USE OF NANOCARRIERS TO ORAL DELIVERY OF VITAMINS

Seniuk I.V., El Mehdi Tolbi, Benzid Yassine
National University of Pharmacy, Kharkiv, Ukraine

Introduction. Inclusion of bioactive agents using lipid nanocarriers is a major technique that is used for oral delivery of nutrient-grade ingredients, such as vitamins, antioxidants, and fatty acids [1]. Vitamins are essential organic micronutrients, many of which function as enzyme cofactors. Many people worldwide take dietary supplements with vitamins to prevent obesity, cardiovascular disorders, osteoporosis, skin aging, and various cancers. Vitamins can be classified as water-soluble or lipid-soluble. The water soluble vitamins are B_1 (thiamine), B_2 (riboflavin), B_3 (niacin), B_5 (pantothenic acid), B_6 (pyridoxal), B_7 (biotin), B_9 (folic acid), and B_{12} (cyanocobalamin), and C. The fat-soluble vitamins are A (retinol, retinal, and retinyl esters), D_2 (ergocalciferol), D_3 (cholecalciferol), E (tocopherol), K_1 (phylloquinone), and K_2 (menaquinone). In addition, these vitamins have many derivatives or analogs that have different bioactivities. The oral bioavailability of most vitamins is relatively low because of their low bioaccessibility, chemical instability, and poor GI absorption [2]. In addition to their low bioavailability, oral vitamins may have erratic absorption profiles, high intra- and inter-subject variations, and absorption that is not dose-dependent, all of which complicate oral administration. However, research in nanomedicine has led to the development of lipid nanocarriers that may improve the bioavailability of oral vitamins.

The aim of the study. To outline the pharmacokinetics of oral vitamins that are formulated using lipid-based nanoparticles.

Methods of research. A literature review has been carried out on modern methods of vitamin delivery.

Main results. Lipid-based nanodelivery systems, such as SEDDSs, nanoemulsions, microemulsions, SLNs, and NLCs, have great promise as oral vehicles for the delivery of bioactive agents because they can increase the solubility and improve bioavailability. Thus, many researchers have examined the effect of lipid nanocarriers on pharmacological or bioactive efficacy, adverse effects that are associated with conventional formulations, and compliance by patients and consumers. The ingredients of lipid nanoparticles include bioactive compounds, lipids, surfactants, aqueous solvents, and cosolvents, and the excipients are usually biocompatible and less toxic to the human body [3].

Self-Emulsifying Drug Delivery Systems (SEDDSs) are the most commonly employed lipid nanocarriers that are used to enhance the oral absorption of vitamins. A SEDDS consists of an anhydrous isotropic mixture of oil, emulsifier, coemulsifier, solubilizer, and active ingredient, in which spontaneously created o/w nanoemulsions or microemulsions with diameters below 300 nm form upon dilution with water under gentle agitation. Their unique ability of self-assembly in the GI fluid makes the drug or nutrient available as nanosized oil droplets, and the high interfacial surface area improves dissolution in the GI environment (**Fig. 1**) [4].

SEDDSs are the most widely used lipid nanoparticles used to improve the oral absorption of vitamins. The self-assembly of nanosystems makes them attractive for the engineering of nanomedicines with distinct physicochemical properties, and

greatly simplifies the optimization of formulations. Previous research examined the use of SEDDSs for oral delivery of five nutraceuticals with poor water solubility (vitamin A, vitamin K_2, coenzyme Q_{10}, resveratrol, and quercetin) [5, 6, 7]. The researchers optimized the formulations to fill gelatin capsules. A dispersion test indicated that all formulations containing nutrients dispersed spontaneously to form microemulsions, with droplet diameter of 25 to 200 nm. For example, vitamin K_2-loaded nanocarriers had an average diameter of about 40 nm [8]. Thus, the development of such formulations is a feasible approach to improve the oral absorption of nutraceuticals with low solubility.

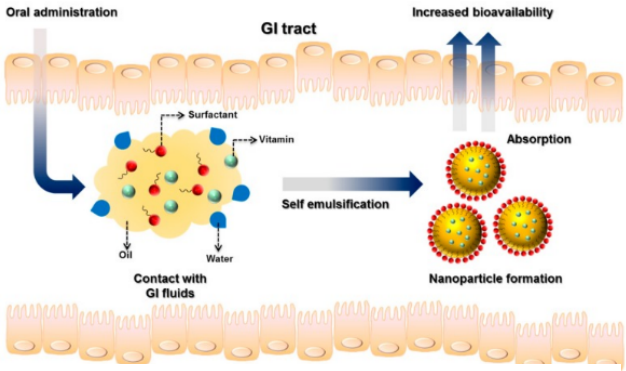

Figure 1. Formation of SEDDSs in the gastrointestinal tract.

Conclusions. When designing different formulations to improve the bioavailability of an oral vitamin, it is essential that the carrier stabilizes the vitamin and improves its transport into circulation. The use of lipid nanoparticles has numerous advantages over conventional formulations for dosing of vitamins, because they are more stable, they can provide sustained release, they can target different tissues, and they provide increased bioavailability. Some important limitations of conventional formulations, such as low solubility and poor epithelium permeation, can also be resolved by the use of lipid nanocarriers. Self-assembled lipid nanoparticles are frequently utilized to improve the oral delivery of vitamins. The type of emulsifier, particle size, interfacial composition, and vitamin concentration are the major factors that impact oral absorption. In the near future, it may be possible to extend the use of lipid nanoparticles by using them as vehicles for other functional nutrients.

References

1. Kumar D.H.L., Sarkar P. (2018) Encapsulation of bioactive compounds using nanoemulsions. Environ. Chem. Lett. 16:59-70.
2. Lopes C.M. et al. (2010) Nanoparticulate carriers (NPC) for oral pharmaceutics and nutraceutics. Pharmazie. 65:75-82.
3. Weber S. et al. (2014) Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for pulmonary application: A review of the state of the art. Eur. J. Pharm. Biopharm. 86:7-22.
4. Pathak K., Raghuvanshi S. (2015) Oral bioavailability: Issues and solutions via nanoformulations. Clin. Pharmacokinet. 54:325-357.
5. Beloqui A. et al. (2016) Nanostructured lipid carriers: Promising drug delivery systems for future clinics. Nanomed. Nanotechnol. Biol. Med. 12:143-161.
6. Tyagi P. et al. (2018) Oral peptide delivery: Translational challenges due to physiological effects. J. Control. Release. 287:167-176.
7. Shearer M.J., Okano T. (2018) Key pathways and regulators of vitamin K function and intermediary metabolism. Annu. Rev. Nutr. 38:127-151.
8. Van Hasselt P.M. et al. (2009) The influence of bile acids on the oral bioavailability of vitamin K encapsulated in polymeric micelles. J. Control. Release. 133:161–168.