



## ADVANCEMENT AND CHARACTERIZATION OF NUTRACEUTICALS AS PHYSIOLOGICAL BENEFITS AGAINST MULTIPLE PATHOGENS; A COMPREHENSIVE REVIEW

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### Abstract

Nutraceuticals are products, which other than nutrition are also used as medicine. A nutraceutical product may be defined as a substance which has physiological benefit or provides protection against chronic disease. Nutraceuticals may be used to improve health, delay the aging process, prevent chronic diseases, increase life expectancy, or support the structure or function of the body. Nowadays, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects. Recent studies have shown promising results for these compounds in various complications. In the present review much effort has been devoted to presenting new concepts about nutraceuticals based on their disease modifying indications. Emphasis has been made to present herbal nutraceuticals effective on hard curative disorders related to oxidative stress including allergy, Alzheimer, cardiovascular, cancer, diabetes, eye, immune, inflammatory and Parkinson's diseases as well as obesity. The recently published papers about different aspects of nutraceuticals as alternative for pharmaceuticals were searched using scientific sites such as Medline, PubMed, and Google Scholar. The used terms included nutraceutical and allergy, Alzheimer, cardiovascular, cancer, diabetes, eye, immune, inflammatory or Parkinson.

Nutraceuticals are items other than sustenance which are additionally utilized as medication.

**Key Words:** herbal nutraceuticals, Nutrients, Pharmaceuticals, Chronic diseases, Therapeutic Efficacy

## Introduction

### History

Nutraceutical is a term derived from “nutrition” and “pharmaceutics.” The term is applied to products that are isolated from herbal products, dietary supplements (nutrients), specific diets, and processed foods such as cereals, soups, and beverages that other than nutrition are also used as medicine (1).



### Concept of Nutraceuticals

In the US, the term “nutraceutical” products are regulated as drugs, food ingredients and dietary supplements. The term is not defined the same in different countries but is usually defined as a product isolated from foods that is generally sold in medicinal forms not usually associated with food. A nutraceutical product may be defined as a substance, which has physiological benefit or provides protection against chronic diseases(1). Nutraceuticals may be used to improve health, delay the aging process, prevent chronic diseases, increase life expectancy, or support the structure or function of the body(2). Nutraceuticals, in contrast to pharmaceuticals, are substances which usually have not patent protection. Both pharmaceutical and nutraceutical compounds might be used to cure or prevent diseases, but only pharmaceutical compounds have governmental sanction(3). A dietary supplement is considered as a product that bears or contains one or more of the following dietary ingredients: A mineral, a vitamin, an amino acid, a medical herb or other botanical, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients. Nutraceuticals are of these nutritional supplements which are used for health purposes other than nutrition(4). Some popular nutraceuticals include ginseng, Echinacea, green tea, glucosamine, omega-3, lutein, folic acid, and cod liver oil. Most nutraceuticals possess multiple therapeutic properties. Nowadays, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects. A market research recently proposed that the worldwide nutraceuticals market is expanding and would reach US \$250 billion by 2018(5). Recent studies have shown promising results for these compounds in various pathological complications such as diabetes(6, 7), atherosclerosis(8, 9), cardiovascular diseases (CVDs),(10, 11) cancer(12, 13), and neurological(14, 15) disorders. These conditions involve many changes, including alterations redox state(16, 17). Most of nutraceuticals have antioxidant activity with the ability to counteract this situation(18, 19). Hence, they are considered as healthy sources of health promotion, especially for prevention of life threatening diseases such as diabetes(20, 21), infection(22, 23), renal(24, 25) and gastrointestinal(26, 27) disorders. In the present review much effort has been devoted to presenting new concepts about nutraceuticals based on their disease modifying indications. Emphasis has been made to present herbal nutraceuticals effective on hard curative disorders related to oxidative stress, including allergy, Alzheimer, cardiovascular, cancer, diabetes, eye, immune, inflammatory and Parkinson’s diseases, as well as obesity.

The focal point of progressing research in the field of nutraceuticals is the examination of atoms that are confined from customary drugs and how they can be useful in incapacitating and degenerative pathologies (28, 29).

Nutraceuticals in adjunction can reinforce the remedial impacts of specific meds when utilized in adjunction by the expansion of a few pathways, like improved re-take-up of restrained monoamines, subsequently giving extraordinary neurobiological impacts(30).

Nutraceuticals, as opposed to drugs, are substances, which for the most part have not patent insurance. Both drug and nutraceutical mixtures may be utilized to fix or forestall sicknesses, however just drug compounds have administrative approval. A dietary enhancement is considered as an item that bears or contains at least one of the accompanying dietary fixings: A mineral, a nutrient, an amino corrosive, a clinical spice or other organic, a dietary substance for use by man to enhance the eating routine by expanding the all-out day by day admission, or a concentrate, metabolite, constituent, concentrate, or mixes of these fixings(31).

In the current survey a lot of exertion has been dedicated to introducing new ideas about nutraceuticals dependent on their sicknesses altering signs. Accentuation has been made to introduce home grown nutraceuticals successful on hard therapeutic messes identified with oxidative pressure, including sensitivity, Alzheimer, cardiovascular, malignancy, diabetes, eye, invulnerable, incendiary and Parkinson's infections, just as heftiness(32).

The quality of life in terms of income, spending and lifestyle has improved with economic development. However, it has also thrown up a major challenge in the form of `lifestyle diseases. The first victim of this lifestyle change has been food habits. Consumption of junk food has increased manifold, which has led to several diseases related to nutritional deficiencies. Nutraceuticals can play an important role in controlling them. No wonder more and more people are turning to nutraceuticals. The term nutraceutical was coined from nutrition and pharmaceutical (Figure 1) in 1989 by Stephen Defelice, founder, and chairman of foundation for innovation in medicine, an American organization which encourages medical health (33-36). According to him "a nutraceutical is any substance that is a food or a part of food and provides medical or health benefits, including the prevention and treatment of disease". Such products may range from isolated nutrients, dietary supplements and specific diets to genetically engineered designer foods and herbal products (33-37). The concept of nutraceutical was started from the survey in U.K., Germany and France and it concluded that diet is rated more highly by consumer than exercise or hereditary factors to achieving a good health. In the U.S. "nutraceutical" was commonly used, but no regulatory definition existed. Its meaning was modified by health ministry of Canada which defines nutraceutical as "a product isolated or purified from the food, generally sold in medicinal form not associated with food and demonstrated to have a physiological benefit .It also provides benefit against chronic disease"(38) .



**Figure 1. Nutraceuticals were coined from nutrition and pharmaceutical.**

## **Nutraceuticals**

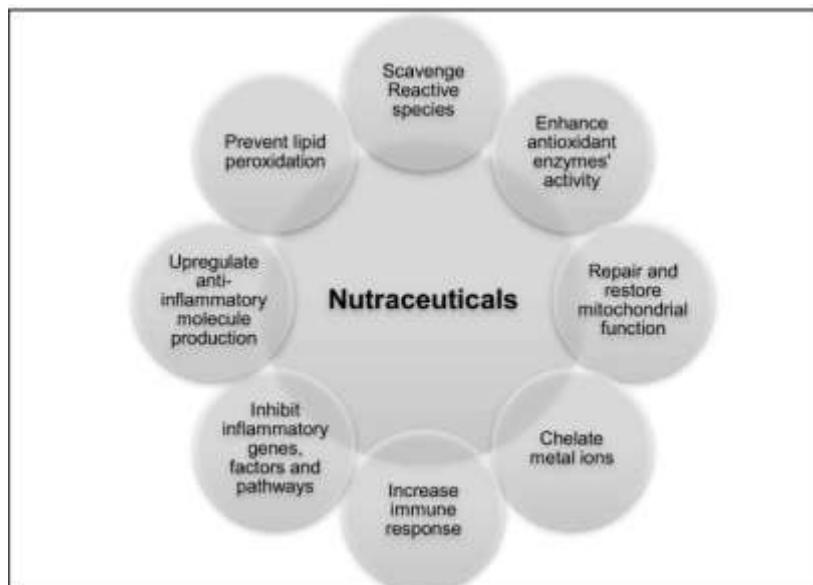
### **Pharmaceuticals Nutrition**

In Britain, the Ministry of Agriculture, Fisheries and Food has developed a definition of a functional food as "a food that has a component incorporated into it to give it a specific medical or physiological benefit, other than purely nutritional benefit (39) . There is a slight difference between the functional foods and nutraceuticals. When food is being cooked or prepared using "scientific intelligence" with or without knowledge of how or why it is being used, the food is called "functional food". Thus, functional food provides the body with the required number of vitamins, fats, proteins, carbohydrates, etc. needed for its healthy survival. When functional food aids in the prevention and/or treatment of disease(s) and/or disorder(s) other than anemia, it is called a nutraceutical. Examples of nutraceuticals include fortified dairy products (e.g. milk) and citrus fruits (e.g. orange juice)(1) .

The DSHEA formally defined "dietary supplement" using several criteria. A dietary supplement: (40)

- is a product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients- a vitamin, a mineral, an herb or other botanicals, amino acids or a dietary substance for use by man to supplement the diet by increasing the total daily intake or a concentrate, metabolite, constituent, extract, or combinations of these ingredients
- is intended for ingestion in pill, capsule, tablet, or liquid form.
- is not represented for use as a conventional food or as the sole item of a meal or diet. • is labeled as a "dietary supplement".

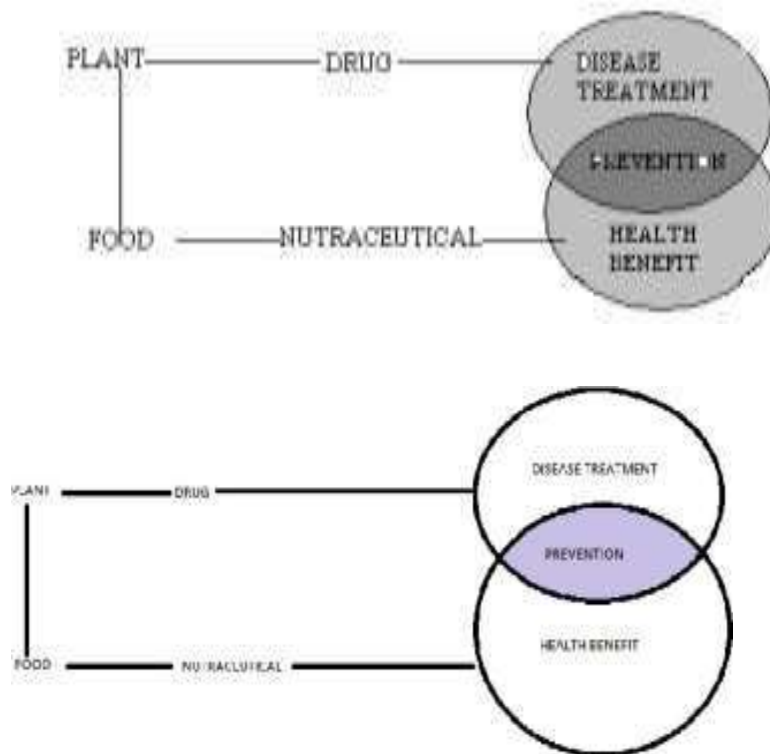
## Benefits



From the consumers' point of view, functional foods and nutraceuticals may offer many benefits:

- May increase the health value of our diet.
- May help us live longer.
- May help us to avoid medical conditions.
- May have a psychological benefit from doing something for oneself.
- May be perceived to be more "natural" than traditional medicine and less likely to produce unpleasant side-effects.
- May present food for populations with special needs (e.g. nutrient-dense foods for the elderly(41).

Bridging the gap between food and medicine Hippocrates highlighted around 2000year ago “Let food be your medicine and medicine be your food” . Nutraceuticals are foods or food ingredients that provide medical or health benefits. This emerging class of products blurs the line between food and drugs (42). They do not easily fall into the legal categories of food or drug and often inhabit a grey. Within European Union (EU) law the legal categorization of a nutraceutical is, in general, made based on its accepted effects on the body. Thus, if the substance contributes only to the maintenance of healthy tissues and organs it may be a food ingredient. If, however, it can be shown to have a modifying effect on one or more of the body’s physiological processes, it is likely to be considered to be a medicinal substance (Figure 2)(43) . Within European Medicines law a nutraceutical can be defined as a medicine for two reasons: 1) It can used for the prevention, treatment or cure of a condition or disease or 2) It can be administered with a view to restoring, correcting or modifying physiological functions in human beings (44) .



**Figure 2. Nutraceuticals inhabit a grey area between the food and drug**

## 2. Nutraceuticals and Its Categories

Nutraceuticals fall under vague natural treatments and are utilized in the anticipation of side effects of less than overwhelming issues to profoundly poisonous harm. Their job as a neuroprotective is all around articulated and profoundly recognized. They can be classified thinking about the accompanying measures(41, 45).

### Categories of nutraceuticals



Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes, and control symptoms. These can be grouped into the following three broad categories(46) :

1. substances with established nutritional functions, such as vitamins, minerals, amino acids, and fatty acids - Nutrients
2. herbs or botanical products as concentrates and extracts – Herbals
3. reagents derived from other sources (e.g., pyruvate, chondroitin sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements, and meal replacements – Dietary supplements. Nutrients:





The most known nutrients are antioxidants, water and fat-soluble vitamins. Many potential benefits have been attributed to antioxidant use in the form of dietary intake or supplementation(47-50). Antioxidants, in general, may be useful in the prevention of cancer and cerebrovascular disease(47) . High dietary intake of vitamin E may prevent Parkinson's disease(48). Agus et al., determined that the oxidized form of vitamin C, dehydroascorbic acid, readily crosses the blood brain barrier(11). These findings have implications for increasing the uptake of antioxidants in the central nervous system; thus, some feel that this has the potential for improving the treatment of Alzheimer's disease. Jialal and Fuller found that the combination of vitamin E, C and beta carotene has been useful in reducing low density lipoprotein oxidation and subsequent atherosclerosis(51) . Vitamin supplement is associated with increased antibody titre response to both hepatitis B and tetanus vaccines because of macrophage and T cell stimulation. Those genetically predisposed to pancreatic cancer have low serum levels of selenium; thus, it is assumed that supplementation with selenium may help to prevent this condition(52, 53). Those suffering from asthma and skin cancer have also been evaluated with selenium for its potential use, although results have been inconclusive(54). Zinc is an essential component of more than a hundred enzymes involving digestion, metabolism and wound healing. L-arginine is a semi-essential amino acid that is a substrate for nitric oxide production. Ceremuzynski et al., demonstrated that supplementation of L-arginine improved exercise capacity in patients, who had angina(55). A list of common nutrients with their health benefits is given in Table 1.

### **Herbals**

Herbals are as old as human civilization and they have provided a complete storehouse of remedies to cure acute and chronic diseases. The knowledge of herbals has accumulated over thousands of years so that today we possess many effective means of ensuring health care. Numerous nutraceuticals are present in medicinal herbs as key components. A list of commonly known herbal and phytochemical products with their therapeutic activity is shown in Table 2.

Herbal extracts, including *β*-sitosterols (found in Saw Palmetto berry), cernilton (pollen extract), and *pygeum africanum* (African plum) have been clinically evaluated for use in the treatment of benign prostatic hyperplasia(56). It has been found that common herbal treatment is in the use of *Echinacea* for the prevention and treatment of colds and flu. A series of five placebo controlled studies evaluating the use of *Echinacea* produced mixed results, which the authors attribute to either the use of healthy volunteers, rather than patients, or the use of extracts that were not standardized or chemically defined monopreparations(57). Ernst suggested that St John's wort is efficacious for mild to moderate depression, but serious concern exists about its interactions with several conventional drugs(58) . *Echinacea* may be helpful in the treatment or prevention of upper respiratory tract infections, but trial data are not fully convincing. Saw Palmetto has been shown in short term trials to be efficacious



Vitamin A	Vitamin D	Vitamin E	Vitamin K
<b>Other Names</b>	<b>Other Names</b>	<b>Other Names</b>	<b>Other Names</b>
Retinol, Retinoic Acid; precursors are Carotenoids	D2, D3/Calciol, Calcidiol, Calcitriol	Alpha-tocopherol	Phylloquinone, menaquinone, memadi- one, naphthoqui- none
<b>RDI</b>	<b>AI</b>	<b>AI</b>	<b>RDI</b>
Women: 700µg/day Men: 900µg/day	Women: 5.0µg/day Men: 5.0µg/day	Women: 7mg/day Men: 10mg/day	Women: 60µg/day Men: 70µg/day
<b>Functions</b>	<b>Functions</b>	<b>Functions</b>	<b>Functions</b>
Vision, skin rejuvenation, bone & tooth growth, reproduction & immunity	Mineralization of bones - Strong bones, immune & neuomuscular function	Antioxidant, stabilization of cell membranes - healthy cells healthy body	Synthesis of blood-clotting proteins and bone proteins
<b>Food Sources</b>	<b>Sources</b>	<b>Food Sources</b>	<b>Food Sources</b>
			

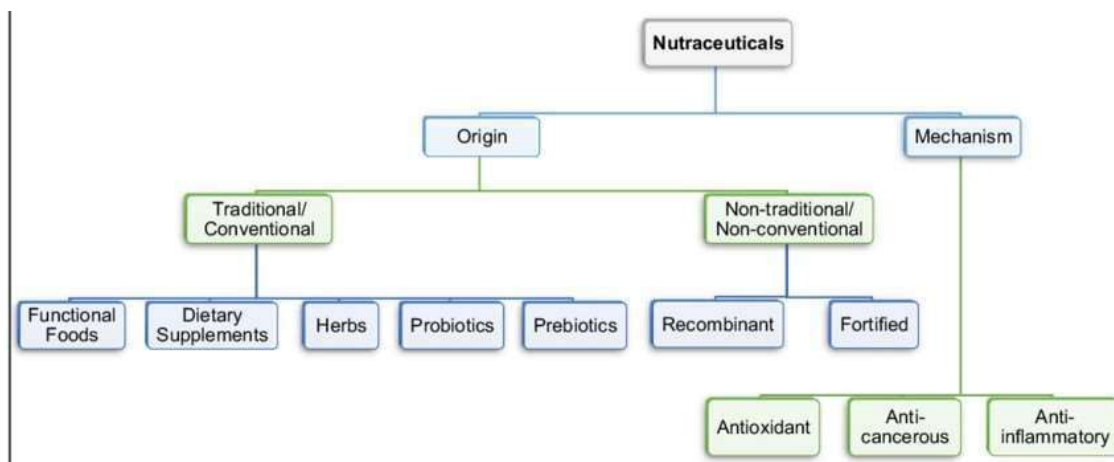
**Fig. showing Fat Soluble Vitamins.**

Compound Therapeutic activity Aloe vera gel Dilates capillaries, anti-inflammatory, emollient, wound healing properties (Aloe vera L. N.L. Burm.) Chamomile Anti-inflammatory, spasmolytic, antimicrobial, wound healing (Matricaria recutita L.) Echinacea Immunostimulant, treatment of cold and flu symptoms (Echinacea purpurea L.) Eleuthera Adaptogen (Eleutherococcus senticosus Rupr. & Maxim., Maxim) Ephedra Bronchodilator, vasoconstrictor, reduces bronchial edema, appetite suppressant (Ephedra sinica Stapf., Ephedra intermedia Schrank., Ephedra equisetina Bunge.) Evening primrose oil Dietary supplement of linoleic acid, treatment of atopic eczema (Oenothera biennis L.) Feverfew Treatment of headache, fever and menstrual problems, prophylactic to reduce frequency, (Tanacetum parthenium L.) severity and duration of migraine headaches Garlic Antibacterial, antifungal, antithrombotic, hypotensive, fibrinolytic, antihyperlipidemic, (Allium sativum L.) anti-inflammatory Ginger Carminative, antiemetic, cholagogue, positive inotropic, treatment of dizziness (Zingiber officinale Rosc.) Ginseng Adaptogen (Panax ginseng , Panax quinquefolius L.) Ginkgo (Ginkgo biloba L.) Vasodilation, increased peripheral blood flow, treatment of post-thrombotic syndrome, chronic cerebral vascular insufficiency, short term memory loss, cognitive disorders secondary to depression, dementia, tinnitus, vertigo Goldenseal Antimicrobial, astringent, antihemorrhagic, treatment of mucosal inflammation, (Hydrastis canadensis L.) dyspepsia, gastritis Horehound Expectorant, antitussive, choleric (Marrubium vulgare L.) Licorice Expectorant, secretolytic, treatment of peptic ulcer (Glycyrrhiza glabra L., G. uralensis Fisch.) Melissa Topical antibacterial and antiviral (Melissa officinalis L.) Plantago seed Cathartic (Plantago arenaria Waldst., Plantago arenaria Kit. Plantago ovata) Slippery elm Mucilaginous demulcent, emollient and nutrient, used to sooth irritated mucous membranes, (Ulmus rubra Muhl.) ulcerations of the digestive tract St. John’s wort Anxiolytic, anti-inflammatory, antidepressant, monoamine oxidase inhibitor (Hypericum perforatum L.) Valerian Spasmolytic, mild sedative, sleep aid (Valeriana officinalis L.) Willow bark Anti-inflammatory, analgesic, antipyretic, astringent, treatment of rheumatic and arthritic (Salix alba L., conditions, headache and gout S. daphnoides Villars, S. pentandra L.).

### CLASSIFICATION OF NUTRACEUTICALS

Regarding the promise of nutraceuticals, they should be considered in two ways: • Potential nutraceuticals • Established nutraceuticals A potential nutraceutical is one that holds a promise of a

particular health or medical benefit; such a potential nutraceutical only becomes an established one after there are sufficient clinical data to demonstrate such a benefit. It is disappointing to note that the overwhelming majority of nutraceutical products are in the 'potential' category, waiting to become established (33). The food products used as nutraceutical are categorized as(41, 61) .



- Probiotic
- Prebiotic • Dietary fiber • Omega 3 fatty acid • Antioxidant

### AREA COVERED BY NUTRACEUTICAL PRODUCTS

All therapeutic areas such as anti-arthritis, pain killers, cold and cough, sleeping disorders, digestion and prevention of certain cancers, osteoporosis, blood pressure, cholesterol, depression and diabetes have been covered by nutraceuticals (Figure 3)(62).

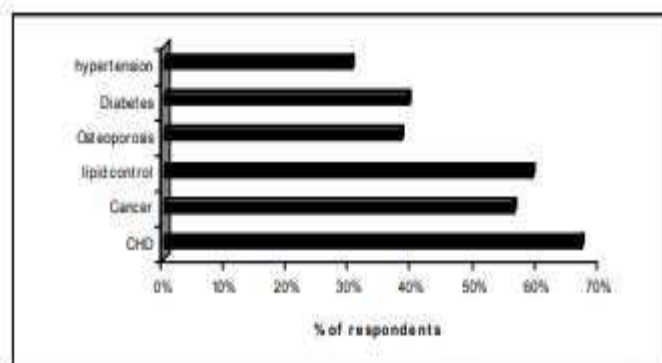


Figure 3. Percentage area covered by nutraceutical products

### NUTRACEUTICALS REVOLUTION

The nutraceuticals revolution began in the early 1980s, sparked off when the actual or potential clinical benefits of calcium, fiber and fish oil were supported by clinical studies published in distinguished medical journals, and when physicians began to educate their colleagues and consumers about these substances via the mass media (33) .

#### Factors effecting Revolution

- Physician - Increased physician acceptance of the medical benefits of nutritional products increased market demand of nutraceuticals.
- Media- The mass media have emerged as the primary sources of medical claims, mass media has now become the powerful and legitimate promotion agency of nutraceutical products (41, 61).



## **RESEARCH AND DEVELOPMENT**

The greatest scientific need in nutraceuticals pertains to standardization of compounds and/or products, to carefully develop and execute clinical studies/trials to provide the basis for health claims for nutraceuticals that impact consumers as well as companies making strategic investments(63). Powerful market forces are fueling the interest in nutraceuticals:(63)

- Rapid advances in scientific knowledge supporting the vital role of diet in health and disease prevention.
- Sky rocketing health care costs.
- An aging population.
- Technical advances in the food industry that are allowing the development of health promoting foods that can be marketed to health-conscious consumers at a premium.
- The changing regulatory environment.

### **Role of R and D in nutraceutical(63)**

- To test safety, purity and potency of products.
- To develop more effective and efficient means of producing ingredients for use in products.
- To develop testing methods for ensuring and verifying the consistency of the dosage of ingredients included in the company's products.
- Develop the new products either by combining existing ingredients used in nutritional supplements or identifying new ingredients that can be used in nutritional supplements.

## **THE FUTURE OF NUTRACEUTICALS**

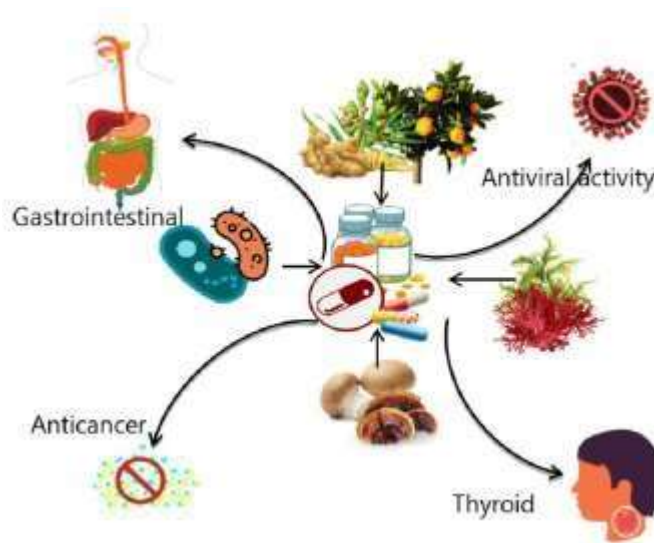
Increasing awareness levels about fitness and health, spurred by media coverage are prompting most people to lead healthier lifestyles, exercise more, and eat healthy. The expanding nutraceutical market indicates that end users are seeking minimally processed food with extra nutritional benefits and organoleptic value. This development, in turn, is propelling expansion in the nutraceutical markets globally. The emerging nutraceuticals industry seems destined to occupy the landscape in the new millennium(63). Its tremendous growth has implications for the food, pharmaceutical, healthcare, and agricultural industries. Many scientists believe that enzymes represent another exciting frontier in nutraceuticals. "Enzymes have been underemployed... they're going to be a hot area in the future." Fermentation technology using microbes to create new food products also represents potential. Global trends to healthy products cannot be reversed. Companies taking the lead by investing strategically in science, product development, marketing and consumer education will not go unrewarded(63).

## **CONCLUSION**

The nutraceutical industry is growing at a rate far exceeding expansion in the food and pharmaceutical industries. In tomorrow's market, the most successful nutraceutical players are likely to be those companies in which functional products are just a part of a broad line of goods satisfying both conventional and health value point. Future demand of nutraceuticals depends on consumer perception of the relationship between diet and disease. Although nutraceuticals have significant promise in the promotion of human health and disease prevention, health professional, nutritionists and regulatory toxicologist should strategically work together to plan appropriate regulation to provide the ultimate health and therapeutic benefit to mankind. Long-term clinical studies are required to scientifically validate nutraceuticals in various medical conditions. The interaction of nutraceuticals with food and drugs is another area, which should be taken into consideration. The effect of different processing methods on the biological availability and effectiveness of nutraceuticals remains to be determined. As like drugs, there should be strict regulatory controls for nutraceuticals.

### **2.1. Food-Based Nutraceuticals or Traditional Nutraceuticals**

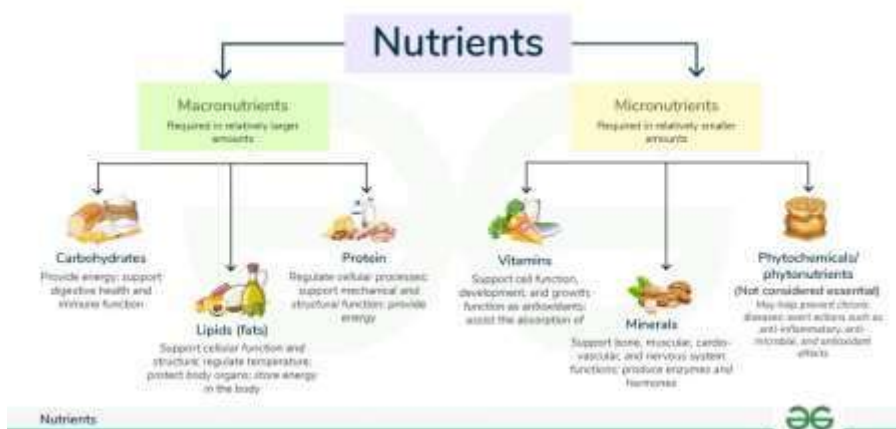
This classification incorporates food items got straightforwardly from nature with no adjustment of their unique constituent structure. These incorporate organic products, vegetables, grains, meat, fish, eggs, and dairy that give a few advantages past fundamental sustenance(64).



## Food-Based Nutraceuticals and their benefits

### 2.1.1. Nutrients

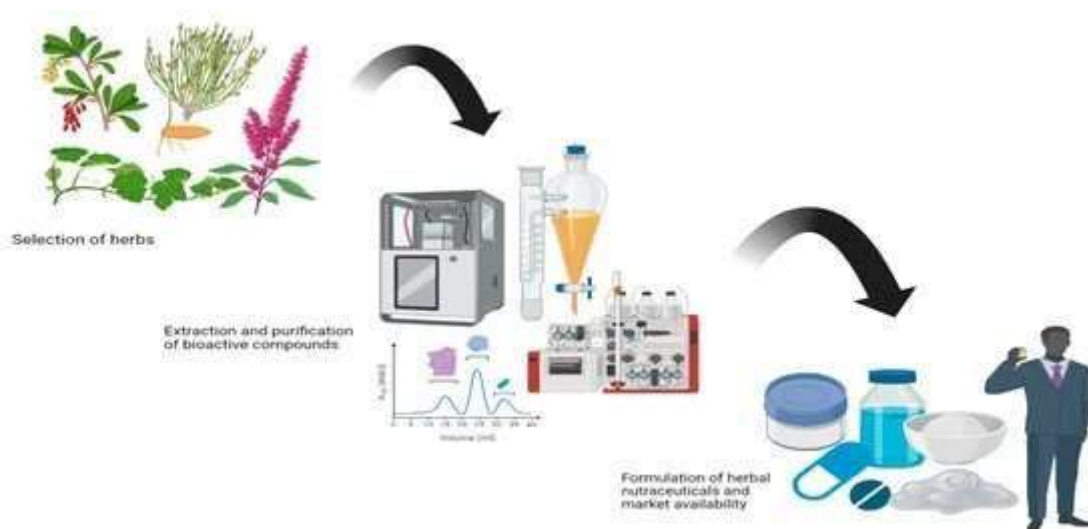
The essential metabolites of substances like minerals, unsaturated fats, nutrients, and amino acids have grounded healthful properties in the metabolic pathways. These supplements in mix with creature and plant items have a few advantages in relieving neurological issues. The planting of supplements can be utilized in forestalling fragile bones, inspiring hemoglobin, and reinforcing muscle power and neuronal transmission. Unsaturated fats and its mixtures improve mind working and help a lessening in cholesterol present in the veins, tending to show its hypolipidemic impacts(64).



### 2.1.2. Herbals or Extracts and Concentrates of Botanical Products

The combination of nutrients and herbals poses an excellent impact on lifestyle-related disorders, including mental health(65). Tannin-containing compounds, like lavender, help in delivering pressure and bringing down pulse. Flavonoids have been clinically demonstrated to forestall diabetes, cardiovascular problems, and kidney irregularities dependent on their cell reinforcement potential, containing compounds, for example, psoralen, which is gotten from parsley and have carminative and diuretic properties. Terpenoid-containing compounds, like peppermint and menthol, are utilized in

respiratory conditions. Numerous other regularly utilized spices, for example, aloe vera, has calming and widening properties, thus it is utilized in injury mending; ephedra has bronchodilator and vasoconstriction impacts, subsequently it is utilized for bronchospasms (29).



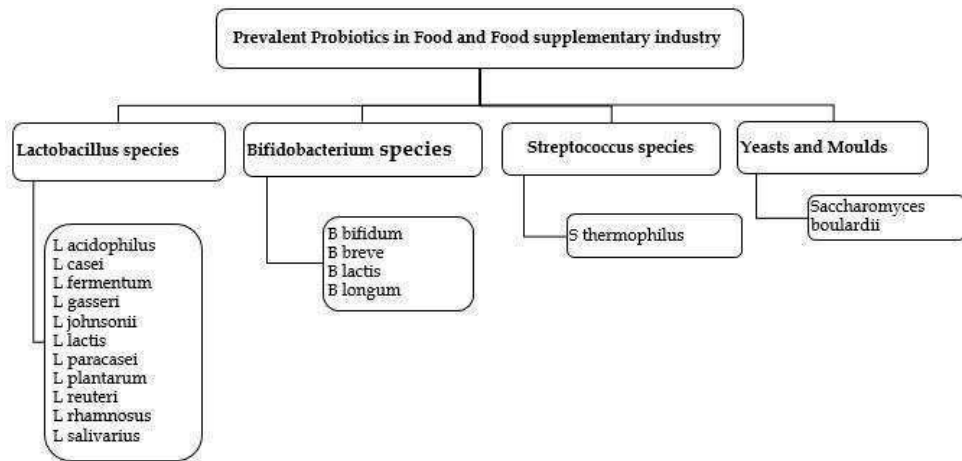
### Schematic diagram of the common steps involved in the extraction of nutraceutical from herbs Reference of figure

Bommakanti, V., Puthenparambil Ajikumar, A., Sivi, C. M., Prakash, G., Mundanat, A. S., Ahmad, F., ... & Rana, S. S. (2023). An overview of herbal nutraceuticals, their extraction, formulation, therapeutic effects and potential toxicity. *Separations*, 10(3), 177.

Home grown items as well as the phytoconstituents they have can likewise be sorted under nutraceuticals, for instance, vegetables contain carotenoids, which support insusceptibility, primarily executioner cells, and have anticarcinogenic properties. They additionally incorporate catalysts and glandular concentrates, and can be burned-through in all dose structures, including containers, powders, tablets, and so on(66).

### 2.1.3. Probiotic Microorganisms

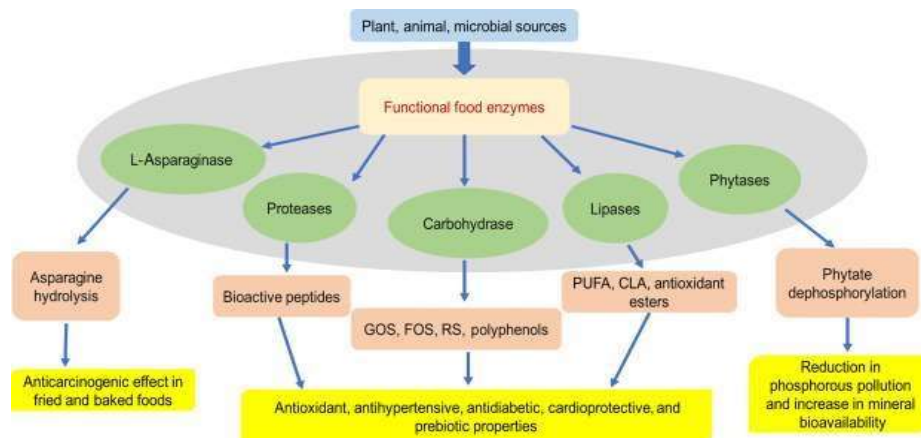
The term probiotic was instituted by the well-known researcher Metchnikoff. They are exceptionally beneficial, corresponding to gastric and digestive physiology. They have anti-infection properties and help in the expulsion of poisonous vegetation from the stomach. A solid eating routine prompts a sound cerebrum and body. The utilization of probiotics has been a forward leap in the administration of gastrointestinal issues. After these outcomes, probiotics have additionally been started for their utilization as enhancements as containers and probiotic drinks. In this way, current probiotics guarantee to be viable in all medical issues from looseness of the bowels to neurological conditions, like wretchedness and Alzheimer's, and are tested for their helpful impacts. There is an incredible need to investigate probiotics, as distributed exploration on their security is inadequate. It is hard to separate the advantages of probiotics from their contraindications. In occurrences with high danger of contamination in patients with compromised safe framework, the probiotics might be tolerably viable restoratively(67).



**Common Probiotic Microorganisms that are used in yogurt, fermented milk products and food-supplementary**

**2.1.4. Nutraceutical Enzymes**

Catalysts or biocatalysts are protein structures and are incorporated by cells. They cause metabolic cycles to happen quicker and are basically valuable in clinical issues identified with the gastrointestinal plot, like gastroesophageal reflux illness, clogging, loose bowels, and so forth Protein supplements give minimal benefits in neurological wellbeing, however as of late, a few treatments have been obtained to fix uncommon issues, like Hunter condition, Gaucher illness, and so forth They are exceptionally practical as they are acquired from the two plants and creature sources. Many benefits are presented upon the utilization of food-based nutraceuticals. Nutraceuticals acquired from food sources, like garlic, ginger, turmeric, dairy items, carotenoids, and so on, are much healthier and can give every one of the fundamental supplements needed by our body. They are effectively accessible in supermarkets and forestall the intensification of extreme life-related issues, like diabetes, and even malignancies. Having great psychological wellness is a need, and a decent eating regimen can be the most engaging choice for neuroprotection.



**Role of enzymatic biosynthesis of nutraceuticals**

Notwithstanding, they represent specific impediments as well. The most focused on downside of food-based nutraceuticals is their security. There is yet a desperate need to investigate useful food varieties for their wellbeing before they are delivered on the lookout for utilization in crude structures. All substances are poison except if burned through in a limited sum. It is clear that a food that is profoundly dynamic as an anticarcinogen can all the while go about as a cardiotoxic. In this way, organization of the ideal portion is suggested (68).

## **2.2. Non-Traditional Nutraceuticals**

These incorporate food varieties acquired from the reproducing of horticultural items and supplements, for example, squeezed orange invigorated with calcium, nutrients, and minerals in grains, and so on social researchers have effectively created methods and have changed the nourishing substance of harvests, and more exploration is being completed to work on the nature of sustenance in crops(69).

### **2.2.1. Fortified Nutraceuticals**

These are the sort of nutraceuticals that are planned from reproducing at the farming level by upgrading supplements, like minerals in grains, expanding calcium, folic corrosive, iron in flour, making milk sustained with cholecalciferol for the treatment of nutrient D inadequacy, and so on(70).

### **2.2.2. Recombinant Nutraceuticals**

Nutraceuticals acquired from the utilization of biotechnology in food items are called recombinant nutraceuticals. These nutraceuticals are among the most utilized classification, including the extraction of supplements from specific food items, like dairy items, cheddar, and bread, to extricate the chemical that is restoratively gainful whenever utilized at ideal levels(28). There are many organizations that orchestrate non-conventional nutraceuticals of low quality to get bigger benefits and edges. Moreover, the bioavailability of improved supplements isn't observed and is by and large poor in different situations. The testing of nutraceuticals isn't quite as controlled as drugs unmistakably demonstrating no characterized guidelines(71).

## **2.3. Based on the Mechanism of Action**

In view of the restorative properties had, nutraceuticals have been additionally grouped into antibacterial, antifungal, cancer prevention agents, mitigating, and against heftiness classifications to recognize their job and evaluate their employments. Food-borne contaminations are the reason for a wide number of passing because of disease. There are numerous bioactive mixtures that have been utilized as an intense antibacterial treatment in the administration of irresistible problems, for example, carsonic corrosive (terpenoids), quercetin (polyphenols), and so on They are obtained from a wide number of fruits and vegetables(72).

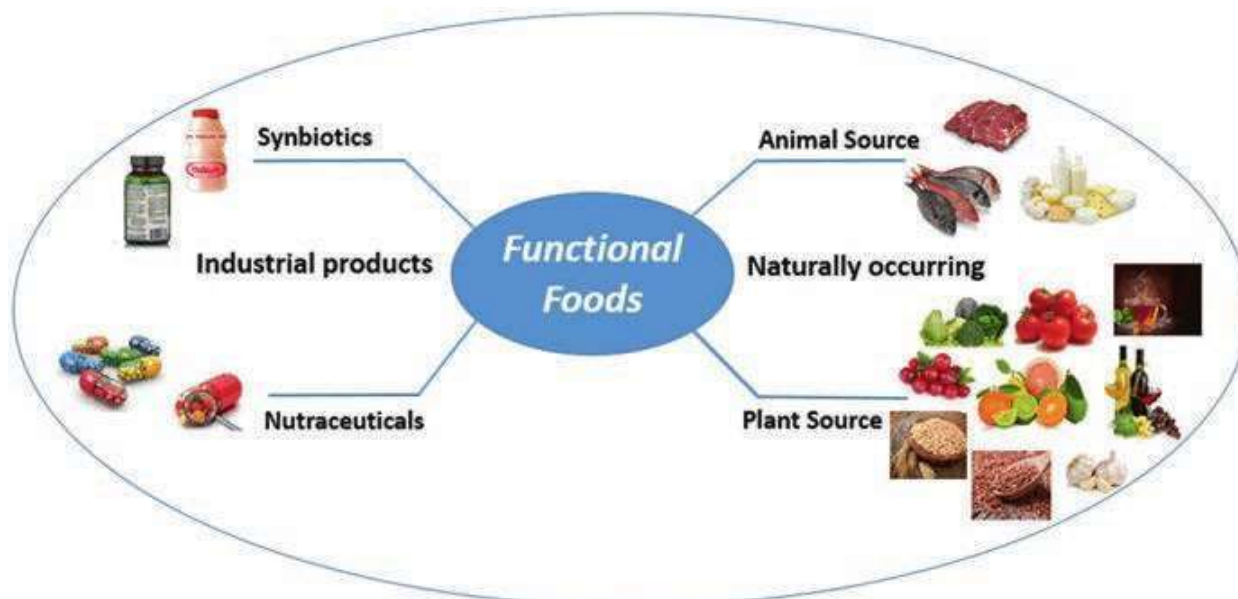
Devouring anything in overabundance goes about as a toxin. The utilization of nutraceuticals dependent on their component of activity is profoundly strong. Devouring any compound for its restorative action will in general diminish the odds of obvious harmful characteristics related to it and advantages the individual for the ideal ailing condition. Furthermore, it prompts checked organization of nutraceuticals and forestalls any poisonous impacts related with high dosages(73).

## **3. Functional Foods**

### **3.1. Concept of Functional Food.**

Utilitarian food is portrayed as any food or food part that can upgrade wellbeing past central sustenance. Such food varieties lessen the danger of way of life related problems by accomplishing physiological capacities past dietary impacts. These food varieties are planned either to forestall or to fix the illness(74).





### Categories of functional foods on the basis of origin

#### Types(75):

- 1)Enriched food items
- 2)Enhanced food wares
- 3)Fortified food item
- 4)Altered food items

### 3.2. Functional Dairy Products.

The buyer will now not think twice about taste or item five star for wellbeing items and the rate is an essential deciding component for rehashed buy. A chief component of dairy items is that clients know them, and many acknowledge that dairy items are sound regular items. Wellbeing experts worldwide rouse a customer to eat at different adjusted get-healthy plans as an option than moment arrangements being looked for, and dairy items are noticeable variables for solid adjusted eating regimens(75). Milk and dairy items make up one of the four prevalent gatherings of dinners that structure a fair eating routine. Additionally, milk is a critical wellspring of protein, B-bunch nutrients, and calcium in a changed eating routine and contains nutrient A, thiamine B1, niacin B3, dimethylglycine B16, folate B9, magnesium, and zinc(76).

### 3.3. Probiotics in Dairy Products.

Gastrointestinal capacities are among the most encouraging focuses on useful food varieties, including those that control the travel time, digestive propensities, and motility of the digestive mucosa just as those that balance epithelial cell multiplication. Stomach related capacities are additionally encouraging objectives identified with adjusted microflora identified with controlling the bioavailability of supplements, tweaking the insusceptible movement of the stomach related framework, or interceding endocrine action of the stomach related framework. Moreover, it is compelling in the therapy of obstruction, anticipation of provocative gastrointestinal issues, and anticancer activity, just as diminishes pulse and brings down cholesterol(77).

### 3.4. Probiotic Yogurt as a Functional Food.

The texture is a critical aspect of yogurt that is acceptable to consumers. Rheological properties affect the texture that affects sensory perception and ultimately consumer acceptance of a product. Right now, the market gives a wide scope of yogurts reasonable for all palates and supper events. Yogurts arrive in a variety of surfaces (like fluid, blended, and set), flavors (like normal, natural product, and oat), and fat substance (like extravagance, low-fat, and sans fat); can be delighted in like a bite or as

a feature of a feast, like sweet or exquisite bites; and are accessible consistently. Along with their acknowledgment as sound and nutritious food, this adaptability added to their far and wide accomplishment in all subgroups of the populace. Acquainting probiotic strains with yogurt is a decent way to deal with producing viable, adequate, and reasonable matured milk. Be that as it may, acquainting new strains with yogurt starter culture might influence the causticity, fragrance insights, and textural properties of the item. The surface is a basic part of yogurt that is adequate to purchasers. Rheological properties influence the surface that influences tangible discernment and eventually buyer acknowledgment of an item(78).

#### **4. Health Benefits of Nutraceuticals**

Nutraceuticals are utilized to achieve advantageous remedial results with decreased incidental effects, as contrasted and other helpful specialists. Utilization of plant-based food sources, nuts, entire grains, cereals, and marine food varieties assumes an imperative part in infection counteraction and wellbeing advancement(79). Some famous nutraceuticals incorporate lutein (for macular degeneration), folic corrosive, and cod liver oil cases. The most famous practical food and drink items incorporate omega-3 eggs, omega-3-improved yogurts, calcium-enhanced squeezed orange, and green tea, to refer to a couple. Most of the nutraceuticals do have various restorative advantages. Nutraceuticals are professed to have physiological advantage or assurance against the accompanying infections:

- 1)CVD
- 2)Cancer
- 3)Diabetes
- 4)Obesity
- 5)Chronic fiery issues
- 6) Parkinson's illness
- 7) Alzheimer's illness

#### **5. Spirulina(80)**

##### **5.1. Synonyms(80)**

“Blue green algae”

##### **5.2. Source of spirulina(80)**

Spirulina is a spiral-shaped microalgae that grows naturally in the wild in warm, freshwater lakes.

##### **5.3. Family(80)**

“Oscillatoriaceae”

##### **5.4. Habitat(80)**

They are found in freshwater and marine habitats, mostly in warmer regions; and are also found in hot springs.

##### **5.6. Cultivation(80)**

1. Most commercial production systems are based on shallow raceways in which spirulina cultures are mixed by a paddle wheel.
2. Spirulina is an economically important filamentous cyanobacterium.
3. The annual production of the algae is about 10,000 tons which makes it the largest microalgal cultivation industry in the world Farming of spirulina

##### **5.7. Chemical constituent(80)**

1. Spirulina is a protein-rich food product (approximately 55-70% dry weight), with a relatively low carbohydrate content of around 15% dry weight.
2. It also contains phycocyanin- containing phycobiliproteins which are thought to be some of spirulina's active ingredients.

3. In addition, spirulina also contains several trace minerals, vitamins, and pro- and pseudo- vitamins phycocyanin.

#### **5.8. Nutraceutical values(80)**

1. Pyocyanin is the main active compound in spirulina. It has powerful antioxidant and anti-inflammatory properties.
2. Its lower blood pressure levels.
3. Spirulina supplements have been shown to be very effective against allergic rhinitis, helping to reduce various symptoms.
4. One study shows that spirulina may be effective against anemia in the elderly.

#### **5.9. Marketing product of spirulina (80)**

1. IMC (International marketing) corporation Indian company
2. Triquetra health Organic spirulina tablet
3. Soft drink of spirulina support by Germany

#### **6. Soya bean(81)**

##### **6.1. Source(81)**

Soya bean is derived from seeds of *Glycine max* (L) Merr. Soya bean is known as Golden bean or super legume of the twentieth century.

##### **6.2. Family(81)**

“Leguminosae”.

##### **6.3. Cultivation(81)**

1. Currently grown in various environments throughout the world.
2. Extensively cultivated in tropical Brazil, sub-tropical central America and southern USA and Canada.
3. Introduction of soybean in most African countries is very recent.

##### **6.4. Habitat(81)**

1. Soya bean cultivation is typically successful climates with hot summers.
2. Optimum growing conditions are mean temp. of 20°-30°c.

##### **6.5. Chemical constituents(81)**

1. Together, protein and soybean oil content account for 56% of dry soybeans by weight (36% protein and 20% fat, table).
2. The remainder consists of 30% carbohydrates, 9% water and 5% ash (table). Soybeans comprise approximately 8% seed coat or hull, 90% cotyledons and 2% hypocotyl axis or germ.

##### **6.6. Nutraceutical values(81)**

1. It prevents prostate cancer
2. It prevents postmenopausal syndrome The phytoestrogen content in soybeans is effective as an estrogen’s replacement. Consume soy regularly to prevent and cure postmenopausal syndromes.
3. It also prevents osteoporosis. It also works as an antioxidant.
4. It also acts as an anti-inflammatory.
5. Reduces high cholesterol level.
6. It also enhances immune function.
7. Broccoli
8. Herbal and Green Tea
9. Ginseng
10. Turmeric
11. Garlic
12. Flax seeds

#### **13. Conclusion**

The objective of this article is to support clinical and wellbeing experts to grow their insight into the properties of useful food varieties as they advance great wellbeing while at the same time assisting with forestalling illness. Useful food varieties that contain physiologically dynamic fixings can

further develop wellbeing, from one or the other creature or plant sources; by supporting wellbeing through counteraction rather than treatment, nutraceuticals and utilitarian food varieties could give an answer for decrease the developing weight on medical services frameworks, although note that practical food sources are not drugs, as they don't mend, fix, or forestall sicknesses. Notwithstanding, nutraceutical items are relied upon to assume a significant part in possible helpful turn of events. Society wellbeing specialists view nutraceutical as anticipation, treatment, and an amazing asset for safeguarding wellbeing and acting versus intense and ongoing sicknesses brought about by sustenance, along these lines improving wellbeing. Nutraceuticals are creating in clinical practice, however progressed concentrates on need to address the significance of drug and clinical issues.

**CONFLICT OF INTEREST:** No

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**REFERENCES:**

1. Kalra EK. Nutraceutical-definition and introduction. *Aaps Pharmsci.* 2003;5(3):27-8.
2. Zhao J. Nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy for improvement of human health: a perspective on plant biotechnology application. *Recent patents on biotechnology.* 2007;1(1):75-97.
3. Chauhan B, Kumar G, Kalam N, Ansari SH. Current concepts and prospects of herbal nutraceutical: A review. *Journal of advanced pharmaceutical technology & research.* 2013;4(1):4.
4. Zeisel SH. Regulation of" nutraceuticals". *American Association for the Advancement of Science;* 1999. p. 1853-5.
5. Hardy G. Nutraceuticals and functional foods: introduction and meaning. *Nutrition (Burbank, Los Angeles County, Calif).* 2000;16(7-8):688-9.
6. Baradaran A, Madihi Y, Merrikhi A, Rafieian-Kopaei M, Nasri H. Serum lipoprotein (a) in diabetic patients with various renal function not yet on dialysis. 2013.
7. Nasri H. Impact of diabetes mellitus on parathyroid hormone in hemodialysis patients. *Journal of Parathyroid Disease.* 2013;1(1):9-11.
8. Madihi Y, Merrikhi A, Baradaran A, Rafieian-Kopaei M, Shahinfard N, Ansari R, et al. Impact of Sumac on postprandialhigh-fat oxidative stress. 2013.
9. Setorki M, Rafieian-Kopaei M, Merrikhi A, Heidarian E, Shahinfard N, Ansari R, et al. Suppressive impact of anethum graveolens consumption on biochemical risk factors of atherosclerosis in hypercholesterolemic rabbits. *International Journal of Preventive Medicine.* 2013;4(8):889.
10. Khosravi-Boroujeni H, Mohammadifard N, Sarrafzadegan N, Sajjadi F, Maghroun M, Khosravi A, et al. Potato consumption and cardiovascular disease risk factors among Iranian population. *International journal of food sciences and nutrition.* 2012;63(8):913-20.
11. Khosravi-Boroujeni H, Sarrafzadegan N, Mohammadifard N, Sajjadi F, Maghroun M, Asgari S, et al. White rice consumption and CVD risk factors among Iranian population. *Journal of health, population, and nutrition.* 2013;31(2):252.
12. Shirzad H, Burton R, Smart Y, Rafieian-kopaei M, Shirzad M. Natural Cytotoxicity of NC-2+ Cells Against the Growth and Metastasis of WEHI-164 Fibrosarcoma. *Scandinavian journal of immunology.* 2011;73(2):85-90.
13. Shirzad M, Kordyazdi R, Shahinfard N, Nikokar M. Does Royal jelly affect tumor cells? *Journal of HerbMed Pharmacology.* 2013;2(2):45-8.
14. Akhlaghi M, Shabaniyan G, Rafieian-Kopaei M, Parvin N, Saadat M, Akhlaghi M. Citrus aurantium blossom and preoperative anxiety. *Revista brasileira de anesthesiologia.* 2011;61:707-12.

15. Roohafza H, Sarrafzadegan N, Sadeghi M, Rafieian-Kopaei M, Sajjadi F, Khosravi-Boroujeni H. The association between stress levels and food consumption among Iranian population. *Archives of Iranian medicine*. 2013;16(3):0-.
16. Baradaran A, Nasri H, Nematbakhsh M, Rafieian-Kopaei M. Antioxidant activity and preventive effect of aqueous leaf extract of Aloe Vera on gentamicin-induced nephrotoxicity in male Wistar rats. *La clinica terapeutica*. 2014;165(1):7-11.
17. Nasri H, Tavakoli M, Ahmadi A, Baradaran A, Nematbakhsh M, Rafieian-Kopaei M. Ameliorative effect of melatonin against contrast media induced renal tubular cell injury. *Pakistan journal of medical sciences*. 2014;30(2):261.
18. Parsaei P, Karimi M, Asadi SY, Rafieian-Kopaei M. Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on post-laparotomy intra-abdominal adhesion in rats. *International Journal of Surgery*. 2013;11(9):811-5.
19. Kafash-Farkhad N, Asadi-Samani M, Rafieian-Kopaei M. A review on phytochemistry and pharmacological effects of *Prangos ferulacea* (L.) Lindl. *Life Sci J*. 2013;10(8s):360-7.
20. Mirhoseini M, Baradaran A, Rafieian-Kopaei M. Medicinal plants, diabetes mellitus and urgent needs. *J HerbMed Pharmacol*. 2013;2(2):53-4.
21. Akbari F, Karimi A, Shahinfard N. Effect of turnip on glucose and lipid profiles of alloxan-induced diabetic rats. *Iranian Journal of Endocrinology and Metabolism*. 2013;14(5):492-7.
22. Bahmani M, Saatloo NV, Maghsoudi R, Momtaz H, Saki K, Kazemi-Ghoshchi B, et al. A comparative study on the effect of ethanol extract of wild *Scrophularia deserti* and streptomycin on *Brucella melitensis*. *Journal of HerbMed Pharmacology*. 2013;2(1):17-20.
23. Karimi A, Moradi M-T, Saeedi M, Asgari S, Rafieian-Kopaei M. Antiviral activity of *Quercus persica* L.: high efficacy and low toxicity. *Advanced biomedical research*. 2013;2.
24. Rafieian-Kopaei M. Metformin and renal injury protection. *Nickan Research Institute*; 2013. p. 91-2.
25. Rafieian-Kopaei M, Baradaran A, Merrikhi A, Nematbakhsh M, Madihi Y, Nasri H. Efficacy of co-administration of garlic extract and metformin for prevention of gentamicin–renal toxicity in wistar rats: A biochemical study. *International journal of preventive medicine*. 2013;4(3):258.
26. Kiani M-A, Khodadad A, Mohammadi S, Ghayour Mobarhan M, Saeidi M, Jafari SA, et al. Effect of peppermint on pediatrics' pain under endoscopic examination of the large bowel. *J HerbMed Pharmacol*. 2013;2(2):41-4.
27. Hosseini-Asl K, Rafieian-Kopaei M. Can patients with active duodenal ulcer fast Ramadan? *Official journal of the American College of Gastroenterology| ACG*. 2002;97(9):2471-2.
28. Abdel-Daim MM, El-Tawil OS, Bungau SG, Atanasov AG. Applications of antioxidants in metabolic disorders and degenerative diseases: Mechanistic approach. *Hindawi*; 2019.
29. Williams RJ, Mohanakumar K, Beart PM. Neuro-nutraceuticals: Further insights into their promise for brain health. *Elsevier*; 2016. p. 1-3.
30. Van Der Burg KP, Cribb L, Firth J, Karmacoska D, Sarris J. Nutrient and genetic biomarkers of nutraceutical treatment response in mood and psychotic disorders: a systematic review. *Nutritional Neuroscience*. 2021;24(4):279-95.
31. Helal NA, Eassa HA, Amer AM, Eltokhy MA, Edafiogho I, Nounou MI. Nutraceuticals' novel formulations: the good, the bad, the unknown and patents involved. *Recent patents on drug delivery & formulation*. 2019;13(2):105-56.
32. Chong LK, Udell LJ, Downs BW. Intellectual property, branding, trademark and regulatory approvals in nutraceuticals and functional foods. *Nutraceutical and Functional Food Regulations in the United States and Around the World: Elsevier*; 2008. p. 403-16.
33. DeFelice SL. The nutraceutical revolution: its impact on food industry R&D. *Trends in Food Science & Technology*. 1995;6(2):59-61.
34. Jack DB. Keep taking the tomatoes—the exciting world of nutraceuticals. *Molecular Medicine Today*. 1995;1(3):118-21.



35. Brower V. Nutraceuticals: poised for a healthy slice of the healthcare market? *Nature biotechnology*. 1998;16(8):728-31.
36. Mannion M. Nutraceutical revolution continues at foundation for innovation in medicine conference. *Am J Nat Med*. 1998;5:30-3.
37. Rishi R. Nutraceutical: borderline between food and drug. *Pharma review*. 2006;2006:51-3.
38. Esther B, Rapport L, Lockwood B. What is nutraceutical. *Pharm J*. 2000;265:57-8.
39. Cockbill C. Food law and functional foods. *British Food Journal*. 1994.
40. Food U, Administration D. Dietary Supplements Health and Education Act of 1994 (Available from:) [http://www.fda.gov/RegulatoryInformation/Legislation/Federal Food Drug and Cosmetic Act FDCAct. Significant Amendments to the FDCAct/ucm148003 htm](http://www.fda.gov/RegulatoryInformation/Legislation/Federal%20Food%20Drug%20and%20Cosmetic%20Act/FDCAct%20Significant%20Amendments%20to%20the%20FDCAct/ucm148003.htm) (Accessed 12 January 2011). 2011.
41. Pandey M, Verma RK, Saraf SA. Nutraceuticals: new era of medicine and health. *Asian J Pharm Clin Res*. 2010;3(1):11-5.
42. Adelaja AO, Schilling BJ. Nutraceuticals: blurring the line between food and drugs in the twenty-first century. *Choices*. 1999;14(4):35-9.
43. Richardson DP. Functional foods--shades of gray: an industry perspective. *Nutrition Reviews*. 1996;54(11):S174.
44. Act A. Dietary Supplement Health and Education Act of 1994 Public Law 103-417 103rd Congress. Public Law. 1994;103:417.
45. Aronson JK. Defining 'nutraceuticals': Neither nutritious nor pharmaceutical. *British journal of clinical pharmacology*. 2017;83(1):8-19.
46. Dureja H, Kaushik D, Kumar V. Development in nutraceuticals. *Indian Journal of Pharmacology*. 2003;35:363-72.
47. Mobarhan S. Micronutrient supplementation trials and the reduction of cancer and cerebrovascular incidence and mortality. *Nutr Rev*. 1994;52(3):102-5.
48. de Rijk MC, Breteler MM, den Breeijen JH, Launer LJ, Grobbee DE, van der Meché FG, et al. Dietary antioxidants and Parkinson disease. The Rotterdam Study. *Arch Neurol*. 1997;54(6):762-5.
49. Agus DB, Gambhir SS, Pardridge WM, Spielholz C, Baselga J, Vera JC, et al. Vitamin C crosses the blood-brain barrier in the oxidized form through the glucose transporters. *J Clin Invest*. 1997;100(11):2842-8.
50. Klein C, Sato T, Meguid MM, Miyata G. From food to nutritional support to specific nutraceuticals: a journey across time in the treatment of disease. *J Gastroenterol*. 2000;35 Suppl 12:1-6.
51. Jialal I, Fuller CJ. Effect of vitamin E, vitamin C and beta-carotene on LDL oxidation and atherosclerosis. *Can J Cardiol*. 1995;11 Suppl G:97g-103g.
52. Burney PG, Comstock GW, Morris JS. Serologic precursors of cancer: serum micronutrients and the subsequent risk of pancreatic cancer. *Am J Clin Nutr*. 1989;49(5):895-900.
53. Mathew P, Wyllie R, Van Lente F, Steffen RM, Kay MH. Antioxidants in hereditary pancreatitis. *Am J Gastroenterol*. 1996;91(8):1558-62.
54. Clark LC, Combs GF, Jr., Turnbull BW, Slate EH, Chalker DK, Chow J, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *Jama*. 1996;276(24):1957-63.
55. Ceremuzyński L, Chamiec T, Herbaczyńska-Cedro K. Effect of supplemental oral L-arginine on exercise capacity in patients with stable angina pectoris. *Am J Cardiol*. 1997;80(3):331-3.
56. Braeckman J. The extract of *Serenoa repens* in the treatment of benign prostatic hyperplasia: A multicenter open study. *Current Therapeutic Research-clinical and Experimental*. 1994;55:776-85.
57. Melchart D, Linde K, Worku F, Sarkady L, Holzmann M, Jurcic K, et al. Results of five randomized studies on the immunomodulatory activity of preparations of Echinacea. *J Altern Complement Med*. 1995;1(2):145-60.

58. Ernst E. The risk-benefit profile of commonly used herbal therapies: Ginkgo, St. John's Wort, Ginseng, Echinacea, Saw Palmetto, and Kava. *Ann Intern Med.* 2002;136(1):42-53.
59. Krinsky DL. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care: American Pharmacists Association*; 2020.
60. Krinsky DL, Ferreri SP, Hemstreet B, Hume AL, Newton GD, Rollins CJ, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-care: American Pharmacists Association*; 2018.
61. Kokate C, Purohit A, Gokhale S. *Nutraceutical and cosmaceutical. Pharmacognosy*, 21st edition, Pune, India: Nirali Prakashan. 2002;542:549.
62. Das L, Bhaumik E, Raychaudhuri U, Chakraborty R. Role of nutraceuticals in human health. *Journal of food science and technology.* 2012;49:173-83.
63. Escott-Stump S. *Nutrition and diagnosis-related care: Lippincott Williams & Wilkins*; 2008.
64. Bhaskarachary K, Vemula SR, Gavaravarapu S, Joshi AKR. Traditional foods, functional foods and nutraceuticals. *Proceedings of the Indian National Science Academy.* 2016;82(5):1565-77.
65. Dohrmann DD, Putnik P, Kovačević DB, Simal-Gandara J, Lorenzo JM, Barba FJ. Japanese, Mediterranean and Argentinean diets and their potential roles in neurodegenerative diseases. *Food research international.* 2019;120:464-77.
66. Montesano D, Rocchetti G, Putnik P, Lucini L. Bioactive profile of pumpkin: An overview on terpenoids and their health-promoting properties. *Current Opinion in Food Science.* 2018;22:81-7.
67. Zucko J, Starcevic A, Diminic J, Oros D, Mortazavian AM, Putnik P. Probiotic–friend or foe? *Current Opinion in Food Science.* 2020;32:45-9.
68. Tapal A, Tiku PK. Nutritional and nutraceutical improvement by enzymatic modification of food proteins. *Enzymes in food biotechnology: Elsevier*; 2019. p. 471-81.
69. Chintale Ashwini G, Kadam Vaishali S, Sakhare Ram S, Birajdar Ganesh O, Nalwad Digambar N. Role of nutraceuticals in various diseases: A comprehensive review. *Int J Res Pharm Chem.* 2013;3:290-9.
70. Gulati OP, Ottaway PB, Coppens P. *Botanical Nutraceuticals,(Food Supplements, Fortified and Functional Foods) in the European Union with Main Focus on Nutrition And Health Claims Regulation. Nutraceutical and Functional Food Regulations in the United States and Around the World: Elsevier*; 2014. p. 221-56.
71. Drake PM, Szeto TH, Paul MJ, Teh AYH, Ma JKC. Recombinant biologic products versus nutraceuticals from plants—a regulatory choice? *British Journal of Clinical Pharmacology.* 2017;83(1):82-7.
72. Gutiérrez-del-Río I, Fernández J, Lombó F. Plant nutraceuticals as antimicrobial agents in food preservation: Terpenoids, polyphenols and thiols. *International journal of antimicrobial agents.* 2018;52(3):309-15.
73. Mandel S, Packer L, Youdim MB, Weinreb O. Proceedings from the “Third International Conference on mechanism of Action of Nutraceuticals”. *The Journal of Nutritional Biochemistry.* 2005;16(9):513-20.
74. Kaur S, Das M. Functional foods: An overview. *Food Science and Biotechnology.* 2011;20:861-75.
75. Henry C. Functional foods. *European Journal of Clinical Nutrition.* 2010;64(7):657-9.
76. L. AYT. Thomas, *Probiotic Dairy Products*, John Wiley & Sons 2017.
77. H. Andersson NGA, Å. Bruce, S. Roos, T. Wadström, and A. E. Wold., ” *Näringsforskning*, vol. 45, no. 1, pp. 58–75.; 2016.
78. Zoumpopoulou G, Tsakalidou E, Thomas L. An Overview of Probiotic Research: Human and Mechanistic Studies. *Probiotic Dairy Products.* 2017:293-357.
79. Khalaf RM, Fakhri MA. Structural and Morphological Investigations of Indium Trioxide Deposited using PLD at Different Pulsed Laser Energies.

80. Ali SK, Saleh AM. Spirulina-an overview. International journal of Pharmacy and Pharmaceutical sciences. 2012;4(3):9-15.
81. Etiosa OR, Chika NB, Benedicta A. Mineral and proximate composition of soya bean. Asian Journal of Physical and Chemical Sciences. 2017;4(3):1-6.