

MANJISTHA (*RUBIA CORDIFOLIA*) - A HELPING HERB IN CURE OF ACNE

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ABSTRACT:

Acne is one of the most prevalent skin ailment affecting almost all teenagers, as it is chronic with frequent remission and exacerbations is often associated with negative psychological consequences, diminished self-esteem and social withdrawal. The Modern measures regarding the treatment of acne are more or less failure. Further it has some limitations, cost effective and many side effects. To overcome from all these, a good herbal approach should be reached. *Manjistha* (*Rubia cordifolia*) can be proven a best remedy to cure acne, due to its *Varnya*, *Raktashodhak*, *Vishaghna*, *Rasayana*, *Krimighna* properties. Certain research papers has also proven that it possess anti-inflammatory, antibacterial, antioxidant and anti-androgenic effects as these are important Pharmacotherapeutic agent to break the pathogenesis of acne.

Key Words: *Manjistha*, Acne, *Varnya*, Anti- inflammatory, *Rubia cordifolia*

INTRODUCTION:

Rubia cordifolia Linn. commonly known as Indian Maddar is a perennial, herbaceous prickly climber with long and cylindrical root with a thin red bark, well known for its versatile action. It is distributed in the Himalayas from Kashmir eastwards and Nilgiris and other hilly districts of India.^[1] One of its unique action is anti-acne effect through anti-bacterial, anti-inflammatory, anti-oxidant and anti-androgen action. The roots and stems are well known source of Anthraquinones, the roots have also been reported as antioxidant, anti-inflammatory, anticancer, immunomodulator and hepatoprotective and are extensively used against blood, urinary and skin diseases.^[2,3] In ancient world, *Manjistha* is reputed as an efficient blood purifier and hence is extensively used against blood, skin and urinary diseases.^[4] Externally, *Manjistha* was applied on major burns, mixed with honey on freckles and blemishes. It remained a potent drug for obstinate skin diseases, erysipelas, leucoderma, and oedema also used as febrifuge and against blood disorders in Ayurveda. Traditionally, it is used in many polyherbal formulations for various ailments and cosmetic preparations because of its inflammatory, antiseptic and galacto-purifier activity.^[5] Root is used externally and internally to gain lustre and glow of the skin and aids to remove pimples, freckles and discoloration.^[6] Traditionally the roots are used to treat various systemic problems and pigmentation anomalies of skin and is an excellent aid in the promotion of complexion. Dried and crushed orange peels, powders of sandal, turmeric and *Manjistha* makes an excellent face pack. The finely crushed root powder along with little honey applied to face for

healing skin tissues damaged by injury or infection. The root powder mixed with ghee, for the medicament of acne.^[7] Vanraji tribes of Kumaun Himalaya use the whole plant pulp rubbed with honey as a cure for acne and dark spots on face.^[8]

Acne, as a family of skin disorder is one of the most prevalent dermatologic diseases in the world. It usually affects almost everybody during the life.^[9] The pathogenesis of acne is complex but dependent on four key factors including androgen-mediated stimulation of sebaceous gland activity, follicular hyperkeratinisation, colonization of the bacterium *Propionibacterium acnes* and inflammation.^[10] Mainly three types of acne: comedonal, nodular and papulopustular. Comedonal is non-inflammatory while nodular and papulopustular are the inflammatory types.^[11] There is a variety of medication for acne vulgaris including topical agents, oral antibiotics, oral retinoid and oral hormonal therapies. The use of natural remedies, particularly herbal medicine, dates back thousands of years. Over the last decade, in view of increasing resistance to existing anti-microbial agents, side effects and sometimes high cost of treatment, interest in medicinal herbs has been progressively increased.^[12,13] There are so many herbal drugs for ant-acne effect, which shows

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Received on: 12/03/15, Revised on: 21/03/15, Accepted on: 28/04/15

broadly four mechanism i.e. anti-inflammatory, anti-oxidant, anti-bacterial and anti-androgenic, among them *Manjistha* is one of important herbal remedy showing all four properties.

MATERIALS AND METHODS:

The following are the process and eligibility criteria for the inclusion of data pertaining to this review: Information extracted from various Ayurvedic treatises, text books of Ayurvedic and modern pharmaceuticals, Pharmacopoeias (Ayurvedic Formulary of India, Ayurvedic Pharmacopoeia of India), available dissertations/thesis were also investigated. A search was undertaken in Google scholar, MEDSCAPE, BMC, Science Direct, MEDLINE (www.pubmed.com)/pubmed database, SCOPMED, and other relevant databases, using keywords like manjistha, rubia cordifolia, acne, ayurveda etc.

Literary observation of Mukhadushika (Acne)

In Ayurveda *mukhadushika* is described under the heading of *Ksudrarogas*. These diseases are called *ksudra* (minor) as they are of lesser severity in comparison to *mahavyadhis* or *vyadhis* (major or medium diseases). The silk cotton tree thorn like eruption on the face due to vitiation of *kapha*, *vata* and *rakta* which are found on the face of adolescent are called as *mukhadushika* or *yauvan pidika*.^[14] In *Ayurvedic samhitas* a very short description is available about the disease *Mukhadushika*. All the *samhitas* have pointed out *kapha*, *vata*, and *rakta* as the causative factor of the disease. In *Sharangadhara Samhita vakrasnigdhatta* (oily face) and *pidika* have been mentioned as due to *shukradhatumala* while *Bhavaprakasa* mentioned due to *svabhav*.^[15,16] The *shalmali* thorn like thick or hard painful eruption, impregnated with *meda*, found on the face of adolescent are called as *mukhadushika*.^[17,18]

Description of Manjistha in Ayurvedic texts

As per '*Charaka Samhita*' the powdered dried roots and fruits are taken internally for the treatment of skin diseases and disorders of spleen.^[19] *Manjistha* is also mentioned in ten *varnya*^[20] drugs and as *Visaghna*^[21] *Jvarahara*.^[22] It is also prescribed for treatment of major burns, fractures and dysentery,^[23] to improve complexion and to treat skin diseases and blood born diseases.^[24,25] *Manjistha* paste is used along with honey in *Vyang*.^[26] It has properties of blood purifying agent and pigment stimulant, tonic and are used in skin and blood diseases.^[27] Ayurvedic pharmacopoeia of India therapeutically indicate it for *Yoni roga* (menstrual disorder), *Kustha* (skin disease), *Sarpavisa* (snake bite), *Visarpa* (herpes virus), *Aksi roga* (eye disease), *Arsa* (haemorrhoids), *Bhagna* (Fracture).^[28] Formulations containing manjistha as main ingredient used for treating skin disease are showing in table-1.^[29-38]

Manjistha is found to be one of the ingredients in majority of the formulas available in market like *Manjisthadi kwatha*, *Mahamanjisthadi kwatha*, *Manjisthadyarka*, *Aravindasava*, *Aswagandharistha*, *Usirasava*, *Candanasava*, *Manjisthadi taila*, *Kadiradikutika*.^[39] Therapeutic indications of *Manjistha* mentioned in Ayurvedic Materia Medica are showing in table-2.^[40]

Research Revelation of Manjistha

1. Anti-acne property

Methanol extract of *Rubia cordifolia* inhibit proliferation of *P. acne*.^[41] It is moderately effective against TNF-alpha and show low activity against IL-8. It is regarded as astringent and useful in external inflammations like ulcers and skin diseases.^[42] The anthraquinone rich fraction of *R. cordifolia* in a gel formulation showed the anti-acne activity against *Propionibacterium acne*, *Staphylococcus epidermidis*, *Malassezia furfur* when compared with standard Clindamycin gel.^[43]

2. Anti-inflammatory activity

The aqueous extract of *R. cordifolia* showed anti-inflammatory effect in rats.^[44] The anti-inflammatory action is because of the presence of rubimallin. The aqueous extract showed anti-inflammatory activity in rats with carrageenan paw oedema in a dose dependent manner, which is comparable to that of phenylbutazone.^[45] It also 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.^[46] Notable nitric oxide scavenging activity was exhibited *in vitro* by some extracts of *R. cordifolia*.^[47] A formulation of manjistin and purpurin from cell culture manifested to have an anti-proliferative action during the rapid development of a model oedema.^[48]

3. Anti-microbial activity

Extract of *R. cordifolia* showed a significant inhibitory activity against *P. acnes* standardized culture. The evaluation was carried out by both dilution method as suggested in MIC, there *R. cordifolia* extract was taken 600 µg/ml. The evidence of anti-acne activity of *R. cordifolia* was further supported by Cup-plate method.^[49] *Rubia cordifolia* was effective against *Klebsiella pneumonia*. The root extracts of *R. cordifolia* have been studied for their antimicrobial activity against various pathogenic bacteria. Sitosterol and daucosterol possess antibacterial activity. The root extracts constituents such as anthraquinones and flavonoids suppressed the activity phytopathogens of *Gossypium*.^[50] Aldehyde acetate, dihydromollugin and rubimallin reported to have significant antibacterial

activity against *Klebsiella pneumonia*.^[51] Ethanol extract inhibited β -Lactamase producing uropathogenic *E. coli*.^[52] The chloroform and the methanol extracts reported to have antibacterial activity on gram-positive strains, although gram negative *Pseudomonas aeruginosa* was also inhibited by the methanol extracts in a dose dependent manner. According to Basu *et al.*, the aqueous extract is active against *Bacillus subtilis* and *Staphylococcus aureus* compared with streptomycin and penicillin G.^[53] The ethanolic whole plant extract also showed same result.^[54] Rubiacordone A reported to have considerable antimicrobial activity against Gram-positive bacteria like *Bacillus subtilis*, *Streptococcus faecalis* and *Bacillus cereus*.^[55] The green synthesized silver nanoparticles using *R. cordifolia* plant root extract was highly inhibiting the bacterial pathogens like *Vibrio alginolyticus*, *Pseudomonas aeruginosa*, *Shigella spp*, *Plesiomonas shigelloides* and *Vibrio parahaemolyticus*. They had highest antimicrobial effect against *Pseudomonas aeruginosa* and *Plesiomonas shigelloides*.^[56]

4. Anti-oxidant activity

Alcoholic extract of root of *Rubia cordifolia* and its constituent rubiadin were found antioxidant property.^{[57],[58],[59]} Hydroxyanthraquinones were the predominant antioxidant phenolic constituents in the root of *R. cordifolia*.^[60] The antioxidant properties of *R. cordifolia* extract for protection against lipid peroxidation and reduced glutathione (GSH) content in rat liver homogenate compared with vitamin E and parabenzoquinone (PBQ).^[61]

Table 1: Formulations containing *Manjistha* as main ingredient used for treating skin disease.

Sl. No.	Formulation	Action	References
1	Laghu Manjisthaadi kwatha, Madhya Manjisthaadi kwatha, Brihat Manjisthaadi kwatha	Treatment of skin diseases	Bhav Prakash samhita Kustharogadhikara/ 99-106 ^[29]
2	Maha Manjisthaadi kwatha	Treatment of skin diseases	Vrindamadhava Vataraktadhikar, 23 /86-87 ^[30]
3	Manjisthadhya tailam	Useful in pidika	Chakradatta 55/61-62 ^[31]
	Mukhkrantimkar lepa	Improves Glowness of face	Chakradatta 55/45 ^[32]
	Haridradavy tailam	Improves Glowness of face	Chakradatta 54/53-55 ^[33]

	Kanak tailam	Cure wrinkles	Chakradatta 54/56-57 ^[34]
	Manjisthadi tailam	Improves Glowness of face	Chakradatta 54/58-60 ^[35]
	Kumkumadi tailam	Glowing face	Chakradatta 54/61-66 ^[36]
	Manjistha with honey	increases complexion	Chakradatta 54/42 ^[37]
4	Raktachandanadi lepa	Improves Glowness of face	Sharangdhar Uttar khand 11/9 ^[38]

DISCUSSION:

Acne vulgaris is an extremely common skin disorder that affects virtually all individuals at least once during life. The incidence of acne peaks at teenage, but substantial numbers of men and women between 20-40 years of age are also affected by the disorder. Acne can have important negative psychosocial consequences for the affected individual, including diminished self-esteem, social withdrawal due to embarrassment and depression.^[62] The use of natural remedies, particularly herbal medicine, dates back thousands of years. Over the last decade, in view of increasing resistance to existing anti-microbial agents, side effects and sometimes high cost of treatment, interest in medicinal herbs has been progressively increases.^[63] The anti-acne effects of *Manjistha (Rubia cordifolia)* include four mechanism i.e. anti-bacterial, anti-inflammatory, antioxidant, and anti-androgen activities. The microbiology of the pilosebaceous unit involves three coexisting groups of microorganisms: Gram-positive, coagulase-negative cocci (staphylococci and micrococci); anaerobic diphtheroids (*Propionibacterium acnes* and *Propionibacterium granulosum*); and lipophilic yeasts (*Pityrosporum* species). The microflora of comedones is qualitatively identical to that of the normal sebaceous follicle. The staphylococci and micrococci are aerobes; therefore, their site of growth within the sebaceous unit is superficial, and these organisms are unable to reside in the anaerobic conditions of the infra-fundibulum where the inflammatory reaction occurs in acne.^[64] The chloroform and the methanol extracts reported to have antibacterial activity on gram-positive strains, although gram negative was also inhibited by the methanol extracts in a dose dependent manner.

Reactive oxygen species (ROS) are subsequently generated from the hypercolonization of *P. acnes*^{[65],[66]} in addition to metabolism in living organisms and from UV exposure. Although ROS perform a useful function in the skin barrier against acne microbes^{[67],[68]} excess formation affects skin condition by activating neutrophil infiltration. ROS including singlet oxygen, superoxide

anion, hydroxyl radical, hydrogen peroxide, lipid peroxide and nitric oxide (NO) play an important role in inflammatory acne as well as in tissue injury. ROS

Table 2: Therapeutic indications of *Manjistha* mentioned in Ayurvedic Materia Medica^[40]

S. No.	Therapeutic effect in Sanskrit Term	Therapeutic effect in Medical Term
1	<i>Varnya</i>	Improves complexion
2	<i>Jvarahara</i>	Anti-pyretic
3	<i>Vishaghna</i>	Remove toxins
4	<i>Mutravirecana</i>	Diuretic
5	<i>Raktasodhana</i>	Blood purifier
6	<i>Rasayana</i>	Rejuvenative
7	<i>Vranaropaka</i>	Wound healing
9	<i>Sonitasthapana</i>	Haemostatic
10	<i>Pittasamsamana</i>	Pacifies pitta doshas
11	<i>Asmaribhedana</i>	Lithagogue
12	<i>Krmighna</i>	Antibacterial and anthelmintic
13	<i>Sothahara</i>	Anti-inflammatory
14	<i>Vedanasthapana</i>	Analgesic
15	<i>Caksusya</i>	Improves vision

stimulate the formation of nuclear factor κ B (NF- κ B)^[69] promote TNF formation^[70] and consequently activate T lymphocytes and keratinocytes. The cytokines IL, TNF, IFN, lipopolysaccharide (LPS), transforming growth factor (TGF) and prostaglandin (PG) are then produced and released.^[71-75] In summary, skin inflammation is initiated by CD4+ in T lymphocytes, regulated by TLRs following neutrophil infiltration which generates ROS and protease enzymes leading to follicular wall rupture of sebaceous glands. This consequently changes the composition of sebum, particularly linoleic acid. Hyperkeratinization is initiated as well as a reduction in desquamation. Subsequently, the proinflammatory cytokines, NF- κ B, IL, TNF, IFN, LPS, TGF, PG and GM-CSF are released causing microcomedones. The resulting microcomedones further develop into comedones and inflammatory lesions.^[76]

Rubia cordifolia contains a wide variety of antioxidants like alizarin, hydroxyl anthraquinones^[77] and rubiadin^[78] which have been using in various medicaments. Hydroxy groups on one benzene anthraquinones to show the activity; its ortho-dihydroxy structure could greatly enhance their effect. 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, catalase and superoxide dismutase

activities etc., which were comparable with that of the combination of vitamin E and C.^[79] Rubiadin prevented lipid peroxidation induced by FeSO₄ and butyl hydroperoxide in a dose dependent manner.^[80,81] Hexane and ethyl acetate fraction of root showed maximum free radical scavenging activity due to anthraquinones and their glycosides present in it. *R. cordifolia* extracts can protect peroxidation and reduced glutathione content in rat liver homogenate compared with vitamin E and parabenzoquinone.^[82]

CONCLUSION:

In present scenario, there is a trend of prescribing combination therapy for many diseases including skin disease. This leads to an increase chances of drug interaction and adverse effects, means there is need to evaluate individual herbal therapy. *Manjistha* (*Rubia cordifolia*) has multiple actions to combat this problem and this will become a new approach in the management of acne. The role of *Manjistha* in supporting skin health is evidenced by traditional and reported activities, which show that it act as potent blood purifier, antioxidant, anti-inflammatory, anti-stress, antimicrobial which can play an important role to cure acne and improve skin health.

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Cite this article as: Vandana Meena, Anand K Chaudhary. Manjistha (*Rubia Cordifolia*) - A helping herb in cure of Acne, *J of Ayurveda and Hol Med (JAHM)*.2015;3(2):11-17.

Source of support: Nil, Conflict of interest: None Declared.