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Transdermal Delivery of Herbal Extracts: A Review on Techniques, Polymers, and Permeation Enhancers

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Abstract: Due to their natural nature, safety, and therapeutic efficacy, herbal medications have become increasingly popular. However, their effectiveness is frequently limited by issues like inconsistent absorption, poor bioavailability, and instability in the gastrointestinal tract. Herbal bioactive can be released through the skin in a controlled and sustained manner with transdermal drug delivery systems (TDDS), which offer a potential approach. The different formulation methods used in herbal TDDS, such as matrix-type patches, reservoir systems, Nano emulsions, and liposomes, are examined in this review. The choice and function of both natural and synthetic polymers are also covered, as is the use of permeation enhancers to increase skin absorption. Highlighted are recent developments in herbal transdermal applications, specifically in the areas of wound healing and antidiabetic treatment. Future prospects, such as nanotechnology, smart delivery systems, and personalized medicine, suggest a bright future for herbal TDDS in contemporary therapeutics, despite ongoing challenges with standardization, skin permeability, and regulatory acceptance.

Keywords: *Transdermal Drug Delivery System, Herbal Extracts, Permeation Enhancers, Polymers, Skin Permeability, Herbal Medicine, Controlled Drug Release, Phytoconstituents, Antidiabetic, Wound Healing.*

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I. INTRODUCTION

Herbal medicine has gained popularity in recent years because of its established therapeutic benefits, low risk of side effects, and all-encompassing approach to healthcare. Herbal extracts, which are made from medicinal plants, have shown impressive effectiveness in treating a range of acute and chronic illnesses, including wounds, diabetes, inflammation, and infections. However, issues like poor bioavailability, first-pass metabolism, and gastrointestinal degradation of phytoconstituents frequently plague the traditional routes of administration, especially oral delivery [1]. A viable substitute for the regulated and prolonged release of synthetic and herbal medications is transdermal drug delivery systems (TDDS). TDDS improves patient compliance and therapeutic efficacy by avoiding the gastrointestinal tract and delivering consistent plasma medication levels. This is especially advantageous for herbal bioactive, many of which are unstable in the digestive tract or poorly soluble in water. Several scientific factors must be taken into account when formulating herbal medications into transdermal systems, such as choosing appropriate methods, polymers, and penetration enhancers to get beyond the skin's natural barrier qualities [2]. Using safe penetration enhancers and biocompatible polymers is essential for optimizing drug delivery without sacrificing skin integrity. The purpose of this paper is to give a thorough overview of the several formulation methods used in herbal transdermal drug delivery, the kinds of polymers used to produce patches, and the function of permeation enhancers in enhancing skin absorption of drugs. It also outlines the difficulties and recent developments in the creation of herbal TDDS, opening the door for more breakthroughs in phytopharmaceutical delivery in the future.

- *Overview of Transdermal Drug Delivery Systems (TDDS)*

Pharmaceutical formulations known as transdermal drug delivery systems (TDDS) are made to transfer active chemicals straight into the bloodstream through the skin barrier. Because TDDS is non-invasive and simple to administer, it offers a number of benefits over conventional methods like oral or injectable, such as sustained drug release, increased bioavailability, and greater patient compliance.

A significant barrier to drug penetration is the skin, especially the topmost layer, the stratum corneum. However, the transdermal route can be an effective way to transport

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some drug molecules, particularly those that are lipophilic, low in molecular weight, and strong in tiny doses. Because of this, TDDS is now the recommended option for medications that need to have their plasma levels regulated for a long time. TDDS can be broadly categorized into various types according to its mechanism and design:

- Matrix-type patches, where the drug is dispersed within a polymer matrix.
- Reservoir systems, which contain a separate drug reservoir and a rate-controlling membrane.
- Adhesive-dispersion systems, in which the drug is incorporated into the adhesive layer.

TDDS present a special chance to enhance the medicinal effects of plant-based compounds when used in herbal medications. The transdermal route can better protect and deliver herbal constituents, which are frequently unstable in the gastrointestinal tract. This results in a more stable and predictable pharmacokinetic profile in addition to increased bioavailability [3]. Integrating herbal actives with TDDS in the context of modern drug delivery signifies a meeting point between traditional and modern medicine and has the potential to increase the acceptance of herbal treatments worldwide.

➢ *Techniques Used in Herbal Transdermal Delivery*

In order to formulate herbal transdermal drug delivery systems, suitable procedures that guarantee effective drug penetration, stability, and therapeutic efficacy must be chosen. Herbal active ingredients, in contrast to manufactured medications, frequently consist of intricate blends of phytochemicals with different molecular weights and solubility profiles. Therefore, a key factor in determining the effectiveness of transdermal distribution is the formulation technique selection [4].

- *Matrix-Type Patches*

One of the most popular methods for transdermal distribution is the matrix system. This approach regulates the drug's release over time by evenly dispersing the herbal extract in a polymeric matrix. Although these patches are simple to make and offer reliable medication release, the integrity of the herbal active ingredients must be preserved by carefully choosing the polymers and solvents. [5,6]

- *Reservoir Systems*

A backing layer and a rate-controlling membrane enclose a drug reservoir in reservoir-type transdermal systems. The drug releases through the membrane at a regulated pace while the herbal extract remains in a semi-solid or gel state. These systems are more complicated and demand great manufacturing precision, even though they provide exact control over drug release [4,7].

- *Microemulsions and Nanoemulsions*

Formulations based on microemulsions and nanoemulsions are becoming more and more common for the delivery of herbal constituents that are poorly soluble. These systems, which are made up of water, oil, surfactants, and co-surfactants, increase the permeability and solubility of phytoconstituents. Better medication diffusion and deeper skin penetration are made possible by their tiny droplet size. [7,8]

- *Liposomes and Niosomes*

These are vesicular systems made up of non-ionic surfactants (niosomes) or lipid bilayers (liposomes). They combine with skin lipids to encapsulate herbal medications and improve their penetration. They are appropriate carriers for herbal actives due to their biocompatibility and capacity to transport both hydrophilic and lipophilic medications [8].

➢ *Polymers Used in Herbal Transdermal Drug Delivery Systems*

The performance and design of transdermal drug delivery systems (TDDS) are heavily reliant on polymers. They affect the mechanical and physicochemical characteristics of the finished product, form the structural matrix of patches, and affect the pace at which active substances are released. Choosing the right polymers is crucial for herbal TDDS in order to preserve the stability and effectiveness of plant-based bioactive [9].

- *Natural Polymers*

Because natural polymers are biocompatible, biodegradable, and have low toxicity, they are frequently used in herbal preparations. Typical natural polymers are as follows:

- ✓ Chitosan: Made from chitin, chitosan has superior antibacterial, bioadhesive, and film-forming properties. Additionally, it improves drug penetration through the skin.
- ✓ Sodium Alginate: Derived from brown seaweed, alginate is used in matrix formulations in conjunction with other polymers and offers good mechanical strength.
- ✓ Gelatin: A protein-based polymer with a high capacity for drug trapping and exceptional film flexibility.
- ✓ Cellulose and starch derivatives: These thickening agents and film formers promote delayed release and even medication distribution [9,10].

➢ *Synthetic Polymers*

Synthetic polymers are frequently employed either alone or in conjunction with natural polymers because they provide greater control over mechanical and release qualities. Typical examples include:

- Hydroxypropyl Methylcellulose (HPMC): This popular film-former offers stable matrix formation and controlled release.
- Polyvinylpyrrolidone (PVP): This substance speeds up medication release, increases film flexibility, and makes herbal extracts more soluble.
- Eudragit Polymers: Used in formulations with prolonged release and pH sensitivity.
- Ethyl Cellulose (EC): Provides long-term release characteristics and resistance to moisture [11,12].

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➢ *Criteria for Polymer Selection*

When selecting polymers for herbal TDDS, the following factors are considered:

- Biocompatibility and non-toxicity
- Good film-forming and mechanical properties
- Controlled drug release behaviour
- Chemical compatibility with herbal extract
- Moisture and oxygen barrier properties

A frequent tactic to strike the ideal balance between performance and safety is to combine natural and synthetic polymers. The perfect polymer should improve permeation, guarantee drug stability, and offer a comfortable user experience [12].

II. PERMEATION ENHANCERS

Overcoming the skin's natural barrier, especially the stratum corneum, which prevents the majority of medications, including herbal bioactives, from penetrating, is one of the main obstacles in transdermal drug administration. Permeation enhancers are chemicals added to transdermal formulations that improve drug absorption without harming or irritating the skin by momentarily and reversibly changing the skin's barrier characteristics [13].

➢ *Mechanism of Action*

Permeation enhancers work through various mechanisms, such as:

- Disrupting the lipid structure of the stratum corneum
- Altering protein conformation within the skin
- Increasing the solubility of the drug in the skin
- Enhancing the partitioning of the drug into the skin [13,14]

➢ *Natural Permeation Enhancers*

Natural enhancers are often preferred in herbal formulations due to their safety and compatibility. Common examples include:

- Essential Oils (e.g., eucalyptus oil, clove oil, peppermint oil): These contain terpenes which effectively disrupt stratum corneum lipids.
- Terpenes (e.g., menthol, limonene, cineole): Proven to enhance skin penetration of both hydrophilic and lipophilic compounds.
- Aloe vera gel: Acts as a moisturizer and mild permeation enhancer.
- Fatty acids (e.g., oleic acid, linoleic acid): Help fluidize the lipid layers of the skin [14].

➢ *Synthetic Permeation Enhancers*

Synthetic agents, though more potent, may carry a higher risk of irritation. Common ones include:

- Dimethyl sulfoxide (DMSO): A powerful solvent that alters skin structure and increases drug flux.
- Propylene glycol and PEG-400: Enhance drug solubility and partitioning into the skin.
- Surfactants (e.g., sodium lauryl sulfate): Reduce surface tension and interact with skin lipids to increase permeability [15,16].

➢ *Evaluation of Enhancer Efficiency*

The effectiveness of a permeation enhancer is assessed based on:

- Increased drug flux across skin in in-vitro permeation studies
- Skin integrity using histopathological or transepidermal water loss (TEWL) tests
- Skin irritation or toxicity studies using animal models or human skin equivalents

The ideal permeation enhancer should significantly improve drug absorption without causing long-term damage or irritation. In herbal TDDS, the use of natural enhancers is especially favorable due to their synergistic compatibility with phytoconstituents [17].

➢ *Evaluation Parameters for Herbal Transdermal Drug Delivery Systems*

A comprehensive assessment of the physical, chemical, and biological characteristics of any transdermal drug delivery system (TDDS) is essential to its success, especiallythosemade with herbal extracts. Patch quality, consistency, efficacy, and safety are guaranteed by these assessments [18].

➢ *Physicochemical Evaluation*

These tests are crucial for ensuring the uniformity and structural integrity of the patch:

- Thickness: Measured using a micrometer at different points for uniformity.
- Weight Variation: Ensures even distribution of drug and excipients.
- Folding Endurance: Indicates the patch's flexibility and mechanical strength.
- Moisture Content and Uptake: Important for shelf-life and stability.
- Drug Content Uniformity: Assesses even distribution of the herbal extract across the patch [18,19].

➢ *Mechanical Properties*

- Tensile Strength: Determines the patch’s strength and durability.
- Elongation at Break: Indicates how much the patch can stretch before breaking [19,20].

➢ *Surface pH*

Patches should have a surface pH close to that of human skin (5.5–6.5) to prevent irritation or allergic reactions [18,20].

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➢ *In-Vitro Drug Release Studies*

Carried out using Franz diffusion cells or similar apparatus:

- Determines the rate and extent of drug release from the patch.
- Provides an idea of sustained/controlled release behaviour [20,21].

➢ *In-Vitro Skin Permeation Studies*

- Uses excised animal or human skin to simulate drug diffusion.
- Measures cumulative amount of drug permeated per unit area over time [19,22].

➢ *Skin Irritation Studies*

- Performed on animal models or using reconstructed human skin models.
- Ensures that the patch and its ingredients do not cause rashes, redness, or other dermatological issues [18,19].

➢ *Stability Studies*

- Conducted under ICH guidelines to assess the patch's physical and chemical stability under different environmental conditions (temperature, humidity, light).

Each of these parameters helps in optimizing the formulation and ensuring that the herbal TDDS is safe, effective, and acceptable for clinical use [22].

III. RECENT RESEARCH AND APPLICATIONS

Research on the potential of herbal extracts in transdermal drug delivery systems (TDDS) has exploded in the last ten years, especially for the treatment of chronic illnesses like diabetes, inflammation, and skin disorders. Innovative transdermal patches that are both patient-friendly and effective have been created by fusing ancient herbal knowledge with contemporary formulation technologies [23,24].

➢ *Herbal TDDS for Antidiabetic Activity*

Several studies have investigated transdermal patches containing plant extracts with known antidiabetic properties:

In comparison to oral forms, herbal patches containing Gymnema sylvestre, Trigonella foenum-graecum (fenugreek), and Momordica charantia (bitter melon) have shown sustained drug release and improved patient compliance. These patches have also been shown to have significant blood glucose-lowering effects [24].

➢ *Wound Healing Applications*

Herbal TDDS have also been widely explored for wound healing purposes:

Plant extracts such as Centella asiatica, Azadirachta indica (neem), Curcuma longa (turmeric), and Aloe vera have been added to hydrogels or transdermal films. These patches help wounds heal more quickly because of their anti-inflammatory, antibacterial, and tissue-regenerative qualities [25,26].

➢ *Use of Novel Carriers*

Recent innovations include:

- Nanoemulsion-based patches with enhanced skin permeation for herbal actives.
- Microneedle-assisted herbal delivery esystems that enhance drug flux through the skin.
- Smart patches capable of pH- or temperature-sensitive release mechanisms [26,27].

➢ *Relevant Example:*

Ricinus communis Studies on transdermal delivery of Ricinus communis leaf extract, which is well-known for its antidiabetic and wound-healing properties, have showed promise. Its phytochemical profile—which is rich in flavonoids, saponins, and glycosides—supports its potential as a bioactive candidate for the development of TDDS, despite the fact that it has received less attention in the literature than other herbs. These developments demonstrate the increasing recognition and usefulness of herbal TDDS in pharmaceutical research, and more study is anticipated to broaden their therapeutic range and commercial application.

➢ *Challenges and Future Prospects*

Herbal transdermal drug delivery systems (TDDS) are a promising way to improve the therapeutic efficacy of plant-based medications, but there are still a number of obstacles in the way of their development and widespread use [28].

➢ *Challenges in Herbal TDDS*

- Complexity of Herbal Extracts: Because herbal extracts are intricate blends of several phytoconstituents, it can be challenging to standardize and regulate uniformity across batches.
- Stability Issues: It can be challenging to maintain long-term stability in transdermal formulations due to the sensitivity of many herbal bioactives to light, heat, and oxidation.
- Limited Skin Permeability: Many herbal compounds require efficient permeation techniques because of their high molecular weight and hydrophilic nature, which make it difficult for them to pass through the stratum corneum.
- Skin Sensitivity and Allergies: When used for extended periods of time, certain herbal ingredients and penetration enhancers may result in dermatitis, irritation, or allergic responses.
- Regulatory and Quality Control Barriers: Complicated regulatory frameworks frequently apply to herbal TDDS. Their acceptance and extensive use are restricted by the absence of worldwide standardization [28,29].

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➢ *Future Prospects*

- Developments in Nanotechnology: Herbal extracts can improve skin permeability, stability, and controlled release when added to nanoparticles, liposomes, or nanoemulsions.
- Smart Transdermal Systems: Real-time regulation of the distribution of herbal drugs may be possible with the development of patches that react to physiological cues (such as pH, temperature, or glucose levels).
- Green and Sustainable Polymers: Growing interest in biodegradable and environmentally friendly polymers may help create herbal TDDS that is safer and more sustainable.
- Personalized Herbal Medicine: AI and digital health monitoring could make it possible to develop transdermal systems that are specifically suited to the requirements and circumstances of each patient.
- International Integration of Ayurveda and Traditional Medicine: As interest in natural therapies grows worldwide, there are more chances to incorporate herbal TDDS into established healthcare systems.

Despite the hurdles, the future of herbal TDDS looks promising. Continued interdisciplinary research, technological innovation, and global collaboration are key to unlocking the full therapeutic potential of herbal-based transdermal systems [29,30].

IV. CONCLUSION

Many of the drawbacks of traditional oral or topical administration are addressed by transdermal drug delivery systems (TDDS), which provide a novel and efficient platform for the delivery of herbal extracts. TDDS greatly increases the bioavailability and therapeutic potential of herbal bioactives by avoiding first-pass metabolism and guaranteeing regulated release.

The main elements and factors in the creation of herbal transdermal systems were emphasized in this review, including the utilization of permeation enhancers, sophisticated delivery methods, and the function of both natural and synthetic polymers. It also looked at new study findings and the expanding use of herbal TDDS in wound healing and the treatment of chronic illnesses like diabetes.

Continuous developments in polymer science, nanotechnology, and formulation techniques are opening the door for safer, more effective, and economically feasible herbal transdermal systems, even while issues like low permeability, extract variability, and regulatory limits still exist.

In addition to improving therapeutic results, combining traditional plant-based medicine with contemporary drug delivery technologies promotes the modernization and worldwide acceptability of herbal healthcare.

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