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EMERGING DEVELOPMETNS IN DRUG DELIVERY SYSTEMS USING SOLID LIPID NANOPARTICLES

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Abstract

Nanomedicine and nano-delivery systems are rapidly growing fields that focus on using small materials for targeted drug delivery and diagnostics, offering significant benefits in treating chronic diseases. These systems enhance treatment effectiveness, reduce costs, and improve patient quality of life. Lipid-based carriers, like solid lipid nanoparticles (SLNs), are becoming popular alternatives to polymeric nanoparticles, especially for delivering lipophilic drugs. SLNs have been successful since the approval of Doxil in 1995 and are showing promise for RNA-based treatments, including mRNA vaccines. They are non-toxic, biodegradable, stable, and designed to improve drug bioavailability while targeting specific tissues. Nanostructured lipid carriers (NLCs) and SLNs are particularly useful for drugs with poor solubility and pharmacokinetic profiles. These carriers can be modified to offer advantages over traditional systems like liposomes. SLNs are versatile, stable, and can incorporate both hydrophilic and lipophilic drugs, with new formulations being developed to address drug resistance. Ongoing research explores their preparation, characterization, and applications in gene therapy, vaccines, and protein delivery. Surface-modified SLNs hold promise for targeted and controlled drug delivery, with future research likely expanding their potential for diagnosing and treating various diseases.

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Introduction

Nanotechnology has revolutionized medicine by enabling precise drug delivery through nanoscale particles, significantly improving treatments like chemotherapy and immunotherapy. By allowing drugs to target specific sites in the body, nanotechnology enhances effectiveness while minimizing side effects. The use of nanoparticles, ranging from 1 nm to 1000 nm, increases surface area and improves drug absorption, distribution, and bioavailability. Biodegradable and biocompatible materials ensure better pharmacokinetics and pharmacodynamics, making treatments safer and more efficient. Solid lipid nanoparticles (SLNs) further enhance drug stability and controlled release [1]. Compared to liposomes, nanoparticles offer superior stability and reliability. Despite its potential, widespread adoption faces challenges such as high costs and regulatory limitations [2]. However, ongoing research aims to develop cost-effective and scalable solutions. As advancements continue, nanotechnology promises to transform medicine by providing safer, more effective and targeted therapies, ultimately improving patient outcomes and revolutionizing pharmaceutical treatments [3].

Solid Lipid Nanoparticles Outline

Phospholipids play a key role in lipid-based drug delivery due to their biocompatibility and multifunctionality. While traditional liposomes face challenges like low drug entrapment, solid lipid nanoparticles (SLNs) offer a promising alternative. SLNs, made of solid lipids, emulsifiers, and active ingredients (50–1000 nm in size), enhance drug bioavailability, targeted delivery, and controlled release while minimizing immune response. They combine benefits from polymeric nanoparticles, liposomes, and microemulsions. Surface modifications improve pharmacokinetics, stability, and drug incorporation, boosting organ-specific drug accumulation. Cyclodextrin enhances solubility and bioavailability. SLNs are stable, effective in chemotherapy, and useful for geneticdiseases, antifungal treatments, and pulmonary drug delivery. Additionally, they are applied in cosmetics for UV protection and skin hydration, showcasing their broad therapeutic potential [4].

Principle of Lipid Nanoparticle Formulation

The formulation of solid lipid nanoparticles (SLNs) depends on interactions between lipids, emulsifiers, and environmental factors like temperature and interfacial forces. Lipids such as fatty acids and triglycerides form the base, while surfactants stabilize the structure. These components influence SLN stability, bioavailability, and drug release. Lipid molecules self-assemble in an aqueous phase, reducing interfacial energy to create stable nanoparticles. The process involves melting solid lipids, mixing with water, and using high-speed agitation to form fine droplets. Surfactants like Tween-80 lower surface tension, enhancing drug loading and stability. By optimizing lipid composition and emulsifiers, SLNs improve drug delivery, offering controlled release, enhanced bioavailability, and reduced toxicity, making them valuable in pharmaceuticals and nanomedicine [5]. To increase the surface of the dispersed particles, the amount of work needed to be done is as follows:

$$W=\gamma \times \Delta A$$

Where;

W =working ergs, γ =surface tension in dynes/cm2,

ΔA =increase in surface area in cm2.

Surfactant selection also based on the HLB scale, as described by Griffin, where a high value denotes hydrophilic molecule and low value indicates a hydrophobic molecule. In the case of non-ionic surfactants whose hydrophilic portion is only polyoxymethylene

$$HLB = \frac{E}{5}$$

Where E is the % by weight of ethylene oxide. In the case of polyhydric alcohol fatty acid esters

$$HLB = 20\left(1 - \frac{S}{A}\right)$$

Benefits and Drawback of SLN's

Benefits

Solid lipid nanoparticles (SLNs) offer numerous advantages due to their nanoscale size, which allows them to evade the reticuloendothelial system (RES) and extend circulation time in the bloodstream. They enhance the bioavailability of poorly water-soluble drugs while protecting sensitive compounds from degradation. SLNs provide a stable environment for both hydrophilic and lipophilic drugs, ensuring controlled and targeted drug release, their simple and scalable formulation, along with the ability to be lyophilized for long-term stability, makes them an effective drug delivery system [6].

Drawbacks

Despite their benefits, SLNs have a dense crystalline lipid matrix, limiting drug loading capacity. Drug-lipid interactions, lipid composition, and miscibility impact encapsulation efficiency. Structural changes over time may alter drug release and stability. High water content in SLN dispersions affects shelf life, requiring stabilizers or lyophilization to maintain integrity [7].

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Processing Methods of SLNs

High-Pressure Homogenization Technique

The high shear homogenization technique, often combined with ultrasonication, is commonly used for solid lipid nanoparticle (SLN) preparation. While simple, it may produce microparticles affecting dispersion quality. Melt emulsification, involving lipid melting, surfactant mixing, and high-shear homogenization, improves SLN formulations. Studies highlight that emulsification time, stirring speed, and cooling conditions influence SLN stability, size, and drug loading efficiency(8)

Hot Homogenization

Hot homogenization, performed above the lipid melting point, is a key technique for preparing solid lipid nanoparticles (SLNs). It begins with a pre-emulsion, where a drug-loaded lipid melt is mixed with an aqueous emulsifier solution using high shear. This pre-emulsion undergoes high-pressure homogenization (HPH) to reduce particle size. Optimal temperature, pressure (500–1500 bars), and homogenization cycles (3–5 passes) are crucial to ensure SLN stability and drug integrity [9].

Cold Homogenization

Cold homogenization is a solid-state lipid processing technique that prevents temperature-induced drug degradation and instability. The drug is first dissolved in a lipid melt, rapidly cooled using dry ice or liquid nitrogen, and ground into microparticles (50–100 microns). These are then dispersed in a chilled emulsification solution and processed via high-pressure homogenization. This method produces larger SLNs with broader size distribution but enhances stability for temperature-sensitive drugs [10].

Solution Emulsification-Evaporation Method

The solvent emulsification-evaporation method is used to prepare solid lipid nanoparticles (SLNs) by forming an oil/water nano emulsion and evaporating the solvent. Lipids and drugs dissolve in an organic solvent, emulsified in an aqueous phase, then evaporated to form SLNs. Ideal for heat-sensitive drugs, it ensures stability and precise size control (~100 nm). However, toxic solvents require careful removal, limiting large-scale production despite high encapsulation efficiency and controlled drug release [10].

Solution-Diffusion Method

The solvent emulsification-dispersion technique, introduced in 2003, is used for preparing solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). It employs water-miscible organic solvents like methyl acetate to dissolve lipids and drugs, forming an oil-in-water emulsion. Upon dilution, the solvent diffuses out, causing lipid precipitation. Solvent removal via lyophilization ensures stable, drug-loaded carriers, enhancing encapsulation efficiency and bioavailability for pharmaceutical applications. [10].

Spray Dry

ay-drying is a cost-effective alternative to lyophilization for converting solid lipid nanoparticle (SLN) dispersions into

medicinal products. Though faster, it may cause particle aggregation due to heat and shear forces. Using lipids with a melting point above 70°C and stabilizers like trehalose prevents this. The double emulsion technique, using a water-in-oil-in-water system, protects drugs during solvent evaporation. Both methods offer effective stabilization for sensitive drugs [10].

Solution Injection Method

The solvent injection method, introduced in 2003, is used to prepare solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). Lipids and drugs dissolve in a water-miscible solvent and are rapidly injected into an emulsifier-containing aqueous phase. Solvent diffusion creates small, stable nanoparticles. Optimizing solvent choice, emulsifier concentration, and injection parameters ensures narrow size distribution and stability, making this method ideal for lipid-based drug delivery [10].

Various Types of Carriers for SLNs

SLNs: Carrier for Biological Drug

Biological drugs, including proteins, peptides, and nucleic acids, often face challenges in absorption and target delivery due to their large molecular sizes and complex structures, limiting their bioavailability and therapeutic effects with traditional methods. To address this, advanced drug delivery systems like nanoparticles, liposomes, and dendrimers are needed. These carriers enhance the stability, absorption, and targeting of biological drugs, ensuring they reach their intended sites with improved efficacy, controlled release, and protection from degradation, ultimately enhancing therapeutic outcomes [11].

SLNs as A Gene Vector Carrier

Solid lipid nanoparticles (SLNs) are emerging as promising non-viral gene delivery vectors due to their safety, stability, and efficiency. Unlike viral vectors, SLNs can cross biological barriers with lower toxicity. Cationic SLNs (cSLNs) have shown high transfection efficiency in gene therapy for diseases like hepatic cell carcinoma. Studies highlight SLNs' ability to bind DNA, enhance delivery, and be surface-modified for targeted therapy, making them ideal for gene delivery applications. [12].

Nanostructure Lipid Carrier

Nanostructured lipid carriers (NLCs) improve upon solid lipid nanoparticles (SLNs) by enhancing drug-loading capacity and stability. Combining solid and liquid lipids creates structural imperfections, preventing drug expulsion and allowing higher encapsulation. NLCs offer sustained drug release, reduced storage-related issues, and better therapeutic efficacy. Despite challenges like cytotoxicity and stability concerns, NLCs are a promising drug delivery system with broad pharmaceutical applications [13].

SLNs as Delivery Vehicles Anti-Fungal Agents

Topical drug delivery with solid lipid nanoparticles (SLNs) enhances dermatologic treatments by improving drug bioavailability and reducing systemic side effects. SLNs effectively deliver antifungals like ketoconazole and fluconazole, offering faster treatment for skin infections. Dual-drug SLN systems, such as clotrimazole with alpha-lipoic acid, combat fungal resistance. SLNs also show promise in treating fungal keratitis by delivering econazole directly to the infection site, improving therapeutic outcomes [15].

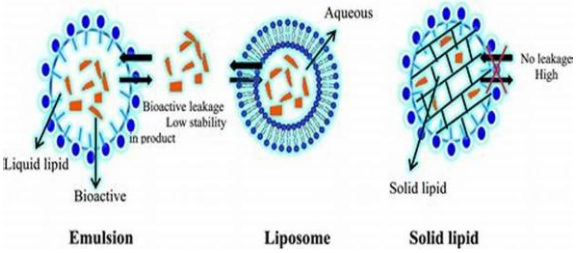

Fig 1: SLNs as Delivery Vehicles Anti-Fungal Agents

Evaluation of SLNs

Particle Size

The physical stability of solid lipid nanoparticles (SLNs) depends on particle size, measured using photon correlation spectroscopy (PCS) and laser diffraction (LD). PCS detects sizes from 3 nm to 3 µm, while LD measures between 100 nm and 180 µm, analyzing light scattering patterns [16].

Zeta Potential

A zeta potential analyzer measures SLN stability by assessing particle charge. SLN dispersions are diluted 50-fold for accuracy. Higher zeta potential prevents aggregation, ensuring stability by enhancing particle repulsion, which reduces the risk of clumping during storage [17].

Surface morphology

Electron microscopy, including SEM and TEM, is used to characterize SLNs. SEM provides 3D images and surface morphology, while TEM reveals shape, size, and internal structure, ensuring accurate analysis of nanoparticle properties [19)].

In Vitro Drug Delivery Release

Drug release from SLNs occurs via diffusion, influenced by formulation factors. SLNs exhibit biphasic release: an initial burst from surface-bound drug, followed by controlled release as the lipid matrix degrades. Techniques like DSC and X-ray diffraction assess lipid crystallization and structural modifications.

Where CrI is the relative degree of crystallinity, I002 is the maximum intensity (in arbitrary units) of the I002 lattice diffraction and lam is the intensity of diffraction in the same units at 28 = 18° [20-21].

Routes of Administration

The SLN technology has made significant advances in the treatment of a wide range of diseases. The encapsulation of

lipophilic and hydrophilic drugs in SLNs reduces their degradation in the body, while also allowing for prolonged strategic drug release. Different types of nanoparticles have been designed for the following applications:

Oral Administration

SLNs can be formulated into oral dosage forms like tablets, capsules, and powders through lyophilization or spray drying.

They enhance drug stability and absorption, protecting compounds like insulin from degradation. SLNs also improve cancer drug delivery, aiding docetaxel and tamoxifen citrate in targeted tumor therapy [22].

Parenteral Administration

Parenteral drug administration is ideal for bioactive compounds with low bioavailability, especially for unconscious patients. Advances in SLNs enable controlled drug release, improving patient adherence and reducing dosing frequency. SLNs enhance peptide drug stability and enable targeted delivery, including doxorubicin, which showed brain-specific distribution when formulated with stealth agents, overcoming oral bioavailability limitations [23].

Pulmonary Administration

Inhalation drug delivery is a non-invasive method that enhances local therapy for airway diseases, bypassing first-pass metabolism and reducing toxicity. A study on pulmonary amikacin-loaded SLNs for cystic fibrosis lung infections showed better kidney safety and longer dosing intervals than intravenous delivery. SLNs also offer alternative administration routes, including ocular and rectal delivery, each with unique advantages for improved drug efficacy and patient adherence [24].

Nasal Route Of Administration

The nasal route is an effective alternative for systemic drug delivery, enhancing absorption and bypassing first-pass metabolism. SLNs improve drug solubility, bioavailability, and blood-brain barrier penetration, making them ideal for CNS diseases like Parkinson's and Alzheimer's. Studies on nasal delivery of bromocriptine, efavirenz, and agomelatine using SLNs show improved bioavailability, offering promising treatments for CNS disorders and HIV [25].

Ocular Route Of Administration

Ocular drug delivery is challenging, but SLNs improve drug penetration, retention, and sustained release without blurring vision. They must meet safety, sterility, and pH requirements. Studies show tobramycin-loaded SLNs enhance drug concentration in the eye, while triamcinolone acetonide-loaded SLNs improve retention and permeability, outperforming commercial formulations for effective ocular treatment [15].

Applications Of Solid Lipid Nanoparticles

Solid Lipid Nanoparticles (SLNs) offer controlled drug release, enhanced bioavailability, and biocompatibility. They are used in drug delivery for oral and topical applications, cancer therapy, antifungal and antiviral treatments, ocular drug delivery, cosmetics, gene therapy, and vaccines. SLNs improve drug stability, targeted delivery, and therapeutic efficacy while reducing toxicity, making them a promising nanocarrier system for various medical and cosmetic applications [12].

Future Perspectives Of SLNs

Solid Lipid Nanoparticles (SLNs) offer a biodegradable, biocompatible drug delivery system capable of carrying both hydrophobic and hydrophilic drugs. They enhance stability, bioavailability, and controlled release, improving treatments while reducing side effects. SLNs show promise in cancer, antiviral, and antifungal therapy. Future advancements in surface modification for targeted delivery and sustained release could revolutionize treatment for chronic diseases, improving patient compliance. As production techniques evolve, SLNs are expected to become more cost-effective and widely accessible, making them a transformative tool in modern pharmacology for safer, more personalized, and efficient therapeutic applications [25].

Conclusion

Solid lipid nanoparticles (SLNs) are promising drug delivery systems that combine the benefits of various colloidal forms, addressing issues like instability and toxicity of traditional nanoparticles. SLNs can be customized with different lipids to control drug release and improve targeting, and they offer stability for long-term use. They can deliver both hydrophilic and lipophilic drugs through multiple routes, including topical, oral, and parenteral administration. SLNs also have potential in imaging and diagnostics, broadening their use in theragnostic. Despite challenges like gelation and degradation, nanostructured lipid carriers (NLCs) are being studied as solutions. With ongoing research, SLNs are expected to play a key role in cancer treatment, providing efficient drug delivery with fewer side effects.

Author Contributions

All authors are contributed equally

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Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

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References

1. Nguyen TT, Duong VA. Solid lipid nanoparticles. Encyclopedia. 2022 May 18;2(2):952-73.
2. Madkhali OA. Perspectives and prospective on solid lipid nanoparticles as drug delivery systems. Molecules. 2022 Feb 24;27(5):1543.
3. Basha SK, Dhandayuthabani R, Muzammil MS, Kumari VS. Solid lipid nanoparticles for oral drug delivery. Materials Today: Proceedings. 2021 Jan 1;36:313-24.
4. Singh Dhakad R, Kumar Tekade R, Kumar Jain N. Cancer targeting potential of folate targeted nanocarrier under comparative influence of tretinoin and dexamethasone. Current Drug Delivery. 2013 Aug 1;10(4):477-91.
5. Phalak SD, Bodke VI, Yadav RE, Pandav SA, Ranaware MA. A systematic review on nano drug delivery system: solid lipid nanoparticles (SLN). International Journal of Current Pharmaceutical Research. 2024;16(1):10-20.
6. Satapathy MK, Yen TL, Jan JS, Tang RD, Wang JY, Taliyan R, Yang CH. Solid lipid nanoparticles (SLNs): an advanced drug delivery system targeting brain through BBB. Pharmaceutics. 2021 Jul 31;13(8):1183.

7. 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.
8. Madkhali OA. Perspectives and prospective on solid lipid nanoparticles as drug delivery systems. Molecules. 2022 Feb 24;27(5):1543.
9. 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.
10. Jahnavi , K. Krishnan , V. Rajashakar , G. S. Burle , K. T. K. Reddy , B. M. Yeruva , G. Dharmamoorthy and O. M. Bagade, "Organometallic Nanoparticulate Delivery: Synthesis, Properties, and Applications," Journal of Applied Organometallic Chemistry, 5 2 (2025): 123-148,
11. Nama S, Chandu BR, Awen BZ, Khagga M. Development and validation of a new RP-HPLC method for the determination of aprepitant in solid dosage forms. Tropical Journal of Pharmaceutical Research. 2011;10(4):491-7.
12. Gindi S, Methra T, Chandu BR, Boyina R, Dasari V. Antiurolithiatic and invitro anti-oxidant activity of leaves of Ageratum conyzoides in rat. World J. Pharm. Pharm. Sci. 2013 Feb 8;2:636-49.
13. Granja A, Lima-Sousa R, Alves CG, de Melo-Diogo D, Nunes C, Sousa CT, Correia IJ, Reis S. Multifunctional targeted solid lipid nanoparticles for combined photothermal therapy and chemotherapy of breast cancer. Biomaterials advances. 2023 Aug 1;151:213443.
14. Burle, G. S., Kakullamarri, P. R., Kothamasu, S. B., Kallam, S. D. M., & Bodapati, A. (2024). Case Study on Regulatory Approaches for New Degradation Impurity Exceeding ICH Thresholds in Solubilized Ibuprofen Capsules During Stability Testing. Journal of International Research in Medical and Pharmaceutical Sciences, 19(3), 70–82
15. Nama S, Chandu BR, Awen BZ, Khagga M. Development and validation of a new RP-HPLC method for the determination of aprepitant in solid dosage forms.Tropical Journal of Pharmaceutical Research. 2011;10(4):491-7.
16. Gindi S, Methra T, Chandu BR, Boyina R, Dasari V. Antiurolithiatic and invitro anti-oxidant activity of leaves of Ageratum conyzoides in rat. World J. Pharm. Pharm. Sci. 2013 Feb 8;2:636-49.
17. Dara SR. An Overview of the Use of Natural Indicators in Acid-Base Titrations. UPI Journal of Pharmaceutical, Medical and Health Sciences. 2024 Jul 23:29-35.
18. Chen YJ, Jin RX, Zhou YQ, Zeng J, Zhang H, Feng QR. Preparation of solid lipid nanoparticles loaded with Xionggui powder-supercritical carbon dioxide fluid extraction and their evaluation in vitro release. Zhongguo Zhong yao za zhi= Zhongguo zhongyao zazhi= China journal of Chinese materia medica. 2006 Mar 1;31(5):376-9.
19. Maiti D, Inamdar MN, Almuqbil M, Suresh S, Asdaq SM, Alshehri S, Al Arfaj SA, Alamri AM, Aldohyan MM, Alqahtani MT, Alosaimi TM. Evaluation of solid-lipid nanoparticles formulation of methotrexate for anti-psoriatic activity. Saudi Pharmaceutical Journal. 2023 Jun 1;31(6):834-44.
20. Carbone C, Cupri S, Leonardi A, Puglisi G, Pignatello R. Lipid-based nanocarriers for drug delivery and targeting: a patent survey of methods of production and characterization. Pharmaceutical patent analyst. 2013 Sep 1;2(5):665-77.
21. Yang S, Zhu J, Lu Y, Liang B, Yang C. Body distribution of camptothecin solid lipid nanoparticles after oral administration. Pharmaceutical research. 1999 May;16:751-7.
22. R. R. Kumar , K. Krishnan , G. S. Burle , P. Samathoti , J. P. Kumar, O. M. Bagade , K. T. K. Reddy and P. Jahnavi, "Biochemical Engineering of Green Nanomaterials for Targeted Drug Delivery and Therapeutic Applications," Journal of Chemical Reviews, 7 2 (2025): 191-215
23. Zhang J, Jiao J, Niu M, Gao X, Zhang G, Yu H, Yang X, Liu L. Ten years of knowledge of nano-carrier based drug delivery systems in ophthalmology: current evidence, challenges, and future prospective. International Journal of Nanomedicine. 2021 Sep 22:6497-530.
24. Jacob S, Nair AB, Shah J, Gupta S, Boddu SH, Sreeharsha N, Joseph A, Shinu P, Morsy MA. Lipid nanoparticles as a promising drug delivery carrier for topical ocular therapy an overview on recent advances. Pharmaceutics 2022; 14 (3): 533 [Internet]. 2022
25. Scioli Montoto S, Muraca G, Ruiz ME. Solid lipid nanoparticles for drug delivery: pharmacological and biopharmaceutical aspects. Frontiers in molecular biosciences. 2020 Oct 30;7:587997.