WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 11, 215-228. Review Article ISSN 2277–7105

AI-BASED OPTIMIZATION OF ALOE VERA GEL NANO-EMULSION FOR TOPICAL DELIVERY

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Article Received on 30 April 2026,
Article Revised on 20 May 2026,
Article Published on 01 June 2026,

https://doi.org/10.5281/zenodo.20438602

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How to cite this Article: Amol Sapkal*[1], Krushna Mhase[1], Chetana Pawar[1], Ms. Kalyani Uttam Chande[2]. (2026). AI-Based Optimization Of Aloe Vera Gel Nano-Emulsion For Topical Delivery. World Journal of Pharmaceutical Research, 15(11), 215–228.

ABSTRACT

Aloe vera has gained considerable attention in pharmaceutical and dermatological applications due to its anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties. However, conventional Aloe vera formulations often face challenges such as poor skin penetration, low stability, and reduced bioavailability of active phytoconstituents, which limit their therapeutic effectiveness. To overcome these limitations, nano-emulsion technology has emerged as a promising approach for improving the solubility, stability, controlled release, and dermal delivery of Aloe vera bioactives. Nano-emulsions, with droplet sizes generally ranging from 20–200 nm, enhance surface area, drug loading capacity, absorption, and overall topical delivery performance. Recent studies have shown that Aloe vera nano-emulsions possess enhanced antimicrobial activity, sustained release properties, improved wound-healing ability, and superior anti-inflammatory effects compared with conventional formulations. This review highlights the phytochemical composition and therapeutic potential of Aloe vera, along with the fundamentals, formulation methods, characterization, and topical applications of nano-emulsion systems. Particular emphasis is placed on the role of Artificial Intelligence (AI) and Machine Learning (ML) in optimizing nano-emulsion formulations. AI-based techniques such as Artificial Neural Networks (ANN), Genetic Algorithms (GA), Response Surface Methodology (RSM), and Design of Experiments (DoE) assist in predicting and optimizing critical formulation parameters including droplet size, polydispersity index, zeta potential, viscosity, stability, and drug release behavior, thereby

reducing experimental effort and development time. In addition, AI-optimized Aloe vera nano-emulsions have shown promising applications in wound healing, anti-acne therapy, anti-aging products, moisturizers, and other cosmeceutical preparations. Overall, the combination of Aloe vera, nano-emulsion technology, and AI-driven optimization offers a promising and advanced strategy for the development of effective topical drug delivery systems.

1. INTRODUCTION

Due to their therapeutic efficacy, safety, and low side effects, the use of herbal medicines has significantly increased in recent years. Aloe vera is one of many medicinal plants, and its antiinflammatory, antioxidant, antimicrobial, and wound-healing qualities have drawn a lot of interest in dermatological and pharmaceutical applications. It is widely used in topical formulations such as creams, gels, and lotions because of its bioactive components, which include polysaccharides, vitamins, enzymes, and anthraquinones.

Aloe vera has therapeutic potential, but its clinical efficacy is frequently constrained by low skin permeability, poor stability, and degradation of active ingredients in traditional formulations.

These difficulties limit its bioavailability and lower its overall effectiveness as a treatment.

Nanotechnology-based drug delivery systems, especially nano-emulsions, have shown promise as carriers for herbal bioactives in order to get around these restrictions. Nano-emulsions, which usually have droplet sizes between 20 and 200 nm, are colloidal dispersions of water and oil stabilized by surfactants. Because of their large surface area and small droplet size, these systems improve stability, solubility, and the ability of active compounds to pass through the skin barrier. Additional benefits of nano-emulsions include enhanced drug loading capacity, regulated release, and higher bioavailability of hydrophilic and lipophilic substances. They are excellent for treating a variety of skin conditions, such as inflammation, infections, and wound healing, because of their capacity to improve dermal and transdermal delivery.

Recent studies have also demonstrated the successful incorporation of Aloe vera into nanoemulsion systems, resulting in improved stability, enhanced antibacterial activity, and prolonged therapeutic effects in topical applications.

However, a number of factors, including droplet size, stability parameters, oil phase composition, and surfactant concentration, are involved in the development of optimized nano-emulsion formulations. Conventional trial-and-error methods are ineffective and time-consuming. In this regard, machine learning and artificial intelligence (AI) have become effective tools for formulation optimization. AI-based models can reduce experimental effort and improve formulation performance by analyzing intricate relationships between formulation variables and accurately predicting ideal conditions.

Therefore, combining Aloe vera with nano-emulsion technology and AI-based optimization is a new and promising way to improve topical medication delivery systems. The current developments in AI-driven optimization of Aloe vera nano-emulsions, as well as their formulation techniques, characterization, and therapeutic uses, are the focus of this review.

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2. Aloe Vera: Phytochemical and Therapeutic Profile

Compound Category	Key example	Concentration (per 100g gel)	Therapeutic Properties
Polysaccharides	Acemannan, mannose-6phosphate, glucomannan, pectic substances	0.1-1.5% dry weight; acemannan up to 0.55%	Wound healing via fibroblast growth and macrophage activation; immunomodulation; antiviral (e.g., HIV inhibition); anti-ulcer effects
Anthraquinone	Aloin (barbaloin), aloe-emodin, aloesin (aloeresin), anthranol	0.1-0.3% in rind; trace in gel	Laxative at >50mg doses; antiinflammatory; antibacterial against pathogens like Staphylococcus; anticancer potential in vitro
Vitamin	A (β-carotene: 5-10 IU/g), C (7-29mg/100g), E (0.2-1mg/100g), B12 (0.3µg/100g), B1, B2, B3, B6, folate	Variable; higher in fresh gel	Antioxidant scavenging ROS; collagen synthesis for skin repair; immune boosting; B12 rare in plants, aids neuropathy
Enzymes	Bradykinase, cellulase, amylase, catalase, peroxidase, oxidase,	Trace amounts; activity peaks in fresh extracts	Reduce swelling (bradykinase); digest sugars/proteins; scavenge

	alkaline phosphatase (up to 92 identified)		H2O2 free radicals; antiinflammatory in arthritis models
Amino acid	18-20 total: lysine (highest), leucine, valine, threonine, phenylalanine, alanine, glycine, glutamic acid, aspartic acid, proline	10-50mg/100g dry weight; all 8 essential present	Tissue repair and collagen formation; neurotransmitter support (glutamic acid); antioxidant via sulfur aminos (methionine, cysteine)
Additional (Lignin, Saponins, Sterols)	Lignin (aloin derivative), saponins, β-sitosterol, campesterol, lupeol	Lignin 0.5%; sterols 0.1-0.3%	Penetrate skin deeply; analgesic/antiarthritic (lupeol); cholesterol-lowering; antifungal saponins

The gel and latex layers of aloe vera contain more than 200 bioactive chemicals. Important phytochemicals include minerals and amino acids for metabolism, polysaccharides like cameraman for immunological support, vitamins A, C, and E for antioxidants, enzymes for reducing inflammation, and anthraquinones like aloin for laxative and anticancer effects. Phytochemical Constituent.

Topical Delivery Applications By getting past the stratum corneum barrier, topical medication delivery systems—especially nanocarriers like liposomes, ethosomes, and microemulsions—improve skin penetration for the treatment of burns, acne, psoriasis, skin hydration, and anti-aging. According to recent preclinical research, these systems offer tailored action, prolonged release, and decreased systemic toxicity. Burns Hydrogels and medical textiles containing medications such as chlorhexidine or 4-aminopyridine allow for localized administration to burn sites, increasing re-epithelialization, lowering inflammation, and speeding up healing without the need for intrusive procedures.

3. Nano Emulsion: Fundamentals

Nano-emulsions are liquid-in-liquid dispersions that are kinetically stable and have droplet sizes of 20–200 nm, though they can occasionally reach 500 nm depending on the source. These are typically water-in-oil (w/o) or oil-in-water (o/w) systems stabilized by one or more surfactants and frequently a cosurfactant.

Nano-emulsions fall into a number of complementary categories. They can be broadly categorized structurally into three types: water-in-oil (W/O), where water droplets are dispersed in a continuous oil phase; oil-in-water (O/W), where oil droplets are dispersed in a continuous aqueous phase; and bicontinuous (bi-continuous) systems, where both water and

oil form interpenetrating micro-domains instead of a clearly dispersed phase. In terms of functionality, nanoemulsions are further divided into two categories: biphasic (simple O/W or W/O systems) and multiple (double) nano-emulsions, such as water-in-oil-in-water (W/O/W) and oil-in-water-in-oil (O/W/O), which offer multi-compartment behavior and the possibility of sequential or controlled release. Physically, they are classified as either turbid/milky (when droplets are slightly larger but still within the nanoscale range) or translucent or transparent (when droplets are very small and light-scattering is minimal). In terms of composition, nano-emulsions can be categorized according to the type of stabilizers they contain, such as non-ionic surfactant-based, ionic surfactant-based, or polymeric/nanoparticle-stabilized systems, each of which affects colloidal stability, biocompatibility, and suitability for use in pharmaceutical, cosmetic, or nutraceutical applications.

Nano-emulsions offer a wide range of advantages that make them superior to many conventional drug-delivery systems. They significantly enhance drug solubility and bioavailability, especially for poorly water-soluble actives, and provide improved physical and chemical stability with longer shelf life. Their nanoscale droplets create a large interfacial area that accelerates drug dissolution and absorption, while protecting encapsulated components from hydrolysis, oxidation, and enzymatic degradation. Nano-emulsions also enable higher drug loading, controlled or targeted delivery, and improved skin penetration for topical/transdermal applications. They are non-toxic, non-irritant, biocompatible, and can be formulated in multiple dosage forms (oral, topical, injectable, nasal, etc.), including taste-masked and cosmetically elegant products. Owing to their ease of scale-up and potential as a simpler alternative to liposomes, nano-emulsions are increasingly important across pharmaceutical, cosmetic, and nutraceutical fields."

Nano-emulsions are typically composed of an oil phase (commonly 5–20% w/w medium-chain or long-chain triglycerides such as coconut, soybean, sesame, or rice-bran oil), an aqueous phase, a surfactant (often non-ionic agents like Tween-80, Tween-20, Span-80, or Brij-96V), and a co-emulsifier or co-solvent (such as ethanol, propylene glycol, PEG, Transcutol-P, or glycerin), with the active drug or bioactive dissolved either in the oil or water phase depending on its solubility; these systems are prepared by high-energy methods such as high-pressure homogenization, ultrasonication, microfluidization, high-energy stirring, or membrane emulsification, which mechanically reduce coarse emulsion droplets to the nanoscale, or by low-energy methods like spontaneous emulsification (solvent

displacement), phase inversion temperature (PIT), emulsion inversion point (EIP/PIC), and cold emulsification, which rely on composition and temperature-driven phase behavior to achieve low interfacial tension and form thermodynamically favored nano-emulsion droplets.

4. Aloevera nano emulsion enhances tropical delivary

Using nano-emulsions of aloevera really helps get its active stuff, like polysaccharides and phenolics, where it needs to go on your skin. Regular gels often have trouble with this, not being stable enough or sinking in well.

These nano-emulsions bring a lot to the table. They keep the active ingredients stable, for starters. And they seem to crank up the antimicrobial and anti-inflammatory punch. Plus, these kinds of formulas can keep releasing the good stuff over time, which is super handy for skincare. Think wound healing or tackling acne. Studies show they keep a pH that's good for skin, somewhere between 5.5 and 7.0. They also hit just the right thickness and are easy to spread.

Compared to regular gels, they're way more stable, even after three months. In tests on rats, their swollen paws went down by as much as 38% when given a dose of 400 mg/kg. That's pretty solid proof they've got some serious anti-inflammatory power.

Nano-emulsions shrink droplet sizes down to the nanometer scale, under 200 nm. This lets them get deeper into the skin barrier than regular Aloe vera gels. We looked at this using in vitro Franz diffusion cells with rat skin. When we used optimized formulas, like one with 3% sodium alginate, we saw 92% of the active stuff released within 12 hours. That's way more than standard gels. Using a bigger surface area and surfactants helps the body absorb the active ingredients better, without causing any irritation.

And this actually makes Aloe vera work better for treating wounds. It also kicks up its antibacterial and soothing powers. This kind of protection stops the active parts of Aloe vera from breaking down too soon.

Studies show chitosan-sodium alginate nanoparticles have better antimicrobial and antiinflammatory effects. They also release the drug consistently, almost like a steady drip. In rat tests, the more you gave them, the better it worked. Higher doses really cut down swelling over a 5-hour period.

Regulated Release

Release profiles for in vitro shows consistent patterns with positive burst followed by diffusion that is sustained. This follows non-fickian or zero order kinetics. Aloe vera was effectively entrapped in optimum nano-gels like Carbopol 940 which released 9 to 92% of Aloe vera over 12 hours. These nano-gels remain stable across temperature changes. This matrix composition actively maintains the reliability of bioactive diffusions and minimizes dosing's repetitiveness.

Application

Wound Healing Applications

Aloe vera nano-gels accelerate tissue regeneration, collagen synthesis, and reduce inflammation in wounds via enhanced antimicrobial action and moisture retention. Curcumin-loaded Aloe nano-emulgels demonstrated superior skin penetrability ($p<0.05$) and in vivo healing in rat models compared to marketed formulations. Stability prevents phase separation, ensuring prolonged therapeutic contact.

Anti-Acne Formulation

Nano-emulsions boost Aloe vera's anti-inflammatory and antibacterial effects against Cutibacterium acnes, often combined with tea tree oil or neem for synergistic action. Zein-based nanocapsules with plant Eos in Aloe formulations enhance ROS scavenging, bacterial inhibition, and transdermal permeation at safe concentrations. These gels reduce acne lesions by targeting overgrowth and oxidation without toxicity.

5. Artificial Intelligence in Pharmaceutical Formulation

Artificial intelligence (AI) refers to sophisticated computational systems that are intended to imitate human intelligence by carrying out tasks like pattern recognition, learning, and reasoning. AI is essential to the analysis of complex, high-dimensional datasets in pharmaceutical formulation because it makes it possible to find non-linear relationships between formulation variables and product performance. Machine Learning (ML), which enables systems to learn from experimental data and make precise predictions without explicit programming, is a crucial aspect of artificial intelligence. Support vector machines, random forests, and regression models are just a few of the machine learning algorithms that have been widely used to predict important quality attributes like particle size, stability, and drug release, thereby drastically reducing experimental trials.

Deep Learning (DL) builds on machine learning (ML) by using multi-layered neural networks to more accurately model complex and non-linear systems. By precisely estimating parameters like droplet size, zeta potential, and release behavior, Artificial Neural Networks (ANN), a wellknown DL approach, have shown superior predictive capability in nano-formulation development. Additionally, predictive modeling forecasts formulation outcomes and optimizes process variables by combining these AI techniques with statistical tools. By establishing quantitative relationships between input variables and responses, techniques like Response Surface Methodology (RSM), ANN, and Genetic Algorithms (GA) facilitate effective formulation design, shorter development times, and enhanced product performance.

Technique	How it Is used in nano-emulsion optimization	Key parameters modeled	Typical responses optimized
Artificial Neural Network (ANN)	Models complex nonlinear relationships between formulation/processing parameters and nano-emulsion properties; reduces experimental runs by predicting optimal conditions.	Oil ratio, temperature, pressure, surfactant concentration.	Droplet size, stability, polydispersity index (PDI); often reported prediction accuracy up to about 95%.
Machine Learning (ML)	Acts as a broader data-driven framework that learns from nano-emulsion datasets to predict "ideal" formulations and accelerate optimization with fewer experiments	Surfactant type, oil/water ratio, homogenization conditions, process variables.	Droplet size, PDI, stability, drug release profile, and manufacturability.
Genetic Algorithm (GA) / ANN–GA	Mimics natural selection to search for optimal surfactant, oil, and process variables, especially in water-in-oil and self-nanoemulsifying systems. Often combined with ANN for enhanced prediction.	Surfactant concentration, oil content, sonication time, pressure, temperature, emulsifier type.	Droplet size, PDI, stability, encapsulation efficiency, and process cost/time.
Response Surface Methodology (RSM)	Fits polynomial equations to experimental data from structured designs (e.g., Box-Behnken, central composite) to model and optimize responses.	Formulation and process variables such as surfactant/oil/water ratios, stirring speed, homogenization pressure.	Droplet size, PDI, zeta potential, % drug entrapment, viscosity, and in-vitro release.
Design of Experiments (DoE)	Provides a structured experimental framework (factorial, mixture, D-optimal designs) to efficiently evaluate multiple variables and identify their interaction effects	Independent formulation and process factors (e.g., oil, surfactant, co-emulsifier, temperature, pressure).	Low particle size, low PDI, acceptable zeta potential, high drug-loading, and stability; significantly reduces trial-and-error development.

6. AI-Based Optimization of Nano-Emulsion

By learning from experimental datasets and forecasting the effects of formulation and process variables without requiring extensive trial-and-error experimentation, AI-based optimization of nano-emulsions focuses on concurrently tuning multiple physicochemical and performancerelated parameters. One of the outputs that is most extensively modeled is droplet size. Machine learning models, particularly Artificial Neural Networks, are trained to predict mean droplet diameter as a function of temperature, pressure, homogenization flow rate, oil ratio, surfactant type and concentration, and mixing time.

These models are reported to achieve high prediction accuracy, allowing for the quick design of nanoemulsions that fall within desired nanoscale size ranges (often 20–200 nm). ANN- or MLbased frameworks are used to determine the ideal combination of surfactant level, co-emulsifier, and process conditions that minimize polydispersity index (PDI), which is regarded as a crucial quality attribute reflecting the uniformity of the droplet size distribution. This results in more monodisperse and physically stable systems. The electrostatic stability of nano-emulsion droplets is inferred from zeta potential, which can be accurately predicted from variables like particle size, surfactant type, pH, ionic strength, and temperature using multiple regression, artificial neural networks, and other machine-learning models. This allows for the selection of surfactant systems and ionic conditions that improve colloidal stability. Predictive models link changes in surfactant/oil ratios, temperature, and homogenization conditions to observed stability indicators like constant droplet size and PDI over time, absence of phase separation, and unchanged visual appearance during storage, enabling the design of robust nano-emulsions appropriate for pharmaceutical and cosmetic use. Physical and long-term stability (creaming, phase separation, aggregation or coalescence) is modeled as functions of formulation composition and process parameters.

AI-based techniques that learn from in vitro release data are increasingly being used to model drug release profiles (e.g., cumulative percent release and release kinetics such as zero-order, first-order, or Higuchi-type behavior); these models assist in fine-tuning the nano-emulsion composition (oil type, surfactant blend, polymer additives, and viscosity modifiers) to achieve sustained, controlled, or targeted release behavior with fewer experimental trials, especially for topical and parenteral delivery systems. Particularly for topical or injectable nanoemulsions, viscosity and rheological behavior are crucial AI-optimized parameters.

Machine learning-based frameworks link oil content, surfactant concentration, co-emulsifier

level, and polymer or thickener type to viscosity and flow properties, allowing formulations with desired spreadability, pumpability, syringeability, or skin adherence to be designed without requiring extensive empirical screening. AI-based optimization enables systematic tuning of droplet size, PDI, zeta potential, stability, drug release, and viscosity by combining ANN, machine learning algorithms, and occasionally genetic algorithm search strategies with traditional formulation-design approaches. This greatly reduces the number of laboratory experiments needed and speeds up the development of high-performance nano-emulsion systems.

In practice, AI-based optimization of nano-emulsions follows a structured, iterative workflow. First, suitable ingredients are selected, such as an oil phase (e.g., medium-chain triglyceride, soybean, or sesame oil), an aqueous phase, one or more surfactants (e.g., Tween-80, Span-80), and a co-emulsifier or co-solvent (e.g., ethanol, propylene glycol, Transcutol-P), along with the active drug or bioactive compound.

Next, critical input variables are defined, including surfactant type and concentration, oil/water ratio, temperature, homogenization pressure, sonication time or stirring speed, and any stabilizers or viscosity modifiers. A dataset of experimental formulations is then compiled, with these inputs mapped to outputs such as droplet size, polydispersity index (PDI), zeta potential, stability, drug release, and viscosity.

This dataset is used to train an AI model (commonly an Artificial Neural Network or another ML algorithm), which learns the nonlinear relationships between the input variables and the quality-of-life attributes; the model is then validated and fine-tuned using separate test and validation sets. Once trained, the model can predict an optimized formulation by exploring the design space (e.g., surfactant concentration, oil ratio, pressure) to identify the combination that simultaneously meets target ranges for droplet size, PDI, zeta potential, stability, release profile, and viscosity.

Finally, the AI-predicted formulation is prepared and tested experimentally in the lab, with measured properties compared to the AI-predicted values; any discrepancy guides refinement of either the model or the experimental conditions, closing the loop. This workflow is used in several nano-emulsion and formulation-design studies to rapidly converge toward high-performance, robust nano-emulsion systems with far fewer experimental runs than classical optimization approaches.

7. Characterization of Aloe Vera Nano-Emulsion

Physicochemical Assessment

To assess the stability and quality of Aloe vera nano-emulsions, physicochemical characterization is crucial. Because nanosized droplets improve drug release and skin penetration, particle size analysis is crucial. Studies have shown that droplet sizes are typically between 20 and 200 nm, indicating that nano-emulsion formation was successful. Formulation stability is assessed using zeta potential; values around ±30 mV indicate good stability because droplet aggregation is prevented. To prevent irritation, the pH of Aloe vera nano-emulsions is typically kept between 5 and 7. Studies on viscosity are also carried out because suitable viscosity enhances topical formulations' spreadability, retention duration, and patient acceptability.

Research on Stability

To assess the physical stability of Aloe vera nano-emulsions under various circumstances, stability studies are conducted. Phase separation, creaming, or cracking are detected through centrifugation studies, and optimized formulations typically exhibit no separation following centrifugation. Aloe vera nano-emulsions remain stable at various storage temperatures with negligible changes in particle size and zeta potential, according to temperature stability studies. Studies on storage stability also verified that nano-emulsion formulations do not significantly deteriorate over long periods of time in terms of appearance, viscosity, and homogeneity.

In Vitro Studies

Aloe vera nano-emulsions' drug release and skin penetration characteristics are assessed in vitro. Because of their large surface area and nanoscale droplets, research studies have reported controlled and sustained release of active constituents from nano-emulsion systems. In comparison to traditional formulations, skin penetration studies demonstrated improved penetration through skin layers, leading to improved topical bioavailability and therapeutic efficacy.

Aloe vera nano-emulsions showed notable anti-inflammatory and wound-healing properties in in vivo experiments. Faster wound contraction, better tissue regeneration, and increased antibacterial activity in topical applications were all demonstrated in experimental studies.

Because aloe vera nano-formulations contain bioactive substances like polysaccharides and

anthraquinones, they also lessen inflammation, redness, and swelling. The potential of Aloe vera nano-emulsions in dermatological and wound healing applications is supported by these findings.

8. AI-Optimized Aloe Vera Nano-Emulsion Applications

Because of their improved stability, increased skin penetration, and controlled drug release, AI-optimized Aloe vera nano-emulsions have demonstrated promising applications in topical drug delivery. According to research, by decreasing droplet size and increasing penetration through skin layers, nano-emulsions increase the bioavailability of active phytoconstituents. For wound healing, anti-inflammatory, antimicrobial, anti-aging, moisturizing, and cosmetic applications, these systems are being thoroughly studied. Additionally, aloe vera nano-emulsions showed improved antibacterial activity against Escherichia coli and Staphylococcus aureus, which makes them helpful for managing infected wounds. In order to minimize experimental trials and increase formulation efficiency, recent studies have emphasized the use of AI and machine learning techniques for optimizing formulation variables like droplet size, surfactant concentration, viscosity, and stability. Because of their enhanced penetration and extended stability, nano-emulsion systems are also being investigated more and more in cosmeceuticals for sunscreens, moisturizers, anti-aging creams, and dermatological preparations.

9. Challenges and Limitations

Aloe vera nano-emulsions and AI-optimized nanoemulgels have a number of drawbacks despite their benefits. According to research papers, nano-emulsions are thermodynamically unstable systems that may experience flocculation, creaming, coalescence, and Ostwald ripening while being stored, all of which can have an impact on the stability of the formulation. In topical applications, high concentrations of surfactants and co-surfactants necessary for stabilization may result in erythema, contact dermatitis, and skin irritation. The high production costs of complex machinery like ultrasonication systems, microfluidizers, and high-pressure homogenizers are another significant barrier. Because nano-emulsions are extremely sensitive to processing conditions, temperature, pH, and composition changes, scale-up and manufacturing reproducibility are still challenging. Furthermore, the commercial translation of nano-emulsion-based topical systems is hampered by a lack of clinical studies, standardized characterization techniques, long-term safety data, and regulatory guidelines. Large experimental datasets, computational know-how, and precise

prediction models are also necessary for AI-based optimization techniques, which may raise complexity and development costs.

10. CONCLUSION

Aloe vera's anti-inflammatory, antimicrobial, antioxidant, and wound-healing qualities make it a promising natural agent for topical medication delivery. Conventional formulations, however, have drawbacks like low skin penetration and poor stability. Studies have shown that by enhancing drug release and interaction with the skin barrier, nano-emulsion systems successfully improve Aloe vera's stability, bioavailability, and dermal penetration. Additionally, by enabling precise formulation parameter prediction, cutting down on experimental trials, and improving product performance, the incorporation of Artificial Intelligence (AI), including machine learning and predictive modeling techniques, has greatly improved formulation optimization.

Aloe vera, nano-emulsion technology, and AI-based optimization therefore constitute a promising and cutting-edge strategy for the creation of effective topical drug delivery systems, with significant potential for upcoming pharmaceutical and cosmetic applications.

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