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***Commiphora mukul*: An Overview**

Ragavi R, Saritha A Surendran*

Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, Cochin, Kerala

*Corresponding Author E-mail: saritha19489@aims.amrita.edu, sarithaasurendran@gmail.com

ABSTRACT:

Guggul (*Commiphora mukul*), a highly valued botanical medicines has been used for centuries in ayurveda to treat several ailments. Various extracts of this drug produces guggulipid in that guggulsterone is the active constituent responsible for its therapeutic activity. *In vivo*, *in vitro* and clinical studies have been conducted to evaluate the pharmacological, phytochemical, and morphological profile of the herb. Studies revealed that guggul contain flavonoids, terpenes, phytosterols etc. producing number of biological activities like anti-inflammatory, antiobesity, antineoplastic, antidiabetic etc. This review is mainly to update information regarding its anti-inflammatory activity.

KEYWORDS: *Commiphora mukul*, guggulsterone, anti-inflammatory activity, flavonoids.

INTRODUCTION:

Guggul is an oleo –gum resin obtained by making deep incisions at the basal part of stem bark of *Commiphora mukul* belonging to the family Burseraceae¹. Ethyl acetate extraction separates the oleo gum resin in to two parts, gum and resin and further separated in to acidic, basic, and neutral fraction containing appropriate fractions of guggulsterone.

PHARMACOLOGICAL PROFILE:

Anti-inflammatory Effect²:

Mukul extract exhibited anti-inflammatory activity as it reduced paw volume induced by formalin in rats. In the carrageen induced rat paw edema model, the 250mg /kg dose of the formulation (rasnadi guggul) showed significant activity ($p < 0.001$) at the end of 5th and 4th hour respectively. It also had an inhibitory action against the granuloma pouch test. New terpenes Myrrhanol A and Myrrhanone A from guggul-gum resins showed potent anti- inflammatory effect on adjuvant induced air pouch granuloma of mice. The study indicated that effect produced by myrrhanol A was greater than hydrocortisone and 5 0% extract of crude resin.

Madusuda et.al determined the inhibitory effects on production of nitric oxide and induction of inducible nitric oxide synthase. The effective biphasic herbal formulation containing *Commiphora mukul* prepared in the form of emulgel exhibited good anti-inflammatory activity and found to be comparable with marketed tacrolimus ointment. E and Z guggulsterones also decreases the level of inflammatory mediators such as MMP-2, nitric oxide and PGE-2, prevents the expression of inflammatory related protein in eye tissues. Guggulsterones inhibit the activation of nuclear factor-kappa B (NF-kappaB), crucial regulator of inflammatory responses³. Guggulosomes prepared using guggul serve as a carrier were loaded with Ibuprofen, sustained release of the drug was observed. Guggulosomes prepared exerts significant anti inflammatory activity at 5 hrs against carageenan injection suggesting that it may have a sustained and synergistic action. Several studies have demonstrated that guggulsterone produce its effect through suppression of cytokines. The crude ethyl acetate extract of gum guggul suppressed inflammatory mediators such as IL-2, TNF- α , IL- β . No inhibition was observed in the case of anti inflammatory cytokine IL-10. Guggul can be used for the treatment of pro-inflammatory chronic diseases as it suppresses activation of pro-inflammatory transcription factor NF-Kb. The proniosomal gel on hydration with water produced niosomal dispersions of average size 30 μm^4 . The entrapment efficiency of guggulipid in pro- niosomal

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gel conducted across semi-permeable membrane revealed the initial faster release followed by slow sustained release of the drug for 8 h duration of study. Evaluation of proniosomal gel for topical anti-inflammatory activity in carrageenan-induced rat hind paw edema model, demonstrated that the proniosomal gel possess fairly good anti-inflammatory activity but not as good as commercial product. However, future studies with inclusion of transcutaneous permeation enhancers in the proniosomal gel formulation may provide a guggulipid loaded proniosomal gel with anti-inflammatory activity comparable to commercial formulations of NSAIDs. Thus, in conclusion, proniosomal formulation of guggulipids holds an immense potential for development of topical herbal anti-inflammatory formulation comparable to topical NSAIDs. The Jerusalem balsam contains 4 plants one of which is myrrh. An external ear mouse model of inflammation was used to examine the anti-inflammatory activity of the balsam. Sabra white mice were injected intraperitoneally, 1hr prior to arachidonic acid administration on the ears (5mg in 5µl of ethanol) significant inhibitory activity on arachidonic acid induced swelling of external mouse ear was observed, both in thickness and in redness, indicating the balsams anti-inflammatory property⁵. A steroidal compound isolated from petroleum ether extract of *Commiphora mukul* showed dose-dependent anti-inflammatory on rat paw oedema which was much more potent than that of the resin fraction. Steroid fraction had a pronounced effect on primary and secondary inflammation induced by Freund's adjuvant; it was less effective than hydrocortisone acetate in the primary phase but more effective in reducing the severity of secondary lesions. The use of the total lipophilic extract, obtained from the resin of *Commiphora mukul* bark, for the preparation of an epicutaneous medicament having anti-inflammatory activity for the treatment of dermatological affections⁵. *Commiphora mukul* is effective in inflammatory bowel disease due to its immunomodulatory, antioxidant, and antibacterial properties and it decreases NF-Kb, Nitric oxide and COX-2. The anti-inflammatory activities of extracts from the resins of four species of the plant family Burseraceae, *Boswellia dalzielii*, *Boswellia carteri* (gum olibanum), *Commiphora mukul*, and *Commiphora incisa*, were studied. The aqueous extracts of the resins of *B. dalzielii*, *C. incisa*, and *C. mukul* significantly inhibited both the maximal edema response and the total edema response during 6 h of carrageenan-induced rat paw edema.

Arthritis:

There are more than 100 different types of arthritis and related conditions. Guggulsterone³ exhibits significant therapeutic effect on osteo arthritis, rheumatoid arthritis

and gout⁶. Ethanolic extract of guggulsterone derivatives were assayed for cyclooxygenase (COX) enzyme inhibitory activities and also inhibit the PGE synthesis. Yogaraja-guggulu is a widely used ayurvedic formulation. In a retrospective study for the frequency of usage, it ranked first in the hospital practice and 2nd in the private practice. This formulation is used in conditions like arthritis, myalgia and hyperlipidemia. It has been shown to have significant anti-inflammatory activity in formaldehyde induced arthritis and croton oil granuloma⁷. Recent study states, although gold compounds are no longer employed for the treatment of arthritis, the larger number of inexpensive natural products such as curcumin (*Curcuma longa*), Boswellic acid (*Boswellia serrata*), guggulsterone (*Commiphora mukul*), Withanolide (*Withania somnifera*), resveratrol (*Vitis vinifera*) can modulate inflammatory responses, but lack side effect, constitute 'goldmines' for the treatment of arthritis. Triphala guggulu formulation proved highly potent inhibitor of hyaluronidase which contribute significantly to cartilage degradation hence act as chondro protective for the treatment of acute arthritis and rheumatism⁸. Triphala extracts were shown to scavenge nitric oxide free radicals in vitro which may account for their anti-inflammatory activity. As per the ayurvedic pharmacopoeia of india part-1, vol-1 important formulations of guggulu are vatari guggulu, yogaraja guggulu, simhanada guggulu, kaishora guggulu, mahayogaraja guggulu, candrphavati and the therapeutic uses were found to be amavata (rheumatism), kustha (skin diseases), prameha (urinary disorders), diseases due to vata dosha/neurologic disorders⁹ (vata vyadi), granthi (cyst), sopho (oedema), gandamala (cervical lymphadenitis), medoroga (obesity).

Osteoarthritis:

Primarily noted in the weight bearing joints (i.e., knees, hips) degeneration of articular cartilage and changes to the subchondral bone. Guggul act as a chondroprotective with less damage to proteoglycane in the epiphyseal plate in period of 2 weeks in experimentally induced osteoarthritis in rats using mono iodo acetate. It reduces pain and stiffness, relieves symptoms of osteo arthritis after one month treatment crucially improves the WOMAC total score and contained to further improvement on long term uses, after treatment with no side effects were reported during the trial¹⁰. In a clinical trial conducted by Sewanti research team in Kerala India, a 1000 mg daily dosage of Rheumat capsules showed reduction in morning stiffness, swelling and pain in 36 patients with moderately to severe arthritis. There was increase in grip strength and range of movements of the joints without any side effects. In a clinical trial, *C. Mukul* capsules administered to a patient with osteoarthritis (OA) of the knee led to

significant improvement without side effects.¹ In a clinical data suggest that elevated levels of hyaluronidase and collagenase type 2 enzymes contribute significantly to cartilage degradation. A study was focused to investigate the chondro protective properties of traditional formulation of Triphala and C. Mukul (TG) for the treatment of acute arthritis and rheumatism¹¹. Triphala extracts were shown to scavenge nitrous oxide free radicals in vitro which may in part account for their anti-inflammatory activity. TG formulation proved highly potent inhibitor of hyaluronidase. The results also proved that TG formulation is a moderate inhibitor of the gelatinase activity of collagenase type 2.

Rheumatoid arthritis:

Peripheral joints are mostly affected. It is characterized by persistent synovitis with diffuse proliferation, hypersensitivity of immune system and in most of the cases, deposition of auto-antibodies to Ig's known as rheumatoid factor, bone erosion, subsequent changes in joint integrity, articular cartilage damage because of synovial inflammation¹². Vatari guggulu displayed significant inhibition of joint swelling in both formaldehyde and Complete Freund's Adjuvant induced arthritis in rats. It also descended the increased WBC count, Rheumatoid factor, Erythrocyte Sedimentation Rate, Cholesterol, Tri glycerides and LDL. With an enhancement of Haemoglobin levels and RBC counts. These effects were found to be dose dependent. Sudard is a polyherbal formulation containing extracts of 11 medicinal plants. Each tablet contains guggulu (c.m)-100mg, rasna-50mg, gandan prasarani-50mg, nirgundi-50mg, ging er-50mg, eranda mula-50mg, chandra sura-30mg, suranjan-30mg, kapilu-10mg, -50mg¹³. Study was carried out to evaluate the anti-inflammatory, analgesic antiarthritic activities of these formulations using different animal models. The results of the study revealed that sudard possesses significant activities in all the tested animal models indicating inhibition of all phases of inflammation¹⁴. A clinical study was undertaken on the effect of tablet Arthnex Forte on rheumatoid arthritis and osteo arthritis. Arthnex Forte was tried in 80 patients in the dose of 2 tablets, t.i.d for 1 month, 2 tablets b.i.d for 1 month and 1 tablet daily from then onwards, with warm water. Arthnex Forte contain 8 plants which are reputed vata hara drugs namely, pluchea lanceolata, Tinospora cordifolia, ricinus communis, cedus deodara, zingiber officinale, sida cordifolia, vitex negundo and commiphora myrrha gum of the 80 patients, 74 patients (92.5%) improved remarkably and 6 patients (7.5%) showed moderate improvement¹⁵.

Gout¹⁶:

Gum resin removes deposit of waste, toxic material in the body including mucus, mineral deposits in the joints

thereby descending the possible causes of sluggishness, inflamed joints and many other conditions.

Anti-hyper lipidemic effect:

Several animal studies showed the significant effect of E and Z guggulsterone on reducing serum lipid levels, Cholesterol levels and preventing cholesterol-induced arteriosclerosis¹⁷. Mechanism of action was found to inhibit liver cholesterol synthesis by acting on HMG-COA, decreased LDL and increased HDL level, increased lipolytic activity in liver and heart, increased excretion of bile acids and cholesterol in the feces. Bio-Active phytoconstituent, cambranoids controls GI absorption of cholesterol and fat antagonist ligand for bile acids receptor called Farnesoid X receptor, important regulator of cholesterol homeostasis¹⁸. Studies on rat said dietary sucrose found to increase the triacylglycerol concentration and lipogenic enzyme activities in liver. L-arabinose significantly prevented these enhances.

Effect on cardiovascular system:

Guggul has cardio protective effect¹⁹ in ischemic patients. Guggul in combination with inula racemosa showed improvement in ECG and reduces chest pain in trials.

Anti-diabetic effect:

Guggulsterone has hypoglycemic effects hence it can be used to treat type 2 diabetes²⁰. Mechanism of action was found to be decreasing insulin resistance in human beings. *Commiphora mukul* administered to diabetes induced rat and has shown improvement in glucose tolerance, decrease in plasma insulin level and reduction in weight gain.

Anti-helminthic activity:

Phyto constituent studies of *Commiphora mukul* reported, Eugenol, ellagic acid alpha-pinene, masumbinoic acid and masumbinone was responsible for its antimicrobial, antibacterial, antiviral and antifungal activities²¹. Muscanone a flavonoid along with naringenin shows good antifungal activity against the fungi candida albicans at 250 micro gram/ml. mansumbinoic acid mansumbinone studied for antibacterial property and observed to be good against number staphylo coccus strains at the concentration below 0.4mg /ml (+-) linalool and alpha-terpineol act against periodontopathic bacteria. It inhibits both gram positive and gram negative bacteria.

Effect on obesity:

It is a state of excess of adipose tissue mass. Important impact on lifestyle related diseases such as glucose intolerance, diabetes, hypertension and some cancers, coronary heart diseases, dyslipidemia. Causes may be the

possible increased energy intake and decreased energy expenditure or the combination of both. *Commiphora mukul*²² produced synergistic effect with *Lagenaria siceraria* causing reduction in body weight and fasting blood glucose, decreased serum levels of cholesterol, triglyceride LDL, VLDL and increased level of HDL.

Anti-neoplastic activity:

Myrrhanone C, a bicyclic tri-terpenoid isolated from the gum resin, has been chemically transformed to synthesize a series of ten novel pyrimidine hybrids and evaluated for their antineoplastic potential²³ against a 6 cancer cell lines namely A-549(lungs), Hela (cervical), MCF-7(breast), ACHN (renal), COLO-205(colon)and B-16 (mouse melanoma) by employing MTT assay. Synthesized compounds displayed significant anticancer activity against all the cancer cell lines tested.

Effect on thyroid gland:

Studies on albino rats had shown the supporting action of *Commiphora mukul* gum resin in normal thyroid health²⁴. The isolated keto-steroid found to enhance the iodine uptake, activities of thyroid peroxidase, and protease and oxygen consumption by its effect on gland.

CONCLUSION:

Guggul known for its medicinal benefits since long time. Many Ayurvedic texts described both useful and side effects of guggul. Results from several studies shown morphological, phytochemical, pharmacological profile and containments like eugenol, guggulsterone etc. These were found to exhibit many therapeutical activities such as anti-inflammatory, antihyperlipidemic, antiobesity, antidiabetic, etc. Its biological activity was found to outweigh its side effects hence it can be proved to produce a positive outcome in future deficits.

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