OLEOGUM RESIN GUGGULU: A REVIEW OF THE MEDICINAL EVIDENCE FOR ITS THERAPEUTIC PROPERTIES

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ABSTRACT
Guggulu is an oleogum resin that exudes spontaneously as a result of injury from the bark of Commiphora wightii Bhandari (Syn : Commiphora mukul Hook. ex Stocks or Balsamodendron mukul Hook. ex Stock). In Ayurveda, guggulu enters into the preparation of several compound medicines most of which are named with suffix ‘guggulu’. It is a complex mixture of steroids, diterpenoids, aliphatic esters, carbohydrates, amino acids and variety of inorganic compounds. Traditionally it is used to treat arthritis, obesity, and other disorders. Guggul has been shown to lower cholesterol and triglycerides. This review is an effort to compile all the available information reported on its macroscopic features, chemical constituents, pharmacological activities, toxicity and adverse reactions.

Keywords: Guggulu, Commiphora wightii, macroscopic features, chemical constituents, pharmacological activities, toxicity, adverse reactions.

INTRODUCTION
Guggulu is an oleogum resin that exudes spontaneously as a result of injury from the bark of Commiphora wightii Bhandari (Syn : Commiphora mukul Hook. ex Stocks or Balsamodendron mukul Hook. ex Stock). Guggul, more popularly known as Bdellium, is derived from the gummy resinous exudate of a plant closely related to myrrh that is found in arid to semi-arid areas of Northern India, Bangladesh and Pakistan1. The Sanskrit definition of the term “guggul” is “one that protects against diseases.” This attests to the wide respect and therapeutic Ayurvedic applications for this botanical, considered the most important for the removal of “ama,” toxic substances which accumulate as a result of sluggish digestion and circulation associated with a slowing of metabolism2,3. Guggul is a resin, the major ingredient in joint care and immuno care that has been regarded as a remedy in Ayurvedic medicine, known to increase white blood cell count and to possess strong immuno-modulating properties. Guggul is one of the “broad spectrum” health products with a wide range of benefits. Mode of action makes this product very helpful not only in protecting against the common cold but also in various other conditions. It has been shown to have remarkable properties as an adjuvant of other types of therapies. In addition, lower cholesterol and triglycerides, while maintaining the HDL to LDL ratio has long known Guggul. It has been subjected to hundreds of clinical studies4.

HISTORY
Veda
Guggul is described as “Agni Sthanam” and used for ‘Dhupa’. In Atharva Veda, it is mentioned that Yaksm and other diseases will not spread to the areas fumigated by Guggulu. ‘Sayana also introduced it as a well known ‘Dhupana dravya’. It was used for the treatement of diseases of cattle5,7,8,9.

Samhita
It is observed that the internal usage of Guggul increased during Samhita period only. Acharya Charaka included Guggul in “Sangya Shapana Maha Kashaya” (Su. 4/48) and in “Kashaya Skandha” (Vi.8/144)7,10. Maharishi Sushruta has described Guggul in the list of seven most important drugs for the treatment of Sthaulya (Su. 15/32). He has prescribed Guggul with Go-mutra in condition of vitiated Vata with Medodhatu dominated Kapha dosha (Chi. 5/35). The drug is also mentioned as highly effective in the treatment of Vrana as a fumigating agent (Su. 5/10-12), Kushtha (Chi. 9/6), Vidradhi (Chi. 17/32), Pratisararathri (Chi. 22/5), Shotha (Chi. 23/12), Gulma (Ut. 42/63)11,12 etc. Acharya Kashyapa has quoted Guggul in different formulations to treat various diseases. Ghrita, Taila, Avaleha, Dhooopana etc. many formulations of it are also described for the treatment of many ‘Bala Rogas’10. Maharishi Bhela has prescribed that Dhoomrapana of Guggul should be taken after bath and after taking meal. He also described the Vana ropana property of Guggul11. Maharishi Harita has elaborated Guggulu in a separate chapter titled “Guggulu Kalpa” (5th Chap.6-8). Here, he has opined that Guggulu from Marudeshma must be collected in Ushna Ritu and Guggulu from hilly areas must be collected in Sheeta Ritu12. Many formulations of Guggul have been mentioned in Sharangadharo Samhita. However, in Vati kalpadhyaya (Sha. Sam. M. Kha. 7), Guggulu has been suggested specifically for the Vati preparation, because it facilitates the binding capacity. Sarangadharo quoted it among the drugs to be used when they are older (Purana)13. Vagbhata has described that it is a drug of choice for Medoroga and Vatavikaras. He has also quoted its Medohara action along with other drugs like Shilajatu, Rasanjana and Brihat panchmula (A. H. Su. 14/23). He has also used Guggul in Sneha vyapada chikitsa (A. H. Su. 16/34) and prescribed Guggulu in diseases produced due to vitiated Vata, Kapha, Medodhatu and in Amavata...
Bhavaprakasha has reported five types of Guggulu on the Rajavallabha Nighantu, Kaiyadeva Nighantu, Grantha:

Mythological origin of Guggul by Guggul is not included any Nighantu.

E. Hiranya, D. Padma, B. Mahane, A. Mahishaksha

These are:

1. Nadi Sameepottha, Which is found near the Sindhu River.
2. Samudra Sameepottha, This is found near the ocean.

Bhavaprakasha has reported five types of Guggulu on the basis of color. These are:

A. Mahishaksha
B. Mahanela
C. Kumuda
D. Padma
E. Hiranya

Each type has its specific color, as Mahishaksha has the color either of Bhringa or Anjana. Mahanee is extremely blue in color, Kumuda type has the color of Kumuda flower i.e. white, Padma looks dark red like ruby color, while Hiranya looks like gold. However, each type of variety has been prescribed for specifically in human and animals.

The Kanaka type has been told as best among all and prescribed to use as medicine in human beings.

Mahishaksha can be used as medicine in humans, Mahaneel and Mahishaksha have been told to be useful in elephants and Kumuda and Padma has been said to be useful in horse.

Synonyms (Paryaya)

Unfolding the hidden meanings of the paryayas or synonyms of the drugs, mentioned in Ayurvedic texts becomes more relevant as these define various characteristics of the drugs and hence help in identifying them.

Rasapanchaka

Rasa: Tikta, Katu
Guna: Laghu, Ruksha, Tikshna, Visada, Sukshma, Sara, Sugandhi (Purana Guggulu) & Snigdha, Picchila (Navina guggulu)
Virya: Ushna
Vipaka: Katu
Dosakarma: Tridosaha
Dhatu karma: Rasayana, vrisya (old Guggulu), lekhana (new Guggulu)
Rogaghnata:

During the administration of Guggulu the patients should be advised not to take Amla rasa, Tikshna guna predominant drug and diet. Should also not drink Madya and to avoid Ajirna bhojana, Maithuna, Vyayama, Atapa sevana and Krodha.

Side effects

On improper use, it gives bad effect to livers and lungs. Long term and higher dose administration of Guggulu may lead to Timira, Mukhasosa, Klaibya, Krisata, asava, amavata, vata vyadhi, prameha, apaci, gandamala, sotha, pitaka, ashmari and kustha.

Sodhana (Purification process) of Guggulu

Different shodhana processes are described for the various drugs in our classics. For the Shodhana of Guggulu, Gomutra, Godugdha, Triphala kasaya, vasa kasaya/svarasa and Nirgundi svarasa with Haridra curna are used as media reported in Ayurvedic Pharmacopoeia of India, Part II, Volume, II; 2008:277.

Scientific Classification

Kingdom: Plantae - Plants
Subkingdom: Tracheobionta – Vascular plants
Superdivision: Spermatophyta – Seed plants
Division: Magnoliophyta – Flowering plants
Class: Magnoliopsida – Dicotyledons
Subclass: Rosidae
Order: Sapindales
Family: Burseraceae – Frankincense family
Genus: Commiphora Species
Commiphora wightii (Arnott.) Brand

Vernacular Names

Bengali: Guggulu, Guggul, Guggal, ranghan turb, Makal, Guggal; Canarese: Guggulu; Dukshini: Gugul, Guggul, Mukul, Ranghan turb; Gujarati: Gugul, Gugal, Bhesaghgala, Guggul, Gugara, Mukul, Ranghanturb, Bhaisoguggul; Hindi: Gugula, Guggul, Guggul, guggulu, Gugava, gugavik, Kukul, Rranghanturb, Gogil, Dhatu karma:
Dosakarma:
Vipaka:
Dosakarma:
Dhatu karma:
Rogaghnata:

Ushna

As. San. Utt. 49.13

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Bhasagulgul; Kannad: Kanthgal, Kangah, Guggul, Ivadol-guggala, Idbol; Marathi: Gugal, Guggal, Guggul, hansaguggul, kantguggul, Mahaishguggul; Sindi: Gugaru; Tamil: Kukkil, Gulak, Guggal, Gulag, Guikula, Maishksahi, maaschi, Kungiliyam; Telugu: Meshakshi, Guikkal, Guggal, Guggal, Gulakula, maishakhim, Mahishak-Gugilamu, Cheetu maishhashi; Arabic: Mukulyahuda, Mulkarjak, Muskilkerarjak, Mogla, Mogal, Mokhit, Aphalatana, Mulk, Ahlatan, Mogal, Arzagialatam; English: Gum guggulu, Indian bdellium, Indian bdellium, salative, Bdellium, Guggul, Borassus, Flabelliformis; Persian: Baijahundanas, Boejahudan; Pharsi: Boejahudan, Buejahudan, Boe, jhoordan, Vorojahudan; Sinhali: Rata dummula, Guggulu, tatayy, Jauya; Unani: Afaleatana, Mikal12,35

Macrosopic Features

Translucent, vernacular or stalactic, tears of varying sizes, reddish yellow or brown in colour, more often occurring in resinous lumps which turn darker in colour on long storage. Fracture-brillte, exposing a rough or waxy surface having a moist unctuous appearance; balsamic odour, acrid, bitter and aromatic taste.36

Traditional Uses

In Ayurvedic, Indian traditional system of medicine, herbs are usually used in combinations37. Yogaraj guggulu is traditionally for detoxifying, treating obesity, joint pain, arthritic conditions, muscle aches, rheumatism, and gout. Punavadi guggulu is for detoxifying the kidneys, eliminating fluid, helping heart conditions, and inflammations. Triphala guggulu is for joint pain, arthritic conditions, muscle aches, rheumatism, and weight loss38. Gum guggul is used as incense, to make lacquers, varnishes, and ointments, as a fixative in perfumes, and in medicine39. Gum guggul is used to treat dysmenorrhea, dyspepsia, endometritis, hypercholesteremia, hypertension, impotence40, bronchitis, caries, catarrh, gingivitis, hay fever, hysteria, inflammation, laryngitis, lochia, mania, pharyngitis, phthisis, pyorrhea, rheumatism, sores, sore throat, stimulant, tonsillitis, tumors, wounds41, bone fractures42, gout, scrofula, sciatica, facial paralysis, diplegia, leprosy, leucodermia, pectoral disorders, otorrhea, epilepsy, fever, strangury, hemorrhoids, dysmenorrheal, amenorrhea, ulcers, anemia, coronary, thrombosis, stomatopathy, pharyngopathy, spermatorrhea, urinary calculus, diabetes, trichosis, to enhance phagocytosis, to increase leukocytes43, to induce abortion44, and as a tonic for the uterus45. Traditional uses of C. mukul include as an anti-inflammatory, antispasmodic46, carminative, emmenagogue, hypoglycemic47, alterative, antiseptic, astringent, sedative, stomachic, carminative, diaphoretic, diuretic, expectorant48, antispasmodic, antisuppurative, aperient, expectorant, a thyroid stimulant49, anthelmintic, deparutive, vulnerary, antisepctic, demulcent, aphrodisiac, stimulant, liver tonic, detergent, anti-spasmodic, hematiniic, diuretic, and lithonotritic50.

Modern Uses

Modern therapeutic uses of guggul include nervous diseases, hemiplegia, leprosy, marasmus, muscle spasms, neuralgia, ophthalmia, pyelitis, pyorrhea, scrofula, skin diseases, spongy gums, ulcerative pharyngitis, hypertension, ischaemia, hypertension, hemorrhoids, and urinary tract disorders45,46. More recently, C. mukul was found to be a relatively safe and effective supplement for osteoarthritis of the knee51. Research studies showed that guggul is effective against aspects of cardiovascular disease. Guggul reduced the stickiness of platelets52. The crude gum guggul and each of the fractions containing the E- and Z-guggulsterones have hypocholesteremic activity: the ethyl acetate extract, the neutral compounds from the extract, the ketonic compounds in the neutral fractions, and that containing the purified E- and Z-guggulsterones49.

Chemical Constituents

A detailed chemical study of guggulu revealed that it is a complex mixture of steroids, diterpenoids, aliphatic esters, carbohydrates, amino acids and variety of inorganic compounds. Besides known sesamin and cholesterol, Sukh Dev et al have isolated Z-guggulsterone, E-guggulsterone, 16 β-hydroxyprogesterone and three new sterols viz. guggulsterols I, II & III50. Later workers have isolated two more new sterols guggulsterol-IV and guggulsterol-V51,52. Besides a new alcohol viz. mukulol53, four steroids too have been isolated from guggulu54. Extracts of the oleoresin include compounds known for their hypolipidemic properties, on which this report focuses the Z- and E-isomers of guggulsterone and its related guggulsterols44. Other types of chemicals that were named as gum guggul constituents were a tetro, nonadecano-1,2,3,4-tetrol, lignans and terpenes. The lignans included guggullignan I; guggullignan II; octadecane-1,2,3,4-tetraol-1-y1 3-(4-hydroxy-3-methoxyphenyl) propanoate, furelic acid [1135-24-6], and sesamin [607-80-7]56,57. The terpenes included mukulol [41943-03-7]; allylcembrol I [39012-00-5]; cembrene A [31570-39-5] (Dev, 1983); cembrene [20016-72-2]; α-camphorene I [532-87-6] (Rücker, 1972); myrcene [123-35-3], and dimyrcene45. Bajaj, A.G et al. 1982 lists the components of the essential oil of C. mukul and their percentages by weight52: α-pinene, 4.75%; myrcene, 3.50%; eugenol, 14.70%; cadinene, 5.50%; geraniol, 6.20%; methyl heptanoate, 17.50%; (+)-α-phellandrene, 5.50%; (+)-limonene, 6.50%; (+)-bornyl acetate, 7.30%; (+)-linalool, 8.70%; methyl chavicol, 5.40%; α-pinene, 4%; 1,8-cineole (eucalyptol), 3.5%; and unidentified compounds. The crude gum guggul was found to contain 2% guggulsterones. Its ethyl acetate extract contains 4% to 4.5% guggulsterones. The neutral subfraction contains 4.2% to 4.7% guggulsterones. The ketonic subfraction of the neutral subfraction contains 35% to 40% guggulsterones, from which the 10% E- and Z-guggulsterones are derived55. E- and Z-Guggulsterones in gum guggul were profiled using ultraviolet (UV) monitoring55. Guggulsterols in gum guggul were identified by 1HNM R, and spectrometers and spectrophotometers were used to gather spectral and analytical data53.

Pharmacology

Lipid-lowering effects

Typical guggulipid preparations contain 2.5-5% of the plant sterols guggulsterones E and Z. These two components have been reported to exert effects on lipids55,56.
Hypocholesterolemic Activity
Crude guggulu was found to possess highly encouraging hypolipaemic activity in rabbits. Crude guggulu and its alcohol soluble fractions caused significant fall in serum cholesterol and serum turbidity with a concomitant increase in the coagulation time and prothrombin time. Fraction A and a steroidal fraction present in guggulu also showed significant hypolipaemic activity in cholesterol fed chicks. Alcoholic extract and a pure steroid isolated from it reduced serum cholesterol level in normal and triton induced hyperlipidemic rats and cholesterol fed hyperlipidemic rabbits. Clinical studies on patients of hypercholesterolemia associated with obesity, ischaemic heart diseases, hypertension, diabetes, etc. showed a fall in total serum cholesterol and serum lipid phosphorous when treated with guggulu. The body weight of the obese ones declined significantly. Other clinical studies showed that the lowering of serum triglycerides was found most encouraging in case of gum guggul in comparison to all the drugs known so far. In a long term clinical study it was found that fraction A of guggulu in cases of hyperlipoproteinemia reduced triglycerides by 36.5% whereas the drug clofibrate brought a reduction of 33.3%. Serum cholesterol was reduced by 26.2% with fraction A treatment when 31.5% was the result with clofibrate. Fraction A enhanced the rate of excretion of cholesterol and also reduced its synthesis.

Anti-fertility activity
Guggulu caused a reduction in the weight of rat uterus, ovaries and cervix with a concomitant increase in their glycogen and sialic acid levels thereby showing that it might be useful as an antifertility agent.

Antioxidant effects
Guggul extracts have been reported to possess antioxidant properties possibly mediating protection against myocardial necrosis.

Platelet effects
Guggulipid has been found to inhibit platelet aggregation and increase .brinolysis.

Anti-inflammatory
Pharmacological studies have shown that the oleoresin is a highly potent antiinflammatory agent as compared to hydrocortisone and butazolidin against Brownlee’s formaldehyde induced arthritis in albino rats. The acidic fraction of the oleo resin was active one whereas the non – acidic and the solid fractions were inactive. The activity of the acidic portion was present even in the adrenalectomised animals. The results of several studies suggest possible anti-inflammatory and antiarthritic activities of guggul.

Thyroid effects
Data from animal models suggest that the guggul constituent guggulsterone Z may stimulate thyroid function. However, results from a recent randomized controlled trial in 103 patients’ reports no difference in thyroid stimulating hormone (TSH) with the use of guggul.

Anti-arthritic Activity
Suddha guggulu administered to 30 patients of rheumatoid arthritis showed complete remission (66.66%) major to minor (23.33% - 10%) improvement besides anti-inflammatory and analgesic properties.

In the treatment of heart diseases
The fraction A and the steroidal component derived from it were studied in experimental myocardial infarction in rats produced by isoprenaline. The results show that guggulu is one of a few drugs which is effective in both hyperlipidemia and myocardial necrosis.

In infective hepatitis
The antagonizing property of guggulu on the liver hypertrophy has been established.

Adverse Effects

Gastrointestinal: In clinical studies and historically, guggul and guggulipid have been associated with diarrhea, loose stools, nausea, vomiting, eructation (belching), and hiccough. Frequency has varied between 10—30%; these symptoms have been observed both with guggul and with guggulipid. Most symptoms have been well controlled with supportive care or treatments such as antacids, although discontinuation is occasionally necessary.

Neurologic/CNS: Headache was reported in 22 of 31 patients (71%) in one study. Restlessness and apprehension were noted in one of 44 patients in a different study.

Endocrine: Stimulation of thyroid function has been noted in animal studies, although a recent human trial reports no effects of guggulipid in thyroid stimulating hormone (TSH) levels after 8 weeks of therapy.

Hematologic: Guggulipid administration has been associated with inhibition of platelet aggregation and increased brinolysis.

Genitourinary: Weight reduction and chemical changes in reproductive organs have been observed in female rats.

Dermatologic: Hyposensitivity skin reactions were noted in a clinical trial, occurring in 5 of 34 patients (15%) receiving 50 mg of guggulsterones three times daily, and in 1 of 33 (3%) of patients receiving 25 mg of guggulsterones three times daily. In most cases, reactions occurred within 48 hours of starting therapy, and resolved spontaneously within 1 week of therapy discontinuation, although one patient required oral steroids.

Renal: A case of rhabdomyolysis has been reported. Rhabdomyolysis may lead to renal failure.

Toxicological Data
Traditional Ayurvedic treatments for obesity were administered in a clinical trial to determine their effectiveness for weight loss. All of the formulations contained gum guggul among its herbal ingredients. Each group except controls were administered triphala guggul (138 mg gum guggul). Group I was administered gokshuradi guggul (35 mg gum guggul); Group II, sinhanad guggul (15 mg gum guggul); Group IV, chandraprabha vati (57.6 gum guggul); and Group III, placebo tablets as a control. The 70 participants experienced a few minor side effects such as nausea and mild diarrhea (eight in treatment groups, two in control group). In a phase I tolerability study of Yogaraj-guggulu (containing 39.87% guggul) with male volunteers (22-28 years old), general tolerability was “good” at doses up to 9 g/day. Three volunteers reported diarrhea; whether intestinal parasites were irritated by Yogaraj-guggulu were not determined. One subject developed rash and pruritus, which was probably not drug-
related since a rechallenge dose failed to reproduce the symptoms and the patient had a past history of urticaria. Another subject had stomatitis; he, however, also had a history of recurrent stomatitis. In other studies reporting no significant side effects, adult obese patients were administered medohar, a guggul formulation, for 30 days for weight loss, and patients with primary hyperlipidemia received gugulipid three times a day for six weeks. A standardized gugulipid extract had a few side effects, including minor gastrointestinal disturbances, such as dyspepsia, fullness. Caution is recommended when using guggul in people with liver disease, inflammatory bowel disease, or diarrhea. It should not be used during pregnancy and it can cause diarrhea, hiccups, apprehension, and restlessness. Gum guggul possibly interacts with several drugs. More side effects are associated with the crude gum guggul. These include skin rashes, irregular menstruation, diarrhea, headache, mild nausea, eructation, hiccough, and with very high doses, liver toxicity.

CONCLUSION

Although the results from this review are quite promising for the use of guggulu as a multi-purpose medicinal agent, several limitations currently exist in the current literature. While recent researchers have focused attention on the anti-inflammatory activity and hypolipaemic activity of guggulu comparatively less work has been done relating to other properties of the drug enumerated in Ayurveda. While guggulu has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use. It is also important to recognize that guggulu may be effective not only in isolation, but may actually have a potentiating effect when given in combination with other herbs or drugs.

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