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Commiphora mukul: An Updated Pharmacological Review

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Abstract

Since time immemorial, herbs play an important role in everyday life. Especially , the medicinal plants play a essential role in development of human culture. Herbs are regarded as important source of ayurvedic medicines. Guggul (*Commiphora mukul*) is used extensively in ayurveda for centuries. It has many pharmacological properties. Many studies have been conducted on guggulu for its anti-inflammatory, anti-obesity, antihyperlipidemic and antidiabetic activities. Present review will discuss the pharmacological properties of guggulu.

Keywords: Guggul; ayurved; antidabetic; pharmacological properties;anti-inflammatory.

Introduction

Many plants are still unknown for their biological and pharmacological properties. Still, the major source of drug discovery comes from natural herbal medicine. The synthetic medicines are having some lacunae because of their side effects. The plant source of guggulu is (*Commiphora mukul*), family- Burseraceae. This tree has been used in ayurvedic medicines for centuries, Guggul is made from the sap (gum resin) of the Commiphora mukul tree, which is native to India. The plant is commonly known as guggul tree and is found in arid areas of India, Bangladesh, and Pakistan. It is found in Rajasthan, Gujarat, Assam, Madhya Pradesh, and Karnataka. It is a small, bushy tree with thorny branches and produces a yellowish gum resin (guggulu) in small ducts located throughout its bark. The trees are tapped by making an incision on the bark. The resin, which flows out, is allowed to harden before it is collected. The tree is tapped from November to January and the resin is collected through May to June **(Sarup *et al.*, 2015).**

Now a days it is used for arthritis, treating high cholesterol and other skin diseases. The phytochemicals present in guggul are mainly responsible for these pharmacological activities. *Guggulu* contains essential oil, resin, gum, and bitter compounds.

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The major chemical constituents of *gugglu* are Z-guggulsterone, E-guggulsterone, guggullignans I & II, gugglu tetrols; mukulol; allylcembrol; c-27 guggulusterols I, II, III; Z-guggulusterol; E-guggulusterol etc. These constituents are responsible for several pharmacological activities like anti-inflammatory, analgesic, cleaning of wound and healing due to its antibacterial action **(Singh *et al.*, 2015)**.

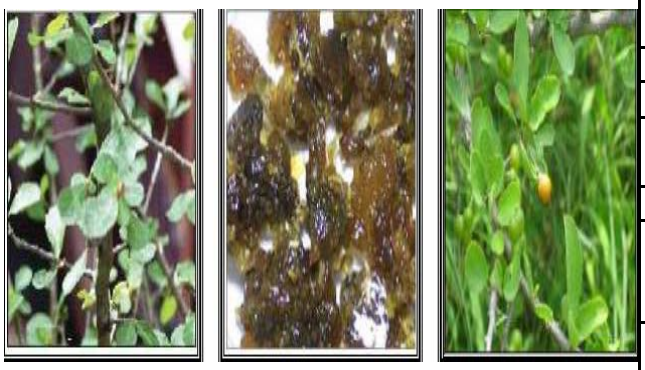

Figure. 1: Leaves, stems, Fruits and gum of Guggul (Bhagyashree *et al.*, 2019, Poonia *et al.*, 2014)

Table 1: A list of few of *Commiphora* species(Poonia *et al.*, 2014; Kirtikar and Basu, 2004; Chopra *et al.*, 2006; Duke *et al.*, 2008; Nadkarni , 2009)

S/No.	Name
1.	*Commiphora mukul* (Hook. ex Stocks) Engl., Syn. *Balsamodendron mukul* (Hook. ex Stocks), *Commiphora wightii* (Arnott) Bhandari
2.	*Commiphora myrrh*, Syn. *Commiphora molmol*
3.	*Commiphora stocksiana* Engl.
4.	*Commiphora berryi* (Arn) Englor Engl., Syn. *Commiphora gileadensis* (L.) C. Chr.
5.	*Commiphora caudata* (Wight & Arn.) Engl.
6.	*Commiphora agallocha* Engl., Syn. *Commiphora roxburghii*
7.	*Commiphora opobalsamum* (L.) Engl., Syn. *Commiphora gileadensis* (L.) C. Chr.
8.	*Commiphora playfairii* (Hook.f.) Engl.
9.	*Commiphora madagascariensis* Jacq.
10.	*Commiphora africana* (A. Rich.) Engl.
11.	*Commiphora angolensis* Engl.
12.	*Commiphora erythraea* (Ehrenb.) Engl., Syn. *Commiphora kataf* (Forssk.) Engl.
13.	*Commiphora humbertii* H. Perrier
14.	*Commiphora boranensis* Vollesen
15.	*Commiphora guidottii* Chiov., Syn. *Commiphora sessiliflora*
16.	*Commiphora harveyi* (Engl.) Engl.
17.	*Commiphora corrugate* J. B. Gillett & Vollesen
18.	*Commiphora habessinica* (O. Berg) Engl.
19.	*Commiphora schimperi* (O. Berg) Engl.
20.	*Commiphora mossambicensis* (Oliv.) Engl.

Bioactive compounds:

The plants contains many phytochemicals of therapeutic importance. These are volatile oil, resins ,gum , a bitter compound and enzyme etc. are found. Solvent extraction using ethyl acetate separates the oleo gum resin into two parts , gum and resin. The gum part is insoluble in ethyl acetate and it is chemically characterized as carbohydrate , and the resinous portion is soluble in ethyl acetate **(Poonia *et al.*, 2014)** Guggul contains mainly a complex mixture of steroids, amino acids, carbohydrates ,aliphatic esters, diterpenoids, and a different inorgranic compounds **(Bhagyashree *et al.*, 2019)**. It also contains E-Guggulsterone , Z-Guggulsterone, Guggulsterol I , Guggulsterol II , Guggulsterol III15, Guggulsterol IV and Guggulsterol-V16,17 . Extracts of guggul oleo gum resin contains the compounds which is known for their hypolipidemic activity. Main reported compounds are E-Guggulsterone , Z-Guggulsterone and other guggulsterone compounds. Other constituents of guggul (oleo gum resin) are Guggul tetrols, Octadecane-1,2,3,4-tetrol, non adecan-1,2,3,4-

tetraols,terpenes and lignans i.e.. Guggullignan I,Guggullignan II , ferulic acid and sesamin21- 23 the essential oil of Commiphora wightii and their percentage present by weight myrcene 3.50%, Alphapinene 4.75%, Methyl chavicol 5.40%, 1,8-cineole (eucalyptol)-3.5% and other unidentified compounds. The following are the percentage of guggulsterones :- Crude gum guggul-2% Ethyl acetate extract-4 to 4.5% Neutral subfraction -4.2 to 4.7% Ketonic subfraction-35 to 40% From this 10% of E-Z Guggulsterones were derived (**Mesrob *et al*., 1998)**.

Traditional Uses of Guggulu

Guggulu is used in Ayurveda since ancient times. The Atharvaveda is the earliest reference that contains its medicinal and therapeutic properties [29]. Description regarding its actions, uses, and indications have been described in numerous Ayurvedic treatises including Charaka Samhita (1000 B.C.), SushrutaSamhita (600 B.C.) and Vagbhata (7th century A.D.)[30]. It has been used to treat obesity, osteoarthritis, rheumatoid arthritis, gout, facial paralysis, sciatica, constipation, haemorrhoids, liver disorders, inflammation, cyst, cervical lymphadenitis, coronary thrombosis, anaemia, diabetes, urinary calculus, increased frequency and turbidity of urine, and skin diseases [31, 32]. It has astringent and antiseptic properties and it also acts as a bitter, stomachic, and carminative when taken internally **(Jaiswal *et al.*,2016)**.

Table 2: Marketed formulation of guggul

Sl. No.	Name	Description
1.	Triphala Guggul	Triphala Guggul is a compound extract (of triphala) to which guggul is added. It is for joint pain, arthritic conditions, muscle aches, rheumatism, and weight loss. (Ayurveda Bazar, India)
2.	Yogaraja Guggul	It is an anti-arthritic herbal supplement useful for joint pain, genito urinary disorders, obesity. (Ayurveda Bazar, India)
3.	Kaishora Guggul	It is used as a blood purifier it is helpful in Athlete's foot and helps in elimination of toxins from the joints. It supports healthy metabolism in the body and maintains healthy white blood cells and liver. (Herbs Forever, USA
4.	Mahayograj Guggul	It is used in the Ayurvedic treatment of joint diseases, skin diseases, piles, sprue, diabetes, gout, fistula, bloating, emaciation, low digestion power, asthma, cold, cough, anorexia, male and female infertility. (http://ayurmedinfo.com/2012/02/17/mahayograj-guggul-benefits)
5.	Navaka Guggul	It is widely used in the Ayurvedic treatment of weight loss, it improves digestion. It is also used to relieve Rheumatoid arthritis. (http://ayurmedinfo.com/2012/05/13/navaka-guggulu-benefits-dosage-how-touse-side-effects-ingredients/)
6.	Singhnad Guggulu	Useful for Lack of Appetite, Abdominal gas, Dysentery, Spasm digestion, gout. (Ayurveda Bazar, India)
7.	Gokshuradi Guggulu	It is an outstanding remedy in urinogenital problems, promoting urine flow, soothing the mucosa, and aiding in the excretion of stones and calculi. It supports kidney and bladder health, detoxification of the urinary tract and also support against enlarged prostate, urinary tract disorders, urinary Stones, inconsistent Urination. (Herbs Forever, USA)
8.	Kanchanara Guggulu	It can be used to address deep-seated kapha imbalances. It supports healthy tissues including muscles, fat and bones as well as the thyroid and the lymphatic system. It is useful in Tumors and Goitre. (Banyan Botanicals, USA)

9.	Trayodashanga Guggul	Useful in Sciatica and nerve related pain, increase the number of red blood cells and used to promote appetite and digestion, increase the number of red blood cells, and aid in removal of undesirable fat in the body. (Ayurveda Bazar, India)
10.	Laxadi Guggul	It is particularly helpful for healing broken bones, fractures, osteophytes removal. It is really an excellent natural formula to enhance calcium deposition on bones. (Ayurveda Bazar, India)
11.	Amrutadi Guggul	Useful in obesity, lowers cholesterol, also beneficial in other conditions like pimples, puss boils, hair follicle boil and buttock boils. (Ayurveda.com)
12.	Saptavinshati Guggulu	It is used for the treatment of any types of worm infestations in the body. And moreover this is beneficial in any age group of patients and is not specifically for a special age group. (Ayurveda Bazar, India)

Pharmacological activities:

Pharmacological effects of c.mukul has been extensively studied in various labs:

Anti-inflammatory Effect:

The anti-inflammatory activity of mukul was studied in carrageen induced rat paw edema model where it reduced paw volume induced by formain. It helps in reducing inflammation at a dose of 250mg /kg bodyweight in carragenan induced paw oedema in rats.(**Raghavi and Surendran, 2018).** Several studies have reported , that guggulsterone exerts its effect through suppression of cytokines .That's why it can be used for proinflammatory chronic diseases as it suppresses the NF kb regulated gene products. **Kimura *et al.*, 2001).**

Antiarthritic effect:

Guggulusterone has marked efficiency in various types of arthritis. There are several types of atrhitis that is known to us. Among those , it has significant therapeutic effect in osteo- arthritis, rheumatoid arthritis and gout. The ethanolic extract of guggulsterone derivatives showed cyclooxygenase (COX) enzyme inhibitory activities and also the PGE synthesis was also inhibited **Patel *et al* .,2015).**

Yogaraja-guggulu ranked first in hospital practice when a retrospective study was conducted for its frequency of usage. It is used for arthritis, myalgia and hyperlipidemia. In formaldehyde induced arthritis and croton oil granuloma , it showed significant anti-inflammatory activity **Sosa *et al* .,1993).**

Anti-hyperlipidemic effect:

Several animal studies report that, guggulu has marked inhibitory effect on liver cholesterol biosynthesis. **(Jain and Gupta, 2006; Orten and Neuhaus ,1982).** There is increased fecal excreation of bile acids(cholic and deoxycholic acids) and cholesterol which lowers the intestinal absorption of fat and cholesterol **(Marks,1990).** It has been reported that, it has significant effect on E and Z guggulsterone which reduces serum lipid levels. It inhibits the enzymes HMG- CoA reductase. It has a preventive role in cholesterol induced arteriosclerosis . **(**Carter ***et al.*,2004).** The antioxidant and protective effect of guggul play an important role in its lipid lowering activity and reduces xanthine oxidase and lipid peroxides and increases superoxide dismutase **(Devlin, 1997).**

Cardioprotective Activity.

Several studies suggest that it had a protective effect on coronary heart diseases **(Jain and Gupta, 2006**) Animal studies report that, in combination with Inula racemosa, it is used to reduce chest pain and dyspnoea of angina pectoris. Studies suggest that guggulsterones acts as effective cardioprotectives. Guggulsterones protected cardiac damage significantly which is measured by reversed blood and heart biochemical parameters when given at a dose of 50 mg/kg (**Chander *et al.*,2003;Sarup *et al.*,2015**).

Anti-diabetic effect:

Studies suggest that, hypoglycemic effects are exerted by guggulsterone which can be used to treat type 2 diabetes **(Raghavi *et al* 2018)**. The alcoholic extract of *C. mukul* when administered at a dose of 200mg/kg for 60 days, there is a reduction in plasma glucose levels in streptozotocin-induced diabetic rats

(Bellamkonda *et al,* .2011).Biochemical parameters such as glycogen content, GTT, glucose homeostatic enzymes (likeglucose-6-phosphatase and hexokinase), insulin release *in vivo*, and the genes which are involved in the metabolism of carbohydrate and lipid clearly demonstrated the hypoglycemic effect. These results indicate that guggulsterone has both hypoglycemic and hypolipidemic effects which can be beneficial in treating type 2 diabetes **(Sharma *et al,* .2009**).

Antimicrobial Activity:

Volatile oil obtained from *C mukul* was found to be highly effective against *Rhyzopertha dominica* which is having a beneficial role as a fumigant. The antibacterial activity of *C. mukul* was best exhibited by its ethanolic extract at 5mg/ml against multidrug-resistant *Klebsiella*] *pneumonia* (**Sharma *et al,* .2010).** Studies indicates, the oleo-gum- resin of guggul has a wide range of activity against both Gram (+) and Gram(-) bacteria because of the various essential oil and 7 sesquiterpenoids compounds present in the oleo-gum-resin. **(Jain *et al,* . 2006).**

Antiatherosclerotic Activity

In atherosclerotic lesions, LDL accumulates and it is the main source of cholesterol accumulation in human foam cells. Several studies suggest that, LDL oxidation is essential for atherogenesis. Guggul contains lipid lowering constituents known as guggulsterones. They effectively inhibited in vitro LDL oxidation. Studies suggest that combination of lipid lowering properties of guggul with antioxidants is beneficial against atherogenesis **(Wang *et al,* .2004)**,

Antioxidant activity

Animal studies suggest that the ethyl acetate extract of Commiphora mukul has good reducing power and anti-lipidperoxidation activity in vitro. Commiphora mukul is extensively used in Indian system of medicines for various activities. Report suggest that it might be due to its protective effect against myocardial necrosis. **(Deng, 2007**; **Nakayama *et al*.,1995; Dubey *et al*.,2009).** It also inhibits the generation of free radical **(Chander *et al*., 2002 ; Singh *et al*.,1994).**

Neuroprotective effect:

It has been reported that , it reverses the streptozotocin induced neuronal damage and also increases glutathione levels in the brains of guggulipid-treated mice significantly, and this effect is attributed to guggulipid for reducing oxidative stress in the brain**(,Sharma,1977; Chaudhary, 2012)**. Above observations , make guggulu a potential target drug for cognition enhancer (**Chaudhary, 2012**).

Hepatoprotective effect: Several studies suggest that leaf and bark of *Commiphora caudate* & *Commiphora mukul* have hepaoprotective activity in CCl4 induced hepatotoxicity in mice (**Chaudhary, 2012)** and replenished the low-level nonprotein sulfhydryl concentration in the liver. The ethanolic extract lowered the serum levels of transaminases, alkaline phosphatase and bilirubin in carbon tetrachloride-induced hepatotoxicity **(Al-howiriny *et al,* .2004)**. Leaves and bark of *Commiphora caudate* & *Commiphora berryi;* gum extract of *Commiphora mukul* have significant hepatoprotective activities etc. **(Balamurugan *et al,* .2010; Shah *et al,* .2012).**

Thyroid-stimulatory effect: Recent studies have shown that guggulsterone stimulates the thyroid gland and restored thyroid activity like an increase in iodine uptake by the thyroid and enhanced the activities of thyroid peroxidase and protease as well as oxygen consumption in hypothyroid rats **(Masten.,2005)**.

Anticancer activity:

Studies suggest that, Myrrhanone C, a bycyclic tri-terpenoid isolated from the gum resin, have potential antineoplastic activities (**Karandikar *et al*.,1960).** Guggulsterone have been found to inhibit inflammation, nuclear receptors, transcription factors and inflammatory cytokines . It has been observed , that it also suppresses the expression of NF-κB-regulated gene products **(Shishodia *et al,.2008).*** Myrrhanone C, a bycyclic tri-terpenoid isolated from the gum resin, has been chemically transformed to synthesize many anticancer compounds that includes a series of ten novel pyrimidine hybrids and synthesized compounds showed significant anticancer activity in 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 (**Karandikar *et al*.,1960).**

Antiobesity effect:

Obesity can be defined as abnormal or excessive fat accumulation that presents a risk to health. It is

among one of the most prevalent problem in the world.

There have been reports, that explain, c. mukul along with Lagenaria siceraria (**Karandikar *et al*.,1960)** causing reduction in body weight. It improves digestion and accelerates metabolism, to pass the food along the git tract quickly. Few reports suggest that , lipophilic extract , when combined with a mixture of phosphate salts , demonstrates noticeable weight loss, fat loss and mood elevating properties (**Brink Williams DesIsles,1998).**

Antifertility Activity:

Research shows when Guggulu administered orally at a dose of (2 and 20 mg/100 g body weight) to female rats, there is reduction in the weight of the uterus, ovaries, and cervix, and there is increased level of glycogen and sialic acid levels in these organs . These studies indicates that guggulu may be useful as an antifertility agent **[Amma *et al.*,1978].**

Skin Diseases:

Gugulipid was found to be effective in the treatment of nodulocystic acne . A Recent study in 21 patients found that gugulipid was very effective in the treatment of nodulocystic acne. Patients with oily faces responded better to the gugulipid treatment [**Thappa and Dogra, 1994].**

Ethnomedical uses:

This tree has been used in indian system of medicine for centuries. Guggulu has been used to treat obesity , osteoarthritis, rheumatoid arthritis , gout, hepatic disorders, inflammation, hyperlipidemic and diabetes , atherosclerosis, sciatica and constipation **(Dev, 1987; Anurekha and Gupta, 2006).** There are many formulations which are available in market.

Inhalation of the fumes burnt guggulu is recommended in hay fever, acute and chronic nasal catarrah , chronic laryingitis , chronic bronchitis. [**Ayurvedic Pharmacopoeia of India, 2007, Dev, 1987; Anurekha and Gupta, 2006).** Guggulu is one of the main drug in many ayurvedic formulations. Gguggulipid is used for heart disease , spondylitis and gout. In India, many guggul formulations are available . Triphala guggulu (for joint pain , rheumatism, weight loss and arthritic conditions), Yograj guggulu (for detoxification ,obesity , rheumatism and gout), Punarvadi guggulu (for detoxification of kidneys, helping heart conditions and inflammations. [**Carter *et al*., Kimura *et al*.2001, Dumond *et al*., 2004].**

Conclusion

Guggul is a very important herb and it is known to mankind since time immemorial for its numerous therapeutic benefits. Various preclinical and clinical studies claim its therapeutic effectiveness. However, further studies are also needed for confirmation of therapeutic claims.

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