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MODERN APPROACHES FOR NUTRACEUTICAL DELIVERY THROUGH NANOTECHNOLOGY

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ABSTRACT

Nutraceuticals are among the rapidly growing areas of healthcare due to increasing interest in natural products and preventive approaches to health. This review provides an overview of the major types of nutraceuticals and highlights their estimated global and Indian market values. It also discusses the key factors that influence the pharmacokinetic and pharmacodynamic behaviour of nutraceuticals. Since many nutraceuticals have poor solubility, stability or bioavailability, there is a growing need for innovative delivery systems. The review examines various nanonutraceutical formulations, such as nanoparticles, nanoemulsions and other advanced dosage forms designed to improve therapeutic performance, in detail. In addition, the emerging patent landscape in nanonutraceutical research is explored, reflecting the rapid development of this field. The applications of advanced nanonutraceutical delivery systems are summarized according to the target organ systems, demonstrating their potential to enhance the effectiveness, safety and targeted delivery of nutraceuticals in modern healthcare.

KEYWORDS: *Nutraceuticals, Advanced delivery systems, Nanonutraceuticals, Applications*

1. INTRODUCTION

Nutraceuticals, a blend of the words 'nutrition' (food component) and 'pharmaceuticals' (drug or dosage form), is a term coined by Stephen DeFelice in 1989 (1). Nutraceuticals are bioactive compounds that may be naturally present in foods or isolated and formulated into dietary products and included as part of the dietary regimen. These agents deliver beneficial and therapeutic actions to health that extend beyond their basic nutritional functions. Some of the biomolecules such as vitamins, polyunsaturated fatty acids (PUFA), secondary metabolites such as alkaloids, carotenoids, polyphenols, flavonoids; minerals, dietary fibres are identified as bioactive substances which provide variety of health benefits (2,3). These substances play a vital role in prevention, control and treatment of cardiovascular diseases such as hypertension, atherosclerosis, respiratory disorders and allergic conditions, gastrointestinal conditions, bone conditions such as osteoporosis, immune and inflammatory disorders, metabolic disorders such as diabetes, obesity etc (4).

Nutraceuticals form an important part of Complementary and Alternative Medicine (CAM) with high focus on preventive healthcare (5). The global market value of nutraceuticals is valued at around USD 685 billion in 2026. It is projected to reach USD 1328 billion by 2035, at a compound annual growth rate (CAGR) of 7.64% (6). Some of the key global market players in the field of nutraceuticals include Nestle, Herbalife Nutrition, Abbott Nutrition and Amway etc.(7). The Indian nutraceutical market is valued at around USD 8 billion of the total global market and is estimated to cross the USD 20 billion by the end of 2030 at a CAGR of 15%. Himalaya Wellness, Dabur and Baidyanath are some of the popular Indian nutraceutical brands (8). The nutraceutical market has seen massive growth post-COVID-19, due to increased consumer demand for natural health products. People are becoming aware of the need to maintain a healthy lifestyle with better routine, decreased or minimal consumption of processed and refined food along with active lifestyle. The nutraceutical industry is supported by the Government of India through Ayushman Bharat and Production-Linked-Incentives Schemes (PLI), thus accelerating a robust startup ecosystem. Development of better quality nutraceutical formulations can be attributed to availability of standardized techniques for validation of plant-based derivatives and herbal extracts (9,10).

2. CONVENTIONAL NUTRACEUTICAL DOSAGE FORMS

This section describes various conventional dosage forms for administration of nutraceuticals. The different forms of edible nutraceuticals are represented in **Fig. 1.** Conventional nutraceutical dosage forms can be broadly classified as shown in **Table 1.**

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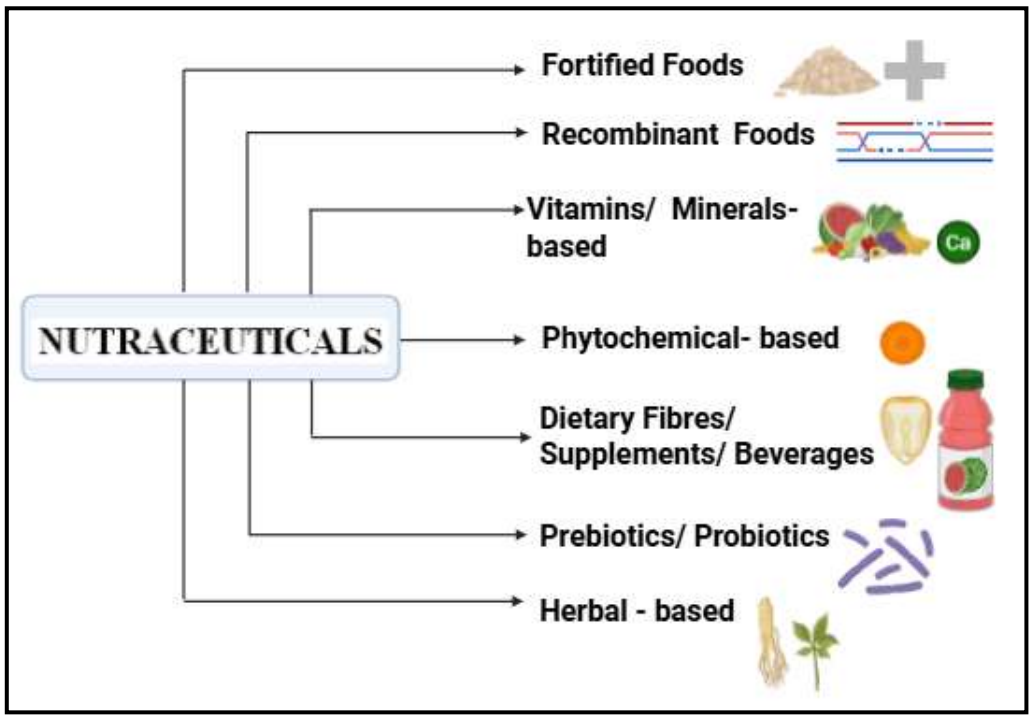

Fig.1: Different Forms of Edible Nutraceuticals

Table 1: Classification of Conventional Nutraceutical Dosage Forms (11–14)

S. No.	Physical state	Dosage forms	Rationale
1.	Solid	Capsules, Tablets, Gummies, Powders, Lozenges	Capsule helps in taste masking, easy administration and better bioavailability of drug. Tablets produce precise dosing of the formulation. Gummies provide high palatability and a child-friendly approach. Powders provide flexible dosing. Lozenges can be explored for better contact time of the formulation in case of oropharyngeal applications.
2.	Liquids	Solutions, Emulsions, Suspensions	Generally prepared by incorporating isolated phytoactive principles in suitable physical form into aqueous or hydroalcoholic herbal extracts.

3. FACTORS AFFECTING DELIVERY OF NUTRACEUTICALS

The following section explains the factors influencing delivery of nutraceuticals, including physicochemical properties. It also discusses pharmacokinetic and pharmacodynamic interactions affecting nutraceutical efficacy.

3.1 Physicochemical Properties

Biomolecules such as omega-3 fatty acids, oil soluble vitamins (Vitamin A, D, E, K) and secondary metabolites such as quercetin, curcumin contain high nutritional value and exhibit high lipophilicity. Phytosterols, fatty alcohols and carotenoids all have high melting points that may lead to unstable formulations (15,16). Appropriate pH conditions ensure maximum drug solubility. Polyphenols, such as curcumin, are poorly soluble in neutral conditions but readily dissolve in an alkaline pH due to deprotonation (17). Ascorbic acid is thermolabile and photolabile. It can undergo reversible oxidation to form dehydroascorbic acid; which further gets irreversibly hydrolyzed to form 2,3- diketogulonic acid (18). LMW molecules are more readily absorbed than HMW molecules; thus, there is a need for specific delivery systems to ensure effective absorption of HMW nutraceuticals (19).

3.2 Pharmacokinetics

3.2.1 Absorption and Distribution

Natural compounds are better absorbed than their synthetic analogues due to the presence of cofactors. The absorption of biologically active nutraceuticals is complex and is affected by various properties such as the molecular size, solubility and the involvement of special transport mechanisms. Nutraceuticals undergo first pass metabolism and digestion to enter into the systemic circulation (20). The nutraceuticals are distributed via human blood vessels to exert their influence on specific target organs and tissues. The systemic circulation involves complex transport across multiple tissue barriers. Factors influencing the distribution of bioactive substances include their molecular size, lipophilicity, protein binding nature etc. (20,21)

3.2.2 Metabolism

Hepatic and extra-hepatic metabolism is more common in nutraceuticals. Phase I of biotransformation is facilitated by cytochrome P450, namely CYP3A4, CYP2D6 and CYP1A2. Phase II reactions transform the metabolites into highly water-soluble forms. The metabolites will have significantly reduced

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pharmacological activity and markedly increased water solubility to facilitate excretion (22). Drugs like resveratrol, piperine and quercetin are known to inhibit CYP3A4 activity, thereby a decreased rate of elimination leads to retention of these substances to toxic levels (23).

3.2.3 Excretion

Water-soluble nutraceuticals are mostly eliminated through renal clearance, which is dependent on glomerular filtration rate and tubular secretion. The lipid-soluble substances are conjugated via hepatic metabolism and eliminated by biliary excretion. Any unabsorbed or metabolized nutraceuticals are excreted in the form of urine and faeces (20). High protein binding nature of the nutraceuticals can result in decreased renal filtration or hepatic clearance (24).

3.3 Pharmacodynamics

When nutraceuticals are administered in combination, with food or drug or other nutraceuticals, can produce synergistic or antagonistic effects. Studies have shown that piperine enhanced the serum concentration, absorption and bioavailability of curcumin in rats and humans without notable side effects (25). However, when garlic is taken concurrently with protease inhibitors (such as indinavir or saquinavir), it is known to decrease blood concentrations of inhibitors, thereby decreasing their overall effectiveness (15). Cinnamon-ginger mixture extract improved the glucose levels, serum triglycerides and other biochemical indicators when administered to gestational diabetic rats (26). A combination of appropriate garlic extract and metformin showed a significant reduction in fasting blood glucose when compared to metformin administration alone. Co-administration of curcumin with piperine or resveratrol improves bioavailability of curcumin, enhancing its anti-inflammatory and anticancer effects (23). A randomized controlled study proved the efficacy of nutraceutical formulation- N247 showed an increase in the serum vitamins and mineral levels over three months (27).

4. NEED FOR INNOVATION IN NUTRACEUTICAL-BASED DOSAGE FORMS

Nutraceuticals are rich in nutrients and biomolecules that can pose formulation challenges (15). **Sec. 3** collectively explains the possible factors affecting the activity and therapeutic efficacy of nutraceuticals. The bioavailability of nutraceuticals is affected by properties such as molecular instability, degradation, poor aqueous solubility, short half-life and rapid metabolism etc. External factors such as food processing and storage conditions can alter the integrity of these compounds prior to ingestion. The concomitant use of nutraceuticals with other drugs or nutraceuticals presents a significant risk of adverse drug reactions (28). These factors minimize the biological effectiveness of nutraceuticals, thereby necessitating the development of advanced innovative drug delivery approaches to enhance their absorption and overall therapeutic impact. As a result, the domain of nanonutraceuticals has emerged to address the current challenges (29–31).

5. NANOTECHNOLOGY IN NUTRACEUTICAL DELIVERY

Nanotechnology offers novel platforms for efficient delivery of nutraceuticals and natural products (32). The incorporation of nanotechnology into nutraceutical delivery science has improved the way bioactive compounds are delivered, protected and absorbed in the human body. These systems are collectively referred to as nanonutraceuticals. Nanotechnology-based nutraceutical delivery systems offer reduced particle size, thus improving surface area, dissolution rate, cellular uptake and ensures controlled release characteristics. It involves the utilization of biocompatible, non-toxic and non-immunogenic materials (lipid, polymer, and protein-based systems) which are generally recognised as safe (GRAS) (29). The ability of nanocarriers, to encapsulate both hydrophilic and lipophilic substances, make them highly versatile platforms for functional food and dietary supplement applications.

Nanoparticles are useful for poorly soluble compounds like curcumin, resveratrol, quercetin, and carotenoids. These systems improve solubility, controlled release, and therapeutic efficacy in disease prevention and health promotion. Polymeric NPs made from synthetic and natural polymers (PLGA, PLA, PCL) deliver nutraceuticals with controlled release and improved bioavailability. These systems suit hydrophobic bioactives such as polyphenols and coenzyme Q10 and allow surface modification for targeted delivery (33). Protein NPs, made from food proteins (e.g., whey, casein, zein), provide biodegradable, biocompatible carriers that bind nutraceuticals via hydrophobic and electrostatic interactions. They protect sensitive bioactives (polyphenols, vitamins) and enhance gastrointestinal stability and release (34). Polysaccharide NPs (e.g., chitosan, alginate) offer mucoadhesion, controlled release, and protection against gastrointestinal degradation, making them ideal for delivering probiotics, antioxidants and herbal extracts with improved stability and absorption (35). Solid Lipid Nanoparticles (SLNs) are lipid matrices solid at room temperature that protect and control the release of lipophilic nutraceuticals (e.g., β-carotene, vitamin E, phytosterols). They enhance stability and bioavailability while using food-grade lipids and surfactants, making them excellent for oral and functional food applications (36).

Nanoemulsions are submicron oil-in-water dispersions that significantly increase the solubility and oral bioavailability of hydrophobic nutraceuticals such as omega-3 fatty acids, coenzyme Q10, and vitamin D. They also provide physical stability and improved absorption via lymphatic transport, benefiting formulations where conventional delivery fails (37). Nanosuspensions consist of pure drug/nutraceutical particles stabilized in a liquid medium, enhancing dissolution rate and absorption of poorly water-soluble nutraceuticals like curcumin and lutein without the need for carriers. This increases oral bioavailability and therapeutic effect (38).

Nanovesicles like liposomes and niosomes encapsulate both hydrophilic and lipophilic nutraceuticals (vitamin C, probiotics, plant extracts), protecting them from enzymatic degradation and enhancing absorption and bioavailability. Their versatility supports oral and topical delivery (39). Nanocrystals are pure crystalline nutraceutical particles reduced to nanoscale, thus increasing surface area and

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dissolution rate. They are particularly effective for hydrophobic compounds like resveratrol, quercetin, and curcumin, improving bioavailability without additional carriers (40). Dendrimers are highly branched, tree-like polymers with tunable surface functionality that allow precise loading and controlled release of nutraceuticals and targeting ligands. They can improve solubility and delivery efficiency for bioactives like antioxidants and vitamins (41). **Fig. 2** outlines the different types of nanonutraceutical delivery systems.

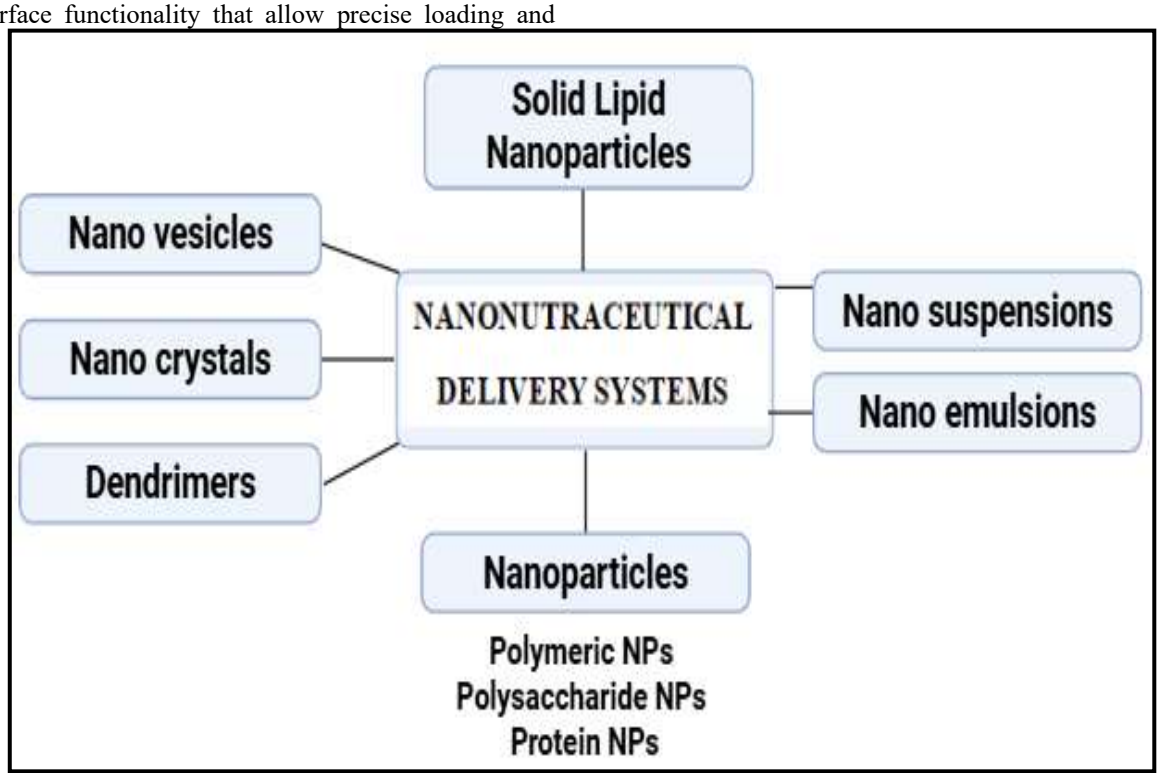

Fig.2: Nanonutraceutical Delivery Systems

6. PATENT LANDSCAPE OF NANONUTRACEUTICALS

The United States of America dominates nanonutraceutical patent filings (61.4%), followed by WIPO (31.7%), highlighting strong innovation and emerging role of nutraceuticals (42). **Table 2** highlights some of the patents based on original research works in nanonutraceuticals.

S. No.	Patent	Year	Work	References
1.	US20250090455A1	2025	Novel saccharide-based, food-form, portable oral delivery systems adhere to gingival, buccal, palatal, or sublingual surfaces, prolonging contact, enhancing small molecule, nutrient, or nutraceutical absorption, increasing bioavailability and therapeutic onset.	(43)
2.	US20240269317	2024	This invention relates to targeted nutraceutical-based treatments addressing chronic diseases. Conventional pharmacological therapies cause side effects, whereas this approach enriches delivery, enhancing efficacy and reducing adverse reactions	(44)
3.	US20220008349A1	2022	The invention covers plant tissue- derived nanoparticles and food powders, focusing on preparation, properties, and applications in food, nutrition, and health.	(45)
4.	WO2021252484A1	2021	This disclosure describes lipid nanoparticle-based formulations (liposomes, solid lipid particles, oil-in-water emulsions) for delivering hydrophobic and hydrophilic therapeutic agents, including vitamins, nutrients, plant extracts, nutraceuticals, and pharmaceuticals.	(46)
5.	US10980267B2	2019	The invention relates to a nanoparticle system and methods for producing advanced nutraceuticals,	(47)

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			enhancing bioactive compound delivery, stability, and absorption, overcoming conventional nutritional supplement limitations	
6.	WO2019129557A1	2019	The controlled nutraceutical delivery system enables oral administration of one or multiple bioactive ingredients, improving solubility, bioavailability, and targeted release in body fluids.	(48)
7.	WO2015057751A1	2015	The invention shows that nanoparticle systems improve nutraceutical delivery by protecting unstable ingredients, enhancing absorption, and helping bioactives cross cell membranes and biological barriers for better health benefits in humans.	(49)

7. APPLICATIONS OF ADVANCED NUTRACEUTICAL DRUG DELIVERY SYSTEMS

In contrast to conventional nutraceutical formulations, advanced drug-delivery systems based on nanotechnology and biotechnology provide site-specific delivery by enhancing the bioavailability and therapeutic efficacy of phytoconstituents. The following section lists out the various applications of advanced nutraceutical systems with respect to specific organ systems. These applications demonstrate the translational potential of nanotechnology and biotechnology based advanced nutraceutical delivery systems, offering targeted, site-specific action with enhanced bioavailability and minimal adverse effects (50).

1. Integumentary System: Cur-NEs/Gel, a protease-triggered self-assembling hydrogel containing curcumin nanoemulsions, enhances skin retention and penetration, effectively alleviates psoriatic inflammation and demonstrates therapeutic potential for the topical treatment of psoriasis and other skin diseases (51).
2. Musculoskeletal System: Curcumin nanoemulsions or hydrogels (Cur-NEs/Gel) enhance joint penetration, reduce inflammation and may provide therapeutic benefits for psoriasis and topical joint inflammation (52).
3. Nervous System: Enhanced-bioavailability curcuminoid formulations, delivered via lipid micelles, solid lipid nanoparticles, or microemulsions, potently induce neurogenesis. They offer a promising therapeutic approach to treat, retard, or prevent age-related neurodegenerative diseases, including Alzheimer's, in both preclinical and human models (53).
4. Endocrine System: Berberine exerts anti-obesity and metabolic benefits by regulating AMPK, gut microbiota and lipid/glucose metabolism, and its therapeutic efficacy is enhanced through nanotechnology-based delivery systems such as lipid nanoparticles and cyclodextrin complexes that overcome bioavailability limitations (54).
5. Cardiovascular System: Nanophytomedicines, such as liposomal curcumin, quercetin, and resveratrol nanoformulations, enhance bioavailability and targeted delivery, providing potent cardioprotective effects in preclinical models of cardiovascular disease (55).
6. Immune System: QuadraMune™, a nutritional supplement, has demonstrated anti-inflammatory and immunomodulatory effects *in-vitro* and pilot *in-vivo* studies and is currently being evaluated in a 500-participant clinical trial for reducing infection risk in individuals at high risk of COVID-19 (56).
7. Respiratory System: Inhalable phytoceuticals inhibit fibroblast-to-myofibroblast transition and profibrotic cytokines in pulmonary fibrosis while enabling targeted lung delivery with reduced systemic toxicity, though formulation optimization and mechanistic studies remain essential (57).
8. Digestive System: Microbiome-responsive nanocarriers enhance the stability, bioavailability, and gut-specific release of nutraceuticals, supporting microbiota modulation, reducing intestinal inflammation, and improving epithelial integrity (58).
9. Urinary System: Chitosan-rosemary oil nanophytosomes offer an eco-friendly, biodegradable alternative for treating multidrug-resistant (MDR) E. coli UTIs by enhancing antibiofilm activity, bioavailability, and nephroprotection while improving bladder/kidney histopathology, though long-term stability optimization remains essential for clinical translation (59).
10. Reproductive System: Curcumin improves reproductive and metabolic health in PCOS by regulating lipid and blood sugar levels through its anti-diabetic, antioxidant, anti-inflammatory, and anti-androgenic effects. Furthermore, nanocurcumin formulation overcomes solubility issues, boosts miR-223–3p, reduces insulin resistance, and supports β-cell and ovarian function, making it a promising therapy (60).

8. CONCLUSION

The limitations of conventional nutraceutical delivery systems in achieving optimal bioavailability, stability and targeted therapeutic outcomes can be addressed using advanced nanotechnology and biotechnology strategies. Nanonutraceuticals protects labile bioactives from degradation, enable controlled release and improve intestinal absorption. The biotechnological strategies including fermentation-derived bioactives, enzyme-assisted alterations, probiotic-based delivery, genetically engineered biomolecules etc. contribute to improved functionality and delivery of nutraceuticals. Overall, novel nutraceutical delivery systems represent a promising avenue in preventive healthcare, connecting nutrition and therapeutics for improving overall health of individuals.

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