OPEN ACCESS
Freely Available Online

JOURNAL OF BIOTECHNOLOGY AND BIOMEDICAL SCIENCE
ISSN NO: 2576-6694

Review

DOI : 10.14302/issn.2576-6694.jbbs-18-2408

Need Of Nutraceuticals / Functional Food Products for Health Benefits to World-Wide People

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Abstract

Improved economic and developed people with their lifestyle have created many challenges of health issues (obesity, osteoporosis, cancer, diabetes, allergies and dental problems), due to selection of different food habits (such as consumption of manifold junk foods). It has created number of health problem (development of many diseases) related to nutritional deficiencies food. Nowadays, people have developed the habit for shifting of synthetic food ingredients to organic foods and ingredients, obtained from natural sources. In this regards, nutraceuticals food or its food products can perform important role in controlling the diseases via fulfilling all the health benefits to many people at worldwide. Incredible dietary supplements as nutraceuticals food (involvement in nutritional, immunologic and physiological functions) can help in prevention or treatment of many diseases (mitigating of gastrointestinal (GI) tract problem), as it is synthesized from raw herbals and lots of rapidly growing industries are reported to synthesize these natural products. And around 100 million people are found to take these products (power of plant based materials) for getting health benefits. It can work as drugs as health benefit of nutraceuticals via regulation/ control for diseases. Global nutraceuticals market had been valued for US$ 165.62 billion in 2014 and it would be grow the value of US$ 278.96 billion by 2021 with compound annual growth rate of 7.3%. This proposed paper will discuss the different types of nutraceuticals food or its functional components involved in prevention or treatment of diseases.

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Running title: Nutraceuticals food products for health

Keywords: Lifestyle; Health issues, Nutritional deficiencies, Diseases, Nutraceuticals foods, Treatment, Prevention.

Received: Sep 30, 2018 **Accepted:** Oct 28, 2018 **Published:** Oct 30, 2018

Editor: Jun Wan, Department of Medical and Molecular Genetics, Indiana University School of Medicine, USA.

Introduction

Stephen De Felice has coined the term nutraceutical for the food product or its functional components exhibiting nutrition and pharmaceutical properties both. Nutraceuticals can be functional food ingredients or dietary supplements, obtained from natural sources (mostly plants origin). It is taken by many people at worldwide for getting the health promotion or benefits and disease risk reduction. Infinite number of bioactive compounds (individually or collectively) are reported with the expected beneficial effects and it has provided many benefits, depending on mechanisms occurred at varied level with their positive effects [1,2]. Phenolic compounds have shown the antioxidant activity via protecting the people from cellular oxidation. Conjugation of bioactives with other active or inactive components has also shown their positive effect as activity of resultant products. And in this regards, phytosterols with docosahexaenoic acid (DHA) are reported to lower cholesterol level in people whereas combination of esters of epigallocatechin gallate with docosahexaenoic acid has shown to arrest colon cancer in mice model. Illustration of the concepts and approaches are used for expected benefits in human being [3].

Significant effects on blood pressure (BP) control have been reported from Dietary Approaches to Stop Hypertension (DASH) in Mediterranean diet as large nutritional interventions. BP-lowering effects from different nutraceuticals product have been studied with specific foods to rich in minerals, lipids, whole proteins, peptides, amino acids, probiotics and vitamins [4]. Further, use of potassium, L-arginine, vitamins C and D, cocoa avonoids, beetroot juice, some probiotics, coenzyme Q10, controlled-release melatonin, aged garlic extract, and coffee has reported for beneficial to health promotion. Other nutraceuticals are also utilized by people to get health benefits which are green tea, fax-seed and resveratrol without any adequate evidence. Chocolate favanols has property to reduce cardiovascular risk. Clinical research is required to identify active nutraceuticals with gained of best cost-effectiveness and risk–benefit ratio [5].

Orthosiphon stamineus has shown significant affect in reduction of mean 24-hour systolic and diastolic BP levels compared to baseline values. Addition of *Orthosiphon stamineus* in combination of nutraceuticals (i.e. policosanol, red yeast rice extract, berberine, folic acid and coenzyme Q(10)) has shown the antihypertensive effect on effective 24-hour BP control in hypertensive patients. Nutraceuticals are free from side effects with valuable strategy for the treatment of blood pressure problem in patients [5,6]. Vascular biology, endothelial and vascular smooth muscle; and cardiac dysfunction have shown their role for initiation and perpetuation of hypertension, cardiovascular disease and target organ damage. But the nutraceuticals food product, nutrient-gene interactions and epigenetic phenomena can provide the predominant factors in promoting the beneficial or reducing the detrimental effects to cardiovascular health and hypertension respectively [7,1].

And macronutrients and micronutrients in food have shown their effect with the capability to prevent, control and treat hypertension via involvement of numerous mechanisms in vascular biology. Functional foods are reported to differ from nutraceuticals but it is required in definite amount for healthy state and survival of people which can get from vitamins, fats, proteins, carbohydrates [8]. Oxidative stress, inflammation and autoimmune dysfunction are reported for initiation and propagation of hypertension and cardiovascular disease. And selected use of functional component in nutraceutical supplements, vitamins, antioxidants and minerals are useful in treatment of hypertension based on complement and optimal nutrition coupled with other lifestyle modifications [9].

Nutraceutical Nature of Food Products or Food Ingredients

Functional foods are the products, possessing physiological benefits to people and its good source can be traditional foods. And nutraceuticals are commodities obtained from natural foods sources with medicinal benefits and it is utilized in form of pills, capsules or liquids with demonstration of physiological benefits and shown in Figure 1**.** In Canada, natural health products have found to promote health benefits which include nutraceuticals and herbal as well as other natural products (plants) [10]. However, functional foods and nutraceuticals are used interchangeably for improving

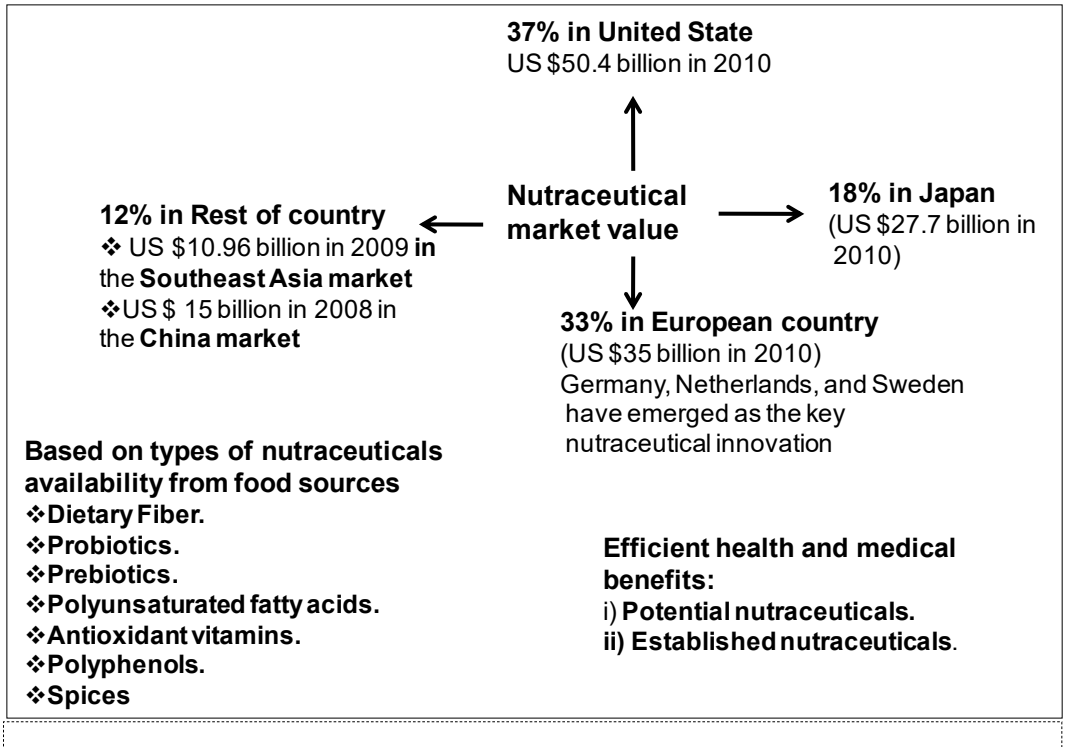

Figure 1. Type of nutraceuticals availability at worldwide from food products [19]

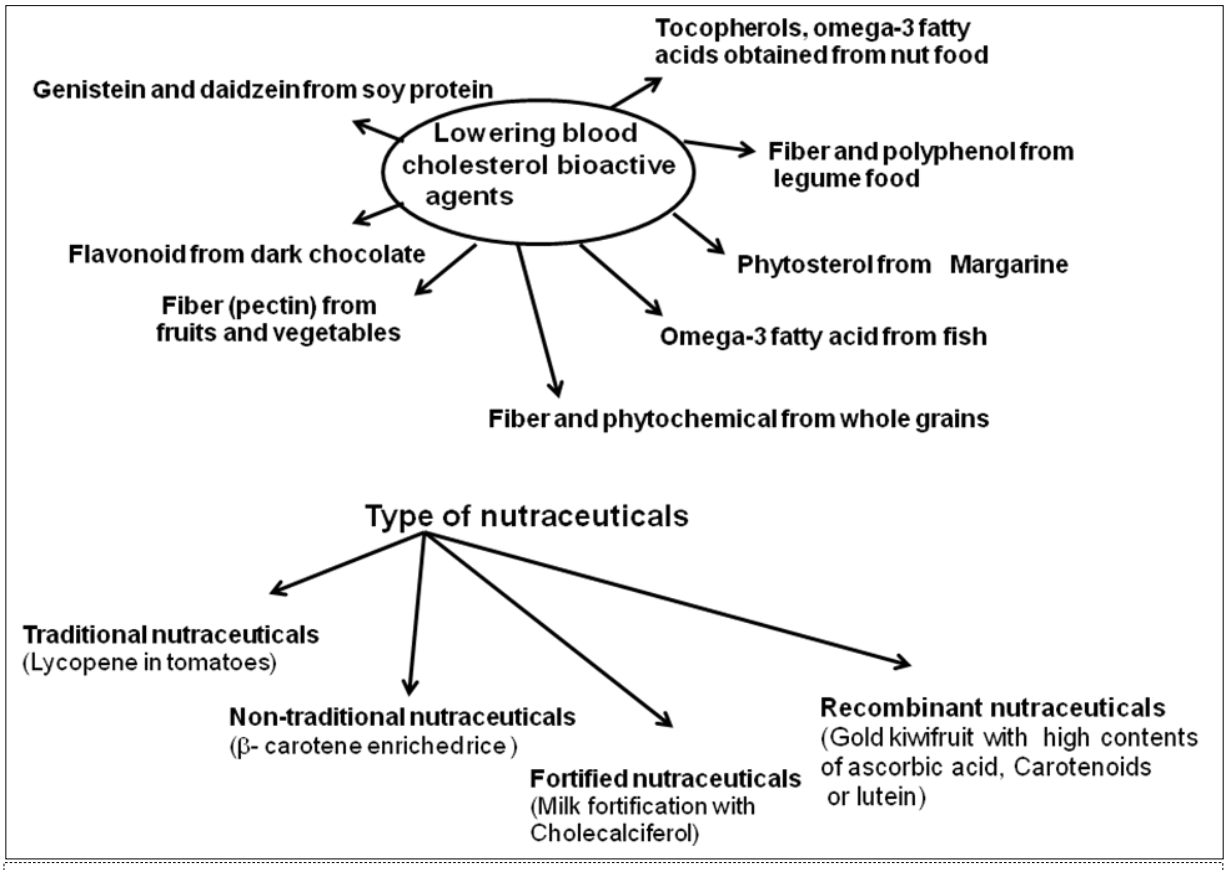

Figure 2. Bioactive components from different food sources help in lowing of blood cholesterol concentration [13, 14].

Table 1. Food sources with neutraceutical properties of different health benefits in many diseases in people

Source of foods	Parts used for	Health benefits	References
1- Allium sativum (Garlic)	Fresh or dried cloves or garlic extracts is utilized by patients	Arteriosclerosis, lowering of cholesterol in blood arteries is shown	[24]
2- ***Capsicum annum*** (Red or Bell pepper)	Fresh and dried fruit powder is used by patient. It is also used as colourant, flavourant, and/or as a source of pungency.	Natural antioxidant, stimulant, dietary antioxidants as health benefits is shown It prevents the blood clots in heart attacks problem	[25, 26]
3- Zingiber officinale, *(Ginger)*	Fresh dried root is used by patient	Help in Indigestion with antioxidant property via having glutathione (GSH) activity and total superoxide dismutase (SOD). Also help in the treatment of liver fibrosis	[27, 28]
4- Phyllanthus emblica *(Amla)*	Fruit pulp or dried fruit is used by patient	Diuretic and anti-ageingis shown and utilized in diabetes, osteoarthritis with chondroprotective potential	[24, 29]
5- Curcuma longa (Turmeric)	Dried root with curcumin compound and chemically known as diferuloylmethane	Helping in Inflammation and indigestion problem with antioxidant property and help in treatment of multiple chronic diseases and has antibacterial agent	[24, 30]
6-Artemisia annua (Artemisia)	Shoot decoction and leaf-derived solvent extracts are used by patient	Anti-malarial and antioxidant property of it is used for remedy against free radical damage (erythrocytes haemolysis)	[24, 31]
7-Matricaria chamomilla (Chamomilla) greek meaning "ground apple"	Dried flower is used by patient	It is used in wound healing, indigestion, insomnia, fever, inflammation, muscle spasms, men-strual disorders, ulcers, rheumatic pain and hemorrhoids	[27, 32]

health with reduction of disease risk through its prevention. They are mostly multi-targeted mixtures and present at low concentration where as pharmaceuticals are uni-targeted and pure compounds with high dose [11].

Polyphenols (catechins~ 30% and epigallocatechin gallate (EGCG) ~59%) are found in dry weight of green tea leaves with multitudes of bioactivities and are highly hydrophilic and poor solubility in lipophylic media with hinderance on its absorption in-vivo state. Acylation of EGCG with selected fatty acids are reported to improve its lipophibicity with its high potential for absorption to expanded application in more diverse systems. These are fats and oils, lipid-based foods and cosmetics as well as biological systems for better cellular absorption and bio-efficacy under physiological conditions and shown in Figure 2 [12].

The esters of phytosterols with omega-3 fatty acids as well as a number of phenolic acids are used as nutraceuticals products. Research and commercial interest has shown in formation of specific combination of phytosterol esters with vegetable oils. Enzymatic or chemoenzymatic preparation of novel phytosterol esters with DHA, other long-chain omega-3 fatty acids have been found more affective or And others with synthesis of phytosteryl caffeates, ferulates sinapates and vannilate (exhibiting food antioxidants) are also utilized for health promotion in people. Phytosteryl oleates with DHA have shown best effect in cholesterol lowering effects. The antioxidant potential of phytosteryl phenolates is influenced by a number of mechanisms for rendering their effects [15]. Food and diet has played a key contribution in promotion of health and lowering of disease state in people. Improved and nutritious full quality of diet has shown viashowing its value in health maintenance. Healthy eating plate by people should be followed with guidance of a balanced meal and it should be contained half of the plate of vegetables and fruits, a quarter of whole grains and the other quarter with healthy proteins. It can lead to a lower risk of heart disease and premature death and shown in Figure 3 [16].

Sustainable health is also reported for healthy and active ageing without the risk of diseases. Healthy foods and functional foods are needed to achieve this health via accomplished by delivering high quality care with improvement of public health and also maintenance of natural resources without severe ecological damage. It can protect and improve health for present and future generations via taking as a healthy nutrition (with functional foods). Minimizing the environmental impact on health and nutrition are required for healthy life [17,18].

Traditional nutraceuticals are made up of the food without any manual changes and its components are natural with some potential of health benefits. Lycopene in tomatoes vegetable are best example. Nontraditional nutraceuticals has capability to boost nutritional content by addition of nutrients, dietary components with improvement of quality of nutrition and b- carotene enriched rice is food example of this class [20].

Fortified nutraceuticals are synthesized from fortification of food components which is completed by addition of micronutrients (trace elements or vitamins) to food. It has enhanced the effectiveness and nutritional value of formulated food products and milk fortification is done with cholecalciferol for treatment of Vitamin D deficiency patients [21]. Application of biotechnology and genetic engineering has helped in recombinant nutraceuticals synthesis which is involved the production of energy providing foods (yoghurt and cheese or extraction of bioactive components) by enzymatic or fermentation technology. Gold kiwifruit has contained high contents of ascorbic acid, carotenoids, lutein and zeaxanthin and it has genetically modified to get it and shown in Table 1 [22, 23]. In this paper, author will discuss some of potential nutraceuticals products which is prepared by biological mean or obtained from some natural plant sources.

Microbial Processes for Lycopene Production

Lycopene is used as functional food with antioxidative and anti-cancer activities / properties, used frequently in nutraceutical, pharmaceutical and cosmetic industries. Chemical synthesis and extraction of lycopene have been done from tomatoes fruits, but microbial production of lycopene is found more economical and sustainable ways. Microbial lycopene production has started from various microbial strain including *Blakeslea*

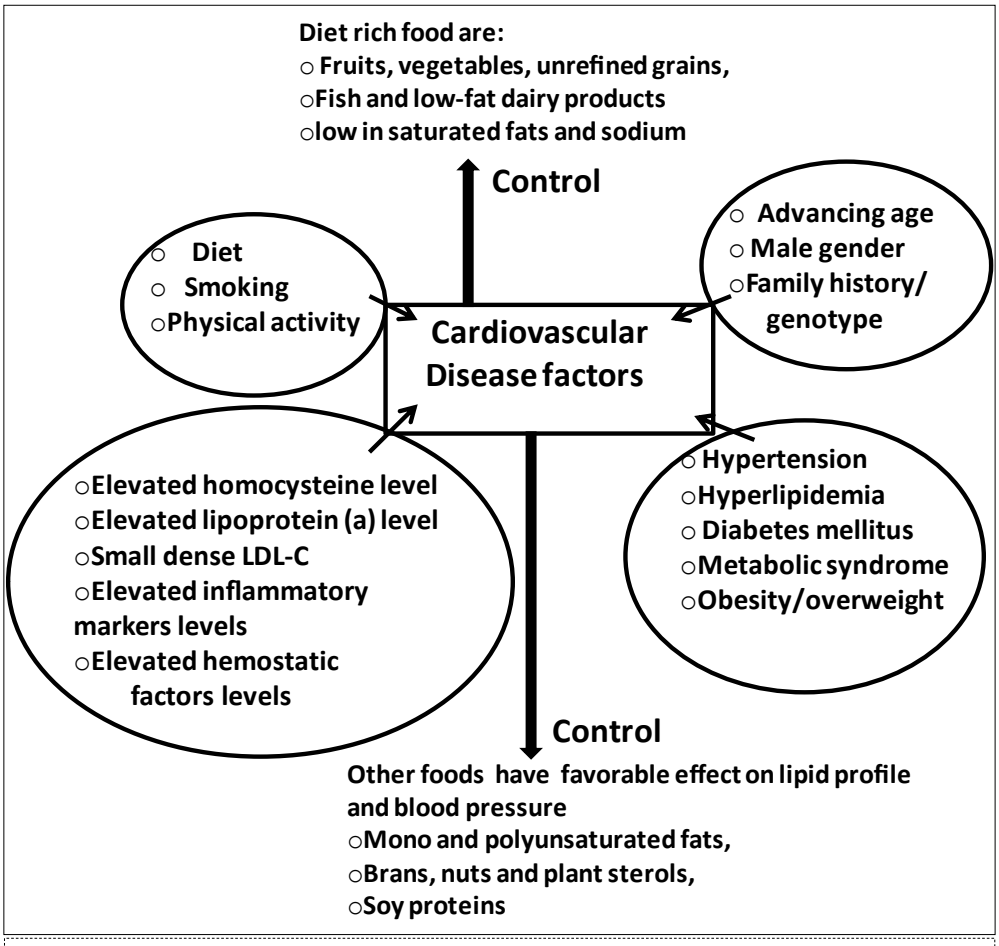

Figure 3. Some nutraceutial sources from food products or its ingredient for reduction of cardiovascular disease with its possible risk factors [14]

trispora, E. coli and *yeasts* [33,34].

Due to food safety issues, use *B. trispora* or *E. coli* (release endotoxin) for lycopene synthesis has been used as active producer but these strains can be utilized via addition of cyclase inhibitors to secure food safety [20]. *Saccharomyces cerevisiae* can be used as industrial organism and it is generally recognized as safe (GRAS) for robust and preferred use with its enhanced lycopene yield (24.41 mg/g DCW) via putting elaborate efforts with directed evolution and copy number variation of *Crt* genes (from *Xanthophyllomyces dendrorhous)*. It has shown that combinatorial engineering in *S. cerevisiae* has helped in construction of a heterologous pathway for enhanced lycopene yield with effective solution [35].

Lycopene biosynthesis pathway has been modified by addition of CrtE, CrtB and CrtI genes (taken from diverse species) in strain of *S. cerevisiae* CEN.PK2 which has helped in (approximately100 %) increasing the cytosolic acetyl-CoA pool compared to parental strain. Screening of CrtE, CrtB and CrtI, for optimal carotenogenic enzyme combination has been done. CrtI from *Blakeslea trispora* (BtCrtI) has shown excellent performance on lycopene production and also lycopene proportion in carotenoid [36]. Expression level of *BtCrtI* has been fine-tuned for evaluation of effect of cell mating types. Distant genetic targets (*YJL*064W (encodes functional protein), *ROX*1 (encodes putative regulator protein of hypoxic, and *DOS*2 (control of single-copy DNA replication)) deletion with up-regulation of stress-responsive transcription factor INO2 (for formation of a complex with the INO1 promoter) have been done for modification of carotenogenic pathway and resulted with enhanced lycopene yield about 22-fold (from 2.43 to 54.63 mg/g DCW). Further fed-batch fermentation has helped the lycopene production yield of 55.56 mg/g DCW in 5-L bioreactors as highest reported yield in yeasts [36,37].

Lycopene is one of member of carotenoid family and used as an efficient antioxidant and singlet oxygen quencher and itsdemand has been increased in the nutraceutical and drug industry. And researchers are putting more efforts to synthesize the effective microbial strain and methods for production of lycopene in cost effective manner at large scale for fulfilling the growing demand. Thermal processing has helped in liberation this carotenoid from complexes with proteins via increasing its bioaccessibilty [38].

In natural process, lycopene content is obtained from fruit peels of guava, papaya, watermelon and red dragon fruit as best sources. UV–vis spectrophotometer has helped in measuring of lycopene content whereas identification of lycopene has done by using high performance liquid chromatography (HPLC). Response surface methodology (RSM) using faced centered composite design (FCCCD) has applied to study the interaction among temperature, time and solid-solvent ratio for maximum lycopene yield (103.1 mg/kg) [39, 40]. In chemical synthesis, the lycopene oleoresin has been saponified using a mixture of propylene glycol and aqueous alkali for getting lycopene crystals fit for human consumption. High Performance Liquid Chromatography has helped in identification of constituents of the total lycopene oleoresin after saponification with lycopene (69.879%) and β-carotene (30.121%) [39,41].

The dehydrated papaya peels has been also utilized for the extraction of lycopene which is standardized for the maximum recovery of the pigment by using response surface methodology with use of three independent variables and their levels based on Face Central Composite Design. Lycopene content in papaya peels has reported to varied between 59.712 to 103.1 mg/kg. In this approach, lycopene are highest values (327 mg/ kg FW) from ripe papaya fruit. Other reports have also claimed for highest level of lycopene (575 mg/kg and 669 mg/kg) from same sources. [42,43].

Bacterium *Rhodospirillum rubrum* is reported as purple non sulfur microbial strain for production of lycopene (up to 2 mg/g (dry weight) of cells or up to15mg/liter of culture) as intermediates in linear pathway for phytoene biosynthesis. This bacterium is gone for desaturation of phytoene via enzyme phytoene desaturase (CrtI) catalysis for leading to neurosporene [44]. Later lycopene is produced via involving only three dehydrogenation steps and not four. Chromosomal insertions of akanamycin resistance cassette into the crtC and crtD region of the partial carotenoid gene cluster are responsible for the downstream processing of lycopene as the major carotenoid. Spectroscopic and biochemical evidence in vivo has shown the lycopene incorporation into the light-harvesting complex1 [44,45].

Combination of rational systems, biological design and random screening approaches has helped to enhance the lycopene levels 18 mg/g (dry weight) to nonlinearly batch-fed of *E. coli* cultures. Introduction up to 40 consecutive copies of heterologous carotenoid biosynthesis pathway genes into the *E. coli* chromosome has shown 14mg of lycopene/g(dry weight). Carbon flow to lycopene in *E. coli* has shown higher titre via introduction of a synthetic regulatory circuit Ntr regulon and it has sensed an intracellular signaling molecule (acetyl phosphate) [46,47].

Phytosterol Synthesis

Phytosterols or plant sterols are belong to family of cholesterol molecules with structural similarity and are found in the cell membranes of plants, playing important roles like cholesterol in humans. Campesterol, sitosterol and stigmasterol are reported most common phytosterols in the human diet. It has acted in the intestine to lower cholesterol absorption and it needs to present in healthy human diets with minimum risk of coronary heart disease [48].

Plant immunity has reported to involve the pathogen-associated molecular pattern (PAMP)-triggered immunity (PTI) and effector-triggered immunity (ETI) which is found to develop the non-host resistance in all members of a plant species due to potentially pathogenic microbes. Increased contents of stigmasterol in leaves of plant has reported through stimulation of sterol C22 desaturation after *Pseudumonas syringae* infection and it attenuates pathogen-induced expression of the defense regulator flavin-dependent monooxygenase-1 enzyme [49,50].

Due to alteration in sterols profile, in plant, has led to alter the control of the efflux of cytoplasmic

nutrients and solutes into apoplastic space without any grown bacterial pathogens. Pathogens have derived of nutrients from host plants with development of relationship between apoplastic nutrient levels and bacterial growth. Membrane leakage and pathogen growth in two different plant species has shown the different concentration of sterol content for plant innate immunity against bacterial infections via regulation of nutrient efflux into the apoplast [51,52].

A species of Arabidopsis plant (*Arabidopsis thaliana*) is reported as sterol methyltransferase 2 mutants and found to involve in sterol biosynthesis with resultant to plant innate immunity against bacterial pathogens. Arabidopsis cytochrome P450 CYP710A1 has capability to encode C22-sterol desaturase which can convert b-sitosterol to stigmasterol due to induced inoculation with nonhost pathogens [53]. An *Arabidopsis Atcyp*710A1 with null mutant has developed both nonhost and basal resistance. But over-expression of AtCYP710A1 has enhanced resistance to host pathogens via involvement of sterols in plant innate immunity against bacterial infections and also has regulated nutrient efflux into the apoplast [54].

Phytosterols are steroid compounds in most of plants with structural and functional similarity to cholesterol of human. Phytosterols can lower the plasma total and LDL-cholesterol levels in human or animals via direct inhibition of cholesterol absorption through displacement of cholesterol from mixed micelles. Stanols in phytosterols are more efficient in lowering cholesterol levels than sterols (unsaturated). Phytosterols have some substitutions at the C24 position on the sterol side chain [55].

Plasma phytosterol in mammalian tissues are low in concentration due to poor absorption from the intestine but faster excretion is reported from the liver. It can be metabolized in the liver of mammals into C21 bile acids via producing health benefits in animals / humans with decreased risk of coronary heart diseases, antiinflammatory activities, induction of apoptosis in cancer cells with disease prevention and treatment. Adverse effects of phytosterols are reported in few group of individuals with phytosterolemia (an inherited lipid disorder) with reduction in plasma levels of nutrients (carotenoids). Phytosterols and their derivatives have promoted the health of man and animals via encouraging their consumption in the population [56,57].

Steroid compounds are widely marketed products of pharmaceutical industry. Highly specific reactions (hydroxylation or ã^{1}-Dehydrogenation) are needed to produce functionalized compounds for therapeutic use and commercial value. The complexity of steroid molecules can be minimized by use of biocatalysts for high regio- and stereo-selectivity of the reactions [58]. The mild conditions are required for bioconversions which led to the development of high yield in biological production processes with environmentally friendly than their chemical synthesis as a major concern of industrialists. Bioconversions are well-established, efforts for increasing the the efficiency of the existing processes as well as to identify new potentially useful bioconversions [58,59].

Prebiotics and Probiotics Food Synthesis

Prebiotic foods are reported as non-digestible foods in human digestive system (onions, garlic, bananas, Jerusalem artichoke, chicory root, beans, and skin of apples, or others prebiotic fiber) and it is mostly reported in small intestine and has capability to stimulate the favourable growth or enhanced the activities of indigenous probiotic bacteria. And it reaches to large colon and it is feed by colonies of beneficial bacteria (probiotic bacteria) and helped in increasing desirable bacteria number in our digestive systems (gut) with association to better health and reduced disease risk [60].

Prebiotic therapies has been reported to cure gut related diseases (constipation relief, suppression of diarrhoea, reduction of the risks of osteoporosis, atherosclerotic cardiovascular disease associated with dyslipidemia, insulin resistance, obesity, and possibly type 2 diabetes) and prebiotics are associated with sufficiently enriched with fibers needed for proper gut work [61].

Probiotics are reported as live and beneficial bacterial culture and their metabolites is naturally created by fermentation in foods and yogurt, sauerkraut, miso soup, kimchi, and others fermented foods are good examples. Recent periods, it is also available in pill form

and also added ingredient in products (yogurt and health drinks). Kefir is found a milk drink with fermented using kefir grains as potent source of probiotics. It contains lactobacilli and bifidobacteria in high numbers with diversity nature (50 different or more types of bacteria) [62].

It has more consistency in drinking food with yoghurt and it is traveling into the digestive tract via colonizing the colon. Currently, consumption of functional foods or nutraceutical food in everyday diet as its parts has demonstrated to potential health benefits. Probiotics are most important and frequently used as functional food compound as it is healthy dairy products and been an excellent source of nutritious foods [63]. Such probiotic dairy foods has beneficially affect on the host by improving survival and implantation of live microbial dietary supplements in the gastrointestinal flora or by selectively stimulating the growth or activating the catabolism. It contains one or a limited number of health-promoting bacteria in the intestinal tract, or by improving the gastrointestinal tract's microbial balance. Current scenario of probiotics and their prospective has shown many potential applications for functional foods for better health and nutrition of the society [64].

Probiotic strains of lactobacilli have been used in clinical practices due to their many health benefits. Probiotic strains of lactobacilli (*Lactobacillus* species) infections are rarely (bacteremia or sepsis) reported in two patients [63]. Probiotic lactobacilli has been subsequently developed and molecular DNA fingerprinting analysis has been performed for *Lactobacillus* strain isolated from blood samples of probiotic strain ingested patient. Invasive disease can be associated with probiotic lactobacilli which should not discourage the appropriate use of Lactobacillus or other probiotic agents and it can cause invasive disease in certain populations [64].

A specific probiotic formulation has been reported to made of *Lactobacillus acidophilus* CL1285, *Lactobacillus casei* LBC80R, and *Lactobacillus rhamnosus* CLR2 (Bio-K+) in market in North America from 1996. These strains has used as commercial products and evaluated for safety, identity, gastrointestinal survival, and stability throughout shelf life [65]. Fermented beverages and the capsules can reduce incidences of antibiotic-associated diarrhea and *Clostridium difficile* infection (CDI) in human as clinical trials. These have shown antimicrobial activity against *C. difficile* and toxin A/B neutralization capacity in vitro with this specific probiotic formulation as bundle of preventive measures to control CDI in healthcare settings [66].

Conclusions

Lifestyle of modern age people have faced many challenges, especially many health issues such obesity, osteoporosis, cancer diabetes, and several chronic gut problems. Problem in life could be developed due to consumption of manifold junk foods which has developed health problem and it is due to nutritional deficiencies in their food. Due to developing of more awareness about food in people, has shifted their synthetic food ingredients to organic foods or ingredients from natural sources. And nutraceuticals food has played important role in controlling such diseases with provider of the health benefits to people. Dietary supplements as nutraceuticals food have helped in nutritional, immunologic and physiological functions with prevention or treatment of diseases of gastrointestinal (GI) tract. Many herbals products with natural products has started to synthesize by many Indian or any other industries in world and more people are getting health benefits. Global nutraceuticals market will be reached the value of US$278.96 billion by 2021. Prebiotics, probiotics (help in development of healthy microenvironment in human with treatment of chronic diseases), lycopene (with potent antioxidant properties) and plant sterol (for lowering the blood cholesterol) has been discussed with their health benefits.

Acknowledgements

Author is main source for writing this manuscript. He has done only all the respective literature paper to writing this manuscript. There is no contribution of any fund or any honorarium money for this paper. But I am thankful to our university to encourage for paper writing.

Conflict of interest

An author has written a cover letter to the editor that is no any conflict of interest to any author or any

associations. There is no any conflict of interest in this manuscript. There is no current or pending relationship to consultant for the company supporting the research or manufacturing products being tested, a financial or managerial interest in such a company, or intellectual property rights.

Abbreviations

BP: Blood pressure;

CDI: *Clostridium difficile* infection;

DASH: Dietary Approaches to Stop Hypertension; DCW: Dry cell weight;

DHA: Docosahexaenoic acid;

EGCG: Epigallocatechin gallate;

ETI: Effector-triggered immunity;

FCCCD: Faced centered composite design;

GI: Gastrointestinal;

GRAS: Generally recognized as safe

GSH: glutathione;

HPLC: High performance liquid chromatography;

LDL: Low density lipid; mg/ kg

FW: Milligram per kilogram fresh weight;

PAMP: Pathogen-associated molecular pattern;

PTI: Pattern-triggered immunity;

RSM: Response surface methodology;

SOD: Superoxide dismutase

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