

Nutraceuticals – A Review on Current Status

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Abstract- *Nutraceuticals refers to foods having a medicinal effect on health of human beings. It consists of food supplements, herbal products, probiotics and prebiotics, medical foods meant for prevention and treatment of diseases. Major nutraceuticals possess multiple therapeutic effect with lacking of unwanted effects hence attract more consumer interest. Increase in shift towards preventive therapies and increasing disposable income, favorable pricing environment growth in pharma retail chain and increase in healthcare spending is mainly responsible for increasing market for nutraceuticals in India, but lack of standardization and awareness, high pricing, marketing and distribution are some challenges. Nutraceutical market is seeing tidal growth mainly in United States, India and European countries. Faster access to this market is possible through business partnership models, effective regulatory compliance and by evaluating key trends and consumer reference.*

Keywords- Nutraceuticals, Prebiotics, Probiotics, Regulatory compliance.

I. INTRODUCTION

Stephen De Felice, MD, the founder and chairman of the foundation for Innovation in Medicine (FIM), Cranford, New Jersey, first used the term "nutraceuticals" in 1989. It is made from of the word's "pharmaceuticals" and "nutrition." His definition states that it is "a food or element of a diet that has pharmacological benefits, including the treatment and prevention of disease." Food has traditionally been used for both nutritional and medicinal purposes by numerous ancient cultures. Actually, the concept of nutritional supplements goes back around 3,000 years! The link between nutrition and health began to gain traction when Hippocrates, the father of modern medicine, recognized it.^{1,2}

A nutraceutical is made from of the word's "nutrient" and "pharmaceuticals." AAFCO, 1996 defines nutrient as a feed component that helps support a human or animal's existence, whereas nutraceutical refers to any non-toxic food ingredient with medically recognized health benefits, such as the prevention and treatment of disease.³ Products that have been separated or refined from food are marketed as medicines that aren't often connected with food. A nutritional supplement

has the physiological advantage of preventing chronic diseases.⁴

Nutraceuticals are products with nutritional and therapeutic properties that are made from food sources. The following terms are also used to refer to nutraceuticals:

- Functional food
- Medical food
- Designer food
- Phytochemicals
- Dietary Supplements²

A broad umbrella word known as "nutraceuticals" is used to describe any food-derived product that offers additional health advantages over and beyond the basic nutritional content present in food.⁴ A nutraceutical might be a food that is naturally high in nutrients, like spirulina, garlic, or soy, or it can be a specific dietary ingredient, such omega-3 fatty acids from salmon. They are also referred to as dietary supplements, nutritional supplements, and healing foods. It includes separated nutrients, dietary supplements, 'designer' foods made through genetic engineering, herbal items, and processed foods like cereals and soups.

Due to their alleged safety and possible medicinal and nutritional advantages, they have attracted a lot of interest.⁵ Nutraceuticals are employed in a wide range of clinical illnesses in addition to lifestyle disorders, such as inflammation, immunodeficiency, allergy, arthritis, malignancies, dyspepsia, depression, sleep issues, hypertension, and blood cholesterol control.⁶

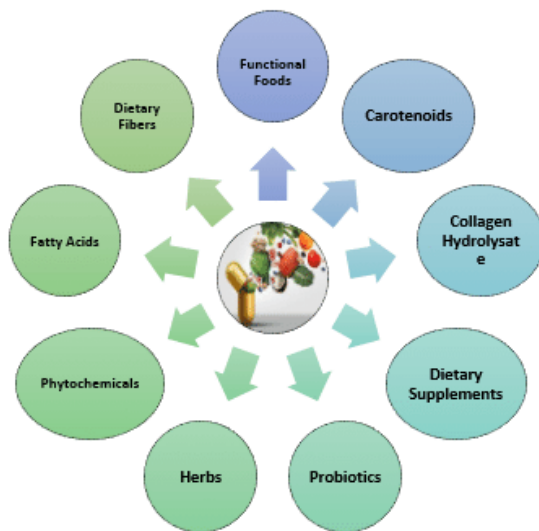
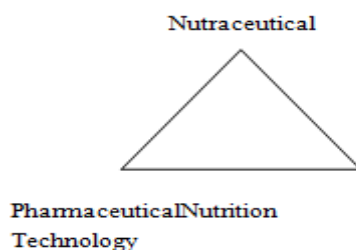


Figure.1: Inter-relationship of various foods as Nutraceuticals

According to the World Health Organization, over 80% of the global population (4.3 billion people) rely on traditional plant-based systems of medicine such as phytochemicals, nutritional components, or as a functional food. A nutraceutical is the antithesis of "junk food."^{7,8} Functional foods are regular foods with added components or substances that offer medical or physiological benefits in addition to their merely nutritional effects. Contrary to medications, which are chemically active compounds used to treat illness, nutritional supplements are primarily preventative or preventive.^{9,10} Instead of using drugs to treat diseases, they offer an alternative strategy that relies on diet to improve overall wellness of the body and treat illnesses. Depending on their pharmacological characteristics and natural sources, nutraceuticals or functional foods can be categorized.^{11,12,13} Nutrients, herbs, nutritional supplements, functional foods, and natural chemicals derived from various medicinal plants are the most popular types of nutraceuticals.¹⁴

The US market for functional foods that are high in nutraceuticals is worth \$250 billion, compared to \$150 billion for drugs. Roughly 29,000 dietary supplements are available in the US, and about 1000 new items enter the market each year.



The nutraceuticals and functional foods have a small distinction. Food is "functional meal" when it is prepared or cooked with "scientific intelligence," whether or not the cook is aware of how or why the food will be used. Thus, functional food gives the body the precise ratio of vitamins, lipids, proteins, carbs, and other nutrients it needs to function properly. Nutraceuticals are functional foods that assist in the prevention and/or treatment of diseases and/or disorders other than anemia. Citrus fruits and fortified dairy products (like milk) are examples of nutraceuticals (e.g., orange juice).¹⁵ The following diseases have been claimed to be protected against by nutraceuticals, or they are said to have physiological benefits (and/or operate as):

- Cardiovascular agents
- Anti-obese agents
- Antidiabetics
- Anticancer agents
- Immune boosters
- Chronic inflammatory disorders
- Degenerative diseases

Benefits:

From the perspective of the consumer, functional foods and nutraceuticals may provide a number of advantages:

- Might improve the nutritional value of our diet.
- Could make us live longer.
- Might enable us to prevent specific medical issues.
- Making a decision for oneself could have psychological benefits.
- May be thought of as more "natural" and less likely to have negative side effects than standard medicine.
- Can provide food for people with particular requirements (e.g., nutrient-dense foods for the elderly).¹⁶

NUTRACEUTICAL CATEGORIES:

(1) Dietary Supplements including botanicals:

- Vitamins, minerals, co-enzyme Q, carnitine
- Ginseng, Ginkgo Biloba, Saint John's Wort, SawPalmetto

(2) Functional Foods:

Food items that are consumed regularly but have health benefits beyond those of traditional nutrition.

Example:Omega-3 milk in prevention of heart disease

- Oats, bran, psyllium and lignin's for heart disease and colon cancer
- Foods/cereals/snacks enriched with soluble fibers, vitamins and minerals
- Stanols (Benecol) in reduction of cholesterol adsorption
- Prebiotics - oligo fructose for control of intestinal flora
- Yogurts - Probiotics for intestinal health.
- Canola oil with lowered triglycerides for cholesterol reduction

(3) Medicinal Foods:

- Transgenic cows and lacto-ferrin for immune enhancement
- Health bars with added medications
- Transgenic plants for oral vaccination against infectious diseases.¹⁷

II. CLASSIFICATION OF NUTRACEUTICALS

Nutraceuticals or functional foods can be classified based on their sources¹⁸

1. Natural or traditional (Based on natural sources, it can be classified as the products obtained from plants, animals, minerals or microbial sources)
2. Unnatural or Non-traditional (Nutraceuticals, as prepared via biotechnology, is called unnatural or non-traditional)
3. Commercial Nutraceuticals

1 Natural or Traditional Nutraceuticals

These are mainly three types-

- 1) Chemical Constituents
 - i) Nutrients
 - ii) Herbal
 - iii) Phytochemicals
- 2) Nutraceutical enzymes
 - i) Chemical constituents
- 3) Probiotic Micro-organisms
- 4) PUFAs
- 5)Antioxidants

1 Chemical constituents:**1.1 Nutrients:**

Amino acids, fatty acids, minerals, and vitamins are among the nutrients in nutraceuticals that have known nutritional objectives. Minerals from plants, animals, and dairy products can help with anemia, osteoporosis, and the development of healthy bones, teeth, and muscles as well as better nerve impulse and heart rhythm.

1.2 Botanicals:

Herbal nutraceuticals promote wellness and fight against chronic illnesses. Astringent, antipyretic, anti-inflammatory, analgesic, and antiarthritic are the most common properties of these. Flavonoids like apiol and psoralen, which are diuretic, carminative, and antipyretic, are found in some herbal remedies. Menthol, an active ingredient found in peppermint (*Mentha Piperita*), aids in the treatment of colds and the flu.¹⁹

1.3 Phytochemicals:

Plant compounds known as phytochemicals have unique biological properties that improve human health. They are additionally known as phytonutrients.²⁰

1.4 Nutraceutical enzymes:

An essential element of life is enzymes. These enzymes originate from microbial, animal, and plant origins.

1.5 Probiotic microbial organisms:

By eliminating the poisonous flora in the intestine and maintaining a pleasant environment, probiotics are crucial for improving life. Many probiotic products, including those made with *Bacillus bulgaricus*, are currently on the market and contain sufficient nutrients to combat a variety of infections and treat a number of human body problems.²¹ These microbes are adaptable bacteria that support wholesome digestion and some nutrient uptake. Most importantly, they work to fight out pathogens like yeast and other bacteria and viruses that could cause disease and form a mutually beneficial relationship with the human digestive system.²²

Probiotics have an antimicrobial effect by affecting the microflora, which prevents the pathogen from adhering to the intestinal epithelium, competing with the pathogen for nutrients necessary for survival, producing an antitoxin effect, and regressing some effects of infection on the intestinal

epithelium, such as secretory changes and neutrophil migration. For instance, probiotics can treat lactose intolerance by increasing the production of Beta-galactosidase, an enzyme that hydrolyzes the irritating lactose into its sugar components.²³

1.6 Poly-unsaturated fatty acids (PUFAs):

Essential fatty acids, such as Omega-3 Fatty Acids, sunflower oil, corn oil, soy oil, and fish oil, are examples of fatty acids with more than one double bond. The omega-3 and omega-6 fatty acid groups make up the category of polyunsaturated fatty acids (PUFAs). Different polyunsaturated fatty acids have different positions for the initial double C-bond. Since they cannot be manufactured by the human body and are necessary for physiological integrity, two PUFAs are referred to as essential fatty acids. One is linoleic acid, which is a member of the N-6 family. The other is an N-3 family member called alpha-linolenic acid (LNA). In the human body, these necessary parent substances can be changed into long-chain fatty acids.²⁴

1.7 Antioxidant:

Antioxidants are essential for maintaining optimal health and wellbeing since they serve as our body's first line of defence against free radical damage. Oxygen is a very reactive atom that can combine with other elements to form potentially harmful compounds known as "Free Radicals," which are found in fruits, vegetables, and fish.

1.7.1 Nutrient derived antioxidants-Ascorbic acid (Vitamin C), tocopherols and tocotrienols (Vitamin E), carotenoids, and other low molecular weight substances like glutathione and lipoic acid.

1.7.2. Antioxidant enzymes - such as superoxide dismutase, glutathione peroxidase, and glutathione reductase, catalyze processes that quench free radicals.

1.7.3. Metal-binding proteins- including ferritin, lactoferrin, albumin, free iron, and copper ions, are listed in Section Various plant meals contain a range of additional antioxidant phytonutrients.

1.7.4. Dietary antioxidants –

- Beta carotene, other carotenoids, and oxycarotenoids
- Vitamin C
- Vitamin E

1.7.5 Metal-binding proteins:

- Ferritin
- Transferrin
- Albumin
- Myoglobin
- Ceruloplasmin
- Metallothionein

2 Unnatural or Non-Traditional Nutraceuticals:

These are the biotechnologically created artificial foods. Samples of food contain bioactive elements which are engineered to create advantages for human wellness. They were divided into two categories.

1. Fortified nutraceuticals
2. Recombinant nutraceuticals

2.1. Fortified nutraceuticals:

These are agrarian-bred nutraceuticals or supplements with additional nutrients and/or additives. Examples include cereals with extra vitamins or minerals, milk fortified with cholecalciferol to treat vitamin D insufficiency, flour fortified with folic acid, and probiotic and prebiotic milk with Bifidobacterium Lactis HN019 to treat severe illnesses such as diarrhoea and respiratory infections.²⁵

2.2 Recombinant Nutraceuticals:

Prebiotic production, bioactive component extraction using enzymes and fermentation techniques, and genetic engineering are all examples of recombinant nutraceuticals. Additionally, current biotechnology is used in the production of foods that provide energy, including bread, wine, fermented starch, yoghurt, cheese, vinegar, and others.²⁶

3 Commercial Nutraceutical:

Commercial Nutraceuticals can be divided as:

1. Dietary supplements
2. Functional food

3.1 Dietary supplements:

They are concentrated sources of nutrients or other compounds that, singly or in combination, have a nutritional or physiological effect. All products that a consumer can purchase over-the-counter are included in dietary supplements.^{27,28} Antioxidants utilised as dietary supplements

or ingestion have been linked to a wide range of possible advantages. In general, antioxidants may be helpful in the prevention of cerebrovascular disease and cancer.^{29,30,31,32}

Drug classification does not apply to dietary supplements. The primary distinction is that, unlike in the case of pharmaceuticals, they do not have therapeutic claims that have been approved. Additionally, dietary supplements may include vitamins, minerals, herbs, or amino acids, all of which are intended to enhance or supplement a person's diet. They are not meant to be used in place of any food or other medications.

3.2 Functional food:

Functional food is described as "any food or food ingredient that may deliver a health advantage beyond the traditional nutrients it contains by the Food and Nutrition Board of the Institute of Medicine of the United States of America. "Food products should be used as part of the regular diet to have beneficial benefits that go beyond basic nutritional function" is the definition of functional food. Physiologically active ingredients can be found in functional foods that come from either plant or animal sources.³³

III. SCOPE OF NUTRACEUTICALS³⁴

The normal physiological function that supports healthy human beings is significantly modified and maintained by nutraceuticals. Dietary fiber, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants, and other diverse kinds of herbal natural foods are some of the food products that are employed as nutraceuticals. Numerous illnesses, including obesity, cardiovascular disease, cancer, osteoporosis, arthritis, diabetes, and cholesterol, are treated with these nutraceuticals. Overall, "nutraceutical" must usher in a new era of medicine and health, one in which the food industry has evolved into a research-focused enterprise.

IV. ROLE OF NUTRACEUTICALS

1. CVS disease:

Grape polyphenols protect and treat vascular disorders. Flavonoids block the ACE and strengthen the tiny capillaries that transport oxygen and vital nutrients to all cells (found in onions, vegetables, grapes, red wine, apples, and cherries).³⁵ Rice bran improves cardiovascular health by lowering (LDL) and raising (HDL) levels of cholesterol in the blood, as well as serum cholesterol levels. The risk of coronary heart disease will increase as the ratio rises. Both lutein and zeaxanthin, which enhance vision and lower the risk of cataracts, are found in rice bran. Additionally encouraging

eye health are the important fatty acids omega-3, omega-6, omega-9, and folic acid found in rice bran. According to reports, a low consumption of fruits and vegetables is linked to a high death rate for CVS.

CVS disease is treated using a variety of nutraceuticals, including:

- Polyphenols
- Polysterol
- Vitamin-E
- Flavonoids
- Curcumin
- Omega-3-fatty acids
- Garlic

2. Diabetes:

In diabetic patients, the usage of ethyl esters of N-3 fatty acids may be advantageous. DHA regulates insulin resistance and is essential for the growth of the neurovascular system.³⁶ Docosahexaenoic acid is an omega-3 fatty acid that is present in cold-water fish like tuna and salmon together with eicosapentaenoic acid (EPA). DHA is essential for the growth of nerve and ocular structures.

To treat diabetes, a variety of nutraceuticals are used:

- Antioxidant
- Vitamin C
- Vitamin D
- Fat
- Calcium
- Carbohydrate
- Protein

3. Cancer:

Flavonoids prevent malignancies brought on by oestrogen by blocking the enzymes that make it. A wide variety of Phyto-pharmaceuticals, often known as "phytoestrogens," are advised to prevent prostate and breast cancer. Curcumin from curry, which is also found in soy foods, and soy isoflavones all have the ability to prevent cancer. In the skin, testicles, adrenal, and prostate, lycopene concentrates to prevent cancer.

Various nutraceuticals are used to treat cancer are:

- Chestnut
- Berries

- Soya
- Greentea
- Garlic
- Ginseng
- Tomato and red pepper

4. Irritable bowel syndrome:

A collection of idiopathic chronic and recurrent inflammatory illnesses of the GIT tract includes Crohn's disease and ulcerative colitis under the umbrella term of "inflammatory bowel diseases/ syndrome."³⁷ Its frequency and prevalence have risen during the past few decades. Any product derived from food sources that asserts additional health benefits above and beyond the inherent nutritional content present in foods is referred to as a nutraceutical. Over the past few decades, evidence has been accumulating that nutraceutical substances have positive benefits on human health. Nutraceuticals, such as herbal products or vitamins, are generally acknowledged as safer alternatives to or supplements to conventional medication, despite the fact that few scientific trials have been conducted on IBD patients.

To treat IBD syndrome, a variety of nutraceuticals are employed, including:

- Curcumin
- Aloe vera
- Garlic
- Honey
- Probiotics
- Minerals

5. Obesity:

The "collection of the unhealthy quantity of body fat" is referred to as obesity, which is a problem for global public health. It is a known risk factor for numerous diseases, including osteoarthritis, cancer, congestive heart failure (CHF), angina pectoris, hypertension, hyperlipidemia, respiratory problems, renal vein thrombosis, and decreased fertility.³⁸

6. Gastro-intestinal disease:

Eating patterns and changes in food production and consumption have an impact on people's health, the environment, and society. Gut health is impacted by diet. Diet plays a role in the development of gastrointestinal problems, including ulcerative colitis, Crohn's disease, irritable bowel syndrome, and celiac disease resistant to gluten therapy. An

individual's general health is determined by their gut health.³⁹ The functions of the human gut include:

- (a) It breaks food down to nutrients,
- (b) It facilitates the absorption of nutrients into the blood through intestinal walls, and
- (c) It prevents foreign and toxic molecules from entering the bloodstream.

Various nutraceuticals are used to treat GIT disease are:

Omega-3-fatty acids
Carbohydrate
Curcumin
Honey
Aloe vera
Minerals
Probiotics
Garlic

7. Osteoporosis:

Osteoarthritis, the most prevalent type of arthritis in the USA, is a crippling joint ailment. In 2004, it was projected that 21 million people were affected, costing an estimated 86 billion dollars in direct and indirect healthcare expenses.⁴⁰

8. Allergies

A condition known as allergy occurs when the body reacts excessively to a substance or food. Flavonoids are a class of polyphenolic compounds that includes quercetin (QR). The group of flavonoids known as flavonols includes QR. It is found in rinds and barks across the plant kingdom. Onions, red wine, and green tea are particularly abundant sources of QR. Natural antihistamine QR works to counteract histamine's effects on the body.

The cause of allergic and inflammatory reactions is histamine. Inflammation brought on by hay fever, bursitis, gout, arthritis, and asthma can be lessened by it.⁴¹ Leukotriene production is reduced and several inflammatory enzymes, such as lipid peroxidases, are inhibited by QR. QR possesses gastroprotective, antiviral, immunomodulatory, anticancer, and anti-inflammatory properties. In people with diabetes, sorbitol buildup has been associated to harm to the nerves, eyes, and kidneys. QR inhibits this enzyme. Additionally, QR has strong antioxidant qualities. It guards against LDL cholesterol deterioration.

The body produces many types of cholesterol and other substances, which QR protects blood vessels from. Heart disease has LDL cholesterol as one of its fundamental causes.

In addition to acting as an antioxidant, QR also scavenges the harmful free radicals that are present in the body. Free radicals can harm blood vessels more easily in people with diabetes.⁴²

V. NUTRACEUTICALS' HEALTH BENEFITS⁴³

- It may improve our diet's nutritional worth,
- lengthen our lives,
- help us avoid certain medical conditions, and
- provide nourishment for people with special dietary demands.

VI. NUTRACEUTICALS IN DRUG DELIVERY:

Since nutraceuticals are mostly absorbed orally, the GI tract's ability to absorb them and what happens to them after first-pass metabolism are the main areas of concern. As a result, the pharmacokinetics and absorption kinetics of these items are yet unknown. Many nutraceutical products are faced with a particular issue as a result, and research into their distribution strategies is currently gaining steam.⁴⁴

The commercialised nutraceutical that contains Milk thistle plant extract and is advised for hepatoprotection is a fairly typical example.⁴⁵ The main bioactive component of the extract, silymarin, degrades in the GIT, which has a significant negative impact on the effectiveness of nutraceuticals.

Diverse bioactives utilised in different nutraceutical formulations, such as alpha-tocopherol, ascorbic acid, curcumin, green tree extract, and lycopene, also exhibit a similar issue. Researchers are therefore working to find a solution by enhancing the effectiveness of nutraceuticals through the use of contemporary medication delivery techniques.⁴⁶

The method of nutraceutical medicine distribution that has been studied and used most frequently is based on nano-technological intervention.⁴⁷ The absorption and distribution kinetics of nutraceuticals are significantly impacted by nanoscale delivery, improving product efficacy and safeguarding nutraceuticals against GIT degradation and the first-pass effect.⁴⁸ Since nutraceuticals are typically administered orally, researchers are exploring nano emulsions-based drug delivery systems and nano micelles to increase the oral bioavailability of these products. Various delivery methods, including phospholipid complexes, liposomes, micelles, and nanoparticles are designed to improve bioavailability enhancements.⁴⁹

VII. REGULATORY ASPECTS

The Dietary Supplement Health and Education Act is the main set of regulations that control the nutraceutical business.

DSHEA was approved in 1994.³

2011's Food Safety and Standard Rule has been published. Regulations regarding food business licencing and registration, manufacturing, packing and labelling, food product standards, etc. have also been issued by the Food Safety and Standard Authority.

Beginning in August 2011, the Food Safety and Standard Rule and Regulations are in effect. This law will motivate manufacturers to conduct clinical research, create trustworthy protocols, and improve their products.

The recently passed Foreign Direct Investment Act of 2012 offers new potential for foreign businesses to manufacture and sell dietary supplements in India.

As a result, the manufacture, distribution, and marketing of nutraceuticals in India are all under the control of a single authority.⁵⁰

VIII. CONCLUSION

Nutraceuticals should be consumed according to their approved suggested consumption because they have been shown to have positive health effects and the ability to prevent disease. In the present self-medication landscape, nutraceuticals play a significant role in therapeutic development, but their success depends on upholding their quality, purity, safety, and efficacy. There is currently a high demand for natural products on the market, a wide range of nutraceuticals have been successfully marketed due to their excellent therapeutic activity against various diseases, and the nutraceutical industry in the food industry and pharmaceutical industry is also growing quickly. Although the effects of the recession have subsided, the worldwide market is currently in a post-recession experimental growth period. The nutraceuticals industry is anticipated to remain in a growth phase, driven by new markets in nations like India, China, Brazil, the United States, Europe, etc. A new idea of "Health for All" has emerged as a result of people changing their thoughts and deciding to adopt a new healthy diet and lifestyle.

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