

MINI-REVIEW

Solid lipid nanoparticles in wound healing:
Mechanistic insights, therapeutic applications,
and translational challengesMaisrh Ali Alrubaye^{1*} and Tha'er Ata^{2*} ¹Pharmacological and Diagnostic Research Center, Faculty of Pharmacy, Al-Ahliyya Amman University, Amman, Jordan²Department of Pharmacy, College of Pharmacy, Amman Arab University, Amman, Jordan

Abstract

Wound healing remains a therapeutic challenge, particularly in chronic and infected wounds, where poor local drug retention, persistent inflammation, oxidative stress, microbial burden, and delayed tissue regeneration reduce the effectiveness of conventional treatments. Solid lipid nanoparticles (SLNs) have emerged as promising lipid-based nanocarriers for topical wound therapy because they combine biocompatibility, protection of labile therapeutic agents, improved local retention, and sustained drug release. This mini-review critically discusses the role of SLNs in modern wound-healing strategies, with emphasis on formulation design, physicochemical properties, mechanisms of action, therapeutic applications, and translational challenges. A narrative literature search was conducted using PubMed, Scopus, and Web of Science to identify relevant studies on SLN preparation methods, wound-healing mechanisms, topical delivery, safety, and clinical translation. SLNs may enhance wound repair through several interconnected mechanisms, including improved wound-bed retention, controlled drug release, interaction with skin and wound barriers, modulation of inflammatory and oxidative pathways, antimicrobial effects, cellular uptake, fibroblast activation, collagen deposition, angiogenesis, and re-epithelialization. Compared with liposomes and polymeric nanoparticles, SLNs offer a practical balance between biocompatibility, physical stability, controlled release, scalability, and cost-effectiveness. However, their clinical translation is still limited by restricted drug loading, lipid polymorphism, formulation instability, sterilization challenges, batch-to-batch variability, and insufficient clinical evidence. Future SLN-based wound therapies may benefit from stimuli-responsive release, artificial intelligence-assisted formulation optimization, personalized wound care, multifunctional theranostic systems, and combination therapy approaches. Nevertheless, standardized evaluation methods, long-term safety studies, scalable manufacturing, and well-designed clinical investigations are required to advance SLNs from experimental wound-healing systems toward clinically applicable products.

Keywords: Advanced drug delivery systems; Nanocarriers; Solid lipid nanoparticles; Topical wound therapy; Wound healing

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1. Introduction

Wound healing is a complex, multistep physiological process that involves hemostasis, inflammation, proliferation, and tissue remodeling.¹ While conventional therapies such as topical antimicrobials and dressings remain central to clinical management, they often fall short in achieving optimal healing—especially in chronic and severe wounds.² Limitations, including poor drug retention, insufficient tissue regeneration, and the rise of antimicrobial resistance, underscore the need for advanced therapeutic strategies.³

Nanotechnology offers a promising paradigm shift in wound care by enabling localized, sustained drug delivery with enhanced bioavailability.⁴ Among various nanosystems, solid lipid nanoparticles (SLNs) have gained significant attention due to their biocompatibility, ability to encapsulate both hydrophilic and lipophilic agents, and their potential for controlled drug release.⁵ SLNs, composed of physiologically tolerated lipids, present an innovative solution to many of the limitations associated with traditional therapies and other nanocarriers.⁶

Although several recent reviews have discussed lipid-based nanoparticles or nanoparticle-based approaches for wound healing, the present mini-review provides a focused discussion of SLNs within this field. Rather than presenting SLNs merely as passive topical drug carriers, this mini-review links their formulation-related characteristics with wound-healing mechanisms and translational considerations. Specifically, this mini-review discusses how SLN design factors, including lipid composition, particle size, surfactant selection, surface charge, drug loading, and incorporation into topical platforms, are related to wound-bed retention, barrier interaction, controlled release, inflammatory and oxidative modulation, cellular uptake, angiogenesis, collagen deposition, and re-epithelialization. Therefore, the mini-review aims to provide an integrated formulation–mechanism–translation perspective on SLNs in wound healing, while also acknowledging remaining challenges related to comparison with other lipid nanocarriers, clinical evidence, scalability, regulatory requirements, and commercialization.

2. Literature search strategy

2.1. Databases searched

A narrative literature search was conducted using major scientific databases, including PubMed, Scopus, and Web of Science. These databases were selected to ensure broad coverage of biomedical, pharmaceutical, and nanomedicine-related literature.

2.2. Search keywords

The search strategy included combinations of the following keywords: “solid lipid nanoparticles,” “SLNs,” “lipid nanoparticles,” “wound healing,” “chronic wounds,” “topical drug delivery,” “skin regeneration,” “infected wounds,” “nanocarriers,” and “controlled drug release.” Boolean operators such as AND and OR were used to combine relevant terms and refine the search results.

2.3. Publication timeframe

Priority was given to peer-reviewed English-language articles published within the last five years to ensure the inclusion of recent advances in SLN-based wound therapy. Selected older articles were also included when they provided essential background information on SLN formulation, preparation methods, physicochemical characterization, or wound-healing mechanisms.

2.4. Inclusion criteria

Studies were included if they discussed at least one of the following aspects: SLN preparation methods, lipid-based nanocarrier characterization, topical or wound-healing applications, drug release behavior, antimicrobial activity, anti-inflammatory effects, safety considerations, or translational challenges related to wound therapy.

2.5. Exclusion criteria

Articles were excluded if they were not directly related to SLNs, wound healing, topical drug delivery, or nanomedicine-based tissue repair. Non-peer-reviewed articles, unrelated studies, and articles with limited relevance to SLN-based wound-healing applications were also excluded.

3. Background and challenges of wound healing

3.1. Limitations of conventional therapies

Conventional wound care therapies, although essential in clinical practice, have significant drawbacks that hamper recovery. Many therapeutic drugs show poor wound-bed penetration, rapid degradation, and low target-site retention—often resulting in subtherapeutic levels during critical healing phases. Overuse of systemic antibiotics has further led to resistant bacterial strains, complicating infection control. Moreover, traditional treatments frequently fall short in providing sufficient tissue regeneration support, particularly in chronic or severe wounds characterized by diminished cellular responses and limited angiogenic activity.⁷

3.2. Need for advanced delivery systems

The limitations of traditional therapies underscore the need for innovative delivery technologies. Advanced systems—especially those leveraging nanotechnology—can enable controlled local delivery of therapeutic agents. These systems overcome issues of drug stability and bioavailability by maintaining effective concentrations essential for tissue regeneration while reducing systemic side effects.⁸

4. Nanotechnology approaches in wound healing

4.1. Nanoparticle-based drug delivery

Nanoparticle-based drug delivery systems offer precise spatial and temporal distribution of active substances, effectively revolutionizing treatment methods. Various nanoparticles have been investigated for wound healing applications, including:

- **Liposomes:** Spherical vesicles with phospholipid bilayers that encapsulate hydrophilic or hydrophobic drugs. Their biocompatibility and ability to merge with cellular membranes enhance medication absorption

and reduce systemic toxicity.⁹

- **Polymeric nanoparticles:** Constructed from biodegradable polymers, these nanoparticles can be customized in terms of particle size, surface charge, and degradation rate, allowing for controlled release of therapeutic agents.¹⁰
- **SLNs:** Combining the advantages of liposomes and polymeric systems, SLNs are formulated with biocompatible lipids that remain solid at physiological temperatures. Their unique matrix stabilizes drugs, controls release, and protects labile compounds.¹¹
- **Other nanocarriers:** Systems such as dendrimers, micelles, and nanogels offer varying payload capacities, targeting capabilities, and release patterns, providing a diverse platform for wound healing applications.¹²

Although liposomes, polymeric nanoparticles, and SLNs have all been explored for wound-healing applications, their clinical relevance depends on differences in stability, drug loading, release behavior, toxicity, scalability, and cost-effectiveness. Table 1 summarizes the main comparative features of these systems and highlights why SLNs may represent a practical compromise between biocompatibility, sustained release, and formulation scalability.^{10,11,13-15}

Table 1. Comparative evaluation of SLNs, NLCs, liposomes, and polymeric nanoparticles for wound-healing applications

Parameter	SLNs	NLCs	Liposomes	Polymeric nanoparticles
Basic structure	Solid lipid matrix stabilized by surfactants	Solid lipid and liquid lipid blend stabilized by surfactants	Phospholipid bilayer vesicles with an aqueous core	Biodegradable or synthetic polymeric matrix
Drug-loading suitability	Suitable mainly for lipophilic drugs; hydrophilic loading may be limited	Generally improved loading due to the less ordered lipid matrix	Can load hydrophilic and lipophilic drugs, but leakage may occur	Flexible loading depending on polymer type and drug-polymer interaction
Stability	Higher physical stability than liposomes, but affected by lipid polymorphism and drug expulsion	Improved stability and reduced drug expulsion compared with SLNs	Lower stability due to vesicle fusion, oxidation, and drug leakage	Generally stable, but may be affected by polymer degradation and aggregation
Skin/wound retention	Good local retention due to lipidic nature and nanoscale size	Good topical retention, especially when incorporated into gels or dressings	Moderate retention; may interact with biological membranes	Variable depending on particle size, charge, and polymer composition
Controlled release	Sustained release through solid lipid matrix	Sustained or more flexible release depending on the solid/liquid lipid ratio	Often faster release unless modified	Sustained release through polymer degradation or diffusion

(Cont'd...)

Table 1. (Continued)

Parameter	SLNs	NLCs	Liposomes	Polymeric nanoparticles
Biocompatibility	High, due to physiological or well-tolerated lipids	High, depending on lipid and surfactant composition	High, due to phospholipid composition	Depends on polymer type and degradation products
Toxicity concerns	Generally low, but surfactant type and concentration are important	Generally low, but formulation complexity may affect tolerability	Oxidation products and instability may affect safety	Possible irritation or toxicity from synthetic polymers, residual solvents, or acidic degradation products
Scalability	Relatively scalable using high-pressure homogenization and related methods	Scalable, but requires optimization of solid/liquid lipid composition	More challenging due to stability and sterilization issues	Scalable, but process complexity varies by polymer and preparation method
Cost-effectiveness	Potentially cost-effective due to simple lipid excipients and scalable methods	Variable; may be higher due to more complex lipid composition	Often higher due to phospholipids and stability requirements	Variable depending on polymer grade and manufacturing process
Main wound-healing advantage	Combines drug protection, sustained release, local retention, and lipid-based biocompatibility	Improved drug loading and reduced crystallinity-related drug expulsion	Excellent biocompatibility and membrane interaction	Strong formulation flexibility and tunable release
Main limitation	Limited drug loading and possible lipid polymorphic transition	More complex formulation optimization than SLNs	Poor long-term stability and drug leakage	Polymer-related toxicity, degradation concerns, and manufacturing complexity

Abbreviations: NLCs: Nanostructured lipid carriers; SLNs: Solid lipid nanoparticles.

4.2. Solid lipid nanoparticles for wound healing

4.2.1. Definition and composition

Solid lipid nanoparticles are nanoscale carriers of active pharmaceutical ingredients composed of a solid lipid matrix stabilized by surfactants. The lipid matrix—typically consisting of triglycerides, fatty acids, or waxes—remains solid at both room and body temperatures, while surfactants reduce surface tension to prevent agglomeration. The formulation's performance, including its release kinetics and bioavailability, is dependent on the chosen lipids, surfactants, and the manner in which the active pharmaceutical ingredient is incorporated.¹⁶

The main physicochemical properties affecting SLN performance are summarized in [Figure 1](#).

4.2.2. Preparation methods

Several techniques have been reported for SLN preparation, and the selection of the method depends on lipid type, drug properties, thermal stability, target particle size, scalability, and compatibility with the final topical wound-healing platform. High-pressure homogenization, microemulsion, and solvent-based methods are among the most described approaches, while solvent injection, ultrasonication/high-shear homogenization, and hot/cold homogenization are also relevant depending on formulation requirements and drug stability. [Table 2](#) summarizes the main preparation methods, advantages, limitations, and pertinent references.

High-pressure homogenization involves dispersing the melted lipid and active compound in an aqueous surfactant phase, followed by size reduction under high shear

Table 2. Summary of SLN preparation methods

Preparation method	Principle	Advantages	Limitations	Pertinent references
High-pressure homogenization	Melted lipid and drug are dispersed in an aqueous surfactant phase and reduced to nanosized droplets under high pressure; cooling solidifies the lipid phase.	Scalable, reproducible, solvent-free, suitable for industrial production.	High energy input; possible degradation of heat- or pressure-sensitive drugs.	17,18
Hot homogenization	Drug is incorporated into melted lipid, followed by emulsification in hot aqueous surfactant solution and homogenization above the lipid melting point.	Suitable for lipophilic and heat-stable drugs; commonly used for SLNs.	Not suitable for thermolabile drugs; possible drug partitioning into aqueous phase.	19,20
Cold homogenization	Drug-loaded lipid melt is rapidly cooled, ground into microparticles, then homogenized in cold surfactant solution.	Reduces thermal degradation and drug loss into the aqueous phase.	Broader particle-size distribution; more complex processing.	21,22
Microemulsion technique	A hot microemulsion containing melted lipid, surfactant/co-surfactant, and water is dispersed into cold water to precipitate SLNs.	Simple process; mild mechanical conditions; useful for laboratory-scale preparation.	Requires relatively high surfactant concentration; possible dilution and stability issues.	23-25
Solvent evaporation	Lipid and drug are dissolved in an organic solvent, emulsified in an aqueous phase, and the solvent is evaporated to form SLNs.	Useful for lipophilic drugs; avoids very high processing temperatures.	Residual solvent risk; solvent toxicity and regulatory concerns.	26,27
Solvent injection	Lipid dissolved in a water-miscible organic solvent is rapidly injected into an aqueous surfactant phase, causing lipid precipitation into nanoparticles.	Simple, rapid, relatively low-energy method; suitable for screening formulations.	Requires organic solvent removal; particle size depends strongly on injection rate, solvent type, and mixing conditions.	28,29
Ultrasonication/high-shear homogenization	Mechanical shear or ultrasonic energy is used to reduce lipid droplets into nanosized particles before solidification.	Simple, accessible, useful for small-scale preparation.	Possible broad particle-size distribution, aggregation, overheating, and metal contamination from probe sonication.	21,30

Abbreviation: SLNs: Solid lipid nanoparticles.

pressure.¹⁶ This method is scalable and suitable for industrial production, although heat and mechanical stress may affect thermolabile compounds.¹⁶ Microemulsion techniques depend on the formation of a hot microemulsion followed by dilution in cold water, leading to lipid precipitation and nanoparticle formation.²³ This approach is relatively simple but may require high surfactant concentrations and may show lower drug-loading efficiency.²³ Solvent evaporation involves dissolving the lipid and drug in an organic solvent, emulsifying the organic phase in an aqueous surfactant phase, and then removing the solvent to form SLNs.³¹ Although useful for lipophilic compounds, residual solvent and toxicity concerns must be considered.

Other techniques include solvent injection, where the lipid dissolved in a water-miscible organic solvent is rapidly injected into an aqueous surfactant phase, allowing lipid precipitation into nanoparticles.²¹ Ultrasonication and high-shear homogenization are also used as simpler laboratory-scale methods, but they may produce broader

particle-size distributions and require optimization to prevent aggregation or metal contamination from probe sonication.³² Hot and cold homogenization approaches may be selected depending on drug stability and solubility; hot homogenization is suitable for heat-stable compounds, whereas cold homogenization can reduce thermal degradation and drug partitioning into the aqueous phase.³³

For wound-healing applications, the preparation method should be selected not only according to particle size and drug loading, but also according to reproducibility, sterilization feasibility, scalability, surfactant safety, and compatibility with final topical systems such as hydrogels, films, foams, or dressings.

Several SLN-based formulations have been investigated for wound-healing applications using different lipid matrices, active ingredients, and particle sizes, as summarized in [Table 3](#).

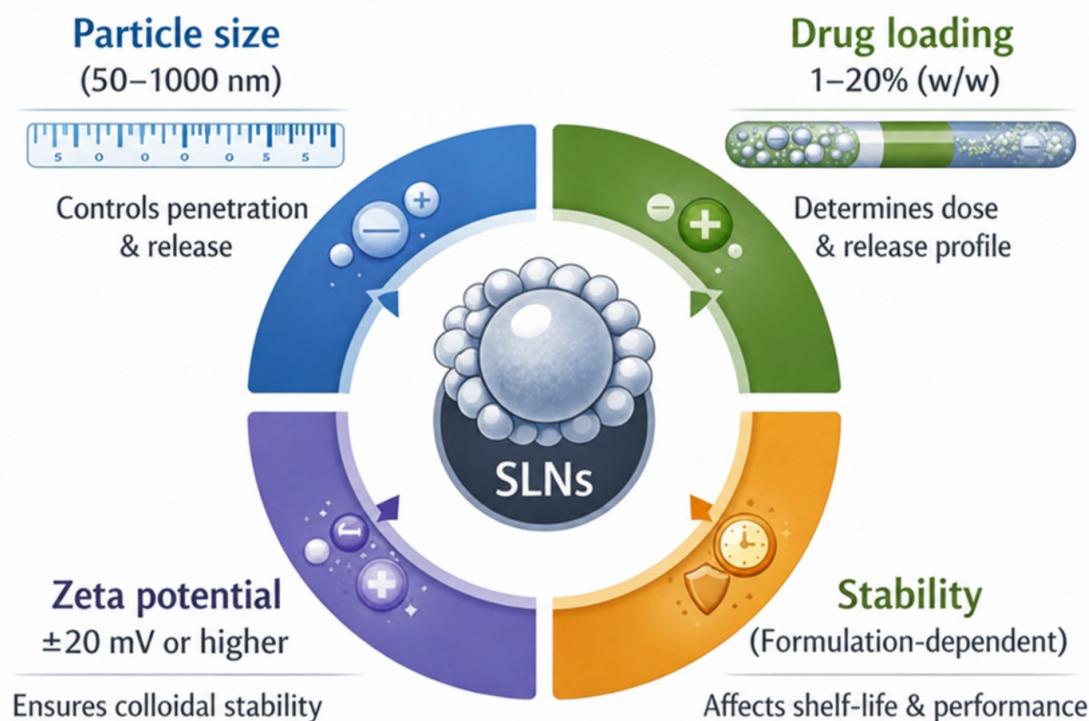


Figure 1. Key physicochemical properties. Image created using ChatGPT 5.0

Table 3. Comparative study data on SLN formulations

Study	Type of lipid used	Particle size (nm)	Loaded substances (active ingredients)
Esposito <i>et al.</i> ³⁴	Tristearin (glyceryl tristearate)	~132 nm (mean $\pm$ 46 nm)	Retinyl palmitate (vitamin A derivative)
Kakkar <i>et al.</i> ³⁵	Compritol 888 ATO (glyceryl behenate)	~97 nm (mean)	Tetrahydrocurcumin (hydrogenated curcumin derivative)
Gad <i>et al.</i> ³⁶	Stearic acid (saturated fatty acid)	~542 nm (optimized SLN size)	Chamomile oil (essential oil with antiseptic/anti-inflammatory properties)
Moglad <i>et al.</i> ³⁷	Stearic acid (long-chain fatty acid)	~263 nm (optimized formulation)	Cefadroxil (first-generation cephalosporin antibiotic)
Sandhu <i>et al.</i> ³⁸	Compritol 888 ATO (glyceryl behenate)	~170 nm (mean $\sim$ 170.1 $\pm$ 26.6 nm)	Curcumin (antioxidant polyphenol)
Makhmalzade <i>et al.</i> ³⁹	Compritol 888 ATO + oleic acid (8% of formulation)	2.88–174 nm (majority < 100 nm)	Deferoxamine mesylate (HIF-1 α agonist to promote angiogenesis)
Abou El-ezz <i>et al.</i> ⁴⁰	Cholesterol (with soy lecithin as emulsifier)	111–202 nm (range for different formulations)	Copper(II) Schiff-base 8-hydroxyquinoline complex (CuSQ)
Salah <i>et al.</i> ⁴¹	Not specified (SLN-integrated topical hydrogel)	190.4 $\pm$ 1.6 nm (optimized formulation)	Amlodipine (vasodilator promoting angiogenesis)

Abbreviations: HIF-1 α : Hypoxia-inducible factor 1- α ; SLN: Solid lipid nanoparticle.

4.2.3. Advantages and limitations

Table 4 shows the advantages and limitations of SLNs in wound healing. Although SLNs provide several benefits, such as better drug stability and controlled release, some formulation challenges remain.^{42–45}

The corresponding advantages and limitations are described in greater detail below:

(i) *Advantages*

- Biocompatibility and biodegradability: Use of physiological lipids minimizes toxicity and ensures safe degradation.
- Controlled drug release: The solid lipid matrix enables sustained and regulated drug release, maintaining therapeutic concentrations while allowing scalable production.
- Protection of labile compounds: Encapsulation shields sensitive drugs from chemical and enzymatic degradation.

(ii) *Limitations*

- Limited drug loading capacity: The crystalline lipid matrix may restrict the incorporation of higher drug amounts.
- Polymorphic transitions: Changes in the lipid's crystalline structure over time can lead to drug expulsion and reduced formulation stability.
- Formulation complexity: Achieving precise control over parameters such as particle size and zeta potential complicates manufacturing.

Solid lipid nanoparticles support wound healing through multiple interconnected mechanisms that involve controlled drug release, enhanced local retention, interaction with wound barriers, modulation of inflammation, and improved cellular uptake.

4.2.4. Solid lipid nanoparticles versus nanostructured lipid carriers in wound-healing applications

Although SLNs and nanostructured lipid carriers (NLCs) are both lipid-based nanocarriers, they differ in lipid matrix organization, which affects their performance in wound-healing applications. SLNs consist of a solid lipid matrix that can protect incorporated drugs and provide sustained release; however, their relatively ordered crystalline structure may restrict drug loading and increase the risk of drug expulsion during storage.⁴⁶ In contrast, NLCs combine solid and liquid lipids, producing a less ordered matrix that may improve drug-loading capacity and reduce crystallinity-related instability.⁴⁷ Nevertheless, NLCs should not be considered universally superior to SLNs because their performance depends on lipid composition,

surfactant selection, drug properties, particle size, release behavior, and compatibility with the final topical dosage form. Therefore, the selection between SLNs and NLCs for wound-healing therapy should be guided by the therapeutic agent, wound type, desired release profile, formulation stability, scalability, and translational feasibility

5. Mechanisms of action of solid lipid nanoparticles in wound healing

5.1. Interaction with the wound barrier and local retention

The lipid-based structure of SLNs facilitates close interaction with the wound surface and surrounding skin layers.⁴⁸ Their nanoscale size allows better distribution within the wound bed, while the lipid matrix improves adhesion and retention of the incorporated therapeutic agent at the application site.⁴² This is particularly important in chronic and exudative wounds, where rapid drug loss from conventional topical formulations may reduce therapeutic efficacy.^{49,50} When incorporated into hydrogels, films, or dressings, SLNs may further prolong contact time and provide a sustained local reservoir for drug delivery.⁵¹

5.2. Controlled drug release and microenvironment modulation

The solid lipid matrix of SLNs acts as a reservoir that regulates the diffusion of encapsulated drugs.⁵² This sustained release helps maintain therapeutic concentrations within the wound microenvironment and reduces rapid drug depletion.⁵³ By providing prolonged local exposure, SLNs can support antimicrobial activity, reduce excessive inflammation, and promote tissue repair processes such as fibroblast migration, collagen deposition, and angiogenesis.⁵⁴

Table 4. Advantages and limitations of solid lipid nanoparticles in wound healing

Advantages	Limitations
High biocompatibility and biodegradability	Limited drug loading capacity due to the crystalline lipid matrix.
Controlled and sustained drug release	Potential for polymorphic transitions leading to drug expulsion.
Scalable production techniques	Formulation complexity requires precise process control.
Protection of sensitive drugs from degradation	Stability challenges under certain storage conditions.

5.3. Modulation of inflammatory and oxidative pathways

Chronic wounds are commonly characterized by persistent inflammation, elevated oxidative stress, and delayed transition from the inflammatory phase to the proliferative phase.⁵⁵ SLNs can improve the local delivery of anti-inflammatory and antioxidant agents, thereby helping to reduce the levels or production of inflammatory mediators and oxidative damage within the wound site.⁵⁶ This may contribute to a more favorable healing environment by limiting prolonged tissue injury and supporting re-epithelialization and extracellular matrix remodeling.⁵⁷

5.4. Cellular uptake and interaction with repair-associated cells

The nanoscale dimensions and lipid composition of SLNs may enhance interaction with cells involved in wound repair, including keratinocytes, fibroblasts, macrophages, and endothelial cells.^{58,59} Cellular uptake may occur through

endocytosis-mediated pathways, allowing encapsulated agents to reach intracellular targets more efficiently than free drugs.⁶⁰ Improved cellular interaction can support key healing events such as keratinocyte migration, fibroblast proliferation, macrophage phenotype modulation, and endothelial cell activity during angiogenesis.⁶¹

As summarized in Figure 2, SLNs may contribute to wound repair through several interconnected pathways, including improved wound-bed retention, sustained drug release, antimicrobial activity, reduction of oxidative stress, modulation of inflammatory mediators, enhanced cellular uptake, fibroblast activation, collagen deposition, angiogenesis, and re-epithelialization.

6. Challenges and future perspectives

6.1. Present limitations

Despite the therapeutic potential of SLNs in wound healing, several formulation-related limitations remain.

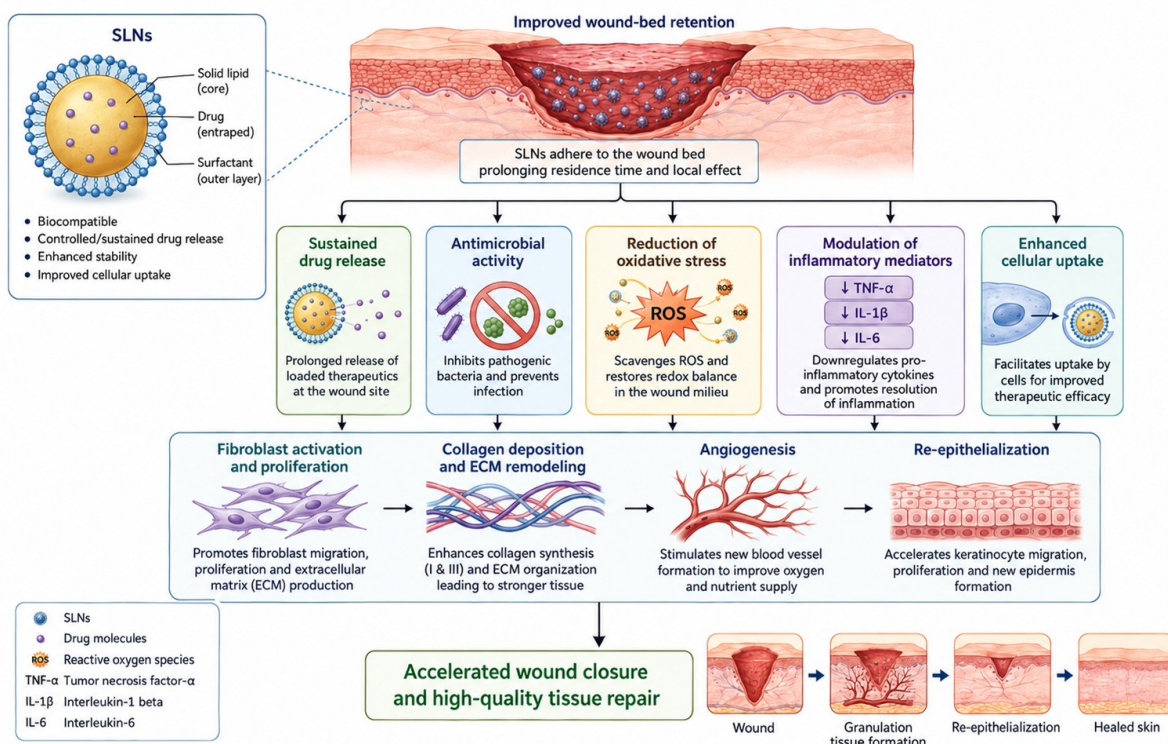


Figure 2. Proposed SLN-mediated wound-healing pathways. The figure summarizes how SLNs may enhance wound repair through improved wound-bed retention, sustained drug release, antimicrobial activity, reduction of oxidative stress, modulation of inflammatory mediators, enhanced cellular uptake, fibroblast activation, collagen deposition, angiogenesis, and re-epithelialization. Image created using ChatGPT 5.0).

Abbreviations: ECM: Extracellular matrix; IL-1β: Interleukin-1 beta; IL-6: Interleukin-6; ROS: Reactive oxygen species; SLNs: Solid lipid nanoparticles; TNF-α: Tumor necrosis factor-alpha.

Lipid polymorphism, drug expulsion, and nanoparticle agglomeration during storage may affect long-term product consistency. In addition, maintaining reproducible particle size, zeta potential, drug loading, and release behavior during scale-up remains a major challenge. Moreover, large-scale production that maintains consistent physicochemical properties requires further process optimization.⁶²

6.2. Safety and toxicology

Safety assessments are crucial for the clinical translation of SLNs. Although the use of biocompatible and biodegradable lipids reduces potential adverse effects, both acute and chronic toxicity must be evaluated. It is also essential to investigate the long-term fate of SLNs and their degradation products to ensure they do not induce immunogenic responses or tissue irritation.⁵

6.3. Regulatory, commercialization, and clinical translation barriers

Despite promising preclinical outcomes, the clinical translation of SLN-based wound-healing formulations remains limited.⁶³ Most developed SLN systems for wound repair are still at the laboratory or animal-study stage, with relatively few formulations progressing toward clinical evaluation.⁸ This gap reflects several regulatory and commercialization challenges, including the need for reproducible large-scale manufacturing, long-term stability, sterilization compatibility, batch-to-batch consistency, and clear quality control specifications for particle size, zeta potential, drug loading, release profile, and lipid polymorphic behavior.⁶⁴⁻⁶⁶

From a regulatory perspective, SLN-based wound products require evidence of safety, local tolerability, absence of irritation or sensitization, and consistent therapeutic performance.⁶⁷ Their final dosage form is also important, since SLNs are often incorporated into gels, films, dressings, or other topical platforms, which may influence regulatory classification, product stability, and clinical evaluation requirements.⁶⁸ Therefore, future studies should move beyond proof-of-concept wound-closure experiments and provide data on manufacturability, storage stability, sterilization, toxicology, and comparative performance against established wound-care products.

6.4. Clinical evidence and formulation failure considerations

Despite encouraging preclinical findings, clinical evidence supporting SLN-based wound-healing products remains limited. Most reported SLN formulations have been evaluated using *in vitro* assays, antimicrobial testing,

ex vivo skin models, or animal wound models, whereas human studies and well-designed clinical trials remain scarce. Therefore, the therapeutic value of SLNs in wound care should be interpreted cautiously until stronger clinical data become available.

Another important translational issue is formulation failure during development. SLN-based wound systems may fail to progress because of low drug-loading capacity, drug expulsion during storage, nanoparticle aggregation, incompatibility with gels or dressings, surfactant-related irritation, or loss of controlled-release behavior after processing.^{63,69} These issues are particularly relevant for wound-care products, where the final formulation must remain stable, non-irritating, easy to apply, and effective under variable wound conditions.

6.5. Future outlook

Future research on SLN-based wound-healing systems should move toward smarter and more clinically adaptable formulations. Stimuli-responsive SLNs represent a promising direction, particularly systems designed to release therapeutic agents in response to wound-specific triggers such as pH changes, bacterial enzymes, oxidative stress, or inflammatory signals.^{70,71} Such responsiveness may allow more precise drug release in infected or chronic wounds while reducing unnecessary exposure to surrounding healthy tissue.⁷²

Another emerging direction is the use of artificial intelligence-assisted formulation optimization. Machine-learning approaches could help predict the influence of lipid type, surfactant concentration, particle size, surface charge, and drug-loading parameters on stability, release behavior, and biological performance. This may reduce experimental trial-and-error and support more reproducible formulation development.⁷³

Personalized wound care may also shape the future use of SLNs. Since wound healing is influenced by patient-specific factors such as diabetes, infection status, inflammation level, and wound exudate composition, SLN formulations may be tailored to deliver antimicrobial, anti-inflammatory, antioxidant, or pro-angiogenic agents according to wound type and healing stage.⁷⁴

Multifunctional theranostic SLNs are another promising concept, combining therapeutic delivery with imaging or diagnostic functions to monitor wound status and treatment response. In addition, combination therapy approaches, where SLNs co-deliver antibiotics, antioxidants, growth-promoting agents, or natural bioactive compounds, may provide broader therapeutic effects for complex wounds.⁷⁵

7. Conclusion

Solid lipid nanoparticles represent a promising platform for wound-healing therapy because they can improve local drug retention, protect unstable therapeutic agents, and provide sustained release at the wound site. Their lipid-based structure and nanoscale properties may support antimicrobial activity, inflammatory modulation, oxidative stress reduction, cellular uptake, collagen deposition, angiogenesis, and re-epithelialization.

The performance of SLNs depends on formulation factors such as lipid composition, surfactant selection, particle size, surface charge, drug loading, and compatibility with topical systems such as hydrogels and dressings. Compared with liposomes and polymeric nanoparticles, SLNs may offer a practical balance between biocompatibility, stability, scalability, and cost-effectiveness.

However, clinical translation remains limited by challenges related to drug loading, lipid polymorphism, long-term stability, sterilization, large-scale manufacturing, regulatory approval, and limited clinical evidence. Future studies should focus on stimuli-responsive SLNs, artificial intelligence-assisted formulation optimization, personalized wound care, theranostic systems, and combination therapy approaches to support the development of clinically applicable SLN-based wound products.

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Conflict of interest

The authors declare no conflict of interest.

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Writing—review & editing: All authors

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Availability of data

Not applicable.

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