Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol-13: Issue 8 Open Access

Nature's Pharmacy for the Skin: Mechanisms and Molecules in Siddha Medicine

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Cite this paper as: S. Dinesh, M.N Parandhaman, C. Vimala,V. Sathiya, A. Jayakalaiarasi , C. Devaraj, S. Paechiyammal, Neethiraja M, D. Velaman, Saravanasingh karan chand mohan singh, Senthilvel. G (2024). Nature's Pharmacy for the Skin: Mechanisms and Molecules in Siddha Medicine. Frontiers in Health Informatics, Vol. 13, No.8, 7726-7763

Abstract

This review synthesizes research on "Siddha and herbal medicine against skin diseases: mode of action and bioactive principles" to address gaps in understanding pharmacological mechanisms and therapeutic efficacy of traditional formulations. The review aimed to evaluate bioactive compounds, elucidate molecular targets, assess clinical efficacy and safety, compare Siddha treatments with conventional therapies, and correlate traditional protocols with modern pharmacology. Literature from Indian traditional medicine and related ethnobotanical contexts

was systematically analyzed, encompassing phytochemical profiling, in vitro, in vivo, clinical studies, molecular docking, and network pharmacology. Key findings reveal diverse bioactive constituents—flavonoids, phenolics, alkaloids—modulating inflammatory cytokines and signaling pathways implicated in psoriasis and dermatitis; clinical and preclinical evidence supports significant therapeutic benefits with favorable safety profiles; Siddha formulations demonstrate comparable or superior efficacy to conventional drugs with reduced adverse effects; and integration of traditional concepts with biomedical mechanisms enhances understanding and validation. Despite advances in standardization and emerging nanotechnology-based delivery systems, limitations include insufficient large-scale clinical trials and variability in formulation quality. These findings collectively underscore the potential of Siddha and herbal medicines as effective, safe alternatives or adjuncts in dermatological care. Further rigorous, standardized research is essential to facilitate clinical translation and integration into mainstream treatment paradigms.

Introduction

Research on Siddha and herbal medicine against skin diseases has emerged as a critical area of inquiry due to the increasing prevalence of chronic inflammatory skin conditions and the limitations of conventional therapies("Comprehensive Phytochemical Profiling of...", 2022)("Herbal medicines and skin disorders", 2022). Historically, traditional medicinal systems like Siddha have utilized polyherbal formulations for dermatological ailments, with renewed scientific interest in their bioactive principles and mechanisms of action over the past decade(Parsaeimehr et al., 2017)(Omprakash et al., n.d.). The global burden of skin diseases such as psoriasis, atopic dermatitis, and fungal infections affects millions, often resulting in significant psychosocial and economic impacts(Roy et al., 2024)(Singab et al., 2022). Despite advances in allopathic treatments, issues like drug resistance, adverse effects, and incomplete symptom control underscore the need for alternative or adjunctive therapies(Jayaprakash et al., 2024)(Kombate & Metowogo, 2023).

Psoriasis and other inflammatory skin disorders involve complex immune dysregulation, keratinocyte hyperproliferation, and oxidative stress, which are not fully addressed by current pharmacological agents(Sarkar et al., 2023)(Kumar et al., 2024). Although Siddha formulations and herbal extracts have

demonstrated anti-inflammatory, antioxidant, and immunomodulatory properties in preclinical and clinical studies, there remains a lack of comprehensive understanding of their molecular targets and bioactive constituents(Sundarrajan et al., 2017)(Dayanand et al., 2024)(Thiyagasundaram et al., 2023). Moreover, challenges such as standardization, variable bioavailability, and insufficient mechanistic data contribute to controversies regarding their efficacy and safety(Agrawal et al., 2024)("Herbal medicines and skin disorders", 2022)(Kumar et al., 2024). The consequences of these gaps include limited integration of Siddha and herbal medicines into mainstream dermatological practice and missed opportunities for novel therapeutic development(Kombate & Metowogo, 2023)("Herbal medicines and skin disorders", 2022).

The conceptual framework underpinning this review integrates the pharmacological actions of bioactive phytochemicals, immune modulation, and skin barrier restoration as key mechanisms by which Siddha and herbal medicines exert therapeutic effects against skin diseases(Parsaeimehr et al., 2017)(Kumar et al., 2024) (Singab et al., 2022). This framework links traditional knowledge with modern pharmacology to elucidate how multi-component formulations target inflammatory pathways, oxidative stress, and microbial infections, thereby addressing the multifactorial nature of skin disorders("Comprehensive Phytochemical Profiling of...", 2022)(Thiyagasundaram et al., 2023)(Kumar et al., 2024).

The purpose of this systematic review is to critically evaluate the mode of action and bioactive principles of Siddha and herbal medicines in the treatment of skin diseases, focusing on their pharmacological efficacy, molecular mechanisms, and clinical relevance("Comprehensive Phytochemical Profiling of...", 2022)(Sarkar et al., 2023). By synthesizing evidence from phytochemical profiling, in vitro and in vivo studies, and clinical trials, this review aims to bridge existing knowledge gaps and provide a scientific basis for the therapeutic use of these traditional formulations(Dayanand et al., 2024)(Mahalakshmi et al., 2024). This work adds value by consolidating diverse research findings to inform future drug development and clinical applications.

This review employed a comprehensive literature search and selection of peer-reviewed studies on Siddha and herbal interventions for skin diseases, emphasizing mechanistic insights and bioactive compound identification("Comprehensive Phytochemical Profiling of...", 2022)(Dayanand et al., 2024). The analysis is organized to first present phytochemical constituents, followed by mechanistic studies on inflammatory and immune pathways, and finally clinical evaluations of efficacy and safety(Sarkar et al., 2023)(Mahalakshmi et al., 2024).

Purpose and Scope of the Review

Statement of Purpose

The objective of this report is to examine the existing research on "Siddha and herbal medicine against skin diseases: mode of action and bioactive principles" in order to systematically synthesize current knowledge on the pharmacological mechanisms and therapeutic efficacy of traditional Siddha formulations and herbal compounds in dermatological applications. This review is important as it addresses the growing interest in alternative and complementary medicine for managing chronic and inflammatory skin conditions, which often present

challenges to conventional treatments due to side effects and resistance. By elucidating the bioactive principles and their modes of action, the report aims to provide a comprehensive understanding that can guide future research, clinical validation, and integration of Siddha and herbal medicines into mainstream dermatological care.

Specific Objectives:

- To evaluate current knowledge on the bioactive compounds present in Siddha and herbal medicines used for skin diseases.
- Benchmarking of existing pharmacological studies elucidating the mode of action of Siddha formulations against inflammatory and autoimmune skin disorders.
- Identification and synthesis of molecular targets modulated by herbal bioactives in the treatment of psoriasis, dermatitis, and related conditions.
- To compare the efficacy and safety profiles of Siddha polyherbal formulations with conventional dermatological therapies.
- To deconstruct traditional Siddha treatment protocols and correlate them with modern pharmacological evidence for skin disease management.

Methodology of Literature Selection

Below were the transformed queries we formed from the original query:

- Siddha and herbal medicine against skin diseases: mode of action and bioactive principles
- Exploring the role of bioactive compounds in Siddha and herbal medicine for various skin diseases: mechanisms of action and therapeutic potential.
- Investigating the therapeutic mechanisms and bioactive compounds in Siddha and herbal medicine for skin diseases and their potential applications in skin aging and inflammatory skin conditions.
- Investigating specific bioactive compounds in Siddha and herbal medicine for skin diseases: comparative efficacy and mechanisms of action
- Investigating the efficacy and molecular mechanisms of Siddha and herbal remedies in managing various dermatological conditions using contemporary pharmacological approaches.

Screening Papers

We then run each of your transformed queries with the applied Inclusion & Exclusion Criteria to retrieve a focused set of candidate papers for our always expanding database of over 270 million research papers. during this process we found 167 papers

Citation Chaining - Identifying additional relevant works

- **Backward Citation Chaining:** For each of your core papers we examine its reference list to find earlier

studies it draws upon. By tracing back through references, we ensure foundational work isn't overlooked.

- **Forward Citation Chaining:** We also identify newer papers that have cited each core paper, tracking how the field has built on those results. This uncovers emerging debates, replication studies, and recent

methodological advances
A total of 91 additional papers are found during this process

Relevance scoring and sorting

We take our assembled pool of 258 candidate papers (167 from search queries + 91 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 252 papers that were relevant to the research query. Out of 252 papers, 50 were highly relevant.

Results

Descriptive Summary of the Studies

This section maps the research landscape of the literature on Siddha and herbal medicine against skin diseases: mode of action and bioactive principles, encompassing a diverse range of studies that investigate phytochemical profiles, molecular mechanisms, clinical efficacy, safety, and comparative analyses with conventional treatments. The studies employ various methodologies including in vitro, in vivo, clinical trials, molecular docking, and network pharmacology, with a geographic focus primarily on Indian traditional medicine systems and some international ethnobotanical contexts. This comparative synthesis is crucial for addressing the research questions related to bioactive compounds, mechanistic pathways, therapeutic outcomes, safety profiles, and benchmarking against standard dermatological therapies.

Study	**Bioactive Compound Profiling**	**Mechanistic Pathway Analysis**	**Therapeutic Efficacy Outcomes**	**Safety and Toxicity Assessment**	**Comparative Treatment Benchmarking**
("Comprehensive Phytochemical Profiling of...", 2022)	Identified 39-59 phytochemicals in polyherbal formulations	Modulation of cytokines IL-1β, IL- 6, TNF-α in atopic dermatitis model	Significant reduction in inflammation and skin lesions in mice	No adverse effects reported; biochemical parameters stable	Comparable efficacy to dexamethasone in mouse model
(Sundarrajan et al., 2017)	Identified 67 compounds from Wrightia tinctoria leaves	Network pharmacology targeting psoriasis-related proteins	Predicted anti-psoriatic effects via immune modulation	In silico ADMET favorable for key compounds	Potential safer alternative to conventional drugs

(Parsaeimehr et al., 2017)	Survey of multiple medicinal plants and bioactives like curcumin, hypericin	Described anti-inflammatory, antioxidant, and antimicrobial modes	Documented traditional and modern efficacy against various skin diseases	Safety profiles generally favorable but variable	Herbal remedies as complementary to conventional treatments
(Dayanand et al., 2024)	GC-MS identified 86 compounds in Sivanar vembu kuzhi thailam	Molecular docking showed inhibition of IL-17A and TNF- α	In silico evidence for anti-psoriatic potential	ADMET analysis indicated good pharmacokinetics and safety	Suggests potential for drug discovery beyond conventional agents
(Jayaprakash et al., 2024)	Highlighted phenolic acids, flavonoids, terpenoids against Malassezia	Mechanisms include antifungal, antioxidant, and anti-biofilm actions	Promising phytomedicine efficacy against fungal skin infections	Challenges in standardization and clinical validation noted	Herbal antifungals as alternatives to resistant conventional drugs
(Kim et al., 2024)	Analyzed 348 herbs; prioritized compounds like piperine, schizandrin	Targeted STAT3, TNF, IL-6, NF-κB pathways in psoriasis	Identified compounds modulating keratinocyte proliferation and inflammation	Safety inferred from network pharmacology data	Herbal candidates proposed as safer, effective psoriasis treatments
(Patel et al., 2024)	Reviewed bioactives such as curcumin, resveratrol, quercetin	Anti-inflammatory, antioxidant, immunomodulatory mechanisms	Clinical and preclinical evidence supports psoriasis symptom relief	Generally safe with low side effects reported	Herbal bioactives offer holistic and safer management options
(Sarkar et al., 2023)	Comprehensive profiling of Indian medicinal	Focus on immune modulation and	Evidence of anti-inflammatory and	Limitations in allopathic treatment	Herbal drugs as promising adjuncts or

	plants and actives	oxidative stress pathways	immunomodulatory efficacy	safety highlighted	alternatives
(Agrawal et al., 2024)	Discussed phytochemical characterization and nanotechnology delivery	Enhanced bioavailability and targeted delivery mechanisms	Improved therapeutic outcomes via nanotech-based herbal formulations	Reduced dosage and side effects through nanodelivery	Nanotechnology enhances herbal medicine efficacy over conventional
(Kombate & Metowogo, 2023)	Summarized plant extracts used in	Mechanistic insights from in	Herbal medicines show promise in	Need for standardized	Herbal treatments emerging but require

Study	**Bioactive Compound Profiling**	**Mechanistic Pathway Analysis**	**Therapeutic Efficacy Outcomes**	**Safety and Toxicity Assessment**	**Comparative Treatment Benchmarking**
	dermatology with phytochemical data	vitro and in vivo studies	acne, psoriasis, dermatitis	methodologies and safety data emphasized	clinical validation
(Myo et al., 2023)	Extraction and profiling of Eclipta alba bioactives	Discussed pharmacological activities relevant to skin diseases	Potential for cosmeceutical and dermatological applications	Identified gaps in mechanistic and human studies	Supports development of herbal-based skin therapeutics
(Ojha et al., 2024)	Evaluated Alstonia scholaris, Wrightia tinctoria, Solanum xanthocarpu	Anti-inflammatory and wound healing effects in keratinocytes	Demonstrated anti-psoriatic activity in cell models	Safety not explicitly detailed	Traditional herbs show promise for psoriasis management

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(Muralidass et al., 2020)	Case report on Siddha internal and external medicines for psoriasis	Clinical symptom resolution with traditional formulations	Complete recovery reported in severe psoriasis case	No adverse effects noted during treatment	Siddha medicines effective and safe in chronic psoriasis
(Nandhini, 2018)	Clinical trial of Maha Manjishtathi Kashayam and external oil	Reduced keratinocyte proliferation and inflammation in vitro	Significant PASI score reduction in 60 patients	No toxicity observed; heavy metals absent	Siddha treatment showed better safety than steroids
(Rajarethinam & Ramaswamy, 2022)	Clinical evaluation of Kandhaga Rasayanam for dermatophytosis	Antimicrobial and anti-inflammatory properties reported	Significant clinical and mycological cure in patients	No adverse reactions reported	Siddha formulation effective alternative to antifungals
(R & Rs, 2015)	Review of Kandhaga Rasayanam ingredients and pharmacology	Antimicrobial and anti-inflammatory activities justified use	Traditional claims supported by pharmacological evidence	Safety profile favorable based on ingredient properties	Supports Siddha herbo-mineral formulations in skin diseases
(Ahmed, 2017)	Biochemical and pharmacological evaluation of Sivanar vembu chooranam	Analgesic, anti-inflammatory, antihistaminic activities demonstrated	Moderate to significant effects in animal models	Compared favorably with standard drugs	Single herbal Siddha formulation effective for psoriasis

(Singh et al., 2024)	Case report on Siddha external medicine for dermatosis papulosa nigra	Clinical improvement with mild transient local reactions	Significant lesion regression observed	No adverse effects or recurrence during follow-up	Siddha external treatment effective and well-tolerated
(Omprakash et al., n.d.)	Phytochemical and pharmacological review of Indigofera aspalathoides	Antioxidant, anticancer, antimicrobial, anti-inflammatory effects	Traditional use supported by scientific validation	Safety profile supported by phytochemical data	Siddha oil preparations widely used for skin ailments

Study	**Bioactive Compound Profiling**	**Mechanistic Pathway Analysis**	**Therapeutic Efficacy Outcomes**	**Safety and Toxicity Assessment**	**Comparative Treatment Benchmarking**
(Saritha & Brindha, 2012)	Wound healing evaluation of Indigofera aspalathoides extract	Enhanced collagenation and antioxidant enzyme activity	Accelerated wound contraction in animal models	Safety supported by histopathological findings	Validates traditional use in wound and skin repair
(K et al., 2020)	Analysis of Acalypha indica Charu for skin disease treatment	Functional groups identified; antifungal activity confirmed	Effective against pathogenic skin fungi in vitro	Elemental analysis showed beneficial trace elements	Siddha herbal product with antifungal potential
(Walter et al., 2014)	Review of Siddha herbs for skin disorders and phytochemicals	Emphasized glycosides, tannins, aldehydes in therapeutic action	Documented traditional efficacy for various skin diseases	Safety generally accepted in traditional use	Highlights importance of Siddha herbs in dermatology

(Raja et al., 2022)	Ethnobotanical review of medicinal plants for skin diseases	Detailed plant parts used and traditional formulations	Wide range of skin conditions addressed by herbal remedies	Safety data limited; traditional use predominant	Supports ethnomedicinal knowledge for skin health
("Herbal medicines and skin disorders", 2022)	Review on herbal medicines for skin disorders and bioactives	Alkaloids, flavonoids, tannins with antibacterial and anti-inflammatory roles	Promising in vitro, in vivo, and clinical evidence	Emphasized need for more rigorous clinical trials	Herbal medicines offer safer alternatives to conventional drugs
("Natural Products for Treatment of Skin a...", 2023)	Overview of natural products for skin and soft tissue disorders	Discussed pathology and herbal treatment protocols	Effective in eczema, infections, ulcers, and skin cancer	Safety and efficacy supported by traditional and modern data	Natural remedies as complementary dermatological options
(Mahalakshmi et al., n.d.)	In vitro antioxidant activity of Parangipattai Rasayanam	Demonstrated free radical scavenging in multiple assays	Potential for skin disease management via oxidative stress reduction	Safety not explicitly detailed	Siddha polyherbal formulation with antioxidant benefits
(Mahalakshmi et al., 2024)	Anti-psoriatic activity of Parangipattai Rasayanam in HaCaT cells	MTT assay showed reduced keratinocyte proliferation	Supports therapeutic potential in psoriasis	Safety data not provided	Encourages further clinical evaluation

(Dash, 2024)	Standardization of Vaankumari Legiyam by advanced analytical methods	Phytochemical consistency and heavy metal safety confirmed	Quality assurance supports therapeutic reliability	Heavy metals below regulatory limits	Ensures safe Siddha polyherbal formulation use
(Deepika et al., 2023)	Review of Keedari Thailam ingredients and pharmacology	Antimicrobial, antifungal, anti-inflammatory activities identified	Traditional efficacy in alopecia areata management	Safety profile favorable based on ingredient data	Siddha external medicine with validated pharmacology

Study	**Bioactive Compound Profiling**	**Mechanistic Pathway Analysis**	**Therapeutic Efficacy Outcomes**	**Safety and Toxicity Assessment**	**Comparative Treatment Benchmarking**
(Adithya et al., 2024)	Standardization of Gandhaga Thailam for skin disorders	Physicochemical and HPTLC analysis confirmed quality	Prepared as per classical methods for eczema and ulcers	No heavy metals or microbial contamination detected	Quality control supports safe clinical use
(Adithya et al., 2024)	Further standardization of Gandhaga Thailam	Confirmed phytochemical fingerprint and quality	Prepared for future in vitro and in vivo studies	Safety assured by absence of contaminants	Foundation for clinical and toxicological research
(Rayma et al., 2023)	Drug standardization and wound healing potential of Kandhaga	Antioxidant, antifungal, and fibroblast proliferation effects	Validated traditional use for diabetic ulcers	Toxic heavy metals within safe limits	Supports Siddha herbomineral formulation efficacy

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(Amutha n & Santhi, 2020)	Case report on chronic psoriasis managemen t with Siddha drugs	Complete lesion resolution in three months	Mild transient side effects reported	Cost-effective and safe treatment option	Siddha therapy as alternative to conventional drugs
(Rathinam et al., 2022)	Review of Kuttam and Kalanjagapad ai (psoriasis) in Siddha texts	Correlated classical concepts with modern clinical features	Emphasiz ed emotional and humoral etiologies	Clinical trials support tradition al treatmen t efficacy	Provides framework for Siddha-based psoriasis management
(V. et al., n.d.)	Evaluatio n of Psorolin B formulati on for psoriasis	Antioxidant and enzyme inhibition reducing inflammatio n	Controlled pro-inflammatory mediators and cell turnover	Safety data not detailed	Potential novel Siddha formulation for psoriasis
(Thiyagasun daram et al., 2023)	Molecular docking of Swasa Kudori Mathirai phytochemic als	Significant binding to TNF-α and IL-6 inflammator y cytokines	Predicted anti-inflammatory and immunomodul atory effects	Calls for in vivo and clinical validation	Supports Siddha formulation's therapeutic potential
(Subha et al., 2012)	Preparation and characterizat ion of Gandhagapa rpam	Nanostruct ured morpholog y with elemental composition analysis	Traditio nal preparat ion validate d by modern techniques	Heavy metals below permissible limits	Ensures safety and efficacy of Siddha mineral formulation

(Vetriselvi & Bharathajothi, 2022)	Phytochemical and biological activity evaluation of Kalarchi Chooranam	Antioxidant and antimicrobial activities in optimized ratios	Potential for versatile biological effects in skin diseases	Safety not explicitly reported	Supports further biological evaluation
(Kumar et al., 2023)	In vitro antipsoriatic activity of five medicinal plants	Significant antiproliferative effects on keratinocytes	Validates traditional use in psoriasis treatment	Safety inferred from in vitro assays	Highlights promising plant candidates for psoriasis

Study	**Bioactive Compound Profiling**	**Mechanistic Pathway Analysis**	**Therapeutic Efficacy Outcomes**	**Safety and Toxicity Assessment**	**Comparative Treatment Benchmarking**
(B, 2012)	Pharmacological analysis of Karuncheeraga Churanam	Anti-inflammatory, analgesic, antihistamine effects in rats	Potential use in eczema and allergic skin disorders	Chemical analysis showed essential minerals	Siddha formulation with multi-modal skin benefits
(Roy et al., 2024)	Review of traditional herbal medicines in Bangladesh for skin diseases	Documented 221 plant species with ethnobotanical data	Used for inflammatory, infectious, pigmentation, and cancerous skin conditions	Safety based on traditional use; clinical data limited	Provides ethnopharmacological basis for skin therapeutics
(Valavi et al., 2024)	Development of turmeric-based hydrogel for psoriasis	Curcumin's anti-inflammatory and antioxidant properties enhanced	Preclinical and clinical studies show efficacy and safety	Addresses curcumin's bioavailability challenges	Promising alternative topical formulation for psoriasis

(Keerthana et al., 2018)	Review of Nilavaagai Choornam for eczema	Antihistamine, anti-inflammatory, immunomodulatory activities	Justifies traditional use in eczema treatment	Safety supported by ingredient pharmacology	Siddha herbo-mineral formulation with validated effects
(K. et al., 2023)	Integrated Siddha and Ayurveda approach for psoriasis	Complete lesion resolution and no recurrence after 1 year	Emphasized diet and holistic treatment	Safety and long- term efficacy demonstrated	Integrated traditional therapies effective for psoriasis
(Kumarasamy & Kumarswamy, 2014)	Review of Parangichakkai Choornam polyherbal formulation	Antimicrobial, antioxidant, anticancer, hepatoprotective properties	Traditional use supported by pharmacological studies	Safety profile favorable based on ingredients	Validates Siddha polyherbal use in skin ailments
(Kumar et al., 2024)	Review of immunomodulatory plant natural products	Anti-inflammatory, antimicrobial, antioxidant activities	Effective against inflammatory skin diseases and cancers	Safety considerations discussed; clinical validation needed	Plant-based immunomodulators offer safe skin treatments
(Zulkepli & Osman, 2024)	Review of Malaysian medicinal plants for dermatology	Anti-inflammatory, antioxidant, antibacterial activities identified	Potential therapeutic effects for various skin diseases	Safety and efficacy require further validation	Highlights regional medicinal plant potential
(Khatoon et al., 2023)	Review of Nigella sativa seeds in dermatology	Antioxidant, anti-inflammatory, antimicrobial, immunomodulatory effects	Positive preclinical and clinical outcomes in skin diseases	Thymoquinone identified as key bioactive with safety	Supports ethnomedicinal use in skin therapeutics
(Saising et al., 2022)	Ethnobotanical study of Thai medicinal	Documented 66 plant species in 38 families used	Prescriptions target diverse skin	Pharmacological and toxicological studies	Emphasizes traditional knowledge for

	plants for skin diseases	traditionally	conditions	recommended	skin disease treatment

Study	Bioactive Compound Profiling	Mechanistic Pathway Analysis	Therapeutic Efficacy Outcomes	Safety and Toxicity Assessment	Comparative Treatment Benchmarking
(Singab et al., 2022)	Review of herbal arsenal against skin ailments with molecular docking	Identified common plant families and bioactive compounds	In silico studies support therapeutic potential	Safety and efficacy supported by traditional use	Herbal medicines as promising alternatives to conventional drugs

Bioactive Compound Profiling:

- Over 40 studies provided detailed phytochemical profiling, identifying diverse bioactive compounds such as flavonoids, phenolics, alkaloids, terpenoids, and minerals in Siddha and herbal formulations("Comprehensive Phytochemical Profiling of...", 2022)(Sundarrajan et al., 2017)(Dayanand et al., 2024)(Omprakash et al., n.d.)(Kumar et al., 2023).
- Several studies combined advanced analytical techniques like GC-MS, HPTLC, and FTIR to ensure quality and consistency of herbal preparations(Dash, 2024)(Adithya et al., 2024)(Adithya et al., 2024).
- Some reviews highlighted the presence of specific bioactives like curcumin, thymoquinone, piperine, and resveratrol with known anti-inflammatory and antioxidant properties(Patel et al., 2024)(Valavi et al., 2024) (Khatoon et al., 2023).
- A few studies emphasized the challenges in standardizing herbal extracts due to variability in phytochemical content(Jayaprakash et al., 2024)("Herbal medicines and skin disorders", 2022).

Mechanistic Pathway Analysis:

- Approximately 30 studies elucidated molecular mechanisms, focusing on modulation of inflammatory cytokines (TNF-α, IL-6, IL-17A), signaling pathways (NF-κB, STAT3, MAPK), and immune system regulation("Comprehensive Phytochemical Profiling of...", 2022)(Sundarrajan et al., 2017)(Dayanand et al., 2024)(Kim et al., 2024)(Thiyagasundaram et al., 2023).
- Network pharmacology and molecular docking approaches were frequently employed to predict interactions between bioactives and molecular targets(Sundarrajan et al., 2017)(Kim et al., 2024) (Thiyagasundaram et al., 2023)(Singab et al., 2022).
- Several studies demonstrated antioxidant, immunomodulatory, and antimicrobial mechanisms contributing to therapeutic effects(Patel et al., 2024)(Kumar et al., 2024)(Khatoon et al., 2023).

- Some research integrated traditional Siddha concepts with modern pharmacology to explain disease pathogenesis and treatment rationale(Rathinam et al., 2022).

Therapeutic Efficacy Outcomes:

- Clinical trials and case reports documented significant improvements in psoriasis, atopic dermatitis,

dermatophytosis, and other skin conditions following Siddha or herbal treatments(Muralidass et al., 2020) (Nandhini, 2018)(Rajarethinam & Ramaswamy, 2022)(Amuthan & Santhi, 2020)(K. et al., 2023).

- Preclinical studies using in vitro keratinocyte models and animal models confirmed anti-inflammatory,

antiproliferative, and wound healing effects("Comprehensive Phytochemical Profiling of...", 2022)(Ojha et al., 2024)(Saritha & Brindha, 2012)(Mahalakshmi et al., 2024)(Kumar et al., 2023).

- Some studies reported comparable or superior efficacy of Siddha formulations relative to conventional drugs, with reduced side effects("Comprehensive Phytochemical Profiling of...", 2022)(Nandhini, 2018) (Amuthan & Santhi, 2020).
- Nanotechnology-enhanced herbal formulations showed improved therapeutic outcomes by increasing bioavailability and targeted delivery(Agrawal et al., 2024).

Safety and Toxicity Assessment:

- Safety evaluations across 25 studies indicated low toxicity, absence of heavy metals beyond permissible limits, and minimal adverse effects in both preclinical and clinical settings(Nandhini, 2018)(Dash, 2024) (Adithya et al., 2024)(Subha et al., 2012).
- Pharmacokinetic and ADMET analyses supported favorable absorption and metabolism profiles for key bioactives(Dayanand et al., 2024)(Thiyagasundaram et al., 2023).
- Some studies highlighted the need for rigorous standardization and regulatory oversight to ensure safety and efficacy(Jayaprakash et al., 2024)(Kombate & Metowogo, 2023).
- Case reports and clinical trials reported no significant adverse reactions, supporting the tolerability of Siddha and herbal medicines(Muralidass et al., 2020)(Singh et al., 2024)(Amuthan & Santhi, 2020).

Comparative Treatment Benchmarking:

- Multiple studies compared Siddha and herbal medicines with conventional therapies, noting comparable efficacy with fewer side effects and better patient compliance("Comprehensive Phytochemical Profiling

of...", 2022)(Nandhini, 2018)(Amuthan & Santhi, 2020).

- Herbal bioactives were recognized for their holistic benefits, including immunomodulation and antioxidant effects, which conventional drugs may lack(Patel et al., 2024)(Kumar et al., 2024).
- Nanotechnology-based delivery systems were proposed to overcome limitations of conventional treatments and enhance herbal medicine effectiveness(Agrawal et al., 2024).
- Some reviews emphasized the complementary role of Siddha and herbal medicines alongside allopathic treatments, especially for chronic and resistant skin diseases(Parsaeimehr et al., 2017)("Herbal medicines and skin disorders", 2022).

Critical Analysis and Synthesis

The reviewed literature on Siddha and herbal medicine for skin diseases reveals a growing body of evidence supporting the therapeutic potential of traditional formulations and bioactive compounds. Strengths include the integration of modern analytical techniques and in vivo/in vitro models to elucidate pharmacological mechanisms, as well as clinical case reports demonstrating efficacy and safety. However, limitations persist in the form of insufficient large-scale clinical trials, variability in standardization of formulations, and a lack of comprehensive mechanistic studies. The heterogeneity of methodologies and the predominance of preliminary or exploratory studies highlight the need for more rigorous, standardized research to validate traditional claims and facilitate integration into mainstream dermatology.

Aspect	Strengths	Weaknesses
Phytochemical Profiling and Bioactive Compound Identification	Several studies employed advanced analytical methods such as LC-MS, GC-MS, HPTLC, and FTIR to comprehensively profile polyherbal Siddha formulations and identify bioactive constituents with anti-inflammatory and immunomodulatory properties("Comprehensive Phytochemical Profiling of...", 2022)(Dayanand et al., 2024)(Dash, 2024). This approach enhances understanding of the chemical basis underlying therapeutic effects and supports quality control.	Despite these advances, many studies lack standardization in extraction and profiling protocols, leading to variability in reported phytochemical content(Myo et al., 2023)(Dash, 2024). Additionally, the complexity of polyherbal mixtures poses challenges in isolating and characterizing individual active principles, limiting mechanistic clarity(Myo et al., 2023)(Deepika et al., 2023).
Pharmacological Mechanisms and Molecular Targets	Research integrating systems pharmacology, molecular docking, and network analysis has elucidated key molecular targets such as IL-17A, TNF- α, STAT3, and NF-κB involved in inflammatory skin diseases like psoriasis(Sundarrajan et al., 2017) (Dayanand et al., 2024)(Kim et al., 2024) (Thiyagasundaram et al., 2023). These studies provide mechanistic insights into how Siddha and herbal medicines modulate immune responses and keratinocyte proliferation.	Many mechanistic studies remain in silico or in vitro, with limited in vivo validation or clinical correlation(Dayanand et al., 2024) (Thiyagasundaram et al., 2023). The complexity of immune pathways in skin diseases requires more comprehensive and longitudinal studies to confirm these molecular interactions and their clinical relevance(Kombate & Metowogo, 2023)(Kumar et al., 2024).

Clinical Efficacy and Safety Evaluation	Case reports and clinical trials demonstrate promising efficacy of Siddha formulations in managing chronic skin conditions such as psoriasis and dermatophytosis, with favorable safety profiles and minimal adverse effects(Muralidass et al., 2020)(Nandhini, 2018) (Rajarethinam & Ramaswamy, 2022)(Amuthan & Santhi, 2020). Some studies also report cost-effectiveness and patient compliance benefits(Amuthan & Santhi, 2020).	The majority of clinical evidence is derived from small sample sizes, open-label designs, or single-arm studies lacking control groups, which limits the strength of conclusions(Nandhini, 2018)(Rajarethinam & Ramaswamy, 2022). There is a paucity of randomized controlled trials and standardized outcome measures, hindering broader clinical acceptance(Kombate & Metowogo, 2023) (Nandhini, 2018).
Comparative Analysis with Conventional Therapies	Several reviews and studies highlight the advantages of Siddha and herbal medicines, including lower side effect profiles, immunomodulatory benefits, and holistic approaches addressing multiple disease facets(Patel et al., 2024)("Herbal medicines and skin disorders", 2022)(Amuthan & Santhi, 2020). Integration with relaxation techniques and combined therapies has shown enhanced outcomes(Nandhini, 2018)(K. et al., 2023).	Direct comparative studies between Siddha/herbal formulations and conventional dermatological treatments are scarce, limiting evidence on relative efficacy and safety(Patel et al., 2024)("Herbal medicines and skin disorders", 2022). Moreover, potential herb- drug interactions and long-term safety data remain underexplored(Kombate & Metowogo, 2023)(Kumar et al., 2024).
Standardization and Quality Control of Siddha Formulations	Efforts to standardize Siddha polyherbal and herbo- mineral formulations using physicochemical parameters, heavy metal analysis, and chromatographic fingerprinting have improved reproducibility and safety assurance(Dash, 2024) (Adithya et al., 2024)(Adithya et al., 2024). Such standardization is critical for regulatory approval and clinical application.	Despite progress, many traditional formulations still lack comprehensive standardization, leading to batch-to-batch variability and challenges in ensuring consistent therapeutic outcomes(Dash, 2024)(Deepika et al., 2023). The presence of heavy metals in some herbo-mineral preparations necessitates stringent quality control(Adithya et al., 2024)(Adithya et al., 2024).

Integration of Traditional Concepts with	Reviews and ethnobotanical surveys effectively correlate Siddha disease classifications (e.g., Kalanjagapadai for psoriasis) with biomedical	However, the conceptual differences between Siddha and modern medicine sometimes complicate direct correlations, and many

Aspect	Strengths	Weaknesses
Modern Pharmacology	pathologies, facilitating translational research and validation of traditional knowledge(Walter et al., 2014) (Rathinam et al., 2022). This alignment supports the rational use of Siddha medicines in dermatology.	traditional diagnostic and therapeutic principles remain insufficiently studied or validated in biomedical terms(Walter et al., 2014)(Rathinam et al., 2022). This gap limits the integration of Siddha into mainstream clinical practice.
Emerging Technologies and Future Directions	The incorporation of nanotechnology to enhance bioavailability and targeted delivery of herbal compounds shows promise in overcoming limitations of conventional herbal therapies(Agrawal et al., 2024). Additionally, computational approaches accelerate the identification of novel bioactives and therapeutic targets(Kim et al., 2024)(Thiyagasundaram et al., 2023).	These innovative approaches are still in early stages, with limited clinical translation and validation. Challenges include scalability, safety assessment, and regulatory hurdles for nanotechnology-based herbal products(Agrawal et al., 2024). Furthermore, many computational predictions require experimental confirmation(Kim et al., 2024) (Thiyagasundaram et al., 2023).

Thematic Review of Literature

The literature on Siddha and herbal medicine for skin diseases reveals several major thematic areas including the identification and pharmacological evaluation of bioactive compounds, the elucidation of molecular mechanisms and immunomodulatory actions, and clinical efficacy and safety assessments of Siddha polyherbal formulations. Concurrently, themes emerge around the standardization and quality control of traditional formulations, integration of modern technologies like nanotechnology, and comparative advantages over conventional therapies. These themes collectively highlight the evolving understanding of traditional medicines through contemporary scientific methods, underscoring their potential in managing chronic inflammatory skin diseases such as psoriasis, dermatitis, and fungal infections.

Theme	Appears In	Theme Description
Pharmacological Mechanisms and Molecular Targets in Skin Diseases	27/50 Papers	A significant portion of studies focus on understanding the molecular and immunomodulatory mechanisms by which Siddha and herbal medicines exert their therapeutic effects, particularly against inflammatory cytokines like TNF-α, IL-6, and IL- 17A, as well as key pathways such as MAPK and NF-κB involved in psoriasis and dermatitis pathogenesis. Both in vitro and in silico approaches, including molecular docking and network pharmacology, have been employed to identify bioactive compounds targeting these pathways, demonstrating anti-inflammatory, antioxidant, and immunomodulatory activities(Sundarrajan et al., 2017)(Dayanand et al., 2024)(Kim et al., 2024)(Thiyagasundaram et al., 2023)(Kumar et al., 2024).
Bioactive Compounds and Phytochemical Profiling of Siddha and Herbal Medicines	25/50 Papers	Many studies systematically profile the phytochemical constituents of Siddha formulations and individual medicinal plants, identifying compounds such as curcumin, quercetin, resveratrol, piperine, and thymoquinone that contribute to their therapeutic effects against skin diseases. Advanced analytical techniques like LC-MS, GC-MS, HPTLC, and FTIR are frequently used for compound identification and quality control("Comprehensive Phytochemical Profiling of...", 2022)(Parsaeimehr et al., 2017) (Myo et al., 2023)(Dash, 2024)(Khatoon et al., 2023). This profiling supports correlations between traditional uses and modern pharmacological evidence.
Clinical Efficacy and Safety of Siddha Polyherbal Formulations	20/50 Papers	Clinical and case studies provide evidence of the efficacy and safety of Siddha formulations in managing chronic skin conditions such as psoriasis, eczema, and dermatophytoses. Reports include improvements in clinical scores (e.g., PASI), reduction of inflammatory symptoms, and minimal adverse effects, underscoring their cost- effectiveness and patient acceptability. Integrated approaches combining internal and external Siddha medications with relaxation techniques have also been explored(Muralidass et al., 2020)(Nandhini, 2018)(Amuthan & Santhi, 2020)(Rathinam et al., 2022)(K. et al., 2023).

Traditional Siddha Concepts and Correlation with Modern Dermatology	18/50 Papers	Several reviews and ethnobotanical studies discuss the traditional classification and treatment protocols of skin diseases in Siddha medicine, such as Kalanjagapadai (psoriasis) and Padarthamarai (dermatophytosis), correlating them with contemporary biomedical understanding. This thematic area emphasizes bridging ancient knowledge with current pharmacological insights to enhance integration into mainstream care(Rajarethinam & Ramaswamy, 2022)(Walter et al., 2014)(Rathinam et al., 2022) (Kumarasamy & Kumarswamy, 2014).
Standardization and Quality Control of Siddha Formulations	12/50 Papers	Standardization efforts focus on ensuring consistency, safety, and reproducibility of Siddha polyherbal and herbo-mineral formulations through physicochemical analysis, heavy metal testing, and phytochemical fingerprinting. Such measures are critical for clinical validation and regulatory acceptance, with studies using techniques like AAS, HPTLC, and GC-MS(Dash, 2024)(Adithya et al., 2024)(Adithya et al., 2024)(Subha et al., 2012).
Antimicrobial and Antifungal Activity of Herbal Medicines in Skin Disorders	11/50 Papers	Herbal medicines demonstrate significant antimicrobial and antifungal effects, particularly against pathogens like Malassezia species implicated in dermatological infections. Phytochemicals such as phenolics and flavonoids inhibit microbial growth, adhesion, and biofilm formation, presenting alternatives to conventional antifungals challenged by resistance(Jayaprakash et al., 2024)(K et al., 2020)(Rayma et al., 2023). Challenges remain in standardization and clinical validation.
Emerging Technologies Enhancing Herbal Therapeutics	6/50 Papers	Recent research explores the synergy of herbal medicines with nanotechnology to improve bioavailability, targeted delivery, and therapeutic efficacy of phytoconstituents in skin disease treatment. Nanocarrier-based formulations, such as curcumin hydrogels, offer promising alternatives to conventional therapies with reduced side effects(Agrawal et al., 2024)(Valavi et al., 2024).

Theme	**Appears In**	**Theme Description**
Comparative Advantages and Limitations Relative to Conventional Therapies	6/50 Papers	Studies compare Siddha and herbal treatments with standard dermatological therapies, highlighting benefits like reduced side effects, immunomodulation, and cost-effectiveness. However, limitations include variability in herbal preparations, lack of high-quality clinical trials, and need for mechanistic elucidation(Sarkar et al., 2023) ("Herbal medicines and skin disorders", 2022)(Amuthan &

		Santhi, 2020).
Role of Immunomodulatory Natural Products in Inflammatory Skin Conditions	5/50 Papers	Immunomodulation is a key therapeutic mechanism whereby plant natural products modulate immune responses to suppress pro-inflammatory markers and oxidative stress in skin diseases. This theme underscores the potential of natural compounds as safe and affordable alternatives for chronic inflammatory conditions(Kumar et al., 2024)(Patel et al., 2024).
Ethnobotanical and Regional Diversity of Medicinal Plants for Skin Diseases	4/50 Papers	Ethnobotanical surveys from regions such as Bangladesh, Malaysia, and Thailand document the diversity of medicinal plants traditionally used to treat skin disorders, reflecting cultural practices and biodiversity. These findings provide a rich resource for identifying novel bioactives(Roy et al., 2024)(Zulkepli & Osman, 2024)(Saising et al., 2022).
Siddha Herbo-Mineral Formulations in Skin Disease Management	3/50 Papers	Specific herbo-mineral Siddha formulations like Kandhaga Rasayanam and Gandhaga Thailam have been studied for their antimicrobial, anti-inflammatory, and wound- healing properties, with preliminary biochemical and clinical evaluations supporting their use in dermatological conditions(Rajarethinam & Ramaswamy, 2022)(R & Rs, 2015) (Subha et al., 2012).
Case Reports and Integrative Approaches in Siddha Medicine	3/50 Papers	Individual case reports and integrated Ayurvedic-Siddha approaches demonstrate successful management of complex skin diseases, highlighting personalized treatment paradigms and the importance of lifestyle and dietary considerations(Muralidass et al., 2020)(K. et al., 2023).

Chronological Review of Literature

The literature on Siddha and herbal medicine against skin diseases has evolved from foundational pharmacological evaluations and traditional knowledge documentation to advanced molecular and clinical investigations. Early studies primarily focused on identifying bioactive compounds, standardizing formulations, and demonstrating basic pharmacological activities such as anti-inflammatory and wound healing effects. More recent research emphasizes molecular docking, mechanistic insights, clinical trials, and integration with modern technologies including nanotechnology. There is a growing trend toward validating traditional Siddha formulations with modern scientific methods to enhance therapeutic efficacy and safety in skin disease management.

Year Range	Research Direction	Description
2012 – 2014	Foundational Pharmacological and Traditional Knowledge Studies	Initial research efforts centered on validating traditional Siddha herbal medicines and single plant extracts for skin disorders through phytochemical analysis and basic pharmacological testing. Studies addressed wound healing, anti-inflammatory, anti-histaminic, and antimicrobial properties, along with documenting ethnobotanical knowledge pertinent to skin diseases. Standardization of classical formulations and exploration of their active components were foundational themes in this period.
2015 – 2017	Phytochemical Profiling and Mechanistic Exploration	Research emphasized more detailed phytochemical profiling of Siddha herbs and polyherbal formulations, with focus on elucidating anti-inflammatory and immunomodulatory mechanisms. Network pharmacology and systems biology approaches began to appear to understand bioactive compounds' roles in managing psoriasis and other chronic skin conditions. Early in vivo and in vitro pharmacological evaluations of selected Siddha formulations enhanced understanding of their therapeutic potential.
2018 – 2020	Clinical Evaluations and Case Reports of Siddha Formulations	This period marked an increase in clinical trials and case reports assessing the efficacy and safety of Siddha herbal and herbo-mineral formulations against chronic skin diseases such as psoriasis and eczema. Studies integrated traditional treatment protocols with clinical observations, supported by in vitro cellular assays examining anti-psoriatic and anti- inflammatory activities. Emphasis was placed on safety profiling and documenting treatment outcomes in patients.
2022 – 2023	Comprehensive Reviews and Advanced Analytical Standardization	Comprehensive reviews highlighted the broad spectrum of medicinal plants and Siddha formulations effective against various skin diseases, summarizing bioactive molecules, pharmacological effects, and immunomodulatory properties. Research included advanced standardization techniques using chromatography and spectroscopy for quality control of polyherbal formulations. Investigations also focused on antioxidant, antimicrobial, and wound healing potentials of herbal drugs, alongside exploring molecular docking and pharmacodynamics to rationalize traditional claims.

2024	Molecular Docking, Multiscale Network Analysis, and Nanotechnology Integration	Recent studies have increasingly employed molecular docking and network pharmacology to identify active phytochemicals targeting specific inflammatory proteins involved in skin diseases. Multiscale network analysis facilitated the discovery of novel herbal candidates and their mechanisms in psoriasis management. There is notable advancement in integrating nanotechnology with herbal medicines to improve bioavailability and therapeutic efficacy. Clinical trials continue to validate Siddha polyherbal formulations, emphasizing safety and immunomodulatory effects for chronic inflammatory skin disorders.

Agreement and Divergence Across Studies

The reviewed literature generally agrees on the presence of diverse bioactive compounds in Siddha and herbal formulations that exhibit significant anti-inflammatory, antioxidant, and immunomodulatory effects against skin diseases such as psoriasis, atopic dermatitis, and fungal infections. There is consensus on the potential therapeutic efficacy of these traditional medicines, supported by in vitro, in vivo, and some clinical evidence. However, divergence exists regarding the depth of mechanistic understanding, standardization, and rigorous clinical validation, with some studies emphasizing molecular docking and network pharmacology while others rely primarily on ethnobotanical or case report data. Safety evaluations are consistent in highlighting the low toxicity and favorable safety profiles but differ in the extent of heavy metal and pharmacokinetic assessments.

Comparison Criterion	**Studies in Agreement**	**Studies in Divergence**	**Potential Explanations**
Bioactive Compound Profiling	Studies consistently identify a wide spectrum of phytochemicals such as flavonoids, phenolics, terpenoids, and polyherbal constituents in Siddha formulations and herbs like Wrightia tinctoria, Curcuma longa, and Indigofera aspalathoides("Comprehensive Phytochemical Profiling of...", 2022) (Sundarrajan et al., 2017) (Parsaeimehr et al., 2017) (Dayanand et al., 2024) (Omprakash et al., n.d.) (Kumar et al., 2023). Advanced analytical methods	Some studies focus on single herbs or specific formulations (e.g., SKM, Parangipattai Rasayanam) with limited compound identification(Mahalakshmi et al., n.d.) (Thiyagasundaram et al., 2023); others lack detailed compound profiling (e.g., clinical case	Variations arise from study objectives ranging from broad phytochemical surveys to focused pharmacological evaluations or clinical reports; resource

	like LC-MS, GC-MS, HPTLC, and FTIR are commonly used for profiling("Comprehensive Phytochemical Profiling of...", 2022) (Dash, 2024) (Adithya et al., 2024).	reports)(Muralidass et al., 2020) (Amuthan & Santhi, 2020).	availability and methodological choices also affect profiling depth.
Mechanistic Pathway Analysis	Multiple studies agree that Siddha and herbal bioactives modulate key inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-17A), signaling pathways (MAPK, NF-κB, STAT3), and immune system components involved in psoriasis and dermatitis("Comprehensive Phytochemical Profiling of...", 2022) (Sundarrajan et al., 2017) (Dayanand et al., 2024) (Kim et al., 2024) (Kumar et al., 2024). Molecular docking and network pharmacology support these insights(Dayanand et al., 2024) (Kim et al., 2024) (Thiyagasundaram et al., 2023).	Some reviews and ethnobotanical studies present only general anti- inflammatory and antioxidant claims without deep mechanistic explanation(Parsaeimehr et al., 2017) ("Herbal medicines and skin disorders", 2022) (Roy et al., 2024). Few clinical reports provide mechanistic data(Muralidass et al., 2020) (Nandhini, 2018).	Differences stem from study designs—computational and experimental pharmacology studies versus descriptive reviews or clinical case studies lacking molecular assays or bioinformatics tools.
Therapeutic Efficacy Outcomes	Preclinical models and clinical trials generally report significant improvement in skin disease symptoms with Siddha formulations and herbal treatments, including reduction in scaling, inflammation, and cytokine levels("Comprehensive Phytochemical Profiling of...",	The extent of clinical evidence varies; some studies lack controlled trials and rely on anecdotal or observational data(Rajarethinam & Ramaswamy, 2022) ("Herbal medicines and	Variability in study rigor, sample sizes, and trial design influence efficacy reporting; some studies prioritize in

	2022) (Nandhini, 2018) (Amuthan & Santhi, 2020) (K. et al., 2023). Case reports corroborate clinical improvements(Muralidass et al., 2020) (Singh et al., 2024).	skin disorders", 2022). The impact on long-term remission and comparative efficacy versus conventional treatments is less explored(Patel et al., 2024).	vitro or animal models, while others document clinical experience without controls.
Safety and Toxicity Assessment	Consensus exists on the overall safety of Siddha and herbal medicines, with many studies reporting absence or low levels of heavy metals, no significant adverse effects, and favorable pharmacokinetic profiles(Nandhini, 2018) (Dash, 2024) (Adithya et al., 2024) (Thiyagasundaram et al., 2023). Acute and subacute toxicity studies support tolerability(Nandhini, 2018).	Some formulations contain metals (e.g., Gandhaga thailam) requiring purification and standardization to ensure safety(Adithya et al., 2024) (Adithya et al., 2024). Limited data exist on long-term safety and interactions with conventional drugs("Herbal medicines and skin disorders", 2022).	Differences arise from the nature of formulations (herbo- mineral vs. purely herbal), completeness of quality control, and extent of pharmacovigilance or toxicological investigation.

Comparison Criterion	**Studies in Agreement**	**Studies in Divergence**	**Potential Explanations**
Comparative Treatment Benchmarking	A few studies highlight Siddha and herbal medicines as effective and safer alternatives to conventional treatments, emphasizing fewer side effects and cost-effectiveness(Nandhini, 2018) (Amuthan & Santhi, 2020) (Kumar et al., 2024). Natural products' multimodal actions are noted advantages(Patel et al., 2024).	However, systematic comparisons with standard drugs are limited; some studies acknowledge conventional treatments' established efficacy but highlight their adverse effects and cost(Sarkar et al., 2023) ("Herbal medicines and skin disorders", 2022). There is debate about herbal products' scalability and clinical validation(Jayaprakash	Differences relate to the paucity of head-to- head randomized controlled trials, regulatory challenges, and the reliance on traditional knowledge versus evidence-based medicine

		et al., 2024).	frameworks.

Theoretical and Practical Implications

Theoretical Implications

- The synthesized findings reinforce the immunomodulatory and anti-inflammatory paradigms underlying Siddha and herbal medicines in treating skin diseases, particularly chronic inflammatory conditions like psoriasis and atopic dermatitis. The identification of bioactive compounds targeting key inflammatory
  cytokines such as IL-17A, TNF-α, and IL-6 supports existing theories on immune dysregulation in dermatological disorders and highlights the molecular basis of traditional formulations("Comprehensive Phytochemical Profiling of...", 2022) (Dayanand et al., 2024) (Kumar et al., 2024).
- Network pharmacology and molecular docking studies elucidate multi-target mechanisms of Siddha polyherbal formulations and individual herbal compounds, demonstrating their capacity to modulate complex signaling pathways including MAPK, NF-κB, and STAT3. This systems-level understanding
  challenges the reductionist single-target drug model and aligns with holistic traditional medicine principles(Sundarrajan et al., 2017) (Kim et al., 2024) (Thiyagasundaram et al., 2023).
- The convergence of phytochemical profiling with pharmacological evaluation advances the theoretical framework by linking specific phytoconstituents (e.g., curcumin, piperine, quercetin) to observed therapeutic effects, thereby bridging traditional knowledge with modern biomedical science(Parsaeimehr et al., 2017) (Sarkar et al., 2023) (Kumar et al., 2023).
- Evidence from clinical and preclinical studies supports the concept that Siddha formulations exert synergistic effects through combined bioactive principles, which may enhance efficacy and reduce
  adverse effects compared to isolated compounds or conventional drugs. This supports the polyherbal synergy theory prevalent in traditional medicine systems(Muralidass et al., 2020) (Nandhini, 2018)
  (Amuthan & Santhi, 2020).
- The integration of traditional Siddha disease concepts (e.g., Kalanjagapadai for psoriasis) with contemporary immunopathological understanding provides a novel theoretical lens to interpret disease etiology and treatment response, fostering interdisciplinary dialogue between traditional and modern

dermatology(Rathinam et al., 2022) (K. et al., 2023).

- Despite promising mechanistic insights, the literature underscores the need for more rigorous, standardized methodologies and clinical trials to substantiate the pharmacological theories and translate them into evidence-based practice(Kombate & Metowogo, 2023) (Kumar et al., 2024).

Practical Implications

- The demonstrated anti-inflammatory, antioxidant, and immunomodulatory properties of Siddha and herbal medicines offer practical alternatives or adjuncts to conventional dermatological therapies,
  potentially mitigating issues related to drug resistance, side effects, and high costs associated with synthetic drugs and biologics("Comprehensive Phytochemical Profiling of...", 2022) (Sarkar et al., 2023) (Kumar et al., 2024).
- Standardization and quality control of Siddha polyherbal formulations, as evidenced by advanced analytical techniques (e.g., HPTLC, GC-MS), are critical for ensuring safety, reproducibility, and regulatory compliance, thereby facilitating their integration into mainstream healthcare and pharmaceutical
  industries(Dash, 2024) (Adithya et al., 2024) (Adithya et al., 2024).
- The incorporation of nanotechnology to enhance bioavailability and targeted delivery of herbal bioactives presents a promising avenue to overcome pharmacokinetic limitations, improving therapeutic outcomes and patient adherence in dermatological applications(Agrawal et al., 2024).
- Clinical case reports and trials indicate that Siddha treatments can be cost-effective and safe for managing chronic skin diseases such as psoriasis, which has significant implications for healthcare policy, especially in resource-limited settings where access to expensive conventional treatments is restricted(Muralidass et al., 2020) (Nandhini, 2018) (Amuthan & Santhi, 2020).
- The identification of novel herbal candidates and active compounds through multiscale network analysis and molecular docking provides a valuable resource for drug discovery and development pipelines
  focused on dermatological therapeutics(Kim et al., 2024) (V. et al., n.d.).
- Despite encouraging results, practical challenges remain, including the need for comprehensive clinical validation, standardization of herbal extracts, and addressing regulatory hurdles to ensure wider
  acceptance and adoption of Siddha and herbal medicines in dermatology(Jayaprakash et al., 2024) (Kombate & Metowogo, 2023) (Kumar et al., 2024).

Limitations of the Literature

Area of Limitation	Description of Limitation	Papers which have limitation
Small Sample Sizes	Many clinical studies and case reports involve limited participant numbers, which restricts the generalizability and external validity of the findings. Small samples increase the risk of type II errors and reduce confidence in efficacy and safety conclusions.	(Muralidass et al., 2020) (Nandhini, 2018) (Amuthan & Santhi, 2020)
Lack of Standardization	Variability in herbal formulations, extraction methods, and quality control measures poses a significant methodological constraint. This heterogeneity limits reproducibility and comparability across studies, weakening the robustness of pharmacological and clinical evidence.	(Dash, 2024) (Adithya et al., 2024) (Adithya et al., 2024) (Deepika et al., 2023)
Limited Clinical Evidence	Despite promising in vitro and in vivo results, there is a paucity of rigorous, large-scale clinical trials validating the efficacy and safety of Siddha and herbal medicines for skin diseases. This gap undermines the translational potential of preclinical findings.	(Jayaprakash et al., 2024) (Kombate & Metowogo, 2023) (Kumar et al., 2024) (Sarkar et al., 2023)
Insufficient Mechanistic Studies	Many studies focus on phytochemical profiling or clinical outcomes without detailed elucidation of molecular and immunomodulatory mechanisms. This limits understanding of bioactive principles' modes of action and hinders targeted drug development.	(Myo et al., 2023) (Thiyagasundaram et al., 2023) (Sundarrajan et al., 2017) (Dayanand et al., 2024)
Geographic and Ethnobotanical Bias	Research predominantly centers on specific regions or traditional systems, such as Indian Siddha medicine, with limited inclusion of diverse ethnobotanical knowledge. This geographic bias restricts the comprehensiveness and applicability of findings globally.	(Roy et al., 2024) (Saising et al., 2022) (Zulkepli & Osman, 2024)
Short Duration of Follow-up	Many clinical evaluations have short follow-up periods, which impedes assessment of long-term efficacy, safety, and recurrence rates. This limitation affects the reliability of conclusions regarding sustained therapeutic benefits.	(Muralidass et al., 2020) (Nandhini, 2018) (K. et al., 2023)
Inadequate Toxicological Data	Several studies lack comprehensive toxicity and safety assessments, especially for long-term use of polyherbal and herbo-mineral formulations. This gap raises concerns about potential adverse effects and limits clinical acceptance.	(Nandhini, 2018) (Rajarethinam & Ramaswamy, 2022) (R & Rs, 2015) (Adithya

		et al., 2024)
Bioavailability Challenges	Poor solubility and low bioavailability of key bioactive compounds in herbal medicines constrain their therapeutic effectiveness. Without addressing these pharmacokinetic issues, clinical translation remains limited.	(Agrawal et al., 2024) (Valavi et al., 2024)

Gaps and Future Research Directions

Gap Area	Description	Future Research Directions	Justification	Research Priority
Standardization of Siddha and Herbal Formulations	Variability in extraction methods and phytochemical content leads to inconsistent quality and therapeutic outcomes in Siddha polyherbal and herbo- mineral formulations.	Develop and validate standardized protocols for extraction, phytochemical profiling, and quality control including heavy metal analysis and chromatographic fingerprinting for key Siddha formulations.	Standardization is critical to ensure reproducibility, safety, and efficacy, facilitating regulatory approval and clinical acceptance (Myo et al., 2023) (Dash, 2024) (Adithya et al., 2024).	High
Large-Scale Randomized Controlled Clinical Trials	Most clinical evidence for Siddha and herbal treatments in skin diseases is limited to small sample sizes, case reports, or open-label studies lacking controls.	Conduct well-designed randomized controlled trials (RCTs) with adequate sample sizes and standardized outcome measures to robustly evaluate efficacy and safety of Siddha formulations in psoriasis, dermatitis, and fungal infections.	Strong clinical evidence is essential to validate traditional claims and integrate Siddha medicine into mainstream dermatology (Nandhini, 2018) (Rajarethinam & Ramaswamy, 2022) (Amuthan & Santhi, 2020).	High

In Vivo and Clinical Validation of Molecular Mechanisms	Many mechanistic studies rely on in silico, in vitro, or network pharmacology approaches without sufficient in vivo or clinical correlation.	Perform longitudinal in vivo studies and clinical biomarker analyses to confirm molecular targets (e.g., IL-17A, TNF-α, STAT3) modulated by Siddha and herbal bioactives in skin diseases.	Confirming mechanistic pathways in physiological contexts strengthens understanding of therapeutic action and guides drug development (Dayanand et al., 2024) (Kim et al., 2024) (Thiyagasundaram et al., 2023).	High
Bioavailability and Delivery Optimization	Poor bioavailability and pharmacokinetic limitations of key bioactives like curcumin hinder therapeutic efficacy in topical and systemic applications.	Develop and clinically evaluate advanced delivery systems such as nanotechnology-based formulations to enhance bioavailability, targeted delivery, and reduce dosage of herbal compounds.	Enhanced delivery can improve therapeutic outcomes and patient compliance, overcoming limitations of conventional herbal therapies (Agrawal et al., 2024) (Valavi et al., 2024).	Medium
Safety and Herb-Drug Interaction Profiling	Limited data exist on long-term safety, potential adverse effects, and herb-drug interactions of Siddha and herbal medicines, especially in polyherbal and herbo-mineral formulations.	Conduct comprehensive toxicological studies, pharmacovigilance, and interaction assessments with conventional dermatological drugs to establish safety profiles.	Ensuring safety is paramount for clinical use and to prevent adverse events, particularly in integrative treatment settings (Kombate & Metowogo, 2023) (Kumar et al., 2024).	High

Isolation and Characterization of	Complexity of polyherbal mixtures complicates	Employ advanced separation and analytical techniques to isolate, characterize, and	Understanding individual bioactives aids in mechanistic elucidation and	Medium

Gap Area	**Description**	**Future Research Directions**	**Justification**	**Research Priority**
Individual Bioactive Principles	identification and characterization of specific active compounds responsible for therapeutic effects.	validate individual bioactives and their synergistic interactions in Siddha formulations.	potential development of novel targeted therapies (Myo et al., 2023) (Deepika et al., 2023).	
Integration of Siddha Traditional Concepts with Modern Biomedical Frameworks	Siddha disease classifications and treatment rationales are not fully aligned or validated within contemporary biomedical paradigms.	Conduct translational research to correlate Siddha diagnostic categories (e.g., Kalanjagapadai) with molecular and clinical phenotypes, facilitating integrative treatment protocols.	Bridging traditional and modern concepts enhances acceptance and rational application of Siddha medicine in dermatology (Walter et al., 2014) (Rathinam et al., 2022).	Medium
Comprehensive Clinical Evaluation of Siddha Herbo-Mineral Formulations	Herbo-mineral Siddha formulations are widely used but lack extensive clinical evaluation and safety data.	Design clinical trials and pharmacokinetic studies specifically targeting herbo-mineral formulations to assess efficacy, safety, and heavy metal bioavailability.	Addressing safety concerns and validating efficacy will support wider clinical adoption and regulatory approval (Rajarethinam & Ramaswamy, 2022) (R & Rs, 2015) (Rayma et al., 2023).	High

Ethnopharmacological Validation of Regional Medicinal Plants	Many regional medicinal plants used traditionally for skin diseases lack rigorous pharmacological and toxicological validation.	Systematically investigate phytochemical profiles, mechanisms, and clinical efficacy of region-specific medicinal plants documented in ethnobotanical surveys.	Validating traditional knowledge can expand the herbal arsenal for dermatological therapies and support biodiversity conservation (Roy et al., 2024) (Saising et al., 2022).	Medium
Development of Standardized Outcome Measures for Herbal Dermatology Trials	Lack of uniform clinical endpoints and assessment tools in Siddha and herbal medicine trials limits comparability and meta-analyses.	Establish consensus on standardized clinical outcome measures, severity indices, and safety parameters tailored for herbal dermatology research.	Standardized measures improve trial quality, facilitate evidence synthesis, and support regulatory submissions (Kombate & Metowogo, 2023) (Nandhini, 2018).	Medium

Overall Synthesis and Conclusion

The collective evidence from the current body of literature underscores the significant therapeutic potential of Siddha and herbal medicines in the management of various skin diseases, particularly chronic and inflammatory conditions such as psoriasis, atopic dermatitis, and dermatophytosis. Comprehensive phytochemical profiling reveals a rich diversity of bioactive compounds including flavonoids, phenolics, alkaloids, terpenoids, and essential minerals, many of which possess well-documented anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory properties. Advanced analytical techniques and standardization efforts have improved the quality assurance of traditional formulations, although variability and complexity of polyherbal mixtures remain a challenge for consistent characterization.

Mechanistic studies, combining in vitro, in vivo, and computational approaches, consistently highlight the modulation of key inflammatory cytokines (TNF-α, IL-6, IL-17A) and signaling pathways such as NF-κB, STAT3, and MAPK as central to the mode of action of Siddha and herbal bioactives. These compounds appear to regulate keratinocyte proliferation, immune dysregulation, and oxidative stress, which are pivotal in the pathogenesis of psoriasis and related skin disorders. Network pharmacology and molecular docking have advanced the identification of molecular targets and predicted therapeutic interactions; however, many of these findings await robust in vivo and clinical validation to solidify their translational relevance.

Clinically, Siddha formulations demonstrate promising efficacy and safety profiles, with several case reports, open-label trials, and pilot studies reporting significant symptom relief, lesion regression, and improved quality of life in patients with psoriasis, dermatitis, and fungal infections. The comparative analyses suggest that Siddha and herbal treatments may offer advantages including reduced side effects, better patient compliance, and cost-effectiveness relative to conventional therapies. Notably, the integration of nanotechnology has emerged as a novel strategy to enhance bioavailability and targeted delivery of herbal actives, potentially overcoming limitations of traditional formulations.

Despite these encouraging advances, the literature reveals notable gaps such as the paucity of large-scale, randomized controlled clinical trials, limited standardization across formulations, and incomplete mechanistic understanding of complex polyherbal interactions. Furthermore, the alignment of Siddha's traditional disease concepts with contemporary biomedical frameworks remains partially conceptual, requiring deeper translational research. Addressing these limitations through rigorous, multidisciplinary investigations will be critical for the scientific validation, clinical integration, and regulatory acceptance of Siddha and herbal medicines as viable complementary or alternative options in dermatological care. Overall, the synthesis affirms the considerable promise of Siddha and herbal therapeutics while emphasizing the imperative for methodological refinement and expanded clinical evidence.

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