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A Comprehensive Review Onsolid Lipid Nanoparticles

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ABSTRACT: Solid lipid nanoparticles provide several prospects for application in medication delivery, clinical medicine, research, and other sciences, marking a substantial breakthrough in the rapidly developing field of nanotechnology. Because of their unique size-dependent properties, lipid nanoparticles may be used to develop innovative therapeutics. The different forms of solid lipid-based nanocarriers, including lipid drug conjugates, solid lipid nanoparticles, and nanostructured lipid carriers, are explained along with their structural variants. Different production methods suitable for the large-scale synthesis and application of solid lipid nanoparticles are addressed. Since SLNs matched hydrophobic (non-polar) active chemicals in terms of affinity and interactions, they were first widely used in this capacity.For the encapsulation of hydrophilic (polar) and semipolar active compounds, SLNs are currently widely used, despite several challenges, such as enhancing their entrapment efficacy. Lipid carriers are another name for solid lipid nanoparticles, or SLNs. Since lipid nanoparticles are regarded as non-toxic, biocompatible, and very simple to manufacture formulations for, their use has grown. SLNs and nano-structured lipid carriers are not biotoxic since they break down spontaneously. They are also extremely stable. Although SLNs and nano-structured lipid carriers are based on lipids and surfactants, they also investigate the influence of these two matrixes on excipient formulation and their pharmacological significance for stability, storage, and innovative theranostic methods.

KEY WORDS : Nanostructured lipid carriers, nanotoxicity, pharmacokinetics, pharmacodynamics, routes of administration, solid lipid nanoparticles

I. INTRODUCTION:

Solid lipid nanoparticles (SLNs), formerly known as lipospheres, are among the most promising pharmaceutical nanocarriers for regulated drug delivery. SLNs often contain lipidic substances that are safe and biodegradable. The capacity of SLNs to transfer a variety of therapeutics, including vaccine antigens, large biomolecules (polysaccharides, etc.), genetic material (DNA/siRNA), and small pharmacological molecules1, is what makes them special. Nanoparticles vary in size from 1 to 100 nanometers and can be composed of metal, carbon, metal oxides, or organic materials. The structure of nanoparticles (NPs) is intricate. There are two or three levels to them: (i) a surface layer functionalized with various metal ions, small molecules, surfactants, or polymers The central area of the core material, which can be purposefully added, is composed ofnanoparticles and differs chemically from the outermost layer2. SLNs combine the advantages of polymeric nanoparticles, emulsions, and liposomes. They offer both the robustness of a solid matrix and the biological compatibility of lipid carriers, avoiding the drawbacks of those drug delivery technologies. Nanomaterials with exceptional biodegradability and biocompatibility are considered the best carriers for drug delivery systems in biomedical applications.

The subsequent characteristics are essential for an ideal nanoparticulate drug delivery system to possess:
(1) Maximum bioavailability of the medication.
(2) Targeting tissues.
(3) Kinetics of release under control.
(4) Very little immunological reaction.
(5) The capacity to provide medications that have historically proven challenging, such as biomolecules, lipophiles, and amphiphiles.
(6) Adequate ability for medication loading.
(7) Satisfactory patient adherence.

Drug delivery has undergone a radical transformation thanks to solid lipid nanoparticles, which combine the best aspects of liposomes, polymeric nanoparticles, and microemulsion. All of the characteristics of lipid nanoparticles are improved through surface modification, increased pharmacokinetic acceptability, inclusion complex

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formation, improved stability pattern, and integration of chemotherapeutic drugs3.

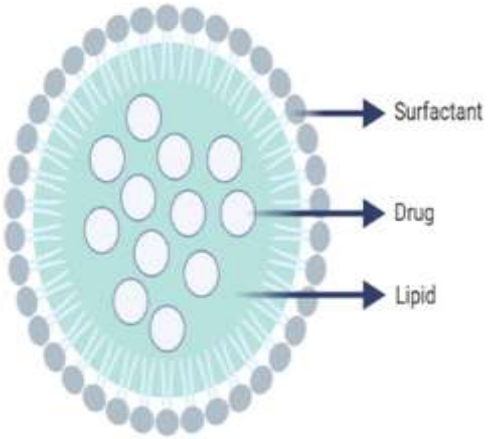

Figure:1 The structure of solid lipid nanoparticles

Solid lipid nanoparticle benefits
• Manage and/or aim for medication release.
• Increase the stability of medications.

High and improved medication content; more economical (less costly than carriers based on polymeric/surfactant materials).
• Easier to obtain regulatory approval and validate.
• SLNs have good biocompatibility and are biodegradable like other lipids.
• Technology based on water (avoid organic solvents)3.

A few drawbacks of SLN are as follows:
(1) low loading capacity for hydrophilic medications;
(2) potential for particle enlargement during storage; and
(3) potential for drug repulsion due to polymeric transformation during storage.
The primary worry with metallic and polymeric nanoparticles is believed to be their harmful consequences, as the lipids employed in the manufacture are frequently categorized as GRAS (Generally Known as Secure) components.

Solid lipid nanoparticles and nanostructured lipid carriers (NLC) are the two primary types of lipid nanoparticles.
Lipid nanoparticles are of 2 types:
SLNs: These consist of solid at room temperature lipids.
NLCs: These consists of mixture of solid and liquid at room temperature lipids.

Two of the main benefits of polymeric nanoparticles, known as SLNs, are their ability to successfully address problems related to the physical and chemical security of medication, medication distribution, and medication consumption. Lipid nanoparticles are brought from solid at the temperature lipids room, fat emulsions, and liposomes
Lipid nanoparticles known as solid lipid nanoparticles (SLNs) are specifically designed to carry polymeric nanoparticles, mainly lipophilic drugs.

METHODS OF PREPARATION OF SOLID LIPID NANOPARTICLES

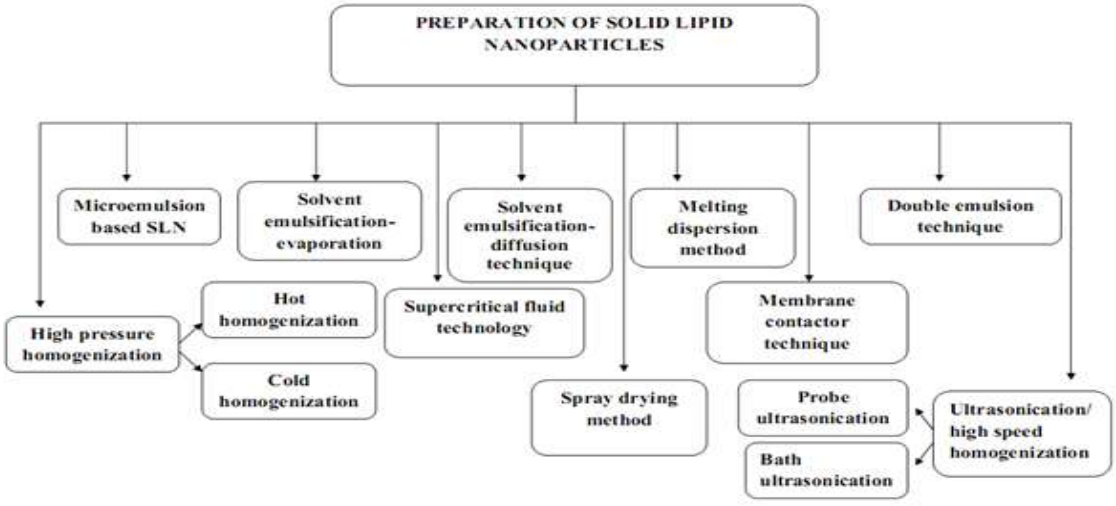

Figure: 2 Methods of preparation

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High pressure homogenization:

SLNs are produced using this dependable and effective process. High pressure homogenizers operate at high pressures (100–2000 bar) to drive a liquid through a tiny opening (a few microns). The fluid accelerates to almost a thousand km/h in a very short amount of time. Very high shear stress and cavitation forces cause disruptions to submicron-sized particles.

Two popular HPH procedures, hot homogenization and cold homogenization, work on the basis of mixing the drug with a lot of lipid melt.[6]

Hot homogenization:

This method involves stirring the drug-loaded, melted lipid (such Ultra Turrax) in an aqueous solution containing surfactants at the same temperature using a high shear device. With a piston gap homogenizer (such a Macron LAB 40, LAB 60, or APV-2000), the pre-emulsion is homogenized and the resulting hot o/w nanoemulsion is cooled to room temperature. SLN is produced when the lipid recrystallizes at normal temperature.

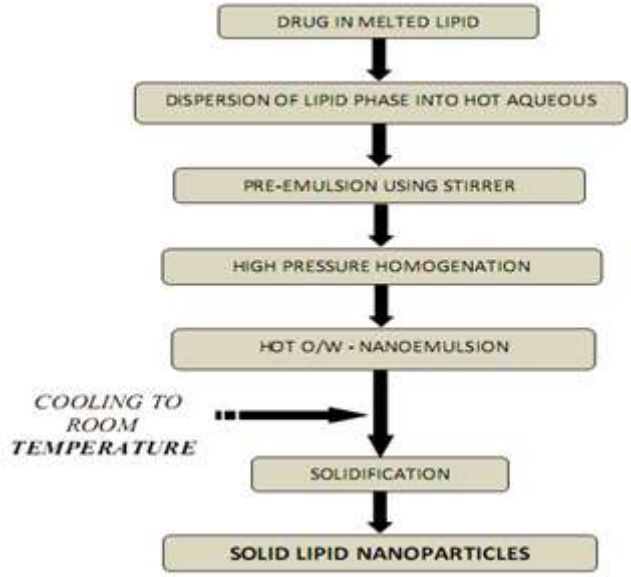

Figure:3 Solid lipid nanoparticles preparation by hot homogenization process[7]

Cold homogenization:

This technique was created to address the problems that came with hot homogenization, such as drug loss during the homogenization process into the aqueous phase, accelerated degradation due to high temperatures, and unknown lipid polymorphisms due to the complexity of crystallization. The initial elementary stage, which is the same as the heat homogenization method, includes the solubilization of the medication in the lipid melt. The next steps are modified: the drug-containing melt is rapidly cooled with the aid of liquid nitrogen or solid carbon dioxide to create a homogeneous drug distribution lipid matrix. The solid is subsequently ground into a fine dust using a ball mill. 50–100 µm is the normal dust size that is reached.The chilled aqueous surfactant disperses the fine dust particles. The SLN synthesis process is now initiated by exposing the dispersion to HPH. However, compared to a hot homogenization procedure, the cold homogenized output frequently has higher particle sizes and a wider size distribution.

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Figure:4 Cold homogenization technique[8]

Method based on microemulsions:

This procedure entails melting the lipid and increasing its temperature to that of the surfactant-containing aqueous phase. By adding an aqueous solution to the lipid phase and gently stirring, microemulsions can be created (Figure 4). SLN can be generated by stirring the microemulsion as it disseminates in cold water (2–10°C). The system is then rinsed with distilled water and filtration to get rid of any last large particles.

Lyophilization is another method the system might use to get rid of extra water. Some disadvantages of this strategy include the employment of surfactants at very high concentrations, the possibility of dilution upon adding the microemulsion to the water, and a decreased concentration of suspended particles. When the microemulsion is being disseminated in cold water (2–10°C), it can be swirled to create SLN. Following that, the system is rinsed and any large particles are removed using distilled water and filtering.

Lyophilization may also be used in the system to remove surplus water. Nevertheless, there are certain drawbacks to this approach, such as the requirement for surfactants in relatively high concentrations, the potential for dilution upon adding the microemulsion to the water, and a reduced concentration of suspended particles.

Emulsification solvent-evaporation:

By dissolving the lipid matrix in an organic solvent that is water-immiscible, the present approach emulsifies the mixture through the aqueous phase. Lipids precipitated in the aqueous media due to the solvent's evaporation at low pressure, which also produced dispersions of nanoparticles (Figure 6). Depending on the chemicals employed in the procedure, nanoparticles with a size range of 100 nm or less are produced. However, the main drawback of this approach is the usage of organic solvents, which could leave the sample containing dangerous residues.

Supercritical fluid method:

This relatively new approach for making SLN has the advantage of processing without the need for a solvent. There are various variants of this platform technology used to manufacture powder and nanoparticles.

To prepare SLN, employ the rapid expansion of supercritical carbon dioxide solutions (RESS) technique. Carbon dioxide (99.99%) was a great solvent choice for this process.

Diffusion of solvent emulsification:

This technique can yield average-sized particles ranging from 30 to 100 nm. The main advantage of this method is that there is no heat generated during the preparation phase. Centrifugation is used to readily separate the lipids using this approach, which modifies the zeta potential to induce coacervation of SLN using an acidic aqueous phase. In a water bath at 50 °C, lipids are normally dissolved in the organic phase. The suspension of the SLN happened quite quickly. After that, the dispersed system can be reconstituted in distilled water by centrifuging the entire system.[10]

Spray drying method:

A different approach than lyophilization, spray drying transforms an aqueous SLN dispersion into a medicinal product. The cost is lower than with lyophilization. This method's high

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temperature, shear forces, and partial melting of the particle cause particle aggregation. Freitas and Mullera[35] recommend utilizing lipids with melting points higher than 70° for spray drying. When 1% SLN was added to a trehalose solution in water or 20% SLN was added to ethanol-water combinations (10/90 v/v), the best results were obtained.11

Membrane contractor technique: Tiny droplets that are separated from the water running tangentially through the membrane hole escape when the melted lipid phase is driven through a membrane's pores at a temperature greater than the lipid's melting point. When droplets are distributed and cooled to room temperature, solid liquid nanoparticles (SLNs) are formed.[12]

Double emulsion-based method:

Warm w/o/w double micro-emulsions can be made in two phases.

Initially, melted lipid, surfactant, and cosurfactant are combined with an aqueous solution containing a medication at a temperature slightly above the melting point of the lipid to generate a transparent system known as w/o microemulsion. In the second step, a solution of water, surfactant, and co-surfactant is mixed with the created w/o microemulsion to create a transparent w/o/w system. SLN can be created by spreading the warm micro double emulsions in the cold and washing the mixture with dispersion medium using an ultra-filtration system. The intrinsic instability of multiple emulsions is caused by the rupture of the layer on the surface, the oil droplets themselves, and the internal water droplets within the oil phase[13]

Accelerated homogenization and/or ultra sonication:

This process starts by mixing the medication with melted fat to produce a concentrated lipid nanoparticle dispersion. This approach is based on dispersing the melted lipid in the warm aqueous phase (about 5 to 10 degrees Celsius above its melting point) including surfactants by high shear homogenization to form an emulsion, hence preventing recrystallization throughout the process. Preparing the pre-emulsion on a lab scale, it was ultrasonicated in a water bath at 0°C using a probe sonicator. Contaminants introduced during ultrasonication were removed by filtering the nanoemulsion (o/w) via a 0.45 µm membrane after it was obtained. They then purchased SLN, which is maintained at 4ºC.[14]

Coacervation technique:

The coacervation method is based on the precipitation of free fatty acids from their micelles in the presence of a surfactant. During this process, a fatty acid salt is uniformly dispersed throughout the stabilizer solution. Once the mixture reached the krafft point of the fatty acid salts, it was continuously stirred until a transparent solution was obtained. The ethanolic solution of the API is then added gradually while being continuously agitated to form a single phase. Then, a coacervation agent or an acidifying solution is added to produce the nanoparticle suspension. The particle size of SLN, which can range from 260 to 500 nm, is determined by the concentration of the micellar solution and the quantity of polymer used for stabilization.[15]

SLN characterization methods:

Parameters	Characterization methods
Particle size	Dynamic light scattering (DLS) Laser diffraction spectroscopy (LD) Coulter counter Nanoparticle tracking analysis (NTA) Flow field fractionation (FFF) Size exclusion chromatography (SEC)
Surface morphology	Scanning electron microscopy (SEM) Transmission electron microscopy (TEM) Atomic force microscopy (AFM)
Surface load	Zeta potentiometer Laser doppler anemometry (LDA)

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Determination of lipid polymorphisms and crystallinity	Differential scanning calorimetry (DSC) X-ray diffraction (XRD) Small angle X-ray scattering (SAXS) Thermal gravimetric analysis (TGA) Nuclear magnetic resonance spectroscopy (NMR) Infrared (IR) and Raman spectroscopy Electron spin resonance (ESR)
Load capacity and entrapment efficiency	High performance liquid chromatography (HPLC) UV spectrophotometer

APPLICATION OF SLNS IN DRUG DELIVERY SYSTEM

1) SLNs are easier to scale up and show long-term stability when compared to other colloidal systems. which implies that they could be important for a range of targeting applications.

2) A systemic approach is frequently used to give anticancer medications. SLNs can be administered intravenously due to their small size. There have been reports that they could be useful as carriers of medication for the treatment of cancer.

3) The physiological lipids that comprise SLNs and the body's already-existing pathways for lipid transport and metabolism dictate the carrier's in vivo destiny. Lipases are essential enzymes for breaking down SLN.

4) The ability of SLNs loaded with camptothecin and methotrexate to target tumors has been reported. It has been observed that paclitaxel prolongs circulation periods.

5) Because SLNs may offer the advantage of delivering the treatment directly to the site of action, they have been used topically to apply a range of pharmaceuticals.

6) Because lipid nanoparticles' surfaces can connect to blood proteins like apolipoproteins, SLNs have the ability to pass the blood-brain barrier. The BBB crossing may then be facilitated by its interacting with endothelial cells. It is known that certain medications, such as tobramycin, doxorubicin, and idarubicin, have these properties.

7) Many drugs are now applied topically utilizing SLNs due to the possible advantage of getting the drug directly to the site of action.

8) The particle nature and sticky qualities of SLNs make them well-suited for use as UV-blocker carriers. In topical formulations, SLNs help to provide improved localization, occlusiveness, controlled release, and increased skin hydration. [16]

II. CONCLUSION:

The ability to encapsulate medications in nanocarriers offers the possibility of targeting particular medications with an innovative drug delivery concept. As a result, researchers are highly interested in solid lipid nanoparticles (SLN) because of their great potential to achieve the objective of controlled and site-specific drug delivery.SLN are very complex systems with unique advantages and disadvantages when compared to other colloidal carriers.SLN systems are designed to address several pharmaceutical challenges, such as enhancing bioavailability, controlling drug release, and optimizing stability. SLNs provide a convenient and economical method of medication administration through several channels to optimize the targeted tissue's effectiveness and reduce any negative effects on adjacent tissues.

REFERENCES:

[1]. Paliwal, R., Paliwal, S. R., Kenwat, R., Kurmi, B. D., & Sahu, M. K. (2020). Solid lipid nanoparticles: a review on recent perspectives and patents. Expert opinion on therapeutic patents, 30(3), 179–194.

[2]. RAJ, R., KOLAY, A., & HAVELIKAR, U. (2023). A REVIEW ON SOLID LIPID NANOPARTICLES. International Journal of Current Pharmaceutical Research, 15(5), 10–16.

[3]. Duan, Y., Dhar, A., Patel, C., Khimani, M., Neogi, S., Sharma, P., Siva Kumar, N., & Vekariya, R. L. (2020). A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems. RSC advances, 10(45), 26777–26791.

[4]. Gabriella F. Punu, Yahdiana Harahap, Qonita Kurnia Anjani, Pietradewi Hartrianti, Ryan F. Donnelly, Delly Ramadon, (2023). Solid Lipid Nanoparticles (SLN): Formulation and Fabrication. Pharmaceutical Sciences and Research (PSR), 10(2), 2023, 55-66.

[5]. Alsaad, A. A., Hussien, A. A., & Gareeb, M. M. (2020). Solid lipid nanoparticles (SLN) as a novel drug delivery system: A

theoretical review. Syst. Rev. Pharm, 11, 259-273.

[6]. Deshmukh, Amol. (2014). Solid Lipid Nanoparticles.Research Journal of Pharmaceutical Dosage Forms and Technology. 6(4): October-December, 2014, 282-285

[7]. D. Thulasi Ram, Subhashis Debnath, M. Niranjan Babu, T. Chakradhar Nath, Thejeswi B. (2012) A Review on solid Lipid Nanoparticles. Research J. Pharm. and Tech. 5(11): Nov. 2012.

[8]. Koduru Trideva Sastri, Gadela Venkata Radha, Sruthi Pidikiti, Priya Vajjhala (2020). Solid lipid nanoparticles: Preparation techniques, their characterization, and an update on recent studies.

[9]. Journal of Applied Pharmaceutical Science Vol. 10(06), pp 126-141, June, 2020.

[10]. Gabriella F. Punu, Yahdiana Harahap, Qonita Kurnia Anjani, Pietradewi Hartrianti, Ryan F.Donnelly, Delly Ramadon (2023). Solid Lipid Nanoparticles (SLN): Formulation and Fabrication. Pharmaceutical Sciences and Research (PSR), 10(2), 2023, 55-66.

[11]. Yadav, Nancy & Khatak, Dr & Sara, U.V.. (2013). Solid lipid nanoparticles- A review. International Journal of Applied Pharmaceutics. 5. 8-18.

[12]. Mukherjee, S., Ray, S., & Thakur, R. S. (2009). Solid lipid nanoparticles: a modern formulation approach in drug delivery system. Indian journal of pharmaceutical sciences, 71(4), 349–358. https://doi.org/10.4103/0250-474X.57282

[13]. Romchat Chutoprapat, Peerawas Kopongpanich and Lai Wah Chan(2022). A Mini-Review on Solid Lipid Nanoparticles and Nanostructured Lipid Carriers: Topical Delivery of Phytochemicals for the Treatment of Acne Vulgaris. Molecules 2022, 27, 3460.

[14]. Mushfiq Akanda, MD Sadeque Hossain Mithu, Dennis Douroumis(2023). Solid lipid nanoparticles: An effective lipid-based technology for cancer treatment. Journal of Drug Delivery Science and Technology, 86 (2023) 104709.

[15]. Deepa MK*, Karthikeyan M*, Abhay AD, Shruti PC, Omkar SD and Satish RC(2020). Comprehensive Review on Solid Lipid Nanoparticles. Annals of Pharmacology and Pharmaceutics, 2020; 5(4): 1190.

[16]. Hernández-Esquivel, R.-A., Navarro-Tovar, G., Zárate-Hernández, E., & Aguirre-Bañuelos, P. (2022). Solid Lipid Nanoparticles (SLN). IntechOpen. doi: 10.5772/intechopen.102536.

[17]. Abhish Bhagwan Jadhav* and A.D savkare (2015). SOLID LIPID NANOPARTICLES AS NOVEL DRUG DELIVERY SYSTEM: AN OVERVIEW. World Journal of Pharmaceutical Research, 2015; 4. 352-370.