Injectable Nutraceuticals: A Novel Frontier in Preventive Health

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Abstract

The world has become more susceptible to micronutrient deficiency and lifestyle diseases in most cases, creating a need to find viable ways of intervening with nutraceuticals. Nevertheless, oral nutraceuticals have significant disadvantages that include low bioavailability, gastrointestinal degradation, unreliable absorption, and compliance. These limitations have heightened the concern on injectable nutraceuticals which is a growing category of parenterally administered vitamins, minerals, peptides, antioxidants and botanical extracts products designed to reach rapid and consistent systemic concentrations. This review brings out the scientific justification, development of formulations and pharmacokinetics advantages of injectable nutraceuticals. Contemporary approaches to delivery such as liposomes, nanoemulsions, cyclodextrin complexes, microspheres, hydrogels, and biopolymer-based carriers play a significant role in increasing the solubility, stability, and prolonged release of bioactive compounds. Mechanically, injectable nutraceuticals have antioxidant, anti-inflammatory, immunomodulatory, and metabolic regulatory effects, which support their use in preventive and integrative care. They are particularly useful in special populations like malabsorption disorders patients, post-operative patients, and patients with high metabolic rates. The threats to their promise can still be seen in the regulatory uncertainty, lack of clinical evidence, and ethical issues in wellness environments, and compliance with GMP should be considered strict. Altogether, injectable nutraceuticals have significant potential of developing precision, high-bioavailability preventive therapies by further research and regulation perfection.

Keywords: Injectable nutraceuticals, parenteral delivery, bioavailability, formulation technologies, preventive healthcare.

1. Introduction

Micronutrient deficiency conditions (MNDs) are faced by over 2 billion people across the globe, impacting morbidity, mortality, and quality of life to a huge extent (1). MNDs are common not only in developed countries but also developing ones and they are known to be silent epidemics (2). This trend is heightened by increasing lifestyle-related diseases like obesity, type 2 diabetes, and cardiovascular diseases and therefore the need to have preventive measures in place (3). Although nutraceuticals could be used in complementary ways in regard to

healthy dieting and exercises, they are useful in disease prevention, but they have been faced with issues surrounding low oral bioavailability, as a result of intestinal permeability, stability and solubility(4). The nutraceutical industry has the opportunity to repurpose the highly developed technologies in the pharmaceutical industry in the delivery of oral drugs to increase the efficacy of these compounds (5). The review shows that there are four main types of nutraceuticals, including fatty acids, micronutrients, phytochemicals and bioactive peptides, and that they are poor solubility and high first-pass metabolism tend to restrict their bioavailability (6). This requires an increase in dosages, which may result not only in side effects but also in a reduction of treatment effects (7). Also, the gastrointestinal milieu has serious biological complications to increased absorption particularly of proteins and peptides administered orally. To enhance the systemic bioavailability and therapeutic efficacy, injectable nutraceuticals (INs) (8) i.e., administered parenterally have been suggested. This method of delivery avoids gastrointestinal barriers, which contributes to better bioavailability and a better pharmacokinetic effect in relation to oral administration (9). The review will attempt to cover in details the injectable nutraceuticals as an upcoming discipline in the therapeutic and preventive medicine including their scientific basis, formulations, dosing factors, and translational prospects (10).

2. Current Scenario of Nutraceuticals

It is projected that the world nutraceutical market will grow to 8.90 % a year to reach $308 billion by 2028 as compared to 149.50 billion by 20219(11). The key segments of the product in this market are vitamins and minerals, which turnover is substantial, especially in Europe as well as proteins, enzymes, and fatty acids. With the outbreak of the COVID-19 pandemic, there was a higher demand among consumers on dietary supplements like zinc, vitamin C, and vitamin D (12) The oral route by which nutraceuticals are delivered still leads in popularity because it is easy to administer; nevertheless, it is not without flaws, including a lack of bioavailability of the compound and gastrointestinal instability. The emergence of transdermal methods is being used as an alternative but has difficulties, namely individual variations of absorption (13). Intravenous nutraceuticals, which include vitamin B12 and vitamin C, are increasingly finding application in clinical practice to address the short-comings of their oral counterparts, and an increasing number of consumers are becoming interested in prevention and anti-aging uses (14). Depending on the country of operation, the regulatory environment of nutraceuticals differs and thus classification of nutraceuticals is also a challenge in comparison with drugs. The FDA considers nutraceuticals as dietary supplements with less strict regulations in the U.S and the FSSAI in India marks them out, although no therapeutic claims are allowed. The EMA in Europe does not have a single category and therefore has a disjointed approach to the regulation; hence necessitating the harmonization of regulations across jurisdictions (15).

3. Limitations of Oral Nutraceutical Delivery

The main cause of poor bioavailability of orally taken drugs are first-pass metabolism and gastrointestinal degradation. Following the oral route, a drug is absorbed in the gastrointestinal system and is transported through the portal vein into the liver where the metabolic process lowers the concentration of active drug to be absorbed into systemic circulation by a significant portion (16). Total causes are the presence of hepatic activity, intestinal activity, the instability of the chemical, and gut wall activity. Food interactions, pH dependency as well as gut microbiota also affect the variable drug absorption as they may modify enzyme activity and drug

solubility and, consequently, influence bioavailability (17). There are also the issues of patient compliance and inability to adhere to certain dosing, particularly in the case of chronic disease, where the lack of understanding of dosing schedules and complicated regimes interfere with adherence (18). The adherence can be promoted with the simplification of drug regimens. The effects of the environmental forces on the stability of the drug include exposure to light and changes in pH that cause biochemical degradation and efficacy loss of bioactive compounds. The activity of enzymes, especially at a certain pH, requires such protective coating as encapsulation in order to enhance the level of stability and bioavailability of these therapeutic agents (19).

4. Injectable Nutraceuticals: Concept, Composition, and Rationale

Injectable nutraceuticals are bioactive compounds that are injected parenterally with essentially required compounds e.g. vitamins, minerals, peptides and amino acids directly getting into the systemic circulation either via intramuscular, intravenous or subcutaneous routes (10). The purpose of these formulations is to reach therapeutic plasma levels within a short period without undergoing gastro intestinal breakdown or first pass metabolism thereby enhancing bioavailability and efficacy (20).

Types include:

4.1 **Intramuscular**: IM injections allow nutraceuticals to enter the skeletal muscle and that part is better absorbed than by oral dosing. There are vitamins such as B-complex, which may construct a depot in the short-term, providing it with slow and prolonged release. However, Glutathione is not a depot and is more rapidly acquired. IM route is usually applied to vitamin B-complex, as well as, some amino-acid formulations (21).

4.2 **Subcutaneous:** Subcutaneous route is one in which the nutraceuticals are carried to the fatty tissue the skin, which leads to slow and gradual absorption. The use of SC is appropriate in low volume antioxidants, peptide and amino-acid preparations which demand gradual absorption into the system (22)**.**

4.3 **Intravenous:** IV route puts the nutraceuticals in the blood, which is a 100 % bioactive route that can act instantly in the body (23). It goes around absorption block and applies to the agents in need of rapid or high plasma concentration, like the high-dose of vitamin C, NAD+, glutathione, and amino-acid infusion. The use of IV administration is usually in the form of a slow infusion to ensure safety and controlled effects of pharmacological activities (24).

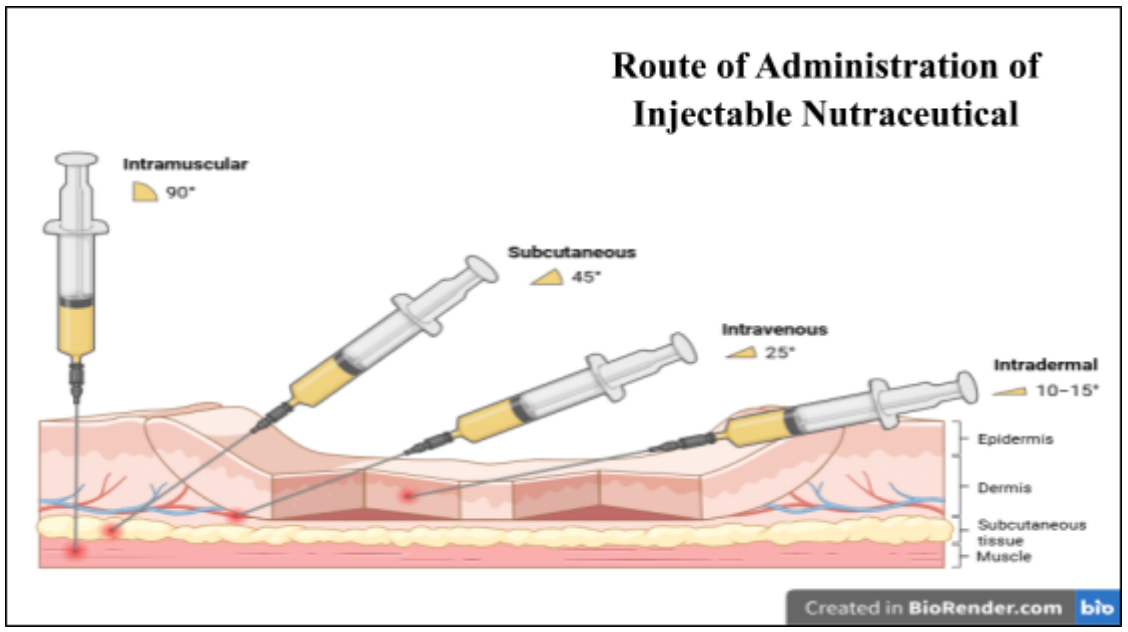

Fig.

1. Route of Administration of Injectable Nutraceutical

5. Formulation and Delivery Innovations

The article talks about different methods of improving solubility and stability of hydrophobic bioactive compounds to increase their therapeutic efficacy (25). It gives prominence on solubilization using liposomes, nanoemulsions, and cyclodextrins as well as pointing out that liposomes, a phospholipid-based carrier, can be used to encapsulate both lipophobic and hydrophilic nutrients, in such a way that bioactive are not dissolved. Use of cyclodextrins in liposomal formulations generates inclusion complexes that increase stability and controlled release and is associated with high bioavailability (26). It is claimed that nanoemulsions expand the surface area of enhancing absorption and stability of poorly water-soluble compounds. Also, it documents the controlled-release injectables such as depot systems, microspheres, and hydrogels that are meant to release nutrients over a long period (27). These systems are meant to extend the therapeutic effects and also decrease the dosing. Bioactives are slowly released into circulation by depot systems which include oil-based injection and use of biodegradable polymeric microspheres (28). Hydrogels have high amount of water, and they are biocompatible, that can be used as a scaffold to sustain constant plasma levels due to the delivery of the nutrients continuously. It also narrates about biopolymer-derived carriers, such as polyethylene glycol, chitosan, and hyaluronic acid, which improve the pharmacokinetics of injectable nutraceuticals (29). PEGylation enhances solubility and half-life in circulation of proteins whereas mucoadhesion and target delivery characteristics are provided by chitosan and hyaluronic acid respectively, decreasing enzymatic degradation (30). Finally, the document proposes the combination systems that can be used to co-deliver the bioactives with synergistic nutrients or bioenhancers (31). Such formulations contain co-factors to increase enzymatic activity and bioavailability by acting via metabolic modulation, so that release of nutrients works in concert to initiate or amplify therapeutic actions, and to reduce the stability problems of the molecules (32).

6. Mechanisms of Action and Preventive Health Benefits

Intravenous nutraceuticals circumvent the gut and provide high bioavailable concentrations that have a direct effect on repairing cells and metabolism. They induce TET-mediated repair of DNA, elevate intracellular NAD+ (Nicotinamide Adenine Dinucleotide) and CoQ10 (CoenzymeQ10) to enhance the energy metabolism of mitochondria, and modify metabolic programs to effective oxidative services (33). They regulate the levels of ROS (Reactive oxygen species) and maintain redox homeostasis and prevent oxidative cell damage. All these alterations result in the enhancement of immune activity, which is improved through the T-cell activation and the Natural killer-cell cytotoxicity, resulting in enhanced cellular resistance, metabolic renewal, and immune monitoring (34).

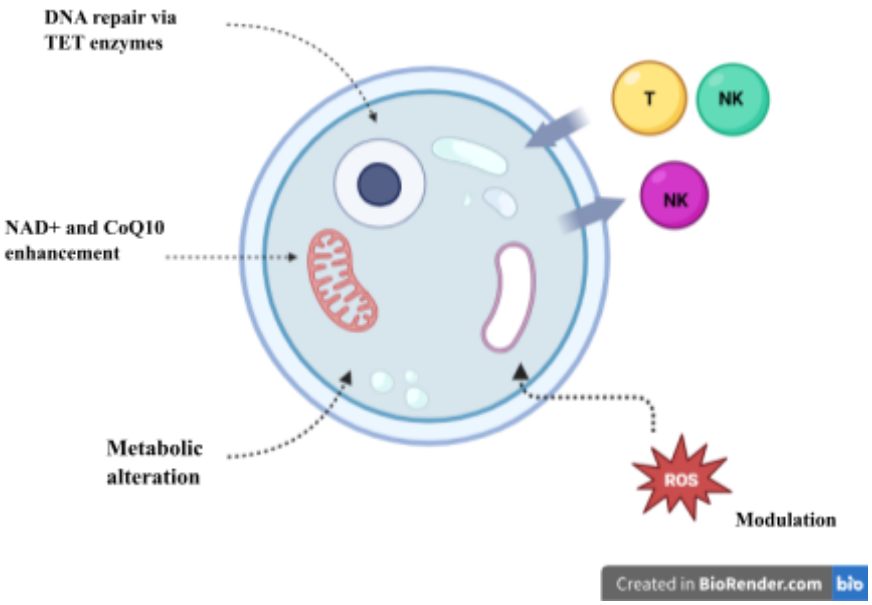

Fig. 2. Mechanism of Action of Nutraceutical

7. Dosing, Pharmacokinetics, and Safety Considerations

The paper explores the effects of parenteral nutraceutical dosage on pharmacodynamics and therapeutic index, highlighting improved absorption kinetics and systemic exposure due to reduced first-pass metabolism (35). Various parenteral routes (intravenous, intramuscular, subcutaneous) enable rapid peak plasma concentrations (Cmax) but pose overdose risks related to vitamin toxicity and infusion reactions, underscoring the need for careful monitoring and individualized dosing (36). Factors such as body mass index and genetic aspects, including pharmacogenetics, significantly influence pharmacokinetics and dosing requirements. For instance, differences in the VDR gene can affect vitamin D dosing, and variations in folate metabolism may necessitate adjustments in folic acid dosage(37). Pharmacokinetic modeling suggests that injectable routes achieve higher plasma concentrations with shorter Tmax compared to oral dosage forms (38).

8. Impact on Medically Compromised and Special Populations

Injectable nutraceuticals provide a solution for patients with malabsorption syndromes, such as Crohn's and celiac disease, by enhancing nutrient absorption and avoiding gastrointestinal obstructions (39). They can rapidly correct nutrient deficiencies, especially important for post-surgical and hospitalized patients with increased nutritional needs. However, these nutraceuticals pose risks, including drug interactions, infection hastening, and monitoring challenges concerning fluid and electrolyte levels (40). Regulatory and ethical issues complicate their use, with significant disparities in manufacturing standards compared to drugs. There is a lack of robust clinical trial data to support their safety and efficacy, and concerns over potential misuse in wellness clinics necessitate cautious patient counselling (41).

9. Future Technologies in Injectable Nutraceuticals

Future advancements in injectable nutraceutical delivery focus on sophisticated formulation platforms and data-guided optimization tools (42). Biodegradable long-acting injectables (LAIs) are emerging as key systems for sustained nutrient release, with current innovations aimed at refining polymer molecular weight, end-group chemistry, and processing parameters to achieve predictable and extended-release profiles (43). In parallel, stimuli-responsive hydrogels are enabling environment-specific, on-demand delivery through in situ gelling mechanisms triggered by pH, redox conditions, or enzymatic activity, thereby improving local tolerability and minimizing undesirable burst release (44).

Lipid-based carriers, including liposomes, solid lipid nanoparticles, and nanoemulsions, continue to evolve through techniques such as PEGylation and remote loading, providing enhanced solubility, protection of labile vitamins or antioxidants, and extended circulation times (45). Increasing interest in co-delivery systems has led to multifunctional formulations in which nutrients are combined with bioenhancers or cofactors (e.g., cyclodextrin complexes, piperine derivatives) to improve uptake, synergistic activity, and dose efficiency(45).

Advances in analytical modelling, such as PK/PD simulation, IVIVC, and Quality-by-Design (QbD), are improving predictability of complex parenteral systems and supporting rational dose design for early clinical translation (46). Finally, emerging work in precision nutraceuticals explores the integration of pharmacogenetic markers such as VDR variants for vitamin D and biomarker-guided regimens to enable individualized parenteral nutrient therapy aligned with patient-specific metabolic and genetic profiles (47).

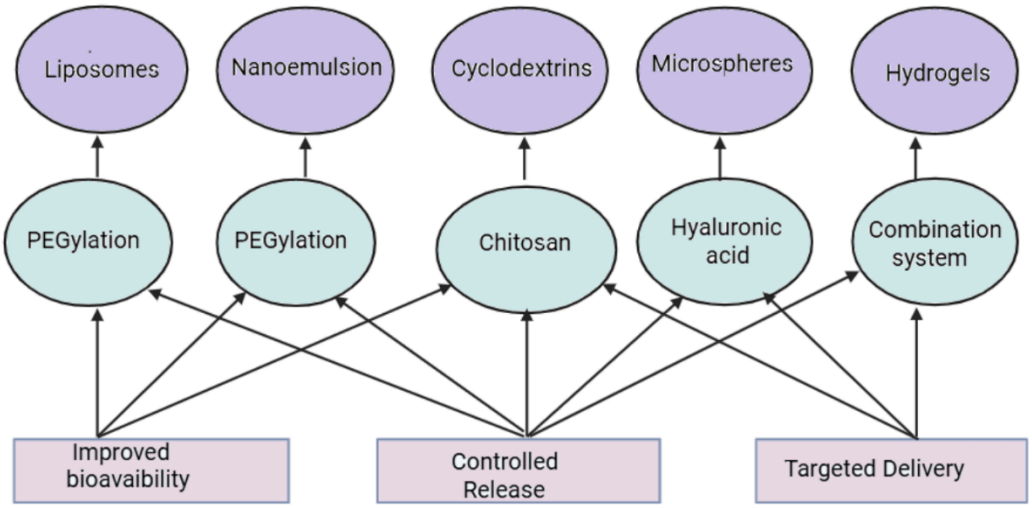

Fig. 3 Modification Strategies in Injectable Nutraceutical Delivery Systems

10. Research Gaps in Injectable Nutraceuticals

Significant research gaps hinder the integration of injectable nutraceuticals into clinical practice, relying mainly on small studies and case reports rather than robust randomized controlled trials(48). Regulatory inconsistencies create uncertainty in standards and quality, leading to variability in manufacturing and labeling. Manufacturing challenges, particularly related to sterility and nutrient stability, are under-reported, and pharmacokinetic data for administered nutrients is incomplete(49). Moreover, the absence of pharmacovigilance systems results in poor adverse event detection, especially outside clinical settings. Formulation issues such as burst release and

complexities in scaling manufacturing are prevalent, along with a lack of standardized dosing and clinical pathways. Ethical concerns regarding misuse and commercialization underline the need for effective oversight and further research (50)

11. Future Perspectives

Future advancements in long-acting nutraceutical injectables will be driven by smart polymers facilitating precise, stimuli-responsive, and sustained release, enhancing patient adherence and tailored medical care. The emergence of nutraceutical pharma hybrids promise integrated preventative and therapeutic advantages through multifunctional delivery systems customized to patient requirements. Large-scale clinical validation and pharmacovigilance databases will be necessary and fundamental to ensure safety, effectiveness, and regulatory approval, supported by cooperative inquiry and big-data analytics**.**

12. Conclusion

Injectable nutraceuticals offer an encouraging bridge between nourishment and medicine by substantially enhancing bioavailability and offering quicker therapeutic effects compared to conventional and customary oral supplements. Advances in formulation science, regulatory frameworks, and clinical validation are expected to redefine precautionary and functional medical care through these injectable systems. Ultimately, the area is poised to transition from oral supplements to evidence-based, precision injectable nutraceutical therapies, allowing more sustainable and personalized condition management. This vision reflects the growing recognition of the advantages of enhanced delivery approaches and the need for strong and durable clinical evidence to support their broader adoption.

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