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Phyto-Pharmacology Profile Of Holarrhena Antidysenterica: A Review

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Abstract

Medicinal plants have been recognized for centuries and are highly regarded worldwide as a valuable source of therapeutic agents for disease prevention and treatment. Holarrhena antidysenterica, commonly known as kauri, kurchi, or kutaj, has been employed since ancient times. Holarrhena antidysenterica (also known as H. pubescens), a member of the Apocynaceae family, is renowned in Ayurveda for its medicinal properties found in its stem bark, leaves, and seeds. Over the years, researchers have isolated various phytochemical compounds from this plant, demonstrating their traditional pharmacological effects, including analgesic, antibacterial, anti-diarrheal, anti-diabetic, antioxidant, anti-urolithic, and anti-inflammatory activities. Furthermore, recent studies have unveiled novel activities such as angiotensin-converting-enzyme inhibition, acetylcholinesterase inhibition, anti-amnesic effects, and neuroprotective properties. This review aims to shed light on the therapeutic potential of Holarrhena antidysenterica for various diseases.

Keywords: Holarrhena antidysenterica, Conessine, Anti-amnesic, Neuroprotective.

INTRODUCTION

Medicinal plants have been revered for thousands of years and are globally valued as abundant sources of therapeutic compounds for preventing diseases and ailments. There is a growing demand for plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics, and more in both developing and developed countries. This trend is driven by the increasing recognition that natural products are generally non-toxic, have fewer side effects, and are readily accessible at affordable prices. One such plant with significant medicinal properties is Holarrhena antidysenterica Linn, belonging to the Apocynaceae family. Commonly known as "Indrajav," "Coneru" in English, and "Vatsaka" in Sanskrit, this shrub is widely distributed across India, thriving at altitudes of up to 4,000 ft. In traditional Indian medicine, this plant has long been employed as an effective remedy for treating dysentery, diarrhea, and intestinal worm infestations (Kavitha D et al., 2004). The tree is particularly renowned for its therapeutic properties, with its seeds and bark extensively used in Ayurveda. The stem bark, referred to as "kurchi" in the Indian subcontinent and "conessi bark" in Europe,

holds a prominent place in traditional Ayurvedic medicine, especially for the treatment of amoebic dysentery. It is valued for its antimicrobial, anti-inflammatory, and analgesic properties (Sharma U. et al., 2009). Other parts of the plant, such as the roots and leaves, are also utilized for medicinal purposes. Both the bark and roots are highly effective in addressing both acute and chronic dysentery, particularly when it involves excessive blood and mucus and is accompanied by colic pain during bowel movements. Additionally, the plant has been recognized for its anthelmintic, appetizing, antidiarrheal, and astringent qualities. Holarrhena antidysenterica has also been documented for its immunomodulatory properties, ability to inhibit larval growth, and utility in combating malaria and vaginitis (Mahato S. et al., 2013).

❖ SCIENTIFIC CLASSIFICATION;

Scientific Classification of Holarrhena antidysenterica (Jamadagni PS et al., 2017):

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Superdivision: Spermatophyta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Subclass: Asteridae
- Order: Gentianales
- Family: Apocynaceae
- Genus: Holarrhena
- Species: Holarrhena antidysenterica

❖ VERNACULAR NAME;

Vernacular Names of Holarrhena antidysenterica (Jamadagni PS et al., 2017):

- English: Tellicherry Bark
- Hindi: Karva Indrajau, Kutaja, Kurchi
- Sanskrit: Indrayava, Kutaja, Sakraparyaaya, Sakraasana, Vatsaka
- Tamil: Kirimllikai, Kutaca-P-Palai, Mlaimllikai
- Telugu: Girimallika, Kodisepala, Kolamukku, Kondamalle, Kutajamu
- Punjabi: Keor, Kewar
- Gujarati: Kadavo Indrajav

❖ PLANT DESCRIPTION;

Description of Holarrhena antidysenterica (Ganapathy PS et al., 2011 and Sinha S et al., 2013):
Holarrhena antidysenterica Linn is a deciduous shrub or small tree that can reach heights of up to 13 meters and have a girth of 1.1 meters, featuring a clear bole (the main trunk of a tree) ranging from 3 to 7 meters in length. The leaves of this plant are 15–30 cm long and 4–12 cm wide. They have an obtuse base, which is often rounded or acute. The leaves exhibit 10–14 pairs of opposite, sessile (without a stalk), elliptic, or ovate nerves. They are oblong, membranous, strong, and have an arched shape. The petioles (leaf stalks) can measure up to 1.5 cm in length. The cymes (inflorescence clusters) of the plant have a diameter ranging from 3 to 6 cm. The seeds of Holarrhena antidysenterica are 1-2 cm long and have a linear or oblong concave shape, along with a long coma. They are light brown and are marked with linear lines. These seeds have a bitter taste.

Fig no.1. Holarrhena antidysenterica plant

❖ ORIGIN AND DISTRIBUTION;

Origin and Distribution of Holarrhena antidysenterica:
Holarrhena antidysenterica is primarily abundant in India, particularly in the Himalayan Mountain ranges. It holds significant traditional and folklore value in India, with its leaves being offered along with rice during the festival of "Nabanna" in the Odisha state of India. This plant is found in various tropical and subtropical regions of Asia and Africa. It can be located in countries such as Burma, Sri Lanka, Pakistan, Nepal, and various parts of Africa. The tree typically blooms and produces flowers during May and July. In India, Holarrhena antidysenterica can be found throughout the country, especially in the deciduous forests of the tropical Himalayas. It thrives at altitudes ranging from 900 to 1250 meters above sea level (Kumar N et al., 2007).

❖ CHEMICAL CONSTITUENTS;

The stem bark and seeds of Holarrhena antidysenterica are known to contain several steroidal alkaloids, including:

1. Conanines
2. 3-Aminoconanines
3. 20-Aminoconanines
4. 3-Aminopregnans
5. 3,20-Diaminopregnanes

Additionally, a new steroidal alkaloid called holadysenterine has been isolated and characterized from this plant. Holadysenterine is represented by the molecular formula C23H38N2O3.
Specifically, the stem bark of Holarrhena antidysenterica contains the following steroidal alkaloids:

1. Conessine (C24H40N2)
2. Isoconessine (C24H40N2)
3. Conessimine/Isoconessimine (C23H38N2)
4. Conarrhimine (C21H34N2) (Yang ZD et al., 2012)

These chemical constituents are responsible for the medicinal properties and therapeutic effects associated with Holarrhena antidysenterica, making it a valuable plant in traditional medicine systems.

❖ PHARMACOLOGICAL ACTIVITIES;

- **Anti-amnesic activity**

Administration of ethanolic extract of Holarrhena antidysenterica seeds for 28 days to the separate groups of STZ significantly decreased the level of AChE as compared to the diseased group, and prevented the rise in MDA levels and GSH depletion in a dose-dependent manner [Mrinal et.al 2016]. Cholinergic dysfunction was assessed by acetylcholinesterase activity. Decreased levels of AChE, prevented levels of MDA and Glutathione showed anti-amnesic properties of Holarrhena antidysenterica.[]

- **Neuroprotective activity**

Treatment with MEHA significantly prevented a fall in body weight as compared to the diabetic control group, The elevated levels of blood glucose and plasma cholesterol levels were significantly depleted, and HbA1C level was considered as a key indicator of AGEs and in the present investigation treatment with MEHA significantly inhibited this elevated level of HbA1c. MEHA-treated rats showed improvement in locomotor activity as compared to their non-treated counterparts indicating the prevention of diabetic neuropathy [Bansal N et al 2016].

- **Acetylcholinesterase inhibitory**

The alkaloidal extract of Holarrhena antidysenterica seeds was subjected to microplate assay for AChE and found to have 91% inhibition of AChE. The alkaloidal extract was subjected to column chromatography over an MCIGEL using a gradient solvent system MeOH–H2O (50%, 60%, 70%, 80%, 90%) (v/v) to afford three fractions (Fr. 1 to Fr. 3). The five compounds were tested for AChE inhibiting activity by the Ellman's method in 96-well microplates [Ellman GL et.al 1961]. The total alkaloidal extract from the seeds of H. antidysenterica strongly inhibited the AChE with an IC50 value of 6.1 μg/mL while huperzine A showed AChE inhibiting activity with an IC50 value of 0.015 μg/mL [Yang ZD, et. al 2012].

- **Antidiabetic activity**

Ethanolic extract of HA significantly reduced plasma glucose levels ½ hr after administration of glucose in euglycemic rats. Diabetic rats showed a decrease in body weight during the experimental period. H. antidysenterica and glibenclamide-treated diabetic group rats showed a significant increase in weight. The decrease in blood glucose level in the treated group decreased the total cholesterol, triglyceride, AST, ALT, urea, and serum creatinine [Umashanker KPd et al 2012]. Methanolic extract of Holarrhena antidysenterica showed the same results in diabetic rats [Mana S et.al 2010]. These parameters are an indication of its better metabolic control and potent antidiabetic anti-diabetic properties. Hepatic glucose-6-phosphatase is an important enzyme in glucose homeostasis [Berg JM et.al 2001] and it is negatively regulated by insulin [Das D. 2002]. After administration of the aqueous extract, significant recovery was noted in these biosensors which may be due to insulin recovery [Ali KM et al. 2009]. Inhibition in the activity of intestinal α-glucosidase is an important strategy to control postprandial hyperglycemia in diabetes. The blood glucose level was significantly lower in acarbose or different doses of hydromethanolic extract treated groups concerning the control group. Phenolic compounds and flavonoids of the extract are responsible for the inhibition of α-glucosidase activity and thereby inhibit glucose absorption in connection with the management of postprandial hyperglycemia [Ali KM et al. 2011]

- **Anti-urolithic activity**

Crude extract of HA in vitro study showed inhibition of DPPH (2,2-Diphenyl-1-Picrylhydrazyl) free radical for antioxidant effect and inhibited lipid peroxidation, induced in rat kidney homogenate. Ha. Cr had no toxic effect on MDCK (kidney epithelial cell lines) cells. In in vivo experiment Ha.Cr had no significant effect on the CaOx crystalluria. The body weight was reduced in stone forming group as compared to the normal saline group. The co-administration of Ha. Cr prevents the loss of body weight. A co-treatment with Ha. Cr reduced polyurea and water intake compared to stone forming group. Oxalate excretion was increased in stone-forming animals, whereas Ca++ excretion was decreased. In histological study Ha.Cr-treated groups, less number of CaOx crystal deposits [Khan A et al. 2012]. Through this article, it can be speculated that the inhibitory effect of the plant extract on CaOx crystal deposition in renal tubules is possibly caused by its antioxidant activity. Thus, these data suggest that the preventive effect of Holarrhena antidysenterica in urolithiasis is mediated through multiple pathways. A few articles are also studied for ulcerative colitis and bleeding piles [Patel MV, et al 2010 & Paranjpe P et al. 2000].

- **Antibacterials activity**

For antibacterial activity, the study was done by studying the zone of inhibition (in mm) observed on three bacteria (Staphylococcus aureus, Salmonella typhimurium, and Escherichia coli). From bark extract, a 10.05 mm inhibition zone was observed showing the highest antibacterial activity against Staphylococcus whereas, in the case of Salmonella and E. coli, it was only 6.65mm and 2.7mm respectively. Holarrhena antidysenterica seed extract with 100% concentration also showed antibacterial activity against Staphylococcus. Callus extracts with 100% concentration showed a 4 mm inhibitory zone against Staphylococcus and its least activity was observed in E. coli with a 3.1mm inhibition zone even at 100% concentration. Results obtained in the present study revealed that three types of extracts of Holarrhena antidysenterica possess potential antibacterial activity against Staphylococcus, Salmonella, and E. coli [3]. Various workers have already shown that plant extracts have antibacterial activity in many aspects [Lin J et.al 1999 & Parekh J et.al 2006].

- **Anti-inflammatory and Analgesic Activity**

Methanolic leaf extract of Holarrhena antidysenterica revealed inhibition of rat paw edema induced by carrageenan. Furthermore, the Methanolic extract of Holarrhena antidysenterica suppressed acetic acid-induced writhing response in dose dose-dependent manner and demonstrated the analgesic effect by improving tail flick latency [Parekh J et al. 2006 & Ganapathy PSS et al. 2010]. Ethanolic extract of H. antidysenterica exhibited an analgesic effect by suppressing the writhing response in albino mice [Shwetha C et.al 2014]. The methanolic bark extract of H. antidysenterica exhibited decreased levels of nitric oxide and malondialdehyde levels and showed increased levels of superoxide dismutase and glutathione in 2,4-Dinitrobenzene sulfonic acid-induced colitis in male albino Wistar rats. The decreased level of nitric oxide thus suggests that reduction in iNOS generation may be responsible for the anti-inflammatory effect. H. antidysenterica treatment also prevented the rupture of goblet cells, inflammatory cellular infiltration, and inflammation in the mucosal layer [Shwetha C et.al 2014].

- **Anti-malarial activity**

Conessine isolated from the stem bark of H. antidysenterica exhibited the greatest anti-plasmodial activity, with reproducible IC50 value 1.3 µg/ml in the in-vitro experiment and 88.95% suppression of parasitemia in vivo experiment when administered at 10 mg/kg. Furthermore, liver function tests were observed due to conessine cytotoxic nature. liver is the most affected organ in the early stage of malaria leading to significant alterations in the host hepatocyte physiology and morphology. Elevated levels of Alkaline phosphatase (ALP) and bilirubin are an indication of hepatocyte damage due to malarial infection. The elevated levels of ALP and bilirubin were significantly depleted at a dose of 30mg/k [. Darji VC et al 20113 & Dua VK et.al 2013].

- **Anti-diarrhoeal activity**

Ethanolic extracts from the seeds of Holarrhena antidysenterica demonstrated a substantial increase in fecal dry weight and a decrease in defecation frequency in rat models with diarrhea induced by castor oil and Escherichia coli, as reported by Sharma et al. in 2015. Aqueous and alcoholic extracts from the bark of this plant have been documented to exhibit antibacterial properties against enteroinvasive E. coli (EIEC), Salmonella enteritidis, Shigella boydii, and Shigella flexneri, as observed in a study conducted [Dey et al.2012]. The commercially available H. antidysenterica preparation known as "kutaja parfait vati" has demonstrated significant efficacy in reducing watery diarrhea and intestinal motility in rats with castor oil-induced diarrhea. Additionally, it exhibited a remarkable 67.55% protection against castor oil-induced enteropooling, as reported [Gupta et al. in 2012].

CONCLUSION;

The existence of diseases has been intertwined with humans throughout history, and the rich treasury of herbal medicines has held untapped potential for decades. This paper delves into the exploration of Holarrhena antidysenterica as a promising medicinal plant, highlighting its extensive range of pharmacological activities that offer potential applications in various medical fields due to their effectiveness and safety. Holarrhena antidysenterica has a longstanding tradition of use in treating diseases such as diarrhea, dysentery, inflammation, and as an antioxidant and anti-malarial agent. However, advancements in technology and experimental research have unveiled additional pharmacological properties of this plant, including anti-amnesic and neuroprotective activities. One of the remarkable aspects of Holarrhena antidysenterica is its composition of unknown chemical constituents. These constituents hold great promise for pharmacists and researchers, offering opportunities to synthesize and formulate novel drugs for the treatment of various other diseases. This underscores the immense potential of traditional herbal medicines and their continued relevance in modern healthcare research and development.

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