**Reviewer’s Comments**

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**New era of medicine: role of nutraceuticals in treatment and prevention of various diseases**

**Abstract**Nutraceutical is a term coined to describe substances which are not traditionally recognized nutrients but which have positive physiological effects on the humanbody. Nutraceuticals are derived from various sources such as medicinal plants, marine organisms, vegetables and fruits. Since ancient times mankind has believed in the role played by the appropriate amount of nutrition in maintaining proper health. In the past few years the increasing interest is seen among the consumers, as they feel that it is a relatively safer way to good health.

The potential of nutraceuticals/functional foods/food supplements in mitigating health problems. Nutraceuticals are alternative to modern medicine. Development of bettercharacterized and research proven products will help enhance consumer confidence in nutraceuticals.

In this review, an attempt has been made to discuss all aspects of nutraceuticals- definition, categories, classification their use in various diseases.

**Key-Words:** Nutraceuticals, Dietary supplements, medicinal plants, health problems.

**Introduction**

Since ancient times people have been aware of the importance of the “right amount of nutrition” in maintaining a healthy lifestyle. Food that is cooked or prepared using "scientific intelligence" the food is called "functional food". It provides the body with the required amount of vitamins, fats, proteins, carbohydrates, etc1. When functional food is used in theprevention and/or treatment of disease(s) and/or disorder(s), it is called a nutraceutical. "Let food be thy medicine and medicine be thy food" These golden words were used around 2500 years ago by Hippocrates, the Father of medicine2. The concept of nutraceuticals was stared from the survey in U.K., Germany and France which concluded that diet is rated more highly by consumers than exercise or hereditary factors for achieving good health3. Since a long time, physicians paid close attention to the role of the daily diet in health maintenance. For example high dietary intake of fruits, vegetables and whole grains is strongly associated with reduced risk of developingchronic diseases, such as cancer and cardiovascular diseases4.

Nutraceuticals is a term coined to describe substances which are not traditionally recognized nutrients but which have positive physiological effects on the human body. Nutraceutical can be defined as, “a food or part of a food that provides medical or health benefits, including the prevention and/or treatment of a disease5. In general nutraceuticals do not easily fall into the legal category of food and drug and often inhabit a grey area between the two. Nutraceuticals includes isolated nutrients, dietary supplements, and diets to genetically engineered “designer” food,herbal products, and processed products such as cereals, soups, and beverages6.

According to Hippocrates “if we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health”. These words of Hippocrates long time ago, summarizes the past, presentand the future of nutraceuticals7.

**Advantages of nutraceuticals**

1. May increase the health value/benefits of our diet8.
2. May help to avoid particular medical conditions.
3. Less unpleasant side-effects9.
4. Easily available and cheap.
5. Provides food for populations with special needs (eg: nutrient-densefoods for the elderly)10.

**Limitations of of nutraceuticals**

1. Nutraceuticals have poor bioavailability, easily eliminate from the body and do not provide sufficient medicinal benefit11.
2. Lack of regulation may compromise the safety and effectiveness ofproducts.
3. Many products are not having proper information about their safety and effectiveness, possible side effects, interaction with prescription medicines or the effect they have on existing medical conditions12.

**Classification of nutraceuticals**

Nutraceuticals can be classified as follows:
**A) On the basis of natural source:**

On the basis of natural source, it can be classified as the products obtainedfrom plants, animals, minerals, or microbial sources13.
**B) On the basis of pharmacological conditions, or as per chemical constituents of the products**

**Dietary supplements**

A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include: vitamins,minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders14.

**Functional food**

These include food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains. Functional foods contain physiologically active components obtained either from plants or animal sources15. Functional foods are fortified or enriched duringprocessing and then marketed. Sometimes, additional complementary nutrients are added, such as vitamin D to milk. This practice restores the nutrient content in a food16.

**NUTRACEUTICALS AND DISEASES**

**1. Nutraceuticals for Cardiovascular Diseases**

Cardiovascular disease (CVD) is now the leading cause of death globally. Nutraceuticals have the potential to significantly reduce the risk of side effects associated with chemotherapy along with reducing the global health care cost. It has been proposed that CVD can be prevented by lifestyle changes, including diet. Certain nutraceuticals affect chronic diseaseand are claimed to have a favourable impact on cardiovascular diseases such as heart attack/ischemia, stroke, coronary artery disease, corpulmonale, hypertension, deep vein thrombosis and/or atherosclerosis17. Nutraceuticals tend to reduce circulating levels of LDL-cholesterol by modulating cholesterol production in the liver (i.e. monacolin, policosanol, red yeast, rice etc.), binding cholesterol within the intestines and/or increasing LDL-c receptor uptake in the liver (i.e. berberina, phitosterols etc.). Excessive consumption of foods that are calorie dense, nutritionally poor, highly processed, and rapidly absorbable can lead to systemic inflammation, reduced insulin sensitivity, and a cluster of metabolic abnormalities, including obesity, hypertension, dyslipidemia, and glucose intolerance. Polyphenols found in grapes and grape derivatives, cocoa and tea are of interest in the prevention of CVD. Phenolic compounds arefound in grapes and these include anthocyanins, flavanols, flavonols, stilbenes and phenolic acids. Anti-oxidants, Dietary fibres, Omega-3 poly unsaturated fatty acids, Vitamins, minerals for prevention and treatment of CVD18.

**2. Nutraceuticals against Alzheimer's disease (AD)**

Alzheimer's disease is the most common and feared form of dementiarepresenting circa 70% of all dementia cases and displaying a dramatic epidemics due to the enormous growth of the aged population worldwide19. Advanced age is often characterized by a decline in a large spectrum of cognitive abilities including reasoning, memory, perceptual speed, and language.

Botanical extracts with anti-amyloidogenic activity, including green tea catechins, turmeric, *Salvia miltiorrhiza*, berry anthocyanins, and Panax ginseng have demonstrated significant efficacy in Alzheimer’s diseases20.

*Bacopa monniera* has been demonstrated as an Ayurvedic nerve tonic, indicating a potential role in helping prevent dementia and serving as a novel memory enhancer.Also, astaxanthin-rich algal biomass, fish oil including omega-3 fatty acids (PUFAs) and krill oil have demonstrated a potential role in preserving memory, sustaining cognitive functions and preventing neuro-inflammatory, neuro-motor and neurodegenerative disorders in humans and animals21.

**3. Nutraceuticals for Diabetes**

Diabetes is a chronic metabolic disorder, where the body is unable to utilize carbohydrate due to absolute or relative lack of insulin, a hormone naturally produced by the ß cell of the islets of langerhans in pancreas. Isoflavones are phytoestrogens have a structural/functional similarity to human estrogen and have been consumed by humans worldwide. Cinnamontea and green tea can help people suffering with diabetes22. Dietary fibers from psyllium have been used for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemia.Omega-3 fatty acids supplementation in type 2 diabetes has a favorable impact in lowering triglycerides and VLDL-cholesterol, and reducing blood pressure and inflammatory markers23.

**4. Nutraceuticals in Parkinson's disease**

Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and other parts of the brain, leading tomotor impairment, cognitive impairment, and dementia. Nutraceuticals can provide neuroprotection via a wide range of proposed mechanisms, such as scavenging of free radicals and ROS, chelation of iron, modulation of cell-signaling pathways, and inhibition of inflammation24.

These nutraceuticals include vitamins C, D, E, coenzyme Q10, creatine, unsaturated fatty acids, sulfur-containing compounds, polyphenols, stilbenes, and phytoestrogens.

Researchers found that curcumin decreases synuclein toxicity and thegeneration of reactive oxygen species (ROS), which are found to be involved in the programmed cell death. It also increases neuronal survival in the *substantia nigra* that is present in the midbrain and have a function in movement. Zingerone is an extract obtained from the ginger root. Researchers found that zingerone inhibits the dopamine reduction in mouse model25.

**5. Nutraceuticals in Hypertension**

Hypertension as “a common condition in which the force of the blood against artery walls is high enough that it may eventually cause health problems, such as heart disease.” Many natural compounds in food, as well as certain nutraceutical supplements, vitamins,antioxidants, or minerals, can mimic drugs, functioning in a similar fashion to a specific class of antihypertensive medications. Melatonin, Hesperidin, pomegranate juice and grape seed extract have shown to be helpful in reducing BP26.

Flavonoids are the natural substances found to reduce stroke and enable smooth cardiac functions. Lycopene present in the carotenoid family, it helps reduce BP and oxidative stress.

Use of garlic helps reduce BP and is also useful in treating patients alreadyon drugs. Clinical studies show that seaweed lower BP within 4 weeks of administration. Sesame reduces BP, arterial stiffness, and improves oxidative defense. Beverages: Tea, coffee, and cocoa – These help reduce BP and improve endothelial function27.

**6. Nutraceuticals with Anti-inflammatory activities**

Inflammation is a process by which the body's white blood cells and substances they produce protect us from infection with foreign organisms, such as bacteria and viruses. It is the response of body tissues to injury or irritation, characterized by painand swelling and redness and heat. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by elevated oxidative stress and inflammatory biomarkers28. Various studies were conducted by many researchers on fish oil, primrose oil, curcumin, fenugreek, liquorice, coriander, tomato, carrot, sweet potato, broccoli, green tea, rosemary, hazelnut, walnut, wheat germ, Beet roots, cucumber fruits, spinach leaves and date for anti-inflammatory properties29. During these studies, changes in inflammatory biomarkers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), seromucoids, fibrinogen, tumor necrosis factor-α (TNF-α), prostaglandin E2), oxidative stress (malondialdehyde), antioxidant status (total antioxidant capacity, vitamin C, vitamin E, retinol, β-carotene), the level of copper (Cu) and zinc (Zn) and colonic microflora in response to the administration of nutraceuticals have been assessed. Studies concluded that the majority of nutraceuticals studied possess beneficial effect toward chronic inflammatory diseases, which might be due to the presence of one or more of the above-mentioned phytochemicals30.

**7. Nutraceuticals in Obesity**

Obesity leads to chronic, excessive adipose tissue expansion resulting in anincrease in the risk for cardiovascular disease, type 2 diabetes mellitus, and other metabolic abnormalities.

Herbal stimulants, such as ephedrine, caffeine, ma huang-guarana, chitosan and green tea help in body weight loss31.

Capsaicin, a biologically active ingredient found in red chili peppers leads to alteration of thermogenesis and lipid metabolism-related proteins in white adipose tissue and skeletal muscle. Thereby it induces thermogenesis and fat oxidation.

A blend of glucomannan, chitosan, fenugreek, G sylvestre, and vitamin C in the dietary supplement signifi cantly reduced body weight32.

**8. Nutraceuticals in Cancer**

As concluded by many researchers’ nutraceuticals, mostly phytochemicals derived from dietary or medicinal plants such as soya bean, garlic, ginger, tea, honeyand others, may have chemopreventive activities33.

Soyfoods source of isoflavones, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. People using large amount of lutein-rich foods such as chicken eggs, spinach, tomatoes, oranges and leafy greens experienced the lowest incidence of colon cancer34. Lycopene prevents cancer, cardiovascular disease, and gastrointestinal tract. It concentrates in the skin, testes, adrenal and prostate where it protects against cancer.

Flavonoids which block the enzymes that produce estrogen reduce of estrogen induced cancers. Isoflavones are a group of phytochemicals that are predominant constituents of a soy-based diet. Among isoflavones, the three major constituents that have beenshown to have remarkable influences in cancer prevention and therapy are genistein, diadzein, and glycitin35.

**Conclusion**Nutraceuticals are the isolated product obtained from foods, and play a vital role in improving health, provides protection against diseases. Nutraceuticals are widely being used rather than medicines because they reduce side-effect and have positive physiological effects on the human body. Since ancient time people were aware of the importance of the “right amount of nutrition” in maintaining a healthy lifestyle. Nutraceuticals are currently receiving recognition for treatment of many diseases such as coronary heart disease, obesity, diabetes, cancer,osteoporosis and other chronic and Parkinson's and Alzheimer's diseases.

In the present scenario of self-medication nutraceuticals play major role in therapeutic development. However for the successful use of nutraceuticals emphasis should be given on their quality, purity, safety and efficacy. In order to have scientific knowledge about the nutraceuticals, publics should be informed/ educated regarding therapeutic efficacy and correct daily doses. There is need to establish a vibrant nutraceuticals research community which is necessary to obtain enormous benefits from the available potential nutraceuticals for all of us

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