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Recapitulation of Nutraceuticals: Overview and Future trend

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ABSTRACT

The exposure of nutrients as medicines in the pharmaceutical world is of prior importance and centres the attention of scientists and researchers toward the health benefits. The demand of these products has been found to be spiked and due to this, the nutraceutical market has become a million-dollar industry at a global level. Majority of the chemical components present in nutraceuticals that may possess beneficial health effects are derived from botanical sources, and will be considered to be natural in form. These products can be as diverse as proteins, peptides, lipids, flavonoids and isoflavanoids, polyphenols and tannins. Additionally, vitamins and minerals, sugar molecules such as glucosamine and chondroitin. As a result, interdisciplinary approaches are now been put in an application to design and develop various dosage forms to deliver these herbal products for the treatment of many disorders. In this review article, an attempt to classify all types of nutraceuticals, followed by their management in the treatment of various diseases has been carried out. It is also important to note that the purification, or not, of the nutraceutical from its natural matrix must also be considered as there may be contaminants/impurities/adulterants present that are deleterious to human health, or whose amounts are regulated by legislation (heavy metals, allergens, toxins). These must also be incorporated into a testing regime to ensure the safety of the product end-user.

Keywords: Nutraceuticals, Fortified food, Health benefits, Regulations, Global market, Quality control

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INTRODUCTION

Contemporary lifestyle and dietary patterns, along with increased technological advancement, pollution and stress, have led to increased susceptibility to a plethora of disorders such as, obesity, hypertension, inflammatory, diabetes, cancers and autoimmune conditions. Recent expansion in the medical sciences has considerably helped in treatment of these complications; however, it has been lately realized that nutrition management may play a major role in prevention as well as in treatment to some extent [1] Nutraceutical is a term formed from the amalgamation of the words “pharmaceutical” and “nutrition” by Dr Stephen Felice in 1989. Others have since tried to further define the term to distinguish and clarify the difference between functional foods, dietary supplements and nutraceuticals. There is now some consensus that a nutraceutical can be loosely defined as “a functional food or supplement that aids in the prevention or alleviation of a disease state or disorder (except for anaemia), and not just supplement the diet” [2]. The actual use of Nutraceuticals is to attain desirable therapeutic outcomes with reduced side effects. About 2000 years ago, Hippocrates emphasized ‘let food be your medicine and medicine be your food’s. Nutraceuticals are used as food or part of food which will provide medical or health benefits including prevention or treatment of disease [3]. The significance of such products has been associated with the treatment of many disorders such as cancer, metabolic problems, cold and cough, depression, coronary heart disease, delayed gastrointestinal emptying, and many more conditions which need special care [4]

The WHO predicted that by 2020 over 65 million people will have dementia and that the prevalence of other neurodegenerative brain diseases, like Alzheimer’s, is also increasing. It is estimated that over 100 million people globally are affected by ‘gut health’ problems, 347 million people worldwide have diabetes. The impact of cardiovascular disease (CVD) is significant. It is the number one cause of death globally [5]

Nutraceuticals has proven their health benefits and disease prevention capability, which should be taken according to their acceptable recommended intake. But their success depends on maintaining on their quality, purity, safety and efficacy [6]

The COVID-19 pandemic has affected various industries severely including nutraceuticals and pharmaceuticals, have vast growth opportunity. Currently the pandemic has successfully shifted consumer preferences worldwide towards health-boosting products. Nutraceuticals are gaining attention globally due to escalating awareness of various health benefits and is becoming popular

among individuals seeking alternative and natural ways to promote and maintain overall health and wellness. [7]

The global nutraceuticals market size was estimated at USD 317.22 billion in 2023 and is projected to grow at a compound annual growth rate (CAGR) of 9.6% from 2024 to 2030. The primary factors driving the market growth are preventive healthcare, increasing instances of lifestyle-related disorders, and rising consumer focus on health-promoting diets. In addition, increasing consumer spending power in high-growth economies is projected to contribute to the growing demand for nutraceutical products [8] China and Japan are predicted to register higher CAGRs of 7.4% and 3.4%, respectively, through 2034. This is due to the growing popularity of nutraceutical products in these nations. Similarly, the nutraceutical CDMO market in India and their emerging nations is expected to progress rapidly. Table 1 summarizes current global markets with a value of nutraceuticals in market share worldwide [9]

Table 1: Current global markets with a value of nutraceuticals in market share worldwide

Country	Value CAGR%
United States	1.8
China	7.4
Japan	3.4
Germany	1.7
Spain	2.8

Currently, the Indian market imports more than it exports; USD 1.5 billion in exports and importing the USD 2.7 billion worth of nutraceuticals. The market is expected to grow at a significant 22% CAGR by 2023. The Indian nutraceuticals industry has been growing at 25% annually during the pandemic. The Foreign Direct Investment (FDI) has also increased from USD 131.4 million (FY12) to USD 584.7 million (FY19) [10]

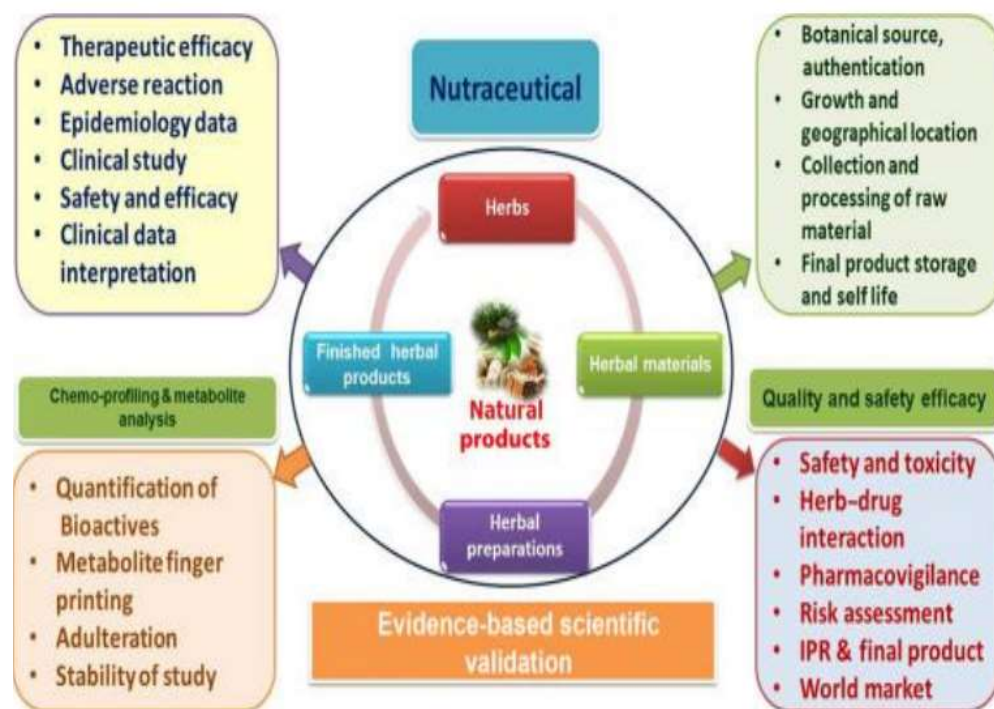
Rediscovering the past of nutraceuticals

Throughout history, civilized societies have devoted a deep interest in, and concern about, the integrity of food supply. Long before the development of the distinct scientific discipline of nutrition, philosophers and later physicians paid close attention to the role of the daily diet in individual and public health [11]. Interestingly, Hippocrates (460–377 BC), the father of modern medicine paved the foundation stone for modern day nutraceuticals through his epic statement “Let food be thy medicine and medicine be thy food”. He was the pioneer to bring forward the concept that specific food can also be the solution for the prevention/ treatment of a disease apart from drug moieties.

Roman Physician Galen enforced trust in the expertise and knowledge base of his profession to design and formulate diet regimen which would maintain health standards of the entire population which further influenced the Islamic medicine. Early nineteenth century marked the initiation of nutrition research by François Magendie. His first work in the field was reported to the Academy of Sciences in 1816, and addressed directly the question as to whether animals could use atmospheric nitrogen to “animalize” ingested foods of low nitrogen content. This modulated scientific minds to think beyond proteins, carbohydrates, fats, and minerals to achieve proper nutrition. This hypothesis was supported by experiments on mice by Nicolai Lunin which produced interesting results. He proved that certain component present in milk was essential for nutrition of mice which cannot be classified as proteins, carbohydrates, fats, and minerals. This fact and similar research findings by several researchers ultimately led to the discovery of the vital nutrient vitamin [12-14].

Ginseng has been another such traditional drug used as chemotherapeutic even today but its history as herbal medicine in china were recorded as early as the Han dynasty, 2,000 years ago.[15]

India is known for its traditional medicinal systems—Ayurveda, Siddha, and Unani. Medical systems are found mentioned even in the ancient Vedas and other scriptures. The Ayurvedic concept appeared and developed between 2500 and 500 BC in India [16]. "Classical scholars have always considered the ancient Greeks, particularly Hippocrates, as being the fathers of medicine but our findings suggest that the ancient Egyptians were practicing a credible form of pharmacy and medicine much earlier. Egyptians valued the medicinal importance of different spices like coriander, fennel, cumin, garlic, turmeric etc. and even considered equivalent to precious metals like gold. The mid-19th century, showed that ancient Egyptian phicians treated wounds with honey, resins and metals known to be antimicrobial [17, 18]. People learned from their experiences and slowly clinical problems were provided with scientific explanations. On many occasions dietary alterations became the remedy instead of medicines. Overall, it can conclude that with the passage of time as scientific knowledge developed, food habits were intelligently modulated for prevention/treatment of disease and this may spark which produced the modern-day nutraceuticals.



Classification of nutraceuticals

Nutraceuticals can be classified based on different criteria, such as their source, chemical composition, mode of action, and health benefits. Here are some common classifications.

- a) The source of origin:
 - plants (garlic, aloe vera, ginger, containing organic acids, salts, tannins, and hormones)
 - animals (oils and proteins),
 - microorganisms (proteins, amino acids, vitamins, probiotics, prebiotics, dietary supplements, and peptides) represented in Table 2&3.
- b) Traditional nutraceuticals: fruits (phenolic compounds, tannins, vitamins, and terpenes), vegetables (minerals, vitamins, organic acids, carotenes, and terpenes).
- c) Non-traditional nutraceuticals: fortified foods (juices, cereals, vitamin additives, and minerals), originated by biotechnological processes (bread; alcoholic beverages such as beer, wine, pulque, tequila, mezcal, and apple or cane vinegar; production of amino acids and other bioceutical derivatives), or recombinant genetic engineering (production of enzymes and obtaining new nutraceutical pathways).
- d) Chemical nature: herbs or spices, nutrients, phytochemicals, enzymes, terpenes (vegetables, fruits, and citrus fruits), phenolic compounds (coffee, spices, seeds, pulp and bunches of grapes, cocoa, red fruits, tea leaves, mango, banana, and spinach), and minerals (legumes,

vegetables, some fruits, and spices). Nutraceuticals such as omega-3 are reported to have more than one mechanism of action.

- e) The mechanism of action: their principle is to maintain and improve the physiological properties of an organism, and they are used in specific medical conditions with varied effects such as anti-inflammatory (ginger and orange peel extract), antimicrobial, osteoprotective, anti-glycemic/antihypertensive (blueberries), antioxidant (broccoli extracts), and anti-hypercholesterolemic (as the β -glucan contained in oats); however, in some cases their toxicity, and synergy, or competition are still unknown. This fatty acid has an anti-inflammatory, anticoagulant, and antithrombotic activity [18,19]. It is naturally in oily fish, shellfish, grains such as soy, canola, and flaxseed, walnut, to name a few and shown in Table 4.

Table 2: Classification of nutraceuticals based on food source (Plant, animal and microorganism)

Classification Based on	Examples	Functional components	Health benefits	Ref.
Source Plant	Carrots,cantaloupe,kale,papaya, tomatoes,pumpkin,	Carotenoids	<ul style="list-style-type: none"> • May protect the body from free radicals which damage cells through oxidation mango • May slow down cognitive decline • • May lower the risk of developing cancer or heart disease 	20,21
	Silymarin	Flavonolignans	<ul style="list-style-type: none"> • antioxidant, anti-inflammatory, immunomodulatory, and hepatoprotective properties, neuroprotective agent, antiviral activity 	22
	Epicatechin	Flavonoid polyphenol	antihypertensive anti-inflammatory activity,	23,24

	Turmeric	Curcumin	antimicrobial agent, against various chronic diseases, including multiple types of cancers, diabetes, obesity, in addition to cardiovascular, lung, neurological, and autoimmune diseases	25-27
Source Animal	Dairy and beef	Conjugated Linoleic acid	reduce body fat deposits and improve immune function	28
	Tuna and salmon	Eicosapentaenoic acid	anticoagulant, cholesterol lowering effects, and anti-inflammatory	
	Sphingolipids	ceramides, sphingomyelins, cerebroside, gangliosides, and sphingosine-1-phosphate	apoptosis and stress responses, stability and insulation of nerve cells, participate in cell-to-cell recognition and signaling, cell migration, proliferation, and immune responses.	29,30
	soybeans, sunflower, canola, corn, rice bran, and cottonseed	Lecithin phosphatidylcholine	high nutritional value as well as their ability to stabilize emulsions and form liposomes.	

Table 3: Classification based on food source(microorganism)

Classification Based on	Examples	Functional components	Health benefits	References
Source Microorganism	<i>Limosilactobacillus reuteri</i> <i>L. helveticus</i> ,	Reuterin calcineurin	antibacterial, antifungal, antiviral, and antiprotozoal peptide activating the transcription of interleukin-2 (IL-2) and participating in the stimulation of the growth and differentiation of T lymphocytes	31

Table 4: Nutraceuticals can be classified on the basis of food source, mechanism of action and chemical nature.

Class/Component	Source	Potential Benefit
Carotenoids	Carrots	Neutralizes free radicals which may cause damage to cells
Alpha-carotene	Various fruits, vegetables Green vegetables	Neutralizes free radicals
Beta-carotene		Contributes to maintenance of healthy vision
Lutein		May reduce the risk of prostate cancer
Lycopene	Tomatoes and tomato products (ketchup, sauces, etc.)	Contributes to the maintenance of healthy vision
Zeaxanthin	Eggs, citrus, corn	May help improve some symptoms associated with osteoarthritis
Collagen Hydrolysate	Gelatine	May reduce risk of breast and/or colon cancer
Dietary Fibre	Wheat bran	Reduces risk of cardiovascular disease (CVD)
Insoluble fibre	Oats	Reduces risk of CVD
Beta glucan	Psyllium	Reduces risk of CVD
Soluble fibre	Cereal grains	Reduces risk of CVD
Fatty Acids	Tuna; fish and marine oils	May reduce the risk of CVD & improve mental, visual functions
Omega-3 fatty acids-DHA/EPA		
Lignans	Flax, rye, vegetables	May protect against some cancers and heart disease
Sulfides/Thiols		
Diallyl sulfide	Onions, garlic, leeks, scallions	Lowers LDL cholesterol, maintains healthy immune system
Allyl methyl trisulfide, Dithiolthiones	Cruciferous vegetables	Lowers LDL cholesterol, maintains healthy immune system
Tannins		
Proanthocyanidins	Cranberries, cranberry products, cocoa, chocolate	May improve urinary tract health May reduce risk of CVD

Conjugated linoleic acid (CLA)	Cheese; meat products	May improve body composition, may decrease risk of certain cancers
Flavonoids		
Anthocyanidins	Fruits	Neutralizes free radicals, may reduce the risk of cancer
Catechins	Tea	Neutralizes free radicals, may reduce the risk of cancer
Flavanones	Citrus	Neutralizes free radicals, may reduce the risk of cancer
Flavones	Fruits/Vegetables	Neutralizes free radicals, may reduce the risk of cancer
Glucosinolates, Indoles, Isothiocyanates		
Sulforaphane	Cruciferous vegetables (broccoli, kale), horseradish	Induces detoxification enzymes, may reduce the risk of cancer
Phenols		
Caffeic acid	Fruits, vegetables, Citrus	Antioxidant-like activities, may reduce risk of degenerative diseases; heart disease, eye disease
Ferulic acid		
Plant Sterols		
Stanol ester	Corn, soy, wheat, wood oils	Lowers blood cholesterol levels by inhibiting cholesterol absorption
Prebiotics/Probiotics		
Fructo-oligosaccharides (FOS)	Jerusalem artichokes, shallots, onion powder	May improve gastrointestinal health
<i>Lactobacillus</i>	Yogurt, other dairy	May improve gastrointestinal health
Saponins		
Saponins	Soybeans, soy foods, soy protein-containing foods	May lower LDL cholesterol; anti-cancer activity
Soy Protein		
Soy protein	Soybeans and soy-based foods	25 grams per day may reduce risk of heart disease
Phytoestrogens		
Isoflavones-Daidzein, Genistein	Soybeans and soy-based foods	May reduce menopause symptoms, such as hot flashes

Nutraceuticals are categorized on the basis of foods available in the market

1. Traditional nutraceuticals
2. Non-traditional nutraceuticals

1. Traditional nutraceuticals are simply natural with no changes to the food. Food contains several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in salmon or saponins in soy. They are grouped on the basis of

I. Chemical Constituents

a) Nutrients

b) Herbals

c) Phytochemicals

II. Probiotic Microorganisms

1. Based on chemical constituents

(a) Nutrients [32]

Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids. Common nutrients and their associated health benefits shown in Table 5 & 6

Table 5: List of nutrients and their relevance

S.No	Nutrients	Health benefits
1.	Vitamin A	Antioxidant, essential, for growth and development and in the treatment of certain skin disorders.
2.	Vitamin E	Antioxidant, helps form blood cells, muscles, lung and nerve tissue, boosts the immune system.
3.	Vitamin K	Essential for blood clotting.
4.	Vitamin C	Antioxidant, for healthy bones, gums, teeth and skin, in wound healing, prevent common cold and attenuate its symptoms.
5.	Vitamin B1	Helps to convert food in to energy, essential in neurologic functions.
6.	Vitamin B2	Helps in energy production and other chemical processes in the body, helps maintain healthy eyes, skin and nerve function.
7.	Vitamin B3	Helps to convert food in to energy and maintain proper brain function.
8.	Vitamin B6	Produce the genetic material of cells, formation of RBCs, maintenance of central nervous system and synthesize amino acids and metabolism of fats, protein and carbohydrates.
9.	Folic acid	Produce the genetic materials of cells, in pregnancy for preventing birth defects, RBCs formation, protects against heart disease.
10.	Calcium	Bones and teeth and maintaining bone strength important in nerve, muscle and glandular functions.
11.	Iron	Energy production, carry and transfer oxygen to tissues.
12.	Magnesium	Healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS).
13.	Phosphorous	Strong bones and teeth, helps in formation of genetic material, energy production and storage.
14.	Chromium	With insulin helps to convert carbohydrates and fats into energy.
15.	Cobalt	Essential component of vitamin B12, but ingested cobalt is metabolized <i>in vivo</i> to form the B12 coenzymes.
16.	Copper	Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from digestive tract.
17.	Iodine	Essential for proper functioning of the thyroid.

(b) Herbals

Herbs or botanical products as concentrates and extracts ordinary herbs and their therapeutic relevance.

Table 6: Nutraceutical classification

Class	Example
Inorganic mineral supplements	Mineral
Vitamin supplements	Vitamins
Digestive enzymes	Enzymes
Probiotics	Lactobacillus acidophyllus
Prebiotics	Digestive enzymes
Dietary fibre	Fibers
Cereals and grains	Fibers
Health drinks	Fruit juice
Antioxidants	Vitamin C
Phytochemicals	Carotenoids
Herbs as functional foods	Soya proteins

Dietary Supplements:

Dietary supplements are items that are taken orally and contain a nutritional element that is meant to enhance the flavour of the food you eat. Black cohosh for menopausal symptoms, ginkgo biloba for memory loss, and glucosamine/chondroitin for arthritis are a few examples of dietary supplements. They also fulfill specialized purposes including meal replacements, weight-loss supplements, and sports nutrition. Vitamins, minerals, herbs or other botanicals, amino acids, enzymes, organ tissues, gland extracts, or other nutritional elements may be found in supplement ingredients. In addition to tablets, capsules, liquids, powders, extracts, and concentrates, they are also available in other dosage forms.[33]

Prebiotics and Probiotic

Probiotics have been used for thousands of years to help support healthy gut bacteria. They are alive microbial feed supplement that helps to maintain a healthy balance of bacteria in the intestines. Some of the most commonly used probiotics come from categories that include lactobacilli, gram-positive cocci, and bifidobacterial. They are used to address gastrointestinal concerns and have even been shown to help reduce the symptoms of cancer, infection, allergy, and asthma.

Prebiotics also help to beneficially alter the bacteria in the gut. They help to promote the healthy growth of bifidobacterial and lactobacillus probiotics in the intestines. Like prebiotics, probiotics also help to address a range of gastrointestinal issues and also play a role in neutralizing toxins, improving intestinal immunity, reducing constipation, and promoting healthy blood cholesterol and lipid levels.

Spices

Several spices are recommended in nutraceutical preparations. Spices play a role in the possible amelioration of health disorders. The medicinal properties of spices include their use as anti-

inflammatory, anti-diabetic, anti-hypercholesterolemic, and anti-carcinogenic agents. Some of the most common nutraceutical spices include fenugreek, garlic, red pepper, turmeric, and ginger. [34]

Fortified Nutraceuticals

Fortification is the practice of deliberately increasing the content of one or more micronutrients (i.e., vitamins and minerals) in a food or condiment to improve the nutritional quality of the food supply and provide a public health benefit with minimal risk to health. As well as increasing the nutritional content of staple foods, the addition of micronutrients can help to restore the micronutrient content lost during processing.

Fortification is an evidence-informed intervention that contributes to the prevention, reduction and control of micronutrient deficiencies. It can be used to correct a demonstrated micronutrient deficiency in the general population (mass or large-scale fortification) or in specific population groups (targeted fortification) such as children, pregnant women and the beneficiaries of social protection programmes. When the vitamins and minerals are not added to the foods during the processing but just before consumption at home or at schools or child-care facilities, it is called point-of-use fortification.

In addition to the micronutrient deficiencies, policies and implementation programmes for fortification need to consider an alignment with policies for the reduction of diet-related noncommunicable diseases. Such is the case of salt iodization, which builds on sodium consumption and, as result, needs to consider strategies for sodium intake reduction.

Recombinant Nutraceuticals

Biotechnology tools have been well applied through a fermentation process in various food materials such as cheese and bread to extract the enzyme useful for providing necessary nutrients at an optimum level. [34]

Bioavailability and functionality of nutraceuticals

Efficacy of any nutraceutical product depends on mainly its bioavailability, referring to rate and extent to which it reaches to the site of absorption and hence the actual functional quantity actually available to the body. Major challenges of incorporating nutraceuticals such as β -carotene, curcumin, vitamins A,D, E and K in food products are their chemical instability during food processing/storage (e.g. sensibility to light, oxygen, heat) or within GI tract (e.g. easily degraded by enzymes, pH), their low water solubility leading to low bioavailability. All these factors can affect the functionality of nutraceuticals' and consequently, hence their health benefits may not be appreciated even when ingested in high amounts. Furthermore, nutraceuticals with unpleasant sensory properties (e.g. polyunsaturated fatty acids) can negatively affect foods' properties and

shelf-life when directly incorporated in food products. Similarly, some of these compounds (e.g. vitamin C) have undesirable interactions with other food components, negatively affecting appearance, texture, mouth feel, stability and bioavailability of other important components in the food product [28]. Investigations on the effect of bioactive ingredients with other food components and the impact of this interaction on the efficacy of bioactive components to act as a drug, is required. These products need faster, accurate, reliable and standardized clinical trials to be performed [35]

Nutraceuticals and Diseases

Cardiovascular diseases

Flavonoids found in onions, vegetables, fruits like grapes, red wine inhibit Angiotensin converting enzymes and strengthen the tiny capillaries that transport oxygen and nutrients to all cells can help prevent cardiovascular disease. Polyphenols found in grapes help to ameliorate and manage arterial diseases. Rice bran promotes cardiovascular health by lowering serum cholesterol levels, lowering the level of (LDL) and increasing the level of (HDL). The greater the ratio, the greater the risk of coronary heart disease. Rice bran includes the antioxidants Lutein and Zeaxanthin,, which improve vision and lower the risk of cataracts and omega-3, omega-6, omega-9, and folic acid, are beneficial to eye health. Low intake of fruits and vegetables is associated with a high mortality in CVD

Allergy

Allergy is a hypersensitive disorder of the immune system. Allergic reactions are caused because of excessive activations of mast cell and basophiles.

Cancer

Present day, cancer has emerged as one of the major public health problems. Pectin is a soluble fiber found in apples has been found to play preventive role against prostate cancer by inhibiting cancer cells from adhering to other cells in the body. Carotenoids and lycopene have antioxidant activity and anticancer effect by decreasing oxidative stress and damage to DNA. Phenolic compounds of natural origin , such as gallic acids, curcumin, ferulic and caffeic acid are observed to possess anticancer activity. Curcumin a polyphenol derived from *Curcuma longa* has been assessed possess anticarcinogenic in addition to the antimicrobial and antioxidative properties.

Obesity

Obesity is a world health problem and causes various serious medical conditions, such as congestive heart failure, hypertension, angina pectoris, hyperlipidemia, osteoarthritis, respiratory disorders and renal failure. Nutraceuticals are recently being researched for their potential in

obesity management. Nutraceuticals such as capsaicin conjugated linoleic acid, psyllium fiber possess potential anti-obese properties. Bioactives components such as ephedrine, caffeine, chitosan and green tea shown good results in facilitating body weight loss.

Neurodegenerative diseases

Neurodegenerative disease indicates a wide range of conditions which primitively affect the neurons. Neurons are building blocks of the nervous system and don't reproduce or replace themselves. Neurodegenerative diseases are characterized by progressive degeneration or death of the neurons and causes damage to the neurons. These diseases are linked with mutated genes, cumulation of abnormal proteins, raised reactive oxygen species or destruction of neurons in specific part of brain [36-38]

Novel herbal drug delivery systems

Numerous approaches in case of new herbal drug delivery system include different types of formulations such as mouth-dissolving tablets, liposomes, phytosomes, pharmacosomes, nanoparticles, microspheres, transfersomes, ethosomes, transdermal drug delivery system (TDDS), and proniosomes.[39]

Current Good Manufacturing Practices (CGMPs) for Food and Dietary Supplements

Following Current Good Manufacturing Practices (CGMPs) help to ensure the safety of food. CGMP regulations generally gives information including appropriate personal hygienic practices, design and construction of a food plant and maintenance of plant grounds, plant equipment, sanitary operations, facility sanitation, and production and process controls during the production of food.

In 1969, FDA established CGMPs in the Code of Federal Regulations (CFR) (21 CFR Part 110). In September 2015, the agency modernized the CGMPs and established them in new Part 117 (21 CFR Part 117), along with new requirements for hazard analysis and risk-based preventive controls which where were issued as part of the implementation of the FDA Food Safety Modernization Act (FSMA). In addition to the CGMPs in Part 117, FDA has issued CGMPs specific to certain types of food.

Quality control

Nutraceutical regulation puts a large responsibility on supplement manufacturers to ensure a high level of quality controls to avoid endangering consumers, not to mention hefty fees and penalties. While specific regulations may vary by country, manufacturers should always take responsibility for traceability and quality control throughout the entire procedure. Many, if not all, risks can be mitigated with thorough testing at each step, including but not limited to:

Ingredients – Testing must begin with pathogen detection (and identification), and quality indicators enumeration for raw materials and ingredients. Contamination from soil and environmental factors are much easier to treat and avoid before materials have moved into production causing wasted time, product, and profit.

Formula – Perhaps the most important step of the production process is the supplement formula, not only the list of finalized ingredients but a functional, repeatable measurement of the level present for each.

Manufacturing – Abiding by the World Health Organization’s Good Manufacturing Processes (GMP) ensures that facilities maintain clean work areas, work to prevent cross-contamination, follow clearly defined processes, etc. Manufacturers who successfully undergo third-party evaluations may receive a NSF or NNFA certification that can be displayed on their respective products.

End-products- Testing (Required & Non-Required) – In cases where rigorous testing is not required, manufacturers are responsible for purity, efficacy, and allergen testing. Manufacturers may choose to obtain a USP Verification Mark, proving that their supplements abide by their label, do not contain harmful levels of contaminants, will be digested in a specified amount of time, and have met by GMP standards. [40, 41]

Nutraceutical regulation

The regulation of nutraceuticals presents a noteworthy challenge to the globalization of nutraceuticals, with a murky and somewhat dissimilar definition of these products that are used in different countries. For example, in Japan, functional foods are defined according to their use of natural ingredients. Comparatively, functional foods in the United States can contain ingredients that are products of biotechnology.

In general, the goals of nutraceutical regulation have been focused on safety and labeling with a lesser emphasis, as compared to pharmaceuticals, on product claims and intended use. This is accomplished through Good Manufacturing Practice (GMP) regulations and a recent increase in enforcement.

Consumers are largely responsible for determining the usefulness and value offered by nutraceuticals. Still, increased regulation related to the quality and safety of these products will significantly benefit the industry and help mitigate the risk of regulatory backlash.

Regulatory rules in different countries

In the United States, the Food and Drug Administration (FDA) tunes nutraceuticals under a different set of regulations as compared to those that cover “conventional” food and drug products.

According to the Dietary Supplement Health and Education Act from 1994 (DSHEA), it is the manufacturer's duty to ensure that a nutraceutical is safe before it is marketed.

The FDA is endorsed to take action against any dangerous product after it reaches the market. Manufacturers have to ensure that the information on the product label is reliable; however, they are not obliged to register their products with the FDA nor get FDA approval before producing or selling nutraceuticals.

In the European Union (EU), food legislation is majority under the shade of the European Food and Safety Authority (EFSA). This legislation concentrates on “food supplements,” which are defined as concentrated sources of nutrients like proteins, minerals, and vitamins, as well as other substances that offer a beneficial nutritional effect. The main EU legislation associated with food supplements is Directive 2002/46/EC.

Novel products from Europe are assumed to have passed stringent European progress and quality requirements. As a result, European nutraceutical companies, which are generally considered leaders in innovation, enjoy the public insight that they are producing the top quality products. In Canada and Australia, nutraceuticals are controlled more closely as a drug than food category.

As with other countries, Indian legislation does not actually ascribe any specific legal status to nutraceuticals. Regulations for nutraceuticals of the Government of India include the Food Safety and Standards Act (FSSA), which was passed in 2006 and has yet to be implemented.

The future prospects of nutraceutical industry

Recently world is becoming more blasé and worldly wise. Foods are found to be more attractive, intriguing and secured to comply the elevated demand of healthy nutrition. With the invention and late advances in Living Modified Organisms (LMOs) and Genetically Modified Foods (GMFs), food for all schedule in the future will be accomplished or rather malnutrition would soon be history but new challenges may emerge. With the dropping-in of tablets as nutrients to provide the body with complete Recommended Dietary Allowance (RDA) including fiber to ensure gastrointestinal or bowel emptying, the prospects of nutraceuticals are boundaryless. The selection of food and nutrition societies for a world nil of lack of food in the future is possible with the potentials of nutraceuticals. Fundamentally, value-added market activity is the increasing impact on the part of consumers as to how nutraceuticals can improve good health. With the established growing public demand for nutraceuticals, not only will consumers in nearby future use supplement products to support overall dietary intake, they are more likely to regard supplementation as an effective way to improve health. The undertone is, would the leading world

economic nations not consider the economic politics and drown this vision or would it be given the attention it so deserves? [42, 43]

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