

Review

# The role of nutraceuticals, functional foods and value added food products in the prevention and treatment of chronic diseases

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The interest in phytochemicals found in plant foods as bioactive components of the diet has expanded in the last few years. This is because they have been linked with the prevention or reduced progression of many chronic diseases, such as cardiovascular disease, cancer and degenerative diseases. Oxidative stress, which could bring about oxidative damage to DNA, protein and lipids has been found to be a major factor in the aetiology of these diseases. Epidemiological evidence shows that observed health benefits of these plant foods on humans, especially fruits and vegetables, are due to the presence of bioactive phytochemicals which today, play an important role in pharmaceutical applications. Research shows that these compounds modulate the risk of chronic disease development by inhibiting reactions mediated by reactive oxygen species (ROS). Consequently, strong recommendations for their ingestion through the diet have become increasingly popular to improve man's health. This article presents a review of the role of nutraceuticals, functional foods and value added food products in the prevention and treatment of chronic diseases. We also summarized the biotechnological approaches for enhancing the level of these bioactive compounds in plants, with a view to improve their nutraceutical value and phytotherapy efficiency.

**Key words:** Antioxidants, degenerative diseases, dietary reference intakes, disease prevention, nutraceuticals.

## INTRODUCTION

Chronic diseases are generally non-communicable diseases (NCDs) of long duration characterized by slow development or progression. These diseases can be prevented and controlled, but not cured. They are

sometimes termed degenerative diseases because the structure or function of the affected tissues or organs progressively deteriorates overtime, whether due to normal bodily wear or lifestyle choices such as exercise

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or eating habits. They often accompany aging, a process which is synonymous with mitochondrial decay and are the consequence of poor nutrition, stress and toxic overload over a long period of time. These diseases include cancer, cataracts, immune system decline, cardiovascular disease, brain dysfunction and atherosclerosis. CVDs, especially atherosclerotic CHD and stroke, are the leading causes of disability and death in developed countries (AHA, 2007) and are projected to be the leading cause of death in the developing world by 2020 (WHO, 2005). Arterial atherosclerosis which primarily affects target organs of the heart, kidney and brain, first develops, until a major cardiovascular catastrophe occurs, leading to morbidity and sudden death. The emphasis so far has been on the functional degeneration of somatic cells during aging, but recently, oxidative damage to DNA lipid and protein has been implicated in the aetiology of these diseases. The level of oxidative DNA damage seems to be roughly related to metabolic rate in a number of mammalian species (Ames, 2001). In fact, one human cell is believed to be exposed to about 105 oxidative hits a day from hydroxyl radical and other such species of oxidants (Lopaczynski and Zeisel, 2001). ROS are normal oxidant by-products of aerobic metabolism, and under normal metabolic conditions about 2 to 5% of oxygen consumed by mitochondria is converted to ROS (Anagnostopoulou et al., 2006). The resulting oxidative stress then permanently modifies the genetic material leading to numerous degenerative or chronic diseases, such as atherosclerosis and cancer (Shanmuganayagam et al., 2007).

More than half of the human population worldwide has no access to a healthy variety of fresh food (Christou and Twyman, 2004), resulting into malnutrition which has become a significant public health issue in most nations, especially the developing world. In malnutrition, increased oxidative stress coupled with chronic inflammation often brings about an increased risk of atherosclerosis (Vinson et al., 2001). Hence, the acronyms MICS (malnutrition inflammation complex syndrome) or MIA (malnutrition inflammation and atherosclerosis syndromes) are used to indicate the combination of these two conditions in patients (Pecoits-Filho, 2002). Very recently, there is a shift towards the optimal nutrition diet because of the growing health issues and there has been an increasing awareness of the populace in most nations of the world about the interplay between nutrition and health. Much scientific evidence indicates that certain bioactive compounds in foods have various disease-fighting properties, which has made consumers worldwide become much more interested in the health benefits of foods. Consequently, dietary reference intakes (DRI) and nutrition recommendations are targeted at disease prevention (EFSA, 2010). Healthy eating guidelines have directed the general public to eat more fresh fruits, vegetables, low fat and high fiber foods throughout the world (WHO,

2003). Food manufacturers therefore tend to produce foods and food products that can satisfy consumer appetite and cravings for health promotion. Such food or food products often carry health claims portraying this attribute and include nutraceuticals, functional foods, value added food products and whole plant foods. The consumption of these foods brings about a reduction in health care costs and supports economic development, especially in rural communities (El Sohalmy, 2012). The health claims on food labels are governed by specific regulations in some countries. For instance, the Food and Drug Administration (FDA) oversees and allows such claims in the United States. We review the role of these foods in the prevention and treatment of chronic diseases. Also, we try to summarize the biotechnological approaches being employed to increase the level of bioactive compounds in food crops, so as to enhance their nutraceutical and functional values, which are important factors in nutritional therapy.

#### **THE BURDEN OF CHRONIC DISEASES AND POSSIBLE INTERVENTION OF NUTRACEUTICALS, FUNCTIONAL FOODS AND VALUE ADDED FOOD PRODUCTS**

Most countries in the world are presently going through a nutritional transition and are affected by double burden of nutritional problems. Under nutrition and specific nutrient deficiencies, especially micronutrient deficiency remain unabated, and simultaneously imbalanced diets and chronic diseases are becoming burdensome and the trend is rapidly increasing globally (Kotilainen et al., 2006). In 2001, chronic diseases were reported to contribute about 46% of the world burden of disease and this has been predicted to increase to 57% by 2020 (WHO, 2002). Most of these diseases now appear earlier in life and affect both the affluent and the poor in developing and developed nations of the world. Chronic diseases are largely preventable diseases. As a result, the promotion of healthy diets, nutrition and lifestyles to reduce the global burden of these diseases is continually being advocated, and a possible way out is the copious consumption of nutraceuticals, functional foods and value added food products, due to their ready availability and diseases preventing characteristics.

Nutraceuticals, which have gained worldwide popularity, have been defined as purified or concentrated food and food products with health-promoting and/or disease-preventing properties beyond their basic nutritional function (Gunther et al., 2004). When consumed, they enhance health and quality of life for people of all ages. Nutraceuticals range from isolated nutrients, dietary supplements, and diets, to naturally occurring substances such as herbals, vitamins, amino acids or their formulations, and processed products such as cereals, soups, and beverages (Kharb and Singh, 2004).

**Table 1.** FOSHU foods and Ingredients (El Sohalmy, 2012).

<b>Carbohydrates</b>	<b>Proteins</b>
Polydextrose	Casein phosphopeptide
Indigestible dextrin	Casein dodecapeptide
Galacto oligosaccharides	Soy protein
Lactulose	<b>Minerals</b>
Lactosucrose	Phosphorus
Isomalto oligosaccharides	Calcium as citrate malate
Maltitol	Heme iron
Palatinose	<b>Others</b>
Soybean oligosaccharides	Rice globulin
Fructo oligosaccharides	Eucommia leaf glycoside
Xylo oligosaccharides	Lactobacillus GG
Wheat bran	

Functional foods have been considered as foods made up of nutrients that confer physiological or medical benefit to the consumers. In fact, any healthy food confirmed to have a health promoting or disease preventing property beyond the basic functions of supplying nutrition is now regarded as a functional food (Martirosyan and Singh, 2015). Nonetheless, it is important to note that there is no universally accepted regulatory definition of the term 'functional foods' to date, despite their wide usage in marketing, and they represent one of the fastest growing segments of the food industry in most nations of the world. Therefore, in addition to providing new options for improving health and well-being, the functional foods sector offers potential for new economic opportunities. These foods often carry a special seal and have been recognized as Foods for Specified Health Use (FOSHU) in Japan (ILSI, 1999). The list of foods or ingredients that qualify for FOSHU status is shown in Table 1.

Value added food products are foods whose nutrients, shape, size or appearance has been scientifically modified from the post-harvest stage of production to improve functionality, and in some cases, reduce consumer preparation time (Feldeisen and Tucker, 2007). They are sometimes termed 'designer foods' and the enhanced phytonutrients usually make them more beneficial health wise.

Whole plant foods are foods obtained solely from plants. Thus, the plant-based diet is made up of fruits, vegetables, tubers, whole grains and legumes with the exclusion or minimal intake of meat, fish, eggs and dairy products (Hu, 2003). It also does not include processed foods or sweets.

Nutraceuticals, functional foods and value added food products are therefore rich repositories of health promoting bioactive compounds. Scientific research show that a large proportion of these compounds often act as antioxidants, and have a role *in-vivo* in modulating disease development by inhibiting ROS mediated reactions, which have been associated with the initiation

and progression of a number of pathological processes (Bajpai et al., 2005). It has been suggested that the protective properties of some of these compounds may be ascribed to a novel mechanism unrelated to their conventional free-radical scavenging abilities (Cooke et al., 2002), and the susceptibility of body tissues to oxidative damage is a reflection of the balance between the extent of pro-oxidant stress and antioxidant levels (Capecka et al., 2005).

Also, from the point of view of food safety, there is growing interest in the practice of using natural antioxidants, especially from herbs and spices, as additives in the food industry. This is not unconnected with their ability to prevent lipid peroxidation (in fat - rich food products), thereby ensuring food stability and prolonged storage time (Olzcan, 2003).

The major bioactive compounds in food crops have been classified on the basis of their activities. Examples include: Carotenoids ( $\alpha$  - and  $\beta$  - carotene,  $\beta$  - cryptoxanthin, lutein, lycopene, and zeaxanthin); Phenols (flavonoids); Cyclic phenolics (chlorogenic acid, ellagic acid, and coumarins); Glucosinolates (sulforaphane, indole-3 carbinol); Saponins; Phytosterols (campesterol,  $\beta$  - sitosterol, and stigmaterol); Sulfides and thiols; Phytoestrogens (isoflavones, daidzenin, genistein, and lignans)(Pradeep and Mallikarjuna, 2012). The carotenoids and flavonoids have been especially implicated in the prevention, control and management of chronic diseases.

Carotenoids comprise an extended group of natural pigments numbering about 600 of which  $\beta$  - carotene is the most prominent. Of this amount, about 50 are consumed in appreciable quantities in human diets (Rimm and Stampfer, 2000). They are present in vegetables, fruits, fungi, algae and bacteria, and are traditionally classified into two large structural groups: the carotenes, which are basically hydrocarbons  $C_{40}H_{56}$  ( $\alpha$  - and  $\beta$  - carotene and lycopene), and the xanthophylls,  $C_{40}H_{56}(OH)_2$ , which include different oxygenated functions in the molecule (lutein, zeaxanthin,  $\beta$ -cryptoxanthin and canthaxanthin). The structures of some prominent carotenoids in human plasma are shown in Figure 1. Carotenoids are responsible for the colour of foods and some occur only in specific plants e.g. lycopene in tomato, pink guava, pink grapefruit, papaya and water melon.

Many studies have shown that individuals with higher dietary intakes of carotenoids have a reduced risk of several chronic diseases (Prakash et al., 2004). The carotenes are generally tissue specific in their biological activity and the xanthophylls serve to protect other antioxidants. The mechanism by which carotenoids protect cells against ROS mediated damage depends largely on physical quenching, a process in which the energy of the excited oxygen is transferred to the carotenoid molecule (Elliott, 2005). In this regard, lycopene has been reported as the most efficient singlet

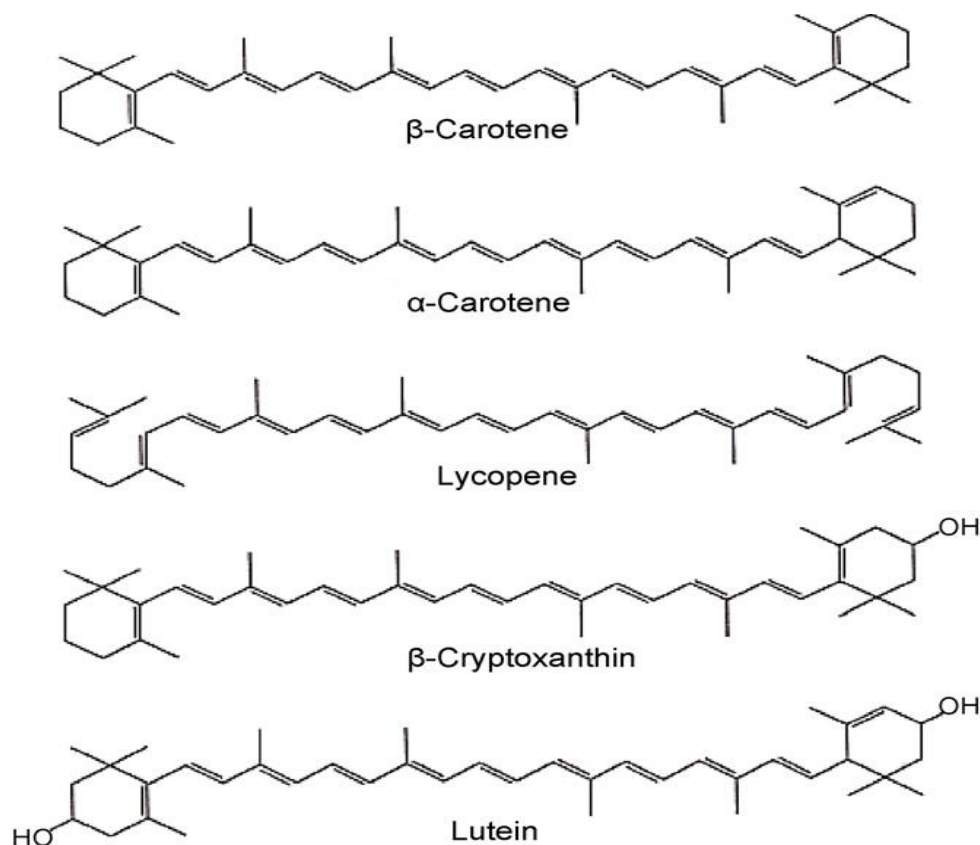


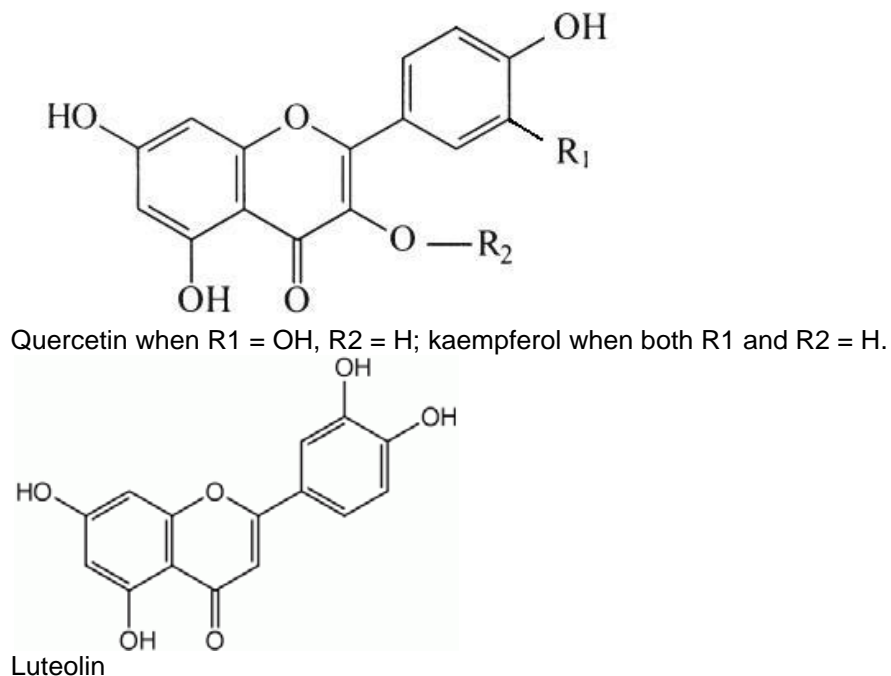
Figure 1. Chemical structures of some common carotenoids.

oxygen quencher among the naturally occurring carotenoids (Prakash and Gupta, 2009).

The major active nutraceutical ingredients in plants are flavonoids. Flavonoids are a family of low molecular weight polyphenolic compounds present in cereals, vegetables, fruits and drinks of plant origin, such as red wine, tea, cocoa and coffee. The compounds are derived from parent compounds known as flavans (Markovic, 2007). About 4000 flavonoids are known and these are classified into six major groups namely flavones, isoflavones, flavanones, flavonols, flavanols (flavan-3-ols) and flavanonols. They are potent antioxidants or free radical scavengers that offer protection against cardiovascular disease by reducing the oxidation of low density lipoproteins (Johnson, 2003). It has been reported that flavonoids may exert local anticarcinogenic effects by acting as intraluminal antioxidants in the intestine (Ren et al., 2003). They may also exert cardioprotective action by preventing or retarding damaging oxidative reactions in cells which is a predisposing factor for the development of CVDs (Di Santo et al., 2003). In particular, studies have shown that Mediterranean diets rich in resveratrol can lower the risk for the development and progression of cardiovascular disease in humans. A few of these compounds are shown in Figure 2.

## HEALTH BENEFITS

Epidemiological evidence shows that regular consumption of functional foods, value added food products and nutraceuticals is associated with a lowered risk of coronary heart disease, obesity, diabetes, cancer, osteoporosis and other chronic age-related degenerative diseases like Parkinson's and Alzheimer's diseases (Prakash and Kumar, 2011). Berry fruits and blackcurrants, for example, are employed in folk medicine for the prevention and treatment of circulatory disorders and inflammatory diseases. These foods are known to play important roles in modulating oxidative stress in disease states. Their observed health benefits has been ascribed to the presence of bioactive compounds (Priya and Santhiya, 2011) which accumulate in plasma and tissues of consumers in relation to dietary intakes and play a role in inhibiting reactions mediated by reactive oxygen species (Ames et al., 1993; Etminan et al., 2004). These compounds, either alone, or synergistically, have much therapeutic potential and exert varying biological and pharmacological effects in human health as anticarcinogenic, anti-inflammatory, anti-diabetic, antioxidants, antifungal, antipyretic, anti-apoptotic, chemopreventive, hepato-protective, hypolipidemic, analgesic, CNS stimulant and stimulation of cellular immunity



**Figure 2.** Chemical structures of some flavonoids.

(Hakiman and Maziah, 2009; Prakash et al., 2012). For instance, tocopherol is useful as an antioxidant therapeutic agent in attenuating the progression of heart attack (Azzi et al., 2003) and heart failure (Ghatak et al., 1996). The vitamin prevents CVDs by reducing platelet adhesion, elevating HDL level in the blood and inhibiting smooth muscle cell proliferation, a predisposing factor in atherosclerosis (Lee et al., 2005). Because they are readily available, cheaper and safer, nutraceuticals, functional foods and value added food products are becoming widely acceptable as alternatives to conventional drugs and pharmaceuticals (Chatterjee et al., 2013). Some of the pharmacological effects are briefly discussed.

### Anticarcinogenic activity

Metabolic syndrome, also known as insulin resistance syndrome, has been identified as an important contributing factor to the progression of some cancers (Singh et al., 2009). Much evidence has been provided to show that a diet rich in fruits and vegetables correlates positively with reduced risk of development of cancer and chronic age-related degenerative diseases (Aberoumand and Deokule, 2010). For instance, vegetable sources like broccoli, cabbage, cauliflower and brussel sprouts with a rich repository of glucosinolates are known to exert a substantial protective support against colon cancer (Doughari, 2012).

Foods and herbs known to have high anticancer activity include ginger, garlic, cabbage, soybeans, fenugreek,

green tea, flaxseed and the umbellifous vegetables (Sakr et al., 2012). Researchers have demonstrated that blueberry anthocyanins, proanthocyanidins, resveratrol, flavonols, and tannins inhibit mechanisms of cancer cell development and inflammation *in vitro* (Arts and Hollman, 2005). Fenugreek, an aromatic herbaceous annual, has also been shown to be cytotoxic against several cancer cell lines inducing apoptosis and cell death (Shabbeer et al., 2009) while lycopene, PUFAs, Co Q10, melatonin and CLA are useful for the preventive treatment of leukaemia, lymphoma, prostate, breast, lung and colon cancers. *In-vivo* studies have shown that hesperidin, a flavonoid glycoside in orange (*Citrus sinensis* L.), and diosmin, its flavone analogue possess anticarcinogenic activity (Tanaka et al., 1997).

### Antidiabetic and gastroprotective effects

The herb and spice crop, fenugreek exhibits insulinotropic and antidiabetic properties (Al-Habori and Raman, 2002) which have been associated with the amino acid, 4-hydroxyisoleucine that occur in this leguminous crop at a concentration of about 0.55%. *In vitro* studies have demonstrated that this amino acid directly stimulates pancreatic  $\beta$ -cells, decreases insulin resistance in muscles and liver by activating insulin receptor substrate-associated phosphoinositide 3-kinase activity. It therefore affects glucose and lipid metabolism and finds use in the control of type- II diabetes, obesity and dyslipidemia (Jette et al., 2009). The effect of aqueous or soluble gel fraction of fenugreek seeds has also been studied on

ethanol-induced gastric ulcer. The seed extract showed significant ulcer protective effect (Tadigoppula et al., 2006), showing that the soluble gel fraction was more effective than Omeprazole, a standard drug in preventing lesion formation.

Flavonoids, especially the polyphenol, quercetin (which is largely present in white wines), has also been reported to possess antidiabetic activity. Vessal et al. (2003) reported that quercetin brings about the regeneration of pancreatic islets and probably increases insulin release in streptozotocin-induced diabetic rats.

### Prevention of LDL oxidation

The progression of atherosclerotic CHD is characterized by oxidative modification of LDL-C (Fillipe et al., 2004). Reducing the risk of CHD therefore entails the inhibition of LDL-C oxidation. Nutraceuticals that are beneficial in the prevention and reduction of symptoms of CHD include GSPE, lycopene, black and green tea and their flavonoids, DHA, EPA, flax lignans, soy protein and isoflavones, coenzyme Q10, pycogenol, DHEA, melatonin, carnitine, resveratrol and lutein (Kharb and Singh, 2004). Specifically, the role of lycopene in the prevention of CVDs has been extensively discussed (Rissanen, 2006). The level of oxidized LDL-C was significantly reduced in subjects ingesting tomato juice, tomato sauce and lycopene oleoresin capsules as sources of lycopene (Agarwal and Rao, 1998).

### Anti-apoptotic activity

Apoptosis, also known as 'programmed cell death' is a series of regulated biochemical events (suicide mechanism) which the cell uses to kill itself. The process takes place under physiological and pathological conditions. Inappropriate apoptosis is often fatal, resulting into disorders like neurodegenerative diseases, myocardial infarction and atherosclerosis in most cases (Kumar and Jugdutt, 2003). Mounting evidence shows that flavonoids inhibit apoptosis in the myocardium (Ishikawa and Kitamura, 2000; Lopez-Lopez et al., 2004) but the mechanism of this effect is not yet fully understood. Some of the proposed mechanisms include abolition of digestion of caspase -3 substrates, free radical scavenging activity, decrease in both oxidative stress and the pro-apoptotic factors C-JUN and JNK.

### Cardioprotective and hepatoprotective effects

One group of bioactive compounds, the phytosterols, found naturally in many plant foods with vegetable oils (particularly unrefined oils), nuts, seeds and grains as the major dietary sources (Piironen et al., 2000) has been

studied for their biochemical roles in chronic diseases. Their cholesterol lowering ability makes them relevant in reducing the risk of incidence of cardiovascular diseases (Xiaobo et al., 2009). The nutraceuticals  $\beta$ -sitosterol (BSS),  $\beta$ -sitosterol glucoside (BSSG) from *Vernonia amygdalina* Del. (bitter leaf) and their mixture (BSS:BSSG) has been shown to possess cardioprotective and hepatoprotective properties, with possible practical application in the management of CVDs (Olaiya et al., 2013a). Reports also indicate that fenugreek, the nutraceutical food plant has hepatoprotective effect. The polyphenolic seed extract of the plant acts as a protective agent against ethanol - induced abnormalities in the liver, demonstrating similar effects as that of silymarin, a known hepatoprotective agent (Thirunavukkarasu et al., 2003).

### MOLECULAR MECHANISM OF ACTION

Disease is the end result of a series of defects in the biochemical machinery of the body. For instance, biochemical and biophysical abnormalities of cell membranes have been implicated in the pathogenesis of hypertension and CVDs. The abnormalities seem to be involved not only in vascular smooth muscle cells but also in circulating blood cells. (Elisaf, 2001).

The mechanism through which nutraceuticals prevent chronic diseases has not been fully elucidated. Many of these phytochemicals have been found to alter antioxidant defence of cells through the induction of DNA repair processes or enzymic antioxidant defence at the gene level. It has been suggested that they may also affect cell cycle progression (Hwang and Bowen, 2004), cell communication (Stahl et al., 2000), hormone and growth factor signaling (Zhang et al., 2002) and apoptosis (Zhang et al., 2003). Lycopene, a potent hypocholesterolemic agent found in tomato has been shown to prevent atherosclerosis by inhibiting LDL-C oxidation (Rissanen et al., 2002). Also, indole-3-carbinol, the most vital and important indole present in broccoli has been found to inhibit the Human Papilloma Virus (HPV) that may cause uterine cancer. This phytochemical acts by blocking the estrogen receptors specifically present in the breast cancer cells as well as down regulating CDK6, and up regulating p21 and p27 in prostate cancer cells. It brings about G1 cell-cycle arrest and apoptosis of breast and prostate cancer cells significantly and enhances the p 53 expression in cells treated with benzopyrene (Dreij et al., 2010). It also depresses Akt, NF-kappaB, MAPK, and Bel-2 signaling pathways to an appreciably good extent (Doughari, 2012).

Many research studies have shown that soy or soy phytoestrogens can inhibit the growth of some cancer cell lines. They are believed to exert actions on a range of biochemical pathways and molecular mechanisms implicated in cell growth, development and survival (Fritz

et al., 2003). This is relevant in the prevention and control of clinically important cancer.

## ENGINEERING PLANTS FOR IMPROVED BIOACTIVE COMPOUNDS PRODUCTION

The prime reason for altering or elevating phytochemicals in plants is associated with their potential benefit to human health. There have been many recent assessments of technologies that abound or that can be developed for increasing plant resources for human consumption. Notably among these is the potential of biotechnology and genetic modification techniques which are being harnessed by the modern man for the production and development of functional foods, and improvement in the level and activity of bioactive compounds in many food plants (Niba, 2003). The technologies include strategies such as biosynthesis pathways engineering, usage of elicitors, large scale cultivation in bioreactor system, root culture, plant cell immobilization, high yielding cell line screening and biotransformation (Peterhansel et al., 2008). Selective breeding and metabolic engineering are also being harnessed by researchers for the development of food crops with improved nutraceutical value such as high vitamin A rice, high-iron rice, improved protein and fatty acid profiles in oil seed crops, legumes and soybeans (Niba, 2003). Currently, there is a shift from genotypes engineered to enhance single nutritional compounds to genotypes with enhanced multiple nutrients. This entails the use of bioregulators, multigene engineering or regulative genetic element with pleiotropic effects, so as to harness the synergistic interactions of these phytochemicals in food crops for their biological activities. It has been suggested that the response of a factor transferred by gene manipulation may be augmented by the use of plant bioregulators, which might act as powerful tools in enhancing the growth, productivity, quality and combating the ill effects generated by various biotic and abiotic stresses in functional food crops in the not too distant future (Olaiya et al., 2013b).

## CONCLUSION

Plants provide directly, or indirectly, about 95% of the world's food supply and plant - based foods with their rich repository of phytochemicals have great beneficial effects on human health (Amrit, 2006). There is increased craving for healthier lifestyle by the populace, and this is only achievable by consuming diets rich in health - promoting compounds. Functional foods, nutraceuticals and value added food products are becoming more popular and readily available in many nations, with a potential large market in a few years to come. The fact that their consumption has been associated with healthy aging, prevention and treatment of chronic diseases

makes them more desirable. However, some food safety issues and concerns have been raised about their use, particularly the herbals (FDA, 2002). This call for effective regulations and legislation to ensure that the health claims is based on sufficiently strong scientific evidence. Efforts should be intensified to communicate their health benefits to the populace so that they can have sufficient information to make wise choices about the foods they eat and enjoy. Research into techniques of enhancing the levels of disease-fighting phytochemicals in food crops should also be sustained. Additionally, the new field of nutrigenomics, which is the application of the sciences of genomics, proteomics, transcriptomics and metabolomics to human nutrition (Kaput and Rodriguez, 2004), may allow the use of information on an individual's genetic make - up for the prediction of personalised nutraceutical and functional food supplementation to prevent or control chronic diseases in the not too distant future.

## Conflict of Interest

The authors declare no conflict of interest.

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## Abbreviations

**BSS**,  $\beta$ -sitosterol; **BSSG**,  $\beta$ -sitosterolglucoside; **CHD**, Coronary Heart Disease; **CLA**, conjugated linoleic acid; **CNS**, central nervous system; **Co Q10**, Coenzyme Q10; **CVDs**, cardiovascular diseases; **DHA**, docosahexaenoic acid; **EFSA**, European Food Safety Authority; **DHEA**, dehydroepiandrosterone; **DNA**, deoxyribonucleic acid; **DRI**, Dietary Reference Intakes; **EPA**, eicosapentaenoic acid; **FAO**, Food and Agriculture Organization of the United Nations; **FDA**, Food and Drug Administration; **FOSHU**, Foods for Specified Health Use; **GSPE**, Grape Seed Proanthocyanidin Extract; **HDL**, high density lipoprotein; **ILSI**, International Life Sciences Institute; **LDL-C**, low density lipoprotein-cholesterol; **MIA**, Malnutrition Inflammation and Atherosclerosis; **MICS**, Malnutrition Inflammation Complex Syndrome; **NCDS**, Non-Communicable Diseases; **PUFAs**, polyunsaturated fatty acids; **ROS**, reactive Oxygen Species; **WHO**, World Health Organization.

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