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REVIEW ARTICLE **OPEN ACCESS**

Medicinal plants as herbal nutraceuticals: A Review

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ABSTRACT

Dietary supplements and supplement industry become major business in recent two decades due to high consumption and awareness of people towards them. Currently, nutraceuticals are obtaining ample attention in views of their nutritional and therapeutic potentials. In prior to production or sales food supplements do not need any registration or approval by the US Food and Drug Administration (FDA). Unlike either foods or drugs, supplements do not need to be registered or approved by the US Food and Drug Administration (FDA) prior to production or sales. Regarding nutraceuticlas liberal of promises has been shown by many studies and they found to promote quality of life in reference to maintaining and promoting optimal health of the mankind. Nutraceuticals can also be used to treat certain health hazards such as cardiovascular diseases, neurodegenerative diseases and cancer also. Present review focuses on their definition, uses, components and therapeutic potentials.

Keywords: *Nutraceuticals, Dietary supplements, Therapeutic potentials.*

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INTRODUCTION

The term "nutraceutical" coined in 1989 by the founder and chairman of the Foundation for Innovation in Medicine (FIM), Cranford, NJ Dr Stephen DeFelice, MD. Basically it means, NUTRITIVE + PHARMACEUTICAL: A food stuff (as a fortified food or dietary supplement) that educes health benefits whereas the concept arose first during the survey conducted in U.K., Germany and France, where consumers give priority to diet then exercise or hereditary factors to achieve a good health [1,2]. In pursuance of Dietary Supplement Health and Education Act (DSHEA) these dietary supplements should bears one or more following dietary ingredients like vitamins, minerals, amino acids, herbs or other botanical, any dietary substance which can supplement the diet of individual by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients [3]. According to European Food Safety Authority (EFSA), only foods that have been labeled with health claims based on studies can be considered nutraceuticals [4]. Image 1 briefly illustrates about the term nutrients from nutrition.

Nutraceuticals are found in a mosaic of products emerging from:

a. Pharmaceutical industries
b. Food industries
c. Herbal and dietary supplement markets
d. Newly merged pharmaceuticals/ agribusiness/nutrition conglomerates

Any nutraceutical may include certain isolated nutrients, dietary supplements, some herbal products and genetically engineered "designer" foods which can be further processed in the form of products such as cereals, soups and beverages. These nutraceutical products are supposed to have influence over most of the therapeutics areas including cold and cough, digestive disturbances, from the prevention of certain cancers, osteoporosis, arthritic, hypertension, cardiac diseases mainly cholesterol, as a pain killer, depression, diabetes and sleeping disorders [5].

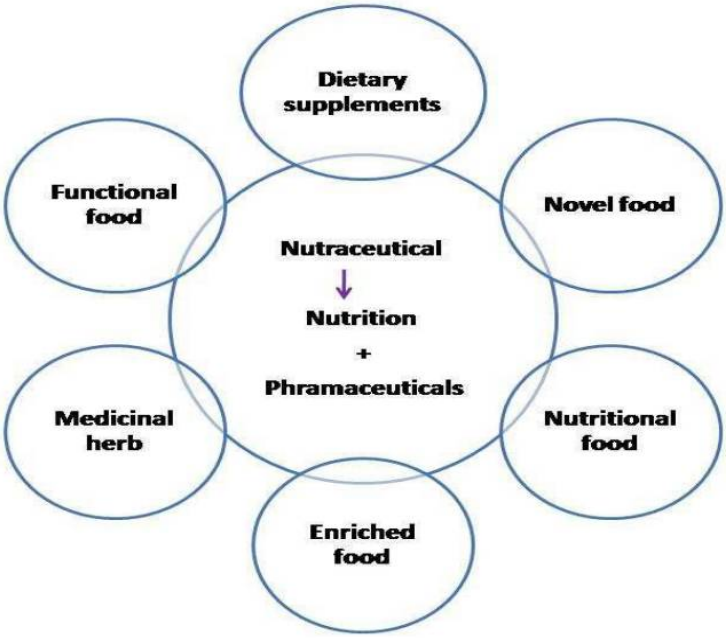
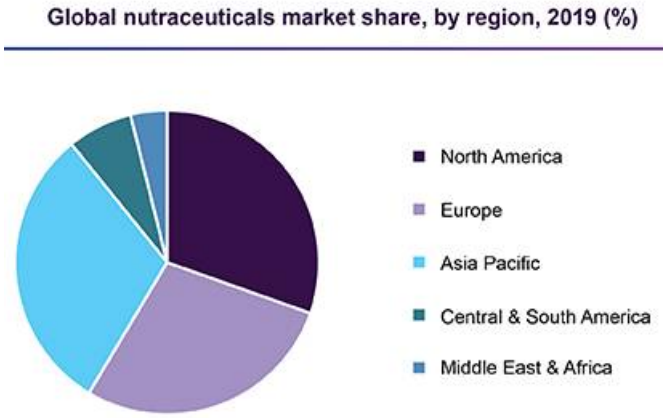


Fig 1: Applications of nutrients to Nutrition

The discovery and development of these nutraceuticals and related products are being utilized by food industries on a grand level mainly due to the current consumer perceptions [6]. Image 1 and 2 is showing the perception of global and Indian market toward emerging nutraceuticals.



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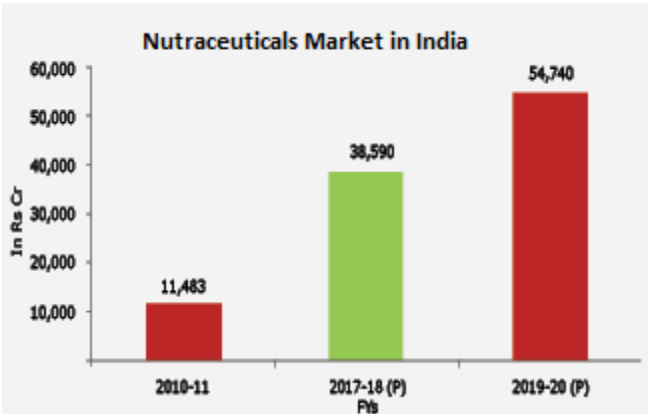

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In many countries Food labelling regulations do not allow food labels to carry health claims which make it hard for food industrials to advertise the benefits of their nutraceutical product without a medical license. To bring a medicine in market will take much long period and is expensive also [7].

Table 1: Inventory regarding certain marketed nutraceuticals

SN	Category	Product
1.	Appetite suppressant	Appetite Intercept (Caffeine, phenylalanine, and tyrosine), Metabolife Ultra Caffeine Free (B-vitamins), Lumatol AC (cacti)
2.	Supplements for hangover	Chaser (Activated calcium carbonate and vegetable carbon)
3.	Calcium supplement	Coral Calcium (Calcium and trace minerals), Calcirol D-3 (Calcium and vitamins)
4.	Immune Booster and immunomodulator	Celestial Healthtone (Dry fruit extract), Chyawanprash (Amla, Ashwagandha, Pippali), Amiriprash (Gold) (Chyawanprash Avaleha, Swarnabhasma and RasSindur), Immulina (Bioactive microalgae complex), Emergen-C (Vitamin), Ester C (Vitamin)
5.	Prebiotics	Clif Bar (Fiber), Cereals, drink mixes, and cereal bars (Fiber), Ensure Fiber (Fiber, digestive health), Builder's Bar (Fiber, Helios Nutrition's Organic Kefir (Bifidogenesis, calcium absorption), Low-fat ice cream sandwiches (Fiber), Luna Bar (Fiber), ZonePerfect Shakes (Fiber)
6.	Probiotics	DanActive (L casei DN114001), Danimals [L rhamnosus GG (infant diarrhea)]
7.	Nutritional supplement	Weight smart (Vitamins and trace elements), GRD (Proteins, vitamins, minerals, and carbohydrates), Proplus (Soy proteins)
8.	Immunity supplement	Immune Assist- complete (Blend of A. blazei, C. sinensis, Coriolusversicolor, L. edodes, Grifola frondosa, and G. lucidum), Mushroom optimizer (Folic acid, mushrooms, and polysaccharides), Omega Women (Antioxidants, phytochemicals (e.g. Lycopene and resveratrol), and vitamins), Agaricus blazie (A. blazei Murill)
9.	Dietary supplement	Olivenol (Natural antioxidant hydroxytyrosol)
10.	Neuropathic pain supplement	PNer plus (Vitamin and other natural supplement)
11.	Protein supplements	Threptin (Diskettes Proteina and Vitamin), Proteinex (Carbohydrates, minerals, pre-digested proteins, and vitamins)
12.	Energy drink	Rox (Caffeine, glucuronolactone, and taurine)
13.	Meal replacement beverage	Snapple-a-day (Vitamins and minerals)
14.	Amino acid supplement	WelLife (Granulated-L-glutamine)
15.	Neurotonic	Biovinca (Vinpocetine)
16.	Anti-depressant	Pure Red Reishi (G. lucidum)

Table source: [8]

IMPACT ON HUMANS

Nutraceuticlas can be categorized as Dietary fibres, probiotics, prebiotics, antioxidant vitamins, polyphenols and spices on the basis of their food sources.

1. Dietary Fibre - Dietary fibres are the food materials including non-starch polysaccharides (NSP) like celluloses, hemicelluloses, gums, pectins, lignin, resistant dextrins and resistant starches obtained from plants and are enable to hydrolyze by gastrointestinal secretions [5].
2. Probiotics – probiotics are live bacteria or yeast used as feed supplements which administrated into host in dose-dependent manner to improve his intestinal microbial balance and proved to decrease systemic conditions like some specific type of allergies, asthmatic condition, cancer and some other infections of ear, and urinary tract [5].
3. Prebiotics – prebiotics are short-chain polysaccharides that are not digested by humans. They alters the composition and metabolism of gut microbiota and help in the improvement of lactose tolerance, helps in combat with constipation, maintains the cholesterol level and amount of lipid in blood,

shows some antitumorous properties, neutralize toxins, and also helps in the stimulation of intestinal immune system [5].

4. Antioxidant vitamins – well known antioxidant vitamins; ascorbic acid, vitamin E and carotenoids prevent from oxidative reactions and their resulting health hazards like cancer, cardiovascular disease and cataract etc. [5].
5. Polyphenols – produced by plants in the form of secondary metabolites and construct a wide range of phytochemicals mainly includes flavonols, flavones, flavan-3-ols, flavanones and anthocyanins etc. These phytochemicals are supposed to possess antioxidant, antiinflammatory, anti-microbial, antitumorous, antidiabetic, cardioprotective activities [5].
6. Spices - dietary spices has a spacious impact over human health when used in minute quantities. They possesses preventive activities against free radicals have chemopreventive, antimutagenic, anti-inflammatory and immunomodulatory activities and shows great impact over human health by influencing their gastrointestinal, cardiovascular, respiratory, metabolic, reproductive and neural systems [5].

Bioactive compounds like carbohydrates, proteins, lipids, vitamins, probiotics, prebiotics, Mushrooms are serves as dietary nutraceuticals whereas herbal nutraceuticlas includes Anthraquinones, alkaloids, tannins, carotenoids, flavanoids and Bitters [9].

Natural products as nutraceuticals

Plants and herbs are the largest resource of phytonutrients and accounts as one of the major resource of nutrients in human food and medicines. Thus phytotherapy or nutritional therapy serves as a new concept of health in recent years. Dietary fibers, allium compounds, betacarotene, flavonoids, folic acid, D-limonene, dithiolthiones, indole-3-carbinol, inositol hexaphosphate, isoflavones, isothiocyanates, lutein, lycopene, phytosterols, selenium, saponins, vitamin-C, and vitamin-E are some common phytochemicals involved during protection from various disease conditions.

Table: 2 List of some medicinal plants used as herbal nutraceuticals

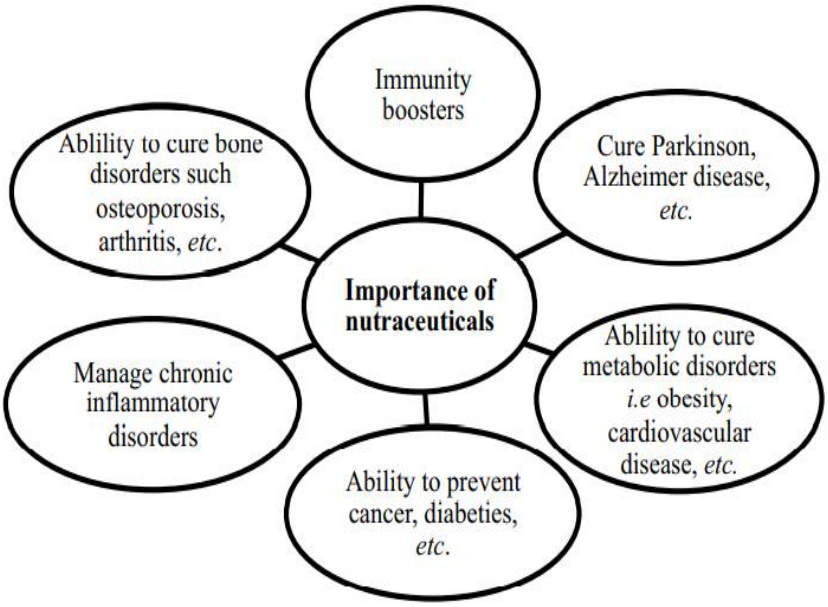
SN	Plant species	Medicinal purpose	Form of use
1.	*Agave americana* (Rambans)	Antiseptic, diuretic	Leaves sap
2.	*Allium sativum* (Garlic)	Chemoprevention, antitumor, antidiabetic, arteriosclerosis prevention, cholesterol-lowering, respiratory infection preventive	Fresh or dried cloves, capsules, odorless tablets, tinctures, aged garlic extracts
3.	*Aloe vera* (Ghritkumari)	First degree burns, cuts and abrasioins, wound healing, antihelminth, antiulcer	Sunscreen, skin-creams, lotions, oral intake
4.	*Asparagus spp.* (Shatavari)	Tonic, astringent	Roots and its modifications
5.	*Boswellia serrata* (Salai guggal)	Asthma prevention, anti-arthritic	Gum-resin
6.	*Calendula spp.* (Pot marigold)	Anti-inflammatory, anti-bacterial, and anti-tumor, skin and cancer treatment	Floweral decoction for wound healing
7.	*Capsicum annuum* (Bell pepper)	Anti-arthritic, anti-oxidant action, nutritious	Fresh and dried fruits, powder
8.	*Centella asiatica* (Gotu kola)	Improves memory, sedative, reduces stress, immunostimulant, wound-healing properties	Herb, powdered, capsules, tablets, tinctures, teas
9.	*Curcuma longa* (Turmeric)	Inflammation reduction, indigestion, anti-oxidant, liver problems	Dried root (whole or powdered)
10.	*Commiphora wightii* (Guggal)	Cardioprotective, anti-inflammatory, rheumatic diseases	Gum-resin
11.	*Echinacea angustifolia, E. purpurea, and E. pallid*	Cold-flu, minor infections, and immunostimulant	Dried whole herb or root, capsules, expresses juice of flowers, tablets, tinctures
12.	*Foeniculum vulgare* (Fennel)	Digestion stimulant	Whole seed, capsules, tinctures
13.	*Glycyrrhiza glabra* (Licorice)	Anti-inflammatory, anti-congestion, relief from cough, and stomach aches	Root powder, capsules, extracts, tablets, tinctures
14.	*Moringa oleifera* (Moringa)	Anti-microbial, anti-viral, hepatoprotective, anticancer, anti-septic, and in treatment of skin diseases	Tree bark, roots, fruit, flower, leaves, seed, and gum
15.	*Nigella sativa*	Analgesic, anticancer, anti-inflammatory, antioxidant antimicrobial, gastro-protective	Seed oil and seed
16.	*Panax ginseng* (Ginseng)	Anti-diabetic, reduces cholesterol, overall health	Dried roots, steamed roots,

		improvement	capsules, extracts, tablets, tinctures, teas
17.	*Rosmarinus officinalis* (Rosemary)	Improves digestion and cures related problems	Leaves, tinctures, extracts
18.	*Phyllanthus emblica* (Amla)	Anti-ageing, anti-diabetic, reduces stress and improves liver functioning	Fruit pulp (fresh and dry)
19.	*Trigonella foenumgraecum* (Fenugreek)	Relieves skin inflammation, anti-diabetic, reduces cholesterol, and improves nutrient absorption	Seed (whole or powdered), capsules, tinctures
20.	*Withania somnifera* (Aashwagandha)	Relieves stress, prevents cataract	Root powder, tea, capsules, tablets, tinctures, extracts
21.	*Zingiber officinale* (Ginger)	Improves digestion, anti-oxidant and controls cholesterol	Roots (fresh or dried), capsule, tablets, tinctures

Table source: [8]

ROLE OF NUTRACEUTICLAS IN VARIOUS DISEASES

The modern human diet comprises higher amount of sugars and saturated fats moreover consumption of fast food items enhance the prevalence of common lifestyle problems such as obesity, atherosclerosis, and heart diseases.



- Cardiovascular Diseases are circumstances of heart and blood vessels. Low consumption of fruits and vegetables founds to support CVDs conditions. Synergetic act of physical workout and intake of nutraceuticals in the form of minerals, vitamins, dietary fibers, antioxidants and omega-3 polyunsaturated fatty acids suggested for the prevention and treatment of cardiovascular Diseases [10].
- A neuronal disorder and most abundant type of dementia, Alzheimer Disease which is also not curable can also be treated with certain antioxidant nutraceuticals containing turmerin, curcumin, lutein, lycopene and βcarotene [8].
- One of the major emerging public health problem cancers can be treated with carotenoid like lycopene with posses preventing role against cancer by decreasing the oxidative stress and prevent DNA from damage. Such compound lycopene founds in many fruits and vegetables like tomatoes, pink grapefruit, guava, watermelon and papaya [8]. Pectin, curcumin are also found from plants and reported to possess anticarcinogenic, antioxidative, and anti-inflammatory properties [8].
- Consuption of high fast foods results in abnormal weight gain called obesity which contributes to several medical issues. Capsaicin conjugated linoleic acid, *Momordica charantia*, *Citrus aurantium* and *Psyllium* fiber are some common nutraceuticlas found to possess efficient anti-obese properties. Certain herbal stimulants like ephedrine, caffeine, chitosan and green tea are also have an emphatic role in facilitating body weight loss [8].
- β-sitosterol, a bioactive phytosterol found to present in plant cell membranes founds to increase the oral glucose tolerance. Oral treatment with this compound results in decreasing the fasting

blood glucose and increasing the fasting plasma insulin level. This antihyperglycemic activity of such compounds is explicit by increasing the levels of circulating insulin within the body. Treatment of these compounds significantly increases pancreatic antioxidants which work for the betterment of diabetic complications and interrupt in its development [11].

- Nutraceutical in Reproductive and Developmental disorder – nutracetical founds to play a potent role in the prevention of birth defects and development of reproductive system from puerility to adulthood in many aspects of the life span. Certain nutraceuticlas are used by infertile individuals (male and female both) as alternative of traditional ART due to their availability and lesser side effects comparatively. Consumption of some determinate compounds like vitamins, amino acids, calcium, zinc, folate at growth phase helps individual in rapid growth, fight against malnutrition and also effective in proper sexual maturity and onset progression of puberty [12].

BIOAVAILABILITY OF NUTRACEUTICALS

Poor or variable bioavailability of nutraceuticals makes them underutilized and unaware about their potential benefits. Certain physiochemical and physiological phenomenon like liberation of food from food matrix, solubility of the component in gastrointestinal fluid, its interaction with the components of gastro-intestine, chemical degradation and permeability of epithelial cells are responsible for the oral bioavailability of nutraceutical (health promoting dietary component). For the betterment of the bioavailability of any nutraceutical product food matrix should be designed in such a way that it retains its bioaccessibility (amount released from food matrix into gastrointestinal tract and become available for absorption for example enters into blood stream), absorption (for absorption compound have to travel through mucus layer, epithelial cell and then into systemic circulation) and transformation (many nutaceuticals are transferred into gastrointestinal tract in inactive form) in gastrointestinal tract (GIT) [13].

Table 3. classification of oral bioavailability of nutraceutical

Classification scheme	Class	Subclass
Biopharmaceutical classification scheme	High solubility and high permeability	
	Low solubility and high permeability	
	High solubility and low permeability	
	Low solubility and low permeability	
Nutraceutical Bioavailability classification scheme	Bioaccessibility	Liberation Solubilization Interaction
	Absorption	Mucus layer Tight junction transport Bilayer permeability Active transporter Efflux transporter
	Transformation	Chemical degradation Metabolism

EFFICACY AND GUIDELINE FOR USING NUTRACEUTICALS

Nutraceuticals can be used without any prescription and regulation. Most of the nutraceuticlas are optimally effective and safe with certain adverse effects like allergies, insomnia, antagonistic effect with certain therapeutic drugs, cardiac arrhythmias, excessive blood thinning etc. [12]. According to the guideline of Food for Special Medical Purpose (FSMP) [14]

- They are naturally occurring ingredients extracted from food sources
- Their consumption has significant effect on health
- Nutraceutical compounds are only applicable for the individual above than 2 years
- Healthy individuals are their targeted population
- Direction of use is orally

- Formed in the form of capsule, tablet, jelly, liquid etc.
- Medical advises are not compulsory
- Claim regarding health function is required
- Claim in reference to cure against any particular disease is not required
- Any hormone or steroid type ingredients are not allowed

ADMINISTRATION OF NUTRACEUTICAL COMPOUND IN BODY

Administration route for any compound generally depends upon the location on which the substance is going to be applied. Common method for administration route includes,

I. **Oral delivery;** most acceptable and preferable route sometimes affect the bioavailability of compound like consumption of lutein with high fat metal increases its absorption within the body and so as lycopene with β carotene. Main consequence of oral delivery is decrement in the bioavailability of compound due its administration route including low stomach pH, collision with degradative, metabolic digestive enzymes and high intestinal pH led researchers to focus on some other emphasis to improve their delivery mechanism [15].

II. **Dermal delivery:** dermal product formed with jutraceutical contains Co-enzyme Q10, ascorbic acid, cucurmine, N-acetylcysteine, genistein and gluconolactone found to have noticeable effect on age associated changes in the skin. Cucurmine also known for its activities against skin cancer, effects of chemotherapy, dermatitis and psoriasis [15].

III. **Opthalmic delivery:** it depends upon the residence time and permeability of given ointment. Inoculation of nutraceutical agent with certain allopathic agents increases intraocular retentiuon time and educes beneficial synergistic effects [15].

NANOTECHNOLOGY BASED APPLICATION FOR NUTRACEUTICAL DELIVERY

Nanoparticle technology is used to increase the potential of any nutraceutical compound as it enhances the solubility and bioavailability of bioactive compound.

I. **Nanosuspension and nanoemulsion:** Significantly used to enhance the solubility of hydrophobic nutraceutical which increase the penetration rate due to increased solubility of compound and larger surface area. Lyophilised nanosuspension of lutein included in creams and gels foe dermal administration and filled into gelatin capsules in pallet form for oral dosing. Nanoemulsions usually made to deliver micronutrients like caretanoids, fat soluble vitamins via oral root of administration.

II. **Nanostructured lipid carriers** These are the nanosized lipid structures made up of lipid matrix having potential for optimum administration of compound via oral, dermal and ophthalmic route. For example nanostructural lipid carrier of cetyl palmetate and capric triacylglycerols used to deliver Co Q10 in dermis which provide excessive physical stability, higher entrapment efficiency and biphasic release pattern for incorporated drug. Nanostreuctured lipid carrier entrapped nutraceutical components get also protection from the impediments of GIT.

III. **Nanomicelles:** Nanomicelles basically provide solubility to insoluble nutraceutical component to increase its potential permeability and bioavailability. A well know example of nanomicelle is quercetine, a bioactive plant metabolite; known for its tremendous clinical properties is poorly commercialized due to its non solubility. To explore nutraceutical benefits of these phytochemical researchers has been developed nanomicelles based delivery system composed of polyethylene glycol (PEG) and phosphotidylethanolmine (PE). These nanomicelles are stable at optimum temperature of GIT and also shows enhanced potential during *In Vivo* clinical studies.

IV. **Nanoparticles, nanocapsules and nano-encapsulation:** most of the phytonutrients founds to be unstable in GIT environment due to their high degradation rate and poor solubility, thus shows limited effects towards certain clinical manifestations. Co-assembled nanovehicles are synthesized to overcome with these circumstances.

STRATEGIES FOR THE FORMULATION OF NUTRACEUTICALS

Prominent formulation design improves the physiochemical characteristics and efficacy of nutraceutical compounds regarding treatment and prevention of concerned health issues. Such nutraceutical formulation strategies include liposomal carrier system, electrospun fiber mats, microsponges and nanosponges, cyclodextrin complexation, biodegradable hydrogels, solid dispersion, self emulsifying drug

delivery system, microparticulate systems and also some nanotechnology based applications as discussed in above section [15].

I. **Liposomal carrier system:** These are phospholipid composed spherical microscopic lipid vesicles basically used to customize pharmacokinetics of certain nutraceuticals depending upon vesicle size, surface charge, composition and concentration of lipid molecules within nutraceutical liposome.

II. **Electrospun fiber mats:** these electrospun fibrous mats mainly designed for the dermal administration of the nutraceutical compound.

III. **Microsponges and nanosponges:** It is type of non-collapsable delivery system containing porous micro and nanospheres. These nanospones are usually hyper cross-linked cyclodextrine polymers forming three-dimensional network.

IV. **Cyclodextrine complexarion:** Cyclodextrines and their derivatives is cage like molecules used as carrier compound to enhance stability, bioavailability, solubility and permeability of nutraceutical compound.

V. **Biodegradable hydrogels:** Vitamins are most common example of these type of formulation that is thermo-labial and successfully transferred at the targeted site for the absorption.

VI. **Solid dispersion:** These are bioactive compounds dispersed in a hydrophilic polymer matrix that increase the dissolution and solubility of the compound.

VII. **Self-emulsifying drug delivery system**: Meant to increase the oral bioavailability of compound by achieving fast self emulsification in aqueous medium that result in extreme improvement in dissolution.

CONCLUSION

There are many inconsistencies and contradictions about the perfect definition of nutraceuticals, moreover it is clear that when functional food aids in the treatment and prevention of any diseased condition than it is termed as nutraceutical. Since more than two decades, scientists are continuously trying to establish benefitial impact of phytochemicals over human health. Researchers have been proved in their investigations that diseases related to esophagus, stomach, lung, endometrium, oral cavity, pancreas, pharynx, and colon can be prevented by combining utilizing fruits and vegetables in daily feeding habits. Furthermore investigations about effect of nutraceuticals on diseased condition and pathogenesis are required. Researches whether these food components can have potency like drugs or not are also need to be confirmed. Faster, accurate, and standardized clinical trials are also need to be performed in order to increase the acceptability of these products in the global market.

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