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A Promising Approach for Improving Solubility and Bioavailability: Solid Lipid Nanoparticles

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ABSTRACT

Background: *This review summarizes the information about Solid lipid nanoparticle which was a novel approach that brings revolutionary changes in the field of pharmaceutical science. Currently, Lipid-based drug delivery has gained more attention for enhancing the solubility and ultimately bioavailability of poorly water-soluble drugs.*

Objectives: *This review represents a new approach for enhancing the solubility as well as bioavailability for oral administration of poor solubility of drugs. This review emphasizes the selection of desired ingredients such as lipid, surfactant/emulsifier, and cosurfactant in the formulation of solid lipid nanoparticles. This review also highlights and discusses the examples of solid lipid nanoparticles loaded drugs which results in prolonged-release, high entrapment efficacy, and stability of a drug and also sheds light on drug targeting to specific tissue by preparing solid lipid nanoparticle which maximizes effectiveness and reduces toxicity while avoiding adverse effects on non-target tissues.*

Conclusion: *Solid lipid nanoparticle was an advanced promising novel drug delivery for improving the bioavailability of poorly soluble drugs which Prolongs the therapeutic activity.*

Keywords: Solid lipid nanoparticle, Bioavailability, Selection of ingredients, Hot homogenization technique, Recent advances of solid lipid nanoparticle.

INTRODUCTION

Physicist Richard Feynman proposed a thought about nanotechnology in 1959 that brings revolutionary changes in the field through future scientific researches [1]. The Drug delivery system was improved by developing colloidal delivery systems such as nanoparticles, liposomes, and micelles. Nanoparticles are solid polymeric, submicronic colloidal framework range between 5-300 nm comprising of macromolecular substances that differ in size 10-1000 nm. The drug was dissolved, adsorbed, entrapped, attached, or encapsulated within the nanoparticle matrix [2]. Nanoparticles were prepared from synthetic or natural polymers and for better drug delivery as well as reduce toxicity. Nanotechnology has been used in various fields such as different diseases and disorders treatments as well as in the medication for therapeutic drug delivery. Pharmaceutical nanotechnology involves nanoscience for developing nanomaterials such as devices, biosensor materials, better drug delivery, diagnostic, and imaging. Nano sized drug delivery system has been created to defeat the following issue: a) changing the drug concentrations due to poor absorption of the drug, rapid metabolism of the drug, and elimination of the drug. b) Drug with poor solubility c) high toxicity of the drug due to distribution in different tissue [3]. Lipids have been used to overcome the difficulties especially for lipophilic pharmaceuticals then these lipid nanoparticles were termed as solid lipid nanoparticles (SLNs) [4].

A specific aspect of poorly water-soluble drugs for *in vivo* performance through oral administration was the hindrance of being dissolved into the GIT fluid. Therefore, the dissolution rate of poorly water-soluble drug increases resulting in the improvement of oral bioavailability [5]. The attributes of lipid nanoparticles for oral and peroral delivery were associated with their adhesive properties. Lipid nanoparticles upon adhering to the GIT wall release the drug on the site of absorption. The cause for expanding the interest of the lipid-based framework involves 1. Increasing Manufacturing scale-up ability. 2. Better characterization of lipid excipients. 3. Oral bioavailability was improved through lipid.

Solid lipid replaced the Liquid lipid to overcome the drawbacks associated with the liquid state of the oil droplets and transformed into solid lipid nanoparticles as shown in Figure 1. They were prepared using physiological biocompatible excipients. Their solid matrix effectively protected the drug-loaded against chemical degradation under rigid biological surroundings and provides the maximum flexibilities in the modification of the release profiles of the drug [2,6-9].

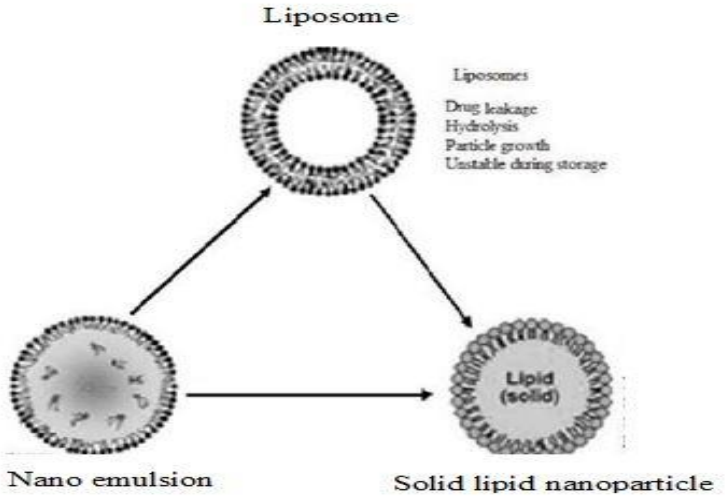

Figure 1: A diagrammatic representation of SLN over emulsion and liposomes [10].

Concept of solid lipid nanoparticles

Solid lipid nanoparticles were first introduced in the 1990s [3] which are composed of physiological lipid, spherical sub-micron ranges between 50 to 1000 nm colloidal carriers dispersed in water or aqueous surfactant solution. Solid lipid nanoparticle was structurally consistent with the solid hydrophobic core within a monolayer of phospholipids coating as shown in Figure 2. The drug was dispersed in the solid high melting fat matrix within the solid core. The hydrophobic chains of phospholipids were implanted within the fat matrix. Both lipophilic and hydrophilic drugs were loaded in SLNs [11]. Solid lipid nanoparticle usually involves the BCS class II and IV [12].

Accordingly, drug mobility reduces in the solid lipid state as compared to the oily phase, hence enhancing the controlled release of loaded drugs. SLN stability can be further improved by the addition of a surfactant coating [13-15].

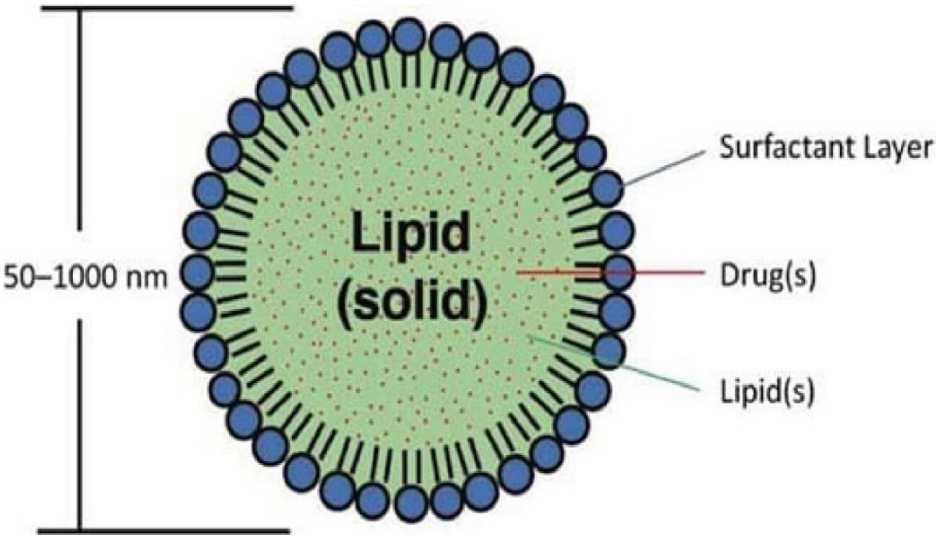

Figure 2: The General structure of solid lipid nanoparticle (SLN) loaded with the drug [16].

SLNs having several advantages for drug delivery which involve lipid chemical stability, enhanced permeability through biological barriers, ability to change their surface, the possibility of co-delivery of a large number of drugs as well as protection of the incorporated drug from degradation [17]. Whereas, SLNs have some disadvantages including drug expulsion during storage. Reestablishment of lipid molecules to form perfect crystal lattice during storage limits the space available for drug incorporation leading to drug expulsion [18,19].

Compositional profile of solid lipid nanoparticles

Lipid and surfactant or stabilizer play an important role in the formulation of solid lipid nanoparticles along with co-surfactant, cryoprotectants, preservatives, and charge modifiers as shown in Figure 3. Surfactants help in stabilizing the SLN structure by decreasing the interfacial tension between the hydrophobic surface of the lipid core and the aqueous environment [11,20].

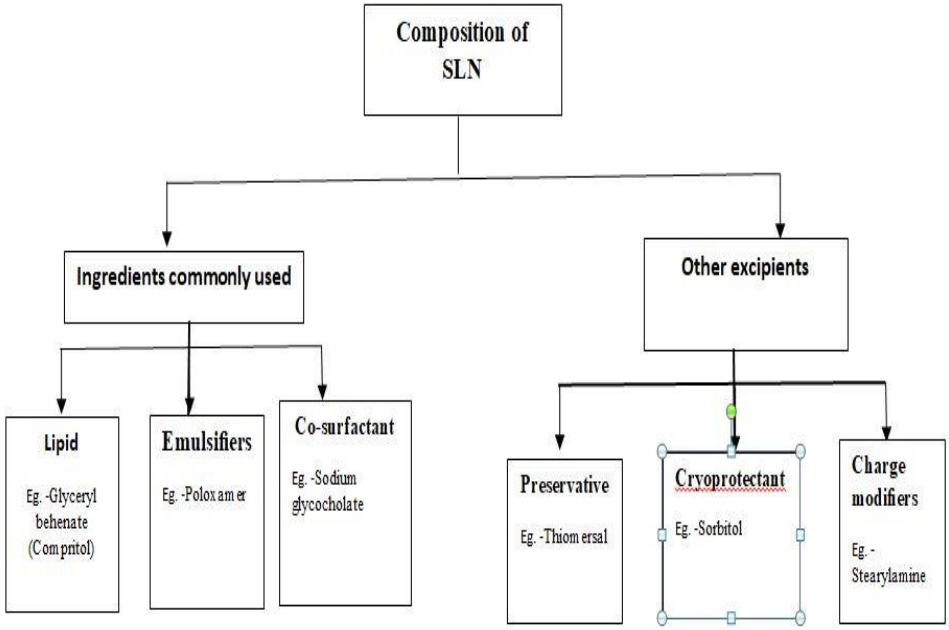

Figure 3: Composition of solid lipid nanoparticles.

Selection criteria for lipids: The lipid plays an important role in lipid nanoparticles that affect their drug loading capacity, and the sustained release of the formulations along with their stability. The solubility of the drug was checked in different lipids for selecting the desired lipid. This was examined by melting the lipid and adding the optimum amount of the drug. The addition of drug was continued until a change in solution was obtained. For Example, efavirenz loaded SLNs were prepared by utilizing glyceryl monostearate as core lipid material because of its solubilizing potential for the drug as it was having higher drug solubility and it holds a large amount of drugs in less quantity of lipids in comparison with other lipids [21].

Selection criteria for emulsifier: The choice of emulsifier and their concentration has greatly affected the nature and stability of SLN. Different emulsifiers and their combination have been used to stabilize the solid lipid nanoparticle. The combination of emulsifiers more accurately avoids particle agglomeration [22]. Phospholipids are not only sufficient due to the geometrical structure of phosphatidylcholine for the formulation of solid lipid nanoparticles which is truncated cone due to its double lipid chains and large head group [23]. The mixture of non-ionic surfactants with lecithin also increased the particle size. The combination of different emulsifying agent's forms mixed films of surfactant at the interface which covers the surface and produces adequate viscosity for increasing the stability [24,25]. The influence of surfactants in the stability of SLNs formulation results in 1.5% Tegocare 450 which was the most effective stabilizer for the Witepsol E 85 solid lipid nanoparticle dispersion as compared to tyloxapol, Tween 80, and Pluronic F68 [26,27] determines there is no ideal emulsifier. So, the choice of emulsifier depends upon the lipid matrix's nature.

Selection criteria for co-emulsifier: Co-surfactant is used for increasing the curvature of the interfacial layer to which emulsifier will form vesicles [23,28] which leads to the reduction of their mobility. Therefore, when there is no external power input to damage the bilayer which reduces its ability to cover newly created surfaces during storage [26]. It is observed that effective co-surfactant will be an amphiphilic molecule that (i) structure of an aromatic ring or lipophilic tail as hydrophobic part of a solid structure which does not increase the mobility of the crystallized lipid at the interface. (ii) a hydrophilic part. It is

predicted that a potent co-surfactant is useful in stabilizing the SLN during the homogenization process and upon polymorphic transition during storage. Bile salts such as sodium glycocholate, sodium taurodeoxycholate are used as co-emulsifier.

METHODS OF PREPARATION

Hot homogenization technique

This technique was performed above the melting point temperature of the lipid referred to as the homogenization of an emulsion. Then a pre-emulsion of the drug-loaded lipid melts and the at the same temperature aqueous phase was formed with the help of high shear mixing device. The nature of the final product is influenced by the nature of pre-emulsion to a high degree and obtained droplets in the size range of a few micrometres. Lower particle sizes formed due to high temperature and the reduced viscosity of the inner phase but the degradation rate of the drug and the carrier also increases due to high temperature. The temperature of the sample was increased 10°C for 500 bars pressure and around 3 to 5 homogenization cycles at 500-1500 bar, this process was repeated several times. The particle size increases on increasing the homogenization pressure, due to particle coalescence which causes high kinetic energy of the particles. Due to the liquid state of the lipid, the primary product was a nano emulsion then cooled at room temperature leads to the formation of solid particles [11,29]. This method was used for incorporating both lipophilic and insoluble drugs but not suitable for hydrophilic medications due to low entrapment efficiency when the hydrophilic drug partitions to the aqueous phase during homogenization. The High entrapment efficiency of ascorbic acid loaded SLN was achieved through the hot homogenization method [30].

Cold Homogenization

Cold homogenization technique was used to overcome the drawbacks of hot homogenization and more appropriate for hydrophilic drugs with particle sizes ranges from 50-100 nm [31]. In this method, the drug exposure to temperature was not dismissed completely due to drug solubilization in melted lipid, and because of the heat generated during the homogenization procedure. Therefore, the drug-loaded in melted lipid was cooled rapidly utilizing fluid nitrogen or dry ice. The rapid cooling produces the drug solid solution which was subsequently powdered to frame micro particles then it was added in a chilled aqueous solution containing emulsifier and homogenized at room temperature for the even allocation of a drug in the lipid lattice [11].

Ultrasonication

In this process, the drug was added to the lipid phase and at the same temperature, the hot aqueous phase was added to the lipid phase which was emulsified through probe sonication. The obtained pre-emulsion was ultrasonicated utilizing probe sonicator through a water bath at a temperature of 0ºC. The temperature kept at 5ºC above the melting point of the lipid to overcome the recrystallization. The acquired Nano emulsion (o/w) was separated through a 0.45µm membrane filter to remove impurities during the procedure [32]. Then SLN obtained was stored at 4ºC. To increase the stability of the formulation then SLN was lyophilized through a lyophilizer to get solidify dried powder and mannitol (5%) as cryoprotector was included in SLNs. Vinpocetine loaded SLN prepared through the ultrasonic-solvent emulsification technique [33].

Microemulsion based method

Microemulsions were composed of lipids, an emulsifier, co-emulsifiers/co-surfactant, and water which formed through stirring an optically transparent mixture at a temperature of 65-70°C. The hot microemulsion is dispersed in cold water at 2-3°C

temperature under mixing. SLN dispersion was utilized as granulation liquid with the granulation process for transferring into the solid product, but too much water needs to be removed in case of low particle content. High-temperature gradient causes fast lipid crystallization and prevents aggregation of particles [34]. Vincristine-Dextran Complex Loaded Solid Lipid Nanoparticles was prepared through the micro emulsion method which was administered to the brain for drug delivery [35]. Ultrafiltration or lyophilization was needed to overcome the drawbacks like diluted final dispersion of SLN. A large amount of surfactant or co-surfactants used is another major disadvantage because it may cause toxicity [36,37].

Solvent emulsification-evaporation method

In Solvent Emulsification-Evaporation Method, the lipophilic material and hydrophobic drug were dissolved in a water-immiscible organic solvent (for example cyclohexane, dichloromethane) and then that is emulsified in an aqueous phase using a high-speed homogenizer. To improve the effectiveness of fine emulsification, the coarse emulsion was quickly gone through the micro fluidizer. Then the organic solvent was evaporated by mechanical stirring at room temperature and reduced pressure (40–60 mbar) (e.g. rotary evaporator) leaving lipid precipitates of SLNs [38]. Here the mean particle size relies upon the concentration of lipid in the organic phase. Resulting in the production of small particle size 25 nm could be obtained with a low lipid load (5%) related to organic solvent and are monodisperse with high encapsulation efficiency.

The major advantage of this technique is the reduction of any thermal stress, which significant for the addition of highly thermolabile drugs. The drawback is the use of an organic solvent that comes in contact with drug molecules and reduces the solubility of the lipid with the organic solvent [39]. Irbesartan loaded solid lipid Nanoparticles prepared using glyceryl monostearate as lipid through solvent emulsification technique followed by probe sonication and characterization is done which results in 73.8% entrapment efficiency showed good bioavailability in Wistar rats and determine optimum stability in the studies [40].

Solvent emulsification-diffusion technique

This strategy utilizes solvent (e.g. benzyl alcohol, butyl lactate) that must be partially miscible with water and carried out either in an aqueous phase or in oil. Both the solvent and water were commonly saturated to ensure the underlying thermodynamic equilibrium of both liquids. The saturation step was performed at a temperature in solubilizing the lipid by heating then both drug and lipid were added in water and emulsified by solvent saturated aqueous solution containing stabilizer with mechanical stirrer resulting in the formation of o/w emulsion then water in ratio from 1:5 to 1:10, were added leads to solvent diffusion into the continuous phase and forms lipid aggregate in the nanoparticles. so, both lipid phase and the aqueous phase was kept at the same high temperature and the diffusion step was performed either at room temperature or at the temperature under which the lipid was dissolved constant stirring is done during the preparation. Lyophilization or vacuum distillation was used for the elimination of the diffused solvent [41].

Supercritical fluid technique

The liquid was used when its pressure and temperature exceed its critical value as a supercritical fluid. The critical point includes 31.5ºC temperature with 75.8 bar pressure was easily accessible and doesn't cause the oxidation of drug material, after the process, it leaves no traces as it was cheap, non-inflammable, ecologically acceptable simple to reuse. Mostly organic solvents such as DMSO were used in this method because they were completely miscible in SCF-CO_2. This innovation contains a few procedures for nanoparticle production such as Rapid Expansion of Supercritical Solution, Aerosol Solvent Extraction

Solvent, Particles from Gas Saturated Solution, Gas/Supercritical Antisolvent Solution Enhanced Dispersion by Supercritical liquid, and Supercritical Fluid Extraction of Emulsions [42].

Solvent injection technique

In this strategy, the solid lipid was dissolved in water-miscible solvent (for example ethanol, acetone, isopropanol) or a water-miscible solvent mixture. Then, this lipid solvent mixture was injected through an injection needle into a stirred aqueous phase with the addition of a surfactant or without surfactant. The resultant dispersion was then separated with a filter paper to remove any excess lipid. The presence of emulsifier within the aqueous phase leads to the formation of lipid droplets at the site of injection and stabilize SLN until solvent diffusion was completed by reducing the surface tension between the organic solvent and an aqueous phase [10,43,44]. The delivery of Hepatitis B surface antigen for vaccination was prepared using the Solvent injection method through administration in the subcutaneous route.

Membrane contractor technique

The liquid phase was pressed above the melting point temperature of the lipid produces little droplets with the help of membrane pore. The aqueous phase was stirred vigorously and inside the membrane module, it tangentially circulates and sweeps away the droplets being formed at the pore outlets. The product was cooled at room temperature leads to the formation of solid lipid nanoparticles. Nitrogen was utilized to create the pressure for the liquid phase and both the phases were put in the thermostat bath to keep up the required temperature. The formulation of polymeric nanoparticles was prepared by this method by utilizing polymerization of dispersed monomers or dispersion of preformed polymers [42].

CHARACTERIZATION

Particle size

Photon Correlation Spectroscopy (PCS) [45-50] and laser diffraction (LD) [49,51-52] are the most useful method for particle size estimation of lipid nanoparticles. Dynamic light scattering was another name of Photon correlation spectroscopy. The fluctuation of the intensity of the scattered light is due to particle movement, which was determined by this method also referred to as quasi-elastic light scattering (QELS). PCS is generally accurate and sensitive method but PCS can measure the only size ranges from few nanometers to about 3 μ [52,53] which is sufficient for a determination of solid lipid nanoparticles. Whereas, laser diffraction can determine larger particle sizes >3 μ; [52,53]. Laser diffraction covers a broad size range from the nanometer to the lower millimeter range (40nm to 2000 micrometer). This strategy depends on the diffraction angle on the particle radius. Smaller particles cause more intense scattering at tremendous angles than the large particles.

Zeta potential

Zeta potential is used for the determination of surface charge of solid lipid nanoparticles through electrophoretic mobility of solid lipid nanoparticles in U type tube at a temperature of 25∘C by using Zetasizer. The zeta potential shows the degree of charge present on suspended particles in the dispersion. The high value of zeta potential confers stability because particles prevent aggregation. The value of zeta potential was almost between (-15.9 to -22.1) [21].

Polydispersity index

SLNs/NLCs are typically polydisperse, which determines the polydispersity index (PI) which is crucial to understand the size distribution of the nanoparticles. As lower the PI value, the more monodispersed the nanoparticle dispersion is. Most of the researchers accept PI value less than 0.3 as the ideal value [54,55]. PI can be determined by PCS [48,50,56].

Shape and morphology

Transmission electron microscopy (TEM), Scanning electron microscopy (SEM) and atomic force microscopy (AFM) are the methods used for the evaluation of the shape and morphology of lipid nanoparticles. These techniques are also used for the evaluation of the particle size and size distribution. SEM uses electron transmission from the sample surface, while TEM uses electron transmission through the sample. Various SEM [57] and TEM [45,46,51,57,58] study indicates the spherical shape of the lipid nanoparticles. Field emission SEM (FESEM) can detect nanometer size range but normal SEM is not very sensitive to the nanometer size range. [59].

AFM maintains a three-dimensional surface profile. AFM gives structural, functional, mechanical, and topographical information about surfaces with nanometer to angstrom scale resolution. This strategy uses the force acting within the surface and a probing tip cause a spatial resolution likely to be 0.01 nm for imaging. Advantages include direct analysis of the originally hydrated, solvent-containing samples is possible without vacuum during the process and the sample shouldn't be conductive. AFM compared with SEM and reported similar particle sizes of the nanoparticles by both techniques [60].

Crystallinity and polymorphism

Differential scanning calorimetry DSC [49,56] and X-Ray diffractometry XRD [56] are the two broadly used methods for the determination of crystallinity and polymorphic behaviour of the parts of the SLNs. DSC involves crystallization and melting behaviour of all solid and liquid constituents of the particles, while the identification of specific crystalline compounds based on their crystal structure done by XRD [61]. DSC based on different lipid modifications acquired different melting points and melting enthalpies. Here, the crystallinity of the particles was measured as crystallinity indexes (CI) and is calculated by the following equation [49,62]

$$CI(\%) = Melting\frac{Enthalpy(SLN)}{Melting\ Enthaply(Bulk\ Material) * Concentration\ (Lipid\ Phase)}$$

This index was not accurate to measure because the particles can crystallize partially in a different modification and the effect is peak separation is not possible in most of the cases [63].

In X-Ray diffractometry, the monochromatic beam of X-ray is diffracted at angles evaluated by the spacing of the planes in the crystals and the type and arrangement of the atoms, which is recorded by a detector. XRD pattern can detect the arrangement of lipid molecules, characterize and identify the structure of drug molecules, lipid, and the phase behaviour [64,65].

Drug Incorporation and Entrapment Efficiency

The entrapment efficiency (EE) was determined by standard analytical techniques such as HPLC, spectrophotometer, or liquid scintillation counting after centrifugation/ultracentrifugation of the aqueous dispersion. The amount of free drug was

identified in the supernatant and the amount of incorporated drug was analysed as a result of the initial drug minus the free drug. The EE was determined by the equation:

$$EE(\%) = \frac{W_{Initial\ Drug} - W_{Free\ Drug} * 100}{W_{Initial\ Drug}}$$

$$Drug\ Loading\ (\%) = \frac{W_{Initial\ Drug} - W_{Free\ Drug} * 100}{W_{Lipid}}$$

where "$W_{Initial\ drug}$" is denoted as the mass of initial drug used for the assay and the "$W_{free\ drug}$" is denoted as the mass of free drug detected in the supernatant after centrifugation of the aqueous dispersion and W_{Lipid} was denoted as the amount of vehicle. SLNs of the lipophilic drug-like mifepristone prepared by ultrasonication and shear homogenization method which showed relative long-term stability as the leakage was very negligible after being stored for one month having more than 87 percent of EE% [66].

In vitro drug release

In-vitro drug release studies are used for quality control studies and the prediction of *in-vivo* kinetics. Due to the very small size of the SLN particles, the release rate investigated *in-vivo* can vary significantly from the release obtained in buffer solution. Thus, *in-vitro* release studies remain useful for quality control and evaluation of the influence of process parameters on the release rate of active components.

ADVANCEMENT IN SLNs

Lipid Drug Conjugates (LDCs)

The fundamental issue with SLNs is the poor loading of drugs because of the partitioning effect. Notwithstanding, profoundly intense hydrophilic drugs in low doses can suitably be incorporated in solid lipid matrix [67]. To overcome this problem, lipid drug conjugates (LDCs) were used, which shows improvement in drug loading capacities of SLN limit up to 33%. For LDC, first, insoluble drug lipid conjugate bulk is prepared by salt formation or via covalent linking. LDCs are spherical and their lipid drug core is stabilized by a surfactant interfacial region. Fatty acids, acylglycerols, waxes, and blend of these are used as core lipids. Surface stabilizers include bile salts, cholesterol, phospholipids, sphingomyelins. The utilization of ligands promotes tissue targeting. LDC facilitates the incorporation of both hydrophilic drugs such as doxorubicin and tobramycin and lipophilic drugs such as progesterone and cyclosporine A [68].

Nanostructured Lipid Carriers (NLCs)

NLCs are the second generation of lipid nanoparticles. Nanostructured lipid carriers (NLCs), formulated with biocompatible solid and liquid lipids (oils) in a usual ratio of 70:30 up to a ratio of 99.9:0.1 at room and body temperature, which is improved generation of solid lipid nanoparticles (SLNs), which provide a delivery system for various active drugs with controlled-release characteristic [67,69]. The objective was to increase drug loading and prevent drug expulsion. Upon addition of a liquid lipid to a solid lipid lead in a less ordered crystal lattice which increased imperfection that results in high drug entrapment and stability during storage. Introducing liquid lipids causes a melting point of depression in comparison with a pure solid lipid. It works at a lower temperature which was the advantage of this method. NLCs involve an interesting advantage of

SLNs such as low toxicity, drug protection, biodegradation, prolong release, and prevent the use of organic solvents in production [70,71]. NLCs can be of three distinct sorts, that is imperfect type, multiple types, and amorphous type [3]. The NLCs have essentially been examined in the topical and dermatological preparations [13] in the delivery of clotrimazole [72,73], ketoconazole [74], another antifungal imidazole [75] and ascorbylpalmitate [76].

Recent advances of solid lipid nanoparticle

SLNs are the most prominent carrier for the delivery of drugs. Incorporation of the drug into solid lipid nanoparticles enhances the efficiency and bioavailability of poorly water-soluble drugs. It is proved that SLNs was an effective drug targeting carrier. There are following various potential areas of application of solid lipid nanoparticles which were elaborated in Table 1.

Table 1: Different applications of solid lipid nanoparticles.

Incorporated drug or substance	Lipid	Method	Application type	Enhancement efficiency	Size (nm)	advantages	References
Paclitaxel	Miglyol812N	solvent emulsification and evaporation technique	targeted carrier for solid tumours	increased efficiency up to 98%	213 nm	encapsulation efficiency is high	[77]
Timolol	Theobroma oil, homolipid	melt emulsification with high-pressure homogenization	Ocular delivery	increased efficiency up to (>44%)	42.9 ± 0.3 nm	improving ocular bioavailability	[78]
Beclomethasone dipropionate	Stearic Acid, Miglyol 812, Compritol 888 ATO, Dynasan 114, Dynasan 118, Gelucire 44/14	high-shear homogenization technique	Pulmonary delivery	increased efficiency up to 99%	150 to 200 nm	high entrapment efficiency	[79]
siRNA	Cholesterol hydrochloride, 3β-[N- (N′,N′-dimethylaminoethane)-carbamoyl]-cholesterol (DC-Chol), Cholesteryl oleate and glyceryl trioleate	modified emulsification-solvent evaporation method	Gene delivery	increased efficiency up to 91%	117.4 ± 11.7 nm	cross the BBB to the tumour site, reduction in tumour volume	[80]
Doxorubicin	Compritol, Stearylamine	hot melting homogenization method using an emulsification-ultrasound	Parenteral delivery	increased efficiency up to 99%	127 ± 14 to 94 ± 1 nm	Improve the antitumor activity and drug release	[81]
Prednicarbate	Precirol, Witepsol, Dynasan 114, Compritol	High-pressure homogenization	Topical delivery	increased efficiency up to (>90%)	144nm	increase the benefit/risk ratio of topical therapy	[82]

Rhodamine B	Stearic acid	Solvent emulsification/evaporative method	Stealth nanoparticles	phagocytic uptake of Solid lipid nanoparticles (SLNs) was better than SSLNs	286.3±48.30nm	stealth SLNs evade phagocytosis of macrophages	[83]
Cucurbitacin B	Compritol 888 ATO	high-pressure homogenization method	liver targeting	increased efficiency up to 63%	135 nm	high entrapment efficiency	[84]
Efavirenz	glyceryl monostearate	solvent evaporation technique	Oral delivery	increased efficiency up to 86%	124.5 ± 3.2 nm	Bioavailability enhanced	[21]
Vinpocetin	Glyceryl monostearate	Ultrasonic-solvent emulsification	Oral delivery	increased efficiency up to 98%	70± 200nm	Bioavailability enhanced	[85]
Lamivudine	stearic acid	solvent evaporation technique	targeted drug delivery to the brain	increased efficiency up to 48.12%	206.4 nm	Bioavailability enhanced	[86]
Carvedilol	Dynasan 114	hot homogenization followed by ultrasonication method	targeted drug delivery	increased efficiency up to 96.03 ± 0.13 to 93.46 ± 0.21%	130.70± 1.80 to 154.40 ± 2.40 nm	sustained and controlled delivery	[87]
Fluconazole	Compritol 888 ATO (glyceryl behenate), pricerol ATO5 (glyceryl palmitostearate)	modified high shear homogenization and ultrasonication method	topical delivery	increased efficiency up to 83.04%	292 ± 500nm	improved skin penetration and increased therapeutic effect	[88]
Calcitonin	Trimyristin	w/o/w emulsion technique	Oral delivery	increased efficiency up to 86%	200 nm	Improvement of the efficiency of such carriers for oral delivery of proteins	[89]
Methotrexate	Stearic acid, Monostearin, Tristearin, Compritol 888	Solvent diffusion method	Oral delivery	increased efficiency up to 72.4 ± 0.14%	120± 167nm	Bioavailability enhanced	[45]

CONCLUSION

From the review, it was evident that during recent years, SLNs has emerged as a promising novel drug delivery system. This review overviews that drugs loaded solid lipid nanoparticle have a high therapeutic activity which maximizes effectiveness while avoiding adverse effects on nontarget tissues. The present paper encompasses the selection of ingredients that affect their drug loading capacity and the sustained release of the formulations along with their stability. This review paper summarizes that SLNs are complex systems with rapidly developing fields of nanotechnology which have the potential for oral delivery to improve GI absorption of poorly water-soluble drugs.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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