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Embrace Nutraceuticals and Live, Reject it and 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, oesteoporosis 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 yoghourt 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 yoghourt 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 yoghourt 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 Szic 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 (Triticumaestivum L), rice (*Oryzasativa L*), maize (*Zeamays 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 nutts, 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, insulin emic, and lipid emic 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* systhesis 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 probiotc 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: Osteoathritis (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 overexpresssion 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 bear 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, cytrolin
Red apple, apple peel, apple and its by products	Soluble fiber, quercetin, catechins, epicatechin, P-cumaric acid, chlorogenic acid, gallic acid, phlordizin, procyanidins
Berries; cranberry, blackberry, black raspberry, blueberry, red raspberry, strawberries	Anthocyanins, tannins, ellagitanins, α-carotene, β-carotene, lutein, delphinidins, pelargonidins, ciyanidins, 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, ω3 fatty acids (docosahexaenoic acid, eicosapentaenoic acid), selenium, taurine
Pomegranate and its byproducts, pomegranate peel and seeds	Anthocyanins, tannins, catechins, gallocatechins, 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-lactorphines, lactoferrin, lactoferricin, α-lactalbumin, β-lactoglobulin, growth factors), conjugated linoleic acids, lactic acid bacteria and bifidobacteria
Olive oil	Oleic acid, ω3 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.

Reference

1. Martin AH (2006) Stair design in the United States and obesity: The need for a change. South Med J 102: 610-614.
2. Eze NM, Maduabum FO, Onyeke NG, Anyaegunam NJ, Ayogu CA, et al. (2017) Awareness of food nutritive value and eating practices among Nigerian bank workers Medicine. Baltimore 96: e6283.
3. Abdel-Salam AM (2010) Functional foods: Hopefulness to good health. American J Food Tech 5: 86-99.
4. Prabu SL, Suriyaprakash TNK, Kumar CD, Kumar SS (2012) Nutraceuticals and their medicinal importance. Intl J Health Allied Sciences 1: 1-6.
5. Popkin BM (2002) Understanding the nutrition transition: Measuring rapid dietary changes in transitional countries. Public Health Nutr 5: 947-952.
6. Maduabum FO (2015) Nutritional awareness of bank workers in Lagos State, Nigeria. Nsukka Nigeria, University of Nigeria.
7. Popkin BM (2006) Physical activity and cardiovascular disease risk profile in women. Am J Epidemiol 146: 322-328.
8. World Health Organisation (2012) Global status report on non-communicable diseases geneva, Switzerland: World Health Organisation.
9. World Health Organisation (2010) Global database on child growth and malnutrition: Forecast of trends Geneva, Switzerland, World Health Organisation.
10. Zhao J (2007) Nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy for improvement of human health: A perspective on plant biotechnology application. Recent Pat Biotechnol 1: 75-97.
11. De Felice Stephen L (1995) The nutraceutical revolution, its impact on food industry. Trends in Food Sci and Tech 6: 59-61.
12. El Sohaimy SA (2012) Functional foods and nutraceuticals-modern approach to food science. World Appl Sci J 20: 691-708.
13. Zeisel SH (1999) Regulation of nutraceuticals. Science 285: 185-186.
14. Mozaffarian D, Prineas RJ, Stein PK, Siscovick DS (2006) Dietary fish and n-3 fatty acid intake and electrocardiographic parameters in humans. J Am Coll Cardiol 48: 478-484.
15. Hollman PCH, Feskens EJ, Katan MB (1999) Tea flavonols in cardiovascular disease and cancer. Proc Soc Exper Biol Med 220: 198-202.
16. Gupta, Pankaj (2016) Functional foods for cancer therapeutics. Nat Prod Chem Res 4: 2.
17. Kalioraa AC, Dedoussisa GVZ, Schmidtb H (2006) Dietary antioxidants in preventing atherogenesis. Atherosclerosis 187: 1-17.
18. De Sousa VMC, dos Santos EF, Sgarbieri VC (2011) The importance of prebiotics in functional foods and clinical practice. Food Nutr Sci 2: 133-144.
19. Cencic A, Chingwaru, W (2010) The role of functional foods, nutraceuticals, and food supplements in intestinal health. Forum Nutr 2: 611-625.
20. Lobo V, Patil A, Phatak A, Chandra N (2010) Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev 4: 118-126.
21. Mazza G (1998) Functional foods. Pennsylvania: Technomic Publishing.
22. Cockbill CA (1994) Food law and functional foods. Br Food J 96: 3-4.
23. Figueroa-Gonzalez I, Quijano G, Ramirez G, Cruz-Guerrero A (2011) Probiotics and prebiotics-perspectives and challenges. J Sci Food Agric 91: 1341-1348.
24. Al-Sheraji SH, Ismail A, Manap MY, Mustafa S, Yusof RM, et al. (2013) Prebiotics as functional foods: A review. J Funct Food 5: 1542-1553.
25. Döderlein A (1892) Das scheidensecret und seine bedeutung f¨ur das puerperal fieber. Centralblatt fur Bacteriologie 11: 699-700.
26. Metchnikoff E (1908) The prolongation of life-optimistic studies. Butterworth-Heinemann, London.
27. Yakult Central Institute for Microbiological Research (1999) Lactobacillus casei Shirota- intestinal flora and human health. Yakult Honsha Co, Ltd, Tokyo.
28. Lilly DM, Stillwell RH (1965) Probiotics growth promoting factors produced by micro-organisms. Science 147: 747-748.
29. Schrezenmeir J, De-Vrese M (2001) Probiotics, prebiotics and synbiotics: Approaching a definition. Am J Clin Nutr 73: 361-364.
30. Fuller R (1989) Probiotics in man and animals. J Appl Bacteriol 66: 365-378.
31. Khan RU, Naz S (2013) The applications of probiotics in poultry production. Worlds Poult Sci J 69: 621-632.
32. Panda SK, Behera SK, Qaku XW, Sekar S, Ndinteh DT, et al. (2017) Quality enhancement of prickly pears (Opuntia sp) juice through probiotic fermentation using Lactobacillus fermentum ATCC 9338 LWT. Food Sci Technol 75: 453-459.
33. FAO/WHO (2001) Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria - Joint Food and Agricultural Organization of the United Nations and World Health Organization Expert Consultation Report C'ordoba,Argentina.
34. Hilliam M (1998) Functional foods in Europe. The World of Ingredients 45-47.
35. Iisakke K (2003) Nutraceuticals and functional foods for demand ingredients. Nutra Cos 2-4.
36. Stanton C, Gardiner G, Meehan H, Collins K, Fitzgerald G, et al (2001) Market potential for probiotics. Am J Clin Nutr 73: 476-483.
37. Challener C (2003) Speciality supplements are the bright spot in US dietary supplement market. Chemical Market Re 3-4.
38. Kaur S, Das M (2011) Functional foods: An overview. Food Sci Biotechnol 20: 861-875.
39. Swati S Mishra, Prafulla KB, Biswabandita Kar, Ramesh CR (2018) Advances in probiotics, prebiotics and

nutraceuticals (1st eds) Innovations in Technologies for Fermented Food and Beverage Industries, Food Microbiology and Food Safety.
40. Heasman, M, Mellentin J (2001) The functional foods revolution. Healthy people Healthy Earthscan Publications Ltd, London 135-147.
41. Menrad, K (2003) Market and marketing of functional food in Europe. J Food Eng 56: 181-188.
42. Evani S (2009) Trends in the US functional foods, beverages and ingredients market. Institute of Food Technologists, Agriculture and Agri-Food, Canada 1-14.
43. Shimizu M (2014) History and current status of functional food regulations in Japan. Food Sci Technol 4: 257-263.
44. Keservani RK, Sharma AK, Ahmad F, Baig ME (2014) Nutraceutical and functional food regulations in India. Food Sci Technol 6: 327-342.
45. Yusuf S, Reddy S, Ôunpuu S, Anand S (2001) Global burden of cardiovascular diseases, part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization Circulation 104: 2746-2753.
46. World Health Organization (2017) World Health Organization Factsheets, Cardiovascular diseases (CVDs).
47. Srivastava Shubhra, Pramod Kumar Sharma, S Kumara Guru (2015) Nutraceuticals: A review. J Chrono Drug Del 6: 1-10.
48. Torrejon, C, Jung, UJ and Deckelbaum, RJ (2007) N-3 Fatty Acids and Cardiovascular Disease: Actions and molecular mechanisms. Prostaglandins Leukot Essent Fatty Acids 77: 319-326.
49. Hdknight SH, Harris WS, Connor WE (1981) The effects of dietary omega 3 fatty acids on platelet composition and function in man: A prospective, controlled study. Blood 58: 880-885.
50. Knapp HR, Reilly IA, Alessandrini P, Fitz Gerald GA (1986) In vivo indexes of platelet and vascular function during fish-oil administration in patients with atherosclerosis. N Engl J Med 314: 937-942.
51. DeCaterina R, Giannessi D, Mazzone A (1990) Vascular prostacyclin is increased in patients ingesting omega-3 polyunsaturated fatty acids before coronary artery bypass graft surgery. Circulation 82: 428-438.
52. Carpentier YA, Portois L, Malaisse WJ (2006) N-3 Fatty acids and the metabolic syndrome. Am J Clin Nutr 83: 1499S-1504S.
53. Woodman RJ, Mori TA, Burke V, Puddey IB, Watts GF, et al (2002) Effects of purified eicosapentaenoic and docosahexaenoic acids on glycemic control, blood pressure, and serum lipids in type 2 diabetic patients with treated hypertension. Am J Clin Nutr 76: 1007-1015.
54. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A (2007) Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. JAMA 298: 299-308.
55. Chan DC, Watts GF, Nguyen MN, Barrett PHR (2006) Factorial study of the effect of n-3 fatty acid supplementation and atorvastatin on the kinetics of HDL, apolipoproteins A-I and apoA-II in men with abdominal obesity. Am J Clin Nutr 84: 37-43.
56. Mori TA, Woodman RJ (2006) The independent effects of eicosapentaenoic acid and docosahexaenoic acid on cardiovascular risk factors in humans. Curr Opin Clin Nutr Metab Care 9: 95-104.
57. Grimsgaard S, Bonaa KH, Hansen JB, Nordoy A (1997) Highly purified eicosapentaenoico acid and docosahexaenoic acid in humans have similar triacylglycerol-lowering effects but divergent effects on serum fatty acids. Am J Clin Nutr 66:649 -659.
58. Geleijnse JM, Giltay EJ, Grobbee DE, Donders AR, Kok FJ (2002) Blood pressure response to fish oil supplementation: Meta-regression analysis of randomized trials. J Hypertens 21: 1493-1499.
59. Ueshima H, Stamler J, Elliott P (2007) Intermap research group food omega-3 fatty acid intake of individuals (total, linolenic acid, long-chain) and their blood pressure: Intermap study Hyper 50:313-319.
60. Von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H (1999) The effect of dietary omega-3 fatty acids on coronary atherosclerosis A randomized, double-blind, placebo-controlled trial. Ann Intern Med 130: 554-562.
61. Eritsland J, Arnesen H, Gronseth K, Fjeld NB, Abdelnoor M (1996) Effect of dietary supplementation with n-3 fatty acids on coronary artery bypass graft patency. Am J Cardiol 77: 31-36.
62. Hjerkinn EM, Seljeflot I, Ellingsen I (2005) Influence of long-term intervention with dietary counseling, long-chain n-3 fatty acid supplements, or both on circulating markers of endothelial activation in men with long-standing hyperlipidemia Am J Clin Nutr 81:583-589
63. Rerksuppaphol S, Rerksuppaphol LA (2015) Randomized doubleblind controlled trial of Lactobacillus acidophilus Plus Bifidobacterium bifidum versus placebo in patients with hypercholesterolemia. J Clin Diagn Res 9: 1-4
64. Golnaz E, Mitra Z, Sharma A (2017) Effects of symbiotic and vitamin E supplementation on blood pressure, nitric oxide and inflammatory factors in non-alcoholic fatty liver disease. EXCLI Journal 16: 278-290
65. World Health Organization (2018) World Health Organization Factsheets, Cancer.
66. Ames BN, Shigenaga MK, Hagen TM (1993) Oxidants, antioxidants, and the degenerative diseases of aging. Proc Natl Acad Sci 90: 7915-7932.
67. Abrams JS, Mooney MM, Zwiebel JA, Korn EL, Friedman SH, et al. (2013) Implementation of timeline reforms speeds initiation of national cancer institute-sponsored trials. J Natl Cancer Inst 105: 954-959.
68. Ames BN, Shigenaga MK (1992) Oxidants are a major contributor to aging. Ann N Y Acad Sci, 663: 85-93.
69. Okada F Inflammation and free radicals in tumor development and progression Redox Rep 2002; 7: 357-366.
70. Mohammad Aghajanpour, Mohamad Reza Nazer, Zia Obeidavi, Mohsen Akbari, Parya Ezati, et al. (2017) Functional foods and their role in cancer prevention and health promotion: A comprehensive review. Am J Cancer Res 7: 740-769.

71. Vel Szic KS, Palagani A, Hassannia B (2011) Phytochemicals and cancer chemoprevention: epigenetic friends or foe. (2nd edi) Phytochemicals-bioactivities and impact on health. InTech, Janeza Trdine 9, 51000 Rijeka, Croatia.
72. Bragg FL, Smith M, Guo Y, Chen Y, Millwood I, et al. (2014) Associations of blood glucose and prevalent diabetes with risk of cardiovascular disease in 500,000 adult Chinese: The China Kadoorie Biobank Diabet Med, 31: 540-551.
73. Mandel S, Packer L, Youdim MBH, Weinreb O (2005) Proceedings from the third int conf mechanism of action of nutraceuticals. J Nutritional Biochem 16: 513-520.
74. Levy J, Bosin E, Feldman B, Giat Y, Miinster A, et al (1995) Lycopene is a more potent inhibitor of human cancer cell proliferation than either α or ß-carotene. Nutr Cancer 24: 257-266.
75. Ewaschuk JB, Walker JW, Diaz H, Madsen KL (2006) Nutrient physiology, metabolism, and nutrientnutrient interactions bioproduction of conjugated linoleic acid by probiotic bacteria occurs in-vitro and in-vivo in mice. J Nutri 136: 1483-1487.
76. Rossi M, Garavello W, Talamini R, La Vecchia C, Franceschi S, et al. (2007) Flavonoids and risk of squamous cell esophageal cancer. Int J Cancer 120: 1560-1564.
77. Santaguida PL, Balion C, Hunt D, Morrison K, Gerstein H, et al. (2005) Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose. Evid Rep Technol Assess 128: 1-11.
78. Evans JL, Goldfine ID, Maddux BA, Grodsky GM (2002) Oxidative stress and stress-activated signaling pathways: A unifying hypothesis of type 2 diabetes. Endocr Rev 23: 599-622.
79. De Faria Maraschin J (2013) Clasification of diabetes in: Ahmad SI, editor Diabetes An Old Dis a New Insight Landes Bio, Springer, 129.
80. Tripathi BK, Srivastava AK (2006) Diabetes mellitus: Complications and therapeutics. Med Sci Monit 12: 130-147.
81. Chen L, Magliano DJ, Zimmet PZ (2011) The worldwide epidemiology of type 2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol 8: 228-236.
82. World Health Organization (2018), World Health Organization Factsheets, Diabetes.
83. Amro Abdelazez, Heba A, Smith EE, Sherif M, Fang-Fang J, et al. (2018) Screening potential probiotic characteristics of lactobacillus brevis strains in vitro and intervention effect on type i diabetes. In Vivo BioMed Res Int 1-20.
84. Barbara Fletcher, Meg Gulanick, Cindy Lamendola (2002) Risk factors for type 2 diabetes mellitus. J Cardiovasc Nurs 16: 17-23.
85. Wu Y, Ding Y, Tanaka Y, Zhang W (2014) Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci, 11: 1185-1200.
86. Kazeem MI, Davies TC (2016) Anti diabetic functional foods as sources of insulin secreting, insulin sensitizing and insulin mimetic agents. J Funct Foods 20: 122-138.
87. Mirmiran P, Bahadoran Z, Azizi F (2014) Functional foods-based diet as a novel dietary approach for management of type 2 diabetes and its complications: A review. World J Diabetes 5: 267-281.
88. Rosén LA, Ostman EM, Björck IM (2011) Effects of cereal breakfasts on postprandial glucose, appetite regulation and voluntary energy intake at a subsequent standardized lunch; focuses on rye products. Nutr J 10: 7.
89. Rosén LA, Silva LO, Andersson UK, Holm C, Ostman EM, et al. (2009) Endosperm and whole grain rye breads are characterized by low post-prandial insulin response and a beneficial blood glucose profile. Nutr J 8: 42.
90. Sadiq Butt M, Tahir-Nadeem M, Khan MK, Shabir R, Butt MS (2008) Oat: Unique among the cereals. Eur J Nutr 47: 68-79.
91. Vanden Langenberg GM, Brady WE, Nebeling LC, Block G, Forman M, et al (1996) Influence of using different sources of carotenoid data in epidemiologic studies. J Am Diet Assoc 96: 1271-1275.
92. Tapola N, Karvonen H, Niskanen L, Mikola M, Sarkkinen E (2005) Glycemic responses of oat bran products in type 2 diabetic patients. Nutr Metab Cardiovasc Dis 15: 255-261.
93. Anderson JW, Bush HM (2011) Soy protein effects on serum lipoproteins: A quality assessment and meta-analysis of randomized, controlled studies. J Am Coll Nutr 30: 79-91.
94. Azadbakht L, Shakerhosseini R, Atabak S, Jamshidian M, Mehrabi Y (2003) Beneficiary effect of dietary soy protein on lowering plasma levels of lipid and improving kidney function in type II diabetes with nephropathy. Eur J Clin Nut, 57: 1292-1294.
95. Bhathena SJ, Velasquez MT (2002) Beneficial role of dietary phytoestrogens in obesity and diabetes. Am J Clin Nutr 76: 1191-1201.
96. Gilbert ER, Liu D (2013) Anti-diabetic functions of soy isoflavone genistein: Mechanisms underlying its effects on pancreatic β-cell function. Food Funct 4: 200-212.
97. Andreasen S, Larsen N, Pedersen ST (2010) Effects of Lactobacillus acidophilus NCFM on insulin sensitivity and the systemic inflammatory response in human subjects. Br J Nutr 104: 1831-1838.
98. Kadooka Y, Sato M, Imaizumi K (2010) Regulation of abdominal adiposity by probiotics (Lactobacillus gasseri SBT2055) in adults with obese tendencies in a randomized controlled trial. Eur J Clin Nutr 64: 636-643.
99. Sanchez M, Darimont C, Drapeau V, Emady-Azar S, Lepage M, et al. (2014) Effect of Lactobacillus rhamnosus CGMCC13724 supplementation on weight loss and maintenance in obese men and women. Br J Nutr 111: 1507-1519.
100. WHO (1998) Obesity: Preventing and managing the global epidemic working group on Obesity Geneva, World Health Organization.
101. World Health Organization (2017) World health organization factsheets, Obesity and overweight.

102. Unnikrishnan AG, S Kalra, Garg MK (2012) Preventing obesity in India: Weighing the options. Ind J Endocrinol Metab 16: 4-6.
103. Gamboa-Gómez CI, Rocha-Guzmán NE, Gallegos-Infante JA, Moreno-Jiménez MR, Vázquez-Cabral BD (2015) Plants with potential use on obesity and its complications. EXCLI J 14:809-831.
104. World Health Organization (2017) World Health Organization Factsheets, 10 facts on obesity.
105. Viner RM, Hsia Y, Tomsic T, Wong ICK (2010) Efficacy and safety of anti-obesity drugs in children and adolescents: Systematic review and meta-analysis. Obesity Rev 11: 593-602.
106. Karthiga T, Venkatalakshmi P, Vadivel V, Brindha P (2016) In vitro anti-obesity, antioxidant and anti-inflammatory studies on the selected medicinal plants. Int J Toxic Pharma Res 8: 332-340.
107. Claire C, Ludivine M, Alina R (2012) Traitement pharmacologique de l'ob´esit´e, Medecine. The J Clin Endo Met 61: 1-12.
108. Kang JG, Park CY (2012) Anti-obesity drugs: A review about their effects and safety. Diab Metab 36: 13-25.
109. Hsu T, Kusumoto A, Abe K (2006) Polyphenol-enriched oolong tea increases fecal lipid excretion. Europ J Clin Nutri 60: 1330-1336.
110. Koo SI, Noh SK (2007) Green tea as inhibitor of the intestinal absorption of lipids: Potential mechanism for its lipid-lowering effect. The J Nutri Biochem 18: 179-183.
111. Ambati S, Yang JY, Rayalam S (2009) Ajoene exerts potent effects in 3T3-L1 adipocytes by inhibiting adipogenesis and inducing apoptosis. Phytother Res 23: 513-518.
112. Arai S (1996) Studies on functional foods in Japan-state of the art. Biosci Biotechnol Biochem 60: 9-15.
113. Thomas PR, Earl R (1994) Enhancing the food supply In: Opportunities in the nutrition and food sciences. National Academy Press, Washington, DC.
114. Ishihara K, Oyaizu S, Fukuchi Y (2003) A soybean peptide isolate diet promotes postprandial carbohydrate oxidation and energy expenditure in type II diabetic mice The Journal of nutrition 133: 752-757.
115. Kazemipoor M, Radzi CWJWM, Cordell GA, Yaze I (2012) Potential of traditional medicinal plants for treating obesity: A review. IPCBEE 39.
116. Birari RB, Bhutani KK (2007) Pancreatic lipase inhibitors from natural sources: Unexplored potential. Drug Disc 12: 879-889.
117. Hansen JC, Gilman AP, Odland JØ (2010) Is thermogenesis a significant causal factor in preventing the globesity epidemic. Med Hypo 75: 250-256.
118. Van Heerden F, Hoodia Gordonii (2008) A natural appetite suppressant. J Ethno 119: 434-437.
119. Haaz S, Fontaine K, Cutter G (2006) Citrus aurantium and synephrine alkaloids in the treatment of overweight and obesity: An update. Obesity Rev 7: 79-88.
120. Abatenh E, Gizaw B, Tsegay Z (2018) Health benefits of probiotics. J Bacteriol Infec Dis 2:8-27.
121. Catherine TD, Mitchell LJ, Divya Sl (2014) Cholesterol assimilation by lactobacillus probiotic bacteria: An in vitro investigation. BioMed ReS Int 1-9.
122. Naheed M, Fatimah H, Narges V (2015) Characterization of indigenous Lactobacillus strains for probiotic properties Jundishapur. J Microbiol 8: 1-7.
123. Vaishnavi K, Krishma M, Rajeswari P (2016) A study on cholesterol degradation by Lactobacillus. Indian J Appl Res 9: 12.
124. Juturu V, Gormley JJ (2005) Nutritional supplements modulating metabolic syndrome risk factors and the prevention of cardiovascular disease. Curr Nutr Food Sci 1:1-11.
125. Merz-Demlow, BE, Duncan AM, Wangen KE (2000) Soy isoflavones improve plasma lipids in normocholesterolemic, premenopausal women. Am J Clin Nutr 71: 1462-1469.
126. Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell, et al. (2006) Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med 354: 795-808.
127. Lei M, Guo C, Wang D, Zhang C, Hua L, et al (2017) The effect of probiotic Lactobacillus casei Shirota on knee osteoarthritis: A randomised double-blind, placebo-controlled clinical trial. Beneficial Microbes 8: 697-703.
128. Dalton-Brewer N (2016) The Role of complementary and alternative medicine for the management of fibroids and associated symptomatology. Curr Obstet Gynecol Rep 5:110-118.
129. Laughlin SK, Schroeder JC, Baird DD (2010) New directions in the epidemiology of uterine broids. Semin Reprod Med 28: 204-217.
130. Evans P, Brunsell S (2007) Uterine fibroid tumors: Diagnosis and treatment. Am Fam Physician 75: 1503-1508.
131. Stewart EA (2001) Uterine fibroids. Lancet 357: 293-298.
132. Buttram VC, Reiter RC (1981) Uterine leiomyomata: Etiology, symptomatology, and management. Fertil Steril 36: 433-445.
133. Carlson KJ, Miller BA, Fowler FJ (1994) The maine women's health study: II outcomes of nonsurgical management of leiomyomas, abnormal bleeding, and chronic pelvic pain. Obstet Gynecol 83: 566-572.
134. Kjerul KH, Langenberg P, Seidman JD, Stolley PD, Guzinski GM (1996) Uterine leiomyomas racial differences in severity, symptoms and age at diagnosis. J Reprod Med 41: 483-490.
135. Zimmermann A, Bernuit D, Gerlinger C, Schaefers M, Geppert K (2012) Prevalence, symptoms and management of uterine fibroids: An international internet based survey of 21,746 women. BMC Womens Health12: 6.
136. Metwally M, Li T (2015) reproductive surgery in assisted conception. Sur J 107.
137. Coronado GD, Marshall LM, Schwartz SM (2000) Complications in pregnancy, labor, and delivery with uterine leiomyomas: A population based study. Obstet Gynecol 95: 764-769.

138. Benson CB, Chow JS, Chang Lee W, Hill JA, Doubilet PM (2001) Outcome of pregnancies in women with uterine leiomyomas identified by sonography in the first trimester. J Clin Ultrasound, 29: 261-264.
139. Bulun SE (2013) Uterine fibroids. The New Eng J Med 369: 1344-1355.
140. Boosz AS, Reimer P, Matzko M, Romer T, Muller A (2013) The conservative and interventional treatment of fibroids. Dtsch Arztebl Int 111: 877-883.
141. Stewart EA, Cookson CL, Gandolfo RA, Rath RS (2017) Epidemiology of uterine fibroids: A systematic review BJOG: An Int J Obst Gyna 8: 221-223.
142. Wise LA, Palmer JR, Harlow BL (2004) Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the black women's health study. Hum Reprod 19: 1746-1754.
143. Wise LA, Radin RG, Palmer JR, Kumanyika SK, Boggs DA, (2011) Intake of fruit, vegetables, and carotenoids in relation to risk of uterine leiomyomata. Am J Clin Nutr 94: 1620-1631.
144. Claudine-Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L (2004) Polyphenols: food sources and bioavailability. Am J Clin Nutr 79: 727-747.
145. Kim DI, Lee TK, Lim IS, Kim H, Lee YC (2005) Regulation of IGF-I production and proliferation of human leiomyomal smooth muscle cells by Scutellaria barbata D Don in vitro: Isolation of flavonoids of apigenin and luteolin as acting compounds. Toxicol Appl Pharmacol 205: 213-224.
146. Roshdy E, RajaratnamV, Maitra S, Sabry M, Allah ASA (2013) A treatment of symptomatic uterine fibroids with green tea extract: A pilot randomized controlled clinical study. Int J Womens Health 5: 477-486.
147. Scalbert A, Williamson G (2000) Dietary intake and bioavailability of polyphenols. J Nutr J Nutri 130: 2073-2085.
148. Landete JM, Curiel JA, Rodr´ıguez H, de-las Rivas B (2014) Aryl glycosidases fromLactobacillus plantarum increase antioxidant activity of phenolic compounds. J Funct Food 7: 322-329.
149. Kasimsetty SG, Bialonska D, Reddy MK (2010) Colon cancer chemopreventive activities of pomegranate ellagitannins and urolithins. J Agri Food Chem 58: 2180-2187.
150. Juranic Z, Zizak Z, Tasic S (2005) Antiproliferative action of water extracts of seeds or pulp of five different raspberry cultivars. Food Chemistry 93: 39-45.
151. Krousel-Wood MA, Muntner P, He J, Whelton PK (2004) Primary prevention of essential hypertension. Med Clin North Am 88: 223-238.
152. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, et al. (2013) Heart disease and stroke statistics-2013 update: A report. American Heart Association Circulation 127: e6-e.
153. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, et al. (2002) Primary prevention of hypertension: Clinical and public health advisory from The National High Blood Pressure Education Program. JAMA 288:1882-1888.
154. Patel AK, Singhania RR, Pandey A (2010) Probiotic bile salt hydrolase: current developments and perspectives. Appl Biochem Biotechnol 162: 166-180.
155. Guo Z, Liu XM, Zhang QX (2011) Influence of consumption of probiotics on the plasma lipid profile: A meta-analysis of randomised controlled trials. Nutr Metab Cardiovasc Dis 21: 844-850.
156. Pinnell SR (2003) Cutaneous photodamage, oxidative stress, and topical antioxidant protection. J Am Acad Dermatol 48: 1-19.
157. Pal HC, Hunt KM, Diamond A, Elmets CA, Afaq F (2016) Phytochemicals for the management of melanoma Mini Rev. Med Chem 16: 953-979.
158. Pandey KB, Rizvi SI (2009) Plant polyphenols as dietary antioxidants in human health and disease oxidative. Med Cell Longev 2: 270-278.
159. Evans JA, Johnson EJ (2010) The role of phytonutrients in skin health. Nutrients 2: 903-928.
160. Fiedor J, Burda K (2014) Potential role of carotenoids as antioxidants in human health and disease. Nutrients 6: 466-488.
161. Grether-Beck S, Marini A, Jaenicke T, Stahl W, Krutmann J (2016) Molecular evidence that oral supplementation with lycopene or lutein protects human skin against ultraviolet radiation: Results from a double-blinded, placebo-controlled, crossover study. Br J Dermatol 176: 1231-1240.
162. Roberts RL, Green J, Lewis B (2009) Lutein and zeaxanthin in eye and skin health. Clin Dermatol 27: 195-201.
163. Schwartz S, Frank E, Gierhart D (2016) Zeaxanthin based dietary supplement and topical serum improve hydration and reduce wrinkle count in female subjects. J Cosmet Dermatol 15: e13-e20.
164. Juturu V, Bowman JP, Deshpande J (2016) Overall skin tone and skin-lightening-improving effects with oral supplementation of lutein and zeaxanthin isomers: a double-blind, placebo-controlled clinical trial. Clin Cosmet Investig Dermatol 9: 325-332.