A Review On: A Smart Herbal Nanotincture: A Polyherbal Nano – Herbosomes Approach for Targeted Dermatological Therapy

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***Abstract*—Herbal medicines have long been employed in dermatological therapy owing to their broad pharmacological activities, favorable safety profile, and patient acceptability. However, the clinical translation of conventional herbal formulations is often limited by poor skin penetration, low bioavailability, instability of phytoconstituents, and lack of site-specific targeting. Recent advances in nanotechnology have opened new avenues for overcoming these challenges through the development of smart nano-delivery systems. Among them, polyherbal nano-herbosomes, formulated as herbal nanotinctures, have emerged as a promising strategy for targeted dermatological applications.**

Nano-herbosomes are lipid-based vesicular systems in which bioactive phytoconstituents are complexed with phospholipids, resulting in enhanced physicochemical stability, improved skin permeation, and controlled release behavior. The integration of multiple herbal extracts in a polyherbal nano-herbosomal system enables synergistic therapeutic effects, addressing multifactorial skin disorders such as acne, psoriasis, eczema, wound infections, hyperpigmentation, and inflammatory dermatoses. Furthermore, smart nanotincture formulations offer advantages such as ease of application, improved patient compliance, enhanced transdermal absorption, and reduced systemic toxicity.

This review comprehensively discusses the concept, formulation strategies, preparation methods, characterization techniques, and mechanism of action of polyherbal nano-herbosomes for dermatological therapy. It also highlights recent research advances, therapeutic applications, safety considerations, regulatory perspectives, and future prospects of smart herbal nanotinctures in targeted skin delivery. The review emphasizes the potential of nano-herbosomal technology as a transformative approach in modern herbal dermatology, bridging traditional medicine with advanced nanopharmaceutical systems.

***Index Terms*—Smart herbal Nanotincture, Nano-herbosomes, Targeted dermatological therapy, Skin targeting.**

I. LITERATURE REVIEW

1.Renu tiruwa , 2016; Nanotechnology defined as a tiny science. Design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale is refers to nanotechnology. Nanotechnology by which we can achieve better therapeutic action, better bioavailability and better patient compliance. Several nanoformulations are successfully used for brain delivery which includes nanoparticles system (polymeric/solid lipid), liposomes, dendrimer's, nanoemulsions, nanosuspension and ligand mediated nanosystems .Nanoparticles are defined as particulate dispersions or solid particles drug carrier that may or may not be biodegradable.

2.MK Dewi, AY Chaerunisaa, M Muhaimin, IM Joni - 2022 - researchgate.net; Phytochemicals or secondary metabolites are substances produced by plants that have been shown to have many biological activities, providing a scientific basis for using herbs in traditional medicine. In addition, the use of herbs is considered to be safe and more economical compared to synthetic medicine. However, herbal medicines have disadvantages, such as having low solubility, stability, and bioavailability

3.Nataliia Hudz, Ewa Makowicz, Mariia Shanaida, Marietta Białoń, Izabela Jasicka-Misiak, Oksana

Yezerska, Liudmyla Svydenko, and Piotr Paweł Wieczorek 2020; Winter Savory (*Satureja montana* L.) has been used in traditional medicine and as a spice or natural food preservative in the Mediterranean region for centuries. In this paper, some technological and analytical aspects of the *S. montana* tinctures development and an evaluation of the essential oil composition are provided. The total phenolic and flavonoid contents and phenolic compounds profile analyzed spectrophotometrically and by high-performance thin-layer chromatography (HPTLC), respectively, were evaluated in the developed tinctures. The results showed that the tinctures prepared from the *S. Montana* herb by maceration or remaceration are rich in polyphenols, and there is an influence of the technological factors (particle size and extraction mode) on the total phenolic and flavonoid contents.

4.Dr. Abhishek Soni, Prof. Dr. Rajender Guleria, Shoaib*, Sanchit Thakur, Sahil and Nikhil Thakur 2024; Nanoparticles such as polymeric micelles or liposomes have been developed with progress in nanotechnology and have been applied to a wide range of fields such as drug/gene delivery. This chapter focuses on applications of these nanoparticles for targeted drug and gene delivery. More recently, nanoparticles have been used to improve immunity, adsorption of active oxygen, adjuvant material, virus neutralization, the blood-brain barrier (BBB) is one of the most essential protection mechanisms in the central nervous system (CNS). It selectively allows individual molecules such as small lipid-soluble molecules to pass through the capillary endothelial membrane while limiting the passage of pathogens or toxins.

5.Sharma Shubham*, Patidar Akshat and Chopra Reet 2023; Despite being widely adopted, traditional medication delivery technologies fall short when compared to more modern, cutting-edge drug delivery techniques in terms of effectiveness. Some medications have a range of optimal concentrations, and within this range, the greatest effect is obtained. If a drug's concentration is above or below this range, it may be harmful or have no therapeutic effect at all. On the other hand, a multidisciplinary approach to the delivery of medicines to the targets in the tissues is becoming increasingly necessary given the relatively modest improvement in the effectiveness of the treatment of severe diseases.

6.Sachin Saggar, Prince Ahad Mir, Nishant Kumar, Apporva Chawla, Jasreen Uppal, Shilpa, and Anmoldeep Kaur 2022;Since ancient times natural herbs were extensively used for the treatment and prevention of various ailments and in past few decades, due to an extensive research in traditional system of medicine various herbal medicines have been developed for the prevention and treatment of diseases, which are environmentally, organically safe and inexpensive.

7. Shaikh Samrin Mohammad Tufail*1, Kashtriya Jayshri Prakash2, Kazi Shifa Abdul Wadood.3 2025; A significant portion of active compounds in herbal medicines shows strong bioactivity in vitro, but much lower effectiveness in vivo due to their poor lipid solubility and unsuitable molecular size. These factors lead to limited absorption and low bioavailability of the active ingredients from herbal extracts. Herbosome technology helps overcome this challenge by improving the bioavailability of herbal extracts. Acting as a link between conventional and advanced drug delivery systems, herbosomes are complexes formed by natural active ingredients and phospholipids (such as phosphatidylcholine and phosphatidylserine), which enhance the absorption of herbal compounds.

AIM:

The developing a Smart Herbal Nanotincture using a Polyherbal Nanoherbosomes Approach for Targeted Dermatological Therapy is to create an advanced dermatological formulation that enhances the delivery, stability, and therapeutic effectiveness of herbal bioactive compounds.[24,25,26]

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II. OBJECTIVES

1. To formulate a stable polyherbal nanotincture using nano-herbosome technology that enhances the solubility, stability, and compatibility of phytoconstituents intended for dermatological use.

2 .To improve targeted skin delivery by enabling better penetration into deeper skin layers through nanoscale particle size, enhancing therapeutic action while minimizing systemic exposure.

3 .To evaluate encapsulation efficiency, particle size, and zeta potential to ensure optimal formulation characteristics necessary for effective cutaneous application.

4. To enhance the therapeutic effectiveness of herbal actives (such as anti-inflammatory, antioxidant, antimicrobial, and wound-healing activities) through synergistic action of the selected polyherbal ingredients.

5. To enable controlled and sustained release of phytoconstituents for prolonged skin interaction, reduced dosing frequency, and improved patient compliance.

6. To compare the performance of the nano-herbosome formulation with conventional herbal tinctures in terms of permeation, stability, efficacy, and safety.

7. To assess the dermatological safety profile of the formulation through suitable in vitro and/or in vivo studies, ensuring biocompatibility, non-irritancy, and suitability for long-term topical use.

8.To explore the potential of the smart nanotincture as an advanced herbal drug delivery platform for treating common dermatological conditions such as acne, eczema, psoriasis, infection-based issues, and oxidative damage-related skin disorders.[24,25,26]

III. NEED OF WORK

Despite the growing popularity of herbal medicines in dermatology, their clinical effectiveness is often limited due to challenges like poor skin penetration, rapid degradation, low bioavailability, and inconsistent therapeutic response. Conventional tinctures deliver active plant constituents superficially on the skin surface, resulting in insufficient absorption into deeper layers where most dermatological disorders originate a smart herbal nanotincture based on a polyherbal nano-herbosomes approach is needed to overcome these limitations and provide improved dermatological therapy. Nano-herbosomes form a phospholipid–herbal complex that enhances lipophilicity, membrane permeability, controlled release, and stability of phytoconstituents. Combining multiple herbs with complementary actions further delivers synergistic therapeutic benefits, such as improved anti-inflammatory, antioxidant, antimicrobial, and wound-healing activities.

Therefore, there is a need for designing a targeted and patient-friendly herbal formulation that can:

i. Enable deep skin penetration and localized delivery of actives.
ii. Protect phytochemicals from chemical and environmental degradation.
iii. Reduce dosing frequency by offering sustained release.
iv. Improve treatment effectiveness for chronic skin conditions.
v. Minimize adverse effects associated with synthetic drugs.

Such innovation can significantly enhance the clinical applicability of herbal dermatological treatments and contribute to the advancement of safe, effective, and smart herbal drug delivery systems.

IV. METHODOLOGY

1. Overview & experimental design:

Use a design-of-experiments (DoE) (e.g., factorial or Box–Behnken) to optimize key formulation variables: Phospholipid: herb ratio, drug loading, hydration volume, sonication time/energy.

Prepare control formulations: (A) conventional polyherbal tincture, (B) blank herbosomes, (C) marketed topical (if available).

2. Materials:

Herbal raw materials / extracts (standardized extracts or concentrates). Note % w/w of marker compounds.

Phospholipid: soya lecithin (phosphatidylcholine) or hydrogenated soybean phosphatidylcholine.

Solvents: ethanol or methanol (analytical grade) for extraction; chloroform / methanol mixture (analytical) for thin-film formation; phosphate buffer (pH 7.4) for hydration.

Edge activators / permeation enhancers (optional): propylene glycol, ethanol, oleic acid. Cryoprotectant for lyophilization: trehalose or mannitol.

Analytical reagents for characterization and bioassays.

3. Preparation of standardized polyherbal extracts (if not using ready extracts):

Dry and powder plant material (shade dry, grind).

Extraction: maceration or Soxhlet with ethanol (70%)

/ hydroalcoholic solvent for 24–48 h. Maintain 1:10 w/v solvent: plant ratio. Filter and concentrate under reduced pressure (rotary evaporator).
Standardize extracts by HPLC/UV for marker phytoconstituents (report mg/g extract).

4. Preparation of nano-herbosomes (Thin-film hydration method -typical, widely used): Complex formation (phytoconstituent–phospholipid complex) (optional step to improve complexation):
Dissolve phospholipid and herbal extract (containing known amount of marker) in chloroform: methanol (2:1). Molar ratio commonly 1:1 or 1:2 (phospholipid: active) — optimize by DoE.
Stir under nitrogen and evaporate solvent to form a thin film on flask wall using rotary evaporator (40–45 °C). Leave under vacuum 2 h to remove traces.
Hydration: Hydrate thin film with phosphate buffer (pH 7.4) or PBS containing small % ethanol/propylene glycol (helps solubilize extract). Typical hydration volume 10 mL per flask; rotate for 30–60 min at 40–45 °C to detach film forming multilamellar vesicles (MLVs). Size reduction: Sonicate (probe sonicator) on ice: pulses of 30 s ON / 30 s OFF for 5–10 min total energy (optimize). Alternatively extrude through polycarbonate membranes (400 → 200 → 100 nm) to obtain small unilamellar vesicles (SUVs).
Optional surface functionalization (to make "smart"):
Add targeting moieties (e.g., hyaluronic acid for CD44 targeting, peptides) by adsorption or covalent coupling. Incorporate thermoresponsive or pH-sensitive lipids if controlled-release triggers are desired.
Purification: Remove free (unentrapped) extract by dialysis (MWCO 12–14 kDa), ultracentrifugation, or gel filtration (Sephadex G-50).
Freeze-drying (optional): Add cryoprotectant (5–10% w/v trehalose), freeze at −80 °C and lyophilize for long- term storage.

5. Formulation of final nanotincture (topical vehicle)
Reconstitute herbosome powder (or use fresh dispersion) into a suitable topical vehicle: hydrogel (carbomer 940), oil-in-water cream, or ointment base. Typical loading: equivalent to 1–5% w/w total herbal extract (adjust per potency).
Ensure pH compatibility (skin target pH ~5.5–6). Add preservatives and antioxidant (e.g., Vitamin E) if required.

V. INTRODUCTION

NDDS is required for herbal medications:
Due to its potential for healing and lower side effects than contemporary synthetic pharmaceuticals, herbal medicines have been utilized for centuries all over the world and are still trusted today. Particularly promising are Ayurvedic treatments, which can be made even more effective by combining them with contemporary pharmacological technologies. Herbal remedies must, however, be created with a more methodical and scientific approach if they are to realize their full potential. Patient compliance may be lowered by the poor stability, low absorption, or frequent administration of many plant-based medications. By adding herbal components to innovative drug delivery systems (NDDS) like liposomes, phytosomes, or nanoparticles, these issues can be resolved. NDDS enhances the bioavailability, lessens toxicity, and more efficiently delivers the herbal active ingredients. And provide long-lasting therapeutic benefits with lower dosages. The development of such sophisticated delivery systems for herbal medicines has drawn more attention from academics in recent years. This strategy enables classic treatments remain relevant in the current pharmaceutical industry while also improving therapeutic outcomes. However, there are still a number of obstacles to overcome before herbal remedies can be completely included into contemporary medicine. These include the limitations of knowing how these substances are absorbed in the body, the absence of standardized procedures for biological and chemical testing, the difficulty of performing clinical studies on herbal medications, and the scarcity of models for assessing their toxicity and safety. Concerns about regulatory permission and the existence of potentially hazardous herbal compounds must also be carefully considered. [4]
Targeted Drug Delivery Systems:-
Targeted drug delivery is a cutting-edge technique for administering medications to patients in a way that increases the concentration of the drug delivered to the targeted body part of interest only (organs, tissues, or cells). This improves treatment efficacy by lowering drug administration side effects. [9]
Targeted drug delivery is a kind of smart drug delivery system which is miraculous in delivering the drug to a patient. This conventional drug delivery system is

done by the absorption of the drug across a biological membrane, whereas the targeted release system is that drug is released in a dosage form [5, 7]. Targeted drug delivery system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body; therefore avoiding any damage to the healthy tissue via the drug. The drug delivery system is highly integrated and requires various disciplines, such as chemists, biologist and engineers, to join forces to optimize this system. When implementing a targeted release system, the following design criteria for the system need to take into account: the drug properties, side effects of the drugs, the route taken for the delivery of the drug, the targeted site, and the disease [5, 6, 8].

Types of Targeted Drug Delivery:-

Passive Targeting

Active Targeting

Passive Targeting:-

It refers to the accumulation of drug or drug carrier system at a specific site such as anti-cancerous drug whose explanation may be attributed to physicochemical or pharmacological factors of the disease.

Drug release or drug actions are limited to selective sites within the body such as a tumour but not the liver.Other examples include targeting of antimalarial drugs for treatment of leishmiansis, brucellosis, and candiadsis [10].

Active targeting:-

Active targeting means a specific ligand receptor type interaction for intracellular localization which occurs only after blood circulation and extravasations. This active targeting approach can be further classified into three different levels of targeting which are -

First order targeting refers to restricted distribution of the drug carrier systems to the capillary bed of a predetermined target site, organ or tissue e.g. compartmental targeting in lymphatics, peritoneal cavity, plural cavity, cerebral ventricles and eyes, joints.

Second order targeting refers to selective delivery of drugs to specific cell types such as tumour cells and not to the normal cells e.g. selective drug delivery to kupffer cells in the liver. [10]

Herbal medicines' physicochemical and biological characteristics:-

Physicochemical Properties:

a) Solubility
b) Stability
c) Lipophilicity and molecular size
d) Partition Coefficient and pKA
e) Crystallinity and particle size
f) Compatibility and interactions

2. *Biological Characteristics:*

a) Pharmacological activity
b) Bioavailability and absorption
c) Metabolism and biotransformation
d) Toxicity and safety
e) Synergism and polyherbal effects
f) Shelf life and biological stability

BENEFITS AND DRAWBACKS OF NDDS IN HERBAL MEDICATIONS

BENEFITS:

1) Increased bioavailability
2) Better stability
3) Sustained and regulated release
4) Targeted medication administration
5) Lessen adverse effects and toxicity
6) Improved adherence to treatment

DRAWBACKS:

1) Complicated production
2) Insufficient uniformity
3) Insufficient clinical data
4) Regulatory and scale-up issues
5) Nanomaterials' potential for toxicity

CHALLENGES TO MODERNIZING AND IMPROVING HERBAL FORMULATIONS:

Despite widespread interest and a long history of traditional use, there are still a number of obstacles in the way of the marketing and acceptance of herbal medicines. Quality issues, manufacturing constraints, and uneven regulatory procedures frequently impede the development of herbal drugs, particularly in wealthy nations.

The following significant issues need to be resolved in order to genuinely update and globalize herbal medicine:

Problems with quality:

Making sure herbal materials are consistently of high

quality is one of the main challenges. The efficacy and purity of herbal medicines can be greatly diminished by issues like adulteration, incorrect plant species identification, inadequate collection techniques, and improper formulation techniques. It is challenging to provide consistent therapy results because of these issues. [11]

Processing and Harvesting Issues:

How plants are cultivated, harvested, and processed has a significant impact on the quality of herbal drugs. Subpar products are frequently the consequence of indiscriminate or unscientific harvesting, poor farming methods, inappropriate pre- and post-harvest management, and a lack of contemporary processing procedures. These problems are prevalent in many areas where customs are still followed without adequate standardization. [11]

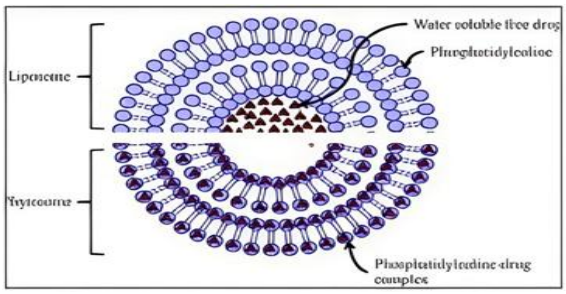
Quality Control Difficulties:

The herbal business continues to face significant challenges related to standardization. Inadequate quality control systems and poor adherence to Good Manufacturing Practices (GMP) are problems faced by many manufacturers. Regulatory rules are frequently poorly understood, particularly by small and medium-sized enterprises. As a result, the legitimacy of herbal medications is still impacted by inconsistent quality testing, documentation, and manufacturing procedures. [11]

APPROACHES IN NOVEL HERBAL DRUG DELIVERY SYSTEMS:

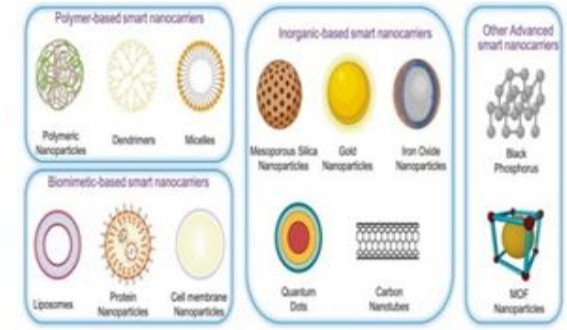
METHODS FOR DEVELOPING NEW HERBAL DRUGS PRESENTLY ACCESSIBLE IN THE MARKET:

HERBOSOMES:



Herbosomes are cutting-edge herbal delivery methods intended to increase the potency, absorption, and duration of plant-based medications. They are created when a phytoconstituent or herbal extract. (*Such as quercetin, curcumin, or silymarin)* is mixed with a phospholipid, like phosphatidylcholine. [12]For example, *curcumin, Silymarin, and Ginkgo biloba extract*

NANOPARTICLES:



Herbal medications are encapsulated in nanoparticles, which are colloidal carriers with particle sizes ranging from 1 to 1000 nm.

Goals: Enhanced bioavailability and solubility, extended circulation, and regulated release.

For instance, *green tea polyphenol nanoparticles and curcumin nanoparticles. [*13]

NANOEMULSIONS:

Nanoemulsions are emulsions that are thermodynamically stable and have droplet sizes smaller than 200 nm.

The goal is to improve the absorption of poorly soluble herbal oils and extracts while offering a quick beginning of action.

For instance, *neem oil and turmeric oil nanoemulsions*. [14]

MUCOADHESIVE SYSTEMS:

Formulations that enable regional or systemic distribution by adhering to mucosal surfaces (buccal, nasal, vaginal, and rectal).

Examples are *herbal nasal gels for allergic rhinitis* and *Aloe vera buccal films for oral ulcers.*

Solid lipid nanoparticles are solid lipid nanocarriers stabilized by surfactants. High stability, controlled release, and high compatibility are the goals.

For instance, quercetin and curcumin SLNs.

TINCTURE:-

Tincture is a liquid extract made by soaking plant or herbal components in ethanol or alcohol [24, 25].

CHARACTERISTICS OF TINCTURE:

Possess a potent scent and hue typical of the utilized herb.

Have no apparent contaminants or silt.
When stored correctly, retain stability and efficacy for at least two to five years.
Have a recognized amount of active phytoconstituents (for pharmaceutical or clinical application standards). [24, 25]
Tincture's pharmacological actions:

I. Quick absorption through mucosal membranes causes a rapid commencement of effect.
II. More stable than herbal extracts in water.
III. Effective transport of polar and non-polar phytoconstituents.
IV. Better bioavailability than decoctions or crude powders.[24,25,26]

ADVANTAGES OF TINCTURE:

i. Long shelf life: If stored correctly, it can last for years.
ii. Easy to use and portable: only a few drops are required.
iii. Rapid absorption, particularly sublingually (under the tongue).
iv. Preserves complete plant chemistry: A wide variety of active chemicals are extracted by alcohol.

DISADVANTAGES OF TINCTURE: -

i. Alcohol content: Not appropriate for young children, expectant mothers, or alcohol-sensitive individuals.
ii. Bitter taste: Strong or disagreeable flavors can be found in some tinctures.
iii. Dosage precision: Needs precise measurement; overdose may result in toxicity or irritation. If the ethanol concentration during extraction is too high, it is not the best option for heat-sensitive chemicals [14, 15, and 20].

NANOPARTICLES:
These are little particles that are invisible to the unaided eye. The range is 1–100 nm. [16, 20]

ROLES OF NANOPARTICLES IN HERBAL DELIVERY:
1. As Carriers of Drugs
2.Safe guarding Sensitive Substances
3. Focused Delivery
4. Sustained and Regulated Release
5. Topical and Skin Uses
6. Diagnostic and Environmental Applications

ADVANTAGES:-
i. Better Medication Stability and Solubility
ii. Regulated and Prolonged Release
iii.Targeted and Site-Specific Activity
iv.Fewer Adverse Effects
v.Increased Bioavailability [20]
vi. Improved Adherence by Patients

DISADVANTAGES:-
i.Potential Safety and Toxicity Issues
ii.Costly and Difficult to Produce
iii.Stability Problems
iv.Uncertain Body Behaviour
v.Regulatory Approval Difficulties
vi. Environmental Issues
vii.Insufficient Long-Term Research [16]

NANO- HERBOSOMES:
INTRODUCTION OF NANO-HERBOSOMES:
Traditional medicines and phytomedicine have been utilized extensively to sustain health in a variety of ways since ancient times. The creation of sophisticated herbal medicine delivery systems has accelerated in recent years with the goal of enhancing the efficient management of human illnesses. Globally, more and more people are using herbal medicines for self-care instead of traditional modern medicine. However, most of the bioactive ingredients in phytomedicine, such as flavonoids, glycosides, and phenolic, are water-soluble, which reduces their efficacy when applied topically or consumed orally. In order to overcome this difficulty, a number of methods have been developed to improve oral bioavailability, including the use of solubility and bioavailability enhancers, chemical structural modification, and the incorporation of lipophilic carriers. Therefore, to enhance the therapeutic potential of these substances, a great deal of study into herbal drug delivery systems is necessary. When compared to traditional herbal extracts, modern formulation technologies help increase the absorption of herbal products, leading to better therapeutic results. In particular, herbosome technology is a major breakthrough that ensures safety while providing increased bioavailability, better therapeutic benefits, and dependable delivery of active substances to target tissues.
"Some" suggests a structure resembling a cell, whereas

"herbo" relates to plants. The majority of physiologically active substances in plants are polar or soluble in water. However, the body frequently exhibits poor absorption of certain water-soluble phytoconstituents, such as flavonoids, tannins, and glycoside aglycones. This is mostly because of their large molecular size, which inhibits passive diffusion, or their low lipid solubility, which restricts their capacity to cross biological membranes that are rich in lipids, eventually leading to limited bioavailability. Herbosomes are a sophisticated herbal mixture that combines phospholipids with active chemicals sourced from plants. When compared to traditional herbal extracts or isolated components, this combination greatly increases their absorption and bioavailability in the body, resulting in increased therapeutic efficacy. Therefore, herbosome technology aids in overcoming the drawbacks of conventional herbal treatments. These cutting-edge, innovative Nano-carrier systems are intended to improve the stability, bioavailability, and targeted delivery of bioactive chemicals found in herbs.

Phospholipids and phytoconstituents combine to generate them (Survanta). [17, 18]

PROPERTIES OF HERBOSOMES:

Natural phytoconstituents and natural phospholipids, most frequently phosphatidylcholine generated from soy, combine to form herbosomes. Certain stoichiometric ratios of phytoconstituents and phospholipids react in an aprotic solvent to form these complexes. The active plant ingredient in this structure attaches itself to the phospholipid's polar head and becomes an essential component of the membrane. Compared to traditional herbal formulations, herbosomes enable better absorption and utilisation inside the body, resulting in more effective therapeutic effects. Herbosomes are an enhanced method of herbal medicine delivery. Pharmacokinetic investigations and human and animal experiments have both shown their increased bioavailability. Herbosomes are lipophilic substances with a certain melting point that exhibit intermediate solubility in lipids and high solubility in non-polar solvents.

Herbosomes, which are fundamentally different from liposomes in terms of composition and properties, create micelle-like structures when exposed to water. [19]

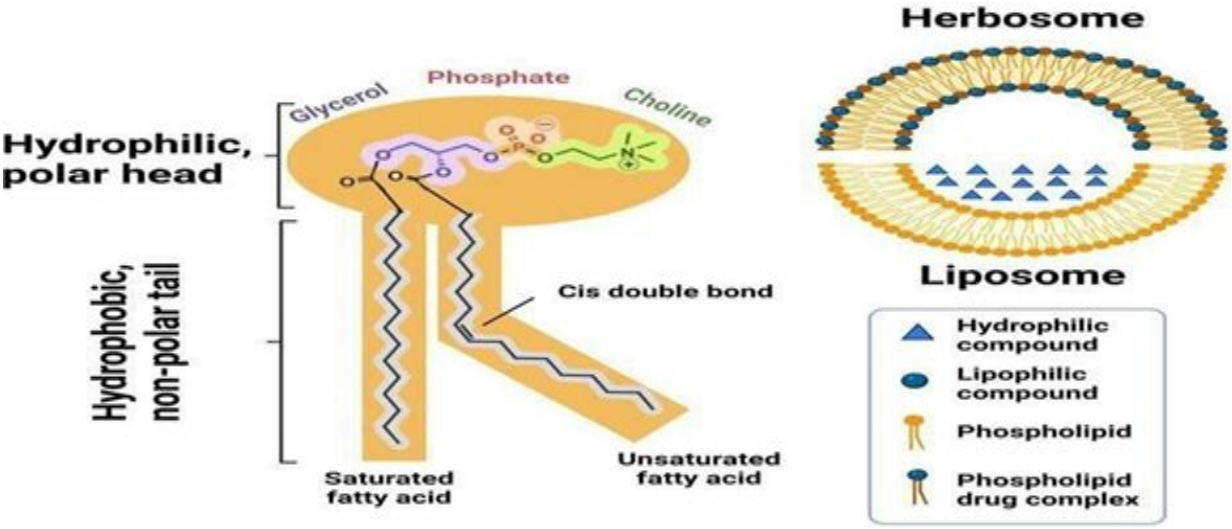
ADVANTAGES:-

i. Enhanced herbal active ingredient bioavailability and absorption.
ii. Improved targeted distribution to particular tissues (brain, liver, skin, etc.)
iii. Minimize adverse effects and the frequency of doses.[20]

APPLICATIONS OF NANO HERBOSOMES: -

i. Neurodefense
ii. Dermatology
iii. Anti-inflammatory and antioxidant

VI. PRINCIPLE OF HERBOSOME FORMATION



PROCEDURE FOR PREPARATION:

1. ANTI-SOLVENT PRECIPITATION TECHNIQUE:

A measured quantity of plant extract and phospholipid was placed in a 100 ml round-bottom flask and refluxed with 20 ml of dichloromethane at a temperature not exceeding 60°C for 2 hours.

After refluxing, the mixture was concentrated down to a volume of 5–10 ml

Then, 20 ml of hexane was slowly added to the concentrated mixture while stirring continuously, which led to the formation of a precipitate.

The precipitate was then filtered, collected, and stored in a desiccator overnight for drying.

Once dried, the precipitate was ground using a mortar and pestle and passed through a #100 mesh sieve to obtain a fine powder.

The final powdered complex was transferred to an amber-colored glass bottle and stored at room temperature.

2. ROTARY EVAPORATION TECHNIQUE:

TO CREATE A THIN FILM, REMOVE THE SOLVENT AT LOW PRESSURE.

The specific amount of plant material and phospholipid were dissolved in 30 ml of tetrahydrofuran in a rotary round bottom flask followed by stirring for 3 hours* at a temperature not exceeding 40°C.

Thin film of the sample was obtained to which n-hexane was added and continuously stirred using a magnetic stirrer.

Precipitate obtained was collected, placed in an amber-colored glass bottle and stored at room temperature.

3. SOLVENT EVAPORATION TECHNIQUE:-

The specific amount of plant material and phospholipids were taken into a 100 ml round bottom flask and refluxed with 20 ml of acetone at a temperature 50-60°C for 2h.

The mixture is concentrated to 5 10 ml to obtain the precipitate which was filtered and collected.

The dried precipitate phytosome complex was placed in an amber-colored glass bottle and stored at room temperature.

4. ETHER-INJECTION TECHNIQUE:-

In this method, the drug-lipid complex is first dissolved in an organic solvent, this solution is then gradually injected into a heated aqueous medium, which leads to the formation of vesicles.

The behavior of amphiphiles depends on their concentration.

At lower concentrations, amphiphiles exist in a monomeric state, while at higher concentrations, they can form various structures such as round, cylindrical, disc, cubic, or hexagonal shapes. [10]

TECHNIQUES FOR PREPARING HERBOSOMES:

Herbosomes are novel complexes that are created by reacting one mole of plant-derived components like flavolignans, either in their pure form or as part of a natural mixture, with three to two moles of natural or synthetic phospholipids, such as phosphatidylcholine, phosphatidylethanolamine, or phosphatidylserine, using aprotic solvents like dioxane or acetone. Once the herbosome complex is formed, it can be precipitated using a non-solvent like aliphilization (freeze-drying) or spray drying. Phospholipids and active plant compounds often have a molar ratio of 0.5 to 2.0 in these complexes, with a 1:1 ratio of phospholipids to flavonoids being the most widely favored for the best complex formation.

EVALUATION AND DESCRIPTION OF HERBOSOMES:

Herbosome formation is influenced by a number of factors, including physical size, membrane permeability, and proportion of entrapped solutes, drug release rate, chemical composition, and the amount and purity of the starting ingredients. Both biological and physical systems are impacted by herbosomes.

MICROSCOPIC AND ADDITIONAL METHODS

1. Visualization: Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) can be used to visualize herbosomes.

2. Vesicle Size and Zeta Potential:

Photon Correlation Spectroscopy (PCS) and Dynamic Light Scattering (DLS) using a computerized system can be used to determine the particle size and zeta potential.

3. Entrapment Efficiency:

The Ultracentrifugation method can be used to evaluate the effectiveness of drug entrapment in herbosomes. [17, 18]

WHY WE CHOOSE HERBOSOMES: -

Herbosomes—also known as phytosomes—are selected over other nano-delivery systems because they are specifically designed to overcome the limitations associated with herbal bioactive compounds. Most phytochemicals are poorly water-soluble, unstable, and have limited skin permeability, which reduces their therapeutic effectiveness in dermatological applications. While several nanocarriers such as liposomes, nanoemulsions, nanoparticles, and ethosomes have been explored for topical delivery, herbosomes offer unique advantages due to their phospholipid–phytoconstituent complex structure rather than simple entrapment. [15]

Unlike liposomes and other carriers where herbal molecules are merely encapsulated, herbosomes form a molecular-level complex between phospholipids and polar phytoconstituents (e.g., flavonoids, polyphenols, and alkaloids). This strong interaction improves:

Bioavailability

Membrane compatibility cutaneous permeation

Chemical stability

Additionally, the phospholipid used in herbosomes is similar to natural skin cell membranes, which facilitates better absorption and targeted delivery of actives into deeper skin layers. This makes them particularly effective for conditions requiring prolonged release and localized action, such as acne, inflammation, infections, and oxidative skin damage.

Herbosomes therefore provide a synergistic mechanism: the herbal extract offers therapeutic benefits, while the phospholipid enhances delivery and supports skin barrier repair—an advantage not seen in most other nanocarriers.Herbosomes are preferred over other nanocarriers because they address a critical pharmacokinetic challenge specific to herbal molecules: low biological affinity and poor membrane transport. Most phytochemicals are highly polar, hydrophilic, and incapable of efficiently crossing the lipophilic skin barrier, resulting in poor therapeutic efficiency when delivered through traditional or even some nanocarrier systems.Unlike nanoparticles, liposomes, or nanoemulsions where herbal actives remain physically entrapped or dispersed, herbosomes create a true molecular complex between the phytoconstituent and phosphatidylcholine via hydrogen bonding. This transforms poorly bioavailable compounds into amphiphilic complexes, meaning they become partly water-soluble and partly lipid-soluble. [17]

This amphiphilic behavior allows herbosomes to: Integrate directly into the skin's phospholipid matrix Cross cell membranes more efficiently.

Achieve higher dermal retention

Deliver the active constituent in its intact, bioactive form

Additionally, the phospholipid component of herbosomes plays a dual role:

✓ As a carrier improving delivery and permeability

✓ As a skin nutrient, helping restore barrier function and reducing irritation.

Thus, herbosomes are chosen not just for enhanced delivery, but because they fundamentally transform the pharmacological behavior of herbal actives, leading to greater therapeutic efficacy with lower dosage and better patient tolerability.

HERBAL EXCIPIENTS:

Excipients are essential non-active components that help achieve stability, bioavailability, and simplicity of administration in medication formulations. Their nature is typically semi-synthetic or synthetic. In recent years, there has been an increase in the usage of herbal excipients made from natural plant sources. Concerns about the safety, biocompatibility, and environmental sustainability of synthetic excipients have sparked an increase in interest. This tendency is also influenced by the pharmaceutical industry's desire for more natural and environmentally friendly formulations. These herbal components are perfect for use in contemporary herbal, nutraceutical, and pharmaceutical formulations because they are non-toxic, renewable, and environmentally friendly. For instance, starches from potatoes or maize can function as disintegrants or fillers, whereas gums from Acacia or Tragacanth can function as natural binders or emulsifiers.[27]

CLASSIFICATION OF HERBAL EXCIPIENTS:

1. Binders:-

Similar to "glue," binders aid in the adhesion of powdered substances so they can be compressed into a solid, stable tablet. Without a binder, the powder would be too loose and disintegrate throughout the tablet-making process.

Natural plant-based binders are frequently used in herbal preparations. These are typically sticky materials derived from plant seeds, leaves, or roots, such as gums, mucilage, or polysaccharides. In addition to being safe, mild, and organically compatible with the body, they aid in keeping the tablet together. [4]
For example, *aloe vera mucilage, pectin, and guar gum.*

2. Herbal disintegrants:
These are natural substances that are added to tablets to aid in their rapid breakdown after ingestion. These agents absorb liquids, expand, or crumble when the pill gets to the stomach, which breaks it up into tiny pieces. This facilitates the medication's quicker release, allowing the body to adequately absorb it.
Herbal disintegrants are safer than many synthetic alternatives because they are derived from plants and are typically non-toxic, biodegradable, and mild on the body. [6]
For instance, *starch from potatoes and maize*.

3. Fillers/Diluents:
When API is in smaller amounts, herbal fillers are added to boost the bulk medication formulation [6]. Their natural nature and minimal toxicity make them advantageous in this process.

4. Emulsifier:
By stabilizing emulsions, herbal emulsifiers stop the separation of the water and oil phases in liquid preparations. Because they are biodegradable and non-toxic, they are favored. [11]
For example, *lecithin, Sapiens, gum acacia, and tragacanth.*
Lubricants: During the tablet-making process, herb lubricants are used to prevent contamination and friction, which facilitates the extraction of tablets from dies and punches [13].
For example, *rice bran oil and castor oil*
.Flavouring and Sweetening ingredients: Herbal excipients for oral medication formulations are flavored and sweetened by natural ingredients [17]. Patients, especially those in pediatric formulations, find the drugs more pleasant thanks to these compounds [18].
For instance, *menthol and stevia.*
Coating Agents: These biodegradable, herbal-based coatings are added to the surface of tablets or capsules to shield the medication, cover up offensive flavors, and improve the dosage form's appearance. For example, *chitosan and shellac.*

ADVANTAGES HERBAL EXCIPIENT: -

- Biodegradable: All living things naturally manufacture these polymers. They don't have any negative consequences on people or the environment.
- Non-toxic and biocompatible chemically speaking, almost all of these plant components are made up of repeating monosaccharide units and are carbs. They are hence non-toxic.
- Economic: Compared to synthetic materials, they are less expensive and require less production.
- Safe and free of side effects: Because they come from a natural source, they are safe and free of side effects.
- Easy availability: Because they are used in numerous industries, they are produced in many nations.[27]
-

DISADVANTAGES HERBAL EXCIPIENT:-

- Microbial contamination: Because they are exposed to the outside world during manufacture, there is a possibility of microbial contamination.
- Variation: Natural polymer production depends on the environment and a number of physical parameters, whereas synthetic manufacturing is a regulated process with set amounts of materials.
- The unregulated rate of hydration: The percentage of chemical constituents in a given substance may change due to variations in the collection of natural materials at different times, as well as variations in geography, species, and climate conditions.
- Slow Process: The production pace cannot be altered because it depends on the environment and numerous other factors. Therefore, the manufacturing of natural polymers is slow.
- Heavy metal contamination: Herbal excipients are frequently linked to the possibility of heavy metal contamination.[27]

DIFFERENCE BETWEEN HERBAL EXCIPIENTS AND SYNTHETIC EXCIPIENTS:[27]

Point of Difference	Herbal Excipients	Synthetic Excipients
Source	Come from plants — leaves, seeds, gums, fruits, bark.	Made in labs and industries through chemical processes.
How body accepts them	Usually, well-tolerated because they are natural.	May sometimes cause irritation or allergies.
Safety	Generally safer and milder with fewer side effects.	May contain chemical residues that need strict control.
Stability	May spoil sooner and need preservatives.	More stable, longer shelf life.
Ease of modification	Harder to chemically modify without losing natural quality.	Easy to tailor and customize properties as needed.
Cost	Often cheaper and easily available locally.	Can be more expensive due to manufacturing steps.
Effectiveness in dosage forms	Multifunctional (same material can act as binder, thickener, stabilizer).	Highly efficient and designed for specific roles.

APPLICATIONS HERBAL EXCIPIENT:

I. Binders: Keep substances in granules and tablets together. Acacia gum and maize starch are two examples.
II. Disintegrants: aid in the breakdown of pills following administration. Agar and guar gum are two examples.
III. Thickening agents: Make liquid compositions more viscous. Tragacanth gum and xanthan gum are two examples.
IV. Suspending agents: Maintain the suspension of solid particles in a liquid.
V. Coating agents: Arrange tablets in a film. Gelatin and natural polymers are two examples.
VI. Sustaining agents: Manage the drug's release rate over time. Guar gum and xanthan gum are two examples.
VII. Fillers/Diluents: Give a formulation more volume, especially if the active ingredient is present in trace amounts. Plant cellulose is one example.
VIII. Gelling agents: They create gels and are frequently utilized in topical medicines such as suppositories.
IX. Protective agents: Keep active substances safe.
X. Flavoring and coloring agents: Improve the taste and look of medications.[27]

NANOTINCTURE:

A nanotincture is a sophisticated herbal formulation that creates nanoscale herbal medication delivery systems by fusing contemporary nanotechnology with the conventional tincture extraction method.

WHY DO WE NEED NANOTINCTURES?

Despite being widely utilized in herbal therapy, traditional tinctures have a number of significant disadvantages:

i. A lot of phytochemicals dissolve poorly in alcohol or water.
ii. When exposed to air or light, they may deteriorate rapidly.
iii. The body's actual absorption capacity is limited by large particle sizes.

Nanotinctures overcome all these by:

i. Reducing particle size → increasing surface area for absorption, nanotinctures get around all of them.
ii. Encapsulating delicate substances to prevent deterioration.
iii. Permitting regulated release → preserving effects that last longer.

PROPERTIES OF NANOTINCTURES:-

i. Particle size: Usually less than 100 nm.
ii. Liquid with a clear or somewhat translucent appearance.
iii. Solvent system: water base, glycerine, or alcohol.
iv. Type of nanocarrier: phospholipid, polymer, or lipid.

APPLICATIONS OF NANOTINCTURE:-

• *Dermatological therapy:-*

Nanotinctures can be used in dermatological therapy to deliver herbal active ingredients like green tea, curcumin, aloe vera, or neem into the deeper layers of the skin. Utilized in formulations for wound healing, anti- inflammatory, anti-aging, and anti-acne.

• *Systemic drug delivery:*

Oral nanotinctures of herbs, such as ginkgo biloba or *ashwagandha*, increase therapeutic action and improve absorption.

• *Antioxidant and immunomodulatory therapy:*

Flavonoid or polyphenol-rich nanotinctures enhance immunity, combat oxidative stress, and promote general well-being.

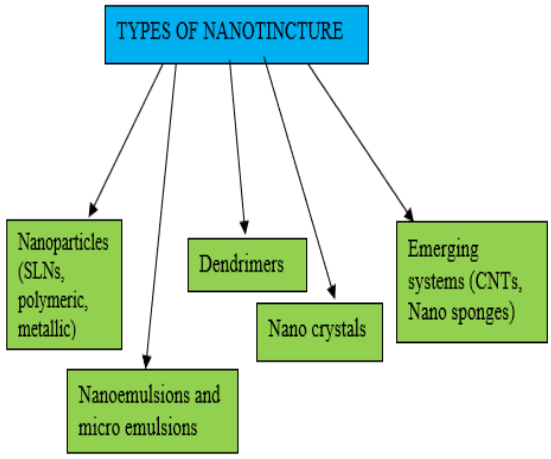
• *Neuroprotective and adaptogenic effects:*

Herbal nanotinctures that can pass through the blood–brain barrier, such as *Bacopa monnieri* or *Withania somnifera*, can improve cognition and reduce stress.

Smart Herbal Nanotinctures:

i. Target particular tissues or receptors
ii. Deliver several herbal actives in a synergistic manner
iii. May be made to be delivered locally and under control (particularly in skin therapy).[14,15,20]

TYPES OF NANO-TINCTURES:-



MATERIALS AND METHOD OF PREPARATION OF NANOTINCTURE (*NIGELLA SATIVA*)

Materials: Nigella Sativa seeds powder, Ethanol (70%),

STEP 1:

Nigella Sativa extract preparation –

1. Weigh 10–20 grams of Nigella sativa seed powder.
2. Pour the powder into a conical flask with a cork.
3. Pour in 100 milliliters of 70% ethanol (1:10 w/v).
4. Shake or macerate the mixture at room temperature with sporadic shaking for seven days. (Soxhlet extraction for four to six hours)
5. Use Wattman filter paper to filter the extract.
6. To eliminate extra solvent, concentrate the filtrate using a rotary evaporator at ≤400C.
7. The resulting hydroalcoholic tincture acts as a foundation for the creation of nanoparticles.

STEP 2:

Nanoparticle production preparation:

There are two popular methods for creating nanoparticles:

1. Preparing the antisolvent:

i. Use the extract solution from Nigella sativa tincture as the organic phase.
ii. Create an aqueous phase with stabilizer (such as PVP-0.5%) and surfactant (such as Tween 80-0.5-1%).
iii. Add the organic phase dropwise to the aqueous phase while stirring magnetically for 30 to 45 minutes, or until a fine dispersion is formed.
iv. Use ultrasonication to lower the mixture's particle size to the nanoscale (100–200 nm).
v. Keep the final Nigella Sativa nanotincture at 40°C in an amber glass vial.

2. Ultrasonication:

i. Combine a tiny amount of surfactant and co-surfactant with Nigella Sativa tincture (oil phase).
ii. Add mixture to water while homogenizing at a high speed (10,000 rpm) for 10 to 15 minutes.
iii. Use probe ultrasonication to shrink droplet size to the nanoscale.
iv. The outcome is a tincture that has been nanoemulsified.

STEP 3:

Filtering and Storage:

Use a 0.22um membrane to filter the finer formulation.

Use a filter to get rid of microbiological pollutants or big particles.

Keep in sterilized amber glass bottles between 4-8^{0}C.

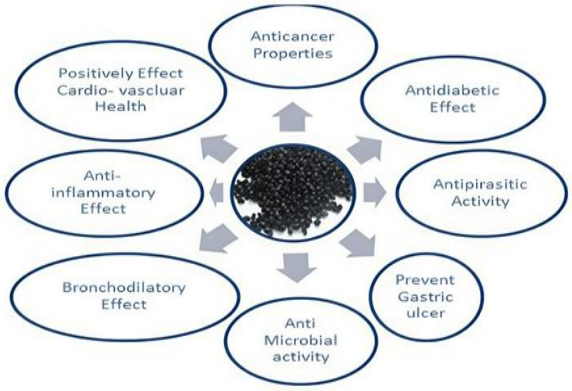


Fig: Health benefits of Nigella sativa

EVALUATION PARAMETERS OF NANOTINCTURE *(NIGELLA SATIVA L.)*:

1. Organoleptic Assessment:
i. Appearance and Colour: Because of thymoquinone and other phytochemicals, *Nigella sativa* typically has a brownish to dark brown colour.
ii.Odor and Clarity: The distinctive herbal scent of *Nigella sativa* is present in a nanotincture. To make sure there isn't any unexpected precipitation or phase separation, we assess clarity.

2. Ph measurement:
5–6.5 is the range for skin compatibility.

3. Viscosity:
Brookfield Viscometer is used to measure viscosity

Particle Size Analysis:
We determine the size of the nanoparticles using tools such as Dynamic Light Scattering (DLS). A stable nanotincture should be between 20 and 200 nm in size.
 # Smaller particles are beneficial:
i. Boost absorption.
ii. Increase stability.
iii. Boost the effectiveness of treatment.

4. Zeta Potential:
Zeta potential provides information on the surface charge of nanoparticles. It aids in stability prediction.
Particles repel one another when the value is high, either positive or negative (e.g., ±20 to ±40 mV).
Particle repel one another
There is less chance of the formulation clumping together.

5. Polydispersity Index (PDI):
0.3-0.6: Moderate uniformity; <0.3: Uniform formulation
0.7: Extremely polydisperse and unstable

6. Entrapment Efficiency (EE %):
Calculates the percentage of active phytoconstituents that are contained within nanoparticles. EE% is calculated by dividing the total drug added by the amount of drug encapsulated. Bioavailability and therapeutic results are enhanced by higher EE%.

$$EE\ \% = (\text{Amount of drug encapsulated} / \text{Total drug added}) \times 100$$

7. Test for Microbial Limit:
Crucial for long-term storage:
Total number of viable
Tests for preservative efficacy may also be carried out on pathogens (E. coli, S. aureus, P. aeruginosa, fungi).

8. Surface Features:
Using TEM/SEM:
Form (polygonal, spherical) Smoothness of the surface
The aggregation pattern verifies the integrity of the nanostructure.

9. In vitro and in vivo Biological Processes:
Depending on the reason:
Reduced inflammation Antibacterial
Healing wounds
Avoid acne Oxidant-rich
When compared to traditional tinctures, nanotinctures should demonstrate improvement.

10. Research on Bio adhesion and Skin Penetration:
For dermatological nanotinctures in particular:
Skin penetration ex vivo confocal imaging
The method of tape-stripping
Determines the nanoparticles' depth of penetration and

retention.

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11. Assessment of Phytochemicals:

Phenolic content overall (TPC) Flavonoids in total Terpenoids, tannins, alkaloids, and saponins (both quantitative and qualitative)

LC-MS and HPLC profiling

Guarantees that following Nano-processing, herbal components are still active.

MECHANISM OF ACTION OF SMART HERBAL NANOTINCTURE: -

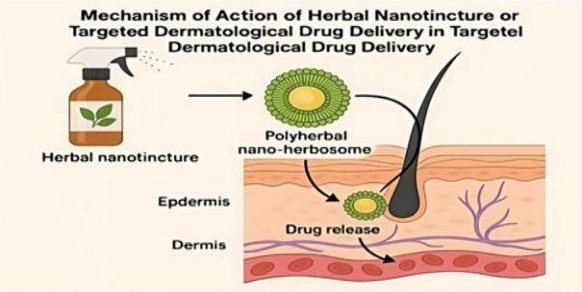

FIG: mechanism of action of smart herbal nanotincture

VII. CONCLUSION

The development of a Smart Herbal Nanotincture through a polyherbal nano-herbosomes approach offers a promising strategy for targeted dermatological drug delivery. By encapsulating multiple herbal bioactive into stable nanoscale herbosomes, this system enhances solubility, permeability, stability, and controlled release of phytoconstituents across skin layers. The improved zeta potential, particle size distribution, and pharmacokinetic profile demonstrate better therapeutic efficacy compared to conventional herbal formulations. This novel approach not only ensures localized action with minimal systemic side effects but also maximizes the synergistic benefits of multiple herbs, making it a sustainable and effective platform for managing dermatological disorders.

The nano-herbosomal formulation exhibited desirable physicochemical characteristics, including nanoscale particle size, uniform morphology, and favorable zeta potential values, confirming both stability and efficiency. High entrapment efficiency and sustained drug release profiles ensured the controlled delivery of multiple phytoconstituents. In vitro antioxidant and antimicrobial studies demonstrated enhanced activity compared to crude herbal extracts, indicating synergistic benefits of the polyherbal combination. Moreover, ex vivo skin permeation studies confirmed improved penetration and retention of bioactive in dermal tissues, validating its potential as a targeted topical therapy.[20,26]

VIII. DISCUSSION

Smart herbal nanotinctures represent a modern fusion of traditional herbal medicine with nanotechnology to improve dermatological treatment. In this approach, multiple herbal extracts are incorporated into Nano-herbosomes, which are complexes of phytoconstituents and phospholipids. These Nano sized carriers mimic the structure of skin lipids, allowing them to merge easily with skin layers and deliver herbal actives more effectively.

The polyherbal combination provides synergistic therapeutic effects such as anti-inflammatory, antioxidant, antimicrobial, and wound-healing benefits—while the nanoscale size enhances penetration through the stratum corneum, which is usually a major barrier for conventional herbal formulations. Nano-herbosomes also protect sensitive plant compounds from degradation, improve their solubility, and enable controlled and targeted release at the diseased skin site.

Overall, smart herbal nanotinctures offer a promising strategy for dermatology by overcoming the limitations of traditional tinctures and ensuring higher bioavailability, deeper skin delivery, and enhanced therapeutic efficiency, especially for chronic skin conditions like acne, eczema, psoriasis, and hyperpigmentation.

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