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Review Article

Evaluation of phytochemical and pharmacological aspects of *Holarrhena antidysenterica* (Wall.): A comprehensive review

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ABSTRACT

Medicinal plants are generating an ever-increasing amount of interest due to the effectiveness, low cost and minimal side-effects associated with drugs derived from them. *Holarrhena antidysenterica* (syn. *H. pubescens*) WALL., belonging to the family Apocynaceae, is commended for the medicinal applications of its stem bark, leaves and seeds in Ayurveda. During the past century, studies on the phytochemical and pharmacological nature of the plant have yielded important results regarding the chemical constituents present and have also verified the traditionally claimed properties associated with the plant viz. analgesic, antibacterial, anti-diarrhoeal, anti-amoebic, anti-inflammatory and anti-haemorrhoidal activities. Moreover, recently some other properties have also been discovered viz. anti-malarial, anti-diabetic, anti-oxidant, anti-urolithic, anti-mutagenic, CNS-stimulating, Angiotensin-converting-enzyme inhibitory and acetylcholinesterase inhibitory activity. This review discusses the findings of studies on the aforementioned properties of the plant in detail and 68 alkaloids isolated from various parts of plant to justify its widespread use in the treatment of a variety of diseases and suggests future lines of research.

1. Introduction

Medicinal plants have been known to exist since centuries, but their importance as a source of vital drugs remained unknown until the establishment of human civilisations. This was followed by the development of ancient medical literature such as the *Rig Veda* and *Sushruta Samhita* in Ayurveda, Dioscorides' *De Materia Medica*, the *Ebers Papyrus* of ancient Egyptians, and the *Pen Tsao* of the Chinese. In India, Ayurveda is the predominant source of traditional medicinal knowledge, in which the central idea is the presence of three "*doshas*", or body systems, named *kapha*, *pitta* and *vata*. The Unani and Siddha systems of medicine also find some importance in certain regions of India, according to which, certain elements

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when present in a balanced state lead to proper health while their imbalance leads to various forms of diseases.[1]

Holarrhena antidysenterica (Roxb. ex Fleming) Wall. (Syn. *Holarrhena pubescens* (Buch.Ham.) Wallrch ex. Don) is commonly known as Tellicherry Bark (English) and Kurchi (Hindi), and belongs to family Apocynaceae. The plant is found in tropical and subtropical regions of Asia and Africa. In India, it can be found throughout the country, especially in deciduous forests of tropical Himalayas, at altitudes ranging from 900 to 1250 m.[2]

H. antidysenterica is being used in Indian ayurvedic medicine system to treat *atisaara* (diarrhoea and dysentery). According to Charaka, the pods have *stanyasodhana* (a lactodepurant), the *indrayava* (seeds) have *ama* and *asthapanopaga* (adjuncts to enema) and the plant contains *vamaka* and *arsoghna*, which have emetic and anti-haemorrhoidal properties respectively. *Susruta* attributes the seeds with having diuretic properties and the plant in general as *sukrasodhana* (sperm-purifier). In the *Susruta Samhita* the plant is described as antiseptic, vermifuge, febrifuge, detoxicant and is believed to cure malignant ulcers, leprosy, diarrhoea and other virulent skin diseases. In modern Ayurveda, the plant is suggested for treating obesity, asthma, bronchopneumonia, hepatosplenomegaly and rheumatism.[3] *H. antidysenterica* is a major ingredient in several Ayurvedic preparations such as *Kutajghan Vati*, *Kutajarista* and *Kutaja churna*, which are used to treat dysentery, diarrhoea, fever and bacterial infections.[4–6] Recently, a number of studies have been done on isolation and characterization of phytochemicals, as well as on several pharmacological properties of *H. antidysenterica* based on experimental trials on animals.

2. Pharmacological properties

2.1. Anti-diabetic efficacy

A recent study reported significant recovery in diabetic rats when they were orally administered with doses of 300 mg/kg and 600 mg/kg of ethanolic extract of seeds. Each week of treatment showed significant decrease in levels of blood glucose, serum cholesterol, triglyceride, aspartate transaminase, alanine transaminase, alkaline transferase, urea, creatinine and uric acid while the weight of the rats increased substantially.[7] Methanolic seed extracts have also shown similar results in streptozotocin-induced rats.[8] Inhibition of α-glucosidase was observed in normoglycemic rats when administered with hydro-methanolic seed extract of *H. antidysenterica*. This enzyme helps in absorption of glucose from intestines and therefore, can play a major role in regulating postprandial diabetes.[9] In another study, no metabolic toxicity of the hydro-methanolic seed extract was reported by glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT) activities in the liver and kidneys.[10]

2.2. Anti-diarrhoeal property

Ethanolic seed extracts of *H. antidysenterica* in castor oil-induced diarrhoea in rats *in vivo* have shown a significant increase in the dry weight of their faeces and reduction in defecation drops. Aqueous and alcoholic bark extracts are also known to act against enteroinvasive *E. coli* (EIEC), *Shigella flexneri*, *Shigella boydii* and *Salmonella enteritidis*.[2] Aqueous and methanolic leaf extracts of *H. antidysenterica* were found to inhibit the growth of diarrhoeal pathogens *Salmonella typhimurium*, *Vibrio cholerae*, *Vibrio alginolyticus*, *Vibrio cholera* 0139, *E. coli* 0157:H7 and *Salmonella typhi*.[11]

2.3. Anti-inflammatory and analgesic property

Methanolic bark extract of *H. antidysenterica* demonstrated decreased nitric oxide and malondialdehyde levels and increased levels of superoxide dismutase and glutathione levels in 2,4-Dinitrobenzene sulfonic acid induced colitis in male albino wistar rats. The rats also resisted rupture of goblet cells, inflammation in mucosal layers and inflammatory cellular infiltration.[12] Furthermore, methanolic leaf extracts demonstrated inhibition of rat paw oedema in carrageenan-induced paw oedema in Swiss albino mice.[13]

H. antidysenterica has been mentioned in Ayurveda to have analgesic effects. Methanol bark extract on Swiss albino mice and wistar rats showed analgesic effects.[14]

2.4. Antioxidant/free radical scavenging property

It has been established that the application of free radical scavenging compounds have healing effect and property of protecting tissue from oxidative damage. Recently in a study that investigated antioxidant property of *H. antidysenterica*, methanolic leaf extracts were found to scavenge superoxide ions and hydroxyl ions as well as reduced capability of converting $Fe^{3+} \rightarrow Fe^{2+}$. Further, the efficiency of these effects was found to be proportional to the concentration of the extract.[15] Hydro-methanolic seed extracts of the plant also showed inhibition of deoxyribose degradation by OH^- ions, inhibition of nitrite formation by competing with O_2, degradation of H_2O_2 and inhibition of lipid peroxidation, all from the ethyl acetate fraction.[16]

2.5. Anti-urolithic property and anti-haemorrhoidal action

Crude aqueous methanolic seed extracts of *H. antidysenterica* significantly decrease the size of calcium oxalate crystals and convert them from calcium oxalate monohydrates (COM) to calcium oxalate dehydrate (COD) *in vitro*. The extract suppresses cell toxicity (induced by COM) and production of lactate dehydrogenase. The extract was tested *in vivo* in male wistar rats, which showed substantial decrease in polyurea, water intake, Ca^{++} excretion and crystal formation.[17]

Stem bark extract of *H. antidysenterica* in the form of "Kutaja tvak churna" showed healing activity in patients suffering from bleeding piles.[18]

2.6. Diuretic property and anti-amoebiasis

Aqueous seed extract of *H. antidysenterica* showed a significant increase in urine output of wistar rats at dosage range of 30–100 mg/kg. A substantial increase was also observed in the amount of Na^+ and K^+ ions excreted through urine of treated rats.[19]