

Nutraceuticals: A Paradigm Revolution in Medicine and Health

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ABSTRACT

Nutraceuticals are usually seen as natural and safe supplements that have the potential to prevent diseases, serve as alternatives to prescription pharmaceuticals, address nutritional deficiencies, or enhance overall well-being. Most nutraceutical products are designed to be taken orally. However, there are concerns regarding their formulation, bioavailability, and targeted distribution to specific sites. The primary factors contributing to the improper delivery of nutraceuticals are their labile nature, limited oral absorption, and lack of target-ability. Nanotechnology presents new opportunities for improvements in various scientific and technological sectors. Several novel phytotherapy and nutraceuticals, such as polymeric nanoparticles, nanocapsules, and nanoemulsions, have been developed applying bioactive and edible components. Nutraceuticals offer significant benefits compared to traditional plant active formulations. These show effects include enhancement of solubility, improved bioavailability, enhanced stability, sustained release, better distribution within tissues, enhanced pharmacological activity, protection against toxicity, and protecting from degradation.

Keywords: Nutraceuticals, Medicinal plants, Nanotechnology, Bioavailability, Dietary Supplements, Microencapsulation.

INTRODUCTION

World Health Organization (WHO) database on Global Health Expenditure, the United States allocated 17% of its resources towards healthcare, whereas India allocated 4% (WHO Indicators). The substantial expenditure on wellness has influenced the attention of both the research and development divisions of global corporations and customers towards food products that offer health advantages.^[1] The "Nutraceutical" is the word firstly created by Stephen Defelice in 1989 via the combination of the words "Nutrition" and "Pharmaceutical." Nutraceuticals are naturally occurring bioactive or chemical compounds that not only have dietary value but also possess qualities that promote health, cure diseases, or prevent them.^[2] Since ancient times, phytomedicines have been a fundamental component of pharmaceuticals; their use has grown because of their medicinal activity and less serious side effects than other medications. Because of their natural origin and few side effects, herbal medications are becoming more and more popular in developed as well as emerging nations.^[3] The development of novel herbal medications has been strongly supported by expanding quickly nanotechnologies. Although many nutraceuticals exhibit poor bioavailability, nutraceuticals are foods and food ingredients that offer health advantages beyond

basic nutrition. Nanotechnology applications have made it possible to get over the difficulties and technological obstacles relevant to the solubility, stability, bioavailability, and distribution of bioactive ingredients in food.^[4] Nutraceutical nanotechnology's exponential rise holds out the possibility of developing novel, potent functional foods as a means of preventing and possibly curing some non-communicable diseases.^[5]

CONCEPT OF NUTRACEUTICALS

A variety of herbs are found in India; traditional systems of medicine in India such as Ayurveda also depend on herbs or medicinal plants. According to natural sources, categories, and chemical groups, herbal nutraceuticals are also called as dietary supplements, nutraceuticals herbals, and dietary fibers. Dietary Supplements, Health, and Education Act (DSHEA, 1994) introduced by FDA, mentioned that dietary supplements must contain more than one content such as vitamins, minerals, amino acids.^[6]

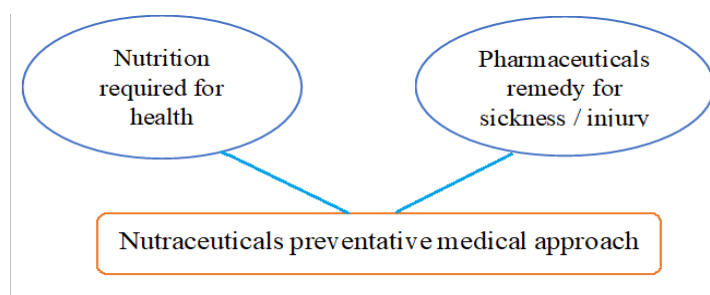


Fig.1: Diagrammatic presentation of Concept of Nutraceuticals

Bioactive compounds as nutraceuticals: Small amounts of bioactive chemicals are found in various foods, particularly in fruits, vegetables, whole grains, and other sources. They provide numerous health advantages beyond their fundamental nutritional value and exhibit diverse medicinal possibilities.^[7] Evidence from epidemiological and animal research indicates that incorporating fruits, vegetables, and whole grains into one's diet can lower their risk of developing chronic diseases attributed to oxidative damage.^[8]

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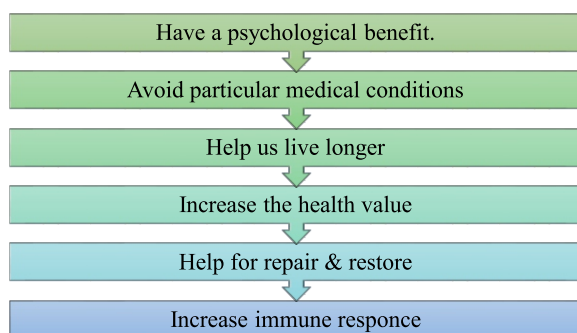
Benefits:

Fig.2: Diagrammatic presentation of benefits of nutraceuticals

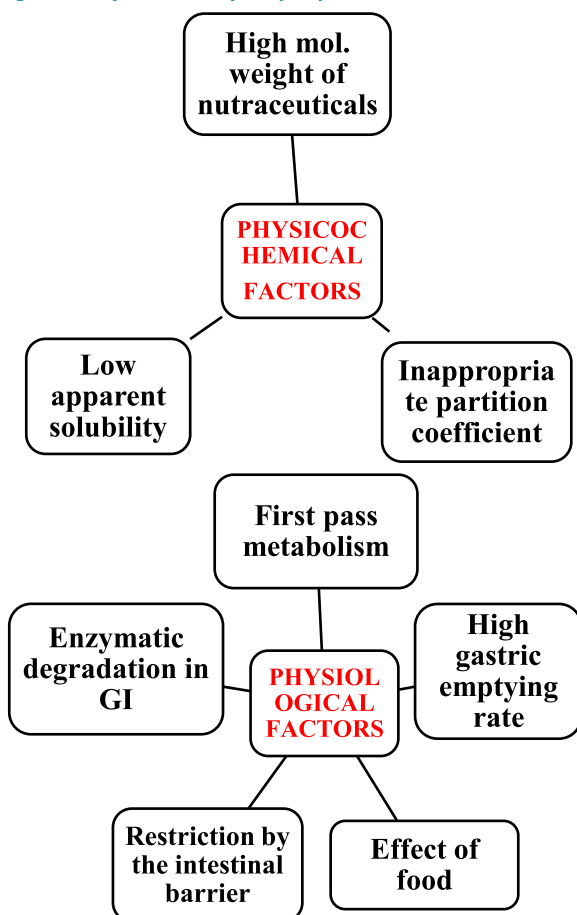


Fig.3: Diagrammatic presentation of factors affecting on nutraceuticals bioavailability

NANO-BASED DELIVERY FOR NUTRACEUTICALS

Nanotechnology is being extensively investigated for its application to enhance stability, solubility, and permeability in nutraceutical, pharmaceutical, and cosmetic applications.^[9] Nanotechnology offers various novel methods and resources that can effectively address the existing gaps in the delivery of nutraceuticals. It provides a promising opportunity to enhance both the products and the techniques employed in the preparation of nutraceuticals, resulting in improved biopharmaceutical properties. Nanoparticles possess distinctive characteristics and significant potential for various applications due to their small size, chemical composition, and surface structure. [10] The nanoformulations have undeniably improved the bioavailability of medications. However, the precise mechanism via which these nano-based formulations enhance the absorption of the active component remains unclear.^[10]

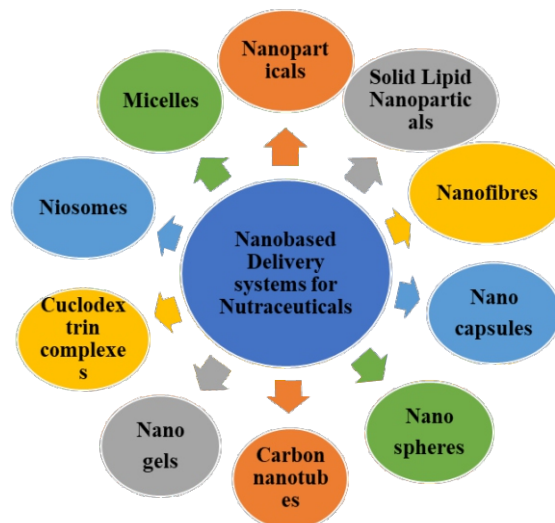


Fig.4: Different Nano-based delivery for nutraceuticals

Nanotechnology to increase nutraceutical bioavailability

Nanotechnological methods can be employed to encapsulate and control the liberation of therapeutic compounds in food and pharmaceuticals, and nutrients. Nanoparticles can exhibit a wide range of structural configurations. The physicochemical properties of these nanoparticles can vary based on the specific materials and procedures employed. The many structural formulations encompass nanolipid dispersions, nanocapsules, nanoemulsions, micelles, nanospheres, nanococheles, coacervates, nanoliposomes.^[11] Nanoform have ability to spread and dissolve by increasing its surface area. Lipid-based formulations enhance absorption by increasing solubility, extending the time they stay in the stomach, promoting transport through the intestinal lymphatic system, modifying intestinal permeability, decreasing the activity of efflux transporters, and reducing metabolism.^[12] The bioavailability of encapsulated bioactive substances typically enhances when particle size housing lowers, owing to their accelerated digestion, capacity to permeate the mucus barrier, or direct absorption by cells.^[12]

Comparing with conventional encapsulation systems, nanoparticles release bioactive molecules more efficiently and have superior defining properties. In addition, particle size directly affects the delivery of compounds to numerous tissues in the organism. Interestingly, several reports suggest that only nanoparticles can be efficiently absorbed into specific cell lines, as opposed to larger microparticles, which significantly reduce their absorption.^[13]

Nutraceutical compound containing nanoparticles can be invented or produce by application of lipid formulations, natural nano materials, technical and sophisticated equipment, bio-polymer nanoparticles, and other types of miscellaneous techniques. Hydrophilic substance or food supplements treat with lipid based nanocarrier for prevention, degradation and breaking of molecules are beneficial method because it increase micellar combinations in lipid bilayer and help in solubilization and reaching target site of action.^[14]

By using various technological methods now a days food industry also improve circulation time of nanocarriers in the gastro intestinal tract. Surface coating in the form of encapsulation prevent the nutraceuticals from degradation and catalytic activity. Studies have demonstrated that lectin's terminal clearance rate in the GIT mucosa decreases when it

covalently binds to poly(methylvinylether)/maleic anhydride carriers, whereas NPs coated with bovine serum albumin exhibit a strong ability to adhere, especially to the stomach mucosa.^[15]

Nanoparticles' main advantages for improving nutrient bioavailability include:^{[16][17]}

- Large surface area enhance bioavailability of in nutraceutical and accelerated digestion in GIT.
- Reducing the size of particles can result in improved permeation through the mucus layer.
- A reduction in particle size can result in the direct uptake of nutraceuticals containing nanoparticles through absorption.
- Reducing the size of particles can result in the production of products which is important for certain dietary products and beverage uses, like enriched waters and soft drinks.
- Including bioactive substances within nanoparticles can potentially enhance their resistance to chemical or biological breakdown.
- Nanoparticle encapsulation can be employed to mitigate their negative interactions with other dietary additives.
- Including bioactive substances within nanoparticles can be useful in avoiding unpleasant taste characteristics.

Encapsulation techniques to safeguard nutraceuticals while they are being digested

Encapsulation is the method in which nutraceuticals/ drug moiety get cover or capsule for protecting the other agents in body such as metabolism process, acid secretion, catalytic activity. It also help to for enhancing activity of and reaching target site of actions. Increase stability, enhanced bioavailability, permeation, reduce toxicity are other important benefits of encapsulation.^[18] Typical encapsulation techniques to safeguard nutraceuticals while they are being digested include;

Microencapsulation: This technique involves encasing the nutraceuticals in small particles or capsules, usually made of proteins, fats, or carbohydrates. In addition to improving stability and minimizing deterioration of the numerous nutrients, microencapsulation can provide balanced ingredient release during digestion. According to the particle size.

Both the microencapsulation (5 to 500 μm) and nanoencapsulation (from 10 to 900 nm) are good for encapsulation procedures. By delivering bioactive chemicals directly to the target site and shielding them from un-favorable surroundings, nano/microencapsulation can increase the bioavailability of these drugs. Extrusion, emulsion, and dehydration are the three primary categories into which microencapsulation processes fall.^[19] nanotechnology is recent method for enhance solubility of hydrophobic as well as hydrophilic nutraceuticals.^[20]

Lipid coating: Coating the nutraceuticals with lipids containing phospholipids or triglycerides can help them become more permeable and protect them from the harsh environment that exists in the digestive system.^[21]

Polymer coating: prevention from degradation through various catalytic enzymes present in stomach the nutraceuticals will cover with polymers its act as barrier and prevent from degradation.

Polymers used in coating the nutraceuticals can serve as a barrier, which prevents degradation through the enzymes and acids that are present in the stomach. This method facilitates the localized release within the intestines.^[22]

Polymeric micelles: Micelles serve as widely employed carriers for nutraceuticals, characterized by a core-shell structure where the hydrophilic head region provides support and stabilization for the hydrophobic core within an aqueous medium. This configuration enhances water solubility while the hydrophobic region serves to carry and protect the encapsulated drug, effectively improving the therapeutic efficacy of drugs associated with central nervous system diseases. The formation of micelles occurs above the critical micelle concentration (CMC) and is thermodynamically stable. It is noteworthy that individual amphiphiles readily form micelles beyond the CMC. However, micelles are not without limitations, notably in terms of low drug-loading efficiency and serum stability. Despite these drawbacks, micelles excel as nanocarriers for lipophilic bioactive.^[23]

Table No. 1: Different types of nanotechnology, mode of action and their applications

Delivery systems	Mode of action	Applications	Ref.
Emulsion based delivery system	Provide balance between attractive and repulsive force. Effectiveness of water insoluble functional ingredient can be improved	Emulsion protect nutrient from degradation, enhance dispersion and improve bioavailability.	[24]
Phospholipid based delivery system	Principle liposomes, solid-lipid nanoparticles, and hydrogel encapsulated lipid bio actives are more palatable due to different physical, chemical and psychological properties.	Fatty acids such as butyric acid have been found to be potent in coronary heart disease have to be delivered.	[25]
Nanocochelete	Encapsulation of lipophilic and hydrophilic compounds give mechanical strength increased safety for chemicals.		[26]
Cocervates	Encapsulation of extremely small lipophilic substances, such as flavoring oils controlled release of substances with bioactive characteristics.		[26]
Hybrid nanoparticles	HNPs demonstrate a unique mechanism of drug release involving disintegration and hydrolytic decomposition on contact with infiltrating water or the release vehicle. This distinctive property is attributed to the presence of a core layer enveloped by multiple layers of shell material.	The formulation of curcumin-based HNPs emerges as a more effective approach in therapeutic applications	[27]
Liposomes	The unique ability of liposomes to hold both lipid-soluble (in the lamellae) and water-soluble (in the aqueous core area) bioactive substances is their most appealing characteristic. By virtue of their biodegradable and biocompatible makeup, liposomes are ideal for delivering medicinal substances.	liposomes in protecting and delivering active ingredients underscore their significance in pharmaceutical and nutraceutical applications, stimulating ongoing research and development efforts to overcome their limitations.	[28]

Nanomaterials used for effective nutrient delivery

Due to the growing demand, foods enhanced and supplemented with nanotechnology are increasingly being introduced. For many years, industries have employed a variety of naturally occurring nanoparticles, such as the casein obtained from milk, lactoglobulins, and phospholipids, which serve as texturizing agents and emulsifiers in the food preparation process.^[29]

Table No. 2: Different nano formulation with their mode of actions and applications

Sr.no	Product	Mode of action	Applications	Ref
1	Aemcolo	Treat microbial infection in GI tract with disturbing flora in the upper portion of the GI tract	Specific dissolution profile which enhance colonic dissipation.	[30]
2	Cordyceps	Useful for strengthening immunity	Dietary supplement	[30]
3	Gen 5G	Contains omega 3 fatty acids like DHA(docosahexaenoic acid) and EPA(eicosapentaenoic acid)	Multi-vitamins and multimineral soft gel capsules	[31]
4	Glenvita 56	Contain lycopene and ginseng	It is multivitamin and multi mineral soft gel capsule use to enhance muscle strength	[31]
5	Multi- X	-	It is useful as immunity booster. Use as multivitamins.	[32]
6	Lubrigen forte	It have vital role to provide joint strength and flexibility because of chondroitin and curcumin as phytoconstituent.	Joint supporting supplement	[33]
7	Coral calcium	Contain calcium and traces minerals	Supplement for Osteoporosis	[34]
8	Albumin bounded paclitaxel nanoparticles	Increases site specific delivery and improved delivery	Application for breast neoplasm	[35]
9	Iron sucrose complexes	Improved dose capacity, improved tolerance	Chronic kidney failure with iron deficiency	[36]
10	Olivenol	Natural antioxidant hydroxytyrosol	Uses as dietary supplements	[37]

Table No. 3: Various common herbal/medicinal plants used as herbal nutraceuticals

Sr No	Medicinal plants	Botanical Name	Phytoconstituents/ Nutraceuticals	Therapeutic action	Ref
1.	Fennel	<i>Foeniculum vulgare</i>	Vita B1, Vita B2, Vita B3 Vita C, Phenols, Flavones, Tannins.	Treating gastrointestinal disorders, Reduce inflammation, Carminative, Diuretic.	[38]
2.	Chaste tree	<i>Vitex agnus-castus</i>	Vitexilactone, Rolundifuran, Ketosteroids, Diterpenoids Vitexin, And Casticin	Carminative, Infertility, Enhance milk secretion Acne.	[39]
3.	Papaya	<i>Carica papaya</i>	Vita A, B1, Vita C, Calcium Hydrate Charcoal, Phosphorus, Iron, Protein, Endopeptidases like papain, glycol endopeptidase,	Treat blood pressure, Anticancer, Malaria Anthelmintic, Anti Antiinflammatory, Free Radical Scavenging, Anti-Sickling,	[40]
4.	Fenugreek	<i>Trigonella foenum-graecum</i>	Alkaloids, Amino acids, Neurin, Vita B12, Vita B9, Vita 7, Vita A.	Hypoglycemic effect Hypocholesterolemic effect Anti-oxidant activity Anti-tumor effect Anti-bacterial	[41]
5.	Bitter Melon	<i>Momordica charantia</i>	Triterpenoids, Glycoside, Phenolic compound, Flavones, Lectins, Sterols	Anticancer activity, Hypoglycaemic agent Anti-bacterial, Antifungal	[42]
6.	Neem	<i>Azadirachta indica</i>	Nimbin, Nimbidin, Nimbolide And Limonoids, Polyphenolic Flavonoids	Antifungal, Anti-inflammatory, Antifungal, Antibacterial Anti-tumour properties	[43]
7.	Okra	<i>Abelmoschus Esculentus</i>	Omega-3 and Omega-6 fatty acids, Sterols, Saturated fat	Diabetes, Cardiovascular disorders, GI problems, Detoxification.	[44]
8.	Buerger's Figwort	<i>Scrophulariabuergeriana</i>	Iridoids and Iridoid glycosides, Phenolic compound.	Pharyngitis, Laryngitis, Neuritis, Sore throat, Rheumatism.	[45]
9.	Garden cress	<i>Lepidium sativum</i>	Phenols, Flavonoids, Terpenoids, alkaloids, saponins, α -pinene, palmitic acid, and linoleic acid	Anticancer, Hepatoprotective, Antidiabetic, Hypoglycaemic, Antioxidant, Antimicrobial, Gastrointestinal activities	[46]
10.	Raspberry	<i>Rubus ellipticus</i>	Phenolics, Flavonoids, Anthocyanins, Tannins Rubinic acid, Rubitic acid, Stigmasterol, Matairesinol, Tocopherol, Morin.	Antidiabetic Activity Antiproliferative and Anticancer Activity Anti-Inflammatory Activity Antifertility Activity Photocatalytic Activity	[47]

THE FUTURE OF NUTRACEUTICALS

The general public's growing consciousness of fitness and health, fostered by media exposure, is inspiring most people to lead better lifestyles, increase their physical activity, and eat more nutrient-dense food. Consumers are increasingly seeking minimally processed food with added nutritional benefits and sensory appeal, as seen by the expanding nutraceutical industry.

^[48] As a result, this progress is fuelling expansion in the global nutraceutical businesses. The rapidly growing nutraceuticals industry is positioned to become the dominant force in the market in the upcoming century.^[49] The nutraceutical firms that are projected to excel in the next sales are those that provide a

diverse array of items that address both conventional and health-related demands, whereas functional products constitute just one facet of their product portfolio. The future market for nutraceuticals depends on how consumers perceive the relationship between nutrition and disease. To fully exploit the potential of nutraceuticals in enhancing human health and avoiding illnesses, it is imperative for health experts, dietician and nutritionists to work strategically and establish suitable rules. By doing so, nutraceuticals can effectively provide the utmost health advantages and curative impacts to humanity. Lack of evidence regarding clinical trial of nutraceutical effectiveness give future scope for research activity.^[49]

CONCLUSION

Acentient history shows various indigenous herbal medicinal plants which give prominent therapeutics action. Recently scientific data also reported that they not have only therapeutic efficacy and medicinal importance apart from this also contain nutritional value. Various phytoconstituent/phytomedicine useful for prevention and treatment of diseases. Nanotechnology is nano particlebased delivery system which improve potency, efficacy solubility, of phytoconstituent and also help to show its target action. Nanotechnology based carrier such as nanoemulsion, sliver nanoparticle, liposomes, nanosome, herbosome show their target specific activity with less toxicity Nanotechnology may improve the aqueous solubility by encapsulating nutraceuticals and prevent oxidation/degradation ultimately improve the health of society.

SUMMARY

Since ancient times, phytomedicines have been an essential source of pharmaceuticals; their use has grown because of their therapeutic activity and fewer adverse effects than other medications. Nanoform have ability to spread and dissolve by increasing its surface area. Lipid-based formulations enhance absorption by increasing solubility, extending the time they stay in the stomach, promoting transport through the intestinal lymphatic system, modifying intestinal permeability, decreasing the activity of efflux transporters, and reducing metabolism.

Several novel herbal formulations and nutraceuticals, such as polymeric nanoparticles, nano capsules, and nan emulsions, have been developed applying bioactive and edible components. Nutraceuticals offer significant benefits compared to traditional plant active formulations.

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