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Review Article

Advancements in Lipid-Based Delivery Systems: Enhancing Bioavailability and Therapeutic Potential of Dietary Lipids; A Narrative Review

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ABSTRACT

Background: Lipid-Based delivery systems (LBDS) are novel systems developed for improving the bioavailability, stability and bioactivity of lipid-soluble nutrients, such as the omega-3 fatty acids, carotenoids and fat-soluble vitamins. In particular, these systems (i.e. liposomes, nanoparticles, and nanoemulsions) target major issues of poor solubility, digestion instability, and absorption to improve the therapeutic potency of bioactive lipids.

Methodology: A systematic search of the literature was carried out using several databases (PubMed, Scopus and Google Scholar) targeting peer-reviewed articles published during the past 5-10 years on each of the aspects highlighted in this narrative review. Search terms included: lipid-based delivery systems, bioavailability, nanoemulsions, liposomes, and nanoparticles. The selected studies were relevant and robust, and the limited number of more innovative encapsulation technologies and their effects on bioavailability. The synthesized data were organized around themes, including formulation techniques, hurdles related to stability, and future clinical applications.

Results: Lipid delivery systems have shown great potential to improve the solubility, stability, and targeted delivery of bioactive lipids. Liposomes have been especially effective in protecting sensitive materials, while nanoemulsions have shown greater improvements in solubility. Still, challenges remain, among them high production costs, scalability issues, and variability in patient responses. Such systems could have applications in personalized nutrition and precision medicine, particularly for targeted delivery and improved therapeutic effects.

Conclusion: Lipid-based delivery mechanisms present a compelling approach for enhancing the bioavailability and therapeutic effectiveness of lipophilic nutrients. Nevertheless, additional investigation is requisite to tackle issues related to scalability, economic feasibility, and regulatory hurdles to comprehensively actualize their potential within the realms of nutraceuticals and individualized medicine.

Keywords: Bioavailability, Lipid based delivery systems, Liposomes, Micro/Nano-emulsions, Nanoparticles

INTRODUCTION

Dietary lipids are necessary macronutrients that not only provide us with energy as the most calorie dense macronutrient, but are also key mediators of overall human health and wellbeing. They play important roles in the absorption and function of fat-soluble vitamins (A, D, E, and K), carotenoids, and function in maintaining physiological functions, immunity, and cellular health. In addition, dietary lipids are known to be structural components of cell membrane to maintain its integrity and fluidity which is necessary for cellular signaling as well as functioning[1]. As metabolic disorders, cardiovascular diseases, and other chronic diseases are becoming increasingly common worldwide, the important health-preserving and disease-preventing role of dietary lipids merits recognition[2].

Lipid intake characterized by certain dietary patterns like Mediterranean diet has been shown widespread effect on health by better cardio-cerebrovascular health, decreased inflammation, and better metabolic profile[3]. The diet focuses on healthy sources of lipids such as omega-3 and omega-6 fatty acids, monounsaturated fat, and polyunsaturated fat from fish, nuts, olive oil, and seeds[4]. Excessive dietary lipid intake, especially of saturated and trans fats, has also been associated with unfavourable human health effects, such as higher levels of low-density lipoprotein (LDL), inflammation, and a variety of risks for obesity and type 2 diabetes[5].

Though essential, human beings face great barriers to the bioavailability of dietary lipids, due to factors including the hydrophobic characteristics of lipids, the instability of lipid structures during digestion, and the low stability of lipids to environmental factors (e.g. oxidation, heat)[6]. The majority of bioactive lipid compounds such as omega-3 fatty acids, carotenoids, and fat-soluble vitamins have low solubility in aqueous systems, which leads to low absorption from the gastrointestinal tract, degradation during storage as well as processing[7]. New strategies of lipid-based delivery systems (liposomes, nanoparticles, and micro/nanoemulsions) are created to overcome them. Such systems present a paradigm shift in ability to increase lipid-soluble compound solubility, stability, absorption, and to enable their targeted delivery and therapeutic potentials[8].

Biologically available compounds can be encapsulated with lipid-based delivery systems to provide a level of protection from degradation and help facilitate bioavailability. One of the most studied candidates as possible delivery vehicles for this route is liposomes (bilayers of phospholipids) due to their known ability to encapsulate lipid-soluble nutrients[9]. Similarly, lipid-based carriers such as nanoemulsions and solid lipid nanoparticles have greatly improved the use of omega-3s and carotenoids into functional foods[10]. This progress not only has enhanced the effectiveness of dietary lipids but also pioneered the opportunity of their application in personalized nutrition and precision medicine[11].

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By novel lipid-based delivery systems this review aims to provide an overview about the analytical relevance of dietary lipids in health and nutrition. It describes how they change their bioavailability, stability & absorption of lipid-soluble nutrients, focusing on their prevention & treatment of diseases. In addition, the limitations of these systems i.e. scalability, cost-effectiveness and regulatory challenges are discussed, followed by future perspectives on improving their application in nutraceuticals and in the field of functional foods. This study highlights the potential role of lipid-based delivery systems in overcoming these factors to facilitate the delivery of bioactive lipids and improve overall public health.

METHODOLOGY

In this review article, a systematic and comprehensive method was adopted to collate, analyze and synthesize up to date research on lipid-based delivery systems. A comprehensive literature search was performed on PubMed, Scopus, and Google Scholar with certain keywords: "lipid-based delivery systems", "bioavailability", "microemulsion", "nanoparticles", and "dietary lipids". Specific filters and Boolean operators were used to ensure relevant scientific literature that is most recent, high-quality, and peer-reviewed studies published within the last decade. We used strict National Institute of Health-Quality Assessment Criteria to select the studies. The review considered studies on lipid encapsulating technologies, their impact on bioavailability and their potential role as therapeutics for improved metabolic health. Excluded articles included articles that were non peer-reviewed, in a language other than English, or were related to dietary lipids or lipid delivery technologies that were unrelated to lipid-based drug delivery. The information extracted focused primarily on the methods of lipidic systems preparation (for example, high-pressure homogenization and nanoprecipitation) and the functional results of bioactive compounds in terms of solubility, uptake, and stability. It also analyzed some key challenges including scalability, cost-effective set up, and formulation stability. Finally, quality assessment of the studies included were conducted using validated tools such as CASP checklist for clinical trials, and AMSTAR guidelines for systematic reviews, resulting in accurate and reliable conclusions. These extracted data were subsequently organized into thematic areas based on delivery system innovations (e.g., liposomes, nano-emulsions, nanoparticles), clinical relevance, and potential for application as functional foods or nutraceuticals. Comparative system analysis revealed variability in system effectiveness relative to published patient outcomes, while also identifying opportunities for further research. The review employed a narrative synthesis and summarised key findings, challenges and opportunities in tables for an integrated overview of the space.

This method allowed a detailed and comprehensive review of the latest development on lipid anchorage systems and its application. The systematic search strategy employed for this review resulted in both a large number of relevant studies, in addition to providing the defined field of encapsulation technologies and effects on bioavailability that merited a detailed systematic review. Quality appraisal tools ensured the credibility of the findings and thematic categorization enhanced the systematic presentation of data. Such a strategy provided a snapshot of the current status of science and the feasibility of the systems based on lipids (e.g. scalability and cost) for production. Moreover, it paved the way for personalized nutrition and functional foods according to the bioactive lipids. The review demonstrated that the unification of research into one narrative might have great potential for enhancing therapeutic outcomes and supporting public health efforts via lipid-based delivery systems. This study is an important piece of the puzzle understanding lipid science, nutraceutical development and precision human nutrition and by being systematic in its design.

RESULTS

The review elucidates the considerable promise of lipid-based delivery systems (LBDS) in enhancing the bioavailability, solubility, and clinical utilization of lipid-soluble nutrients. Micro- and nano-emulsions were observed to significantly augment the solubility and absorption of hydrophobic bioactive compounds, including carotenoids. Nevertheless, their vulnerability to oxidative degradation and instability under certain environmental conditions presents constraints, which may be mitigated through the formulation of more stable delivery systems. Liposomes exhibited pronounced protective properties for delicate bioactive entities and facilitated effective nutrient transport. However, elevated production costs and challenges related to scalability persist as formidable obstacles, despite the potential for advancements in manufacturing that could yield more economically viable and targeted liposomal technologies.

Nanoparticles facilitate precise delivery mechanisms and enhance therapeutic efficacy while minimizing adverse effects; however, discrepancies in particle size and the complexities of production persist as barriers to achieving consistent outcomes. Dietary lipids, particularly omega-3 and omega-6 fatty acids, have been reaffirmed to provide significant metabolic and cardiovascular advantages. Nevertheless, individual metabolic variability, coupled with the excessive intake of detrimental fats, constrains their widespread applicability in the absence of tailored strategies. Ultimately, lipid-based nutraceuticals have been recognized as promising agents for the provision of superior nutrition and therapeutic benefits. However, the lack of adequate long-term safety data and prevailing regulatory ambiguities pose substantial challenges. In spite of these obstacles, the systems examined underscore considerable opportunities, including biofortification, the formulation of personalized nutrition regimens, and the growth of the nutraceutical market through the innovation of lipid-enriched functional foods.

Table I: Insights, Challenges, and Opportunities in Lipid-Based Delivery Systems for Nutrients and Therapeutic

Aspect	Key Insights	Challenges	Opportunities
Micro/Nano-emulsions[6]	Boost the bioavailability and solubility of lipid-soluble elements, such as carotenoids	Potential for oxidation and limited stability in specific circumstances	Creation of more stable formulations to extend their shelf life
Liposomes[4]	Prevent the deterioration of bioactive substances and enhance the delivery of nutrients	Expensive production costs and difficulties with large-scale manufacturing	More accurate targeting, cost-effective, scalable liposome production techniques
Nanoparticles[3]	Deliver medication precisely, enhance therapeutic results, and have few adverse consequences	Variability in size and cost, coupled with intricate manufacturing procedures, provide uneven outcomes	Therapeutic administration that is precisely tailored to particular tissues or cells
Dietary Lipids[7]	The benefits of omega-3 and omega-6 fatty acids for diabetes, inflammation, and cardiovascular health	Overconsumption of unhealthy fats, variability in individual lipid metabolism	Foods biofortified with healthy fats and customized nutrition plans
Lipid-Based Nutraceuticals[8]	Improved nutrition and therapeutic advantages are provided by lipid-based functional meals	Inadequate studies on the long-term consequences of consuming large amounts of fat and regulatory obstacles	Development of lipid-rich functional foods and expansion of the nutraceutical market

DISCUSSION

Lipid delivery systems have revolutionised dietary lipid (omega-3 fatty acids, carotenoids and vitamins) delivery, bioavailability, stability and functional attributes. Such evolutions have overcome significant pitfalls such as low solubility, instability, and narrow absorption spectrum of lipid-soluble compounds and offer innovative methods for nutritional and therapeutic functions[1,2]. Bioactive lipids can be emulsified with novel lipid-based delivery systems, including liposomes, nanoparticles, and micro/nanoemulsions, which can improve their solubility profiles and provide specific compartments and sites of action in the body[3,4]. These stable formulations — produced, e.g. by high-pressure homogenization, solvent evaporation or spontaneous emulsification — are capable of efficiently delivering the nutrients to their target tissues[5,6].

Enhancement of omega-3 fatty acids bioavailability are among the most mentioned benefits of these systems and such bioavailability improvement should suggest high potential use of these systems as treatments for metabolic disease, inflammation and cardiovascular diseases[7,8].

Liposomes are vesicles of phospholipids with dietary lipids that are protected from degradation via an optimized technique such as thin-film hydration or reverse-phase evaporation[9]. Likewise, nanoparticles that are formed upon emulsifting the lipid solutions in presence of surfactants, offer a relatively stable and more effective delivery strategy for lipid soluble nutrients with enhanced uptake[10,11]. In contrast, nanoemulsions are very efficient at improving solubility of hydrophobic compounds so they can be incorporated into functional foods and nutraceuticals[12,13].

Although highly efficacious, lipid-based delivery systems are limited by their stability, scalability and cost efficiency. Stability problems, especially during processing and storage, are still a major challenge since lipid formulations may easily degrade via oxidative degradation and phase separation under an unfavorable environment[14,15]. Besides, the steep synthesis expenses involved in sophisticated delivery methods such as liposomes and nanoparticles inhibit their bulk application, especially in the field of nutraceuticals[16,17]. These systems become more difficult to apply on a larger scale due to the variability in individual lipid metabolism, which is dependent upon factors such as genetics, physiology and diet[18].

Personalized medicine represents a promising approach to detail lipid-based therapies to individual metabolic profiles for improved results[19,20]. To illustrate, there is some evidence of the benefits of nanoemulsion-based omega-3 fatty acid formulations for decreasing inflammation and promoting lipid metabolism in metabolic syndrome[21,22]. Thus, studies that investigate the interaction of lipid-based delivery systems with gut microbiota are especially interesting as these systems can modulate the gut status affecting metabolic pathways at the systemic level[23].

The introduction of lipid-based delivery systems into nutraceuticals and functional foods might be an exciting opportunity to provide people with health-promoting dietary solutions in response to the increasing health consciousness of consumers. Encapsulated omega-3 fatty acids or carotenoids fortified foods can not only overcome the existing nutrient deficiency but also provide additional therapeutic advantages[24]. Such micro/nanoemulsions have been used to develop fortified beverages with improved storage and in vivo stability and bioavailability of lipophilic nutrients upon consumption.

Future studies will need to tackle the difficulties linked to such systems—namely, developing cheap and scalable production techniques. Solving these bottlenecks will mainly depend on innovations based on green synthesis techniques, biopolymers

and machine learning based approaches for optimization[25]. The widespread acceptance and approval of lipid-based delivery systems will also need some pre-defined protocols for assessment of safety, efficacy and stability.

Lipid-based delivery systems have the potential for revolutionising nutrition and medicine by improving the bioavailability and bioactivity of lipid soluble nutrients and bioactive compounds. Despite the promise of these agents, numerous hurdles must still be overcome before they can be fully realized, including formulation stability, high manufacturing costs, and interindividual differences in lipid metabolism. With the development of these systems and their continued advances, these systems will provide a foundational next step in the measures of precision nutrition, molecular medicine, and evolutionary vitamins by design of novel nutraceuticals and functional foods. The use of these technologies may eventually result in gains in public health by addressing both preventative and clinical lifestyle interventions for chronic diseases[26].

CONCLUSION

Lipid-based delivery mechanisms present a compelling approach for enhancing the bioavailability and therapeutic effectiveness of lipophilic nutrients. Nevertheless, additional investigation is requisite to tackle issues related to scalability, economic feasibility, and regulatory hurdles to comprehensively actualize their potential within the realms of nutraceuticals and individualized medicine.

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