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Review Article

Kutaja in Paediatric Infectious Diarrhoea: A Narrative Review of Phytochemistry, Antimicrobial Activity, Antisecretory Action and Clinical Evidence

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Abstract:

Background: Acute infectious diarrhoea remains an important cause of illness and nutritional decline in children. Oral rehydration, continued feeding and appropriate zinc supplementation are the foundations of care. *Kutaja* (*Holarrhena pubescens*, commonly reported as *H. antidysenterica*) is widely used in Ayurveda for diarrhoeal and dysenteric disorders. Objective: To critically examine its Ayurvedic basis, phytochemistry, antimicrobial activity, possible antisecretory and antimotility effects, safety, and paediatric clinical evidence. Methods: A narrative review of classical sources, official standards, WHO guidance, phytochemical studies, experimental pharmacology and clinical reports was undertaken. Evidence was interpreted according to study design and paediatric relevance. Results: Steroidal alkaloids, especially conessine, are prominent constituents. Extracts and isolated alkaloids show activity against several bacteria, including enteropathogenic *Escherichia coli*. Animal models also suggest reduced stool output, intestinal fluid accumulation and excessive motility. However, extract composition varies, some mechanistic findings come from polyherbal products, and modern trials of standardised *Kutaja* monotherapy in children are lacking. Conclusion: *Kutaja* is a plausible adjunctive research candidate, but it should not replace oral rehydration, nutrition, zinc or indicated antimicrobial therapy. Child-specific dose, quality, pharmacokinetic and safety data are required before routine evidence-based use can be claimed.

Keywords: *Kutaja*; *Holarrhena pubescens*; paediatric diarrhoea; conessine; antimicrobial activity; Ayurveda

Introduction

Diarrhoea is the passage of unusually frequent loose or watery stools and is commonly caused by viral, bacterial or parasitic infection. In children, the immediate danger is not the number of stools alone but the resulting loss of water and electrolytes. The World Health Organization (WHO) therefore places

clinical assessment, low-osmolarity oral rehydration solution (ORS), continued feeding and age-appropriate zinc at the centre of management[1]. WHO also identifies acute watery diarrhoea, bloody diarrhoea and persistent diarrhoea as clinically important patterns[2].

The causes and consequences of childhood diarrhoea vary across settings. Large multicountry studies show that the pathogen profile changes with age, geography and disease severity[3,4], while repeated episodes contribute to malnutrition and remain part of a substantial global child-health burden[5]. These differences matter when a plant medicine is evaluated. An extract that inhibits a bacterium in vitro cannot be assumed to treat viral gastroenteritis, and an agent that reduces secretion cannot replace treatment for severe dehydration or invasive disease.

Kutaja is among the best-known Ayurvedic drugs used for loose stools, mucus and dysenteric features. Modern studies provide a credible pharmacological signal, particularly from its steroidal alkaloids. Yet the literature often combines traditional use, laboratory inhibition, animal models and small clinical observations as though they were equivalent.

Aim and Objectives

The aim was to critically review *Kutaja* in paediatric infectious diarrhoea. The objectives were to describe its Ayurvedic and botanical context; summarise major constituents; examine antimicrobial, antidiarrhoeal, antisecretory and motility-related findings; assess paediatric clinical relevance and safety; and identify priorities for standardised clinical research.

Review Method

A narrative review was undertaken using classical Ayurvedic texts, official monographs, WHO guidance and modern biomedical literature. Search terms included "*Kutaja*," "*Holarrhena pubescens*," "*Holarrhena antidysenterica*," "conessine," "paediatric diarrhoea," "enteropathogenic *Escherichia coli*," "antidiarrhoeal," "antisecretory," "intestinal motility," "amoebiasis" and related combinations. Primary experimental and clinical reports were preferred for specific claims, while recent reviews were used to map phytochemistry and safety.

Clinical Framework for Childhood Diarrhoea

The clinical priority is correction and prevention of dehydration. The established glucose-sodium transport principle allows ORS to replace water and electrolytes even during secretory diarrhoea [6]. Reduced-osmolarity ORS lowers stool output and vomiting compared with older formulations [7]. Zinc can shorten the course of diarrhoea in many settings, although effects vary with age, nutritional status and population [8,9]. Continued breastfeeding and feeding help protect nutritional status.

Antibiotics are not routinely indicated for uncomplicated acute watery diarrhoea. They are reserved for defined situations, including bloody diarrhoea and selected confirmed or strongly suspected infections, guided by severity and local recommendations [10,11]. A child with shock, lethargy, inability to drink, persistent vomiting, severe malnutrition, blood in stools, suspected sepsis or prolonged symptoms needs prompt medical assessment. Any study of *Kutaja* should therefore add it to, rather than replace, proven care.

Table 1: Clinical patterns and the appropriate place of Kutaja research

Clinical pattern	Immediate management priority	Relevance of current Kutaja evidence
Acute watery diarrhoea	Assess dehydration; ORS, feeding and WHO-recommended zinc[1,6]	Antisecretory or stool-reducing benefit is plausible but unproven in children
Bloody diarrhoea	Medical assessment and indicated antimicrobial treatment[1,11]	Laboratory antibacterial activity cannot replace diagnosis or antibiotics
Persistent diarrhoea	Assess nutrition, infection and underlying disease	Traditional use may justify research; clinical evidence is insufficient

Severe dehydration or shock	Urgent protocol-based rehydration and referral	No role as a substitute or reason to delay emergency care

Ayurvedic and Botanical Context

Traditional rationale

Ayurvedic texts discuss diarrhoeal disorders mainly under *Atisara*, with related consideration of *Pravahika* and *Grahani*. Clinical reasoning includes stool character, *Dosha*, strength of the patient and the state of *Agni* [12-14]. *Kutaja* bark and seeds are traditionally used when stools are frequent, poorly formed, mucoid or dysenteric. Modern *Dravyaguna* texts and the Ayurvedic Pharmacopoeia describe the drug and its gastrointestinal indications [15,16].

Botanical identity and plant part

The accepted botanical name is *Holarrhena pubescens* Wall. ex G.Don (family Apocynaceae); *H. antidysenterica* is widely retained in Ayurvedic and pharmacological literature as a synonym [17]. Bark and seeds are the most studied parts for gastrointestinal use, but their chemical profiles are not interchangeable. Authentication, plant part, harvest conditions and extraction solvent must therefore be stated in every experimental or clinical report.

Phytochemistry and Standardisation

Reviews consistently identify steroidal alkaloids as the characteristic chemical group of *Holarrhena*. Reported constituents include conessine, conessimine, conimine, isoconessimine, kurchicine, holarrhenine and related bases, alongside tannins, phenolics and other secondary metabolites [18-21]. Conessine is the best-known marker, but a traditional bark powder, a decoction, a seed extract, an alkaloid-rich fraction and purified conessine are different interventions. Recent assessment of conessine likewise emphasises formulation, toxicology and clinical-validation gaps [22].

Early isolation work established the chemical diversity of bark alkaloids [23,24], and later analytical studies identified conessine, isoconessimine, kurchessine and additional compounds in characterised material[25]. This diversity makes a single-dose label such as "*Kutaja* extract" inadequate.

Table 2: Major constituent groups and their research relevance

Constituent or group	Reported relevance	Interpretive caution
Conessine	Marker steroidal alkaloid; antibacterial and resistance-modifying activity reported[22]	Purified conessine is not equivalent to classical bark preparations
Conessimine, conimine and isoconessimine	Part of the alkaloidal profile of bark and seeds[18-25]	Content changes with plant part and extraction
Other steroidal alkaloids	May contribute antimicrobial or motility-related activity	Individual compounds have limited paediatric data
Tannins and phenolics	May add astringent, antioxidant or anti-inflammatory effects	Mechanisms in human infectious diarrhoea are not established
Whole standardised extract	Most relevant bridge to a traditional product	Requires batch fingerprinting and contaminant control

Preclinical Evidence

Antimicrobial activity

Methanolic bark extract, fractions and conessine have inhibited several tested microorganisms, although susceptibility differed among species [26]. Isolated steroidal alkaloids also show antibacterial activity [27]. Studies against multidrug-resistant enteropathogenic bacteria provide an additional signal that deserves investigation [28]. However, disc diffusion, minimum inhibitory concentration and resistance-modifying assays answer different questions and cannot be compared without standardised methods.

Conessine has shown direct activity against enteropathogenic *E. coli* (EPEC) in vitro [29]. An

alkaloid fraction from seeds also inhibited clinical EPEC isolates and altered bacterial plasmid, whole-cell and outer-membrane protein profiles in the experimental system [30]. These findings are biologically interesting, but the concentrations achieved in agar or broth may not occur in a child's intestine after an oral dose. They also do not predict activity against rotavirus, norovirus or every bacterial cause of diarrhoea.

Antidiarrhoeal activity

Ethanolic seed extract reduced the severity of castor-oil-induced diarrhoea in rats at selected doses. The same study reported benefit in an experimentally induced *E. coli* diarrhoea model[31]. Alkaloidal preparations also reduced wet stools in castor-oil models[30]. These results support a pharmacological effect on diarrhoeal physiology, but animal dose-response findings cannot be converted directly into a safe paediatric dose.

A decoction study found effects on diarrhoeagenic *E. coli*, including disruption of characteristic EPEC microcolonies and changes in toxin-related behaviour, without complete prevention of adherence[32]. This is useful because it points beyond simple bacterial killing, but it remains an experimental result rather than evidence of clinical cure.

Motility and secretion

Compounds and extracts from *H. antidysenterica* seeds have demonstrated inhibitory effects on intestinal peristalsis in experimental testing[33]. Reduced motility can lengthen contact time for absorption and reduce stool frequency. Excessive motility suppression, however, may be undesirable in invasive infection; a symptom benefit should not be confused with pathogen clearance.

Secretory diarrhoea develops when chloride and water secretion exceeds absorptive capacity. Bacterial toxins may activate cyclic nucleotide pathways and alter epithelial ion transport[34,35]. Contemporary reviews of secretory diarrhoea identify several epithelial transport targets but do not establish a specific, clinically validated ion-channel action for *Kutaja*[36]. Direct mechanistic claims should therefore remain cautious.

A polyherbal formulation containing *Holarrhena* reduced faecal output, intestinal transit, enteropooling and enterotoxin-associated secretion in rats and cell-based systems[37]. A fermented polyherbal preparation with *H. antidysenterica* as a major constituent also reduced ricinoleic-acid-induced diarrhoea and showed in-vitro antibacterial activity[38]. These studies support the plausibility of combined antisecretory and motility effects, but the activity cannot be assigned to *Kutaja* alone.

Table 3: Evidence map for *Kutaja* in infectious diarrhoea

Evidence level	What the literature suggests	What it does not establish
Traditional use	Long, specific use in *Atisara*, *Pravahika* and related disorders	Modern paediatric efficacy or a safe standardised dose
Phytochemistry	Reproducible presence of steroidal alkaloids, including conessine	Which constituent or combination drives clinical benefit
In-vitro antimicrobial studies	Activity against EPEC and other tested bacteria[26-30]	Clinical eradication, activity against all pathogens or effective intestinal exposure
Animal diarrhoea models	Reduced wet stools and severity in castor-oil and experimental *E. coli* models[30,31]	Effectiveness in naturally acquired paediatric diarrhoea
Polyherbal mechanistic studies	Antisecretory and antimotility signals[37,38]	A single-drug *Kutaja* mechanism
Clinical evidence	Historical signal in intestinal amoebiasis/giardiasis	Contemporary randomised paediatric efficacy

Clinical Evidence and Paediatric Applicability

Clinical evidence is the weakest part of the literature. A 1986 report described 40 patients with amoebiasis and/or giardiasis treated with *Kutaja* and reported

symptomatic and parasitological responses [39]. The study is historically relevant, but it predates current standards for allocation concealment, diagnostic stratification, reporting of co-interventions and adverse-event surveillance.

Children should not be treated as small adults. Age changes body-water reserve, gastrointestinal physiology, hepatic metabolism and renal clearance. Malnutrition and recurrent infection can further alter risk. A traditional dose expressed as powder or decoction cannot be translated automatically to an alkaloid-standardised extract. There are no adequate data to claim that *Kutaja* shortens paediatric diarrhoea, reduces hospitalisation or is safe across infancy and childhood.

Safety, Quality and Clinical Boundaries

Historical use does not remove the need for product-specific safety assessment. A paediatric preparation should define botanical identity, plant part, extraction method, alkaloid profile, dose and duration. It should also meet limits for microbial contamination, pesticides, aflatoxins, heavy metals and adulterants. WHO guidance on good agricultural and collection practices provides a useful upstream quality framework[40], while the Ayurvedic Pharmacopoeia provides the relevant identity and purity standard[16]. The safety of purified conessine should not be inferred from that of traditional bark preparations. Potential interactions with antibiotics, zinc and other medicines are poorly characterised. For current practice, *Kutaja* must not delay ORS, referral, diagnostic testing or indicated antimicrobial therapy. It should also not be used to suppress bloody diarrhoea without medical assessment.

Research Priorities

The next useful step is not another general efficacy claim. It is a staged development programme. First, an authenticated bark or seed preparation should be manufactured with a reproducible chromatographic and alkaloid specification. Nonclinical toxicology and age-appropriate formulation work should precede paediatric dose finding. Pharmacokinetic studies should determine whether conessine and related alkaloids are absorbed, remain mainly within the gut, or produce relevant systemic exposure.

A subsequent trial should compare standard care plus standardised *Kutaja* with standard care plus matching placebo. Children must be classified by dehydration, duration and, where feasible, stool pathogen. Primary outcomes could include time to last unformed stool and stool frequency at 24 and 48 hours. Secondary outcomes should include ORS use, vomiting, need for antibiotics, admission, recurrence and adverse events. Severe disease should be excluded or managed according to protocol without withholding treatment.

Table 4: Proposed sequence for paediatric clinical development

Stage	Essential work	Progression criterion
1. Product definition	Authenticate plant and part; specify extract ratio, fingerprint and alkaloid range	Three or more reproducible pilot batches
2. Nonclinical safety	Dose-range, target-organ, genotoxicity and interaction assessment	Justified no-observed-adverse-effect range
3. Early clinical work	Adult tolerability followed by cautious age-appropriate dose finding	Acceptable exposure and adverse-event profile
4. Paediatric adjunctive trial	Standard care plus *Kutaja* versus standard care plus placebo	Clinically meaningful benefit without delayed care or excess harm
5. Confirmatory research	Multicentre, pathogen-stratified trial with longer safety follow-up	Reproducible efficacy and defined target population

Discussion

Kutaja is a rational candidate for research because its traditional gastrointestinal use is specific, its major chemical class is identifiable, and experimental studies show both antibacterial and antidiarrhoeal signals. The strongest direct evidence concerns chemistry, laboratory antibacterial activity and

animal models. These findings make the plant more than a historical curiosity, but they do not make it a proven paediatric treatment.

The most likely explanation is multi-target activity. Steroidal alkaloids may contribute direct or resistance-modifying antimicrobial effects; other constituents may influence secretion, motility or inflammation. That model remains provisional. Studies of multi-ingredient products must not be used as proof of *Kutaja*-only action, and isolated-conessine results must not be presented as whole-plant clinical evidence.

Interpretation must also follow the clinical phenotype. A stool-reducing effect could be useful in uncomplicated watery diarrhoea when hydration is protected, but it cannot clear a virus and must not mask invasive disease. Evidence in amoebiasis may not apply to bacterial or viral gastroenteritis. This heterogeneity is why future trials should use pathogen and severity stratification rather than enrol every child under the broad label of infectious diarrhoea.

The defensible current position is therefore narrow: *Kutaja* may be studied as an adjunct to evidence-based paediatric care. Its use should be tied to a defined preparation, a measured dose and active safety monitoring. Claims of cure, replacement of antibiotics, or proven paediatric efficacy are not supported by the present evidence.

Limitations

This is a narrative rather than systematic review, and the available studies are heterogeneous in plant part, extraction, organism, dose and outcome. Several early reports have limited methodological detail. Direct human mechanistic studies and modern paediatric randomised trials are lacking.

Conclusions

Kutaja (*Holarrhena pubescens*/*H. antidysenterica*) has a long Ayurvedic association with diarrhoeal and dysenteric disorders. Modern work identifies a chemically rich steroidal-alkaloid profile and demonstrates antibacterial, stool-reducing and motility-related effects in laboratory and animal models. Conessine is an important marker, but it should not be treated as a complete explanation for the action or safety of traditional preparations.

Clinical evidence in children remains insufficient. *Kutaja* should not replace ORS, continued feeding, WHO-recommended zinc, referral or indicated antibiotics. Its most promising role is as a standardised adjunct evaluated in carefully designed, pathogen-aware paediatric trials. Such research must establish product identity, dose, pharmacokinetics, interactions and safety before routine evidence-based use can be claimed.

Declarations

Ethics approval and consent to participate

Not applicable. This narrative review did not involve human participants, human data, human tissue or animals.

Consent for publication

Not applicable.

Availability of data and materials

No new datasets were generated or analysed. All information discussed in this review is available in the cited sources.

Competing interests

The author(s) declare that they have no competing interests.

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