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Kutaja (*Holarrhena Antidysenterica*): From ayurveda to modern pharmacology: A review

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Abstract
Holarrhena antidysenterica (L.) Wall. ex A. DC. (Family Apocynaceae), commonly known as Kutaja or Kurchi, is an important medicinal tree extensively employed in the traditional systems of medicine, particularly Ayurveda, Siddha, and Unani, for the management of gastrointestinal disorders. The stem bark and seeds have been traditionally prescribed for the treatment of diarrhoea, dysentery, amoebiasis, intestinal helminthiasis, inflammatory bowel disorders, fever, skin diseases, and several metabolic ailments. Owing to its long-standing therapeutic significance, *H. antidysenterica* has attracted considerable scientific attention, resulting in extensive investigations on its pharmacognosy, phytochemistry, pharmacology, and quality control. The present review critically compiles and updates the available information on the taxonomy, botanical characteristics, ethnomedicinal applications, pharmacognostic features, phytochemical constituents, pharmacological properties, clinical evidence, toxicity, and standardization of *H. antidysenterica*. The plant is particularly rich in steroidal alkaloids, including conessine, conessidine, holarrhine, kurchicine, kurchine, and holarrhimine, which are primarily responsible for its potent antiamoebic, antidiarrhoeal, antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, and anticancer activities. Recent advances employing chromatographic fingerprinting, metabolomic profiling, molecular docking, DNA barcoding, and nanotechnology-based formulations have further strengthened the scientific basis for its therapeutic applications and quality assurance. Experimental investigations have also demonstrated promising hepatoprotective, antidiabetic, neuroprotective, gastroprotective, and antimicrobial properties, indicating the plant's potential beyond its classical use in gastrointestinal diseases. Despite encouraging pharmacological evidence, well-designed multicentric clinical trials, standardized herbal formulations, comprehensive toxicological assessments, and conservation strategies remain limited. Moreover, sustainable harvesting practices and molecular authentication are essential to prevent adulteration and ensure the quality of herbal raw materials. This review integrates classical knowledge with recent scientific developments, identifies existing research gaps, and highlights future opportunities for developing evidence-based phytopharmaceuticals from *Holarrhena antidysenterica*. The compiled information may serve as a valuable reference for researchers, pharmacologists, ethnobotanists, clinicians, and pharmaceutical industries engaged in medicinal plant research and herbal drug development. The review is based on classical pharmacognostic literature and incorporates updated scientific evidence to provide a comprehensive perspective on this pharmaceutically important medicinal species.

Keywords: *Holarrhena antidysenterica*, Kutaja, apocynaceae, conessine, ethnomedicine, phytochemistry, pharmacology

Introduction
Medicinal plants have served as the foundation of traditional healthcare systems for millennia and continue to play a pivotal role in contemporary drug discovery. The World Health Organization (WHO) estimates that approximately 80% of the global population relies on herbal medicines for primary healthcare, particularly in developing countries where medicinal plants remain affordable and culturally acceptable. India, one of the world's megadiverse countries, possesses nearly 7–8% of global biodiversity and harbours more than 7,500 medicinal plant species utilized in Ayurveda, Siddha, Unani, and diverse folk medicinal traditions (World Health Organization [WHO], 2019; Sharma *et al*., 2004) [15, 23].

Holarrhena antidysenterica (L.) Wall. ex A. DC. (Apocynaceae), commonly known as Kutaja, Kurchi, Kuda, or Indrayava, is among the most valued medicinal trees in Indian traditional medicine. Although modern taxonomic databases currently recognize it as *Holarrhena pubescens* Wall. ex G. Don, the name *H. antidysenterica* continues to be widely adopted in pharmacological, ethnobotanical, and Ayurvedic literature.

The therapeutic importance of *H. antidysenterica* has been recognized since ancient times and is extensively documented in classical Ayurvedic texts such as the *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, and *Bhavaprakasha Nighantu*. The stem bark (Kutaja Twak) and seeds (Indrayava) are prescribed for the management of diarrhoea (*Atisara*), dysentery (*Pravahika*), intestinal parasitic infections, inflammatory bowel disorders, skin diseases, fever, haemorrhoids, and several metabolic disorders (Sharma *et al*., 2004 [15] Jamadagni *et al*., 2017) [9]. Recent reviews further recognize the species as an important medicinal resource with broad therapeutic applications extending beyond gastrointestinal diseases.

Botanically, *H. antidysenterica* is a deciduous laticiferous shrub or small tree distributed throughout tropical and subtropical regions of the Indian subcontinent. It commonly inhabits dry deciduous forests, scrublands, open woodlands, and the lower Himalayan foothills up to an altitude of approximately 1,200 m. The species is distinguished by its rough grey bark, opposite elliptic leaves, fragrant white flowers, paired cylindrical follicles, and silky-haired seeds adapted for wind dispersal. Classical pharmacognostic investigations have also established reliable anatomical characteristics of the bark for distinguishing genuine crude drug material from common adulterants such as *Wrightia tinctoria* and *W. tomentosa*.

Phytochemical investigations over the past several decades have revealed that *H. antidysenterica* is an exceptionally rich source of steroidal alkaloids. More than thirty alkaloids have been isolated, including conessine, conessidine, holarrhine, holarrhimine, kurchicine, conimine, and conkurchine. Among these, conessine is considered the principal bioactive marker responsible for many of the plant's pharmacological activities. Recent phytochemical studies employing LC–MS/MS, metabolomics, and chromatographic fingerprinting have expanded the understanding of its chemical diversity and have facilitated the standardization of herbal formulations.

Extensive pharmacological investigations have validated numerous traditional claims associated with *H. antidysenterica*. Experimental studies have demonstrated significant antiamoebic, antidiarrhoeal, antimicrobial, antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, gastroprotective, neuroprotective, immunomodulatory, and anticancer activities. Particularly noteworthy is the recent discovery that conessine functions as an inhibitor of bacterial multidrug efflux pumps, thereby restoring antibiotic susceptibility in resistant bacterial pathogens and highlighting its potential role in combating antimicrobial resistance.

Despite encouraging experimental evidence, the translation of these findings into clinical practice remains limited. Most pharmacological investigations have been confined to *in vitro* studies and animal models, whereas well-designed randomized clinical trials, comprehensive toxicological evaluations, and standardized phytopharmaceutical formulations remain relatively scarce. Furthermore, increasing commercial demand has intensified concerns regarding adulteration, sustainable harvesting, and quality assurance of crude drug materials. Consequently, modern authentication techniques such as DNA barcoding, metabolomic profiling, and chromatographic fingerprinting are increasingly recommended for ensuring the quality, safety, and efficacy of herbal products.

The present review critically summarizes classical knowledge together with recent scientific advances concerning the taxonomy, botanical characteristics, ethnomedicinal applications, pharmacognosy, phytochemistry, pharmacological activities, quality control, clinical evidence, and future therapeutic prospects of *Holarrhena antidysenterica*. The review also identifies current research gaps and highlights opportunities for developing evidence-based phytopharmaceuticals from this pharmaceutically important medicinal species.

Botanical Description

Holarrhena antidysenterica (L.) Wall. ex A. DC. (currently accepted as *Holarrhena pubescens* Wall. ex G Don according to modern taxonomic databases) belongs to the family Apocynaceae, order Gentianales. It is a deciduous laticiferous shrub or small tree attaining a height of 4–12 m, occasionally reaching 15 m under favourable environmental conditions. The species is indigenous to the Indian subcontinent and is widely distributed in India, Nepal, Sri Lanka, Bangladesh, Myanmar, Thailand, and several other tropical Asian countries. It predominantly occurs in tropical dry deciduous forests, open woodlands, scrub forests, and lower Himalayan regions up to approximately 1,200 m elevation.

The stem is erect, cylindrical, profusely branched, and covered with rough grey to pale brown corky bark that exudes copious white milky latex upon injury. Mature bark is irregularly fissured, bitter in taste, and constitutes one of the principal medicinally important plant parts. Pharmacognostic studies have shown that the bark possesses tangential bands of stone cells, narrow cork cells, abundant calcium oxalate crystals, laticiferous ducts, and non-lignified pericyclic fibres, which serve as important diagnostic features for authentication and differentiation from adulterants including Wrightia tinctoria and Wrightia tomentosa.

Holarrhena pubescens **(Safed Kuda)**

Leaves are simple, opposite, decussate, broadly elliptic to ovate-oblong, measuring approximately 10–30 cm long and 5–15 cm wide. The lamina is coriaceous, dark green and glabrous on the adaxial surface, while the abaxial surface is paler and pubescent. The margin is entire, the apex acute to acuminate, and the venation is pinnate with 10–20 pairs of conspicuous lateral veins. Latex canals are abundantly distributed throughout the leaf tissues, a characteristic feature of members of the Apocynaceae.

Flowering generally occurs from March to June, depending upon climatic conditions and geographical location. The flowers are fragrant, bisexual, actinomorphic, pentamerous, and borne in terminal or axillary corymbose cymes. The corolla is salver-shaped, creamy white to pure white, becoming yellowish with age. Pollination is primarily mediated by bees, butterflies, and other nectar-feeding insects, contributing to successful sexual reproduction.

The fruit consists of paired slender cylindrical follicles, 15–45 cm long, which split longitudinally upon maturity to release numerous linear-oblong seeds. Each seed bears a tuft of silky white hairs (coma) that facilitates efficient wind dispersal. Fruiting generally extends from May to August, enabling natural regeneration under suitable environmental conditions.

The plant develops a deep taproot system with extensive lateral roots, conferring considerable drought tolerance and enabling successful establishment in dry tropical ecosystems. Ecologically, it contributes to forest stability, supports pollinator diversity, and provides habitat for various insects and birds.

Among the different plant parts, the stem bark and seeds are of greatest medicinal importance. These organs contain high concentrations of biologically active steroidal alkaloids, particularly conessine, conessidine, holarrhine, holarrhimine, and kurchicine, which are largely responsible for the plant's antiamoebic, antidiarrhoeal, antimicrobial, anti-inflammatory, and immunomodulatory activities. Seasonal and age-dependent variations in alkaloid content have been reported, emphasizing the importance of appropriate harvesting time for obtaining high-quality crude drugs.

Taxonomy and Nomenclature

Holarrhena antidysenterica (L.) Wall. ex A DC. is an important medicinal species belonging to the family Apocynaceae, one of the largest angiosperm families comprising over 5,000 species distributed among approximately 375 genera. The genus *Holarrhena*, established by Robert Brown in 1810, consists of several species distributed mainly in tropical Africa and South to Southeast Asia. Among them, *Holarrhena antidysenterica* is the most extensively investigated medicinal species owing to its remarkable therapeutic applications in traditional medicine. Recent taxonomic revisions based on morphological evidence and herbarium studies recognize *Holarrhena pubescens* Wall. ex G. Don as the accepted scientific name, whereas *H. antidysenterica* (L.) Wall. ex A. DC. is treated as its synonym. Nevertheless, the latter name continues to be widely used in Ayurvedic literature, pharmacopoeias, ethnobotanical studies, and pharmacological investigations, and therefore remains acceptable in medicinal plant research (Kew Science, 2026 [10] Pawar *et al*., 2024) [13].

Taxonomic Classification

Rank	Classification
Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Gentianales
Family	Apocynaceae
Subfamily	Apocynoideae
Tribe	Malouetieae
Genus	*Holarrhena* R.Br.
Species	*Holarrhena pubescens* Wall. ex G Don (= *Holarrhena antidysenterica* (L.) Wall. ex A.DC.)

The generic name *Holarrhena* is derived from the Greek words holos (entire) and arrhen (male), referring to the floral morphology, whereas the specific epithet *antidysenterica* reflects its long-recognized efficacy against dysentery. Modern molecular and taxonomic databases, including the International Plant Names Index (IPNI), World Flora Online (WFO), and Plants of the World Online (POWO), currently recognize *H.* pubescens as the accepted nomenclature while listing H. antidysenterica as a synonym.

Distribution, Ecology and Conservation

Holarrhena antidysenterica is widely distributed throughout tropical and subtropical Asia and parts of eastern and southern Africa. Its natural range extends across India, Nepal, Sri Lanka, Bangladesh, Pakistan, Myanmar, Thailand, Cambodia, Laos, Vietnam, and southern China. Within India, the species occurs abundantly in the Western Ghats, Eastern Ghats, Central Indian forests, Himalayan foothills, and dry deciduous forests from sea level to approximately 1,200–1,300 m above mean sea level (Kew Science, 2026) [10].

The species thrives under tropical dry deciduous climatic conditions receiving annual rainfall between 600 and 2,000 mm. It grows well in sandy loam, lateritic, gravelly, and rocky soils with good drainage and tolerates prolonged drought because of its deep taproot system. It commonly occurs in open forests, scrublands, riverine forests, woodland margins, and secondary vegetation. Ecologically, the plant serves as an important nectar source for bees and butterflies during flowering, while its wind-dispersed seeds facilitate natural regeneration and colonization of disturbed habitats.

Although *Holarrhena pubescens* is currently categorized as Least Concern (LC) globally owing to its broad geographic distribution, local populations are declining in several parts of India due to unsustainable bark harvesting, habitat degradation, forest fragmentation, and increasing commercial demand from the herbal pharmaceutical industry. Excessive removal of stem bark often results in mortality of mature trees, thereby reducing natural regeneration. Conservation strategies should therefore emphasize sustainable harvesting, cultivation through agroforestry systems, ex situ conservation, germplasm preservation, and community-based management programmes. The use of DNA barcoding and chromatographic fingerprinting has further strengthened species authentication and conservation planning by minimizing adulteration in the herbal drug trade.

Vernacular Names

Holarrhena antidysenterica is widely recognized throughout the Indian subcontinent and neighbouring countries under various vernacular names, reflecting its extensive ethnomedicinal importance.

Language	Vernacular name
Sanskrit	Kutaja, Vatsaka, Girimallika
English	Kurchi, Conessi Tree, Kurchi Bark Tree
Hindi	Kutaj, Kuda
Marathi	Kuda
Gujarati	Kado, Indrajav
Bengali	Kurchi
Punjabi	Kewar
Kannada	Kodasige
Malayalam	Kodagapala
Tamil	Kudasappalai
Telugu	Kodise
Odia	Kurei
Assamese	Dudhkhuri

The seeds are widely known in Ayurveda as Indrayava, a highly valued crude drug prescribed in formulations intended for the treatment of diarrhoea, dysentery, intestinal infections, and digestive disorders. The remarkable diversity of vernacular names across different linguistic regions reflects the widespread utilization of this medicinal species in indigenous healthcare systems for several centuries.

Traditional and Ayurvedic Uses

Holarrhena antidysenterica occupies a distinguished position in Ayurveda and is classified as one of the most effective herbal remedies for disorders affecting the gastrointestinal tract. Classical Ayurvedic texts, including the *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, and *Bhavaprakasha Nighantu*, describe the stem bark (Kutaja Twak) and seeds (Indrayava) as potent Deepana (digestive stimulant), Grahi (absorbent), Atisarahara (antidiarrhoeal), Krimighna (anthelmintic), Jwaraghna (antipyretic), Raktapittahara, and Kaphahara drugs. The bark is primarily indicated in chronic diarrhoea, amoebic dysentery, inflammatory bowel disorders, piles, intestinal parasitic infections, and chronic gastrointestinal inflammation, whereas the seeds are widely employed in treating fever, dysentery, jaundice, skin disorders, and urinary ailments.

Besides Ayurveda, the plant is extensively utilized in Siddha, Unani, and numerous tribal healthcare systems throughout India. Traditional formulations containing *Holarrhena* bark have been used to treat cholera, abdominal colic, haemorrhoids, ulcers, bronchitis, chronic fever, anaemia, skin diseases, and metabolic disorders. The dried bark is considered stomachic, astringent, febrifuge, and antiamoebic, while powdered seeds are prescribed for chronic diarrhoea and intestinal worm infestations. Modern pharmacological studies have validated many of these traditional therapeutic claims, particularly those relating to antidiarrhoeal, antimicrobial, anti-inflammatory, and antiamoebic activities.

Ethnomedicinal Importance

The ethnomedicinal significance of *Holarrhena antidysenterica* extends across South Asia and Africa, where different indigenous communities have utilized various plant parts for centuries. Tribal groups including the Santals, Bhils, Gonds, Baigas, Oraons, and several Himalayan communities employ the bark, leaves, roots, fruits, and seeds for the treatment of diarrhoea, dysentery, amoebiasis, stomach ache, intestinal worms, fever, diabetes, skin infections, jaundice, anaemia, and snake or dog bites. Traditional healers frequently prepare decoctions, powders, infusions, and paste formulations using bark and seeds either alone or in combination with other medicinal plants.

Recent ethnopharmacological investigations have demonstrated that the therapeutic efficacy of *H. antidysenterica* largely arises from its rich content of steroidal alkaloids, particularly conessine, conessidine, holarrhine, and holarrhimine. These compounds exhibit broad-spectrum antimicrobial, anti-inflammatory, antioxidant, immunomodulatory, antidiabetic, gastroprotective, and anticancer activities, thereby providing scientific support for many traditional medicinal applications. Furthermore, contemporary studies have highlighted the potential of conessine as an inhibitor of bacterial multidrug efflux pumps, suggesting an important role in combating antimicrobial resistance. Consequently, *Holarrhena antidysenterica* represents a valuable bridge between traditional ethnomedicine and evidence-based phytopharmaceutical development, warranting further clinical investigations and sustainable conservation efforts.

Pharmacognosy and Quality Standards

Pharmacognostic standardization is an indispensable component of herbal drug authentication and quality assurance, particularly for medicinal plants susceptible to adulteration and substitution. *Holarrhena antidysenterica* (syn. *Holarrhena pubescens*) has been extensively investigated because its stem bark is frequently adulterated with *Wrightia tinctoria* and *W. tomentosa* owing to their close morphological resemblance (Prasad & Kaul, 1956; Atal & Sethi, 1962; Jamadagni *et al*., 2017 [9] Pawar *et al*., 2024) [13].

Macroscopically, the bark is greyish-brown to reddish-brown, bitter in taste, and possesses numerous transversely elongated lenticels and irregular fissures. Microscopically, it is characterized by tangential bands of stone cells, calcium oxalate crystals, laticiferous ducts, narrow cork cells, non-lignified pericyclic fibres, and bi- to triseriate medullary rays, all of which serve as reliable pharmacognostic markers for authentication (Prasad & Kaul, 1956; Bhutani, 1984; Jamadagni *et al*., 2017) [9].

Modern pharmacognostic evaluation incorporates HPTLC, HPLC, LC–MS/MS, FTIR spectroscopy, DNA barcoding, and metabolomic fingerprinting for authentication and quality assurance of crude drugs and herbal formulations (Sinha *et al*., 2020; Pawar *et al*., 2024) [13, 17, 18, 19]. Conessine has been accepted as the principal phytochemical marker for standardization owing to its abundance and pharmacological significance (Mustafa *et al*., 2026) [12].

Phytochemistry

Phytochemical investigations over the last century have established *Holarrhena antidysenterica* as one of the richest natural sources of steroidal alkaloids within the family Apocynaceae. More than thirty structurally related steroidal alkaloids have been isolated from different plant parts, particularly the stem bark, seeds, roots, leaves, and fruits. Besides alkaloids, the species also contains flavonoids, phenolic compounds, tannins, coumarins, triterpenoids, sterols, glycosides, resins, amino acids, and several volatile constituents. Steroidal alkaloids constitute the major bioactive chemical class responsible for most of the reported pharmacological activities.

1. Steroidal Alkaloids

Steroidal alkaloids constitute the principal bioactive constituents of *Holarrhena antidysenterica*. More than thirty alkaloids have been isolated from various plant parts, including conessine, conessidine, conessimine, isoconessimine, holarrhine, holarrhimine, kurchicine, conimine, conkurchine, holacetine, and antidysentericine (Chaturvedi *et al*., 1980, 1981; Bhutani, 1984; Jamadagni *et al*., 2017 [9] Pawar *et al*., 2024) [13].

2. Conessine

Conessine is the major steroidal alkaloid of *Holarrhena antidysenterica* and serves as the official chemical marker for quality control. It exhibits antiamoebic, antimicrobial, anti-inflammatory, antidiarrhoeal, neuroprotective, anticancer, and antioxidant activities (Basu & Jayaswal, 1968 [1] Chaturvedi *et al*., 1981 [3] Jamadagni *et al*., 2017 [9] Mustafa *et al*., 2026) [12]. Recent investigations have demonstrated that conessine inhibits bacterial multidrug efflux pumps, thereby restoring antibiotic susceptibility in multidrug-resistant bacteria (Mustafa *et al*., 2026) [12].

3. Holarrhine

Holarrhine is another biologically important steroidal alkaloid occurring mainly in the bark and roots. Experimental studies indicate antimicrobial, antioxidant, anti-inflammatory, and antiamoebic properties, and it is believed to contribute synergistically with conessine in therapeutic preparations (Chaturvedi *et al*., 1981 [3] Jamadagni *et al*., 2017 [9] Pawar *et al*., 2024) [12].

4. Conessidine
Conessidine possesses potent antiamoebic activity against *Entamoeba histolytica* and contributes significantly to the traditional efficacy of Kutaja preparations. It is also considered an important chemotaxonomic marker of the genus *Holarrhena* (Basu & Jayaswal, 1968; Chaturvedi *et al*., 1981 [3] Pawar *et al*., 2024) [13].

5. Kurchicine
Kurchicine has demonstrated antiamoebic, antimicrobial, hypotensive, and anti-inflammatory activities. Although comparatively less investigated than conessine, it contributes substantially to the pharmacological profile of *Holarrhena* extracts (Chopra *et al*., 1933; Chaturvedi *et al*., 1981 [3] Jamadagni *et al*., 2017) [9].

6. Minor Phytochemicals
Besides steroidal alkaloids, *Holarrhena antidysenterica* contains flavonoids, phenolic acids, tannins, triterpenoids, phytosterols, glycosides, amino acids, coumarins, and volatile constituents. These metabolites collectively contribute antioxidant, hepatoprotective, antimicrobial, gastroprotective, and anti-inflammatory properties (Daniel *et al*., 1978; Narayanan & Naik, 1981; Sinha *et al*., 2020; Pawar *et al*., 2024) [13, 17, 18, 19].

7. Recent Metabolomic Reports
Recent metabolomic investigations using UHPLC–QTOF–MS, LC–MS/MS, GC–MS, and HPTLC have considerably expanded the phytochemical profile of *Holarrhena pubescens*. Comparative metabolite profiling has demonstrated that secondary branches possess chemical fingerprints comparable to stem bark, suggesting a sustainable alternative for medicinal utilization (Sulaiman *et al*., 2025) [20]. Integration of metabolomics with network pharmacology, molecular docking, transcriptomics, and chemometric analyses has further facilitated the identification of bioactive metabolites and improved quality control of herbal formulations (Pawar *et al*., 2024 [13] Mustafa *et al*., 2026) [12].

Pharmacological Activities
Holarrhena antidysenterica (syn. *Holarrhena pubescens*) has attracted considerable scientific interest because of its broad spectrum of pharmacological activities, many of which substantiate its long-standing use in traditional medicine. The therapeutic potential of the plant is primarily attributed to its steroidal alkaloids, particularly conessine, conessidine, holarrhine, kurchicine, and related compounds, along with phenolics, flavonoids, tannins, and triterpenoids (Chaturvedi *et al*., 1981 [3] Jamadagni *et al*., 2017 [9] Pawar *et al*., 2024) [13].

1. Antidiarrheal Activity
The stem bark and seeds of *H. antidysenterica* have been extensively used in Ayurveda for the treatment of diarrhoea and dysentery. Experimental studies have demonstrated that alcoholic and aqueous extracts significantly reduce intestinal motility, inhibit intestinal fluid secretion, and improve water absorption. The astringent action of tannins, together with the antimicrobial and anti-inflammatory properties of steroidal alkaloids, contributes to its remarkable antidiarrhoeal efficacy (Chopra *et al*., 1933; Singh & Chaturvedi, 1982 Jamadagni *et al*., 2017) [9, 16].

2. Antiamoebic Activity
Among all pharmacological properties, antiamoebic activity is the most thoroughly investigated. Conessine exhibits potent activity against *Entamoeba histolytica* by disrupting protozoal metabolism and inhibiting parasite proliferation. Experimental studies have confirmed that conessine is more effective than several other alkaloids isolated from the plant, validating the traditional use of Kutaja in amoebic dysentery (Basu & Jayaswal, 1968; Datta & Iyer, 1968 [1] Mustafa, 2026) [12].

3. Antimicrobial and Antifungal Activities
Extracts of *H. antidysenterica* exhibit broad-spectrum antibacterial activity against several Gram-positive and Gram-negative pathogens, including *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, and *Pseudomonas aeruginosa*. Recent investigations have shown that conessine inhibits bacterial multidrug efflux pumps, thereby restoring antibiotic susceptibility in resistant bacterial strains. The seed oil also exhibits antifungal activity against several pathogenic fungi, including *Microsporum gypseum* and *Keratinomyces ajelloi* (Deshmukh & Jain, 1981 [6] Sinha *et al*., 2020; Mustafa *et al*., 2026) [12, 17, 18, 19].

4. Anthelmintic Activity
Traditional healers have long prescribed bark and seed preparations to eliminate intestinal worms. Although early investigations reported variable efficacy against some helminths, subsequent studies indicate that alkaloid-rich extracts possess moderate anthelmintic activity by interfering with neuromuscular function and energy metabolism of parasitic worms (Dhar *et al*., 1968 [7] Jamadagni *et al*., 2017) [9].

5. Anti-inflammatory and Antioxidant Activities
The plant possesses significant anti-inflammatory activity through suppression of pro-inflammatory cytokines, cyclooxygenase pathways, and oxidative stress. Steroidal alkaloids, flavonoids, and phenolic compounds also exhibit strong antioxidant activity by scavenging reactive oxygen species and enhancing endogenous antioxidant enzymes, thereby protecting tissues against oxidative damage (Sinha *et al*., 2020; Pawar *et al*., 2024) [13, 17, 18, 19].

6. Anticancer and Antidiabetic Activities
Recent studies have demonstrated cytotoxic activity of *Holarrhena* extracts against several human cancer cell lines, suggesting their potential role in cancer chemoprevention. Additionally, experimental investigations have reported significant hypoglycaemic effects, possibly mediated through enhanced insulin sensitivity, inhibition of carbohydrate-metabolizing enzymes, and antioxidant mechanisms (Dhar *et al*., 1968 [7] Jamadagni *et al*., 2017 [9] Pawar *et al*., 2024) [13].

7. Hepatoprotective, Neuroprotective and Immunomodulatory Activities
Extracts of *H. antidysenterica* have shown hepatoprotective effects against chemically induced liver injury by reducing lipid peroxidation and restoring antioxidant defence systems. Emerging evidence also indicates neuroprotective and immunomodulatory properties, which may be attributed to steroidal alkaloids capable of modulating inflammatory mediators and oxidative stress pathways. These findings

suggest potential applications in neurodegenerative and immune-mediated disorders, although further clinical validation is required (Sinha *et al*., 2020; Mustafa *et al*., 2026) [12, 17, 18, 19].

8. Gastroprotective and Antiviral Activities

Traditional use of *Holarrhena* in gastrointestinal disorders is supported by studies demonstrating gastroprotective effects through enhancement of mucosal defence, reduction of gastric acidity, and inhibition of inflammatory mediators. Although antiviral activity against certain viruses has been reported to be limited in early investigations, modern phytochemical studies suggest that purified alkaloids may possess broader antiviral potential requiring further investigation (Dhar *et al*., 1968 [7] Pawar *et al*., 2024) [13].

Clinical Evidence

Despite extensive traditional use and encouraging preclinical investigations, clinical evidence supporting the therapeutic efficacy of *Holarrhena antidysenterica* remains relatively limited. Most available clinical studies have evaluated standardized bark and seed preparations in the management of acute and chronic diarrhoea, amoebic dysentery, inflammatory bowel disorders, and gastrointestinal infections. Several clinical observations have reported significant improvement in stool frequency, abdominal pain, intestinal inflammation, and recovery from amoebic dysentery following administration of Kutaja formulations (Chopra *et al*., 1956 [4] Sharma *et al*., 2004) [15]. Experimental and clinical studies further support the antiamoebic efficacy of conessine-containing preparations against *Entamoeba histolytica* (Datta & Iyer, 1968 [5] Jamadagni *et al*., 2017) [9]. However, most published studies involve small sample sizes, inadequate randomization, and limited follow-up. Therefore, well-designed multicentric randomized controlled clinical trials employing standardized phytopharmaceutical preparations are necessary to establish efficacy and safety according to contemporary evidence-based medicine (Pawar *et al*., 2024 [13] Mustafa *et al*., 2026) [12].

Toxicology

Toxicological investigations indicate that *H. antidysenterica* possesses a comparatively wide safety margin when administered at recommended therapeutic doses. Acute and subacute toxicity studies have demonstrated low toxicity of aqueous and alcoholic bark extracts in experimental animals, with no significant alterations in biochemical, hematological, or histopathological parameters (Jamadagni *et al*., 2017) [9]. Nevertheless, administration of excessively high doses of purified alkaloids, particularly conessine, may produce gastrointestinal irritation, nausea, vomiting, dizziness, and neurological manifestations due to central nervous system stimulation (Mustafa *et al.,* 2026) [12]. Comprehensive chronic toxicity, reproductive toxicity, mutagenicity, teratogenicity, and pharmacokinetic studies remain insufficient and warrant further investigation before widespread pharmaceutical application.

Standardization

Standardization is essential for ensuring the quality, safety, and reproducibility of herbal medicines. The stem bark and seeds of *H. antidysenterica* are officially recognized in the Ayurvedic Pharmacopoeia of India, where diagnostic macroscopic, microscopic, physicochemical, and phytochemical parameters have been established (Government of India, 2001) [8]. Conessine is widely accepted as the principal chemical marker for quality assessment and quantitative standardization. Modern analytical techniques such as High-Performance Thin-Layer Chromatography (HPTLC), High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), LC–MS/MS, and chromatographic fingerprinting provide reliable methods for authentication and quantification of bioactive constituents (Sinha *et al*., 2020; Pawar *et al*., 2024) [13, 17, 18, 19]. Standardized cultivation, harvesting season, drying procedures, and storage conditions are equally important for maintaining consistent phytochemical composition.

DNA Barcoding and Authentication

Accurate authentication of medicinal plants has become increasingly important because of the widespread adulteration of herbal raw materials. DNA barcoding has emerged as a powerful molecular tool for species identification independent of morphological characteristics. Universal barcode regions including rbcL, matK, ITS, and psbA–trnH have been successfully applied for authentication of medicinal plants and differentiation from closely related adulterants (Kress *et al*., 2005 [11] CBOL Plant Working Group, 2009) [2]. Integration of DNA barcoding with chromatographic fingerprinting, metabolomics, and microscopic analysis provides a robust quality assurance strategy for commercial *Holarrhena* preparations (Pawar *et al*., 2024) [13].

Adulteration and Quality Control

Commercial bark of *Holarrhena antidysenterica* is frequently adulterated with morphologically similar species such as *Wrightia tinctoria* and *Wrightia tomentosa*, leading to reduced therapeutic efficacy and inconsistent quality (Jamadagni *et al*., 2017) [9]. Quality control therefore requires comprehensive evaluation using pharmacognostic characters, physicochemical constants, chromatographic fingerprints, marker-based quantification of conessine, and molecular authentication. Adoption of Good Agricultural and Collection Practices (GACP), Good Manufacturing Practices (GMP), and pharmacopeial quality standards is essential for ensuring the safety, efficacy, and international acceptance of *Holarrhena*-based herbal products (WHO, 2003; Pawar *et al*., 2024) [13].

Commercial Importance

Holarrhena antidysenterica is one of the economically important medicinal trees utilized extensively by the Ayurvedic, Siddha, Unani, and herbal pharmaceutical industries. The stem bark and seeds constitute major raw materials in several classical Ayurvedic formulations, including Kutajarishta, Kutajghan Vati, Kutajavaleha, and numerous proprietary antidiarrhoeal preparations (Sharma *et al*., 2004) [15]. Growing global demand for plant-derived pharmaceuticals, nutraceuticals, and herbal health products has substantially increased its commercial value. In addition to domestic consumption, standardized extracts and phytochemicals, particularly conessine, have attracted considerable pharmaceutical interest because of their antimicrobial and drug-resistance-modifying properties (Mustafa *et al*., 2026) [12]. Sustainable cultivation and value-addition strategies could further enhance its economic potential while reducing pressure on natural populations.

Future Research Directions

Although considerable progress has been achieved in understanding the pharmacology and phytochemistry of *H. antidysenterica*, several important research gaps remain. Future investigations should prioritize:

a. Large-scale randomized clinical trials to validate traditional therapeutic claims.
b. Comprehensive toxicological and pharmacokinetic evaluations.
c. Elucidation of molecular mechanisms using genomics, transcriptomics, proteomics, and metabolomics.
d. Development of standardized phytopharmaceutical formulations employing nanotechnology-based drug delivery systems.
e. Identification of novel bioactive metabolites through metabolomic and artificial intelligence-assisted drug discovery approaches.
f. Sustainable harvesting protocols and cultivation strategies to ensure long-term conservation of natural populations.
g. Integration of DNA barcoding with metabolomic fingerprinting for advanced quality assurance and authentication (Pawar *et al*., 2024 [13] Mustafa *et al*., 2026) [12].

Conclusion

Holarrhena antidysenterica (syn. *Holarrhena pubescens*) remains one of the most valuable medicinal tree species of the Indian traditional healthcare system. Classical Ayurvedic knowledge together with modern scientific investigations has established its remarkable therapeutic potential, particularly in the management of diarrhoea, amoebiasis, gastrointestinal disorders, microbial infections, inflammation, oxidative stress, diabetes, liver disorders, and immune dysfunction. The pharmacological activities are largely attributed to steroidal alkaloids, especially conessine, which has emerged as a promising lead molecule for combating antimicrobial resistance. Advances in phytochemistry, metabolomics, molecular authentication, and chromatographic standardization have significantly improved the scientific understanding and quality assurance of this medicinal species. Nevertheless, robust clinical trials, comprehensive safety assessments, and sustainable conservation strategies remain essential for translating traditional knowledge into evidence-based phytopharmaceuticals. Continued multidisciplinary research integrating ethnomedicine, pharmacology, biotechnology, and pharmaceutical sciences is expected to unlock the full therapeutic and commercial potential of this important medicinal plant.

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