Biointerface Research in Applied Chemistry
Open-Access Journal (ISSN: 2069-5837)

Review
Volume 13, Issue 1, 2023, 51
https://doi.org/10.33263/BRIAC131.051

Nano Lipid Carrier in Augmenting the Bioavailability of Functional Bio-compounds

Amin Abbasi [1], Sahar Sabahi [2], Nayyer Shahbazi [3,*], Atefeh Karimi [4], Hasan Barkhordari [4]

[1] Student Research Committee, Department of Food Science and Technology, National Nutrition and Food Technology Research Institute, Faculty of Nutrition Science and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Department of Nutritional Sciences, School of Allied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[3] Department of Food Science, Faculty of Agriculture Engineering, Shahrood University of Technology, Shahrood, Iran
[4] Department of Food Safety and Hygiene, School of Public Health, Zanjan University of Medical Sciences, Zanjan, Iran
* Correspondence: nayer.shahbazi@gmail.com (N.S.);

Scopus Author ID 57217107334

Received: 12.11.2021; Accepted: 15.12.2021; Published: 30.01.2022

Abstract: Foods have a fundamental role in maintaining the health and well-being of the host, as well as functional foods, due to their unique inherent feature, have been considered in promoting nutritional value and biological properties. The present study aimed to review the role of encapsulation technology in removing the limitation of consumption of lipid-based functional foods by using the lipid-nanocarriers strategy. In the food industry, functional ingredients cannot be added directly to the food matrix to produce products that have acceptable sensory characteristics and desirable health benefits. Therefore, various technologies have been developed to improve aqueous solubility, protect against degradation and oxidation, and increase the bioavailability of functional lipid-based foods. In this respect, encapsulation technology is one of today's most applied technologies. This technology stabilizes functional compounds, prevents undesirable interactions in the food matrix, and plays a fundamental role in their effective transmission by food. Among the various strategies for encapsulation, lipid nanocarrier systems can be widely used. The encapsulation of functional lipid compounds by nanotechnology can, in addition to removing the limitation of adding these compounds in the food system, improve their oxidative stability, which in turn enhances the nutritional value of food, regulates release in the gastrointestinal tract, increases intestinal absorption, and develops functional food formulations. Consequently, play a significant role in establishing and promoting host health status.

Keywords: nanotechnology; functional foods; nanostructured lipid carrier; encapsulation.

1. Introduction

Functional bio-compounds include a wide range of nutrients such as vitamins, minerals, plant-derived constituents (polyphenols and carotenoids), prebiotics, probiotics, and postbiotics that play an effective role in disease prevention improve health status. With the passage of time and changes in the lifestyle, the demand of consumers also changes, and they choose foods that meet the basic needs of hunger and provide nutrients, increase the promotion of physical and mental health as well as prevent some chronic diseases, which reveal the importance of the functional foods [1-4]. Bioactive food compounds are known to be natural compounds that have biological activities and, in some cases, have significant nutritional value.

The results of studies indicated that these bio-compounds possess a wide range of biological functions, such as reducing the risk of acute/chronic diseases, establishing gut homeostasis, and maintaining health and safety in society. Food bioactive compounds can be divided into some categories, such as flavorings, odors, colors, and preservative agents. When added to food and beverage matrices in certain and standard amounts, can improve nutritional value and shelf life [5-7]. In this regard, lipid-based functional foods due to the presence of essential nutrients in high amounts, including unsaturated fatty acids (linoleic, linolenic, and oleic fatty acids) and also due to the clinical functions of these compounds in the combat against various cancers, obesity, diabetes, and cardiovascular diseases has always been the focus of nutritionists and food scientists. However, these lipophilic compounds have limited consumption in food systems due to low solubility in water, low bioavailability, high sensitivity to biologically harmful agents such as oxidation, non-combination with other hydrophilic compounds, or having an unpleasant taste [8,9].

On the other hand, several technologies have been developed to improve water solubility, protect against oxidation and increase bioavailability, which is one of the most widely used technologies is encapsulation [10-12]. Among the various strategies for encapsulating bioactive compounds, nanocarrier systems have been developed worldwide for the efficient delivery of lipophilic compounds. Nanoparticles with a particle size of fewer than 500 nanometers are suitable for use in the food industry. Due to their very small size, Nanoparticles do not block light transmission, have a low precipitation rate, and have higher bioavailability than larger particles [13-15]. Other benefits of nanoparticles include improved water solubility, increased shelf life, increased intestinal absorption, and controlled release [8,16,17].

In recent years, the use of liposome production technology has been investigated by many researchers in various fields of medicine and the food industry. Liposomes consist of two closed spherical layers separated from fluid regions. The structure of liposomes is similar to that of biological cell membranes. Hydrophobic groups are trapped toward each other, and hydrophilic groups are trapped around the material and accumulate around the liquid environment, forming lipid wells or liposomes [18]. In the structure of liposomes, mainly phospholipids and especially phosphatidylcholine are used as the most important phospholipid in eggs and soybeans. Due to the equal size of the head and tail, this compound creates a uniform structure in the liposome. The addition of cholesterol increases the stability and decreases the permeability of the liposome membrane. The presence of this compound causes the liposome structure to be more compact and the volume of the encapsulated material to be reduced. The presence of anionic compounds such as phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid, and cationic compounds such as diacetyl phosphate and phosphatidylethanolamine leads to electrostatic repulsion, reduction of accumulation, improvement of stability. As a result, more liposome is trapped inside the cheese clot [19-21]. Cheese is one of the oldest dairy products of human production, which has a special place in people's nutrition. With time, the desired aroma, taste, texture, and special therapeutic properties are created in the product. Depending on the type of cheese and its different characteristics, the ripening period of ripe cheeses in the world lasts from a few weeks to several months and even years [22]. The ripening process is a complex, lengthy and costly process. It is economically very important to shorten the ripening period of the cheese without damaging its aroma, taste, and texture [23].

Increasing the amount of lipase, protease, and peptidase enzymes into the cheesecloth is an effective key in accelerating the ripening of the cheese. However, non-uniform distribution and loss of enzymes in whey are among the most important problems of enzyme utilization [24]. Encapsulation of the mentioned enzymes is the solution to overcome this limitation. The first paper on the microencapsulation of enzymes in liposomes was published by Cesa and Wiseman in 1970. In this study, lysozyme microencapsulation in fat vesicles with changes in fat composition and a total load of fat vesicles was investigated [25,26]. The use of liposomes as carriers to transport enzymes protects the enzyme from abnormalities and controls the reaction rate between the enzyme and the substrate. This goal is pursued by microencapsulating proteolytic enzymes during cheese production [27]. When nanocarriers are added to food or carrier systems, they must be considered in terms of stability in food formulation, non-toxicity, biodegradability, and stability during food processes [28]. Among colloidal nanocarriers, Nanostructured Lipid Carrier (NLC) is one of the most suitable delivery systems due to its high encapsulation efficiency, acceptable physicochemical stability, and controlled release [29]. Studies in nanotechnology and the encapsulation of food compounds have led to the development of functional compounds and increased their health effects. While introducing the functional lipid compounds, the present review study surveys the different strategies for adding these compounds to the food matrix and the role of nanostructured lipid carriers in increasing the bioavailability of functional lipid compounds.

2. Lipid-based Functional Foods

The concept of nutraceuticals was coined in 1989 from a combination of the words "nutrition" and "pharmaceutical". Generally considered a food or part of a food that has physiological properties and valuable biological activity and can increase health or reduce the risk of disease, in addition, to having basic nutritional properties. They also have an effective role in the prevention or treatment of chronic diseases. Despite the urgent need, these substances are compounds that the host body cannot make. Their deficiency in the body also causes diseases such as learning disabilities, mental retardation, blindness, and premature death [30-32]. It is noteworthy that reducing dietary fat to create a healthy diet causes a lack of fat-soluble nutrients, including fat-soluble vitamins, antioxidants, and polyunsaturated fatty acids [33-35]. Therefore, to meet the body's need for essential nutrients and solve the resulting problems, low-fat and non-fat foods can be enriched with essential and valuable micronutrients. Enrichment is the addition of one or more essential micronutrients to foods at levels higher than naturally present in the food or not at all [36]. Functional components include a group of food compounds, including vitamins, bioactive peptides, minerals, phytochemicals (polyphenols and carotenoids), prebiotics, probiotics, and postbiotics, and is associated with disease prevention and health promotion [37,38].

On the other hand, most food-drug compounds cannot be added to foods and beverages in pure form due to their low solubility, sensitivity to degradation during the process, shelf life, digestion, and low bioavailability [39]. Therefore, to eliminate these disadvantages, encapsulation systems were created. The use of new encapsulation methods, solubility, resistance to oxidation and isomerization, and the bioavailability of fat-soluble vitamins and carotenoids, especially betacarotene, is significantly increased [28,40,41].

3. The Adding Strategy of Functional Compounds into the Food Matrix

3.1. Encapsulation of functional compounds.

Encapsulation is the process of trapping active agents within carriers. It is a useful tool for improving the delivery of bioactive substances (antioxidants, minerals, vitamins, phytosterols, lutein, fatty acids, and lycopene) and living cells (probiotics) through foods [42,43]. Encapsulation can be defined as the technology of packing liquid, solid and gaseous materials inside small capsules. These capsules release their contents in controlled amounts over long periods and under special conditions in the target areas [44,45]. This technique separates reactive materials from other food system components and controls their release [46,47]. The materials used in the design of the capsules' shell supporting must be edible, biodegradable, and create a barrier between the internal phase and the environment. Of all the substances, polysaccharides, proteins, and lipids have the widest range of uses in food encapsulation, which preserve the natural and intrinsic properties of the product [48]. The particles produced usually have a diameter of a few nanometers to a few hundred micrometers [19]. Micro/nanoencapsulation has been developed to create a boundary to prevent adverse chemical reactions and the controlled release of bioactive compounds, especially vitamins [49,50]. The diameter of the capsule in microencapsulation is 5-300 μm. Still, due to the reduction of particle size in nanoencapsulation, the surface-to-volume ratio increases, so the reactions are several times faster and also the optical properties and electrical of the material will change [51].

3.2. Novel approaches in the transmission of functional compounds.

Proper selection of the process, emulsifiers, and other used compounds is the most important factor in obtaining particles with the desired size and color for any type of application. Of course, accurate and correct process control is also necessary during the formulation process [52]. Nanosystems are divided into three groups based on wall material: lipid and surfactant-based nanocarriers, polysaccharide-based nanocarriers, and protein-based nanocarriers [53]. Lipid and surfactant-based nanocarriers are composed of the following materials: nanoliposomes, nanoemulsions, solid lipid nanoparticles (SLN), nanostructured lipid carriers, micelles, automated emulsion drug delivery system, and nanosuspension. Polysaccharide-based nanocarriers include polysaccharide nanoparticles and polysaccharide micelles. Protein-based nanocarriers also consist of casein micelles and various complex proteins such as albumin, gelatin, whey protein, soy protein, milk serum protein, and corn. Because each of these systems has specific advantages such as encapsulation efficiency, particle stability, aqueous solubility, oral uptake, and bioavailability, understanding the properties of core compounds and nanosystems is essential to designing the best lipophilic food-drugs delivery system (Table 1).

Table 1. Differences and similarities of different emulsions (macro-emulsion, micro-emulsion, and nanoemulsion).

Features	macro-emulsion	micro-emulsion	nanoemulsion
Appearance	Formulation dependent	Transparent	Transparent/Semi-transparent
Production methods	Normal homogenization	Low energy emulsification	High energy emulsification
Diameter size	0.5-100 micrometers	10-100 nanometers	20-200 nanometers
Thermodynamic stability	Unstable	Stable	Unstable (kinetically stable)

Dendrimers are a family of three-dimensional polymers and nano dimensions characterized in solution by a compact spherical structure. The word cascading molecules was used instead of a dendrimer, but the best word is "dendrimer". Although the origin of dendrimers can be thought of as linear polymers and then branched polymers, the amazing structural properties of dendrimers and macromolecules with many branches are quite different from traditional polymers' properties. Despite the use of polymers in drug delivery systems, dendrimers have more benefits than them. They have limited polydispersity and nanometer dimensions, making it easier to cross biological barriers [54]. Dendrimers can carry target molecules by receptors on their surface or encapsulate them in cavities between branches [55]. Unlike linear polymers, dendrimers are macromolecules that branch from one nucleus, and all branches eventually reach a central nucleus. In making dendrimers, their size and molecular mass can be precisely controlled. The presence of many terminal branches increases the solubility, miscibility, and reactivity of dendrimers. The solubility of dendrimers is strongly influenced by the nature of the surface groups, for example, the presence of hydrophilic groups causes the dendrimers to be soluble in polar solvents, and the hydrophobic terminal groups cause the dendrimers to be more soluble in non-polar solvents. The importance of dendrimers is characterized here that the therapeutic effectiveness of any drug depends on its good solubility in the body's aqueous environment. Many substances with strong therapeutic properties are available, but they are not used for therapeutic purposes because they are insoluble. Water-soluble dendrimers can bind to hydrophobic molecules with antifungal or antibacterial properties. There is a possibility of releasing the bound drug due to contact with the targeted living organisms, and therefore these complexes are considered drug delivery systems [56,57].

Recently, various cells such as monocytes, macrophages, erythrocytes, neutrophils, dendritic cells, and stem cells have been used as new drug carriers. Cellular drug delivery systems have several benefits: environmental compatibility, reduced immune stimulation, long and controlled half-life, and inherent targeting of inflamed, injured, and cancer cells. Mononuclear cells such as dendritic cells, monocytes, and macrophages have a strong tendency to swallow foreign material and collect damaged, inflamed, and cancerous cells. Cytokines released from these damaged parts, especially in the absence of oxygen, cause the uptake of monocytes and macrophages. These cells can also cross impermeable barriers, such as the blood-brain barrier. Therefore, these cells are very suitable for targeted drug delivery and to improve and enhance the effect of a drug without inducing immune reactions. Cells can typically be used for drug delivery in three ways. In the first method, drugs enter the cells in the form of endocytosis and are transported to the site of injury, placing drug molecules on the cell surface and its release after reaching the damaged tissue is the second method. The third approach is using genetically modified cells as biological plants that release therapeutic proteins at the site of injury [58,59].

3.3. NLC lipid nanocarriers.

The fast crystallization process reduces the solubility of the drug and leads to the ejection of the drug from the lipid nanoparticles, especially when the drug concentration in the nanosystem is very high. Most drugs have a higher solubility in liquid lipids than solid lipids. NLC is the same as modified SLN, and in the lipid phase, it contains both solid lipids (fat) and liquid lipids (oil) at room temperature [60]. NLC, or oil-loaded SLN, contains liquid lipid droplets that are partially crystallized and have a less regular or amorphous solid crystalline structure and was developed to overcome the limitations of SLN in the late 1990s [61] (Figure 1), (Table 2).

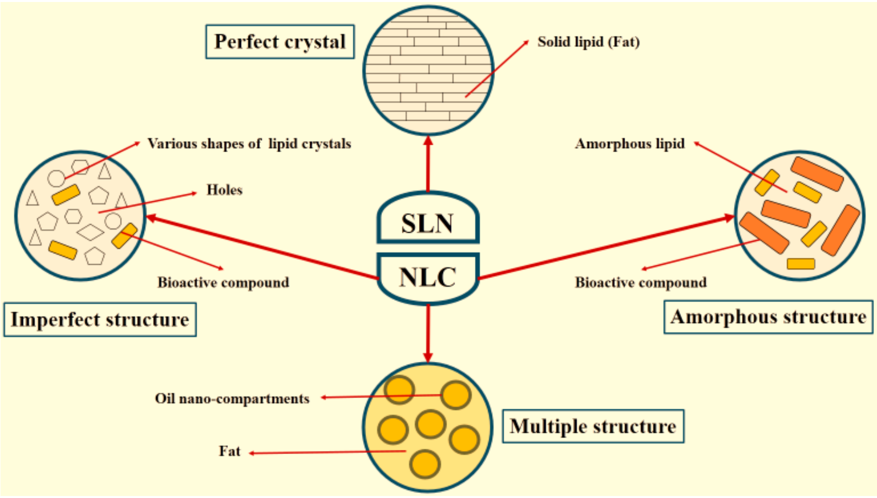

Figure 1. Schematic of the structure of different types of nanoformulations. Solid lipid nanoparticles (SLN) compared to lipid nanocarriers (NLC) (incomplete structure, irregular structure, multiple structures).

Table 2. Main components of NLC formulation.

Different types of NLC structure's components	
Liquid oil	Soybean oil, medium-chain triglycerides, capric acid, caprylic acid, oleic acid, alpha-tocopherol, vitamin E, corn oil, squalene
Solid lipids	Stearic acid, carnauba gum, glyceryl tristearate, tri-stearin, acetyl palmitate, glyceryl monocaprate, glyceryl palmitostearate, glyceryl behenate, propylene glycol monostearate
Surfactant/Emulsifier	Tween 80, lecithin, poloxamer 188, polyglyceryl-3-methyl glucose distearate, sodium dodecyl sulfate, sodium deoxycholate, tween 20

Among the advantages of using this type of structure is controlling and releasing active agents and vitamins and increasing the permeability of the stomach wall to pharmacological and nutritional factors [62,63]. Despite the presence of liquid oil, the structure of NLC at room temperature and body temperature are in the form of solid particles dispersed in the aqueous phase. Due to the incomplete crystal structure of lipids in NLC, it is expected that the space for placing the active compound in the lipid-oil mixture and the loading capacity will increase, and the release of the encapsulation compounds will decrease during the storage period. By replacing lipid lattice compounds, the release index of active compounds can be easily adjusted [64]. Much research has been done on the use of NLC in the food industry that includes the following: the production of lipid nanocarriers containing vitamin A palmitate [62], optimization of NLC formulations containing lutein [65], production of beta-carotene nanostructured lipid carriers using grape seed and squalene oil [66] and the production of nanostructured lipid carriers containing quercetin.

4. Application of Nanostructured Lipid Carriers to Increase the Bioavailability of Functional Compounds

Among various strategies for the effective delivery of lipophilic functional substances, the application of nanocarrier systems is becoming more widespread around the world. Due to their small size, these compounds improve aqueous solubility, increase shelf life in the gastrointestinal tract, improve physicochemical stability in the gastrointestinal tract, increase intestinal permeability, controllable release into the gastrointestinal tract, intracellular and intercellular release [8]. When nanocarriers are added to the food system, stability in food formulation, non-toxicity, biodegradability, and application in different food process systems should be considered [28]. Figure 2 shows the types of nanosystems used for the lipophilic functional compounds. Injectable application: SLN compounds are generally injected into a vein, muscle, or subcutaneously.

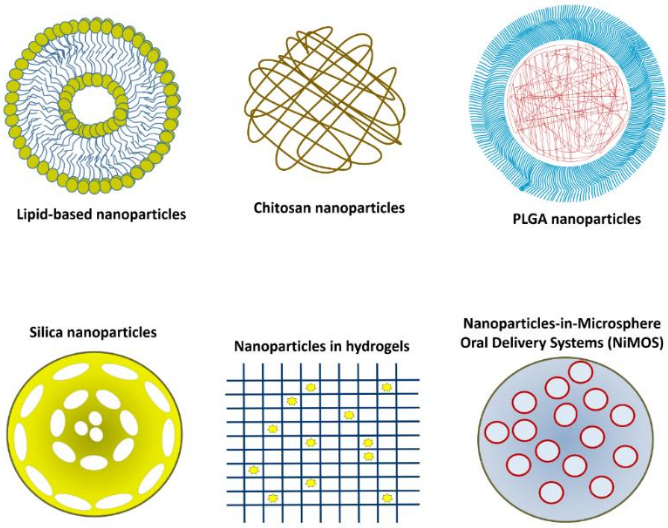

Figure 2. Different nanosystems for loading and transporting beneficial lipophilic compounds.

Because the particle size is less than one micrometer, these systems can be used with minimal risk of blood clots leading to embolism. The particle size for intravenous injection should be less than five micrometers to prevent embolism [67]. Oral application: the use of these systems is very effective because of their ability to regulate drug release as it passes through various parts of the gastrointestinal tract and protects against the chemical breakdown of drugs prepared for bile, such as peptide drugs. According to reports, the release of the drug in the laboratory lasted from a few minutes to 7 weeks. Decomposition of SLN prepared with the wax matrix is slower than glyceride matrices [68]. Oral application of lipid nanoparticles can be in tablets, pellets, or capsules. Due to the stomach conditions (the presence of acid and strong ionic force), the environment will be suitable for the accumulation of particles. Food is also expected to have a significant effect on the performance of lipid nanoparticles, although there are insufficient valid data in this regard. Unfortunately, few studies have been performed on the effect of gastric and pancreatic lipase on the in vivo breakdown of nanoparticles [69]. Respiratory application: Liu *et al*. In 2008, by loading insulin into the SLN, they introduced it as a carrier for respiratory application and systemic transport of proteins [70]. Topical application: SLN lipid nanoparticles, due to their physiological or degradable fats, are considered as high tolerance carrier systems for dermal applications potential of lipid nanoparticles is proven in targeting the skin, controlling its release, reducing skin side effects, and protecting active compounds. It has been shown that the small particle size in lipid nanoparticles improves the presence of nanoparticles in direct contact with the stratum corneum and ensures the entry of encapsulated agents into the skin [71].

5. Potential Application of Lipid Nanosystems in the Production of Functional Foods

The application of nanotechnology in various aspects of food science has accelerated at the beginning of the third millennium [72]. The potential benefits of using nanotechnology in food science include many aspects, including packaging materials, effective nutrient release systems, Improved bioavailability formulations, and new tools in cell-molecular biology [73]. Nanotechnology in food processing means the encapsulation of active and nutrient compounds with nano- and micro-sized edible coating and these particles into food matrices. Nanosystems have several advantages over macro systems. Nanocarriers appear to be single-component, thermodynamically stable or show long-term kinetic stability. These systems have a higher level and potentially improve the solubility and bioavailability of bioactive materials. Finally, nano delivery systems enhance controlled release and improve the targeting of encapsulated food components [74]. In the scientific literature, a range of approximately larger than 600 nanometers has also been reported for nanocarriers. Systems containing 600-nanometer particles in the human gastrointestinal tract have similar effects to 1-100 nm particles. Nanocarrier systems have valuable aspects in nanotechnology in functional compounds, cosmetics, and the food industry. These systems are generally divided into two groups: polymer systems and fat-based systems. Due to the toxicity of polymers and the lack of optimal large-scale production methods, low acceptance of desirable biopolymers, and the need to use organic solvents, the amount of products offered is limited compared to the past. In addition, most bioactive compounds (fatty acids, carotenoids, tocopherols, flavonoids, polyphenols, fat-soluble vitamins, and functional compounds), flavorings, and preservatives are hydrophobic. The most desirable colloidal dispersions in the aqueous environment (type of oil in water) are required to encapsulate lipophilic compounds. Also, the presence of digestible lipids facilitates the absorption of bioactive compounds in the small intestine because these lipids increase the number of mixed micelles available, which leads to the dissolution and transfer of more hydrophobic compounds [75]. A study on the effect of bacterial and fungal proteases encapsulated in liposomes on cheddar ripening showed that tissue improvement and proteolysis in cheese occur faster than in the control sample. Observation of the electron microstructure performed using a transmission electron microscope showed that the microstructure of cheeses containing liposomes was less compact. The liposomes were located on the common surface of casein fat. The study of the peptide pattern showed that bitter and astringent peptides accumulated in cheddar cheeses derived from protease-containing liposomes, and their amount depends on the type and concentration of enzyme added. Investigation of organoleptic properties during the ripening period of cheese reveals that the aroma and flavor of all cheese samples improved, and no bitterness and bad taste (except in cases where the enzyme concentration is high) was observed during the three months ripening period [76]. During the ripening of cheddar cheese, a part of the enzyme is removed from the liposome by destroying some liposomes, and depending on the type of enzyme and its concentration, the ripening of the cheese intensifies. Therefore, according to the ripening time of cheese, casein and high molecular weight peptides are broken down into water-soluble peptides and then converted into small peptides and amino acids. As a result, all indicators of proteolysis depth increase. Although the amount of compounds that make up the astringent taste is zero at the beginning, during the ripening of the cheese, the amount of these compounds increases and its amount in cheeses containing liposomes containing the enzyme and the control sample is similar to each other. It is noteworthy that these compounds depend on the amount of enzyme added. By developing the appropriate concentration of the enzyme, the development of compounds that cause astringent taste can be controlled. However, due to the acceleration of proteolysis in cheddar cheeses with liposomes containing enzymes, the amount of compounds that cause bitter taste is more than the control. During the first two months, the amount of these compounds increases and then decreases [77]. Salminen *et al*. have investigated the potential of saponins extracted from Quillaja Saponaria to replace yolk salts in surfactant formulations to increase the physical and oxidative stability of omega-3 NLC carriers. The results showed that omega-3 encapsulation by the NLC method reduced the formation of lipid hydroperoxides, propanal, and hexanal by 72, 53, and 57%, respectively, compared to emulsion fish oil in water (without encapsulation) [78]. Therefore, much attention has been focused on lipid-based nanocarriers, including nanoemulsions, liposomes, solid lipid nanocarriers (SLN), and nanostructured lipid carriers (NLC). In this regard, NLC has advantages over other lipid nanocarriers under certain conditions. The historical development of colloidal carrier systems is shown in figure 3. These lipid nanoparticles have sizes of 40 to 1000 nm, are spherical, and consist of solid lipid phase and surfactant. Dispersed phase, solid fat, and surfactant are used as emulsifiers.

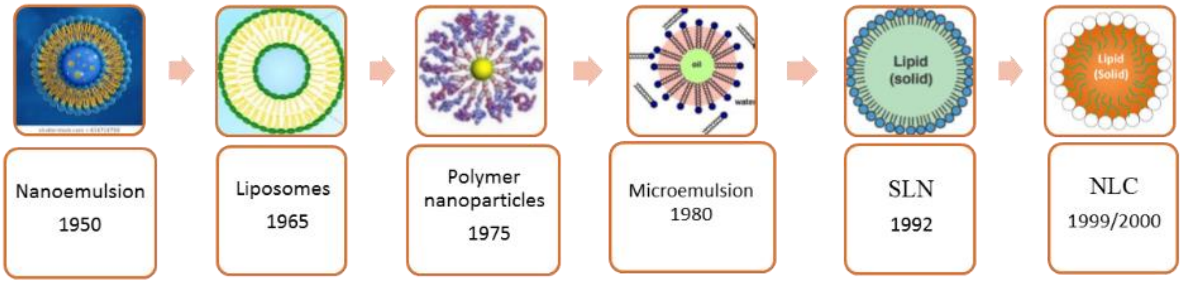

Figure 3. Diagram of the historical progress of colloidal carrier systems.

6. Advantages of Using Lipid Nanocarriers

The use of nanocarriers in enriching foods with beneficial compounds such as fat-soluble vitamins (A, D, E, K), which have known effects in reducing the risk of chronic diseases, can be done with high efficiency. Numerous other benefits include control of release at a specific location and time, stability of the encapsulation product against light, heat, and oxygen during the process and storage within the food matrix, increased solubility of hydrophobic compounds in an aqueous environment such as beverages and low-fat milk and bioavailability have them higher [79]. This technique is used in various fields of the food industry, pharmacy, and cosmetics. Food applications include the following: achieving a uniform color in food, inhibiting pH change, changing ionic strength and extreme temperatures, encapsulating flavors or odors, and separating reactive species from each other. In addition, while nanoencapsulation increases the dispersibility and distribution of water-insoluble compounds, it should not affect the product's sensory properties, color, and taste [80]. Preservation of the encapsulated compound during the process of transfer to the food and during storage should be at the highest level, and against the amount of release in the place of absorption should be optimal. For the transmission systems (drug, food, and genes) to be effective, the encapsulation compounds must be made from natural materials, inexpensive, nanoscale, prevent premature decomposition, and in terms of safety and health, should be generally recognized as safe. Release systems must be compatible with other compounds in the system in terms of physicochemical and qualitative properties of the final product (appearance, texture, taste, and shelf life). The important point is that in nanotechnology, the small particle size is desired and the change in the intrinsic properties of the particle along with the change in its size should be considered [81]. The NLC formulation aims to produce particles embedded in solid lipid oil, which increases the loading capacity and controls the release of the functional compounds. In this case, the effective substance is dissolved in the oil and simultaneously encapsulated by solid lipids [82]. The lipid mixture in NLC has a slower polymorphic transfer and a lower crystallization coefficient. In addition to the presence of oil in the NLC core, the improvement in these properties may be due to the spherical shape of the particles. Thus NLC may increase encapsulation efficiency, loading of functional compounds, and physical stability. NLC appears to be a valuable choice for improving chemical stability, bioavailability, and controlled release of lipid-friendly functional compounds in food matrices. NLC immobilizes biomolecules in a solid particle matrix and protects bioactive compounds against degradation [83]. As a physical barrier, the lipid matrix may protect encapsulated sensitive active compounds from destructive agents in the aqueous phase. NLC is a new system for controlled release in the food entry phase.

7. Conclusion

The present study considers a new field of research in lipid nanocarriers with a limited number of articles in this field. The information extracted for this study is extracted from 30 articles in line with the purpose of the study. Using nanotechnology, it is possible to make changes in food, add the desired additives in very small sizes and manipulate the physical contents of food. As a result, the quality of food and digestion and absorption of food in the body is improved, and new products are obtained in different flavors and colors. Also, for effective intestinal delivery and absorption and increasing the bioavailability and stability against oxidation of functional lipid foods, the microencapsulation method is the most efficient method, which also preserves the natural and intrinsic properties of the product over time. One nanoscale lipid carrier is NLCs, which have many advantages over other colloidal carriers. High-pressure hot homogenization, as well as high shear force, is the most common method for the production and preparation of lipid nanocarriers. The position of the active compound in nanostructured lipid carriers is different. This difference is mainly due to the composition of the formulation components, such as the chemical nature of the formulation components, lipids, surfactants, and the manufacturing method. Medium-chain triglycerides and oleic acid are the most commonly used oils in the production of NLC, and the most common solid lipids used in the preparation of NLC are glyceryl behenate glyceryl palmitostearate, glyceryl monostearate/monoesterin, acetyl palmitate, and stearic acid. As mentioned, among lipid nanocarriers, NLC has shown more stability and loading percentage than SLN, liposomes, and emulsions, especially at 25 °C, and is a new system for controlled release in the food entry phase. Further studies are needed to determine the optimal methods for producing lipid nanocarriers and evaluate the safety criteria and biological activity in different hosts.

Funding

This research received no external funding.

Acknowledgments

The authors would like to express their thanks to the Research Vice-Chancellor of Shahid Beheshti University of Medical Sciences for the financial support of this study.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Homayouni Rad, A.; Aghebati Maleki, L.; Samadi Kafil, H.; Fathi Zavoshti, H.; Abbasi, A. Postbiotics as novel health-promoting ingredients in functional foods. *Health Promot Perspect* **2020**, *10*, 9-229, https://doi.org/10.15171/hpp.2020.02.
2. Homayouni Rad, A.; Samadi Kafil, H.; Fathi Zavoshti, H.; Shahbazi, N.; Abbasi, A. Therapeutically effects of functional postbiotic foods. *Clinical Excellence* **2020**, *10*, 33-52.
3. Maqsood, S.; Adiamo, O.; Ahmad, M.; Mudgil, P. Bioactive compounds from date fruit and seed as potential nutraceutical and functional food ingredients. *Food chemistry* **2020**, *308*, https://doi.org/10.1016/j.foodchem.2019.125522.
4. Homayouni Rad, A.; Aghebati Maleki, L.; Samadi Kafil, H.; Abbasi, A. Postbiotics: A novel strategy in food allergy treatment. *Critical reviews in food science and nutrition* **2021**, *61*, 492-499, https://doi.org/10.1080/10408398.2020.1738333.
5. McClements, D.J. Recent advances in the production and application of nano-enabled bioactive food ingredients. *Current Opinion in Food Science* **2020**, *33*, 85-90, https://doi.org/10.1016/j.cofs.2020.02.004.
6. Bhowmick, S.; AlFaris, N.A.; ALTamimi, J.Z.; ALOthman, Z.A.; Aldayel, T.S.; Wabaidur, S.M.; Islam, M.A. Screening and analysis of bioactive food compounds for modulating the CDK2 protein for cell cycle arrest: Multi-cheminformatics approaches for anticancer therapeutics. *Journal of Molecular Structure* **2020**, *1216*, https://doi.org/10.1016/j.molstruc.2020.128316.
7. Rad, A.H.; Aghebati-Maleki, L.; Kafil, H.S.; Abbasi, A. Molecular mechanisms of postbiotics in colorectal cancer prevention and treatment. *Critical reviews in food science and nutrition* **2021**, *61*, 1787-1803, https://doi.org/10.1080/10408398.2020.1765310.
8. Oehlke, K.; Adamiuk, M.; Behsnilian, D.; Gräf, V.; Mayer-Miebach, E.; Walz, E.; Greiner, R. Potential bioavailability enhancement of bioactive compounds using food-grade engineered nanomaterials: a review of the existing evidence. *Food & function* **2014**, *5*, 1341-1359, https://doi.org/10.1039/C3FO60067J.
9. Karimi, N.; Jabbari, V.; Nazemi, A.; Ganbarov, K.; Karimi, N.; Tanomand, A.; Karimi, S.; Abbasi, A.; Yousefi, B.; Khodadadi, E. Thymol, cardamom and Lactobacillus plantarum nanoparticles as a functional candy with high protection against Streptococcus mutans and tooth decay. *Microbial pathogenesis* **2020**, *148*, https://doi.org/10.1016/j.micpath.2020.104481.
10. Jiang, T.; Liao, W.; Charcosset, C. Recent advances in encapsulation of curcumin in nanoemulsions: A review of encapsulation technologies, bioaccessibility and applications. *Food Research International* **2020**, *132*, https://doi.org/10.1016/j.foodres.2020.109035.
11. Rad, A.; Abbasi, A.; Javadi, A.; Pourjafar, H.; Javadi, M.; Khaleghi, M. Comparing the microbial quality of traditional and industrial yoghurts. *Biointerface Research in Applied Chemistry* **2020**, *10*, 6020-6025, https://doi.org/10.33263/briac104.020025.
12. Abbasi, A.; Aghebati-Maleki, L.; Homayouni-Rad, A. The promising biological role of postbiotics derived from probiotic Lactobacillus species in reproductive health. *Critical Reviews in Food Science and Nutrition* **2021**, 1-13, https://doi.org/10.1080/10408398.2021.1935701.
13. Yang, Y.; Leser, M.E.; Sher, A.A.; McClements, D.J. Formation and stability of emulsions using a natural small molecule surfactant: Quillaja saponin (Q-Naturale®). *Food Hydrocolloids* **2013**, *30*, 589-596, https://doi.org/10.1016/j.foodhyd.2012.08.008.
14. Loh, B.; Gondil, V.S.; Manohar, P.; Khan, F.M.; Yang, H.; Leptihn, S. Encapsulation and delivery of therapeutic phages. *Applied and Environmental Microbiology* **2020**, *87*, e01979-01920, https://doi.org/10.1128/AEM.01979-20.
15. Fathi-zavoshti, H.; Douroud, N.; Shahbazi, N.; Abbasi, A. Evaluating the role of postbiotics as a new generation of probiotics in health and diseases. *Journal of Ardabil University of Medical Sciences* **2020**, *19*, 381-399, https://doi.org/10.29252/jarums.19.4.381.
16. Mohammadian, M.; Waly, M.I.; Moghadam, M.; Emam-Djomeh, Z.; Salami, M.; Moosavi-Movahedi, A.A. Nanostructured food proteins as efficient systems for the encapsulation of bioactive compounds. *Food Science and Human Wellness* **2020**, *9*, 199-213, https://doi.org/10.1016/j.fshw.2020.04.009.
17. Homayouni-rad, A.; Oroojzadeh, P.; Abbasi, A. The Effect of Yeast Kluyveromyces marxianus as a Probiotic on the Microbiological and Sensorial Properties of Set Yoghurt during Refrigerated Storage. *Journal of Ardabil University of Medical Sciences* **2021**, *20*, 254-268, https://doi.org/10.52547/jarums.20.2.254.
18. Weston, M.; Mazur, F.; Chandrawati, R. Monitoring of Food Spoilage Using Polydiacetylene-and Liposome-Based Sensors. *Smart Sensors for Environmental and Medical Applications* **2020**, 81-102, https://doi.org/10.1002/9781119587422.ch5.
19. Wilkinson, M.; Kilcawley, K. Mechanisms of incorporation and release of enzymes into cheese during ripening. *International Dairy Journal* **2005**, *15*, 817-830, https://doi.org/10.1016/j.idairyj.2004.08.021.
20. Homayouni Rad, a.; Aghebati Maleki, L.; Samadi Kafil, H.; Abbasi, A.; Khani, N. Postbiotics as a Safe Alternative to Live Probiotic Bacteria in the Food and Pharmaceutical Industries. *HBI_Journals* **2021**, *26*, 132-157.

21. Ozma, M.A.; Khodadadi, E.; Pakdel, F.; Kamounah, F.S.; Yousefi, M.; Yousefi, B.; Asgharzadeh, M.; Ganbarov, K.; Kafil, H.S. Baicalin, a natural antimicrobial and anti-biofilm agent. *Journal of Herbal Medicine* **2021**, *27*, https://doi.org/10.1016/j.hermed.2021.100432.
22. Fox, P. Proteolysis during cheese manufacture and ripening. *Journal of Dairy science* **1989**, *72*, 1379-1400, https://doi.org/10.3168/jds.S0022-0302(89)79246-8.
23. Azarnia, S.; Robert, N.; Lee, B. Biotechnological methods to accelerate Cheddar cheese ripening. *Critical Reviews in Biotechnology* **2006**, *26*, 121-143, https://doi.org/10.1080/07388550600840525.
24. Mozafari, M.R.; Khosravi-Darani, K.; Borazan, G.G.; Cui, J.; Pardakhty, A.; Yurdugul, S. Encapsulation of food ingredients using nanoliposome technology. *International Journal of Food Properties* **2008**, *11*, 833-844, https://doi.org/10.1080/10942910701648115.
25. Walde, P.; Ichikawa, S. Enzymes inside lipid vesicles: preparation, reactivity and applications. *Biomolecular engineering* **2001**, *18*, 143-177, https://doi.org/10.1016/S1389-0344(01)00088-0.
26. Mohammadian, M.; Dabbagh Moghaddam, A.; Sharifan, A.; Dabaghi, P.; Hadi, S. Different forms of whey protein aggregates as curcumin delivery systems: evaluation of free radical scavenging activity and drug release kinetics. *Biointerface Research in Applied Chemistry* **2020**, *10*, 5490-5495, https://doi.org/10.33263/BRIAC103.490495.
27. Sforzi, J.; Palagi, L.; Aime, S. Liposome-Based Bioassays. *Biology* **2020**, *9*, https://doi.org/10.3390/biology9080202.
28. McClements, D.J.; Decker, E.A.; Park, Y.; Weiss, J. Structural design principles for delivery of bioactive components in nutraceuticals and functional foods. *Critical reviews in food science and nutrition* **2009**, *49*, 577-606, https://doi.org/10.1080/10408390902841529.
29. Müller, R.; Petersen, R.; Hommoss, A.; Pardeike, J. Nanostructured lipid carriers (NLC) in cosmetic dermal products. *Advanced drug delivery reviews* **2007**, *59*, 522-530, https://doi.org/10.1016/j.addr.2007.04.012.
30. Rashid, A.; Ali, V.; Khajuria, M.; Faiz, S.; Gairola, S.; Vyas, D. GC–MS based metabolomic approach to understand nutraceutical potential of Cannabis seeds from two different environments. *Food Chemistry* **2021**, *339*, https://doi.org/10.1016/j.foodchem.2020.128076.
31. Pinakin, D.J.; Kumar, V.; Suri, S.; Sharma, R.; Kaushal, M. Nutraceutical potential of tree flowers: A comprehensive review on biochemical profile, health benefits, and utilization. *Food Research International* **2020**, *127*, https://doi.org/10.1016/j.foodres.2019.108724.
32. Leylabadlo, H.E.; Heravi, F.S.; Soltani, E.; Abbasi, A.; Kafil, H.S.; Parsaei, M.; Sanaie, S.; Ahmadian, Z.; Ghotaslou, R. The role of gut microbiota in the treatment of irritable bowel syndrome. *Reviews in Medical Microbiology* **2021**, *33*, e89-e104, https://doi.org/10.1097/MRM.0000000000000284.
33. Considine, T.; Patel, H.A.; Singh, H.; Creamer, L.K. Influence of binding conjugated linoleic acid and myristic acid on the heat-and high-pressure-induced unfolding and aggregation of β-lactoglobulin B. *Food chemistry* **2007**, *102*, 1270-1280, https://doi.org/10.1016/j.foodchem.2006.07.022.
34. Abbasi, A.; Aghebati-Maleki, A.; Aghebati-Maleki, L.; Yousefi, M. Probiotic intervention as a potential therapeutic for managing gestational disorders and improving pregnancy outcomes. *Journal of Reproductive Immunology* **2020**, *143*, https://doi.org/10.1016/j.jri.2020.103244.
35. Aleshkov, A.V.; Ivashkin, M.; Zhebo, A.V.; Burik, M. Technology and characteristics of boiled sausages enriched with dietary fibers of Plantago Psyllium l. *Biointerface Research in Applied Chemistry* **2020**, *10*, 5715-5723, https://doi.org/10.33263/briac104.715723.
36. Gonnet, M.; Lethuaut, L.; Boury, F. New trends in encapsulation of liposoluble vitamins. *Journal of Controlled Release* **2010**, *146*, 276-290, https://doi.org/10.1016/j.jconrel.2010.01.037.
37. Rad, A.H.; Abbasi, A.; Kafil, H.S.; Ganbarov, K. Potential pharmaceutical and food applications of postbiotics: A review. *Current pharmaceutical biotechnology* **2020**, *21*, 1576-1587, https://doi.org/10.2174/1389201021666200516154833.
38. Rad, A.H.; Maleki, L.A.; Kafil, H.S.; Zavoshti, H.F.; Abbasi, A. Postbiotics as promising tools for cancer adjuvant therapy. *Advanced Pharmaceutical Bulletin* **2021**, *11*, https://doi.org/10.34172/apb.2021.007.
39. Livney, Y.D. Nanostructured delivery systems in food: Latest developments and potential future directions. *Current Opinion in Food Science* **2015**, *3*, 125-135, https://doi.org/10.1016/j.cofs.2015.06.010.
40. Abbasi, A.; Hajipour, N.; Hasannezhad, P.; Baghbanzadeh, A.; Aghebati-Maleki, L. Potential in vivo delivery routes of postbiotics. *Critical Reviews in Food Science and Nutrition* **2020**, 1-39, https://doi.org/10.1080/10408398.2020.1865260.
41. Abbasi, A.; Rad, A.H.; Ghasempour, Z.; Sabahi, S.; Kafil, H.S.; Hasannezhad, P.; Rahbar Saadat, Y.; Shahbazi, N. The biological activities of postbiotics in gastrointestinal disorders. *Critical Reviews in Food Science and Nutrition* **2021**, 1-22, https://doi.org/10.1080/10408398.2021.1895061.
42. de Vos, P.; Faas, M.M.; Spasojevic, M.; Sikkema, J. Encapsulation for preservation of functionality and targeted delivery of bioactive food components. *International dairy journal* **2010**, *20*, 292-302, https://doi.org/10.1016/j.idairyj.2009.11.008.
43. Delshadi, R.; Bahrami, A.; Tafti, A.G.; Barba, F.J.; Williams, L.L. Micro and nano-encapsulation of vegetable and essential oils to develop functional food products with improved nutritional profiles. *Trends in Food Science & Technology* **2020**, https://doi.org/10.1016/j.tifs.2020.07.004.

44. Desai, K.G.H.; Jin Park, H. Recent developments in microencapsulation of food ingredients. *Drying technology* **2005**, *23*, 1361-1394, https://doi.org/10.1081/DRT-200063478.
45. Akbari-Alavijeh, S.; Shaddel, R.; Jafari, S.M. Encapsulation of food bioactives and nutraceuticals by various chitosan-based nanocarriers. *Food Hydrocolloids* **2020**, *105*, https://doi.org/10.1016/j.foodhyd.2020.105774.
46. Badea, G.; Lăcătuşu, I.; Badea, N.; Ott, C.; Meghea, A. Use of various vegetable oils in designing photoprotective nanostructured formulations for UV protection and antioxidant activity. *Industrial Crops and Products* **2015**, *67*, 18-24, https://doi.org/10.1016/j.indcrop.2014.12.049.
47. Weiss, J.; Decker, E.A.; McClements, D.J.; Kristbergsson, K.; Helgason, T.; Awad, T. Solid lipid nanoparticles as delivery systems for bioactive food components. *Food biophysics* **2008**, *3*, 146-154, https://doi.org/10.1007/s11483-008-9065-8.
48. Nedovic, V.; Kalusevic, A.; Manojlovic, V.; Levic, S.; Bugarski, B. An overview of encapsulation technologies for food applications. *Procedia Food Science* **2011**, *1*, 1806-1815, https://doi.org/10.1016/j.profoo.2011.09.265.
49. Katouzian, I.; Jafari, S.M. Nano-encapsulation as a promising approach for targeted delivery and controlled release of vitamins. *Trends in Food Science & Technology* **2016**, *53*, 34-48, https://doi.org/10.1016/j.tifs.2016.05.002.
50. Gharehbeglou, P.; Jafari, S.M.; Homayouni, A.; Hamishekar, H.; Mirzaei, H. Fabrication of double W1/O/W2 nanoemulsions loaded with oleuropein in the internal phase (W1) and evaluation of their release rate. *Food Hydrocolloids* **2019**, *89*, 44-55, https://doi.org/10.1016/j.foodhyd.2018.10.020.
51. Neethirajan, S.; Jayas, D.S. Nanotechnology for the food and bioprocessing industries. *Food and bioprocess technology* **2011**, *4*, 39-47, https://doi.org/10.1007/s11947-010-0328-2.
52. Tamjidi, F.; Shahedi, M.; Varshosaz, J.; Nasirpour, A. Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. *Innovative Food Science & Emerging Technologies* **2013**, *19*, 29-43, https://doi.org/10.1016/j.ifset.2013.03.002.
53. Huang, Z.; Huang, Y.; Wang, W.; Fu, F.; Wang, W.; Dang, S.; Li, C.; Ma, C.; Zhang, X.; Zhao, Z. Relationship between particle size and lung retention time of intact solid lipid nanoparticle suspensions after pulmonary delivery. *Journal of Controlled Release* **2020**, *325*, 206-222, https://doi.org/10.1016/j.jconrel.2020.06.004.
54. Ambekar, R.S.; Choudhary, M.; Kandasubramanian, B. Recent advances in dendrimer-based nanoplatform for cancer treatment: A review. *European Polymer Journal* **2020**, *126*, https://doi.org/10.1016/j.eurpolymj.2020.109546.
55. Clemons, T.D.; Singh, R.; Sorolla, A.; Chaudhari, N.; Hubbard, A.; Iyer, K.S. Distinction between active and passive targeting of nanoparticles dictate their overall therapeutic efficacy. *Langmuir* **2018**, *34*, 15343-15349, https://doi.org/10.1021/acs.langmuir.8b02946.
56. Liu, Y.; K Tee, J.; NC Chiu, G. Dendrimers in oral drug delivery application: current explorations, toxicity issues and strategies for improvement. *Current pharmaceutical design* **2015**, *21*, 2629-2642, https://doi.org/10.2174/1381612821666150416102058.
57. Yousefi, M.; Narmani, A.; Jafari, S.M. Dendrimers as efficient nanocarriers for the protection and delivery of bioactive phytochemicals. *Advances in colloid and interface science* **2020**, *278*, https://doi.org/10.1016/j.cis.2020.102125.
58. Batrakova, E.V.; Gendelman, H.E.; Kabanov, A.V. Cell-mediated drug delivery. *Expert Opin Drug Deliv* **2011**, *8*, 415-433, https://doi.org/10.1517/17425247.2011.559457.
59. Kelly, C.; Jefferies, C.; Cryan, S.-A. Targeted liposomal drug delivery to monocytes and macrophages. *Journal of drug delivery* **2011**, *2011*, https://doi.org/10.1155/2011/727241.
60. Müller, R.H.; Radtke, M.; Wissing, S.A. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Adv Drug Deliv Rev* **2002**, *54 Suppl 1*, S131-155, https://doi.org/10.1016/s0169-409x(02)00118-7.
61. Souto, E.B.; Baldim, I.; Oliveira, W.P.; Rao, R.; Yadav, N.; Gama, F.M.; Mahant, S. SLN and NLC for topical, dermal, and transdermal drug delivery. *Expert Opin Drug Deliv* **2020**, *17*, 357-377, https://doi.org/10.1080/17425247.2020.1727883.
62. Pezeshki, A.; Ghanbarzadeh, B.; Mohammadi, M.; Fathollahi, I.; Hamishehkar, H. Encapsulation of vitamin A palmitate in nanostructured lipid carrier (NLC)-effect of surfactant concentration on the formulation properties. *Advanced Pharmaceutical Bulletin* **2014**, *4*, https://doi.org/10.5681/apb.2014.083.
63. Weber, S.; Zimmer, A.; Pardeike, J. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for pulmonary application: a review of the state of the art. *European Journal of Pharmaceutics and Biopharmaceutics* **2014**, *86*, 7-22, https://doi.org/10.1016/j.ejpb.2013.08.013.
64. Chen, C.; Han, D.; Cai, C.; Tang, X. An overview of liposome lyophilization and its future potential. *Journal of controlled release* **2010**, *142*, 299-311, https://doi.org/10.1016/j.jconrel.2009.10.024.
65. Liu, C.-H.; Wu, C.-T. Optimization of nanostructured lipid carriers for lutein delivery. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* **2010**, *353*, 149-156, https://doi.org/10.1016/j.colsurfa.2009.11.006.

66. Lacatusu, I.; Badea, N.; Ovidiu, O.; Bojin, D.; Meghea, A. Highly antioxidant carotene-lipid nanocarriers: synthesis and antibacterial activity. *Journal of Nanoparticle Research* **2012**, *14*, 1-16, https://doi.org/10.1007/S11051-012-0902-9.
67. Dal Magro, R.; Ornaghi, F.; Cambianica, I.; Beretta, S.; Re, F.; Musicanti, C.; Rigolio, R.; Donzelli, E.; Canta, A.; Ballarini, E. ApoE-modified solid lipid nanoparticles: A feasible strategy to cross the blood-brain barrier. *Journal of Controlled Release* **2017**, *249*, 103-110, https://doi.org/10.1016/j.jconrel.2017.01.039.
68. Zhou, K.; Yan, Y.; Chen, D.; Huang, L.; Li, C.; Meng, K.; Wang, S.; Algharib, S.A.; Yuan, Z.; Xie, S. Solid lipid nanoparticles for duodenum targeted oral delivery of tilmicosin. *Pharmaceutics* **2020**, *12*, https://doi.org/10.3390/pharmaceutics12080731.
69. Mehnert, W.; Mäder, K. Solid lipid nanoparticles: production, characterization and applications. *Advanced drug delivery reviews* **2012**, *64*, 83-101, https://doi.org/10.1016/j.addr.2012.09.021.
70. Yadav, P.; Yadav, A.B. Preparation and Optimization of Insulin Loaded Solid Lipid Nanoparticles for the Targeted Delivery of Insulin to the Lungs for Diabetes Treatment via Inhalation. In: *Composite Materials for Extreme Loading*. Springer: **2022**; pp. 73-86, https://doi.org/10.1007/978-981-16-4138-1_6.
71. Shrotriya, S.; Ranpise, N.; Satpute, P.; Vidhate, B. Skin targeting of curcumin solid lipid nanoparticles-engrossed topical gel for the treatment of pigmentation and irritant contact dermatitis. *Artificial cells, nanomedicine, and biotechnology* **2018**, *46*, 1471-1482, https://doi.org/10.1080/21691401.2017.1373659.
72. Shimoni, E. Nanotechnology for foods: delivery systems. In: *Global issues in food science and technology*; Elsevier: **2009**; pp. 411-424, https://doi.org/10.1016/B978-0-12-374124-0.00023-5.
73. Hosseini, S.A., Abbasi, A., Sabahi, S. and Khani, N. Application of Postbiotics Produced By Lactic Acid Bacteria in the Development of Active Food Packaging. *Biointerface Research in Applied Chemistry* **2021**, *12*, 6164-6183.
74. Mozafari, M.R.; Flanagan, J.; Matia-Merino, L.; Awati, A.; Omri, A.; Suntres, Z.E.; Singh, H. Recent trends in the lipid-based nanoencapsulation of antioxidants and their role in foods. *Journal of the Science of Food and Agriculture* **2006**, *86*, 2038-2045, https://doi.org/10.1002/jsfa.2576.
75. McClements, D.J.; Xiao, H. Potential biological fate of ingested nanoemulsions: influence of particle characteristics. *Food Funct* **2012**, *3*, 202-220, https://doi.org/10.1039/c1fo10193e.
76. Kheadr, E.E.; Vuillemard, J.C.; Deeb, S.A.E. Accelerated Cheddar cheese ripening with encapsulated proteinases. *International Journal of Food Science and Technology* **2000**, *35*, 483-495, https://doi.org/10.1046/j.1365-2621.2000.00398.x.
77. Kheadr, E.; Vuillemard, J.; El-Deeb, S. Impact of encapsulated enzyme cocktails on Cheddar cheese ripening. *Food Research International* **2003**, *36*, 241-252, https://doi.org/10.1016/S0963-9969(02)00166-7.
78. Salminen, H.; Helgason, T.; Kristinsson, B.; Kristbergsson, K.; Weiss, J. Formation of solid shell nanoparticles with liquid ω-3 fatty acid core. *Food Chem* **2013**, *141*, 2934-2943, https://doi.org/10.1016/j.foodchem.2013.05.120.
79. Hoseinnejad, M.; Jafari, S.M.; Katouzian, I. Inorganic and metal nanoparticles and their antimicrobial activity in food packaging applications. *Critical reviews in microbiology* **2018**, *44*, 161-181, https://doi.org/10.1080/1040841x.2017.1332001.
80. Rashid, A.; Javed, I.; Ayaz, M.; Abdullah, M.; Saeed, F.; Yousuf, M.R.; Imran, M.; Bader Ul Ain, H.; Anjum, F.M. Probing the physicochemical and sensorial properties of pasteurized milk via nanoparticles. *International Journal of Food Properties* **2019**, *22*, 825-842, https://doi.org/10.1080/10942912.2019.1607374.
81. Liu, J.; Hu, W.; Chen, H.; Ni, Q.; Xu, H.; Yang, X. Isotretinoin-loaded solid lipid nanoparticles with skin targeting for topical delivery. *International journal of pharmaceutics* **2007**, *328*, 191-195, https://doi.org/10.1016/j.ijpharm.2006.08.007.
82. Garcês, A.; Amaral, M.H.; Sousa Lobo, J.M.; Silva, A.C. Formulations based on solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for cutaneous use: A review. *European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences* **2018**, *112*, 159-167, https://doi.org/10.1016/j.ejps.2017.11.023.
83. Vieira, R.; Severino, P.; Nalone, L.A.; Souto, S.B.; Silva, A.M.; Lucarini, M.; Durazzo, A.; Santini, A.; Souto, E.B. Sucupira Oil-Loaded Nanostructured Lipid Carriers (NLC): Lipid Screening, Factorial Design, Release Profile, and Cytotoxicity. *Molecules* **2020**, *25*, https://doi.org/10.3390/molecules25030685.