A Review on Pharmacognostic and Therapeutic Uses of *Rubia cordifolia*


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**ABSTRACT**

In today’s time research on plants has increased globally. There are thousands of plant species having good potential offering direct therapeutical effect individually or in combinations. *Manjith* a herbal drug also known as Indian madder with its botanical name *Rubia cordifolia* is an age old ethno-medicinal plant in India used as anti-oxidant, anti-inflammatory, anticancer, anti-bacterial, anti-androgenic, immune-modulator, hepatoprotective, astrigent, tonic, antiseptic, de-obstructant, anti-dysenteric and efficient blood purifier, hence is extensively used against blood, skin and urinary diseases. This study is aimed at assessing the scientific evaluation of desi *Rubia cordifolia* in the course of pharmacognostical analysis to identify its various parts and to differentiate it from various adulterants, which mainly covers the macroscopic and microscopic features and its medicinal properties which are due to its richness in phytoconstituents such as quinines (anthraquinones), glycosides, saponins, tanins, alkoids, hexapeptides, triterpenoids, steroids, phenols, and saccharids.

**Keywords:** *Rubia cordifolia*, Manjith, Footh, ethno medicinal plant, Unani, pharmacological study

**INTRODUCTION**

With an increasing use of modern medicines, last few decades has shown resistance in different pathologies, their related side effects and high cost of treatment, all this has led to change the focus to the type of medication to be used, progressively herbal medicine. Which in itself plays a basic role in preparation of different herbal formulation. In rural areas indigenous plants plays an important role in maintaining health and improving life. But identifying the drug with classical literature sometimes become difficult hence leading to misidentification of the plant, which may be due to complexities in herbal nomenclature. One such herbal drug which is rich in medicinal properties and is used in number of formulations for treating different ailments is Manjith. Manjith also known as *Footh* in Unani system of medicine, is a species of flowering plant in the coffee family, Rubiaceae. It has been cultivated for a red pigment derived from the roots. 1 Rubia denotes 'red' as their internal use imparts red color to breast milk and urine. 2 Roots of this plant having high medicinal value are recognized as official. It is ethno-medicinal plant, being used in Unani system of medicines for thousands of years. The drug is used for treating different ailments like arthralgia, arthritis, cephalalgia, cough, discolouration of the skin, dysmenorrhoea, emmenagogue, leucorrhoea, neuralgia, strangury, pectoral diseases, pharyngitis, general debility, hepatopathy, intermittent fevers, ophthalmopathy, otopathy, splenopathy, slow healing of broken bones, tubercular conditions of the skin and mucous tissue, tuberculosis and urethrorrhrea 3 leucoderma, ulcers, urinary discharges, jaundice, and piles. 4 alzheimer, diabetes, cancer, acne, inflammation, allergy, enterocolitis, bacterial and viral infections. The aim of writing this review is to learn how to differentiate it from other related species and to bring attention to its multiple medicinal properties so that more benefits could be achieved from it.

**TAXONOMICAL CLASSIFICATION:**

Kingdom: Plantae

Class: Dicotyledoneae

Subclass: Sympetalae

Order: Rubiales
Family: Rubiaceae  
Genus: Rubia  
Species: cordifolia

VERNACULAR NAMES
- Arabic- Aroque sabagh and Foo ul sabagh  
- Persian-Roomans  
- English-Indian Madder  
- Hindi-Majit and Manjit  
- Bengali-Manjistha  
- Urdu-Manjith  
- Malayalam-Manjetti and Poont  
- Marathi-Manjestha  
- Kashmiri-Manjito  
- Manipuri-Moyam  
- Nepali-Manjito

DISTRIBUTION
Rubia cordifolia linn is a flowering plant species from indigenous system of medicine. It commonly is known as Common Madder. Rubia cordifolia is a perennial climber, prickly or scabrous herb plant with red rhizomatous base and roots, distributed in temperate and tropical forests of Africa and Asia especially in the hilly regions with an altitude ranging up to 3500 m while in south India adjacent to rivers and streams of upper ghat.

DESCRIPTION

The stem

The stems are often many yards long, rough, grooved, becoming slightly woody at the base, bark white, petioles quadrangular, divaricately branched, prickly-hispid, especially on the angles. Sometimes are glabrous and shining. It is slender, four angled with sharp recurved prickles on the ridges.

In transverse section of the stem it is seen as circular and smooth in outline. The Pyramidal hairs are present on the epidermis. Sclerenchymatous hypodermis is present in the stems, at its corner. The cortex is chlorenchymatous, hence photosynthetic. The periderm formed of rectangular cell which are compactly arranged, thin walled and well developed with 4 to 11 layers. The periderm is followed by 8 to 12 layers of flattened compactly arranged parenchymatous cell, and is composed of xylem vessels in some section. Primary xylem is present towards the centre characterized by small vessels with xylem parenchyma cells.

Phloem parenchymal cells are very compactly arranged. Shape may vary from rectangular to spindle. The cortex is narrow and is 12 to 80 layered of longitudinally stressed, flattened parenchymatous cells. The secondary phloem is well developed and made up of 6-7 layers unlike primary phloem.

Medullary rays are uniseriate. Perimedullary sheath is narrow and it is made up of round or irregular thin-walled cells. Secondary xylem is made up of vessels, tracheids, fibers and xylem parenchyma. Vessels are large and uniformly arranged. Here larger vessels are at periphery and smaller one are towards inner boundary. It is diffusely porous and are completely cylindrical. Cambium ring of the stem is represented by two layers.

The root

Roots are long, cylindrical, flexuous, with a thin red bark. It is brittle, hard splinterly in texture and hard to break. External bark gets peeled easily. Its surface is longitudinally furrowed. When peeled off inner surface is furrowed and dark purple in colour. Then cleaned and dried in the sun. The cross-section of roots showed an outer 5-7 layer of cork tissue, which is known for storing tannin. Cambium is devoid of medullary rays. It has narrow cortex. The presence of anthraquinones is responsible for the red coloured appearance of the root.

Mizaj (Temprament)

Garam 2 (hot) and Khushk 2 (dry)
The leaves

Leaves are highly variable, ovate lanceolate, 5-7 nerved, 2-10 cm long and 2-5 cm broad, occurring in whorls of 4-6. Leaf base is slightly cordate. The lower leaves are larger than upper. The margins are with minute white prickles. Leaf is composed of single layer of epidermis and is covered with cuticle and possess pyramidal hairs. Leaf section showed single layered epidermis and also single layer of Palisade cells which are compactly packed, whereas the spongy cells are multilayered and loosely arranged. The dorsal aspect of midrib is made up of collenchymatous cells, which are found in 2-4 layers. Vascular bundles are collateral and closed, conjoint and definite in numbers.

The flower

Flowers are cymes, fragrant, minute, whitish or greenish yellow. Plant carries flower and fruit in the month of August and October.

The fruit

At the time of ripening the fruit is didymous or globose, smooth, shining and purplish black. It is fleshy, succulent and has red juice.

- Taste
  Sweet Bitter-acrid

- Biomarkers of Rubia cordifolia responsible for therapeutical activities.
  1. Rubiadän – Hepato-protective - Antioxidant
  2. Alizarin – Anti-genotoxic
  3. Mollugin - Antiadipogenesis – Antiplatelet
  4. Alizarin, mollugin, lucidin - Potent COX-2 inhibitor
  5. RA-70029 RA-XI, XII, XIV - Antitumor
  6. 1-hydroxytectoquinone - Anti-inflammatory

- Substitute
  Kababa and Tij

- Toxic
  Urinary bladder

- Correctives
  Kateera and Aneeson

The constituent which is responsible for providing red colour to the herb is purpurin, while a yellow principle, a glucoside is manjistin, alzirin and garancin responsible for orange-red, and xanthine for yellow colour. These colouring property of the plant was the reason that it was used for the commercial purpose as a dye stuff in old days. Some of the commonly used forms in USM are:

  a) Joshandah of Manjith used for Mudire baul wa haiz
  b) Safoofe Manjith 3gm given with Sikanjabeen for Mufatte Sudah and Yarqan (deobsturent and Jaundice)
  c) Manjith along with vinegar works well for leukoderma and vitiligo.

Some of the Classical Unani formulations which has R. cordifolia as an important ingredient:

- Halwae Gheekwar
- Dawaul Kurkum kabir
- Safoof Khas
- Safoof Musafi khaas
- Majoon Dabeedul ward
- Majoon Suparipak
- Arq Anannas
- Roghan Ahmar Jadeed
- Sadri
• Agras Mur 31
• Majoon Alkula 32
• Majoon e Hafiz ul Ajsad 32

**Traditional uses:**

There are numerous Indian folk medicines which are composed of Genus Rubia for treating ailments like healing wounds, inflammation, and skin infections.

Traditionally the plant has been used as an anthelmintic, anti-septic, constipating, diuretic, astringent, thermogenic, anti-dysenteric, anti-inflammatory, antipyretic, analgesic, anodyne, galactopurifier, febrifuge, rejuvenating and tonic. 33

• In other Indigenous Systems

Charak a vedic physician has used its dry fruit to treat ailment of spleen and skin disorders. 34 In classic Ayurvedic script Sushruta samhita it is documented for bleeding piles.

Mollugin one of the active component was commonly used in Chinese medicine for the treatment of inflammatory diseases like arthritis and uteritis. 35

In Tibetan system of medicine, the stem is used to treat blood disorders, spreading fever of kidneys and intestines. 36

In Philippines decoction of root is used to treat urinary disorders, while in Korea, to treat rheumatism, jaundice and urinary disorders. 37

Whereas in India, use to treat irregular menstruation and ear diseases in Sikkim, 38 to relieve uterine pain in tribes of Maharashtra, 39 tribes of Kerala use it to treat skin diseases, 40 to treat diarrhoea and dysentery in Odisha, 41 in Konda Dora tribes of A.P pills are used which are orally administered on empty stomach to treat jaundice 42 Vanraj tribes of Kumaun Himalaya use it with honey as a cure for acne and dark spots on face. 43

The administration of root decoction in the treatment of diabetes has been documented in 2010 survey. 44

It is an excellent expectorant especially used in infants to relieve cough, cold and respiratory problems. 45 In the Cape Province, natives take a decoction of the leaf or root for pleurisy and other inflammatory conditions of the chest. 12

Roots were used for treating stones of kidney, bladder and gall bladder. 46

*R. cordifolia* decoction is used to reduce scarring of the umbilical cord post birth. Primarily done in Uganda. 47

It has been used to provide relief from heat and itching in eczema, psoriasis, scabies and herpes. It has shown successful results in the treatment of vitiligo when given with honey. 26

**PHYTOCHEMISTRY**

This includes anthraquinones, iridoids, hexapeptides, rubiprasins, quinones, and triterpenoids. 48 Anthraquinone, anthraquinone glycoside, naphthaquinone, naphthaquinone glycoside, furomollugin, mollugin, alizarin, lucidine, pimeveroside, ruberythric acid, purpurin, xanthopurpurin, cyclohexapeptide, alkaloid and lignan have been reported from rubia species. 49 Rubiadin is the major chemical constituent of this plant considered as a marker compound used in the quality control of this plant. 50 Purpurin is the major anthraquinone present in *Rubia cordifolia*. 1 Coumarins have been reported for the first time in roots and stems of *R. cordifolia*. It lacked flavonoids, which was a major finding in its another species, i.e. *R. tinctorium*. Which is frequently used as a substitute of *R. cordifolia*. 51

The roots contains many quinones, like mangustin, alizarin, mollugin, furomollugin, 1-hydroxy, 2-methoxy anthraquinone, 3-dimethoxy 2 carboxy anthraquinone, rubiprasin A, B, C. 52

Some newly found anthraquinones in its roots are cordifoliol and cordifadiol. While purpurin is the major anthraquinone to be extracted from it.

**PHARMACOLOGICAL ACTIONS**

1. **Anti-inflammatory Effect**

During a rapid development of a model edema, manjistin along with purpurin has shown anti-proliferative action. 48

There is involvement of inflammatory mediators in the conditions like arthritis, asthma and in different inflammatory disorders, which are produced through lipoxygenase enzyme pathway. In a study the aqueous extract of rubia has been found effective in inhibiting the pathway. 53

The extract *Rubia cordifolia*, Linn. was used to study the anti-inflammatory effect in rats with carrageenan paw oedema. Where animals were given ethanolic and alcoholic extract of the rubia. Chronic administration of ethanolic extract decreased the humoral and cell-mediated immune response, phagocytosis, phagocytosis index. 54

2. **Wound Healing Activity**

Root extract of *R. cordifolia* has reported to be effective wound healer in experimental models. 55

A formulation of *R. cordifolia* along with some other herbal drugs were tested for their wound healing properties, where it proved to be capable of contracting the wound and promote epithelisation. 56

Ethanolic extract and the hydrogel formulation of roots were found to be effective in the functional recovery and healing of wounds and also showed histo-pathological alterations. 57

3. **Diuretic**

The hydro-alcoholic extract as well as the ethanol extract has shown significant electrolyte excretion and increase in urine volume in a dose dependent manner. 58

In another experiment to see the diuretic activity of the hydro-alcoholic extract of roots of *R. cordifolia*, dose of the extract was given according to weight of the animal, the extract showed a significant dose dependent increase in urine volume and electrolyte excretion. And showed better clearance or creatinine than furosemide. 59

4. **Antimicrobial**

Root extract of *R. cordifolia* has shown its effectiveness against various pathogenic bacteria’s, like Klebsiella pneumonia, its constituents such as anthraquinones and flavonoids suppressed the active dphytopathogens of Gossypium, daucosterol possess antibacterial activity. 60

The green synthesized silver nanoparticles using root extract of *R. cordifolia* was highly effective against bacterial pathogens like Pseudomonas aeroginosa, Shigella spp, Plesiomonas shigelloides and Vibrio parahaemolyticus, and they had highest antimicrobial effect against Pseudomonas aeroginosa and Plesiomonas shigelloides. 61

The chloroform and the methanolic extracts reported to have antibacterial activity on gram-positive strains, although gram
negative was also inhibited by the methanolic extracts in a dose dependent manner. The extract is significantly active against Bacillus subtilis and Staphylococcus aureus compared to streptomycin and penicillin G. 62

Many compounds have been isolated from the roots of R. cordifolia L by established chemical and spectroscopic methods, where many compounds showed antibacterial activities. 63

Though furomollugin and mollugin has little effect on the viability of the cells, but it strongly suppresses the secretion of hepatitis B surface antigen in human hepatoma Hep3B cells. 64

5. Radioprotective

When R. cordifolia extract was administered intraperitoneally before the radiation exposure it provided significant protection against radiation induced lipid peroxidation, hemopoietic injury and genotoxicity. The alcoholic extract of R. cordifolia possess significant radioprotective potential, that might be due its antioxidant, anti-inflammatory, metal chelation and free radicle scavenging potential. 65

The aqueous extract of R. cordifolia effectively prevents Single strand breaks induced in plasmid pBR322 DNA following ionizing radiations. 66

Highest antioxidant potential of R. cordifolia leaves is found in methanolic extract. This free radical scavenging protocol is efficient for R. cordifolia and makes it potent for the production of biologically active compounds at a comparable rate to commercially available antioxidants. 67

6. Anti-Adipogenic

Anti-adipogenic activity of 2-carbomethoxy-2 3- epoxy-3- prenly-1, 4-naphthoquinone (CMEP-NQ) was found to be effective on apoptosis, cell viability and adipogenesis in 3T3-L1 preadipocytes. 1

R. cordifolia extract in treated animals has lead reduction in Lipid peroxidation in the kidney and liver tissues. 24

7. Gastro-protective

R. cordifolia extract has shown significant protection against gastric ulcer in a much better way than ranitidine in an experiment done on rats. 68

In an experiment where wistar rats were used and were treated the chloroform extract of R. cordifolia, it can be attributed to decrease gastric acid along with strengthening of the mucosal defensive mechanism by prostaglandin synthesis and antioxidant potency of the drug. 69

In a study where hydroalcoholic extract of R. cordifolia was tested upon animals, it suggested that it can protect indomethacin-induced enterocolitis in rats and may be beneficial in patients with inflammatory bowel diseases. 70

8. Anti-convulsant

In an experiment, rats where tested by giving them chemoconvulsants and maximum electric shock. But when they were given triterpenes, extracted from R. cordifolia, it inhibited the seizures by raising the brain GABA and Serotonin (5-HT). 71

9. Immunity enhancing activity

The ethanolic extracts of the whole plant of R. cordifolia was given to rat model, who were given immunosuppressive drug, phosphamidon. The extract improved both type of immunity, cell-mediated and humoral. Also a significant suppression of DTH (Delayed type hyper sensitivity reaction) was noticed. It was observed that the extracts, of the plant acted as a potentiator of DTH. 11

In another study the administration of ethanolic plant extracts to cyclophosphamide exposed animals resulted in enhanced immune responses. 72

10. Antioxidant

Anti-oxidant present in abundance in the root of R. cordifolia is rubiadin a dihydroxyantraquinones, which prevents lipid peroxidation induced by FeSO4 and t-butylhydroperoxide (t-BHP) in a dose dependent manner. 58

It also contains antioxidants like alizarin and rubiadin, which prevents peroxidation. 73

The antioxidants present in herb significantly inhibits FeSO4 induced lipid peroxidation and glutathione depletion. This antioxidant property is due to direct interaction with iron. 74

The study highlighted the importance of R. cordifolia as an alternative system of medicine for parkinsonism due to its significantly active antioxidant property, that might be due to its anticholinergic action. Phenolic compounds are responsible for the action. 75

Hexane and ethyl acetate fractions of root showed maximum free radical scavenging activity due to the presence of anthraquinones and glycosides in it. Hence R. cordifolia extract can protect peroxidation and can reduce glutathione content in rat liver homogenate compared to vitamin E and parabenzoquine. 76

11. Anti-acne

Mentholic extract of R. cordifolia has shown anti-proliferative action against Propionibacterium. acnes. 77

It is proved to be effective against TNFalpha and mildly against IL-8.

It is regarded as astringent and useful in external inflammations, skin diseases. 78

12. Anti-cancerous

R. cordifolia had shown an increase in leukocyte count in leucopenia 79 R. cordifolia is reported to be active against a diversified panel of cancer cell lines, such as P388, L1210, L5178Y, B16 melanoma, Lewis lung carcinoma, and sarcoma 180. 80

Mollugin an active antiproliferative principle, obtained by bioassay-monitored fractionation using a human colon cancer (Col2) cell line. 81

R. cordifolia is promisingly cytotoxic and they might have antitumor activity against myeloid leukaemia and Histolytic lymphoma. 82

Chloroform extract of R. cordifolia consists of mollugin, furomollugin and dehydro-a-laphone. Mollugin inhibits passive cutaneous anaphylaxis (PCA) and dose protection of mast cell from degranulation in rats. It also exhibited considerable activity against lymphoid leukaemia (P338) in mice. 83

The methylene chloride fraction from the roots of R. cordifolia showed strong cytotoxicity against HT-29 and MCF-7 cell lines, as well as DNA topoisomerase I and II inhibitory activities. 84

13. Hepatoprotective activity

Aqueous-menthol extract of R. cordifolia was used to investigate hepatoprotective activity against acetaminophen
and CC14-induced hepatic damage, which proved to be protective in nature. 

It has been found to be effective against acute and chronic hepatitis caused by the hepatitis B virus (HBV) in human hepatoma cells (Hep 3B). The quinone derivatives were thought to be the active components. 

The quinone derivatives are known to have hepatoprotective effect in animals. In an experiment methanolic extract has shown protective action against the liver thioacetamide-induced hepatotoxicity. 

The study indicated that rubiadin has hepatoprotective action against carbon tetrachloride induced hepatic damage in rats. There was decreased activity of glutathione S-transferase and glutathione reductase; and they were restored towards normalization. Rubiadin inhibited the elevation of hepatic malondialdehyde formation and depletion of reduced glutathione content in the liver, in a dose dependent manner. 

14. Anti-proliferative activity

In an experiment Rubiadin was isolated from the roots of R. cordifolia, where it has shown to possess in vitro antiproliferative activity. Rubiadin was subjected for the inhibition of the enzyme EGFR tyrosine kinase in molecular docking, which is one of the targets for inhibition of cancer cells. 

Ethyl acetate (EA) fraction of Radix Rubiae strongly suggests its anti-psoriatic activity since it inhibits cell growth and promotes terminal differentiation in cultured human keratinocytes. 

15. Anti-diabetic activity

In an experiment, animal model was tested with alcoholic extract of root of R. cordifolia, where it was found to have promising anti-diabetic activity. The extract of roots was given to normal, glucose fed and alloxan induced diabetic rats, where it showed decrease in blood glucose level, it reduced the blood sugar level in alloxan treated diabetic rats as well, indicates that the extract has an extra pancreatic effect. 

The rats when treated with Aqueous extract of Rubia cordifolia improved oral glucose tolerance by compared to glucose fed animals, exogenously injected insulin along with the drug extract caused potentiation of hypoglycaemic effect as compared with alone insulin treatment. 

The leaf extract decreased the blood glucose level compared to the glibenclamide in both normal fasted rats and alloxan-induced diabetic rats. The extract also showed a favourable effect on glucose disposition in glucose-fed hyperglycemic rats. There was also reduction in serum cholesterol and triglyceride levels, whereas elevation in serum high density lipoprotein and protein level in diabetic rats. 

16. Nephroprotective Activity

In an experiment where swiss albino rat model was used, hydro-alcoholic extract of Rubia cordifolia has shown decrease in intensity of displatin induced nephrotoxicity due to antioxidiant property present in the drug. There were remarkable changes in the serum creatinine and urea levels. 

Hydro alcoholic extract of R. cordifolia can protect against ethylene glycol induced urolithiasis as it reduced and prevented the growth of urinary stones, because it significantly reverts the increased calcium and oxalate levels and number of calcium oxalate crystals depots in the kidney tissue of calculogenic rats. 

17. Cardioprotective

It can work in arrhythmias because it has got spasmyloytic activity which is suggestive of presence of calcium channel blocker like constituents in this plant. 

Diuretic activity of Rubia cordifolia, has proven to be effective against the management of oedema, therefore it could be alternative therapy in the management of congestive heart failure (CHF). Also Antihyperglycemic and antihyperlipidemic effects of rubia can also work cardiomypathy and diabetic macrovascular disease. 

CONCLUSION

Recently there is increase in use of traditional medicines to cure various ailments and prescribing combination therapy for many diseases. This has led to an increase chance of drug interaction and adverse effects, means there is need to evaluate individual herbal therapy. Rubia cordifolia is an ethno botanical plant which is abundant in constituents which are having marvellous properties to treat different pathologies and to combat them. The plant is well tested for its efficacy and is believed to be safe for human use. But there are many adulterants present in the market by its name. So as to get the required results it is necessary to avoid any such interchanging for that pharmacogonstical study is need to be done properly. The reported phytochemicals and pharmacological studies supports its long traditional use due to presence of anthraquinones, glycosides, saponins, steroids, phenols, and flavonoids etc, which are responsible for different actions like potent blood purifier, antioxidant, anti-inflammatory, immune modulator, antistress, antimicrobial, hypoglycemic, hepatoprotective, anti-cancerous, cardio and nephro protective. More studies are yet to be done on these active components to explore the therapeutic potential of the plant. And this review might help to open more doors of research in future.

REFERENCES


18. Nabi MG; Makhanmal muradat wa murrayk (Khasa Advia), Matha Iterekha Delhi.


