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SOLID LIPID NANOPARTICLES AS A NOVEL DRUG DELIVERY SYSTEM: A COMPREHENSIVE REVIEW

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ABSTRACT

Alternative drug delivery methods to colloidal carriers including liposomes, emulsions, and polymeric micro- and nanoparticles include solid lipid nanoparticles (SLNs). One of the most cutting-edge methods for addressing drug delivery's targeting and bioavailability problems is the use of SLNs. This review covers every important aspect of SLNs, including their manufacturing processes, various SLN models, drug incorporation, loading capacity, and drug release, as well as the most recent characterization techniques, their uses, and developments in the delivery of biological drugs, such as gene vectors, novel adjuvants for vaccines, proteins, and peptides with SLNs. According to the data that is now available, SLNs have a wider chance of success in the future since they can be readily created with a variety of features that have a huge potential for targeting and diagnosing a wide range of disorders. With the current conversation that reframes the potential of SLNs and compiles the various research findings of SLNs in tabular form along with the approved patent technologies of SLNs, this review will assist aspiring researchers in learning about the unexplored areas of SLNs.

KEYWORDS: Solid lipid nanoparticles (SLNs), Method of preparation, Surfactants, TEM, PCS.

INTRODUCTION

Nanotechnology and Nanoparticles: Nanotechnology is the study of extremely small particles, or nanoparticles. In the past few years, research in nanoscience has advanced quickly across a wide range of product categories. Colloidal particles, often known as nanoparticles, are tiny particles with sizes ranging from one to a thousand nm.[1] They are made from natural or synthetic polymers and are perfect for minimizing toxicity and improving drug delivery. This approach allows for the oral delivery of medications, which can enhance the related drugs' therapeutic index, tolerability, specificity, and efficacy.[2]

Every field of medicine, including endocrinology, cardiology, immunology, pulmonology, ophthalmology, and oncology, has greatly benefited from the use of nanoparticle-based drug delivery systems. Additionally, highly specialized fields like tumor targeting, gene delivery, brain targeting, oral vaccine formulations, and many others have also benefited. Nanoparticle based formulations are an emerging approach that utilizes a broad range of technique and procedures aimed for diagnosis of disease and novel drug delivery.[1,3]

Researcher mainly focused on development of nano-particle-based systems for drugs which have oral bioavailability issues due to the hydrophilic nature of the GIT. For such type of medicine they have tried different chemical structure, proteolytic enzyme inhibitors, using permeation enhancers, decrease in hepatic first-pass metabolism, alteration in GIT transit duration, and designing modern drug delivery methods to enhance absorption and bioavailability of medicine. The pharmacokinetics of drugs via nanoparticles has exhibit that they can enhance circulation time, extend residence time and half-life, decrease clearance, and eliminate pre-systemic metabolism at the site of absorption.[2,3]

The nanoparticles are made to be able to regulate their size, shape, charge, and lipophilicity in addition to having an easy time passing through the GI membrane. Numerous nanoparticulate systems are used in nanotechnology, including micelles, cell ghosts, liposomes, niosomes, lipoproteins, metal-oxide nanoparticles, microcapsules, and numerous nano-assemblies.[4]

However, there are certain drawbacks to nanoparticle-based drug delivery systems, such as dendrimers, quantum dots, etc. These include the need for organic solvents during the synthesis process, which can leave residues that are cytotoxic, and the challenge of scaling up manufacturing processes for some particular nanoparticles. Drug delivery systems based on lipids appear to be a possible solution to these issues. Lipid-based delivery systems range from simple oil solutions to mixes of oils, surfactants, co-surfactants, and co-solvents. Solid lipid nanoparticles (SLNs) for the

treatment of various illnesses were developed in order to address all of the aforementioned issues.[1-3]

Lipid based Nanoparticles drug delivery system:[5,6] Since lipids may be synthesized with small particle size and shape and are known to enhance oral drug absorption, lipid-based drug delivery systems hold great potential. This system includes a variety of products, ranging from straightforward oil solutions to intricate blends of oils, co-solvents, surfactants, and oils.

Drugs are typically dissolved in a mixture of two or more excipients, such as triglyceride oils, partial glycerides, surfactants, or co-surfactants, in lipid formulations intended for oral administration. Lipid-based delivery systems are becoming more and more popular for the oral delivery of lipophilic, poorly water soluble medications. Lipidic dose forms' increased oral bioavailability could be the result of various processes.[5,6]

The main mechanism is usually the avoidance, either partially or completely, of the slow breakdown process that causes hydrophobic medicines in solid dosage forms to have limited bioavailability. The medicine should ideally be able to stay dissolved as it passes through the digestive system thanks to the lipidic formulation.

Emulsions, which are conventional lipid-based systems, are inadequate in addressing the issues associated with lipophilic medications, including poor patient compliance, low stability, and poor solubility. Novel lipid-based carriers were developed in response to the need for new carrier systems. The lipid and surfactant-based formulation strategy garnered attention among the other approaches since it has been shown to be effective in enhancing the oral bioavailability of medications with low aqueous solubility.[7-9]

Table 1: Lipid based formulation and their particle size.

Formulation	Particle Size
Solid lipid nanoparticles (SLNs)	1-1000 nm
Nanostructured lipid carriers (NLC)	50-300 nm
Liposomes	50~1,000 nm
Self micro-emulsifying drug delivery system(SMEDDS)	>50 nm
Self emulsifying drug delivery system (SEDDS)	100-200 nm
Micro emulsions	10-300 nm
Macro emulsions	1000~10,000 nm
Micelles	5~50 nm

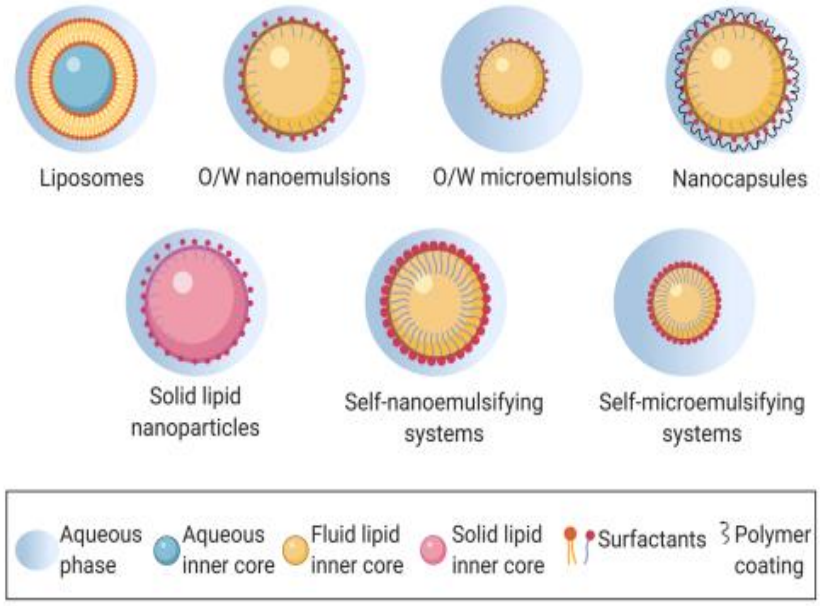

Figure 1: Classification of lipid-based nanoparticle drug delivery systems[10]

In solid lipid nanoparticles, lipid matrix consists of a solid lipid or a mixture of solid lipids which form almost a perfect crystalline structure. In nanostructured lipid carrier, lipid matrix is composed of a blend of a solid lipid and an oil leading to a crystal structure with more imperfections and therefore with more room for drug accommodation. Solid lipid carrier and nanostructured lipid carrier retain the advantages of traditional liposomes and niosomes such as high absorption and biocompatibility, while overcoming issues of stability commonly encountered with liposomes.[1,8,11]

Table 2: Comparison of various nanotechnology based formulations

Property	SLNs	Liposomes	Polymeric Nano- articles	Nano Emulsions	Nano- Suspensions
Ability to deliver hydrophobic and hydrophilic drugs	Yes	Yes	Yes	Yes	Only hydrophobic drugs
Physical stability	Good	Poor	Good	Moderate	Good
Biological stability	Moderate	Poor	Good	Moderate	Moderate
Biocompatibility	Good	Good	Moderate	Good	Moderate
Drug targeting	Moderate	Moderate	Moderate	Poor	Poor
Drug loading	High	Low to moderate	Moderate	High	High
Ability to deliver biotechnological therapeutics	Moderate	Moderate	Moderate	Poor	No
Oral delivery	Possible	Not possible	Possible	Possible	Possible
Parenteraldelivery	Possible	Possible	Possible	Possible	Possible

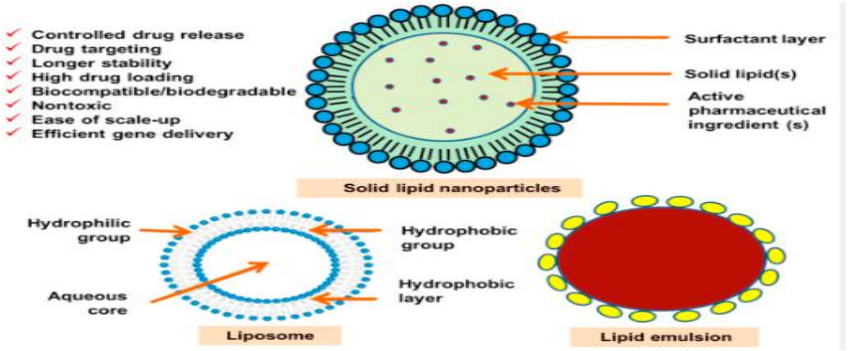

Figure 2: Diagrammatic representations of advantages of SLNs over other nanotechnology.

Solid lipid Nanoparticles[12]

Solid lipid nanoparticles (SLN) have a high drug loading capacity and facile permeability, making them an important field of nanotechnology in drug delivery for the treatment of chronic illnesses. The physiological lipids (triglycerides, fatty acids, or waxes) in the sub-micron size range of 50–500 nm colloidal carriers make up the SLNs. These lipids are distributed in water or an aqueous surfactant solution. One of the most often used methods for enhancing the oral bioavailability of poorly water soluble medications is the use of SLNs, which are thought to be the most effective lipid-based colloidal carriers. Drugs that are lipophilic or hydrophilic can be distributed across the solid hydrophobic lipid core of SLNs. Compared to polymeric nanoparticles, they exhibit lower systemic toxicity and greater biocompatibility because they are made of a physiological solid lipid emulsion system by eliminating organic solvents to the greatest extent possible. Owing to their small size (50–500 nm), they are directly absorbed from the intestines through the lymphatic system, avoiding the liver and spleen's metabolism. This increases the medications' bioavailability. Since SLNs can cross the blood-brain barrier if their diameter is less than 50 nm, they have been extensively researched as a potential treatment for brain diseases. Because solid lipids, modified pharmaceuticals, and additional components are used in a certain ratio to create a specific physicochemical state with the longest diffusion pathway and regulated drug release, SLNs containing drugs also exhibit a sustained release feature.[13,14]

Advantages of solid lipid nanoparticle[15]

- SLNs escape RES bypassing liver and spleen filtration due to their unique physicochemical properties.
- Feasibilities of carrying both lipophilic and hydrophilic drugs.
- SLNs have better long term stability and ease of upgradability by immobilizing within and resulting a stable formulation.
- Drug formulations are cost-effective during scale-up processes.
- Use of biodegradable physiological lipids which decreases the danger of acute and chronic toxicity and avoidance of organic solvents in production method.
- Site specific delivery of drugs, enhanced drug penetration into the skin via dermal application.
- More affordable (less expensive than polymeric/surfactant based carriers): The lipid raw materials for SLNs are cheaper than the polymers.
- They have no reports of any acute or chronic toxicity due to lipid matrix.
- Easy to manufacture than bipolymeric nanoparticles.

- Protection of chemically labile agents from degradation in the gut and sensitive molecules from outer environment.

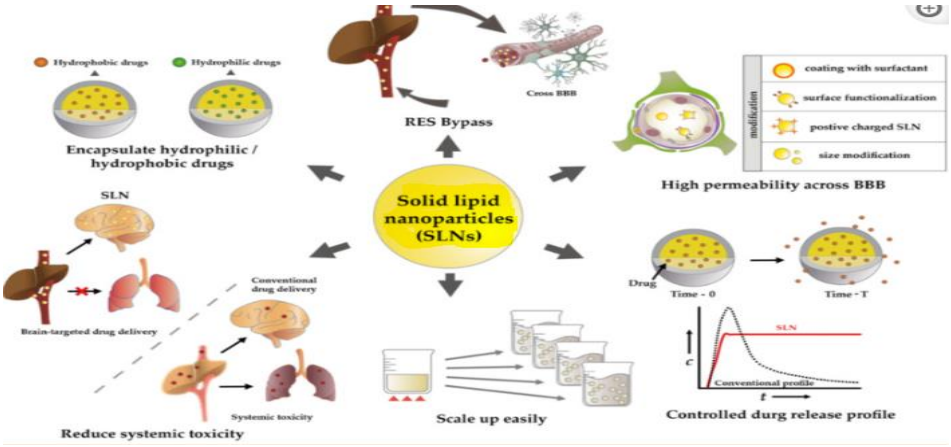

Figure 3: Advantages of solid lipid nanoparticle.

Excipients used in solid lipid nanoparticles: A mixture of solid lipids and surfactant is used to create solid lipid nanoparticles. The main ingredients utilized to create SLNs include lipids, surfactants/stabilizers, charge modifiers, cryoprotectants, and co-surfactants. Surfactants aid in stabilizing the SLN structure by lowering the interfacial tension between the hydrophobic surface of the lipid core and the aqueous environment. To stabilize the lipid dispersion, emulsifiers of all classes (in terms of charge and molecular weight) have been employed. It has been discovered that using multiple emulsifiers together may more effectively avoid particle agglomeration.[16]

Table 3: Ingredients used in SLNs-based formulations.[15]

Ingredients	Examples
Lipid component	Stearic acid, Beeswax, Glyceryl trilaurate, Glyceryl trimyristate, Glyceryl, behenate (Compritol), Glyceryl tripalmitate, Hardened fat (Witepsol E85, H5 and W35), Monostearate monocitrate, Solid paraffin, Behenic acid.
Surfactant/Emulsifiers	Phosphatidyl choline, Soy and Egg lecithin, Poloxamer, Poloxamine, Polysorbate 80.
Co-surfactant	Sodium dodecyl sulphate, Tyloxopol, Sodium oleate, Taurocholate sodium salt, Sodium glycocholate, Butanol.
Preservative	Thiomersal.
Cryoprotectant	Gelatin, Glucose, Mannose, Maltose, Lactose, Sorbitol, Mannitol, Glycine, Polyvinyl alcohol, Polyvinyl pyrrolidone.
Charge modifiers	Dipalmitoyl phosphatidyl choline, Stearylamine, Dicetylphosphate, Dimyristoyl phophatidyl glycerol.

Methods of preparation of SLN: SLNs can be created in a number of ways. In general, there are two popular methods for creating SLNs. Before the SLNs are formulated, the medication is first dissolved in the melted solid lipid in the first method. In this strategy, the SLNs are formulated using techniques such double emulsion, microemulsion, high-pressure homogenization, and high-speed homogenization. In the second method, the medication and solid lipid are dissolved in a suitable solvent before the SLNs are produced. The SLNs are prepared with the aid of a surfactant using double emulsion and microemulsion-based techniques such solvent injection, solvent evaporation, thin film, and supercritical fluid extraction, after which the solvent is evaporated.[16-18]

1. High pressure homogenization
   - Hot homogenization
   - Cold homogenization

2. Ultra-sonication/high speed homogenization
3. Solvent evaporation method
4. Solvent emulsification-diffusion method
5. Microemulsion based method
6. Spray drying method
7. Double emulsion method
8. Precipitation technique

Physiochemical Characterization of SLN's[18-20]

1. Particle Size and Shape: The most effective methods for determining particle size are laser diffraction (LD) and photon correlation spectroscopy (PCS). Electron microscopy was employed to ascertain the SLNs' shape.

A. Photon Correlation Spectroscopy (PCS): Dynamic light scattering, or PCS for short, is a technique that quantifies how much the intensity of scattered light varies due to particle motion. The measuring of particles in the 3 nm–3 mm range can be accomplished with this approach. The PCS apparatus is made up of a detector, a temperature-controlled sample cell, and a laser source. Light scattered over surfaces is detected using a photomultiplier as a detector. The intensity of the light scattering from the particles determines the PCS diameter.

B. Electron Microscopy: Transmission of Scanning Electron Microscopy To ascertain the physical characteristics of nanoparticles, such as their shape and morphology, electron microscopy is employed. It makes it possible to determine the distribution and size of the particles. Whereas TEM employs electrons that are communicated through the sample, SEM uses electrons that are transmitted from the sample's surface. The size limit of detection for TEM is smaller.

Table 4: Methods of particle size measurement of SLN.

Sr. No	Method	Principle	Measured size
1	Light scattering	Light Interaction	50 nm-1µm
2	Laser light diffraction	Light Interaction	1-1000 µm
3	Scanning electron microscope	Microscopy	50 nm-100 µm
4	Atomic force microscopy	Microscopy	10 nm-1µm
5	Analytical ultracentrifugation	Centrifugation	20 nm-1µm
6	Capillary electrophoresis	Electrophoresis	20-500 nm

2. Measurement of zeta potential: Predictions regarding the colloidal dispersion's storage stability are made possible by the measurement of the zeta potential. Because of electric repulsion, charged particles (high zeta potential) are generally less prone to aggregate. The Zeta potential measurement tool most commonly used is the Malvern Zetasizer. Zeta potentials of -25 mV and higher are necessary for the formulation to fully stabilize electrostatically.[21]

3. Determination of incorporated drug (drug loading and entrapment efficiency)[20,21]

Measuring the amount of drug included in nanoparticles is crucial since it influences the release property of the particles. Following the removal of the free drug and solid lipids from the aqueous medium using ultracentrifugation, centrifugation filtration, or gel permeation chromatography, the amount of drug encapsulated per unit weight of nanoparticles is calculated. Standard analytical techniques including spectroscopy and HPLC procedures can be used to assay the medication.

Two parameters expressing the efficiency of drug loading are most widely used. Entrapment efficiency is the amount of the drug incorporated in the particles divided by its overall amount in the formulation.

$$EE = \frac{Actual\ amt.\ Of\ drug\ in\ formulation - soluble\ unencapsulated\ drug}{Amount\ of\ drug\ added\ during\ formulation} \times 100$$

Drug loading capacity (DL) is another parameter that expresses the amount of drug in the particles divided by the weight of total carrier system (all ingredients taken together). DL is also expressed in %.

$$L = \frac{Actual\ amount\ of\ encapsulated\ drug \times 100}{Amount\ of\ lipid\ used\ to\ prepare\ the\ formulation}$$

4. Measurement of degree of crystallinity and lipid modification[16,22,23]

It has been well-established for decades that there is a relationship between drug incorporation and release rates, as well as between thermodynamic stability and lipid packing density. The majority of the methods rely on measurements from differential scanning calorimetry (DSC) and X-ray diffractometry (XRD).

5. In vitro drug release from SLNs[24,25]

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

a) Dialysis bag diffusion technique.
b) Reverse dialysis bag technique.
c) Agitation followed by ultracentrifugation or centrifugal ultra-filtration

Applications of SLNs[26,36]

- **Cancer Chemotherapy by using SLNs**

The in-vitro and in-vivo efficacy of several chemotherapeutic drugs that have been encapsulated in the form of SLNs has been assessed by several scientists.43 SLNs are a good vehicle for delivering chemotherapeutic agents because of a variety of features,

including increased drug efficacy, better pharmacokinetics, improved drug stability, and encapsulation of chemotherapeutic medicines with a variety of physicochemical qualities that reduce in vitro toxicity. SLNs are used to address issues related to anticancer compounds, such as normal tissue toxicity, reduced stability, inadequate specificity, and a high rate of treatment resistance. One of the main challenges in targeting organs other than bone marrow and solid malignancies is the RES macrophages' quick clearance of colloidal particles.[26,27]

✓ **SLNs in brain tumor and cancer:** The main problem associated with anti-cancer drugs is difficulty in effective transport of across the BBB, resulting in lower therapeutic efficacy. A broad range of medicine and their modification have been investigated for their ability to treat glioblastoma, such as the SLNs of etoposide and paclitaxel. In vitro studies demonstrated that these had an enhanced inhibitory effect on the proliferation of glioma cell lines, which was performed more efficiently than when using the free drug alone.[24,28]

✓ **SLNs as targeted carrier for anticancer drug to solid tumor:** SLNs have been to be useful as drug carriers. Tamoxifen is an anticancer drug incorporated in SLN to prolong the release of drug after IV administration in breast cancer. Tumor targeting has been achieved with SLN loaded with drugs like methotrexate and camptothecin.[44]

✓ **SLNs in breast cancer and lymph node metastases:**[29,30] Mitoxantrone SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of the drug in breast and lymph node cancer.

➢ **SLNs as potential new adjuvant for vaccines:** To enhance the immune response of vaccine adjuvants are used. New developments in the adjuvant area are the emulsion systems. These are O/W emulsions that degrade rapidly in the body. Being in the solid state, the lipid components of SLNs will be degraded more slowly providing a longer lasting exposure to the immune system.[3]

➢ **Solid lipid nanoparticles for delivering peptides and proteins:** Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN. Formulation of protein SLNs confers enhance stability, prevent proteolytic degradation, sustained release can achieved of incorporated molecules. Peptides as cyclosporine A, insulin, calcitonin and somtostatin have been incorporated into solid lipid particles and are currently under investigation. There are several local or systemic therapeutic.[32]

➢ **SLN for Topical application:** SLNs and NLCs are very attractive colloidal carrier systems for skin applications due to their various desirable effects on skin besides the characteristics of a colloidal carrier system. During the last few years, SLNs have been studied with active compounds such as Vit E, tocopherol acetate, retinol, clotrimazole, triptolide, and phodphyllotoxin for topical application.[33] SLNs used for topical preparation for various drugs such as anticancers, imidazole, ketoconazole tropolide, glucocorticoids, vitamin A, isotretinoin, antifungals etc. By using glyceryl derivative vitamine A-loaded SLNs can be prepared.[34]

➢ **Solid lipid nanoparticles for parasitic diseases:** SLNs and NLCs are effective alternative to liposomes mainly due to their better stability profile, ease of scalability and commercialization and relative cost efficacy. Both the formulation shows particulate nature and inherent structure which exhibit good potential in the treatment of parasitic infections. Parasitic diseases (malaria, leishmaniasis, tryanosomiasis) can treated by using SLNs.[31,32]

➢ **Oral SLNs in anti-tubercular chemotherapy:** Drugs such as isonizide, rifampicin, pyrazinamide-loaded SLNs systems, were able to reduce the dosing frequency and also improve patient compliance. By using the emulsion solvent diffusion technique these anti-tubercular drugs loaded SLN are prepared.[35] The nebulization in animal by incorporating the above drug in SLN also reported for improving the bioavailability of the drug.

➢ **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. The in vivo study showed that skin hydration will be increased by 31% after 4 weeks by addition of 4% SLN to a conventional cream. SLN and NLCs have proved to be controlled release innovative occlusive topicals.[36,37]

➢ **SLN for potential agriculture application:** Artemisia arborescens extract when incorporated in SLNs, were able to decrease the rapid evaporation compared with emulsions and the systems have been used in agriculture as a suitable carrier of ecologically safe pesticide.[38]

CONCLUSION AND FUTURE PROSPECTS: SLN formulations are currently primarily employed as a drug delivery method for medications that are poorly soluble. Low toxicity, targeted medication delivery, controlled release, and the ability to incorporate hydrophilic or lipophilic medicines are all advantages of using nanoparticles. This review concentrated on the range of features of SLNs and how they can be utilized to encapsulate different medications. This page discusses many methods for preparing SLNs, their evaluation, characterisation parameters, and applications in various fields. Because they improve intestinal absorption and shield the encapsulated medications, SLNs are therefore a viable option for delivering poorly-soluble molecules orally. A combination of lipid or fatty acid with non-

ionic emulsifiers has been shown to reduce the lipase-mediated degradation of SLNs after oral administration. According to the main applications reported in the literature, the use of SLNs to target drug delivery to the brain has increased in importance as alternative carriers for polymeric nanoparticles. Because of the SLN potential for facilitating controlled drug delivery to a target tissue and its biocompatibility, there will be much investigation in improvement of quality, efficacy, and safety profile of drugs using them in the future.[39] A front line of research should merely be focused on the development of surface-modified SLNs for future perspectives. If properly explored, a very well-designed, SLNs seems to be a promising carrier that may open a new benchmark in treatment, diagnosis, and as a carrier for biological drugs.

Conflicts of interest: The authors declare no conflict of interest.

REFERENCES

1. Mukherjee S, Ray S, Thakur R. Solid lipid nanoparticles: A modern formulation approach in drug delivery system. Indian J. Pharm. Sci; 2009; 71: 349-360.
2. Garud A, Singh D, Garud N. Solid Lipid Nanoparticles (SLN): Method, Characterization and Applications. International Current Pharmaceutical Journal, 2012; 1(11): 384-393.
3. Duan A, Dhar A, Patel C. A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems. RSC Adv; 2020; 10: 26777-26791.
4. Farokhzad OC, Langer R. Impact of nanotechnology on drug delivery. ACS Nano, 2009 Jan 27; 3(1): 16-20.
5. Pavankumar AR, Parthiban S. A modern review on solid lipid nanoparticles as novel controlled drug delivery system. Ijrpns, 2014; 3(4): 313-325.
6. Sultana S, Mohammed S, Begum AS. Review of Solid Lipid Nanoparticles. International Journal for Research Trends and Innovation, 2020; 5(5): 88-103.
7. Ekambaram P, Abdul Hasan A, Priyanka K. Solid Lipid Nanoparticles: A Review, Sci. Revs. Chem. Commun, 2012; 2(1): 80-102.
8. Kamble MS. Solid lipid nanoparticles and nanostructured lipid carriers - an overview. Int J of Pharm Chem and Bio Sci; 2012; 2(4): 681-691.
9. Shah C, Shah V, Upadhyay U. Solid lipid nanoparticles: a review current pharma research, 2011; 1(4): 351-368.
10. Plaza-Oliver M, Santander-Ortega MJ, Lozano MV. Current approaches in lipid-based nanocarriers for oral drug delivery. Drug Deliv. and Transl. Res, 2021; 11: 471–497.
11. Chutoprapat R, Kopongpanich P. 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.
12. Tekade RK, Maheshwari R, Tekade M. Chapter 8 - Solid Lipid Nanoparticles for Targeting and Delivery of Drugs and Genes. Academic Press, 2017: 256-286.
13. Yadav N, Khatak S, Singh U. Solid Lipid Nanoparticles- A Review. International Journal of Applied Pharmaceutics, 2013; 5(2): 8-18.
14. Surender V, Deepika M. Solid lipid nanoparticles: a comprehensive review. Journal of Chemical and Pharmaceutical Research, 2016; 8(8): 102-114.
15. Mishra V, Bansal KK, Verma A, Yadav N, Thakur S, Sudhakar K, Rosenholm JM. Solid Lipid Nanoparticles: Emerging Colloidal Nano Drug Delivery Systems. Pharmaceutics, 2018 Oct 18; 10(4): 191.
16. Guerrero DQ, Morlán ZU, Gómez GL. Solid Lipid Nanoparticles: An Approach to Improve Oral Drug Delivery. J Pharm Pharm Sci; 2021; 24: 509-532.
17. Sachin J, Gupta V. Solid Lipid Nanoparticles – Preparation, Applications, Characterization, Uses in Various Cancer Therapies, Research Journal of Pharmaceutics and Technology, 2013; 6: 825-837.
18. Hu L, Tang X, Cui F. Solid lipid nanoparticles (SLNs) to improve oral bioavailability of poorly soluble drugs. J Pharm Pharmacol, 2010; 56(12): 1527–35.
19. Sinha VR, Srivastava S, Goel H, Jindal V. Solid Lipid Nanoparticles (SLN'S) – Trends and Implications in Drug Targeting. International Journal of Advances in Pharmaceutical Sciences, 2010; 1: 212-238.
20. P. Rabinarayan, S. Padilama, Production of SLNs-Drug Loading and Release Mechanism. Journal of Chemical and Pharmaceutical Research, 2010; 2(1): 211-227.
21. Naseri N, Valizadeh, HP. Solid Lipid Nanoparticles and Nanostructured Lipid Carriers: Structure Preparation and Application. Adv. Pharm. Bull; 2015; 5: 305–313.
22. Jaiswal S, Gupta GD. Recent advances in solid lipid nanoparticles and challenge. Indo ame J of Pharm Res; 2013; 3(12): 1601-1611.
23. Thukral DK, Dumoga S, Mishra AK. Solid lipid nanoparticles: promising therapeutic nanocarriers for drug delivery. Curr Drug Deliv; 2014; 11(6): 771-91.
24. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. Eur J Pharm Biopharm, 2000 Jul; 50(1): 161-77.
25. Salah E, Abouelfetouh MM, Pan Y. Solid lipid nanoparticles for enhanced oral absorption: A review. Colloids Surf B Biointerfaces, 2020 Dec; 96: 111-118.
26. Murthy RS. Solid lipid nanoparticles as carriers for anti-cancer drugs to solid tumours. Drug Deliv; 2005; 12: 385–92.

27. Pandey S, Shaikh F, Gupta A, Tripathi P, Yadav JS. A Recent Update: Solid Lipid Nanoparticles for Effective Drug Delivery. Adv Pharm Bull, 2022 Jan; 12(1): 17-33.
28. Kaur IP, Bhandari R, Bhandari S, Kakkar V. Potential of solid lipid nanoparticles in brain targeting. J Control Release, 2008 Apr 21; 127(2): 97-109.
29. Reddy JS, Venkateswarlu V. Novel delivery systems for drug targeting to the brain. Drugs Future, 2004; 29: 63–83.
30. Jain V, Kumar H, Anod HV. A review of nanotechnology-based approaches for breast cancer and triple-negative breast cancer. J Control Release, 2020 Oct 10; 326: 628-647.
31. Shankar R, Joshi M, Pathak K. Lipid Nanoparticles: A Novel Approach for Brain Targeting. Pharm Nanotechnol, 2018; 6(2): 81-93.
32. Scioli Montoto S, Muraca G, Ruiz ME. Solid Lipid Nanoparticles for Drug Delivery: Pharmacological and Biopharmaceutical Aspects. Front Mol Biosci, 2020 Oct; 30(7): 987-997
33. Paliwal R, Paliwal SR, Kenwat R, Kurmi BD. Solid lipid nanoparticles: a review on recent perspectives and patents. Expert Opin Ther Pat; 2020 Mar; 30(3): 179-194.
34. Eldem T, Speiser P, Hincal A. Optimization of spray-dried and congealed lipid microparticles and characterization of their surface morphology by scanning electron microscopy. Pharm Res; 1991; 8: 47–54.
35. Jenning V, Gysler A, Schafer-Korting M, Gohla S. Vitamin A loaded solid lipid nanoparticles for topical use: Occlusive properties and drug targeting to the upper skin. Eur J Pharm Biopharm, 2000; 49: 211–218.
36. Shinde PB, Gunvantrao DS, Vivekanand SM. Lipid Based Nanoparticles: SLN/NLCs-Formulation Techniques, Its Evaluation and Applications. Int. J. Creat. Innov. Res. All Stud, 2019; 1: 20–31.
37. Puglia C, Bonina F. Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals. Expert Opin Drug Deliv; 2012 Apr; 9(4): 429-41.
38. Assali M, Zaid AN. Features, Applications, and Sustainability of Lipid Nanoparticles in Cosmeceuticals. Saudi Pharm. J; 2022; 30: 53–65.
39. Lai F, Wissing SA, Muller RH, Artemisia arborescens essential oil-loaded solid lipid nanoparticles for potential agriculture application: Preparation and characterization. AAPS Pharm Sci Tech, 2006; 7: 21-27.