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Haldina cordifolia: A potential plant in drug discovery research

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Abstract

Ailments are the always together companions of the life. The labors to heal ailments and the aspiration to attain liveliness and prolonged existence encouraged the early man to explore the natural surroundings. In his pursuit, the herbs became the early medicines of the man. Astonishingly, still 80% of the world population relies on traditional medicines. World Health Organization encourages the traditional medicines as they are economical, easily and copiously available, and also comparatively free from side effects. There are many medicinal herbs and spices, which find place in day-to-day uses, many of these, are used as herbal remedies. Some insignificant ailments like common cold; cough etc. may be cured by herbal remedies with employ of medicinal properties of spices. The effectiveness of herbal remedies brought us interest to study this vital plant which has numerous therapeutic ranges and has also provide researcher for the future scope of work. *Haldina cordifolia* is very important plant having wide range of activities and can be helpful for finding novel molecules in drug discovery research.

Keywords: *Haldina cordifolia*, astringent, refrigerant, diuretic, demulcent, aphrodisiac etc.

Introduction

There are numerous biologically active plants symbolize a rich resource of drugs independently or in combination have been suggested in a variety of therapeutically treatment for the management of diverse diseases. *Haldina cordifolia* is an India, Ceylon, Thailand, and Burma; spread in varied deciduous forests second-hand by conventional healers for the management of chronic cough, and uses in jaundice, stomachache, fodder and swelling in stomach, the roots are astringent and constipating, and are useful in diarrhea and dysentery [1]. The bark is acrid, bitter, astringent, refrigerant, vulnerary, diuretic, demulcent, aphrodisiac and tonic. It is useful in vitiated conditions of pitta, wounds and ulcers, stranguary, skin disease, gastropathy, fever and burning sensation. In the literature, *Haldina cordifolia* is described as to have wide range of medicinal applications. It has been used as antiamebic, anti-inflammatory, antinociceptive, ant fertility. This article explains the evidence based information regarding the phytochemistry, pharmacological activity and medicinal uses of this plant [2].

In ancient times, medicinal plants have been used all over the world as unique sources of medicines and may constitute the most common human use of biodiversity. According to the World Health Organization (WHO), 80% of people in developing countries still depend on local medicinal plants to fulfill their primary health needs. In India, there are about 550 tribal communities covered under 227 ethnic groups residing in about 5000 villages in different forest and vegetation types. India with its glorious past of traditional medicinal system and use pattern of different plants is one of eight major centers of origin and diversification of domesticated taxa. Having rich biodiversity and is one of the world's twelve mega diversity countries [3]. Besides that, there is a global consensus on the benefits of phytopharmacy and at present medicinal plant. Occupy a key position in plant research and medicine. Many plants species which are extensively used as medicine need phytochemical investigation to search active medicaments. Many plants species containing active ingredient of medicinal values are yet to be discovered. This fact prompted us to undertake phytochemical investigation of plants for the research [4]. A wide range of medicinal plant parts is used for extract as raw drugs and they possess varied medicinal properties. The different parts used include leaves, root, stem, flower, fruit, twigs exudates and modified plant organs. While some of these raw drugs collected in larger quantities and traded in the market as the raw material for many herbal industries [5]. Herbal medicinal which is the use of medicinal plants or drugs from medicinal plants in the treatment and cure of sickness and diseased conditioned [4]. The herbal products today symbolize safety in contrast to the synthetics that are regarded as unsafe to human and environment. Although, herbs had been priced for their medicinal, flavoring and aromatic qualities [5].

Herbal medicine is a major component in all indigenous people's traditional medicine and a common element in Ayurvedic, Homeopathic, Unani, Naturopathic, and Traditional Oriental [6]. In rubiaceae family containing plants are used as medicinal use and contain the secondary metabolites. Rubiaceae is by far the largest family in the flowering plants order gentianales. It is also the oldest family that branched off on the gentianales family tree. The family rubiaceae comprises about 450 genera and 6500 species and includes trees, thousand infrequently herbs 7-10. Among the many plants *Haldina cordifolia* is one from Rubiaceae family. Synonym: *Adina Cordifolia* (Roxb.), Local name: Kadami, Haldu, English name: Yellow Teak, Saffron Teak. A large deciduous tree, under good conditions grows, over 30 m., but is normally about 14-20 m tall, leaves up to 25 cm or more across, broadly oval or circular in shape, acute at the apex, heart-shaped at the base, slightly hairy especially when young, green or tinged with red or pink; nerves a strong one running from the base to the tip of the leaf and 5-6 pairs of lateral ones, which unite in a wavy line near the margin of the leaf. Leaves come out in pairs, one on either side of a branch, their stalks connected by a pair of stipules. These are two leaf-like structures, up to 2.5 cm. long, enclosing and protecting the very young leaves and shoot apex; when the stipules fall away, they leave two clear lines, each encircling half of the branch. Leaf stalks are 5-10 cm, long. Flowers are insignificant individually, being very small; but they come out in balls 2-3 cm. across; the tiny flowers are yellow or yellowish in color, often tinged with pink. When the little flowers open out, the most prominent parts are the styles, which form a sort of halo round the floral ball. Fruits are minute, forming an almost solid ball, which when ripe is black or nearly black. Leaves are shed about February, and the tree remains leafless until about may-june; the stipules covering the buds are than very conspicuous. Flower balls are at their best from June to August. After the fruit proper has been shed at about the beginning of June of the following year, the fruit-heads appear black and are about 12 mm. across: the rains of the monsoon may bring them down and prepare the tree for the new flower balls.

The chemical constituents of in *Haldina cordifolia* Root and Bark are oleoresin, essential oil, cellulose, β -sitosterol [13]. The shade dried bark powder of *Adina cordifolia* was extracted with ethanol and ethanolic extract was fractionated with different solvents. Phytochemical screening of ethanolic extract and its four fractions reveals the presence of Alkaloids, flavonoids, saponins, terpenes, tannins, carbohydrates [14]. All the fractions of ethanol extract were screened for their hepatoprotective effect against CCl₄ induced hepatotoxicity in wistar albino rats. The degree of hepatoprotectivity was measured by using biochemical parameters like serum transaminases (SGOT and SGPT), alkaline phosphates, total protein and total bilirubin in the treated groups, and morphological parameters as change in liver weight and liver volume. The ethanol extract and butanol fraction shows significant hepatoprotective activity as comparable with against CCl₄ induced hepatotoxicity as evident by restoration of serum transaminases, alkaline phosphates, total protein and total bilirubin. Histopathology of the liver tissue further supports the biochemical finding confirming the hepatoprotective potential of these two fractions. The present study shows that ethanol extract and butanol fraction of *Adina cordifolia* is significantly capable of restoring integrity of hepatocytes indicated by improvement in physiological parameter of hepatocytes. The acetone and

aqueous extracts of *Haldina cordifolia*, belonging to the family rubiaceae, were studied for hepatoprotective activity against wister rats with liver damage induced by ethanol. Active principle from root bark of *Haldina cordifolia* was extracted in benzene and ethyl acetate and was seen to exhibit antiameobic activity with IC₅₀ values of 2.92 and 2.50 μ g/ml, respectively [16]. Studied extractives of some forest produce including acetone and alcohol extracts of bark and roots of *Dalbergia stipulacea*, leaves of eucalyptus hybrid and *Adina cordifolia*, ursolic acid and bryonolic acid were evaluated as insect antifeedant against poplar defoliator *Clostera cupreata* (Lepidoptera: Notodontidae). Ursolic acid (separated from Eucalyptus hybrid leaves extract) has shown maximum Anti-feedant activity and gave over 92 per cent protection of poplar leaves from its pest. It was followed by alcohol and acetone extracts of eucalyptus hybrid leaves, bryonolic acid, acetone extract of *D. stipulacea* bark, alcohol extract of *A. cordifolia* leaves [8]. Studied on the plants like *Adina cordifolia*, *Asparagus racemosus*, *Aegle marmelos*, *Cassia Tora*, *Dillenia pentagyna*, *Valeriana wallichii* showed little activity (5 to 8mm) against some pathogenic microorganisms [17]. Isolation of 7-hydroxycoumarin and 7-beta-D-glucosyl coumarin, respectively. Umbelliferone was converted into 7-acetoxycoumarin, which on treatment with aluminum chloride afforded 7-hydroxy-8-acetylcoumarin. A new series of thiosemicarbazones of 7-hydroxy-8-acetylcoumarin with different thiosemicarbazides were synthesized. Umbelliferone was also converted into its methoxy derivative (7-methoxycoumarin). Subsequently, the entire compound assessed antiameobic activity [13]. Studied on Evaluation of Anti-inflammatory potential of *Adina cordifolia* bark. Carried studies Petroleum ether and ethyl acetate extracts of *Adina cordifolia* bark were screened for anti-inflammatory and analgesic activity. Studied on extract of *Adina cordifolia* leaves and Bark using the solvent Dichloromethane and methanol shows the activity against micro-organism. A new Indole alkaloid from the heartwood of *Adina cordifolia*. *Haldinia cordifolia* stem had been evaluated for its antiulcer potential. Enzyme assay-guided fractionation of the chloroform extract yielded 7-hydroxycoumarin as the active constituent which showed interesting HqrKq ATPase inhibitory activity. Studied on Preliminary pharmacology of acetone extract fraction of wood of *Adina cordifolia*. Four compounds isolated from the stem of *Adina cordifolia* were identified as stigmasta-5, 22-diene-3 β -O-rhamnopyranosyl-(1D-xylopyranoside, α -amyrin, octacosanol, and naringenin-7-methyl-ether-4'- α -L4) - β -O- α -L-rhamnopyranoside on the basis of spectral and chemical evidence [25]. Studied on Four compounds isolated from the stem of *Adina cordifolia* were identified as stigmasta-5, 22-diene-3P-O-a-rhamnopyranosyl-(1-4)-P-Dxylopyranoside, α -amyrin, octacosanol, and naringenin-7 methyl ether - 4'-O-a-rhamnopyranoside on the basis of spectral and chemical evidence.

The acetone and ethanol extracts from the leaves of *Adina cordifolia* i.e. Aqueous Extract of *Haldina cordifolia* and Ethanolic extract of *Haldina cordifolia* respectively were evaluated for anticancer activity against Ehrlich Ascites Carcinoma (EAC) bearing Swiss albino mice [7]. The extracts were administered at the doses of 500 mg/kg body weight per day for 14 days after 24 h of tumor inoculation. 24 h after the last dose, with fasting, the mice were sacrificed. The study deals with the effect of Aqueous Extract of *Haldina cordifolia* and Ethanolic extract of *Haldina cordifolia* on mean survival time, peritoneal cell count, hematological studies, tumor

volume, tumor weight, tumor cell count, body weight and *In vitro* cytotoxicity. Aqueous Extract of *Haldina cordifolia* and Ethanolic extract of *Haldina cordifolia* caused significant decrease in tumor volume, tumor weight, tumor cell count, body weight and it prolonged the life span *i.e.* mean survival time of EAC-tumor bearing mice and normal peritoneal cell count in normal mice. Hematological profile converted to more or less normal levels in Aqueous Extract of *Haldina cordifolia* Ethanolic extract of *Haldina cordifolia* treated mice. Aqueous Extract of *Haldina cordifolia* and Ethanolic extract of *Haldina cordifolia* also exhibited significant cytotoxic activity at 200 μ g/ml, but higher cytotoxic activity was found in Aqueous Extract of *Haldina cordifolia*. The results indicate that Aqueous Extract of *Haldina cordifolia* and Ethanolic extract of *Haldina cordifolia* exhibited significant anticancer activity in EAC-bearing mice.

Hydro alcoholic activity extract of *Haldina cordifolia* was shown significant activity in alloxan induced diabetes rats [8]. The extract showed activity at the doses of 500 mg/kg body weight. A numbers works carried out for the anti-diabetic activity and many medicinal plants and their metabolites are used for the treatment of diabetes in different system of medicines however many other active ingredients obtained from plants have not been characterized. *Haldina cordifolia* was given to diabetic rats continuously for 15 days which resulted in dose dependent reduction of blood sugar level compared to diabetic control rats. The extract was found to contain tannins, phenolic compounds, flavonoids, saponins, gums and mucilage etc. These constituents are thought to be responsible for anti-diabetic activity. The anti-diabetic effect of majority plant are due to their ability to restore the function of pancreatic tissue by causing an insulin secretion or inhibit the intestinal absorption of glucose. This may be one of the mechanism of *Haldina cordifolia* extract.

There are many factors which are responsible for the liver damage or injuries such as chemicals and drugs. In the present study ethanol was used to induce hepatotoxicity, since it is clinically relevant. Ethanol produces a constellation of dose related deleterious effects in the liver (Leo *et al.*, 1982). The majority of ethanol is metabolized in the liver and individuals who abuse alcohol by routinely drinking 50-60 g (about 4 to 5 drinks) of ethanol per day are at risk for developing alcoholic liver disease. In addition, both acute and chronic ethanol administration cause enhanced formation of cytokines, especially TNF-alpha by hepatic Kupffer cells, which have a significant role in liver injury, Besides the development of fatty liver (steatosis), another early sign of excessive ethanol consumption is liver enlargement and protein accumulation, both of which are common findings in alcoholics and heavy drinkers (Baraona *et al.*, 1975; Baraona *et al.*, 1977). Elevated levels of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) are indications of hepatocellular injury (Yue *et al.*, 2006). Aqueous Extract of *Haldina cordifolia* and AQEAC at a dose of 500 mg/kg, caused a significant inhibition in the levels of SGOT and SGPT towards the respective normal range and this is an indication of stabilization of plasma membrane as well as repair of hepatic tissue damage caused by ethanol. On the other hand suppression of elevated ALP activities with concurrent depletion of raised bilirubin level and an increase in the total plasma protein content suggests the stability of biliary dysfunction in rat liver during hepatic injuries with toxicants. These results indicate that Aqueous Extract of *Haldina cordifolia* and AQEAC preserved the structural integrity of the hepatocellular membrane and liver cell

architecture damaged by ethanol which was confirmed by histopathological examination [9]. Phytochemical screening revealed that Aqueous Extract of *Haldina cordifolia* and Aqueous Extract of *Haldina cordifolia* contains active pharmacological constituents such as flavonoids, alkaloids, phytosterols and phenolic compounds. However, it has been already reported that such phytoconstituents like phenolic compounds, flavonoids, tannins in various experimental models. Therefore it has been suggest that the hepatoprotective activity shown by the Aqueous Extract of *Haldina cordifolia* and Aqueous Extract of *Haldina cordifolia* can be because of these active phytoconstituents present in the plant which is being also confirmed by the biochemical and histological parameters. The aqueous extract has shown more promising effect as compared to ethanol extracts of leaves of *Adina cordifolia* [10]. The plant selected for the present study has demands for further phytochemical as well as pharmacological research such isolation of principle active phytoconstituents, evaluation of various pharmacological activities. Out of these aspects some respective parameters are already in process at our organization [11].

Since *H. cordifolia* also had shown same but less anti-ulcer activity in comparisons to *Rhizophora mangle*. So, it may be considered that *H.cordifolia* also have tannins or polyphenolic compounds which are responsible for its anti ulcer property. In this study, contrast to it the pretreatment with hot water and cold water extract, at doses of 55.5 mg/kg and the body weight 120kg decreased the ulcerated area to high dose-cold extract (1.170 \pm 0.35) and high dose-hot extract (1.015 \pm 0.205), followed by low dose-cold extract and low dose-hot. This was compared to the effect exerted by standard control (Omeprazole) (0.735 \pm 0.185). Based on the comparison with the *R. mangle* it is expected that the wound healing capacity of *Haldina cordifolia* during ulcer is due to several mechanisms, such as coating the wound, forming complexes with proteins of cell wall, chelating free radicals and imprudent oxygen species, stimulating the retrenchment of the wound and increasing the formation of new capillaries and fibroblasts [14].

The result indicated the crude extract of the corresponding plant species studied showed antibacterial activities towards gram positive bacteria (*Bacillus subtilis*) and multi drug resistant *Staphylococcus aureus*. The resistance of gram negative bacteria enterohemorrhagic *Escherichia coli* and *pseudomonas aeruginosa* to plant extract was not unexpected as in general, this class of bacteria is more resistant than gram positive bacteria. Such resistance could be due to the permeability barrier provided by the cell wall of the membrane accumulation mechanism. Infection caused by *pseudomonas aeruginosa* especially those of multi drug resistance are among the most difficult to treat with conventional antibiotics. Growth of *P. aeruginosa* was remarkably inhibited by the methanolic extract of *Haldina cordifolia*. It seems very likely the antibacterial compound extracted from *Haldina cordifolia* may inhibit bacteria a different mechanism than that of currently used antibiotics and may have therapeutic values as an antibacterial agent against multi drug resistant bacterial strains [15].

Haldina cordifolia had been extensively used for its reported biological action in indigenous organization of medicine. The at hand investigation was carried out to discover the anti-inflammatory effect of methanolic extract of *Haldina cordifolia* in albino rats. The anti inflammatory activity was evaluated by means of acute inflammatory model like carrageenan Induced paw edema and chronic inflammatory

model like cotton pellet induced granuloma respectively. The methanolic extract in different doses (100,200, and 400 mg/kg, p.o) exhibited dose dependent and significant anti-inflammatory activity in acute (Carrageenan induced hind paw edema <math>p < 0.05</math>) and chronic (cotton pellet granuloma formation, $p < 0.05$) model of inflammation^[16].

Haldina cordifolia is tree species belonging to the family rubiaceae. The paste of the stem bark or leaves heal deep wounds and jaundice, stomach ache, malarial fever, swelling in stomach and root is useful for dysentery and the direct seeding of *Adina cordifolia* failed due to low viability. Due to destructive mode of harvesting, *Adina cordifolia* is included in threatened species. Thus there is need to save this plant from being extinct. *Adina cordifolia*, apical buds were used as explants for *in vitro* establishment. The explants collected in the month of march to june were surface sterilized by 5% (v/v) Tween-20 for 5 minute, 0.1% Bavistin for 5 minute, 0.1% (w/v) HgCl₂ for 1 minute and 70% ethanol for 1 minute and placed on the surface of Murashige and Skoog (MS) medium containing different combination of hormone BAP and NAA. The maximum survival rate of explants was observed 66.67% at 1 mg/L BAP. The shoot length was highest in MS medium supplemented 2mg/L BAP alone and 0.5mg/L NAA^[17].

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