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RESEARCH PAPER

Evaluation of lipid nanocarriers in the form of SLN and their application in drug delivery

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ABSTRACT

Currently, most drugs reach to their place where they can have their desired effects through traditional methods and systemic absorption. Drugs are associated with many problems and complications in drug delivery systems the aim of which is reducing the frequency of drug usage and optimizing the effect of the drug. Therefore, by providing effective drug concentrations in the damaged organ, the therapeutic effect of the drug is enhanced and its degradation is reduced. In addition, this maintains the circulation of the drug in the blood for a longer time and can diminish its side effects. There are different types of drug delivery systems (DDS) of most advanced types for nanostructured carriers in design and fabrications. Solid lipid nanoparticles (SLN) form colloidal drug carrier systems are an alternative to colloidal carriers such as liposomes, emulsions, and micro polymeric components. For the synthesis of these particles, many methods are applied which provide the possibility of loading various hydrophobic and hydrophilic drugs inside the lipid nanoparticles. In this article, various methods and application of these lipids in targeted drug delivery system are reviewed.

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INTRODUCTION

Conventional methods of drug delivery system (DDS) in the body mainly work through two digestive (pills, capsules, and syrup) and non-digestive (such as injections, eye drops, and topical creams) ways at specific intervals of drug consumption [1-3]. Most of these methods have various paths in drug release and delivery in the body during exposure to the acidic environment of the stomach, passing through the tough junctions of the cells of the intestinal wall and entering the intrahepatic cycle [2-4]. Most drugs reach their place of effect through traditional methods and systemic absorption and the wasted drug reaches it place through the digestive system, circulatory system, and intermediate tissues. When the drug dose is increased unrealistically, the amount of the drug is more than the required amount for treatment [5-8]. The foundations of this attitude are based on the fact that the drug of sufficient concentration enters the blood circulation and eventually reaches the cite of action for treating the disease [9-13]. The process of targeted drug delivery helps to maintain the level of appropriate drug concentration for a longer period of time and reduces many limitations of conventional treatment such as the number of used doses and the

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Table 1: Characteristics of nanocarriers

	Characterization parameters	Instrumentation/ Analytical methods
1	Shape and surface morphology	Transmission electron microscopy (TEM)
		Scanning electron microscopy (SEM)
		Phase contrast optical microscopy (PCM)
		Atomic force microscopy (AFM)
		Freeze fracture microscopy (FFM)
2	Molecular weight	Gel permeation chromatography (GPC)
3	Surface charge and electrophoretic mobility	Laser light scattering technique
4	Vesicle size and size distribution	Electron microscopy (SEM/TEM)
		Optical microscopy
		Photon correlation spectroscopy (PCS)
5	Surface hydrophobicity	Hydrophobic interaction chromatography
		Two phase partition
		Radiolabel probe
		Contact angle measurement
		X-ray photoelectron spectroscopy
6	Electrical surface potential and surface pH	Zeta potential measurement
		pH sensitive probes
7	Density	Gas pycnometer
8	Rheology	Viscometer
9	*In-vitro* release	Dialysis membrane
		Dissolution test apparatus

initial concentration of the drug as well as the side effects resulting from the simple release of the drug in an uncertain systemic distribution [14-17]. Each targeted delivery system includes a drug, carrier, and targeting ligand in which the distribution, metabolism, and cellular absorption of the drug are determined according to the physicochemical properties and biological behavior of the carrier and ligand. Therefore, the design of an appropriate carrier and ligand increases the efficiency of the drug in the diseased tissue and reduces the toxicity of the drug in other healthy tissues [18-21]. Due to the small size (10-1000 nm) of nanocarriers, they are highly suitable for drug delivery and improving the efficiency of treatment by encapsulated drugs. In Table 1, characteristics, instrumentation and more analytical methods for nanocarriers are listed. Colloidal drug carriers as one of the DDS have been widely considered in the fields of medicine, pharmacy, and dentistry in recent years. In addition, to overcome many problems caused by the low solubility of hydrophobic drugs, these carriers have been able to acquire high attractiveness for the use of various drugs in lipophilic drugs. Among these drug carriers, solid lipid nanoparticles (SLN) are significant [22-27]. These SLN have been successfully employed to deliver a variety of lipophilic drugs and sometimes hydrophilic drugs. Since the beginning of 1990s, SLN have been created as an alternative pharmaceutical agent for drug delivery approaches compared to conventional colloidal systems such as emulsions, liposomes, microparticles, and polymer nanoparticles [28-333]. SLN nanoparticles are made of solid lipids (lipids that are solid at room and body temperatures) and are stabilized by surface activators.

DRUG DELIVERY SYSTEM

Using conventional DDS has no control over the time, place, and speed of drug release at specific time intervals. In addition, the drug delivery to the target tissue should satisfy the patient's need for treatment until the next dose and fluctuations in the concentration of the drug may exceed the therapeutic range and result in more side effects [32-37]. On the other hand, many drugs are unstable, toxic, and their effectiveness period is short; some drugs may also have solubility problems. In recent years, the importance of DDS has grown. The significant point about DDS is that each of the medicinal systems has its own unique chemical, physical, and morphological properties. Further, chemical interactions such as hydrogen

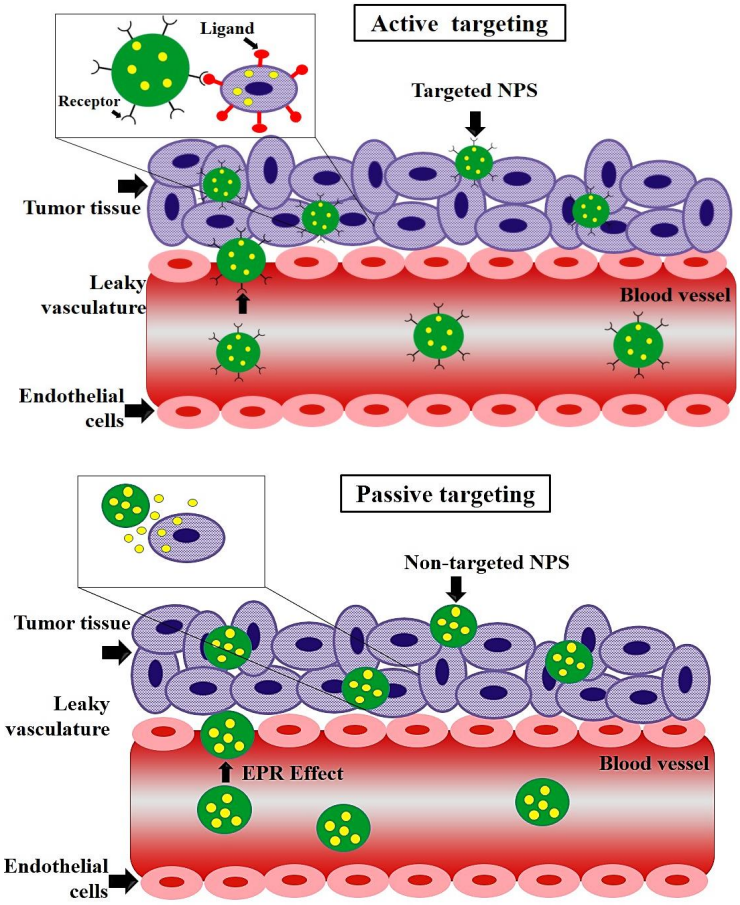

Fig. 1: Comparison of active and passive targeting

and covalent bonds or physical interactions such as electrostatic and Van Der Waals interactions have different binding tendencies toward polar and non-polar drugs. Furthermore, other factors such as the chemical composition of nanoparticles and various forms of systems are related to the drugs which play a key role in the controlled release profile of the drug [38-43]. Theoretically, any targeted DDS should have two features: increasing drug efficiency in diseased tissue and reducing drug toxicity in other healthy tissues. In the new field of dental materials, pharmaceuticals applications, molecular biology, polymer chemistry, and nanotechnology are combined with targeted drug delivery to develop these systems. In general, a targeted DDS includes a drug, a carrier, and a targeting ligand. The biological behavior of carriers and ligands determines how it is metabolized, distributed, and absorbed by cells. For this reason, the successful preparation of carriers and targeting ligands allows drug delivery to target cells [44-50]. Targeted drug delivery can be performed using different methods from simple and local to complex applications (carriers specifically targeted by ligands). Drug delivery mechanisms are generally divided into three categories including physical targeting, passive targeting, and active targeting. Fig. 1 shows the comparison of active and passive targeting mechanisms. Passive targeting is the presence of target ligands on the surface of nanoparticles which can lead to the active targeting of nanoparticles to the receptors which are present in the cell or target tissue, thus increasing cellular accumulation and uptake. Physical targeting is conducted by forces such as electric field, magnetic field, ultrasound, heat, and light (external forces) in order to accumulate or disperse the medicinal agent in the desired location [51-57]. It seems that among these cases, the use of magnetic field, light and ultrasound waves is more widely used. Among these fields, the magnetic field has found wide commercial

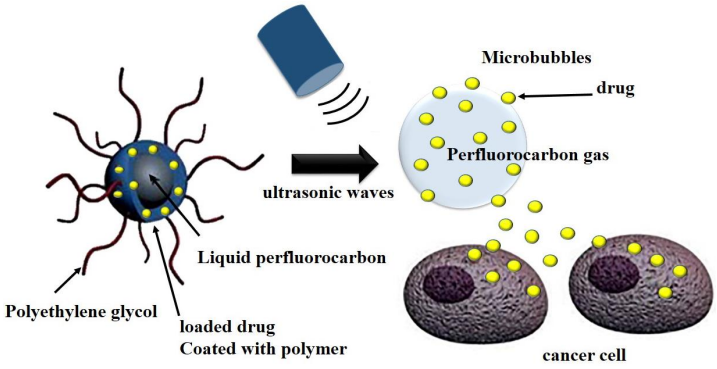

Fig. 2: Sending ultrasound waves to microbubbles and drug release in cancer tissue

applications due to its cheapness and easy approaches. Fig. 2 displays the process of sending ultrasound waves to microbubbles and drug release in cancer tissue. In passive targeting, the drug carrier complex is directed to the desired location through the blood stream under the influence of properties such as molecular location, shape, temperature, and pH concentration. The main targets are cell membrane receptors, cell membrane lipid components, and cell surface antigens. In fact, passive targeting occurs when the desired tissue has unique physiological properties. Nano-systems can use structural features of tumor tissue for passive targeting. In addition to this method, there are other methods for passive drug targeting. Methods such as inactive enzyme targeting (conversion of the inactive form of the drug into the active form due to the presence of a special enzyme), acidity of the environment (release of the drug due to the difference in pH conditions in the treated tissue), temperature difference (according to the temperature conditions of the tissue), and other methods which depend on the specificities of the conducted tissue [58-62]. The most advanced targeting approach in DDS is active targeting, which makes the structure by connecting receptor target molecules to drug delivery systems. In this method, the drug can be transferred completely specifically to the treated tissue, intracellular or specific molecules. The mechanism, drug carriers for ligands such as antibodies or monoclonal fragments, peptides, nucleic acids (aptamers) or small molecules (such as folic acids) are directed to the receptors. This method is more important in the treatment of primary tumors that have not yet metastasized.

TARGETED DRUG DELIVERY WITH SLN

The results of recent clinical and pre-clinical research demonstrate that targeted drug delivery systems are a wonderful method for treating a variety of life-threatening diseases. Targeted drug delivery include nanoscale carriers, targeted prodrugs, and cellular carriers. In current years, the preparation of nanoparticles and nanostructures as carriers for drug delivery system has been investigated by many researchers. Since these structures are suitable for targeted drug delivery and biocompatibility due to the size of particles being smaller than cells, protecting the drug molecule, controlling and slowing down the release of the drug. Due to the ability to pass through biological barriers to deliver the drug to the target tissue and cell, increasing the durability of the drug in the bloodstream, targeted drug delivery and biocompatibility can be considered as a highly effective drug delivery system, which increases the therapeutic efficiency of the drug [63-66].

One of the limitations in the use of nanoparticles is the creation of a structure called corona when nanoparticles enter the blood, which is due to the existence of non-specific interactions between the coating of nanoparticles and proteins that circulate in the bloodstream. The removal of nanoparticles from blood circulation is carried out by the reticuloendothelial system. The most common methods employed for bypassing the reticuloendothelial system are the formation of nanoparticles with a natural surface charge, covering the surface of the nanoparticles with various hydrophilic surfactants such as polysorbate and polyethylene glycol (PEG), and using nanoparticles smaller than 90 nm [54-57]. Nanoparticles with these characteristics are called hidden, which

Table 2: Examples of fatty substances and emulsifiers used in SLN preparation

lipid	Hard fats	Emulsifier
Lipids Literature	Witepsol® W 35	Soybean lecithin (Lipoid® S 75, Lipoid® S 100)
Triglycerides	Witepsol® H 35	Egg lecithin (Lipoid® E 80)
Tricaprin	Witepsol® H 42	Phosphatidylcholine (Epikuron® 170, Epikuron 200)
Trilaurin	Witepsol® E 85	Poloxamer 188
Trimyristin	Glyceryl monostearate (Imwitor®900)	Poloxamer 182
Tripalmitin	Glyceryl behenate (Compritol® 888 ATO)	Poloxamer 407
Tristearin	Glyceryl palmitostearate (Precirol® ATO 5)	Poloxamine 908
Hydrogenated coco-glycerides	Cetyl palmitate	Tyloxapol
	Stearic acid	Polysorbate 20
	Palmitic acid	Polysorbate 60
	Decanoic acid	Polysorbate 80
	Behenic acid	Sodium cholate
	Acidan N12	Sodium glycocholate
		Taurocholic acid sodium salt
		Taurodeoxycholic acid sodium salt
		Butanol
		Butyric acid
		Dioctyl sodium sulfosuccinate
		Monooctylphosphoric acid sodium

circulate in the blood for a longer period of time and are able to bypass the reticuloendothelial system. Nanoparticles should be non-inflammatory, non-immunogenic, biocompatible, and biodegradable. Many nanometric structures have been studied and manufactured for drug delivery system among the most important ones used as carriers.

SLN are colloidal structures with an average size of 10 to 1000 nm; the average size of dispersed SLN particles increases with the rise in lipid melting point which is consistent with the general theory of homogenization given the high viscosity pressure of the dispersed phase. They usually consist of a solid hydrophobic with a phospholipid monolayer coating in which the core can contain a drug dissolved or dispersed in a lipid network with a high melting temperature and a phospholipid layer. In the absence of phospholipid, surface activator is used in the preparation of lipid nanoparticles. In this case, the synthesized phospholipid, which has biphilic characteristics, is placed in the outer layer of SLN where the hydrophilic part of the phospholipid is placed towards outer layer and its hydrophobic end is placed towards the inner core. The constituents of SLNs formulation include lipids, water, and surfactant. The main ingredient of the aqueous phase is deionized water to which other water-soluble substances are added depending on the characteristics and applications of each formulation and various types of aqueous surfactants among these substances. Surfactant results in the final stability of SLN and the optimal placement of fat and water phases together. The type of surfactant and its concentration have a significant impact on the quality of the size of the SLN particles. Higher concentrations of emulsifiers reduce surface tension and facilitate particle separation during homogenization [59-66]. Due to the ability of these nanoparticles to carry active substances and drugs in their lipid part, these nanoparticles protect the target substance from environmental damage. Therefore, this range of nanoparticles can be utilized to carry the medicine and increase its effectiveness. Drug delivery by

Table 3: Salient characteristics and limitations of SLN

Composition	Salient features	Benefits	Limitations/challenges
Physiological lipid	Avoidance of organic solvents	Organic solvents not required for formulation	Low drug loading capacity
Dispersed in water or in an aqueous surfactant	Potential wide application spectrum (dermal, per oral, intravenous)	Greater stability and bioavailability	Drug expulsion during storage
	High pressure homogenization as an established production method		High water content
			Low capacity to load hydrophilic drug

SLN is influenced by a number of factors including the method of sample preparation, type of lipid, and the applied active substance. Table 2 shows examples of fatty substances and emulsifiers used in the preparation of SLN.

Lipase enzyme is one of the important enzymes that affects these structures in the body. Different lipids have different degradation rates using this enzyme. As an example, the longer the lipid chain, the slower the breakdown of the enzymes. The degradation rate is reduced in the presence of some emulsifiers that act as lipid barriers [32]. The benefits of using these carriers include the increased shelf life of the drug, non-toxicity of the carrier, and not using organic solvents related to their removal after preparation. In addition, these materials are easier to make compared to other biological biopolymers and liposomes. SLNs enhance the accessibility of encapsulated bioactive substances and protect encapsulated drugs from unstable chemical compounds, which are formed during the preparation process. Encapsulated materials may have exactly the same pharmaceutical structure in the original emulsion and may not change in nature [61-65]. A major advantage of these carriers over polymeric nanoparticles is that they are composed of body-compatible lipid compounds which reduce chronic and acute toxicity. These carriers have less storage and leakage problems compared to systems such as liposomes. Further, they are effectively used for the transfer of proteins and peptides, and SLNs avoid the high costs required for the preparation of liposomes [66-71]. Table 3 lists other salient features and limitations of SLN.

PREPARATION OF SLN FOR DRUG DELIVERY SYSTEM

To prepare this type of nanoparticles, various methods used to include hot and cold high-pressure homogenization in which a very high-pressure mechanism used for microemulsion technique, emulsification-solvent evaporation, and ultrasonication. In the technique of ultrasonic waves before sonication, homogenization under high shears is also applied. The observations have demonstrated that the nanoparticles created by this method are homogeneous, spherical, and 60% of the products are below the size of 500 nm. Furthermore, the formulation exhibits a prolonged release and some SLN production methods are discussed in the section below [39, 40]. Fig. 3 shows the classification of SLN preparation methods.

High-pressure homogenization method

Hot homogenization method

Hot homogenization is performed by applying high pressure by the homogenizer at a temperature above the melting point of the lipids. Using this method, the lipid content in the environment reaches from 5% - 10% to 40%. In the primary emulsification, the drug is loaded on the melted polymers. Then, emulsifiers are added to the reaction medium at the same temperature as those containing ingredients for fragmenting lipids. High pressure homogenization for primary emulsion is performed at a temperature above the melting point of the lipids [41-42]. First, the primary emulsion with coarser particles is formed followed by high pressure homogenization; the homogenization process is performed with a

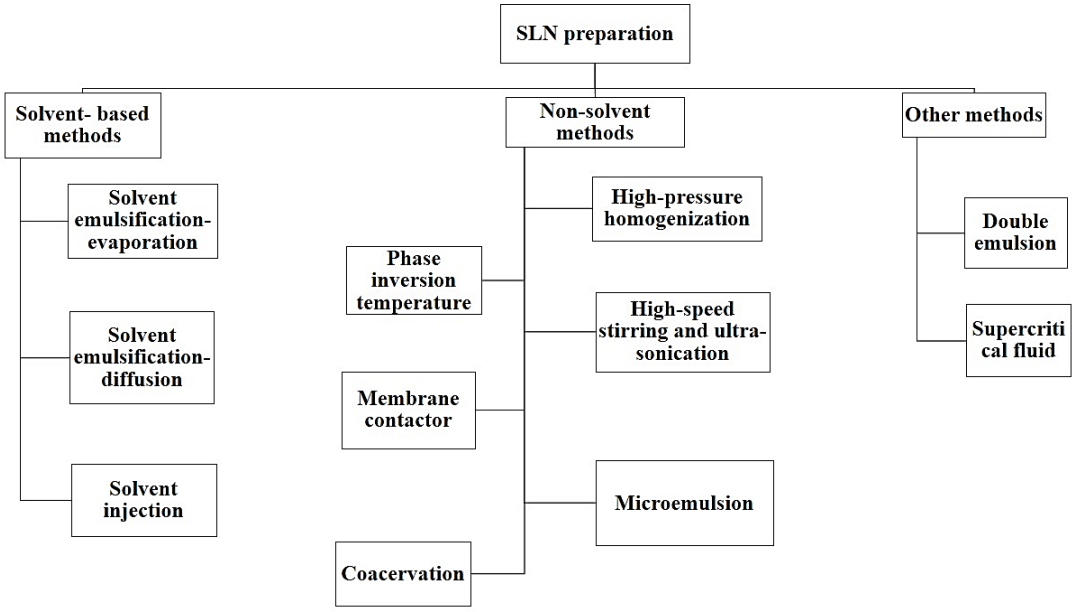

Fig. 3: Classification of SLN preparation methods

pressure ranging from 100 to 1500 o/w bar. Cooling the obtained nano-emulsion at room temperature leads to the crystallization of fat and the formation of lipid nanoparticles. The quality of the primary emulsion has a significant impact on the size of fat droplets and the final quality of the product. The higher the temperature of this process and the lower the viscosity of the lipid phase, the smaller the particle size and the faster the drug delivery and biodegradability. Generally, in order to obtain good quality products, the emulsion is placed in the high-pressure homogenizer (HPH) device for 3 to 5 times. Applying more than 3 to 5 cycles of HPH has a negative impact on the samples and the size of the samples increases; however, an important problem which arises is the degradation of active pharmaceutical compounds at high temperature [42-45]. This technique can be used for lipophilic drugs and insoluble drugs; however, it is not suitable for hydrophilic drugs. During homogenization, the hydrophilic component of the drug tends to the aqueous phase, and the drug entrapment efficiency diminishes. In addition, homogenization can be conducted at a temperature slightly lower than the melting point of fat (a temperature lower than 5 to 10°C), which seems to lead to fat softening during the process of composition for hydrophilic drugs. The homogenization temperature should be chosen carefully because hydrophilic drugs may be lost [43-55].

Cold homogenization method

Cold homogenization is designed to solve the problems caused by hot homogenization. In hot homogenization, high temperature leads to the decomposition of drugs and reducing their loading on nanoparticles. In addition, this temperature leads to the inactivation of part of the drug as well as multiple complex changes in the crystallization stage in the emulsion. This method can be used for hydrophilic drugs and many heat-sensitive drugs which can be introduced into the lipid nanoparticles by this technique, since the drugs are exposed to heat for a relatively short time. To solve these problems, several steps have been added to the cold homogenization method. The first step in hot and cold homogenization is quite similar. In the second stage, the entire primary emulsion is rapidly cooled by liquid nitrogen or dry ice to distribute the drug in the lipid matrices, which increase the brittleness of the fat and simplify the milling process. After grinding, it can be microparticles with the size of approximately 50 to 100 microns dispersed in a cold aqueous solution of surfactant. Comparing the size of the final particles, the size of the particles in cold homogenization is larger than that in hot homogenization; however, its advantage is lesser exposure time of the drugs to high temperature

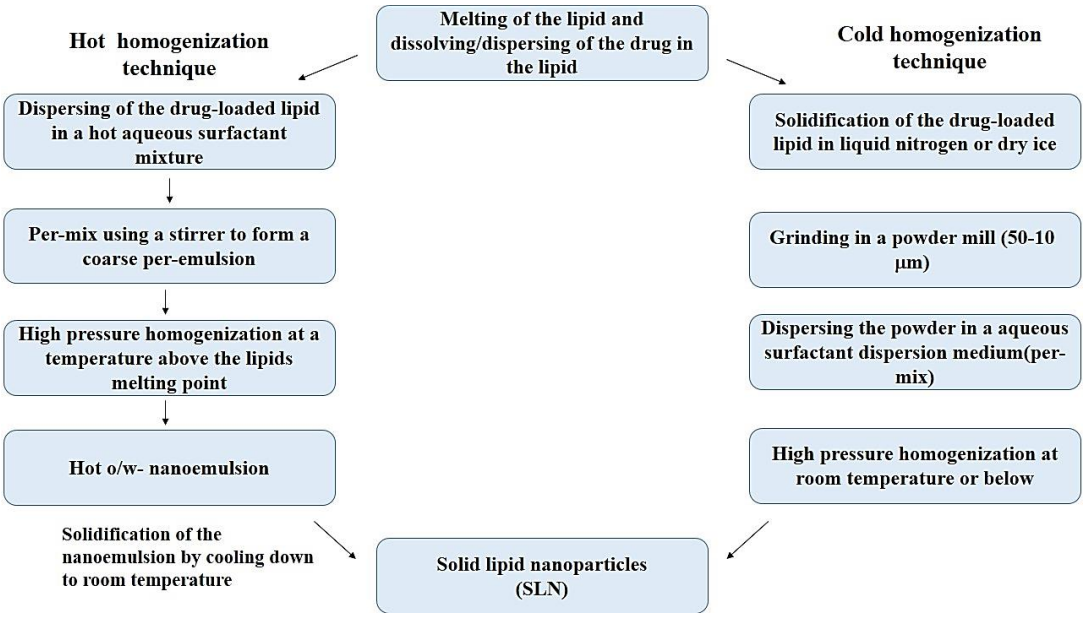

Fig. 4: Preparation of SLNs by cold and hot homogenization

[51-64]. Most of the nanoparticles produced by hot homogenization have a particle size below 500 nm and the content of micro particles is low. On the contrary, coarser size particles with more particle size distribution are observed in SLNs obtained by cold homogenization compared to hot homogenization. The characteristics of hot homogenization include low particle size distribution, low production of microparticles, and high dispersion of lipid particles. The advantages of using high pressure homogenization (hot and cold), compared to other methods, are the possibility of measurement and evaluation, access to the homogenization production line in the industry, and the approval of the homogenization equipment by regulatory authorities. According to the research results, increasing the homogenization temperature may decrease the particle size, and usually increasing the temperature reduces the viscosity of the fat and liquid phases [48-50]. Fig. 4 demonstrates the preparation of SLNs by cold and hot homogenization.

Preparation of SLN based on supercritical fluid

One of the prominent characteristics of supercritical fluid is its low viscosity and surface tension, as well as its high solubilizing power. In this technique, SLN and the drug are dissolved in a supercritical liquid, which is usually carbon dioxide, then transferred to a large chamber for rapid expansion of the supercritical liquid. This rapid expansion leads to the supersaturation of the drug, resulting in precipitation in the form of fine particles [62-66]. The characteristics of supercritical fluid include its high solubilizing power, low viscosity, and surface tension.

Double emulsion method

The double emulsion method, known as the W/O/W technique, is used to load hydrophilic drugs. The drug and stabilizer, which is used to prevent the drug from entering the external phase during solvent evaporation, are enclosed in the internal aqueous phase. The aqueous solution containing the drug along with the stabilizer is emulsified using a stirrer at a high speed and temperature. Then, the w/o emulsion is dispersed in the aqueous phase containing the stabilizer as the extrinsic phase of the w/o/w emulsion at a temperature of 2 to 3°C under a mechanical stirrer until lipid nanoparticles are obtained. Then, lipid nanoparticles are purified by diaphilization. The fabrication of lipid nanoparticles with a larger particle size and the existence of a hydrophilic end layer differentiate the nanoparticles produced by this method from the nanoparticles produced by other methods [56-58, 67-73].

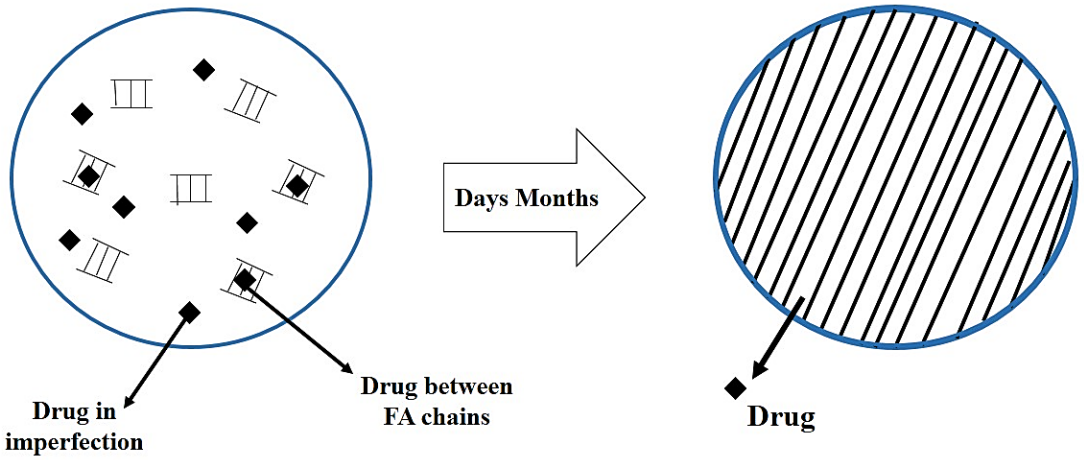

Fig. 5: Mechanism of drug excretion during storage from SLN, changing state to regular lipid crystal

Spray drying method

This method is performed for lipids with a melting point higher than 70°C. An organic solvent is used to dissolve the drug and SLN particles, which sprayed in a chamber with controlled pressure and temperature. This technique is cheap, easy, and fast which can be employed at industrial scales. In the spray drying method, lipid particles are incompletely melted and the best concentration of trehalose solution and water is predicted to be 1% to 2%. The type of solvent, temperature and evaporation pressure of solvent, viscosity of polymer and drug solution, concentration of polymer in polymer solution and spraying pressure can affect polymer changes and particle size. The biggest problem of this method is the removal of a large amount of medicine due to the adhesion of nanoparticles to the wall of the spray chamber [59-61]. Fig. 5 demonstrates the mechanism of drug excretion during storage from SLN, changing the state to regular lipid crystal.

APPLICATIONS OF SLNS IN DRUG DELIVERY

Injection application

In the last two decades, lipid nanoparticles have become a suitable alternative for pharmaceutical and dental systems such as liposome and emulsion. It has demonstrated favorable properties. Generally, SLNs are injected subcutaneously, intramuscularly, or intravenously. Because the size of the particles is less than 1 micrometer and the size of the particles for intravenous injection must be below 5 micrometers to prevent embolism, these systems can have a minimal risk of blood clots. Characteristics such as high drug loading, increased flexibility in the modulation of the drug release profile, convenient manufacturing, biocompatibility, directivity, and finally the complete removal of the remnants of the drug from the circulatory system, introduce these nanoparticles as a suitable and safe method in injectable applications [8-63].

Oral applications of SLN

The use of these systems is very effective because of their ability to improve bioavailability, long-term persistence in the blood plasma level, regulation of drug release while passing through different parts of the digestive system, as well as protection against chemical decomposition of drugs [63, 43]. In a study conducted by Müller et al. [64] for improving the oral formulation of cyclosporine compared to the commercial Neural/Optoral sandimum, it was shown that in the commercial type of the drug, the plasma peak of the drug had reached its maximum (1000 nm) after 2 hours while the use of the drug loaded in SLN had had minimal dispersion.

The present study indicates that the use of SLN as a drug carrier for oral use creates minimal distribution in the bioavailability of the drug and prevents it from reaching the maximum plasma peak that was created by eating the drug with the previous formulation. After drug loading, these nanoparticles are dispersed and soluble in water or after converting into forms such as tablets, capsules or powder [65]. Considering the conditions of the stomach (the presence of acid and having strong ionic strength), it may be a suitable environment

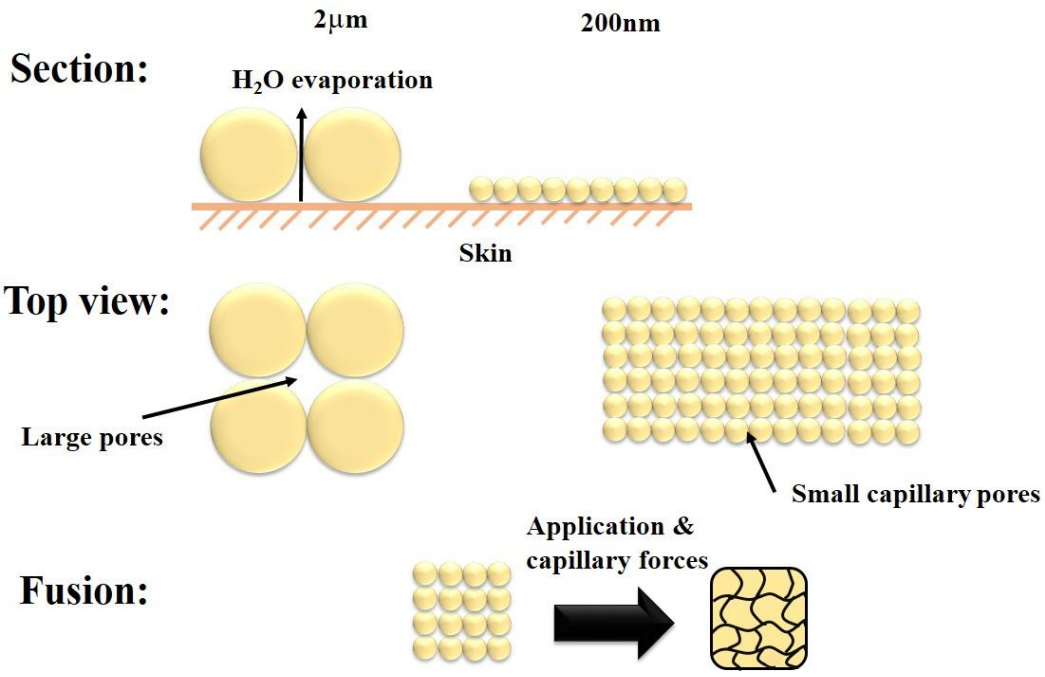

Fig. 6: Model of film formation on the skin for 2 mm and 200 nm lipid particles (in cross-section (top) and from above (middle)), a new model of nanoparticle fusion into a non-porous film (bottom).

for particles to accumulate. Unfortunately, there have been few *in vivo* studies on the effect of gastric and pancreatic lipase on the *in vivo* decomposition of nanoparticles [66-73].

Topical application

A large part of the potential of applying SLN is their use as topical products in addition to medicinal uses and cosmetic products. Lipid nanoparticles are considered as carrier systems with high tolerance for skin applications due to having physiological or degradable fats. The capacity of lipid nanoparticles has been proven in terms of skin targeting, controlled release, low skin side effects, and protection of active ingredients [68-76]. The small size of lipid nanoparticles improves direct contact with the stratum corneum of the skin and allows the penetration of encapsulated agents into the skin. Furthermore, SLN can be added to existing commercial products without changing its formulation, such as cosmetic day cream, where the addition of SLN increases its coverage [74-78]. The results of the study by Muller et al. [44] indicated that adding SLN to pure commercial formulation increases skin moisture by 24% and stabilized commercial formulation by 32%. Fig. 6 shows the model of film formation on the skin and a new model of fusion of nanoparticles into a non-porous film.

Ophthalmic administration

In the case of ophthalmic drugs including eye drops due to the limited duration of the presence of the drug in the eye, poor bioavailability is a fundamental requirement for improving the effectiveness of drugs by increasing the rate of drug penetration and maintaining an appropriate therapeutic level. By increasing the viscosity of the drug delivery system, the presence time of the drug becomes longer, which may bring disadvantages such as preventing the penetration of the drug and its insufficient effectiveness. Complications related to toxicity have also made it difficult to use suspensions containing nanoparticles that improve adhesion properties and can provide optimal effectiveness [75-79]. Lipid nanoparticles are superior to others due to their ability to be sterilized through autoclaving, appropriate biocompatibility due to the use of physiological lipids which improve drug tolerance with low side effects. In addition to the aforementioned applications, the use of these nanoparticles in gene therapy, the loading of anti-

cancer drugs, dental treatment, and food industry has developed the application of this nano system day by day [77-79].

CONCLUSION

The presence of active drug cannot guarantee effective drug delivery in the patient's body. Therefore, an effective and efficient DDS must transfer the active drug to the desired tissue so that the drug starts to be effective at a certain time and place. Due to the fact that the old DDSs are less able to achieve these goals, using new systems with optimal drug delivery features is drawing attention of many researchers. Such systems can change the way of drug's release, speed, distribution, and even the occurrence of adverse effects. They use nanostructured carriers as one of the newest and most advanced types of drug release systems. However, the high cost of preparation and lack of safe polymers allowed the nanocarriers for drug delivery systems. Using lipid nanoparticles is an appropriate solution to overcome these limitations. The possibility of SLN synthesis by different methods has made various hydrophobic and hydrophilic drugs loaded inside lipid nanoparticles. Among the various methods used to prepare these lipid nanoparticles, the methods based on not using organic solvent are more suitable. In addition, cold high pressure homogenization methods and solvent evaporation emulsification methods are suitable methods for temperature sensitive drugs. In short, SLN has a wide range of application and advantages over other nanocarriers.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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