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Review Article

Exploring the Use of Herbal Medicines in the Context of Dermatokinetic Research

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ABSTRACT

Herbal therapy is the application of herbal remedies to prevent and treat illness. It encompasses a variety of practices, from the use of standardized and treated herbal extracts to traditional and popular medicines used worldwide. Many skin conditions and wounds are treated with herbal extracts and isolated plant compounds. Different portions of plants, such as stems, leaves, flowers, roots, or seeds, are used in herbal medicine, also known as botanical medicine or phytomedicine, to treat and prevent diseases. Improved general health and well-being are common goals of using herbal remedies. They are accessible in various forms, including dried or fresh plants, tablets, capsules, teas and extracts. Herbal remedies consist of vitamins, minerals, herbs, or mixtures of these that are taken orally. Herbs like *Arnica Montana, German chamomile,* St. John's Wort, Evening Primrose and others have been used in studies to treat dermatological conditions like dermatitis, acne, wounds, burns and psoriasis. Additionally, to evaluate the pharmacokinetics of topical formulations and comprehend their penetration and distribution in the skin layers, dermatokinetic research techniques like the tape stripping technique, microdialysis, vasoconstrictor assay and confocal laser scanning microscopy have been used. Dermatokinetic research aims to lighten topically applied herbal compounds' pharmacokinetic properties and bioavailability by examining their Absorption, Distribution, Metabolism and Excretion (ADME). Dermatokinetic studies, which assess herbal compounds' systemic exposure and potential toxicity, helps establish safe dosage schedules and formulation techniques.

Keywords: Herbal medicine, Dermatokinetics, Herbal remedies, Skin metabolism, Skin absorptions.

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INTRODUCTION

When applied topically, dermatokinetic research examines the Absorption, Distribution, Metabolism and Excretion (ADME) of herbal ingredients. This provides insights into the compounds' bioavailability, pharmacokinetic characteristics and modes of action in the skin.[1] Dermatokinetic study is crucial for understanding the efficacy and safety of topical medications, cosmetics and skincare products.[2] People have used herbal therapy to treat skin conditions for thousands of years. India has records pertaining to Ayurvedic medicine since approximately 3000 BC. Ayurvedic drugs integrate both holistic and physiological principles. It is based on the hypothesis that the five energy components of earth, water, fire, air and space make up the universe and also make up the human body.[3] Dermatokinetics is the study of the kinetics of herbal compounds applied to the skin. It has become an important field of research. With a rich history spanning millennia across diverse cultures, herbal medicine presents a vast reservoir of bioactive compounds with promising therapeutic potential for a range of dermatological conditions.[4]

Numerous factors influence the bioavailability of topical and transdermal drugs. Physicochemical properties of the drug (pKa, logP, solubility and molecular weight), the type of formulation and the rate-limiting membrane stratum corneum, the application site, the enzyme presence in the structures of the skin and the formulation's excipients are among them. The medication needs to cross multiple layers in order to penetrate deeper layers of the skin after being applied topically or transdermally. A variety of permeability enhancement strategies are used to increase the amount of medication transported into the stratum corneum. For the delivery of drugs topically and transdermally, estimating the amount of drug retained in skin layers is essential. To determine how well the medication penetrates the different skin layers, it is necessary to divide the skin into layers.[5]

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IMPORTANCE IN HERBAL MEDICINE OF DERMATOKINETIC STUDY

Investigations into dermatokinetics shed light on how herbal compounds cross the epidermal layer. It is possible to create delivery systems that are more effective by developing an understanding of the factors that affect absorption, such as molecular size, lipophilicity and formulation characteristics.[6] Dermatokinetic studies are useful in determining safe dosage schedules and formulation techniques by evaluating the systemic exposure and potential toxicity of herbal compounds.[7] Dermatokinetic studies aid in the creation of formulations with enhanced skin penetration and bioavailability by describing the kinetics of herbal ingredients in various formulations (like lotions, gels and ointments).[8]

HERBAL MEDICINES

Herbal medicine, also known as botanical medicine or phytomedicine, makes use of various plant parts, including leaves, stems, flowers and roots, or seeds, to treat and prevent diseases.[9] Herbal remedies are frequently used to improve overall health and well-being. They can be taken in various forms, including pills, capsules, teas, extracts and dried or fresh botanicals (Figure 1).[10] Herbal medicines can be consumed orally and include vitamins, minerals, herbs, or combinations of these. Plants or parts of plants used for flavor, aroma, or medicinal purposes are one definition for them. Herbal medicines are not like pharmaceuticals in that they are not subject to the premarketing safety and efficacy standards that conventional drugs are. Globally, herbal remedies have grown significantly, with a growing number of individuals using these products to treat a wide range of health issues in medical practices across national borders.[11] A plant that contains biologically active secondary metabolites or active ingredients is called a medicinal Plant. Parts or the entire plant may have therapeutic value. Medicinal preparations containing active ingredients derived from herbal plants are known as herbal medicine. Any portion or the whole plant can be used to make the product. Preparations made from herbal byproducts, such as oils, gums and other secretions, are also included in herbal medicine.[12]

TYPES OF HERBS USED IN DERMATOKINETIC STUDY

Aloe vera

The perennial green herb known as *Aloe vera*, also known as *Aloe barbadensis* Miller of the family *Xanthorrhoeaceae*, is a common plant in hot, dry climates in the Canary Islands, Southern Mediterranean, Middle East and North Africa. It has bright yellow tubular flowers. A colorless, mucilaginous gel made from *aloe vera* leaves is frequently used in medical and cosmetic applications. *Aloe vera* contains over seventy-five different compounds: vitamins A, C, E and B12; enzymes (catalase, amylase and peroxidase); minerals (zinc, copper, selenium and calcium); sugars (monosaccharides like mannose-6-phosphate and polysaccharides like glucomannans); anthraquinones (aloin and emodin); fatty acids (lupeol and campesterol); hormones (auxins and gibberellins); and other substances (salicylic acid, lignin and saponins).[13] *Aloe vera* has been used as a medicine since 1500 BC and has been used in many nations, including Mexico, Greece and China. It has also been used as traditional medicine for centuries to treat various diseases and skin conditions.[14] *Aloe vera* is well-known for its ability to heal wounds, reduce inflammation and moisturize. The reasons behind its medicinal benefits are the presence of vitamins, glycoproteins and polysaccharides. *Aloe vera* is frequently used to relieve sunburn, hydrate parched skin and accelerate the healing of wounds. Studies on dermatokinetics concentrate on how well it penetrates the skin and distributes bioactive substances to the intended tissues (Figure 2).[15] *Aloe vera* can promote healing, reduce inflammation and inhibit thromboxane, an enzyme that prevents wounds from healing, according to *in vitro* research and studies on living things.[16]

Figure 1: Herbal Medicines used in dermatokinetic study.

When *Aloe vera* 3% ointment was applied topically to patients suffering from acute radiation proctitis brought on by pelvic radiotherapy, the symptoms of diarrhea and urgency in the stools were reduced.[17]

Calendula officinalis

Calendula's flavonoids, saponins and volatile oils are responsible for their anti-inflammatory, antimicrobial and antioxidant characteristics. Topically applied *calendula* extracts relieve irritated skin, heal small wounds and lessen dermatitis and eczema symptoms. The leaves and flowers of *C. officinalis* are said to have antipyretic, anti-arthritic, antiepileptic and antibacterial properties in the Ayurvedic and Unani medical systems. *C. officinalis* has been employed in conventional and homeopathic medication for the treatment of duodenal ulcers, varicose veins, poor vision, hemorrhoids and irregular menstruation. *Calendula* flowers were used to treat liver obstructions, snake bites and heart strengthening during the middle Ages.[18]

From ancient times, *Calendula officinalis*, or *marigold*, has been applied topically and accepted as an antiseptic and wound healer by Commission E, the German regulatory body. Herpes zoster, burns, boils, rashes, wounds, ulcers and varicose veins can all be treated with a topical preparation of marigold. Gargles made from marigolds are applied to soothe sore lips and throats. Additionally, marigold is frequently applied topically to treat mild skin inflammations such as diaper dermatitis. The course of treatment involves applying a lotion or ointment obtained by mixing 100 g of ointment with 2.5-5 g of floral heads several times a day.[19]

Turmeric

Turmeric extracts are used in skincare products for their ability to reduce the *Curcuma* species has been found to possess a variety of advantageous pharmaceutical characteristics, such as non-inflammatory, anti-cancer, insulin-resistant, low in cholesterol, non-thrombotic, preventative, sedative, dilated, counter-rheumatic, low blood pressure, antibacterial, antiviral, protective agent, larvicidal, pesticide, antigens and antityrosinase actions for many different conditions.[20] Turmeric has numerous medicinal benefits in Ayurvedic practices, such as boosting the body's general energy, lowering gas, removing worms, improving the digestive system, managing menstruation, easing arthritis and breaking down gallstones. In many South Asian countries, it is used as an antiseptic and antibacterial treatment for cuts, burns and bruises. Turmeric stimulates the digestive system. It significantly increased the actions of amylase, chymotrypsin and lipase in the pancreas when taken as a dietary supplement. Additionally, combining turmeric with other spices like cumin, black pepper, red chili and coriander significantly increased the flow of bile and the secretion of bile acid.[21]

Neem

Neem (*Azadirachta indica*) belongs to the family *Meliaceae* and its abundance in antioxidants is thought to play a part in its health-promoting properties. Neem's ability to heal acne, ease eczema and reduce itching makes it a popular ingredient in skincare products. It serves as a natural insect deterrent as well. Plant-based or natural products have a significant impact on disease prevention and treatment by increasing antioxidant activity, preventing bacterial growth and changing genetic pathways.[22] Throughout history, neem has been utilized to treat infections and illnesses like smallpox. Neem compounds have

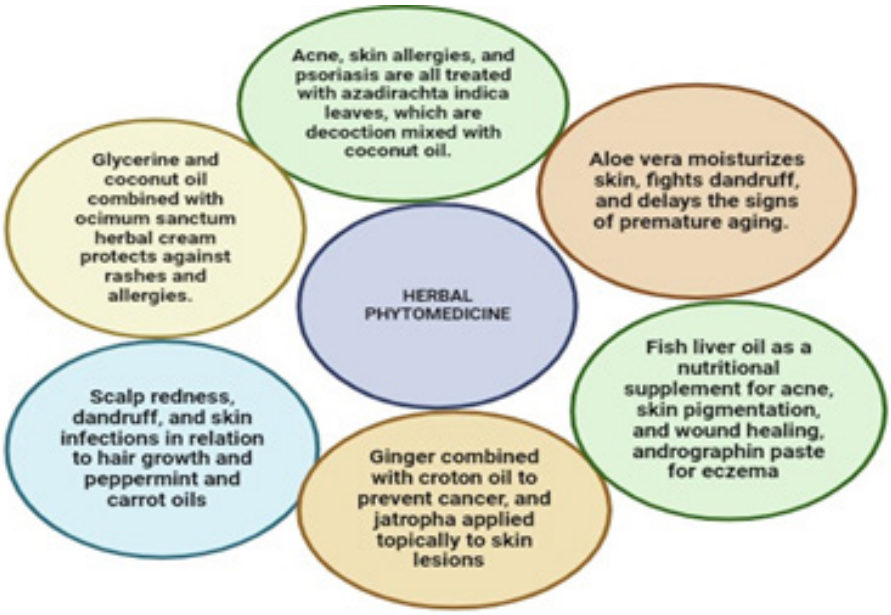

Figure 2: Herbal remedies against skin infections.

been shown to exhibit several advantageous qualities, such as antitumor, hypoglycemic, anthelminthic, anti-inflammatory, antiarthritic, antipyretic, antiviral, spermicidal and anti-gastric ulcer. An extract from neem bark has the ability to lessen inflammation and pain.[23]

DERMATOLOGICAL DISORDERS WITH DIFFERENT HERBAL TREATMENTS

Dermatitis

Dried flowers of other species, such as *Arnica montana* of arnica, are the source of arnica. While external use preparations are secure and efficient, oral use, even at low dosages, carries substantial health risks. Since ancient times, people have applied arnica, an anti-inflammatory medication, to boils, scratches, bug bites, inflamed gums, hemorrhoids, sore muscles and sore joints. It is also a common ingredient in psoriasis and seborrheic dermatitis preparations.[24] From ancient times, the daisy family member *German chamomile* (*Matricaria recutita*) has been used topically and topically to cure a range of illnesses, including dermatitis, mouth or skin inflammation and gastrointestinal tract symptoms.[25] *Chamomile* from Germany is known to possess a vital blue oil that includes flavonoids, α-bisabolol, chamazulene and sesquiterpene alcohol, which is responsible for its anti-arthritic, healing of wounds and antibacterial properties. In animal experiments, these compounds demonstrated anti-inflammatory and antispasmodic effects, partly because they inhibited lipoxygenase and cyclooxygenase *in vitro*.[26]

Hypericum perforatum

Traditionally, burns and wounds are treated with hypericum oil, which is made from St. John's wort. The lipophilic derivative of phloroglucin, hyperforin, exhibits antibacterial, anti-inflammatory and keratinocyte differentiation-promoting characteristics.[27] According to recent studies, this herb may also be useful in treating bacterial and viral infections, cancer, disorders associated with inflammation and other conditions. It may also act as a neuroprotective and antioxidant. Between the eighteenth and nineteenth centuries, the use of SJW as a herbal remedy persisted in Europe and eventually expanded across other continents. It was frequently prepared into tinctures and teas to treat gastritis, anxiety, depression, insomnia and water retention.[28]

Evening Primrose

The oil of evening primrose has an excessive γ-linolenic acid content, which is beneficial for AD. It finds application in topical products as well as internal use. The impact of evening primrose oil on AD has been the subject of only a few excellent research studies. Just recently, a meta-analysis of the body of literature determined that evening primrose oil has a moderate impact on AD itching, scaling and crusting.[29]

Acne

Because of their natural astringency, tannins are applied topically to treat acne. Bark extract from witch hazel (*Hamamelis virginiana*) is a popular home remedy is prepared by decocting one cup (0.24 L) of water and five to ten grams of herb. The bark of English walnut and white oak trees can be used to make similar astringents. You can use these preparations twice or three times a day, but they should be strained before use.[30]

Wounds and Burns

The *Aloe vera* leaves (*A. vera*) yield a latex and a gel. For centuries, burns and wounds have been treated topically with the gel that is extracted from the leaf's center core. The bitter yellow liquid known as latex, which is derived from the leaf's inner skin, is typically offered as a powder after drying with strong laxative properties. Additionally, it has been discovered that *Aloe vera* expedites the healing process of frostbite, surgically created wounds and chronic leg ulcers.[31] Since ancient times, honey has been applied topically to help heal Injuries, including burns, ulcers incibitus and contaminated wounds. It has been discovered to possess antifungal and antibacterial properties *in vitro*, targeting common surgical wound-infecting microorganisms.[32] Many herbs have tannins in them, which function as astringents and help the wounds stop bleeding and seeping. A number of frequently mentioned plants that contain tannin and may be beneficial when applied topically to wounds include Chinese rhubarb, the leaf of English walnut, goldenrod, tea from Labrador, lavender, mullein, the bark of oak trees and yellow dock.[33]

Birch bark

The molecular level elucidation of betulin's wound healing properties has demonstrated a positive effect on all three stages of the healing process of wounds, namely the state of inflammation and the keratinocyte stages of migration and differentiation. About 22% of the betulin in the cork tissue of the birch bark is available sustainably on a scale of several hundred thousand tons per year from the wood-processing industry in Northern Europe.[34]

Psoriasis

Psoriasis is a multifactorial, chronic, inflammatory skin disorder brought on by hyperproliferative epidermis responses resulting from immature keratinocyte development and hyperactivation.[35] *Mahonia aquifolium*, the *Oregon grape*, has anti-inflammatory and antibacterial qualities due to the presence of berberine. It has been demonstrated that symptoms of psoriasis like redness, scaling and itching can be lessened by topical ointments containing Oregon grape extract. *Aloe vera* gel helps lessen inflammation in psoriasis lesions and soothe irritated skin. It might also help hydrate dry, scaling skin and relieve irritation and discomfort.[36]

Araroba tree

The scientific name for the araroba tree is *Andira araroba*. Traditional medicine has long utilized it to treat various conditions, including psoriasis. Chrysarobin, the active component of araroba tree bark, has been shown to have antipsoriatic qualities.[37]

The anthracene derivative dithranol (also known as anthralin) is the most effective topical treatment for psoriasis. Chrysarobin, derived from the bark of the araroba tree, which grows in the rainforests of the Amazon, was the source of this material.[38]

Barberry bark

A shrub native to Northern America is the barberry *Mahonia aquifolium*. Native American psoriasis patients used it for centuries. Traditional European and North American medicines include tinctures and ointments made from the bark of Mahonia. Its medicinal use is attributed to the presence of isoquinolone alkaloids, such as jatorrhizamine, palmatine, berberine, beramine and magnoflorine, in the root and wood. In particular, its ability to reduce inflammation has made it popular in the treatment of dermatological conditions.[36]

Rosacea

Rosacea is an inflammatory skin disease that primarily affects the small superficial skin vessels and sebaceous glands on the face. There are various clinical variations of rosacea, such as telangiectatic, papulopustulous and erythematous variants. It is typified by redness, flushing, acne, pustules and dilated blood vessels. Phymas, or thickening of the skin with enlargement, are common in the eyes and, in certain cases, can also affect the nose. Numerous factors, including genetics, immunological response, microorganisms, environmental influences and neurovascular dysregulation, are recognized as etiological contributors to the development of rosacea.[39]

Green Tea

Green tea, or *Camellia sinesis*, commonly known as green tea, has anti-inflammatory and anti-cancer qualities. Catechins are the primary antioxidant agents found in *Camellia sinesis*, among other physiologically active compounds. Green tea's health-promoting qualities result from its polyphenol content, specifically its flavonol and flavanol content. Their anti-inflammatory and antioxidant properties are supported by *in vitro* and clinical research.[40]

DERMATOKINETIC RESEARCH METHODS

The amounts of drugs in the skin's layers are estimated using the dermato-pharmacokinetic method. The stratum corneum is the drug permeation membrane that sets a rate limit even though it may not be the site of action. Similar to pharmacokinetic studies conducted on blood and urine is dermato-pharmacokinetics. The drug's uptake and the point at which management is stopped determine the skin kinetics. Methods using dermatopharmacokinetics assume three mechanisms: i) The stratum corneum's actions as the membrane that limits the rate at which drugs absorb; ii) The drug's concentration at the stratum corneum directly influences the drug's diffusion into the dermis; iii) Dermatological effects of the drug are demonstrated by its concentrations in the stratum corneum, epidermis and dermis. The maximum concentration of medicine in the skin layers, or Cmax and Tmax, is among the parameters of dermato-pharmacokinetics (Figure 3).[41]

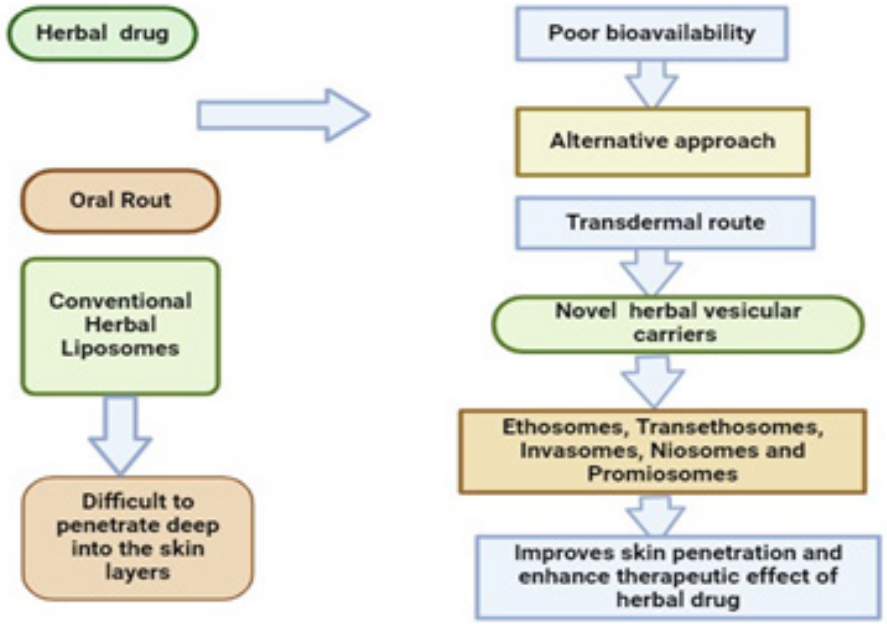

Figure 3: Applications of herbal drug delivery.

Tape stripping technique

Applying tape stripping to cutaneous biology involves several tasks, including assessing gene expression, dermatopathology inspection, barrier function assessment, pH profile assessment and skin of animal examination as a model for the skin of humans. Additionally, it offers a substitute for evaluating the regional bioavailability or bio equivalency of topically administered medications whose intended target is the underlying viable tissues. The standardized version of this technique works well for figuring out the topical formulations' DPK, which shows that the drug's concentration is in the SC layers that tape stripping gradually removes. This technique is an easy, fast, rapid and comparatively non-distant way to evaluate the standard and effectiveness of medications, emulsifiers and skin-care products after the application of topical dermatology.[42]

Microdialysis

A less intrusive method called microdialysis has been brought to dermatological studies as a beneficial *in vivo* instrument for evaluating topical formulations' bioavailability and bioequivalence. This method has been effectively used to evaluate the pharmacokinetic and pharmacodynamic response and the cutaneous administration of various substances both internal and external to tissues' extracellular spaces. In fact, this technique allows for evaluating the local pharmacokinetic profile of topical medication absorption from every sampling site by monitoring drug action site concentrations of free drug throughout time. Human volunteers have successfully used the microdialysis method to look into the penetration of various organic solvents and the histamine is released topically in reaction to different topical stimuli. This could be used to assess skin metabolism, quantify the dermal inflammatory mediators, measure drugs or other substances absorbed through the skin and provide an alternate medication administration method.[43]

Vasoconstrictor assay

The blanching assay on human skin, also called the vasoconstrictor test, is a tried-and-true technique for evaluating topical products' safety and effectiveness in clinical trials. The vasoconstrictor assay method complies with the FDA's *in vivo* bio equivalency guidelines for topical dermatological glucocorticoids. A hilltop chamber (about 1.2 cm) was applied with a predetermined volume of formulation or sample and secured up to the epidermis using sticky tape.[44]

Confocal laser scanning microscopy

Microscopy using Confocal Laser Scanning is another crucial instrument for evaluating DPK parameters. It is not necessary to prepare the skin to produce optical sections in order to obtain confocal images using fluorescent medications or probes. Confocal pictures are available in the perpendicular plane or the plane that runs parallel to the sample's surface. This technique has been extensively employed to evaluate distribution or penetration of drugs in the layers of skin subsequent to topical administration of microbes, particles of nanoscale and vesicular structures, including liposomes and niosomes, among others.[45]

CONCLUSION

In the context of dermatokinetic research, the study of herbal remedies presents a potential therapeutic benefit as well as significant side effects. We have clarified the effectiveness, safety issues, mechanisms of action and potential uses of herbal remedies in dermatology through this analysis. Herbal medicines are a promising alternative method of treatment for a range of dermatological conditions because they are a rich source of bioactive compounds with many different pharmacological effects. Botanical extracts have a great deal of potential to replace or supplement traditional treatments due to their antimicrobial, wound-healing and anti-arthritic qualities. Due to the widespread and expanding use of natural-derived substances worldwide, herbal remedies require a thorough and rigorous assessment of their safety issues and pharmacological characteristics.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ADME: Absorption, Distribution, Metabolism and Excretion; **AD:** Atopic dermatitis; **SC:** Sub-cutaneous layer; **DPK:** Dermatopharmacokinetic.

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