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Pharmacological Review on Indium Bdellium

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Abstract: *Currently, a day to day life increasing used of herbal drug and ayurvedic remedies or derived medicine as natural instead of synthetic products in all over the world. indium bdellium also known as guggul belong to family burseraceae obtain from gum resin (sap) of the commiphora mukul and commiphora wightii. It contained wide range of chemical constituents diterpenoids, triterpenoids, steroids, long-chain aliphatic tetrols, aliphatic esters, ferulates, lignans, carbohydrates. This review article focus on the pharmacological actions like hypolipidemic activity, effect on platelet aggregation and fibrinolytic activity, thyroid stimulatory activity, anti-inflammatory and anti-arthritic activity, anti-oxidant activity, anti-atherosclerotic activity, cardioprotective activity, cytotoxic activity, anti-fertility activity, skin diseases, anti-hyperglycemic activity, anti-microbial activity.*

Keywords: Indium bdellium, Guggul, Pharmacology, Review, Chemical Constituents.

I. INTRODUCTION

Indium bdellium obtained as an extraction of oleo-gum resin from the spontaneously injury to stem and branches of Commiphora wightii (Arnott) Bhandari and Commiphora mukul (Hook. Ex Stocks); Family, Burseraceae. The plant is commonly known asguggul tree and is found in arid areas of India, Bangladesh, and Pakistan. In India, it is found in Gujrat, Rajasthan, Madhya Pradesh,Assam, 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 Sanskrit term "guggul" is "one that protects against diseases". Guggul is a small tree with various branches normaly grow upto two or three meters long. The tree go on without any foliage for several years. it grows well in sandy to slit loam soils, which are reach in matters. The tree is tapped from November to January and the resin iscollected through May to June. A guggul tree yields between250 to 500 g of dry resin during each collection season [3,4].

In Indian traditional system of medicine, guggulu hasbeen used for thousands of years in the treatment of arthritis, inflammation, gout, rheumatism, obesity, and disorders oflipids metabolism [5]. It is known by different names like guggula, guggul, guggal, gugar, and Indium bdellium [6]

Guggulu occurs in vermicular pieces of pale yellow or brown coloured mass with aromatic odour and bitter astringent taste; when fresh it is viscid and golden coloured. It should produce not more than 5 percent of total ash and 1percent of acid-insoluble ash. It yields not less than 27 percentof alcohol-soluble matter and not less than 53 percent of water-soluble matter. The genuine samples of guggulu contain1 percent of volatile oil [4] and between 1.0 and 1.5 percent of guggul sterones (Z and E) [5]

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Synonyms: Gumgugul, Salai-gogil.

Biological Source:
Guggal is a gumresin obtained by incision of the bark of Commiphora mukul (H. and S.) Engl., belonging to family Burseraceae.
Guggul is known by different names in different languages such as:

- In Hindi: – Guggul.
- In Marathi: – Guggala.
- In Tamil: – Gukkulu.
- In Telugu: – Guggipannu.
- In Sanskrit: – Guggulu.
- In English: – Indian bdellium.
- In Kannada: – Kanthagana.
- In Gujarati: – Gugal

Geographical Source:
The tree is a small, thorny plant distributed throughout India.

Collection:
Guggal tree is a small thorny tree 4 to 6 feet tall branches slightly ascending. It is sometimes planted in hedges. The tree remains without any foliage for most of the year. It has ash-coloured bark, and comes off in rough flakes, exposing the innerbark, which also peels off. The tree exudes a yellowish resin called gum guggul or guggulu that has a balsamic odor. Each plant yields about one kilogram of the product, which is collected in cold season

Characteristics: Guggal occurs as viscid, brown tears; or in fragment pieces, mixed with stem, piece of bark; golden yellow to brown in colour. With water it forms a milk emulsion. It has a balsamic odour and taste is bitter, aromatic.

Chemical Constituents
Major –
Volatile oil consisting myrecene, dimyrecene, polymyrecene; Resin (Z-Guggulsterone, E-Guggulsterone, Z-Guggulusterol, Guggulusterol I-V)5.
Others –
20-α-Hydroxy-4-pregnen-3-one; 20-β-hydroxy-4-pregnen-3-one; 16-β-hydroxy-4,17(20)Z-pregnadien-3-one; 16-α-hydroxy-4-pregnen-3-one; cembrene A; mukulol;
Quercetin; 3-O-α-L-arabinoside; 3-O-α-L-rhamnoside; 3-O-β-D-glucoronide; ellagic acid; pelargonidin-3; α-camphorene; cambrene; Chloestrol; guggulsterols I, II, III15, 6-7.
One reviewer also says that there is the components of the essential oil found in C. mukul . The essential oil with their percentages by weight as shown- α-pinene (4.755); myrcene (3.50%); eugenol (14.70%); cadiene (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-pineol (4%); 1,8-cineole (3.5%); and unidentified compounds8. The seed of C. wightii contains 9.8 ± 0.7% oil. The esters of fatty acids shows the presence of 46.62% saturated fatty acids and 51.40% unsaturated fatty acids. The fatty acid composition is capric acid (3.50%); myristic acid (14.51%); palmitic acid (6.68%); steric acid (4.705%); arachidic acid (3.185%); behenic acid (14.05%); myristoleic acid (1.34%); palmitoleic acid (12.07%); oleic acid (14.15%); eicosenoic acid (0.11%); linoleic acid (22.34%); and alpha linol acid (1.37%)9.

Veda
Guggul is described as “Agni Sthana” and used for ‘Dhupa’. In Atharva Veda, it is mentioned that Yaksma 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 cattle2,3,5,6

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Samhita

It is observed that the internal usage of Guggul increased during Samhita period only. Acharya Charaka included Guggul in "Sangya Sthapana Maha Kashaya" and in "Kashaya Skandha". Maharishi Sushruta has described Guggul in the list of seven most important drugs for the treatment of Sthaulya. He has prescribed Guggul with Go-mutra in condition of vitiated Vata with Medodhatu dominated Kapha dosha. The drug is also mentioned as highly effective in the treatment of Vrana as a fumigating agent, Kushtha, Vidradhi Pratisaranartha, Shotha , Gulma etc. Acharya Kashyapa has quoted Guggul in different formulations to treat various diseases. Ghrita, Taila, Avaleha, Dhoopana etc. many formulations of it are also described for the treatment of many 'Bala Rogas'10Maharishi Bhela has prescribed that Dhoomrapana of Guggulu should be taken after bath and after taking meal. He also described the Vrana ropana property of Guggulu11. Maharishi Harita has elaborated Guggulu in a separate chapter titled "Guggulu Kalpa" . Here, he has opined that Guggulu from Marudesha must be collected in Ushna Ritu and Guggulu from hilly areas must be collected in Sheeta Ritu12. Many formulations of Guggulu have been mentioned in Sharangadhara Samhita. However, in Vati kalpadhyaya , Guggulu has been suggested specifically for the Vati preparation, because it facilitates the binding capacity. Sarangadhara quoted it among the drugs to be used when they are older (Purana).

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. He has also used Guggul in Sneha vyapada chikitsa and prescribed Guggulu in diseases produced due to vitiated Vata, Kapha, Medodhatu a

II. PHARMACOLOGICAL ACTIVITIES

Hypolipidemic Activity

The lipid lowering effect of gug-gulu with special reference to atherosclerosis and obesity(medoraga) was first reported in a doctorate thesis submittedto the Banaras Hindu University (BHU) in January 1966.Earlier to this work, guggulu was well known as an Ayurvedicdrug for the treatment of various types of arthritis. Thiswork was inspired by a rather obscure shloka in Sanskritin the well-known Ayurvedic treatise Sushruta Samhita. Theshloka deals in an extraordinarily lucid and scientific manner, with the etiology, pathogenesis, and treatment of obesityand associated lipid disorders and their complications. The hypolipidemic activity was shown in animals as well as inpatients of obesity and hypercholesterolemia [20].In carefully planned studies carried out (over a period oftwo years) on rabbits, in which hyperlipidemia was induced by feeding cholesterol (in hydrogenated vegetable oil), itwas demonstrated for the very first time that crude guggulucould not only lower significantly the serum cholesterol in hypercholesterolemic rabbits but also protected these animalsagainst cholesterol-induced atherosclerosis at the fatty streakstage. It also reduced the body weight of the animals. Asimilar trend to reduce significantly the serum cholesterollevels in patients with obesity and hypercholesterolemia was found in clinical studies with crude guggulu. The CentralDrug Research Institute (CDRI), Lucknow, has been engagedin chemical, pharmacological, and clinical studies on guggulu[20].Gugulipid, an ethyl acetate extract of the oleoresin,standardized at CDRI, has been marketed in India since 1988 as a hypolipidemic agent. It contains Z-guggulsterones and$E$-guggulsterones which are purported to be the compounds responsible for the hypolipidemic activity of the guggulu. Gugulipid contains not less than 4 percent and not morethan 6 percent of guggulsterones ($Z$and E). The decision touse the ethyl acetate extract rather than two guggulsterone was primarily for commercial reasons and was also because of the fact that other components of the ethyl acetate extractshowed synergistic (hypolipidemic) effect [20]. A number ofclinical studies were carried out to confirm hypolipidemicactivity of guggulu and gugulipid [21]. The findings ofmulticentric clinical trials carried out with gugulipid at seven different centres in India coordinated in collaboration withCDRI confirmed the role ofgugulipid as a hypolipidemicagent .

Effect on Platelet

Aggregation and Fibrinolytic Activity.The purified steroid mixture from guggulu completely inhib-ited ADP, adrenaline, or serotonin induced platelet aggrega-tion. No difference was observed between the effectivenessof the steroid mixture and the purifiedguggulsterone E or$Z$. The effect of guggulsterones E and Z was very similar to the inhibitory effect of clofibrate. This finding has therapeuticvalue in myocardial infarction and thromboembolism .The effect of guggulu on fibrinolysis and platelet adhe-siveness in coronary heart disease was studied. Guggulufraction A (pet ether extract) in daily dose of 1 g wasadministered to healthy individuals (group I) and to patientsof coronary artery disease (CAD) (group

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II) for a period of 30days. Serum fibrinolytic activity increased, while the platelet adhesive index decreased, which was statistically significantin 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 disease [19].

Thyroid Stimulatory Activity

Administration of ethano-lic extract of guggulu to the female albino mice for 15 days enhanced the triiodothyonine (T3) concentration and T3/T4ratio, while no marked change in the concentrations of serumthyroxine (T4) was observed [47]. *Z*-Guggulsterone wasshown to be responsible for the thyroid stimulatory action of guggulu. Administration of isolated *Z*-guggulsterone to ratsled to significant increase in all thyroid function parameters, namely, uptake of iodine by the thyroid, enzymes involved inthe synthesis of thyroid hormones, and tissue oxygen uptake,thus suggesting thyroid stimulatory action [18].

Anti-Inflammatory and Antiarthritic Activity

Theresults of several studies confirm anti-inflammatory andantiarthritic activities of guggulu [13, 15, 25, 49–52]. The 50percent aqueous methanolic extract was found to exhibitan anti-inflammatory effect on adjuvant-induced air pouch granuloma in mice. The methanolic extract inhibited nitricoxide production in lipopolysaccharide activated mouseperitoneal macrophages [15]. A crystalline steroid wasisolated from the petroleum ether extract and tested in ratsfor inhibition of inflammation induced by Freund's adjuvant.It inhibited the full development of the primary lesions in adjuvant arthritis and also reduced the severity of secondarylesions as compared with the untreated control group.Guggulosomes prepared using guggul with ibuprofenby bath sonication and trituration methods were studiedfor anti-inflammatory activity. It was clearly shown tha tguggulosomes had more efficacy than ibuprofen and both and ibuprofen had synergistic effect.The study proved that guggul could serve as a carrier for entrapping drugs and for their sustained release action [17].

Antioxidant Activity

The antioxidant property of gug-gulu helped stop the oxidation of cholesterol and subsequenthardening of the arteries, reduced the stickiness of platelet,and also lowered the risk of coronary artery disease [16]. Italso enhanced the production of thyroxin and triiodothyro-nine; these hormones increase the metabolism of carbohy-drates and protein synthesis and help in lowering the lipidactivity .The antioxidant activity was attributed to the presence ofguggulsterones. It was tested in vitro against the formation of oxygen free radicals. The oxidation of human LDL inducedby Fe2+ or by rat peritoneal macrophages caused marked formation of lipid peroxidation products. Guggulsterone(50 μM) prevented the generation of thiobarbituric acid reactive substances and lipid hydroperoxide of low density lipoprotein in above system. However, it did not protect lipids against the formation of conjugated dienes, the initial step of lipid peroxidation cascade. Guggulsterone significantly inhibited the reaction of lipid peroxidation in liver micro-somes challenged with Fe2+ and sodium ascorbate

Antiatherosclerotic Activity

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 invitro LDL oxidation (as discussed under antioxidant action). Thus the combination of antioxidant and lipid-loweringproperties of guggulu makes it especially beneficial against atherogenesis [15].

Cardioprotective Activity

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 50 mg/kg significantly protected cardiac damage as assessed by the reversal of bloodand heart biochemical parameters in ischemic rats [14].

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Cytotoxic Activity

Ferulates, important bioactive con-stituents identified from the guggulu gum, were reported to play a significant role in in vitro cytotoxicity by decreasing the cell viability in MCF-7 (breast) tumor cells, PC-3 (prostate) tumor cells, and parental and transfected P 388 cells [13]. Therefore, ferulate compounds are used in themethod 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-picryl hydrazyl (DPPH) radicals [12]. Treatment with gugulipid 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 possiblerole in apoptosis and cancer prevention [12]. The results ofthis study indicated that guggulsterone inhibited prolifera-tion of PC-3 cells in culture by causing apoptosis, whereasa normal prostate epithelial cell line is resistant to growth inhibition and apoptosis induction by this phytoconstituent.These observations provided rationale for further preclinicaland clinical evaluation of guggulsterone for its efficacy againstprostate cancer [11].

Antifertility Activity

Guggulu administered orally (2 and 20 mg/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 agent [10].

Skin Diseases

Administration of gugulipid was reported to be effective in the treatment of nodulocystic acne. A study in 21 patients found that gugulipid was as effective as tetracycline in the treatment. The patients with oily faces responded better to the gugulipid treatment [9]

Antihyperglycemic Activity

Administration of alcoholic extract of C. mukul at a dose of 200 mg/kg for 60 continuous days reduced plasma glucose levels in streptozotocin-induced diabetic rats [8]. 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 diabetes [7].

Antimicrobial Activity

The volatile oil of C mukul was found to be highly effective against Rhyzopertha dominica which suggested its role as a fumigant. The ethanolic extract of C. mukul exhibited best antibacterial activity at 5 mg/ mL against multidrug-resistant Klebsiella pneumonia [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 bacteria [1]

Formulation	Manufacturer by	composition	uses
GUGULIPID 	SABINSA Corporation	**Guggul Resin, Dalchini, Bhumi Amla, Sonth, Marich, Pippali**	Lipid lowering agent.anti-atherogenic, dietary supplement

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	Nishan products	Guggal Dhoop Are Manufactured Using Pure And Natural Gugle, Herbs And Fine Essense Oils Etc	Scent, air fragrance , purifier of atmosphere
	Premium Quality Nutraceuticals and Herbal Formulations	Guggul extract 400mg. commiphora wightii, guggul sterons >2.5%	normal cholesterol levels, normal function of joints and connective tissues

III. ACKNOWLEDGMENTS

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IV. 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. Indium Bdellium is traditional medicines for the treatment of inflammation, arthritis, obesity, microbial infection, wound, pain,fractures, tumor, and gastrointestinal diseases. It is one of the oldest and the most prominent herbs in Ayurvedic medicine. Guggulu is a versatile drug and, because of its paranormal properties, it is very valuable in treating variety of disorder

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