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A REVIEW ON NANO HERBAL FORMULATION- FUTURISTIC APPLICATIONS

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ABSTRACT

Herbal medicines have gained widespread attention due to their therapeutic potential and perceived safety compared with synthetic drugs. However, their clinical application is often limited by challenges such as poor solubility, low bio availability, instability, and inadequate skin penetration when delivered through conventional dosage forms. In recent years, nanotechnology-based drug delivery systems have emerged as a promising approach to overcome these limitations. Nano formulations can enhance the topical and trans-dermal delivery of herbal bio active compounds by improving skin permeation, stability, controlled release, and therapeutic efficacy. This review presents a comprehensive overview of nano-enabled delivery systems developed for the topical administration of herbal medicines. Various nano formulation strategies—including liposomes, ethosomes, phytosomes, nano emulsions, transfersomes, niosomes, lipid nanoparticles, and polymeric nanocarriers—are discussed with respect to their formulation principles, advantages, and applications. Herbal medicines, favorite for their perceived effectiveness and lower cost compared to the conventional treatments, are gaining global popularity. However, many active compounds in these medicines have limitations, such as slow absorption, to a targeting, and instability in certain environments. Making the therapeutic application challenging, herbal medicine contains ingredients that work together to treat diseases. To improve patient adherence and reduce the need for frequent reasons, a gradual and systemic approach to drug delivery is necessary, requiring innovative methods . Additionally, the review highlights safety concerns, toxicity evaluation, and regulatory challenges associated with herbal nano formulations, emphasizing the need for standardized guidelines to ensure their safe clinical translation.

KEYWORDS: Tropical drug delivery, Herbal drug delivery, Nano formulation, Nano technology, Skin permeation.

INTRODUCTION

The use of herbal medicines has gained significant acceptance among the general population, largely due to the belief that these therapies are inherently safer and better tolerated than synthetic drugs. Herbal remedies are often associated with a reduced incidence of adverse effects and have been supported by an increasing volume of clinical evidence demonstrating their therapeutic value across diverse disease conditions. Nevertheless, herbal medicines present several limitations that restrict their widespread clinical application. Conventional allopathic treatments remain the preferred option for managing acute and life-threatening conditions due to their rapid and predictable therapeutic outcomes. Additionally, the unsupervised use of herbal products poses potential risks, including overdose resulting from non-standardized dosing, toxicity due to improper preparation, and adverse effects arising from incorrect plant identification or inappropriate selection of plant parts. The absence of stringent regulatory frameworks and quality control measures further complicates the safe and effective use of herbal medicines. These challenges highlight the need for advanced formulation strategies capable of improving the safety, efficacy, and reproducibility of herbal drug delivery, thereby facilitating their integration into modern therapeutic practice. Herbal nanoformulations

are classified mainly by their core material (inorganic, lipid, polymeric, carbon), structure (nanoparticles, nanomicelles, liposomes, dendrimers, nanogels, quantum dots, nanocages), or dimension (0D, 1D, 2D, 3D). Common types include lipid-based carriers (liposomes, solid lipid nanoparticles), polymeric systems (PLGA nanoparticles, nanogels), inorganic ones (metal NPs, quantum dots), and advanced structures like exosomes, all designed to enhance herbal drug solubility, stability, and targeted delivery.

CLASSIFICATION BY CARRIER TYPE
LIPID BASED
: Liposomes, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), Nanoemulsions, Phytosomes (lipid-compatible complexes).

POLYMERIC
Polymeric Nanoparticles (PNPs, nanospheres, nanocapsules), Polymeric Micelles, Dendrimers, Nanogels (cross-linked polymers).

INORGANIC
Metal nanoparticles (gold, silver), Quantum Dots (QDs), Mesoporous Silica Nanoparticles (MSNs).

CARBON BASED
Carbon nanotubes.

BIODERIVED
: Exosomes (natural lipid vesicles).

CLASSIFICATION BY STRUCTURE/DIMENSION

ZERO DIMENSION (0D)): Nanosized dots (e.g., quantum dots) where all dimensions are nanoscale.

ONE DIMENSION (1D): Nanofibers, nanorods, nanotubes.

TWO DIMENSION(2D): Nanosheets, nanofilms, nanolayers.

THREE DIMENSIONl (3D): Bulk nanomaterials like nanoparticles, nanocomposites, etc.. Classification by Formulation Strategy

Encapsulation: Drugs are enclosed within a carrier (e.g., nanocapsules, liposomes, micelles).
Dispersion: Drug dispersed as nanoparticles (e.g., nanocapsules, nanosuspensions). Complexation: Forming molecular complexes (e.g., phytosomes).

TYPES
Herbal nanoformulations use tiny carriers like liposomes, polymeric nanoparticles, solid lipid nanoparticles (SLNs), micelles, nanocapsules, and dendrimers to enhance herbal medicine efficacy by improving solubility, bioavailability, stability, and targeted delivery, overcoming limitations of traditional forms like extracts, and are classified mainly as lipid-based, polymer-based, or inorganic.

Types of herbal nano formulation
Lipid based/nano carriers
Liposomes/Nanoliposomes: Vesicles made of lipid bilayers, excellent for encapsulating both water-soluble and fat-soluble herbal compounds, improving stability and delivery. Solid Lipid Nanoparticles (SLNs) & Nanostructured Lipid Carriers (NLCs): Solid lipid matrices that offer controlled release and improved bioavailability, reducing toxicity. Nanoemulsions/Nanosuspensions: Tiny oil-in-water or water-in-oil droplets, increasing drug solubility and absorption.

Polymer based nano carriers
Polymeric Nanoparticles/Nanospheres: Solid colloidal particles made from biodegradable polymers (like PLGA) that protect the herbal drug and allow for sustained release. Nanocapsules: Vesicles with a polymeric shell, offering controlled and sustained release. Polymeric Micelles: Formed by amphiphilic block copolymers, ideal for poorly water-soluble herbal compounds.

Dendrimes: Highly branched, tree-like polymers that provide precise drug loading and targeted release.

Nanogels: Crosslinked polymer networks that swell in water, offering sustained release and biocompatibility.

Inorganic nano carriers
Metal nano particles: Used for specific interactions, diagnostics, and synergistic effects, though careful assessment is needed.

Quantum: Semiconductor nanocrystals used in imaging and sensing, sometimes incorporated with herbs.

Hybrid & nano particles
Phytosomes: Complexes of herbal extracts with phospholipids, improving absorption (e.g., Indena's technology).

Exosomes: Natural lipid vesicles from cells, promising for targeted delivery.

NANO FORMULATION FOR TOPICAL DELIVERY OF HERBAL MEDICINES
LIPOSOMES
Liposomes are spherical vesicles composed of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic compounds. They enhance skin hydration, improve drug penetration, and reduce irritation. Liposomes have been extensively investigated for delivering herbal extracts and phytoconstituents in dermatological applications.

ETHOSOMES

Ethosomes are lipid vesicles containing a high concentration of ethanol, which enhances skin permeability by fluidizing the stratum corneum lipids. Ethosomal formulations have demonstrated superior penetration compared to conventional liposomes and are effective carriers for herbal activities requiring deeper skin delivery.

PHTYOSOMES

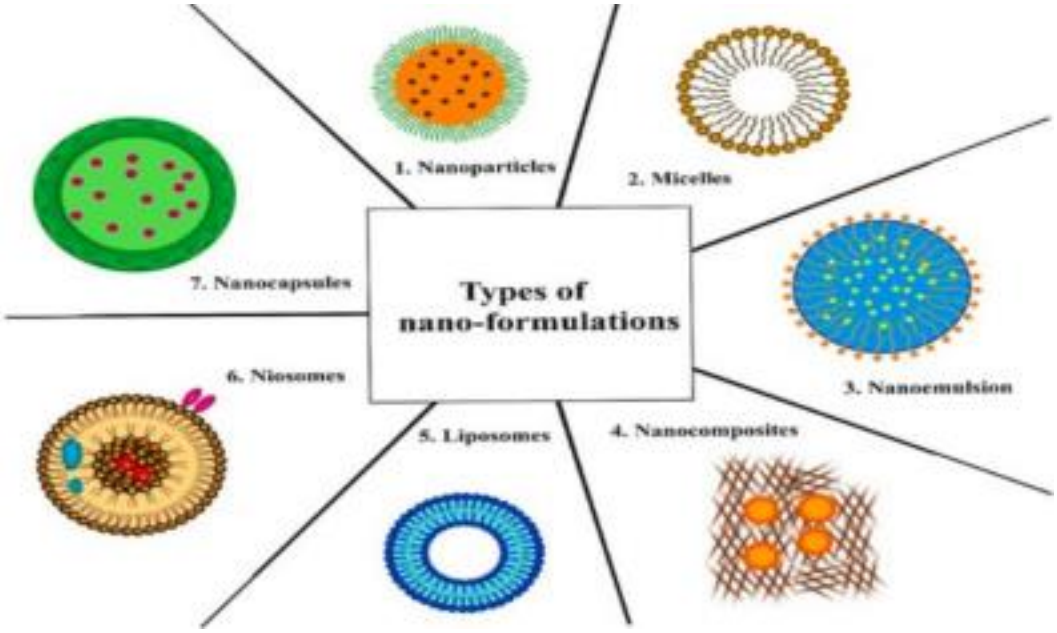
Phytosomes are complexes formed between phospholipids and phytochemicals, improving the solubility and bioavailability of poorly absorbed plant constituents. These systems enhance the stability and dermal absorption of herbal compounds, making them suitable for topical use.

NANO EMULSION

Nanoemulsions are thermodynamically stable systems with droplet sizes in the nanometer range. They offer high surface area, improved solubilization of lipophilic herbal compounds, and enhanced skin penetration. Their low viscosity and optical clarity make them attractive for cosmetic and pharmaceutical formulations.

TRANSFEROSOMES

Transfersomes are ultra-deformable vesicles capable of penetrating the skin through narrow pores without compromising vesicle integrity. Their flexibility allows efficient transdermal delivery of herbal bioactives.



ADVANTAGES

1. Enhanced drug delivery
2. Increased bio availability and solubility
3. Enhanced stability &protection
4. Targeted & control release
5. Reduced toxicity and side effects
6. Better permeability
7. Better cellular uptake
8. Enhancing synergistic pharmacological actions

DISADVANTAGES

1. High cost
2. Scaling challenges
3. Oxidative stress
4. Immune reactions

MECHANISM OF SKIN PENETRATION ENHANCEMENT

Herbal medicines are widely used in contemporary healthcare for managing various skin conditions, including dermatitis, psoriasis, skin infections, and acne. However, the skin acts as a strong protective barrier, limiting drug penetration. To overcome this limitation and enhance trans-dermal absorption, novel drug delivery systems have been developed.

Epidermis

The skin serves as a protective barrier against external physical, chemical, and biological threats and acts as the first line of defense against microorganisms and harmful substances. It also plays a vital role in regulating body temperature, maintaining fluid balance, synthesizing vitamin D, and functioning as a sensory organ for detecting pain, pressure, and temperature. Although skin thickness varies across the body, it is typically about 1.5 mm thick and consists of three primary layers.

The epidermis is composed of five layers—stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. It contains keratinocytes, melanocytes, macrophages, and tactile epithelial cells. Keratinocytes produce keratin, a fibrous protein that protects the skin and contributes significantly to the poor absorption of hydrophilic drugs due to the epidermal barrier.

Dermis

Beneath the epidermis lies the dermis, a connective tissue layer rich in collagen and elastic fibers. It contains sweat glands, hair follicles, connective tissue, and an extensive capillary network. The

The papillary surface of the dermis forms epidermal ridges, increasing skin surface area and playing a crucial role in drug absorption due to its vascularity.

Subcutaneous tissue or hypodermis

The subcutaneous tissue, or hypodermis, consists mainly of adipose and areolar tissue, nerve endings sensitive to pressure, and large blood vessels. Although not considered part of the skin, it connects the dermis to underlying muscles and bones, serves as a fat storage depot, provides insulation, and protects deeper tissues from physical injury.

SKIN ANATOMY AND PATHWAY DRUG TRANSPORT

Corneocytes, which are terminally differentiated keratinocytes, are arranged within highly organized lipid layers and play a crucial role in the skin's barrier function. The stratum basale represents the deepest viable layer of the epidermis, with a typical thickness of approximately 0.06–0.8 mm, and contains metabolically active cells. During the process of keratinization, these cells gradually migrate upward from the basal layer, undergo morphological changes, lose viability, and eventually form the stratum corneum.

The dermis lies beneath the epidermis and has a thickness ranging from 0.3 to 0.5 mm. It consists primarily of collagen and elastic fibers that provide structural support. This layer contains sweat glands, hair follicles, connective tissue, and an extensive capillary network. The papillary region of the dermis forms epidermal ridges, increasing the surface area of the skin. The presence of blood vessels within this layer is particularly significant when considering the skin as a potential site for drug absorption.

The subcutaneous tissue, also referred to as the hypodermis, constitutes the deepest layer and is composed mainly of adipose and areolar tissue. It contains large blood vessels and pressure sensitive nerve endings. Although not considered a true component of the skin, it connects the dermis to underlying muscles and bones. This layer functions as an energy reservoir, provides thermal insulation, and protects deeper tissues from mechanical injury.

Routes of Transdermal Drug Penetration

Drug molecules can penetrate the skin through three primary pathways, as described in previous studies and illustrated schematically in Figure 1.

Intercellular lipid pathway

The stratum corneum acts as the principal barrier to skin permeation. The intercellular spaces within this layer contain flexible, hydrophobic lipid domains arranged in a less ordered manner. These lipid regions facilitate the diffusion of lipophilic molecules across the skin. Hydrophilic compounds, in contrast, tend to diffuse laterally along these lipid interfaces and may utilize the spaces between corneocytes and their surrounding membranes.

Transcellular pathway

In this route, hydrophilic drugs traverse the skin by passing directly through corneocytes, following the path of least resistance. Transport occurs through small aqueous channels between adjacent corneocyte clusters. As these gaps expand, a greater quantity of the drug can permeate the skin. Follicular pathway.

Although initially regarded as a minor route due to the limited surface area occupied by hair follicles (approximately 0.1%), follicular penetration has gained increasing attention in recent years. Nanoparticles and drug molecules can enter hair follicles, either enhancing drug absorption or obstructing follicular openings to regulate chemical entry through this pathway.

Most nanoformulations exploit one or more of these penetration routes to achieve effective drug delivery across the skin.

Nano carriers

Nanocarriers are particulate systems with sizes typically ranging from 1 to 100 nm that encapsulate or transport active substances. They are widely employed as drug delivery vehicles for various administration routes, including transdermal delivery. In topical formulations, nanocarriers can enhance localized therapeutic effects, target deeper skin layers, and facilitate drug transport across the skin to achieve systemic therapeutic outcomes.

FACTORS

Factors Influencing Nano-Based Drug Delivery Systems

Particle Size, Particle Size Distribution, and Zeta Potential.

Drug release behavior, formulation stability, and cellular uptake are significantly influenced by the size and shape of nanoparticles. Various processing conditions, such as temperature and the viscosity of both organic and aqueous phases, play a crucial role in determining these characteristics (Reis et al., 2006; Maestrelli et al., 2009).

Zeta potential is an important parameter used to assess the stability of nanoparticle colloidal systems (Attama et al., 2007). It represents the electrokinetic potential at the shear plane, which is the interface where the compact layer of charged particles surrounding the nanoparticle meets the diffuse layer.

Particle size analysis can be performed using several

analytical techniques. One commonly used method is dynamic light scattering (DLS), which measures fluctuations in light scattering intensity caused by the random Brownian motion of particles suspended in a medium Microscopic techniques are widely employed to obtain real-time images of nanoparticles, with electron microscopy and atomic force microscopy being the primary methods used. Among electron microscopy techniques, transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are the most commonly applied. In TEM, a high-energy electron beam generated from an electron gun passes through the specimen mounted on a conductive grid, producing an image. The transmitted electrons are captured using imaging detectors such as fluorescence screens or CCD cameras. SEM, on the other hand, involves the interaction of the electron beam with the surface of the specimen, resulting in a three-dimensional image. For non conductive samples, coating the particle surface with materials such as platinum, gold, or graphite improves image clarity (Kim et al., 2018).

Atomic force microscopy (AFM) operates using a cantilever with a nanoscale tip that oscillates across the sample surface. Piezoelectric actuators regulate scanning in the X and Y directions, while oscillation along the Z-axis enables surface profiling. AFM provides qualitative information such as particle size, morphology, height, and surface texture of nanoparticles. Additionally, with suitable statistical analysis, quantitative data can also be obtained.

SURFACE PROPERTIES

The surface charge of nanoparticles significantly influences their interaction with cell membranes. Due to varying electrostatic interactions, nanoparticles generally exhibit a strong affinity for cellular membranes (Bernfield et al., 1999). Negatively charged sulphated proteoglycans and phosphatidylcholine present on cell surfaces play a crucial role in cellular migration, proliferation, and motility. As cell membranes contain large negatively charged domains, they tend to repel negatively charged nanoparticles. In contrast, positively charged nanoparticles markedly enhance cellular uptake. However, non-specific adsorption at positively charged sites and the formation of nanoparticle aggregates can also increase the uptake of negatively charged nanoparticles.

Nanoparticles can be engineered to possess specific surface properties that influence cellular uptake and intracellular distribution. By modifying surface charge, it is possible to direct nanoparticles toward particular intracellular targets such as mitochondria, lysosomes, or the cytoplasm.

A variety of techniques have been utilized for the formulationofnanophytomedicines. These methods include complex coacervation, co-precipitation, salting-out, nanoprecipitation, solvent emulsification–diffusion, supercritical fluid technology, and self-assembly techniques. Among these, the most widely used and extensively discussed methods are high-pressure homogenization (HPH), solvent emulsification–evaporation, and solvent emulsification–diffusion technique.

HIGH PRESSURE HOMOGENIZATION

High-pressure homogenization employs pressures ranging from 100 to 200 bars to force a coarse drug-containing emulsion through a narrow micro-sized gap using a microfluidizer. The high energy stream enters a disruption unit where particle size reduction occurs due to intense collision and cavitation forces, resulting in particles in the submicron range. The final characteristics of the product depend on parameters such as applied pressure, number of homogenization cycles, and drug concentration. This method offers several advantages, including good reproducibility, uniform particle size distribution, reduced processing time, and suitability for continuous production. In this technique, the melted lipid—maintained approximately 5–10 °C above its melting point—acts as a solvent medium for the drug during both hot and cold homogenization processes.

SOLVENT EMULSIFICATIONn–EVAPORATION TECHNIQUE

This technique is particularly advantageous for thermolabile drugs as it minimizes thermal stress during processing. However, the use of organic solvents may limit lipid solubility due to possible interactions with drug molecules. In this method, a water-immiscible organic solvent is used to dissolve the lipophilic material and hydrophobic drug. The resulting solution is emulsified into an aqueous phase using high-speed homogenization. Subsequently, the organic solvent is removed by evaporation under reduced pressure with continuous stirring at room temperature, leading to the formation of solid lipid nanoparticles.

SOLVENT EMULSIFICATION–DIFFUSION TECHNIQUE

This process begins with the mutual saturation of water and a partially water-miscible solvent. The drug and lipid are then dissolved in the solvent-saturated aqueous phase, followed by emulsification using mechanical stirring. To facilitate solvent diffusion into the continuous aqueous phase, water is added, resulting in nanoparticle formation due to lipid precipitation.

EXAMPLES OF HERBS USED IN HERBAL NANO FORMULATIONS

1. Nano curcumin
2. Nano ashwagandha
3. Nano ginger
4. Ginsing
5. Quercetin
6. Berberine
7. Triptolide
8. Ginkgo biloba

METHODS USED IN PREPARATION OF HERBAL NANO FORMULATIONS: Techniques Used for the Preparation of Nanopharmaceuticals:

1. Complex coacervation method

Complex coacervation is a spontaneous phase separation process occurring in colloidal systems due to interactions between two oppositely charged polyelectrolytes upon mixing in an aqueous medium.

The process mainly involves three steps

Formation of three immiscible chemical phases

Deposition of the liquid polymer coating onto the core material

Rigidization of the polymer coating.

2. Co precipitation method

The co-precipitation method is a modification of the complex coacervation technique and is used for the preparation of nanoscale core–shell particles. This method has been reported to provide good dispersion stability for poorly water-soluble drugs.

3. Salting out method

This method is based on the principle that the solubility of a non-electrolyte in water decreases upon the addition of an electrolyte. Acetone is commonly used as a water-miscible solvent due to its excellent solubilizing properties and its efficient separation from aqueous solutions by the salting-out technique. The diffusion of acetone from the droplets is a critical step; upon dilution with excess water, this diffusion generates interfacial turbulence, leading to polymer aggregation and nanoparticle formation.

4. Nano precipitation method

With increasing interest in biodegradable nanoparticles for drug delivery applications, extensive investigations have been conducted to understand nanoparticle formation using the solvent displacement method. This technique is based on the interfacial deposition of a polymer following the displacement of a semi-polar, water-miscible solvent from a lipophilic solution. This displacement reduces interfacial tension between the phases, increases surface area, and leads to the spontaneous formation of small organic solvent droplets without the need for mechanical stirring.

5. Solvent emulsification-diffusion method

This method involves the preparation of an oil-in-water (o/w) emulsion in which the oil phase, containing a polymer such as PLGA dissolved in an organic solvent, is emulsified with an aqueous phase containing a stabilizer using a high-shear mixer. Subsequent addition of water induces diffusion of the organic solvent, resulting in nanoparticle formation.

: Solvent emulsification–diffusion method

6. Supercritical fluid method

Supercritical fluids (SCFs) are substances used above their thermodynamic critical temperature and pressure, exhibiting properties of both liquids and gases. Carbon dioxide is the most commonly used SCF. These methods enable the production of particles with smooth surfaces, small particle size, narrow size distribution, and good flow properties. Techniques such as Rapid Expansion of Supercritical Solutions (RESS), Supercritical Anti-Solvent (SAS), and Particles from Gas Saturated Solutions (PGSS) are commonly employed to obtain fine, monodisperse powders.

7. High pressure homogenization method

In this method, lipids are subjected to high pressure (100–2000 bar), generating intense shear stress that disrupts particles into submicron or nanometer-sized ranges. High-pressure homogenization is a reliable and powerful technique for large-scale production of nanostructured lipid carriers, lipid drug conjugates, solid lipid nanoparticles (SLNs), and parenteral emulsions.

8. Self assembly method

Self-assembly is a physicochemical process in which pre-existing disordered components such as atoms or molecules spontaneously organize into ordered nanoscale structures through physical or chemical interactions, without any external intervention.

9. Emulsion solvent evaporation method

This method involves two main steps. First, the polymer solution is emulsified into an aqueous phase. Second, the organic solvent is evaporated, inducing polymer precipitation and formation of nanospheres. The nanoparticles are collected by ultracentrifugation, washed with distilled water to remove stabilizer residues or free drugs, and lyophilized for storage. A modified version, known as the high-pressure emulsification and solvent evaporation method, involves homogenization of the emulsion under high pressure followed by solvent removal through stirring. Particle size can be controlled by adjusting the stirring rate, dispersing agent type and concentration, phase viscosity, and temperature. However, this method is mainly applicable to lipophilic drugs and faces scale-up limitations. Commonly used polymers include PLA, PLGA, poly(caprolactone) (PCL), and poly(β-hydroxybutyrate) (PHB).[1]

10. Double emulsions and evaporation method

The conventional emulsion–solvent evaporation method exhibits poor entrapment efficiency for hydrophilic drugs. To overcome this limitation, the double emulsion technique is employed. This method involves the emulsification of an aqueous drug solution into an organic polymer solution under vigorous stirring to form a water-in-oil (w/o) emulsion. This primary emulsion is then added to a second aqueous phase under continuous stirring to form a water-in-oil-in-water (w/o/w) emulsion. The solvent is subsequently removed by evaporation, and the nanoparticles are isolated by high-speed centrifugation. The resulting nanoparticles must be thoroughly washed before lyophilization. Factors such as the amount of hydrophilic drug, stabilizer concentration,

polymer concentration, and aqueous phase volume significantly influence nanoparticle characteristics.

EVALUATION TESTS

Particle size measurement

The particle size of nanoemulsions was determined using light scattering techniques by measuring scattering intensity at a scattering angle of 90°. The viscosity of the dispersion was found to be 0.8872, and the count rate was recorded as 382.1 kcps.

Zeta potential measurement

The zeta potential of the prepared formulations was measured at 25 °C to evaluate the surface charge and stability of the nanoemulsions.

Thermodynamic stability studies

Nano formulation were subjected to various thermodynamic stability tests to assess their physical stability:

Heating–Cooling Cycle: Formulations were exposed to six heating–cooling cycles between 4 °C and 45 °C, with storage at each temperature for 48 hours. Samples were examined for signs of phase separation or precipitation.

Centrifugation Test: Formulations that remained stable after heating–cooling cycles were centrifuged at 3500 rpm for 30 minutes. Samples without phase separation were selected for further studies.

Viscosity determination

The viscosity of nanoemulsion formulations was measured using a Brookfield viscometer operated at 10 rpm for 3 minutes using spindle no. 62.

Drug content determination

An accurately measured 0.01 ml of the formulation was dissolved in 10 ml of dichloromethane to prepare the stock solution. One milliliter of this solution was further diluted with dichloromethane up to 10 ml. The absorbance was measured spectrophotometrically at 243 nm, and the drug content was calculated.

PH determination

The pH of the formulations was measured using a digital pH meter. The formulation was placed in a beaker, and the electrode was immersed into the sample. Readings were recorded, and the procedure was repeated three times for each formulation. The average value was reported as the pH.

In vitro drug release study

In-vitro permeation studies were carried out using a Franz diffusion cell fitted with a cellophane membrane. The membrane was placed between the donor and receiver compartments. About 150 mg of the nanoemulsion was placed in the donor compartment, while the receiver compartment contained 60 ml of phosphate buffer (pH 7.4). The receiver medium was continuously stirred at 100 rpm using a Teflon-coated magnetic stirrer, and the temperature was maintained at 37 ± 0.5 °C. Samples of 2 ml were withdrawn at predetermined intervals and replaced with fresh buffers. Drug content was analyzed using a UV spectrophotometer at 243 nm.

Evaluation parameters for Gels

Rhelogical study

The viscosity of the gel formulation was determined using a Brookfield viscometer at 10 rpm for 3 minutes using spindle no. 64.

PH determination

The pH of the gel was measured using a digital pH meter. Measurements were performed twice for each formulation, and the average value was recorded.

Evaluation parameters for nano formulation gels

Physical appearance

Colour: Evaluated against black and white backgrounds.

Odour: Assessed by mixing a small quantity of gel with water and smelling. Consistency: Checked by applying the formulation onto the skin.

Homogeneity: Evaluated visually for the presence of aggregates after storage. Greasiness: Determined by topical application on the skin.

Phase Separation: Examined visually for any separation.

Drug content determination

Ten grams of gel formulation were transferred into a volumetric flask containing 20 ml of dichloromethane and stirred for 30 minutes. The volume was made up to 100 ml and filtered. One milliliter of the filtrate was diluted to 10 ml with dichloromethane, and absorbance was measured at 243 nm. Drug content was then calculated.

PH determination

The pH of the nanoemulgel was determined using a digital pH meter. Measurements were performed three times for each formulation, and the average value was recorded.

SAFETY CONSIDERATIONS

When assessing novel topical herbal nanoformulations, a comprehensive safety evaluation is essential. Toxicity concerns may arise either from the nanosystem components or from the herbal drug itself. In addition to the active herbal constituents, nanoparticles may enter systemic circulation, where they could interact unpredictably with immune system cells or induce the generation of free radicals. There is also a risk of toxicity associated with commonly used nanomaterials, including metallic nanoparticles such as gold, silver, and titanium, as well as carbon-, silicon-, polymer-, and protein-based nanocomponents.

These nanomaterials may exhibit cytotoxic effects not only on skin cells such as keratinocytes and fibroblasts but also on immune cells and other organs Furthermore,

the potential environmental impact of nanocomponents requires careful consideration. Nanoparticles may enter soil and aquatic environments through leaching from formulations or during routine activities such as washing and bathing, thereby posing potential risks to plants, aquatic organisms, and human health Carbon-based nanoparticles and fullerenes have already been reported to exhibit ecotoxicological effects. As each nanoformulation consists of distinct nanocomponents, establishing uniform safety guidelines is challenging. Therefore, every formulation must be individually assessed based on its specific nanomaterial composition. The development of validated in vitro safety evaluation methods for each nanocomponent, along with comprehensive toxicity studies of nanoparticulate systems, is critically important.

CONCLUSION

The integration of nanotechnology with herbal medicine addresses key limitations of traditional formulations, including low absorption, poor stability, and non-targeted delivery. Nanoherbal systems such as liposomes, nanocapsules, and nanoemulsions enhance the therapeutic efficacy and bioavailability of herbal compounds by enabling precise and stable delivery to target sites. These advancements have shown significant potential in areas such as cancer treatment, where they exploit the enhanced permeability and retention (EPR) effect to facilitate drug accumulation in tumor tissues, and in dermatology, where they improve drug stability and controlled release. Additionally, nanoherbal formulations in the food industry enable more effective delivery of bioactive compounds, offering both nutritional and functional benefits. Despite these promising developments, challenges remain regarding safety and the understanding of long-term effects. Ongoing research is therefore essential to address concerns related to interactions between nanoherbal formulations and biological systems, as well as their environmental impact. In conclusion, nanoherbal technology represents a new era in healthcare and nutrition, offering the potential for safer and more effective therapeutic and nutritional solutions, provided that continued investigation ensures their responsible development and use.

This review highlights how the rapidly advancing field of nanomedicine and innovative drug delivery systems is addressing the pharmacological limitations associated with conventional herbal formulations. Nanoformulations not only help overcome challenges such as poor bioavailability and instability of phytochemical constituents but also enhance dermal and transdermal drug delivery by effectively bypassing the skin barrier. Although research in this area is still at an early stage, it demonstrates significant promise for topical nanoformulations to deliver herbal constituents in a targeted manner, thereby achieving both localized and systemic therapeutic effects.

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