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### RESEARCH ARTICLE

#### A REVIEW STUDY OF MEDICINAL USES OF MANJISHTHA (RUBIA CORDIFOLIA).

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#### Abstract

Herbal medicines have good efficacy, safety and lesser side effects. They have great demand in developed world for primary health care. India has rich traditional knowledge, heritage of herbal medicines and large biodiversity. *Rubiocordifolia Linn.* is a flowering plant species. It is commonly known as *Manjishtha*. Roots and stems are active part of plant. Plant has many pharmacological actions like blood purifier activity, anticancer, astringent, anti-acne, anti-inflammatory, anti-microbial, antidysentric, antiseptic, nephroprotective, antirheumatic and hepatoprotective properties. This review article presents the information on synonyms, microscopic, macroscopic, chemical constituents, uses and pharmacological actions of *Manjishtha*.

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#### Introduction:-

*Rubiocordifolia Linn.* is a flowering plant species. It is commonly known as *manjishtha*. Roots and stems are active part of plant. Plant has many pharmacological actions like blood purifier activity, anticancer, astringent, anti-acne, anti-inflammatory, anti-microbial, antidysentric, antiseptic, nephroprotective, antirheumatic and hepatoprotective properties.

Charaka has included *manjishtha* in *varnya*<sup>1</sup>, *vishaghna*<sup>2</sup> and *jwarahara mahakashaya*<sup>3</sup> while *sushrua* has included in *priyangwadi*<sup>4</sup>, *pitta sanshamana varga*<sup>5</sup> and *ambawashtadi gana*<sup>6</sup>.

#### Material and methods:-

References related to proposed title are collected from classical texts of *ayurveda*. Various publications, internet, books, research papers and proceedings of seminars related to the topic are collected.

#### Plant profile:-

Kingdom : plantae  
Class : dicotyledoneae  
Order : rubiales  
Family : rubiaceae  
Genus : rubia  
Species : cordifolia

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**Synonyms:-**

Jingi, yojanavalli, samanga, raktanga, bhandi, vikasa, vastraranjani, manjetha, rakta, indianmaddar, manjitha.

**Morphological description:-**

Origin and habitat<sup>7</sup>:-

It is a deciduous climber with weak flexible stem upto 10 feet high and .25 inch diameter. Basal portion of stem is usually persistent and often softly woody. Branches are quadrangular, remoeselyscabrid or glabrous. Leaves 4 inch whorl, two often larger and with longer petioles, long, ovate, acute, base cordate, scabrid or smooth strong basal nerves. Flowers are less than 1 inch in diameter, dark red or pinkish brown, in terminal cymose, leafy panicles. Fruits are globose, dark purple or black fleshy, succulent, with red juice.

Geographical distribution-

It is commonly occurring throughout the hilly regions of india, ascending to 8000 ft. Frequently in the himalayan region of country from the north west frontier eastwards on the himalaya and south to ceylon and the malay, also in china, japan, java and tropical africa<sup>8</sup>. It occurs throughout india (dehradun, kashmir, nagpur, malva), nepal, shrilanka, iran, afghanistan. It is propagated by seeds and stem cutting.

According to *Rajnighantu*, *manjishtha* has four types: chola, yojani, konchi and sinhali<sup>9</sup>. *Manjishtha* has also three species: *rubiadifolia* (indianmaddar), *rubiakane* (asianmaddar) and *rubiactinctorum* (european or africanmaddar)<sup>10</sup>.

**Phytochemicals:-**

Different classes of bioactive compounds such as anthraquinones and their glycosides, naphthoquinones and glycosides, terpenes, bicyclic hexapeptides, iridoids, carboxylic acids (malic, citric, quinic, rosmarinic acids) and saccharides (xylose, ribose, fructose, glucose, sucrose, primverose) were isolated from various parts of *R.Cordifolia*<sup>11</sup>. Saponins and some naphthene derivatives are also isolated. It contains alizarin, pseudopurpurin, rubiadin along with glucoside, lucidine, purpurin and manjisthin<sup>12</sup>.

Quinones:- the plant contains quinines, mainly anthraquinone glycosides and include 1-hydroxy 2-methoxy anthraquinone, 1, 4- dihydroxy-2- methyl-5-methoxy anthraquinone, 1,3- dimethoxy 2- carboxyanthraquinone and rubiadin.

Iridoids:- 6-methoxygeniposidic acid is found along with manjistin, garancin and alizarin. Oleananestriterpinoid:- rubiprasin a, b, and c along with arboranestriterpinoids, like rubiarbonol a, b, c, d, e and f have been isolated.

Bicyclic hexapeptides:- the compounds having antitumour activity have been isolated and identified chemically.

Anthraquinones:- the colouring matter present in the roots of *R. cordifolia* is a mixture of purpurin (trihydroxyanthraquinone) and manjistin (xanthopurpurin-2-carboxylic acid). The roots contain small amounts of xanthopurpurin or purpuroxanthin and pseudopurpurin (purpurin-3- carboxylic acid). The plant also contains dihydromollugin, mollugin, rubilactone. Purpurin, belonging to the lipocalin family of proteins, is a fast dye for cotton printing and forms complexes with various metal ions. It is a glycosaminoglycan binding protein as well as a retinol binding protein.

Alizarin, or 1, 2-dihydroxyanthraquinone or mordant red, is the red dye originally derived from the root of the madder plant. In 1869, it became the first natural pigment to be duplicated synthetically. *R. cordifolia* yielded anthraquinones namely, 1-hydroxy-2 carboxy 3-methoxyanthraquinone, 1-hydroxy-2 methyl 6 or 7-methoxy-anthraquinones. The other compounds were oleanolic acid acetate,  $\beta$ -sitosterol, and scopoletol. Ten fatty acids with saturated and unsaturated long chains were also identified.

**Formulations and preparations:-**

Mahamanjisthaadikwatha, laghumanjisthadikwath, manjisthadichurna, manjisthadipana, manjisthadhyatailam, manaktaila, jatyadi ghrita, chandanadi tail, pindataila, bala tail, kumkumadi tail, phalasarpi ghrita, phalkalyanaghrita, chandanasaava, ashwagandharistam, devdarvarishtam, eladyarishtam, madhookasawam, manjisthasavam, usheerasavam, erimedaditaila, dashamoolarishta etc.

**Traditional uses in different systems of herbal medicine:-**

In traditional Korean system of medicine, the root is used to treat rheumatism, jaundice and menstrual disorders. In the Philippine system, a decoction of root is drunk as a remedy for urinary disorders<sup>13</sup>. The natives of the Republic of South Africa take a decoction of the leaf or root for pleurisy and other inflammatory conditions of the chest. The stem is used in the Tibetan system of medicine in the treatment of blood disorders and spreading fever of kidneys and intestines<sup>14</sup>.

Unani system of medicine:- *R. cordifolia* has been prescribed for paralysis, dropsy, jaundice, amenorrhoea, urinary tract obstructions, skin disorders, menstrual disorders (excessive or painful bleeding), renal stone, urinary disorders and blood detoxification.

Chinese system of medicine:- roots help menstrual flow, promote blood circulation, promote urination, stop coughing blood or vomiting blood, nose bleeding. The plant is also useful in treatment of missing menses due to blood stasis, pain and inflammation caused by bleeding and blood circulation stasis, injuries from impacts and in jaundice and edema<sup>15</sup>. The herb is internally used for abnormal uterine bleeding, internal and external haemorrhage, bronchitis, and rheumatism<sup>16</sup>.

Ethnoveterinary usage:- *R. cordifolia* is used in the treatment of liver fluke, dysentery, maggots, wounds and intestinal worms in animals.

**Ayurvedic properties<sup>17, 18, 19</sup>:-**

Rasa	Madhura, Tikta, Kashaya
Guna	Guru, Ruksha
Virya	Ushna
Vipaka	Katu

Doshagnata: Kapha-Pittahara

Rogagnata: Charmavikara, Raktavikara, Kushtha, Jvara, Mutrakricha, Prameha, Visarpa, Shotha, Raktatisara.

Karma : Rakta-Prasadana, Raktashodhaka, Varnya, Kaphagna, Vishaghna, Krimighna, Svarya, Vrishya, Shothaghna, Kushthaghna, Pramehaghna, Stambhana, Artavajanana, Rasayana, Shonitasthapana.

Therapeutic uses: it is blood purifying agent and pigment stimulant. It is useful in diseases of blood and skin. It is used in Yoni Roga, Akshiroga, Shleshmajashotha, Manjishthameha, Raktatisara, Kushtha, Visarpa, Prameha, Sarpavisha, Bhagna, Arsha, Vyanga.

**Pharmacological activity:-****Anti-acne property:-**

The anti-acne activity of anthraquinone rich fraction of *R. cordifolia* in a gel formulation against propionibacterium acne, staphylococcus epidermidis, malassezia furfur is proved when compared with standard clindamycin gel<sup>20</sup>.

**Anti-arthritis property:-**

The anthraquinones rich fraction of ethanolic extract of *R. cordifolia* has imperative anti-arthritis potential and showed edema inhibition in induced arthritic model, which is similar to a standard non-steroidal anti-inflammatory drug, aspirin<sup>21</sup>.

**Anti-cancer property:-**

Anticancer activities of various fractions of *R. cordifolia* roots extracts was demonstrated through in vitro and/or in bioassays based on animal models. The crude aqueous extracts demonstrated growth inhibitory activity on selected cancer cell lines as well as on normal human mammary epithelial cells<sup>22</sup>.

**Anti-convulsant activity:-**

In modern medicine, *R. cordifolia* was reported to have anticonvulsant activity. Triterpenes inhibited seizures induced by maximum electric shock, electrical kindling and various chemoconvulsants in rats. Brain GABA and serotonin (5-HT) contents were raised by the compound proves its anticonvulsant property<sup>23</sup>.

**Anti-diabetic:-**

Alcoholic extract of root and leaf extracts were found to have promising antidiabetic activity against animal models. The extract of roots reduced the blood sugar level in alloxan treated diabetic rats, indicates that the extract has an extra pancreatic effect<sup>24</sup>. The aqueous root extracts 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<sup>25</sup>. Serum cholesterol and triglyceride level were decreased where as serum high density lipoprotein and protein levels were increased in diabetic rats<sup>26</sup>.

**Anti-inflammatory activity:-**

Rubiocordifolia root extract has been used as anti-inflammatory agent because of the presence of rubimallin. It inhibited the lipoxygenase enzyme pathway, which catalyses the production of various inflammatory mediators such as leukotrienes that are involved in asthma, arthritis, and other inflammatory disorders, and the production of cumene hydroperoxides<sup>27</sup>.

**Wound healing activity:-**

The root extract of *R. cordifolia* was reported as an effective wound healing principle in experimental models as wound healer<sup>28</sup>. 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<sup>29</sup>.

**Anti-microbial activity:-**

The root extracts of *R. cordifolia* have been studied for their antimicrobial activity against various pathogenic bacteria. Sitosterol and daucosterol possess antibacterial activity. Rubiacordone a reported to have considerable antimicrobial activity against gram +ve bacteria like *bacillus subtilis*, *streptococcus faecalis* and *bacillus cereus*<sup>30</sup>. The green synthesized silver nanoparticles using *R. cordifolia* plant root extract was highly inhibiting the bacterial pathogens like *vibrio alginolyticus*, *pseudomonas aeruginosa*, *shigella* spp, *pleiomonas* v and *vibrio parahaemolyticus*. They had highest antimicrobial effect against *pseudomonas aeruginosa* and *pleiomonas shigelloides*<sup>31</sup>.

**Anti-oxidant activity:-**

*Rubiocordifolia* contains a wide variety of antioxidants like alizarin, hydroxyl anthraquinones and rubiadin which have been using in various medicaments. The study of in vivo antioxidant activity and its influence on ethanol-induced immuno-suppression showed that the concurrent daily administration of madder prevented the decrease of humoral and cell-mediated immune response, phagocytosis index, leukocyte count, glutathione content etc., which were comparable with that of the combination of vitamin e and c<sup>32</sup>.

**Anti-peroxidative activity:-**

Solvent free alcoholic extract of *R. cordifolia* showed antiperoxidative property in rat liver homogenate<sup>33</sup>.

**Anti-platelet activating effect:-**

In ayurvedic system, the plant is prescribed to cure blood related ailments. Partially purified fraction of the whole plant inhibits the action of platelet activating factor at its receptor level either by its blocking or by desensitization property<sup>34</sup>.

**Anti-proliferative property:-**

Aqueous, ethanolic extract of root reported to have significant anti-proliferative effect. Mollugin found to be an active antiproliferative principle by bioassay-monitored fractionation. It did not exert cytotoxicity to human fibroblast cell line<sup>35</sup>.

**Antistress and nootropic activity:-**

Alcoholic extract enhanced brain  $\gamma$ -amino-n-butyric acid levels and decreased brain dopamine and plasma corticosterone levels<sup>36</sup>. The extract inhibited acidity and ulcers caused due to cold restraint stress.

**Anti-ulcer activity:-**

The effect of alcoholic extracts of roots of *R. cordifolia* and its antiulcer potential on alcohol, ibuprofen, cold restraint stress and pyloric ligation-induced gastric lesions was studied along with ranitidine, a standard drug<sup>37</sup>.

The extract showed substantial and significant protection against gastric ulcers in all the models compared to ranitidine.

**Antiviral activity:-**

The naphtha-hydroquinones are reported to have antiviral activity. 6-hydroxy group and a pyran or furan ring of furomollugin and mollugin strongly suppressed the secretion of hepatitis b surface antigen, in human hepatoma hep3b cells. The methanolic extracts of leaves have minimum inhibitory concentration of different virus using hel cell cultures and vero cell cultures<sup>38</sup>.

**Diuretic activity<sup>39,40</sup>:-**

To substantiate the traditional claim, the hydroalcoholic root extract of *R. cordifolia* was evaluated for its diuretic property and got positive results. The hydroalcoholic extract as well as the ethanol extract showed significant increase in urine volume and electrolyte excretion in a dose dependent manner compared with the reference drugs.

**Gastroprotective activity:-**

*Rubiacordifolia* has both gastroprotective and ulcer healing properties. Triterpenoids present in root extracts are potent antiulcer and antioxidant compound which can be clinically explored<sup>41</sup>.

**Hepatoprotective activity:-**

The quinone derivatives from *R. cordifolia* reported to have hepatoprotective effect on animal systems. Animal model studies proved that the methanolic extract protects the liver thioacetamide-induced hepatotoxicity<sup>42</sup>. The aqueous-methanol extract has 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<sup>43</sup>.

**Immuno-modulating activity:-**

The alkaloids, cardiac glycosides, tannins, flavonoids and phenols present in *R. cordifolia* are responsible for enhanced immuno-modulation. Ethanolic extracts of the whole plant were administered to rats to test immunosuppressive activity and showed enhanced cell mediated and humoral immuno-potentiating activity<sup>44</sup>. Hence *R. cordifolia* can be utilized as a source of immunity enhancing drug.

**Neuroprotection:-**

*Rubiacordifolia* has been reported to contain a wide variety of antioxidants and exhibited strong free radical scavenging properties against reactive oxygen and nitrogen species. The herb attenuate oxidative stress mediated cell injury during oxygen glucose deprivation and exert the above effects at both the cytosolic as well as at gene expression level and may be an effective therapeutic tool against ischemic brain damage<sup>45</sup>. The alcoholic extract decreases the neuro-degeneration and helps in memory retention activity<sup>46</sup>.

**Radiation protection:-**

Oxidative stress induced by oxygen derived reactive oxygen species produces several adverse effects which are highly implicated in several degenerative diseases such as cancer. The therapeutic applications of *r.Cordifolia* extract provide significant protection against radiation induced lipid peroxidation, hemopoietic injury and genotoxicity when administered intra-peritoneally before the radiation exposure<sup>47</sup>.

**Calcium channel blocker(s) in R. cordifolia:-**

The calcium channel antagonistic activity of a crude root extract of *R. cordifolia* was tested in isolated tissue preparations. The extract (0.1–3mg/ml) augmented spontaneous contractions of guinea pig atria, rabbit jejunum and rat uterus in a concentration-dependent manner.

**Nephrotoxicity:-**

The hydro-alcoholic extract of *rubiacordifolia* could decrease the intensity of cisplatin induced nephrotoxicity in swiss albino mice. The extract could significantly decrease the cisplatin induced nephrotoxicity as inferred from the tissue antioxidant status in the drug administered animals. Remarkable change was observed in serum creatinine and urea levels.

**Other uses:-**

Apart from its medicinal value, this plant has also been used as natural colorants in food, medicated oils, syrups etc. Root derived dye also used as textile and hair dye. Madder extracts is commonly used as a colorant for confections and soft drinks, because of its advantageous resistance to heat and light. The persuasive antioxidant activity of madder is effectively exploited in food industry as chemo-preventive agents. *R. cordifolia* can be used as a single drug to cure chikungunya fever<sup>48</sup>. Leaf extract is used during cataract of eyes, conjunctivitis and also to clean the eyes. In patients with eczema, the topical application of the plant caused reduction in the severity of score and oedema, exudation and itching being significantly relieved.

Crude methanolic extract suppressed the spontaneous contractions of guinea-pig atria, rabbit jejunum and rat uterus in a concentration dependent manner. The indicated spasmolytic activity similar to that of verapamil, a standard  $Ca^{++}$  channel blocker, suggests the presence of calcium channel like constituents in the plant, which may be responsible for the folkloric use of this plant for disintegration of urinary stones<sup>49</sup>. Psoriasis is a skin disease associated with hyper proliferation and aberrant differentiation of keratinocytes. The in vitro and in vivo findings together, the preclinical study confirms that ethanol fraction is a promising antipsoriatic agent.

**Conclusion:-**

*Manjishtha* is very important drug, which is described from ancient time. *Acharya* had already known the importance of *manjishtha* in the therapeutic management. Hence they used single or in combination in the form of *churna*, *kwath*, *lepa*, *ghrita*, *taila* etc. Used internally or externally to cure and prevent various diseases. The multiple benefits of *rubiacordifolia* made it a true miracle of nature. It has several effects like anti-oxidant, anti-inflammatory, anti-acne, anti-arthritis, anti-cancer, anti-convulsant, anti-diabetic, anti-microbial, anti-peroxidative, anti-proliferative, anti-stress, anti-ulcer, anti-viral, diuretic, gastroprotective, neuroprotective, immune modulating, radiation protective, hepatoprotective wound healing etc. Properties.

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