Current Pharmaceutical Research (CPR)
Vol 2, Issue 1, January-March 2026
Journal Homepage: https://cpr.org.in/

Synergizing Ethno-medicine and Technology: Transdermal Herbal Formulation against Scabies

[1]Avidit Sharma, [1]Namita Bakshi, [1]Pallavi Chandel[*], [1]Mohita Thakur

[1] *School of Pharmacy, Deshbhagat University, off to NH-44, Amloh Road, Mandi Gobindgarh District Fatehgarh Sahib, Punjab- 14, Mandi Gobindgarh, Punjab 147301, India.*

Keywords

Ethnomedicine, Transdermal drug delivery, Herbal formulations, Nanocarriers, Artificial intelligence.

Abstract

Scabies is a highly contagious parasitic skin disease that continues to impose a substantial global health burden, particularly in resource-limited, overcrowded, and displaced populations. Despite the availability of conventional scabicides such as permethrin and ivermectin, treatment outcomes are increasingly compromised by drug resistance, poor ovicidal activity, adverse effects, and low patient adherence. These limitations highlight an urgent need for safer, more effective, and accessible therapeutic alternatives. Ethnomedicine offers a rich repository of plant-based agents with proven antiparasitic, anti-inflammatory, antibacterial, and wound-healing properties; Their clinical translation is often constrained by poor skin penetration, variability, and lack of standardization. This review explores the strategic integration of ethnomedicinal knowledge with modern transdermal drug delivery technologies for the management of scabies. Emphasis is placed on advanced delivery platforms such as nanocarriers (liposomes, ethosomes, phytosomes), microneedle-mediated systems, and quality-by-design–based formulation strategies that enhance dermal penetration, bioavailability, controlled release, and patient compliance. The emerging role of artificial intelligence and machine learning in formulation optimization, skin permeability prediction, and rational selection of herbal actives is discussed as a transformative approach to accelerate development and improve therapeutic precision. Collectively, the convergence of ethnomedicine, transdermal technology, and data-driven optimization presents a promising, sustainable, and culturally acceptable paradigm for scabies management. Such integrative strategies have the potential to overcome current therapeutic gaps, reduce disease burden, and support global efforts aligned with neglected tropical disease control and universal health coverage.

***Corresponding Author:**
Ms. Pallavi Chandel (pallavichandel1921@gmail.com)
ORCID: 0009-0000-5819-6016

Article Info
Received: 06 February 2026; Received in revised form: 28 March 2026; Accepted: 29 March 2026; Available online: 31 March 2026; Volume: 2; Issue: 1; Pages: 41-62.

ISSN: 3049-2955/The authors © 2026, under exclusive license to the Sprout Publication
DOI: https://doi.org/10.63785/2026.2.1. 4162

1. Introduction

1.1 Global Epidemiology and Socioeconomic Impact

Scabies, an infection caused by a mite, Sarcoptes scabiei, is a paradigmatic example of neglected tropical disease, the etiology of which is based on a complex of biological, socioeconomic, and infrastructural decadence [1]. The intrusion of the cutaneous substrate then the embryonic differentiation of oocytes, accomplishes the continuation of the intractable pruritus, pain, and skin-related lesions, which provokes a self-perpetuating cycle of chronic morbidity. The socioeconomic deprivation, overcrowding, low health literacy, and inefficiency of the health-care delivery systems are closely tied to the epidemiologic manifestation of this condition [2]. Globally, scabies infests over 200 million people simultaneously and has been estimated to have 400-600 million cases of incidence every year, thus perpetuating endemic populations as well as epidemic bursts. The illness occurs in all the continents and classes of the population; however, the load is disproportionately in poor, overcrowded areas. Some settings include Ethiopia, India and Indonesia which have had greater prevalence of up to 35 percent particularly in paediatric patients, among refugees, and tribal populations [3]. The issue of outbreaks of scabies also occurs in high-income scenarios in institutions, such as nursing homes, hospitals, and in prisons, hence demonstrating permanency of the environmental and

social determinants [4]. In tropical areas with limited resources, the prevalence of scabies may be as high as 10 percent among children, which makes scabies a societal-health, as well as a child equity issue [5].

Scabies has enormous socioeconomic impacts, which are very manifold. Physician visits, treatment plans, and the financial cost of wrong diagnosis are direct expenses, whereas the cost of interrupted education, lost income, sleep deprivation, loss of mental health and social stigma are indirect [6]. Long-term lesions are a factor in the social isolation and developmental delays in children with the diagnosed condition. The secondary bacterial superinfections as a result of dermal injury can result in severe sequelae of acute glomerulonephritis or rheumatic heart disease hence increasing the cost and mortality rates in health-care [7]. The Global Burden of Disease conducted in 2015 estimated scabias to cause about 0.21 percent of global Disability-Adjusted Life Years (DALYs), with the greatest burden of the disease being found in Asia, Oceania, and Latin America [8].

Ethnomedical strategies constitute cluster strategies wherein the traditional botanical-based remedies are incorporated in the modern transdermal preparations, offering a promising source of therapeutic value [9]. It is used in gels, creams, and patches with essential oils and phytochemicals like tea tree oil, neem, eugenol, and geranial that have acaricidal and anti -inflammatory effects and show good compliance and few negative incidents in both human and animal research [10]. The Emerging therapy functioned as trial efficiency, which was fast and was registered in India with community-based experimentation of neutraceutical gels fortified with plant extracts [11]. It is also supported by veterinary models that highlight the fact that such interventions can be scaled up in resource-sustained settings that need to be cost-effective, easy to use and store, and culturally consistent, which accompany public-health education efforts in relation to neglected diseases [12].

Table 1 summarizes key findings from global, regional, and population-based studies on scabies, highlighting prevalence and incidence estimates, high-risk regions and populations (including displaced and school-aged groups), behavioral and environmental risk factors, health and socioeconomic impacts, post-pandemic trends, and policy implications. Collectively, the evidence underscores substantial global burden, marked geographic and population heterogeneity, and the need for integrated control strategies within universal health coverage frameworks [13].

Table 1: Global epidemiology, burden, and determinants of scabies.

S. No.	Finding / Metric	Region / Population	Key Insight / Impact	References
1.	Global prevalence estimate	Worldwide	~11.9 % pooled prevalence across studies; highest in Western Pacific	[14],
2.	Total affected worldwide	Global	>200 million affected at any time with ~455 million annual incidence	[15]
3.	High-risk region	Oceania	~17.9 % prevalence, highest among regions	[16]
4.	Post-COVID resurgence	Lazio, Italy	Significant increase in cases 2021–2023	[17]
5.	Refugee populations	Displaced settings	Highest pooled prevalence ~23 %	[18]
6.	Asia	Displaced / general	~25 % prevalence in Asia among displaced	[19]
7.	Africa	Displaced / general	~7 % prevalence among displaced	[20]
8.	School-aged children	Combined groups	~15 % in child/adult populations	[21]
9.	Pooled odds related to behaviors	Global	Contact history, lack of hygiene ↑ risk	[22]
10.	Shared sleepers/clothing risk	Community settings	2.5–3.4× risk with sharing habits	[23]
11.	Inequity not reliably linked	Countries	Socioeconomic status not always assoc. with prevalence	[24]
12.	Trend in Europe	Belgium	Rising national incidence 2000–2023	[25]
13.	Age distribution	Finland	Incidence trends vary by age	[26]
14.	Children highest burden	Fiji, Panama	Extreme point prevalence in young children	[27]
15.	Secondary infection risk	Global	Bacterial complications add clinical burden	[28]
16.	DALYs	Global	Millions of DALYs reported (GBD 2021)	[29]
17.	Health systems strain	Low-resource countries	Outbreaks exacerbate service loads	[30]

18.	Outbreak volatility	Post-pandemic	Reduced then rapid resurgence in some regions	[31]
19.	Risk in overcrowding	Refugee camps	Transmission driven by crowding/hygiene barriers	[32]
20.	Gender distribution	Local analyses	Females sometimes show higher incidence locally	[33]
21.	Geographic hotspots	Iran province	Rising prevalence over years in specific areas	[34]
22.	Hospital outbreaks	High-income settings	Institutional outbreaks reported	[35]
23.	Socioeconomic effect	Sudan study	Poverty, hygiene, access impact prevalence	[36]
24.	Child morbidity	School populations	Burden leads to missed school days	[37]
25.	Stigma and isolation	Global narrative	Social and psychological effects reported	[38]
26.	Secondary disease sequelae	Diverse settings	Potential for severe complications	[39]
27.	Economic cost	Resource-poor health systems	Treatment costs and lost productivity	[40]
28.	Neglect as NTD	WHO designation	Recognized in neglected tropical disease roadmap	[41]
29.	Variation by SDI	Burden studies	Middle SDI regions often highest rates	[42]
30.	Policy implications	Universal health coverage	Calls for integration of control measures	[43]

1.2 Treatment Gaps in Current Dermatological Approaches

The existing dermatological solutions to scabies have enormous gaps that pose challenges towards proper management of the scabies disease; which is a highly contagious disease of the skin [44]. Scabies is a disease affecting millions of people across the globe, especially when it comes to the more vulnerable groups of people in the resource- restricted regions, but the current therapies seem not to be effective, owing to factors like treatment resistance, poor compliance, low ovicidal activity, and adverse effects. Standard methods of treatment are mainly based on topical scabicides such as permethrin and benzyl benzoate, or on systemic ivermectin [45]. Although these medications have demonstrated effectiveness and efficiency, new literature cites increased cases of treatment failure and development of resistance particularly against permethrin and ivermectin, making the control of scabies difficult in most parts of the world [46]. The major shortcoming of the existing therapies is that they do not completely eliminate the life cycle of the mite especially the eggs [47]. The vast majority of conventional acaricides are efficient in killing adult mites but do not have ovicidal qualities, which results in resounding infestation and subsequent frequent application [48]. Such therapeutic gap tends to lead to extended treatment courses that are cumbersome and disruptive to adherence even in overcrowded or low-income settings, where several rounds of treatment or a course of treatment are not only inaccessible, but unaffordable. In addition, topical scabicides need to be applied carefully on the entire body surface and failure to do so or partly is a typical failure mode. Recurrent contact during multiple weeks also enhances the chances of washing off the product or renewal of the untreated contacts in the household [49].

Another issue is adverse effects. As effective as they are, lindane, permethrin and ivermectin which are commonly used in the treatment have been reported to cause side effects including skin irritation to systemic toxicity [50]. Their safety profiles limit their application in vulnerable groups such as young children, pregnant women and those with liver impairment and as such, thereby limit the choice of treatment to the at-risk groups [51]. The most extreme form of scabies is the so-called crusted scabies, which is very common in immunocompromised people and presents even more of a therapeutic challenge since topical scabicides cannot enter softened skin in thickness and there is no agreement among the disciplines on how to dodge the most required treatment regimens [52]. Also, the high frequency of the application of the same scabicides in the whole world adds selective pressure to mites, providing resistance and leaving first- line medications of minimal use in the long term [53]. The potential remedies to these gaps have been in ethnomedicine and herbal alternatives [54]. Melaleuca alternifolia (tea tree oil) which is traditional medicinal plant demonstrates promising acaricidal, anti-inflammatory, and antibacterial effects that may substitute or supplement treatment of scabs. As an illustration, tea tree oil has been shown to have better in vitro mite-killing efficacy than permethrin and ivermectin and could possess greater symptom mitigation and decrease treatment regimen [55]. Nevertheless, there have been barriers to the integration of herbal therapies into formal treatment guidelines due to the problem of bioavailability, standardisation, and mode of delivery

[56]. This is where the prospect of implementation of ethnomedicine together with the progressive pharmaceutical methods- transdermal delivery system lies [57].

Transdermal available herbal preparations increase the dermal flux of active herbal phytoconstituents, control of dosage, contact time, and reduction of systemic exposure, thereby defeating numerous limitations of traditional therapies, and pure herbal application [58]. They offer convenient application to the user, minimise ill reactions of the dermatology, and may act on both the eggs of the mite and adult leading to their elimination by prolonged release of bioactive substances [59]. The solution to this part of the treatment gaps would be more intensive research in order to maximize the transdermal herbal preparations, prove their efficacy in scale based clinical trials, and put down standards of production to guarantee authenticity. Simultaneous approaches in the field of public health should be focused on effective application methods, treatment of the household contacts, and education in improving the compliance and preventing reinfestations. Finally, the ethical combination of ethnomedicine and technology can be used to determine safer, more effective, accessible, and sustainable treatments of scabies to overcome the gap in dermatological treatments, particularly in the high-burden, resource-poor environments [60].

1.3 Rationale for Integrating Ethnomedicine and Modern Technology

Incorporating ethnomedicine into current technology and especially using transdermal herbs is an interesting and the needed approach towards the development of treatment of scabies [61]. The logic behind such integration lies in the fact that it will overcome major shortcomings of the traditional therapies and take advantage of the merits of traditional knowledge and new pharmacological approaches. Sarcoptes scabies causes scabies, which is popular parasitic skin infection that affects the skin of millions of people all over the world, particularly in the poor and congested environment. Currently used scabicidal agents such as permethrin and ivvermectin are also effective but there are also increasing concerns about them such as resistance to drugs, low ovicidal efficacy, lack of safety in susceptible groups and additionally lack of availability in low-resource states. The restriction breeds a dire need to find alternative or adjunctive therapy which is safe, effective, culturally acceptable and economically valid [62]. The medieval application of natural products and medicinal plants, ethnomedicine, is a well-explored but poorly utilized source of antiparasitic, anti-inflammatory, antibacterial, and wound-healing bioactive compounds [63]. Historically, there are several plants that are used across numerous cultures in the treatment of skin infestations (as well as inflammation), these plants include Melaleuca alternifolia (tea tree), Azadirachta indica (neem), Curcuma longa (turmeric), and Tinospora cordifolia [64].

A large number of in vitro and in vivo experiments have proved acaricidal effects of these botanical extracts on scabies mites, and positive outcomes on alleviating symptoms and prevent further infections [65]. Conventional herbal treatment, however, has difficulties when used crudely in that there is difficulty in penetrating the skin, dosing remains irregular, and quality variability- concerns that preclude its substantial clinical use and acceptance. Contemporary pharmaceutical technology especially the transdermal drug delivery systems presents solutions that can these challenges at bay [66]. Transdermal delivery systems such as crams, gels, patches boost penetration of herbal actives across the stratum corneum to target locations in the skin, enhancing bioavailability and owing to increased therapeutic efficacy. They also enable smart, controlled, and sustained release and the frequency of dosing is lowered, and patient adherence is enhanced [67]. Notably, transdermal implementation equals decreased systemic absorption and therefore lowers the chances of systemic toxicity commonly developed by the oral antiparasitics. With this technology, it is now possible to standardize and optimize ethnomedicinal compounds to enhance their reproducibility, stability, and scalability to use in clinical applications [68]. Ethnomedicine with modern transdermal technology synergy is in line with some of the priority aspects in addressing the unexplored linkage of most neglected tropical conditions by implementing a strategy focused on scabies through resource-deprived areas [69]. It offers culturally congruent remedies that are likely to be well accepted within a society that is accustomed to traditional remedies yet have no access or trust in synthetic drugs [70]. Integration can enhance health equity by providing herbal-based remedies that are scientifically proven effective and safe and enable the community to take control in the management of diseases. Plant-based therapies are also environmentally friendly as they are biodegradable, which is beneficial to the sustainability of the whole world, as compared to synthetic agents that have more harmful effects on the environment [71].

2. Mechanisms of Action of Selected Herbal Agents

Transdermal herbal compounds can be viewed as an effective approach toward integrating ethnomedicine and technology to address scabies, most likely through exploiting multifunctional multi-herbs with known bioactivities. Tea tree oil (Melaleuca alternifolia), Tulsi (Ocimum sanctum), Aloe vera, Leucas aspera, Cedrus deodara and geraniol belonging to the family Apiaceae have been found to have key antiscabietic activities such as acaricidal, anti-inflammatory, antioxidant, antibacterial and wound remedy activities. The prominent features of tea tree oil are it has a strong in vitro acaricidal effect, activity against various scabies resistant strains, and multi-mode action destroying mites, reducing secondary infection by bacteria, soothing itching, and healing lesions caused by anti-inflammatory action on terpinen-4-ol [72].

The aloe vera has proven to have similar effects to benzyl benzoate, which mends the skin, and alleviates pruritus because of its capacity to heal wounds and moisturize the skin[73]. The effects of Leucas aspera and Cedrus deodara are scabicidal in nature as well as anti-inflammatory and this combined with Strychnos nux-vomica and Pongamia pinnata has provided significant clinical outcomes in terms of symptom alleviation. These herbal agents can be incorporated with modern technology such as nanoemulsion and vesicular drug delivery system to penetrate the skin deeply to cause long lasting and target acaricidal effects and to reduce the side effects of the system to the rest of body [74]. Further future advances in patch medications depend on drug delivery efficiency and patient compliance by making use of a new generation of polymers e.g., HPMC and PVA [75]. Moreover, organic molecules such as geraniol show safe, full-crossed clinical remission in current research and this highlights how they can be utilized as safe, effective alternative medical treatment to conventional therapies [76]. Using the blend of ethonomedicine knowledge and technology, including maximally effective extraction, nano-formulation, and precise controlled drug delivery, the management of scabies in cases with limited resources and reported resistance will be transformed by transdermal herbal products, utilizing both the tradition and the innovation of natural medicine practices [77].

2.1 Antiparasitic and Anti-inflammatory Activities

Scabies is a transmittable skin infection by the miticule Sarcoptes scabiei which usually infects vulnerable groups all over the globe with the exception of children in tropical and impoverished regions [78]. Traditional allopathic therapy with permethrin and ivermectin is useful and has side effects, a growing resistance, and inaccessibility. The integration of ethnomedicine, which is the traditional plant-based medicine and current transdermal drug delivery technologies, is a promising alternative treatment method that is safer, more efficient, and efficient. The ethnomedicinal plants are widely used because of their bioactive compounds that have antiparasitic as well as anti-inflammatory effects [79]. These twin facts are important as scabies mite does not only lead to parasitism but long-term inflammatory reactions on the skin [80]. Herbal formulation of anti-inflammatory agents diminishes the redness, itching, and the secondary infection by bacteria to increase the patient comfort and recovery. To exemplify, terpenoids and flavonoids that are found in compounds of the tea tree oil, aloe vera, and others, prevent the performance of mites and regulate the inflammatory process [81]. Recent developments put emphasis on transdermal herbal preparations as topical-specific agents that promote the rapid penetration of bioactive substances into the skin [58]. This approach boosts the absorption rates of the drug, lowers the levels of systemic exposure and side effects, and allows the constant delivery, thus enhancing adherence to the treatment process [82]. In one research a 2 percent herbal ointment was presented as a method to cure scabies in less than a month when the intensity was applied twice per week, which showed the prospective of low-frequency and effective dosing with few side effects. Transdermal patches containing extracts of plants such as tulsi and Centella asiatica have also been prepared and tested to be better in penementation through the skin. Gel preparations of the tea tree oil have demonstrated better acaricidal (killing mites) effects than regular treatment, and other antibacterial and anti-inflammatory effects, lessening the load of scabies and eliminating secondary infections. Nevertheless, it should be formulated properly to reduce the exposure to sensitization, especially among children [83]. New technologies in drug discovery based on ethnomedicinal knowledge are, therefore, important towards the creation of new anti-scabies medications. Such a synergy will use traditional herb advantages combined with modern drug delivery to overcome the weak points of synthetic drugs such as resistance and side effects. These integrative patterns can also be implemented to mass administration of drugs to the endemic regions to enhance the access of effective and safe scabies control [84].

2.2 Role in Skin Barrier Repair and Immune Modulation

Scabies is a skin infestation by the mite, Sarcoptes scabiei which permeates the skin barrier and initiates a complicated immune reaction that usually causes inflammation, itching and secondarily, infection [80]. Treatment of mites does not just involve eliminating the mites but also involves repairing of the skin barrier and the immune system to ease inflammation and restore skin homeostasis [85]. The skin is a dual function barrier (particularly the top-most layer, which is the stratum corneum) that functions as a vital physical immunological barrier against infection by pathogens [86]. Scabies mites may cause damage to this barrier which will break its functionality and can create microbial colonization and worsen immune dysregulation. In the treatment plan, it is vital to restore the skin barrier integrity to diminish the symptoms and avert recurrence. This healing is done by fortifying structural proteins such as filaggrin and involucrin that are useful in supporting the protective role of the skin and hormonal balance of hydration [87].

Ethnomedicine presents a tremendous source of herbal agents, which have barrier-repair as well as immunomodulatory effects [88]. Anti-inflammatory effects of many herbal extracts including neem oil, tea tree oil, aloe vera, and other traditional polyherbal preparations can be attributed to the anti-inflammatory effect of the extracts on mediators, including NF-KB, inflammatory cytokines, and adhesion molecules that mediate skin inflammation. These botanicals also facilitate wound healing and skin regeneration in stimulating keratinocyte migration and excessive immune responses which in turn facilitates the re-establishment of normal skin architecture. The effect of these herbal compounds can be increased significantly by the use of technological advances in transdermal drug delivery.

Nanotechnology, nanoemulsions and transethosomal formulation enhance diffusion of herbal actives through the tough barrier layer of skin and ensures deep penetration into deeper layers of skin and must also be sustained [89]. The bioengineering methodology allows overcoming the inherent constraints of phytochemical absorption to enable more efficient mites and localized inflammations to be suppressed with less systemic side effects [90]. The integrative interface between the immunomodulatory and skin repair potential of ethnomedicine and the development of current transdermal delivery development approaches towards novel compound formulations capable of addressing scabies in a more holistic manner lies in a synergistic approach to addressing the issue [90]. These formulations offer the effect of anti-scabies but at the same time promote the skin healing process and immune control lead to secondary infections that may cause chronic inflammation and immune responses, leading to a better patient outcome with a better degree of safety and convenience [91].

2.3 Synergistic Interactions among Phytoconstituents

Cumulative activity of phytoconstituent is central to augmenting the effect of ethnomedicine particularly when synthesized together with superior technologies in drug delivery like transdermal herbal preparations in addressing diseases like scabies [92]. Ethnomedicine depends upon the multifaceted combinations of bioactive compounds, and phytoconstituents, of plant derivatives the summation of which in bioactivity can work wonders beyond those of their individual counterparts because of the synergies of action between most of them [93]. Studies have shown that the phytoconstituents of herbal extract do not operate in isolation, but rather interact synergistically to enhance the solubility, absorption and the bioavailability of the active compounds; which are among the determining factors in transdermal delivery system [93]. As an illustration, membrane permeability may be altered by some flavonoids, phenolic acids, and terpenes in plant extract to prevent the biodegradation of other bioactives, easier penetration into the skin and extended bioactivity of topical formulations used in treating scabies. The research indicated that the increased efficacy of herbal formulations in the treatment of skin ailments including scabies is due to the combined action of numerous phytochemicals on a variety of therapeutic pathways that include anti-microbial, anti-inflammatory, and antipruritic mechanisms [94].

Essential oils such as carvacrol and geranium extracts bring in robust antimicrobial functions whereas flavonoids and tannins bring antioxidant and anti-inflammatory functions which enhances skin repair and alleviates irritation on skin often caused by scabies mites [95]. This multidimensional activity is an example of the potential uses of ethnomedicine which makes use of natural synergy inherent in plants which is frequently lacking in modern pharmacology when single compounds are isolated.Technologically, transdermal formulations give a very good platform on which to harness on these synergies [96]. The skin is a complicated barrier that should be formulated with careful consideration to maintain maximum delivery of herbal actives. Phytoconstituent-derived enhancements in drug permeation can be achieved by themselves. Plants such as Tinospora cordifolia, Centratherum anthelminticum among others that are traditional effective against scabies have led to the development of herbal transdermal patches and gels. Such formulations have a limited number of side effects than synthetic medicines and can be used less often and with a lot of efficacy depending on the prolonged absorption of the phytochemicals used which is attributed to the synergistic effect [97].

In addition, phytochemical synergy not only enhances better treatment results but is also useful in reducing drug resistance, which is one of the challenges in the treatment of infectious and parasitic skin diseases such as scabies. Various phytoconstituents have been shown to act in combination with traditional antiparasitic drugs or in the herbal preparations to overcome the resistance mechanisms in microbial cell membrane or enzymatic resistance [98]. As an example, various bioactive agents can act on various locations in the mite or skin inflammation pathway, and slow down the emergence of resistance. Phytochemical interactions can be better understood and optimized by combining the traditional herbal wisdom with the modern scientific methods, such as a higher level of chromatography, and computational modelling. This combined strategy would lead to development of more effective and safer transdermal herbal products due to prediction of synergies and antagonies among phytoconstituents which would also increase therapeutic efficacy in clinical applications against scabies and other skin related illnesses [99].

3. QbD-Based Formulation Design

Quality by Definite (QbD) is a methodology based on science, which tries to guarantee pre-defined quality of products by comprehending and regulating formulation and process variables [100]. QbD offers a stringent guideline through which to combine the ethnomedicinal with the contemporary pharmaceutical technology to develop optimized, effective and safe drug delivery systems under the context of designing transdermal herbal formulations to treat scabies [101]. The herbal preparations used to treat scabies are based on the anti-parasitic, anti-inflammatory, antibacterial and skin-soothing properties of bioactive phytochemicals found in both non-Western and Western systems of medicine including the Unani and Ayurveda medicine [102]. These botanicals contain essential oils, extracts, and purified plant compounds that have been proven to have known effectiveness against scabies mites Sarcoptes scabiei and skin lesions associated with them [103]. Formulation design using QbD principles starts by defining a Quality Target Product Profile (QTPP), the process of identifying important quality attributes (CQAs) such as drug content uniformity,

release rate, skin permeation, and stability. The identification of critical material attributes (CMAs) and critical process parameters (CPPs) are performed with the help of risk assessment tools (Failure Mode and Effects Analysis, FMEA, et cetera) [104]. This aids developers to devise experimental integrity to maximize essential variables such as the concentration of the herbal extract, selection of the permeation enhancers, polymer matrix structure, and patch or gel thickness so as to increase their effectiveness and acceptability by the patient [105].

A number of studies indicate QbD use in the herbal transdermal patches, nanogels. An example of this is that a study developed herbal transdermal patches by extracting plants that have anti-inflammatory properties and anti-arthritic properties, and casting them in solvents to get uniform, flexible and controllable drug release films through optimum solvents and polymer combinations [106]. The other study incorporated synergistic herbal extracts in nanogel preparations, which took a chance and capitalized on their joint effects of anti-inflammatory and analgesic on the traditional pharmaceuticals to enhance skin permeation and self-release and reduce systemic side effects [107]. The recent updates involve the use of nanocarriers such as solid lipid nanoparticles (SLNs), liposomes and nanosponges in herbal transdermal gels to improve the bioavailability and site-specific skin delivery of herbal actives. These technologies are compatible with principles of the QbD framework and permit the control of the drug release kinetics and enhance the stability and skin retention. It is demonstrated that clinical assessments of polyherbal topical products in the treatment of scabies reveal a great occurrence of reduction in itching/skin lesions and parasitism load with fewer adverse effects, which validates the therapeutic capacity of such QbD-optimized herbal products [108].

4. Nanocarriers: Liposomes, Ethosomes, and Phytosomes

Liposomes, ethosomes, and phytosomes are the best examples of nanocarriers that are essential in the increased delivery of transdermal drugs using herbs, particularly in combining technology and ethnomedicine in the treatment of illnesses like scabies [109]. These nanocarriers enhance the stability, permeability and bioavailability of the drug as well as delivering its specific targeted applications via the skin barrier, and these issues related to the standard herbal formulations of the past in terms of their effective penetration through the skin barrier [110]. Assemblage of lipids and cholesterol the liposomes are spherical vesicles with bilayer membranes constituted by the main components of phospholipids and cholesterol that can entrap both hydrophilic and lipophilic drugs [111]. They ensure the active drug does not degrade honestly and increase controlled delivery, and increase the absorption of the drug by fusing with the lipid layers of the skin. Ethosomes are an altered liposome consisting of a high content of ethanol (20-45%), this renders the vesicles highly deformable and allows the vesicles to infiltrate further into the layers of the skin [112]. This ethanol is also a permeation enhancer in that the lipid bi-layer of skin is destabilized permitting entry of ethosomes of health promoting bioactives deep within the circulatory system, avoiding skin irritation [113]. Ethosomes offer a better encapsulation efficiency, have more prolonged retention and enhanced patient compliance as compared to traditional liposomes, which explains the reason why ethosomes is an enhanced and a viable choice with regard to transdermal drug delivery systems [114].

In contrast to the ethosomes, the phytosomes are chemically attached between the phospholipids, such as phosphatidylcholine and phytochemicals which ensure the stability of the complex and increased penetration of the phytosomes through the skin barrier. The ability of the phytosomes to enter through the skin layers in large numbers due to the strong lipid affinity and flexibility of the vesicles can increase the efficacy of the herbal drugs by means of optimizing the pharmacodynamics and pharmacokinetics [115]. The phytosomes are very small and deformable hence they are very useful in delivery of poorly soluble herbal drugs transdermally which give targeted and controlled delivery. These nanocarriers are used in ethnomedicine and transdermal scabias herbal preparation, the traditional herbal knowledge is used in combination with the modern technology to circumvent the drawbacks of traditional herbals such as low bioavailability and low skin absorption [116]. An example is the synergistic activity of ethosomal gels impregnated with herbal extracts (e.g. luliconazole/clove extracts) in the management of skin infection, due to their ability to allow deeper drug penetration and prolonged retention of the drug at the site of insult [117]. Not only improves its therapeutic effectiveness, but also minimizes the systemic side effects of either oral or topical therapy [118].

Phytosome-based preparations increase the delivery of antimicrobial phytoconstituents in ethnomedicinal plants, penetration of this antimicrobial through the stratum corneum and localized effect on parasites such as scabies causes. Elastic, deformable vesicles delivered by the transferosome and ethosome systems can cross the skin barrier without causing chemical irritation to increase the efficacy of bioactive herbal productsv [119]. All in all, nanocarriers (liposomes, ethosomes and phytosomes) are superior delivery systems that have played an instrumental role in enhancing transdermal delivery of herbal medicines through improving the stability, permeability, targeted delivery, and sustained release of these compounds [120]. The technologies provide a good prospect towards integrating ethnomedicine with nanotechnology in the development of highly effective herbal transdermal preparations against such diseases as scabies and show greater bioavailability, patient compliance and synergy with pharmacologic therapy [121].

The figure 1 illustrates (left) traditional herbal formulations (gel, lotion, and patch), where limited penetration across the stratum corneum results in reduced bioavailability of active compounds at the site of scabies mite infestation, and (right) nanocarrier-based systems (liposomes, ethosomes, and phytosomes), which enhance skin permeation, improve dermal targeting, and increase local bioavailability of herbal actives, leading to improved therapeutic efficacy against scabies mites [122].

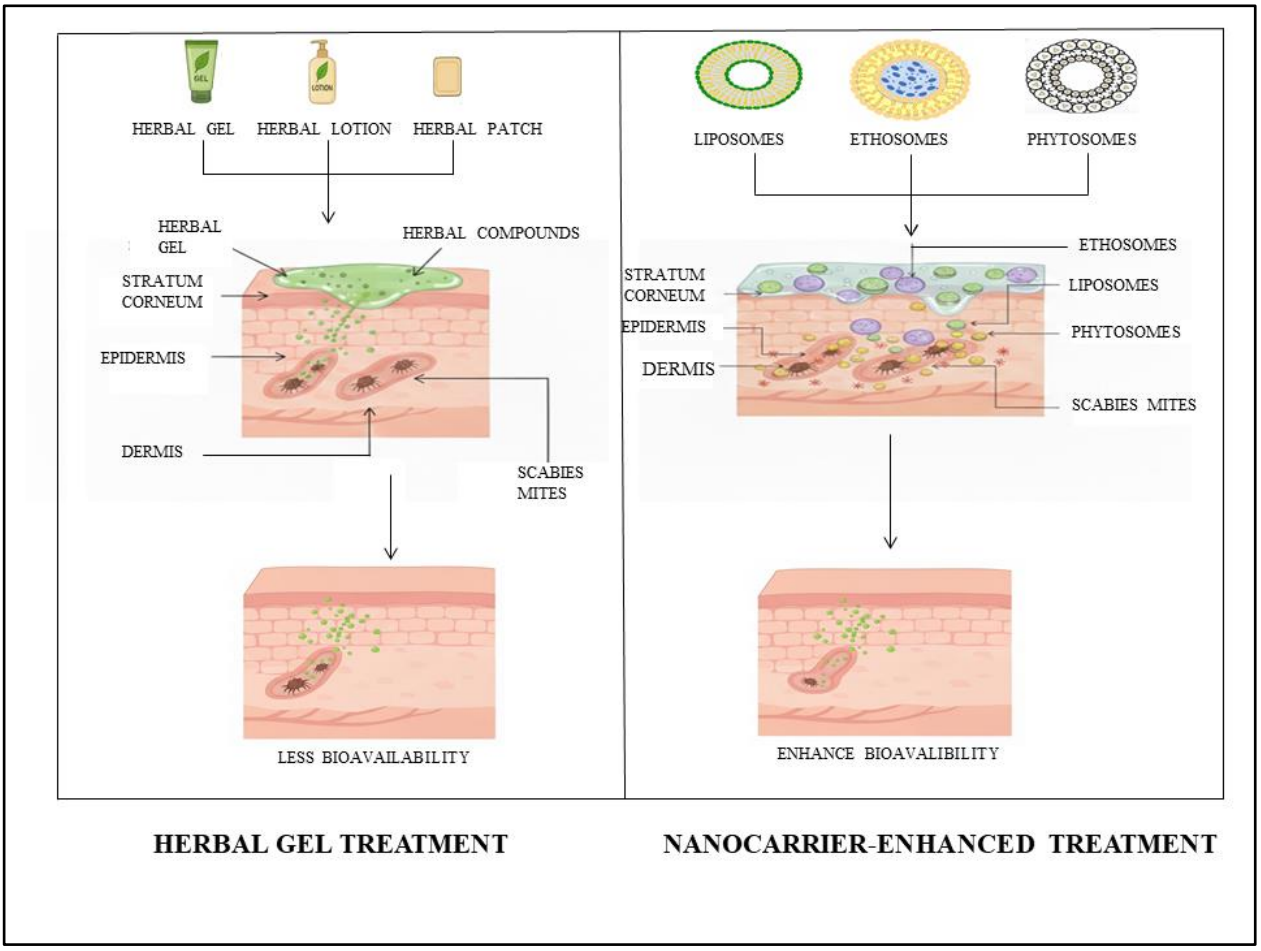

Figure 1: Schematic comparison of conventional herbal topical therapy and nanocarrier-enhanced delivery for scabies management.

5. Integration of Emerging Technologies

5.1 Microneedle-Mediated Systems

Microneedle (MN) is an innovative technology of transdermal drug administration. It enhances the efficacy and accuracy of herbal drugs having been employed in conventional ethnomedicine to cure skin diseases, such as scabies [123]. The large issue that microneedles fix is that the stratum corneum, the outermost stratum of the skin, is impermeable to most phytochemicals that are active [124]. Microneedles enable the herbal actives to enter directly into the deeper epidermis or dermis by formation of tiny channels [125]. What comes out is increased bioavailability and quicker action as far as therapy is concerned, greater than the normal topical creams [126]. Due to impermeability of the liver, the drug would need lesser doses since the drug does not undergo the 1st pass metabolism by the liver, the side effects will be lesser to those that occur in the body. The micro needles systems are herbal based systems that synthesize natural healing properties of plant extract with a cutting-edge technology that manufactures dissolvable or coated micro needles [127]. These micro needles could be designed to release antiphrastic compounds as well as anti-inflammatory compounds into the skin layers in which the Sarcoptes scabies mites inhabit in a sustained localized mode of delivery [128]. Direct delivery enhances the drug absorption and reduces the time till the therapeutic effect, being superior to the conventional use of the oral or ointment routes [129]. In the case of scabies, a variety of phytochemicals (turmeric, neem, tulsi) have been found to have antiparasitic, anti-inflammatory, and wound-healing effects [130]. Corporation of these compounds in microneedle patches develops a painless, least invasive, and easy to administer method of therapy [131]. It also decreases the compliance issues which are due to a high dosage frequency or the side effects of chemical acaricides [132]. According to some research, the incorporation of nanoparticle carriers into our micro needles helps to increase penetration and release of herbal antimicrobials, in turn, increasing the efficacy and reducing microbial resistance [133]. Another advancement is the micro needle biosensors. Due to these devices, it is possible to monitor the level of infections, drugs, and therapeutic response in real-time, creating an individual scabies treatment plan [134]. Microneedle wearable sensors are simple to

use at home or in the field and effective ethnomedical interventions are also available [135]. Comprehensively, the revolution of microneedle-mediated transdermal delivery is a synergistic one. It is a combination of the sophistication of the herb remedies together with the precision technology and this deals with the drawbacks of the existing scabies cures. The strategy provides enhanced skin permeation, controlled delivery, hence, enhances patient compliance, and a lower systemic exposure, which results to safer and effective management of diseases [136].

The figure 2 depicts the fabrication and mechanism of action of a smart microneedle system, including a blank microneedle array integrated with an electronic control unit (drug-release controller), loading of herbal drugs into the microneedles, and application onto the skin. Upon attachment, the microneedles enable controlled and sustained transdermal delivery of herbal actives into the dermis, resulting in enhanced penetration, targeted release at the infestation site, and a reduction in scabies mites following treatment compared with the pre-treatment condition [137].

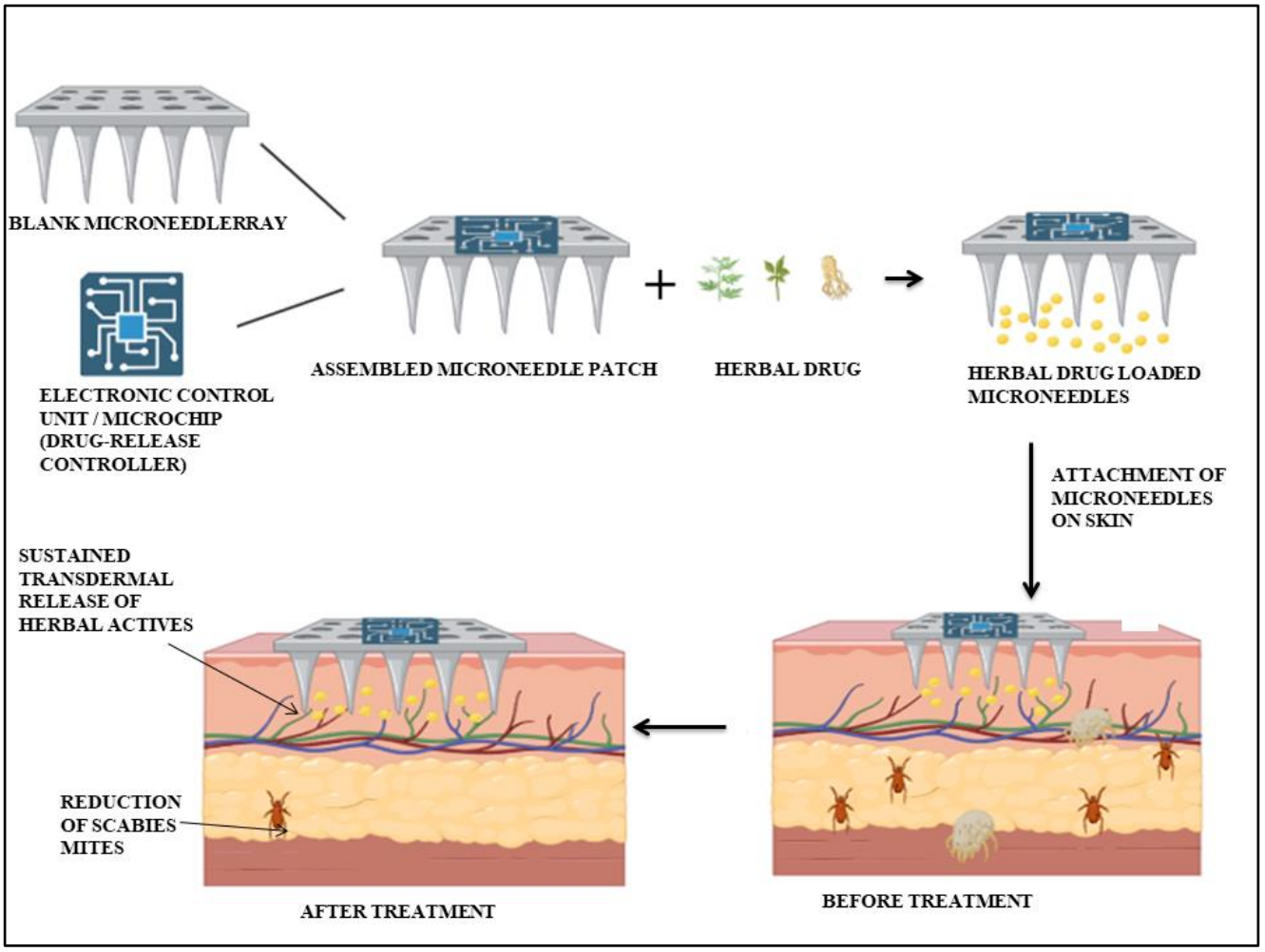

Figure 2: Conceptual illustration of an electronic-controlled herbal microneedle patch for scabies therapy.

5.2 3D Bioprinted Skins for Preclinical Modeling

Preclinical dermatological studies have benefited significantly due to a significant integration of emerging technologies, such as the use of three-dimensional bioprinted skin models, with the ability to significantly complement ethnomedicinal concepts with the high-tech approaches investigated in transdermal herbal concoctions against scabies [138]. Three-dimensional bioprinted skin is a high-end, biomimetic platform, which strongly mimics the cellular physiology and performances of the human epidermis, thus making it an ideal preclinical platform, which can be used to evaluate transdermal formulations, enhance their efficacy, safety, and tailor medicine [139]. Making skin constructs printed skin models in pharmacological testing as an involves bio printing followed by sequential deposition of living cells, such as fibroblasts, keratinocytes and endothelial cells, into bioinks which replicate the extracellular matrix [140]. The technology leads to cellular migration, proliferation, and differentiation which enable the production of skin tissues with multi-layered epidermis and dermis, vascularized and pigmented assemblies that are very similar to native human skin [141]. It is important to note that bio printed skins have been programmed to mimic physiological and pathological states including wound healing, inflammatory, and drug permeation dynamics which are essential in testing the efficacy of a transdermal herbal preparation against cutaneous infestations such as scabies [142]. Some studies have shown the usefulness of three dimensional bio improvement over the old-fashioned two dimensional

cultures and animal models, by giving species-specific and human-relevant information [143].

Recent improvements evolve on the vascularized skin-on-chip models that are produced using sacrificial bio printing, which offers more real-life skin barrier properties and immunogenicity to topical therapeutic, which is sensitive to the preclinical evaluation of anti-scabies herbal formulae [144]. Herbal preparations have therapeutic potential in ethno medical terms, as they have anti-inflammatory, anti-microbial, and anti-pruritic effects, which is necessary in the treatment process of scabies, a parasitic skin infection that is associated with rash and severe itching. These bioactive phytochemicals are effectively penetrated into the cutaneous layers using transdermal delivery systems which are optimized to get maximal absorption through the skin. Three-dimensional bio printed skin skins would also allow effective considerations of formulation penetration, efficacy and toxicological profiles to be assessed in advance before clinical use, enabling traditional remedies to be validated in a modern scientific paradigm [145].

Three-dimensional bio printed skin patches that are multifunctional, incorporating polycaprolactone; chitosan derivatives and curcumin have shown impressive therapeutic effects of the treatment of wounds and prevention of infections, thus indicating the strategy that could be made to maximize the delivery and efficacy of herbal formulations in the treatment of scabies [146]. These patches facilitate tissue regeneration by facilitating an increase in the polarization of macrophages, neovascularization, and collagen remodelling, which eventually leads to therapeutic outcomes to refractory dermatological conditions [147]. Altogether, convergent three-dimensional bio printing combined with ethno medicine uses the structural and functional reliability of bio printed skin to emulate disease pathology and assess herbal transdermal products [148]. This synergy overcomes the drawbacks of traditional testing paradigms because it will allow personalized, mechanistic examination of drug-skin interactions, which will cut down on the use of animal models and accelerate the generation of safer and more effective scabies treatment [149].

5.3 AI-optimized formulation algorithms

The adoption of artificial intelligence (AI) and machine learning (ML) methods are inculcating the paradigm shift in designing transdermal drug delivery system (TDDS), especially in herbal formulation with the objective of treating scabies [150]. Computational algorithms analyse big biochemical, physicochemical, and molecular data phasing to propose the best combination of health-achieving herbal constituents, excipients, and penetration enhancers to maximize therapeutic effects, increased drug permeation of the stratum corneum [151]. This constitutes a significant advancement opposed to traditional trial-and-error methods, which allowed fast design of formulations that are resource-efficient and have a higher bioavailability and clinical success [152]. The appropriate AI models such as artificial neural networks, deep neural networks and quantitative structure-activity relation (QSAR) models are used to model cutaneous permeability and drug-skin interactions [153]. They also use customized factors including skin type, level of hydration, age, etc, which they use to tailor transdermal herbal formulations to individual patient parameters, and to facilitate the maximum benefit of therapy. This can be achieved by sensor-integrated patches that have been designed to have AI functionality to control the process of drug release in real time, based on continuous monitoring of feedback data supplied by the skin microenvironment, hence maintaining steady efficacy and minimizing adverse effects [154].

In the context under investigation (scabies control), AI will help optimize herbal formulae based on ethno medicine, and increase their penetration and anti-scab-activity against Sarcoptes scabies. They are made-to-order such combinations of bioactive herbal extracts fortified with essential oils, AI-selected penetration promoting agents, and superior delivery systems like liposomes and micro needles [155]. Empirical research has documented close to 100 percent clinical cure and in less than a month of treatment and lower usage and no side effects compared to conventional chemical modalities [156]. The formulation workflow is based on AI that can provide a proper balance of the herbal ingredients to be safe and effective considering the pharmacokinetic variables such as solubility, stability, and dermal absorption. Besides, AI predicts both molecular interaction and permeation kinetics at complex formulations, stabilizing and maintained release profiles. Transdermal patches or ointments are therefore able to reach long-lasting therapeutic effects with lower dosage rate [157]. Researchers are working to create advanced systems of herbal transdermal delivery that are both environmentally friendly, cost-efficient, and patient-compliant by balancing the holistic understanding of ethno medicinal herbs and are state-of-the-art on AI optimization algorithms [158].

This table 2 outlines key AI/ML algorithms and computational concepts applied across formulation design, optimization, and evaluation, including prediction of drug release, skin permeability, bioavailability, stability, safety, and excipient compatibility. Collectively, these approaches enhance data-driven decision-making, reduce experimental burden, support multi-objective optimization, and accelerate the development of effective and safe herbal transdermal delivery systems [159].

Table 2: Applications of artificial intelligence and machine learning algorithms in herbal and transdermal formulation development

S. No.	Algorithm / Concept	Application in Formulation	Outcome / Relevance	References
1.	Machine Learning (ML)	Predict drug/compound release profiles	Improves prediction of formulation outcomes	[160]
2.	Supervised ML	Predict excipient and drug interactions	Guides formulation choices	[161]
3.	Decision Trees / RF	Classification of formulation data	Helps select optimal compositional factors	[162]
4.	Deep Neural Networks	Formulation property prediction	Models complex patterns in data	[163]
5.	Bayesian Optimization	Multi-objective optimization	Finds best trade-offs in design	[164]
6.	Reinforcement Learning	Sequential herbal planning (chronic diseases)	Adaptive optimization of prescription	[165]
7.	Gradient-Boosting Models	Enhanced prediction accuracy	Useful for skin permeability predictions	[166]
8.	QSAR Modeling	Predict molecular suitability for transdermal delivery	Helps identify herbal actives fit for skin absorption	[167]
9.	Predictive Skin Permeability Models	ML regression/clustering	Tailors patch composition to skin characteristics	[168]
10.	Ensemble Learning	Combines models to improve performance	Better generalization across datasets	[169]
11.	Predictive Analytics	Forecast formulation stability	Anticipates long-term performance	[170]
12.	Explainable ML	Interpretable optimization results	Facilitates actionable formulation insights	[171]
13.	Digital Twin / Simulation	Virtual testing of formulations	Reduces lab iterations	[172]
14.	Active Learning	Efficient data use to improve models	Reduces need for large labeled datasets	[173]
15.	Generative AI models	Design novel excipient combinations	Suggests unseen design combinations	[174]
16.	Multi-omics Integration	AI guides network pharmacology	Enhances understanding of herbal synergies	[175]
17.	AI for bioavailability optimization	Higher phytochemical absorption targets	AI signals high performing nanoformulations	[176]
18.	Predictive Bioactivity Models	Suggest active herbal components	Prioritizes compounds for transdermal efficacy	[177]
19.	ML in extraction optimization	Improve extraction yields from herbs	Increases active concentration for formulation	[178]
20.	Bayesian vs. Gradient Methods	Compare optimization strategies	Enables selection of best algorithm per goal	[179]
21.	Regression Models	Linking physicochemical features and outcomes	Helps predict optimal patch property values	[180]
22.	Clustering for grouping compounds	Identifying similar actives	Reduces complexity in candidate selection	[181]
23.	Predictive modelling for drug release	Forecasts release kinetics	Critically useful for transdermal release profiles	[182]
24.	AI-driven excipient screening	Finds compatible carriers	Enhances formulation success rates	[183]

25.	Multi-objective optimization	Balances adhesion, release, stability	Addresses competing formulation goals	[184]
26.	Cross-validation techniques	Ensures model robustness	Improves predictive confidence	[185]
27.	Digital formulator platforms	Automated in-silico formulation design	Reduces manual experiments	[186]
28.	Predictive Toxicity Models	Anticipate safety profiles	Crucial for herbal compound safety	[187]
29.	Natural Language Processing (NLP)	Extract and curate literature/formulation knowledge	Enhances data mining	[188]
30.	AI-integrated clinical trial design	Adaptive RCT optimization	Improves evidence quality of herbal formulations	[189]

6. Future Prospective

The convergence of ethno medicine, advanced transdermal technologies, and artificial intelligence presents a transformative pathway for the future management of scabies, particularly in high-burden and resource-limited settings [190]. Building on the foundations discussed in this work, several forward-looking directions can be envisioned to enhance therapeutic effectiveness, accessibility, and sustainability [191].

First, standardization and regulatory harmonization of herbal transdermal formulations will be critical. Although ethno medicinal agents such as tea tree oil, neem, turmeric, and aloe Vera demonstrate strong ant parasitic and anti-inflammatory potential, variability in plant sources, extraction methods, and phytochemical composition remains a major barrier to widespread clinical adoption. Future research should prioritize pharmacopeial standardization, robust quality-by-design (QbD) frameworks, and alignment with regulatory guidelines to ensure batch-to-batch consistency, safety, and reproducibility [192].

Second, next-generation delivery platforms are expected to play an increasingly important role. Nanocarriers, smart microneedle patches, and hybrid systems combining vesicular carriers with microneedles may enable deeper skin penetration, ovicidal activity, and sustained localized delivery, addressing one of the key limitations of current scabicides [193]. Future innovations may include biodegradable, self-dissolving microneedles loaded with polyherbal Nano formulations, offering painless application, improved compliance, and suitability for mass drug administration campaigns [194].

Third, AI-driven and data-centric formulation development represents a major future opportunity. Machine learning, digital twins, and generative AI models can be further integrated to predict skin permeability, optimize excipient–herb compatibility, and balance competing formulation goals such as adhesion, stability, release kinetics, and safety. As datasets grow, explainable AI and active learning approaches will allow formulation scientists to move from empirical design toward rational, personalized transdermal therapies tailored to skin type, age, and disease severity [195].

Fourth, advanced preclinical and translational models such as 3D bioprinted skin and skin-on-chip platforms are expected to reduce reliance on animal testing and accelerate clinical translation [196]. These systems can model scabies pathology, immune responses, and drug–skin interactions with higher human relevance, enabling rapid screening of herbal Nano formulations and microneedle systems before large-scale trials [197].

Fifth, integration with public health strategies will determine real-world impact. Future scabies control programs could incorporate culturally accepted herbal transdermal products alongside education, contact tracing, and household-level interventions [198]. Cost-effective, shelf-stable herbal patches or gels could be particularly valuable in refugee camps, schools, and rural communities, supporting WHO's neglected tropical disease roadmap and universal health coverage goals. Finally, systems-level and precision approaches may redefine scabies management. The integration of multi-omics data, network pharmacology, and AI-guided clinical trial design could elucidate synergistic phytochemical interactions, minimize resistance development, and strengthen evidence quality for herbal therapeutics [199]. In the long term, wearable or sensor-integrated transdermal systems may enable real-time monitoring of treatment response and adaptive dosing, ushering in a new era of personalized, technology-enabled ethnomedicine [200].

Conclusion

Combining ethnomedicine with modern transdermal drug delivery innovations represents an opportunity and a pioneering method of the successful management of scabies as a neglected tropical disease with serious global health and socioeconomic costs. The shortcomings of traditional treatments (resistance of drugs, low ovicidal impact, adverse reactions and lack of compliance with patients) support the high demand of less harmful and more effective options. Ethnomedical plants are extremely promising sources of bioactive compounds with antiparasitic, anti-inflammatory, antimicrobial, and wound-healing activity, but their therapeutic translation has been impaired by low skin

penetration and no formulation standardization. Recent transdermal systems such as nanocarriers, microneedles and QbD systems are major improvements to dermal delivery, stability and controlled delivery of herbal actives, which leads to improved treatment outcome and compliance. Simultaneously, new instruments including artificial intelligence and 3D bioprinted skin samples are making the process of formulation optimization, prediction of permeability, and preclinical validation faster. This is a synthesis of the ancient information with technological advancement that forms a sustainable, culturally agreeable, and precision-focused paradigm of therapeutic treatment. As clinical validation is sustained, regulatory convergence, and the integration of new treatment options with public health, transdermal herbal preparations have a high potential of filling the current gaps in treatment, lessening the burden of disease, and enhancing the global effort to control neglected tropical diseases.

Acknowledgment
The authors would like to express their sincere gratitude to their respective institutions for providing the necessary support and resources for the successful completion of this review. Special thanks to the collaborative efforts and contributions of all co-authors for their valuable insights and dedication throughout the preparation of this manuscript.

Author Contribution
AS: writing, reviewing and editing; **NB:** Conceptualisation; **PC:** Study concept or design; **MT:** Visualisation.

Conflict of Interest
The authors declare no conflict of interest.

Source of Funding
There is no funding available to conduct this study.

Data Provenance and Authenticity
Data are taken from credible peer-reviewed sources, systematically extracted, and verified as authentic.

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