A Review: Solid Lipid Nanoparticles

NIKITA AUTADE[1], VIKAS KUNDE[2]
[1, 2]*Department of pharmaceutics PRES'S College of Pharmacy (for Women), Chincholi, Nashik.*

Abstract— Solid lipid nanoparticles (SLNs) have emerged as promising carriers for poorly water-soluble drugs and cosmetic active ingredients. This review provides an extensive overview of SLNs, including their introduction, advantages, disadvantages, aims, methods of preparation, characterization techniques, and routes of administration. SLNs offer several advantages, such as controlled drug release, increased drug stability, high drug payload, and versatility in administration routes. Various preparation methods, including high-pressure homogenization, ultrasonication, solvent evaporation, and others, highlight the flexibility in production techniques. Characterization methods ensure quality control and provide insights into particle size, distribution, crystallinity, and surface properties. Furthermore, SLNs exhibit promising applications in pharmaceuticals, cosmeceuticals, vaccine delivery,agriculture, and targeted drug delivery for cancer treatment. Their ability to enhance drug bioavailability, reduce side effects, and provide sustained release makes them attractive for diverse therapeutic needs. Despite their advantages, SLNs have limitations such as limited drug loading capacity and potentialparticle growth. However, ongoing research aims to overcome these challenges and further optimize SLNs for clinical applications. In conclusion, SLNs represent a versatile and promising drug delivery system with potential applications across various fields. Continued research and development efforts are necessary to fully harness the benefits of SLNs and address existing limitations, ultimately advancing drug delivery technology and improving patient outcomes.

Index Terms- Solid lipid nanoparticles, nanotechnology, characterization technique, administration routes, Pharmaceutical applications.

I. INTRODUCTION

Solid lipid nanoparticles (SLNs) serve as an innovative carrier system for water-insoluble medications and cosmetic active ingredients. Nanoparticles, colloidal particles with sizes ranging from 10 to 1000 nm, are primarily composed of synthetic or natural polymers, making them idealfor enhancing drug delivery efficiency and reducing toxicity [1]. Solid lipid nanoparticles (SLNs) have emerged as a versatile alternative to liposomes for drug carriers. Manufactured from synthetic or natural polymers, they are well-suited for optimizing drug delivery and minimizing toxicity. Their successful use relies on their ability to penetrate anatomical barriers, sustain release of contents, and maintain stability at the nanometer scale. However, challenges such as the scarcity of approved safe polymers and high costs hinder their widespread clinical application. To address these limitations, lipids have been proposed as an alternative carrier, especially for lipophilic drugs, giving rise to SLNs. These lipid nanoparticles are gaining attention among formulators worldwide [2].

The reasons for the increasing interest in lipid-based system are many
– fold and include.

1. Lipids enhance oral bioavailability and reduce plasma profile variability.
2. Better characterization of lipoid excipients.

An improved ability to address the key issues of technology transfer and manufacture scaleup. Solid lipid nanoparticles are one of the novel potential colloidal carrier systems as alternative materials to polymers which is identical to oil in water emulsion for parenteral nutrition, but the liquid lipid of the emulsion has been replaced by a solid lipid shown on[3]

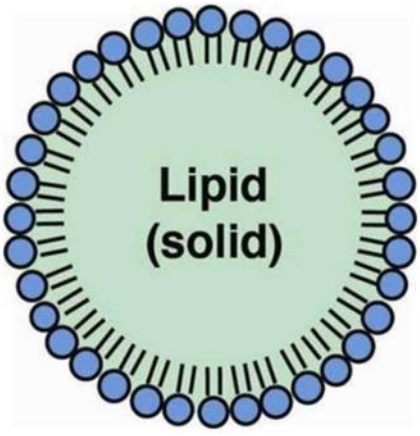


Figure 1. Structure of Solid Lipid Nanoparticle (Sln)

They have many focal points, for example, great biocompatibility, low danger and lipophilic medications are better conveyed by Solid lipid nanoparticles and the framework is physically stable

1.1. Advantages of SLN [15,16,19]

Incorporation of biodegradable physiological lipids. Elimination of organic solvents from the production process.

Versatile application methods including oral, intravenous, and dermal administration. Enhancement of bioavailability for poorly water-soluble substances. Exceptional biocompatibility enhancing pharmaceutical stability.High drug content without the need for special solvents.

Versatility in application.
Decreased required dosage frequency.
SLNs have better stability and ease of upgradability to production scale as compared to liposome. Very high long-term stability.

It is easy to manufacture than bipolymeric nanoparticles.

Better control over release kinetics of encapsulated compound. Large scale productionis possible Lyophilization possible.

1.2. Disadvantages of SLN [15,16,19]

Limited drug loading capacity due to the crystalline structure of solid lipids.
Adjustment of drug release profile.
Risk of drug expulsion during storage due to the formation of perfect crystals. Particle growth.
Unpredictable tendency for gelation.

Elevated water content in solid lipid nanoparticle dispersions. Relatively high-water content of the dispersions (70-99.9%)

II. AIMS OF SLN'S [17]

The aim of SLNs is to provide controlled and sustained drug release, influenced by factors such as drug partition coefficient, particle size, drug dispersion within the lipid matrix, crystallization behavior, and drug incorporation model. Additionally, SLNs aim to offer flexibility in drug release profiles, achieved through different production methods and formulation parameters. Thedevelopment of SLNs, including new generation SLNs like nanostructured lipid carriers (NLCs), aims to enhance drug loading capacity, prolong release duration, and optimize drug release kinetics to meet specific therapeutic needs while minimizing burst effects and improving patient compliance.

Certainly! Here are some points outlining the aims of solid lipid nanoparticles (SLNs)-

- Possibility of controlled drug release.
- Increased drug stability.
- High drug pay load
- No bio-toxicity of the carrier.
- Avoidance of organic solvents.
- Incorporation of lipophilic and hydrophilic drugs.

III. METHODS OF PREPARATION OF SOLID LIPID NANOPARTICLES

The strategy for preparing solid lipid nanoparticles (SLNs) involves a range of techniques, including high shear homogenization, ultrasonication, microemulsion-based SLN preparation, supercritical fluid technology, spray drying, solvent emulsification/evaporation, solvent injection method, and solvent emulsification-diffusion[7]. methods employ processes such as lipid precipitation and solvent removal, with various parameters such as lipid concentration, temperature, and type of organic solvent and emulsifier influencing particle size control. SLNs are formulated from lipids, emulsifiers, and water/solvent using these diverse techniques.

3.1 High-pressure homogenization [8,9]

3.1.1 Hot homogenization.

3.1.2 Cold homogenization.

3.2 Ultrasonication/fast Homogenization

Test Ultrasonication.

3.2.1 Shower Ultrasonication.

3.3 Solvent evaporation method.

3.4 Solvent emulsification-diffusion method.

3.5 Supercritical fluid method.

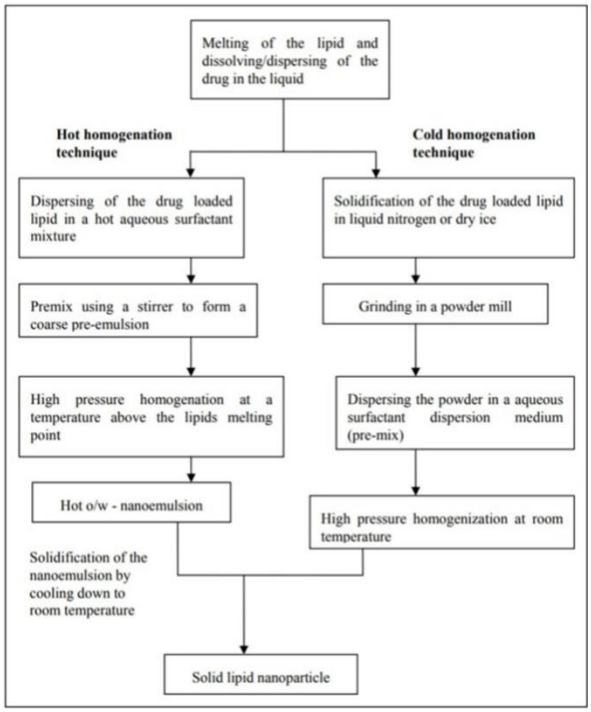
3.6 Microemulsion based method.
3.7 Spray drying method.
3.8 Double emulsion method.
3.9 Precipitation technique.
3.10 Film-ultrasound dispersion.

3.1.1 High-Pressure Homogenization (HPH)-
HPH is a reliable and powerful technique, used for production of solid lipid nanoparticles. Highpressure homogenizers push liquid at high pressures (100 – 2000 bar), through a narrow gap (in the range of few microns). The fluid accelerates over a very short distance under very high shear stress and cavitation forces disrupt the particles down to the submicron range. Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated[4,31]

A. Hot homogenization
Temperatures higher than the melting point of the lipid are selected for this process and can subsequently be considered as the homogenization of an emulsion. An aqueous surfactant is used for the combination of lipid and drug at the same temperature. A device for high shear mixing is used to prepare a hot pre-emulsion, resulting in an emulsion of oil in water type. Then, the product is left for cooling, and this leads to the initiation of crystals of lipid and then the formation of SLNs. For the production of perfect SLNs, 3–5 cycles of homogenization at a pressure of 500–1,500 bar are necessary (Akanksha et al., 2012). One should always be aware that there is a rise in temperature with HPH. With the rise in the number of cycles or the pressure, there is a growth in the particle size. This is due to attractive forces between the particles which are due to the energy of moving the particles (Siekmann and Westesen, 1994). Finally, cooling of the nanoemulsion to room temperature is done, where the recrystallization of lipids occurs and this leads to the formation of nanoparticles[5]

B. Cold homogenization
Cold homogenization has been 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 nanoemulsion leading to several modifications and/or super cooled melts. In this technique the drug containing lipid melt is cooled, the solid lipid ground to lipid microparticles and these lipid microparticles are dispersed in a cold surfactant solution yielding a presuspension. 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. [6]

Comparison of hot and cold homogenization processes (Maa F et al., 1996)



3.2. Ultrasonication/fast Homogenization
The preparation of solid lipid nanoparticles (SLNs) can also be achieved through ultrasonication or highspeed homogenization techniques . However, to attain smaller particle sizes, a combination of both ultrasonication and high-speed homogenization is often necessary. Despite its effectiveness, this approachcomes with significant drawbacks, including potential metal contamination and physical instability such as particle growth upon storage.[11] This could be improved by higher surfactant concentrations, which in order might be correlated with toxicological problems after parenteral administration. A further disadvantage is potential metal contamination due ultra sonication.[15]

3.3. Solvent evaporation method.

The solvent emulsification-diffusion method serves as a primary approach for crafting polymeric nanocarriers. In 2003, Trotta et al. pioneered its application in fabricating SLNs and NLCs [12]. Typically, this technique employs organic solvents that exhibit partial miscibility with water, such as methyl acetate, ethyl acetate, isopropyl acetate, benzyl alcohol, and butyl lactate. Initially, the organic solvent and water achieve mutual saturation to establish the initial thermodynamic equilibrium of both phases. Lipids and drugs are dissolved in the water-saturated solvent, subsequently emulsified in the aqueous phase (solvent-saturated water containing a stabilizer) under stirring, forming an o/w emulsion. Dilution of the emulsion with water (volume ratio ranging from 1:5 to 1:10) facilitates solvent diffusioninto the continuous phase. Spontaneous formation of SLNs and NLCs occurs due to lipid precipitation, after which solvent removal is achieved through lyophilization or vacuum distillation [12,13,14].

3.4. Solvent emulsification-diffusion method.

This technique yields particles with average diameters ranging from 30 to 100 nm. Its significant advantage lies in the avoidance of heat during the preparation process.[16]

3.5. Supercritical fluid method.

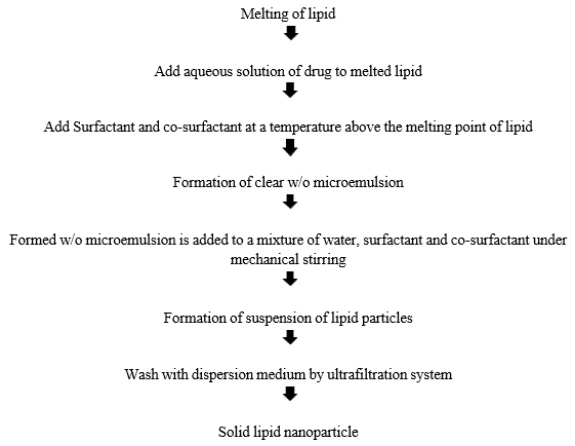
The supercritical fluid method offers an alternative approach to preparing SLNs through particles from gas-saturated solutions (PGSS). This technique presents several advantages, including the avoidance of solvent usage, obtaining particles as dry powder rather than suspensions, and operating under mild pressure and temperature conditions. Carbon dioxide serves as an ideal solvent choice for this method.[18]

The supercritical fluid method, also known as particles from gas saturated solutions (PGSS), offers an alternative approach to preparing SLNs. Its advantages include: [21]

1. Elimination of solvent usage.
2. Production of particles as dry powder, rather than suspensions.
3. Operation under mild pressure and temperature conditions.
4. Utilization of carbon dioxide solution as an effective solvent for this technique

3.6. Microemulsion based method.[19]

The microemulsion-based method relies on diluting microemulsions, which are two-phase systems consisting of inner and outer phases (e.g., o/w microemulsions). These are created by stirring an optically transparent mixture at 65-70°C, typically comprising a low melting fatty acid (e.g., stearic acid), an emulsifier (e.g., polysorbate 20), co-emulsifiers (e.g., butanol), and water.[24] The hot microemulsion is dispersed in cold water (2-3°C) under stirring. While SLN dispersion can be utilized as a granulation fluid for transferring into solid products (tablets, pellets) via the granulation process, excessive water removal may be necessary in cases of low particle content. High-temperature gradients promote rapid lipid crystallization and prevent aggregation. However, due to the dilution step, achievable lipid contents are significantly lower compared to HPH-based formulations.



Advantages

Low mechanical energy input.Theoretical stability.

Disadvantages

Extremely sensitive to change.

Labor intensive formulation work. Low nanoparticle concentrations.

3.7 Spray drying method.

Utilizing the spray drying method involves dissolving or dispersing the lipid excipient and the active ingredient (such as glibenclamide, etoricoxib, estradiol) in an organic solvent. This mixture is then

atomized into warm filtered air, eliminating the solvent from the droplets and resulting in solid microparticles. The process requires lipids with high melting points (> 70 °C) to prevent the meltingof lipid microparticles during spraying, which could limit the method's applicability in lipid microparticle preparation [10].

3.8 Double emulsion method [20]

The double emulsion-based method involves preparing warm w/o/w double microemulsions in two steps. Firstly, a w/o microemulsion is formed by adding an aqueous solution containing the drug to a mixture of melted lipid, surfactant, and co-surfactant at a temperature slightly above the lipid's melting point to obtain a clear system. In the second step, the formed w/o microemulsion is added to a mixture of water, surfactant, and co-surfactant to obtain a clear w/o/w system. SLNs can be obtained by dispersing the warm micro double emulsions in cold water, then washed with dispersion medium using an ultrafiltration system. Multiple emulsions inherently suffer from instabilities due to coalescence of internal aqueous droplets within the oil phase, coalescence of oil droplets, and rupture of the layer on the surface of internal droplets. However, for SLNs production, stability for a few minutes is crucial, achieved during the time between the preparation of clear double microemulsions and their quenching in cold aqueous medium.

3.9 Precipitation technique

In the precipitation method, glycerides are first dissolved in an organic solvent, such as chloroform. This solution is then emulsified in an aqueous phase. Upon evaporation of the organic solvent, the lipids precipitate, forming nanoparticles.[21]

3.10 Film-ultrasound dispersion

The lipid and drug were dissolved in appropriate organic solutions. After decompression, rotation, and evaporation of these solutions, a lipid film formed. Subsequently, the aqueous solution containing the emulsions was added. Finally, ultrasound with the probe diffuser was utilized, resulting in the formation of Solid Lipid Nanoparticles (SLN) with uniform particle size.[28]

IV. CHARACTERIZATION OF SOLID LIPID NANOPARTICLES (SLNS)

Accurate and thorough characterization of SLNs is crucial for quality control measures. Yet, this task poses significant challenges due to the colloidal size of the particles and the intricate, dynamic nature of the delivery system. Key parameters assessed for SLNs comprise particle size, size distribution kinetics (zeta potential), degree of crystallinity and lipid modification (polymorphism), presence of additional colloidal structures (micelles, liposomes, supercooled melts, drug nanoparticles), distribution process timelines, drug content, in-vitro drug release, and surface morphology.

1. Particle size and Zeta potential

Particle size and zeta potential can be effectively measured using photon correlation spectroscopy (PCS) and laser diffraction (LD). These techniques are widely utilized for routine particle size assessments.[24] While the Coulter method is seldom employed for SLN particle size measurement due to challenges in assessing small nanoparticles and the requirement of electrolytes, which can potentially destabilize colloidal dispersions. PCS, also referred to as dynamic light scattering, quantifies fluctuations in the intensity of scattered light resulting from particle movement. This method covers a size range from a few nanometers to approximately 3 microns, making it suitable for characterizing nanoparticles but not larger microparticles. Larger particles can be observed using LD measurements, which rely on the relationship between diffraction angle and particle radius (Fraunhofer spectra). Smaller particles exhibit more intensescattering at high angles compared to larger ones. LD offers the advantage of covering a broad size range from nanometers to the lower millimeter range.[22]

2. Electron microscopy-

Electron microscopy techniques, such as scanning electron microscopy (SEM) and transmission electron microscopy (TEM), offer direct observation capabilities for nanoparticles. SEM excels in morphological examination, while TEM boasts a smaller size limit of detection and serves as a valuable

validation tool for other methods. However, it's essential to consider the statistically small sample size and the impact of vacuum conditions on the particles when utilizing these techniques for structural analysis.[32]

3. Atomic force microscopy (AFM)

This method involves scanning a probe tip, incredibly sharp at the atomic level, over a sample to generate a topographical map based on the interaction forces between the tip and the surface. The probe can either be dragged across the sample (contact mode) or allowed to hover just above it (non-contact mode), with the specific force employed distinguishing among subtechniques. The AFM offers ultra-high resolution, enabling the mapping of samples based on properties beyond size, such as colloidal attraction or resistance to deformation, rendering it a highly valuable tool.[28]

4. Dynamic light scattering (DLS)-

Dynamic Light Scattering (DLS), also known as quasi-elastic light scattering, captures changes in scattered light intensity on a microsecond timescale. These changes stem from the interference oflight scattered by individual particles experiencing Brownian motion and are quantified through an autocorrelation function. Typically, this function is fitted to an exponential model, or a modified version, where the resulting decay constant(s) correlate with the diffusion coefficient.

Notable advantages include rapid analysis, absence of calibration requirements, and sensitivity to submicrometer particles.[30]

5. Static light scattering (SLS)/Fraunhofer diffraction –

Static light scattering (SLS), also known as Fraunhofer diffraction, is an ensemble technique that involves collecting the scattered light pattern from a solution of particles and fitting it to electromagnetic equations, primarily focusing on size determination. While SLS offers speed androbustness, it demands a higher level of cleanliness compared to dynamic light scattering (DLS), along with prior knowledge of the particles' optical characteristics.[32]

6. Differential scanning calorimetry (DSC)

The geometric scattering of radiation from crystal planes within a solid allows for the determination of the presence or absence of the former, thus enabling the assessment of crystallinity degree. Differential scanning calorimetry (DSC) is utilized to discern the nature and speciation of crystallinity within nanoparticles by measuring glass transition and melting point temperatures.[29]

7. Acoustic methods

Acoustic spectroscopy, as another ensemble method, gauges size by assessing the attenuation of sound waves, employing physically relevant equations for fitting. Moreover, it can detect the oscillating electric field from charged particles' movement influenced by acoustic energy, offering insights into surface charge.[22]

8. Nuclear magnetic resonance (NMR) –

Nuclear magnetic resonance (NMR) is a versatile technique utilized for discerning both the size and qualitative characteristics of nanoparticles. Its capacity for chemical shift selectivity enhances sensitivity to molecular mobility, thereby offering valuable insights into the physicochemical composition of individual components within the nanoparticle structure.[32]

V. ROUTE OF ADMINISTRATION

1. Parenteral administration-

Parenteral administration of peptide and protein drugs circumvents enzymatic degradation in the gastrointestinal tract. Due to short half-lives, frequent parenteral dosing is required. Researchers explore non-parenteral routes like transdermal and nasal delivery. SLNs offer controlled release, good tolerability, and storage stability, making them promising for systemic and targeted drug delivery.

They enhance drug bioavailability and reduce side effects, making them attractive for pharmaceutical applications. Several companies develop SLN-based products for gene transfer and treating infectious diseases, aiming to enhance efficacy and minimize adverse effects.[17]

2. Oral Administration-

Oral adminstration solid lipid nanoparticles (SLNs) offers versatility, allowing administration as aqueous dispersion or incorporation into various dosage forms such as tablets, pellets, capsules, or sachet powders. In tablet production, aqueous SLN dispersion can replace granulation fluid or be transformed into powder form (e.g., via spray drying) for inclusion in tableting mixtures. SLN dispersion serves as a wetting agent in pellet extrusion, while SLN powder can fill hard gelatin capsules or be directly produced in liquid PEG 600 for soft gelatin capsules. Sachets may utilize spray-dried or lyophilized powders. The stomach's microclimate promotes particle aggregation due to acidity and high ionic strength, potentially affected by food, although no experimental data on this issue are currently available.[18]

3. Rectal administration-

Rectal administration is preferred in certain circumstances when a rapid pharmacological effect is needed, or for pediatric patients due to its easy application. This route can be chosen alongside parenteral administration.[21]

4. Topical adminstration-

Solid Lipid Nanoparticles (SLNs) offer numerous advantages when administered topically. Their small particle size enables close interaction with the stratum corneum, enhancing drug penetration into deeper skin layers. Moreover, SLNs facilitate sustained drug release, reducing systemic absorption while exhibiting occlusive properties that minimize transdermal water loss. This occlusion fosters improved skin hydration, easing symptoms such as atopic eczema and enhancing overall skin appearance. Integration of SLNs into conventional topical formulations has yielded promising outcomes, with controlled drug release achievable through polymorphic transitions manipulation.

Additionally, SLNs modify skin structure, augmenting stratum corneum thickness and fortifying the drug penetration barrier. Research indicates enhanced drug targeting and protection against degradation with SLNs, underscoring their potential as a carrier for various topical medications.

Rheological analysis underscores the suitability of SLNs dispersions for topical administration, particularly at higher lipid concentrations. Furthermore, SLNs and Nanostructured Lipid Carriers (NLCs) hold promise in delivering drugs like clotrimazole, with SLNs demonstrating superior occlusive capacity compared to NLCs.[25]

5. Ocular administration-

Colloidal drug delivery systems, like polymeric nanoparticles and SLN, are utilized to enhance the bioavailability of drugs administered ocularly. Surface characteristics of nanoparticles play a crucial role in their interaction with ocular mucosa. SLN, with their biocompatibility and muco-adhesive properties, prolong the residence time of drugs on the cornea, aiding in ocular drug targeting.

Research shows significant enhancement in drug bioavailability, such as tobramycin and pilocarpine, when delivered via SLN. Incorporating poorly water-soluble drugs into SLN results in high loading capacity and prolonged drug release. Industrial efforts include incorporating antibiotics like gentamicin into SLN for their antimicrobial properties, exemplified by products like OcusolinTM from AlphaRx, currently in preclinical development.[26]

VI. APPLICATIONS

Solid lipid nanoparticles (SLNs) offer superior stability and scalability for production compared to liposomes, making them highly valuable for various targeting strategies. These properties are crucial for diverse applications. SLNs serve as the foundation for colloidal drug delivery systems, boasting biodegradability and the ability to be stored for at least one year. They excel in delivering drugs to the liver in vivo and to phagocytic cells in vitro[23]. The potential applications of SLNs are numerous, including

1) SLNs for topical use

Lipid nanoparticles (SLNs) find applications in topical delivery of various drugs, including anticancer agents [16], vitamin-A, isotretinoin, and flurbiprofen. By incorporating glyceryl behenate, nanoparticles loaded with vitamin A can be effectively formulated, enhancing penetration with sustained release. Isotretinoin-loaded lipid nanoparticles have been developed specifically for topical drug delivery. Moreover, the production of flurbiprofen-loaded SLN

gel for topical application presents a promising approach, enabling targeted delivery to the site of action and potentially achieving higher tissue concentrations.[19]

2) SLNs as cosmeceuticals

Cosmetic applications involve protecting the skin from harmful UV radiation, with UV-A causing premature aging and UV-B leading to burns, erythema, and cancer. UV blockers utilize chemical absorption and physical reflection mechanisms. Solid Lipid Nanoparticles (SLNs) emerge as innovative carriers, particularly for UV blockers. Crystalline cetylpalmitate SLNs reflect and scatter UV radiation independently, offering photoprotection without molecular sunscreens. Incorporating sunscreens into SLNs enhances photoprotection synergistically, with a three-fold increase observed with Eusolex 4360. Physical sunscreens like titanium dioxide can also complement SLN formulations. SLNs demonstrate superior UV reflection compared to traditional emulsions.

Incorporating molecular sunscreens in SLNs decreases release rates compared to emulsions, enhancing skin penetration. Tape-stripping methods reveal formulation-dependent release rates, with SLNs providing sustained release, ensuring prolonged sunscreen action on the skin surface. In vivo tests confirm SLNs' efficacy in delivering sunscreens for prolonged skin protection.[25]

3) SLN as vaccine carriers-

For an extended period, researchers have pursued particulate carriers as means for protein antigens delivery. Considerable efforts have focused on formulating vaccines using various biodegradable polymeric nanoparticles and microparticles. These carriers release antigens in a controlled manner, offering adjuvant properties via parenteral or mucosal routes. Yet, challenges persist, such as cost and toxic solvents in production. Among biodegradable polymers, PLA/PLGA microspheres are widely used for antigen delivery. Liposomes have also emerged as potent adjuvants, inducing immune responses against bacterial and viral antigens. Lipidated antigens, mimicking viral particles, enhance both humoral and cellular immune responses. Despite progress, further exploration is needed for lipid-based systems in vaccine development.[27]

4) SLNs for potential agriculture application-

SLN, or Solid Lipid Nanoparticles, present a promising avenue for potential applications in agriculture. Extracted from Artemisia arborescens L., essential oils when integrated into SLN demonstrate a notable decrease in rapid evaporation compared to emulsions. These systems serve aseffective carriers for ecologically safe pesticides, demonstrating their utility in agricultural practices. The formulation of SLN utilized Compritol 888 ATO as the lipid component, along with either Poloxamer 188 or Miranol Ultra C32 as surfactants, showcasing a versatile approach to their preparation.[30]

5) SLNs as a targeted carrier for anticancer drug to solid tumors-

Solid lipid nanoparticles (SLN) serve as targeted carriers for anticancer drugs in solid tumors. For instance, Tamoxifen, an anticancer drug, is encapsulated within SLN to extend drug release following intravenous administration for breast cancer treatment. SLN loaded with drugs such as methotrexate and camptothecin have demonstrated effective tumor targeting.[29]

6) Solid lipid nanoparticles for delivering peptides

Stable lipid particulate systems, including solid lipid nanoparticles (SLN), lipid microparticles (LM), and lipospheres, have been explored as alternative carriers for therapeutic peptides, proteins, and antigens. Research in this area suggests that under optimized conditions, these systems can incorporate hydrophobic or hydrophilic proteins and meet the criteria for an effective particulate carrier system. Proteins and antigens intended for therapeutic use can be combined or adsorbed onto SLN and administered via parenteral routes or alternative methods such as oral, nasal, and pulmonary routes. Formulating proteins in SLN offers improved stability, protects against proteolytic degradation, and enables sustained release of the incorporated molecules and proteins.

CONCLUSION

solid lipid nanoparticles (SLNs) present a versatile and promising platform for drug delivery and cosmetic applications. Their ability to enhance drug stability,

provide controlled release, and improve bioavailability makes them valuable in pharmaceutical formulations. Despite challenges such as limited drug loading capacity and potential particle growth, ongoing research is addressing these limitations and optimizing SLNs for clinical use.

The diverse methods of preparation and characterization techniques discussed in this review highlight the flexibility and robustness of SLN production processes. Moreover, the wide range of administration routes, including parenteral, oral, topical, rectal, ocular, and potential agricultural applications, underscores the broad applicability of SLNs in various fields.

Overall, SLNs offer significant advantages over conventional drug delivery systems, including improved drug efficacy, reduced side effects, and enhanced patient compliance. With continued research and development, SLNs hold great promise for revolutionizing drug delivery technology and improving therapeutic outcomes across a wide range of medical and cosmetic applications.

REFERENCES

[1] Lingayat, V. J., Zarekar, N. S., & Shendge, R. S. (2017). Solid lipid nanoparticles: A review. *Nanoscience and Nanotechnology Research, 2*(2), 67-72.

[2] Sarangi, M., & Padhi, S. (2016). Solid lipid nanoparticles: A review. *Journal of Critical Reviews, 3*(3), 5-12.

[3] Hanumanaik, M., Patel, S., & Ramya Sree, K. (2013). Solid lipid nanoparticles: A review. *IJPSR, 4*(3), 928-940.

[4] Kakadia, P., & Conway, B. (2014). Solid lipid nanoparticles: A potential approach for dermal drug delivery. *American Journal Of Pharmacological Sciences, 2*(5), 1-7.

[5] Sastri, K. T., Radha, G. V., Pidikiti, S., & Vajjhala, P. (2020). Solid lipid nanoparticles: Preparation techniques, characterization, and an update on recent studies. *Journal of Applied Pharmaceutical Science, 10*(06), 126-141.

[6] Teja, V. R. C., Chowdary, V. H., Raju, Y. P., Surendra, N., & Vardhan, R. V. (2014). A glimpse on solid lipid nanoparticles as drug delivery systems. *Journal of Global Trends in Pharmaceutical Sciences, 5*(2), 1649-1657.

[7] Omray, L. (2014). Formulation and characterization of solid lipid nanoparticles for transdermal delivery of testosterone. *International Journal Of Pharma Sciences And Research (Ijpsr), 5*, 323-328.

[8] Pragati, S., Kuldeep, S., & Satheesh, M. (2009). Solid lipid nanoparticles: A promising drug delivery technology. *International Journal of Pharmaceutical Sciences and Nanotechnology, 2*(2),509-516.

[9] Meyer, E., & Heinzelmann, H. (1992). Scanning force microscopy. *Surface Science, Scanning Tunneling Microscopy II*, 99-149.

[10] Scalia, S., Young, P. M., & Traini, D. (2015). Solid lipid microparticles as an approach to drug delivery. *Expert Opinion on Drug Delivery, 12*(4), 583-599.

[11] Kamboj, S., Bala, S., & Nair, A. (2010). Solid lipid nanoparticles: An effective lipid-based technology for poorly water-soluble drugs. *International Journal Of Pharmaceutical Sciences Review And Research, 5*(2), 78-90.

[12] Trotta, M., Debernardi, F., & Caputo, O. (2003). Preparation of solid lipid nanoparticles by a solvent emulsification–diffusion technique. *International Journal of Pharmaceutics, 257*, 153–160.

[13] Hu, F. Q., Yuan, H., Zhang, H. H., & Fang, M. (2002). Preparation of solid lipid nanoparticles with clobetasol propionate by a novel solvent diffusion method in aqueous system and physicochemical characterization. *International Journal of Pharmaceutics, 239*, 121–128.

[14] Duong, V. A., Nguyen, T. T. L., Maeng, H. J., & Cortesi, R. (2020). Preparation of solid lipid nanoparticles and nanostructured lipid carriers for drug delivery and the effects of preparation parameters of solvent injection method. *Molecules, 25*(20), 4781.

[15] Swathi, G., Prasanthi, N., Manikiran, S., & Ramara, N. (2010). Solid lipid nanoparticles: Colloidal carrier systems for drug delivery. *IJPSR, 1*(12), 01-16.

[16] Yadav, P., Soni, G., Mahor, A., Alok, S., Singh, P., & Verma, A. (2014). Solid lipid nanoparticles: An effective and promising drug delivery system- A review. *IJPSR, 5*(4), 1152-1162.

[17] Üner, M., & Yener, G. (2007). Importance of solid lipid nanoparticles (SLN), in various administration routes and future perspectives. *International Journal of Nanomedicine, 2*(3), 289–300.

[18] Reddy, R., & Shariff, A. (2013). Solid lipid nanoparticles: An advanced drug delivery system. *IJPSR, 4*(1), 161-171.

[19] Ramteke, K., Joshi, S., & Dhole, S. (2012). Solid lipid nanoparticles: A review. *IOSR Journal Of Pharmacy, 2*(6), 34-44.

[20] Yadav, N., Khatak, S., & Singh, S. (2013). Solid lipid nanoparticles: A review. *International Journal of Applied Pharmaceutics, 5*(2), 8-18.

[21] Ekambaram, P., Sathali, A., & Priyanka, K. (2011). Solid lipid nanoparticles and lipid nanostructures overview. *Scientific Review &Chemical Communication, 2*, 216-220.

[22] Akanksha, G., Deepti, S., & Navneet, G. (2012). Solid lipid nanoparticles: Method, characterization and applications. *International Current Pharmaceutical Journal, 1*, 384–393.

[23] Sailaja, A. K., Amareshwar, P., & Chakravarty, P. (2011). Formulation of solid lipid nanoparticles and their applications. *Current Pharmaceutical Research, 1*(2), 197-203.

[24] Rani, P. S., & Lakshmi, P. V. (2020). A review on solid lipid nanoparticles – A new model approach for effective drug delivery. *European Journal of Pharmaceutical and Medical Research, 7*(8), 331-339.

[25] Manjunath, K., Reddy, J. S., & Venkateswarlu, V. (2005). Solid lipid nanoparticles as drug delivery systems. *Methods Findings Exp Clin Pharmacol, 27*, 127-144.

[26] Üner, M., & Yener, G. (2007). Importance of solid lipid nanoparticles (SLN), in various administration routes and future perspectives. *International Journal of Nanomedicine, 2*(3), 289–300.

[27] Almeida, A. J. A., & Souto, E. (2007). Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advances in Drug Delivery Reviews, 59*, 478-490.

[28] Rewar, S., Mirdha, D., & Rewar, P. (2014). Solid lipid nanoparticles: A novel potential carrier approach. *Asian Journal of Research in Chemistry and Pharmaceutical Sciences, 2*(4), 108-117.

[29] Bhattacharya, S., & Prajapati, B. G. (2014). A review on solid lipid nanoparticles (SLNs). *International Journal of Pharmaceutical Research and Bio-Science (IJPRBS), 3*(6), 445-465.

[30] Reddy, A. P., Parthiban, S., Vikneswari, A., & Senthilkumar, G. P. (2014). A modern review on solid lipid nanoparticles as novel controlled drug delivery system. *International Journal of Research in Pharmaceutical and Nano Sciences, 3*(4), 313-325.

[31] Mishra, B., Patel, B. B., & Tiwari, S. (2010). Colloidal nanocarriers: A review on formulation technology, types and applications toward targeted drug delivery. *Nanomedicine: NMB, 6*(1), 9-24.

[32] Soni, K., Kukereja, B. K., & Kapur, M. (2015). Lipid nanoparticles: Future of oral drug delivery and their current trends and regulatory issues. *International Journal of Current Pharmaceutical Research, 7*(1), 1-18.