NANOLIPOSOMES AS A SMART DELIVERY SYSTEM OF NUTRACEUTICAL SUPPLEMENTS

Elwira Lasoń*

Department of Chemical Engineering and
Technology, Cracow University of Technology,
Warszawska 24, 31-155 Krakow, Poland
*e-mail: elwira.lason@pk.edu.pl

Abstract

Numerous essential nutraceuticals have poor oral bioavailability, which significantly reduces their effectiveness as health-promoting agents. Different nanoparticles can be used to produce delivery systems that enhance oral bioavailability through a number of mechanisms such as improving nutraceutical solubility in intestinal fluids, increasing nutraceutical stability in foods and the gastrointestinal tract, or facilitating nutraceutical absorption. Nanoliposomes are a category of nanoparticles that, used in various fields from pharmaceuticals to food and cosmetics, have become the subject of growing interest in the field of nanotechnology. In the health industry, they are especially used as ingredients in the manufacturing process. Nanoliposomes were mainly incorporated into food products to improve the texture, taste, and smell of certain flavours, however, research suggests a promising future for the use of these lipid nanostructures in nutraceutical applications. One of the main advantages of using them in the nutraceutical industries is the fact that they can enrich food and beverages with bioactive substances without negatively affecting the sensory characteristics of the original product. Moreover, the nanometric size of nanoliposomes makes them transparent, which is very useful for fortifying clear drinks with hydrophobic nutraceuticals or those with an undesirable taste or odour. Therefore, the use of nanoliposomes can be extended to the nutraceutical field by functionalizing them with bioactive compounds known for their health and beauty benefits.

Keywords: *nanomaterials, nanoliposomes, nutraceuticals, targeted delivery, encapsulation*

Introduction

Based on current knowledge about successful applications of liposomes in the pharmaceutical and biomedical industries, scientists have started applying this type of vehicle for the encapsulation and controlled delivery of nutraceuticals. Distinguishing nutraceuticals from dietary supplements is not always simple and often leads to consumer confusion, therefore, some general information about nutraceuticals must be pointed out.

Nutraceuticals are defined as nutrient and non-nutrient compounds in food that have health-promoting, disease-preventive, or medicinal properties. The most popular nutraceuticals are compounds derived from whole foods, usually vegetables and fruits, with anti-oxidant or anti-inflammatory properties, which are suggested to provide protection against chronic diseases. They can be isolated and purified to make a dietary supplement or added to a processed food to increase the amount of nutrients and non-nutrient compounds in the diet [1,2].

In turn, dietary supplements are defined as products that are consumed together with the regular diet to provide additional health-prompting nutrients, which contain dietary ingredients including vitamins, minerals, amino acids, herbs, and botanicals. Dietary supplements are usually ingested in the form of capsules, tablets, liquids or powder form, and are labelled as being supplements [3].

In fact, the definition "nutraceutical" is derived from the combination of the words "nutrition" and "pharmaceutical" and was established by Stephen DeFelice in 1989. According to DeFelice, founder and chairman of the Foundation for Innovation in Medicine (FIM), nutraceuticals can be used to improve health, delay the ageing process, prevent chronic diseases such as obesity, increase life expectancy, or support the physique or function of the body [4,5].

Currently, nutraceuticals are of great interest due to their nutritional potential, safety, and medicinal effects. Although nutraceuticals have shown promising results in the treatment of various complications, their uncontrolled use may not remain without side effects and therefore they should be strictly regulated as prescription drugs [6]. However, most nutraceuticals are not pharmaceutical drugs and are therefore treated as food [7]. The food sources used as nutraceuticals are all natural and can be classified as dietary fiber, prebiotics, probiotics, polyunsaturated fatty acids, minerals, amino acids and peptides, carotenoids, vitamins, phytochemicals, and species [8,9].

The nutraceutical industry, including nutritional supplements and natural, herbal products, is growing rapidly. It has been stated that the global nutraceutical market will reach $ 340 billion by the end of 2024, growing at a Compound Annual Growth Rate (CAGR) of 7.2% from 2016 to 2024 and the main market factors related to the significant development of this sector are: better healthcare, growing popularity for nutrition and increasing demand for nutraceuticals [10].

Employing nutraceuticals or dietary therapeutics as complementary medicines is called nutritional therapy thanks to its certain healing mechanisms. The health benefits of nutraceuticals are vast, ranging from antioxidant and anti-inflammatory action to reduce the risk of skin disorders or alleviate skin ageing in the case of skin health and beauty, to cardiovascular support and anticancer effect [11,12]. TABLE 1 provides some examples of nutraceutical compounds in food along with their health benefits.

[Engineering of Biomaterials 172 (2024) 09]

doi:10.34821/eng.biomat.172.2024.09

Submitted: 2024-09-19, Accepted: 2024-10-22, Published: 2024-10-24

TABLE 1. Examples of popular nutraceuticals in foods and their therapeutic benefits [7,11,13-16].

Nutraceutical	Food source	Health benefits
lycopene	carrots, tomatoes	cardiovascular support, anticancerogenic
lutein and zeaxanthin	parsley, spinach, kale, egg yolk, einkorn, corn	antioxidant, eye health issues, anticancerogenic
β-Carotene	carrots, pepper	antioxidant
sulfurophane and other glucosinolates	broccoli, cabbage, brussels sprouts, and cauliflower	anticancer
catechins, theaflavins, thearubigins	teas (green and black)	antioxidant, anticancer
long-chain omega-3 (n-3) fatty acids	fatty fish (salmon, mackerel) and fish oil, flax seed	anti-inflammatory, antiarthritic
lignans	flax seed, sesame	anti-inflammatory, antioxidant, anticancer
allicin and related sulfur-containing compounds	garlic	anti-inflammatory, anticancer, antihyperlipidemic
quercetin, anthocyanins, organosulfur compounds	onion	anticarcinogenic, antibiotic, anti-inflammatory, antidiabetic, cardioprotective
Isoflavones and soy protein	soybeans	anti-atherosclerotic, antihyperlipidemic
conjugated linoleic acid (CLA), lactoferrin	dairy foods, red meat	anti-obesity, anticancer, cardiovascular support
naringin, naringenin,	citrus fruits	anti-inflammatory, anticancer, hepatoprotective
piperine, zingerone	black pepper, ginger	hepatoprotective, anticancer,
diadzein, genistein, phytoestrogens	soybean, flax, lucerne, vegetables	bone health or osteoporosis, anticancerogenic, reduce menopause symptoms

To ensure consumer satisfaction, nutraceuticals and dietary supplements must satisfy several requirements. Long-term storage, stability during processing and after time, ease of incorporation, and effectiveness at low concentrations are the most common needs. That is why in the formulation of many pharmaceuticals, cosmeceuticals, and nutraceuticals, one of the most applied technologies is encapsulation. The protection of unstable nutraceutical compounds from degradation and activity loss has been studied extensively during the last few years, especially in microcapsule systems. Nevertheless, targeted controlled release can be achieved more efficiently by using nanoencapsulation techniques [17]. The amount of bioactive/nutraceutical compound required to exhibit a specific effect when encapsulated is much less than the amount of unencapsulated compound and this is very useful when dealing with expensive nutraceuticals. Reactive or sensitive ingredients such as omega-3 acids and antioxidants can be protected through encapsulation by nanocarrier systems like nanoliposomes [18].

Encapsulation of nutraceuticals in nanoliposomes

Generally, liposomes and nanoliposomes possess the same physical, structural, and thermodynamic properties that are determined by their components and suspension media. The phrase nanoliposome has been introduced to fully refer to nanoscale lipid vesicles, as liposome is a general expression covering many classes of lipid vesicles in the size range from tens nanometres to several micrometres. In comparison to liposomes, nanoliposomes provide more surface area and have the potential to increase solubility, improve bioavailability, and controlled release with precise targeting of the encapsulated ingredient. Both, liposomes and nanoliposomes require a contribution of energy when it comes to preparation technique, and due to the fact that they are dynamic structures with the tendency to aggregate, vesicles prepared in nanometric size ranges may become micrometric during storage. Nevertheless, nanoliposomes should have an acceptable stability profile to retain their size in the nanometric range [19].

The encapsulation of nutraceuticals in nanoliposomes can be achieved principally through two different mechanisms [20]:

I. passive encapsulation, where the bioactive compound is entrapped during the vesicle formation process;
II. active or remote loading, where bioactive compound is loaded into intact (preformed) vesicles.

The passive entrapment mechanism relies on the ability of nanoliposomes to capture a definite aqueous volume during capsule formation. For water-soluble ingredients, the encapsulation efficiency (EE) after passive entrapment is proportional to the aqueous volume enclosed by the nanoliposomes. On the other hand, it depends on the phospholipid concentration, lamellarity, and morphology of the vesicles. For less water-soluble ingredients or lipophilic compounds, which react with the lipid phase of the bilayer, EE will depend more on the phospholipid concentration and the type of nanoliposome preparation method [20].

In the case of a remote (active) loading mechanism, the bioactive ingredient is loaded in the preformed nanoliposome with an additional trans-membrane potential as the driving force [21]. Various chemical gradients can be used as an inflow driving force depending on the physicochemical properties of the bioactive ingredient. As an example, ammonium sulphate [22] and calcium acetate [23] are suitable for remote loading of weak bases and acids, respectively, while chemically modified β-cyclodextrins can be used as a novel remote loading approach to incorporate hydrophobic nutraceuticals like curcumin into liposomes [24].

Use of nanoliposomes for the targeted delivery of nutraceutical molecules

Nanoliposomes have several advantages that determine their use as vehicles of bioactive compounds, not only in nutraceuticals to improve their textural and organoleptic properties but also in the organism, by using the fusion properties of nanoliposomes to cell membranes. These vehicles have previously been used for a long time by food products consumed, including maternal milk containing liposomes. The difference with the nanoliposomes that require to be vectorized in the human body is the need to cross the intestinal barrier in order to reach the target cell or tissue [25].

Targetability is a very useful feature of liposomes and nanoliposomes. Targeting nutraceutical molecules to the site where their action is required *in vitro* or *in vivo* is necessary to achieve the appropriate concentration of bioactive ingredients at the target site for their optimal effectiveness. Appropriate and targeted release increases the efficacy of the nutraceuticals, expands the scope of their use, and ensures optimal dosage, thereby improving the profitability of the product. Two types of targeting encapsulated nanoliposome from the cell membrane can occur [20]. The first is active transport, which involves internalization through receptors on the cell surface [26] (e.g., by incorporation of antibodies). The second type of transfer is passive and occurs through the fusion of the lipid bilayer of nanoliposomes with cell membranes, which mainly involves nanoliposomes of smaller sizes [27] (e.g., targeting based on particle size).

The use of nanoliposomes for targeted active ingredient delivery has several advantages over direct conjugation of the targeting ligand to the therapeutic agent. The availability of functional groups for direct conjugation of the ligand to the therapeutic molecule may be limited, making the coupling chemistry problematic. In addition to this, when directly conjugated therapeutic agents are taken, generally only a single active molecule is delivered [28]. Meanwhile, multiple nutraceutical molecules can be delivered after internalization in a single nanoliposome. Undoubtedly, another great advantage of using nanoliposomes is the diversity of molecules that can be encapsulated. It can be hydrophobic molecules in the membrane of nanoliposomes, or hydrophilic molecules in the core or on the surface of nanoliposomes. Nanoliposomes can be given many functions by incorporating two types of bioactive molecules. As an example, Suntres and Shek proved that two antioxidants of different natures, α-tocopherol (hydrophilic) and glutathione (hydrophobic), could be integrated into a single liposomal vesicle [29].

Application of nanoliposomes in the nutraceutical supplements industry

Based on the successful applications of nanoliposomes in the biomedical pharmaceutical industries, researchers have begun to use nanoliposomes for the encapsulation and controlled delivery of nutraceuticals [30]. One of the main advantages of using this type of vesicles in the nutraceutical industries is the fact that they enable the enrichment of food and beverages with bioactive substances (e.g., omega fatty acids from fish) without negatively affecting the sensory characteristics of the original product [18]. The nanometric size of nanoliposomes makes them transparent which is very useful, for example, for fortifying clear drinks with hydrophobic nutraceuticals or those with an undesirable taste or odour [31]. Another unique advantage of nanoliposomes is that they can be produced using safe ingredients obtained from natural sources such as eggs, soy, or milk. Thus, they have the potential to obtain regulatory approval to be used in food-grade products [7]. Nanoliposome lipids used in nutraceuticals can be derived from animal or plant raw materials.

In the first case, marine fats are especially interesting because fatty fish such as salmon, mackerel, herring, tuna, and sardine are rich in omega-3 including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Plant sources, e.g., flax and chia, are rich sources of precursors to these fatty acids, including the essential fatty acids linoleic and alpha-linolenic acids, which cannot be synthesized in the organism. Omega-3 fatty acids play an important role in the functioning of the human body and have been used in the prevention of aging-related diseases, such as cardiovascular and neurodegenerative diseases, including Alzheimer's disease [32,33]. Some of the advantages of nanoliposome application in the area of nutraceutical supplements are shown in FIG. 1.

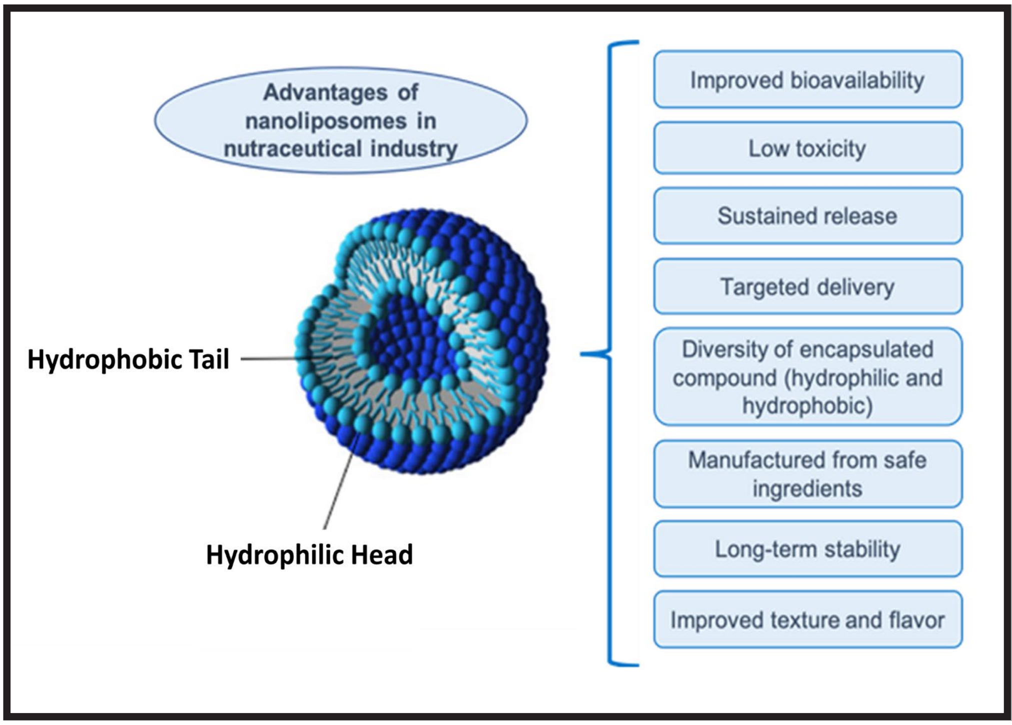

FIG. 1. Advantages of nanoliposomes application in the area of nutraceutical supplements.

Liposomes and nanoliposomes have attracted huge interest for their application in the nutraceutical industry. They are suitable for the encapsulation and delivery of carotenoids, so their effects are often studied in the case of these nutraceuticals [34,35]. Carotenoids have several potential health benefits, such as anti-inflammatory and anticancer effects, and are also beneficial in the treatment of age-related muscle degeneration and cataracts. However, as a nutraceutical, carotenoids are relatively unstable in food matrices and susceptible to light, oxygen, and auto-oxidation [36,37]. Tan and co-workers [34] successfully encapsulated carotenoids (lutein, β-carotene, lycopene, and canthaxanthin) in liposomal structures and investigated in vitro the interactions between carotenoid structure and concentration inside the vesicles and bioaccessibility. The greatest bioaccessibility was observed for lutein, followed by β-carotene, lycopene, and canthaxanthin. The same authors [35] studied the storage stability and in vitro release behaviour of carotenoids encapsulated in lipid vesicles in simulated gastrointestinal media. They observed that carotenoids exhibited different encapsulation efficiencies into the lipid vesicles, which were in the order of: lutein > β-carotene > lycopene > canthaxanthin. A similar trend for their antioxidant activity against lipid peroxidation during preparation was also observed. Release studies demonstrated that the lipid vesicles strongly retain β-carotene and lutein, in contrast to lycopene and canthaxanthin, where this effect was not observed [35]. Hamadou et al. [38] successfully created β-carotene-loaded nanoliposomes using phospholipids from eggs and marine animals as compositional components. Marine phospholipids were more effective for encapsulation than their counterparts. Nanoliposomes with a lower average size and polydispersity index, better ability to inhibit lipid peroxidation and better stability at 4°C for 70 days were also obtained from marine phospholipids [38].

Antioxidants are another class of nutraceuticals for which liposome encapsulation technology significantly improves their nutritional value. In vivo oxidation is different from that which affects the lipids in our food products. Reactive oxygen species (ROS) are produced by leukocytes and play a role in cell signalling and bacterial defence. They are usually metabolized and removed by antioxidant control mechanisms. Still, approximately 1% of ROS escape these mechanisms and poses a risk of damaging surrounding tissues and accelerating cell ageing [39]. Several studies have demonstrated the use of antioxidants in the prevention of age-related diseases, including Alzheimer [25]. Wenzel et al. [40] have shown in their in vitro study the positive effects of antioxidant (trans-resveratrol) on oxidative stress when injected in large concentrations, but the same assays on animals or humans performed in vivo show considerably reduced effects than expected [40]. This could be caused by the low bioavailability of the antioxidant, including difficulty in crossing cell membranes, and rapid elimination from the bloodstream without reaching the damaged target tissue. For this reason, targeted delivery via nanoliposomes is required to reach the desired tissue.

Nanoliposomes can be used to encapsulate both hydrophilic and hydrophobic compounds and therefore may be suitable for encapsulating antioxidants for targeted effects. An example of such an antioxidant is curcumin, known for its anti-inflammatory, chemoprotective, and anticancer properties and its effects on Alzheimer's disease. Since curcumin is hydrophobic and has very low solubility in aqueous solutions, its encapsulation in nanoliposomes has been shown to improve the bioavailability of this nutraceutical [41]. Another interesting nutraceutical - allicin, was also successfully encapsulated in nanoliposomes using the reverse phase evaporation process and sonication. Allicin, extracted from fresh garlic, has been studied for its effects on lipoprotein homeostasis, inflammatory and oxidative stress, and the prevention of arteriosclerosis [42].

Nanoliposomes are suitable nanocarriers for improving the stability and therapeutic potential of betanin. Betanin is a natural bioactive compound with anti-diabetic effects and high antioxidant activity. Betanin-loaded nanoliposomes revealed a relatively good sustained release profile in the simulated gastric and intestinal fluids. *In vitro* digestion stability of betanin and its antioxidant activity were significantly improved by liposomal encapsulation [43].

In other studies, an example of the bifunctional nanoliposomal antioxidant formulation containing ascorbic acid (vitamin C) and α-tocopherol (vitamin E) has been presented [44,45]. As nanoliposomes are able to incorporate and deliver both vitamin E and vitamin C to a site of action, they provide a synergistic effect. Since oxidation occurs first at the water/oil interface, if the nanoliposome is located at this interface, the α-tocopherol in the membrane can reduce the peroxy radicals before the radicals initiate oxidation. Ascorbic acid entrapped in the aqueous regions of the nanoliposome can regenerate α-tocopherol [44].

Hydrophilic compounds such as green tea catechins were also successfully encapsulated in nanoliposomes [46]. Encapsulation efficiency (EE) was over 70%, but the size of the vesicles increased significantly upon encapsulation of catechins. The formulation was added to milk during low-fat hard cheese production and almost no catechin was lost in the whey [46].

Liposomal nutraceuticals and appropriate claims

The claims regarding health benefits and commercialization of nanoliposomes may involve both well-being benefits and disease prevention. These claims can be attributed to the fatty acid composition of nanoliposomes, including omega-3 fatty acids and other polyunsaturated fatty acids, as well as the encapsulated nutraceutical compound [23]. The claims may be general in nature, based on known literature or established results, or may be based on specific health claims made by the company, known as an "exclusive promise". This statement must be substantiated by solid evidence, and only the creators have the exclusive right to use this claim. It is not obligatory to use any claim, but then other means of communication must be used, such as citing research to promote sustainable nutraceuticals and demonstrate the health benefits of prepared omega-3 fatty acid rich nanoliposomes from naturally sourced marine by-products [25,47].

Conclusions

The enormous potential of nanoliposome delivery systems is rapidly being discovered in nutraceutical industries, and especially in light of global health problems, its use for effective disease prevention and health promotion is necessary and unpreventable. The knowledge and experience gained in this field illustrate the potential application of these lipid nanostructures in nutraceutical approaches, where nanoliposomes as natural vesicles can be used and modified to improve tissue accessibility to deliver bioactive compounds with known health and beauty benefits. There is no doubt that diverse uses of nanoliposomes and their applications offer new perspectives for encapsulation and nutraceutical delivery.

Statement

This paper did not receive a specific grant from any funding agency in the public, commercial, or non-profit sectors.

References

[1] Camire M.E., Childs N., Hasler C.M., Pike L.M., Shahidi F., Watkins B.A.: Nutraceuticals for Health Promotion and Disease Prevention. Council for Agricultural Science and Technology 24 (2003) 1-6.

[2] Ronis M.J.J., Pedersen K.B., Watt J.: Adverse Effects of Nutraceuticals and Dietary Supplements. Annu Rev Pharmacol Toxicol. 58 (2018) 583-601.

[3] Mukherjee P.K., Harwansh R.K., Bahadur S., Duraipandiyan V., Al-Dhabi N.A.: Factors to Consider in Development of Nutraceutical and Dietary Supplements. Pharmacognosy 34 (2017) 653-661.

[4] Brower V.: Nutraceuticals: Poised for a healthy slice of the healthcare market? Nat. Biotechnol. 16 (1998) 728-731.

[5] Kalra E.K.: Nutraceutical-definition and introduction. AAPS PharmSci. 5 (2003) E25.

[6] Pérez-Sánchez A., Barrajón-Catalán E., Herranz-López M., Micol V.: Nutraceuticals for Skin Care: A Comprehensive Re-view of Human Clinical Studies. Nutrients 10(4) (2018) 403.

[7] Khorasani S., Danaei M., Mozafari M.R.: Nanoliposome technology for the food and nutraceutical industries. Trends in Food Science & Technology 79 (2018) 106.

[8] Das L., Bhaumik E., Raychaudhuri U., Chakraborty R.: Role of nutraceuticals in human health. J. Food Sci. Technol. 49 (2012) 173-183.

[9] Chavez-Mendoza C., Sanchez E.: Bioactive compounds from mexican varieties of the common bean (Phaseolus vulgaris): Implications for health. Molecules 22 (2017).

[10] Variant Market Research. Available online: https://www.variantmarketresearch.com/report-categories/food-beverages/nutraceuticals-market/ (accessed on 4 Sept. 2024).

[11] Shinde N., Bangar B., Deshmukh S., Kumbhar P.: Nutraceuticals: A Review on current status. Research J. Pharm. and Tech. 7(1) (2014) 110-113.

[12] Boelsma E., Hendriks H.F., Roza L.: Nutritional skin care: Health effects of micronutrients and fatty acids. Am. J. Clin. Nutr. 73, (2001) 853-864.

[13] Sarin R., Sharma M., Singh R., Kumar S.: Nutraceuticals: Review, International Research Journal Pharmacy 3(4) (2012) 95-99.

[14] Abdel-Aal el-S.M., Akhtar H., Zaheer K., Ali R.: Dietary sources of lutein and zeaxanthin carotenoids and their role in eye health. Nutrients. 5(4) (2013) 1169-85.

[15] Conaway C.C., Getahun S.M., Liebes L.L., Pusateri D.J., Topham D.K., Botero-Omary M., Chung F.L.: Disposition of glucosinolates and sulforaphane in humans after ingestion of steamed and fresh broccoli. Nutr Cancer. 38(2) (2000) 168-178.

[16] Rodríguez-García C.; Sánchez-Quesada C.; Toledo E.; Delgado-Rodríguez M.; Gaforio J.J.: Naturally Lignan-Rich Foods: A Dietary Tool for Health Promotion? Molecules 24 (2019) 917.

[17] Mozafari M.R., Flanagan J., Matia-Merino L., Awati A., Omri A.W., Suntres Z.E., Singh H.: Recent trends in the li-pid-based nanoencapsulation of antioxidants and their role in foods. Journal of the Science of Food and Agriculture 86(13) (2006) 2038-2045.

[18] Rasti B., Erfanian A., Selamat J.: Novel nanoliposomal encapsulated omega-3 fatty acids and their applications in food. Food Chemistry 230 (2017) 690.

[19] Mozafari M.R., Mortazavi S.M., Nanoliposomes: From fundamentals to recent developments, Trafford Pub. Ltd., Oxford, 2005.

[20] Maherani B., Arab-Tehrany E., Mozafari M.R., Gaiani C., Linder M.: Liposomes: A Review of Manufacturing Techniques and Targeting Strategies. Current Nanoscience 7(3) (2011) 436-452.

[21] Zhang W., Wang G., Falconer J.R., Baguley B.C., Shaw J.P., Liu J., Xu H., See E., Sun J., Aa J., Wu Z.: Strategies to maximize liposomal drug loading for a poorly water-soluble anticancer drug. Pharm Res. 32(4) (2015) 1451-1461.

[22] Bolotin E.M., Cohen R., Bar L.K., Emanuel N., Ninio S., Barenholz Y., Lasič D.D.: Ammonium Sulfate Gradients for Efficient and Stable Remote Loading of Amphipathic Weak Bases into Liposomes and Ligandoliposomes. Journal of Liposome Research 4 (1994) 455-479.

[23] Clerc S., Barenholz Y.: Loading of amphipathic weak acids into liposomes in response to transmembrane calcium acetate gradients. Biochimica et Biophysica Acta (BBA) - Biomembranes 1240(2) (1995) 257.

[24] Odeh F., Nsairat H., Alshaer W., Alsotari S., Buqaien R., Ismail S., Awidi A., Al Bawab A.: Remote loading of curcuminin-modified β-cyclodextrins into liposomes using a transmembrane pH gradient. RSC Adv. 9 (2019) 37148-37161.

[25] Bondu C., Yen F.T.: Nanoliposomes, from food industry to nutraceuticals: Interests and uses. Innovative Food Science and Emerging Technologies 81 (2022) 103140.

[26] Wang G., Wu B., Li Q., Chen S., Jin X., Liu Y., Zhou Z., Shen Y., Huang P.: Active Transportation of Liposome Enhances Tumor Accumulation, Penetration, and Therapeutic Efficacy. Small. 16(44) (2020) 2004172.

[27] Vieira A.M., Silvestre O.F., Silva B.F., Ferreira C.J., Lopes I., Gomes A.C., Sárria M.P.: pH-Sensitive Nanoliposomes for Passive and CXCR-4-Mediated Marine Yessotoxin Delivery for Cancer Therapy. Nanomedicine 17(10) (2022) 717-739.

[28] Aveling E., Zhou J., Lim Y., Mozafari M.R.: Targeting Lipidic Nanocarriers: Current Strategies and Problems. Pharmakeftiki 19 (2006) 101-109.

[29] Suntres Z.E., Shek P.N.: Alleviation of paraquat-induced lung injury by pretreatment with bifunctional liposomes containing alpha-tocopherol and glutathione. Biochem Pharmacol. 52(10) (1996) 1515-1520.

[30] Shukla S., Haldorai Y., Hwang S.K., Bajpai V.K., Huh Y.S., Han Y.K.: Current Demands for Food-Approved Liposome Nanoparticles in Food and Safety Sector. Front. Microbiol. 8 (2017) 1.

[31] Livney Y.D.: Nanostructured delivery systems in food: latest developments and potential future directions. Current Opinion in Food Science 3 (2015) 125.

[32] Wood A.H.R., Chappell H.F., Zulyniak M.A.: Dietary and supplemental long-chain omega-3 fatty acids as moderators of cognitive impairment and Alzheimer's disease. Eur J Nutr. 61(2) (2022) 589-604.

[33] Djuricic I., Calder P.C.: Beneficial Outcomes of Omega-6 and Omega-3 Polyunsaturated Fatty Acids on Human Health: An Update for 2021. Nutrients 13(7) (2021) 2421.

[34] Tan C., Zhang Y., Abbas S., Feng B., Zhang X., Xia S.: Modulation of the carotenoid bioaccessibility through liposomal encapsulation. Colloids Surf B Biointerfaces 123 (2014) 692-700.

[35] Tan C., Xue J., Abbas S., Feng B., Zhang X., Xia S.: Liposome as a delivery system for carotenoids: comparative antioxidant activity of carotenoids as measured by ferric reducing antioxidant power, DPPH assay and lipid peroxidation. J Agric Food Chem. 62(28) (2014) 6726-6735.

[36] Xianquan S., Shi J., Kakuda Y., Yueming J.: Stability of lycopene during food processing and storage. J Med Food 8(4) (2005) 413-422.

[37] Molteni C., La Motta C., Valoppi F.: Improving the Bioaccessibility and Bioavailability of Carotenoids by Means of Nanostructured Delivery Systems: A Comprehensive Review. Antioxidants 11 (2022) 1931.

[38] Hamadou A.H., Huang W.C., Xue C., Mao X.: Comparison of β-carotene loaded marine and egg phospholipids nanoliposomes. J. Food Eng. 283 (2020) 110055.

[39] Berger M.M.: Can Oxidative Damage Be Treated Nutritionally? Clinical Nutrition 24 (2005) 172-183.

[40] Wenzel E., Soldo T., Erbersdobler H., Somoza V.: Bioactivity and metabolism of trans-resveratrol orally administered to Wistar rats. Mol Nutr Food Res. 49(5) (2005) 482-494.

[41] Hasan M., Elkhoury K., Kahn C.J.F., Arab-Tehrany E., Linder M.: Preparation, Characterization, and Release Kinetics of Chitosan-Coated Nanoliposomes Encapsulating Curcumin in Simulated Environments. Molecules 24 (2019) 2023.

[42] Lu Q., Lu P.M., Piao J.H., Xu X.L.: Chen J., Zhu L., Jiang J.G.: Preparation and physicochemical characteristics of an allicin nanoliposome and its release behavior. Lebensmittel-Wissenschaft & Technologie 57 (2014) 686-695.

[43] Amjadi S., Abbasi M.M., Shokouhi B., Ghorbani M., Hamishehkar H.: Enhancement of therapeutic efficacy of betanin for diabetes treatment by liposomal nanocarriers. Journal of Functional Foods 59 (2019) 119.

[44] Chawda P.J., Shi J., Xue S., Quek S.Y.: Co-encapsulation of bioactives for food applications. Food Quality and Safety 1(4) (2017) 302-309.

[45] Niki E.: Role of vitamin E as a lipid-soluble peroxyl radical scavenger: in vitro and in vivo evidence. Free Radic Biol Med. 66 (2014) 3-12.

[46] Rashidinejad A., Birch E.J., Sun-Waterhouse D., Everett D.W.: Delivery of green tea catechin and epigallocatechin gallate in liposomes incorporated into low-fat hard cheese. Food Chem. 156 (2014) 176-183.

[47] Passeri E., Elkhoury K., Jiménez Garavito M.C., Desor F., Huguet M., Soligot-Hognon C., Linder M., Malaplate C., Yen F.T., Arab-Tehrany E.: Use of Active Salmon-Lecithin Nanoliposomes to Increase Polyunsaturated Fatty Acid Bioavailability in Cortical Neurons and Mice. Int. J. Mol. Sci. 22 (2021) 11859.