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Rubia Cordifolia An Ethnopharmacological Review

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ABSTRACT

Rubiacordifolia, belongs to family *Rubiaceae*, commonly known as Indian Madder and Manjistha in Sanskrit. It is perennial, herbaceous prickly climber with long and cylindrical root with a thin red bark. Various parts of *Rubiacordifolia* have been suggested in the Indian system of medicine for a number of diseases. The roots and stems are well known source of Anthraquinones. The roots have also been reported to possess antioxidant, anti inflammatory, anticancer, immunomodulatory and hepatoprotective activities. This plant has been pharmacologically screened for anti-acne, anti-convulsant, anti-ulcer, anti-diabetic, anti-microbial, anti arthritic, anti-platelet and wound healing activities. This review will be helpful in the development of polyherbal formulation as well as for conducting further research to explore the therapeutic potential of *Rubiacordifolia*.

Keywords: Manjistha, *Rubiacordifolia*, Diseases, Antihyperlipidemic.

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INTRODUCTION

Rubiocordifolia Linn is the commonly used plant present throughout the hilly tracts of India. The stems are often many yards long, rough, grooved, becoming slightly woody at the base. Bark is white, petioles quadrangular, sometimes prickly on the angles, glabrous and shining. Fruits are 4-6 mm, didymous or globose, smooth, shining and purplish black when ripe. The roots of the plant are sweet, bitter, acrid and used as anti-inflammatory,¹ haemostatic,² antidysenteric, antipyretic, analgesic, anthelmintic, improves the voice, complexion and cures the *Kapha*. It was found that the plant is useful to treat various inflammatory diseases of the uterus, vagina, eye, ear and blood. It is also used in the treatment of leucoderma, ulcers, urinary discharges, jaundice, and piles. The *Ruberythric acid* is one of the major constituents of the root and is widely used as phytotherapeutic drug in the treatment of calcium containing stones in the urinary tract. *Rubiocordifolia* is used in Ayurveda as an ingredient of popular formulations like Chandanasava, Ashwagandha, Arishtha, JatyadiGhrita, JatyadiTaila, PhalaGhrita, PindaTaila.

Botanical Description

Rubiocordifolia is a perennial climbing herb; roots are long, cylindrical, with a thin red bark, stems very long, rough, grooved, branches scandent, quadrangular, often prickly on angles. Leaves in whorls of 4, ovate, 4-9 x 1.5-3.5 cm, lower leaves longer than the upper, scabrous above, margins with minute prickles. Flowers are small, greenish, in terminal, paniced cymes. Fruits are didymous or globose, 4-6 mm in diameter, purplish black when ripe. The *Rubiocordifolia* plant leaves and roots are shown in figure 1, 2 and 3.



Figure 1: *Rubiocordifolia* whole plant



Figure 2: Leaves of *Rubiacordifolia* Figure 3: Roots of *Rubiacordifolia*

PHYTOCHEMICAL CONSTITUENTS

The roots of *Rubiacordifolia* contain anthraquinones and cyclic peptides. Main anthraquinone constituents are munjistin, purpurin, and pseudopurpurin. Some New anthraquinones namely 1-hydroxy-2,7-dimethylantraquinone, 2-hydroxy-6-methylantraquinone, 2,6-dihydroxyanthraquinone, 1-hydroxy 2-methylantraquinone, nordamnacanthal, physcion, 1,4-dihydroxy 6-methyl-antraquinone, 1,4-dihydroxy 2-methylantraquinone, 1,5-dihydroxy 2-methylantraquinon, 3-prenyl methoxy 1,4-naphthoquinone, 1-hydroxy 2-methoxy anthraquinone, 1,4-dihydroxy 2-methyl 5-methoxy anthraquinone or 1,4-dihydroxy 2-methyl 8-methoxy anthraquinone, 1,3-dimethoxy 2-carboxy anthraquinone and rubiadin have been isolated from *Rubiacordifolia* roots.^{3,4,5,6} A new anthracene derivative, rubiasin was isolated from the roots and stems of *Rubiacordifolia*.⁷ Naphthoquinones, naphthohydroquinones and naphthohydroquinones dimmers have also been identified in the roots. Two new naphthoquinones, 2-carbamoyl-3-methoxy-1, 4- naphthoquinone and 2-carbamoyl-3-hydroxy-1, 4-naphthoquinone were isolated from the methanol extract of *Rubia cordifolia*.⁸ Two pentacyclitriterpenes, Rubicoumaric acid and rubifolic acid was isolated from *Rubia cordifolia*.⁹ A new iridoidglucoside, 6 Methoxygeniposidic acid was isolated from the roots of *Rubia cordifolia*.¹⁰ Mollugin and dehydro- α -lapchone was isolated from the chloroform fraction of *Rubiacordifolia* (Linn.) roots.¹¹ Four naphthoic acid esters namely rubilactone, 3'-carbomethoxy-4'-hydroxy-naphtho 1',2'-2,3 furan, dihydromollugin and 3-carbomethoxy-2-(3'-hydroxy) isopentyl-1,4-naphthohydroquinone-1-O - β -D-glucoside were isolated from the roots of *Rubia cordifolia*.¹² The structure of phytochemical constituents are shown in figure 4 and 5.

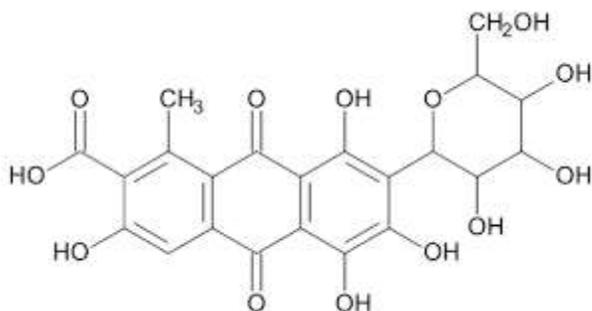


Figure 4: (Ruberythric acid)

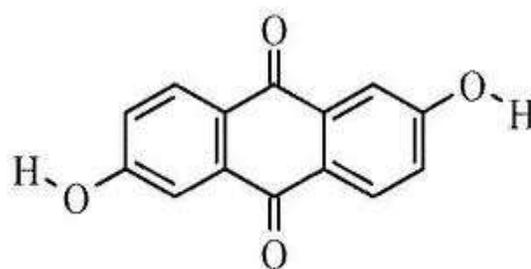


Figure 5:(2,6-Dihydroxyanthraquinone)

PHARMACOLOGICAL ACTIVITIES

Radiation protection activity

The intra-peritoneal administration of *Rubiacordifolia* extract was found to provide significant protection against radiation induced lipid peroxidation, hematopoietic injury and genotoxicity.¹³

Anti-acne activity

The anthraquinone fraction of *Rubiacordifolia* gel formulation has found to show anti acne activity against *Propioni bacterium acne*, *Staphylococcus epidermidis* and *Malassezia furfur*.¹⁴

Immuno-modulating activity

The alkaloids, cardiac glycosides, tannins, flavonoids and phenols in *Rubiacordifolia* are responsible for enhanced immune-modulation. The ethanolic extract of the whole plant found to exhibit immunosuppressive activity, cell mediated and humoralimmuno-potentiating activity.¹⁵ The extracts of *Rubiacordifolia* and *Rubiadianthus* were found to inhibit the IgE production in peanut-allergic mice. In another study revealed that, the administration of ethanolic plant extract to cyclophosphamide exposed animal was found to enhance immune responses.¹⁶

Anti-convulsant Activity

Rubiacordifolia was reported to have anticonvulsant activity due to presence of Triterpenes, which inhibited seizures induced by maximum electric shock and various chemo-convulsants in rats. Brain GABA and serotonin (5-HT) contents were raised by the compound.¹⁷

Diuretic activity

The hydroalcoholic root extract of *Rubiacordifolia* was found to possess diuretic property.^{18,19} An another study showed that the hydroalcoholic extract and the ethanolic extract increased urine volume significantly and electrolyte excretion in a dose dependent manner.²⁰

Anti-peroxidative activity

The alcoholic extract of *Rubiacordifolia* was found to show anti-peroxidative property in rat liver homogenate.²¹

Anti-arthritic activity

The ethanolic extract of *Rubiacordifolia* was found to show paw edema inhibition in induced arthritic model.²²

Neuroprotective activity

Extract of *Rubiacordifolia* was found to have good antioxidant and strong free radical scavenging properties against reactive oxygen and nitrogen species.^{23,24}

Anti-diabetic activity

Alcoholic extract of root and leaf extracts were found to have promising antidiabetic activity in alloxan treated diabetic rat model.²⁵ The aqueous root extract was found to normalize hyperglycemia, hyper triglyceridemia, enhanced transaminases of liver and kidney, hypochromic microcytic anemia, and loss of body weight in streptozotocin -induced diabetic rat models.²⁶ The leaf extract of *Rubiacordifolia* was found to decrease the blood glucose level compared to the glibenclamide normal fasted rat and alloxan-induced diabetic rats.²⁷ Methanolic root extract of *Rubiacordifolia* was found to possess antiglycation, antioxidant and anti-diabetic activities.²⁸

Anti-ulcer activity

The alcoholic root extract of *Rubiacordifolia* was found to have antiulcer potential on alcohol, ibuprofen, cold-restraint stress and pyloric ligation-induced gastric lesions models.²⁹ In polyherbal formulations, the ulcerogenicity effect in rats shown significantly lesser ulcer effect even at very high dosage as compared to that of aspirin.³⁰

Anti-inflammatory activity

The aqueous root extract of *Rubiacordifolia* was found to have anti-inflammatory activity in rats.³¹ It also exhibited the inhibition of lipooxygenase enzyme pathway which is responsible for anti-inflammatory action.³²

Gastroprotective activity

Rubiacordifolia has both gastroprotective and ulcer healing properties.³³ Triterpenoids present in root extracts were found potent antiulcer and antioxidant compound.³⁴ The methanolic extract and the chloroform fraction possessed reduction in ulcer index, lipid peroxidation, and increase in the mucin content.³⁵

Anti-proliferative activity

The antiproliferative property was also tested on A-431 cells (epidermal carcinomoid cells) and 3T3 fibroblast cells. The extract of *Rubiacordifolia* was found to inhibit the phorbol 12-myristate 13-acetate induced expression of c-fos genes in A-431 cells due to the inhibition of DNA

synthesis.³⁶ The active constituent Mollugin was found to be an active antiproliferative principle by bioassay-monitored fractionation.³⁷

Anti-microbial activity

The root extract of *Rubiacordifolia* was found to have antimicrobial activity against various pathogenic bacteria. Sitosterol and daucosterol possessed antibacterial activity. The root extracts constituents such as anthraquinones and flavonoids were found to suppress the activity of phytopathogens of *Gossypium*.³⁸ Aldehyde acetate, dihydromollugin and rubimallin were reported to have significant antibacterial activity against *Klebsiella pneumoniae*.³⁹ Ethanolic extract of *Rubiacardifolia* was found to inhibit β -Lactamase producing uro-pathogenic *E. coli*.⁴⁰ The chloroform and the methanolic extracts of *Rubiacardifolia* reported to have antibacterial activity on gram-positive strains and gram negative *Pseudomonas aeruginosa* in a dose dependent manner. The aqueous extract of *Rubiacordifolia* was found to be active against *Bacillus subtilis* and *Staphylococcus aureus*.⁴¹ *Rubiacordone* was reported to have considerable antimicrobial activity against Gram positive bacteria like *Bacillus subtilis*, *Streptococcus faecalis* and *Bacillus cereus*. The green synthesized silver nano particles using *Rubiacordifolia* plant root extract were reported to have highly inhibitory activity of the bacterial pathogens like *Vibrio alginolyticus*, *Pseudomonas aeruginosa*, *Shigella* spp, *Plesiomonas shigelloides* and *Vibrio parahaemolyticus*.⁴²

Antiviral activity

The methanolic extracts of leaves of *Rubiacardifolia* were found to have minimum inhibitory concentration of different virus using HEL cell cultures and Vero cell cultures.⁴³ Thenaphthoquinones were also reported to have antiviral activity.

Wound healing activity

The root extract of *Rubiacordifolia* was reported to possess wound healing property.⁴⁴ Ethanolic extract and the hydrogel formulation of roots were found to be effective in the functional recovery and healing of wounds and also lead to histo-pathological alterations.⁴⁵

Antistress and nootropic activity

Alcoholic extract of *Rubiacordifolia* was found to enhance brain γ -amino-n-butyric acid levels and decreased brain dopamine and plasma corticosterone levels.⁴⁶ The extract also inhibited acidity and ulcers caused due to cold restraint stress. The animals treated with alcoholic extract were found to spend more time in open arm in elevated plus maze model, which antagonized scopolamine induced learning and memory impairment.⁴⁶

Anti-platelet activating effect

Partially purified fraction of the whole plant was found to inhibit the action of platelet activating factor at its receptor level either by its blocking or by desensitization property.⁴⁷

Hepatoprotective activity

The quinone derivatives from *Rubiaccordifolia* were reported to have hepatoprotective effect on animal systems. The methanolic extract of *Rubiaccordifolia* was found to protect the liver from thioacetamide induced hepatotoxicity.⁴⁸ The aqueous and methanol extract was to active active against acetaminophen and CCl₄-induced hepatic damage in rats.⁴⁹ The methanolic extract also found to preventive in CCl₄-induced prolongation in pentobarbital sleeping time.⁵⁰ It has been also found to be effective against acute and chronic hepatitis caused by the hepatitis B virus by interfering with the secretion of hepatitis B surface antigen in human hepatoma cells.⁵¹

Other uses of *Rubiaccordifolia*

1. Powdered dried roots and fruits are used in the treatment of skin diseases and disorder of spleen.
2. It is used for the treatment of major burns, ulcers and bone fractures.
3. It is considered tonic, antitussive, and useful in chronic low fevers.
4. The roots are used internally in the treatment of abnormal uterine bleeding, internal and external hemorrhage, bronchitis, rheumatism, stones in the kidney, bladder and gall, dysentery etc. The plant is used in the treatment of blood disorders.
5. The roots are alterative, antiphlogistic, astringent, diuretic, expectorant, styptic and vulnerary.

CONCLUSION

The above collected information regarding the uses and pharmacological activities of *Rubiaccordifolia* is immensely useful for further studies. In the present scenario, ethno-botanical and traditional uses of natural compounds, especially of plant origin have received much attention, as they are well tested for their efficacy and are generally believed to be safe for human use. It is best classical approach in the search of new molecules for management of various diseases. Thorough screening of literature available on *Rubiaccordifolia* depicted the fact that it is a popular remedy among the various ethnic groups, Ayurvedic and traditional practitioners for treatment of various ailments. Researchers are exploring the therapeutic potential of this plant as it has more therapeutic properties which have not been investigated. This review will be helpful in the development of polyherbal formulation as well as for conducting further research to explore the therapeutic potential of *Rubiaccordifolia*.

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