Parijataka Beeja Lepa For *Indralupta* (Alopecia Areata): An Integrative Conceptual Review Of *Ayurvedic* Evidence And Modern Scientific Perspectives

Dr. Apurva Yelavi[1], Dr.Virendra Pawar[2], Dr. Harshavardhan Wagaj[3], Dr. Ashwini Jadhav[4], Dr. Dattatray L Shinde[5*]

[1]Student PG diploma D. Dermatology, Bharti Vidyapeeth (Deemed to be University) College of Ayurveda Pune, Maharashtra, India

[2]**M.D Ph.D**, Associate Professor Dept.of Kayachikitsa,Bharati Vidyapeeth (Deemed to be University) College of Ayurveda Pune, Maharashtra,India. (0009-0001-7812-2724)

[3]**MD**, Assitant. Professor, Dept of Panchkarma ,Bharati Vidyapeeth (Deemed to be University) College of Ayurved ,Pune, Maharashtra,India. (0009-0002-6099-1750)

[4]**MD**, Assistant .Professor,Dept of Kayachikitsa ,Bharati Vidyapeeth (Deemed to be University) College of Ayurved ,Pune, Maharashtra,India. 0009-0000-7353-9654

[*5]**MD Ph.D,** Professor and HOD Department.of Kayachikitsa,
Bharati Vidyapeeth (Deemed to be University) College of Ayurved Pune, Maharashtra, India.

[*]**Corresponding Author**
Dr. Dattatray L. Shinde
MD Ph.D, Professor and HOD Department of Kayachikitsa,
Bharati Vidyapeeth (Deemed to be University) College of Ayurved Pune, Maharashtra, India.
dattatray.shinde@bharatividyapeeth.edu (0009-0006-3614-4876)

Abstract

Alopecia areata is a relapsing, immune-mediated, non-scarring hair-loss disorder in which collapse of hair-follicle immune privilege and cytotoxic inflammatory signalling interrupt the anagen phase. In Ayurveda, the clinically comparable presentation is commonly discussed as Indralupta, where Vata-Pitta-associated hair shedding is followed by Kapha-Rakta obstruction of Romakupa and failure of regrowth. Parijataka Beeja Lepa, prepared from Nyctanthes arbor-tristis L. seeds, is considered in this review as a standardisable topical research candidate rather than an established treatment. The principal research gap is the absence of an authenticated and standardised Parijataka seed formulation supported by validated solubility, release, follicular-deposition, target-engagement, dermal-safety and controlled clinical-efficacy data. The research aim is to develop a scientifically defensible and analytically testable framework for investigating Parijataka Beeja Lepa in Indralupta correlated with alopecia areata. The objectives are to integrate historical and classical evidence with modern immunopathogenesis; describe seed phytochemistry and representative molecular structures; compare extraction and isolation methods; evaluate formulation-relevant solubility and analytical standardisation; examine pharmacological plausibility; compare the proposed Lepa with established treatments; and define a staged translational research programme. Reported seed constituents include arbortristosides, phenolic compounds, sterols and lipid fractions with preclinical antioxidant, anti-inflammatory, anti-allergic and immunomodulatory activities. An ethyl-acetate seed fraction has shown measurable phenolic content and free-radical-scavenging activity, although these in-vitro findings do not establish scalp delivery or hair regrowth. No validated equilibrium-solubility dataset or controlled clinical trial of Parijataka Beeja Lepa for alopecia areata was identified. Authentication, physicochemical testing, solvent screening, HPTLC/HPLC method validation, dermal safety assessment, follicular mechanistic studies and controlled trials using SALT and trichoscopic outcomes are therefore required. Until such evidence is generated, the formulation should remain investigational and should not replace established dermatological diagnosis or evidence-based treatment.

Keywords: Indralupta; alopecia areata; Parijataka; Nyctanthes arbor-tristis; Beeja Lepa; arbortristoside; phytoconstituents; solubility; HPLC; standardisation.

How to cite this article: Yelavi A, Pawar V, Wagaj H, Jadhav A, Shinde DL. Parijataka Beeja Lepa for Indralupta (alopecia areata): an integrative conceptual review of ayurvedic evidence and modern scientific perspectives. Int J Drug Deliv Technol. 2026;16(72s): 162-179. DOI: 10.25258/ijddt.16.72s.21

1. Introduction

Alopecia areata (AA) is an acquired inflammatory disorder characterised by sudden or progressive non-scarring hair loss from the scalp or other hair-bearing sites [20]. The most recognisable presentation consists of one or more smooth, sharply demarcated round or oval patches, although diffuse, ophiasis, totalis and universalis patterns also occur [21]. Exclamation-mark hairs, broken hairs, black dots and yellow dots may

occur at active margins, while nail pitting, trachyonychia or ridging may indicate greater disease burden [21].

The lifetime occurrence of AA is commonly estimated near two per cent, and population studies demonstrate variation in incidence and healthcare use across age, sex, ethnicity and socioeconomic groups [28]. The disorder may begin at any age, frequently starts in childhood or early adulthood and follows an unpredictable course with spontaneous regrowth, relapse or progression [20]. Hair loss does not usually impair organ function, but it can substantially alter self-image, interpersonal interaction, educational participation, employment and health-related quality of life [29].

Current management includes topical and intralesional corticosteroids, systemic corticosteroids in selected rapidly progressive disease, topical minoxidil as an adjunct, anthralin, contact immunotherapy and systemic immunomodulatory treatment [34]. Oral JAK-pathway inhibitors have produced clinically meaningful hair regrowth in subsets of patients with severe AA, but response is incomplete, relapse can occur and treatment requires safety screening and monitoring [36]. The limitations of current therapy create a legitimate need for safe and standardised topical adjuncts, but any traditional formulation must be examined with the same standards of authentication, reproducibility, safety and outcome measurement applied to modern products [50].

Indralupta is described in Ayurvedic literature as a disorder of the scalp and hair in which aggravated Vata and Pitta initiate hair shedding and Kapha associated with Rakta subsequently obstructs the follicular pathway and prevents regrowth [1]. This sequence is clinically useful because it separates the phase of active hair fall from the phase of persistent failure of regrowth [1]. The analogy with AA should remain cautious because Dosha, Rakta and Romakupa are Ayurvedic functional concepts and are not literal equivalents of cytokines, immune cells or anatomical plugs [1].

Parijataka, botanically identified as Nyctanthes arbor-tristis L. of the family Oleaceae, is a medicinal tree used in Ayurveda and regional systems of medicine [5]. Its seeds contain iridoid glycosides, phenolic constituents, sterols and lipid-associated compounds, and preclinical studies describe antioxidant, anti-inflammatory, anti-allergic and immunomodulatory effects [10]. These findings offer biological plausibility for a topical research formulation, but they do not prove delivery to the human follicle or clinical hair regrowth [8].

1.1 Historical background

Descriptions of circumscribed hair loss appear in early medical traditions, including ancient Egyptian papyri that recorded remedies for patch-like alopecia [45]. Celsus described a serpiginous and circumscribed form of alopecia in the first century, providing an early clinical distinction from diffuse baldness [45]. Thomas Bateman later published an influential modern clinical description of circular alopecic patches in 1817, while nineteenth- and twentieth-century debate progressively shifted from parasitic and neurogenic explanations toward immunological concepts [45].

The modern understanding of AA developed through histopathological recognition of perifollicular lymphocytic inflammation, experimental models, genetic association studies and demonstration of hair-follicle immune-privilege collapse [26]. The identification of CD8+NKG2D+ T-cell activity and IFN-gamma/IL-15 signalling helped establish the JAK–STAT pathway as a therapeutic target [22]. The recent targeted-therapy era therefore represents the latest stage in a long transition from descriptive morphology to mechanism-based intervention [31].

Ayurvedic descriptions developed through a different conceptual system and emphasised the sequence of Dosha disturbance, Kesha-patana and obstruction of Romakupa [1]. The Sushruta formulation remains historically important because it links an initiating phase of hair loss with a subsequent failure of regeneration [1]. An integrative review can compare the clinical sequence and therapeutic objectives of the two systems without claiming that their explanatory categories are identical [1].

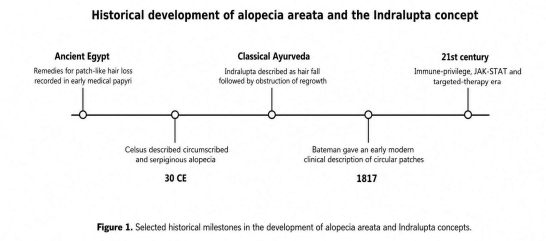

Figure 1. The alopecia areata milestones are based on a published historical review [45]. The Indralupta milestone follows the classical description in Sushruta Samhita [1].

1.2 Review of literature and rationale

The literature relevant to Parijataka Beeja Lepa is distributed across classical Ayurvedic texts, botanical reviews, phytochemical isolation studies, preclinical pharmacology, modern AA pathogenesis and contemporary treatment trials [2]. No single publication establishes the complete chain from authenticated Parijataka seed to standardised topical exposure, follicular target engagement and controlled clinical hair regrowth [5]. The purpose of the present synthesis is therefore to identify which links are supported, which are inferential and which require direct experimentation [8].

Table 1. Representative literature informing the Parijataka Beeja Lepa research concept

Source	Evidence type	Principal finding	Interpretation for this review

Source	Evidence type	Principal finding	Interpretation for this review
Sushruta Samhita	Classical description	Vata–Pitta-associated hair shedding followed by Kapha–Rakta obstruction of Romakupa [1].	Provides the traditional disease sequence but not modern clinical efficacy.
Purushothaman et al., 1985	Seed isolation	Arbortristoside A and B were isolated as iridoid glucosides from N. arbortristis [7].	Supports marker selection and structural standardisation.
Das et al., 2008	Isolated constituent / animal models	Arbortristoside A showed anti-inflammatory and antinociceptive activity [9].	Supports biological plausibility but not topical scalp efficacy.
Vajravijayan et al., 2013	Seed extracts / in-vitro assays	Ethyl-acetate extract showed antioxidant and membrane-stabilising effects [8].	Provides comparative assay data and solvent-selection rationale.
Gupta et al., 1995	Isolated arbortristosides	Anti-allergic activity was reported in preclinical experiments [10].	Suggests immune interaction but not disease-specific suppression.
Khan et al., 1995	Extracts and iridoid glucosides / mice	Immunomodulatory effects were observed in systemic candidiasis models [11].	Demonstrates immune activity with uncertain direction for autoimmunity.
Rathore et al., 2007	Different plant organs / murine arthritis	Cytokine modulation varied among plant parts [12].	Supports organ-specific comparison and cautions against extrapolation.
Gupta et al., 2024	Isolation, crystallography and RP-HPLC	Arbortristoside A was structurally validated by X-ray crystallography [48]. It was quantified using an RP-HPLC method [49].	Supports analytical quality control and marker-based batch comparison.
AA reviews and guidelines	Human disease evidence	Hair-follicle immune-privilege collapse and cytotoxic T-cell signalling are established [22]. Validated clinical outcomes are defined in current guidance [31].	Defines biological targets, diagnosis and outcome measures.
JAK-inhibitor phase 3 trials	Randomised clinical trials	Baricitinib produced SALT-defined responses in phase 3 trials [36]. Ritlecitinib produced SALT-defined responses in its pivotal trial [37]. Deuruxolitinib produced SALT-defined responses in THRIVE-AA1 [38].	Provides an evidence benchmark but not a direct comparator for an untested Lepa.

The literature converges on three research premises: Indralupta provides a traditional topical-treatment rationale, Parijataka seed contains chemically identifiable constituents and AA provides measurable inflammatory and clinical targets [1]. The literature also

reveals three major gaps: absence of validated aqueous-paste chemical release data, absence of scalp penetration and follicular target-engagement data, and absence of controlled human efficacy data [8]. A scientifically defensible review must therefore separate tradition, constituent identification, preclinical activity and clinical proof at every stage [31].

1.3 Research Gap

No controlled clinical study has evaluated a standardised Parijataka Beeja Lepa in alopecia areata using validated outcomes such as SALT scoring, trichoscopy and relapse assessment [5].

Seed-specific literature does not establish chemical release from an aqueous Lepa, penetration across scalp skin, follicular deposition or engagement of alopecia-areata-relevant inflammatory targets [8].

Validated equilibrium-solubility, pH-solubility, stability and vehicle-compatibility data for arbortristoside A and other representative seed constituents in scalp-relevant media remain unavailable [47].

A formulation-specific analytical specification linking botanical identity, HPTLC/HPLC marker content, batch consistency and biological performance has not yet been established [49].

The central translational gap is therefore the absence of an authenticated, standardised and dermally safe formulation connected sequentially to mechanistic follicular evidence and controlled human clinical outcomes [50].

2. Research Aim and Objectives

2.1 Research Aim

The research aim is to develop a scientifically defensible, analytically standardised and clinically testable framework for evaluating Parijataka Beeja Lepa as an investigational topical adjunct in Indralupta correlated with alopecia areata [1].

2.2 Research Objectives

- To review the classical Ayurvedic description, historical development and modern immunopathogenesis of patchy non-scarring alopecia [45].
- To describe the botanical, Ayurvedic and seed-specific phytochemical profile of Nyctanthes arbor-tristis [4].
- To present the chemical structures and physicochemical implications of representative seed constituents [7].
- To compare extraction, fractionation and isolation methods used for Parijataka phytoconstituents [7].
- To propose a formulation-relevant solubility study without presenting unmeasured values as established data [47].
- To develop an analytical standardisation plan consistent with WHO, ICH and EMA quality principles [52].
- To critically evaluate pharmacological actions relevant to inflammatory and oxidative aspects of AA [8].
- To compare the proposed investigational Lepa with established AA treatments and validated outcome measures [31].
- To address the identified translational gaps by defining dermal-safety requirements, mechanistic endpoints, clinical outcomes and a staged programme for preclinical and controlled clinical evaluation [31].

3. Materials and Methods

This manuscript was prepared as a structured conceptual and narrative review integrating classical Ayurvedic sources with contemporary scientific literature [1]. Classical sources included Sushruta Samhita, Sharngadhara Samhita and Nighantu literature describing Indralupta, Lepa Kalpana and Parijataka [2]. Modern sources included peer-reviewed primary studies, systematic reviews, clinical guidelines, regulatory documents and official quality-control guidance [31].

Search concepts included “alopecia areata”, “Indralupta”, “hair follicle immune privilege”, “CD8 NKG2D”, “IFN-gamma”, “IL-15”, “JAK-STAT”, “oxidative stress”, “Nyctanthes arbor-tristis seed”, “arbortristoside”, “extraction”, “solubility”, “HPTLC”, “HPLC”, “LC-MS”, “anti-inflammatory”, “antioxidant”, “immunomodulatory”, “Lepa Kalpana” and “topical herbal formulation” [49]. Priority was assigned to primary phytochemical studies, randomised clinical trials, systematic reviews and recognised quality guidelines [31]. Unsupported promotional claims, duplicated secondary summaries and reports lacking identifiable methods were not used to establish efficacy [31].

Evidence was classified as classical textual evidence, chemical identification, in-vitro or animal pharmacology, human AA evidence or direct Parijataka-Lepa clinical evidence [2]. Each conclusion was restricted to the level of evidence available, and proposed actions were labelled as hypotheses when direct topical or clinical evidence was absent [8]. Numerical data were included only when a source provided identifiable methods and the measurement was relevant to comparison or analytical planning [8].

Table 2. Evidence domains and permissible levels of inference

Evidence domain	Examples
Classical textual evidence	Indralupta sequence and Lepa principles [2].
Phytochemical evidence	Iridoid glycosides, sterols, phenolics and seed lipids [5].
In-vitro / animal pharmacology	Antioxidant, anti-inflammatory, anti-allergic and immunomodulatory models [10].
Human AA evidence	Guidelines and trials of corticosteroids, minoxidil, immunotherapy and JAK inhibitors [34].

Evidence domain	Examples
Direct Parijataka Lepa clinical evidence	No adequate controlled trial identified [5].

4. Ayurvedic Concept of Indralupta

4.1 Classical definition and textual basis

Sushruta places Indralupta among Kshudra Roga and describes a compact sequence involving all three Dosha and Rakta [1]. The classical passage states that Pitta associated with Vata reaches Romakupa and causes hair shedding, after which Kapha associated with Rakta obstructs the follicles and prevents new hair from arising [1]. The description supports a two-stage conceptual model consisting of Kesha-patana followed by impaired regeneration [1].

रोमकूपानुगं पित्तं वातेन सह मूर्च्छितम्।
प्रच्यावयति रोमाणि ततः श्लेष्मा सशोणितः ॥३३॥
रुणद्धि रोमकूपांस्तु ततोऽन्येषामसम्भवः।
तदिन्द्रलुप्तं खालित्यं रुज्येति च विभाव्यते ॥३४॥ [1]

4.2 Nidana, Dosha, Dushya and Samprapti

Classical texts do not provide a single exhaustive list of causes exclusive to Indralupta, so Nidana analysis is usually derived from factors that disturb Vata, Pitta, Kapha and Rakta and from broader scalp-disorder descriptions [1]. Irregular diet, excessive heat exposure, sleep disturbance, psychological stress, incompatible food patterns, poor scalp hygiene and constitutional susceptibility may be considered contributory within an Ayurvedic assessment [1]. Modern clinical modifiers such as atopy, autoimmunity, infection, medication exposure and nutritional disturbance should be evaluated separately and should not be collapsed into Dosha terminology [20].

Vata may be interpreted as facilitating instability and displacement of the hair shaft, while Pitta may be associated with inflammatory heat and tissue disturbance [1]. Kapha may represent persistence, coating or functional obstruction, while Rakta indicates involvement of the skin-associated tissue domain and inflammatory manifestations [1]. Twak, Kesha and Romakupa constitute the principal local sites, and Rasavaha and Raktavaha functional channels may be considered during systemic assessment [1].

A practical Samprapti sequence is: Nidana produces Dosha Prakopa; Vata and Pitta localise at the scalp and disturb Kesha anchoring; patchy Kesha-patana occurs; Kapha and vitiated Rakta sustain Avarodha at Romakupa; and regrowth becomes delayed or absent [1]. This sequence is a classical functional model and should not be interpreted as a histological statement that physical mucus or blood blocks a follicular opening [1].

4.3 Rupa and differential diagnosis

The typical clinical correlation is circumscribed loss of hair over a smooth, non-scarring surface with absent or delayed regrowth [1]. Scale, pustules, marked erythema, scarring, pain or loss of follicular openings should prompt reconsideration of the diagnosis [20]. Differential diagnosis includes tinea capitis, trichotillomania, androgenetic alopecia, telogen effluvium, traction alopecia, secondary syphilitic alopecia and cicatricial alopecias [21].

Table 3. Clinical differentiation of alopecia areata from selected mimics

Condition	Typical clues	Reason for exclusion before Lepa
Alopecia areata	Smooth non-scarring patches, exclamation hairs and possible nail changes [20].	Target condition for the proposed research concept.
Tinea capitis	Scale, broken hairs, inflammation, lymphadenopathy or fungal evidence [20].	Requires antifungal treatment; an empirical paste may delay care.
Trichotillomania	Irregular patches with hairs of unequal length and a behavioural context [20].	Requires behavioural and psychological management.
Androgenetic alopecia	Patterned miniaturisation and a chronic distribution [20].	Different pathobiology and different outcome measures.
Telogen effluvium	Diffuse shedding after a systemic or physiological trigger [20].	Requires identification of the precipitating factor.
Cicatricial alopecia	Loss of follicular openings, erythema, scale, pustules or scarring [20].	Urgent diagnosis is required to prevent irreversible loss.
Traction alopecia	History of sustained mechanical tension and marginal distribution [20].	Removal of the mechanical cause is primary.

5. Modern Concept of Alopecia Areata

5.1 Hair cycle and immune-privilege collapse

AA affects a hair follicle that is usually anatomically preserved, which explains why regrowth remains possible even after extensive shedding [20]. The lower anagen follicle normally maintains relative immune privilege through low major-histocompatibility-complex expression, local immunosuppressive mediators and restricted immune surveillance [23]. In AA, this privilege collapses, antigen presentation increases and

the anagen bulb becomes vulnerable to inflammatory attack [22]. The hair cycle shifts prematurely toward catagen and telogen rather than undergoing immediate permanent destruction [20].

5.2 Cellular and cytokine pathways

CD8+ T cells expressing NKG2D are central effectors in experimental and human AA, while CD4+ subsets, dendritic cells, mast cells and innate immune populations can amplify or regulate disease [22]. IFN-gamma promotes follicular antigen presentation and chemokine expression, while IL-15 supports cytotoxic lymphocyte activation and persistence [22]. JAK–STAT signalling transmits many of these cytokine signals and provides a mechanistic basis for the efficacy of systemic kinase inhibitors in severe disease [22]. Other mediators, including tumour necrosis factor, IL-2, IL-12, IL-18 and CXCL9/10/11, may contribute in a stage- and patient-dependent manner [22].

5.3 Genetic, environmental and oxidative factors

AA is polygenic, and association studies implicate HLA regions, ULBP genes, CTLA4 and other innate and adaptive immune loci [26]. Environmental or physiological triggers may precipitate disease in a susceptible person, although a single trigger is often not identifiable [20]. AA is associated with atopic disease, autoimmune thyroid disease, vitiligo and other immune-mediated conditions [44]. Oxidative-stress studies report altered lipid peroxidation and antioxidant defence markers, but association does not prove that antioxidant treatment alone reverses AA [42].

6. Cautious Ayurvedic–Modern Correlation

Indralupta and AA share a clinically meaningful pattern of patchy non-scarring hair loss with potential preservation of the follicular structure [1]. The Vata–Pitta phase may be compared conceptually with destabilisation of anagen hair production under inflammatory signalling, while Kapha–Rakta Avarodha may be compared with a persistent perifollicular environment that prevents productive cycling [1]. These are analogical comparisons at the level of clinical sequence and therapeutic objective, not one-to-one anatomical or molecular identities [1].

Table 4. Cautious correlation between Indralupta and alopecia areata

Ayurvedic element	Modern observation	Interpretive caution
Vata–Pitta reaches Romakupa	Inflammatory destabilisation of the anagen follicle [22].	The concepts are not biochemically identical.
Kesha-patana	Non-scarring shedding and dystrophic hair formation [20].	AA may show several patterns and spontaneous remission.
Kapha–Rakta Avarodha	Persistent perifollicular immune signalling and delayed anagen re-entry [22].	AA is not caused by a simple physical plug.
Romakupa retains capacity	Follicle is often preserved despite immune attack [20].	Regrowth remains possible but is not guaranteed.
Dosha-shamana and Rakta-prasadana	Reduction of local inflammatory disturbance and restoration of homeostasis [1].	Clinical benefit requires validated outcome measurement.

7. Parijataka: Botanical and Ayurvedic Drug Profile

7.1 Identity and distribution

Parijataka is botanically identified as Nyctanthes arbor-tristis L. and belongs to the family Oleaceae [5]. Common names include night-flowering jasmine, coral jasmine, Harsinghar, Harshringar, Shiuli and Pavalamalli, although the plant is not a true Jasminum species [5]. It is a shrub or small tree with opposite rough leaves, fragrant white flowers with an orange corolla tube and a flat bilobed capsule whose lobes generally contain one seed [5]. The species is widely cultivated in South Asia and parts of Southeast Asia [5].

Leaves, flowers, bark, roots and seeds have all been used in regional medicine, but plant-part substitution is scientifically unacceptable because each organ may have a different chemical profile and pharmacological activity [5]. The present concept focuses on the seed because seed-specific studies identify iridoid glucosides, phenolic material, sterols and lipid fractions [5]. Botanical authentication and a retained voucher specimen are essential because vernacular names can be shared with unrelated ornamentals [50].

7.2 Ayurvedic properties and traditional uses

Nighantu descriptions commonly assign Tikta and Katu Rasa, Laghu and Ruksha Guna, Ushna Virya and Katu Vipaka to Parijataka, although textual variation should be acknowledged [4]. The drug is traditionally discussed in conditions involving Jvara, Gridhrasi, Sandhivata, Krimi, pain and inflammation [4]. A universally accepted classical designation of Parijataka Beeja as Keshya was not firmly established in the sources reviewed [5]. The proposed hair-supportive effect is therefore a research hypothesis based on local use and seed pharmacology rather than a claim of explicit classical indication [4].

8. Phytochemical Profile and Structural Presentation

Seed chemistry is less extensively characterised than leaf chemistry, but several constituent classes have been repeatedly reported [5]. Arbortristoside A and arbortristoside B are iridoid glucosides first isolated from the seeds and remain important candidate markers [7]. Reviews and primary studies also describe hydroxyloganin-related iridoids, nyctanthoside-related glycosides, nyctanthic acid, polysaccharide fractions, beta-sitosterol and glycerides or fatty acids such as linoleic, oleic, stearic, palmitic and myristic acids [5]. The identity and abundance of these compounds depend

on plant source, maturity, drying, extraction solvent and analytical method [5].

Arbortristoside A has a reported molecular formula of C27H34O13 and a molecular mass near 566.5 g/mol, reflecting a polyoxygenated glycosidic structure with both polar and aromatic ester features [56]. Beta-sitosterol has a predominantly lipophilic steroidal skeleton with a single hydroxyl group and is therefore expected to partition preferentially into non-polar or lipid-rich phases [57]. Nyctanthic acid has a pentacyclic lipophilic skeleton with a terminal carboxylic-acid group, indicating limited neutral-water affinity but potential pH-dependent ionisation [58]. These structural observations guide solvent selection, but they do not replace experimentally measured equilibrium solubility [47].

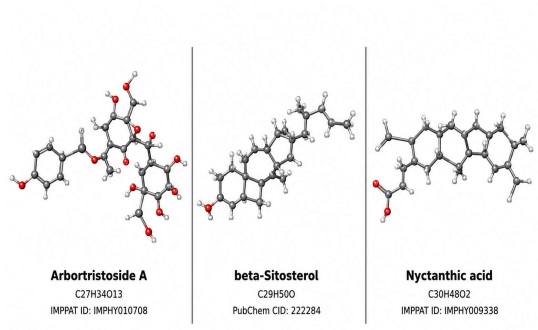

Figure 2. The arbortristoside A structure follows the IMPPAT record [56]. The beta-sitosterol structure follows PubChem [57]. The nyctanthic acid structure follows IMPPAT [58].

Table 5. Major reported phytoconstituent classes of Parijataka seeds and research relevance

Class	Representative constituents	Physicochemical implication	Potential relevance
Iridoid glycosides	Arbortristoside A and B; hydroxyloganin-related compounds [7].	Relatively polar polyoxygenated structures; candidate HPLC/HPTLC markers.	Anti-inflammatory, anti-allergic or immunomodulatory plausibility [10].
Phenolic constituents	Total phenolic fraction and phenylpropanoid-related glycosides [8].	Often extracted by hydroalcoholic or intermediate-polarity solvents.	Redox activity and radical scavenging [8].
Sterols	Beta-sitosterol [14].	Lipophilic; expected in non-polar or lipid fractions.	Anti-inflammatory activity has been reported from plant-derived beta-sitosterol [14].
Fatty acids and glycerides	Linoleic, oleic, stearic, palmitic and myristic components [5].	Lipophilic and vehicle-relevant; may affect spreadability and occlusion.	Formulation role is plausible but hair-specific activity is unproven.
Triterpenoid acid	Nyctanthic acid [58].	Lipophilic skeleton with an ionisable carboxyl group.	Potential analytical marker or supportive constituent; direct AA relevance is unknown.
Polysaccharide fractions	Seed-associated carbohydrate fractions [5].	Water-dispersible or colloidal behaviour may influence paste rheology.	May affect texture and hydration; biological relevance requires direct testing.

9. Methods Used for Extraction and Isolation of Phytoconstituents

9.1 Raw-material processing

Mature fruits should be collected from an authenticated source, and the separated seeds should be cleaned, dried under controlled conditions and milled to a defined particle-size range [50]. Drying temperature and duration should be recorded because excessive heat may alter glycosides, phenolics and unsaturated lipids [5]. The powdered seed should be tested for foreign matter, moisture, total ash, acid-insoluble ash, extractive values, microbial load, pesticide residues, heavy metals and aflatoxins before extraction [50].

9.2 Literature-derived extraction sequence

A published isolation approach used successive extraction with petroleum ether, chloroform and ethanol to separate constituents broadly according to polarity [47]. The ethanolic extract yielded 26.5% w/w relative to the starting material in that study [47]. Further liquid–liquid fractionation with diethyl ether, ethyl acetate and n-butanol concentrated the polar iridoid fraction, and the n-butanol fraction represented 50.32% of the ethanolic extract in the reported process [47]. Subsequent

trituration, washing and crystallisation from chloroform:methanol in a 1:1 ratio produced an arbortristoside-A-rich isolate reported at 5.25% of the relevant processed fraction [47]. These percentages have different denominators and should not be plotted or compared as if they were direct mass-balance equivalents [47].

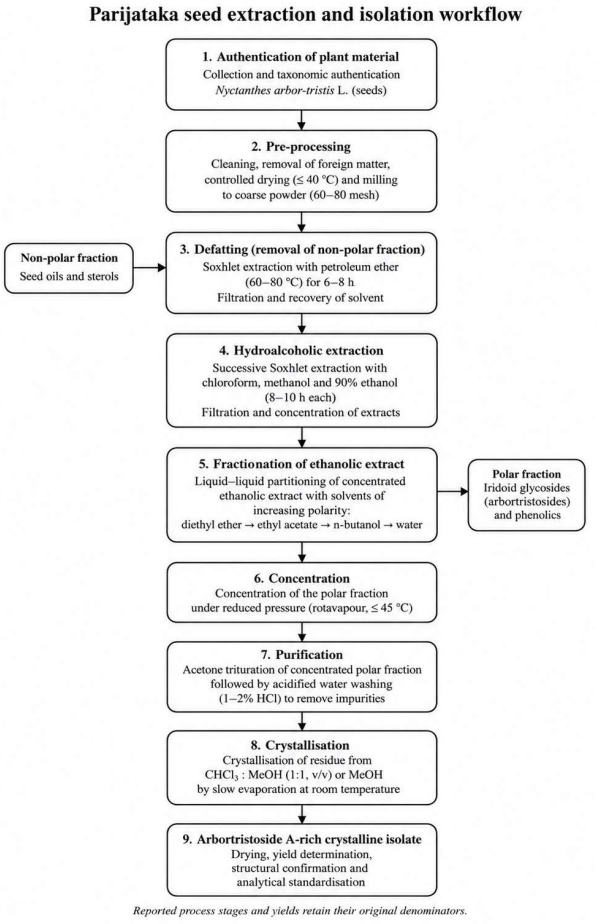

Figure 3. Literature-derived extraction and isolation workflow for Parijataka seed phytoconstituents [47].

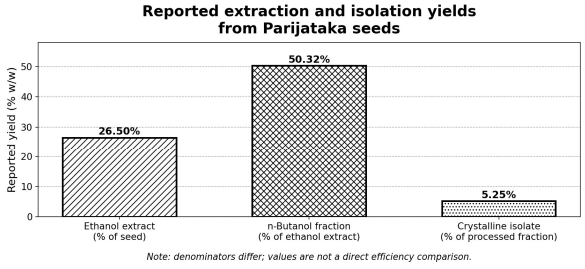

Figure 4. Reported yield-related values from an arbortristoside-A isolation workflow are shown with their original denominators [47].

Table 6. Comparison of extraction and formulation approaches

Approach	Main chemical domain	Advantage	Important limitation
Aqueous maceration / fresh Lepa	Water-soluble glycosides, sugars and colloidal components.	Directly compatible with classical paste preparation and low solvent toxicity.	Lower chemical reproducibility, short microbiological stability and uncertain recovery of lipophilic constituents [52].
Hydroalcoholic extraction	Polar and moderately polar iridoids and phenolics.	Good screening range and easier concentration than water alone.	Residual-solvent control and extract-to-drug ratio must be defined [50].
Ethyl-acetate extraction	Intermediate-polarity phenolics and selected glycosides.	The seed study showed strong antioxidant and membrane-stabilising activity in this fraction [8].	The extract may not represent the composition of an aqueous Lepa.
Non-polar extraction	Seed oils, fatty acids, glycerides and sterols.	Useful for lipid profiling and formulation studies.	Less suitable for direct recovery of highly oxygenated glycosides.
Successive extraction and fractionation	Sequential separation by polarity.	Supports constituent mapping, marker isolation and mechanistic testing [47].	More complex, solvent-intensive and less representative of traditional preparation.

Approach	Main chemical domain	Advantage	Important limitation
Standardised extract hydrogel	Defined extract dispersed in a controlled topical base.	Potentially superior dose uniformity, release and stability.	Requires preservative compatibility, dermal safety and regulatory-quality development [50].

9.3 Proposed extraction-screening study

1. Prepare matched extracts from the same authenticated seed batch using purified water, 50% ethanol, 70% ethanol, 90% ethanol, ethyl acetate and a non-polar solvent under controlled drug-to-solvent ratio, temperature and time [8].
2. Calculate percentage extractive yield on a dry-weight basis and record moisture-corrected mass balance [50].
3. Compare HPTLC fingerprints, total phenolic content and arbortristoside-A peak area across extracts [8].
4. Evaluate antioxidant activity at matched dry-extract concentrations and report IC50 with confidence intervals or standard deviation [8].
5. Select the candidate topical extract by a predefined balance of chemical recovery, dermal compatibility, stability and biological activity rather than by the strongest single in-vitro assay [52].

10. Solubility and Formulation-Relevant Study

10.1 Literature-informed solubility considerations

No validated equilibrium-solubility dataset for arbortristoside A, beta-sitosterol, nyctanthic acid or a standardised Parijataka seed extract in scalp-relevant media was identified in the reviewed literature [48]. The absence of numerical data is important because extraction yield, apparent dispersion and true molecular solubility are different properties [50]. A clear solution, a colloidal dispersion and a suspension may each appear visually uniform but have different release and penetration behaviour [50].

The multiple hydroxyl and glycosidic groups of arbortristoside A suggest higher affinity for polar solvents than the predominantly hydrocarbon frameworks of beta-sitosterol and nyctanthic acid [48]. The aromatic ester and aglycone region of arbortristoside A may nevertheless limit complete water solubility and may create a need for hydroalcoholic, surfactant-assisted or cosolvent systems [48]. Beta-sitosterol is expected to show very low neutral-water solubility and preferential solubilisation in oils, surfactant micelles or organic solvents [57]. Nyctanthic acid is expected to be poorly soluble in neutral water in its unionised form, with increased apparent solubility possible at a pH that promotes carboxylate formation, subject to chemical stability and dermal tolerability [58]. These are structure-based expectations and must be verified experimentally [47].

Table 7. Qualitative solubility expectations derived from structure and extraction behaviour

Material	Structural basis	Expected behaviour	Required confirmation
Arbortristoside A	Multiple hydroxyl groups and a glycosidic aromatic ester are present in the recorded structure [56].	Water / aqueous buffer: potentially dispersible to moderately soluble; hydroalcoholic media: expected higher recovery.	Qualitative expectation only; perform equilibrium and kinetic solubility testing.
Beta-sitosterol	A predominantly lipophilic sterol skeleton contains one hydroxyl group [57].	Water: expected very low; oil, surfactant or organic phase: expected higher.	Measure in selected oils and surfactant systems; avoid assuming extraction equals solubility.
Nyctanthic acid	A pentacyclic lipophilic skeleton contains a terminal carboxylic acid [58].	Neutral water: expected low; alkaline buffer may increase apparent solubility through ionisation.	Evaluate pH-solubility and chemical stability together.
Crude seed powder	Mixture of hydrophilic, lipophilic and colloidal components [5].	Forms a suspension/paste rather than a true solution.	Characterise particle size, sedimentation, rheology and extractable marker release.
Standardised seed extract	Composition depends on extraction solvent and concentration [8].	Solubility depends on marker profile, residual matrix and vehicle.	Report extract-to-drug ratio, solids content and marker concentration.

10.2 Proposed experimental solubility protocol

A shake-flask method is recommended because it can distinguish equilibrium solubility from transient dispersion when sampling and filtration are carefully controlled [51]. Excess test material should be added to each medium, agitated at a defined temperature, sampled at multiple time points and considered at equilibrium only when consecutive measurements remain stable [51]. Samples should be centrifuged or filtered through a validated low-binding membrane, diluted within the validated HPLC range and quantified against an authenticated marker standard [49].

Table 8. Proposed solubility-study design for Parijataka seed markers and extracts

Parameter	Proposed specification
Test materials	Arbortristoside-A reference or enriched isolate, standardised extract and seed powder release sample [48].
Media	Purified water; citrate or phosphate buffers spanning dermally acceptable pH; 10%, 20% and 40% ethanol-water; selected non-ionic surfactant solutions; and candidate oils.
Temperature	25 ± 2°C for formulation screening and 32 ± 1°C to approximate scalp-surface conditions.
Equilibration	Agitate with excess solid and sample at 2, 6, 12, 24 and 48 hours until a plateau is demonstrated.
Separation control	Validate centrifugation or membrane filtration for absence of adsorption and particle carry-over [51].
Quantification	Validated RP-HPLC-UV or LC-MS assay for arbortristoside A, with dilution integrity and system suitability [49].
Reported outputs	Micrograms per millilitre or milligrams per millilitre, pH after equilibration, recovery, mean ± standard deviation and visible phase state.
Interpretation	Select a vehicle that balances solubility, release, stability, scalp tolerability and consistency with the intended Lepa concept.

10.3 Topical release and follicular-access study

Equilibrium solubility alone does not predict delivery from a paste because release depends on vehicle viscosity, particle size, binding to excipients, drying and contact time [50]. A membrane-release study should compare fresh aqueous paste, hydroalcoholic gel and extract hydrogel at equal marker dose [49]. Ex-vivo skin or follicular-deposition studies should quantify marker recovery in the stratum corneum, follicular casts, epidermis and receptor phase without assuming that receptor-phase appearance is required for a local effect [51]. The study should include mass balance and recovery controls so that loss by degradation or adsorption is not misclassified as poor penetration [51].

11. Analytical Evaluation and Standardisation

11.1 Raw-drug quality evaluation

A reproducible Lepa begins with a reproducible seed material, so pharmacognostic identity and contaminant testing must precede pharmacological interpretation [50]. Macroscopy should document seed size, shape, colour, surface characteristics and internal morphology, while microscopy should establish diagnostic tissue features and powder characters [50]. Physicochemical constants should include loss on drying, total ash, acid-insoluble ash, water-soluble extractive and alcohol-soluble extractive values [50]. Safety specifications should cover microbial quality, aflatoxins, pesticide residues, elemental impurities and foreign matter [50].

11.2 Chromatographic fingerprint and marker assay

HPTLC can provide a rapid batch-comparison fingerprint and should include a system-suitability approach, reference marker track, densitometric profile and documented Rf acceptance window [50]. RP-HPLC-UV is suitable for quantitative marker analysis when specificity, linearity, range, accuracy, precision, detection capability and robustness are demonstrated according to ICH Q2(R2) [49]. A recently reported HPLC method for arbortristoside A provides a starting point, but the method must be transferred, verified and validated for the laboratory, matrix and formulation actually used [49]. LC-MS may be added for identity confirmation and impurity profiling, especially when multiple iridoids co-elute or ultraviolet spectra are insufficiently selective [48].

11.3 Structural confirmation of arbortristoside A

A published isolation study described ultraviolet absorption maxima at approximately 206, 227, 300 and 308 nm for the isolated material [47]. The same study reported infrared bands near 3424, 2950, 1719, 1662, 1633, 1514, 1450, 1377, 1216, 1177, 1050, 877, 835, 750 and 591 cm−1, consistent with hydroxyl, carbonyl, aromatic and glycosidic functional groups [47]. Nuclear magnetic resonance and mass spectrometric data were used as orthogonal evidence for structural assignment [47]. Subsequent X-ray crystallographic analysis provided additional structural validation of arbortristoside A isolated from N. arbor-tristis seeds [48].

Table 9. Proposed analytical specification framework

Domain	Test	Purpose
Identity	Macroscopy, microscopy, DNA barcoding where needed and voucher specimen [50].	Prevents substitution or adulteration.

Domain	Test	Purpose
Physicochemical constants	Loss on drying, ash values and solvent extractives [50].	Defines batch consistency and storage suitability.
Contaminants	Microbial limits, aflatoxins, pesticides, heavy metals and foreign matter [50].	Establishes baseline safety.
HPTLC fingerprint	Reference-marker co-chromatography and densitometric profile [50].	Rapid identity and batch-comparison tool.
HPLC marker assay	Arbortristoside-A quantification with validated system suitability [49].	Supports dose normalisation and stability testing.
LC-MS / MS	Accurate-mass or fragmentation confirmation [47].	Improves specificity and impurity characterisation.
UV / FTIR / NMR	Orthogonal identity tests for isolated marker [47].	Supports structural confirmation.
Particle size	Laser diffraction or sieve analysis for powder and microscopy for morphology.	Controls surface area, abrasiveness and release.
Formulation tests	Appearance, pH, viscosity, spreadability, microbial quality, marker uniformity and preservative efficacy [50].	Establishes topical product reproducibility.
Stability	Marker assay, degradation products, pH, viscosity and microbial quality under defined storage [50].	Defines shelf life and packaging.

11.4 Method-validation plan

The quantitative method should demonstrate specificity by showing separation of the marker from matrix peaks, degradation products and vehicle components [51]. Linearity and range should cover the expected sample concentration and all planned dilution steps [51]. Accuracy should be evaluated by recovery at multiple levels, and precision should include repeatability and intermediate precision across analysts, days or instruments [51]. Robustness should examine small deliberate changes in mobile-phase composition, flow rate, temperature and wavelength where technically relevant [51]. A stability-indicating method should include stress conditions appropriate for a glycosidic herbal marker without generating conditions so extreme that they become mechanistically irrelevant [49].

12. Pharmacological Actions Relevant to the Research Hypothesis

12.1 Anti-inflammatory and membrane-stabilising activity

An ethyl-acetate seed extract showed concentration-dependent protection in a human red-blood-cell membrane-stabilisation assay, an in-vitro screening method used to estimate anti-inflammatory potential [8]. The reported concentration producing 50% inhibition was 7.19 ± 1.71 mg/mL for the ethyl-acetate extract in that assay [8]. Arbortristoside A also showed anti-inflammatory and antinociceptive activity in experimental models [9]. These findings justify targeted studies of inflammatory mediators, but they do not demonstrate suppression of the IFN-gamma/IL-15/JAK–STAT circuit in human AA [22].

12.2 Antioxidant activity and comparative data

The seed-extract study reported total phenolic content of 206.81 ± 1.11 mg catechol equivalents per gram for the ethyl-acetate extract [8]. Reported IC50 values for the same extract were 338.82 micrograms per millilitre for superoxide scavenging, 363.32 micrograms per millilitre for hydroxyl-radical scavenging, 459.91 micrograms per millilitre for DPPH scavenging and 545.03 micrograms per millilitre for nitric-oxide scavenging [8]. A lower IC50 indicates greater activity within a given assay, but IC50 values from different radical systems should not be treated as directly interchangeable measures of clinical potency [8]. Oxidative stress is associated with AA, making these data mechanistically relevant, although no evidence shows that radical scavenging by a seed extract alone restores hair-follicle immune privilege [42].

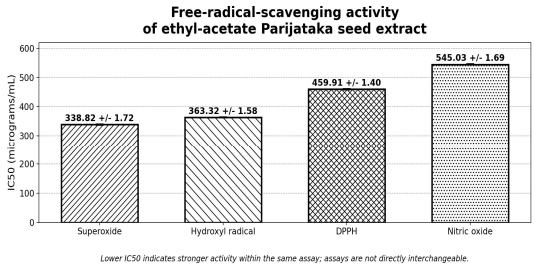

Figure 5. Comparative in-vitro IC50 values and reported errors for antioxidant assays of the ethyl-acetate Parijataka seed extract [8].

12.3 Immunomodulatory and anti-allergic activity

Arbortristosides showed anti-allergic activity in preclinical work, and plant extracts or iridoid glucosides altered immune responses in animal infection models [10]. Oral seed extract enhanced non-specific immune responses in a fish model [13]. These studies show that Parijataka constituents interact with immune pathways,

but the direction of an immune effect may differ according to species, dose, extract and model [10]. Broad immune stimulation cannot be assumed beneficial in an autoimmune disorder, so AA-relevant studies must directly examine pathogenic T-cell activation and follicular signalling [22].

12.4 Antimicrobial, wound-healing and analgesic activities

Antibacterial activity has been reported for selected N. arbor-tristis extracts, particularly from leaves and flowers [16]. Leaf-based wound-healing work and a crocetin phytosome derived from flower calyx support broader skin-repair research, but these findings are not seed-specific evidence for AA [18]. Beta-sitosterol isolated from the plant has demonstrated analgesic and anti-inflammatory activity in experimental models [14]. These actions may contribute to formulation or tolerability hypotheses, but none establishes a direct hair-growth effect [14].

12.5 Hair-growth-specific evidence gap

No robust controlled human study was identified showing that Parijataka seed paste induces clinically meaningful regrowth in AA [5]. Future work should measure human dermal-papilla-cell viability, outer-root-sheath keratinocyte viability, oxidative stress, beta-catenin/Wnt signalling, VEGF, IGF-1, alkaline phosphatase and hair-shaft elongation in organ culture [20]. AA-specific models should additionally examine IFN-gamma, IL-15, CXCL10, MHC expression, NKG2D ligands and JAK/STAT phosphorylation [22]. A result in a general antioxidant assay should not be described as a hair-growth result unless these follicular and clinical endpoints are demonstrated [8].

Table 10. Comparative interpretation of reported pharmacological actions

Action	Evidence	Possible relevance	Main limitation
Anti-inflammatory	Membrane stabilisation and experimental anti-inflammatory activity [8].	Potential reduction of local inflammatory stress.	No direct AA cytokine or topical follicular study.
Antioxidant	Radical-scavenging and lipid-peroxidation assays [8].	Potential support of redox balance.	Chemical assays do not prove tissue exposure or regrowth.
Anti-allergic	Arbortristoside preclinical activity [10].	Suggests modulation of hypersensitivity pathways.	Not equivalent to suppression of AA autoimmunity.
Immunomodulatory	Animal infection and fish immune-response models [11].	Confirms immune interaction.	Direction and relevance to AA are uncertain.
Antinociceptive	Arbortristoside-A experimental activity [9].	May be relevant to inflammatory discomfort.	Pain is not a primary AA endpoint.
Antimicrobial / repair	Studies mainly involving non-seed parts [16].	May inform scalp-supportive formulation research.	Indirect and plant-part-specific evidence.
Hair growth	No adequate controlled human seed-Lepa study identified [5].	Justifies hypothesis generation only.	Efficacy remains unproven.

13. Concept of Lepa Kalpana

Lepa is a topical Ayurvedic dosage form prepared by triturating fresh material or finely powdered dry drug with a suitable liquid medium and applying the paste to the affected site [2]. Classical descriptions distinguish Lepas by purpose and recommend attention to freshness, smoothness, thickness, direction of application and time of removal [2]. Local application offers prolonged contact and may limit systemic exposure compared with internal administration, but local irritation and sensitisation remain possible [52].

Pratiloma application, in a direction opposite to hair growth, may improve contact around follicular openings when performed gently without abrasion [2]. A new layer should not be placed over a dried old layer, and the paste should be removed when it approaches drying rather than being left until excessive cracking or adhesion occurs [2]. These classical principles can be translated into defined mass per square centimetre, controlled contact time, documented vehicle and standardised removal [2].

Table 11. Classical Lepa principles and modern research translation

Classical principle	Research translation
Fine Kalka or Churna with Drava	Authenticated seed, defined drying, sieve size and seed-to-vehicle ratio [2].

Classical principle	Research translation
Fresh preparation	Prepare immediately or develop a preservative-validated standard gel [2].
Pratiloma application	Part hair and apply gently against hair direction without abrasion [2].
Defined thickness	Use a reproducible mass per square centimetre in research.
Remove near drying	Specify contact time during pilot work and rinse gently [2].
Avoid layering or prolonged occlusion	Use a single application on clean dry scalp during early safety studies [2].
Consider patient factors	Record AA phenotype, activity, sensitivity, allergy history and concomitant therapy [31].

14. Proposed Preparation and Application of Parijataka Beeja Lepa

14.1 Research prototype

The following preparation is proposed only as a research prototype and not as a proven clinical prescription [5]. Authenticated seed powder should be passed through a defined sieve and mixed with a measured volume of purified water to obtain a smooth non-dripping paste [50]. An initial ratio of 1 g seed powder to approximately 1.0–1.5 mL water may be explored during rheological optimisation rather than treated as a fixed traditional standard [50]. The final ratio should be selected from spreadability, adhesion, drying time, marker-release and irritation data [49].

Purified water is the least confounded vehicle for an initial safety study because it has minimal independent pharmacological action and supports a clear vehicle control [50]. A standardised extract hydrogel may later provide superior dose uniformity, release and microbiological stability [52]. Sesame oil, aloe gel or other media should be studied separately because each vehicle changes solubility, penetration, occlusion and irritation potential [50].

14.2 Proposed pilot application procedure

1. Confirm dermatologist diagnosis of limited patchy AA and document baseline SALT score, standardised photographs, trichoscopy and disease activity [21].
2. Perform a patch test with the standardised preparation and vehicle control before scalp exposure, with delayed-reaction review where feasible [50].
3. Clean and dry the target patch, then apply a measured dose to the alopecic area plus a predefined margin without contact with eyes, mucosa or broken skin [50].
4. Apply gently in the Pratiloma direction without microneedling, scraping, vigorous rubbing or bloodletting during the initial safety phase [2].
5. Maintain contact for a short predefined period, such as 20–30 minutes in early tolerability work, and remove with lukewarm water before excessive drying [2].
6. Begin with a low application frequency and escalate only after review of burning, erythema, pruritus, scaling, folliculitis and other adverse effects [52].
7. Do not withdraw effective standard treatment in an uncontrolled manner, and define rescue criteria before enrolment [31].

14.3 Formulation quality attributes

The topical product should have defined appearance, pH, viscosity, spreadability, homogeneity, particle size, marker content, microbial quality and drying time [50]. Dose uniformity is especially important because a traditional spoonful or finger-thickness description cannot support a reproducible clinical trial [50]. A preserved hydrogel should undergo preservative-efficacy testing and packaging compatibility, while a fresh paste should have a strict use period and microbial-risk control [50].

15. Probable Mode of Action

15.1 Ayurvedic level

Tikta–Katu, Laghu–Ruksha and Ushna attributes described for Parijataka may conceptually counter Kapha-dominant stagnation and support local Dosha-shamana [4]. Local application may be interpreted as acting at Romakupa to reduce Kapha–Rakta Avarodha and restore a favourable scalp environment [1]. Rakta-prasadana is used here as an Ayurvedic functional interpretation of reduced local disturbance rather than a literal claim of blood purification [1]. A Keshya effect remains hypothetical because it has not been directly established for Parijataka seed in controlled human research [5].

15.2 Pharmaceutical level

A moist paste can increase contact between seed material and the scalp and transiently hydrate the stratum corneum [50]. Fine particles increase surface area for in-situ extraction, while endogenous seed lipids may affect spreading and occlusion [5]. Follicular deposition will depend on particle size, marker solubility, vehicle, dose, contact time and drying behaviour [49]. Excessive drying may increase adhesion, hair pulling and irritation, so overnight exposure is not justified during early investigation [2].

15.3 Modern biological hypothesis

The primary modern hypothesis is that iridoid and phenolic constituents may reduce oxidative and inflammatory stress around the follicle [8]. A secondary hypothesis is preservation of dermal-papilla and outer-root-sheath cell viability, thereby supporting anagen re-entry [20]. These hypotheses must be tested by marker delivery, cell viability, ROS, cytokines, JAK/STAT phosphorylation, MHC expression and hair-organ-culture endpoints [22]. No current evidence

demonstrates that topical Parijataka seed preparation inhibits AA-specific CD8+NKG2D+ T cells in humans [22].

16. Comparative Study with Existing Treatments

Comparative interpretation must distinguish an investigational botanical paste with no controlled AA trial from treatments supported by guidelines and randomised studies [31]. A theoretical advantage such as low systemic exposure cannot be treated as an established safety advantage until dermal absorption, irritation and sensitisation are measured [50]. The proposed Lepa should initially be studied as an adjunct or in carefully selected limited disease rather than described as an alternative equivalent to corticosteroids or JAK inhibitors [31].

Table 12. Comparison of the proposed Lepa with established or commonly used AA treatments

Intervention	Evidence level	Principal role	Important limitation	Position in research
Topical corticosteroid	Guideline-supported for localised scalp AA [31].	Local anti-inflammatory action.	Skin atrophy, telangiectasia or folliculitis with inappropriate use.	Evidence-based local comparator.
Intralesional triamcinolone	Commonly used for small adult patches [31].	Direct delivery to active patches.	Pain, atrophy, pigment alteration.	Useful active comparator but invasive.
Topical minoxidil	Adjunctive evidence with variable study quality [34].	Supports hair growth rather than primary immune suppression.	Irritation, hypertrichosis and incomplete response.	Potential adjunct comparator.
Contact immunotherapy	Systematic-review evidence in extensive disease [39].	Deliberately redirects local immune response.	Eczema, lymphadenopathy, pigment change and repeated visits.	Specialist treatment, not suitable for casual combination.
Systemic JAK inhibitor	Phase 3 and regulatory evidence in severe AA [36].	Targets cytokine signalling central to disease.	Systemic monitoring and class warnings.	Highest mechanistic evidence benchmark.
Parijataka Beeja Lepa	Classical rationale and preclinical seed evidence only [1].	Proposed local antioxidant and anti-inflammatory support.	Uncertain dose, release, penetration, efficacy and sensitisation.	Investigational; requires controlled testing.

16.1 Selected quantitative trial benchmarks

Quantitative trial data provide a useful benchmark for the magnitude and time course expected in severe-AA studies, but cross-trial comparisons are limited by population and design differences [36]. In BRAVE-AA1 and BRAVE-AA2, the proportions achieving SALT ≤20 at week 36 were 38.8% and 35.9% with baricitinib 4 mg, 22.8% and 19.4% with baricitinib 2 mg, and 6.2% and 3.3% with placebo, respectively [36]. In the ritlecitinib pivotal trial and regulatory analysis, approximately 23% of participants receiving 50 mg once daily achieved SALT ≤20 at week 24 compared with about 1.5–1.6% receiving placebo [37]. In THRIVE-AA1, 29.6% of participants receiving deuruxolitinib 8 mg twice daily and 41.5% receiving 12 mg twice daily achieved SALT ≤20 at week 24 compared with 0.8% receiving placebo, although the approved and clinically relevant dose must follow current regulatory labelling [38]. These systemic-treatment outcomes should not be used to predict a response rate for Parijataka Lepa [36].

Table 13. Selected quantitative clinical-trial benchmarks for severe alopecia areata

Study / intervention	Assessment time	Endpoint	Reported response
Baricitinib BRAVE-AA1	Week 36	SALT ≤20	4 mg: 38.8%; 2 mg: 22.8%; placebo: 6.2% [36].
Baricitinib BRAVE-AA2	Week 36	SALT ≤20	4 mg: 35.9%; 2 mg: 19.4%; placebo: 3.3% [36].

Study / intervention	Assessment time	Endpoint	Reported response
Ritlecitinib pivotal study	Week 24	SALT ≤20	50 mg once daily: approximately 23%; placebo: approximately 2% [37].
Deuruxolitinib THRIVE-AA1	Week 24	SALT ≤20	8 mg twice daily: 29.6%; 12 mg twice daily: 41.5%; placebo: 0.8% [38].
Parijataka Beeja Lepa	Not established	No validated response endpoint	No controlled human response rate is available [5].

17. Discussion

The conceptual strength of Parijataka Beeja Lepa lies in the convergence of a classical follicular disease sequence, a recognised topical dosage-form principle and seed constituents with preclinical biological activity [2]. This convergence is sufficient to justify research but is insufficient to justify a therapeutic claim [5]. The most defensible conclusion is that the formulation represents a standardisable hypothesis whose critical variables can be measured [49].

The distinction between active hair fall and failure of regrowth is useful in both classical and modern frameworks [1]. Active AA may require control of perifollicular immune activity, while a stable patch may require support of anagen re-entry and cosmetic recovery [20]. Future studies should stratify disease by activity, duration, extent, ophiasis pattern, nail involvement, atopy and previous treatment because a single response estimate may obscure clinically important subgroups [21].

The seed-specific evidence remains uneven because different studies used crude extracts, isolated compounds, different solvents, different species and different administration routes [8]. The ethyl-acetate fraction showed strong in-vitro antioxidant and membrane-stabilising activity, but a fresh water paste will extract a different chemical spectrum [8]. The arbortristoside isolation studies support marker chemistry and analytical control, but an isolated-compound animal result cannot be transferred directly to a topical powder [48].

Solubility is a central translational issue because a constituent must leave the plant matrix and enter a vehicle phase before diffusion or follicular deposition can occur [49]. A preparation can have high total marker content but low release if the marker remains trapped in particles or precipitates during drying [52]. Conversely, a highly soluble marker may leave the vehicle rapidly but fail to remain at the target site [52]. The optimal product therefore requires a balance of solubility, release, retention, stability and tolerability rather than maximisation of a single parameter [52].

Immunomodulation requires particular caution because enhancement of host defence in an infection model may be irrelevant or undesirable in an autoimmune condition [11]. A useful AA intervention should reduce pathogenic inflammatory signalling without injuring follicular keratinocytes or provoking allergic contact dermatitis [22]. Direct testing against IFN-gamma/IL-15-induced changes, CXCL10 expression, JAK/STAT phosphorylation and NKG2D-ligand pathways is therefore more informative than broad labels such as “immunity booster” [22].

Clinical trials should use SALT, standardised global photography and trichoscopic hair density rather than patient impression alone [20]. Terminal-to-vellus ratio and target-patch hair count can help distinguish fine vellus growth from cosmetically meaningful terminal regrowth [20]. Quality of life, treatment satisfaction, adverse effects, relapse after discontinuation and time to response should be prospectively defined [29]. A follow-up period of sufficient duration is essential because visible hair growth and relapse occur over months rather than days [31].

18. Research Gaps and Future Scope

18.1 Stage 1: botanical and analytical development

- Authenticate seed material by pharmacognostic methods and retain a voucher specimen [50].
- Establish physicochemical constants, contaminants and batch-to-batch fingerprints [50].
- Select arbortristoside A as a provisional marker while confirming whether it is sufficiently abundant, stable and specific [48].
- Validate HPTLC and HPLC methods according to ICH Q2(R2) and define acceptance criteria [49].
- Complete solvent screening, equilibrium-solubility testing and marker-release studies [49].

18.2 Stage 2: formulation and dermal safety

- Compare fresh aqueous paste, aqueous extract gel and hydroalcoholic extract gel at matched marker dose [49].
- Evaluate pH, viscosity, spreadability, drying time, microbial quality, preservative efficacy and stability [50].
- Conduct reconstructed-human-epidermis irritation testing, sensitisation assessment and phototoxicity evaluation where appropriate [50].
- Measure particle morphology and friction because seed powder may abrade sensitive or inflamed scalp [50].
- Perform controlled patch testing in healthy volunteers before exposure in AA patients [50].

18.3 Stage 3: mechanistic and follicular studies

- Use human dermal papilla cells, outer-root-sheath keratinocytes and follicle organ culture [20].

- Model inflammatory stress with IFN-gamma and IL-15 and quantify JAK/STAT phosphorylation, MHC expression and CXCL10 [22].
- Measure cellular ROS, antioxidant defence, viability, apoptosis and inflammatory cytokines [22].
- Assess anagen-associated markers, hair-shaft elongation and reversible versus cytotoxic effects [20].
- Conduct follicular-deposition and skin-mass-balance studies with the validated marker assay [49].

18.4 Stage 4: controlled clinical evaluation

Clinical development could begin with a small randomised, vehicle-controlled, assessor-blinded pilot in adults with limited stable patchy AA [31]. Safety and tolerability should be the primary early objectives, with target-patch hair density or SALT change as exploratory efficacy outcomes [20]. A subsequent study could compare Lepa plus standard topical corticosteroid with vehicle plus standard therapy, provided that marker dose, application method and rescue criteria are standardised [31]. A multicentre trial should be considered only after formulation stability, dermal safety and mechanistic plausibility are established [52].

19. Safety, Precautions and Limitations

Seeds can contain concentrated secondary metabolites and proteins capable of irritation or sensitisation [50]. The scalp is more vulnerable when scratched, infected, inflamed, microneedled or exposed to potent topical medicines [31]. Botanical identity and contaminant control are therefore prerequisites rather than optional enhancements [50].

- Use only authenticated and contaminant-tested material in a defined formulation [50].
- Perform patch testing before scalp use and document delayed reactions where feasible [50].
- Do not combine initially with dermarolling, Prachchhana, chemical irritants or contact immunotherapy because barrier disruption can increase absorption and toxicity [39].
- Exclude fungal infection and cicatricial alopecia before enrolment [20].
- Refer rapidly progressive, extensive, eyebrow/eyelash, childhood or diagnostically uncertain disease for specialist dermatological evaluation [31].
- Do not claim equivalence to corticosteroids, minoxidil or JAK inhibitors without direct comparative trials [34].
- Stop treatment for significant burning, erythema, swelling, blistering, folliculitis or systemic symptoms [52].

The main limitations of this review are the scarcity of seed-specific studies, heterogeneity of extracts, absence of dermal pharmacokinetics, absence of validated numerical solubility data and lack of controlled human hair-regrowth trials [5]. Classical properties are subject to interpretive variation, and modern correlations remain analogical rather than identity statements [1]. Numerical in-vitro results should not be converted into clinical dose recommendations without pharmacokinetic and safety data [8].

20. Conclusion

Indralupta and alopecia areata share a clinically meaningful pattern of patchy non-scarring hair loss with impaired regrowth, although their theoretical frameworks are not identical [1]. Parijataka seeds contain iridoid glycosides, phenolic constituents, sterols and lipid fractions, and preclinical studies report antioxidant, anti-inflammatory, anti-allergic and immunomodulatory activity [10]. Structural and analytical literature supports marker-based standardisation with arbortristoside A and orthogonal chromatographic and spectroscopic confirmation [48].

The reviewed evidence does not establish that Parijataka Beeja Lepa induces clinically meaningful hair regrowth or modifies AA-specific immune pathways in humans [5]. The intervention should therefore remain an investigational concept until solubility, release, dermal safety, follicular target engagement and controlled clinical outcomes are demonstrated [52]. The appropriate next step is a staged programme of authentication, analytical validation, formulation development, mechanistic testing and carefully controlled clinical research [50]. Established dermatological diagnosis, counselling and evidence-based treatment should not be replaced by an unvalidated preparation [31].

References

1. Sushruta. Sushruta Samhita. Nidana Sthana, Kshudraroga Nidana, chapter 13, verses 33–34. In: Shastri AD, editor. Varanasi: Chaukhambha Sanskrit Sansthan; reprint edition.
2. Sushruta. Sushruta Samhita. Sutra Sthana, Vranalepabandhavidhi, chapter 18. In: Acharya YT, editor. Varanasi: Chaukhambha Surbharati Prakashan; reprint edition.
3. Sharngadhara. Sharngadhara Samhita. Uttara Khanda, Lepa-related chapter. In: Murthy KRS, translator. Varanasi: Chaukhambha Orientalia; reprint edition.
4. Chunekar KC, Pandey GS, editors. Bhavaprakasha Nighantu of Bhavamishra. Varanasi: Chaukhambha Bharati Academy; reprint edition.
5. Agrawal J, Pal A. Nyctanthes arbor-tristis Linn—A critical ethnopharmacological review. J Ethnopharmacol. 2013;146(3):645–658. doi:10.1016/j.jep.2013.01.024.
6. Tipugade O, Sawale J, Jadhav N. Nyctanthes arbor-tristis Linn.: comprehensive insights into its medicinal, phytochemical and safety profiles. Nat Prod Res. 2026;40(11):3338–3351. doi:10.1080/14786419.2025.2456086.
7. Purushothaman KK, Mathuram V, Sarada A. Arbortristoside A and B, two iridoid glucosides from Nyctanthes arbor-tristis. Phytochemistry. 1985;24(4):773–776.
8. Vajravijayan S, Udayakumar M, Prabakaran A, Thangaraju N. Anti-inflammatory, antioxidant and free radical scavenging activities of

Nyctanthes arbor-tristis Linn. seed extract under in vitro conditions. Sch Acad J Biosci. 2013;1(6):242–250.
9. Das S, Sasmal D, Basu SP. Anti-inflammatory and antinociceptive activity of arbortristoside-A. J Ethnopharmacol. 2008;116(1):198–203.
10. Gupta PP, Srimal RC, Srivastava M, Singh KL, Tandon JS. Anti-allergic activity of arbortristosides from Nyctanthes arbor-tristis. Int J Pharmacogn. 1995;33(1):70–72.
11. Khan ZK, Manglani A, Shukla PK, Puri A, Saxena RP, Tandon JS. Immunomodulatory effect of plant extracts and iridoid glucosides from Nyctanthes arbor-tristis against systemic candidiasis in mice. Pharm Biol. 1995;33:297–304.
12. Rathore B, Paul B, Chaudhury BP, Saxena AK, Sahu AP, Gupta YK. Comparative studies of different organs of Nyctanthes arbor-tristis in modulation of cytokines in a murine model of arthritis. Biomed Environ Sci. 2007;20(2):154–159.
13. Kirubakaran CJW, Alexander CP, Michael RD. Enhancement of non-specific immune responses and disease resistance on oral administration of Nyctanthes arbor-tristis seed extract in Oreochromis mossambicus. Aquac Res. 2010;41(11):1630–1639.
14. Nirmal SA, Pal SC, Mandal SC, Patil AN. Analgesic and anti-inflammatory activity of beta-sitosterol isolated from Nyctanthes arbor-tristis leaves. Inflammopharmacology. 2012;20(4):219–224.
15. Rathee JS, Hassarajani SA, Chattopadhyay S. Antioxidant activity of Nyctanthes arbor-tristis leaf extract. Food Chem. 2007;103(4):1350–1357.
16. Nair R, Kalariya T, Chanda S. Antibacterial activity of some selected Indian medicinal flora. Turk J Biol. 2005;29:41–47.
17. Khatune NA, Haque ME, Mosaddik MA. Antibacterial activity and cytotoxicity of Nyctanthes arbor-tristis flowers. Fitoterapia. 2001;72(4):412–414.
18. Varadkar M, Gadgoli C. Preparation and evaluation of wound healing activity of phytosomes of crocetin from Nyctanthes arbor-tristis in rats. J Tradit Complement Med. 2022;12(4):354–360. doi:10.1016/j.jtcme.2021.10.002.
19. Bharti M, Saxena RC, Baghel OS, Saxena R, Apte KG. Wound healing activity of leaf of Nyctanthes arbor-tristis Linn. Int J Pharm Sci Res. 2011;2(10):2694–2698.
20. Pratt CH, King LE Jr, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nat Rev Dis Primers. 2017;3:17011. doi:10.1038/nrdp.2017.11.
21. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: Part I. Clinical picture, histopathology, and pathogenesis. J Am Acad Dermatol. 2010;62(2):177–188. doi:10.1016/j.jaad.2009.10.032.
22. Rajabi F, Drake LA, Senna MM, Rezaei N. Alopecia areata: a review of disease pathogenesis. Br J Dermatol. 2018;179(5):1033–1048. doi:10.1111/bjd.16808.
23. Bertolini M, McElwee K, Gilhar A, Bulfone-Paus S, Paus R. Hair follicle immune privilege and its collapse in alopecia areata. Exp Dermatol. 2020;29(8):703–725.
24. Ma T, Zhang T, Miao F, et al. Alopecia areata: pathogenesis, diagnosis, and therapies. MedComm (2020). 2025;6(5):e70182. doi:10.1002/mco2.70182.
25. Kim SY, et al. Alopecia areata: from immunopathogenesis to emerging therapeutic approaches. Front Immunol. 2025;16:1681163.
26. Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. Nature. 2010;466(7302):113–117. doi:10.1038/nature09114.
27. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. Clin Cosmet Investig Dermatol. 2015;8:397–403. doi:10.2147/CCID.S53985.
28. Thompson AR, Tziotzios C, Nesnas J, Randall R, Czachorowski M, Messenger AG. Lifetime incidence and healthcare disparities in alopecia areata: a UK population-based cohort study. Br J Dermatol. 2024;191(6):924–935. doi:10.1093/bjd/ljae307.
29. Toussi A, Barton VR, Le ST, Agbai ON, Kiuru M. Psychosocial and psychiatric comorbidities and health-related quality of life in alopecia areata: a systematic review. J Am Acad Dermatol. 2021;85(1):162–175. doi:10.1016/j.jaad.2020.06.047.
30. Rencz F, Gulacsi L, Pentek M, et al. Alopecia areata and health-related quality of life: a systematic review and meta-analysis. Br J Dermatol. 2016;175(3):561–571.
31. Harries MJ, et al. British Association of Dermatologists living guideline for managing people with alopecia areata 2024. Br J Dermatol. 2025;192(2):190–230.
32. Cranwell WC, Lai VW, Photiou L, et al. Treatment of alopecia areata: an Australian expert consensus statement. Australas J Dermatol. 2019;60(2):163–170.
33. Delamere FM, Sladden MJ, Dobbins HM, Leonardi-Bee J. Interventions for alopecia areata. Cochrane Database Syst Rev. 2008;(2):CD004413.
34. Freire PCB, Riera R, Martimbianco ALC, Petri V, Atallah AN. Minoxidil for patchy alopecia areata: systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2019;33(9):1792–1799. doi:10.1111/jdv.15545.
35. Yee BE, Tong Y, Goldenberg A, Hata T. Efficacy of different concentrations of intralesional triamcinolone acetonide for

alopecia areata: a systematic review and meta-analysis. J Am Acad Dermatol. 2020;82(4):1018–1021.
36. King B, Ohyama M, Kwon O, et al. Two phase 3 trials of baricitinib for alopecia areata. N Engl J Med. 2022;386(18):1687–1699. doi:10.1056/NEJMoa2110343.
37. King B, Zhang X, Harcha WG, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b–3 trial. Lancet. 2023;401(10387):1518–1529. doi:10.1016/S0140-6736(23)00222-2.
38. King B, Senna MM, Mesinkovska NA, et al. Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: results from the phase 3 THRIVE-AA1 trial. J Am Acad Dermatol. 2024;91(5):880–888. doi:10.1016/j.jaad.2024.06.097.
39. Lee S, Kim BJ, Lee YB, Lee WS. Hair regrowth outcomes of contact immunotherapy for patients with alopecia areata: a systematic review and meta-analysis. JAMA Dermatol. 2018;154(10):1145–1151. doi:10.1001/jamadermatol.2018.2312.
40. US Food and Drug Administration. Olumiant (baricitinib) prescribing information for severe alopecia areata. Silver Spring, MD: FDA; 2022.
41. US Food and Drug Administration. Litfulo (ritlecitinib) prescribing information. Silver Spring, MD: FDA; 2023; and Leqselvi (deuruxolitinib) prescribing information. Silver Spring, MD: FDA; 2024.
42. Acharya P, Mathur MC. Oxidative stress in alopecia areata: a systematic review and meta-analysis. Int J Dermatol. 2020;59(4):434–440. doi:10.1111/ijd.14753.
43. Ma Y, et al. Oxidative stress and alopecia areata. Front Med (Lausanne). 2023;10:1181572. doi:10.3389/fmed.2023.1181572.
44. Lee S, Lee H, Lee CH, Lee WS. Comorbidities in alopecia areata: a systematic review and meta-analysis. J Am Acad Dermatol. 2019;80(2):466–477.e16.
45. Broadley D, McElwee KJ. A “hair-raising” history of alopecia areata. Exp Dermatol. 2020;29(3):208–222. doi:10.1111/exd.14073.
46. Callander J, Yesudian PD. Nosological nightmare and etiological enigma: a history of alopecia areata. Skin Appendage Disord. 2018;4:236–244. doi:10.1159/000485080.
47. Das S, Das S, Singh AP, et al. Arbortristoside-A: a promising bioactive moiety from Nyctanthes arbor-tristis Linn. against hemorrhoid. Pharmacogn Mag. 2021;17(76):695–699. doi:10.4103/pm.pm_573_20.
48. Gupta D, Vikram VN, Lama P, et al. Isolation of Arbortristoside-A from Nyctanthes arbor-tristis seeds and structural validation by X-ray crystallographic analysis. Nat Prod Res. 2024;38(18):3237–3243. doi:10.1080/14786419.2023.2228985.
49. Gupta D, Singh S, Tiwari AK, et al. Quantification of Arbortristoside-A isolated from Nyctanthes arbor-tristis using HPLC: method development and pharmaceutical applications. J Chromatogr B Analyt Technol Biomed Life Sci. 2024;1233:123985. doi:10.1016/j.jchromb.2023.123985.
50. World Health Organization. Quality control methods for herbal materials. Geneva: WHO; 2011.
51. International Council for Harmonisation. ICH Q2(R2): Validation of Analytical Procedures. Geneva: ICH; 2023.
52. European Medicines Agency. Guideline on quality of herbal medicinal products/traditional herbal medicinal products. Revision 3. Amsterdam: EMA; 2022.
53. European Medicines Agency. Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products. Revision 3. Amsterdam: EMA; 2022.
54. Vivek-Ananth RP, Mohanraj K, Sahoo AK, Samal A. IMPPAT 2.0: an enhanced and expanded phytochemical atlas of Indian medicinal plants. ACS Omega. 2023;8(9):8827–8845. doi:10.1021/acsomega.3c00156.
55. Kim S, Chen J, Cheng T, et al. PubChem 2023 update. Nucleic Acids Res. 2023;51(D1):D1373–D1380. doi:10.1093/nar/gkac956.
56. IMPPAT. Phytochemical record for Arbortristoside A, IMPHY010708. IMPPAT 2.0; accessed 24 July 2026.
57. National Center for Biotechnology Information. PubChem Compound Summary for CID 222284, beta-Sitosterol. Bethesda, MD: NCBI; accessed 24 July 2026.
58. IMPPAT. Phytochemical record for Nyctanthic acid, IMPHY009338. IMPPAT 2.0; accessed 24 July 2026.
59. World Health Organization. Guidelines for selecting marker substances of herbal origin for quality control of herbal medicines. WHO Technical Report Series 1003, Annex 1. Geneva: WHO; 2017.