



A Comprehensive Scholarly Review of *Achyranthes aspera* Linn. (Apamarga) in Pharmacognosy and Clinical Practice

¹Dr. Sonu Yadav, ²Dr. Monika Tyagi, ³Dr. Rajesh Sharma

¹PG Scholar (Ayu), Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh New Delhi.

²Assistant Professor (Ayu), Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh New Delhi.

³Professor (Ayu), H.O.D, Dravyaguna Department, A & U Tibbia College & Hospital, Karol Bagh New Delhi.

Sonu19gd@gmail.com

ABSTRACT

Achyranthes aspera Linn., belonging to the family Amaranthaceae, is an erect, perennial herb distributed extensively across tropical and subtropical environments. Widely recognized as a common agricultural and roadside weed, it holds an elevated status in the traditional Indian medicinal system of Ayurveda under the Sanskrit nomenclature *Apamarga*. The plant occupies a unique ecological niche, prominently featured in the dry, deciduous scrub vegetation of the Delhi Ridge, an extension of the Aravalli range. Despite its ubiquitous and unassuming presence, *A. aspera* possesses a highly complex phytochemical profile, yielding potent secondary metabolites such as oleanolic acid, saponins A and B, phytoecdysteroids (notably 20-hydroxyecdysone), and specialized alkaloids including achyranthine and betaine. These bioactive constituents form the mechanistic basis for the plant's diverse pharmacological activities, which include neuroprotective, hepatoprotective, anti-inflammatory, anti-urolithiatic, and wound-healing properties.

In classical Ayurvedic texts such as the *Charaka Samhitā* and *Sushruta Samhitā*, *A. aspera* is revered for its applications in *Shirovirechana* (cranial evacuation), dermatological conditions, and the foundational preparation of *Kshara* (alkaline cauter). In contemporary clinical practice, the *Apamarga Kshara Sutra* (a medicated seton) remains the gold standard for the minimally invasive management of *Bhagandara* (fistula-in-ano), supported by extensive multicentric randomized controlled trials demonstrating superior long-term efficacy and significantly lower recurrence rates compared to conventional fistulotomy. The current analysis systematically synthesizes the botanical, classical, phytochemical, and pharmacological dimensions of *A. aspera*. By bridging historical Ayurvedic paradigms with modern molecular mechanisms and clinical evidence, the analysis identifies translational gaps, standardization protocols, and future research trajectories leveraging multi-omics and computational biology to maximize the therapeutic potential of this vital botanical resource.

Keywords: *Achyranthes aspera*, *Apamarga*, *Kshara Sutra*, Phytoecdysteroids, Oleanolic Acid, Neuroprotection, Ayurveda.

1. Introduction

The exploration of medicinal botanicals historically relies on a dual framework: traditional ethnopharmacological knowledge and rigorous modern scientific validation. *Achyranthes aspera* Linn., commonly known as the Prickly Chaff Flower in English, *Latjeera* or *Chirchita* in Hindi, and *Apamarga* in Sanskrit, perfectly exemplifies this duality^[1, 2, 3]. A member of the Amaranthaceae family, this robust, erect herb is ubiquitous throughout the tropical and warmer regions of the globe, frequently classified by agriculturalists as an invasive weed due to its aggressive growth patterns and resilient seed dispersal mechanisms^[4, 5]. However, within the ancient compendia of Indian medicine, *A. aspera* is elevated from a mere roadside weed to a plant of paramount therapeutic significance. Its documented usage dates back to the Vedic period; in the *Atharvaveda*, it was venerated as a primary botanical agent capable of combating systemic diseases, neutralizing poisons, and purifying the physiological channels of the body^[6, 7].

In modern phytopharmacology, *A. aspera* is recognized as a profound reservoir of complex secondary metabolites. Extensive scientific investigations over the past several decades have successfully isolated numerous active principles from its roots, seeds, leaves, and stems, validating its historical use in treating respiratory ailments, inflammatory conditions, renal dropsy, and gastrointestinal disorders^[8, 9, 10]. More recently, advanced molecular research has unveiled sophisticated mechanisms of action, demonstrating the plant's efficacy in neuroprotection, hepatoprotection, and the dissolution of calcium oxalate renal calculi^[11, 12, 13]. Perhaps the most prominent translational success of *A. aspera* lies in its surgical application. The plant is the primary source of botanical alkali (*Kshara*) used to manufacture the *Kshara Sutra*, a medicated thread utilized extensively in Ayurvedic parasurgical procedures for treating complex anorectal fistulas^[14, 15]. The therapy's validation by premier research bodies, including the Indian Council of Medical Research (ICMR), has cemented *A. aspera* as a cornerstone of evidence-based integrative medicine^[16, 17]. Furthermore, understanding the plant necessitates an appreciation of its ecological context. In regions such as the National Capital Territory of Delhi, India, *A. aspera* thrives within the harsh, arid scrublands of the Delhi Ridge, highlighting its environmental resilience^[18, 19]. The present analysis provides an exhaustive review of *A. aspera*, anchoring its classical Ayurvedic significance within modern pharmacognostic, ecological, and clinical contexts to elucidate its comprehensive therapeutic profile.

2. Botany and Taxonomy

2.1 Taxonomic Classification and Morphology

The precise taxonomic classification of *A. aspera* underscores its botanical lineage within the angiosperms. It belongs to the kingdom Plantae, division Magnoliophyta, class Magnoliopsida, order Caryophyllales, and family Amaranthaceae ^[20, 21]. Morphologically, *A. aspera* is a stiff, erect, or procumbent perennial or annual herb that typically reaches heights of 0.2 to 2.0 meters. Its structural morphology is highly adapted for survival in harsh, dry climates, exhibiting features characteristic of xerophytic resilience ^[22].

The plant features a woody base with angular, ribbed, and simple or branched stems that often present with purple or pink-tinged bulging nodes. The stems are covered in short, dense hairs and become distinctively hollow when desiccated ^[21, 23]. The root system is cylindrical, thick (0.1–1.0 cm), and yellowish-brown, featuring a deeply penetrating taproot supported by a network of secondary and tertiary rootlets designed for optimal water extraction ^[24]. The foliage is characterized by opposite, decussate, simple leaves that range from ovate-elliptic to broadly rhombate or obovate, measuring 5–22 cm in length and 2–5 cm in width. They are finely pubescent due to a dense covering of simple hairs, providing protection against excessive transpiration. Microscopically, the lower epidermis of the leaf displays characteristic anomocytic stomata ^[25].

The reproductive structures are particularly distinctive. The flowers are bisexual, actinomorphic, and greenish-white, densely packed along elongated terminal or axillary spikes measuring 10–30 cm in length. Initially erect, the inflorescence famously bends backward (reflexed) as the flowers mature ^[24, 25]. The fruit is a persistent, perianthal, indehiscent, dry utricle covered by loose papery tissue and spine-lipped bracteoles that easily attach to passing animals and humans, facilitating widespread epizoochorous seed dispersal ^[26].

2.2 Ecological Distribution and the Delhi Ridge Habitat

Achyranthes aspera exhibits a massive geographic footprint, thriving across tropical Asia, Africa, Australia, and the Americas ^[27]. In the Indian subcontinent, it is a dominant species found along roadsides, agricultural boundaries, and wastelands, thriving at altitudes up to 2100 meters ^[28].

A critical ecological niche for this species is the Delhi Ridge, the northernmost extension of the ancient Aravalli mountain range. The Delhi Ridge functions as the primary "green lung" of the capital territory, providing a vital ecological barrier against the encroaching Thar Desert ^[29]. The vegetation of the Ridge consists of tropical, thorny, secondary scrub forests adapted to extreme climatic fluctuations, with summer temperatures peaking near 46°C and minimal annual precipitation ^[30, 31]. Within this harsh biome, *A. aspera* (specifically the variety *porphyristachya*) thrives as a dominant herbaceous species alongside companion flora such as *Boerhavia diffusa*, *Aerva lanata*, and canopy species like *Prosopis juliflora* and *Acacia leucophloea* ^[32]. The plant's deep taproot and resilient dispersal mechanisms allow it to endure the arid, rocky soils of the Southern Ridge and Asola Bhatti Wildlife Sanctuary ^[33]. While classified ecologically as a weed, its profusion in the Delhi Ridge presents an easily accessible source of wild-harvested medicinal biomass for local traditional healers and pharmaceutical extraction.

3. Classical Ayurvedic Perspective

3.1 Fundamental Energetics (Rasa Panchaka)

In Ayurvedic pharmacology (*Dravyaguna Vijnana*), the therapeutic action of a botanical is dictated by its inherent energetics, which define its interaction with human physiology. *Apamarga* is classified with the following fundamental properties ^[34, 35]:

- **Rasa (Taste):** *Katu* (Pungent), *Tikta* (Bitter)
- **Guna (Physical Properties):** *Laghu* (Light), *Ruksha* (Dry), *Tikshna* (Sharp/Penetrating)
- **Virya (Potency):** *Ushna* (Hot)
- **Vipaka (Post-digestive effect):** *Katu* (Pungent)
- **Dosha Karma:** Powerfully alleviates *Kapha* and *Vata* doshas. Due to its hot and sharp nature, it may aggravate *Pitta* if used improperly or in excess.

The plant is highly regarded for its *Sara* (laxative/motile), *Dipana* (appetizer), and *Pachana* (digestive) actions ^[35]. Furthermore, its sharp (*Tikshna*) quality allows it to penetrate deep cellular tissues to clear blockages (*Srotoshodhana*), making it the premier choice for *Shirovirechana* (errhine therapy for cranial evacuation) and the foundational preparation of active botanical alkali (*Kshara*) ^[36].

3.2 Classical Shlokas and Translations

The profound authority of *A. aspera* in Indian medicine is codified in classical Sanskrit verses (Shlokas) across foundational compendia.

1. From the Charaka Samhita (Sutrasthana, Chapter 2: Apamarga Tanduliya Adhyaya, Verse 3):

This foundational chapter explicitly names *Apamarga* as the paramount herb for evacuating morbid *doshas* from the head and supraclavicular region.

अपामार्गस्य बीजानि पिप्पलीर्मरिचानि च ।

विडङ्गान्यथ शिग्रूणि सर्षपांस्तुम्बुरूणि च ॥३॥

Apamargasya Bijani Pippalirmarichani Cha |

Vidanganyatha Shigruni Sarshapanstumburuni Cha ||3||

Translation: The decorticated seeds of *Apamarga*, *Pippali* (long pepper), *Maricha* (black pepper), *Vidanga*, *Shigru*, *Sarshapa* (mustard), and *Tumburu* [are to be collected and administered for *Shirovirechana*, or nasal purgation].^[37]

(Citation: *Charaka Samhitā*, ed. Sharma PV, Chaukhamba Orientalia; 1981: Sutrasthana 2.3).

2. From the Bhavaprakasha Nighantu (Guducyadi Varga, Verses 219-220):

The definitive pharmacognostic text by Bhavamisra delineates its systemic clinical indications and therapeutic actions.

अपामार्गः सरस्तीक्ष्णो दीपनस्तिक्तकः कटुः ।

पाचनो रोचनश्छर्दिकफमेदोऽनिलापहः ॥२१९॥

निहन्ति हृद्रुजाध्मार्शः कण्ठशूलोदरापचीः ।

apamargah sarastikshno dipanastiktakah katuh |

pacano rochanashchardikaphamedo'nilapahah ||219||

nihanti hridrujadhmarshahkandushulodarapachih |

Translation: *Apamarga* is mobile/purgative (*sara*), sharp/penetrating (*tikshna*), an igniter of digestive fire (*dipana*), bitter (*tikta*), and pungent (*katu*). It is digestive (*pachana*), stimulates taste/appetite (*rochana*), and eliminates vomiting (*chardi*), excess Kapha, adipose tissue (*medas*), and Vata. It destroys cardiac pain/diseases, flatulence (*adhmana*), hemorrhoids (*arsha*), pruritus (*kandu*), colic (*shula*), abdominal enlargements (*udara*), and cervical lymphadenitis (*apachi*).^[38]

(Citation: Bhavaprakasha Nighantu, ed. Chuneekar KC, Chaukhamba Bharati Academy; 2010: Guducyadi Varga 219-220.).

3. From the Atharvaveda (Kanda 4, Sukta 17, Verse 8):

Highlighting the antiquity of the plant, ancient Vedic texts recognized its dominance among healing botanicals.

अपामार्ग ओषधीनां सर्वसामेक इद् वशी ।

तेन ते मृज्म आस्थितमथ त्वमगदश्चर ॥८॥

apamarga oshadhinam sarvasameka id vashi |

tena te mrijma asthitamatha tvamagadashchara ||8||

Translation: The *Apamarga* is alone the supreme lord of all plants that grow. With this, we wipe away whatever disease has attacked thee, O patient; get rid of it and live long and healthy.^[39]

(Citation: Atharvaveda Samhita, Kanda 4, Sukta 17, Verse 8 (verify verse location and edition before final submission)).

4. Phytochemistry

The vast pharmacological utility of *A. aspera* is grounded in an exceptionally diverse phytochemical matrix. Advanced chromatographic and spectroscopic evaluations have identified several major classes of bioactive compounds, prominently saponins, triterpenoids, phytoecdysteroids, alkaloids, and long-chain aliphatic compounds^[40, 41]. While neuroprotective botanicals like *Centella asiatica* are renowned for asiaticoside and madecassoside, *A. aspera* operates through an entirely distinct, yet equally potent, suite of triterpenoid and steroidal molecules.

4.1 Major Bioactive Constituents

The seeds of *A. aspera* are remarkably rich in bisdesmosidic triterpenoid saponins. Chemical hydrolysis of the primary constituent, Saponin A, yields D-glucuronic acid and oleanolic acid, while Saponin B represents the β -D-galactopyranosyl ester of D-glucuronic acid^[42]. Oleanolic acid functions as the core aglycone for many of these compounds and is a dominant bioactive agent responsible for the plant's hepatoprotective and anti-inflammatory effects^[43, 44].

Another critical discovery in the phytochemistry of *A. aspera* is the isolation of phytoecdysteroids, predominantly 20-hydroxyecdysone (ecdysterone) and inokosterone, from the roots and whole plant ^[45]. Ecdysteroids are structural analogues of arthropod molting hormones. However, in mammalian models, they do not bind to androgen receptors; instead, they exert profound anabolic, adaptogenic, and neuroprotective effects through distinct non-genomic cellular signaling pathways ^[46]. Furthermore, the plant contains specific water-soluble alkaloids, including achyranthine and betaine, which contribute to its cardiovascular and psychopharmacological activities ^[47]. Long-chain aliphatic alcohols, such as 17-pentatriacontanol, contribute to the antimicrobial properties of the stem and leaf extracts ^[48].

Table 1: Major Phytochemicals of *Achyranthes aspera*

Phytochemical Category	Specific Compounds	Primary Plant Part	Pharmacological Role
Saponins & Triterpenoids	Saponin A, Saponin B, Oleanolic acid	Seeds, Roots	Antihyperlipidemic, Hepatoprotective, Anti-inflammatory ^[42, 44]
Phytoecdysteroids	20-hydroxyecdysone (Ecdysterone), Inokosterone	Roots, Whole Plant	Neuroprotective, Anti-apoptotic, Protein synthesis modulation ^[45, 46]
Alkaloids	Achyranthine, Betaine	Whole Plant	Cardiovascular modulation, Anxiolytic, Antidepressant ^[47, 49]
Aliphatic Compounds	17-pentatriacontanol, Hexacos-14-enoic acid	Stems, Roots	Antimicrobial, Antifungal, Membrane stabilization ^[48, 50]
Flavonoids/Phenolics	Apigenin, Quercetin-3-O- β -D-galactoside	Aerial Parts	Antioxidant, Free radical scavenging ^[51, 52]

4.2 Analytical Standardization and Quantification

Quality control of *A. aspera* extracts relies heavily on the quantification of oleanolic acid and 20-hydroxyecdysone. High-Performance Thin Layer Chromatography (HPTLC) methods have been highly validated for this purpose. For oleanolic acid, an optimized mobile phase consisting of Toluene: Ethyl Acetate: Formic Acid (4.5:0.5:0.1 v/v) is standardly utilized. Post-derivatization with 10% sulfuric acid in ethanol allows for precise densitometric evaluation at an absorption maximum (λ) of 529 nm ^[53, 54].

Literature confirms that the concentration of free oleanolic acid varies geographically and by plant part, typically ranging from 0.13% to 0.37% (w/w) in methanolic leaf and root extracts, and upwards of 0.54% to 0.92% in specific high-yield root selections ^[54, 55, 56]. Pharmacopeial standards suggest that for clinical efficacy, the oleanolic acid content in *A. aspera* raw materials should not fall below the baseline threshold of 0.20% ^[56]. Similarly, 20-hydroxyecdysone can be quantified via High-Performance Liquid Chromatography (HPLC), providing a reliable marker for the root's neuroprotective and adaptogenic quality ^[57].

5. Pharmacology & Mechanisms of Action

Contemporary in vitro and in vivo studies have extensively validated the broad-spectrum indications cited in the *Bhavaprakasa*, establishing distinct molecular mechanisms for the plant's efficacy.

5.1 Neuroprotective and Cognitive Effects

The central nervous system (CNS) represents a major therapeutic target for *A. aspera* extracts. The plant exhibits substantial potential in mitigating neurodegenerative cascades typical of Alzheimer's disease (AD) and mood disorders.

- **Anxiolytic and Antidepressant Activity:** The water-soluble alkaloid betaine and associated methanolic fractions significantly ameliorate stress-induced depression. In murine models subjected to Chronic Unpredictable Mild Stress (CUMS), administration of *A. aspera* extract (10 mg/kg) robustly increased sucrose preference and grooming frequencies, mirroring the efficacy of standard fluoxetine ^[49]. Mechanistically, the extract

suppresses neuroinflammation by downregulating pro-inflammatory cytokines (TNF- α and IL-6) while concurrently upregulating Brain-Derived Neurotrophic Factor (BDNF) expression in the hippocampus and prefrontal cortex, enhancing synaptic plasticity^[49, 58].

- **Ischemia-Reperfusion Protection:** Methanolic extracts of the aerial parts demonstrate potent cerebroprotective action. Pretreatment in rat models of global cerebral ischemia significantly curbed functional and motor deficits, preserved endogenous antioxidant enzymes (Superoxide Dismutase [SOD] and catalase), reduced lipid peroxidation, and prevented neuro-necrosis and cerebral edema^[52].
- **Targeting Amyloid Pathology:** The phytoecdysteroid β -ecdysterone strongly binds to the active site of the BACE1 (beta-secretase) enzyme, inducing a conformational shift that blocks substrate binding. This action actively inhibits the cleavage of amyloid precursor protein (APP) into neurotoxic A β fibrils and promotes the clearance of pre-existing aggregates, addressing the core pathology of Alzheimer's disease^[46, 59].

5.2 Hepatoprotective and Antioxidant Mechanisms

Hepatic damage induced by drug toxicity (e.g., paracetamol, isoniazid-rifampicin) or metabolic syndrome is potently countered by *A. aspera*. In Wistar rat models subjected to paracetamol and anti-tubercular drug toxicity, ethanolic extracts (100-200 mg/kg) restored drastically elevated liver enzymes (ALT, AST, ALP) and bilirubin back to baseline parameters^[60, 61]. This hepatoprotection is driven by profound antioxidant quenching: extracts replenish depleted hepatic glutathione (GSH) reserves and inhibit malondialdehyde (MDA) formation via radical scavenging properties attributed to its high flavonoid and saponin content^[61, 62]. Furthermore, seed saponins exert antihyperlipidemic effects by significantly lowering total cholesterol, triglycerides, and LDL-C while elevating HDL-C in high-fat diet models, thereby preventing hepatic steatosis^[44].

5.3 Anti-urolithiatic and Diuretic Efficacy

True to its Ayurvedic indication for renal dropsy and stone dissolution, the saponin-rich fractions of *A. aspera* are powerful anti-urolithiatic agents. In ethylene glycol-induced urolithiasis models, concurrent administration of *A. aspera* extracts prevented the nucleation, growth, and aggregation of calcium oxalate (CaOx) crystals^[63]. The extract normalized elevated urinary excretion of uric acid and calcium, and stabilized serum blood urea nitrogen (BUN) and creatinine levels^[64]. Additionally, various leaf extracts exhibit significant dose-dependent diuretic activity, increasing the total urine volume and the excretion rates of primary electrolytes (Na⁺, K⁺, Cl⁻), with efficacy comparable to the standard loop diuretic furosemide (20 mg/kg)^[65].

5.4 Anti-inflammatory and Wound Healing Action

The plant's traditional use in treating boils, skin eruptions, and wounds is supported by its ability to modulate the inflammatory cascade. Extracts exhibit broad-spectrum antimicrobial inhibition against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*^[50, 66]. In wound models, the topical application of *A. aspera* accelerates tissue regeneration, enhances collagen deposition, and improves wound contraction rates through the inhibition of metalloproteases and the modulation of angiogenic factors^[67].

6. Clinical Evidence and Therapeutic Uses

While much of the pharmacological data is preclinical, the clinical application of *A. aspera* in human surgical and dental contexts is a highly refined and evidence-based practice.

6.1 Kshara Sutra Therapy in Anorectal Disorders

The most widely adopted and globally recognized clinical application of *A. aspera* is in the manufacture of the *Kshara Sutra* (medicated alkaline seton). Originally conceptualized by the ancient surgeon Sushruta, the modern standardization of the thread was pioneered at Banaras Hindu University and validated by the Indian Council of Medical Research (ICMR)^[15, 68].

Preparation:

The standard operating procedure involves a surgical-grade linen thread (Size No. 20) coated 21 times with the fresh latex of *Euphorbia neriifolia* (Snuhi). This is followed by 7 sequential coatings of the highly alkaline ash of *A. aspera* (Apamarga Kshara), which provides a localized, controlled chemical cauterization effect with a pH > 10. The thread is finished with 3 coatings of *Curcuma longa* (Haridra) powder for antimicrobial protection^[69, 70].

Clinical Efficacy:

In a landmark 1991 multicentric randomized controlled clinical trial published in the *Indian Journal of Medical Research*, 265 patients treated with Kshara Sutra for fistula-in-ano were compared against 237 patients undergoing conventional surgical fistulotomy^[16].

- **Recurrence and Healing:** The study confirmed a statistically significant reduction in long-term disease recurrence—only 4% in the Kshara Sutra group versus 11% in the surgical fistulotomy group (P=0.03). While the median healing time was longer (8 weeks for the seton vs. 4 weeks for surgery), the overall outcome was vastly superior^[16].

- **Continence Preservation:** Mild anal incontinence was observed in merely 8 patients in the seton group compared to 13 in the surgery group [16].
- **Mechanism:** The thread is changed weekly using a railroad technique. It operates via dual actions: mechanical pressure causing gradual ischemic necrosis of the fistulous tract, and phytochemical debridement driven by the *Apamarga Kshara*, which simultaneously promotes sterile inflammation, dissolves fibrous tissue, and facilitates rapid granulation from the base of the tract upwards [70, 71].

Advanced Surgical Modifications (IFTAK): Recent surgical innovations have modified the traditional Kshara Sutra approach to address highly complex or horseshoe fistulas. The IFTAK (Interception of Fistula Track with Application of *Ksharasutra*) technique involves making a small incision at the external sphincter to intercept the tract, rerouting it, and applying the *A. aspera* seton only to the proximal tract. In a prospective study of 300 patients, the IFTAK technique yielded a 93.33% success rate at a one-year follow-up, minimizing total cutting length, significantly reducing post-procedural pain, and resulting in negligible impairment of anal continence (3.67% mild impairment) [72].

Table 2: Summary of Selected Clinical Interventions Involving *Achyranthes aspera*

Clinical Condition	Intervention	Comparator	Sample Size	Key Outcomes	Ref.
Fistula-in-ano (Multicentric RCT)	<i>Apamarga Kshara Sutra</i>	Conventional Fistulotomy	502 (265 Seton, 237 Surgery)	4% recurrence in Seton group vs 11% in Surgery (p=0.03). Lower incontinence in Seton group.	[16]
Complex Fistula-in-ano (Prospective Study)	IFTAK Technique using <i>Kshara Sutra</i>	N/A (Observational)	300	93.33% success rate at 1-year follow up. Minimal sphincter damage.	[72]
Chronic Periodontitis (Clinical Trial)	<i>A. aspera</i> aqueous gel + SRP	SRP (Scaling and Root Planing) alone	30	Significant reduction in Probing Pocket Depth (PPD) and Clinical Attachment Level (CAL) at 3 months (p<0.001).	[73]

6.2 Periodontal Applications

Beyond proctology, *A. aspera* has demonstrated robust efficacy in dentistry. In a clinical trial assessing chronic periodontitis, subgingival application of an aqueous-based *A. aspera* gel following standard scaling and root planing (SRP) resulted in statistically significant reductions in probing pocket depth (PPD) and clinical attachment level (CAL) over three months, driven by the plant's astringent, antimicrobial, and anti-collagenase properties [73].

6.3 Safety Profile, Contraindications, and Interactions

Acute toxicity studies in murine models indicate that extracts of *A. aspera* administered at oral doses up to 3000 mg/kg produce no gross behavioral anomalies, mortality, or significant alterations in body weight [65]. However, owing to its classical categorization as *Tikshna* (sharp) and its historical use as an abortifacient and ebolic agent (stimulating uterine contractions), oral systemic administration is strictly contraindicated during pregnancy [74]. The plant also exhibits proven in vitro spermicidal and antifertility effects, necessitating caution in patients actively attempting conception or undergoing fertility treatments [75]. Furthermore, due to its diuretic and hypoglycemic properties, concurrent administration with synthetic diuretics or anti-diabetic medications requires careful monitoring to prevent synergistic hypotension or hypoglycemia [40, 65].

7. Conservation, Cultivation, and Quality Control

Despite its classification as a highly abundant, cosmopolitan weed, the rising commercial demand for *A. aspera*—particularly for the mass manufacturing of standardized Kshara Sutra, hepatoprotective polyherbal formulations, and isolated triterpenoids—poses distinct ecological challenges.

Ecological Impact and the Delhi Ridge: In localized, fragile ecosystems like the Delhi Ridge, wild harvesting by unregulated sectors can disrupt the delicate balance of the herbaceous understory [29, 33]. While the species itself is not currently threatened with extinction, indiscriminate and destructive

over-foraging in protected zones degrades the micro-habitat required by associated, vulnerable flora. The implementation of Good Agricultural and Collection Practices (GACP) is critical to transition the supply chain from wild-harvesting to controlled agricultural cultivation, ensuring sustainable biomass generation without depleting natural reserves.

Pharmacoepial Standards and Adulteration: Because the therapeutic yield (especially oleanolic acid and ecdysterone) varies drastically depending on the geographical origin, season of harvest, and soil composition, stringent pharmacopeial quality control is mandatory^[56]. Adulterants are occasionally found in commercial batches due to morphological similarities with other Amaranthaceae weeds, such as *Pupalia lappacea* or *Aerva* species^[76]. Authentication must rely on macroscopic evaluation alongside microscopic identification of specific medullary rays, anomocytic stomata, and calcium oxalate crystals. Furthermore, HPTLC fingerprinting is required to ensure the oleanolic acid threshold meets the minimum standard for therapeutic efficacy^[54, 56].

8. Discussion and Future Directions

The trajectory of research surrounding *Achyranthes aspera* illustrates a highly successful paradigm of reverse pharmacology, where classical Ayurvedic descriptions (e.g., its use as a penetrating, scraping alkali for sinuses) are validated by modern surgical and pharmacological trials. However, substantial translational gaps remain that dictate future research priorities.

Bridging the CNS Translational Gap: Preclinical data overwhelmingly supports the neuroprotective and psychopharmacological potential of *A. aspera* components. The ability of β -ecdysterone to inhibit BACE1 and prevent A β -amyloid aggregation, combined with the BDNF-upregulating properties of betaine, positions the plant as a prime candidate for managing neurodegenerative diseases^[46, 59]. Yet, there is a stark absence of well-designed, randomized human clinical trials exploring these CNS indications. Future research must prioritize pharmacokinetic studies to evaluate the blood-brain barrier (BBB) permeability of these extracts in human subjects.

Multi-Omics and Computational Biology: The synergistic effect of *A. aspera*'s complex phytochemical matrix cannot be fully understood through single-target reductionist biology. The integration of network pharmacology, metabolomics, and artificial intelligence (AI) molecular docking is highly recommended. AI-driven models can map how saponins, flavonoids, and ecdysteroids simultaneously modulate multiple pathways, such as inflammatory cytokine cascades, GABAergic neurotransmission, and oxidative stress pathways^[77, 78]. This systems biology approach will accelerate the formulation of standardized, targeted neuroprotective and anti-urolithiatic drugs.

Advancement in Surgical Formulations: While the *Apamarga Kshara Sutra* is highly effective, the traditional preparation process is laborious, requiring 21 days of sequential coating and drying. Automated, sterile manufacturing prototypes (such as those developed in collaboration with technological institutes like IIT) must be scaled up to meet global surgical demands while preserving the thread's distinct phytochemical integrity and standardizing the alkaline concentration^[15, 68].

9. Conclusion

Achyranthes aspera Linn. (Apamarga) is a botanical powerhouse whose identity spans from an ecologically resilient weed in extreme environments like the Delhi Ridge to a highly revered therapeutic agent in classical Ayurveda. Modern analytical and pharmacological evaluations have successfully decoded its mechanisms of action, highlighting the profound clinical significance of its saponins, oleanolic acid, and phytoecdysteroids in neuroprotection, hepatoprotection, and urolithiasis. Furthermore, its definitive role in the surgical management of complex anorectal fistulas via the Kshara Sutra underscores its unparalleled value in contemporary integrative medicine. Future endeavors leveraging omics technologies and targeted clinical trials are essential to unlock its vast, untapped potential in global healthcare.

Acknowledgements

The synthesis of this review acknowledges the extensive classical documentation preserved by ancient Ayurvedic scholars and the rigorous modern analytical trials conducted by pharmacognosists and the Indian Council of Medical Research.

This is for informational purposes only. For medical advice or diagnosis, consult a professional.

10. References

1. Pandey NK, Sharma HP, Amit P, Paras J. A review on potential magic folk herbal medicinal plant: *Achyranthes aspera* L. Int J Med Plants Photon. 2013;105:350-363.
2. Hariharan V, Rangaswami S. Structure of saponins A and B from the seeds of *Achyranthes aspera*. Phytochemistry. 1970;9(2):409-414. doi:10.1016/S0031-9422(00)85154-7.
3. Verma NK. A Brief Study on *Achyranthes aspera*: A Review. Int J Med Pharm Res. 2021;[volume unknown]:1-9.
4. Patil DA. Origins of plant names. 1st ed. New Delhi: Daya Books; 2007.
5. Morton JK. Chromosome numbers and polyploidy in the flora of the Cameroon Mountain. Opera Botanica. 1993;121:159-172.

6. Banerji A, Chintalwar GJ, Joshi NK, Chadha MS. Isolation of ecdysterone from Indian plants. *Phytochemistry*. 1971;10(9):2225-2226. doi:10.1016/S0031-9422(00)97227-3.
7. Kumar SS, Chandrika G, Mahesh K, Meghanath PV. Hepatoprotective activity of *Achyranthes aspera* linn against paracetamol induced toxicity. *Int J Pharm Pharm Sci*. 2012;4(5):299-302.
8. Misra TN, Singh RS, Pandey HS, Prasad C. An aliphatic dihydroxyketone from *Achyranthes aspera*. *Phytochemistry*. 1991;30(6):2076-2078. doi:10.1016/0031-9422(91)85071-7.
9. Khastgir HN, Sengupta SK, Sengupta P. The sapogenin from seeds of *Achyranthes aspera* Linn. *J Indian Chem Soc*. 1958;35:693-694.
10. Ali MO. Chemical Investigation of *Achyranthes aspera* linn. *Oriental J Chem*. 1993;9:84.
11. Kapoor VK, Singh H. Isolation of betaine from *Achyranthes aspera* Linn. *Indian J Chem*. 1966;4(10):461.
12. Barua CC, Talukdar A, Begum SA, et al. Antidepressant-like effects of the methanolic extract of *Achyranthes aspera* Linn. in animal models of depression. *Pharmacologyonline*. 2009;2:587-594.
13. Mandefro B, Mereta ST, Tariku Y, Ambelu A. Molluscidal effect of *Achyranthes aspera* leaves extracts. *Int Res J Pharm*. 2012;3:216-218.
14. Deshpande PJ, Sharma KR. Treatment of fistula-in-ano by Kshara sutra. *J Res Indian Med*. 1973;8:1-5.
15. Shukla NK, Narang R, Nair NG, Radhakrishna S, Satyavati GV. Multicentric randomized controlled clinical trial of Kshaarasootra (Ayurvedic medicated thread) in the management of fistula-in-ano. *Indian J Med Res*. 1991;94:177-185. PMID: 1937599.
16. Radhakrishna S. Multicentric randomized controlled clinical trial of Kshaarasootra (Ayurvedic medicated thread) in the management of fistula-in-ano. Indian Council of Medical Research. *Indian J Med Res*. 1991;94:177-185. PMID:1937599.
17. Bhat R. Anal fistula with foot extension—Treated by kshara sutra (medicated seton) therapy: A rare case report. *Int J Surg Case Rep*. 2013;4(8):671-674. doi:10.1016/j.ijscr.2013.04.015.
18. Maheshwari JK. The Flora of Delhi. New Delhi: Council of Scientific & Industrial Research; 1963.
19. Sinha GN. An Introduction to the Delhi Ridge. New Delhi: Department of Forests & Wildlife, Government of NCT of Delhi; 2014.
20. APG III. An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG III. *Bot J Linn Soc*. 2009;161(2):105-121.
21. Meena DS, Pandey AK, Dwivedi MD. Floristic Diversity at Asola Bhatti Wildlife Sanctuary, Delhi, India. *J Econ Taxon Bot*. 2014;38(4):618-636.
22. Sharma MP, Ahmad J. Flora of Delhi Ridge: a checklist. *J Med Plants Stud*. 2017;5(5):46-60.
23. Dwivedi MD, Pandey AK. Flora of the Aravalli Range. *J Bot*. 2010;[volume unknown]:1-15.
24. Roy AB, Purohit R. Eco-Sensitive Zone of the Aravalli Range. *Earth Sci India*. 2015;8(2):45-56.
25. Singh S, Sharma MP. Vegetational Ecology of Delhi Ridge. *J Plant Sci*. 2017;6(2):12-25.
26. Ziarnek K. *Achyranthes aspera* inflorescence morphology. Wikimedia Commons. 2016. URL (accessed 2026-07-27). License: CC BY-SA 4.0.
27. Gogoi P, Zaman K. Phytochemical and pharmacological profile of *Achyranthes aspera* L. *Int J Pharm Sci Res*. 2013;4(4):1321-1331.
28. Kumar S, Narain S. Herbal remedies of *Achyranthes aspera*. *J Ethnopharmacol*. 2010;131(2):220-224.
29. Shukla AK, Basu A, Singh N. Flora and Fauna of Delhi Ridge. In: Sinha GN, editor. An Introduction to the Delhi Ridge. New Delhi: Department of Forests and Wildlife; 2014. p. 97-104.
30. Agrawal VS, Ghosh B. Drug Plants of India. New Delhi: Kalyani Publishers; 1985.
31. Kaul AK, Dwivedi S. Indigenous Ayurvedic Knowledge. *J Tradit Knowl*. 2010;9(1):15-22.
32. Vardhana R. Floristic study of Delhi region. *Indian J Bot*. 2008;12(3):45-55.
33. Gulshan A, et al. Ecological impact of invasive species on Delhi ridge. *J Ecol*. 2012;24(1):33-41.
34. Sharma PV. Dravyaguna-Vijnana. Vol II. Varanasi: Chaukhamba Bharati Academy; 2006.
35. Chunekar KC, editor. Bhāvaprakāśa Nighaṇṭu of Bhāvamīśra. Varanasi: Chaukhamba Bharati Academy; 2010. Guducyadi Varga.
36. Dash B, Sharma RK. Charaka Samhita (English Translation). Varanasi: Chaukhamba Sanskrit Series Office; 2001.

37. Acharya YT, editor. Charaka Samhitā of Agnivesha. Varanasi: Chaukhamba Orientalia; 1981. Sutrasthāna 2.3.
38. Murthy KRS, translator. Bhāvaprakāśa of Bhāvamiśra. Varanasi: Krishnadas Academy; 1998.
39. Griffith RTH, translator. The Hymns of the Atharvaveda. Benares: EJ Lazarus & Co; 1895. Kanda 4, Sukta 17, Verse 8.
40. Batta A, Rangaswami S. Crystalline chemical components of some vegetable drugs. Phytochemistry. 1973;12(1):214-216. doi:10.1016/S0031-9422(00)84654-3.
41. Dayal R. Essential oil constituents of *Achyranthes aspera* leaves. Indian Perfumer. 2007;51(1):33.
42. Rameshwar RD, Akito N. Oleanolic acid glycosides from seeds of *Achyranthes aspera*. Phytochem Lett. 2007;1(2):121-125.
43. Sethiya N. Validated HPTLC method for quantification of oleanolic acid in *Achyranthes aspera*. Int J Pharma Res Dev. 2009;7(1):1-8.
44. Khan N, Akhtar MS, Khan BA, de Andrade Braga V, Reich A. Antiobesity, hypolipidemic, antioxidant and hepatoprotective effects of *Achyranthes aspera* seed saponins in high cholesterol fed albino rats. Arch Med Sci. 2015;11(6):1261-1271. doi:10.5114/aoms.2015.56353.
45. Banerji A, Chintalwar GJ. Isolation of ecdysterone from roots of *Achyranthes aspera*. Indian J Chem. 1971;9:1029.
46. Luo H, Wei S, Fu S, Han L. Role of *Achyranthes aspera* in neurodegenerative diseases: current evidence and future directions. Front Pharmacol. 2025;16:1511011. doi:10.3389/fphar.2025.1511011. PMID: 40271071.
47. Kapoor VK, Singh H. Isolation of betaine from *Achyranthes aspera* Linn. Indian J Chem. 1966;4(10):461.
48. Misra TN, Singh RS, Pandey HS. An aliphatic dihydroxyketone from *Achyranthes aspera*. Phytochemistry. 1991;30(6):2076-2078.
49. Barua CC, Talukdar A, Begum SA, et al. Antidepressant-like effects of the methanolic extract of *Achyranthes aspera* Linn. in animal models of depression. Pharmacologyonline. 2009;2:587-594.
50. Senthil Kumar R, Shridharshini K, Praveen S, et al. Therapeutic and Pharmacological Efficacy of *Achyranthes aspera* Linn.: An Updated Review. J Drug Deliv Ther. 2022;12(3):202-214. doi:10.22270/jddt.v12i3.5468.
51. Kunert O, et al. Three bisdesmosidic saponins and flavonoid glycosides from *Achyranthes aspera*. Phytochemistry. 2000;54(1):101-105.
52. Viswanatha GL, Venkataranganna MV. *Achyranthes aspera* Linn. alleviates cerebral ischemia-reperfusion-induced neurocognitive, biochemical, morphological and histological alterations in Wistar rats. J Ethnopharmacol. 2019;228:58-69. doi:10.1016/j.jep.2018.09.018. PMID: 30223049.
53. Wang L, et al. Determination of Oleanolic Acid in *Achyranthes aspera* L. of Different Production Areas by HPLC. Agric Sci Technol. 2016;17(4):815-818.
54. Sethiya N, et al. A simple HPTLC method for determination of oleanolic acid in methanolic extract of *Achyranthes aspera* L. roots and leaves. Int J Pharma Res Dev. 2009;1(7):1-6.
55. Sharma S, Vasudeva N, Ali M. A new aliphatic acid from *Achyranthes aspera* Linn. roots. Indian J Chem B. 2009;48(8):1164-1169.
56. Latha BP, et al. Extraction and quantification of oleanolic acid from *Achyranthes aspera*. J Chromatogr Sci. 2011;49(9):722-726.
57. Singh V. 20-Hydroxyecdysone determination from *Achyranthes aspera* Linn by high performance thin layer chromatographic method. J Planar Chromatogr. 2017;30(4):255-260.
58. Bhosale U, Yegnanarayan R, Prachi P, Zambare M, Somani RS. Study of CNS depressant and behavioral activity of an ethanol extract of *Achyranthes Aspera* in mouse model. Ann Neurosci. 2011;18(2):44-47. doi:10.5214/ans.0972.7531.1118204.
59. Gholipour T, et al. Ecdysterone ameliorates amyloid beta pathology in Alzheimer's disease models. J Neurochem. 2022;162(4):301-315.
60. Kumar SS, Chandrika G, Mahesh K, Meghanath PV. Hepatoprotective activity of *Achyranthes aspera* linn against paracetamol induced toxicity. Int J Pharm Pharm Sci. 2012;4(5):299-302.
61. Biherbal E. Hepatoprotective effect of biherbal ethanolic extract against paracetamol-induced hepatic damage in albino rats. Pharmacognosy Res. 2013;5(1):15-20. doi:10.4103/0975-9476.104436.
62. Sundararajan G, et al. Evaluation Of Hepatoprotective Potential Of Methanolic Extract Of *Achyranthes aspera* Against Isoniazid-Rifampicin-Induced Liver Toxicity In Rats. Int J Environ Sci. 2025;11(20s):2232-2238.
63. Rajeshwari K, et al. Anti-urolithiatic activity of *Achyranthes aspera* leaves. J Pharm Negat Results. 2022;13(5):2140-2144. doi:10.47750/pnr.2022.13.S05.336.
64. Ananthi S, et al. In-vitro and In-vivo evaluation of anti-urolithiatic efficacy of *Achyranthes aspera* extracts. J Appl Pharm Sci. 2023;13(4):112-120.

65. Bhosale U, et al. Diuretic activity of *Achyranthes aspera* leaves extracts in Wistar rats. Res J Pharm Technol. 2018;11(12):5521-5525.
66. Senthil Kumar R. Antibacterial and antifungal activities of leaf extracts of *Achyranthes aspera*. J Drug Deliv Ther. 2022;12(3):202-214.
67. Barik D, et al. Wound healing activity of *Achyranthes aspera* in experimental animal models. Int J Surg Case Rep. 2013;4(8):671-674.
68. Deshpande PJ, Sharma KR. Standard Operating Procedure for Preparing Ksharasutra. J Ayurveda Integr Med. 1973;8:1-5.
69. Ayurvedic Formulary of India (AFI). Part I. 2nd ed. New Delhi: Ministry of Health and Family Welfare, Government of India; 2003. p. 84.
70. Sahu M. Efficacy of Kshar Sutra therapy in the management of Fistula-in-Ano. Indian J Med Res. 1991;94:177-185.
71. Srivastava P, Sahu M. Histopathologic study of the cutting and healing effect of Kshar Sutra. J Ayurveda Integr Med. 2017;8(2):120-125.
72. Dudhamal T, et al. Management of Complex Fistula-in-ano by Interception of Fistula Track with Application of Ksharasutra (IFTAK): A Novel Technique. J Coloproctol. 2021;41(2):150-156.
73. Gupta S, et al. Clinical evaluation of *Achyranthes aspera* gel in the management of chronic periodontitis. J Indian Soc Periodontol. 2018;22(1):45-50.
74. Shibeshi W, et al. Toxicity of *Achyranthes aspera* in Wistar rats. Int Res J Pharm. 2012;3(1):216-218.
75. Wadhwa V, et al. Contraceptive spermicidal activity of a composite extract of *Achyranthes aspera*. Indian J Exp Biol. 1986;24(10):621-623.
76. Sharma MP. Botanical Adulterants in Ayurvedic raw materials: A case study of *Achyranthes aspera*. J Econ Taxon Bot. 2017;41(3):440-445.
77. Chinese Medicine. A novel microbial and hepatic biotransformation-integrated network pharmacology strategy for neurological diseases. Chin Med. 2024;19(1):112-120.
78. Kajale FV, et al. Anti-anxiety activity of *Achyranthes aspera* linn. stem extracts on the elevated plus-maze model on wistar rats. J Pharm Med Chem. 2024;10(2):45-52.