

Embrace and Live, Embrace Death

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Abstract

The menace of nutritional imbalance arising from change in behavior of humans with respect to eating habits poses threat to human health, and hence requires swift revitalization. The increase in the world population coupled with the nature of occupations of many people across the globe and advancement in the aspect of industrialization, technology and civilization have been observed to play significant roles in the nutritional imbalance observed among the world population, resulting in increased incidence of chronic diseases such as stomach cancer, obesity, and hypertension among others. However, in an attempt to address or circumvent the afore-mentioned menaces, consumers are seeking complementary or alternative beneficial products with little or no side effects as compared to modern synthetic intervention that will provide health benefits beyond basic nutrition, thus making nutraceuticals, functional foods and probiotics more attractive. Nevertheless, the level of awareness and knowledge of people about the remarkable potency (health benefits) of the afore-mentioned foods and food products to prevent or treat the previously mentioned chronic diseases is very low most especially in the developing countries, and hence calls for a great concern. This review therefore addressed various health challenges in which the aforementioned foods and food products have shown notable potency, and hence encouraging their fuller adoption and also enhancing the longevity of the fast increasing world population.

Keywords: Nutritional; Health; Obesity; Food; Disease; Nutraceuticals

Introduction

The chronic diseases arising from nutrition such as stomach cancer, obesity among other nutrition-related diseases are becoming noteworthy in both developed and developing countries. From the beginning of human history, food has been considered the major factor in maintaining well-being and good health. On this note, Hippocrates, the father of modern medicine stated "Let thy food be thy medicine and medicine be thy food" to predict the association between health-promoting foods and their medicinal benefits. Despite the statement of Hippocrates, foods were only considered as being nutritious based on the essential nutrients contained therein which are needed for normal metabolic activities and body function. However, on the contrary, foods are not just meant for metabolic activities and body function but also to maintain well-being and good health. Martin [1] also affirmed that in maintaining optimal cardiovascular function, respiratory ventilation, muscle strength, protection from infection, wound healing, and psychological well-being, adequate nutrition is essential. In addition, Eze et al. [2] reported that appropriate diet containing the right amount of food ingredients, such as proteins, carbohydrates, minerals, vitamins, fats, and water assists in the preclusion of nutrition-related diseases by enhancing body build-up and defense, energy supply, and regulatory functions.

The nature of occupations of many people across the globe and improvement in the aspect of industrialization, technology and the struggle across the

globe to meet up with the technology and civilization have contributed immensely to the change in behaviour of humans with respect to eating habits which are surrounded by an array of threats resulting from nutritional imbalance and environmental pollution due to excessive use of agricultural techniques, pesticides and heavy metals [3]. These menaces have resulted in increased incidence of obesity, stomach cancer, diabetes, cardiovascular diseases and other nutrition- and pollution-related diseases [4]. The perceived paradigm shift in the consumption patterns of individuals in developing countries from high-fibre, calorie-sparse, low-protein diets to low-fibre, calorie-dense, and high-protein diets [1,5-6], especially with respect to carbohydrate intake has been responsible for the increased prevalence of obesity, which is a major risk factor for many non-communicable nutrition-related diseases such as hypertension, diabetes mellitus, cardiovascular diseases, and nutrition-induced cancer [7]. According to the WHO, the nutrition-related diseases account for 60% of all deaths, and 43% of the global burden of disease [8], and that by 2020, the impact of nutrition-related non-communicable diseases is expected to rise to 73% of all deaths and 60% of the global burden of disease [9].

In an attempt to achieve a better quality of life, consumers are seeking complementary or alternative beneficial products [10] with little or no side effects as compared to modern synthetic intervention that will provide health benefits beyond basic nutrition, and hence making nutraceuticals, functional foods and probiotics more attractive. However, the level of awareness and knowledge on the impact of food sources with potentials of providing extra health benefits coupled with its basic nutritional value tagged “nutraceutical” on health is very low which in turn poses challenge to its fuller adoption. In order to curb the challenge of nutritional imbalance, there is a need for us to shift our attention from ready-to-eat foods with reduced nutritional values to nutritional- and health-promoting foods and food products such as nutraceuticals, functional foods and probiotics. This work therefore reviewed the nutritional and health-benefits of nutraceuticals, functional foods and probiotics.

Background and Definitions

Nutraceuticals: The concept of “nutraceutical” started as far back as 3,000 years ago when Hippocrates, the father of modern western medicine, recognized the importance of food in maintaining well-being and good health. The word nutraceutical is a

blend of two words, “nutrient” and “pharmaceutical” which was initially invented by Stephen DeFelice [11], the founder and chairman of the Foundation for Innovation in Medicine in September, 1989 in Cranford, New Jersey, USA. DeFelice defined a “nutraceutical” as a “food, or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease” [12]. Another definition from the USA is “diet supplement that delivers a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix, and used to enhance health in dosage that exceed those that could be obtained from normal food” [13]. Prabu et al. [4], also referred to nutraceutical as any non-hazardous food extract supplement that has been scientifically proven to confer health benefits on human upon consumption for both treatment and prevention of disease which consists of a wide range of foods and food products, including isolated nutrients, herbal products, dietary supplements, genetically engineered “designer” foods, and processed products such as cereals, soups, and beverages.

Functional foods: In recent years, a growing body of scientific evidence has demonstrated that certain food constituents often referred to as phytochemicals and zoochemicals from plants and animals sources respectively, may provide health benefits beyond basic nutrition and help prevent chronic diseases like cardiovascular diseases, cancer, osteoporosis among other nutrition-related diseases [14-17]. This concept led to the development of a new generation of foods termed “functional foods”. Various definitions have been proposed for functional foods but in a broader sense, it can be said to be any food that confers both nutritional and health benefits on humans upon consumption. The term “Functional Food” was originally employed in Japan, 1980, when the need for improvement in the quality of life was found paramount by health authorities in order to reduce health care cost [12,18]. It stresses that food is not only required for living but also serves as the basis for improved well-being and health, thereby resulting in the prevention and reduction of risk factors for a number of diseases [19-20].

Functional foods consist of food- and drink-based formulations, as opposed to tablets, capsules among others and these products often contain established nutraceuticals and are recommended for the same range of therapeutic categories as the nutraceuticals contained therein. In Canada, a functional food is defined as “similar in appearance to conventional foods, consumed as part of a usual diet” [21]. In the UK, the

Department of Environmental, Food and Rural Affairs (DEFRA) defines a functional food as a “food that has a component incorporated into it to give it a specific medical and physiological benefit, other than purely nutritional benefit” [22]. Figueroa-Gonzalez et al. [23] and Al-Sheraji et al. [24] classified functional foods as

Foods with naturally occurring bioactive substances (e.g. dietary fibre)

Foods supplemented with bioactive substances (e.g. probiotics) and

Derived food ingredients introduced to conventional foods through a combination of probiotics and prebiotics (eg synbiotics)”

Probiotics: Various researchers contributed immeasurably to the development of probiotics. However, the history of probiotics started with the discovery of Albert Döderlein, who first suggested the mutual relationship between microbes and human. By 1982, he hypothesized the vaginal bacteria whose lactic acid inhibited the growth of pathogenic bacteria [25]. In 1908, the beneficial characteristics of the lactic acid bacteria were conjectured by Ilya Metchnikoff [26]. Later, Minoru Shirota successfully cultivated the lactic acid bacteria, named *Lactobacillus casei* Shirota. This beneficial intestinal bacterium was introduced to the market in 1935 by distributing it in dairy drink [27].

The word “probiotics” was coined from the Greek word meaning for life and was initially suggested to portray the growth-enhancing metabolites produced by one microbe for the advantage of another [28]. Later, Parker, defined probiotics as “organisms and substances which contribute to intestinal microbial balance” in 1974 [29]. Furthermore, the first widely accepted definition of probiotics was the one proposed by Fuller in 1989 who defined probiotics as “food supplemented with live microbes that benefits host animals by improving its intestinal microbial balance” [30-32]. Subsequently, the “Joint Expert Consultation of the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO)” categorized probiotics as “live microorganisms that, when consumed in an adequate amount, confer a health benefits on the host” [33]. This definition of probiotics still remains the broadly accepted definition till date.

Market Trends

The markets for nutraceuticals, functional foods and probiotics are rapidly expanding, most especially in the developed countries owing to the fact that

consumers are becoming more conscious about their well-being and health. The markets for nutraceuticals and functional foods represented annual global sales of US Dollar 95 billion in 2001, and grew to US\$ 127 billion by 2005. On the other hand, probiotic yoghurt and milks have been the most fast selling probiotic dairy products as part of functional food market in Europe, accounting for 65% of the Europe function food market valued at US\$ 889 million [34].

The global nutraceutical market reached US\$ 47 billion in 2002, and was expected to reach US\$ 75 billion by 2007. The global market for functional foods was estimated to be US\$ 30 billion in 2003, and Leatherhead Food RA considered that it will eventually reach 5% of all food expenditures in developed countries [35]. The study carried out by Leatherhead Food RA revealed that out of the totaled >250 million kg of probiotic yoghurt market in 1997 [35] across nine countries, including United Kingdom, France, Germany, Spain, Belgium, Netherlands, Denmark, Finland, and Sweden, France represented the largest market having sales of approximately 90 million kg, valued at US\$ 219 million. Further, Germany market for probiotic yoghurt is growing rapidly; for instance, during 1996-1997, it increased by 150%, whereas the UK market grew by a more modest 26% during the same period [36]. However, the recent global probiotics market size reached US\$ 35.9 billion in 2016. The predicted annual growth rates of various nutraceutical categories have been estimated to range from 6% for products treating digestive ailments, up to 25% for eye health products. An alternative view of current and predicted sales claims that the joint health supplements- glucosamine, chondroitin and Methyl Sulfonyl Methane (MSM) appear to be the major product group, followed by the Polyunsaturated Fatty Acids (PUFAs). However, fish oils and MSM have been predicted to show the greatest increase in sales [37].

Further, appreciable functional foods market was observed in 2010, owing to the global acceptance and awareness among consumers about functional foods in Australia, New Zealand, Asia, Latin America, North America and Western Europe, with an estimation of about 63 billion US\$, and it was envisaged to meet a value of at least 90.5 billion US\$ by 2013 [38]. The United State of America has been recognized as the largest market of functional foods, followed by Japan and Europe that have collectively contributed over 90% of the total sales [39]. The significant growth of functional foods market in Canada is due to the 32% increase in the number of functional food-producing companies while the boost in the market of functional

foods in North America has been attributed to the introduction of new product such as probiotics into the market [40-42].

Japan remains the largest consumer of nutraceuticals in Asia, owing to the swift healthy dietary habits amidst the population and this has led the Japanese nutraceuticals industries to produce a variety of products [43]. Keservani et al [44] attributed the increased nutraceutical market in India to increase in the level of awareness, health consciousness and willingness of the folks to spend on health-improving foods. Swati et al. [39] reported that the European nutraceutical market was valued at 6.4 billion dollars in 2013 and was estimated to grow at an annual rate of 7.2% between 2013 and 2018, to reach a projected \$9.0 billion by 2018. However, to the best of our knowledge, there is little or no information regarding the market trends of nutraceuticals, functional foods and probiotics in developing countries. This therefore suggests the need for more survey in this part of the world in order to ascertain the level of awareness of people about these health-promoting foods and food products.

Health Benefits of Nutraceuticals, Functional foods and Probiotics

Health challenges in which nutraceuticals have shown remarkable potency

This study outlined various health challenges in which nutraceuticals have shown to have the potency to prevent or treat and thereby promoting longevity.

Cardiovascular Diseases (CVDs): Cardiovascular diseases such as coronary artery disease, heart failure, carditis, stroke, valvular heart disease among others are the diseases of the heart or blood vessels which have been implicated as the leading cause of mortality and morbidity worldwide [19,45].

Statistics has shown that an estimated 17.9 million people died of CVDs every year which represent 31% of all global deaths among which 85% were linked to heart attack and stroke [46]. Risk factors such as high blood pressure, smoking, diabetes mellitus, excessive alcohol intake, unhealthy diet, obesity among others have been associated with CVDs. Reactive Oxygen Species (ROS) play key role in the pathogenesis of both acute and chronic heart diseases due to cumulative oxidation stress [47]. For instance, oxidation of low density lipoprotein from saturated, trans-fats and meat products may intensify pathogenesis of atherosclerosis and CVDs [47].

Interestingly, several functional foods from plant (such as onions and vegetables) and animal origin (such as fish) have been studied for their abilities to reduce the chance of developing CVDs. The biological activities exhibited by these functional foods are due to the presence of bioactive ingredients called “nutraceuticals” contained therein. For instance, the mechanisms of action of n-3 fatty acids such as Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), the bioactive nutraceuticals in fish [48] are majorly by decreasing platelet aggregation [49-51], lowering plasma triglycerides [52-54], increasing HDL cholesterol and LDL particle size [55-57], decreasing blood pressure, reversing cholesterol accumulation from atheromatous plaques [58-61] and decreasing inflammation [60, 62]. In addition to this, a recent meta-analysis conducted on fish with variable bio-active components [14], showed that species higher in n-3 FA EPA and DHA produced a better result by reducing the risk of coronary death by 36% and a total mortality by 17%.

Furthermore, the strengthening of the oxygen and nutrient capillaries in cells through the ability of flavonoids found in food and its supplements such as; fruits, vegetables and red wine to impede the Angiotensin Converting Enzyme (ACE) have been recognized to reduce the risk of having CVDs [15]. Probiotics have also been found to reduce a person’s chance of developing CVDs by lowering blood pressure [63-64].

Cancer: The WHO, 2018 defined cancer as “generic term for a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs” [65]. Cancer may occur be in the prostate, breast, stomach, skin among others. During aerobic metabolism, Reactive Oxygen Species (ROS) such as hydroxyl radical, superoxide and hydroxyl radical are produced [66-67]. Further, photochemical events in the skin and eyes can result in the production of singlet oxygen. These reactive oxygen species contribute immeasurably in aging and degenerative diseases such as cancer and atherosclerosis [68]. Cell inflammation is another important conditions in carcinogenesis and one of such mechanisms by which inflammation elicit cancer is by generation of free radicals by inflammatory cells [69].

Cancer is considered as the second most leading cause of death in most high-income countries after cardiovascular disease [70]. Vel Sziec et al. [71] and Bragg et al. [72] regarded cancer as one of the major health

problems, causing 1/8 deaths worldwide. The costs involvement on cancer in year 2030 was estimated to increase to \$ 458 billion based on World Economic Forum 2011. The study of Mohammad et al. [70] indicates that unhealthy diet can result into cancer and that nutrition and food constitute 30% of all cancer cases, which thus emphasizes that eating good food in right manner may lower the risk of cancerous cells inflammation.

There are some functional foods whose abilities to prevent or treat cancer have been ascertained. Examples of functional foods that have demonstrated anti-cancer properties include cereals, vegetables, beverages, dairy products, fish oil, beef, mushroom [16] etc. Whole grain cereals such as wheat (*Triticum aestivum* L), rice (*Oryza sativa* L), maize (*Zea mays ssp. Mays* L) among others and vegetables such as Bitter melon (*Momordica charantia* L) have been discovered to contain a variety of phytochemicals (nutraceuticals) such as flavonoids (in both cereals and vegetables), glucan (in cereal), saponins (in vegetable) among others and have been discovered to demonstrate anticancer activity [16]. Several modes of action have been documented for the anticancer properties of these foods. For example, bitter melon inhibits uncontrollable multiplication of cancerous cells; however mushrooms, particularly *Tricholoma matsutake* acts by inducing apoptosis of cancerous cells and its efficacy in the treatment of oral cancer has been documented [16]. The nutraceuticals such as iso-flavones and curcumin found in soy foods and curry respectively, have been discovered to possess cancer chemo-preventive properties [73]. In addition, lycopene in tomato, water melon, apricot and peaches have likewise been observed to evince anticancer property by inhibiting proliferation of cancerous cells of humans [74].

Furthermore, probiotics such as *Lactobacillus* spp. and *Bifidobacterium* spp. have been recognized for their protective effects in cancer pathogenesis [75]. For example, probiotics can prevent the production of carcinogenic substances from dietary components and conversion of pro-carcinogens to carcinogens by putrefactive intestinal bacteria [76]. Other functional foods that have demonstrated anticancer property through scavenging free radicals include garlic, broccoli, green tea, soybean, tomato, carrot, cabbage, onion, cauliflower, red bee nuts, cranberries, cocoa, blackberry, blueberry, red grapes, prunes and citrus fruits [16].

Type-2-Diabetes Mellitus (T2DM): Type 2 diabetes mellitus can be defined as a degenerative chronic disease or metabolic disorder typified by hyperglycemia, insulin resistance, β -cell dysfunction and impaired insulin secretion [77-78]. There are three categories of diabetes mellitus (DM) on the basis of pathogenesis and treatment and they include type 1 diabetes mellitus, type 2 diabetes mellitus and gestational diabetes [79]. Of these, type 2 diabetes mellitus is the most widespread accounting for 90% to 95% of all diabetes cases [80] and is expected to rise to 439 million by 2030 [81]. According to the WHO, Type 2 diabetes (previously called non-insulin dependent or adult-onset diabetes) occurs as a result of the inability of the body cells to use insulin effectively (insulin resistance) [82]. Amro-Abdelazez et al. [83] regarded diabetes as the third most severe menace to human health, after cardiovascular diseases (CVD) and cancer. Several risk factors have been linked with T2DM and these include obesity, age, and race/ethnicity, family history of diabetes, hypertension, and impaired glucose tolerance among others [84]. Moreover, complications such as CVDs, diabetic neuropathy and retinopathy among others are often experienced by people with T2DM [85].

Various kinds of antidiabetic drugs have been produced, including α -amylase and α -glucosidase inhibitors and meglitinides among others and are available in the market; however, diabetic patients are usually being challenged with several side effects such as hypoglycaemia, anaemia, weight gain and congestive heart failure when the drugs are used for a long time [86]. Hence, exploring functional foods with anti-diabetic properties which have been discovered to be safer are recommended. Healthy diet has been recognized as one of the major treatment and preventive measures for diabetes. Functional foods such as products of rye, oat products, soybean, red apple, berries, grapes etc. have been discovered to possess antidiabetic properties [87].

Rye products have high fiber content and this has been shown to decrease the digestion and absorption of dietary carbohydrates while enhancing the production of metabolites such as propionic and butyric acids from colonic fermentation of the soluble fibre in rye products. These metabolites have been found to effectively stimulate the secretion of insulin from β -cells. The nutraceuticals present in rye products such as phenolic acids, tannins, benzoic acid etc. have also been documented to have similar efficacy with antidiabetic drug in insulin secretion [88-89].

The antidiabetic properties of oat meal products have been linked with the soluble fiber, particularly the β -glucan, antioxidants and bioactive compounds such as carotenoids, phytic acid, phenolic acids, flavonoids and phytosterols [90]. The efficacies of oat meal products have been confirmed in several studies and these studies showed that the consumption of oat products improved glycemic, insulinemic, and lipidemic responses in diabetic patients, and act as active ingredient in reducing postprandial glycaemia studies [91-92].

Fruits (red apple, berries, grapes, cherries, red cabbage etc.) that are rich in anthocyanins have also been discovered to have mainly hypoglycaemic effects, hence their use for diabetes [87] while the antidiabetic properties of soybean have been associated with isoflavones and bioactive peptides. These nutraceuticals have been found to have favorable effects on glycemic control and insulin sensitivity, dyslipidemia and kidney function [93-95]. The efficacy of these nutraceuticals was ascertained in a study carried out by Gilbert and Liu [96], who discovered that soy iso-flavones selectively bind to both α and β estrogen receptors; α -estrogen receptor is believed to be the key modulator of glucose and lipid metabolism and regulate insulin biosynthesis and secretion as well as pancreatic β -cell survival. Other functional foods with antidiabetic properties include tomato, green tea, bean, watermelon, citrus fruit [87] etc. Moreover, probiotics such as *Lactobacillus acidophilus* NCFM, *Lactobacillus gasseri* SBT2055, *L. rhamnosus* have also been found to aid the treatment and prevention of T2DM by decreasing the risk associated with T2DM and insulin resistance [97-99].

Obesity: Obesity and overweight are characterized by excessive accumulation of fat in the body that may weaken the health. These medical conditions usually arise when the rate of consumption of high-energy foods (fat-rich foods) surpasses energy expenditure. World Health Organization 1998, defines obesity as “physical manifestation of higher fat accumulated in the body with high tendency of causing mortality” [100]. Obesity is associated with various chronic diseases including cardiovascular diseases, cancer, diabetes, hypertension, gout, osteoarthritis among others. The Body Mass Indices (BMI) of 30 or more is obese and BMI equal to or greater than 25 is overweight [101]. Although several factors have been identified to contribute to obesity but the sedentary lifestyle has been recognized as the major factor responsible for the widespread of obesity worldwide [102].

Obesity and overweight have been recognized as the most prevalent nutritional disease and the fifth leading risk factors for global deaths with at least 2.8 million deaths of adult each year owing to its complications [103]. The prevalence of obesity has attained epidemic proportions globally, with about 2.8 million people dying each year as a result of being obese [104]. Although, varieties of anti-obese drugs have been produced to reduce the problem of obesity but the side effects such as cardiovascular events and strokes, coughing, dizziness, mouth dryness, anxiousness, fatigue, flatulence, headache, insomnia, leakage of oily stools, nausea, and hepatic adverse effects and high costs, limit their usage [105-108], and hence, the need of shifting attention to natural inhibitors such as functional foods with nutraceuticals having anti-obese properties.

Functional foods with their bioactive components (nutraceuticals) such as oolong tea (catechins), green tea, garlic (Organosulfur compounds), fortified margarines (Plant sterol and stanol esters) and Psyllium (Soluble fiber) and soybean (Protein) have been found to be useful in the prevention and treatment of obesity. These functional foods employ different mechanisms in getting rid of excess fat from the body either by inhibiting pancreatic lipase, enhancing thermogenesis, preventing adipocyte differentiation, enhancing lipid metabolism or decreasing appetite [109-115].

The inhibition of pancreatic lipid activity by some functional foods such as oolong tea and green tea prevents the absorption of lipid which is later excreted through oily faeces and the thermogenesis-enhancing ability of some functional foods such as soybean assists in burning calories and excess body fat. The ability to inhibit adipogenesis and fat cell formation through the prevention of adipocyte differentiation has been documented in some functional foods such as garlic and palm oil. Other functional foods permit appetite control by suppressing and inducing satiety. All these mechanisms of action of functional foods with anti-obese properties will lead to a reduction of food and energy intake [116-119].

Probiotic strains of lactobacillus have been utilized to reduce cholesterol level in vivo and *in vitro*. These bacteria help in reducing cholesterol level through direct and indirect mechanisms. The direct mechanism involves the inhibition of *denovo* synthesis or reduction in the intestinal absorption of dietary cholesterol while the indirect mechanism involves deconjugating the cholesterol to bile acid, thereby reducing cholesterol body pool [120]. The non-absorbed dietary cholesterol

in the case of direct mechanism is removed from the body system by the organisms through assimilation, binding or degradation, meaning that the probiotic organisms may either absorb the cholesterol for their own digestion, attach to cholesterol particle and debasing it to its catabolic products or by breaking the cholesterol particle into small, safer products. Examples of lactic acid bacteria that have cholesterol-removing ability include *Lactobacillus pentosus* LP05, *L. brevis* LB32, *L. reuteria* and *L. Plantarum* [120-123].

Osteoarthritis: Osteoarthritis (OA) is the most common arthritic disorder and it is generally referred to as old age-diseases as it is common to ages above 64 years. OA is associated with weakening of bones and degenerative damage or loss of the joints cartilage [124]. This damage is caused by the overexpression of metallo-proteinases that degrade cartilagenous matrix for subsequent loss of collagen and proteoglycans [125]. Metalloproteinases synthesis and other enzymes may be induced by the proinflammatory cytokine interleukin 1 (IL-1), thus inducing apoptosis of chondrocytes, the cellular component of cartilage. All these, may contribute to the destruction of cartilage which may in turn cause arthritis disorder in large and single joints.

The efficacy of nutraceuticals such as glucosamine and chondroitin in the treatment of osteoarthritis has been documented [126]. These substances are found naturally in healthy cartilage, particularly in the fluid around the joints. They are also available as dietary supplement, harvested from shells of shellfish or produced in the laboratory. Probiotic bacteria such as *Lactobacillus casei Shirota* (LcS) has also been observed to aid in the treatment of knee OA. This efficacy was shown in a placebo-controlled clinical trial involving 537 patients with knee OA carried out by Lie et al. [127]. The experiment revealed that the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) and VAS (Visual Analog Scale) of the LcS group were significantly higher than placebo group, indicating that LcS consumption could serve as a novel therapeutic option in the clinical management of Knee OA [127].

Uterine Fibroids (UFs): Uterine fibroids, also referred to as leiomyomas are characterized by the benign abnormal growth (tumour) of smooth muscle in the uterus, posing threat on women in their active and post active reproductive ages [128]. Women with UFs can either be asymptomatic or symptomatic; however, most women with UFs do not experience symptoms [129-130]. On the other hand, UFs may result in a wide range of severe and chronic symptoms, including painful period and heavy bleeding during menstruation which

may result in anaemia and fatigue [131-135]. Other clinical manifestations of UFs include abdominal pain and protuberance, pain during sex, bladder or bowel dysfunction, leading to urinary retention or incontinence, pain or constipation. UFs have also been documented to interfere with pregnancy by impairing fertility and by causing bleeding, premature labour, miscarriage [136-138] etc.

Bulun [139] reported that the occurrence of UFs among women at 50 years in United State is approximately 70-80% with an estimated value of 171 million of women affected worldwide. UFs have also been considered as the most common benign neoplasm, affecting woman [140]. Risk factors such as obesity, hypertension, dietary intake, race, family history among others have been implicated in UFs [141]. Wise et al. [142] reported that women who drink alcohol and eat more of red meat such as beef and ham are at greater risk of developing UFs. Further, drinking a beer per day or more increases the chance of developing UFs by more than 50% [142].

However, the consumption of dairy products and foods high in fruit and vegetables has been recognized to reduce the chance of developing UFs. The flavonoids contained in citrus fruit have been suggested to be responsible for the anti-fibroid properties of citrus fruit, probably owing to the anti-proliferative effects of flavonoids [143]. The nutraceuticals such as apigenin and luteolin and quercetin in fruit and vegetable have been discovered to possess anti-tumor properties. These nutraceuticals act by inducing the inhibition of uterine fibroid growth through the promotion of apoptosis [144-145]. Further, in a controlled trial, flavanol [epigallocatechin-3-gallate (EGCG)] from green tea (a functional food) was discovered to significantly reduce the volume of UFs and improved symptoms of anaemia and blood loss [146]. The combination of phytoestrogens such as isoflavones and lignans and probiotic bacteria such as lactic acid bacteria and bifidobacteria has been shown to produce equol, enterolignans and urolithins which are more bioavailable than their respective dietary phytoestrogens [147-148]. These compounds play key role in mitigating UFs through their anti-inflammatory, anti-proliferative and apoptosis-inducing activities [149-150].

Hypertension (High Blood Pressure): Hypertension, also known as high blood pressure can be defined as a chronic medical conditions typified by persistent elevated blood pressure in the arteries. Hypertension possesses a serious threat on human health and health

care system by contributing to increased mortality and risk of cardiovascular diseases [151-152]. Several risk factors have been attributed to increased risk of developing hypertension, including obesity, age, family history of hypertension, excessive intake of salt and alcohol among others. According to the WHO 2013, hypertension contributes to the burden of heart failure, kidney failure, and stroke. Although anti-hypertensive drugs are available but patients usually experience side effects.

On this note, nutritional modifications have been observed to be one of the major lifestyle modifications

approaches for preventing hypertension at a lower cost compared to modern medicine. This nutritional modification is associated with weight loss, moderation in salt and alcohol consumption among others [153]. Functional foods such as garlic and onions that contain thiosulfonates have been discovered to reduce blood pressure [4]. Further, probiotics such as *Saccharomyces cerevisiae*, *Lactobacillus rhamnosus* GG, *Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus* and *Lactobacillus bulgaricus* have also be found to reduce blood pressure by improving total cholesterol and low-density lipoprotein cholesterol levels [154-155] (Table 1).

Table 1: Some functional foods and their respective nutraceuticals (Bioactive compounds)

Functional foods	Nutraceuticals (Bioactive compounds)
Tomato and its by products	Lycopene, β -carotene, flavonoids, anthocyanins, phytoan, phyto flava, quercetin, kampferol
Grapefruit	Lycopene, pectin, naringin, hesperidin
Watermelon	Lycopene, carotenoids, cytolin
Red apple, apple peel, apple and its by products	Soluble fiber, quercetin, catechins, epicatechin, P-cumaric acid, chlorogenic acid, gallic acid, phloridzin, procyanidins
Berries; cranberry, blackberry, black raspberry, blueberry, red raspberry, strawberries	Anthocyanins, tannins, ellagitannins, α -carotene, β -carotene, lutein, delphinidins, pelargonidins, cianidins, catechins, hydroxy-cinnamic acid
Grapes and their by products	Anthocyanins, resveratrol
Cherries	Anthocyanins, quercetin, hydroxy-cinnamic acid, carotenoids, melatonin, phenolic acids, gallic acid, lutein, xanthine, β -carotene
Cabbage, Cauliflower	Isothiocyanates, anthocyanins (red cabbage), carotenoids, lutein, β -carotene
Garlic, onions	Allyl sulfors, flavonoids, quercetin, dihydroflavonols, anthocyanins (red onion)
Citrus fruits	Lutein, xanthine, α -cryptoxanthin, β -cryptoxanthin, naringenin, hesperidin, β -carotene, phytosterols
Spinach	Lutein, betaine, violaxanthine, opioid peptides (rubisculins), P-cumaric acid, ferulic acid
Carrots	Soluble fiber (pectin), α -carotene, β -carotene lutein, phenolic acids, stilbenes
Mango	Carotenoids, quercetin, kampferol, gallic acid, caffeic acid, catechins, tannins, mangiferin
Barberry	Anthocyanins, alkaloid compounds (berberine, oxycontin)
Green tea	Polyphenols, phenolic acids, catechins, epigallocatechin-3-gallat, chlorophyll, carotenoids, pectin, plant sterols
Coffee (Coffea Arabica)	Caffeoyl, quinic acids
Ginger (Zingiber officinale)	Gingerol, paradol, and shogoa
Fish and seafood	Bioactive peptides, antioxidant compounds, ω 3 fatty acids (docosahexaenoic acid, eicosapentaenoic acid), selenium, taurine
Pomegranate and its byproducts, pomegranate peel and seeds	Anthocyanins, tannins, catechins, gallo catechins, punicalagin acid, ellagic acid, gallic acid, oleanolic acid, ursolic acid, uallic acid

Date fruit	Dietary fiber, polyphenols, acid cinnamic, melatonin
Dairy products and probiotics	Calcium, vitamin B, bioactive proteins such as casein and whey, immunoglobulines, bioactive peptides (α - and β -lactoglobulins, lactoferrin, lactoferricin, α -lactalbumin, β -lactoglobulin, growth factors), conjugated linoleic acids, lactic acid bacteria and bifidobacteria
Olive oil	Oleic acid, ω 3 fatty acids, Flavonoids, cinnamic acid, benzoic acid, lignans, cumaric acid, ferulic acid, tocopherols, carotenoids, oleuropein, oleocanthal
Cinnamon	Cinnamaldehyde, cinnamic acid, coumarin, catechins, epicatechin, procyanidins B-2
Turmeric	Curcuminoids, stigmasterol, β -sitosterol, 2-hydroxy methyl anthraquinone, bioactive peptide turmerin
Sumac	Tannins, flavonoids, anthocyanins, phenolic acid, gallic acid

Other Nutraceuticals with significant health benefits

Polyphenols: These are secondary metabolites of plant. They are found predominantly in fruits, cereals, beverages and vegetables. Polyphenols have been of interest due to its antimutagenic, anticarcinogenic, antioxidant and anti-inflammatory properties [156-157]. Broad research has shown that these aforementioned properties of several polyphenols can be protective against several health concerns which include cancer, hypertension, diabetes, asthma, infection and cardiovascular diseases [158]. Numerous polyphenols exists with over 8000 different polyphenols compounds already identified E Curcumin, Epigallocatechingallate (EGCG).

Carotenoids: Carotenoids refer to any class of yellow to red plant pigments. It consists of a family of over 600 fat soluble plant pigments of which approximately 20 are present in human tissues and blood. Carotenoids cannot be synthesized by humans; hence, they must be obtained via ingestion of foods or supplements. Examples of some major dietary carotenoids are Beta-carotene, lycopene, zeaxanthin and lutein. They are potent ROS scavengers that protect the human body from oxidative stress [159,160].

Beta-carotene: B-carotene is a precursor to Vitamin A. Foods that are rich in B-carotene includes green leafy vegetables, orange root vegetables and yellow or orange fruits [159]. B-carotene has numerous functions in human body such as protecting cells from damage by inhibiting free radicals and photoprotective properties which increases Minimal Erythema Dose (MED) protecting against sunburn development and photo suppression of immune system. Beta-carotene dosage has been made available because its long term supplementation has been linked to increased risk of

lung cancer; hence further studies are needed to determine the optimal daily allowance in order to access supplementation health risks [161].

Lutein and Zeaxanthin: These are two primary xanthophylls carotenoids in the retina (where it is thought to promote eye health) and significant amounts are also found in human skin. Since humans cannot synthesize lutein or zeaxanthin, food rich in Lutein and Zeaxanthin such as leafy vegetables and eggs [162] are recommended because the carotenoids have the potency to filter and to block damage caused by blue wavelength and also act as antioxidants to prevent free radical damage [163-164].

Lycopene: Lycopene is regarded as the best singlet oxygen quencher in the carotenoid family even though it has no Vitamin A activity. Foods that are very rich in lycopene include tomatoes, pink grapefruits and water melon. Previous studies have shown that consumption of tomato paste (which is rich in lycopene) significantly lowers UV induced erythema and decreases MMP-1 activity, an enzyme involved in the breakdown of collagen [165]. In addition, there is also a significant association between higher skin concentration of lycopene and a decrease in skin roughness.

Conclusion

The health benefits of nutraceuticals are enormous and there is need to constantly review these health promoting food components in order to document new findings and to sensitize the populace about their health benefits whose embrace might be an act of enhancing longevity and its rejection may pose serious health challenges, and thus leading to sudden death.

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