trans*-anethole, palmitic acid, oleic acid, linoleic acid, nigellidine, nigellicine, nigellimine N-oxide, nigellimine, etc (Kalonji, 2021). Aromatics in black seed include thymoquinone, β-pinene, α-pinene, thymol, α-thujene, carvacrol, *p*-cymene, dihydrothymoquinone, *trans*-anethole, etc. (Kalonji, 2021). Clinical trials have shown that black seeds benefits temporarily lower blood pressure (systolic and diastolic), however, evidence is little about black seed extracts to reduce LDL, total cholesterol, and triglycerides (Sahebkar et al., 2016).

3.6. Vegetables

Vegetables are considered as nutraceuticals given the many essential nutrients and phytochemicals present. Generally low in calories and high in vitamins, minerals, dietary fiber, and important phytochemicals, vegetables either eaten raw or cooked (Saiwal et al., 2019) and regularly consumed can help decrease in incidence of cardiovascular diseases, stroke, cancer, etc (Büchner et al., 2010). Vegetables, such as broccoli, cauliflower, zucchini, pumpkin, kale, spinach, scent leaves, etc., contain antioxidants, including vitamin A, C, and E, as well as polyphenols (Büchner et al., 2010). Vegetables also contain antinutrients and toxins like oxalic acid, enzyme inhibitors (of protease, amylase, cholinesterase, etc.), tannins, cyanide and precursors of cyanide, α-chaconine, α-solanine, etc, which can be managed by processing methods (Saiwal et al., 2019). Many phytochemicals in vegetables have excellent nutraceutical properties, ranging from the carotenoids in carrot, lycopene in tomato, etc (Jeong et al., 2013). Carotenoids are classified into two; carotenes and xantophylls, which are present in vegetables (Arya et al., 2019). Carotenes, e.g., beta carotene, and xanthophylls, e.g., astazanthin, zeaxanthin, canthaxantin, cryotpxanthin, etc., have a wide range of nutraceutical/health benefits (Arya et al., 2019). Carotenes α-, β-, ɣ-, ϒ- lycopene and lutein have protective effects against prostate, breast, uterine, colorectal, and lung tumors/cancers (Yoon et al., 2012).

Xanthophylls protect vitamin A, and E, as well as many other carotenoids from oxidation. Some xanthophylls, particularly canthaxantin, migrate to skin and protect it from harm by sunlight. Cryptoxanthin protects uterine, cervical, and vaginal tissues (Arya et al., 2019). Glucosinolates are commonly found in vegetables belonging to the family Cruciferae. They help induce the detoxifying enzymes in the liver, cytokines and white blood cells, and thus help boost immunity. Dithiolthiones, sulforaphane, and isothiocyanates are glucosinolates biotransformation products involved in blocking enzymes responsible for tumour growth in the lung, breast, gastrointestinal tracts, and liver (Arya et al., 2019). Phytosterols, present in green and yellow vegetables and their seeds, can effectively compete with dietary cholesterol absorption through intestines, and help to ease the excretion of cholesterol from the body, to alleviate cardiovascular disease risks (Awaishesh et al., 2013).

3.7. Nuts

Nuts are considered as nutrient dense foods with natural mix of important bioactive compounds/nutrients, which can range from vegetable protein, fat-soluble bioactives, polyunsaturated fats, minerals, dietary fibre, vitamins, to many other phytochemicals (Chang et al., 2016; Ros et al., 2021). Common nuts include tree nuts, almonds, macadamia nuts, cashews, pistachios, Brazil nuts, macadamias, pecans, cashews, walnuts, hazelnuts, pine nuts, etc. Their components synergistically and favorably influence vascular and metabolic physiology pathways, improve cardiovascular prognosis, and reduce the risk of cancer and cardiovascular diseases (Ros et al., 2021). Consumption of nuts also has moderate ameliorative effects on inflammation, endothelial function, blood pressure (BP), and glycaemic control, with beneficial effects on depression and cognitive function (Del Gobbo et al., 2015). For example, consuming 30 g of nuts per day, such as walnuts, hazelnuts, and almonds, could significantly lower the risk of many cardiovascular diseases (CVDs), including stroke, myocardial infarction. Including nuts in regular diets reduce the risk of stroke by 45%(Ros et al., 2021).

Nuts like almonds, cashews, etc., are very useful source of magnesium, very important in blood pressure management. Nuts are also enriched with oil, largely after vegetable oils as richest natural plant food oils (Kornsteiner-Krenn et al., 2013; ARS, 2019). The fatty acids in nuts are salutary with low amounts, largely between 4% and 16% (Ros et al., 2021). With about 10g/100g, walnuts are enriched with α-linolenic acid, a plant-based omega-3 fatty acid (Ros, 2010). Bioactive macronutrients in nuts provide medicinal and nutraceutical benefits to human body via frequent consumption (Ros et al., 2021). Dietary fibre via nut consumption help in body detoxification, prevention of diverticulosis, as well as promotion of intestinal health, etc (Ros, 2010). Nuts contain folate, including peanuts (ARS, 2019). Hazelnuts and almonds contain ample vitamins with antioxidant properties, such as tocopherol. Most polyphenolic compounds found in nuts outer peel, between the nut and the shell, which makes it a better reason to consume unpeeled, raw nuts (Del Gobbo et al., 2015; Estruch et al., 2018; Moreau et al., 2018; Ros and Hu, 2013Becerra-Tomás et al., 2019).

3.8. Whole grains

According to Shahidi (2009), the consumption of whole grains should be encouraged given the many important nutrients, including dietary fiber. Whole grains consumption supplies high nutrients such as dietary fiber, which when included in, for instance, breakfast can improve the intake of micronutrient and reduce disease risks such as type 2 diabetes mellitus (T2DM), coronary heart disease, etc (Aune et al., 2016; Priebe and McMonagle, 2016; Shahidi, 2009; Williams et al., 2014; Zeng et al., 2018). The regular consumption of whole grains may also lower increased triglyceride levels and LDL (Aune et al., 2016), which helps to tackle diabetes, obesity, and hypertension (Kelly et al., 2017), given the presence of the many bioactive phytochemicals, including phenolic acids, carotenoids, tocopherols, alkylresorcinols, benzoxazinoids, phytosterols, and lignans, as well as many derivatives of cinnamic and benzoic acids, flavonoids, flavanols and flavones (Luthria et al., 2015; Mey et al., 2021; Belobrajdic and Bird, 2013; Xu et al., 2022), some of which are found at the (grain) outer structures, especially the aleurone layers and pericarp seed coat (Zhu and Sang, 2017; Zabolotneva et al., 2022). Phenolic acids in most grains are concentrated in embryo cell walls and bran, and mostly exist in insoluble bound form, with soluble-conjugated and free forms at minor levels (Mey et al., 2021; Xu et al., 2022). Other phytochemicals in wholegrains that may play a protective role against diseases include several carotenoids, such as α- carotene, lutein, β-carotene, zeaxanthin, and β-cryptoxanthin (Belobrajdic and Bird, 2013).

Examples of whole grains would include major cereals, such as wheat (durum, kamut, farro einkorn, emmer, spelt), barley (hulled, dehulled), rice (brown, black, red, etc.), rye, oats, and corn/maize; minor cereals, such as millets, job's tears, canary grass, fonio, sorghum, wild rice, triticale, and teff, as well as pseudocereals (Priebe and McMonagle, 2016; Shahidi, 2009; Zeng et al., 2018). For instance, oats contain good amounts of phenolic acids, phytosterols, vitamin E, carotenoids, soluble dietary fiber (especially β-glucan), flavonoids, etc. (Sang and Chu, 2017). Maize (corn) also contain important phytochemicals, for instance, in corn silk and corn seeds (Nawaz et al., 2018; Bujang et al., 2021; Miranda et al., 2021). Despite proteins from cereals having low biological value given the reduced essential amino acids (Shewry and Hey, 2015), pseudocereals proteins have high nutritional value, closely similar to casein, a major protein in milk (Saturni et al., 2010). Amaranth and quinoa are among the most nutrient dense grains because of their high content of quality proteins, which have high amounts of essential amino acids, including lysine (Robin et al., 2015).

3.9. Fermented foods

Fermented foods, such as yoghurt, sauerkraut, soy products, tempeh, kefir, barley, kimchi, rice bran, kombucha, etc., are rich in nutraceuticals (Islam et al., 2019), which have immune-modulatory, antioxidant, chemoprotective, anti-inflammatory, cardioprotective, immune boosting, and anticancer, and antidiabetic properties. Microorganisms mostly used for fermentation include yeasts and lactic acid bacteria, which help to enhance nutrient bioavailability and functioning of bioactive compounds (Islam et al., 2019). Besides fermentation of vegetable milk substitutes obtained from chickpeas and broad beans, DPPH radical scavenging ability significantly increased after enzymatic hydrolysis for both legumes. Lactic fermentation results in increased DPPH radical scavenging activity, with promising health benefit (Vasilean et al.,2021).

Another important fermented nutraceutical is yogurt, which has beneficial bacterial strains that make it a potent probiotics source. The fermented food matrix of yogurt makes it unique, where it helps to enhance nutrient digestion and absorption (Fernandez and Marette, 2017). Consumption of yogurt is associated with a low risk of type 2 diabetes mellitus and decreased weight gain (Fernandez and Marette, 2017). Yogurt benefits digestive health, strengthens immune system, protects against osteoporosis, as well as promotes weight management, etc. An example is sauerkraut, which is high in vitamins K and C; the process of sauerkraut fermentation improves nutrients bioavailability, thus making sauerkraut more beneficial than cabbage (Lipski, 2013).

Additionally, there is the example of citrus blended vinegars (CBVs), which has been understood to significantly decrease the lipid accumulation and intracellular triglyceride, and improved anti-obesity gene levels. Citrus blended vinegars also exerted anti-aging activities, largely by increasing cell lifespan and viability, while reducing senescence-related genes expression under oxidative stress induced by H_2O_2 (Yun et al., 2021). By studying the influence of fermentation of pasteurised papaya puree with different lactic acid bacterial strains, Mashitoa et al. (2021) was able to prepare papaya as puree, thereafter pasteurised, and fermented for 2 days at 37 °C, then stored at 4 °C for 7 days. The lactic acid bacteria strains included *Leuconostoc pseudomesenteroides*, *Weissella cibaria*, and *Lactiplantibacillus plantarum*. Non-fermented samples at 0, 2, and 7 days were used as controls. The fermentation by *Weissella cibaria* and *Lactiplantibacillus plantarum* increased the recovery (%) of ferulic acid, vanillic acid, catechin, chlorogenic acid, epicatechin, quercetin, ellagic acid, and syringic acid in intestinal fractions in comparison with the *Lactiplantibacillus plantarum* and 7 day-non-fermented sample. The papaya puree fermented with *Leuconostoc pseudomesenteroides* had the highest inhibitory effects on α-glucosidase activities followed by that of *Lactiplantibacillus plantarum*.

3.10. Honey

Honey is the viscous and sweet edible secretion made by bees, mostly honey bees (Grüter, 2020), and widely considered in herbal and traditional medicine as an antibiotic (Boukraâ, 2014). Natural honey usage as a nutraceutical is largely associated with its nutritional and bioactive compositions, as well as its therapeutic properties. Due to the floral diversity in their sources of pollen, bees might have the capability of choosing nectar varieties with positive effects on overall health (Berenbaum and Calla, 2021). Organic acids are the major acids in honey, constituting around 0.17 to 1.17%

of the mix, with the most prevalent being gluconic acid produced by glucose oxidase actions. Other organic acids present include succinic, palmitic, formic, capronic, valeric, propionic, acetic, pyroglutamic, malic, lactic, citric, and butyric acids, among others, most of which have antimicrobial, gut pH modulation, and health promoting properties (Boukraâ, 2014).

Honey has been shown to possess antibacterial properties against gram+ve and gram–ve bacteria (Nolan et al., 2019; Okpala, 2019). Honey are believed to possess such components as hydrogen peroxide, and methylglyoxal, which are believed to be under preliminary studies for potential antibiotic application (Anfang et al., 2018). Honey could also control the side effects of chemotherapy or radiation therapy used in cancer treatment (Bardy et al., 2008). Honey comprises calories majority from fructose, which does not increase weight gain, although it can temporarily increase blood sugar level (Sievenpiper et al., 2012). Honey is reported to help treat several ailments, such as skin burns, gastric disturbances, skin wounds, and ulcers (Pećanac et al., 2013). Honey possesses a number of bioactive compounds, such as pinobanksin, caffeic acid, p-coumaric acid, kaempferol, galangin, apigenin, quercetin, chrysin, gallic acid, eugenol, naringin, luteolin, syringic acid, isorhamnetin, pinocembrin, and ferulic acid; which have antioxidant, anticancer, antidiabetic, anti-inflammatory, immune boosting, blood pressure lowering, antihistamine, antimicrobial, cognitive, cardioprotective, and nervous improving properties (Martinez-Armenta et al., 2021).

3.11. Seafood (fish)

Seafood (fishes) have several roles as nutraceuticals, including fatty fish, such as salmon, trout, herring, and sardines. They generally have high levels of essential fatty acids, including omega-3 fatty acids, that reduce the risks of cardiovascular diseases (heart diseases) and can improve the health of infants when consumed by pregnant or breastfeeding women (Ellis, 2021). Anchovies, cod, mackerel, etc. are good choices. Fish oil products contain fatty acids mixtures with high omega-3 (*n*-3) polyunsaturated fatty acids (PUFAs). Part of the main ingredients include polyunsaturated fatty acids, which include the n-6 series, such as linoleic acid, arachidonic acid precursor, a prostaglandins source, thromboxanes, and leukotrienes, and the *n*-3 series, such as α-linolenic acid, and highly unsaturated fatty acids (HUFA) (Telessy, 2019). The omega-6 fatty acids in fish oil, such as cod liver oil, is >5%, while omega-3 is 20–25%. In general, daily foods contain 5–20 times much omega-6 highly unsaturated fatty acids than omega-3 highly unsaturated fatty acids (Beydoun et al., 2015).

Generally, seafood contains many nutrients with nutraceutical properties, including proteins, peptides, long-chain omega-3 polyunsaturated fatty acids, copper, zinc, calcium, essential amino acids, vitamin B_{12}, sodium, iodine, selenium, potassium, etc. (Venugopal, 2018). Commercial processing of fish produces approximately over 30 million metric tonnes of discards containing fish skin, fin, intestines, bones, shell, head, etc. (Kim, 2017; Venugopal, 2018; Ashraf et al., 2020). The discards of seafood provide some important compounds like collagen, chitosan, chitin, gelatin, calcium, protein hydrolyzates, carotenoids, oil, enzymes, peptides, etc., all of which have promising nutraceutical properties (Sachindra and Mahendrakar, 2015; Hamed et al., 2015; Suleria et al., 2016; Anal, 2017). There is increased interest on nutraceuticals from seafood for functional formulations to alleviate, prevent, and/or treat many diseases (Suleria et al., 2016). Black Sea anchovy processing constitutes about 32% (w/w) discards containing the frame, viscera, and head. They contain protein, fat, lysine, leucine, polyunsaturated fatty acids, and minerals. The discards of Black Sea anchovy are used as the raw material for fish oils, protein powder, mineral supplements, and protein hydrolyzates (Gencbay and Turhan, 2016; Stephen et al., 2022).

Most seafood also produce many secondary metabolites, including terpenoids, alkaloids, peptides, sulfated polysaccharides, carotenoids, etc., which contribute to their survival (Venugopal, 2018). These secondary metabolites have many bioactivities/benefits as nutraceuticals, including neuroprotective, anti-atherosclerotic, antihypertensive, antioxidant, anticancer, antimicrobial, anticoagulant, antiviral, anti-inflammatory, anti-obesity, appetite-suppressing, muscle relaxant, cardioactive, antidiabetic, hypotensive, analgesic, antibiotic, and immunomodulatory properties (Correia-da-Silva et al., 2017; Ashraf et al., 2020; Stephen et al., 2022). Sourcing medicinal compounds and nutraceuticals from seafood, including tilapia, perch, mollusks, sea slugs, bryozoans, salmon, shrimp, tunicates, tuna, sponges, etc., has increased recently with the aim and potentials of controlling several diseases (Suleria et al., 2016). By-products from lobster processing are considered as valued sources of bioactive compounds with potentials for nutraceutical, medicinal, pharmaceutical, and pharmacological applications (Awuchi et al., 2022).

4. Major bioactive components of nutraceuticals

Foods and agricultural commodities contain bioactive constituents mostly responsible for their nutraceutical functions. Major bioactive components of nutraceuticals are shown in Table 3, which include dietary fibre, essential fatty acids, minerals, phytochemicals, pre-/probiotics, as well as vitamins. We briefly discuss these, with examples specific to the context of nutraceuticals.

4.1. Minerals and vitamins (antioxidant)

Largely, minerals are believed to demonstrate diverse potentials in human homeostasis and metabolism. As mineral deficiency can lead to many disease conditions/disorders, the adequate intake would help maintain a healthy body (Gharibzahedi and Jafari, 2017) . Important nutraceutical functions can come from such minerals like calcium, sodium, potassium, magnesium, phosphorus, sulfur, and chloride, including trace minerals, such as iodine, zinc, iron, copper, cobalt, manganese, selenium, fluoride,etc. The biological and physiological processes of minerals suggest nutraceutical roles especially for people within 31 to 50 years, male or female (not pregnant, not lactating), which is further depicted in Table 4 (Schlenker and Gilbert, 2014; Minister of Health, Labour and Welfare, Japan, 2015; Food and Nutrition Board, 2020).

There are promising human health benefits associated with minerals, which are found in various foods. For instance, iodine fortification of salt has led to significant decrease in the goiter incidence (Gómez-Galera et al., 2013). Selenium exerts natural effects through incorporating into seleno-proteins, which play significant role in regulating ROS and redox states practically in every tissue. Zinc plays an important role in several body functions, for example, immune cells function and growth. Given its role in homeostasis well regulated in every cell, when zinc is compromised, making the human body vulnerable to cancer, autoimmune diseases, infections, and allergies (Bhowmik et al., 2010). Moreover, some vitamins are known to have strong antioxidant properties, like vitamins E and C. Despite many foods containing them, food fortification with like vitamins A, E, D, etc. would improve health and help prevent such disease conditions as heart disease, vision

Table 3. Major bioactive components of nutraceuticals

Bioactive component	Examples	Nutraceutical effects	References
Dietary fiber	Mucilages, beta-glucan, pectin, cellulose, hemicellulose, lignin	Fiber binds to excess fat and glucose, moving them to large intestine for defecation via stool. Fiber also helps in body detoxification mechanisms and prevention of diverticulosis. Fiber helps prevent excess fats and sugar in the blood, thus, reducing the risks of CVDs, obesity, and T2DM.	He et al., 2010; Ambuja and Rajakumar, 2018
Essential fatty acids	Alpha-linolenic acid, linoleic acid, docosahexaenoic acid, eicosapentaenoic acid, docosapentaenoic acid, etc.	Essential fatty acids perform many important functions in the body, including cardioprotective, immune boosting, antimicrobial, metabolic, heart promoting, anti-inflammatory, and health promoting functions. Adequate intake of essential fatty acids has many health and nutraceutical benefits, including improvement in brain health, reduced depression, reduced joint pain from rheumatoid arthritis, improved cognition, improved heart health, reduced risk of atherosclerosis, reduced risk of heart disease, reduction in triglycerides, reduced inflammation, improved blood pressure, etc.	Hengeveld et al., 2018; Herrera Vielma et al., 2021; Joshi et al., 2022
Minerals	Calcium, sodium, potassium, magnesium, phosphorus, sulfur, chloride, iodine, zinc, iron, copper, cobalt, manganese, selenium, fluoride, etc.	Minerals play many biological and physiological roles and have many potentials in homeostasis and metabolism. See Table 4 for the nutraceutical roles of specific minerals	Gharibzahedi and Jafari, 2017
Phytochemicals	Polyphenols, alkaloids, glycosides, terpenes and terpenoids, etc.	Many phytochemicals exert important impacts on human and animal health system and provide many medicinal benefits on health, including helping in preventing and/or treating physiological disorders and many diseases. Many phytochemicals have antioxidant, cardioprotective, immune boosting, antimicrobial, metabolic, heart promoting, anti-inflammatory, and health promoting properties, among others.	Howes et al., 2020; Yeh et al., 2022
Prebiotics	Resistant starch, oligosaccharides (galacto-oligosaccharides, inulin, and fructo-oligosaccharides), guar gum, pectin	In the colon, they serve as substrates for many beneficial bacteria, resulting in improved colon-pH reduction and short-chain fatty acids production, and act as selective stimulants to their proliferation. The short-chain fatty acids also have antioxidant (ROS scavenger), antiproliferative (regulation of apoptosis, signal transduction, and gene expression), and anti-inflammatory (reduced PGE2 and pro-inflammatory cytokines) properties.	Kellow et al., 2014; Zaman et al., 2015
Probiotics	*Lactobacillus plantarum, Leuconostoc argentinum, Leuconostoc citreum, Lactobacillus brevis, Pediococcus pentosaceus, etc.*	Probiotics have been associated with the prevention and/or treatment of many diseases and conditions, including diarrhea (antibiotic-induced diarrhea, travellers diarrhea, acute diarrhea), Crohn's disease, lactose intolerance, *Helicobacter pylori* infection, pouchitis, ulcerative colitis, metabolic diseases (e.g., dyslipidemia, obesity, diabetes mellitus), impaired immunity (allergic conditions), respiratory tract infections, neurological and mental health conditions, acute otitis media, allergies (eczema, milk allergy, etc.), depression and anxiety, dermatitis (eczema), childhood asthma, bacterial vaginosis, high blood pressure, inflammatory bowel disease, etc.	Cuello-Garcia et al., 2015; Saez-Lara et al., 2015; Dolan et al., 2016; Parker et al., 2016; Williamson et al., 2017; Robles-Vera et al., 2017; Lin et al., 2018; Guo et al., 2019; Scott et al., 2019; Ansari et al., 2020; Collinson et al., 2020
Vitamins	Vitamins A, E, D, etc.	Vitamins improve health and can prevent diseases such as heart disease, vision loss, cancer, osteoporosis, immune system suppression, osteoarthritis, T2DM, and CVDs, and improves survival and quality of life. Antioxidant vitamins, such as vitamins C and E, inhibit oxidation process in the body and prevent the actions of reactive oxygen species (ROS) and free radicals, thus ensuring overall health and the prevention of many acute and chronic diseases.	Öztürk, 2017; Xiao and Li, 2020

Table 4. Common nutraceutical roles of minerals in biological and physiological processes for people within 31 to 50 years, male or female (not pregnant, not lactating)

Dietary element	High nutrient density dietary sources	Category	Excess	Deficiency	Recommended Dietary Allowance (RDA)/ Adequate intake (AI) Male/Female [mg]
Calcium	Milk, dairy products, eggs, green leafy vegetables, fish with bones (sardines, salmon, etc.), tofu, thyme, nuts, seeds, oregano, etc.	Builds bone; needed for healthy muscle, digestive system, and heart; helps in blood clotting; supports function and synthesis of blood cells	hypercalcaemia	hypocalcaemia	1,000
Chlorine	Table salt (NaCl)	Needed for hydrochloric acid production in the stomach, as well as in the functions of cellular pump	hyperchloremia	hypochloremia	2,300
Chromium	Broccoli, meat, grape juice, whole grains, etc.	Involved in the metabolism of glucose and lipid	Chromium toxicity	Chromium deficiency	0.035/0.25
Cobalt	Required in synthesizing vitamin B12, however, as bacteria are required for vitamin B12 synthesis, it is normally regarded as part of vitamin B12 that is obtained from consuming foods from animal sources (e.g., eggs)	Enzyme with *cobalt* as its essential cofactor takes part in translation regulation; also, *cobalt* may be an oxygen sensor constituent.	Cobalt poisoning	Cobalt deficiency	none
Copper	Liver, oysters, seeds, nuts, seafood, legumes, whole grains, etc.	Required cytochrome c oxidase co-factor. Along with iron, copper helps the body to form red blood cells (RBCs). Helps in maintaining healthy blood vessels, bones, iron absorption, nerves, and immune functions	Copper toxicity	Copper deficiency	0.9
Iodine	Iodized salt, seaweed (kombu, kelp), eggs, grains	Required for synthesizing thyroid hormones, which control many body functions such as growth, development, etc.	Hyperthyroidism, iodism	Goiter, iodine deficiency	0.150
Iron	Meat, nuts, seafood, dark chocolate, beans, etc.	Required for several proteins, including enzymes, especially hemoglobin for the prevention of anemia. Involves in synthesizing hemopglobin for new RBCs	iron overload disorder	iron deficiency	8/18
Magnesium	Spinach, whole grains, legumes, avocado, nuts, seeds, peanut butter, etc.	Required for bones and for ATP processing. Essential for muscle and nerve functions, and helps in maintaining carbohydrates metabolism, bone health, regulating blood sugar, etc.	hypermagnesemia	hypomagnesemia, magnesium deficiency	420/320

Table 4. Common nutraceutical roles of minerals in biological and physiological processes for people within 31 to 50 years, male or female (not pregnant, not lactating) - *(continued)*

Dietary element	High nutrient density dietary sources	Category	Excess	Deficiency	Recommended Dietary Allowance (RDA)/ Adequate intake (AI) Male/Female [mg]
Manganese	Grains, nuts, leafy vegetables, coffee, legumes, seeds, tea, etc.	Required superoxide dismutase co-factor. Involves in metabolism of amino acids, glucose, cholesterol, and carbohydrates. Involves in bone formation, scavenging reactive oxygen species, immune response, and reproduction. Involves in blood clotting and hemostasis	manganism	manganese deficiency	2.3/1.8
Molybdenum	Legumes, nuts, whole grains, etc.	Required for proper xanthine oxidase, sulfite oxidase, and aldehyde oxidase functioning. Oxygen transfer reaction functions	Molybdenum toxicity	Molybdenum deficiency	0.045
Phosphorus	Red meat, poultry, fish, dairy foods, oats, bread, rice. Often occurs as phosphate	A constituent of bones, DNA, ATP, energy processing, cells, etc. Helps keep heartbeat steady, kidney filter wastes, energy storage, tissue repair and development, breakdown of macromolecules, etc.	hyperphosphatemia	hypophosphatemia	700
Potassium	Sweet potato, lentils, milk and dairy products, potato, carrot, beans, tomato, prune, orange, seafood, banana, etc.	Systemic electrolyte. Essential in ATP coregulating with sodium. Involves in regulating water balance, heart functions, muscle contractions, etc.	hyperkalemia	hypokalemia	4,700
Selenium	Brazil nuts, meats, grains, seafoods, milk and dairy products, organ meats, eggs, etc.	Essential to antioxidant enzymes activity, including glutathione peroxidase	selenosis	selenium deficiency	0.055
Sodium	Table salt (NaCl), milk, spinach, sea vegetables, etc.	Systemic electrolyte. Essential in ATP coregulating with potassium. Plays role in muscle and nerve functions	hypernatremia	hyponatremia	1,500
Zinc	Oysters, nuts, poultry, milk and dairy products, whole grains, red meat, etc.	Required for many enzymes, including matrix metalloproteinases, carbonic anhydrase, liver alcohol dehydrogenase, zinc finger proteins, etc.	zinc toxicity	zinc deficiency	11/8

Sources: Schlenker and Gilbert (2014); Minister of Health, Labour and Welfare, Japan (2015); Food and Nutrition Board (2020).

loss, cancer, osteoporosis, immune system suppression, osteoarthritis, T2DM, and CVDs (Öztürk, 2017). Antioxidant vitamins, by inhibiting oxidation processes, prevent the actions of reactive oxygen species (ROS)/free radicals (Xiao and Li, 2020). Given that over 2 billion individuals globally are believed as deficient in at least one micronutrient (Arshad et al., 2021), the sufficient intake of vitamins would help save lives, and maintain livelihood. Strong vitamin fortification should improve the vitamins bioavailability, with no unwanted reaction (Knijnenburg et al., 2019).

4.2. Essential fatty acids

Essential fatty acids (EFAs) are fatty acids that animals, including humans, must consume as required for good health, but unable to synthesize. Two major EFAs with important nutraceutical properties include omega-3 fatty acid known as alpha-linolenic acid (ALA) and omega-6 fatty acid known as linoleic acid (Kaur et al., 2014). The adaptation of EFAs help to produce eicosanoids (that influence inflammation and cellular functions); lipoxins, eicosanoid derivatives, produced by the lipoxygenase pathway from omega-6 fatty acids and resolvins from omega-3 (in acetylsalicylic acid presence, downregulating inflammation); endocannabinoids (that affect behavior, inflammation, mood, etc.); and, neuroprotectin D, epoxyeicosatrienoic acids, neurofurans, hepoxilins, isoprostanes, and isofurans (Kaur et al., 2014; Joshi et al., 2022; Herrera Vielma et al., 2021; Chen et al., 2021).

EFAs perform many important functions in the body, including cardioprotective, immune boosting, antimicrobial, metabolic, heart promoting, anti-inflammatory, and health promoting functions (Reiffel and McDonald, 2006; Joshi et al., 2022). In the US, for example, the Adequate Intake (AI) for omega-3 fatty acids relies on the median intake for adult women and men are 1.1 g/day and 1.6 g/day, respectively. For omega-6 fatty acids, the AI is for linoleic acid, and relies upon the median intake; 14 g/day and 17 g/day for old men (50 years and above) and younger men respectively; 11 g/day and 12 g/d for women (above 50) and for younger women, respectively (James et al., 2019). By help prevent the clumping together of blood platelets, omega-3 fatty acids as EFAs improve brain health, reduce joint pain from rheumatoid arthritis, and improve cognition, heart health, and reduce risk of heart disease, triglycerides, inflammation, etc (Hengeveld et al., 2018).

4.3. Dietary fibre and prebiotics

Dietary fiber comprises of polysaccharides found in several foods of plant origin ,like mucilages, beta-glucan, and pectin considered as soluble, whereas cellulose, hemicellulose, and lignin considered insoluble (Chawla and Patil, 2010). Foods fortified with fiber are understood to help improve their nutraceutical properties, nutrient profile, structural properties, shelf life, and sensory qualities (Ambuja and Rajakumar, 2018). Passing undigested and unabsorbed into the large intestine, dietary fiber functions to work against many disease/health conditions in human, by binding to excess fat and glucose, moving them to large intestine for defecation via stool. Also, fiber also helps the human's detoxification mechanisms, as well as prevents excess fats and sugar in the blood, thus, reducing the risks of CVDs, obesity, and T2DM (He et al., 2010; Ambuja and Rajakumar, 2018).

Among dietary fibers, include prebiotics considered as plant-based carbohydrates, poorly metabolized and/or absorbed, and nondigestible in the small intestine. Fermented in the colon, however, prebiotics facilitate local microbes that produce lactic acid. Common prebiotics include resistant starch, oligosaccharides (galacto-oligosaccharides, inulin, and fructo-oligosaccharides), guar gum, and pectin. Prebiotics are largely characterised by their water-holding capacity, viscosity, fermentability (in the colon), water-solubility, as well as their capacity to support probiotics (Kuo, 2013). As substrates for many beneficial bacteria in the colon, prebiotics help improve colon-pH reduction and short-chain fatty acids production that provide energy to mucosal cells, and stimulating (mucosal) blood flow. Short-chain fatty acids possess antioxidant (ROS scavenger), antiproliferative (regulation of apoptosis, signal transduction, and gene expression), and anti-inflammatory (reduced PGE2 and pro-inflammatory cytokines) properties (Kellow et al., 2014; Pandey et al., 2015; Zaman et al., 2015).

4.4. Phytochemicals (bioactive compounds)

Many foods with nutraceutical properties, including vegetables, herbs (medicinal plants), fruits, whole grains, and beans, contain important phytochemicals that provide human body systems with excellent physiological and health benefits (Howes et al., 2020; Awuchi and Twinomuhwezi, 2021; Messaoudi et al., 2022; Rafiq et al., 2022; Yeh et al., 2022). For instance, salicin that was originally extracted from white willow tree's bar, later produced synthetically to become aspirin, has pain-relieving and anti-inflammatory properties. An important cancer drug, Paclitaxel, is isolated from English yew tree. Besides, phytochemicals with established body functions have also been considered as essential micronutrients (Palermo et al., 2014; U.S. Food and Drug Administration, 2017). While some phytochemicals do serve as nutraceuticals in ageing-related cognitive functions (Howes et al., 2020; Yeh et al., 2022), some interfere with nutrients' absorption and are considered as antinutrients (Palermo et al., 2014; U.S. Food and Drug Administration, 2017). Generally speaking, phytochemicals like polyphenols, alkaloids, glycosides, terpenes and terpenoids, etc., have proven nutraceutical, therapeutic, and medicinal properties, even though some are also toxic even in small doses (US Department of Agriculture, 2016).

4.5. Probiotics

Probiotics provide health benefits and their function in the food industry and healthcare system remains broad, from probiotic medical foods, probiotic drug, probiotic animal feed, probiotic infant formula, probiotic snack, probiotic dietary supplement, to probiotic food, etc. (de Simone, 2018). Live probiotic cultures are among constituents of fermented dairy products, probiotic-fortified foods, and other fermented foods, mostly administered/consumed orally, even though other forms of dosage do exist. Most action mechanisms of probiotics range from competing with pathogens, antimicrobial agents' production, reducing gastrointestinal discomfort, antagonizing gastrointestinal pathogens, immunmodulation, to modifying toxins/toxin-receptors (Carding et al., 2015; Durchschein et al., 2016; Turck et al., 2019). Probiotics have been associated with helping in preventing as well as treating many diseases and conditions, from diarrhea (antibiotic-induced diarrhea, travellers diarrhea, acute diarrhea), Crohn's disease, lactose intolerance, *Helicobacter pylori* infection, pouchitis, ulcerative colitis, metabolic diseases (e.g., dyslipidemia, obesity, diabetes mellitus), impaired immunity (allergic conditions), respiratory tract infections, neurological and mental health conditions, to acute otitis media, as well as allergies (eczema, milk allergy, etc.) (Cuello-Garcia et al., 2015; Saez-Lara et al., 2015; Dolan et al., 2016; Parker et al., 2016; Williamson et al., 2017; Ro-

bles-Vera et al., 2017; Lin et al., 2018; Guo et al., 2019; Scott et al., 2019; Ansari et al., 2020; Collinson et al., 2020).

Many fermented products (industrial and traditional) possess lactic acid bacteria (LAB). Examples include dairy products (e.g., yogurt, buttermilk, kefir), vegetables (e.g., sauerkraut, kimchi pao cai, pickled vegetables), soy products (e.g., miso, soy sauce, tempeh), etc. (Breidt et al., 2013; Shiby and Mishra, 2013; Swain et al., 2014). For instance, kimchi contains probiotic bacteria such as *Weissella* spp., *Leuconostoc* spp., and *Lactobacillus* spp. Sauerkraut contains probiotic bacteria such as *Weissella* spp, *Lactobacillus coryniformis*, *Leuconostoc mesenteroides, Lactobacillus paraplantarum, Lactobacillus plantarum, Leuconostoc argentinum, Leuconostoc citreum, Lactobacillus brevis, Pediococcus pentosaceus, etc*. Another example is kefir that contains *Leuconostoc* species, *Lactococcus lactis*, *Lactobacillus kefiranofaciens, Lactobacillus helveticus, Lactobacillus acidophilus, Lactobacillus delbrueckii* subsp. *bulgaricus, Streptococcus thermophilus, Bifidobacterium bifidum,* etc. (Guzel-Seydim et al., 2011; Bauer, 2017). Pao cai contains the probictics *L. fermentum, L. lactis*, *Lactobacillus brevis, Leuconostoc mesenteroides, L. pentosus, L. plantarum, etc.* Buttermilk contains *L. bulgaricus or Lactococcus lactis*. Kombucha contains acidic bacteria believed to be probiotics (Bauer, 2017), and contains *Zygosaccharomyces* sp., *Gluconacetobacter xylinus*, *Gluconobacter oxydans, Acetobacter aceti*, and *Acetobacter pasteurianus* (Jayabalan et al., 2014). Despite the Generally Recognised As Safe (GRAS) status by relevant authorities across countries, the use of probiotics still demands some caution given the associated risks especially among vulnerable population (Doron and Snydman, 2015; Didari et al., 2014; Scourboutakos et al., 2017).

5. Formulation of nutraceuticals, especially functional foods

While some natural foods with nutraceutical effects, e.g., fruits and vegetables, often may not require formulation, many nutraceuticals are developed or formulated in nutraceutical industries. Food formulation is among critical aspects of food processing, which demands different techniques, especially for nutraceuticals such as the formulation of functional foods. Many technologies, including novel technologies such as 3D printing, have helped to enhance the production of nutraceuticals (Morya et al., 2022a,b). Our major focus in this section is on functional foods. The formulation of nutraceuticals such as functional foods can be designed to remove and/or replace some ingredients, add bioactive compounds, and/or reduce some components; thereby obtaining:

1. *Enhanced food*: in this case, the bioactive compound content is improved using some breeding practice (such as omega-3 in eggs), genetic practice (such as vitamin A in rice), and/or agricultural practice;
2. *Light food*: in this case, there is intentional reduction in an undesired component's concentration (such as low/reduced sugar, low/reduced fat);
3. *Fortified/enriched food*: in this case, the bioactive compound (such as calcium, iodine, specific vitamins, probiotics, prebiotics, etc.) is added (fortified) or its concentration is increased (enriched); (McClements et al., 2015).

For the replacement/removal of ingredient, among the major concerns include excess sugar consumption, which have been overcome by many available recipes including non-nutritive sweeteners (such as aspartame, sucralose, acesulfame-K), low-calorie carbohydrates (such as maltodextrin, polydextrose, oligofructose), or a combination of both (Luo et al., 2019). Fat mimetics for the modulation of lipid digestion and/or the reduction of calorie intake is another area of research interest (Guo et al., 2017; Martins et al., 2018). Organogels, emulsions as well as fat replacement are among ingredients able to resolve the second formulation interventions' target (bioactive compounds delivery)(Salvia-Trujillo et al., 2017; Calligaris et al., 2020). Additionally, phenolic-enriched ingredients for glycemic response control include bakery products formulated using spent coffee grounds, apple pomace, onion skin, etc. (Martinez-Saez et al., 2017; Alongi et al., 2019).

6. Health benefits involving disease prevention by nutraceuticals

6.1. Early development/growth, cognitive functions, and immune boosting

In early development, nutrition has short- and long-term effects on body development, functions, growth, and composition. Pregnancy, childbirth, and breast milk composition are affected by food consumption. Pregnancy along with the succeeding postnatal months are critical for development of sensory, cognitive abilities, immune responses, maturation, nervous system, intestinal growth, and bone mass (Koletzko et al., 2019; Abrahams and Lund, 2022). Some nutraceuticals are formulated to provide adequate nutrient intake to both child and mother, e.g., folic acid addition to baked products, cereals, flour, etc., to prevent the occurrence of neural tube defects in newborn (Dessie et al., 2017). Nutraceuticals that are considered immune boosters include extracts from coneflowers, *Echinacea purpurea, E. angustfolia*, *E. pillida*, fruits, vegetables, *Astragalus membranaceus*, berries, *Astragalus mongolicus*, etc. *Astragalus* stimulates stem cells' transformation and development in the lymph and marrow tissues to very active immune cells. Soy isoflavones have received special interest as potent better alternatives to the modulators of synthetic selective estrogen receptor presently used in hormone replacement therapies (Limer and Speirs, 2004; Sionek et al., 2021).

Several plants, e.g., cannabis, balm, ginseng, guarana, valerian, etc., and foods components, e.g., theophylline, theobromine, caffeine, and cannabinoids, have established positive effects on mental health and cognitive performance (Thaung Zaw et al., 2017; Barfoot et al., 2019). More so, the effects of probiotics and herbal medicines on immune defense and the functions of intestinal epithelial cells have opened novel use of nutraceuticals, such as probiotics in clinical applications. For instance, probiotics are effective against recurring *Clostridium difficile* induced infection and children's infectious diarrhea. Probiotics supplementation may potentiate lymphoid tissue's maturational signals and enhance the balance of anti- and pro-inflammatory cytokines (Carding et al., 2015; Durchschein et al., 2016; Turck et al., 2019). Besides probiotics acting on intestinal flora to maintain normal balance, immune functions can be enhanced by dietary fiber, antioxidants, vitamins, honey, polyphenols, etc (Dwyer et al., 2015; Singla et al., 2019; Das et al., 2020).

6.2. Diabetes mellitus (DM)

Nutraceuticals have shown to be effective in preventing and managing/treating DM. Type 2 diabetes mellitus (T2DM), the most common DM, constitute over 95% of all DM cases, and has been linked to obesity. The number of those suffering from DM worldwide is increasing, especially T2DM (Roshan and Stanton, 2013; Tavafi, 2013; Nasri et al., 2014; Bahmani et al., 2014). Several

herbal supplements, herbal medicines, and dietary measures have been scientifically shown to ameliorate T2DM in preclinical and clinical studies, although only few have been proved effective in controlled randomized clinical trials (Rafieian-Kopaei and Nasri, 2013; Rahimi-Madiseh et al., 2014). Isoflavones are phytoestrogens similar in functions and structures to estrogen. Soy isoflavones consumption is associated with lower rate of T2DM incidence and mortality (Awuchi et al., 2021; Egbuna et al., 2021). Omega-3 fats are believed to decrease glucose tolerance in those at risk of DM. Insulin is required for the long chain omega-3 fatty acids synthesis; as a consequence, the heart might be affected by their depletion in DM. Omega-3 fatty acids ethyl esters may be beneficial against DM. Lipoic acid has antioxidant properties and is used in treating diabetic neuropathy. It appears effective for long-term diet-based protection against DM complications. Psyllium dietary fibers are widely used to reduce levels of lipid in hyperlipidemia, as pharmacological supplement, for glucose control in people with DM, to aid reduction in weight, as food ingredients, among other uses. Many extracts from plants, including cinnamon, bitter melon, *Toucrium polium*, etc., treat and/or prevent T2DM (Nasri and Rafi, 2013; Salvia-Trujillo et al., 2017; Calligaris et al., 2020).

6.3. Alzheimer's disease (AD) and Parkinson's disease (PD)

Alzheimer's disease (AD) affects some individuals worldwide. It is among the most commonly known dementia, affecting memory and mental functions. AD is mostly diagnosed in those aged 65 years and above, however, early-onset Alzheimer's may manifest early. AD affects women more compared with their men counterpart, at about 2:1 ratio. Oxidative stress may potentiate many neurodegenerative disorders such as AD. Antioxidant compounds with nutraceutical properties, including curcumin, turmerin, β-carotene, lutein, lycopene, etc., may ameliorate diseases such as AD by preventing and/or curbing oxidative stress. There are growing belief that use of nutraceuticals can slow dementia development, including AD. Many medicinal plants, including *Zizyphus jujube*, *Lavandula officinalis,* have been reported to slow and ameliorate AD, memory loss, and learning difficulties (Rabiei et al., 2013; Rabiei et al., 2014).

Parkinson's disease (PD), or Parkinson's, is a central nervous system's degenerative disorder that affect motor system (Han et al., 2018). The motor symptoms are caused by the dopamine-generating cells' destruction in substantia nigra. The obvious symptoms include movement-related symptoms such as shaking, rigidity, difficulty in walking/gait, behavioral and thinking problems, and slow movement (Tambasco et al., 2018; Orgeta et al., 2020). PD mostly affect the older population, especially those aged 50 and above. Although current scientific information is insufficient to recommend nutritional supplementation for PD, some nutrients have shown promising outcomes in preliminary trials (Tambasco et al., 2018; Orgeta et al., 2020). Vitamin E, creatine, and glutathione may have protective effects against PD. Caffeine in coffee, tea, etc. may protect against PD with a better risk reduction reported with larger caffeinated beverages' intake, including coffee (Costa et al., 2010).

6.4. Allergy

Allergic reactions would occur when the immune system of an individual reacts to typically harmless compounds or substances. Allergy is distinctive due to excess activation of some white blood cells known as basophils and mast cells by immunoglobulin E, an antibody. The allergic reactions cause an inflammatory response, which can be uncomfortable or dangerous (May and Dolen, 2017; Greer et al., 2019). Quercetin prevents damage to low-density lipoprotein, blood vessels in particular (Khatri, 2021). LDL is among the major causes of heart disease. Quercetin is a strong antioxidant that scavenge free radicals, and is beneficial in ameliorating allergy. Other foods and compounds with nutraceutical properties against allergy include guduchi, honey, tinospora, stinging nettle, omega 3's, spirulina, probiotics, Pycnogenol, grape seed extract, capsaicin, astragalus, etc. (National Center for Complementary and Integrative Medicine, 2017; Khatri, 2021).

6.5. Cardiovascular diseases

Cardiovascular diseases (CVDs) are among the greatest global healthcare challenges. Major CVDs include atherosclerosis, angina, peripheral vascular diseases, myocardial infarction (heart attack), stroke, hypertension, etc. Most nutraceuticals have the capacity to prevent CVDs as well as promote cardiovascular health. They are usually formulated to reduce fat contents in the foods/products, mostly by reducing *trans* unsaturated fatty acids and/or saturated fatty acids, and also by the addition of omega-3 fats, increasing phytostanol/phytosterol, and reducing cholesterol or substituting it with phytosterols (Shahbazian, 2013). Foods rich in antioxidant, including flavonoids, have potential nutraceutical effects against CVDs, including inhibiting cell-to-cell adhesion factors' formation, modifying the immune-competent cells' activities, inhibiting LDL oxidation, etc. Adequate intake of antioxidants, vitamins, dietary fiber, polyunsaturated fatty acids (especially omega-3 fats), and minerals, coupled with physical exercise can prevent and/or treat CVDs. Polyphenols play roles in cell signaling and cellular metabolism, and can reduce the risk of arterial disease (Shahbazian, 2013).

Some phytochemicals are understood to possess preventive and treatment effects against CVDs. Flavonoids are commonly found in plant foods such as berries, vegetables, red wine, black grapes, pomegranate, onion, cherries, endives, apples, cruciferous, and grapefruits. They occur as flavanones, flavonols, and flavones, and play a major role in preventing and treating CVDs (Gharipour et al., 2013; Khosravi-Boroujeni et al., 2013). Flavonoids block cyclooxygenase enzymes (the enzymes that break prostaglandins), block angiotensin-converting enzyme (ACE), and prevent aggregation of platelet. They have protective effects on the vascular systems that carry nutrients and oxygen to cells (Nasri et al., 2014). Stilbenes, anthocyanins, tetrahydro-β-carbolines, proanthocyanidins (tannins), serotonin, melatonin, hesperidin, beta carotenes, and dietary indoleamines exert health benefits against diseases such as CVDs (Pla-Pagà et al., 2019). Intake of flavonoids has been significantly inversely correlated with death due to the incidence of coronary heart disease and myocardial infarction. The levels of flavonoids found in commonly consumed plant foods may reduce mortality risk from coronary heart disease, including among the elderly (Rafieian-Kopaei et al., 2013). For instance, *Zingiber officinalis* rhizome (ginger) - commonly used condiment in several foods/beverages with medicinal as well as nutraceutical effects, has shown to be promising against CVDs given tis potent anti-inflammatory and antioxidant properties. Buckwheat seeds possess phytosterols, flavonoids, flavones, proteins and thiamin-binding proteins, etc (Rahimi et al., 2013). Omega-3 fatty acids in fish affect plasma lipid profile and CVDs, including arrhythmias. Octacosanol in fruits, plant leaves, and whole grains lowers lipid, without any side effect (Heidarian et al., 2013). Phytosterol competes with dietary cholesterols by blocking its uptake and promoting its excretion and removal from the body. Phytosterols (plant

sterols) are found in plants such as vegetables (green and yellow especially), seeds, etc (Khosravi-Boroujeni et al., 2013).

6.6. Obesity

Obesity is understood to take place when excessive fat in body accumulate to the extent of having harmful effects on the health of the affected individual. It is characterized by a Body Mass Index (BMI) of 30 and above. Obesity is a major public health concern and the leading cause of preventable death globally, with its rates increasing in both adults and children (Chiolero, 2018; von Bubnoff, 2021). Obesity contributes to the risk of several disorders, including hyperlipidemia, angina pectoris, congestive heart failure, respiratory disorders, hypertension, reduced fertility, renal vein thrombosis, cancer, and osteoarthritis (Chiolero, 2018; Kassotis et al., 2020). Obesity is mainly treated by losing weight via lifestyle changes, such as increased physical exercise and dietary prescription (US Department of Health and Human Services, 2017; Arnett et al., 2019; von Bubnoff, 2021).

Nutraceuticals like *Psyllium* fiber, *Momordica charantia,* capsaicin conjugated linoleic acid, tea, etc, are believed to possess anti-obesity potentials (Yannakoulia et al., 2019; Yoshino et al., 2020). Although excess intake of foods high in calories, including soft drinks, processed foods, snacks, etc., causes addition of weight, increased physical activity and restriction of calorie are moderately helpful in obesity management (Bojanowska and Ciosek, 2016; Arnett et al., 2019). Stimulants from plant sources, including caffeine, green tea, ma huang-guarana, ephedrine, chitosan, etc., can facilitate loss in body weight. Other foods with nutraceutical effects, including berries, avocado, ginger, fruits, vegetables, nuts, pomegranate, olive oil, etc., have anti-obesity properties (Konstantinidi and Koutelidakis, 2019). Bioactive compounds in these foods, including quercetin, capsaicin, oleuropein, polyphenols, ascorbic acid, anthocyanins, gallic acid, caffeine, and catechins, can contribute to obesity prevention, weight loss, and the associated metabolic consequences (Konstantinidi and Koutelidakis, 2019; Zhang et al., 2022).

6.7. Eye disorders

Some nutraceuticals are able to protect, prevent, and /or ameliorate eye disorders. Healthy lifestyle involving diets rich in antioxidants, including lutein, zeaxanthin, and omega-3 fatty acids may be beneficial against age-related macular degeneration. Nutraceuticals high in polyphenols have antioxidant properties (Barredo et al., 2017). Herbs and their extracts, including *Allium* spp., green tea, coenzyme Q10, carotenoids (especially β-carotene and lycopene), polyphenols, vitamins E and C, honey, etc., have antioxidant properties beneficial against age-related macular degeneration (Barredo et al., 2017). Astaxanthin prevents oxidative damage to the heart, boosts immune system function, and prevents degenerative diseases (e.g., AD). Lutein, a carotenoid, occurs in many fruits and vegetables such as carrots, squash, sweet potatoes, corn, mangoes, tomatoes, leafy greens, collards, kale, etc. (Bernstein et al., 2015). Zeaxanthin is found in foods such as honeydew, egg yolks, spinach, collard greens, corn, kiwi, kale, broccoli, lettuce, fruits, cabbage, green peas, brussel sprouts, green beans, etc (Bernstein et al., 2015).

6.8. Cancer

Cancer remains characterized by abnormal growth of cells that can spread to or invade other body parts. In 2020, cancer accounted for around 10 million deaths (almost one in every six deaths worldwide), and is the leading cause of death globally (World Health Organization, 2022). Several dietary/nutraceutical recommendations are available to reduce the risks of cancer (Yasmin et al., 2021).Dietary recommendations for preventing cancer usually emphasize on fruit, vegetables, fish, herbs, and whole grains, and the avoidance of refined carbohydrates processed, pickled foods, animal fats, red meat (lamb, pork, beef) (Kushi et al., 2012; IARC Staff, 2015; Sciacovelli et al., 2020; Tammela and Sage, 2020). Besides carotenoids having antioxidant properties effective for preventing cancer, plant nutraceuticals rich in genistein, isoflavones, biochanin, daidzein, etc., would inhibit the growth of prostate cancer cells (Shirzad et al., 2013). Lycopene is a potent singlet oxygen quencher, and can concentrate in the skin, adrenal, prostate, and testes, where it prevents cancer (Shirzad et al., 2013). Another carotenoid is lycopene, found in foods like tomatoes, papaya, water melon, pink grapefruit, and guava equally protects against cancer by reducing/preventing oxidative stress and DNA damage (Shirzad et al., 2013).

Additionally, β-carotene has the highest antioxidant property among the carotenes. α-carotene and ε-carotene have 50 to 54% and 42–50% respectively antioxidant activity as β-carotene, the latter found in tomatoes, carrots, spinach, cantaloupe, broccoli, sweet potatoes, lettuce, winter squash, and oranges (Lee et al., 2019; Kim et al., 2021). Chronic inflammation has been associated with increase in the risk of cancer risk, and is associated with the suppression of the immune system, which also increases the risk of cancer development. Ginseng found in some foods has anti-inflammatory properties that targets several key factors in inflammation-to-cancer processes (Lee et al., 2019; Kim et al., 2021).

Many phytochemicals such as polyphenols, including flavonoids, have anticancer properties. Flavonoids in plant foods, including Citrus fruit, have cancer protective properties mainly due to their antioxidant activities (Choudhari et al., 2020). Saponins have antitumor, anti-inflammatory, and antimutagenic activities that can reduce cancer risk, by preventing the growth of cancer cells (Kooti et al., 2017; Choudhari et al., 2020). Saponins are found in peas, soapberry, soybeans, soapbark, soapwort, clover, spinach, tomatoes, alfalfa, potatoes, etc. Saponins are mainly commercially extracted from *Quillaja saponaria* and *Yucca schidigera.* Tannins helps to detoxify carcinogens and remove damaging free radicals. Tannins found in grapes, blackberries, cranberries, blueberries, lentils, and tea are proven anticarcinogenic properties that prevent cancer (Kooti et al., 2017; Subramaniam et al., 2019). Glucosinolates and their hydrolytic products, such as isothiocyanates and indoles, which is found in adequate cruciferous vegetables' intake', can help lower the risk of lung and colorectal cancers. Glucosinolates bio-transformation products, including isothiocyanates, sulforaphane, and dithiol thiones, would block tumor growth promoting enzymes, especially in liver, stomach, esophagus, breast, colon, and lung. Moreover, sulfur containing compounds in garlic boost the body immunity, decrease atherogenesis, reduce platelet stickiness, and ultimately reduce the risk of cancer. Sulforaphane in broccoli reduces the risk of breast and prostate cancers (Giordano and Tommonaro, 2019). Besides, curcumin in *Curcuma longa* (turmeric) has anticarcinogenic, anti-inflammatory, and antioxidant, properties (Giordano and Tommonaro, 2019).

6.9. Health conditions associated with inflammation and microbial infections

Inflammation, characterized by heat, swelling, redness, and pain, is among the body tissues complex biological response to harmful

stimuli, e.g., irritants, damaged cells, and pathogens - also a protective response that involves molecular mediators, blood vessels, and immune cells (Hannoodee and Nasuruddin 2020; Pahwa et al., 2020; Adetuyi et al., 2021). Nutraceuticals with tested influence on osteoarthritis include S-adenosylmethionine, ginger, chondroitin, glucosamine, soybean, etc.(Rafieian-Kopaei, 2014). Essential fatty acids, such as omega-3 and omega-6 fatty acids, play an important role against many inflammatory diseases via the generation of inflammatory responses' modulatory molecules, such as leukotrienes, interleukins, and prostaglandins (Rouhi-Broujeni et al., 2013). Gamma linolenic acid is used for the treatment of inflammatory and autoimmune diseases. Preformed Gamma linolenic acid is found in green leafy vegetables, nuts, and vegetable oils, including hemp seed oil, blackcurrant *Oenothera biennis* oil, borage oil, etc. Gamma linolenic acid metabolizes to dihomogamma linlenic acid that undertakes cyclooxygenase and lipoxygenase enzymes mediated oxidative metabolism to generate anti-inflammatory eicosanoids (Rouhi-Broujeni et al., 2013). Many herbs have anti-inflammatory properties like gentianine from Gentian root, as well as bromolain in pineapple, stinging nettle, etc (Rouhi-Broujeni et al., 2013).

Many nutraceuticals have established antiviral, antibacterial, antifungal, and anti-parasitic properties, including quercetin, resveratrol, palmitoylethanolamide, curcumin, N-acetyl cysteine, epigallocatechin gallate, etc. (Zhong et al., 2011; Hesselink, 2013; Moghadamtousi et al., 2014; Jayawardena et al., 2020; Kavitha et al., 2021). A diet rich in essential nutrients, such as essential fatty acids, vitamins, minerals, phytochemicals, protein, etc., can reduce the risk of chronic diseases associated with microbial infection, as well as the severity of their infection. Nutraceuticals can help create balanced diets, which would equally help to improve immune functions and maintain healthy respiratory system (Singh et al., 2021). Lactoperoxidase, bovine lactoferrin (Mehra et al., 2021), and artificially altered milk proteins, including β-lactoglobulin, α-lactalbumin, and serum albumin have antimicrobial properties against some viruses by binding to the viral cellular receptors, and inhibit the absorption and replication of the viruses. Phytochemicals have been employed for the treatment of many microbial diseases, such as helminthiasis, scabies and myiasis (Akram et al., 2021; Palai et al., 2021).

7. Concluding remarks

In this overview, we presented natural nutraceuticals, their major bioactive components, formulation, and health benefits for disease prevention. By briefly differentiating among nutraceuticals, we attempted to make readers understand the importance all these nutraceuticals in human health and wellbeing. In addition to common nutraceuticals and their biological properties, major bioactive components of nutraceuticals and their health benefits and disease prevention were also presented. While many strategies for nutraceutical formulations are available to enhance the functionality of foods, one of the main challenges in implementing novel industrial products globally appears to be insufficiency of knowledge about the applicability and complexity of food matrix. Overall, nutraceuticals' healing actions are largely due to the components present, including dietary fiber, essential fatty acids, minerals, phytochemicals, prebiotics, probiotics, vitamins, proteins, and carbohydrates. Despite the diversity of recommended nutraceuticals and their bioactive components, there is continuous need for industries to seek for avenues to meet up with the increasingly dynamic expectations of consumers, which steadily possess great challenge. The effectiveness of some nutraceuticals still requires further investigation, including control clinical trials and randomized studies, especially their bioactive components and medicinal effects against specific disease conditions.

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Conflict of interest

The authors have declared no conflict of interest.

Author contributions

Chinaza G. Awuchi was associated with conceptualisation; data curation; formal analysis; investigation; project administration; resources; methodology; and wrote the original draft; Charles Odilichukwu R. Okpala was associated with formal analysis; investigation; methodology; supervision; and reviewed and edited the final manuscript.

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