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ADVANCES IN LIPID NANOPARTICLE-BASED DERMAL DELIVERY: FORMULATION, CHARACTERIZATION, AND THERAPEUTIC APPLICATIONS OF SOLID LIPID NANOPARTICLES AND NANOSTRUCTURED LIPID CARRIERS.

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ABSTRACT

The use of lipid nanoparticles particularly solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have become current tools of promoting the delivery of dermal drugs and cosmetic use. The systems are meant to address the shortcomings of the traditional topical formulations by raising the drug solubility, stability, and penetration through the stratum corneum. SLN which is a type of solid lipids give a rigid structure that controls the release of the drug, but NLC which is a mixture of both solid and water lipid gives an imperfect structure that increases drug loading capacity and the reduction of drug release. Different methods of preparation, such as high-pressure homogenization, microemulsion process, and solvent-based methods allow to create stable and efficient systems of nanoparticles. The intercellular and follicular penetration of the nanoscale size and lipid composition of SLN and NLC leads to better therapeutic effects because of their high ability to adhesively penetrate the skin and be absorbed by the follicles. They have shown a lot of potential in the treatment of dermatological disorders like psoriasis, acne, fungus, and skin cancer, and also find extensive use in cosmetic preparations as anti-aging, sun protection and skin care. The mentioned advantages notwithstanding, the issues of stability, scalability, and regulation standardization can still be observed and require further studies and optimization. In making sure that these nanocarrier systems are safe, effective and reproducible, regulatory and quality control factors are significant. In general, SLN and NLC are potential and universal methods of dermal delivery that overcome the immobilization between conventional formula and the modern age of nanotechnology-based therapeutic formulas.

Key words: Solid lipid nanoparticles, Nanostructured lipid carriers, Dermal drug delivery, Lipid nanocarriers.

INTRODUCTION

The nanocarrier systems based on lipids have become a new breakthrough in the field of dermal drug delivery and cosmetic science as they are innovative strategies to address the shortcomings of the traditional topical formulations. Two of such systems have received much interest, i.e. solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), which are characterized by their special physicochemical,

Biocompatibility and capacity to increase the effectiveness of active compounds used on the skin.

The skin specifically the stratum corneum is a very efficient barrier that limits the penetration of most therapeutic and cosmetic compounds hence limiting bioavailability and clinical efficacy. SLN and NLC have been developed to overcome these difficulties to enhance the penetration, controlled release and targeted delivery of drugs across epidermal and dermal layers. (Viegas C, *et al.*, 2023) SLN consist of solid lipids, and these lipids are in a solid state at both room temperature and body temperature, which offers a rigid matrix, and can be used

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to entrap lipophilic drugs, whereas NLC is a second generation system which consists of a mixture of solid lipids and liquid lipids, which forms a less ordered lipid matrix and is able to entrap more drugs. These lipid nanoparticles do not only enhance the stability of sensitive ingredients, like vitamins, antioxidants and peptides, but provide occlusive effects that enhance skin hydration and deeper penetration. Moreover, they have a nanoscale size that permits the proximity to the skin surface, which enhances residence time and diffusion via intercellular lipid routes. (Chutoprapat R, *et al.*, 2022) SLN and NLC are also commonly used in anti-aging formulations, sunscreens and moisturizing products in the cosmetic sector and in the pharmaceutical sector, find application in the management of a wide range of skin disorders, such as psoriasis, acne, fungal infections and inflammatory conditions. The fact that they are less damaging to the system and enhance the localized drug action is very beneficial to them in dermal therapy. With the ongoing development of research, lipid nanoparticles are gaining popularity as convenient and useful vehicles that can fill the divide between conventional topical preparations and high-technology nanotechnology-based delivery vehicles, ushering in the next generation of dermal therapeutics and cosmeceuticals. (Prajapati A *et al.*, 2024)

Composition and Structural Characteristics of SLN and NLC

The composition and the structure of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are crucial in defining their ability to perform as dermal delivery systems. Usually SLN consist of the physiologically compatible solid lipids e.g. triglycerides (e.g. tristearin), fatty acids (e.g. stearic acid), waxes and mixtures of glycerides that stay solid at room temperature and body temperature. Surfactants or emulsifiers, including polysorbates (Tween) poloxamers, lecithin or bile salts, stabilize these lipids, lowering interfacial tension and inhibiting aggregation of the particles. SLN are structurally well-organized crystalline lattices which confer rigidity and encapsulate drugs, but could limit drug loading and cause expulsion of the drug during storage because of lipid polymorphic changes. (Tiwari A, *et al.*, 2023) To address these shortcomings, Second generation lipid nanoparticles, NLC, came into existence using a mixture of both solid and liquid lipids (oils) including medium-chain triglycerides, oleic acid, or isopropyl myristate. This mixture forms an imperfect and less ordered lipid matrix containing structural defects that increase the accommodation of the drugs and decrease the likelihood of drug expulsion. On the basis of their internal arrangement, NLC can be categorized into three, i.e., imperfect type, amorphous type and multiple (oil-in-fat-in-water) type each with a particular advantage in terms of drug loading and release behavior. Nanoscale

size of SLN and NLC (usually 50-1000 nm) gives large surface area contributing to the close contacts with the skin and improved penetration. (Souto EB, *et al.*, 2020) Also, their lipidic environment resembles the stratum corneum composition, which enhances biocompatibility and affinity with the skin. Dispersant stability also depends on the presence of surfactants, particle size, stability, and zeta potential, among which, is important to ensure the stability of dispersion. Altogether, the personalized structure and individual peculiarities of SLN and NLC make them effective versatile carriers to be used in the context of the dermal and transdermal drug delivery applications. (Dobrev M, *et al.*, 2020)

Methods of Preparation and Formulation Techniques

Different methods have been developed in the preparation and formulation of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) to develop stable nanoscale systems with ideal drug loading and release properties. High-pressure homogenization (HPH) is one of the most commonly used procedures, which can be carried out either in hot or cold; in hot homogenization, the lipid phase is melted and homogenized in a hot aqueous surfactant solution and then subjected to high-pressure processing, but cold homogenization is suitable with thermolabile compounds because the drug-lipid mixture is solidified and then milled and homogenized at room temperature or below. Microemulsion-based methods are also widely used, in which a warm microemulsion of the combination of melted lipids, surfactants, co-surfactants, and water is dispersed in cold water to cause the precipitation of nanoparticles. (Queiroz MDCV & Muehlmann LA, 2024) Other methods can be applied such as solvent emulsification-evaporation and solvent diffusion methods which are useful especially in incorporating lipophilic and moderately hydrophilic drugs where organic solvents are applied to dissolve lipid phase before the emulsification and afterward removal of the solvent. Further reduction in particle size and enhancement of uniformity can be achieved by ultrasonication or high speed stirring but in some cases these techniques can lead to broader size distributions. Also, large scale production and enhanced stability have been suggested using supercritical fluid technology and spray drying. The formulation materials, which include solid, liquid lipids, surfactants, and co-surfactants play a major role in affecting the physicochemical characteristics, such as particle size, polydispersity index, zeta potential and the encapsulation efficiency. (Hernández-Giottonini KY *et al.*, 2020) Process parameters should be optimized such as temperature, pressure, homogenization cycles, and cooling rate in order to have reproducible and stable formulations. Moreover, to augment the performance and shelf-life of SLN and NLC systems, addition of functional additives (penetration enhancers, antioxidants,

or preservatives) can be used. In general, lipid nanoparticles can be tailored to individual needs of dermal and transdermal drug delivery systems due to the range of available preparation techniques. (Talele P, *et al.*, 2025)

Mechanisms of Skin Penetration and Drug Release

The mechanisms of skin penetration and drug release from solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are governed by their nanoscale size, lipid composition, and interaction with the skin's barrier structure, particularly the stratum corneum. These lipid nanoparticles enhance dermal delivery primarily through three pathways: intercellular, transcellular, and follicular routes. Due to their small particle size and large surface area, SLN and NLC form a close adhesive film on the skin surface, increasing residence time and promoting drug diffusion. One of the key mechanisms is the occlusive effect, wherein the lipid nanoparticles create a thin hydrophobic layer that reduces transepidermal water loss (TEWL), leading to increased skin hydration. (Munir M, *et al.*, 2023) This hydration causes swelling of the stratum corneum, thereby loosening its tightly packed lipid structure and facilitating enhanced drug penetration through intercellular pathways. Additionally, the lipid composition of SLN and NLC closely resembles the natural lipids of the skin, allowing them to integrate into the stratum corneum and disrupt its barrier function in a controlled manner, further enhancing permeability. The presence of surfactants and penetration enhancers in the formulation can also fluidize the lipid bilayers, improving drug transport across the skin. Drug release from SLN is typically characterized by a biphasic pattern, with an initial burst release due to drug present on or near the particle surface, followed by a sustained release from the solid lipid matrix. In contrast, NLC, owing to their less ordered and imperfect lipid matrix, provide higher drug loading and more controlled and prolonged release profiles, minimizing drug expulsion during storage. Furthermore, follicular targeting plays a significant role, as nanoparticles can accumulate in hair follicles and sebaceous glands, acting as drug reservoirs for prolonged release. Overall, SLN and NLC facilitate enhanced dermal penetration and controlled drug delivery through a combination of occlusion, lipid interaction, nanoscale effects, and

targeted follicular deposition, making them highly effective carriers for topical and transdermal applications.

Advantages of SLN and NLC in Dermal Applications

Nanostructured lipid carriers (NLC) and solid lipid nanoparticles (SLN) have a lot of potential in dermal delivery due to the benefits that they have. Their great biocompatibility and biodegradability due to their physiological lipids composition, which is generally considered as safe (GRAS) is one of the major advantages since the risks of irritation and toxicity are limited when used topically. Their small size of nanoparticles allows an intimate contact with the stratum corneum, increasing adhesion on the skin surface and drug penetration. One of their major strengths is their high occlusive properties that minimise transepidermal water loss (TEWL) and enhance skin hydration resulting in enhanced permeability of active compounds. Controlled and sustained drug release is also offered by SLN and NLC, and helps to maintain the therapeutic drug levels during a longer period, decreases the dosing schedule, and improves patient compliance. (Tang Q, *et al.*, 2023) Besides, these systems can inhibit the decomposition of sensitive active ingredients like antioxidants, vitamins, peptides as well as drugs that are not stable to light, oxidation or environmental factors. The NLC in this case, have increased drug loading capacity and decreasing drug expulsion during storage, because they have lower ordered lipid matrix than SLN. The other important benefit is that they can deliver drugs to particular layers of skin, such as the hair follicle and sebaceous glands, which is especially useful when it comes to local skin disorders like acne and alopecia. SLN and NLC can also be used to increase the solubility of poorly water-soluble drugs and hence increase their bioavailability. Formulation wise, incorporation of these lipid nanoparticles into different dermal dosage forms, which include creams, gels, lotions and sprays, is simple and hence offers flexibility in the development of products. (Eroğlu C, *et al.*, 2023) Their non-greasy property, better skin touch and increased beauty appeal adds to their acceptability in cosmetic use. In general, the improved delivery system, stability, safety, and friendliness to patients make SLN and NLC the best replacement of traditional topical formulations.

Table 1: Composition and Structural Differences between SLN and NLC

Parameter	Solid Lipid Nanoparticles (SLN)	Nanostructured Lipid Carriers (NLC)
Lipid Composition	Only solid lipids (e.g., triglycerides, stearic acid, waxes)	Mixture of solid and liquid lipids (e.g., oils like oleic acid)
Structural Arrangement	Highly ordered crystalline matrix	Imperfect, less ordered matrix with structural defects
Drug Loading Capacity	Limited due to tight crystal packing	Higher due to imperfect structure
Drug Expulsion	Possible during storage (polymorphic)	Reduced risk of drug expulsion

	transition)	
Types	Homogeneous matrix	Imperfect, amorphous, multiple types
Stability	Moderate (affected by crystallization)	Improved stability
Flexibility in Formulation	Limited	High flexibility
Suitability	Best for lipophilic drugs	Suitable for both lipophilic and moderately hydrophilic drugs

Tables 2: Methods of Preparation of SLN and NLC

Method	Principle	Advantages	Limitations
High-Pressure Homogenization (HPH)	Lipid phase homogenized under high pressure (hot/cold methods)	Scalable, reproducible, no organic solvents	High energy input, not ideal for heat-sensitive drugs (hot method)
Microemulsion Technique	Formation of warm microemulsion followed by dispersion in cold water	Simple, uniform particle size	Requires high surfactant concentration
Solvent Emulsification-Evaporation	Lipid dissolved in organic solvent, emulsified, then solvent removed	Good for thermolabile drugs	Residual solvent concerns
Solvent Diffusion Method	Diffusion of solvent into aqueous phase leads to nanoparticle formation	Mild conditions	Requires solvent handling
Ultrasonication/High-Speed Stirring	Mechanical size reduction using shear forces	Simple, cost-effective	Broad size distribution
Supercritical Fluid Method	Use of supercritical CO ₂ for particle formation	Solvent-free, eco-friendly	Expensive equipment
Spray Drying	Conversion into dry powder form	Improved stability, storage	Thermal stress possible

**Figure1: Advantages of SLN and NLC in Dermal Applications**

Pharmaceutical Applications: Treatment of Skin Disorders and Drug Delivery

Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have demonstrated significant potential in pharmaceutical applications for the treatment of various skin disorders and enhancement of dermal drug delivery. These lipid-based nanocarriers enable targeted and controlled delivery of therapeutic agents to specific layers of the skin, thereby improving treatment efficacy while minimizing systemic side effects. In inflammatory skin conditions such as psoriasis, dermatitis, and eczema, SLN and NLC facilitate sustained release of anti-inflammatory drugs like corticosteroids and immunomodulators, reducing dosing frequency and improving patient compliance (Fathi F, *et al.*, 2024). In acne management, these carriers enhance the penetration of antibacterial and keratolytic agents such as retinoids and antibiotics into hair follicles and sebaceous glands, which are the primary sites of infection and inflammation. Similarly, in fungal infections, lipid nanoparticles improve the solubility and skin retention of antifungal drugs, thereby enhancing therapeutic outcomes. SLN and NLC are also extensively explored for the delivery of anticancer agents in skin cancers, where they enable localized targeting, reduce drug toxicity, and enhance drug stability. Furthermore, these systems are used in transdermal drug delivery for systemic therapy, allowing drugs to bypass hepatic first-pass metabolism and maintain consistent plasma drug levels. Their ability to encapsulate both lipophilic and hydrophilic drugs broadens their application spectrum. In wound healing and burn management, SLN and NLC formulations promote tissue regeneration by delivering bioactive molecules such as growth factors, antioxidants, and antimicrobial agents directly to the affected site. Additionally, they protect labile drugs from degradation and enhance their bioavailability. The follicular targeting capability of these nanoparticles further supports their use in conditions like alopecia. Overall, SLN and NLC represent versatile and efficient carriers in modern dermatological therapy, offering improved drug delivery, enhanced therapeutic efficacy, reduced adverse effects, and better patient adherence compared to conventional topical formulations. (Araujo VHS, *et al.*, 2020)

Stability, Safety, and Toxicological Considerations

The stability, safety and toxicological characteristics of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are key parameters that define their appropriateness as dermal and transdermal delivery systems. The aspects of physicochemical stability of these lipid nanoparticles are determined by the size of the particle, polydispersity index, zeta potential, lipid crystallinity, and storage conditions. The highly ordered nature of crystalline structure of SLN can allow this polymorphic transition in

the storage of the product which results to drug expulsion as well as reduction in the loading capacity of the product, but NLC with their less ordered structure will show better stability as well as less likelihood of drug leakage. The decision on the type of lipids and surfactants is a key factor in the stability of dispersion as well as the dispersion prevention of aggregation or coalescence of particles. Regarding safety, SLN and NLC are typically said to be biocompatible and non-toxic since they are done with physiological lipids and the commonly accepted excipients that are usually known to be safe in topical application. (Madkhali OA, *et al.*, 2022) they are not highly irritating and can be used to improve the hydration of the skin when well-formulated, as they are the occlusives. Nevertheless, toxicological factors also need to take into account the possibility of skin irritation, sensitization, and long-term exposure symptoms, in particular, in case the high doses of surfactants or penetration enhancers are applied. (Mura P, *et al.*, 2021) The size of these carriers on the nanoscale is also subject to question as to how they interact with skin cells and have a potential to penetrate deeper tissues and thus requires close consideration in regards to in vitro and in vivo studies. Moreover, lipid degradation can be oxidized, which may impact stability and safety and hence the use of antioxidants in the formulation design is essential. Toxicological evaluations, such as cytotoxicity, dermal irritation, sensitization tests, and others, are mandatory as required by regulatory agencies to confirm the safety of products. In general, although SLN and NLC have positive safety profile and enhanced stability in contrast to traditional systems, intensive characterization and optimization are necessary in order to reduce risks and assure consistent performance in dermal applications.

Comparison Between SLN and NLC Systems

The stability, safety and toxicological characteristics of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are key parameters that define their appropriateness as dermal and transdermal delivery systems. The aspects of physicochemical stability of these lipid nanoparticles are determined by the size of the particle, polydispersity index, zeta potential, lipid crystallinity, and storage conditions. The highly ordered nature of crystalline structure of SLN can allow this polymorphic transition in the storage of the product which results to drug expulsion as well as reduction in the loading capacity of the product, but NLC with their less ordered structure will show better stability as well as less likelihood of drug leakage. (Chauhan I, *et al.*, 2020) The decision on the type of lipids and surfactants is a key factor in the stability of dispersion as well as the dispersion prevention of aggregation or coalescence of particles. Regarding

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Challenges and Limitations in Dermal Formulations

Despite their promising advantages, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) face several challenges and limitations in dermal formulation development that must be carefully addressed to ensure optimal performance. One of the primary limitations of SLN is their highly ordered crystalline structure, which can lead to low drug loading capacity and drug expulsion during storage due to lipid polymorphic transitions. Although NLC were developed to overcome this issue, they may still exhibit formulation complexity and variability depending on the ratio of solid to liquid lipids. Another significant challenge is the physical instability of nanoparticle dispersions, including aggregation, gelation, and particle growth over time, which can affect product consistency and efficacy. The selection and concentration of surfactants are critical, as excessive amounts may cause skin irritation or toxicity, while insufficient levels can compromise stability. Scale-up and manufacturing reproducibility also present challenges, particularly in maintaining uniform particle size distribution and encapsulation efficiency during large-scale production. Additionally, the high cost of specialized equipment such as high-pressure homogenizers and the need for stringent process control can limit industrial applicability. From a dermal delivery perspective, variability in skin permeability among individuals, as well as differences in skin condition, age,

and disease state, can influence the performance of SLN and NLC formulations. Furthermore, limited penetration into deeper skin layers may restrict their effectiveness for certain therapeutic targets requiring systemic delivery.

(Doustvaghe YK, *et al.*, 2024) Stability issues such as lipid oxidation and hydrolysis can further compromise product shelf-life, necessitating the inclusion of stabilizers and antioxidants. Regulatory challenges also exist due to the evolving guidelines for nanotechnology-based products, requiring extensive characterization and safety evaluation. Overall, while SLN and NLC offer significant potential, overcoming these formulation, stability, scalability, and regulatory challenges is essential for their successful translation into commercial dermal products.

Regulatory Aspects and Quality Control Requirements

Quality control regulations and solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in dermal preparations are of high importance in order to be safe, efficacious and even homogenous, especially as they belong to the category of dermal preparations that are classified under nanotechnology-based drug delivery systems. The regulatory frameworks of such products are regulated by bodies like the US Food and Drug Administration (FDA), European Medicines Agency (EMA) and other regional authorities which prioritize a risk-based approach to the nanomaterials. (Sha'At F, *et al.*, 2025) Based on the fact that no harmonized guidelines have been established that are specifically dedicated to SLN and NLC, those systems are assessed in the context of the implemented pharmaceutical and cosmetic regulations, with the guidance documents serving as the supplementary means of the nanotechnology. Regulatory evaluation is dedicated to the extensive characterization of the nanocarriers such as the size distribution of the particles, polydispersity index, zeta potential, morphology, surface properties, and drug loading efficiency because these parameters affect the product performances and safety significantly. Quality control testing can be also used to test the physical and chemical stability such as lipid crystallinity, polymorphic transitions and possible expulsion of drugs during storage. (Pérez-Moreno AM, *et al.*, 2024) To prove functionality in dermal applications, in vitro release experiments, permeation experiments with appropriate skin models, as well as evaluation of occlusive characteristics are required. Also, topical products should be provided with microbiological quality, preservatives efficacy, and contaminants absence. Safety wise, toxicological testing is required and carries with it studies on dermal irritation, sensitization, cytotoxicity, phototoxicity, and risks of long-term exposure. (Nasiri F, *et al.*, 2020) The possibility of nanoparticle entry into the systemic circulation and

contact with skin cells should also be strictly evaluated with the help of approved experimental models. Another requirement is Good Manufacturing Practice (GMP) compliance, which ensures reproducibility, scalability and batch-to-batch consistency, especially when producing in large scale. Characterization and quality control is usually done by the use of analytical methods, including dynamic light scattering (DLS), electron microscopy, differential scanning calorimetry (DSC), and high-performance liquid chromatography (HPLC). Moreover, regulatory submissions should also provide specific information regarding formulation composition, manufacturing processes, control strategies and stability data as required by International Council for harmonisation (ICH) guidelines (Venkatesan KB, *et al.*, 2025). The labeling requirements might also have to reveal the existence of nanomaterials, especially in cosmetic products. In general, strict regulatory controls and sound quality control mechanisms are inevitable in the safe and effective developmental, approval, and commercialization of SLN-based and NLC-based dermal formulations.

CONCLUSION

The nanoparticle-derived systems, specifically, the solid lipid nanoparticles (SLN), and nanostructured lipid carriers (NLC) have become a groundbreaking technology in the area of dermal drug delivery, which provides a versatile, efficient, and biocompatible medium of pharmaceutical and cosmetic usage. These nanocarriers overcome the innate constraint of traditional topical formulations particularly the stratum corneum barrier function by facilitating drug penetration, enhancing bioavailability and controlled release and sustained release of active compounds. These properties

of SLN and NLC are unique in terms of their structure and their capacity to entrap a variety of therapeutic factors, which has made them useful in numerous treatment of skin diseases, both inflammatory and infectious as well as cancers confined to a specific region. In addition, their occlusive nature and skin-compatible lipid profile increase hydration and increase the rate of interaction with the skin, which also improves the therapeutic effect. Although these benefits are possessed, there are still a number of challenges such as the formulation stability, expulsion of the drug, mass production and standardization of regulations. The control of particle size, the lipid composition, and the production parameters must be done with a high degree of accuracy to guarantee performance consistency and safety. Also, there should be a complete assessment of the clinical and business viability of such nanocarriers by long term toxicological assessment and standardized regulatory systems. The future of SLN and NLC is likely to be expanded by the introduction of new formulation strategies that may involve the use of functional lipids, ligand-targeting, and hybrid systems. In future dermatological treatment, emerging technologies, including stimuli responsive systems and customized nanomedicine applications can also increase their context. In general, SLN and NLC can be viewed as a major step forward into the dermal delivery system, which comes between the conventional topical formulations and those developed based on nanotechnology. These lipid nanoparticles have enormous potential to revolutionize the history of skin-targeted drug delivery and cosmeceutical development with further research, optimization and regulatory alignment and eventually resulting in effective, safer, and more patient friendly forms of treatment.

REFERENCES

- Araujo VHS, Delello Di Filippo L, Duarte JL, Spósito L, Camargo BAFD, Da Silva PB, Exploiting solid lipid nanoparticles and nanostructured lipid carriers for drug delivery against cutaneous fungal infections. *Critical Reviews in Microbiology* 2020; 47: 79–90.
- Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. *Adv Pharm Bull* 2020; 10: 150–165.
- Chutoprapat R, Kopongpanich P, Chan LW. 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.
- Dobrev M, Stefanov S, Andonova V. Natural Lipids as Structural Components of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers for Topical Delivery. *CPD* 2020; 26: 4524–4535.
- Doustvaghe YK, Haeri A, Sisakht MM, Amirkhani MA, Vatanpour H. Recombinant human epidermal growth factor-loaded liposomes and transferosomes for dermal delivery: Development, characterization, and cytotoxicity evaluation. *Drug Development Research* 2024; 85.
- Eroğlu C, Sinani G, Ulker Z. Current State of Lipid Nanoparticles (SLN and NLC) for Skin Applications. *CPD* 2023; 29: 1632–1644.
- Fathi F, Machado TOX, De A C Kodel H, Portugal I, Ferreira IO, Zielinska A, et al. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for the delivery of bioactives sourced from plants: part I – composition and production methods. *Expert Opinion on Drug Delivery* 2024; 21: 1479–1490.

- Hernández-Giottonini KY, Rodríguez-Córdova RJ, Gutiérrez-Valenzuela CA, Peñuñuri-Miranda O, Zavala-Rivera P, Guerrero-Germán P, PLGA nanoparticle preparations by emulsification and nanoprecipitation techniques: effects of formulation parameters. *RSC Adv* 2020; 10: 4218–4231.
- Madkhali OA. Perspectives and Prospective on Solid Lipid Nanoparticles as Drug Delivery Systems. *Molecules* 2022; 27: 1543.
- Munir M, Zaman M, Waqar MA, Khan MA, Alvi MN. Solid lipid nanoparticles: a versatile approach for controlled release and targeted drug delivery. *Journal of Liposome Research* 2023; 34: 335–348.
- Mura P, Maestrelli F, D'Ambrosio M, Luceri C, Cirri M. Evaluation and Comparison of Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) as Vectors to Develop Hydrochlorothiazide Effective and Safe Pediatric Oral Liquid Formulations. *Pharmaceutics* 2021; 13: 437.
- Nasiri F, Faghfoury L, Hamidi M. Preparation, optimization, and in-vitro characterization of α -tocopherol-loaded solid lipid nanoparticles (SLNs). *Drug Development and Industrial Pharmacy* 2020; 46: 159–171.
- Patel D, Patel B, Thakkar H. Lipid Based Nanocarriers: Promising Drug Delivery System for Topical Application. *Euro J Lipid Sci&Tech* 2021;123: 2000264.
- Pérez-Moreno AM, Aranda CJ, Torres MJ, Mayorga C, Paris JL. Immunomodulatory potential of rapamycin-loaded mesoporous silica nanoparticles: pore size-dependent drug loading, release, and in vitro cellular responses. *Drug Deliv and Transl Res* 2024; 14: 3467–3476.
- Prajapati A, Kumar D. A Comprehensive Review of the Use of Nanoparticles in Cosmeceutical Science. *JOPIR* 2024; 2: 030–037.
- Queiroz MDCV, Muehlmann LA. Characteristics and Preparation of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers. *JNT* 2024; 5: 188–211.
- Sha'At F, Miu D, Eremia MC, Neagu G, Albulescu A, Albulescu R, Fabrication and Evaluation of Polyhydroxyalkanoate-Based Nanoparticles for Curcumin Delivery in Biomedical Applications. *Molecules* 2025; 30: 1216.
- Souto EB, Baldim I, Oliveira WP, Rao R, Yadav N, Gama FM, SLN and NLC for topical, dermal, and transdermal drug delivery. *Expert Opinion on Drug Delivery* 2020; 357–377.
- Talele P, Jadhav A, Sahu S, Shimpi N. Experimental approaches to evaluate solid lipid nanoparticle-based drug delivery systems. *Anal Methods* 2025; 17: 1451–1466.
- Tang Q, Xu F, Wei X, Gu J, Qiao P, Zhu X, et al. Investigation of β -caryophyllene as terpene penetration enhancer: Role of stratum corneum retention. *European Journal of Pharmaceutical Sciences* 2023; 183: 106401.
- Tiwari A, Palaria B, Tiwari V, Aslam R, Kumar A, Sahoo BM,. Nanostructured Lipid Carriers: A Promising Carrier in Targeted Drug Delivery System. *CNM* 2023; 8: 23–43.
- Venkatesan KB, Alamelu S, Srinivasan MK, Pachaiappan P. Nerolidol loaded beta cyclodextrin nanoparticles: a promising strategy for inducing apoptosis in breast cancer cells (MCF-7). *Journal of Biomaterials Science, Polymer Edition* 2025; 36: 2021–2051.
- Viegas C, Patrício AB, Prata JM, Nadhman A, Chintamaneni PK, Fonte P. Solid Lipid Nanoparticles vs. Nanostructured Lipid Carriers: A Comparative Review. *Pharmaceutics* 2023; 15: 1593.