

## REVIEW ARTICLE

# Enhancement of Permeation for Skin Rejuvenation using Herbal Drugs

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### ABSTRACT

*The skin, the largest organ of the human body, serves as a multifunctional barrier that protects against physical, chemical, and microbial insults while maintaining homeostasis through thermoregulation, hydration, and sensory perception. Despite these essential roles, the skin's barrier—particularly the stratum corneum—remains a significant obstacle to the effective delivery of therapeutic agents. This limitation is especially relevant in skin rejuvenation, where there is a rising demand for safe and effective treatments to counteract premature aging caused by environmental stressors, ultraviolet radiation, and lifestyle-related damage. Conventional approaches such as synthetic topical creams, chemical peels, and laser therapies provide only partial benefits and are often associated with adverse effects or limited long-term efficacy. Consequently, there has been a growing shift toward herbal drugs and phytoconstituents, which are valued for their natural origin, safety, and diverse pharmacological properties, including antioxidant, anti-inflammatory, collagen-stimulating, and photoprotective effects. To enhance their therapeutic potential, recent research has focused on innovative permeation strategies. Nanoformulations such as liposomes, niosomes, nanoemulsions, and solid lipid nanoparticles improve the stability, bioavailability, and controlled release of herbal actives. Chemical penetration enhancers, including natural oils and surfactants, modify the lipid structure of the stratum corneum to facilitate drug diffusion. Additionally, advanced physical methods like microneedles, iontophoresis, and sonophoresis provide minimally invasive options for deeper penetration without compromising safety. This review highlights the mechanisms, benefits, limitations, and future perspectives of these strategies, emphasizing the integration of herbal therapeutics with modern delivery technologies to develop novel, safe, and scientifically validated skin rejuvenation formulations.*

**Keywords:** Skin barrier, Transdermal delivery, Skin rejuvenation, Herbal drugs, Phytoconstituents

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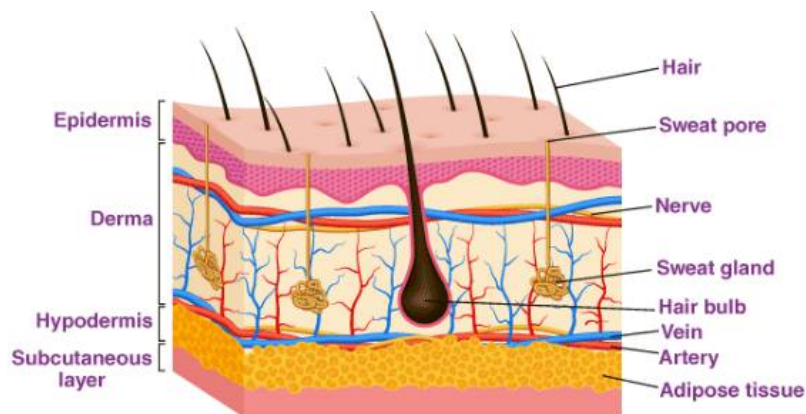
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### INTRODUCTION

The skin is the largest organ of the human body, covering an average surface area of 1.5–2.0 m<sup>2</sup> in adults and accounting for nearly 15–20% of total body weight. It performs multiple functions essential for survival, including acting as a mechanical and chemical barrier, regulating water and electrolyte balance, providing thermoregulation, synthesizing vitamin D, and serving as a sensory interface with the external environment [1]. Structurally, the skin is composed of three major layers: the epidermis, dermis, and hypodermis. The outermost epidermis, particularly the stratum corneum, is primarily responsible for barrier function, restricting the entry of external agents and preventing transepidermal water loss. The dermis provides tensile strength and elasticity through its collagen and elastin fibers, while the hypodermis serves as insulation and energy storage [2].

With advancing age, the skin undergoes intrinsic aging (genetically programmed changes) and extrinsic aging (environmentally induced changes, primarily due to ultraviolet radiation, pollution, and lifestyle factors). These processes result in reduced collagen synthesis, fragmentation of elastin, increased activity of matrix metalloproteinases (MMPs), and decreased hydration levels, leading to visible signs such as wrinkles, sagging, pigmentation, and loss of firmness [3]. Furthermore, oxidative stress plays a central

role in accelerating skin aging by promoting cellular damage, lipid peroxidation, and mitochondrial dysfunction [4].



**Figure No. 1 Diagram of Skin (Labelled Structure)**

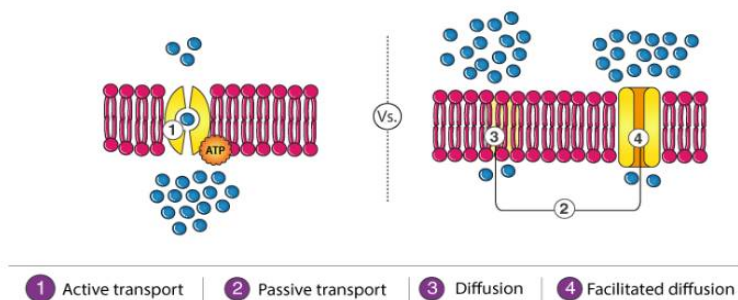
Although a wide range of synthetic and procedural interventions—including retinoids, chemical peels, botulinum toxin, dermal fillers, and laser therapies—are available for skin rejuvenation, they are often associated with drawbacks such as high costs, adverse effects, limited patient compliance, and concerns regarding long-term safety [5]. These challenges have fueled growing interest in herbal drugs and natural phytoconstituents as safer, sustainable, and cost-effective alternatives. Herbal agents possess diverse pharmacological activities such as antioxidant, anti-inflammatory, collagen-stimulating, depigmenting, and photoprotective effects, which make them highly suitable for incorporation into cosmeceutical formulations [6].

In recent years, there has been a global surge in consumer demand for herbal cosmetics and natural formulations, driven by a preference for products perceived as safe, eco-friendly, and ethically sourced. According to market surveys, the herbal skincare industry has shown significant growth, with projections estimating it to surpass USD 150 billion by 2030, largely fueled by rising awareness of skin health, aging concerns, and increasing preference for chemical-free formulations [7]. Particularly, ingredients such as aloe vera, turmeric, green tea, centella, ginseng, and bakuchiol have gained widespread popularity as natural anti-aging and skin-rejuvenating agents [8]. This trend is further supported by regulatory encouragement toward green chemistry and sustainability in cosmetic industries worldwide.

Despite their promise, the clinical utility of herbal drugs in skin rejuvenation remains limited due to their poor permeability across the stratum corneum, low bioavailability, instability, and poor solubility. These challenges necessitate innovative formulation approaches, including nanoformulations, penetration enhancers, and advanced physical methods, to maximize the therapeutic potential of phytoconstituents in skin care applications [9].

Thus, the current review emphasizes the physiological barriers of skin, explores the mechanisms of permeation, and provides an in-depth discussion on herbal drugs and advanced formulation strategies for effective skin rejuvenation. By integrating traditional herbal knowledge with modern transdermal delivery systems, it is possible to develop safe, effective, and patient-friendly therapeutic options that meet the rising global demand for natural skincare solutions.

#### SKIN PERMEATION MECHANISMS:



**Figure no. 2 Permeation Mechanisms**

The skin, while serving as the first line of defense against environmental aggressors, simultaneously acts as a formidable barrier to the entry of xenobiotics and therapeutic agents. The **stratum corneum**, the outermost layer of the epidermis, is the principal component that limits penetration. It has been widely

described as a "brick and mortar" structure, where the corneocytes (bricks) are embedded in an intercellular lipid matrix (mortar). This lipid matrix, composed primarily of ceramides, cholesterol, and free fatty acids, provides both hydrophobicity and rigidity, rendering the skin relatively impermeable to most molecules [7].

For topical and transdermal drug delivery systems, understanding the precise mechanisms by which molecules traverse this barrier is critical for the rational design of formulations. The major recognized pathways include passive diffusion, active transport, and vesicular transport, each influenced by the physicochemical properties of the molecule and the physiological state of the skin.

### **PASSIVE DIFFUSION**

Passive diffusion is the dominant and most extensively studied pathway of skin permeation. It relies on Fick's law of diffusion, which states that the rate of diffusion is directly proportional to the concentration gradient across the barrier and inversely proportional to its thickness [8]. In the context of skin, drug molecules move from an area of high concentration in the formulation to an area of lower concentration in the viable epidermis and dermis.

The ability of a molecule to diffuse passively depends on several physicochemical parameters:

- **Molecular Weight:** Molecules with a molecular weight below 500 Daltons permeate the skin more effectively, which is often referred to as the "500 Dalton rule." Larger molecules struggle to pass through the tightly packed stratum corneum lipids [10].
- **Lipophilicity:** Moderately lipophilic compounds (log P between 1 and 3) are best suited for diffusion, as they can partition into the lipid bilayers while still maintaining solubility in the aqueous environment of deeper skin layers [11].
- **Ionization:** Unionized molecules penetrate more readily than ionized ones, as charged species face resistance from the hydrophobic lipid matrix [12].
- **Solubility:** Adequate solubility in both lipid and aqueous phases is necessary for efficient permeation, making amphiphilic molecules favorable candidates.

Classic examples of drugs that rely on passive diffusion include hydrocortisone, nicotine, and estradiol. In herbal medicine, small lipophilic phytoconstituents such as terpenoids, flavonoids, and essential oil components are known to diffuse effectively through this pathway [13].

### **ACTIVE TRANSPORT**

Unlike passive diffusion, active transport involves the movement of molecules across the skin barrier against their concentration gradient, necessitating energy input in the form of adenosine triphosphate (ATP). This process is mediated by specialized membrane-bound carrier proteins, such as ATP-binding cassette (ABC) transporters, solute carrier (SLC) transporters, and ion channels [9].

Although active transport plays a comparatively minor role in dermal delivery, it becomes significant in the transport of specific molecules, especially hydrophilic nutrients, ions, and small peptides. For instance:

- **Glucose transporters (GLUTs)** have been implicated in the dermal uptake of sugar molecules.
- **Sodium-potassium ATPases** regulate ion exchange and contribute indirectly to drug permeation.
- **Efflux pumps**, such as P-glycoprotein, may reduce drug accumulation by actively pumping xenobiotics back out of cells [14].

Recent research also suggests that certain phytoconstituents may interact with these transport systems, thereby modulating drug penetration. For example, flavonoids have been reported to influence P-glycoprotein activity, potentially altering the dermal absorption of co-administered compounds [15].

### **VESICULAR TRANSPORT**

Vesicular transport encompasses processes such as endocytosis and exocytosis, which involve the active uptake and release of substances through vesicle formation at the cell membrane.

- **Endocytosis:** Molecules are engulfed by the cell membrane, internalized into vesicles, and transported across cellular compartments. This is particularly relevant for large biomolecules such as proteins, polysaccharides, and nanoparticles [16].
- **Exocytosis:** Vesicles within cells fuse with the plasma membrane to release their contents extracellularly, aiding in the clearance or secretion of molecules.

This pathway is highly significant for nanocarriers, such as liposomes, ethosomes, and solid lipid nanoparticles, which are designed to exploit vesicular uptake mechanisms. For example, studies have demonstrated that curcumin-loaded liposomes can penetrate skin layers more effectively via endocytosis, resulting in enhanced therapeutic outcomes [17].

## APPENDAGEAL PATHWAY

In addition to the three classical mechanisms, an often-overlooked route is the appendageal or transappendageal pathway, which includes drug transport through hair follicles, sweat glands, and sebaceous glands. Although this route contributes only about 0.1% of the total skin surface area, it provides a shunt pathway for the delivery of ions, large molecules, and particulate carriers [18].

Hair follicles, in particular, act as reservoirs, allowing prolonged retention of nanoparticles and lipophilic herbal extracts. This mechanism is especially advantageous in conditions such as acne, where targeted delivery to sebaceous glands is desirable [19].

### Other Factors Influencing Skin Permeation

Beyond intrinsic mechanisms, physiological and environmental factors profoundly affect permeation:

- **Hydration:** Increased hydration of the stratum corneum disrupts lipid packing, leading to enhanced permeability. Herbal humectants like aloe vera gel and hyaluronic acid are often used in formulations for this purpose [20].
- **Temperature:** Elevated skin temperature increases lipid fluidity, thereby improving molecular diffusion. Conversely, cold conditions reduce permeability.
- **Barrier Integrity:** Diseased or damaged skin (eczema, psoriasis, wounds) exhibits compromised barrier function, which can significantly increase drug absorption but may also raise safety concerns [21].
- **Age:** Infant skin is more permeable than adult skin due to incomplete barrier development, whereas elderly skin often shows reduced lipid content and hydration, altering drug penetration profiles [22].

**Table No.1: Factors Influencing Skin Permeation**

Category	Factors	Effect on Skin Permeation
<b>Physicochemical Factors</b>	- Molecular size / weight - Lipophilicity (log P) - Ionization (pKa) - Solubility (aqueous & lipid)	- Small, moderately lipophilic, unionized molecules permeate better. - High solubility improves diffusion.
<b>Formulation Factors</b>	- Drug concentration - Vehicle/base type - pH of formulation - Use of permeation enhancers (e.g., DMSO, ethanol, surfactants)	- Higher concentration enhances diffusion gradient. - Suitable vehicles improve partitioning. - Enhancers disrupt stratum corneum to increase permeation.
<b>Biological Factors</b>	- Skin site (thickness, hair follicles) - Age (infants & elderly more permeable) - Skin hydration - Blood flow & metabolism	- Thin, highly vascularized, and hydrated areas show higher permeation. - Age-related changes alter barrier function.
<b>Physiological/Environmental Factors</b>	- Temperature - Humidity - Skin condition (diseased, damaged, inflamed)	- Increased temperature and humidity enhance diffusion. - Damaged/inflamed skin allows higher penetration.

## HERBAL DRUGS FOR SKIN REJUVENATION

Herbal drugs have been used for centuries in traditional medicine and are increasingly recognized in modern dermatology and cosmetology for their ability to promote skin health and rejuvenation. Derived from plants, these bioactive compounds possess a wide range of pharmacological activities including antioxidant, anti-inflammatory, photoprotective, wound-healing, and collagen-stimulating effects, all of which are critical for maintaining youthful and healthy skin. Unlike synthetic agents, herbal compounds are generally considered safer, biodegradable, and better tolerated, making them attractive candidates for incorporation into cosmeceutical formulations [23].

Below, we discuss in detail the major herbal drugs widely studied for their skin-rejuvenating potential.

### ALOE VERA (*ALOE BARBADENSIS* MILLER)

Aloe vera is one of the most extensively used medicinal plants in skin care. Its gel contains aloins, acemannan, and polysaccharides, which contribute to its biological activities. Aloe vera enhances fibroblast proliferation, stimulates collagen and elastin synthesis, and accelerates wound healing. Its strong antioxidant and anti-inflammatory properties counteract reactive oxygen species (ROS) and reduce UV-induced skin damage. Clinically, Aloe vera gel has been used in moisturizing creams, anti-aging products, and after-sun lotions for improving skin hydration, elasticity, and wrinkle reduction [24].

**GREEN TEA (*CAMELLIA SINENSIS*)**

Green tea extract, rich in catechins such as epigallocatechin gallate (EGCG), is well known for its antioxidant and photoprotective effects. EGCG inhibits matrix metalloproteinases (MMPs), enzymes that degrade collagen and elastin, thereby preventing wrinkle formation and loss of elasticity. It also reduces UV-induced oxidative stress, protecting the skin from photoaging. Green tea polyphenols further demonstrate anti-inflammatory activity by modulating NF- $\kappa$ B and MAPK pathways. Topical formulations containing green tea extract have been shown to improve skin tone, firmness, and reduce erythema caused by sun exposure [25].

**TURMERIC (*CURCUMA LONGA*)**

Turmeric, traditionally used in Ayurveda, contains the active compound curcumin, which exhibits strong antioxidant, anti-inflammatory, and anti-carcinogenic properties. Curcumin inhibits NF- $\kappa$ B signaling, reduces oxidative stress, and suppresses melanogenesis, thereby providing skin-lightening effects. It has also been reported to enhance wound healing and collagen deposition. Curcumin-based creams and nanoformulations are increasingly incorporated into anti-aging products for reducing pigmentation, evening skin tone, and imparting a natural glow [26].

**GINSENG (*PANAX GINSENG*)**

Ginseng is highly valued in traditional Chinese medicine for vitality and longevity. Its bioactive components, ginsenosides and saponins, enhance collagen synthesis, improve microcirculation, and act as powerful antioxidants. These properties help reduce wrinkles, improve skin elasticity, and support skin barrier function. Ginseng extracts are widely used in serums and creams for anti-aging, hydration, and skin revitalization. Clinical evidence suggests that regular topical use of ginseng-based formulations can visibly reduce fine lines and improve overall skin appearance [27].

**CENTELLA ASIATICA (*GOTU KOLA*)**

Centella asiatica, also known as Gotu Kola, is rich in asiaticoside and madecassoside, which stimulate fibroblast proliferation, enhance wound healing, and increase type I and III collagen production. This makes it particularly effective in improving skin firmness, reducing wrinkles, and healing scars. Its antioxidant and anti-inflammatory effects further protect against premature aging. Centella-based creams and gels are commonly recommended for improving skin elasticity and reducing stretch marks and scars [28].

**POMEGRANATE (*PUNICA GRANATUM*)**

Pomegranate extract contains punicalagins and ellagic acid, both of which are potent antioxidants with anti-inflammatory and photoprotective properties. These compounds protect against UV-induced skin damage, enhance collagen production, and improve skin hydration. Pomegranate seed oil is particularly beneficial for improving skin tone, restoring elasticity, and reducing oxidative stress. Studies have demonstrated that regular topical application reduces photoaging signs such as pigmentation and fine wrinkles [29].

**GRAPESEED (*VITIS VINIFERA*)**

Grapeseed extract is abundant in proanthocyanidins and resveratrol, known for their antioxidant activity and ability to inhibit collagen degradation. These compounds also increase skin hydration and promote firmness. Resveratrol, in particular, has been studied for its anti-aging properties through activation of the SIRT1 longevity gene pathway, which enhances mitochondrial function and cellular repair. Grapeseed oil and extract are widely used in moisturizers, serums, and sunscreens for anti-aging and skin brightening effects [30].

**LICORICE (*GLYCYRRHIZA GLABRA*)**

Licorice extract contains glabridin and liquiritin, compounds with strong tyrosinase-inhibiting activity that effectively reduce melanin production and hyperpigmentation. In addition, its antioxidant and anti-inflammatory properties protect against oxidative stress and irritation. Licorice extract is widely used in formulations for skin brightening, pigmentation reduction, and even skin tone. Clinical studies suggest it can be as effective as hydroquinone but with a better safety profile [31].

**NEEM (*AZADIRACHTA INDICA*)**

Neem is known for its azadirachtin and nimbidin content, which provide antibacterial, antifungal, antioxidant, and anti-inflammatory effects. Neem-based formulations are widely used for acne control due to their ability to reduce sebum secretion and prevent bacterial colonization. Additionally, neem extracts help improve skin texture, reduce scars, and support wound healing. Neem oil and leaf extracts are commonly incorporated in anti-acne and detoxifying skincare products [32].

**ROSE (*ROSA DAMASCENA*)**

Rose extracts and essential oils contain flavonoids, vitamin C, and aromatic oils with hydrating, soothing, and antioxidant properties. Rose water is traditionally used as a natural toner, while rose oil enhances

skin hydration and radiance. Its anti-inflammatory and calming effects make it suitable for sensitive and aging skin. Rose-based formulations promote skin rejuvenation, imparting a natural glow and reducing stress-related dullness [33].

**Table No.2 : Table of herbal drugs for skin rejuvenation**

Herbal Drug	Major Active Constituents	Mechanism of Action	Skin Rejuvenation Benefits
<b>Aloe vera</b>	Aloin, acemannan, polysaccharides	Promotes fibroblast proliferation, increases collagen synthesis, antioxidant, anti-inflammatory	Hydration, wound healing, anti-wrinkle
<b>Green Tea (<i>Camellia sinensis</i>)</b>	Epigallocatechin gallate (EGCG), catechins	Antioxidant, inhibits MMPs, UV protection, reduces ROS	Prevents photoaging, maintains elasticity
<b>Turmeric (<i>Curcuma longa</i>)</b>	Curcumin	Inhibits NF- $\kappa$ B, reduces oxidative stress, anti-inflammatory	Brightening, anti-aging, reduces pigmentation
<b>Ginseng (<i>Panax ginseng</i>)</b>	Ginsenosides, saponins	Stimulates collagen synthesis, antioxidant, improves microcirculation	Reduces wrinkles, improves skin elasticity
<b>Centella asiatica (<i>Gotu Kola</i>)</b>	Asiaticoside, madecassoside	Promotes fibroblast proliferation, enhances wound healing, increases collagen type I/III	Anti-wrinkle, scar healing, firmness
<b>Pomegranate (<i>Punica granatum</i>)</b>	Punicalagins, ellagic acid	Potent antioxidant, anti-inflammatory, photoprotective	Improves skin tone, prevents UV-induced aging
<b>Grapeseed (<i>Vitis vinifera</i>)</b>	Proanthocyanidins, resveratrol	Antioxidant, inhibits collagen degradation, increases skin hydration	Firmness, anti-wrinkle, anti-aging
<b>Licorice (<i>Glycyrrhiza glabra</i>)</b>	Glabridin, liquiritin	Tyrosinase inhibition, antioxidant, anti-inflammatory	Skin brightening, reduces pigmentation
<b>Neem (<i>Azadirachta indica</i>)</b>	Azadirachtin, nimbidin	Antibacterial, antioxidant, reduces inflammation	Acne control, improves skin texture
<b>Rose (<i>Rosa damascena</i>)</b>	Flavonoids, vitamin C, essential oils	Antioxidant, hydrating, soothing	Skin hydration, rejuvenation, glow

## STRATEGIES TO ENHANCE SKIN PERMEATION

The skin's barrier function, primarily governed by the stratum corneum, is a major challenge for the efficient delivery of herbal drugs. Many phytoconstituents suffer from poor aqueous solubility, low lipophilicity, or high molecular weight, which limits their ability to penetrate deeply into the skin. To overcome these barriers, several innovative strategies have been developed to improve stability, permeability, and therapeutic efficacy of herbal actives. These strategies broadly include nanoformulations, chemical penetration enhancers, and physical enhancement techniques [34].

### NANOFORMULATIONS

Nanoformulation-based approaches have gained significant attention in recent years due to their ability to encapsulate bioactive herbal compounds, protect them from degradation, and enhance their skin permeation:

- **Liposomes:** Spherical phospholipid vesicles that improve solubility of both hydrophilic and lipophilic herbal constituents. For example, liposomal curcumin enhances antioxidant activity and penetration into deeper skin layers.
- **Niosomes and Ethosomes:** Non-ionic surfactant-based vesicles (niosomes) and ethanol-rich vesicles (ethosomes) provide greater skin fluidity and improved permeation of herbal actives like quercetin and ginseng extracts.
- **Nanoemulsions:** Thermodynamically stable oil-in-water or water-in-oil systems that enhance solubility of poorly water-soluble phytochemicals. Neem oil and tea tree oil nanoemulsions have shown improved anti-acne efficacy.
- **Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs):** Provide controlled drug release and protect unstable compounds (e.g., resveratrol, curcumin) from oxidation, thereby improving skin rejuvenation outcomes [35].

These carriers not only facilitate improved diffusion across the stratum corneum **but also increase** residence time within the skin layers, resulting in sustained therapeutic action.

#### **CHEMICAL PENETRATION ENHANCERS**

Chemical penetration enhancers (CPEs) transiently alter the lipid structure of the stratum corneum, thereby increasing drug permeation:

- **Surfactants** (e.g., sodium lauryl sulfate, polysorbates) disrupt lipid packing and improve solubility of herbal actives.
- **Solvents** (e.g., ethanol, propylene glycol, dimethyl sulfoxide) increase skin hydration and lipid fluidity, enhancing diffusion of phytoconstituents like flavonoids.
- **Fatty Acids and Terpenes** (e.g., oleic acid, menthol, limonene) integrate into the lipid bilayer, increasing its fluidity. Menthol, for instance, is frequently used with herbal actives to improve dermal delivery [36].

Although effective, safety remains a concern since excessive use of enhancers can cause irritation or barrier disruption. Therefore, careful optimization of concentration and formulation is required.

#### **PHYSICAL ENHANCEMENT METHODS**

Physical approaches to skin permeation offer minimally invasive but highly effective strategies for improving drug delivery. These include:

- **Microneedles:** Create microchannels in the stratum corneum without reaching nerve endings, thus being painless yet highly effective. Herbal actives such as curcumin and aloe vera extracts have shown enhanced delivery via microneedle-assisted systems.
- **Iontophoresis:** Uses a low-level electric current to drive ionizable herbal compounds across the skin, enhancing penetration of charged phytoconstituents.
- **Sonophoresis (Ultrasound-mediated delivery):** Employs ultrasound waves to temporarily disrupt skin lipids and enhance permeability of macromolecules and nanoparticles.
- **Fractional Laser-Assisted Delivery:** Creates controlled microthermal zones that act as conduits for herbal actives, significantly enhancing penetration and therapeutic effect [37].

These physical methods are increasingly combined with nanoformulations to create synergistic effects, achieving higher bioavailability, targeted delivery, and prolonged action of herbal compounds.

#### **FUTURE PERSPECTIVES**

The integration of herbal drugs with advanced permeation-enhancing technologies represents a promising frontier in dermatological research and cosmeceutical development. While substantial progress has been made in understanding the mechanisms of skin permeation and developing novel delivery systems, several opportunities remain to improve efficacy, stability, and patient compliance of herbal-based formulations.

One important future direction is the optimization of formulation parameters in nano-delivery systems, such as particle size, surface charge, encapsulation efficiency, and release kinetics. Tailoring these attributes can significantly influence the penetration depth, bioavailability, and therapeutic action of phytoconstituents. Furthermore, innovations in green nanotechnology, utilizing biodegradable and plant-derived polymers, can enhance both safety and sustainability of cosmeceutical products [38].

Another key area involves mechanistic elucidation. Although numerous studies have demonstrated the effectiveness of herbal nanoformulations in enhancing skin permeation, the exact cellular and molecular pathways remain underexplored. Advanced analytical techniques, such as confocal microscopy, Raman spectroscopy, and molecular docking studies, can help clarify interactions between phytoconstituents and skin lipids or proteins [39].

Equally important is the translation of preclinical findings into clinical studies. Large-scale, randomized clinical trials are essential to validate the safety and efficacy of these formulations. Currently, most data are derived from *in vitro* and animal models, which may not fully reflect human skin physiology. Clinical evidence will be crucial for gaining regulatory approval and wider acceptance of herbal-based transdermal products [40].

Future research should also focus on synergistic combinations of herbal drugs with conventional skincare ingredients, such as retinoids, hyaluronic acid, or peptides. These combinations may provide additive or even synergistic effects in combating multiple pathways of skin aging, thereby improving overall skin rejuvenation outcomes [41]. Moreover, personalized skincare, guided by advances in genomics, metabolomics, and artificial intelligence, holds potential for tailoring herbal-based treatments to individual skin types and conditions [42].

In summary, the future of herbal skin rejuvenation lies in multidisciplinary approaches that combine traditional knowledge with cutting-edge formulation technologies, advanced analytical tools, and clinical

validation. Such efforts are expected to pave the way for next-generation cosmeceuticals that are not only effective and safe but also sustainable and widely acceptable in the global market.

## CONCLUSION

Enhancing skin permeation remains one of the most critical challenges in the effective delivery of therapeutic agents for skin rejuvenation. The skin's barrier, particularly the stratum corneum, offers remarkable protection but simultaneously restricts the penetration of bioactive molecules, including herbal constituents. Overcoming this challenge is essential to harness the full therapeutic potential of herbal drugs in modern dermatology and cosmeceuticals.

Herbal drugs hold distinct advantages due to their natural origin, broad spectrum of pharmacological activities, biocompatibility, and consumer acceptance. Compounds with antioxidant, anti-inflammatory, collagen-stimulating, and photoprotective properties provide a holistic approach to skin health by addressing multiple pathways of aging simultaneously. However, their clinical application is often limited by poor permeability, low stability, and reduced bioavailability.

The advent of novel formulation technologies, such as nanoformulations, chemical enhancers, and physical methods, provides viable solutions to these limitations. By combining herbal therapeutics with permeation-enhancing systems, researchers can achieve improved delivery, sustained release, and targeted action. Moreover, the integration of these strategies with advanced scientific tools, clinical validation, and personalized skincare approaches holds promise for developing next-generation cosmeceuticals that are effective, safe, and sustainable.

In conclusion, the future of skin rejuvenation lies in bridging traditional herbal wisdom with modern delivery technologies. Such an approach not only offers innovative solutions for overcoming skin barrier challenges but also aligns with the growing global demand for natural, eco-friendly, and evidence-based skincare products.

**CONFLICT OF INTEREST-** The authors declared no conflict of interest

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