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Review Article

Commiphora wightii (Arn.) Bhandari. Review of Its Botany, Medicinal Uses, Pharmacological Activities and Phytochemistry

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ABSTRACT

The oldest remedies identified to mankind are herbal medicines. India is recognized worldwide for its Ayurvedic treatment. As only little studies are done on this plant, the purpose of current review is to make accessible up-to-date information on, botany, morphology, ecological biodiversity, medicinal uses, phytochemistry and pharmacological activities on diverse parts of *Commiphora wightii* (Arn.) Bhandari (*C. wightii*). This review was assembled using scientific literature from electronic search engine such as Springerlink, BioMed Central, PubMed, Scopus, ScienceDirect, Scielo, Medline and Science domain. Supplementary literatures were obtained from books, book chapters, dissertations, websites and other scientific publications. *C. wightii* (Syn. *Commiphora mukul* Hook. ex. Stocks) or *Guggulu* tree. *C. wightii* is a shrub or small tree belonging to *Burseraceae* family. *C. wightii* contains volatile oil, gum resin, guggulipids, guggulsterones, guggulsterols, mukolol and other steroids. *Guggulu* is very much used in *Ayurvedic* system of medicine as astringent, anti-septic, expectorant, aphrodisiac, carminative, anti-spasmodic, emmenagogue. In *Ayurveda*, it is the best among herbs that are used for *Medoroga* and *Vata* disorders. It is widely used for obesity and it is also known as fat burning agent all over the world. It helps to lower cholesterol and triglycerides level. It is very effective in rheumatoid arthritis, gout and sciatica. It is also one of the most important *Rasayana* of *Ayurveda*. In addition it treats sluggish liver, stimulates libido, nervous diseases, bronchial congestion, cardiac and circulatory problems, weak digestion, wounds, abscess, foetid ear, fractures, gynaecological problems and various skin diseases. *C. wightii* is a very important and trustworthy herb in *Ayurvedic* medicine. This alternative system of medicine is gaining increasing fame universal. There is a required to isolate active constituents, their biological test, molecular mechanisms, experimental defense and legalization of therapeutic uses of *C. wightii*. The collected information will be obliging to locate up study protocol for current drugs and *Ayurvedic* formulation extension in remedial and luxury a variety of ailments. Clinical trials for the reported preclinical studies should be executed immediately to further validate the claims on humans.

Keywords: *Commiphora wightii*, Phytochemistry, Pharmacological activity, Ayurveda, Medicinal uses**Article Info:** Received 11 June 2019; Review Completed 21 July 2019; Accepted 23 July 2019; Available online 15 August 2019**Cite this article as:**

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Introduction

Plants are significant to human being for his life. Plants are incessantly an ordinary source of medicine in the usage of traditional preparations. All plants phyla create official and illegal product of therapeutic significance. The antiquity of herbal medicine is as very old as human society. The treasure of India is stored in the huge natural flora, which has been advantage to mankind. India is almost herbarium of the planet^{1,2}. Although the biologically active phytoconstituents of certain herbal drugs are unidentified, they are prescribed normally owing to their effectiveness, least side effects in clinical information and moderately very low costs³. Ornamental plants are grown for decorative purposes in gardens and scenery design projects, as house plants, for cut flowers and specimen exhibit. Ornamentals and flowers harvests are not only grown for the exhibit of

aesthetic features, but also have nutritive and therapeutic properties. There has been rehabilitated interest in utilizing garden environments having therapeutic value, as therapeutic entities to improve the process of healing that occurs in healthcare environments. The use of plant complexes for pharmaceutical purpose has steadily increased in India, about 85% of individuals from urbanized countries use customary medicine, which involves compounds resulting from medicinal plants⁴. Flowering trees are now being browbeaten in the customary medicine and their curative potentials are well recognized. *C. wightii* with common names Indian bdellium tree, *Gugal*, *Guggul*, *Guggulu*, is a flowering plant belonging to family *Burseraceae*. The *Guggul* plant may be found from northern Africa to central Asia, but is most common in Northern India. It prefers arid and semi-arid climates and is tolerant of poor

soil. It is a shrub or small tree, reaching a maximum height of 3m, with thin papery bark. *C. wightii* produces a resinous sap known as gum *Guggul*. The extract of this gum, called guggulipid or gugglipid, has been used in *Ayurvedic* medicine abundantly. *C. wightii* contains essential oil, resin, gum, and bitter compounds. The major chemical constituents of *C. wightii* are Z- guggulsterone, E-guggulsterone, guggullignans I & II, gugglu tetrols; mukulol; allylcembrol; c-27 guggulsterols I, II, III; Z-guggulsterol; E-guggulsterol etc. These constituents are responsible for several pharmacological activities like anti-inflammatory, analgesic, cleaning of wound and healing due to its antibacterial action. *C. wightii* is a natural health product used primarily to reduce elevated blood cholesterol levels. It has been used for many years as a hypocholesterolaemic agent in India. *C. wightii* is one of the best rewarding herbs for *Vata* diseases. Various preparations of *C. wightii* used in sciatica, hemiplegia, gout, rheumatic diseases, facial paralysis etc. *C. wightii* is beneficial in cleansing and healing of wounds and to reduce oedema due to its anti-inflammatory and anti-septic properties. In digestive ailments also like anorexia, flatulence, worm infestations, piles etc, it works well^{5,6}. *C. wightii* is known as *Marudeshya* because it is a plant which grows in arid zone. It exudes a gum resin coming out of cavities (*Kaushika*, *Ulukhala*, *Kumbholukhala*) in form of particles (*Kananiryasa*) reddish black in colour (*Mahishaksa*, *Kalaniryasa*). It removes a number of ailments (*Guggulu*) particularly obesity (*Palankasa*) and is antiseptic (*Rakshoha*) as fumigation. It is also used as incense in god's worship (*Devadhupa*)⁷. *C. wightii* is known as *Ulukhala* because it exudes a gum-resin which comes out from cavities. The resin is the best medicine, so it is known as *Pura*. It is also known as *Durg* because it is a plant which grows in arid zone⁸. The classification of *C. wightii* consist of domain: Eukaryota, kingdom: Plantae, sub-kingdom: Tracheobionta, division: Magnoliophyta, class: Spermatopsida, sub-class: Magnoliidae, order: Sapindales, genus: Commiphora, family: Burseraceae, species: wightii⁹. The vernacular names of the plant is Mukul, Guggul, Gugal, Gogil, (Hindi), Gukkal, Gukkulu, Maishakshi (Tamil), Guggala, Gulag, Mukul (Marathi), Gugal, Gugali, Gugar, Guggul, Mukul, (Gujarat), Gugul, Mahisaksh, Maisakshi (Telgu) Aflatan, Moql, Moqlearzaqi, Muklearabi (Arabic), Bhavabhishta, Bhutahara, ect (Sanskrit)¹⁰. Therefore, in this study, the ethnopharmacological review of *C. wightii* was carried out aimed at providing a detailed précis of the botany, ethnomedicinal uses, pharmacological activities and chemical composition of the species.

Research methodology

To recognize pertinent information on the botany, medicinal uses, phytochemistry and biological activities of *C. wightii*, a review was compiled based on scientific literature from various sources including Google Scholar, Web of Science, SciFinder, Scopus, Science Direct, PubMed, Scielo, Springerlink, Google Patents, Espacenet, BioMed Central (BMC) and Medline. The keywords used for recognition of relevant data included dissimilar scientific name and synonyms, common English names, and the terms: biological activities, medicinal uses, ethnobotany, ethnopharmacology, medicinal, pharmacology, phytochemistry and therapeutic value, *C. wightii*, *Commiphora mukul* Hook. ex. Stocks. Further literatures were obtained from books, book chapters, theses, websites and conference proceedings.

Occurrence and distribution

The *C. wightii* plant present in arid and semi arid climate and it's tolerant of poor soil. The *C. wightii* plant mainly distributed in arid area of northern Africa to central Asia, but

it most common in Rocky track of western India and Eastern Himalayas. In central Asia the *C. wightii* plant is distributed in arid areas of India, Bangladesh and Pakistan. In India it plant found in arid, Rocky tracts of Rajasthan, Gujarat, Maharashtra, Madhya Pradesh and Karnataka. According to Ayurveda, there are five type of Guggul namely; Krishnan (black), Peet Varn (Yellow), Neel (blue), Kapish (light brown) and Rakt (blood red). It is propagated by seeds and root cuttings¹¹⁻¹³.

Morphology

C. wightii is a woody shrub or a small tree which grows to the height of 2-3 metres, much branched with characteristics silvery and paper like bark-peelings. Branches are knotty and crooked, divaricate, usually ending in a sharp spine. **Leaves:** The leaves are rhomboid-ovate, 1-3 foliate, serrate-toothed in the upper part, smooth and shining, the lateral leaflets when present less than half the size of the terminal ones. **Flowers:** Flowers in the fascicles of 2-3; pedicels very short. Calyx campanulate, glandular, hairy; lobes are 4-5 in number, triangular, as long as the tube. Petals are brownish red, broadly linear, nearly thrice the length of the calyx, reflexed at the apex. Stamens are 8-10 in number, alternatively long and short, half the length of the petals. Disk, 8-10 lobed, the alternate sinuses deeper and in these are inserted the shorter stamens. Ovary oblong-ovoid, attenuated into the style. **Fruits:** The fruits are small, red in colour when ripe, ovoid drupes. Each plant produces about 0.5 to 1kg of oleo-gum resin which is collected from January to March. **Gum Resin:** Pale yellow to brown aromatic gum resin obtained from the bark of the plant. Agglomerated tears of resin are somewhat transparent, with waxy surface and brittle in nature. Gum-resin is thick, scented, burnt on fire, liquifies in sun heat. When dissolved in water, it turns milky white¹⁴⁻¹⁶.

Macroscopic and microscopic features

Macroscopic *C. wightii* occurs in vermicular pieces of pale yellow or brown colored mass with aromatic odour and bitter astringent taste; when fresh it is viscid and golden colored. Makes milky emulsion in hot water and readily burns. Tears of varying sizes, reddish yellow or brown in color, more often occurring in resinous lumps which turn darker in color on long storage. Fracture-brittle, exposing a rough or waxy surface having a moist unctuous appearance; balsamic odour, acrid, bitter and aromatic taste.

Microscopic Foreign matter Not more than 4 %; Total Ash Not more than 5 %; Acid-insoluble ash Not more than 1%; Alcohol-soluble extractive Not less than 27 %; Water-soluble extractive Not less than 53%; Volatile oil Not less than 1%, v/w and between 1.0 and 1.5 percent of guggulsterones (Z and E)^{17,18}.

Phytochemical constituents

C. wightii contains diterpenoids, triterpenoids, steroids, longchain aliphatic tetrols, aliphatic esters, ferulates, lignans, carbohydrates, and a variety of inorganic ions besides minor amounts of sesamin and other unidentified constituents.

1. Volatile oil and its terpenoidal constituents

Monoterpenoids The gum resin of *C. wightii* yields about 0.4% of essential oil by steam distillation and its chief components are myrcene, dimyrcene, and polymyrcene¹⁹. Other components of the oil are eugenol, d-limonene, α -pinene, (\pm) linalool, cineole, α -terpineol, d- α -phellandrene, methylheptanone, bornyl acetate, (\pm) geraniol, and some other unidentified compounds²⁰.

Sesquiterpenoids The gum resin of *C. wightii* has been reported to contain bicyclic sesquiterpene, cadinene²⁰.

Diterpenoids Diterpenoid constituents from guggulu include α -camphorene, cembrene-A, cembrene²¹ and other cembrenoids. Cembrene-A is one of the most elementary tetraenes derived from geranylgeranyl pyrophosphate by C-1 to C-14 cyclization. Mukulol (allylcembrol) is a new cembrene alcohol which was isolated from the aerial parts and also from the resin of guggulu^{22,23}. The allylcembrol structure was established by spectral analysis and mild dehydration which yielded cembrene. Other isolated cembrene type diterpenes include isocembrol and 4-epiisocembrol. (1*E*, 4*E*, 8*E*)-4,8,14-Trimethyl-11-(1-methylethyl)-4-methoxycyclotetradeca-1,4,8-triene, (2*E*, 12*E*)-2,7,13-trimethyl-9-(1-methylethyl)-15-oxabicyclo [12.1.0] pentadeca-2,12-diene-7-ol and (4*Z*, 6*E*)-4,7,12,15,15-pentamethylbicyclo [9.3.1] pentadeca-4,6-diene-12-ol were novel compounds obtained by bioassay-guided isolation from hexane-soluble portion of the methanol extract of guggulu²⁴.

Triterpenoids Polypodane-type triperpenes, myrrhanol A, B, and C, myrrhanone A, myrrhanone B, myrrhanone A acetate, commipherol, commipherin, and octanordammarane triperpenoid, epimansumbinol have been isolated from the gum resin. The isolation of two more triterpenoid components has been reported, which are identified as mansumbinone and mansumbinoic acid²⁵⁻²⁸. The absolute stereo structure of myrrhanol A was determined to be (3*S*, 5*S*, 8*R*, 9*R*, 10*S*)-3, 8,30-trihydroxypolypoda-13*E*, 17*E*, 21*E*-triene. Myrrhanol B is 30-oic acid of myrrhanol A with altered stereostructure at C-5 (5*R* in contrast to 5*S* in myrrhanol A). Myrrhanone A and B are 3-keto analogue of myrrhanol A and B, respectively²⁶. A myrrhanone derivative, (13*E*, 17*E*, 21*E*)-8-hydroxypolypoda-13, 17, 21-trien-3-one and a myrrhanol derivative, (13*E*, 17*E*, 21*E*)-polypoda-13, 17, 21-trien-3, 18-diol have also been isolated²⁴.

2. Steroids Isolation of several steroidal constituents has been reported from the gum resin. The major constituents include E-guggulsterone, Z-guggulsterone, guggulsterol-1, guggulsterol-II, guggulsterol-III, guggulsterol-IV, guggulsterol-V and guggulsterol-VI. Other isolated steroids are 20 α -hydroxy-4-pregnen-3-one, 20 β -hydroxy-4-pregnen-3-one, and 16 β -hydroxy-4, 17 (20)-Z-pregnadien-3-ones which has been designated as Z-guggulsterol²⁹⁻³². Progesterone and related steroids, 4-pregnene-3, 16-dione, (20*R*)-20-acetoxy-4-pregnene-3,16-dione, 16 β -acetyloxy-4,17(20)-trans-diene-3-one, 3 α -acetyloxy-5 α -pregnan-16-one and 20*R*,22*R*-dihydroxycholest-4-en-3-one have also been isolated²⁷. Cholesterol has also been reported. Three new and recently isolated steroids are guggulsterone-M, dihydro guggulsterone-M and guggulsterol-Y²⁸. The steroidal constituents have been related with hypolipidemic and anti-inflammatory activities of the drug²⁴.

3. Flavonoids An ethanolic extract of trunk of *C. wightii* was separated on column packed with silica gel to give a new antifungal flavone named muscanone along with known naringenin. Muscanone was found to be active against *C. albicans* in microbial sensitive assay. The major flavonoid components of the flowers of *C. wightii* were identified as quercetin, quercetin-3-O- α -L-arabinose, quercetin-3-O- β -D-glucuronide, quercetin-3-O- β -D-galactoside, quercetin-3-O- α -L-rhamnoside and pelargonidin-3, 5, di-O-glucoside^{32,33}.

4. Guggultetrols A crystalline material was isolated from the saponified gum resin which was characterized as a mixture of octadecan-1,2,3,4-tetrol, nonadecan-1,2,3,4-tetrol and eicosan-1,2,3,4-tetrol with minor amount of other

components, possibly lower (C-16 and C-17) and higher (C-21 and C-22) homologous tetrols. These compounds constitute a new class of naturally occurring lipids, guggultetrols. They are long-chain linear aliphatic tetrols with hydroxyl functions at C-1, C-2, C-3, and C-4 positions. Through derivatization and preparative GLC, guggultetrol-18 and guggultetrol-20 were obtained in pure form. A mixture of two ferulates ($n = 16, 17$) with an unusual skeleton was found to be responsible for the cytotoxic action of the drug. They have been isolated from cytotoxic fraction of ethyl acetate extract of guggulu. It was identified as a mixture of esters based on homologous longchain tetrols and acid^{34,35}.

5. Lignans Two lignans, sesamin²⁹ and diayangamin³⁶ have been reported from guggulu. Also, 5,5-tetrahydro-1*H*,3*H*-furo[3,4-*c*]furan-1,4-diylbis[7- (methoxy)-1,3-benzodioxole] has been reported from methanolic extract of guggulu²⁴.

6. Sugars Complete hydrolysis of gum part of resin yielded L-arabinose, D-galactose, L-fructose (traces) and 4-O-methyl-D-glucuronic acid. Graded hydrolysis of the gum furnished an aldobiouronic acid [6-O-(4-O-methyl- β -D-glucopyranosyluronic acid)-D-galactose]. Hydrolysis of methylated gum furnished 2,3,4,6-tetra-O-methyl-Dgalactose, 2,3-di-O-methyl-L-arabinose, 2,3,4-tri-O-methyl-D-galactose, 2,4-di-O-methyl-D-galactose, and 2,3,4-tri-O-methyl-D-glucuronic acid in the ratio of 1 : 1 : 1 : 2 : 1. The provisional structure showed the gum to be a highly branched polysaccharide containing 1-6, 1-3, and 1-5 type of linkage^{37,38}.

7. Amino Acids *C. wightii* was extracted with alcohol and the extract after removal of the solvent was partitioned between water and ether. The aqueous fraction was chromatographed and it showed the presence of various amino acids. The amino acids detected were cystine, histidine, lysine, arginine, aspartic acid, serine, glutamic acid, threonine, alanine, proline, tyrosine, tryptophan, valine, leucine, and isoleucine³⁹.

Cultivation

C. wightii is sought for its gummy resin, which is harvested from the plant's bark through the process of tapping. In India, *C. wightii* is cultivated commercially. It can successively be propagated by vegetative means. The rooting initiates 21 days after sprouting and 300mm, long 15 and 15mm diameter cutting gives the maximum rooting. As it is a plant of arid zone, there is no necessity of irrigation upto the middle of November except during drought. However, if there is the winter shower, there is a necessity of irrigation to plants of one to five years of age group. The plants of 6-7 years of age group require irrigation only in summer season. Irrigation can be done either by head load method or water tank method^{40,41}.

Medicinal uses

The use of *C. wightii* plant in the treatment of diseases occupies an important place in ayurveda, the traditional medicine system of india. The Atharvaveda one of the four well known holy scriptures (Vedas) of the Hindus, the Atharvaveda is the earliest reference for it medicinal and therapeutic properties⁴². Detailed description regarding its action, use and induction as well as the varieties of guggul have been described in numerous Ayurvedic treat including Charaka samhita (1000 BC), Sushruta Samhita (600 BC and Vagbhata seventh century AD). In addition, various medical lexicons were return between twelfth and fourteen centuries AD. It responsible for reducing fat, indicated for healing Bone Fracture to inflammation, Arthritis, Atherosclerosis, Obesity, Hyperlipidemia, Rheumatism, Haemorrhoids,

Urinary disorder, skin disease high cholesterol, neuro-degeneration, Parkinson's diseases, mongolism and ageing process⁴³⁻⁴⁸. *C. wightii* is a gum resin, historically used for antiseptic and deep penetrating action in the treatment of elevated blood cholesterol and Arthritis. *C. wightii* is effective as weight loss and fat burning agent. It increase white blood cell count and possess strong disinfecting properties. Used as a carrier and combined with other herbs to treat specific condition^{44,49,50}. Traditionally, *C. wightii* plant is given in the form of YOG, where in *C. wightii* is mixed with other drug's along with castor oil or Indian clarified butter. The YOG could also be prepared by cooking the *C. wightii* with water, and other herbal drug powder. Popular Ayurvedic formulated containing *C. wightii* are: Yograj gugguluvati, Pachamrit ioh guggulu, Kaishore gugguluvayi, Triphla guggulu and Sinha gugguluvati⁵¹. *C. wightii* has been a key component in ancient Indian Ayurvedic system of medicine and now widely use in Morden medicine for treatment of heart ailments. But *C. wightii* as it's locally known, has become so scarce because of its overuse in it two habitats in india where it found-Gujarat and Rajasthan. The extract, called guggulipid, comes from the *C. wightii* tree and has been used in Ayurvedic medicine, a traditional Hindu medicine, for nearly 3000 years in India. Today it existence is threatened because of low seed production in an adverse natural condition and recent environmental change due to rainfall pattern and increasing level of atmospheric pollution. This plant species is fighting for its survival in the natural habitat since a long time. Attempts have been made in this direction by number of researchers including under present investigation towards its natural populations, germ-plasm collection, cultivation techniques, Phytosociology and regeneration potentialities etc. at different site of Western Indian Thar desert^{44,52}. The oleo-gum resin commonly known as "gum guggul" or "Indian Myrrh" is the economically important product of Indian bdellium. The oleo-gum is collected as exudates from woody stem. A plant generally takes 10 years to reach tapping maturity under the dry climate conditions. The thick branch is incised during the winter to extract the oleo-gum resin. Guggul gum is a mixture of 61% resin, and 29.3% gum, in addition to 6.1% water, 0.6% volatile oil and 3.2% foreign matter⁵³.

Reported pharmacological activities

➤ Hypolipidemic/ Hypocholesterolaemic activity

1. Crude *Guggulu* was reported to possess highly encouraging hypolipaeamic activity in rabbits⁵⁴.
2. Anion exchange property detected by means of chloride retention and bile acid sequestrating activity in the oleoresin fraction hypocholesterolaemic activity⁵⁵.
3. Crude drug as well as its two fractions (alcohol soluble and alcohol insoluble) were found to cause a significant fall in serum cholesterol and serum turbidity with a concomitant increase in the coagulation time and prothrombin time. The alcohol insoluble fraction was slightly more potent in this respect than alcohol soluble fraction as well as crude *Guggulu*⁵⁶.
4. PE fraction A (petrol-soluble), B (alkali washed neutral portion) and C (petrol-insoluble) were given to 8 week old male white leg horn chicks for 2-3 weeks in hypercholesterolaemia induced by atherogenic diet. All fractions lower the serum cholesterol, but fraction A is most potent and B is the least potent⁵⁷.
5. Alcohol extract and two pure fractions (a terpenoid and a steroid) isolated from the PE extract showed that

the steroid fraction was highly potent as hypolipaeamic agent lowering the serum cholesterol by 69.3% as well as the c/p ratio. The alcohol extract could lower the cholesterol by 59.2% whereas the Terpenoid lowered it by 54.3%⁵⁸.

6. The alcohol extract of *Guggulu* when orally administrated to Indian domestic pigs kept on standard atherogenic diet over a period of six weeks effectively reduced the total serum cholesterol and also serum beta-lipoprotein fraction and significantly altered the lipoprotein ratio⁵⁹.
 7. The steroidal compound isolated from fraction A of PE extract reduced the lipid content (Viz., total lipids, cholesterol, TG and phospholipids) of both hepatic and aortic tissues. The response was doses-dependent and the maximum effect was noted at 10mg/kg⁶⁰.
 8. Fraction A of PE extract of *C. mukul*, effectively lowered serum lipids, cholesterol, phospholipids and triglycerides in monkeys fed with cholesterol diet⁶¹.
 9. Alcoholic extract (25-50 mg/kg orally), reduced serum cholesterol level in normal and hyperlipaemic rats and rabbits. Further, a resin fraction, a pure steroid and fraction F isolated from crude extract showed hypocholesterolaemic effect on normal and triton-induced hyperlipaemic rats^{62,63}.
 10. The hypolipidemic activity was shown in animals as well as in patients of obesity and hypercholesterolemia⁶⁴.
 11. A number of clinical studies were carried out to confirm hypolipidemic activity of guggulu and guggulipid^{65,66}.
 12. In another study, highly significant reduction in levels of mean serum cholesterol and triglyceride was observed in groups of animals receiving high-fat diet for one month along with guggulu, which clearly demonstrated its hypolipidemic activity. Additionally, administration of guggulu partially reversed the atherosclerosis in the aorta that was induced by high-fat diet⁶⁷.
 13. Clinical studies on *C. mukul* showed its hypolipidemic effect and the outcome of change in lipid profile upon its administration. This study showed significant decrease in total cholesterol and LDL cholesterol after treatment with guggulu⁶⁸.
 14. The hypolipidemic activity of the isomers *E*-guggulsterone and *Z*-guggulsterone has also been studied in animal models. Administration of guggulsterone (*Z* and *E*) significantly lowered serum lipid levels of rats with either triton (WR-1339) or cholesterol-induced hyperlipidemia⁶⁹.
- #### ➤ Effect on Platelet Aggregation and Fibrinolytic Activity
1. The purified steroid mixture from guggulu completely inhibited ADP, adrenaline, or serotonin induced platelet aggregation. No difference was observed between the effectiveness of the steroid mixture and the purified guggulsterone *E* or *Z*. The effect of guggulsterones *E* and *Z* was very similar to the inhibitory effect of clofibrate. This finding has therapeutic value in myocardial infarction and thromboembolism⁷⁰.
 2. The effect of guggulu on fibrinolysis and platelet adhesiveness in coronary heart disease was studied.

Guggulu fraction A (pet ether extract) in daily dose of 1 g was administered to healthy individuals (group I) and to patients of coronary artery disease (CAD) (group II) for a period of 30 days. Serum fibrinolytic activity increased, while the platelet adhesive index decreased, which was statistically significant in healthy individuals and in CAD patients. In view of this, guggulu fraction A may be a useful therapeutic agent in the management of coronary artery disease⁷¹.

➤ **Thyroid Stimulatory Activity**

1. Administration of ethanolic extract of guggulu to the female albino mice for 15 days enhanced the triiodothyronine (T3) concentration and T3/T4 ratio, while no marked change in the concentrations of serum thyroxine (T4) was observed⁷².
2. Z-Guggulsterone was shown to be responsible for the thyroid stimulatory action of guggulu. Administration of isolated Z-guggulsterone to rats led to significant increase in all thyroid function parameters, namely, uptake of iodine by the thyroid, enzymes involved in the synthesis of thyroid hormones, and tissue oxygen uptake, thus suggesting thyroid stimulatory action⁷³.

➤ **Anti-inflammatory and Anti-arthritis activity**

1. Oleoresin was found to be highly potent anti-inflammatory agent, as compared to hydrocortisone and butazolidin against Brownlee's for maldehyde-induced arthritis in albino rats⁷⁴.
2. Oleoresin fraction possessed significant anti-arthritis and anti-inflammatory activities, the minimum effective dose being 12.5mg/100g body weight. Only the acidic fraction showed significant activity while the monoacid and solid fractions were inactive⁷⁵.
3. The Steroidal compound isolated from PE extract possessed significant anti-inflammatory activity on carrageenin-induced rat-paw oedema^{76,77}.
4. The results of several studies confirm anti-inflammatory and antiarthritic activities of guggulu⁷⁸⁻⁸².
5. The 50 percent aqueous methanolic extract was found to exhibit an anti-inflammatory effect on adjuvant-induced air pouch granuloma in mice. The methanolic extract inhibited nitric oxide production in lipopolysaccharide activated mouse peritoneal macrophages⁸³.
6. Guggulosomes prepared using guggul with ibuprofen by bath sonication and trituration methods were studied for anti-inflammatory activity. It was clearly shown that guggulosomes had more efficacy than ibuprofen and both guggul and ibuprofen had synergistic effect. The study proved that guggul could serve as a carrier for entrapping drugs and for their sustained release action⁸⁴.
7. Several animal studies have demonstrated the effectiveness of guggulu extract in standard osteoarthritis (OA) models. The authors had conducted both animal and clinical investigations of guggulu for OA prior to this study. The goal of this study was to determine the effectiveness of guggulu for reduction of pain, stiffness, and other symptoms that arise from OA⁸⁵.

➤ **Antiatherosclerotic Activity**

1. LDL has been found to accumulate in atherosclerotic lesions and is the major source of the cholesterol accumulation in human foam cells. There is evidence that LDL oxidation is essential for atherogenesis and the antioxidants that prevent this oxidation may either slow down or prevent atherogenesis. Guggulsterones, the lipid-lowering components of guggulu, effectively inhibited *in vitro* LDL oxidation (as discussed under antioxidant action). Thus the combination of antioxidant and lipid-lowering properties of guggulu makes it especially beneficial against atherogenesis⁸⁶.

➤ **Cardioprotective Activity**

1. Guggulsterones are shown to be effective cardioprotectives. Myocardial necrosis induced by isoproterenol in rats caused marked increase in serum creatine phosphokinase and glutamate pyruvate transaminase. Phospholipase, xanthine oxidase, and lipid peroxides were simultaneously enhanced in ischemic heart following depletion of glycogen, phospholipids, and cholesterol. Treatment with guggulsterone at a dose of 50mg/kg significantly protected cardiac damage as assessed by the reversal of blood and heart biochemical parameters in ischemic rats⁸⁷.

➤ **Antifertility Activity**

1. Guggulu administered orally (2 and 20mg/100 g body weight) to female rats decreased the weight of the uterus, ovaries, and cervix, whereas glycogen and sialic acid levels in these organs increased. This suggested that guggulu may be useful as an antifertility agent⁸⁸.

➤ **Skin Diseases**

1. Administration of guggulipid was reported to be effective in the treatment of nodulocystic acne. A study in 21 patients found that guggulipid was as effective as tetracycline in the treatment. The patients with oily faces responded better to the guggulipid treatment⁸⁹.

➤ **Antihyperglycemic Activity**

1. Administration of alcoholic extract of *C. mukul* at a dose of 200mg/kg for 60 continuous days reduced plasma glucose levels in streptozotocin-induced diabetic rats⁹⁰.
2. A study showing effect of guggulsterone isolated from *C. mukul* in high-fat diet induced diabetic rats has also been reported. Different biochemical parameters like GTT, glycogen content, glucose homeostatic enzymes (like glucose-6-phosphatase and hexokinase), insulin release *in vivo*, and expression profiles of various genes involved in carbohydrate and lipid metabolism clearly demonstrated the hypoglycemic effect. The results suggested that guggulsterone has both hypoglycemic and hypolipidemic effects which can help cure type II diabetes⁹¹.

➤ **Antimicrobial Activity**

1. The volatile oil of *C. mukul* was found to be highly effective against *Rhizopertha dominica* which suggested its role as a fumigant. The ethanolic extract of *C. mukul* exhibited best antibacterial activity at 5mg/ml against multidrug-resistant *Klebsiella pneumonia*⁹².
2. An active compound, 5(1-methyl,1-aminoethyl)-5-methyl-2-octanone, of the methanolic extract of guggulu gum possessed significant antibacterial

activity against Gram-positive bacteria and moderate activity against Gram-negative bacteria⁹³⁻⁹⁵.

➤ Cytotoxic Activity

1. Ferulate compounds are used in the method for prevention and treatment of abnormal cell growth and proliferation of inflammation, neoplasia, and cardiovascular disease. Ethyl acetate extract showed significant *in vitro* cytotoxicity. A fraction showing cytotoxic activity was characterized as a mixture of two ferulates with an unusual skeleton by spectral and chemical methods. This fraction also showed moderate scavenging effect against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals⁹⁶. Treatment with guggulipid significantly inhibited the viability of human prostate cancer cell line LNCaP (androgen dependent) and its androgen-independent variant (C-81) with IC₅₀ of 1 μM (24 h treatment), thus indicating its possible role in apoptosis and cancer prevention⁹⁶. The results of this study indicated that guggulsterone inhibited proliferation of PC-3 cells in culture by causing apoptosis, whereas a normal prostate epithelial cell line is resistant to growth inhibition and apoptosis induction by this phytoconstituent. These observations provided rationale for further preclinical and clinical evaluation of guggulsterone for its efficacy against prostate cancer⁹⁷.

Substitutes and Adulterants

Oleo-gum resin obtained from *Boswellia serrata* Roxb. (*Salai guggulu*) is the major adulterant. It is distinguished by its yellowish green, golden or milky tears, seldom amalgamated into lumps and a characteristic turpentine like odour. Gum-oleo-resin of *Commiphora myrrha* (Nees) Engl. imported from Africa and constituting the drug Hirabole or bole of commerce is sometimes mixed with *Guggulu*. Similarly, gum-oleo-resin obtained from *Commiphora roxburghii* (Arn) Engl., occurring in central and eastern India is sold by the name of *Guggulu*. The former is distinguished by large tears of yellowish brown colour, exposing, on fracture, a brown surface having white markings, while the latter has a bluish tinge and a feeble balsamic odour⁹⁸.

Possible Reasons for Its Decline

Several reasons are cited for the plant being listed as endangered species and some of these are considered to be of greater consequences affecting its population survival. The various factors are: slow growth, poor seed-setting and seed germination rate, lack of cultivation, unsustainable over-exploitation, excessive and unscientific tapping method, invasion of alien species⁹⁹⁻¹⁰¹. These have been listed below.

1. Unscientific method of tapping and overexploitation
2. Low seed setting
3. Regeneration through seeds
4. Invasion of alien species
5. Others
 - ✓ Narrow extent of occurrence, small area of occupancy and severe fragmentation, as other reasons for conservation threat and extinction risk.
 - ✓ It has never been brought under cultivation.
 - ✓ The changing environment and existing natural populations of this species has been affected by climatic conditions, soil erosion, low rainfall, termite

infestation, over-grazing by domestic animals and mining activities.

Safety and Toxicity

It has been mentioned in Ayurvedic texts that administration of raw guggulu may sometimes lead to skin rashes, irregular menstruation, diarrhoea, headache, mild nausea, and, with very high doses, liver toxicity¹⁰². In order to overcome the side effects of raw guggulu, Ayurveda describes a number of purification processes (shodhan vidhi) in different "dravyas," that is, fluids, which not only take care of the adverse effects but also enhance the therapeutic activity¹⁷. It is also mentioned in Ayurvedic texts that guggulu must be purified before incorporation into herbal formulations. There are a large number of commercial polyherbal anti-inflammatory formulations which are using guggulu as the chief ingredient⁸². The clinical trials done with standardized gum guggul extracts reported transient side effects such as skin rashes, diarrhoea, and irregular menstruations. A report also states that, out of 22 individuals receiving 2160mg guggulu daily for 12 weeks, 10 persons experienced one or another side effect including gastrointestinal distress, fatigue, and skin rash¹⁰³. Skin rashes have also been reported in other trials using 1-2 g guggulipid (ethyl acetate fraction) daily for a month. This study did not report any intestinal distress¹⁰⁴. Although generally accepted as relatively safe, caution may be warranted during guggul consumption. There is little or no information on toxicity with the use of guggulu.

Conclusion

In the present review, we have made an effort to provide the morphological, phytochemical, ethnopharmacological and pharmacological information on *C. wightii*, a tree used conventionally for medicinal purposes. A variety of extracts and chemical compounds of the plant have shown Hypolipidemic/ hypocholesterolaemic activity, Effect on platelet aggregation and fibrinolytic activity, thyroid stimulatory activity, antioxidant, antibacterial, cytotoxic, anti-inflammatory and hypoglycaemic activities. Its phytochemical composition indicates the presence of diterpenoids, triterpenoids, steroids, longchain aliphatic tetrols, aliphatic esters, ferulates, lignans, carbohydrates, and a variety of inorganic ions besides minor amounts of sesamin and other unidentified constituents. A large number of compounds have been isolated from *C. wightii* and shown to possess assorted biological properties. In addition, crude extracts of the plant and their solvent fractions are connected with diverse pharmacological activities. Ethnopharmacological research on *C. wightii* is heartening as phytochemical profiling, nutritional and biological activities of the species could support the documented medicinal uses, nutritional and nutraceutical properties of *C. wightii*. Comprehensive research on phytochemical properties, biological activities, pharmacokinetics and clinical trials of *C. wightii* is required as this will present further confirmation for the nutritional, ethnopharmacology and nutraceutical potential of *C. wightii*. Further research should center on experimental *in vitro*, *in vivo* studies and toxicological evaluation of *C. wightii* and its phytochemical compounds.

Conflict of interest

The authors declare that no conflict of interest is associated with this work.

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