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SOLID LIPID NANOPARTICLES-A TARGETED CARRIER- A REVIEW

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ABSTRACT

Solid lipid Nanoparticles (SLN) have emerged as a targeted drug delivery system with several applications within the field of pharmaceuticals, cosmetics, research, clinical drugs and different allied sciences. The review comprises an overview on the potential advantages and the disadvantages of solid lipid nanoparticles, drug incorporation models, method of preparation, secondary production steps, characterization, application and drug toxicity of solid lipid nanoparticles. SLN comprises the solid and lipid materials which were incorporated and by producing them as a Nanoparticle it is widely used in many of the disease conditions nowadays. Different production strategies that area unit appropriate for big scale production and applications of solid macromolecule nanoparticles area unit delineated. There is a specific analytical techniques for characterization of solid nanoparticles like Scanning electron microscopy (SEM) and differential scanning calorimetry a. If fittingly investigated, solid macromolecule nanoparticles might open new vistas in medical aid of advanced diseases.

KEYWORDS

Solid lipid nanoparticles, Drug release, Preparation, Characterisations, Application and Toxicity aspects.

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INTRODUCTION

Nowadays formulation scientists facing various challenges in improving the low solubility and bioavailability of the newly invented drugs. To overcome above problems is to formulate the new particulate carrier system. The existence of different colloidal drug carrier systems may raise the queries to the scientists about suitable carrier system for a desired purpose. The accompanying viewpoints ought to be contemplated[1].

Drug loading capacity
Sufficient drug targeting
In vivo fate of the carrier system (interaction with the surrounding biological fluid, degradation rate, accumulation in organs, etc)
Toxicity, acute as well as chronic
Large scale production[2].

Nanoparticles are solid colloidal particles. Which are available in range from 10 to 1000nm (1.0µm), in which the active drug or biologically active material are dissolved, entrapped, and/or to which the active principle is adsorbed or attached. Goal of nanotechnology is same as that of medicine: to diagnose as accurately and early as possible and to treat as effectively as possible without any side effects using controlled and targeted drug delivery approach[3].

Nowadays, Lipid-based nanocarriers are an acceptable approach and have gained significance in the current era because of their various prominent properties, such as low toxicity, improved bioavailability, high biocompatibility, high drug-loading efficiency, and high protection from degradation in the gastro intestinal tract. Various lipids used for the preparation of lipid nanocarriers are those which are biodegradable and showing biocompatibility in physiological media or biological fluid[4].

To overcome the limitations of polymeric nanoparticles, lipids are incorporated as a carrier, especially for lipophilic pharmaceuticals. These lipid nanoparticles also called as solid lipid nanoparticles (SLNs).

It is the new generation of submicron-sized lipid emulsions in which the liquid lipid has been replaced by a solid lipid. SLN gives a properties like small size, large surface area, high drug loading capacity, interaction of phases at the interfaces, and they are attractive for their potential to improve the performance of pharmaceuticals, nutraceuticals and other materials[5].

Drug Delivery System developed using Nanotechnology principles are:
Nanoparticles,
Solid Lipid Nanoparticles,
Nanosuspension,
Nanoemulsion,
Nanocrystals[3].

Classification of Nanoparticles
Polymeric nanoparticles
Solid lipid nanoparticles
Metal nanoparticles
Ceramic nanoparticles
Carbon based nanoparticles[5].

SOLID LIPID NANOPARTICLES

Solid lipid nanoparticles were discovered by Gasco and Muller in 1991 it represent an alternative carrier system to tradition colloidal carriers[6]. Lipids have been used as an alternative carrier for polymeric nanoparticles, particularly for lipophilic pharmaceuticals and lipid nanoparticles are known as solid lipid nanoparticles (SLNs)[7]. The system consists of spherical solid lipid particles in the ranges of nanometer it is dispersed in water or in aqueous surfactant solution. It is identical for oil-in-water type emulsion for parenteral nutrition but the liquid lipid of the emulsion has been substituted by a solid lipid, which yields a Solid Lipid Nanoparticles. SLNs are colloidal particles derived from oil-in-water emulsions by replacing liquid lipids with a lipid matrix that is solid at body temperature and stabilized by the use of surfactants. SLN are prepared by a combination of lipids, fatty alcohol, wax, triglycerides and surfactants[5].

The rationales for the increasing interest in lipid based system are:
Lipids reduce plasma profile variability and enhance oral bioavailability.
Better characterization of lipoid excipients.
An improved ability to address the issues of technology transfer and manufacture scale-up[8].

ADVANTAGES OF SLNs

SLNs particularly those in the range of 120 -200nm are not taken up readily by the cells present in the RES and thus bypass liver and spleen filtration.
The feasibility of incorporating both hydrophilic and hydrophobic drugs.
The carrier lipids are biodegradable and safe.

Avoidance of organic solvents.
Feasible for large scale production and sterilization.
The SLNs can be decreases the danger of acute and chronic toxicity.
It is easy scale up and excellent biocompatibility.
Enhanced bioavailability of entrapped bioactive compounds.
Controlled and targeted release of the incorporated drug can be achieved.
Better control over release kinetics of encapsulated compound.
Drug stability of SLNs for three years has been developed. This is of more importance compared to the other colloidal carrier systems.
Excellent reproducibility with use of different methods as the preparation procedure[9,10].

DISADVANTAGES OF SLNs

Relatively high water content of the dispersions (70-99.9%).
Poor drug loading capacity.
Drug expulsion after polymeric transition during storage.
The low capacity to load water soluble drugs due to partitioning effects during production process.
Particle-particle aggregation due to small size and large surface area.
Difficult in physical handling.
Limited drug loading and burst release[9].
Rationale for research of nanotechnologies in drug delivery includes:
Decrease in toxicity while maintaining therapeutic effects.
Specific drug targeting and delivery.
Biocompatibile and greater safety.
Development of safe medicine[11]

DRUG RELEASE OF SOLID LIPID NANOPARTICLES

These SLNs mainly depends on the chemical nature of the active ingredient and lipid, nature and concentration of surfactants, the solubility of active ingredient in the melted lipid and type of production and the production temperature. Therefore 3 incorporation models have been proposed for study[12].

Homogenous matrix model

The SLN is derived from a solid solution of lipid and active ingredient. A solid solution can be produced by the cold homogenation method. A lipid blend containing the active material in a molecularly dispersed form is produced. After solidification of this blend, it is ground in its solid state to avoid or minimize the enrichment of active molecules in different parts of the lipid nanoparticles.

Drug enriched shell model

It is produced by the hot technique, and the active ingredient concentration in the melted lipid is low during the cooling process of the hot o/w Nanoemulsion the lipid will precipitate first, leading to a steadily increasing concentration of active molecules in the remaining melt, an outer shell will solidify containing both active and lipid. The particle enrichment in the outer area which causes burst release. The percentage of active ingredient in the outer shell is adjusted in a manner of controlled shell model is the incorporation of coenzyme.

Drug enriched core model

Core model can be produced while the active ingredient concentration in the lipid melt is high and relatively close to its saturation solubility. In most conditions cooling down of the hot oil droplets will reduce the solubility of the active in the melt. Active molecules precipitate leading to the formation of a drug enriched core when the saturation solubility exceeds.

PREPARATIONOF SOLID LIPID NANOPARTICLE

The activity of SLNs mainly depends on the method of preparation which in turn influences the particle size, drug release, drug stability, drug loading capacity etc. More approaches available for the production of finely dispersed lipid nanoparticle dispersions[13].

Methods of preparation[3]

High pressure homogenization

oHot homogenization
oCold homogenization
Ultrasonication/high speed homogenization
oProbe ultrasonication
oBath ultrasonication
Solvent evaporation method
Solvent emulsification-evaporation method
Supercritical fluid method
Microemulsion based method
Spray drying method
Double emulsion method
Precipitation technique
Film-ultrasound dispersion

High pressure homogenization

The High pressure homogenization is a powerful technique used for the first time for production of SLNs. High pressure homogenizers uses to push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). The fluid accelerates with a very short distance to very high velocity (over 1000Km/h). Very high cavitation forces and Shear stress disrupt the particles down to the submicron range. Commonly 5-10% lipid content is used but up to 40% lipid content has also been investigated.

HPH is of two types-hot homogenization and cold homogenization. In both cases, a preparatory step involves the drug incorporation into the bulk lipid by dissolving or dispersing the drug in the lipid melt.

Hot homogenization

Hot homogenization is carried out at temperatures above the melting point of the lipid thus produces homogenised emulsion. A pre emulsion that contains drug loaded lipid melt and the aqueous emulsifier phase is obtained by high-shear mixing device. High pressure homogenization of the pre-emulsion is carried out at temperatures above the melting point of the lipid. Due to the decreased viscosity of inner phase and high temperature result in lower particle size. At high temperatures degradation rate of the drug and the carrier is increased. Increasing the homogenization pressure or the number of cycles often results in an increase of the particle size due to high kinetic energy of the particles. The hot homogenization technique can be used for lipophilic and insoluble drugs. This technique is not applicable for incorporation of hydrophilic drugs into SLNs. Homogenization results in low entrapment efficiency because of higher portion of drugs in water.

Cold homogenization

It has developed to overcome various problems associated with hot homogenization such as: Temperature-induced drug degradation, drug distribution into the aqueous phase during homogenization, Complexity of the crystallization step of the nano-emulsion leading to several modifications and super cooled melts. In this strategy the medications containing the liquefied lipid is cooled, the strong lipid ground to lipid microparticles and these lipid microparticles were scattered in a chilly surfactant arrangement yielding a pre-suspension. Then this pre-suspension is homogenized at or below room temperature, the gravitation force is strong enough to break the lipid microparticles directly to solid lipid nanoparticles.

Ultrasonication/high speed homogenization

The SLNs are also prepared by ultrasonication and/or high speed homogenization techniques. For the smaller particle size combination of both ultrasonication and high speed homogenization is required. It reduces shear stress but has some disadvantages like potential metal contamination, physical instability like particle growth upon storage. In this probe sonicator or bath sonicator is used[14].

Solvent evaporation method

SLN can also be prepared starting from emulsion precursor, whose organic phase is constituted by a solvent, which can be either volatile or partially water miscible. O/W or W/O/W emulsions can be prepared: O/W emulsions are used for lipophilic drugs that are dissolved in the inner organic phase of the system, together with the lipid. W/O/W emulsions are suitable for hydrophilic drugs that are dissolved in the inner aqueous phase, while the lipid is dissolved in the intermediate organic phase of the multiple system. Nanoparticles are formed when the solvent is removed either by evaporation (solvent

evaporation technique for volatile solvents) or by water dilution (solvent diffusion technique for partially water miscible solvents): owing to solvent removal lipid precipitates as nanoparticles encapsulating the drug[15].

Solvent emulsification-evaporation method

The particles with a diameters of 30-100nm can be prepared by this technique. Voidance of heat during the preparation is the most important advantage of this technique. In this technique lipid is, are generally dissolved in the organic phase in water bath at 50°C and used an acidic aqueous phase in order to adjust the zeta potential to form coacervation of the SLNs, and then easy separation by centrifugation. The SLN suspension was quickly produced. The entire dispersed system can then be centrifuged and re-suspended in distilled water[16].

Supercritical fluid method

This is a new technique for SLN production. It has the advantage of solvent-less processing. There are several variations in this platform technology for preparation of powder and nanoparticles. SLN can prepared by the rapid expansion of supercritical carbon dioxide solutions (RESS) method. Carbon dioxide (99.99%) was the good choice as a solvent for this method[14].

Microemulsion based method

This method is based on the dilution of microemulsions. As micro-emulsions are two-phase systems composed of an inner and outer phase (e.g. microemulsions). Microemulsion are produced by stirring an optically transparent mixture at 65-70°C, which composed of a low melting fatty acid (e.g. stearic acid), an emulsifier (e.g. polysorbate 20), co-emulsifiers (e.g. butanol) and water. The hot micro emulsion is dispersed in cold water (2-3°C) under stirring. SLN dispersion can be used as granulation fluid for transferring in to solid product (tablets, pellets) by granulation process, but in case of low particle content too much of water needs to be removed. High-temperature facilitate rapid crystallization of lipid and prevent aggregation. Due to the dilution step achievable lipid contents are considerably lower compared with the HPH based formulations.

Spray drying method

It is an alternative and cheaper technique to the lyophilization process. This recommends the use of lipid with melting point more than 70ºC. The best results were obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixture. The addition of carbohydrates and low lipid content favor the preservation of the colloidal particle size in spray drying. The melting of the lipid can be minimized by using ethanol–water mixtures instead of pure water due to cooling leads to small and heterogeneous crystals, the lower inlet temperatures[17].

Double emulsion method

A novel method based on solvent emulsification-evaporation has been used to prepare the hydrophilic loaded SLN. The encapsulated drug with a stabilizer to prevent the partitioning to external water phase during the solvent evaporation in external water phase of double emulsion (w/o/w). This method is particularly used for achieving high incorporation of hydrophilic molecule.

Precipitation technique

Solid lipid nanoparticles can also be produced by a precipitation method which is characterized by the need for solvents. The glycerides will be dissolved in an organic solvent (e.g. chloroform) and the solution will be emulsified in an aqueous phase. After evaporating the organic solvent the lipid show precipitation forming nanoparticles[18].

Film-ultrasound dispersion:

The drugs with lipids were transfer to suitable organic solutions, then subsequently decompression, rotation and evaporation of the organic solution, a lipid film is formed, then the aqueous solution containing the emulsions was added. Using the ultrasound with the probe to diffuser at last, a small and uniform particle of SLN is formed[11].

Membrane contactor technique

The liquid phase was pressed at a temperature above the melting point of the lipid through the membrane pores which forms the small droplets. SLNs were formed by cooling the preparation at

room temperature. Here both the aqueous and organic phases were placed in the thermostated bath to maintain the required temperature and nitrogen was used to create the pressure for the liquid phase More recently, a process known as nanotemplate engineering technology (NET) is developed in which "direct cooling" is utilized. The process consists of three steps.

Melting a pharmaceutically acceptable matrix comprised of lipids, polymers.

Adding pre-heated water with stirring to form the o/w microemulsion.

Cooling to room temperature with stirring to generate the SLNs[5].

Solvent Injection technique

It is a new approach to prepare SLNs. This method of preparation the solid lipid was dissolved in water-miscible solvent (e.g. ethanol, acetone, isopropanol) or a water-miscible solvent mixture. Then this organic solvent mixture was slowly injected through an injection needle in to stirred aqueous phase with or without surfactant. The dispersion was filtered through a filter paper in order to remove excess lipid. The aqueous medium with surfactant helps to produce lipid droplets at the site of injection and stabilize the formed SLNs until the solvent diffusion was completed by reducing the surface tension[19].

Secondary production steps[20]

Freeze drying

Lyophilization is a promising way to increase the chemical and physical stability over extended period of time. Lyophilization were choosen as a best method to achieve long term stability for a product containing hydrolysable drugs or a suitable product per oral administration. Hence transformation to solid state would prevent the Oswald ripening and avoid hydrolytic reactions.

In freeze drying of the product, all the lipid matrices were fully used to form a larger solid lipid nanoparticle with wider size distribution which is due to presence of aggregates between the particles. During the freeze drying process, the removal of water promote the aggregation of the solid lipid nanoparticles.

Sterilization

Sterilization of the nanoparticles must be desirable for parenteral administration and autoclaving to formulations containing heat-resistant drugs. Effects of sterilization on particle size have been investigated and it was found to cause a distinct increase in particle size.

Characterization of SLN's[21,22]

Particle size analysis

Many techniques are available for particle size analysis and zeta potential like scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunneling microscopy (STM) and photon correlation spectroscopy (PCS). To determine the particle size the best suitable methods are Photon correlation spectroscopy (PCS) and laser diffraction (LD). PCS is also known as dynamic light scattering which measures the fluctuation of the intensity of the scattered light, which is caused by particle movement.

Zeta potential

Zeta potential estimation can be completed utilizing zeta expected analyzer or zetameter. Zeta potential provides information about the magnitude of the electrostatic repulsion or attraction between particles in the aqueous suspension of SLN. Zeta potential can serve as an important parameter in the predictions for long term stability of the formulations. High values of zeta potential (e.g., more than +30mV or less than-30mV) can stabilize the colloidal suspension by electric repulsion, Electric repulsion generally results in less contact between the particles and less aggregation. For example colloidal systems that containing steric stabilizers which express good and long term stability when the zeta potential is as low as around 0mV.

Electron Microscopy

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) provide way to directly observe nanoparticles. SEM is however better for morphological examination. TEM has a small size limit of detection. Transition electron microscopy and light microscopy both are

based on same principle but one difference is that in light microscopy light is used instead of electron.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) which is used to measures differences in the amount of heat required to increase the temperature of a sample compared to a reference. Contrasts in heat stream might be positive or negative and are introduced as capacity of the temperature. During phase transition there were differences in the samples when compared to the reference. The rate of crystallinity is estimated using DSC by comparing the melting enthalpy/g of the bulk material with the melting enthalpy/g of the dispersion.

X-ray diffraction

A useful technique to exclude aggregate of more than 1μm and substantial polymorphic β1 transition form to stable; thus help in characterizing the crystalline nature of the compound and determine the polymorphic shifts present. X-beam diffraction (XRD) assume an unmistakable job since they can give auxiliary data on the scattered molecule.

Entrapment efficiency

By measuring the concentration of free drug in the dispersion medium the entrapment efficiency of the drug is determined. Ultracentrifugation carried out using the Centrisart, that consist of filter membrane (molecular weight cutoff 20,000Da) at the base of the sample recovery chamber. The SLNs along with encapsulated drug remain in the outer chamber and aqueous phase moves into the sample recovery chamber. The HPLC or UV spectrophotometer method was used to measure the amount of the drug present in the aqueous phase.

Static light scattering (SLS)/Fraunhofer diffraction

In this method the pattern of light scattered from a solution of particles is collected and fit to fundamental electromagnetic equations in size is the primary variable. This method is fast but it requires advanced knowledge of particles optical qualities and more cleanliness than DLS.

Nuclear magnetic resonance (NMR)

The size and the qualitative nature of nanoparticle can be determine by NMR. The selectivity gave by the synthetic move supplements the affectability to atomic versatility to give data on the physicochemical status of segments inside the nanoparticle.

Dynamic light scattering (DLS)

DLS otherwise called PCS records the variety in the force of the dissipated light on the microsecond time scale. The variation results from interference of light scattered by individual particles under the influence of Brownian motion and quantified by completion of an auto correlation function. The advantage of the method are the lack of required calibration, sensitivity to sub micrometer particles and speed of analysis.

Atomic force microscopy (AFM)

In this method, a probe tip with atomic scale sharpness is rastered across a sample to produce a topological map based on the forces at play between the tip and the surface. The probe can be dragged across the sample (contact mode), or allowed to hover just above (noncontact mode), with the exact nature of the particular force employed serving to distinguish among the sub techniques. From this approach, ultra-high resolution is obtainable which has ability to map a sample according to properties in addition to size, e.g., colloidal attraction or resistance to deformation, makes AFM a valuable tool[23].

Storage stability of SLN

The physical properties of SLN's during prolonged storage can be determined by monitoring changes in zeta potential, particle size, drug content, appearance and viscosity as the function of time. External parameters such as temperature and light appear to be of primary importance for long term stability. The zeta potential ought to be in the middle of - 100 to + 100mV for a scattering to remain truly steady.4°C - Most favorable storage temperature. 20°C - Long term storage did not result in drug loaded SLN aggregation or loss of drug. 50°C - A rapid growth of particle size is observed[24].

EVALUATION PARAMETERS

Various methods used to study the *in vitro* release of the drug are,

In vitro drug release

Dialysis tubing

In vitro drug delivery could be accomplished utilizing dialysis tubing. The strong lipid nanoparticle scattering is put in pre - washed dialysis tubing which can be airtight fixed. The dialysis sac is then dialyzed against a reasonable disintegration medium at room temperature, the examples are pulled back from the disintegration medium at appropriate stretches, centrifuged and examined for the medication content utilizing a reasonable logical technique.

Reverse dialysis

In this method various little dialysis sacs containing 1ml of disintegration medium are set in SLN scattering. The SLN's are then dislodged into the medium.

Franz Diffusion Cell

The SLN's dispersion is placed in the donor chamber of Franz diffusion cell fitted with a cellophane membrane.

Parameter Method of Analysis[23]

Molecular weight gel chromatography, X-ray photoelectron spectroscopy, Surface element analysis Electrophoresis, Laser Doppler anemometry.

Statistical Analysis

Size and entrapment efficiency of SLNs are compared using the Student's t-test. Statistical analyses are also performed.

Stability Studies

Drug loaded SLNs are stored at 25°C for 6 months and average size and entrapment efficiency are determined.

Effect of Sterilization:

To see the effect of sterilization on particle size, zeta potential and entrapment efficiency, blank and drug dispersions are autoclave at 121°C for 20 min.

APPLICATION OF SOLID LIPID NANOPARTICLE[5]

For ocular drug delivery

SLNs can improve the corneal absorption of drugs and progress the ocular bioavailability of both hydrophilic and lipophilic drugs.

As gene vector carrier

Cationic solid lipid nanoparticles can well bind de-oxy ribo nucleic acid (DNA) directly via ionic interaction and intervene gene transfection and can be used in the gene vector formulation.

A targeted carrier for solid tumors

SLNs have been accounted for to be helpful as medication transporters to treat neoplasms.

Anti-tubercular chemotherapy

SLNs-based drug delivery is pulmonary delivery of antimicrobials to treat tuberculosis, a serious lung infection caused by Mycobacterium tuberculosis is another prominent example.

For topical use

Skin SLN items show gigantic planned for treating dermatological conditions by focusing on corticosteroids to dermal malady locales while diminishing fundamental medication retention.

For Parenteral Application

SLN are very suitable for systemic delivery because they consist of physiologically well-tolerated ingredients and they have good storage capabilities after lyophilization and/or sterilization.

SLNs as cosmeceuticals

The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers[25]. The *in vivo* study showed that skin hydration will be increased by 31% after 4 w* by the addition of 4% SLN to a conventional cream. SLN and NLCs have proved to be controlled release innovative occlusive topicals[26]. Vitamin A Produces better localization in upper layers of skin with glyceryl behenate SLNs compared to conventional formulations.

SLNs for potential agriculture application

Fundamental oil separated from Artemisia arboreseens when joined in SLN had the option to decrease the fast vanishing contrasted and emulsions and the frameworks broadly utilized in

horticulture as a reasonable transporter of biologically safe pesticides.

SLN as potential new adjuvant for vaccines

Adjuvants are used in vaccination to enhance the immune response. The safer new subunit vaccines are less effective in immunization and. Therefore, effective adjuvants are required. New developments in the adjuvant area are the emulsion systems. These are oil-in-water emulsions which degraded rapidly in the body. Being in the strong express the lipid parts of SLNs will be debased all the more gradually giving a more drawn out enduring introduction to the invulnerable framework[27,28].

SLN applied to the treatment of malaria

Despite the fact that we live in an era of advanced technology and innovation, infectious diseases, like malaria, continue to be one of the greatest health challenges worldwide. The disadvantages of ordinary jungle fever chemotherapy is to build up various medication obstruction and the vague focusing to intracellular parasites, bringing about expanded portion prerequisites and ensuing heinous harmfulness. Nanosized transporters have been utilized in extraordinary consideration with the intend to limit the reactions of medication treatment, for example, helpless bioavailability and the selectivity of medications. Many nanosized drug delivery systems have already proved their effectiveness in animal models for the treatment and prophylaxis of malaria. Taking into account the peculiarities of malaria parasites, the focus is placed particularly on lipid-based e. g., liposomes, solid lipid nanoparticle.

TOXICITY ASPECTS OF SOLID LIPID NANOPARTICLES

Materials used in drug delivery systems should be biocompatible and assessment of biocompatibility is an obligatory viewpoint to address. The toxicity of a formulation must be resolved by the in-vivo studies, an assortment of In-vitro toxicological assays, performed in selected cell lines, produce helpful data. These tests are broadly acknowledged as first markers of toxicity[29].

Cytotoxicity of SLNs

Assurance of cell toxicity or cell viability are the regular test for the confirmation of biocompatibility or toxicity. SLN prepared using glyceryl monostearate are tested for their cytotoxicity. *In-vitro* test performed on monkey kidney epithelial cells (VERO) and acute lymphoblastic leukemia cells (L1210) using MTT assay. The 50% inhibitory concentration (IC50) of SLN was found to be 0.7 and 0.4mg/mL in VERO cells and 0.5 and 0.3mg/mL in L1210 cells, after 24 and 48 h of incubation, respectively[30]. In another study SLNs prepared using Softisan® 154 and soy lecithin by high-pressure homogenization technique were tested on MCF-7 and MDA-MB231 for the toxicity. The IC50 values reported in this study for MCF-7 cells were found to be approximately 0.28, 0.26, 0.22mg/mL after 24, 48 and 72 h, respectively. Similarly, IC50 values observed for MDAMB-231 cells were found to be about 0.29, 0.29, 0.27mg/mL after 24, 48, and 72 h, respectively. It tends to be inferred that the lipid used to plan nanoparticle has noteworthy impact on the cytotoxicity of acquired SLNs[5].

Impact of Surface Charge

The interaction between the colloidal nanoparticles and cells depend on the surface charge of the particles. Cationic surfactants used in SLNs can create deformities in membrane integrity and sensitize the immune system[31].

Effect of Composition on Cell Viability

Identification of the surfactants utilized for SLNs, regarding biocompatibility as well as for the dependability or timeframe of realistic usability, is something significant for the SLNs framework. Pluronic ® F68 and Tween80 were utilized in effective, oral fluid, and semisolid dose structures. Evaluation of the two surfactants (Pluronic ® F-68 and Tween 80) for cell reasonability joined in SLNs was made. Pluronic ® F-68 in SLNs has indicated great security and 90% cell reasonability, though Tween 80 in SLNs with same lipid structure has demonstrated better steadiness yet with 50% cell suitability[32]. The nature of surfactant used in SLNs

and duration of contact time of SLNs with cells will influences the cell viability percentage.

Genotoxicity

Several studies showed that SLN does not produce damage to DNA or gene related toxicity. Dolatabadi *et al* and Bhushan *et al*. investigated SLN with negative charge by incubating with A549 cells, and found that these did not produce any toxicity or harm to genome DNA determined by gel electrophoresis[33].

However, a report showed DNA damage by acetyl shikonin-bearing SLN, which instigated an increase in comet development in A549 cells. SLN-encapsulated drug further increased the DNA damage[34].

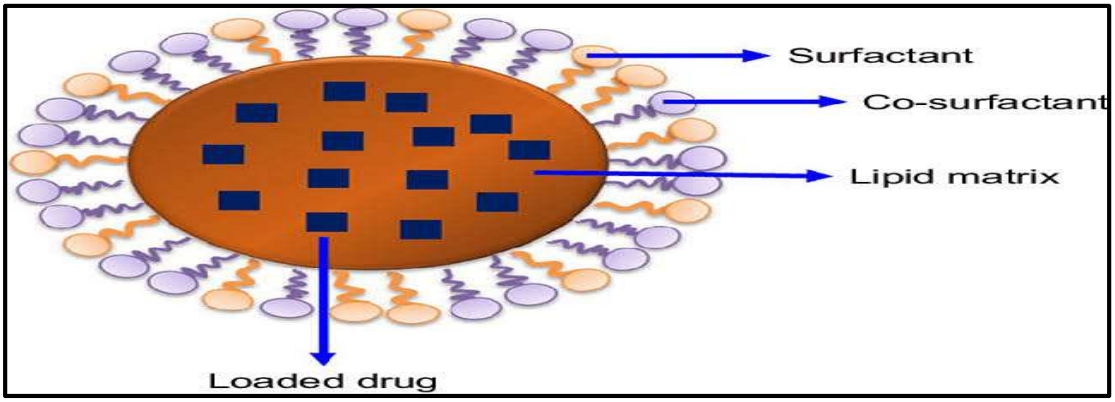
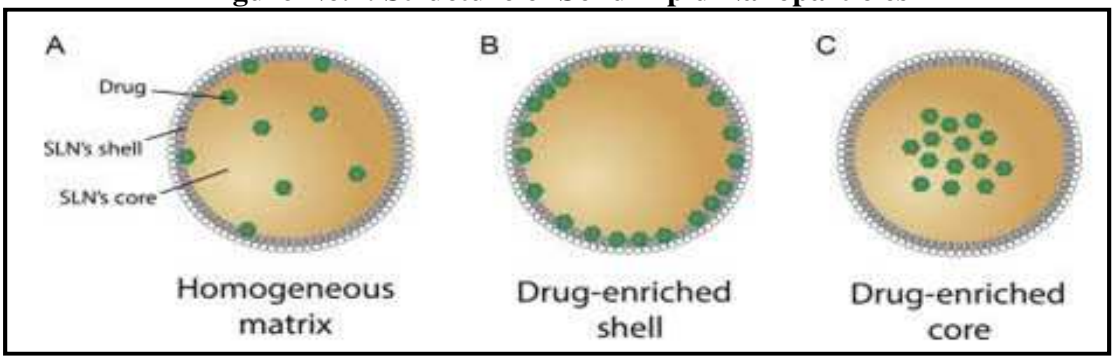


Figure No.1: Structure of Solid Lipid Nanoparticles



CONCLUSION

The SLN are exciting carrier systems for encapsulating bioactive substances and hence widely used nowadays. The present review has concentrated on newer approach of Nanoparticles including Solid Lipid Nanoparticle its advantages, disadvantages, principle of drug release, preparation, characterization, application and toxicity aspects etc. As SLN have potential of controlled drug delivery to a target tissue, there will be a vast area of investigation in improvement of quality, efficacy and safety of drug in future.

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CONFLICT OF INTEREST

There is no conflict of interest.

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