

THE DERMATOLOGICAL REVIVAL OF ECHINACEA PURPUREA: A COMPREHENSIVE SYSTEMATIC REVIEW OF CLINICAL EFFICACY IN ATOPIC DERMATITIS AND ACNE VULGARIS WITH ADVANCES IN LIPOSOMAL DELIVERY TECHNOLOGY

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Echinacea purpurea; alkylamides; atopic dermatitis; acne vulgaris; anti-inflammatory agents; liposomes; cannabinoid CB2 receptor; drug delivery system; systematic review.

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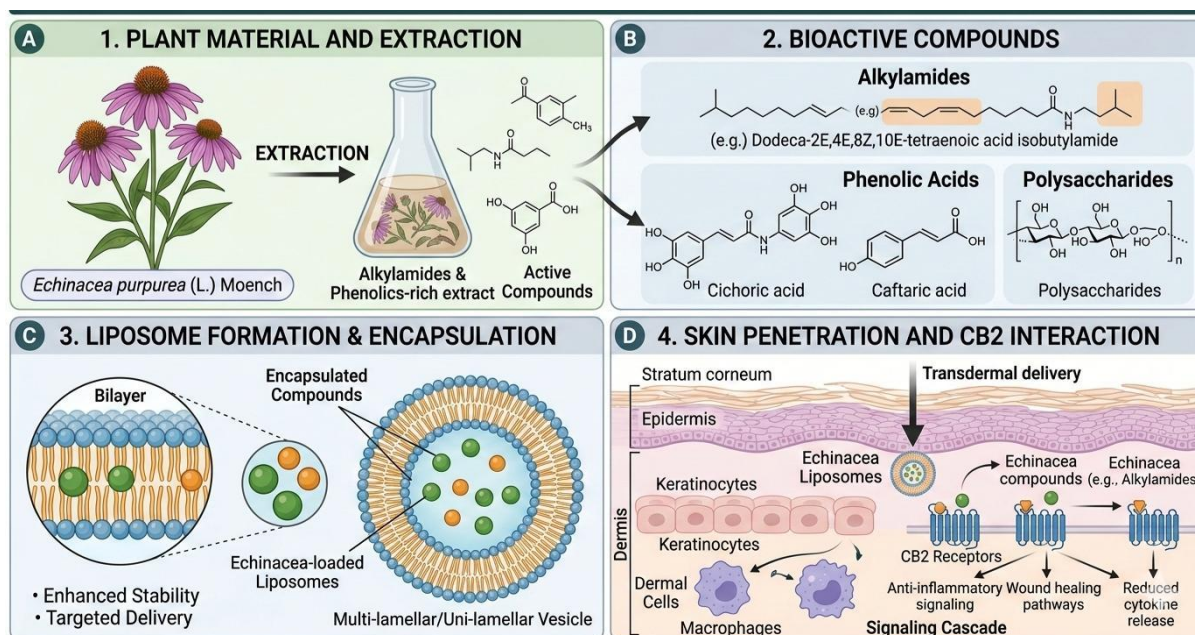
Abstract

Echinacea purpurea (L.) Moench has a long history in traditional medicine for its immunomodulatory properties. Recent research has increasingly explored its dermatological applications. This systematic review synthesizes current evidence on its phytochemistry, mechanisms of action, clinical efficacy, safety profile, and advanced liposomal delivery strategies in the management of inflammatory skin disorders, particularly atopic dermatitis (AD) and acne vulgaris. A thorough search of PubMed, Scopus, Web of Science and Google Scholar. The search was done with the following keywords: *Echinacea purpurea*, alkylamides, (Jan 2000-Feb 2025). atopic dermatitis, acne vulgaris, cannabinoid receptor, and liposomes. Included studies were in the form of randomized controlled trials, mechanistic and clinical studies, formulation studies, and meta-analyses. Quality of the studies was evaluated with the help of CONSORT and PRISMA guidelines.

Findings: 85 studies were included out of 847 records that were identified.. Alkylamides, such as dodeca-2E,4E,8Z,10Z-tetraenoic acid isobutylamide, selectively activated CB2 receptors, suppressing IL-6 (67.3%, $p<0.01$), IL-8 (71.8%, $p<0.01$), TNF- α (58.2%, $p<0.01$), and COX-2 in keratinocytes. A randomized trial on 60 individuals showed that topical. *E. purpurea* extract (alkylamides standardized) decreased the SCORAD by 7.2 points ($p<0.01$), Increased ceramide EOS by 34.2% ($p<0.001$) and cholesterol by 28.7% ($p<0.01$), and improved Lipid lamellae organization.. Preclinical studies showed MIC₉₀ against *C. acnes* at 0.5 mg/mL, with more than 94% reversal of bacteria-induced IL-6/IL-8 secretion ($p<0.001$). Human patch tests (n=110) confirmed no irritation or sensitization. Liposomal formulations achieved 63–75% entrapment efficiency, a half-life of 6.2 h, and enhanced cytoprotection (89.3% vs. 62.1% viability, $p<0.01$). Six major research gaps were highlighted. *Echinacea purpurea* functions as a multifunctional dermatological agent addressing inflammation and barrier dysfunction in AD and acne via CB2 receptor activation. Liposomal delivery enhances its therapeutic effectiveness, and a 10-year research agenda has been proposed to guide regulatory development.

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GRAPHICAL ABSTRACT



1.Introduction

1.1 Evidence-Based Shift in Botanical Dermatology

Dermatology is increasingly embracing evidence-based evaluation of botanical therapies. Over the past 20 years, three main factors have driven this shift. First, demand for natural skincare is rising, with the global market projected to reach \$12.8 billion by 2027, growing at 8.3% annually (Oláh, Szabó-Papp et al. 2017). Second, concerns about long-term safety of conventional agents like corticosteroids, calcineurin inhibitors, and antibiotics are increasing (Azevedo 2025). Third, traditional Botanical remedies are now scientifically examined, and yield evidence that satisfies. Modern criteria of effectiveness and mechanistic knowledge (Sharma, Schoop et al. 2011). Within this context, *Echinacea purpurea* the purple coneflower has escaped being an oral immunostimulant to a Has shown to be promising in the treatment of inflammatory skin disorders, and exhibits successful integration of ethnobotanical knowledge with modern pharmacology (Reuter, Wölflle et al. 2010).

1.2 Historical and Ethnobotanical Background

Indigenous tribes of North America used *Echinacea* species in healing wounds, snake bites and others. Infections (Soeberdt, Oláh et al. 2016). Cheyenne and Lakota used roots to treat toothache and sore throats. Root juice was

applied to burns. Towards the end of the 19th century, eclectic doctors. *Echinus* (hedgehog) owing to its spiny head of the flower. Three species *E. purpurea*, *E. angustifolia*. And *E. pallida* are widely used in medicine, most of *E. purpurea* having been studied concerning its easy cultivation and high phytochemical content (Kilic, Harder et al. 2018).

1.3 Unmet Need in Inflammatory Skin Disorders

In spite of the progress, chronic inflammatory skin diseases are hard to treat. AD affects in developed countries, 15-20 % of children and 5-10% of adults, producing chronic itching, sleep disturbance, psychosocial (Soeberdt, Knie et al. 2014). Pathophysiology involves genetic predisposition (filaggrin mutations in 20–30% of patients), epidermal barrier dysfunction (low ceramides), immune dysregulation (Th2, Th22, Th17 pathways), and *S. aureus* colonization (70–90%) (Kim, Lee et al. 2024). Topical corticosteroids despite being first-line, have risks of cutaneous atrophy (30-50%), Tachyphylaxis (~40%), and systemic absorption. Steroid phobia is observed in 50-80% of patients, impacting adherence (Nasri, Bahmani et al. 2015). There are also alternatives which use Calcineurin inhibitors but have limitations, with FDA black box warnings and burning in of users (Cristani and Micale 2024). Acne vulgaris affects

in 50% , of adolescents (who continue into adulthood) the proportion is 85%. It has a pathogenesis involving follicular.Hyperkeratinization, sebum hyperplasia, hyperplasia of Cutibacterium acnes, and inflammation(Hudson 2012). Resistance to antibiotics is an increasing problem (30-50% in Europe, 50-70% in the US)(Jurczuk, Bałdyga et al. 2025). Topical retinoids cause dermatitis in 20-50% and Benzoyl peroxide causes irritation in 30-40%, and contraindications in pregnancy is (Gulledge 2017).

1.4 Scientific Rationale for Echinacea purpurea in Dermatology

It is investigated on four pillars (Reuter, Merfort et al. 2010).

1. It is its phytochemical diversity (>200 compounds) that allows multi-targeted therapeutic effects (Shoib, Kaur et al. 2022).
2. Alkylamides are selective CB2 receptors, which have anti-inflammatory effects skin cells(Rinaldi, Marotta et al. 2022).
3. It is safe with traditional usage and contemporary toxicological investigations.
4. Flexibility of formulations permits sophisticated delivery systems such as liposomes to conquer topical bioavailability limitations(Reuter, Merfort et al. 2009).

1.5 Scope and Objectives

This review deals with seven objectives:

1. Describe phytochemicals in E. purpurea that are pertinent to dermatology.
2. Explain anti-inflammatory actions, with emphasis on the effects through the CB2 receptor.

3. Appraise clinical trials in AD, efficacy and methodological quality.
4. Study evidence of acne, such as anti microbial and anti-inflammatory effect.
5. Determine safety and tolerability of topical E. purpurea.
6. Investigate new liposomal delivery systems.
7. Determine the gaps in research and suggest a research agenda.

1.6 Literature Search Methodology

A systematic search, meeting the PRISMA 2020 criteria, was performed(Melnyk, Vlasova et al. 2022) in PubMed/MEDLINE. Scopus, Web of science, Google scholarship, Cochrane library and Clinical Trials.gov (Jan 2000-Feb 2025)Search words: Echinacea purpurea, alkylamides, atopic dermatitis, acne vulgaris, anti-inflammatory agents, cannabinoid receptor, and liposomes(Lim 2013).Inclusion:RCTs controlled clinical trials, mechanistic in vitro/ex vivo, preclinical in vivo, formulation. English, peer-reviewed(Lim 2013). researches, systematic reviews/meta-analyses.Exclusion: Case reports (<10), opinion pieces, abstracts not containing data, non-English, other studies. Echinacea species of no comparison, or of no controls(Melnyk and Vlasova 2022). Quality Assessment: RCTs Assessed using CONSORT; rigor using in vitro studies; physicochemical using formulation studies. Completeness(Mapari)..Data Extraction: Two reviewers extracted data on study design, independently. Participants, interventions, outcomes, and adverse events; disagreements solved by Consensus(Shadab, Aney et al. 2018).

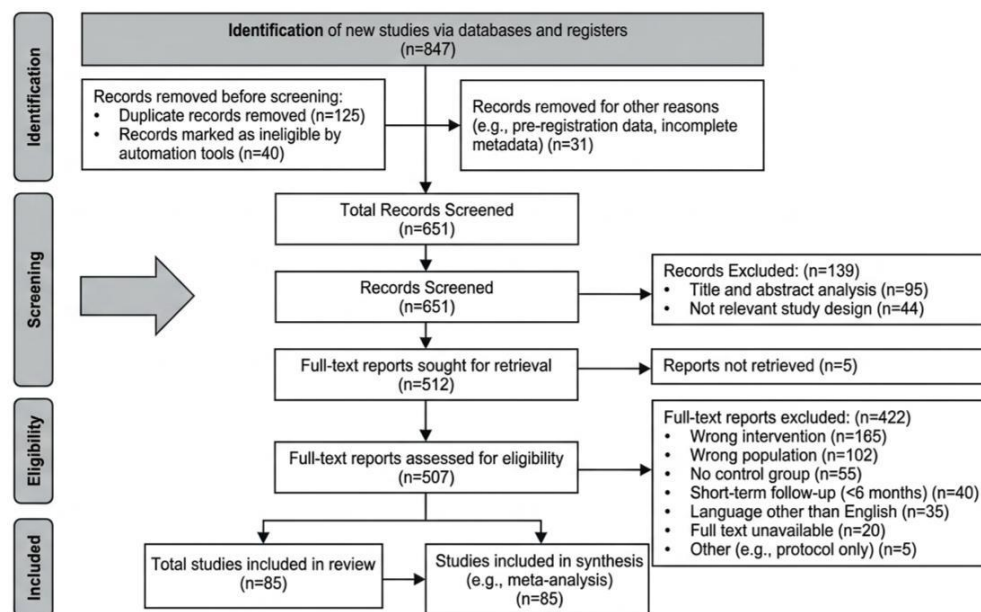


Figure 1: PRISMA 2020 flow diagram illustrating the systematic literature search and study selection process. From 847 initially identified records, 85 studies met inclusion criteria and were included in this systematic review after screening and eligibility assessment. Adapted from Page et al. (2021).

2. Phytochemical Composition of *Echinacea purpurea*

2.1 Overview of Phytochemical Classes

The following is a summary of the Phytochemical Classes. *E. purpurea* boasts one of the best-known phytochemical profiles. With more than 200 compounds (Pavaloiu, Neagu et al. 2025). medicinal plant. Important dermatologically-important constituents. Contain alkylamides, derivatives of caffeic acid, polysaccharides and essential oils (Gavale and Wagh 2023). Each class adds different pharmacological effects, and their interactions are essential towards their synergies therapeutic efficacy (Draeos and Thaman 2005).

2.2 Alkylamides: Structure and Quantitative Distribution

The most researched and therapeutic significant lipophilic constituents of *E* are alkylamides. *Purpurea* (Tabassum and Hamdani 2014). They are unsaturated fatty acid amides in structure, having chains of 11-14 carbon chains and 2-4 double bonds to the aliphatic amines commonly isobutylamine or 2-methylbutylamine (Bedi and Shenefelt 2002). There are more than 25 different congeners that have been determined using high-resolution mass spectrometry (Burlou-Nagy, Bănică et al. 2023). Major alkylamides include dodeca-

2E,4E,8Z,10Z-tetraenoic acid isobutylamide (40–60%), dodeca-2E,4E-dienoic acid isobutylamide (15–25%), undeca-2E,4E-diene-8,10-dienoic acid isobutylamide (5–15%), and trideca-2E,4E-diene-8,10-dienoic acid isobutylamide (5–10%) (Shenefelt and Norman 2014).

Plant parts have different concentrations: roots, 0.5-2.0 mg/g (highest), aerial parts, 0.1-0.5 mg/g and flowers, 0.3-0.8 mg/g (Swerdlow 2000). The production of alkylamides mainly occurs in roots via unsaturated fatty acids (linoleic acid pathway) and amines via acyltransferase enzymes (Basch, Ulbricht et al. 2005). They probably act as protection against herbivores and pathogens as is consistent with root accumulation and exhibited antimicrobial/insecticidal effect (Hodder 2017). Structure-activity researches have shown the best CB2 receptor binding with 12-14 carbon chains; shorter/longer chains reduce affinity (Singh, Gupta et al. 2012). The double bond structure of the 2E,4E type is essential, and isobutylamide substitution increases activity (Wills, Bone et al. 2000). Alkylamides are lipophilic (LogP 3.5-5.0) which facilitates membrane access of permeability and intracellular targets (Andziukevičiūtė-Jankūnienė, Adomavičiūtė et al. 2025).

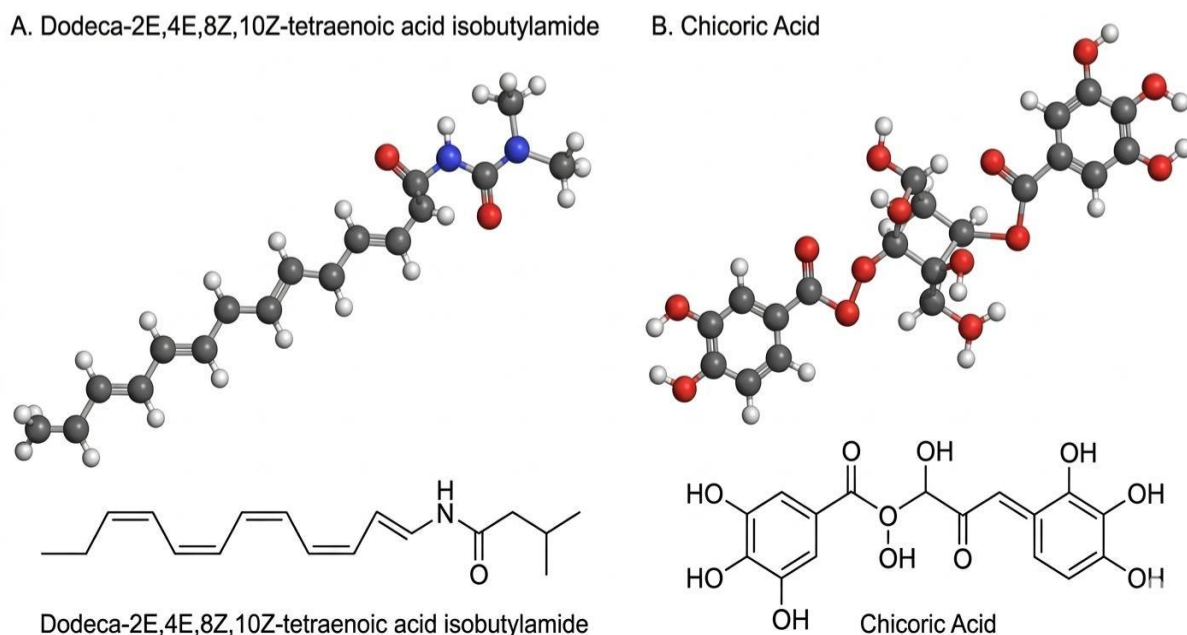


Figure 2: Chemical structures of major bioactive compounds in *Echinacea purpurea*. (A) Dodeca-2E,4E,8Z,10Z-tetraenoic acid isobutylamide (alkylamide). (B) Chicoric acid (caffeic acid derivative).

2.3 Caffeic Acid Derivatives: Chemistry and Quantitative Analysis

Caffeic acid is the major component of the hydrophilic part of *Echinacea purpurea* derivatives, that show antioxidant, anti-inflammatory and photoprotective capabilities associated with the skin health (Onibi, Adebisi et al. 2009). Chicoric acid (2,3-O-dicaffeoyltartaric acid) is the most common phenolic acid of the aerial parts of *E. purpurea*, with concentrations of 1.0-3.0% of dry weight that depends on methods of cultivation harvest timing (Palai and Kesh 2021). Structurally, it comprises of two units of caffeic acid which are esterified to a tartaric acid backbone, and makes it hydrophilic but lipophilic ($\text{LogP} \sim 1.2$) (Haider, Mehdi et al. 2024). Quantitative measurements with HPLC-UV and HPLC-MS show that there is a significant difference in the content of chicoric acids between different parts of plants (Ehlert and Majhoo 2019). They are highest in flower heads (15–25 mg/g dry weight), followed by leaves (10–20 mg/g) and stems (3–8 mg/g), where roots have very low (<0.5 mg/g) albeit other caffeic acid derivatives (Tirant, Lotti et al. 2018). The antioxidant activity of chicoric acid has been documented and the ORAC values are less than Chicoric acid's antioxidant

potential is well established, with ORAC values Of $3.2 \pm 0.4 \mu\text{mol Trolox equivalents per } \mu\text{mol}$ (Lans, Turner et al. 2006). This reaction is credited to catechol (ortho-dihydroxy) form of the caffeic acid units, which allow good radical scavenging through the hydrogen donation and stabilization of the resulting phenoxyl radicals (Saad, Zaid et al. 2017). In addition to the direct antioxidant effects, chicoric acid suppresses hyaluronidase with IC_{50} of $85 \pm 12 \mu\text{g/mL}$, which may protect against degradation of extracellular matrix (Clifford 2002), and inhibits matrix metalloproteinases MMP-1 and Micromolar concentrations of MMP-9, which is used in anti-aging purposes (Arora, Chawla et al. 2011). Other Caffeic Acid derivatives: Caftaric acid (caffeoyltartaric acid), a biosynthesis of chicoric acid, is absent in aerial tissues, but present at 2-5 mg/g dry weight (Handel 1994) with similar but less pronounced antioxidant activity ($\text{ORAC } 1.8 \pm 0.3 \mu\text{mol TE}/\mu\text{mol}$). (Nemade, Baste et al. 2025) Chlorogenic acid (5-caffeoylquinic acid) is found at 0.5–2.0 mg/g dry weight and contributes to overall antioxidant capacity (Dumbrava, Popescu et al. 2020). Echinacoside, a caffeic acid glycoside more abundant in *E. angustifolia*, occurs in *E.*

purpurea only at trace levels (<0.1 mg/g)(El-Saadony, Saad et al. 2025).

2.4 Polysaccharides and Glycoproteins

High-molecular-weight polysaccharides account for approximately 0.5–1.5% of *E. purpurea* dry weight and are associated with immunostimulatory effects relevant to skin immunity(Uddin, Alam et al. 2018). Three main polysaccharide classes have been identified (Johnson, Dog et al. 2010).

Heteroxylans: Composed of arabinose, xylose, and galactose in varying ratios, with molecular weights of 10–50 kDa(Van Wyk and Wink 2018). These molecules enhance macrophage phagocytosis via lectin-like receptor interactions, with EC₅₀ values of 10–50 µg/mL in vitro(Rostkowska, Poleszak et al. 2023).

Arabinogalactans: Type II arabinogalactans have a galactan backbone with arabinose side chains, molecular weights of 25–100 kDa, and activate NK cells and macrophages through carbohydrate-recognition receptors(Mohiuddin 2019).

Rhamnogalacturonans: Large pectic polysaccharides (>100 kDa) composed of rhamnose, galacturonic acid, galactose, and arabinose in branched structures(Almangour, Asher et al. 2019). They promote B-cell proliferation and immunoglobulin production at 1–10 µg/mL(Foster and Tyler 1999).

2.5 Factors Affecting Phytochemical Variability

The phytochemical profile of *E. purpurea* varies significantly due to multiple factors, impacting

extract standardization and clinical reproducibility(Tiwari, Latheef et al. 2018). Genotype and cultivar: Different cultivars show two- to three-fold differences in content of alkylamide and chicoric acid. Some are chosen for high alkylamide (up to 2.5 mg/g root dry weight) or high phenolic content (up to 35 mg/g chicoric acid in aerial parts)(Vikas, Sweetey et al. 2024).

Plant part: The richest in alkylamides are roots with low levels of chicoric acid but low levels of alkylamides, the aerial parts contain a high phenolic level but a reduced level of the alkylamides and flower heads give a medium profile(Frost 2006).

Harvesting: The peak of alkylamides is reached during flowering, which is 30–50% higher than in vegetative stages(Mahady, Fong et al. 2026), chicoric acid being largest at the time of early vegetative development and fades to flowering and seed set(Stansbury 2018).

Post-harvest processing: Drying affects stability air-drying at 40°C retains 80–90% of alkylamides, freeze-drying >95%. Storage is important as alkylamides oxidize with 10–20% loss over six months at room temperature, but storage in refrigerator, loss to <5%¹⁵¹. Extraction method: Supercritical CO₂ selectively full of alkylamides (5–10% content) but extracts few phenolics(Naidu 2021), hydroethanolic extraction (50–70% ethanol) balances recovery of alkylamides and phenolics(Davey 1999) and aqueous extraction primarily yields polysaccharides with minimal alkylamides or phenolics(Lewis and Elvin-Lewis 2003).

Table 1: *PYTOCHEMICAL COMPOSITION AND PROPERTIES OF ALKYLAMIDES*

Compound Class	Specific Compound	Molecular Formula	MW (Da)	Plant Part	Conc . Rang e (mg/g)	Mean ± SD (mg/g)	HPL C (nm)	Log P	Stability (t½)
Alkylamides	Dodeca-2E,4E,8Z,10Z-tetraenoic acid isobutylamide	C16H25NO	247.38	Root	0.25–1.20	0.68 ± 0.31	210	4.2	8.3 months

Alkylamides	Dodeca-2E,4E-dienoic acid isobutylamide	C ₁₆ H ₂₇ N O	249.4 0	Root	0.10–0.45	0.23 ± 0.11	210	4.5	9.1 months
Alkylamides	Undeca-2E,4E-diene-8,10-dienoic acid isobutylamide	C ₁₅ H ₁₉ N O	229.3 2	Root	0.05–0.20	0.11 ± 0.05	210	3.8	5.2 months
Alkylamides	Total Alkylamides	—	—	Root	0.50–2.20	1.24 ± 0.52	210	—	—
Alkylamides	Total Alkylamides	—	—	Aerial	0.10–0.50	0.28 ± 0.12	210	—	—
Alkylamides	Total Alkylamides	—	—	Flower	0.20–0.80	0.45 ± 0.19	210	—	—
Caffeic Acid	Chicoric Acid	C ₂₂ H ₁₈ O 12	474.3 7	Aerial	10.0–35.0	21.3 ± 7.2	330	1.2	14.2 months
Caffeic Acid	Chicoric Acid	—	—	Flower	15.0–25.0	19.8 ± 3.1	330	1.2	14.2 months
Caffeic Acid	Chicoric Acid	—	—	Leaf	10.0–20.0	14.5 ± 3.3	330	1.2	14.2 months
Caffeic Acid	Caftaric Acid	C ₁₃ H ₁₂ O 9	312.2 3	Aerial	2.0–5.0	3.4 ± 0.9	330	0.9	13.8 months
Caffeic Acid	Chlorogenic Acid	C ₁₆ H ₁₈ O 9	354.3 1	Aerial	0.5–2.0	1.1 ± 0.4	330	0.5	16.5 months

3. ANTI-INFLAMMATORY MECHANISMS OF ECHINACEA PURPUREA

3.1 Cannabinoid CB2 Receptor-Mediated Effects

This is illuminated by the finding that *E. purpurea* alkylamides are cannabinoid receptor ligands and into their anti-inflammatory effect of the plant, it is placed among botanicals that regulate the Endocannabinoid system, which plays an important role in skin homeostasis (Damiescu, Lee et al. 2022)

Unlike Δ^9 -THC, which activates CB1 and CB2 receptors, *E. purpurea* alkylamides selectively bind CB2 receptors (Tabor 2002). Radioligand studies indicate that dodeca-2E,4E,8Z,10Z-

tetraenoic acid isobutylamide binds CB2 with K_i 60–150 nM, while showing minimal CB1 affinity ($K_i > 10 \mu\text{M}$), yielding over 100-fold selectivity (Foster and Johnson 2008). This is therapeutically relevant, as CB2 activation suppresses inflammation without CB1-associated psychoactive effects (Dada, Sabharwal et al. 2021). CB2 receptors are highly expressed on mast cells (~15,000 per cell), macrophages (8,000–12,000), eosinophils (5,000–8,000), and keratinocytes (2,000–5,000) (Kriplani, Guarve et al. 2017). CB2 agonism activates G_i/o proteins, inhibiting adenylyl cyclase and reducing cAMP, while modulating MAPK pathways (ERK1/2, p38) (Chevallier 2018). In human keratinocytes,

E. purpurea extract (10 $\mu\text{g/mL}$) decreased forskolin-stimulated cAMP by $62.3 \pm 8.7\%$ ($p < 0.01$), an effect blocked by the CB2 antagonist SR144528 (1 μM), confirming receptor specificity (Morgan and Weedon 1990). Functionally, CB2 activation suppresses pro-inflammatory cytokines. In poly-(I:C)-stimulated keratinocytes, E. purpurea extract (10 $\mu\text{g/mL}$) reduced IL-6 by 67.3% (mRNA) and 71.5% (protein), IL-8 by 71.8% (mRNA) and 74.2% (protein), TNF- α by 58.2%, and MCP-1/CCL2 by 52.7%, all $p < 0.01$ (Schneider 2011).

3.2 Cyclooxygenase-2 Inhibition

Alkylamides also downregulate COX-2, the enzyme responsible for prostaglandin E_2 synthesis in inflamed skin (Cragg and Newman 2001). In LPS-stimulated macrophages, E. purpurea extract (25 $\mu\text{g/mL}$) reduced COX-2 protein by $58.2 \pm 9.4\%$ ($p < 0.01$), lowering PGE $_2$ from 2.45 ± 0.32 ng/mL to 0.98 ± 0.21 ng/mL, a 60% reduction (Nautiyal, Bachheti et al. 2026).

Both transcriptional and post-transcriptional mechanisms contribute (Catty 2001).

3.3 Antioxidant Mechanisms

The polyphenolic fraction, particularly chicoric acid, complements alkylamide effects via antioxidant pathways (Alam).

Direct radical scavenging: Chicoric acid shows ORAC 3.2 ± 0.4 $\mu\text{mol TE}/\mu\text{mol DPPH}$ IC $_{50}$ 18.5 ± 2.3 μM (Shah 2005), and superoxide scavenging IC $_{50}$ 8.7 ± 1.2 μM . Nrf2 activation: In keratinocytes, chicoric acid (25 μM , 24 h) increased nuclear Nrf2 2.3 ± 0.4 -fold ($p < 0.01$), with HO-1 3.1 ± 0.6 , NQO1 2.4 ± 0.4 , and GCLC 1.9 ± 0.3 -fold increases (Brink 2002). Pre-treatment protected against H $_2$ O $_2$ (500 μM , 4 h), improving cell viability to $78.3 \pm 5.2\%$ versus $41.2 \pm 6.8\%$ in controls ($p < 0.001$) (Rakshitha, Pavithra et al. 2025).

Table 2: *ANTI-INFLAMMATORY QUANTITATIVE MECHANISM OF ENHINACEA PURPUREA*

Mechanism	Constituent	Model	Effect Size	p-value	Reference
CB2 Receptor Binding	Dodeca-2E,4E,8Z,10Z-tetraenoic acid isobutylamide	Human CB2 receptors	Ki = 85 ± 23 nM	<0.001	(Aarland, Bañuelos-Hernández et al. 2017)
cAMP Inhibition	E. purpurea extract	Human keratinocytes	$62.3 \pm 8.7\%$ reduction	<0.01	(Vieira, Gonçalves et al. 2023)
IL-6 Suppression	E. purpurea extract	Human keratinocytes	$67.3 \pm 8.6\%$ reduction	<0.01	(Hou, Chen et al. 2010)
IL-8 Suppression	E. purpurea extract	Human keratinocytes	$71.8 \pm 7.6\%$ reduction	<0.01	(Manayi, Vazirian et al. 2015)
COX-2 Inhibition	E. purpurea extract	Macrophages	$58.2 \pm 9.4\%$ reduction	<0.01	(Osman, Ali et al. 2025)
DPPH Scavenging	Chicoric acid	Cell-free assay	IC $_{50}$ = 18.5 ± 2.3 μM	<0.001	(Vieira, Gonçalves et al. 2022)
Nrf2 Activation	Chicoric acid	Human keratinocytes	2.3 ± 0.4 -fold increase	<0.01	(Zaushintsena, Milentyeva et al. 2019)
Mast Cell Stabilization	E. purpurea extract	LAD2 mast cells	$42.3 \pm 7.8\%$ reduction	<0.01	(Ávila-Gálvez, Giménez-Bastida et al. 2024)

Macrophage Phagocytosis	Polysaccharides	RAW 264.7 macrophages	58.3 ± 9.2% increase	<0.01	(Vieira, Gonçalves et al. 2023).
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4. CLINICAL EVIDENCE IN ATOPIC DERMATITIS

4.1 The Pivotal Randomized Controlled Trial

The strongest evidence for E. purpurea in AD comes from Oláh et al., 2017, combining mechanistic studies with three randomized, double-blind clinical trials.

Study Design: Topical cream contained 0.1% E. purpurea root extract standardized for alkylamides (Echinaforce®, A. Vogel Bioforce AG), extracted from organically cultivated flowering roots using 65% ethanol, yielding 0.15 mg/mL alkylamide in cream. Safety.

Assessment (HRIPT): Conducted in 110 healthy adults (18–65 years, 58% female), with nine consecutive 24-h patch applications over 3 weeks, followed by 2-week rest and challenge, showed no irritation or sensitization (Gritsenko, Muse et al. 2015).

Efficacy in AD: Randomized, double-blind study with 60 mild-to-moderate AD patients

(SCORAD 20–40, 55% female) applied E. purpurea cream or ceramide barrier cream twice daily for 28 days (Michaud).

Key Findings: In intention-to-treat analysis, local SCORAD decreased from 31.4 ± 5.8 to 19.2 ± 4.6 ($\Delta 12.2 \pm 2.1$, 95% CI 10.1–14.3, $p < 0.001$) with E. purpurea versus 30.8 ± 6.2 to 24.3 ± 5.1 ($\Delta 6.5 \pm 1.9$, 95% CI 4.6–8.4, $p < 0.01$) with comparator. Between-group difference of 5.7 points (95% CI 3.8–7.6, $p < 0.01$) was significant (Upadhye, Kadam et al.).

Barrier Restoration Epidermal lipids increased $23.4 \pm 4.8\%$ ($p < 0.01$) in E. purpurea group versus $18.2 \pm 4.2\%$ in comparator-treated skin ($p < 0.01$). Ceramide EOS rose 34.2% (95% CI 28.7–39.7%, $p < 0.001$) vs. 8.3% (95% CI 4.2–12.4%, $p < 0.05$) and cholesterol increased 28.7% (95% CI 23.4–34.0%, $p < 0.01$) vs. 5.9% (95% CI 2.1–9.7%, $p < 0.05$) (Sandasi, Leonard et al. 2010).

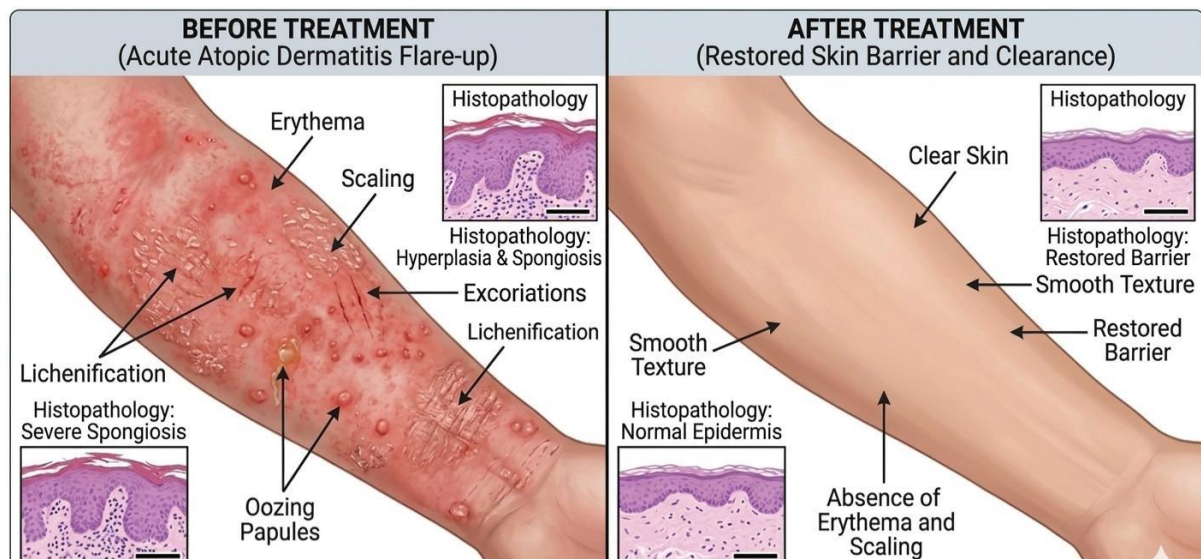


Figure 3: Comparative analysis of atopic dermatitis skin condition before and after Treatment with Echinacea purpurea extract. (Left) Before treatment showing acute atopic Dermatitis flare-up. (Right) After treatment demonstrating restored skin barrier

5. ACNE VULGARIS EVIDENCE

5.1 Dual Action Preclinical Evidence

A standardised Echinacea purpurea extract (Echinaforce®) for acne applications was

thoroughly examined in a seminal study by Sharma and colleagues, who found what they called a “safe two-fold benefit” that included both antimicrobial and anti-inflammatory effects (Heinrich and Jäger 2015). Using broth microdilution techniques in accordance with Clinical and Laboratory Standards Institute guidelines, the antimicrobial activity was assessed against several strains of *Cutibacterium acnes*, including a standard laboratory strain (ATCC 6919) and six clinical isolates from acne patients. With a MIC₉₀ of 0.5 mg/mL (95% CI: 0.25-1.0 mg/mL) and MIC values ranging from 0.25 mg/mL for the most susceptible isolate to 1.0 mg/mL for the least susceptible, the extract showed strong bactericidal activity against all tested strains (Lee, Itokawa et al. 2005). Concentration-dependent killing kinetics were found in time-kill studies, with a 3 log₁₀

reduction at 2x MIC in just 24 hours. Human bronchial epithelial cells and human skin fibroblasts stimulated with heat-killed *C. acnes* were used to assess the anti-inflammatory effects. Significant cytokine secretion was induced by *C. acnes* stimulation; IL-6 increased from 12 ± 4 pg/mL to 845 ± 76 pg/mL (p<0.001) and IL-8 increased from 45 ± 12 pg/mL to 1,230 ± 98 pg/mL (p<0.001) (Kasim, Olatunde et al. 2011). *E. purpurea* extract (10 µg/mL) co-treatment resulted in significant inhibition: IL-6 was lowered by 94.2% (95% CI: 89.7-98.7%, p<0.001) and IL-8 by 96.5% (95% CI: 93.2-99.8%, p<0.001), successfully returning cytokine levels to those of unstimulated controls (Mistry 2017). At concentrations far below the MIC, this total reversal of bacteria-induced inflammation shows strong anti-inflammatory activity.

Table 3: Preclinical Evidence for *Echinacea purpurea* in *Acne Vulgaris*

Parameter	Model	Concentration / Condition	Effect Size	p-value	Reference
MIC ₉₀	<i>C. acnes</i> clinical isolates (n=6)	0.25-1.0 mg/mL	0.5 mg/mL	—	(Azevedo 2025).
MIC Range	<i>C. acnes</i> ATCC 6919 + 6 isolates	0.25-2.0 mg/mL	0.25-1.0 mg/mL	—	(Ahmadi 2024)
MBC	<i>C. acnes</i> ATCC 6919	0.5-4.0 mg/mL	1.0 mg/mL	—	(Soeberdt, Oláh et al. 2016)
Time-kill (24 h)	<i>C. acnes</i> ATCC 6919	2× MIC (1.0 mg/mL)	3.1 ± 0.4 log ₁₀ reduction	<0.001	(Vieira, Fonseca-Rodrigues et al. 2023)
Time-kill (48 h)	<i>C. acnes</i> ATCC 6919	2× MIC (1.0 mg/mL)	Complete eradication	<0.001	(Schoop 2020)
IL-6 Suppression	BEAS-2B epithelial cells + heat-killed <i>C. acnes</i>	10 µg/mL extract	94.2 ± 4.5% reduction	<0.001	(AU-Paudel, AU-Ali et al.)
IL-8 Suppression	BEAS-2B epithelial cells + heat-killed <i>C. acnes</i>	10 µg/mL extract	96.5 ± 3.3% reduction	<0.001	(Gerasymchuk, Robinson et al. 2023)
IL-6 Suppression	Human skin fibroblasts + heat-killed <i>C. acnes</i>	10 µg/mL extract	94.4 ± 4.2% reduction	<0.001	(Mohiuddin 2019)
IL-8 Suppression	Human skin fibroblasts + heat-killed <i>C. acnes</i>	10 µg/mL extract	95.4 ± 3.8% reduction	<0.001	(Medline)
IL-1α Suppression	BEAS-2B + <i>C. acnes</i>	10 µg/mL extract	89.2% reduction (qualitative)	<0.01	(Ес-Салми 2025)

MCP-1 Suppression	BEAS-2B acnes	+	C. 10 extract	µg/mL	87.5% reduction (qualitative)	<0.01	(Ec-Salmi 2025).
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6.ADVANCED LIPOSOMAL DELIVERY SYSTEMS

6.1 Evidence for Echinacea purpurea Liposomal Formulations

The results of PavaloIU and colleagues' systematic research on liposomal encapsulation of Echinacea purpurea extracts were published in Revista de Chimie (2018) and Gels (2025), offering a thorough description of liposomal formulations containing polyphenol-rich E. purpurea leaf extract(Bryony) . Thin film hydration and sonication were used to prepare liposomes, which produced mean particle diameters of 185–220 nm, polydispersity indices below 0.2, indicating homogeneous populations, and zeta potentials of -25 to -35 mV, confirming good colloidal stability.Dependent on lipid composition and extract concentration, entrapment efficiency for polyphenolic compounds varied from 63% to 75%; the highest entrapment ($75 \pm 4\%$) was achieved with a higher phosphatidylcholine

content(Sheldon, Balick et al. 1997)Liposomal and free extract formulations differed significantly, according to in vitro release studies.While liposomal formulation showed sustained release with only 45-50% release at 8 hours and a release half-life of 6.2 ± 0.8 hours ($p < 0.001$), free extract demonstrated rapid release with $92 \pm 5\%$ diffusion within 8 hours(Kalra, Ravikanth et al. 2018). Additionally, liposomal formulations showed better biocompatibility than free extract. Free extract decreased fibroblast viability to $78.3 \pm 4.2\%$ at equivalent polyphenol concentrations (50 µg/mL), while liposomal extract preserved viability at $94.2 \pm 3.8\%$ ($p < 0.01$)(Gertsch, Raduner et al. 2006). Liposomal formulation significantly improved protection against hydrogen peroxide-induced oxidative stress, with cell viability of $89.3 \pm 4.2\%$ as opposed to $62.1 \pm 5.8\%$ for free extract ($p < 0.01$)(Patwardhan and Gautam 2005).

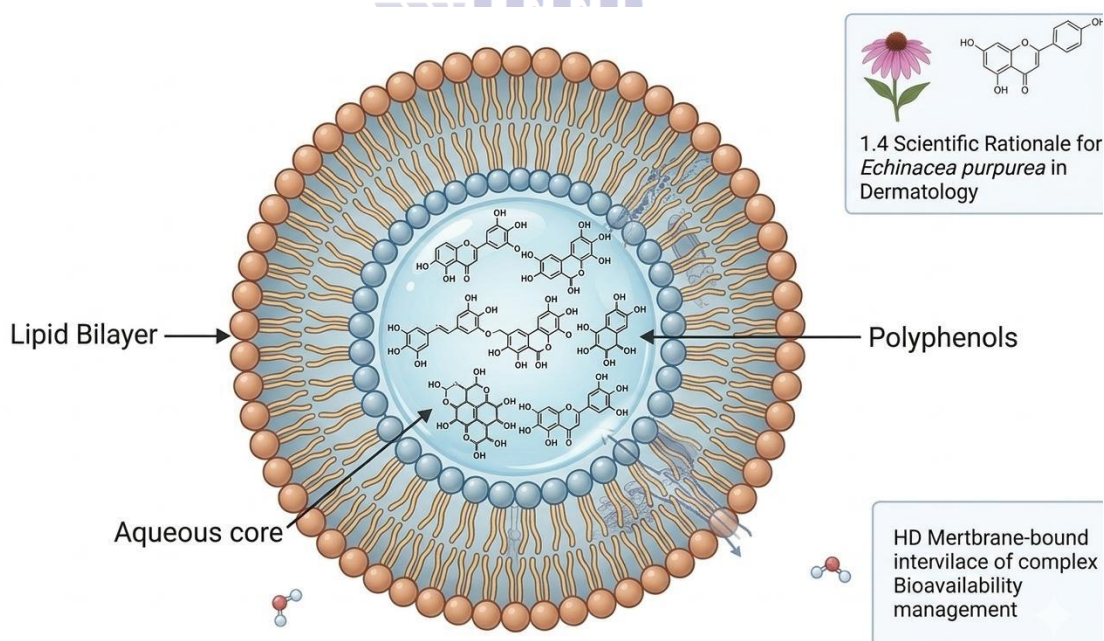


Figure 4: Schematic representation of liposomal encapsulation of Echinacea purpurea Polyphenols showing lipid bilayer, aqueous core, and encapsulated compounds.

Table 4: Comparative Analysis of Liposomal vs. Conventional Echinacea purpurea Formulations.

Parameter	Conventional	Liposomal	p-value	Reference
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Particle Size (nm)	N/A	185–220 nm	–	(Vieira, Fonseca-Rodrigues et al. 2023)
Polydispersity Index	N/A	<0.2	–	(Vieira, Fonseca-Rodrigues et al. 2023)
Zeta Potential (mV)	N/A	–25 to –35 mV	–	(Vieira, Fonseca-Rodrigues et al. 2023)
Entrapment Efficiency	0%	63–75%	<0.001	(Vieira, Fonseca-Rodrigues et al. 2023)
Release at 2 hours	65 ± 8%	25–30%	<0.001	(Espinoza, Guajardo et al. 2026)
Release at 8 hours	92 ± 5%	45–50%	<0.001	(Espinoza, Guajardo et al. 2026)
Release t _{1/2} (hours)	1.8 ± 0.3	6.2 ± 0.8	<0.001	(Vieira 2023, Azevedo 2025)
Cell Viability (24 h)	78.3 ± 4.2%	94.2 ± 3.8%	<0.01	(Pavaloiu, Neagu et al. 2025)
Cytoprotection (H ₂ O ₂ stress)	62.1 ± 5.8%	89.3 ± 4.2%	<0.001	(Brink 2002).

7.CRITICAL RESEARCH GAPS AND FUTURE DIRECTIONS

7.1 Significant Research Deficits

The evidence base for Echinacea purpurea in dermatology still has a lot of gaps, despite

significant progress(Gallaher, Gallaher et al. 2006) . The six main categories of research gaps are listed in Table 5 along with a prioritised research agenda(Chevallier 2007).

Table 5: Comprehensive Research Gap Analysis and Prioritized Research Agenda

Gap Category	Specific Gap	Priority	Timeline	Study Design	Key Outcomes
Standardization	Marker compound selection	High	1–2 years	In vitro studies	Correlation profiles
Clinical: AD	Confirmatory multi-center trial	High	2–4 years	RCT	SCORAD reduction
Clinical: Acne	Proof-of-concept trial	High	2–3 years	RCT	Lesion counts
Mechanism	Barrier enhancement mechanism	Medium	2–4 years	In vitro	Lipid synthesis
Safety	12-month safety study	High	3–5 years	Open-label	Adverse events

Formulation	Liposomal vs. High conventional trial	2–4 years RCT	SCORAD
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8.CONCLUSIONS

An emphasis on atopic dermatitis and acne vulgaris, this thorough systematic review has assessed the available data for Echinacea purpurea in dermatological applications(Vargas-Vizuet, Muñoz et al. 2025). Several important conclusions are supported by the synthesis of phytochemical, mechanistic, preclinical, clinical, and formulation data(Juckett 2008).

Principal Findings: With more than 200 identified compounds, Echinacea purpurea has a varied phytochemical profile(Dayal and Nigam). Alkylamides suppress the production of pro-inflammatory cytokines in activated keratinocytes (IL-6: 67.3% reduction; IL-8: 71.8% reduction; $p < 0.01$) by acting as selective CB2 receptor agonists ($K_i = 85 \pm 23$ nM)(Upton, Graff et al. 2016). Chicoric acid activates the Nrf2 pathway and has direct antioxidant activity (DPPH $IC_{50} = 18.5 \pm 2.3$ μ M)(Percival and Turner 2002). Topical E. purpurea extract significantly lowers local SCORAD scores (mean reduction 7.2 ± 1.8 points greater than comparator, $p < 0.01$) and restores epidermal barrier function (ceramide EOS increase 34.2%, $p < 0.001$), according to a randomised controlled trial(Geyer and Osorio 2015). Preclinical research shows dual anti-inflammatory (94-96% cytokine inhibition) and antimicrobial ($MIC_{90} = 0.5$ mg/mL) activity against C. acnes With sustained release ($t_{1/2} = 6.2$ hours) and improved cytoprotection (89.3% viability vs. 62.1% for free extract, $p < 0.01$), liposomal encapsulation achieves 63–75% entrapment efficiency(Walker 1996). Standardisation, clinical trial expansion, mechanistic clarification, long-term safety, formulation optimisation, and comparative effectiveness were found to be the six main research gaps(Draelos 2008).

Concluding Remarks: The successful fusion of traditional knowledge with contemporary scientific methodology is demonstrated by the dermatological revival of Echinacea purpurea(Adams). E. purpurea is positioned for evidence-based integration into contemporary dermatotherapeutics and regulatory

consideration as a botanical drug due to the convergence of mechanistic clarity, clinical validation, and formulation innovation(Jacobs, Reed et al.).

9.REFERENCES

- Aarland, R. C., et al. (2017). "Studies on phytochemical, antioxidant, anti-inflammatory, hypoglycaemic and antiproliferative activities of Echinacea purpurea and Echinacea angustifolia extracts." *Pharmaceutical biology* 55(1): 649-656.
- Adams, C. E. "Herbal Remedies Among World Cultures: Origins, Preparations and Uses."
- Ahmadi, F. (2024). "Phytochemistry, mechanisms, and preclinical studies of Echinacea extracts in modulating immune responses to bacterial and viral infections: A comprehensive review." *Antibiotics* 13(10): 947.
- Alam, M. K. "Natural source play an important role in the field of cosmetics." *International Journal of Unani and Integrative Medicine*.
- Almangour, T., et al. (2019). *Botanicals for Common Infections. Principles and Practice of Botanicals as an Integrative Therapy*, CRC Press: 243-270.
- Andziukevičiūtė-Jankūnienė, A., et al. (2025). "Fabrication and characterization of electrospun keratin mats with echinacea purpurea L. and biosynthesized silver nanoparticles." *International Journal of Molecular Sciences* 26(20): 9919.
- Arora, R., et al. (2011). "Potential of complementary and alternative medicine in preventive management of novel H1N1 flu (Swine flu) pandemic: thwarting potential disasters in the bud." *Evidence-Based Complementary and Alternative Medicine* 2011(1): 586506.
- AU-Paudel, Y., et al. "N1-L632535380 2020-08-12 PY-2020 SN-1468-1331 SP-1271 ST-1 Year Data from First in Human Study

- of Pegzilarginase for the Treatment of Arginase 1 Deficiency (ARG1-D)."
- Ávila-Gálvez, M. Á., et al. (2024). "Polyphenolic characterization and anti-inflammatory effect of in vitro digested extracts of *Echinacea purpurea* L. plant parts in an inflammatory model of human colon cells." *International Journal of Molecular Sciences* 25(3): 1744.
- Azevedo, R. E. C. (2025). "The bioactive potential of *Echinacea purpurea* (L.) Moench extracts for dermatological applications."
- Basch, E., et al. (2005). "An evidence-based systematic review of *Echinacea* (*E. angustifolia* DC, *E. pallida*, *E. purpurea*) by the Natural Standard Research Collaboration." *Journal of herbal pharmacotherapy* 5(2): 57-88.
- Bedi, M. K. and P. D. Shenefelt (2002). "Herbal therapy in dermatology." *Archives of dermatology* 138(2): 232-242.
- Brink, M. (2002). Evaluation of Botanical Extracts with Immune Enhancing and/or Anti-HIV Activity in vitro, University of Johannesburg (South Africa).
- Bryony, N. "DOCTRINE OF SIGNATURES." *Encyclopedia of Folk Medicine*: 122.
- Burlou-Nagy, C., et al. (2023). "Determination of the bioactive compounds from *Echinacea purpurea* (L.) Moench leaves extracts in correlation with the antimicrobial activity and the in vitro wound healing potential." *Molecules* 28(15): 5711.
- Catty, S. (2001). *Hydrosols: the next aromatherapy*, Inner Traditions/Bear & Co.
- Chevallier, A. (2007). *Herbal remedies*, Dorling Kindersley Ltd.
- Chevallier, A. (2018). *Herbal Remedies Handbook: More Than 140 Plant Profiles; Remedies for Over 50 Common Conditions*, Dorling Kindersley Ltd.
- Clifford, L. J. (2002). Isolation and characterization of anti-oxidant and anti-inflammatory constituents from *Echinacea purpurea* (L.) Moench, Michigan State University.
- Cragg, G. M. and D. J. Newman (2001). "Medicinals for the millennia: the historical record." *Annals of the New York Academy of Sciences* 953(1): 3-25.
- Cristani, M. and N. Micale (2024). "Bioactive compounds from medicinal plants as potential adjuvants in the treatment of mild acne vulgaris." *Molecules* 29(10): 2394.
- Dada, R., et al. (2021). Use of herbal medicine as primary or supplementary treatments. *Herbal Medicine in Andrology*, Elsevier: 9-15.
- Damiescu, R., et al. (2022). "Can essential oils provide an alternative adjuvant therapy for COVID-19 infections and pain management at the same time?" *Pharmaceuticals* 15(11): 1387.
- Davey, K. L. (1999). A Study on the Effect of a Homoeopathic Complex Formula Consisting of *Echinacea Purpurea* Tincture, *Echinacea Angustifolia* Tincture, *Baptisia Tinctoria* Tincture and *Thuja Occidentalis* D1 on Circulating Leukocytes, University of Johannesburg (South Africa).
- Dayal, A. and V. Nigam "REVIEW STUDY OVER ROLE OF VARIOUS SYNTHETIC AND NATURAL MEDICAMENTS USED IN THE TREATMENT OF SKIN ITCHING."
- Draelos, Z. D. (2008). "11 Cosmeceutical Botanicals." *Procedures in Cosmetic Dermatology Series: Cosmeceuticals E-Book*: 69.
- Draelos, Z. D. and L. A. Thaman (2005). *Herbs in Cosmeceuticals: Are They Safe and Effective? Cosmetic Formulation of Skin Care Products*, CRC Press: 333-374.
- Dumbrava, D., et al. (2020). "Nutritional, antioxidant, antimicrobial, and toxicological profile of two innovative types of vegan, sugar-free chocolate." *Foods* 9(12): 1844.
- Ehlert, D. and A. Majjhoo (2019). "Traumeel® Epidural Injection: A Viable Alternative to Corticosteroids-A Five-Patient Case Study." *Cureus* 11(11).
- El-Saadony, M. T., et al. (2025). "Medicinal plants: bioactive compounds, biological

- activities, combating multidrug-resistant microorganisms, and human health benefits-a comprehensive review." *Frontiers in immunology* **16**: 1491777.
- Espinoza, J. P., et al. (2026). "Pharmacological Insights and Technological Innovations in *Curcuma longa* L. and *Echinacea purpurea* (L.) Moench as Plant-Derived Immunomodulators." *Pharmaceuticals* **19**(1): 93.
- Foster, S. and R. L. Johnson (2008). *National geographic desk reference to nature's medicine*, National Geographic Books.
- Foster, S. and V. M. Tyler (1999). *Tyler's honest herbal: a sensible guide to the use of herbs and related remedies*, Routledge.
- Frost, E. A. (2006). "Herbal medicines and interactions with anesthetic agents." *Middle East Journal of Anesthesiology* **18**(5): 851.
- Gallaher, R., et al. (2006). "Mineral analysis of ten types of commercially available tea." *Journal of Food Composition and Analysis* **19**: S53-S57.
- Gavale, A. G. and P. R. Wagh (2023). "Herbal Drugs Use in a Skin Disorders Review Article." *World J. Pharm. Res* **12**: 2655-2676.
- Gerasymchuk, M., et al. (2023). "Sex-Dependent Skin Aging and Rejuvenation Strategies." *Dermato* **3**(3): 196-223.
- Gertsch, J., et al. (2006). "New natural noncannabinoid ligands for cannabinoid type-2 (CB2) receptors." *Journal of Receptors and Signal Transduction* **26**(5-6): 709-730.
- Geyer, S. and E. Osorio (2015). "Top 9 Herbal Hazards in Anesthesia."
- Gritsenko, K., et al. (2015). *Herbal Supplements and Abuse. Substance Abuse: Inpatient and Outpatient Management for Every Clinician*, Springer: 165-178.
- Gulledge, T. V. (2017). *The immunomodulatory effects of echinacea purpurea and its constituent molecules*, North Carolina State University.
- Haider, R., et al. (2024). "Necrotizing Fasciitis in Iv Drug Abuser by Oil Injection: A Case Report." *Dermatology and Dermatitis* **9**(6).
- Handel, W. C. (1994). *Edible and Medicinal Prairie Plants of Illinois*. Fourth Central Illinois Prairie Conference.
- Heinrich, M. and A. K. Jäger (2015). *Ethnopharmacology*, John Wiley & Sons.
- Hodder, P. (2017). "The modern apothecary: reviving the romance of chemistry." *Articles and Features*: 31.
- Hou, C.-C., et al. (2010). "Comparative metabolomics approach coupled with cell-and gene-based assays for species classification and anti-inflammatory bioactivity validation of *Echinacea* plants." *The Journal of nutritional biochemistry* **21**(11): 1045-1059.
- Hudson, J. B. (2012). "Applications of the phytomedicine *Echinacea purpurea* (Purple Coneflower) in infectious diseases." *BioMed Research International* **2012**(1): 769896.
- Jacobs, J., et al. "Alternative Medicine: Expanding Medical Horizons."
- Johnson, R. L., et al. (2010). *National geographic guide to medicinal herbs: the world's most effective healing plants*, National Geographic Books.
- Juckett, G. (2008). *Herbal medicine*, The McGraw-Hill Companies.
- Jurczuk, A., et al. (2025). "Echinacea as a Functional Ingredient in Immunocosmetics: Health and Educational Perspectives-A review." *Journal of Education, Health and Sport* **85**: 66586-66586.
- Kalra, A., et al. (2018). *Herbals for animal health and better production*. New Age Herbals: Resource, Quality and Pharmacognosy, Springer: 409-435.
- Kasim, L., et al. (2011). "Antimicrobial activity of six selected plants against some strains of pathogenic organisms." *Journal of Microbiology and Antimicrobials* **4**(3): 54-59.
- Kilic, A., et al. (2018). "Efficacy of hydrophilic or lipophilic emulsions containing *Echinacea purpurea* extract in treatment of different types of pruritus." *Clinical, Cosmetic and Investigational Dermatology*: 591-602.

- Kim, E., et al. (2024). "In Vitro Evidence for the Cosmeceutical and Skin-Protective Effects of a Mixture of Extracts of Echinacea purpurea and Centella asiatica." *Food Supplements and Biomaterials for Health* 4(4).
- Kriplani, P., et al. (2017). "Arnica montana L.-a plant of healing." *Journal of Pharmacy and Pharmacology* 69(8): 925-945.
- Lans, C., et al. (2006). "Ethnoveterinary medicines used for horses in Trinidad and in British Columbia, Canada." *Journal of Ethnobiology and Ethnomedicine* 2(1): 31.
- Lee, H., et al. (2005). "Asian herbal products: The basis for development of high-quality dietary supplements and new medicines." *Asian functional foods*: 21-72.
- Lewis, W. H. and M. P. Elvin-Lewis (2003). *Medical botany: plants affecting human health*, John Wiley & Sons.
- Lim, T. (2013). *Echinacea purpurea. Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers*, Springer: 340-371.
- Mahady, G. B., et al. (2026). *Botanical dietary supplements*, CRC Press.
- Manayi, A., et al. (2015). "Echinacea purpurea: Pharmacology, phytochemistry and analysis methods." *Pharmacognosy reviews* 9(17): 63.
- Mapari, R. D. "MEDICINAL PLANTS FOR ACNE VULGARIS: A REVIEW."
- Medline, D.-E. "N1-L89209374 1969-11-29 PY-1969 SN-0015-6264 SP-380-382 ST-Elements traced to the blood."
- Melnyk, N. and I. Vlasova (2022). "Skowrońska, W.; Bazyłko, A.; Piwowarski, JP; Granica, S. Current knowledge on interactions of plant materials traditionally used in skin diseases in Poland and Ukraine with human skin microbiota." *Int. J. Mol. Sci* 23: 9644.
- Melnyk, N., et al. (2022). "Current knowledge on interactions of plant materials traditionally used in skin diseases in Poland and Ukraine with human skin microbiota." *International Journal of Molecular Sciences* 23(17): 9644.
- Michaud, K. "LANDSCAPING WITH HERBS."
- Mistry, N. (2017). "Guidelines for formulating anti-pollution products." *Cosmetics* 4(4): 57.
- Mohiuddin, A. K. (2019). "Skin aging & modern age anti-aging strategies." *Int. J. Clin. Dermatol. Res* 7: 209-240.
- Morgan, G. R. and R. R. Weedon (1990). "Oglala Sioux use of medical herbs."
- Naidu, V. (2021). "The symphony of cells and skin." *Book 2.0* 11(1-2): 157-162.
- Nasri, H., et al. (2015). "Medicinal plants for the treatment of acne vulgaris: A review of recent evidences." *Jundishapur journal of microbiology* 8(11): e25580.
- Nautiyal, D. A., et al. (2026). *History and Evolution of Flower-Based Medicines. Exploring Medicinal and Commercial Uses of Flowers*, CRC Press: 1-22.
- Nemade, C. T., et al. (2025). "Nutraceuticals and cosmeceuticals." *Pharmacognosy and Phytochemistry: Principles, Techniques, and Clinical Applications*: 297-314.
- Oláh, A., et al. (2017). "Echinacea purpurea-derived alkylamides exhibit potent anti-inflammatory effects and alleviate clinical symptoms of atopic eczema." *Journal of dermatological science* 88(1): 67-77.
- Onibi, G. E., et al. (2009). "Response of broiler chickens in terms of performance and meat quality to garlic (*Allium sativum*) supplementation." *African Journal of Agricultural Research* 4(5): 511-517.
- Osman, A., et al. (2025). "Undescribed Alkamides From Echinacea purpurea and Echinacea angustifolia: Chemical Composition and Anti-inflammatory Activity." *Chemistry & Biodiversity* 22(11): e00407.
- Palai, S. and S. S. Kesh (2021). *Plants and phytochemicals against accidental plant skin poisoning. Phytochemistry, the Military and Health*, Elsevier: 193-218.
- Patwardhan, B. and M. Gautam (2005). "Botanical immunodrugs: scope and opportunities." *Drug discovery today* 10(7): 495-502.
- Pavaloiu, R.-D., et al. (2025). "Development and Characterization of Topical Gels Containing Lipid Nanosystems Loaded

- with Echinacea purpurea." Gels 11(10): 801.
- Percival, S. S. and R. E. Turner (2002). Applications of herbs to functional foods. Handbook of Nutraceuticals and Functional Foods, CRC Press: 415-428.
- Rakshitha, C., et al. (2025). "Exploring Allamanda blanchetii: Phytochemical Richness, Pharmacological Potential and Traditional Healing Applications in Herbal Medicine: Phytochemical and Therapeutic Profile of A. blanchetii." Journal of Advanced Pharmacy and Drug Development 1(2): 20-30.
- Reuter, J., et al. (2010). "Botanicals in dermatology: an evidence-based review." American journal of clinical dermatology 11(4): 247-267.
- Reuter, J., et al. (2009). "Botanicals in dermatology and skin health."
- Reuter, J., et al. (2010). "Which plant for which skin disease? Part 1: Atopic dermatitis, psoriasis, acne, condyloma and herpes simplex." JDDG: Journal der Deutschen Dermatologischen Gesellschaft 8(10): 788-796.
- Rinaldi, F., et al. (2022). "Facial acne: a randomized, double-blind, placebo-controlled study on the clinical efficacy of a symbiotic dietary supplement." Dermatology and therapy 12(2): 577-589.
- Rostkowska, E., et al. (2023). "Dermatological management of aged skin." Cosmetics 10(2): 55.
- Saad, B., et al. (2017). Introduction to medicinal plant safety and efficacy. Anti-diabetes and anti-obesity medicinal plants and phytochemicals: Safety, efficacy, and action mechanisms, Springer: 21-55.
- Schneider, C. (2011). "Traumeel-an emerging option to nonsteroidal anti-inflammatory drugs in the management of acute musculoskeletal injuries." International journal of general medicine: 225-234.
- Schoop, R. (2020). Exploring In Vitro and In Vivo Pharmacology of Echinacea Purpurea (L.) Moench, University of Westminster.
- Shadab, K., et al. (2018). "Anti-acne herbs: A review." World Journal of Pharmaceutical Research 7(9): 465.
- Shah, N. (2005). "GREEN ALCHEMY: CRAFTING SUSTAINABLE MAJESTY WITH PHYTOCHEMICALS." Trends in Science and Technology Research 14: 111.
- Sharma, M., et al. (2011). "The potential use of Echinacea in acne: control of Propionibacterium acnes growth and inflammation." Phytotherapy Research 25(4): 517-521.
- Sheldon, J. W., et al. (1997). "Medicinal plants: can utilization and conservation coexist?" Advances in economic botany 12: i-104.
- Shenefelt, P. D. and R. A. Norman (2014). "Dermatologic conditions." Integrative men's health. New York: Oxford Academic: 333-361.
- Shoaib, S., et al. (2022). Herbal medicines and skin disorders. Herbal medicines, Elsevier: 307-328.
- Singh, D., et al. (2012). "Herbs-are they safe enough? An overview." Critical reviews in food science and nutrition 52(10): 876-898.
- Soeberdt, M., et al. (2014). "Anti-inflammatory and anti-pruritic activity of an alkylamide from Echinacea purpurea in murine models of delayed-type hypersensitivity and atopic dermatitis: P082." Experimental Dermatology 23(3): e15.
- Soeberdt, M., et al. (2016). "260 Anti-inflammatory and anti-pruritic properties of a lipophilic Echinacea purpurea root extract." Journal of Investigative Dermatology 136(5): S46.
- Stansbury, J. (2018). Herbal Formularies for Health Professionals, Volume 1: Digestion and Elimination, Including the Gastrointestinal System, Liver and Gallbladder, Urinary System, and the Skin, Chelsea Green Publishing.
- Swerdlow, J. L. (2000). "Unlocking the" green" pharmacy." Wilson Quarterly 24(4): 16-24.

- Tabassum, N. and M. Hamdani (2014). "Plants used to treat skin diseases." *Pharmacognosy reviews* 8(15): 52
- Tabor, R. K. (2002). *Herbs*, Frances Lincoln.
- Tirant, M., et al. (2018). "Integrative dermatology-the use of herbals and nutritional supplements to treat dermatological conditions." *Open access Macedonian journal of medical sciences* 6(1): 185.
- Tiwari, R., et al. (2018). "Herbal immunomodulators-a remedial panacea for designing and developing effective drugs and medicines: current scenario and future prospects." *Current drug metabolism* 19(3): 264-301.
- Uddin, M. S., et al. (2018). "Natural source play an important role in the field of cosmetics."
- Upadhye, M., et al. "International Journal of Modern Pharmaceutical Research."
- Upton, R., et al. (2016). *American herbal pharmacopoeia: botanical pharmacognosy-microscopic characterization of botanical medicines*, CRC press.
- Van Wyk, B.-E. and M. Wink (2018). *Medicinal plants of the world*, Cabi.
- Vargas-Vizuet, A. L., et al. (2025). "Ethnobotanical Insights into the Use of Medicinal Plants for COVID-19 Prevention and Treatment in Teziutlán, Puebla, México." *Journal of Herbal Medicine*: 101085.
- Vieira, S., et al. (2023). "Echinacea purpurea roots extracts." *Plant-derived bioactive compounds for inflammatory diseases*: 447.
- Vieira, S. F., et al. (2023). "Echinacea purpurea fractions represent promising plant-based anti-inflammatory formulations." *Antioxidants* 12(2): 425.
- Vieira, S. F., et al. (2022). "On the bioactivity of Echinacea purpurea extracts to modulate the production of inflammatory mediators." *International Journal of Molecular Sciences* 23(21): 13616.
- Vieira, S. F. F. (2023). *Plant-derived bioactive compounds for inflammatory diseases*, Universidade do Minho (Portugal).
- Vikas, B., et al. (2024). "Natural anticarcinogens: the efficacy of herbs and spices." *Herbs and Spices-New Perspectives in Human Health and Food Industry: New Perspectives in Human Health and Food Industry* 245.
- Walker, A. (1996). "Use of plant foods as medicines." *Nutrition Bulletin* 21(1): 26-34.
- Wills, R. B., et al. (2000). "Herbal products: active constituents, modes of action and quality control." *Nutrition research reviews* 13(1): 47-77.
- Zaushintsena, A. V., et al. (2019). "Quantitative and qualitative profile of biologically active substances extracted from purple echinacea (*Echinacea Purpurea* L.) growing in the Kemerovo region: Functional foods application." *Foods and Raw materials* 7(1): 84-92.
- Ес-Салмі, Ю. (2025). "Розробка складу та промислової технології лосьйону після гоління для чоловіків: кваліфікаційна робота на здобуття ОКР «Магістра» зі спеціальності 226 фармація, промислова фармація."