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Review Article

EXPLORATION IN PHARMACOLOGICAL SCREENING OF *RUBIA CORDIFOLIA* VERSES AYURVEDIC DOCUMENTATION: A COMPARATIVE VALIDATION

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ABSTRACT

Manjishtha is one of the most clinically practiced herbs in Ayurveda System of Medicine. It is also immensely documented in Ayurvedic traditional literature for various diseases. Out of its entire therapeutic spectrum, herb is famous for its activity on various skin diseases/blood disorders. The Latin name of Manjishtha is *Rubia cordifolia* Linn (Family: Rubiaceae) and is commonly sold under the trade name 'Majith' in Indian Market. In recent period many experiments were carried out in different field like Pharmacognosy, Pharmacology, Chemistry, etc to trace out valuable components from this plant. Being one of the major herbs in Ayurveda, it has attracted many researchers to explore its potential in Pharmacological field. It is observed that most of the screened Pharmacological results were seemed to be already documented in Ayurveda directly or indirectly since centuries. This documentation is mostly in the form of Sanskrit Sutra and carries large concealed information for those who understand the conceptual depth of Ayurveda. Here is a review of screened information verses Ayurvedic literature which is validating the claims made by the ancient sages.

Keywords: Manjishtha, *Rubia cordifolia*, pharmacological screening, Ayurvedic Validation

INTRODUCTION

Manjistha is known to the Indian think tankers since Vedic period. The references are found in Atraireya Aranyaka. The herb was also used in a ritual and ceremonial part of Indian cultural activity like Upanayana Samskara. The Ksatriyas (warriors) are expected to wear the cloths colored with Manjista which is a sign of victory. As a commercial point of view it is identified as artificial coloring agent since many decades[1]. The drug is known by many synonyms like Vikasa, Jinghi, Samanga, Kalameshi, Mandukaparni, Yojanavalli, etc. In recent past researches were carried out to explore potential chemical constituents of the drug and many compounds have been extracted from this plant[2,3]. The efforts were also made to standardize the plant and its components through various Pharmacognostic studies[4-7]. Apart from this clinical trials were also carried out to see the effect of the herb for claimed activities[8]. Some researchers also made the review of work done till date on Manjishtha[9]. The most important and majority of researches were done in the field of pharmacological screening systematic review of published pharmacological evaluation on Manjishtha along with parallel references from Ayurvedic classics is as follows.

PHARMACOLOGICAL ACTIVITY	DIRECT OR INDIRECT CLASSICAL REFERENCES	AYURVEDIC INTERPRETATION: AN APPLIED THERAPEUTIC FEATURE
Anti-acne property: This activity was proved regarding its Anthraquinone rich fraction in a gel formulation[10]. The activity was exhibited against *Propionibacterium acne, Staphylococcus epidermidis, Malassezia furfur*	Kaphaghna, Vatapittaghna[51], Shopha[42,44,47,49], Visarpa[42,44-47], Kushtha[42,44-47,49], Raktavilara[43,44], Varna kruta[44,45,47],	Manjishtha can become drug of choice for all Tridoshaja (tri-humor) diseases. It reduces the inflammation underlying all skin diseases, herpes and any blood disorders. It improves the complexion by improving the quality of blood
Anti-arthritic property: it was established regarding its anthraquinones rich fraction of ethanolic extract and showed paw edema inhibition in induced arthritic model[11]	Kaphaghna[51], Shopha[42,44,45,47,49], Rasayani[50]	It can be a good drug of choice for rheumatoid arthritis than plain arthritis. By this way it is useful in all inflammatory conditions and increases the immunity.
Anti-convulsant Activity: The Triterpenes present in the *R. cordifolia* inhibited seizures induced by maximum electric shock, electrical kindling and various chemoconvulsants in rats[12]	Vatapittaghna[51], Akshiroga[42,43,44,48],, Shopha[42,44,45,47,49], Rasayani[50]	It is suitable for all obstructive pathological conditions (Upastambhita) responsible for convulsions. It reduces the inflammation and act as immunity booster for nervous tissues. Its action on eyes (Akshi) indicates that the drug have action at the level of Majja Dhatu (Source of nerve tissue)
Anti-diabetic: The Alcoholic[13], Acquous[14] and Methanolic[15] extract of root along with leaf extracts[16] of the plants showed Antidiabetic activity against animal models	Kaphaghna, Vatapittaghna[51], Shopha[42,44,45,47,49] Meha[42,43,44,45,48], Kushtha[42,44,45,46,47,49], Vrana[42,43,44,45,48], Rasayani[50]	The direct reference is related with Meha (frequency of urine). Apart from this it take care of all inflammatory conditions in diabetes, diabetic ulcers, diabetic dermatopathy, etc. It is one of the important herbs for regular intake in diabetes as Rasayana.

Anti-microbial activity: the extracts suppressed the activity phytopathogens of *Gossypium*[17,] *Klebsiella pneumonia*.[18], *E. coli*.[19], *streptomycin* and *penicillin* G.[20], *Pseudomonas aeroginosa* and *Plesiomonas shigelloides*.[21]	Kaphaghna[51], Akshiroga[42,43, 44,48], Kushtha[42,44,45,46,47,49], Vrana[43,44,45,48]	The herb is purely against Kapha (platform for microbs growth) and hence directly or indirectly it will cover all the range of microbial growth. The action of inflammatory condition of Eyes, ear, wound, etc shows that there are many microbial floras yet to be screened for the action.
Anti-inflammatory activity: The aqueous root extract showed anti-inflammatory activity in rats[22]. It also exhibited the inhibition of the lipoxygenase enzyme pathway[23] responsible for Anti-inflammatory action	Kaphaghna, Vatapittaghna[51], Karnaroga[42,44,45], Akshiroga[42,43,44,48], Yoniroga[42,44-46], Shopha[42,44,45,47,49], Visarpa[42,44-47] Meha[42,43,44,45,48], Kushtha[42,44-47,49], Arsha[42], Vrana[42,44,45,48], Raktatisara[42,44-46], Raktavikara[43,44], Swara krut[44,45,49], Varna krut[44,45,47], Mutrakruchchh[49], Rasayani[50], Jwaranashana[41,46,48,50]	Any inflammatory process in the body, especially related with blood mechanism the herb will be useful. The wide range of inflammatory diseases mentioned in Ayurveda for Manjishtha is the proof of its activity.
Wound healing activity: The Ethanolic root extract is effective wound healing principle[24]	Kaphaghna, Vatapittaghna[51], Akshiroga[42,43,44,48], Yoniroga[42,44-46], Visarpa[42,44-47], Meha[42,44,45,48], Kushtha[42,44-47,49], Vrana[42-45,48], Raktavikara[43,44]	The drug directly acts on blood diseases like skin diseases, wound diseases, etc. In that sense it improves the quality of blood and resolves any underline pathogen responsible for non-wound healing
Anti-oxidant activity: antioxidants like alizarin, hydroxyl anthraquinones[25] and rubiadin[26]	Kaphaghna, Vatapittaghna[51], Meha[42-45,48], Rasayani[50]	The drug is Rasayana in nature. It means Rasa (body fluids) and Ayana (proper circulation and nutrition). Hence will act on any pathological condition
Anti-platelet activating effect: inhibits the action of platelet activating factor at its receptor level either by its blocking or by desensitization property.[27]	Kaphaghna, Vatapittaghna[51], Shopha[42,44,45,47,49], Raktatisara[42,44-46] Raktavikara[43,44], Jwaranashana[41,46,48,50]	Improving quality of blood is also a part of preventing platelet aggregation. Having Ushna Veerya (Hot In nature) and Katu Vipaka is also helpful for anti-platelet action
Antistress and nootropic activity: Alcoholic extract enhanced brain ϒ-amino-n-butyric acid levels and decreased brain dopamine and plasma corticosterone levels.[28]	Kaphaghna, Vatapittaghna[51], Kushtha[42,44-47,49]	There is no direct reference of the herb on anti-stress but by curing the skin diseases it prevents the psychological distress which is the major issue in dermatology.
Anti-ulcer activity: alcoholic extracts of roots of *R. cordifolia* and its antiulcer potential on alcohol, ibuprofen, coldrestraint stress and pyloric ligation-induced gastric lesions was studied along with ranitidine, a standard drug.[29]	Kaphaghna, Vatapittaghna[51], Yoniroga[42,44-46], Kushtha[42,44-47,49], Vrana[42,43-45,48], Raktavikara[43,44]	Manjishtha is a strong bitter in taste which is one of the major property for Pittahara. Pitta is responsible for the ulcers formation. Hence any ulcerative disease like cervical erosion (Yoniroga) or wounds (Vrana), etc the Manjishtha will be useful.
Antiviral activity: The naphthohydroquinones are reported to have antiviral activity[30]	Kaphaghna, Vatapittaghna[51], Shopha[42,44,45,47,49], Visarpa[42,44-47], Raktavikara[43,44]	Viral infection is the main factor for herpes disease (Visarpa). Hence not only Visarpa but also other underline viral infections related with Rakta Vikara, etc the drug will be useful.
Diuretic activity: *R. cordifolia* was evaluated for its diuretic property and got positive results.[31,32]	Shopha[42,44,45,47,49], Meha[42,43,44,45,48], Mutrakruchchh[49]	It is very surprising the see that the Manjishtha is useful for restricting excessive urine (e.g. in Meha) and promoting urination (e.g. Mutrakruchchh). Hence the drug is under Rasayana category. Ultimately it regulates the urine mechanism and prevents underline pathology.
Gastroprotective activity: gastroprotective and ulcer healing properties.[33], Triterpenoids present in root extracts are potent antiulcer and antioxidant compound which can be clinically explored.[34]	Kaphaghna, Vatapittaghna[51], Arsha[42],	Manjishtha is Ushna Veerya (helpful for digestion), Tikta Rasa (useful in endo-toxins -Ama) and hence indirectly helpful in improving Gastro-intestinal functions. The activity on Arsha indicates that It improves the portal circulation.
Hepato-protective activity: quinone derivatives from *R. cordifolia* reported to have hepatoprotective effect. methanolic extract protects the liver[35]	Visarpa[42,44-47], Meha[42,43,44,45,48], Kushtha[42,44-47,49], Raktatisara[42,44,45,46], Raktavikara[43,44], Varna kruta[44,45,47]	According to Ayurveda Yakrut (Liver) is the place for Rakta (Blood), hence any blood diseases as per Ayurveda like Visarpa, Kushtha, Vrana, Raktatisara, etc there is a involvement of Liver. The drug is strongly hepatoprotective in this connection
Immuno-modulating activity: The alkaloids, cardiac glycosides, tannins, flavonoids and phenols present in *R. cordifolia* are responsible for enhanced immuno-modulation [36, 37]	Kaphaghna, Vatapittaghna[51], Visarpa[42,44-47] Meha[42,43-45,48], Kushtha[42,44-47,49], Raktavikara[43,44], Rasayani[50]	As explained earlier Manjishtha is Rasayana in nature. It is taking care of each and every biochemical mechanism related with explained diseases and hence become immunity booster for those diseases and in general.
Neuroprotection: Found to be good antioxidant and exhibited strong free radical scavenging properties against reactive oxygen and nitrogen species. It is observed that it may be an effective therapeutic tool against ischemic brain damage.[38, 39]	Akshiroga[42-44,48], Rasayani[50]	The action on Akshi (a part of Majja Dhatu in Ayurveda) is an indirect reference of the drug having action on Neurons. The drug is also a Rasayana and hence will be helpful for any Tridoshaja dominant neurological deficit in body.
Radiation protection: 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.[40]	Rasayani[50], Jwaranashana[41,46,48,50]	This is novel information where as such no directly comment observed in the Ayurvedic texts. Indirectly it can be predicted that the drug shows its radiation protection activity through curing Vyang (Sunburn?), Kushtha, which may cause due to environmental radiations.

DISCUSSION

Most of the time the information documented in Ayurvedic classics can be justified by pharmacological screening but sometimes the information given in the text may not be reproducible in animal models. Such positive activity screening carried out using modern perspective is used to justify the rationality of Ancient sciences like Ayurveda. On the contrary negative results were used to disqualify the claims of traditional medicines. Thinking on high attitude being the researcher we must assess the area and intention of respective sciences for their documentations and experimentations. It is very clear that the purposes of Pharmacological screening of herbs are mostly done to trace out certain compounds and their systematic research for isolation and characterization. Later it may be administered in quantum (extract) form or can be further planned for synthetic preparation. The principles, theories, methods, patterns with intention and aim of Pharmacology are entirely different to conduct the studies in compare with any Traditional System of Medicine. In the same way the Traditional System of Medicine like Ayurveda also have their own philosophy, ideology, principles, methods and understanding which is entirely and conceptually different from Pharmacological study. It believes in 'Drug as a Whole' than any fraction of the herb. Hence claiming or disclaiming or commenting on the rationality of the system is not justified. The correlation about the activity and their application can be applicable in Drug discovery. Generally, the processes of Drug Discovery for finding a therapeutic effective molecule is time consuming, costly and have its own limitations through existing methods. It is assessed that if drug discovery research is associated with traditional Ayurvedic approaches with multidisciplinary knowledge, it may reduce the burden in many pharmacologic research organizations. It can be assumed that the traditional scientists who claimed the activity of herb hundreds of year back may have carried out such pharmacological experiments but in different style than existing methods. This may be the reason where most of the claims are still found to be experimentally valid and clinically effective. In this review on Manjishtha shows various pharmacological activities and can be utilized for modification in failed drug discovery methods.

CONCLUSION

The Ayurvedic documentation on the herbal drugs is described in the Sutra form (Sanskrit quotation). The knowledge of Sanskrit, medical background and expertise in Dravyaguna (Ayurvedic therapeutics) can become the benchmark for ideal interpretation of the Ayurvedic Sutras. These Sutras contain the conceptual and broad meanings. Applying the exact information in a personified disease condition is an art of the Vaidya (Ayurvedic Doctor). The knowledge of modern science and Ayurvedic literature can enlarge the futuristic research in Pharmacology. Manjishtha can be better studied and applicable with scientific reasoning in most diseases by studying this kind of review.

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