



## NUTRACEUTICALS: THE INDIAN PERSPECTIVE

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**Abstract:** Nutraceuticals are alternate beneficial compounds which provide additional health benefits apart from normal nutritional values. The concept of nutraceuticals is gaining momentum now but its roots can be traced back to Ayurveda the Indian system of Medicine. From isolated nutrients, dietary supplements to genetically engineered “designer” foods, herbal products and processed products such as cereals, soups and beverage are all considered as Nutraceuticals. When these functional foods aid in prevention or treatment of a disease they become nutraceuticals. Nutrigenetics is a nascent area of “personalized medicine.” Probiotics, dietary supplements, photochemical rich source provide major health benefits. Despite far reaching effects of nutraceuticals, it still lacks a proper generalized definition and standard guideline, which can be universally accepted. Different examples from diverse categories of nutraceuticals, their function in various disease and pharmacological properties are highlighted. In this review an attempt has also been made to discuss the about the Nutraceutical industry in our country focusing on the regulations and market scenario which show the potential of this promising field .

**Index Terms:** Nutraceutical, Ayurveda, functional foods, Nutrigenomics, Regulations

### I. INTRODUCTION

Around 2000 year ago Hippocrates gave a befitting statement “Let food be your medicine and medicine be your food” bridging the gap between food and medicine. Naturally available bioactive materials which provide certain demonstrated physiological benefits or prevent the onset or reduce the risk of a disease are beyond their nutritional role are known as Nutraceutical. Stephen Defelice, the chairperson of the Foundation for Innovation in Medicine (New York, US)[1], coined the term Nutraceutical by amalgamation of two words Pharmaceuticals and Nutrition. The concept of nutraceutical in gaining momentum now, its roots can be traced back to Ayurveda the Indian system of Medicine The association of nutraceutical with traditional medicine supported by current modern medical research, is bound to bring the long lasting consumer acceptance whole heartedly [19]. From isolated nutrients, dietary supplements to genetically engineered “designer” foods, herbal products and processed products such as cereals, soups and beverage are all considered as Nutraceutical[1]. Consumers are concerned about their health, as there is an emergence of Lifestyle diseases, the disease which arise due a certain way of living. Nutraceuticals have the power to control them. Revelations about the side effects of synthetic drugs and chemotherapeutics employed diseases like diabetes, cancer and heart problems which are prominent lifestyle diseases, have alerted many people all over the world and efforts are on the rise to find alternatives. They rarely have any side effects. Relatively long half-life, most of them easily available without prescription. This approach is believed to be more natural than using prescription drug. Some people turn to these products when treatments for specific illnesses have failed. Nutraceuticals increase the health value of the diet and aids in restoring, correcting or modifying physiological functions of human beings. They are often confused with Nutritional food. Nutritional foods are foods, which are, produce using the scientific knowledge to just increase the nutritional value of food. When these functional foods aid in prevention or treatment of a disease they become nutraceutical.[8]. Nutraceutical are consumed as capsules, pills, tablets and functional foods are ordinary foods. If a phytochemical is enclosed in a food, it is a functional food but if the same phytochemical is present in a capsule, it is a nutraceutical.[3]. The classification of nutraceuticals with respect to the promising potential they present is of two types 1. Potential Nutraceuticals 2. Established Nutraceuticals. A nutraceutical that holds a promise of a particular health or medical benefit is a potential nutraceutical it becomes an established nutraceutical after there is ample of clinical data to reinforce such a benefit.[17]

### II. Classification of Nutraceuticals

For easier understanding nutraceutical are classified into many different categories

## 2.1 Traditional Nutraceuticals

These are the naturally available foods, which are not modified in. They bioactive compounds which confer additional health benefit along with fulfilling primary nutritional needs. They consist of three main groups Chemical constituents, Probiotic microorganisms and Nutraceutical enzymes[24]

### 2.1.1 Chemical constituents

Chemical constituents include nutrients, herbs and phytochemicals from natural sources.

**2.1.1.1 Nutrients:** This group contains general nutrients like carbohydrates, lipids, peptides amino acids vitamins and minerals, which we obtain through our daily diet. Such nutrients in Japan are referred to as FOSHU or *Foods for Specific Health Use* [8] . Fruits, dairy products, vegetables meat ,fish oil and fish products contain all the essential nutrients of our diet which are very beneficial in curing diseases like osteoporosis, anaemia [23]cardiovascular diseases, diabetes mellitus, different types of cancer.[10]

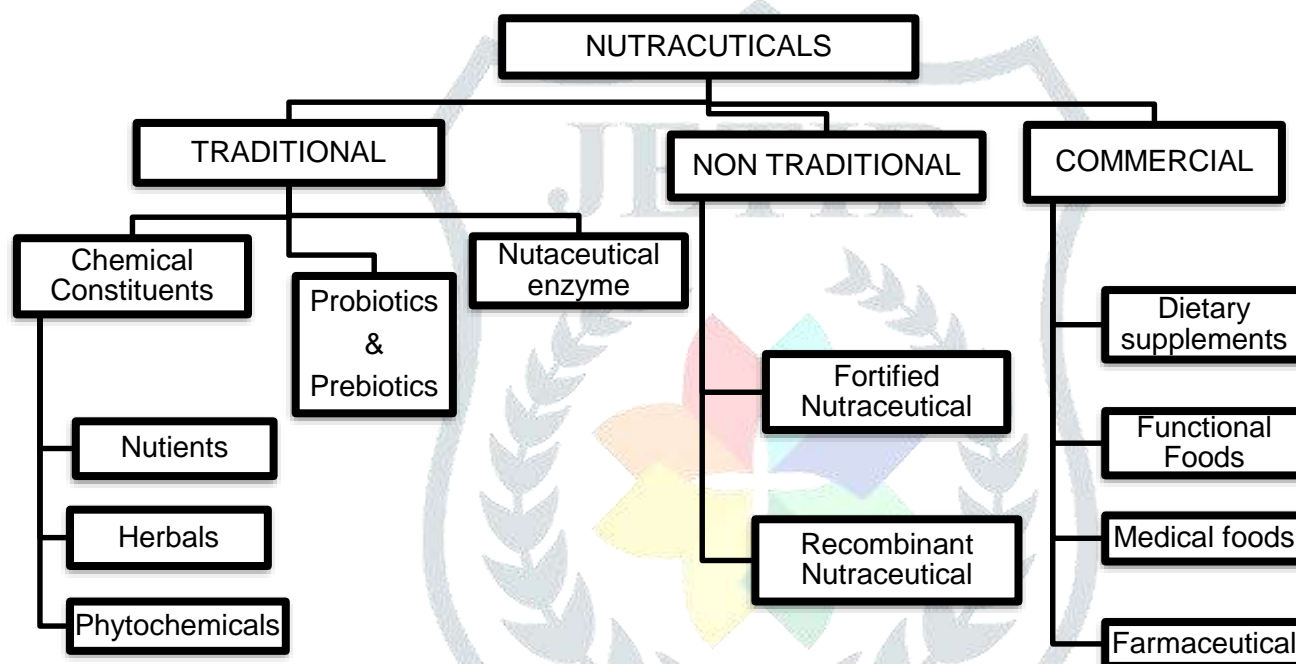


Fig no 1 - General Nutraceutical classification

Various nutrients along with their benefits and sources are listed as follows[7][8][23]

TABLE NO: 1 - List of Nutrients, their sources and benefits

NUTRIENT	SOURCE	EFFECT
CARBOHYDRATES [DIETARY FIBERS]:  1.SOLUBLE FIBERS gums and pectin	Whole grain barley and oats, strawberries and bananas	They can help to control body weight, absorption by forming indigestible mass witch traps Digestive enzymes, cholesterol, starch, glucose and toxins and expel them through the faces.
INSOLUBLE FIBERS cellulose and hemicelluloses	Bran, leafy and vegetables or fruit skins of apples and pears	Help in lowering blood cholesterol. Promotes bowel regularity and keeps GI track clean .Reduces the risk of constipation. Low risk of developing diabetes colorectal cancer
FATTY ACIDS: 1.Omega-3 fatty acids i.e. Docosapentaenoic acids [DPA]	Fish oils	Reduces blood pressure and Cardiovascular disease risk. Contributes t improved memory function. Plays a role in reducing Alzheimer’s disease. Anti-cancer effects on breast, colon and prostate cancer.

2.Linoleic and Linolenic acids	Canola, soybean Sunflower,peanuts and almonds	Increased Cardiovascular benefits Rich in anti-oxidants and maintains integrity of organs ,blood vessels and genes
PROTEINS AND PEPTIDES	Buckwheat and soybean	Act as indigestible substances to trap and expel (through feces) toxins and bile, which reduces the re-absorption of cholesterol intestinal tract
	Bioactive soybean peptides	antimicrobial and antifungal properties, blood pressure lowering effects, cholesterol-lowering ability, antithrombotic and immunomodulatory effects
VITAMINS VITAMIN A	Organ meats, dairy products	Antioxidant, essential for growth development and maintenance of healthy vision, skin and mucous membranes, Useful in cancer treatment and certain skin disorders.
VITAMIN [THIAMIN]	B1 Grain products, pork, legumes	Important for neurologic functions
VITAMIN B2 [RIBOFLAVIN]	Dairy products, meat, fish, legumes	Involved energy production and maintains healthy eyes, skin and nerve function
VITAMIN B3 [NIACIN]	Meat, fish, poultry, nuts • Nuts,beans,peas,lentils,meats,poultry, dairy products	Helps to convert food in to energy and maintain proper brain function Cholesterols, steroids and fatty acids synthesis. Crucial for intraneuronal acetylcholine synthesis
VITAMIN B5 [PANTOTHENIC ACID]	Meat, fish, poultry, legumes, bananas	Helps to produce essential proteins and convert protein in to energy
VITAMIN B6	Legumes, grains, leafy greens, oranges	Necessary to produce the genetic materials of cells, essential in first three months of pregnancy for preventing birth defects, helps in red blood cell formation, protects against heart disease
VITAMIN B9 [FOLATE]	Meat, fish, poultry, eggs, dairy products	Helps to produce the genetic material of cells and red blood cells formation Maintenance of central nervous system and synthesize amino acids and is involved in metabolism of fats, protein and carbohydrates
VITAMIN B12		
VITAMIN C L-ASCORBIC ACID	Citrus fruit, strawberries, broccoli	Antioxidant in nature necessary for promoting healthy bones, gums, teeth and skin, helps in wound healing, and may prevent common cold.
VITAMIN D	Fluid milk, margarine, fatty fish and fish Oils	Responsible for formation of bones and teeth along with helping in absorption and use calcium
VITAMIN E Tocopherol	Vegetable oils, almonds, sunflower seeds	Antioxidant, helps in the formation of blood cells, muscles tissue, lung tissue and nerve tissue, boosts the immune system and maintains reproductive organs.
VITAMIN K	Leafy greens, soy and canola oils	Helps in blood clotting
MINERALS CALCIUM		Most important component of bone and teeth. Also maintains bone strength Important in nerve, muscle and glandular functions as it acts as chemical messenger
IRON		Involved in energy production, part of ETS, carries, and transfers oxygen to tissues.
MAGNESIUM		Pivotal role in nerve and muscle function and bone development may help prevent premenstrual syndrome

PHOSPHOROUS	(PMS).
CHROMIUM	Supporting material of bones and teeth. Present DNA,RNA structure and is involved in ATP production and storage
COBALT	Convert carbohydrates and fats into energy.
COPPER	Component of Vitamin B12
IODINE	Haemoglobin and collagen production plays a role in proper functioning the heart and energy production. Supports absorption of iron from digestive tract.
	Involved in thyroid function

### 2.1.1.2 Herbals:

Ancient history provides a lot of information about herbals, which improve the quality of life and help in preventing various diseases. Herbals are the product that have been obtained from plant various plant parts through extraction. Herbs like ginger, garlic, wheat grass etc are used as the source of these products. [10].Ginger (*Zingiber officinale*) contains Gingerol which helps in soothing headaches, motion sickness, nausea, vomiting& is vascular conditions, cold and arthritis, along with acting as an antimicrobial and antifungal agent. Another famous ancient herb used is Holy basil or Tulsi (*Ocimum sanctum Linn.*)whose Leaf and stem have Eugenol and acts as an anti-asthmatic, anti-inflammatory, antibacterial and antifungal agents. Also Neem (Azadirachta indica), whose Stem, fruit and leaves are Quercetin and  $\beta$ -sitosterol rich is Antifungal, anti-bacterial, anti-inflammatory, anti-arthritic, antipyretic, hypoglycaemic, antigastric and antitumor activities.[20]Apart from the given examples other potential herbals with their benefits are listed in the following table.[10][20]

TABLE NO: 2 - List of Herbals, their sources and benefits

HERBAL	BENEFITS
Aloe Vera gel ( <i>Aloe Vera L. N.L.Burm.</i> )	Dilation of capillaries, emollient, anti-inflammatory and wound healing properties
Turmeric <i>Curcuma longa</i>	Rhinitis, wound healing, common cold, skin infections, liver and urinary tract diseases, and as a blood purifier'
Coriander <i>Coriandru m sativum L.</i>	Anti- microbial, Antidiabetic, Anxiolytic, anti- depressant, neuro- protective, anti- mutagenic, anti- epileptic, anti- hypertensive, anti- inflammatory and diuretic
Curry leaf <i>Murraya koenigii L.</i>	Anti-diabetic, antioxidant, antifungal, antimicrobial, cytotoxic properties, anti-inflammatory, antitumor promoting, anti-hypercholesterolemia, kidney pain relief, hepato protective activities
Cinnamon <i>Cinnamomum zeylanicum</i>	Anti-inflammatory, anti-diabetic, antimicrobial, anticancer, lipid lowering, cardiovascular disease-lowering compound and have activities against neurological disorders, such as Parkinson's and Alzheimer's disease
Lavender <i>Lavandulaangustifolia</i>	Contains tannin for curing depression, hypertension, stress cold, cough and asthma.
Willow bark <i>Salix nigra</i>	Contains Salicin as an anti-inflammatory, analgesic, antipyretic, astringent and anti-arthritic agent
Parsley <i>Petroselinumcrispum</i>	Contains Apiol and is diuretic, used in flavouring and aromatic food additives
Ashoka <i>Saraca indica</i>	Antihyperglycemic, antipyretic, antibacterial, antihelminthic

### 2.1.1.3. Phytochemicals

Phytochemicals are the finest choice as a nutraceutical. Carotenoids like Lycopene and carotenes (carotenes) and lutein ( xanthophylls)have antioxidant potentials which help in the prevention of free radical initiated diseases, like atherosclerosis,cataracts, age-related muscular degeneration, and multiple sclerosis.Lycopene, found in of tomatoes and tomato products, is involved in decreasing the development of cervical,colon, prostate, rectal, stomach, and other types of cancers. Flavonoids, like flavones, flavonols, flavanones, flavanonols, and anthocyanins are antioxidant, anti-mutagenic and show free-radical scavenging activities.[15]Quercetin is a well-known flavone ,present in apples and onions is used for curing breast cancer, lung cancer, liver cancer, and cervical and colon cancer[10]. Berries rich in anthocyanins,

exhibit a range of beneficial effects on: visual capacity, cognitive brain function, obesity, ulcer protection, cardiovascular risk, and cancer prevention. Resveratrol, which was first isolated from the roots of Hellebore (*Veratrum grandiflorum* O. Loes) and detected in wine showed some cardioprotective effects. It has anticancer potential and can prevent or reduce a wide range of cardiovascular diseases, and ischemic damage well as increase the resistance to stress. Ellagic acid (EA) has effects on blood pressure and clotting. It is found in strawberries pomegranate raspberries & is a powerful antioxidant agent. Proanthocyanidins, present in grapes, apples, strawberries, beans, nuts, cocoa, and wine are involved in increasing in the antioxidant activity of plasma, decrease of LDL-cholesterol fraction and oxidative stress-derived substances, improvement of endothelium vasodilatation, decrease of blood pressure, maintenance of endothelium function, etc. Catechin is a very (proanthocyanidin) abundant component in green tea, is a strong antioxidants that inhibit damage to DNA and blood vessels, thereby reducing the risks of cancer development and cardiovascular diseases, respectively[9]. Some essential phytochemicals as potential nutraceuticals are compiled as follows.[9][10]

**TABLE NO: 3- List of Phytochemicals, their sources and benefits**

PHYTOCHEMICAL	TYPE	SOURCE	BENEFITS
CAROTENOIDS	Lycopene	Tomato, tomato products	Reduce blood pressure, anti-mutagenic, prevents cancer, cardiovascular and neurodegenerative diseases
	Eluting	Green vegetables	Maintains health
	Beta carotene	Fruits and vegetables	Neutralization of free radicals
PHENOLICS	Flavones [Quercetin]	Beet root, guava, pear, papaya, watermelon	Treatment of hypertension, atherosclerosis, type 2 diabetes and dementia lower risk of cardiovascular disease and cancer, ,
	Flavonoids	Apple, plum, spinach, cauliflower, onion	Help to control blood sugar level, contain cancer fighting compound, boost bone density, antibacterial property and immune response
	Catechins	Green tea, Red wine, Beans, Apricot, Cherry, Grape, Peach, Apple, Red raspberry, Strawberry, Blackberry	Anti-mutagenic, anticancer, antidiabetic, anti-inflammatory, antiobesity.
	Isoflavone Phytoestrogen	Soy-bean and soy based products	Menopause symptoms, such as hot flashes. Protect against heart disease and some cancers; lower LDL and total cholesterol
POLY PHENOL	Resveratrol	Grapes, wine	Free radical scavenging capacity preventing lipid peroxidation; inhibition of platelet aggregation; vasodilatation; bacterial, antiviral and antihelminthic; increase of the cognitive capacity of brain and neuroprotection
ELLAGIC ACIDS		Pomegranate, strawberry and raspberry	Protection against cardiovascular diseases decrease in atherosclerosis risk factors such as hypertension, platelet aggregation, oxidative stress, and blood lipid profiles
ANTIOXIDANTS	VITAMIN C	Lemon, cranberry, blueberry, Mango	Help in control weight, prevent kidney stone, and reduce risk of cancer. Lower blood pressure, maintains brain function, improve memory, anti-diabetic, and reduce muscle damage. Urinary tract protection and clears the skin, eye health, helps in diabetes, improve digestion and boost immune system.

### 2.1.2 Prebiotics & Probiotics

The good bacteria found in the body along with the bacteria which are important to keep these good bacteria healthy are pre & probiotic bacteria

### 2.1.2.1 Probiotics

Bacteria living in our gut make Vitamin K and help to keep the immune system proper. Intestinal dysbiosis due to antibiotic therapy, stress and poor dietary choices results in overgrowth of bad bacteria and yeast. Restoration of these bacteria in our digestive tract is possible through ingestion of probiotics. Probiotics are live microbial supplements, when ingested in a particular concentration improves the balance and maintains the stability of the intestinal microbial flora. They are referred as 'good bacteria'. Probiotics are usually of human origin, commonly gram-positive organism and can survive even after passing through acid and bile. They show antagonist action against pathogenic or carcinogenic bacteria by adhering to intestinal cells and displace pathogens to form a symbiotic relationship with human GIT. They exhibit antimicrobial effect by modification of the micro flora, prevent adhesion and compete for nutrients with the pathogen, making their survival tedious. Asthma & sensitivity reactions along with infections of urinary tract are reduced. Gastrointestinal (GI) infections like diarrhoea and intolerance related to lactose is eased. Fermented milk products like Yogurt, sauerkraut have probiotic organism like lactobacilli Spp. Other examples include Streptococcus subsp, Enterococcus spp & Bifidobacteria spp. [4][8][110][20] Additional probiotic organisms along with their effects on human health are given below [4]

TABLE NO: 4- List of Probiotic organisms and their effects

BACTERIA	EFFECTS
<i>L. acidophilus</i>	Used in treatment diarrhoea, bacterial vaginosis. Reduces urinary tract infections in children Lowers the effect of irritable bowel syndrome symptoms Anti-microbial against Staphylococcus aureus, Salmonella, E. coli, Candida albicans
<i>L. delbrueckii bulgaricus</i>	Enhances systemic immunity Has antimicrobial action against E. coli, Helicobacter pylori Exhibited antimutagenic activities and is protective in action because of lactic acid production
<i>L. brevis</i>	Synthesizes Lactic acid along with Vitamins D and K
<i>L. casei</i>	Used in treatment of functional constipation and antibiotic-associated diarrhoea . Restores of vaginal flora of patient with bacterial vaginosis . Has protective function against Salmonella infection, rotavirus infections, clostridium infection, synovitis and is immunomodulatory action. Produce vitamins B1 and B2
<i>L. lactis</i>	Bactericidal and Fungicidal action to the pathogens . Used for cytokine delivery
<i>B. infantis</i>	Lowers irritable bowel syndrome symptoms Simulates the production of cytokines that affect the immune system, Antimicrobial action against clostrida, salmonella and shigella.
<i>B. longum</i>	Used in prevention and treatment of necrotizing enterocolitis in newborns. Reduces symptoms of irritable bowel syndrome. Anti-inflammatory properties protecting the cells lining your mucous membranes. Present in breast milk, and hence colonizes the infant gut Prevents Colon cancer
<i>E. faecium</i>	Used in treatment of antibiotic-associated diarrhoea Decreased duration of acute diarrhoea from gastroenteritis . Prevent infection by Salmonella enteric ssp. Produces bacteriocin[ inhibitory substances] which is antimicrobial activity against Gram-positive bacteria.
<i>S. thermophilus</i>	Reduction of irritable bowel syndrome symptoms . Used in fermented milk products. Reduces necrotizing enterocolitis in preterm infants and lowers the risk of bleeding

### 2.1.2.2 Prebiotics

Prebiotics are responsible to keep the probiotic organisms healthy. They are non-digestible foods, mostly oligosaccharides that move through the GI and promote the growth of beneficial bacteria. Galacto and fructo oligosaccharides (GOS), (FOS), pyrodextrins, Stachyose and raffinose are some common examples of prebiotics [23]. Allium, Banana, Tomatoes and chicory roots have high FOS. reduction of constipation, neutralization of toxins, stimulation of intestinal immune system, maintaining blood cholesterol levels, antitumor properties, blood lipids and lactose tolerance are benefits conferred by the Prebiotics. [8][10][20]

### 2.1.3 Nutraceutical enzymes

Enzymes are natural catalyst and without them, our bodies will cease to function. Blood sugar disorders, digestive problems and obesity symptoms are eliminated by enzyme supplements. These enzymes are derived from microbial, plant and animal sources. Glucoamylase from *A. niger* or *Saccharomycopsis fibuligera* increases digestive capacity.  $\alpha$ - Galactosidase found beans, cabbage, Brussels sprouts, broccoli, asparagus, other vegetables, and whole grains digests non-digestible sugars such as raffinose and stachyose. Lysozyme a component of saliva, tears, egg white, and many animal fluids is anti bacterial in nature. [16][24]

## 2.2 Non-traditional Nutraceuticals

The food products are modified artificially by using biotechnological methods. They are either modified genetically for are biofortified. This category has two classes first Fortified nutraceutical and second Recombinant Nutraceutical.

### 2.2.1 Fortified nutraceutical

The fortified foods are the foods that supply the body with essential amount of vitamins, minerals, carbohydrates, proteins and other required nutritional elements to improve the health status or treat and/or prevent anemia. They are produced by either agricultural breeding or nutrients are added to a food.

Eg. Fortified milks for lowering risk of osteoporosis, Vita Kids Bread fortified with MEG-3[24]

### 2.2.2 Recombinant Nutraceutical

Genetically engineered plants, their metabolites, Fermentation products like yogurts, sauerkraut, cheese, breads etc which have bioactive compounds involved in prevention of diseases along are all recombinant nutraceutical.

Eg. Gold kiwifruit with high level of Ascorbic acid, carotenoids lutein and zeaxanthin. Potatoes having tuber-specific expression of a seed protein. Golden mustard having a deficiency of Vitamin A is combined with a soybean ferritin gene to increase its content [24]

## 2.3 Commercial Nutraceuticals

Due to a very huge and growing market. pharmaceutical companies are now trying to manufacture nutraceutical. there is now abundant evidence that supports the role of various foods/food components in promoting human health and hence the R&D of various companies are focused in making such products. This category includes four four classes.

### 2.3.1 Dietary supplements:

Concentrated nutrients in the form of a capsule or a liquid, derived from food products are called dietary supplements. Dietary Supplement Health and Education Act (DSHEA) passed in 1994 does not permit FDA to consider a new product a “drug” or “food additive” if it falls under the definition of a “dietary supplement”. According to DSHEA a dietary supplement. refers to a product (excluding tobacco) meant to supplement the diet that containing a vitamin, minerals ,amino acids or herbs or it can also be a a concentrate, metabolite, constituent, extract, or combination of any ingredient. They are not conventional foods and are labelled as dietary supplements. [14] . Resveratrol supplements are sold as capsules, Isoflavone supplements are sold as pills, tablets, extracts. [9] Some commercially available products are as follows.[7]

TABLE NO: 5 - List of some dietary supplements found in country

DIETARY SUPPLEMENT (PRODUCT)	CATEGORY	COMPANY NAME
Threptin® Diskettes	Protein supplement	Raptakos, Brett & Co. Ltd., Mumbai, India
GRD®	Nutritional supplement	Zydu Cadila Ltd. Ahmedabad, India
Proteinex®	Protein supplement	Pfizer Ltd., Mumbai, India
Calcirol D-3®	Calcium supplement	Cadilla healthcare limited, Ahmedabad, India

### 2.3.2 Functional foods

Food which are taken as part of the usual diet and have beneficial effects that go beyond traditional nutritional effects are called as called as functional foods. If functional foods help in the prevention of a disease them they become nutraceutical. Rather than taking dietary supplements, Functional foods designed by enrichment or fortification process allow consumers to to consume food close to their natural state. Probiotic yogurt, Increased antioxidant levels in fruit juices; cereals wheat, oat, barley and fenugreek with high amounts of dietary fibre.omega3 fatty acid rich milk are all functional foods. [8][19]

### 2.3.3 Medicinal foods

The food intended for the specific dietary management of a disease or conditions, which require distinctive nutritional needs and cannot be fulfilled by normal diet, are medicinal foods. According to the FDA, these foods are formulated to be consumed or internally administered only in the presence of a medical practitioner and are not available over the top for the consumers.[14] Eg.Axona for Alzhimers, Limberal for osteoarthritis [25]

### 2.3.4 Farmaceuticals

This word is a combination of Farm and pharmaceuticals. It is refers to the use genetically modified crops and to produce medically important compounds through oral vaccinations. [14]

### III. Production and analysis of nutraceuticals

A multidimensional approach is required in production of nutraceutical. During processing, the product is fused with of the whole food containing the desired property. Another way is the extraction of the bioactive compound from one food and incorporating it into another food, which increase its physiological benefits by helping in prevention of a disease [14]. Bio fortification [23] through conventional breeding techniques or genetic engineering are advanced ways of production of nutraceutical .Mostly nutraceutical are manufactured as pills, supplements or powders etc.

Structural Analysis of each entity in formulation is difficult as they are an agglomerate of chemical entities and identification and quantification of all components is tedious Also, to detect, define and identify an impurity and assess whether it is harmful to the consumer or not is a necessity and hence increases the need of advanced analytical techniques [4].To maintain a of uniform quality, quantity and standardization of nutraceutical along with their identification and collection is very crucial as composition of active principle of plants changes with respect to various environmental factors. For the identification, characterization of structure and bioactivity, quantification, product development & quality control advanced analytical techniques are required. [3] Analytical techniques for handful nutraceutical compound with their matrices are enlisted as follows.[3]

TABLE NO: 6- List of some nutraceutical found in different matrix, their bioactivityand analytical technique used in their analysis

NUTRACEUTICAL	MATRIX	HEALTH BENEFITS	ANALYTICAL TECHNIQUE
<b>Plant-sterols (Phytosterols)</b>	Vegetable-oil (olive,sunflower, rice )	Decrease cholesterol associated with LDL anti-cancer activity and immune modulation and inflammation	GC [FID,MS]
<b>Milk lipids(PUFA &amp;other fatty acids)</b>	Milk	Immunesuppressant, Antiinflammatory Anti microbial	HPLC-MS/MS,GC/LC
<b>β-carotene</b>	Orange juice	Antioxidant, immunomodulation and cancer prevention	LCxLC-DAD-MS(APCIIT-TOF-MS)
<b>Lycopene</b>	Tomato products	Antioxidant, anti-cancer	HPLC (UV,DAD) NMR, ESI-MS/MS, HPTLC
<b>Vitamin C (L-Ascorbic acid)</b>	Fruits	Antioxidant	HPLC (UV/Vis, VWD)
<b>Tocopherol Vitamin E</b>	Vegetables & Vegetable oils	Antioxidant, antitumor, hypocholesterolemic potential cardiovascular disease treatment and angiogenic disorders	HPLC (PDA,FLD, VWD, MS), GCFID
<b>Amino acid</b>	Sprouts	Effects on nervous system, Antioxidant, anti cancer	HPLC (UV/Vis,MS) MEKC-LIF,MCE
<b>Peptide</b>	Fishes	Anti hypertensive Anticoagulant activity Antioxidant	HPLC-MS/MS,QTOFMS, GPC, HPLC-FLD
<b>Anthocyanins</b>	Fruits	Antioxidant	HPLC-DAD
<b>Catechins</b>	Green tea	Antioxidant	GC-MS
<b>Isoflavone</b>	Soy milk	Estrogenic activity	HPLC-DAD
<b>Resveratrol</b>	Grapes	Antioxidant	HPLC-DAD
<b>Flavanoids</b>	Cranberry	Antioxidant	HPLC-DAD-MS, NMR
<b>Phenolic acids</b>	Rice	Antioxidant	HPLC-DAD-MS/MS

### IV. Concept of Nutrigenomics

Nutrigenomics is a new developed field by the combination of genome science and technology and involves the study of interaction between the dietary components and genome, which causes changes in proteins, and other metabolites.Nutrigenetics, is a nascent area of “personalized medicine”providing opportunities in nutraceutical product development. Developing nutraceutical based on the gene-based differences in response to dietary components that are most compatible with health based on individual genetic makeup is Nutrigenomics.Modification of the gene expression due the interaction of nutrients and botanicals with genome has provided a great impetus for nutrigenetic research and nutraceutical development based on nutrigenetic.[26]



## V. Pharmacology: efficacy and adulteration

Enhancement of overall health, to fill dietary nutrient gaps, stimulate immune health and boost energy are the main reason Nutraceutical are consumed. Scientific communities need to have access to rigorous and reliable information of the experimental and clinical pharmacology of nutraceuticals. The clinical evidences are evaluated according to individual nutraceutical Claims that nutraceutical are harmless because they are natural is misleading, as the most potent poisons or toxins are naturally occurring molecules. Use of dietary supplements can possibly lead to drug interactions. Dietary supplements-prescribed drug interactions can have both a pharmacokinetic and pharmacodynamic basis as that of normal drug interactions. Most significant safety concern posed by dietary supplements is that of adulteration. Mixing the dietary supplement with over the top drugs or un declared prescription to enhance a therapeutic claim is common and can have a deleterious effect on the individual.[2]

## VI. Bioavailability

Oral bioavailability is the primary stage of nutraceutical bio efficiency involving the release of nutraceutical from food matrices or nanocarriers in gastrointestinal fluids, their solubilisation and their interaction with other components of gastrointestinal fluids absorption by the epithelial layer and their chemical and biochemical transformations into epithelial cells[6]. Their direct incorporation into food products is limited as they often exhibit low water solubility and stability along with low bioavailability due to limited accessibility, poor absorption and or chemical transformation within the gastrointestinal tract. This renders their health benefits extremely difficult to be realized by the consumers. Different factors can compromise the bioavailability of a compound, Insufficient gastric residence time, low permeability and/or solubility within the gastrointestinal (GI) tract and instability during food processing/storage or in GI tract can compromise the bioavailability. Without the use of an appropriate delivery nutraceutical do not exhibit the promised bioactive properties system. Choosing an adequate encapsulation procedure is crucial, as many nutraceutical are sensitive to heat and to high temperature, which could cause loss of their bioactivity. The designing delivery systems for nutraceutical having the required physical and chemical stability as well as food-grade status, cost effectiveness and technological feasibility can involve numerous challenges. Protection of the encapsulated nutraceutical Compatibility with the food matrix, Controlled release capacity, High loading capacity, Bioavailability are the factors to be considered Tailor made approach should be followed, to design a delivery system suitable for a specific nutraceutical depending upon the physicochemical-properties(e.g.solubility,chemical interactions and stability) and on the final application. Delivery systems for food applications can be divided in two groups:[11]

### Lipid and surfactant-based carriers

- Emulsions,
- Liposomes,
- Solid lipid particles,
- Nanostructured lipid carriers and self-dispersing lipid formulations

### Biopolymer-based carriers (i.e. polysaccharide and protein-based carriers), hydrogels

- Protein-polysaccharide complex and polymeric micelles.
- Nanolaminated systems.

### Release of nutraceutical takes place by following ways

- Diffusion-controlled release
- Swelling-controlled release
- Erosion-controlled release:
- Fragmentation-controlled release.
- Dissolution-controlled release

Absorption of nutraceutical occurs in Small intestine.[11]

## VII. Nutraceuticals in treatment of diseases

Globalization and economic development has led to an improvement in the quality of life. As a ripple effect there was an emergence of life style diseases like Obesity,CVD. Consumption of junk food increased the number of nutritional deficiencies. Industrialization was the root of allergies reaction.Nutraceuticals could play a pivotal role in controlling them. They can also be used in preventing diseases like cancer [14]. In recent times the application of stem cell therapy in curing various disease very famous, it is found that nutraceutical can affect growth and proliferation which can stimulate stem cells to reach healing and regenerating goals Dose-related effect of blueberry, green tea, carnosine, and vitamin D3 on proliferation with human bone marrow have been reported[5].Nutraceutical can also be used as immune boosters. A broad range of phyto-estrogens are recommended in prevention of various diseases extracts from the coneflowers, or herbs of the genus Echinacea, Goldenseal extract, Extracts of elderberries are used as Immune boosters or as anti viral agents and promote wound healing[18] Some biological components from natural sources which can be used as potential nutraceuticals in disease treatment are mentioned in the following table.[18]

TABLE NO: 7- List of nutraceutical used in the treatment of diseases, their sources and effects

DISEASE	NUTRACEUTICAL	SOURCE	EFFECTS
Cardiovascular diseases (CVD)	Flavanoids	onion, endives cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries and berries	block the angiotensin-converting enzyme protect the vascular system and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cells. Flavonoids block the enzymes that produce estrogen, thus reducing the risk of estrogen-induced cancers.
	Hesperidin	Sweet oranges	Used in venous insufficiency and Haemorrhoids in combination with a flavones glycoside called diosmin. Analgesic and anti-inflammatory activity
	[6]-Gingerol	Ginger	antioxidant and anti-inflammatory activities, and some of them exhibit cancer preventive activity, hypertension and palpitations.
	Phytosterols	Buckwheat	Compete with dietary cholesterol by blocking the uptake as well as facilitating its excretion from the body. Phytosterols in diet have the potential to reduce the morbidity and mortality from cardiovascular disease
	Dietary fibre	Defatted rice bran	Acts as a laxative and has cholesterol lowering. Involved in prevention or alleviation of cardiovascular disease, diabetes, diverticulitis and colon cancer.
	PUFA	Milk and eggs	Production and rebuilding of cells, to reduce blood pressure, lower cholesterol and triglycerides, reduce the risk of blood clots and prevents arthritis, arrhythmias, and other cardiovascular disease
	Octacosanol		It has gastro protective and lipid lowering effects
OBESITY	Ephedrine caffeine,	Dietary supplement coffee	Facilitating weight loss
	Dietary fibres	Buckwheat seeds	Helping in losing weight and prevents the risk of constipation
DIABETES	Isoflavones	Soybeans	Lower incidence and mortality rate of type II diabetes, heart disease, osteoporosis and certain cancer
	Omega 3 fatty acids	Milk and eggs	Reduce glucose tolerance in patients
	Docosahexanoic acid	Milk and eggs	Modulates insulin resistance and is also vital for neurovisual development
	Lipoic acid	Spinach, Broccoli and red meat	Universal antioxidant, used in the treatment of diabetic neuropathy
	Dietary fibre		Aids in weight reduction, for glucose control in diabetic patients and to reduce lipid levels in hyperlipidemi

	Mineral Mg		Reduces diabetes risk and improves insulin sensitivity;
CANCER	Flavanoids	Citrus fruits	antioxidant
	Beta carotene	Carrots, spinach, lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, oranges, and winter squash	offer protection against lung, colorectal, breast, uterine and prostate cancers
	Tannins	Blackberries blueberries, cranberries, grapes, lentils, tea and Wine	Detoxify carcinogens and scavenge harmful free radicals
	Pectin	Apples	Prevent prostate cancer metastasis by inhibiting the cancer cells from adhering to other cells in the body.
	Ellagic acids	strawberries, cranberries, walnuts, pecans, pomegranates	Anti-carcinogenic used in alternative medicine to prevent cancer
	Glucosinolates	Brussels sprouts, broccoli, cauliflower, cabbage, watercress, oilseed rape, and mustard	Lower risk of lung and colorectal cancer .They also regulate white blood cells and cytokines
	Thiosulfonates	Garlic and onions	anticarcinogenic properties, ant platelet activity, antithrombotic activity, antiasthmatic and antibiotic effect
	Curcumin	Turmeric	chemo preventive properties, anticarcinogenic, ant oxidative and anti-inflammatory properties, suppress proliferation of a wide variety of tumor cells
	Saponins	Peas, soybeans, and some herbs	antitumor and antimutagenic activities
	Sulphur containing Compounds	Garlic	Sulforaphane has been reported to reduce the risk of breast cancer and prostate cancer
INFLAMMATORY DISORDER		Cat's claw	Anti-inflammatory agent
	Resveratrol	Blue berry	It acts as an anti-inflammatory agent, antifungal
	Gamma linolenic acid	Breast milk	Anti inflammatory
ALLERGY	Quercetin	Tea, Chocolates	Anti histamine, anti-inflammatory, antiviral, immunomodulatory, anticancer and gastroprotective activities, potent antioxidant

PARKINSON	Vitamin E	Vegetables	may be protective against Parkinson's disease
	Gutathione	Spinach,avaca dos and asparagus	Determine its effect on nerve and its power as an antioxidant
ALZHEIMER'S	$\beta$ -Carotene, curcumin, lutein, lycopene, turmerin	All types of vegetables	Neutralizing the negative effects of oxidative stress, mitochondrial dysfunction, and various forms of neural degeneration
Osteoarthritis	Glucosamine (GLN) and chondroitin sulfate (CS)	Shellfish,Supplements	Regulates gene expression and synthesis of NO and PGE2,which makes them antiinflammatory

### VIII. Need for standard guidelines and regulatory protocol for nutraceutical sale

Nutraceutical are mostly referred to as pharma-foods, indicating that an official and unanimous definition is missing and this definition needs to be distinct than that for other food derived categories. An officially shared and accepted definition of nutraceutical is still missing. As nutraceutical are robust tools, which can be used beyond the diet because they provide a bunch benefits to prevent and treat diseases and can be administered before the drugs. They can be fruitful in treating patients who may not eligible for conventional pharmaceutical therapy. Hence, it is of dire importance to define nutraceutical unequivocally and draft universal regulations. Assessment of safety, mechanism of action and efficacy of nutraceutical should be backed up with clinical data. The claims on Many nutraceutical are mainly unsubstantiated due to a lack of studies on possible mechanisms of action and in vivo research confirming the claimed beneficial health effects on specific pathological conditions. The data reported in the literature, mainly comes from in vitro studies not in vivo generally on focused on single food constituents (micronutrients) and are based on the assumption that micronutrients can be considered safe for consumption. There is also the possibility of contaminants of inorganic and organic origins in these products as nutraceutical are mainly derived from plants. Moreover, the ingredients themselves may cause health problems because of lack of bioavailability studies, and proper information on possible unwanted side effects should be provided on the label. Considering all the reasons above it is imperative to have more information on how these products should be formulated, marketed and regulated. Each country which is involved in the nutraceutical market uses different guidelines and regulations for production and export thus a nutraceutical in one country could be a pharmaceutical in another. A clear and shared regulation system allowing the identification and classification of these products at an international level that clearly indicates requirements for quality, efficacy, mechanism of action and safety could benefit potential consumers as well as the industry.[21]

#### 8.1. Regulatory bodies in India

- 1. Food Safety and Standards Act (FSSA):**FSSA foundation regulates the safety and standards along with manufacture, storage, distribution, sale and import of food and nutraceutical
- 2. Indian Pharmacopoeia:**Provides safety and quality standards for compounds like plant extracts and phytochemicals
- 3. Federation of Indian Chambers of Commerce and Industry (FICCI):**FICCI has drafted improved regulatory framework for validation of product claims, which meets consumer demands
- 4. Centre for Food Safety and Applied Nutrition (CFSAN)**
- 5. Diverse process of New Dietary Ingredient (NDI)**
- 6. NIN (National Institute of Nutrition):** Mainly focuses on studies of protein energy malnutrition [PEM], nutrition situation in our country and management and prevention methods for nutritional problems
- 7. FDTRC (Food and Drug Toxicology Research Centre):** Conducts studies drug nutrient interactions (drug metabolism, toxicity)

HADSA (Health Food and Dietary Supplements Association), NNMB (National Nutrition Monitoring Bureau), Indian Health Foods and Dietary Supplements Association (INHADSA). Indian Council of Medical Research (ICMR) is also some of the important regulatory bodies of our country. [4]

#### 8.2 The Indian food and safety stadard Act

Despite being the world's second largest producers of fruits and vegetable only 2% of perishable agriculture, products are processed in India compared to 80% in the United States. In mid 1990's various laws related at both state level and national level in the food sector. In 1998, unified legislation under a single food regulatory authority was recommended in the Prime Minister's council on trade and industry and finally in 2005, Indian Food Safety Standard Bill 2005 was signed into law, which promised a major impact on the Indian food processing industry. **The Indian Food Safety and Standard Act came into enforcement in 2006** with an objective to introduce a single structure of food and bestow scientific development to the food sector. Article 22 from chapter IV of the act addresses nutraceutical, functional food,

dietary supplements and the need to regulate them. It also throws light on the guidelines on how to manufacture, sell, or distribute or import these products. According to this act Nutraceutical, include novel foods, genetically modified articles of food, irradiated food, organic food and food for special dietary uses, functional food, and nutraceutical and health supplements. Articles 23 and 24 address the packaging and labelling of food and restriction of advertisement regarding these foods. This law led to unification of the original eight laws with alignment of international regulations and science-based standards with a clarity and uniformity on novel food areas and helped to curb corruption. [13]

### 8.3 Regulatory requirements

There are three major regulatory requirements namely, product assessment, licence and registration and health claims and labels are involved.

#### 8.3.1 Product assessment

To perform product assessment as per Indian regulation, imperative to examine each active principles and additive in the context of their permissibility, standards and dosage of allowed as per the therapeutic, prophylactic, or RDA for Indians. In addition, for manufacturers who are unclear whether their products will be classified as food or food supplement or drug, The Food Safety and Standards Rules 2011 highlights the regulatory enforcement structure and procedures that central government proposes to make. Documentation of the extracts used and authenticating it the by concerned authority, collection of the samples in the presence of a witness and dispatching it to the concerned authority followed by food analysis. If the analysis is, delayed the authorities and finally adjudication proceedings i.e. holding enquiry, appeal procedure, hearing, etc decide further proceedings.[13]

#### 8.3.2 License and registration

Licensing and registration processes for nutraceutical, varies depending on the number of parameters. For the product to be registered in India product registered in India Import licensing Manufacturing licensing, Marketing licensing along other state and national level clearances/licenses are required.[13]

#### 8.3.3 Health claims and labels

The major element to be focused on while entering Indian market is claims developing health and label claims as per Indian guidelines. Based upon the regulatory assessment of the product, India-specific label content and claims have been developed.[13]

“Health claims” refers to a relationship between the active component or food constituent and health. Nutrient content claim, Reduction of disease claim, Structure/Function claim are considered here

**Nutrition Content Claim:** Points towards beneficial nutritional properties of a food. A Claim is defined as a statement that affirms a relationship between food and health e.g. "It help lower cholesterol"

**Reduction of Disease Claim:** Any claims implying that that the consumption of dietary supplements prominently reduce the risk factor in the development of human disease.

**Structure/Function Claim:** Claim on label of a food or dietary supplement about and its effects on the human body structure come under Structure Claims.[27]

## IX. Indian Nutraceutical Market

15% of the population is undernourished in the country and through initiatives like Integrated Child Development Services (ICDS), National Health Mission (NHM) and the mid-day meal scheme the government is trying to reduce the same. India loses nearly US\$12 billion in Gross Domestic Product (GDP) to malnourishment. This propels the need for nutraceutical in the country. The nutraceutical market in India is expected to be around \$ 18 billion in 2025 because of rising demand for dietary supplements from upper and middle class. India has a unique advantage of rich heritage and knowledge and since it is home to largest number of US FDA approved plants located outside the US raw materials are easily available for favouring growth in herbal extract manufacturers demonstrate a strong presence as a preferred supplier in export markets, make India a daunting contender in the global nutraceutical market.[12]

Ranbaxy laboratory, Abbott India, Nicolas Piramal, Dr Reddy's lab and Pfizer, Dabur India, Zandu, Baidynath, GSK Consumer healthcare, Heinz, Yakult ,Danone, Amul, Amway, Zydus wellness, EID Parry and Herbalife, Patanjali are they major players ruling the Indian Nutraceutical Market.[22]

## X. Challenges

Tailoring products to domestic tastes and preferences, vegetarianism, Halal or Hindu dietary practices, traditional remedies, flavour and formulation preferences reflecting social and cultural diversity, or reluctance to see functional benefits in staple foods are the challenges which arise due to psychological state of the major population of our country[4] Poor infrastructure, logistic and tight food regulation are barriers of growth in food sector a myriad of food regulatory policies by makers and enforcement agencies prevailing in different sectors of the food industry contributed to considerable indecision among the consumers, producers and retailers and business which proved to be detrimental to the growth of the functional food and nutraceutical industry in the country[13]

## XI. CONCLUSION

The nutraceutical market is still very nascent in India, with limited participation from indigenous manufacturers and lower awareness about foods for special dietary use. In this scenario, there is a need to come up with new marketing strategies for nutraceutical. If these products are put forth by, highlight its natural components in ad campaigns it could be picked up more ceremoniously by the Indian consumers because of our strong Ayurvedic background. More investments in Research and Development along with production should be given. Proper documentation with assessment that no fake health claims are being made is also essential. The development of Nutraceutical market can be the epitome of the 'MAKE IN INDIA' imitative and this can create new opportunities in the field of Biotechnology. With 'immunity' has become the new buzzword as the world battles the COVID-19 pandemic, the demand for nutraceutical across the globe has increased manifold. As a country, having an indigenous knowledge in the form of Ayurveda along with being a repository of herbs and spices have a potential to be a Nutra-Hub in the making what needed is more incentives and promotion of nutraceutical is need.

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