



## PHARMACOLOGICAL ACTIVITY AND CLINICAL PHARMACOLOGY OF KUTAJA (HOLARRHENA ANTIDYSENTERICA LINN.)- A REVIEW

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## ABSTRACT

As per WHO, in developing nations, almost 4000 million people strongly believed in the effective actions of herbal remedies and they use them on daily basis. Ayurvedic system of medicine is accepted as the ancient written medical system that is also supposed to be more effective in mostly cases than modern therapies and Ayurveda has been recognized throughout the world in the current era due to its wide spectrum therapeutic utility mainly using plant-based medicine in various disease. Information of Medicinal plant usage is available in various literature of Ayurveda like Samhitas, Nighantus etc. to cure different ailments as well as for the prevention of diseases. The plant *Holarrhena antidysenterica* Linn. (Family Apocynaceae), also known as “Indrajav”, ‘Coneru’ in English, and Kutaja in Sanskrit, is found out india up to a height of 4,000 feet. According to Raja Nighantu, there are two types of Kutaja namely Sita and Asita Kutaja,<sup>1</sup> which are botanically identified as *Holarrhena antidysenterica* Linn. And belonging to the family Apocynaceae. Acharya Charaka also mentioned the two varieties of Kutaja

(Pum and Sthree Kutaja)<sup>2</sup> which are botanically identified as *Holarrhena antidysenterica* Linn. and *Wrightia tinctoria* R Br respectively. The plant Kutaja in general is used in the management of Rakthapitha, Atisara, Kushta, Jwara, Visarpa etc. Hence there is the need of collecting the information present in the various texts in a systematic way to encourage further study on this drug from a different perspective and better utilization of this drug.

**Keywords:** Kutaja, *Holarrhena antidysenterica* Linn., *Wrightia tinctoria* R Br, Sita Kutaja, Asita Kutaja, Antimicrobial, Pharmacological activity.

## INTRODUCTION

Literary research can be considered as the basis of conceptual studies and the fundamental step of any research work. This includes - a collection of data from all the available oldest literature as well as published research works. In the Ayurveda texts, around 1200 – 1500 drugs have been incorporated in a scattered way. For executing any research on those drugs, the initial step is together all the information available about the drug to have an idea of its usage in different ailments through different therapeutic modifications as well to prevent the further repetition of proven studies. Thereby helps in the better utility of the drug clinically. Thus, the study current was initiating together information on the plant Kutaja for discovering its different therapeutic uses as well as for utilising it clinically for human beings. In classical texts like- the Samhitas, Nighantus, and recent books on Ayurveda, drug information (like- the synonyms, types, properties, therapeutic actions, Amayika prayoga) on kutaja is collected.

Some synonyms of kutaja like -

कुटजः कूटजः कीटो वत्सको गिरिमल्लिका | कालिङ्गः  
शक्रशाखी च मल्लिकापुष्प इत्यपि |

इन्द्रो यवफलः प्रोक्तो वृक्षकः पाण्डुरद्रुमः  
॥101॥<sup>3</sup>(भावप्रकाशनिघण्टु-गुडूच्यादिवर्ग)

The therapeutic utility of Kutaja is mentioned in Brihatrayees, Laghutrayee and Nighantus.

कुटजःकटुकोरूक्षोदीपनस्तुरोहिमः|अर्शोऽतिसारपित्तास्र  
कफतृष्णामकुष्ठनुत् ॥१०२॥<sup>4</sup>(भावप्रकाशनिघण्टु-  
गुडूच्यादिवर्ग)

Traditionally, it has been used to treat Atisara (diarrhoea), Jwaratisara (secondary diarrhoea), Arsa (blood or blood-related disorders), Pravahika (amebiasis), Trasnā (thirst), sukrasodhana (sperm-purification), Kusthahara (skin disease), Deepan (enhance digestion function), Vatarakta (cures gout) and Jantujit (relieves from worm infestation).

## GEOGRAPHICAL DISTRIBUTION-

*Holarrhena antidysenterica* is an indigenous plant of the tropical Himalayas. It is mainly found in tropical India, Burma, Sri Lanka, Pakistan, Nepal, and Africa. In India, it is found growing in Assam, Uttar Pradesh, down to Travancore.<sup>5</sup>

MORPHOLOGY(PHARMACOGNOSY)-



Fig. 1

Fig. 2

*Holarrhena antidysenterica* is an evergreen woody, aromatic, deciduous, and lactiferous small shrub or tree having greyish-brown and rough stem bark. The stem of the plant is whitish soft. It has 10- 20 cm long leaves which are simple and ovate to elliptical in shape and are obtusely acuminate. Flowers are small and white in colour and present in terminal corymbose cymes having a diameter of 7.5- 15 cm. The corolla tube is about 4-13cm long whose base is slightly inflated. The lobes are almost of equal length as of corolla tube and having a rounded apex. The follicles are almost 20-38 cm in length giving the appearance of two slender pencils that come from an anode which have white spots over it. The fruits are small. Numerous flat, 1-2cm long seeds are released from the brown hair when the dried fruit opens up in a split manner. The seeds are light brownish and linear/oblong concave with a long coma-like structure having linear lines over them. The seeds have a bitter taste.<sup>6, 7, 8, 9</sup>

### PHARMACODYNAMICS

Gilani et al. studied the crude hydro-alcoholic extract of *Holarrhena antidysenterica* and its fractions on isolated Guinea pig ileum.<sup>10</sup> They described the presence of both gut stimulant and relaxant activities in the extract. They concluded that these gut stimulant and relaxant activities are possibly mediated through the activation of histamine receptors and Ca (++)

channel blockade, respectively. Using activity-directed fractionation, it was revealed that the spasmogenic component was present in the aqueous fraction, while the spasmolytic component was found in the organic fraction. Ali et al. reported the inhibition of alpha glycosidase and thereby reduced the absorption of carbohydrates as possible mechanism of action of *Holarrhena antidysenterica* seed extract.<sup>11</sup>

### EXPERIMENTAL PHARMACOLOGY

#### In vivo pharmacology

*Kutaja* has been widely studied for its antidiabetic activity which is mainly found in seed extract and mostly the ethanolic extract of seeds at the dosage of 300 mg/kg has been proved beneficial. Aqueous, petroleum ether, and methanolic extracts of *Kutaja* seeds are known to have anti-hyperglycaemic and anti-hyperlipidaemic activities at the dosage of 250 mg/kg body weight (BW) in rats. In another study, the methanolic extract of *Holarrhena antidysenterica* seeds moderately protected against streptozotocin-induced diabetes at the dose of 300 mg/kg BW in rats. Its antidiabetic property was attributed to quercetin, which is used as a marker compound for *Kutaja*<sup>12, 13, 14, 15</sup>. The effect of hydro methanolic (2:3) extract of seeds of *holarrhena antidysenterica* Linn. on alpha-glycosidase activity in starch-loaded rats was studied where the extract exhibited the inhibition of alpha glycosidase activity, thus decreasing carbo-

hydrate absorption from the intestine, which in turn prevents postprandial hyperglycaemia comparable to acarbose (a modern medicine).<sup>16</sup>

### In vitro pharmacology

The in vitro cytotoxic activity of ethanolic, hydroalcoholic, and aqueous extracts of *holarrhena antidysenterica* leaves against 14 human cancer cell lines, namely, A 549, COLO-205, DU-145, HeLa, HEP-2, IMR-32, KB, MCF-7, NCI-H23, OVACAR-5, SiHa, Sk-N-MC, SW-620, and ZR-75-1, from nine different tissues, namely, breast, colon, cervix, central nervous system, lung, liver, oral, ovary, and prostate, was studied. The ethanolic extract was found beneficial against lung, colon, liver, oral, ovarian, cervical, and neural cancer cell lines. Hydro-alcoholic extract also showed similar results except on ovarian cancer cell line. The aqueous extract showed more than 50% growth inhibition in lung and colon cancer cell lines. Further fractions of the extract were studied, and it was observed that, chloroform-soluble fraction showed the highest anticancer potential against human cancer cell lines.<sup>17</sup> The in vitro antiplasmodial activity of *Holarrhena antidysenterica* whole plant extracts (chloroform and petroleum ether) using parasite lactate dehydrogenase (LDH) assay was studied. The extracts significantly reduced parasitaemia in Plasmodium berghei-infected mice as compared to chloroquine with ED50 value at 18.29 mg/kg BW where the chloroform extract showed a significant activity with IC50 value at 16 µg/ml. The cytotoxic effect on rat skeletal muscle myoblast cells (L6 cells) was studied, and no cytotoxicity was observed up to 16 µg/ml.<sup>18</sup> A similar study was performed by Dua et al. on *conessine*, an alkaloid isolated from the *Holarrhena antidysenterica* bark.<sup>19</sup> The study reports antiplasmodial activity, with IC50 value at 1.9 µg/ml using schizont maturation and 1.3 µg/ml using parasitic LDH assay. The alkaloid showed cytotoxicity with its IC50 value at 14 µg/ml, against L6 cells of rat skeletal muscle myoblast. The antidiarrheal activity of *Holarrhena antidysenterica* root bark decoction was studied on three strains of Escherichia coli, i.e., EPEC-B170, ETECTX1 (078: H 12), and ETEC B 831-2, on a culture of HEPr. *Holarrhena antidysen-*

*terica* inhibits the stable toxin production and prevents its intestinal secretions, which leads to a decrease in the virulence of enterotoxigenic (ETEC) strains. Thus, it can be concluded that *Holarrhena antidysenterica* gives protection against multiple stages of diarrhea.<sup>20</sup> Srivastava and Saxena studied the in vitro activity of the aqueous extract of *Holarrhena antidysenterica* seeds against E. coli, Shigella, Staphylococcus aureus, and Salmonella typhi organisms and found it highly effective against these pathogens responsible for diarrhea.<sup>21</sup> In another study, alcoholic and aqueous extracts of the *Holarrhena antidysenterica* stem bark were reported to have an antibacterial activity against 10 enteric pathogens at the dosage of 200 mg/ml.<sup>22</sup> The ten enteric pathogens used for the study were S. aureus, Vibrio cholerae 01, V. cholerae 0139, enteroinvasive E. coli, enteropathogenic E. coli, S. typhimurium, S. enteritidis, Shigella flexneri, Sh. boydii, and Pseudomonas aeruginosa.

### CLINICAL PHARMACOLOGY STUDIES –

दीपन पाचनं कुष्ठज्वरविसर्पशूलनुत् गुदकीलकवातास्र  
श्रमलोहितनाशनम्            ॥            कै.नि.            कुटजः  
कफपित्तास्रत्वग्दोषार्शोतिसारनुत्            ।            तद्बीजं  
रक्तपित्तातिसारज्वरहरम् हिमम् ॥ सो.नि.

According to Ayurvedic texts (kaiyadeva & Shodala Nighantu) it is clinically used in deepan (enhance digestion function), pachan (digestion), kustha (skin disease), Jwar (fever), Visharpa (skin disease), shool (pain), gudkilak (piles), Vatasra (gout), shram (fatigue), lohit nashan (Hyperbilirubinemia), twagdosha (skin disease), atisara (diarrhoea) and Raktpitta (blood disorder).

A lot of clinical studies have already been done on kutaja (*Holarrhena antidysenterica*) such as Singh (1985) reported the clinical efficacy of Kutaja stem bark extract in forty patients of clinical amebiasis and giardiasis. The extract was found to improve 70% of clinical symptoms (symptoms such as loose motions, constipation, flatulence, abdominal cramping, diminished appetite, and mucus in stools related to these infections) when given at 4 g/day per adult in three divided doses for 15 consecutive days.<sup>23</sup> Cha-



turvedi and Singh reported various side effects observed in four clinical individuals given 4 g powder of *Holarrhena antidysenterica* bark in three divided doses for 15 consecutive days. The symptoms were sensation of heat in abdomen and head, nausea, flatulence, constipation, agitation, nervousness and insomnia, vertigo, syncope, weakness and emptiness, xerostomia, and lightness of body. One patient reported a decrease in body temperature.<sup>24</sup> Pal et al. also observed that the *Holarrhena antidysenterica* stem bark powder administered to patients with bleeding piles at a dose of 4 g twice a day for 2 weeks each showed significant efficacy.<sup>25</sup> Panda et al. reported a reduction in glycosylated haemoglobin after administration of ethanolic extract of *Holarrhena antidysenterica* seeds to a 65-year-old woman for 48 consecutive days, suggesting that *Holarrhena antidysenterica* seeds have a promising action against mild-to-moderate type II diabetes mellitus.<sup>26</sup>

## CONCLUSION

The plant *Holarrhena antidysenterica* Linn. has the potential to develop drug against various enteric, skin diseases and diabetes.

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