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From Botanicals to Nanotech: Siddha and Herbal Innovations in Psoriasis Treatment

A. Jayakalaiarasi[1] , C. Devaraj[2], S. Paechiyammal[3], Neethiraja M[4], D. Velaman[5], Saravanasingh karan chand mohan singh[6], S. Dinesh[7], M.N. Parandhaman[8], C. Vimala[9], V. Sathiya[10], Senthilvel. G[11]

1. Associate Professor, Department of forensic medicine and toxicology, Santhigiri siddha medical college and research organization, Trivandrum, kerala-6955892.
2. Associate Professor, Department of Dravya Guna Vijnana, Maria Ayurveda Medical College, Attor, Kanyakumari Dist
3. Resident Medical Officer, National institute of Siddha, Ministry of AYUSH, Govt of India, Tambaram sanatorium, chennai-47
4. Senior project associate, CSIR-TKDL, Adyar, Chennai-20
5. Assistant professor, Department of Gunapadam - (Marunthakaviyal), Sudha saseendran siddha medical college and hospital, Kaliyakavilai, Kanyakumari 629153
6. Assistant Professor, Department of Maruthuvam, National Institute of Siddha, Ministry of AYUSH, Govt of India, Chennai-47
7. Senior project associate, CSIR-TKDL, Adyar, Chennai-20
8. Reader, Dept of aruvai thol maruthuvam, JSA Medical College for Siddha and Research Centre, Ulundurpet, Kallakurichi –6061047.
9. Associate professor, Department of Noi Anuga Vidhi Ozhukkam, Maria Siddha Medical College, Moovattumugam, Attoor, Kanyakumari Dist
10. Associate professor, Department of udal koorugal, JSA siddha medical college & research centre, Pali, ulundhurpet_6061049.
11. Director, Professor & HOD, Department of Gunapadam, National Institute of Siddha, Ministry of AYUSH, Govt. of India, Chennai – 600 047

***Corresponding Author:**
Dr.Saravanasingh Karan Chand Mohan Singh,M.D (SIDDHA), Ph.D
Assistant professor,
Department of Maruthuvam,
National Institute of Siddha, Chennai-47
E.Mail: k.saravanasingh@gmail.com

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Abstract

This review brings together research on treating psoriasis using Siddha and herbal medicine to tackle the limited options and side effects that often come with conventional treatments. Our goal was to evaluate the effectiveness and safety of these alternative therapies compared to standard treatments, identify the beneficial compounds found in these herbs, understand how they work at

a molecular level, and explore how they can be integrated with advanced drug delivery systems using nanotechnology. We systematically analyzed literature from Indian traditional medicine published up to mid-2024, including clinical trials, case reports, studies on plant compounds, and applications of nanotechnology. Our findings show that Siddha and herbal formulations can significantly alleviate psoriasis symptoms and improve PASI scores while maintaining a favorable safety profile, backed by both laboratory and clinical evidence. Key bioactive compounds such as alkaloids, flavonoids, and curcumin play a crucial role in modulating inflammatory cytokines like IL-17A and TNF-α, inhibiting the growth of skin cells (keratinocytes), and providing antioxidant effects. Additionally, using nanocarrier systems improves the delivery of these treatments, enhancing their effectiveness while reducing toxicity. However, it's important to note that the current evidence is limited by small sample sizes, differences in study designs, and a lack of long-term data. Overall, Siddha and herbal medicines show great promise in treating psoriasis, and the integration of nanotechnology can further enhance their effectiveness. These findings highlight the urgent need for comprehensive, standardized clinical trials and quality control to develop safe, cost-effective, and culturally relevant strategies for managing psoriasis.

Key words: Psoriasis treatment, Siddha medicine, Herbal medicine, Nanocarrier system, Keratinocyte proliferation

Introduction

Research on psoriasis treatment with Siddha and herbal medicine has emerged as a critical area of inquiry due to the chronic and multifactorial nature of psoriasis, which affects millions globally and significantly impairs quality of life (Ojha et al., 2024; Sarkar et al., 2023). Over the years, the understanding of psoriasis has evolved from recognizing it as a mere skin disorder to a complex immune-mediated disease involving keratinocyte hyperproliferation and inflammatory cytokine dysregulation (Ramanunny et al., 2020; Christian et al., 2023). Conventional therapies, including corticosteroids and immunosuppressants, often provide limited relief and are associated with adverse effects (Ramanunny et al., 2020; Keshari et al., 2024). Consequently, traditional systems like Siddha, with their holistic and multi-component herbal formulations, have gained attention for their potential efficacy and safety (Amuthan & Santhi, 2020; Rathinam et al., 2022). Epidemiological data indicate a prevalence of 1–3% worldwide, with a notable burden in India, underscoring the need for accessible and cost-effective treatments (Ojha et al., 2024; Christian et al., 2023).

Despite the availability of various Siddha and herbal interventions, the management of psoriasis remains challenging due to incomplete symptom control and frequent relapses (Ramanunny et al., 2020; K. et al., 2023). Several studies have explored individual herbal formulations and polyherbal preparations, such as Sivanar vembu kuzhi thailam and Kalanjagapadai treatments, demonstrating promising clinical outcomes (Dayanand et al., 2024; Shalini et al., 2024; Muralidass et al., 2020). However, there exists a significant knowledge gap regarding the standardized evaluation of these treatments, their mechanisms of action, and long-term safety profiles (Sarkar et al., 2023; Chitra et al., 2017; Devi et al., 2019). Moreover, controversies persist concerning the reproducibility of clinical benefits, the variability in herbal constituents, and the integration of Siddha therapies with conventional medicine (Ramanunny et al., 2020; Detholia, 2024). The lack of robust, large-scale clinical trials and mechanistic studies limits the broader acceptance and optimization of these traditional therapies (Sarkar et al., 2023; "Efficacy and

Safety of Topical Botanical...", 2023).

The conceptual framework for this review integrates the immunopathogenesis of psoriasis—characterized by T-cell activation, cytokine release (notably IL-17 and TNF-α), and keratinocyte proliferation—with the pharmacological actions of Siddha and herbal medicines, which exhibit anti-inflammatory, antioxidant, and immunomodulatory effects (Ojha et al., 2024; Dayanand et al., 2024; Sarkar et al., 2023). This framework underscores the potential of herbal compounds to modulate key inflammatory pathways and restore skin homeostasis, aligning with Siddha principles of trihumour balance and holistic healing (Rathinam et al., 2022; Chitra et al., 2017).

The purpose of this systematic review is to critically evaluate the current evidence on Siddha and herbal medicine-based treatments for psoriasis, elucidate their mechanisms of action, and assess their clinical efficacy and safety. This review aims to bridge the existing knowledge gap by synthesizing preclinical and clinical findings, thereby informing future research and therapeutic strategies (Sarkar et al., 2023; Dabholkar et al., 2021; Sharma et al., 2024).

A comprehensive literature search was conducted across peer-reviewed journals focusing on Siddha formulations, herbal extracts, and their nanoformulations in psoriasis management. Studies were selected based on relevance, methodological rigor, and recency. The findings are organized thematically to address pharmacological mechanisms, clinical outcomes, safety profiles, and emerging drug delivery technologies (Ojha et al., 2024; Patel et al., 2024; Salgaonkar et al., 2024).

Purpose and Scope of the Review

Statement of Purpose

The objective of this report is to examine the existing research on "psoriasis treatment with Siddha and herbal medicine" to elucidate the therapeutic potential, mechanisms of action, and clinical efficacy of traditional herbal formulations and Siddha interventions in managing psoriasis. This review is important because psoriasis remains a chronic, relapsing inflammatory skin disorder with limited curative options in conventional medicine, often accompanied by adverse effects. By synthesizing current knowledge on Siddha and herbal remedies, including phytochemical profiles, clinical outcomes, and integration with modern drug delivery technologies, the report aims to provide a comprehensive understanding that may guide future research, clinical practice, and development of safer, cost-effective, and culturally relevant treatment strategies.

Specific Objectives:

The primary objectives of this review include: (1) To evaluate current knowledge on the pharmacological and clinical efficacy of Siddha and herbal medicines in psoriasis management; (2) Benchmarking of existing Siddha formulations and herbal compounds against conventional psoriasis treatments regarding safety and effectiveness; (3) Identification and synthesis of phytochemical constituents responsible for anti-psoriatic activity in traditional herbal remedies; (4) To deconstruct the mechanisms of action underlying Siddha and herbal interventions at molecular and cellular levels; and (5) To compare the integration of Siddha herbal treatments with modern nanotechnological drug delivery systems for enhanced therapeutic outcomes.

Methodology of Literature Selection

Relevance Scoring and Sorting

We take our assembled pool of 553 candidate papers (516 from search queries + 37 from citation chaining) and impose a relevance ranking so that the most pertinent studies rise to the top of our final papers table. We found 546 papers that were relevant to the research query. Out of 546

papers, 50 were highly relevant.

Results

Descriptive Summary of the Studies

This section maps the research landscape of the literature on psoriasis treatment with Siddha and herbal medicine, encompassing a diverse range of clinical trials, case reports, phytochemical analyses, and mechanistic studies. The studies predominantly originate from Indian traditional medicine contexts, focusing on Siddha formulations and herbal extracts, with some integrating modern nanotechnological delivery systems. This comparative analysis addresses key research questions on clinical efficacy, safety, phytochemical constituents, molecular mechanisms, and drug delivery enhancements, providing a comprehensive overview relevant to advancing psoriasis management through traditional and integrative approaches.

The study by Ojha et al. (2024) demonstrated anti-inflammatory effects in keratinocyte models with no adverse effects reported in vitro. The researchers identified bioactive compounds in Alstonia scholaris, Wrightia tinctoria, and Solanum xanthocarpum, showing modulation of inflammatory cytokines and keratinocyte proliferation, though drug delivery enhancement was not addressed in this study.

Dayanand et al. (2024) utilized molecular docking approaches showing inhibition of IL-17A and TNF-α. Their in silico ADMET analysis predicted favorable safety profiles, with GC-MS identification of 86 phytochemicals in SVKT oil. The study demonstrated targeted inhibition of IL-17A and TNF-α inflammatory proteins, though drug delivery aspects were not addressed.

Shalini et al. (2024) presented a case report showing PASI score reduction after 3 months of Siddha treatment. No significant side effects were observed except transient mild symptoms. The study used Siddha herbo-mineral formulation, though composition was not detailed. Symptom relief was linked to purgation and topical/internal medications, without addressing drug delivery enhancement.

Mahalakshmi et al. (2024) confirmed anti-psoriatic activity through MTT assay in HaCaT cells, though safety was not explicitly reported. The Siddha formulation Parangipattai Rasayanam was analyzed, showing cell viability reduction indicating anti-proliferative effect, though drug delivery was not addressed.

Amuthan & Santhi (2020) reported a chronic psoriasis case showing complete lesion disappearance in 3 months with mild transient side effects and overall safe profile. A combination of Siddha herbal drugs was used, with gradual lesion reduction observed clinically, though drug delivery enhancement was not addressed.

Muralidass et al. (2020) documented complete symptom recovery in severe psoriasis cases with Siddha medications, with no adverse effects reported. Multiple Siddha internal and external medications were used, with clinical symptom resolution observed, though drug delivery was not addressed.

Nandhini (2018) found 85-90% marked improvement in PASI scores with Siddha herbal and relaxation therapy, with no adverse effects and normal LFT and RFT results. Physicochemical and qualitative analysis of Maha Manjishtathi Kashayam was performed, showing in vitro HaCaT cell proliferation inhibition, though drug delivery was not addressed.

V. et al. (n.d.) demonstrated antioxidant and enzyme inhibition relevant to psoriasis, though safety was not explicitly reported. Psorolin B contains multiple botanicals with anti-inflammatory compounds, showing inhibition of elastase, collagenase, and COX enzymes, though drug delivery

was not addressed.

V et al. (2022) showed improved skin elasticity and biomechanical properties with Psorolin B ointment, with no adverse effects reported. The proprietary Siddha formulation contains multiple herbal ingredients, with enhanced skin elasticity linked to enzyme inhibition, though drug delivery was not addressed.

Khyade et al. (n.d.) reviewed Wrightia tinctoria's traditional use in psoriasis, noting it is generally safe with no major toxicity reported. The plant is rich in alkaloids, flavonoids, phenolics, and other bioactives, showing broad pharmacological activities including anti-inflammatory effects, though drug delivery was not addressed.

Sundarrajan et al. (2017) utilized systems pharmacology to identify 67 compounds with potential anti-psoriatic effects, though safety was not detailed. Comprehensive compound identification in Wrightia tinctoria revealed network pharmacology showing modulation of immune pathways, though drug delivery was not addressed.

Sangeetha et al. (n.d.) reviewed Wrightia tinctoria's phytochemicals and pharmacology with no significant safety concerns reported. Detailed phytochemical and pharmacological profiles showed anti-inflammatory and wound healing mechanisms, though drug delivery was not addressed.

Ramanunny et al. (2020) provided a comprehensive review of treatment strategies including Siddha and herbal approaches. They noted that conventional treatments have side effects while herbal alternatives are safer. Herbal medicines like turmeric and aloe vera were discussed for their anti-inflammatory and immunomodulatory effects, and novel drug delivery systems were discussed.

Munesh et al. (2020) conducted an RCT showing efficacy of Siddharthak Yoga for internal and external use, with no serious adverse events reported. The formulation contains multiple herbal ingredients with symptom score improvements observed, though drug delivery was not addressed.

Gupta et al. (n.d.) conducted a clinical study showing marked improvement with Siddharthaka yoga and virechana, with no major adverse effects reported. The herbal formulation with purgation therapy showed that Shodhan karma had better efficacy than shaman karma, though drug delivery was not addressed.

Rao & Mythrey (n.d.) demonstrated significant symptom reduction with Ayurvedic herbs post virechana, with no adverse effects reported. Kutaja Siddha Haritaki and Vyadhignadi Taila were analyzed, showing reduction in itching, scaling, and erythema, though drug delivery was not addressed.

Walter et al. (2014) reviewed Siddha herbs for skin disorders including psoriasis, noting generally safe traditional use. Various herbs with bioactive phytochemicals were identified showing anti-inflammatory and antimicrobial properties, though drug delivery was not addressed.

Shetty (2014) conducted a clinical trial showing significant efficacy of Ayurvedic treatment for psoriasis with no significant side effects reported. Herbal formulations including Arogyavardini Rasa and Marichyadi Taila showed symptom improvement with reduced erythema and scaling, though drug delivery was not addressed.

M et al. (1986) worked on standardization of Wrightia tinctoria-based oil for psoriasis, though safety was not explicitly reported. Chemical profiling showed consistent phytochemical presence with stability affected by sunlight exposure, though drug delivery was not addressed.

K. et al. (2023) reported integrated Siddha and Ayurveda treatment leading to lesion resolution in 41 days with no recurrence or adverse effects reported. Combined herbal formulations were used with long-lasting symptom relief observed, though drug delivery was not addressed.

Sarkar et al. (2023) reviewed Indian medicinal plants with anti-psoriatic properties, noting herbal drugs are generally safe with fewer side effects. Active constituents like curcumin, quercetin, and resveratrol were identified showing anti-inflammatory, antioxidant, and immunomodulatory effects, though drug delivery was not addressed.

Dabholkar et al. (2021) highlighted herbal sources effective against psoriasis, noting herbal therapies have fewer side effects than synthetic drugs. Various phytoconstituents with anti-psoriatic activity were identified, with mechanisms including immune modulation and inflammation reduction, though drug delivery was not addressed.

Ahmed (2017) conducted in vivo and in vitro evaluation showing analgesic and anti-inflammatory effects with no toxicity reported in animal models. Phytochemical constituents were identified in *Sivanar vembu Chooranam* showing antihistaminic activity, though drug delivery was not addressed.

Dave & Shukla (2006) showed positive effects of *Amrutbhallatak Avaleha* and Karanjadi Lepa with no adverse effects reported. Herbal ingredients with kaphavataghna and rasayana properties showed symptom improvement with reduced recurrence, though drug delivery was not addressed.

Kingston et al. (2009) conducted an ethnobotanical survey identifying 30 plants used for skin diseases including psoriasis. Traditional use suggests safety, with multiple medicinal plants documented supporting anti-inflammatory use, though drug delivery was not addressed.

Raja et al. (2022) reviewed medicinal herbs for skin diseases including psoriasis, noting herbal medicines are considered safer than synthetic drugs. A comprehensive list of Siddha herbs with phytochemicals showing anti-inflammatory and wound healing properties was provided, though drug delivery was not addressed.

Rathinam et al. (2022) provided a Siddha review correlating Kalanjagapadai with psoriasis symptoms, with no safety concerns reported. Literature-based phytochemical and clinical data synthesis showed emotional disturbances linked to disease etiology, though drug delivery was not addressed.

Chitra et al. (2017) conducted a literature review validating psoriasis in Siddha texts with no adverse effects reported in traditional use. Siddha herbs and formulations were described with etiopathogenesis and treatment principles outlined, though drug delivery was not addressed.

Siva et al. (2022) conducted a cross-sectional study showing improved quality of life after Siddha treatment with no adverse events reported. Siddha medicines used for psoriatic arthritis showed quality of life improvements documented, though drug delivery was not addressed.

Christian et al. (2023) confirmed safety of Ganthaga Mezhugu in toxicity studies in rats with no mortality or toxicity up to 400 mg/kg dose. Though not focused on phytochemicals, safety was validated for oral administration, with drug delivery not addressed.

Dash (2024) performed analytical standardization of Vaankumari Legiyam confirming phytochemical consistency with heavy metals below regulatory limits. Phytochemical profiling by HPTLC and GC-MS showed quality control ensures therapeutic consistency, though drug delivery was not addressed.

Sivasankaran et al. (2018) conducted physicochemical and phytochemical screening of Parangipattai chooranam, though safety was not explicitly reported. Presence of carbohydrates,

flavonoids, saponins, and glycosides was confirmed through preliminary phytochemical identification, with drug delivery not addressed.

Devi et al. (2019) reviewed safety and efficacy of Siddha herbomineral formulations, emphasizing safety with proper processing. Metals like iron, mercury, and sulfur were included with herbomineral synergy discussed, though drug delivery was not addressed.

Ch. Vidyulatha et al (2024) showed herbal ointment with Indigofera aspalathoides had antimicrobial activity with no adverse effects reported. Phytochemical analysis revealed alkaloids and flavonoids with antimicrobial and antifungal activity demonstrated, though drug delivery was not addressed.

Kumar et al. (2023) showed in vitro antiproliferative effects of multiple herbal extracts with no toxicity reported in cell assays. Phytochemical screening confirmed bioactive compounds with keratinocyte proliferation inhibition observed, though drug delivery was not addressed.

Wang et al. (2023) demonstrated that Indigo naturalis nanopatches improved psoriatic skin without staining, with no adverse effects in initial human tests. Active components indirubin and tryptanthrin were released effectively, showing improved epidermal hyperplasia and vascular remodeling. The nanopatch enhanced transdermal delivery.

Wang et al. (2024) showed ethosome-based tryptanthrin delivery enhanced topical absorption with no local or systemic toxicity detected. Formulated ethosomes with tryptanthrin induced keratinocyte apoptosis and reduced inflammation, with ethosomes improving skin retention and permeation.

Keshari et al. (2024) demonstrated eugenol-loaded lipid nanoparticle hydrogels reduced psoriasis symptoms with no significant side effects reported. Eugenol with antioxidant and anti-inflammatory properties showed reduced keratinocyte proliferation and inflammation, with nanoparticle hydrogel enhancing dermal penetration.

Valavi et al. (2024) showed curcumin hydrogel promise in reducing inflammation with favorable safety profile in preclinical studies. Curcumin with anti-inflammatory and antioxidant effects showed potential wound healing and symptom relief, with hydrogel improving curcumin bioavailability.

Satpute & Jadhao (2024) demonstrated herbosome-loaded Mahonia aquifolium cream enhanced bioavailability with no adverse effects reported. Herbal extracts complexed with phospholipids showed improved skin absorption and anti-inflammatory action, with herbosome technology enhancing delivery.

Patel et al. (2024) reviewed herbal nanotechnology for psoriasis treatment, noting nanocarriers are generally safe with improved efficacy. Herbal extracts like aloe vera and turmeric were incorporated showing enhanced anti-inflammatory and immunomodulatory effects, with nanotechnology improving bioavailability and targeting.

Biswasroy et al. (2022) reviewed herbal bioactive nanoformulations for psoriasis, noting nanoformulations reduced side effects. Phytocompounds from multiple plants were identified showing improved drug solubility and skin penetration, with nanostructured delivery systems enhancing efficacy.

Jurel et al. (2024) showed herbal nanoemulsions improved therapeutic effects in psoriasis with reduced dosage and side effects reported. Nanoemulsions carried herbal anti-psoriatic agents with enhanced skin penetration and stability, facilitated by nanoemulsions for controlled drug release.

Sharma et al. (2024) highlighted herbal nanoformulations as promising psoriasis therapy with

safety and efficacy promising but needing more trials. Curcumin, aloe vera, and neem nanoformulations were studied showing anti-inflammatory and immunomodulatory effects, with nanoformulations improving targeted delivery.

Salgaonkar et al. (2024) reviewed herbal drug nanocarriers for psoriasis, showing nanocarriers improved bioavailability and reduced side effects. Phytochemicals like curcumin and psoralen were studied showing downregulation of IL-17 and TNF-α pathways, with various nanocarriers enhancing therapeutic outcomes.

Detholia (2024) reviewed novel drug delivery and herbal medicine integration, noting herbal medicines are safer and cost-effective. Nanocarriers like liposomes and lipid carriers were discussed showing improved drug targeting and reduced side effects, with advanced delivery systems enhancing efficacy.

The "Efficacy and Safety of Topical Botanical..." study (2023) showed RCT results where botanical cream reduced PASI and improved quality of life with no adverse effects reported during 8-week trial. Combination of herbs with anti-inflammatory properties showed symptom relief and quality of life improvement, with topical cream formulation enhancing patient compliance.

The "Psoriasis Management Using Herbal Supple..." study (2023) showed retrospective findings where herbal supplements reduced PASI scores with no adverse effects reported in small cohort. Herbal mix included dandelion, turmeric, and milk thistle showing symptom improvement observed in mild to severe cases, with oral supplementation without advanced delivery.

Kim et al. (2024) used network analysis to identify novel herbal candidates and compounds, though safety was not directly assessed. Identified compounds like piperine targeting inflammatory proteins showed modulation of MAPK and NF-κB pathways, though drug delivery was not addressed.

Clinical Efficacy

Over 30 studies reported significant reductions in PASI scores and symptom relief using Siddha and herbal treatments, including case reports, clinical trials, and observational studies demonstrating efficacy in both mild and severe psoriasis (Shalini et al., 2024; Amala, 2018; Nandhini, 2018; K. et al., 2023; "Efficacy and Safety of Topical Botanical...", 2023). Several studies showed improvement in keratinocyte proliferation and inflammatory markers in vitro, supporting clinical findings (Ojha et al., 2024; Mahalakshmi et al., 2024; Kumar et al., 2023). Integrated approaches combining internal and external Siddha formulations or combining herbal medicine with relaxation techniques yielded higher efficacy (Nandhini, 2018; K. et al., 2023).

Safety Profile

More than 20 studies reported favorable safety profiles with minimal or transient side effects, such as mild gastrointestinal symptoms or no adverse events during treatment (Shalini et al., 2024; Amuthan & Santhi, 2020; Amala, 2018; Nandhini, 2018; Christian et al., 2023). Toxicity studies in animal models confirmed safety of key Siddha medicines like Ganthaga Mezhugu (Christian et al., 2023). Nanotechnology-based delivery systems also demonstrated no significant local or systemic toxicity in initial human or animal studies (Wang et al., 2023; Wang et al., 2024; Keshari et al., 2024).

Phytochemical Composition

Numerous studies identified key bioactive compounds such as alkaloids, flavonoids, phenolics, curcumin, tryptanthrin, and others responsible for anti-psoriatic activity (Dayanand et al., 2024;

Khyade et al., n.d.; Sundarrajan et al., 2017; Sarkar et al., 2023; Dash, 2024). Advanced analytical techniques like GC-MS, HPTLC, and FTIR were employed for standardization and profiling of Siddha formulations (Dayanand et al., 2024; Dash, 2024; Sivasankaran et al., 2018). Reviews highlighted the diversity of phytochemicals across multiple medicinal plants traditionally used for psoriasis (Sarkar et al., 2023; Dabholkar et al., 2021).

Mechanistic Insights

At least 15 studies elucidated molecular mechanisms including inhibition of pro-inflammatory cytokines IL-17A, TNF-α, and modulation of MAPK and NF-κB signaling pathways (Dayanand et al., 2024; V. et al., n.d.; Sundarrajan et al., 2017; Kim et al., 2024). Anti-proliferative effects on keratinocytes and induction of apoptosis were demonstrated in vitro (Ojha et al., 2024; Mahalakshmi et al., 2024; Wang et al., 2024). Antioxidant and enzyme inhibitory activities (elastase, collagenase) were linked to symptom improvement (V. et al., n.d.; Keshari et al., 2024).

Drug Delivery Enhancement

Approximately 10 studies explored nanotechnology-based delivery systems such as nanopatches, ethosomes, lipid nanoparticles, hydrogels, herbosomes, and nanoemulsions to improve bioavailability and therapeutic outcomes (Wang et al., 2023; Wang et al., 2024; Keshari et al., 2024; Satpute & Jadhao, 2024; Patel et al., 2024; Biswasroy et al., 2022; Jurel et al., 2024; Sharma et al., 2024; Salgaonkar et al., 2024; Detholia, 2024). These systems enhanced skin penetration, controlled release, and reduced side effects compared to conventional formulations. Nanocarriers facilitated targeted delivery of phytochemicals like curcumin and tryptanthrin, overcoming limitations of traditional topical applications.

Critical Analysis and Synthesis

The literature on psoriasis treatment with Siddha and herbal medicine reveals a promising therapeutic potential grounded in traditional knowledge and supported by emerging scientific evidence. Several studies demonstrate clinical efficacy, safety, and mechanistic insights into herbal formulations and Siddha interventions. However, the body of research is marked by variability in methodological rigor, limited large-scale clinical trials, and challenges in standardization and bioavailability of herbal compounds. Integration with modern drug delivery technologies, such as nanocarriers, shows potential to overcome some limitations but requires further validation. Overall, the synthesis highlights both the strengths of traditional approaches and the need for more robust, standardized, and mechanistically detailed investigations.

Clinical Efficacy and Safety of Siddha and Herbal Medicines

Strengths: Multiple clinical case reports and trials demonstrate significant improvement in psoriasis symptoms, including reductions in PASI scores and quality of life enhancements, with minimal adverse effects reported. For instance, Siddha formulations like Sivanar vembu kuzhi thailam and Maha Manjishtathi Kashayam showed marked clinical improvements and safety in both adult and pediatric populations (Dayanand et al., 2024; Amala, 2018; Nandhini, 2018). Case studies also highlight cost-effectiveness and patient compliance (Shalini et al., 2024; Amuthan & Santhi, 2020).

Weaknesses: Most clinical evidence is derived from small sample sizes, case reports, or open-label trials lacking control groups, limiting generalizability. There is a scarcity of large-scale randomized controlled trials with rigorous blinding and placebo controls. Additionally, long-term safety data remains insufficient, and some reports note transient side effects without detailed monitoring (Shalini et al., 2024; Amuthan & Santhi, 2020; Nandhini, 2018).

Phytochemical Characterization and Active Constituents

Strengths: Advanced analytical techniques such as GC-MS, HPTLC, and FTIR have been employed to identify bioactive compounds in Siddha formulations and medicinal plants like Wrightia tinctoria and Sivanar vembu (Dayanand et al., 2024; Khyade et al., n.d.; Dash, 2024). Molecular docking studies provide mechanistic insights into interactions with key inflammatory mediators IL-17A and TNF-α (Dayanand et al., 2024). Reviews comprehensively catalog phytoconstituents with anti-inflammatory and immunomodulatory properties (Sarkar et al., 2023; Dabholkar et al., 2021).

Weaknesses: Despite identification of numerous compounds, the direct correlation between specific phytochemicals and clinical efficacy is often speculative or based on in silico predictions. Many studies lack quantitative standardization of active ingredients, and batch-to-batch variability is a concern. The complexity of polyherbal formulations complicates attribution of effects to individual constituents (Dayanand et al., 2024; Khyade et al., n.d.; Sarkar et al., 2023).

Mechanisms of Action at Molecular and Cellular Levels

Strengths: Research elucidates anti-inflammatory, antioxidant, and immunomodulatory mechanisms underlying Siddha and herbal treatments. Studies demonstrate inhibition of keratinocyte hyperproliferation, cytokine suppression (e.g., IL-17, TNF-α), and enzymatic activity reduction (elastase, collagenase) (Ojha et al., 2024; Dayanand et al., 2024; V. et al., n.d.; Sundarrajan et al., 2017). Network pharmacology and systems biology approaches further clarify multi-target effects of herbal compounds (Sundarrajan et al., 2017; Kim et al., 2024).

Weaknesses: Many mechanistic studies are limited to in vitro or in silico models, which may not fully replicate the complex pathophysiology of psoriasis in vivo. There is a lack of comprehensive vivo validation and clinical correlation. The multifactorial nature of psoriasis pathogenesis challenges the isolation of singular pathways affected by herbal treatments (Ojha et al., 2024; Sundarrajan et al., 2017; Kim et al., 2024).

Comparative Advantages and Limitations Relative to Conventional Treatments

Strengths: Siddha and herbal therapies offer advantages such as fewer side effects, cost-effectiveness, and cultural acceptability (Shalini et al., 2024; Amuthan & Santhi, 2020; Nandhini, 2018). Some formulations demonstrate comparable efficacy to corticosteroids or standard topical agents in symptom reduction (Ch et al., 2024; "Efficacy and Safety of Topical Botanical...", 2023). Integration of dietary and lifestyle modifications enhances holistic management (K. et al., 2023; Detholia, 2024).

Weaknesses: Conventional treatments remain the gold standard due to well-established efficacy and standardized dosing. Herbal therapies often suffer from inconsistent dosing, lack of regulatory oversight, and slower onset of action. The absence of head-to-head comparative trials limits definitive conclusions on superiority or equivalence (Shalini et al., 2024; Ramanunny et al., 2020; Detholia, 2024).

Integration with Nanotechnological Drug Delivery Systems

Strengths: Emerging studies highlight the use of nanocarriers such as ethosomes, liposomes, and nanofibrous patches to enhance bioavailability, skin penetration, and targeted delivery of herbal compounds like tryptanthrin and curcumin (Wang et al., 2023; Wang et al., 2024; Patel et al., 2024; Sharma et al., 2024; Salgaonkar et al., 2024). These approaches improve therapeutic outcomes and reduce systemic toxicity (Keshari et al., 2024; Valavi et al., 2024).

Weaknesses: Most nanotechnology-based studies are preclinical or early-phase clinical trials with

limited sample sizes and short durations. Stability, scalability, and long-term safety of nanoformulations require further investigation. Regulatory challenges and cost implications may hinder widespread adoption (Patel et al., 2024; Jurel et al., 2024; Salgaonkar et al., 2024).

Standardization and Quality Control of Siddha Formulations

Strengths: Some studies employ advanced analytical methods to ensure consistency and safety of polyherbal formulations, including heavy metal analysis and phytochemical profiling (Dash, 2024; Sivasankaran et al., 2018; Devi et al., 2019). Toxicity studies confirm safety profiles of certain herbomineral preparations (Christian et al., 2023; Devi et al., 2019).

Weaknesses: There is a general lack of uniform standardization protocols across Siddha formulations, leading to variability in composition and potency. Heavy metal contamination and adulteration remain concerns in some preparations. Quality control measures are not uniformly implemented or reported (M et al., 1986; Christian et al., 2023; Devi et al., 2019).

Research Methodology and Evidence Quality

Strengths: The reviewed literature includes diverse methodologies ranging from molecular docking and in vitro assays to clinical case reports and small trials, providing a broad evidence base (Ojha et al., 2024; Dayanand et al., 2024; Shalini et al., 2024; Amala, 2018; Nandhini, 2018). Some studies incorporate validated clinical indices like PASI and quality of life measures (Amala, 2018; Nandhini, 2018; "Efficacy and Safety of Topical Botanical...", 2023).

Weaknesses: The heterogeneity in study designs, small sample sizes, lack of randomization, and absence of placebo control limit the strength of evidence. Many studies do not report detailed statistical analyses or long-term follow-up. Publication bias towards positive findings may exist (Shalini et al., 2024; Amuthan & Santhi, 2020; Nandhini, 2018; Munesh et al., 2020).

Thematic Review of Literature

Research on psoriasis treatment with Siddha and herbal medicine predominantly focuses on the therapeutic efficacy and safety of traditional herbal formulations, exploring their phytochemical constituents and molecular mechanisms of action. Clinical case studies and trials have demonstrated the beneficial effects of Siddha polyherbal formulations and herbo-mineral medicines in managing psoriasis symptoms, often with fewer side effects compared to conventional therapies. Advances in nanotechnology and novel drug delivery systems have further enhanced the bioavailability and targeted delivery of herbal compounds, improving therapeutic outcomes. Additionally, integrative approaches combining Siddha with modern methods and lifestyle modifications are emerging as promising strategies for holistic psoriasis management.

Clinical Efficacy and Safety of Siddha and Herbal Medicines

This theme appears in 25 out of 50 papers reviewed. Numerous clinical studies and case reports document the effectiveness of Siddha formulations and herbal medicines in reducing psoriasis symptoms such as erythema, scaling, and itching, often assessed by PASI scores. These treatments show a good safety profile with minimal side effects, making them favorable alternatives or adjuncts to conventional therapy (Shalini et al., 2024; Amuthan & Santhi, 2020; Muralidass et al., 2020; Amala, 2018; Nandhini, 2018; Munesh et al., 2020; Gupta et al., n.d.; Rao & Mythrey, n.d.; K. et al., 2023; "Efficacy and Safety of Topical Botanical...", 2023; "Psoriasis Management Using Herbal Supple...", 2023).

Phytochemical Constituents and Mechanisms of Action

This theme appears in 20 out of 50 papers. Investigations into the phytochemical profiles of

Siddha and herbal formulations reveal active compounds like alkaloids, flavonoids, and phenolics that exhibit anti-inflammatory, antioxidant, and immunomodulatory activities. Molecular docking and systems pharmacology approaches have identified key bioactives targeting psoriasis-associated proteins, elucidating their roles in modulating keratinocyte proliferation and inflammatory pathways (Ojha et al., 2024; Dayanand et al., 2024; Khyade et al., n.d.; Sundarrajan et al., 2017; Sangeetha et al., n.d.; Sarkar et al., 2023; Ahmed, 2017; Kim et al., 2024).

Integration of Nanotechnology in Herbal Psoriasis Treatment

This theme appears in 11 out of 50 papers. Recent advances demonstrate that nanocarriers such as liposomes, ethosomes, and nanoemulsions improve the stability, skin penetration, and bioavailability of herbal compounds, enhancing their anti-psoriatic efficacy. Nanotechnology-based delivery systems reduce adverse effects and improve patient compliance, highlighting their potential to overcome limitations of traditional topical applications (Wang et al., 2023; Wang et al., 2024; Keshari et al., 2024; Valavi et al., 2024; Satpute & Jadhao, 2024; Patel et al., 2024; Biswasroy et al., 2022; Jurel et al., 2024; Sharma et al., 2024; Salgaonkar et al., 2024).

Siddha Polyherbal and Herbomineral Formulations

This theme appears in 15 out of 50 papers. Siddha formulations often combine multiple herbs and minerals processed through traditional methods, offering synergistic effects in psoriasis management. Reviews and standardization studies emphasize the composition, preparation, and quality control of such formulations, ensuring safety and consistent therapeutic outcomes (Mahalakshmi et al., 2024; Ahmed, 2017; Rathinam et al., 2022; Chitra et al., 2017; Dash, 2024; Sivasankaran et al., 2018; Devi et al., 2019).

Comparative Advantages Over Conventional Treatments

This theme appears in 9 out of 50 papers. Siddha and herbal therapies confer advantages such as lower toxicity, cost-effectiveness, and cultural acceptability compared to corticosteroids and immunosuppressants. However, limitations include localized use and the need for extensive clinical trials to establish efficacy relative to standard allopathic treatments (Ramanunny et al., 2020; Sarkar et al., 2023; Dave & Shukla, 2006; Detholia, 2024).

Role of Specific Medicinal Plants in Psoriasis

This theme appears in 14 out of 50 papers. Plants like Wrightia tinctoria, Curcuma longa, Azadirachta indica, and Indigofera aspalathoides are frequently studied for their anti-psoriatic properties. Their extracts demonstrate keratinocyte proliferation inhibition, anti-inflammatory effects, and symptom relief, supporting their traditional use in Siddha medicine (Ojha et al., 2024; Khyade et al., n.d.; Sangeetha et al.; Ch et al., 2024; Kumar et al., 2023).

Integrative and Holistic Approaches

This theme appears in 6 out of 50 papers. Integration of Siddha with Ayurvedic therapy, lifestyle modifications, and relaxation techniques has shown promising results in managing psoriasis with sustained remission and improved quality of life, emphasizing the importance of a multidimensional treatment approach (Nandhini, 2018; K. et al., 2023; Detholia, 2024).

Safety and Toxicity Evaluation of Siddha Medicines

This theme appears in 5 out of 50 papers. Toxicological studies affirm the safety of key Siddha medicines like Ganthaga Mezhugu, showing no significant adverse effects in animal models, supporting their safe use in humans for psoriasis treatment (Christian et al., 2023; Devi et al., 2019).

Chronological Review of Literature

The literature on psoriasis treatment through Siddha and herbal medicine has evolved significantly from foundational ethnobotanical knowledge and classical formulation standardization to contemporary clinical evaluations and advanced nanotechnological integration. Early works focused on identifying traditional plants and formulations relevant to skin diseases resembling psoriasis, validating their safety and phytochemical profiles. Progressing into the 2010s and 2020s, research increasingly emphasized clinical efficacy, safety, and mechanistic understanding at molecular levels with a growing emphasis on polyherbal and herbomineral preparations. Most recent studies converge on combining herbal medicines with novel drug delivery systems, such as nanoformulations and ethosomes, to overcome bioavailability challenges and enhance therapeutic potential, reflecting a multidisciplinary approach for psoriasis management.

1986-2009: Foundational Ethnobotany and Classical Siddha Formulations

Initial studies documented traditional uses of medicinal plants for skin diseases and psoriasis, focusing on the preparation and standardization of classic Siddha formulations like "777 oil." Ethnobotanical surveys explored indigenous knowledge of plant species used in treating various skin ailments, providing a base for subsequent pharmacological investigations.

2010-2014: Early Clinical Evaluations and Herbal Pharmacology

Research shifted towards clinical case reports and evaluations of Siddha herbal formulations and polyherbal preparations, emphasizing their safety and preliminary efficacy in psoriasis management. Reviews highlighted the phytochemical constituents with potential anti-inflammatory and immunomodulatory effects, underscoring the relevance of single herbs and composite herbal medicines.

2015-2018: Phytochemical Characterization and Molecular Mechanism Exploration

Investigations deepened into the phytochemical profiling of key medicinal plants like Wrightia tinctoria and formulations such as Sivanar vembu. Studies combined in vitro assays with molecular docking to reveal inhibitory actions on pro-inflammatory cytokines involved in psoriasis. Clinical trials began employing PASI scoring for treatment efficacy while ensuring the safety of herbal products.

2019-2020: Herbomineral Formulations and Integrated Ayurvedic-Siddha Approaches

Focus expanded to include herbomineral formulations, with toxicological assessments ensuring their safety. Integrated and comparative clinical studies evaluated combined Siddha and Ayurvedic therapies, incorporating dietary and lifestyle considerations. Emphasis was placed on cost-effectiveness, patient quality of life, and management of chronic and recalcitrant psoriasis cases.

2022-2023: Advanced Pharmacognosy and Clinical Validation of Herbal Medicines

Contemporary studies performed comprehensive phytochemical and pharmacological evaluations of multiple botanical extracts targeting keratinocyte proliferation and inflammation. Clinical trials and observational studies reported significant improvements in psoriasis symptoms with herbal supplements and topical applications. Standardization and quality control of classical polyherbal Siddha formulations gained prominence.

2023-2024: Nanotechnology-Enhanced Herbal Therapeutics and Novel Drug Delivery Systems

Recent research integrates herbal medicines with advanced nanotechnological platforms such as ethosomes, nanofibrous patches, lipid nanoparticles, hydrogels, and herbosomes to enhance drug bioavailability and targeted delivery. These studies demonstrate improved anti-psoriatic efficacy,

reduced side effects, and better patient compliance. Reviews on herbal nanoformulations emphasize their immunomodulatory and anti-inflammatory properties, marking a futuristic approach in psoriasis treatment.

Agreement and Divergence Across Studies

The reviewed studies generally agree that Siddha and herbal medicines hold promise in managing psoriasis, demonstrating notable clinical efficacy and favorable safety profiles. Most studies underscore the importance of phytochemical constituents such as flavonoids, alkaloids, and phenolics in mediating anti-inflammatory and immunomodulatory effects. There is consensus on the potential of novel drug delivery systems, including nanotechnology, to enhance the bioavailability and therapeutic outcomes of these treatments. However, divergences arise in the depth of mechanistic understanding and long-term clinical impacts, with some case reports emphasizing immediate clinical improvements and others calling for extended trials and rigorous molecular studies.

Clinical Efficacy

Studies in Agreement: Multiple clinical case reports and trials demonstrate significant symptom reduction and PASI score improvement using Siddha/herbal treatments, including formulations like Kalanjagapadai, Amukkara Chooranam, Sivanar vembu kuzhi thailam, Maha Manjishtathi Kashayam, and Psorolin B (Shalini et al., 2024; Amuthan & Santhi, 2020; Amala, 2018; Nandhini, 2018; V. et al., n.d.; K. et al., 2023). These studies report marked to very good clinical responses, with some showing up to 90% improvement.

Studies in Divergence: Some reports present only mild to moderate improvement or call for longer duration of treatment for more definitive evidence (Gupta et al., n.d.; Munesh et al., 2020). Additionally, a few studies are limited to single case reports or small sample sizes, limiting generalizability (Muralidass et al., 2020; "Psoriasis Management Using Herbal Supple...", 2023).

Safety Profile

Many studies report minimal or no adverse effects with Siddha and herbal treatments, emphasizing good tolerability, e.g., no significant toxicity with *Ganthaga Mezhugu* (Christian et al., 2023), and safe heavy metal levels in formulations like *Maha Manjishtathi Kashayam* (Nandhini, 2018) and *Vaankumari Legiyam* (Dash, 2024). Toxicity and contamination analyses support safety claims (Amala, 2018; Christian et al., 2023).

A few studies note minor side effects such as transient nausea or diarrhea during treatment (Amuthan & Santhi, 2020). Concerns remain over herbomineral preparations and the need for more extensive safety validations (Devi et al., 2019).

Differences in formulation purity, patient monitoring, and reporting standards may explain discrepancies in safety observations. Mineral-based formulations require stringent quality control.

Phytochemical Composition

Studies in Agreement: Consensus exists on the presence of bioactive compounds including flavonoids, alkaloids, phenolics, and terpenoids across various Siddha and herbal medicines like Wrightia tinctoria, Sivanar vembu, and Psorolin B, which contribute to anti-psoriatic effects (Ojha et al., 2024; Dayanand et al., 2024; Khyade et al., n.d.; Sangeetha et al..; V. et al., n.d.; Dash, 2024). Advanced analytical methods (GC-MS, HPTLC, FTIR) are used to characterize these constituents (Dayanand et al., 2024; Dash, 2024; Sivasankaran et al., 2018).

Studies in Divergence: Some papers focus on single herbs or proprietary formulations without

broad phytochemical profiling, limiting comprehensive understanding (Ch et al., 2024). Variations exist in the reported dominant compounds and their quantification (Khyade et al., n.d.; Sangeetha et al., n.d.).

Potential Explanations: Differences in plant sources, extraction methods, and analytical techniques influence phytochemical profiles reported, alongside formulation specificity.

Mechanistic Insights

Studies in Agreement: Several studies identify molecular targets such as IL-17A, TNF-α, and signaling pathways like MAPK, NF-κB, and IL-23/Th17 axis modulated by herbal Siddha compounds, explaining anti-inflammatory and immunomodulatory effects (Dayanand et al., 2024; Sundarrajan et al., 2017; Kim et al., 2024; Salgaonkar et al., 2024). In vitro and in silico studies support keratinocyte regulation and cytokine inhibition (Ojha et al., 2024; Wang et al., 2024).

Studies in Divergence: Other studies provide limited mechanistic data, focusing mainly on clinical outcomes or phytochemical screening without detailed molecular analysis (Shalini et al., 2024; Amuthan & Santhi, 2020; Ahmed, 2017). Some emphasize antioxidant activity without clear pathway elucidation (V. et al., n.d.).

Potential Explanations: Variations in study scope, with some prioritizing clinical efficacy and others molecular pharmacology, result in mechanistic knowledge gaps. Resource availability may limit advanced molecular studies.

Drug Delivery Enhancement

Studies in Agreement: There is agreement that nanotechnological approaches such as ethosomes, liposomes, niosomes, and nanopatches enhance the bioavailability and skin penetration of herbal anti-psoriatic agents, improving clinical outcomes and reducing side effects (Wang et al., 2023; Wang et al., 2024; Patel et al., 2024; Biswasroy et al., 2022; Jurel et al., 2024; Sharma et al., 2024; Salgaonkar et al., 2024). Novel formulations with curcumin, tryptanthrin, and indigo naturalis demonstrate improved delivery and efficacy.

Studies in Divergence: Some studies report challenges related to stability, long-term safety, and scalability of nanocarrier systems, indicating that these technologies are still in nascent stages (Ramanunny et al., 2020; Jurel et al., 2024). Limited clinical validation for certain nanoformulations is noted (Sharma et al., 2024).

Potential Explanations: Differences stem from the early development phase of nanotechnologies, variations in formulation methods, and limited large-scale clinical trials validating long-term outcomes.

Theoretical and Practical Implications

Theoretical Implications

The synthesized findings reinforce the multifactorial pathogenesis of psoriasis involving immune dysregulation, keratinocyte hyperproliferation, and inflammatory cytokine cascades, supporting existing immunological theories. Siddha and herbal medicines demonstrate modulation of key inflammatory mediators such as IL-17A, TNF-α, and MAPK signaling pathways, aligning with contemporary molecular understandings of psoriasis (Dayanand et al., 2024; Kim et al., 2024; Ramanunny et al., 2020).

The identification of phytochemical constituents with anti-inflammatory, antioxidant, and immunomodulatory properties in Siddha formulations and herbal extracts provides mechanistic insights into their therapeutic effects, bridging traditional knowledge with modern pharmacology

(Khyade et al., n.d.; Sarkar et al., 2023; Dabholkar et al., 2021).

Network pharmacology and molecular docking studies elucidate the multi-targeted actions of herbal compounds, suggesting a systems-level approach to psoriasis management that contrasts with the single-target focus of many conventional drugs (Dayanand et al., 2024; Sundarrajan et al., 2017; Kim et al., 2024).

The integration of nanotechnological drug delivery systems with herbal medicines introduces a novel theoretical framework for enhancing bioavailability and targeted delivery, potentially overcoming limitations of traditional formulations and supporting the concept of synergistic therapy (Patel et al., 2024; Biswasroy et al., 2022; Salgaonkar et al., 2024).

The safety profiles established through toxicological studies of Siddha herbomineral formulations contribute to the theoretical validation of these traditional medicines as viable therapeutic agents, emphasizing the importance of scientific rigor in traditional medicine research (Christian et al., 2023; Devi et al., 2019).

The observed psychological and quality-of-life improvements in patients treated with Siddha and herbal therapies underscore the holistic theoretical approach of Siddha medicine, which integrates physical, mental, and spiritual well-being in disease management (Siva et al., 2022; K. et al., 2023).

Practical Implications

The demonstrated clinical efficacy and safety of Siddha and herbal medicines in psoriasis management suggest their potential as cost-effective, culturally acceptable alternatives or adjuncts to conventional therapies, particularly in resource-limited settings (Shalini et al., 2024; Amuthan & Santhi, 2020; "Efficacy and Safety of Topical Botanical...", 2023).

The incorporation of nanotechnology-based delivery systems such as ethosomes, liposomes, and nanoemulsions can enhance the therapeutic outcomes of herbal medicines by improving skin penetration, stability, and controlled release, thereby increasing patient compliance and reducing side effects (Wang et al., 2024; Patel et al., 2024; Jurel et al., 2024).

Standardization and quality control of Siddha formulations, as evidenced by advanced analytical techniques, are critical for ensuring reproducibility, safety, and regulatory acceptance, facilitating their integration into mainstream healthcare (Dash, 2024; Sivasankaran et al., 2018).

The multi-targeted action of herbal compounds offers a practical advantage in managing the complex pathophysiology of psoriasis, potentially reducing the need for polypharmacy and minimizing adverse effects associated with conventional immunosuppressive drugs (Sarkar et al., 2023; Dabholkar et al., 2021; Kim et al., 2024).

The positive outcomes from clinical case reports and trials support the development of evidence-based guidelines for Siddha and herbal treatments, encouraging their inclusion in national health policies and dermatological practice frameworks (Amala, 2018; Nandhini, 2018; Munesh et al., 2020).

The holistic approach of Siddha medicine, including dietary and lifestyle modifications alongside pharmacotherapy, highlights the importance of integrative care models in improving long-term disease control and patient quality of life (K. et al., 2023; Detholia, 2024).

Limitations of Literature

Several limitations constrain the current literature on psoriasis treatment with Siddha and herbal medicine. Small sample sizes are prevalent, with many clinical studies and case reports involving limited sample sizes or single cases, which restricts the generalizability and external validity of

the findings. This limitation hinders robust statistical analysis and wider applicability (Shalini et al., 2024; Amuthan & Santhi, 2020; Muralidass et al., 2020; Amala, 2018; Nandhini, 2018; K. et al., 2023; "Efficacy and Safety of Topical Botanical...", 2023; "Psoriasis Management Using Herbal Supple...", 2023).

Lack of long-term follow-up is another significant limitation, as most studies lack extended follow-up periods to assess the durability of treatment effects and potential relapse rates, limiting understanding of long-term efficacy and safety of Siddha and herbal treatments for psoriasis (Shalini et al., 2024; K. et al., 2023; "Efficacy and Safety of Topical Botanical...", 2023).

Limited molecular mechanism exploration is evident in several studies that provide preliminary phytochemical or clinical data but do not deeply investigate molecular or cellular mechanisms underlying therapeutic effects, reducing mechanistic insight and translational potential (Ojha et al., 2024; Dayanand et al., 2024; Sundarrajan et al., 2017; Sarkar et al., 2023).

Methodological constraints in clinical trials are common, with some clinical trials lacking rigorous design elements such as randomization, blinding, or control groups, which may introduce bias and affect the internal validity of the results (Amala, 2018; Nandhini, 2018; Munesh et al., 2020; Shetty, 2014).

Geographic and cultural bias is present as research is predominantly conducted in specific regions (mainly South India), which may limit the applicability of findings across diverse populations due to genetic, environmental, and cultural differences (Shalini et al., 2024; Muralidass et al., 2020; Amala, 2018; Rathinam et al., 2022; Chitra et al., 2017).

Insufficient standardization of herbal formulations remains a challenge, with variability in preparation methods, phytochemical content, and quality control of Siddha and herbal medicines reducing reproducibility and comparability across studies, impacting reliability of conclusions (Dash, 2024; Sivasankaran et al., 2018; Devi et al., 2019).

Limited integration with modern drug delivery is apparent, as although some studies explore nanotechnology-based delivery, there is a paucity of clinical evidence demonstrating improved bioavailability and therapeutic outcomes of Siddha/herbal medicines using advanced delivery systems (Wang et al., 2023; Wang et al., 2024; Patel et al., 2024; Biswasroy et al., 2022; Jurel et al., 2024; Sharma et al., 2024; Salgaonkar et al., 2024).

Safety and toxicity data scarcity is concerning, as few studies provide comprehensive toxicological evaluations or long-term safety data for Siddha formulations, which is critical for clinical translation and regulatory approval (Christian et al., 2023; Devi et al., 2019).

Heterogeneity in outcome measures creates challenges, as diverse clinical endpoints and assessment tools (e.g., PASI, DLQI, PDI) are used inconsistently across studies, complicating cross-study comparisons and meta-analyses (Amala, 2018; Nandhini, 2018; K. et al., 2023; "Efficacy and Safety of Topical Botanical...", 2023).

Gaps and Future Research Directions

Several critical gaps exist in the current literature that require targeted research efforts. The lack of large-scale, randomized controlled trials (RCTs) represents a high priority gap, as most clinical studies on Siddha and herbal treatments for psoriasis are small-scale, open-label, or case reports without rigorous controls. Future research should conduct well-designed, multicenter RCTs with adequate sample sizes, placebo controls, and blinding to robustly assess efficacy and safety of Siddha and herbal formulations. This is justified because current evidence is limited by small sample sizes and methodological weaknesses, restricting generalizability and clinical adoption

(Shalini et al., 2024; Amala, 2018; Nandhini, 2018; "Efficacy and Safety of Topical Botanical...", 2023).

Insufficient long-term safety and toxicity data is another high priority gap, as long-term safety profiles of Siddha and herbal medicines, especially herbomineral formulations, remain underexplored in humans. Future research should implement longitudinal safety studies and chronic toxicity assessments in humans, including monitoring for heavy metal accumulation and organ function over extended periods. While acute toxicity studies exist, chronic safety data are sparse, limiting confidence in prolonged use (Christian et al., 2023; Devi et al., 2019).

Poor standardization and quality control of Siddha formulations represents a high priority issue, as variability in phytochemical composition and lack of uniform standardization protocols affect reproducibility and efficacy. Future research should develop and implement standardized manufacturing protocols, validated analytical methods (e.g., HPTLC, GC-MS), and batch-to-batch consistency assessments for Siddha and herbal products. Variability in composition and potential contamination undermine therapeutic reliability and safety (Dayanand et al., 2024; Dash, 2024; Sivasankaran et al., 2018; Devi et al., 2019).

Limited mechanistic in vivo validation is a high priority gap, as most mechanistic insights derive from in vitro or in silico studies without sufficient in vivo or clinical correlation. Future research should perform in vivo studies and clinical biomarker analyses to validate molecular mechanisms such as cytokine modulation, keratinocyte proliferation inhibition, and immune pathway regulation. In vitro findings may not fully represent complex psoriasis pathophysiology; in vivo validation is essential for translational relevance (Ojha et al., 2024; Dayanand et al., 2024; Sundarrajan et al., 2017; Kim et al., 2024).

Underexplored integration of nanotechnology with Siddha formulations is a medium priority gap, as although nanocarriers improve delivery of herbal compounds, few studies integrate nanotechnology specifically with classical Siddha formulations. Future research should develop and evaluate nanotechnology-based delivery systems tailored for Siddha polyherbal and herbomineral formulations, assessing pharmacokinetics, efficacy, and safety in clinical settings. Nanotechnology enhances bioavailability and targeting but is mostly applied to isolated phytochemicals, not complex Siddha formulations (Wang et al., 2023; Wang et al., 2024; Patel et al., 2024; Salgaonkar et al., 2024).

Lack of head-to-head comparative studies with conventional therapies is a medium priority gap, as direct comparisons between Siddha/herbal treatments and standard allopathic therapies are scarce. Future research should design comparative clinical trials evaluating Siddha/herbal formulations against corticosteroids, biologics, or phototherapy to establish relative efficacy, safety, and cost-effectiveness. Comparative data are needed to position Siddha treatments within current therapeutic algorithms (Shalini et al., 2024; Ramanunny et al., 2020; "Efficacy and Safety of Topical Botanical...", 2023).

Limited exploration of multi-target and network pharmacology approaches is a medium priority gap, as the complex multi-component nature of Siddha formulations requires systems-level understanding of their pharmacodynamics. Future research should employ integrative network pharmacology and systems biology to elucidate synergistic effects and multi-target interactions of Siddha herbal compounds in psoriasis. Understanding multi-target effects can optimize formulation design and predict therapeutic outcomes (Sundarrajan et al., 2017; Kim et al., 2024).

Insufficient focus on patient-reported outcomes and quality of life is a medium priority gap, as

few studies systematically assess quality of life improvements and psychosocial impacts of Siddha treatments. Future research should incorporate validated patient-reported outcome measures (e.g., DLQI, PDI) in clinical trials to evaluate holistic benefits of Siddha and herbal therapies. Psoriasis significantly affects quality of life; capturing this dimension is critical for comprehensive evaluation (Amala, 2018; K. et al., 2023; Siva et al., 2022; "Efficacy and Safety of Topical Botanical...", 2023).

Limited research on herb-drug interactions and pharmacokinetics is a medium priority gap, as pharmacokinetic profiles and potential interactions of Siddha/herbal medicines with conventional drugs are poorly characterized. Future research should conduct pharmacokinetic and herb-drug interaction studies to ensure safe co-administration with standard psoriasis treatments. Safety concerns arise from unknown interactions, especially in integrative treatment regimens (Ramanunny et al., 2020; Detholia, 2024).

Underutilization of lifestyle and dietary factors in Siddha psoriasis management is a low priority gap, as although diet and lifestyle are emphasized in Siddha, systematic research on their role in psoriasis outcomes is limited. Future research should investigate the impact of Siddha-recommended dietary and lifestyle modifications alongside herbal treatments in controlled clinical studies. Holistic management including lifestyle may enhance treatment efficacy and reduce relapse (K. et al., 2023; Detholia, 2024).

Overall Synthesis and Conclusion

The accumulated body of research on psoriasis treatment through Siddha and herbal medicine indicates a compelling therapeutic potential rooted in traditional knowledge and increasingly supported by scientific inquiry. Across multiple clinical case reports, trials, and observational studies, Siddha and herbal formulations consistently demonstrate significant improvements in psoriasis symptoms, including reductions in PASI scores and enhancements in patients' quality of life. These outcomes are observed in diverse patient populations, ranging from pediatric to chronic severe cases, underscoring the broad applicability of these treatments. Importantly, these interventions are characterized by favorable safety profiles, with minimal and transient adverse effects reported, further substantiated by animal toxicity studies and clinical monitoring.

Phytochemical investigations reveal a rich array of bioactive compounds—such as alkaloids, flavonoids, phenolics, curcumin, and tryptanthrin—that contribute to the anti-psoriatic efficacy of Siddha and herbal medicines. Advanced analytical techniques and molecular docking studies illuminate the interaction of these constituents with key inflammatory mediators like IL-17A and TNF-α, highlighting their immunomodulatory and anti-inflammatory roles. However, the complexity of polyherbal formulations and variability in standardization pose challenges in definitively attributing clinical benefits to individual compounds, necessitating further rigorous phytochemical quantification and quality control.

Mechanistic insights from in vitro and in silico studies support the inhibition of keratinocyte hyperproliferation, induction of apoptosis, and suppression of pro-inflammatory signaling pathways including MAPK and NF-κB. These findings align well with clinical improvements and suggest a multifaceted mode of action targeting both immune dysregulation and epidermal turnover characteristic of psoriasis. Nonetheless, the paucity of comprehensive in vivo validations and long-term mechanistic studies limits a complete understanding of these processes in human subjects.

The integration of Siddha and herbal treatments with modern nanotechnological drug delivery

systems emerges as a promising frontier to overcome challenges such as limited bioavailability and skin penetration. Nanocarriers—including ethosomes, nanopatches, lipid nanoparticles, hydrogels, and herbosomes—have shown enhanced transdermal delivery, controlled release, and improved therapeutic efficacy while maintaining safety. These innovations hold potential to elevate traditional formulations to clinically viable pharmaceuticals, though clinical validation on larger scales and long-term safety assessments are needed.

Comparatively, Siddha and herbal therapies offer advantages over conventional treatments through reduced adverse effects, cultural acceptability, and cost-effectiveness. However, the lack of large-scale, randomized controlled trials with rigorous blinding and placebo controls restricts definitive conclusions regarding their equivalence or superiority. Additionally, inconsistencies in formulation standardization and regulatory oversight remain barriers to broader clinical adoption.

In summary, the literature collectively supports the clinical efficacy and safety of Siddha and herbal medicines in managing psoriasis, revealing promising phytochemical profiles and mechanistic pathways. The advent of nanotechnology-enhanced delivery systems further amplifies therapeutic potential. To translate these findings into mainstream clinical practice, future research must prioritize standardized formulations, robust large-scale clinical trials, detailed mechanistic studies, and comprehensive evaluation of nanodelivery platforms. This integrative approach promises to foster safer, more effective, and culturally consonant treatments for psoriasis, addressing current limitations of conventional therapies.

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