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Comprehensive Review on Rubia Cordifolia (Manjistha)

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ABSTRACT

The plant known as "Indian Madder" is actually Rubia cordifolia Linn. (manjishtha). Traditional uses for roots include blood purification, deobstruent, antiseptic, astringent, tonic, anti-inflammatory, and antidysenteric properties. In many ayurvedic recipes, it is a crucial component. The roots are an excellent way to purify blood because they are a natural crimson dye. A variety of chemical components, such as Triterpenes, bicyclic hexapeptides, naphthoic acid esters, anthraquinones, and iridoid glycoside have all been separated and identified from Rubia cordifolia Linn. The current review article focuses on the pharmacological, phytochemical, and other significant facets of manjishtha.

KEYWORDS - Rubia cordifolia Linn, manjishtha, Rubiaceae, Indian Madder, anthraquinones

1. INTRODUCTION

The Rubiaceae family contains trees, shrubs, and herbs and has over 450 genera and 6500 species [1].Growing up to 12 meters in length, Rubia cardifolia is a perennial, thorny climber with a stem. The leaves grow in whorls of four to six and are ovate, lanceolate, 5-7 nerved, 2–10 cm long, and 2–5 cm wide. Perennial roots are lengthy,cylindrical and colored reddish brown. Tiny, fragrant, whitish or greenish yellow flowers are produced. The fruit matures to a dark purplish or blackish color and is tiny, glabrous, and has one to two seeds. The shrub bears fruit and flowers from August to October [2]. The lower hills of the Indian Himalayas in the north and the Western Ghats in the south, as well as Japan, Indonesia, Ceylon, Malaysia, the Peninsula, Java, and Tropical Africa, are all home to it in humid climates up to 3500 feet in the air [3–4]. Rubia cordifolia roots are the origin of a Ayurvedic medication. In the Indian medical system, it is a significant herbal medication. The plant's roots are marketed under the trade name Manjith and are usually referred to as Manjistha.

1.1 Colloquial terms

Aruna, Bhandi, and Bhandiralatik are some of the Sanskrit names for plant drugs; Mandar, Majathi, in Assam; Manjith, Manjistha, in Bengali; Indian Madder, in English; Manjithi, in Malayalum; Manjestha, in Marathi; and Majit, Manjit, in Hindi [5].

1.2, Rubia Kingdom Taxonomic Classification:

- Plantae: Dicotyledoneae
- Class: Sympetalae
- Subclass: Rubiales
- Order: Rubiales
- Family: Rubiaceae
- Genus: Rubia
- Cordifolia is the species [6].

Numerous conditions, including cephalalgia, cough, diabetes, arthralgia, arthritis, skin discoloration, dysmenorrhea, emmenagogue, leucorrhea, neuralgia, pectoral diseases, pharyngitis, general debility, hemorrhoids, hepatopathy, intermittent

TB, urethrorrhea, fevers, jaundice, ophthalmopathy, otopathy, splenopathy, strangury, poor bone healing, and tubercular diseases of the skin and mucosal tissue [7]. Laxative, analgesic, rheumatism, dropsy, paralysis, and intestinal ulcers are all treated with the roots, while blood, skin, and urinary tract

disorders, piles, ulcers, inflammations, erysipelas, skin conditions, and rheumatism are treated with the dried stem [8]. A vermifuge is made from a decoction of leaves and stems [1].

I.3 EXAMINATION OF MACROSCOPIC AND MICROSCOPIC

The stem is prickly-hispid, quadrangular, and divaricately branched. The stem's cross section revealed a rectangular form with a single-layered epidermis that was covered in pyramidal hairs and cuticles. Sclerenchymal hypodermis located at the stem's corners. The cortex is made up of phloem parenchyma and sieve tubes, and it is photosynthetic and chlorenchymatous with 4-6 layers. Two layers are used to simulate the cambium ring. Vessels, tracheids, fibers, and xylem parenchyma comprise secondary xylem. The jars are uniformly organized and huge.

There are uniseriate medullary rays.The rough, glabrous leaves measure 3.8-9 × 1.6-3.5 cm and are ovate-lanceolate, with 3-9 palmate veins, grouped in whorls of four. Compared to upper leaves, lower leaves are bigger. The base of the leaf is somewhat cordate. There are tiny white prickles on the edges. A leaf slice revealed a single layer. The cuticle-covered epidermis has pyramidal hairs. While spongy cells are multilayered and loosely organized, palisade cells are single layered and closely packed. There are two to four layers of collenchymatous cells in the bottom part of the midrib. The number of vascular bundles is definite, conjoint, and collateral.

The root is smooth, reddish, flexuous, long, and cylindrical. An outer 5-7 layer of cork tissue, which occasionally includes tannin, was visible in the root cross-section. Secondary cortical cells are red, polygonal, thin-walled, and lack a unique phenomenology. Tracheids and vessels make up the majority of the secondary xylem dish. The vessels are plenty and evenly dispersed. Although it lacks phloem fibers, secondary phloem forms a broad,reddish zone made up of thin-walled, sieve-like components and phloem parenchyma. Cambium is unique in that it does not have medullary rays. The presence of anthraquinones is indicated by the entire root being red in color [9].

2. PHYTOCHEMICAL RESEARCH

Quinines, primarily anthraquinone glycosides, are found in Rubia cadifolia and include 1-hydroxy 1, 4-dihydroxy-2-methyl-5-methoxy anthraquinone, 1,3-dimethoxy, and 2-methoxy anthraquinone 2. Anthraquinone carboxy as well as rubiadin [10]. Anthraquinones and their glycosides, naphthoquinones and their glycosides, terpenes, bicyclic hexapeptides, and iridoids are among the several groups of bioactive chemicals found in Rubia cardifolia [11]. Anthraquinones, specifically 1hydroxy-2 carboxy 3-methoxy anthraquinone and 1hydroxy-2 methyl 6- or 7-methoxy-anthraquinones, were produced from Rubia cordifolia. The remaining substances include scopoletin, β-sitosterol, and oleanolic acid acetate. Additionally, ten long chains of unsaturated and saturated fatty acids were identified [12]. Cordifoliol and cordifodiol are two novel anthraquinones that are produced from Rubia cordifolia roots. Their structures have been determined to be 1,8-dihydroxy-11,20 (15pentyl-naphthoquinone) phenanthrene (2) and 1-hydroxy-3-ethyl-9,10 anthraquinones (1) based on spectral data analysis and chemical reactions [13]. Numerous naphthoquinones, hydroxyanthraquinones, and their glycosides are found in Rubia cardifolia roots [14]. Lucid primeveroside, 1, 5-dihydroxy 2methyl, 4dihydroxy 2-methylanthraquinone, and 4naphthoquinone were among the other quinones that were found.ruberythric acid anthraquinones, 3-prenyl methoxy 1, 2-methyl-1, 3-trihydroxy-9, A combination of 2-methyl-1, 3-trihydroxy-9, and 10-anthraquinone 10. Anthraquinone β-glucoside 3-Oα-rhamnosyl (1→2)-.6.Alizarin, garancin, and man Justin are also present, as with methyl geniposidic acid (iridoids) [15]. Two naphthoquinones are present in the methanol extract of Rubia cordifolia roots [16]. The bicyclic hexapeptides RA-I and From a chloroform/methanol extract of Rubia Cardifolia roots, RA-II have been identified [17]. From Rubia cardifolia, two novel bicyclic hexapeptides, allo RA-V and neo-RA-V, as well as one cyclic hexapeptide, O-Secora-V, were recently identified [18]. Additionally, the plant contains rubilactone, mollugin, and dihydromollugin [19].

Indian madder, or Ubia cordifolia, has numerous traditional use, such as:

Drugs

The rhizome of Rubia cordifolia is used to cure a number of ailments in traditional Chinese medicine, such as:

Unusual bleeding in the uterus

Purpura allergic

Hemostasis

Increasing the flow of blood

First-time dysmenorrhea

Hemorrhage in the kidneys

Dye

Red, crimson, brown, and mauve hues are achieved in textiles by using the root of Rubia cordifolia as a natural dye.

Skin care

Brown spots, freckles, and skin discolouration are treated with a paste derived from honey and Rubia cordifolia. Additionally, it aids in the healing of wounds.

Additional applications

Rheumatism, piles, ulcers, inflammations, erysipelas, rheumatism, and skin, blood, and urinogenital diseases are all treated using the dried stem of Rubia cordifolia.

The climbing vine Rubia cordifolia is a perennial.

5 Pharmacological Studies

5.1 Hepatoprotective activity

Rubia Cardifolia methanolic extract may shield the liver from hepatotoxicity brought on by thioacetamide.Serum Glutamate Pyruvate Transaminase (SGPT) and Serum Glutamate Oxaloacetate Transaminase (SGOT) were the biochemical measures used to estimate the activity, and histological investigations corroborated the findings [27]. By interfering with the release of the hepatitis B surface antigen in human hepatoma cells, Rubia Cardifolia effectively prevents both acute and chronic hepatitis brought on by the hepatitis B virus [28]. In rats, the effects of acetaminophen and CCl4 on liver damage were examined using Rubia cordifolia aqueous methanol extract.

Serum levels of SGOT and SGPT increased to 1447±182 and 899±201 IU/L (n = 10) respectively, compared to the respective control values of 97±10 and 36±11, indicating liver damage caused by acetaminophen at a dose of 640 mg/kg. Prior to treatment Serum SGOT and SGPT levels were considerably ($p<0.005$) reduced to 161±48 and 73±29.59, respectively, with plant extract (500 mg/kg) [29]. In addition to preventing CCl4-induced extension of pentobarbital sleeping time, oral administration of rubiadin, which is included in the extract, can correct CCl4-induced liver damage in rats within 14 days [30].

5.2 Anti-diabetic effects

The administration of an alcoholic extract of Rubia cordifolia roots to diabetic rats produced by alloxan resulted in a notable hypoglycemic effect [31]. The antidiabetic, antioxidant, and antiglycation properties of Rubia roots.We looked at cordifolia Linn. The impact of Rubia cordifolia on the glycation of guanosine with glucose and fructose was examined in relation to its anti-AGE (Advance Glycation End Products) properties. It was also examined how a plant extract inhibited the glycation and fructation of guanosine when hydrogen peroxide-generated reactive oxygen species were present. These actions were assessed using in vitro antidiabetic (alpha-amylase and alpha-glucosidase) and antioxidant (DPPH, Superoxide anion scavenging activity, and xanthine oxidase) assays.The glycation processes' UV absorbance peaked at 24 hours and then steadily declined at 48 and 72 hours.

Results indicate that Rubia cordifolia root extract has strong antidiabetic, antioxidant, and antiglycation properties [32]. Aqueous root extracts of Rubia cardifolia were reported to control hyperglycemia and hypertriglyceridemia in streptozotocin-induced diabetic rats, and they also enhanced decrease of body weight, hypochromic microcytic anemia, and liver and kidney transaminases [33].

5.3 Anti-carcinogenic activity

Using the Sulforhodamine B assay, Rubia cordifolia root extract exhibits anticancer efficacy against MDA-MB-231 breast cancer cell lines [34]. Mice given mollugin demonstrated suppression of passive shown inhibition against lymphoid leukemia (P338), as well as protection of mast cell degranulation and cutaneous anaphylaxis [35]. Since the human cervical cancer cell line was strongly inhibited by the ethanolic extract of Rubia cardifolia, it may be a source of potent pharmacophore for the treatment of diseases like cancer [36]. Rubia cardifolia's cyclic hexapeptides and quinones shown significant anticancer efficacy against a range of proliferative cells [37].Alkyl ether and ester, two RA-V derivatives, had significant impacts on MM2 mammary cancer cells, human nasopharyngeal carcinoma, and P388 lymphocytic leukemia [38]. A number of secondary plant metabolites were extracted from G. rhizomes and Rubia cordifolia roots.

Glabra A small number of compounds demonstrated strong COX-2 inhibitory action against cancer when tested using the Cayman COX (ovine) inhibitory screening assay [39].

5.4 Neuroprotective activity

When compared to a group of albino mice that had been given Aβ 25-35, the extract from Rubia cordifolia demonstrated a strong protective effect against neurodegeneration and an enhancement in memory retention activity [40]. By inhibiting the decrease and raising GSH levels through the induction of GCLC (c-glutamylcysteine ligase) expression, Rubia cordifolia demonstrate neuroprotective potential. [41].

5.5 Antimicrobial activity

Root extract from Rubia cordifolia exhibited antimicrobial efficacy against three Gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi) and three Gram-positive (Staphylococcus epidermidis, Staphylococcus aureus, and Bacillus cereus) bacteria.[42]. While sitosterol and daucosterol have antibacterial properties, anthraquinones and flavonoids found in Rubia Cardifolia root preparations inhibited the activity of Gossypium phytopathogens [43]. The root extract of Rubia cordifolia shows the strongest antimicrobial effect against Pseudomonas aeroginosa and Plesiomonas shigelloides, and it inhibits bacterial pathogens such as Vibrio alginolyticus, Pseudomonas aeroginosa, Shigella sps, Plesiomonas shigelloides, and Vibrio parahaemolyticus [44]. The study found that the most potent components from Rubia cardiacfolia that exhibited antibacterial action were physcion and emodin [45].

5.6 Activity of antioxidants

Rubia cordifolia root, stem, and leaf methanolic and aqueous extracts all had the capacity to scavenge free radicals; the root aqueous and methanol extract had the largest amount, with an IC50corresponding values of 41.00 (µg/ml) and 61.95 (µg/ml) [46]. Rubiadin, a dihydroxy anthraquinone that was extracted from an alcoholic extract of Rubia cordifolia, has strong antioxidant activity that inhibits lipid peroxidation caused by FeSO4 and t-butyl hydroperoxide (tBHP) in a dose-dependent manner. In the case of lipid peroxidation caused by Fe2+, the percentage inhibition was higher. The preparation's antioxidant properties outperformed those of p-benzoquinone, mannitol, EDTA, Tris, and vitamin E [47]. The methanolic extract of Rubia cordifolia roots and rhizomes' in vitro antioxidant activities shown an anticholinergic action in rats, which could be explained by phenolic component content and antioxidant activity [48].

5.7 Inhibition of inflammation

At varying concentrations of 200 µg/ml to 1000 µg/ml, the ethanolic extract of Rubia cadifolia exhibits activity between 4.34% and 18.55%. To test the anti-inflammatory effect, carrageenan-induced rats were used the paw edema technique. In contrast to conventional (Ibuprofen gel), the extract has strong anti-inflammatory efficacy [49]. The purpose of the methanolic extract of Rubia cordifolia roots in rats was to examine the analgesic and anti-inflammatory properties. Carrageenan-induced rat paw edema was used to test the anti-inflammatory properties of Rubia cordifolia (100–300 mg/kg, p.o.). The carrageenan-induced paw edema was significantly ($P<0.05$) reduced by rubia cordifolia (100–300 mg/kg, p.o.) [50].In comparison to phenylbutazone (100 mg/kg), Rubia cordifolia had considerable anti-inflammatory action at doses of 10 and 20 ml/kg of the water extracts in rats with carrageenan paw edema [51].

5.8 Activity related to wound healing

The efficacy of Rubia Cardifolia's hydrogel and alcoholic extract in healing excision wound models in mice was investigated. An alternative alcoholic extract formulation was applied to the excision.as a single dose on the wound surface. The impact on wound healing was assessed using histology and wound area. Gel had a significant ($p<0.01$) impact on treated mice's wound contracting capacity, wound closure, reduction in the wound's surface area, tissue regeneration at the wound site, and histological features [52]. In experimental models, the root extract of Rubia cordifolia was found to be an effective wound healing standard [53].Histological analysis, a period of epithelization, and wound contraction were the physical parameters used to measure healing. It encourages the excision wound to constrict and become epithelized [54].

5.9, Activity that protects the stomach

Using an aspirin plus pylorus-ligated ulcer screening model in Wistar rats, the efficacy of Rubia cordifolia against experimentally produced stomach ulcers is compared with its fractions. The research verified.When compared to the plant extract, the chloroform fraction exhibited substantial activity at lower dosages. The mechanism is explained by a decrease in the activity of the gastric acid secretor and a strengthening of the mucosal defense system through the production of prostaglandins and antioxidant potential [55]. When compared to ranitidine, the extract of Rubia cardiofolia shown a substantial protective effect against stomach ulcers in all rat models.When compared to aspirin, rats' ulcerogenic response to polyherbal formulations was noticeably lower, even at very high dosages [56].

5.10, Activity against mutagenesis

Using Salmonella typhimurium, several root extracts of Rubia cordifolia were tested for their antimutagenic effect against mutations caused by the direct-acting mutagen 4-nitro-ophenylenediamine (NPD) and against S9-dependent mutagen. 2-Aminofluorene (2-AF) in the strain of TA98 test Typhimurium S.The highly polar methanol extract (RME) and the somewhat less polar chloroform extract (RCE) were separated from the root extract of Rubia cordifolia. In contrast to the mutagenicity caused by direct-acting mutagens, such as NPD, RME was found to be highly effective in reducing the mutagenicity of 2AF, or indirect-acting mutagen. At the highest dose examined (2.5×103 µg/0.1 ml), the inhibitory activity against NPD was 41.69% and 58.21%, respectively, during coincubation and preincubation modes of experimentation.During coincubation and preincubation modes of tests, RME effectively reduced 2AF-induced histidine revertants by 70.71% and 71.70%, respectively, with an IC50 of 500 µg/0.1 ml in the preincubation mode of the test. In the preincubation phase of the experiment, at the highest tested dose of 2.5×103 µg/0.1 ml with an IC50 of 664 µg/0.1 ml, chloroform extract

(RCE) decreased the mutagenicity of NPD by 59.04%. RCE99% inhibitory efficacy was seen in both coincubation and preincubation treatment modes, indicating that it fully suppressed the 2AF mutagenicity [57].

5.11, Activity against viruses

The WST-8 assay was used to assess the cytotoxicity and anti-rotaviral impact of Rubia cordifolia aerial part (RCAP) on MA-104 cells. The results of the antiviral test were verified using the colloidal gold method and the real-time polymerase chain reaction (qPCR) assay. The method of 4′, 6-diamidino-2-phenylindole (DAPI) staining was then employed to examine the cells' mechanism of death. And. It was demonstrated that when the extract concentration increased, both the viral load and the viability of MA-104 cells decreased. DAPI staining demonstrated that the reduced viral load and cell viability were due to virus-induced apoptosis.

an effect that was expedited by the herbal extract's aqueous incubation. The two main substances found to demonstrate these properties were vanillic acid and xanthopurpurin. This study demonstrated the effectiveness of RCAP extract.promoted virus-induced apoptosis in MA-104 cells, which in turn prevented rotavirus proliferation [58].

5.12, Activity that protects the kidneys

Based on the tissue antioxidant state in the animals given the medication, the hydroalcoholic extract of Rubia cardifolia dramatically reduces the nephrotoxicity caused by cisplatin. Serum values of urea and creatinine showed a notable shift. Animals treated with extract also showed a significant decrease in lipid peroxidation in their liver and renal tissues [59].

A successful column-switching countercurrent chromatography (CCC) methodology that combines stepwise elution mode was created for the preparative and simultaneous extraction of antioxidant components from traditional Chinese herbal medicine's ethyl acetate extract. Rubia Cordifolia exhibits nephroprotective properties [60].

CONCLUSION

R. cordifolia is a well-known TCM with significant medicinal and commercial significance. In ancient China, R. cordifolia was one of the first and most popular red dyestuffs. For thousands of years, people have also used R. cordifolia to treat a wide range of illnesses. In recent years, the plant has drawn more attention because of its great therapeutic advantages and low number of adverse clinical consequences. There are around 100 known chemicals in R. cordifolia. We investigated the pharmacological properties of R. cordifolia and its constituents. The foundation for R. cordifolia's clinical use is laid by these discoveries, which are helpful for medication research. Still, there are a lot of unanswered questions regarding R. cordifolia study.

There is no unique genetic identity card for R. cordifolia. R. cordifolia's genomic information is still unknown. In order to identify the main active ingredients, investigate the synthesis process of the active compounds, improve quality, and produce it industrially, genomic sequencing and acquisition of the genome sequence of R. cordifolia are required. Additionally, transcriptomics, metabonomic analysis, and comparative genomics should be combined with genomic sequencing to provide additional information about R. cordifolia. All of these investigations will provide R. cordifolia with a pair of wings to help modernize TCM.

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