



A Review on Medicinal Importance of Guggulsterone in Guggul (*Commiphora wightii*)

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ABSTRACT

Guggulsterone is a plant sterol obtained from gum resin of Guggul. To treat various disorders, including internal tumors, obesity, liver disorders, malignant sores and ulcers, urinary complaints, intestinal worms, leucoderma, sinuses, edema, and sudden paralytic seizures the gum resin which is obtained from Guggul plant used for thousand years in ayurveda. Guggulsterone has been identified a bioactive components of this gum resin. For the regulation of bile acids and cholesterol metabolism it works as antagonist of nuclear receptors such as farnesoid X receptor. It also inhibits the cancers cells by activating p38 pathway, protein kinase and nuclear kappa cells for causing apoptosis which results in cell proliferation. Guggulsterone eradicated cholesterol metabolites bile acids from the liver by upregulating bile salt export pump and also proposed a system of anti-inflammatory effect by repression of NF- κ B activation. Guggulsterone activates 3T3L1 adipocytes which leads to mitochondrial biogenesis which leads to weight loss. This review paper reveals the importance of Guggul due to its medicinal value which aimed to clarify the role of Guggulsterones in chronic diseases and its mode of action which helps in the future research studies.

Keywords: cancer, antiinflammatory, hyperlipidemia, weight loss.

INTRODUCTION

From the past few decades the world has substantially seen an exponential increase in population rise, inadequate supply of drugs, prohibitive cost of treatments, side effects of several synthetic drugs and the economic forum has



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always stated that the resources on earth are limited, an optimum use of available technology and new modificants will enhance the productivity to three folds and this has popularised the use of plant materials in sectors of medicines and agriculture for wide variety of human ailments.(Soni and Swarnkal 2006).

Due to its rare or minimal side effect treating with medicinal plant contemplates very safe and important fact arises that herbal treatments is independent of any age groups. Guggul (*Commiphora wightii*) comes under the critically endangered species and considered as important medicinal plant.(Tomar et al.,2021) It is mostly found in Bangladesh ,Pakistan, Rajasthan, Gujarat, Assam, Madhya Pradesh, and (Kulloli and Kumar, 2013).Guggulis having complicated mixture of minerals, gum, terpenes, sterols (Guggulsterol -I,-II,-III,-IV,-V), essential oils, sterones (Z-, E-, M-Guggulsterone, and dehydro Guggulsterone-M), ferrulates, lignans, and flavanones.(Shishodia et al., 2008).One of the main sterol of Guggul is Guggulsterone. It plays a vital role which controls the synthesis and transport of bile acidby suppressing the physiological action of the nuclear hormone receptor i.e FXR (Sinal and Gonzalez, 2002; Urizar et al., 2002).It also has been reported that it found for exerting theanti-metastatic effect by reducing the level of MMP-9, COX-2, and VEGF (Shishodia and Aggarwal, 2004). It also modulates the expression of anti-apoptotic genes for inducing apoptosis (Shishodia and Agarwal, 2004).

This review paper summarizes the medicinal importance of Guggulesterone for treatment of human health such as followingtreating inflammatory conditions, diabetes, weight loss, hypothyroidism, cancer, hyperlipidemia and also has the future possibilities for obtaining herbal medicines for the health benefits of the people.

For treatment of hyperlipidemia

Guggul considered the important medicinal plant due to its various medicinal properties.In asia Guggul have been widely used for cholesterol-lowering agents and their popularity is increasing in the United States. Guggulsterones - E and -Z are responsible for the lipidlowering properties of Guggul in human blood. To evaluate the effects of Guggulsterone on disorders of lipid metabolism, studies are finding out. The study of Singh *et al.* (2007) reveals that Guggulsterone (25 mg/kg body weight for 10 days) lowered serum cholesterol and triglyceride levels by 27% and 30%, respectively. Chander *et al* (2002) examine the effect of Guggulsterone decreased serum levels of LDL and very low-density lipoprotein. To understand the role of Guggulsterone for the treatment of hyperlipidemia the following pathway Fig. 1.

As we all can see in fig.1 that Guggulesterone activates FXR receptor factor which is metabolism regulator found in liver and intestine which regulates protein coding gene i.e CYP7 α 1 which modulates the enzyme 7 α hydrolase for synthesis of bile acid from cholesterol and also upregulate the bile salt export pump.FXR receptor also activates bile acid binding protein gene 1-BABP for cholesterol homeostasis which treated with α PPAR leads to uptake of bile salt. (Urizar et al.,2002; Chaudhary 2012;Satyavati et al.,1969)

For the treatment of Cancer

For modern drug development Identification of active principles and their molecular targets from traditional medicine is carried out. Gum resin from *Commiphora wightii* (syn *C. mukul*) has been used for centuries in Ayurveda to treat internal tumors .Guggulsterone has been identified as one of the major active components of this gum resin. Evidence has been presented through findings to suggest that Guggulsterone can suppress tumor initiation, promotion and metastasis.Crasto (2012)arecent study revealedthat gugulipid which is extracted from *Commiphora mukul*, and mostly used in lowering the cholesterol level effect.Studies also revealed that Guggulsterone recently act as inhibitor for cancer growth invivo and invitro condition and also through the understanding of anti-cancer activity leads to treat different types of human cancer. Shishodia (2007).Guggulsterone suppressed proliferation of tumor cells through inhibition of DNA synthesis, producing cell cycle arrest in the S phase. Silva et al (2014) while investigating the role of bone lipids in breast cancer migration to bone showed that the FXR antagonist Z-Guggulsterone prevented migration of these cells and induced apoptosis in breast cancer cells.To understand the role of Guggulesterone for the treatment of cancer the following pathway is Fig.2. As we can see in fig .2 that



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Guggulesterone plays a role for inhibition of cancer cells by activating MAPK pathway which is mitogen activated protein kinase which produce pro apoptotic genes and causes apoptosis .it activates protein kinaseB and NF-Kb pathway which is nuclear factor kappa light chain enhancer of activated b cells.Both MAPK and protein kinase produce cytochrome c and which activate caspase activation and causes cell proliferation. Nf-Kb pathways also produce anti apoptotic genes results in cell proliferation. (Miller et al., 2019; Shishodia 2008; Murthy et al., 2021).

For the treatment of inflammatory conditions

For the treatment of inflammatory conditions Guggulesterone played a vital role by exerting its anti-inflammatory effects through suppression of cytokines. To better understand the role of Guggulsterone on cytokineinduced inflammation, Lv et al. (2015) studied the effect of Guggulsterone on IL-1 β - and IFN- γ -induced beta-cell damage in the islets of Langerhans.Denget al, (2007) reported that guggulsterone eradicated cholesterol metabolites bile acids from the liver by upregulating bile salt export pump.and also proposed a system of antiinflammatory effect by repression of NF- κ B activation by Guggulsterone.Neuder LE et.al (2009) examinesGuggulesterone induce LPS-stimulated macrophageand manipulate the expression of proinflammatory cytokines and suppress the mrna expressions of IL-1 β , TNF- α , and iNOS.

For the treatment of Weight loss

Guggulhad been used as a weight loss aid in Ayurvedic medicine and in 2008 lab study found that the active ingredient in Guggul preparations did cause fat cells to break down. Some studies support the claim that Guggul can be beneficial for weight loss.Urizar et.al (2019) study reveals that taking Guggulsterone phosphate supplement alongside regular exercise led to a significant reduction in fat mass.Miller and Samuels, (2019),studied the understanding of anti-obesity effects of Guggulesterone and direct and indirect stimulation of M2 macrophage polarization. And establish the potential anti-obesity effects of Guggulesterone.To understand the role of Guggulesterone for the treatment of weight loss the following pathway is fig.3.

As we can see in fig .3 that Guggulesterone activates 3T3L1 adipocytes which leads to mitochondrial biogenesis in which cells increase mitochondrial numbers and it regulates the upregulation of UCP1 for ATP synthesis and reuptake of catecholamine leads to weight loss(Miller et al.,2019;Sethi 2011)

CONCLUSION

For treating chronic diseases such as hyperlipidemia, obesity and also inhibit cancer cells as well as in improving the immune system Guggulesterone played a vital role.Due to minute immunomodulatory effect of Guggulesteronefurther research is required obtaining herbal medicinesfor the health benefits of the people.

REFERENCES

1. Chander R, Khanna AK and Pratap R (2002): Antioxidant activity of guggulsterone, the active principal of guggulipid from Commiphora mukul. *J Med Arom Plant Sci* 24: 370-374.
2. Chander R, Rizvi F, Khanna AK and Pratap R (2003): Cardioprotective activity of synthetic guggulsterone (E and Zisomers) in isoproterenol induced myocardial ischemia in rats: A comparative study. *Indian J Clin Biochem* 18: 71-79,
3. ChaudharyG (2012). Pharmacological Properties of Commiphora wightii Intern. *J. of Pharma and Pharmaceutical Sciences*. 4(3), 73-75.
4. CrastoAM(2012) .Gugulipid, an extract of ayurveda medicine plant commiphora mukul as a potent agent for cancer chemoprevention and cancer chemotherapy. *Med chem* 2:e105



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5. Deng R, Yang D, Radke A, Yang J and Yan B (2007): The hypolipidemic agent guggulsterone regulates the expression of human bile salt export pump: dominance of transactivation over farsenoid X receptor-mediated antagonism. *J Pharmacol Exp Ther* 320: 1153-1162.
6. DengR (2007) Therapeutic effects of guggul and its constituent guggulsterone: cardiovascular benefits. *Cardiovasc Drug Rev* 25:375–390.
7. Kulloli RN and Kumar S (2013). *Commiphora wightii*(Arnott) Bhandari:A threatened plant of conservation concern.*J.MEDI.RES.* 7(28):2043-2052)
8. Lv N, Song MY, Kim EK, Park JW, Kwon KB and Park BH (2008): Guggulsterone, a plant sterol, inhibits NF-kappaB activation and protects pancreatic beta cells from cytokine toxicity. *Mol Cell Endocrinol* 289(1-2): 49-59
9. Miller CN, Samuels JS, Azhar Y, Parmar A, Shashidharamurthy R, Rayalam S (2019). Guggulsterone activates adipocyte beiging through direct effects on 3T3-L1 adipocytes and indirect effects mediated through RAW264.7 macrophages. *Medicine* 6 (1), 22
10. Murthy BR,Yelavarthu PR,Devanna N,Basha DJ (2021).Design of Guggul lipid loaded chitosan nanoparticles using box-behnken design .*Journal of Pharmaceutical Research International*33(18):53-67
11. Neuder LE,Keecher JM,Eckert RE,Trujillo JC,Jones SL (2009). Role of p38 MAPK in LPS induced pro-inflammatory cytokine and chemokine gene expression in equine leukocytes.*Veterinary Immunology and Immunopathology* vol 129.
12. Satyavati.G.V, Dwarakanath. C, Tripathi.S. N.(1969) Experimental studies on the hypocholesterolemic effect of *Commiphora mukul* Engl. (guggul). *Indian Journal of Medical Research* Vol.57 pp.1950-1962
13. Shishodia S, Aggarwal BB. (2004) Guggulsterone inhibits NF-kappaB and IkappaBalpha kinase activation, suppresses expression of anti-apoptotic gene products, and enhances apoptosis. *J Biol Chem* 279:47148–47158.
14. Shishodia S, ,Harikumar.KB, Dass.S, . Ramawat.KG and Aggarwal.B(2008) The Guggul for Chronic Diseases: Ancient Medicine, *Modern Targets Anticancer Research* (6A) 3647-3664;
15. Shishodia S and Aggarwal BB (, 2004): Guggulsterone inhibits NFKappaB and IkappaBalpha kinase activation, suppresses expression of anti-apoptotic gene products, and enhances apoptosis. *J Biol Chem* 279: 47148-47158
16. Shishodia S, Sethi G, Ahn KS and Aggarwal BB (2007): Guggulsterone inhibits tumor cell proliferation, induces S-phase arrest, and promotes apoptosis through activation of c-Jun N-terminal kinase, suppression of Akt pathway, and down-regulation of antiapoptotic gene products. 74: 118-130,
17. Singh SV, Choi S, Zeng Y, Hahm ER and Xiao D (2007): Guggulsterone-induced apoptosis in human *Biochem Pharmacol* prostate cancer cells is caused by reactive oxygen intermediate dependent activation of c-Jun NH2-terminal kinase. *Cancer Res* 67: 7439-7449
18. Silva J, Dasgupta S, Wang G, Krishnamurthy K, Ritter E and Bieberich E (2006): Lipids isolated from bone induce the migration of human breast cancer cells. *J Lipid Res* 47: 724- 733.
19. Soni.V, Swarnkar, P. L(2006),conservation strategies for *Commiphora wightii*. An important medicinal plant species *Medicinal Plant Conservation* Vol.12 pp. 40-42
20. Tomar UK,Singhal H,Gaur A,Saini LS (2021).Population Density,Genetic Diversity and Hot Spots of *Commiphora wightii* (arnott) Bhandari in Rajasthan State.*Journal of applied Research on Medicinal and Aromatic Plants* Vol.25.
21. Urizar NL, Liverman AB, Dodds DT, Silva FV, Ordentlich P, Yan Y, Gonzalez FJ, Heyman RA, Mangelsdorf DJ, Moore DD. (2002) A natural product that lowers cholesterol as an antagonist ligand for FXR. *Science* 296:1703–1706





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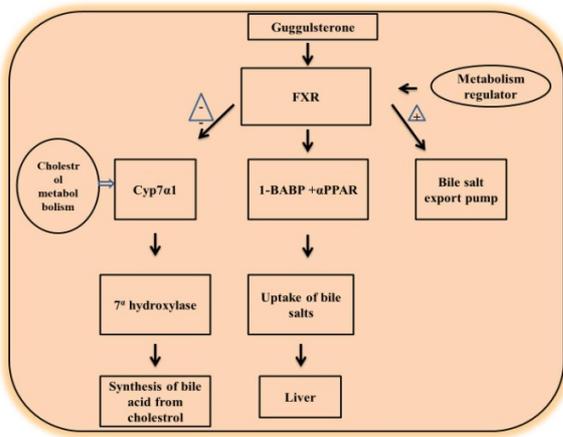


Fig.1. Guggulsterone treating hyperlipidemia

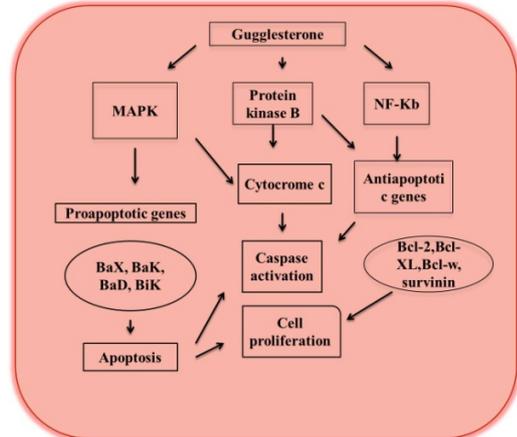


Fig .2. Guggulsterone for treating cancer

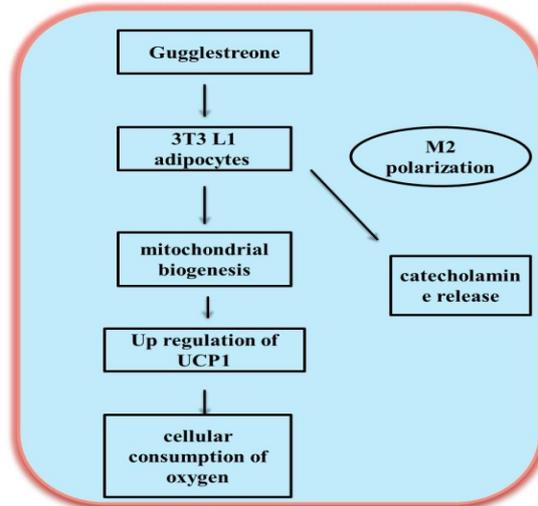


Fig .3. Anti-obesity

