ABSTRACT

‘Guggul’ a common name for all Commiphora species, is the bioactive oleo-gum-resin responsible for the therapeutic effects. Gum, essential oils, flavonoids, ellagic acid, camphorene, cembrene, diterpene hydrocarbon, diterpene alcohol, Z-guggulsterone, E-guggulsterone, guggulsterol-I, II, & III, cholesterol, etc are present. Guggul was introduced as a medicine in 1966, and but approved as a hypolipidemic drug for marketing in India in 1986. Commercially ayurvedic formulations of guggul are Triphala guggulu, Yogaraj guggulu, Kaishor guggulu, Punavadi guggulu, etc. used for detoxification, treating obesity, arthritic conditions, muscle aches, rheumatism, gout, eliminating fluid, helping heart conditions, and inflammations. Now it has been used to treat hypercholesterolemia, impotence, bronchitis, catarrh, sores, tumors, wounds bone fractures, facial paralysis, ulcers, anemia, diabetes, and as a tonic for the uterus, etc. The result from clinical and preclinical studies support the therapeutic claims for gum guggul as mentioned in Ayurveda. However, future clinical studies are required to confirm these claims.

Keywords: Anti-obesity, Anti-rheumatic, Commiphora, Guggulsterone, Gum Guggul, Hypolipidemic

INTRODUCTION

Various Commiphora species belonging to family Burseraceae are the sources of Oleo-gum-resin known as guggul. The name Commiphora originates from the Greek words kommi (means ‘gum’) and phero (means ‘to bear’). The majority of the species yield a fragrant oleo-gum-resin following damage to the bark. More than 200 species of Commiphora are native to the seasonally dry tropics of India, Africa, and Arabia from which majority yields a fragrant oleo-gum-resin on damage to the bark (listed in Table 1)1. The few synonyms of oleo-gum-resin from Indian origin are listed in table 2. In India, guggul grows wildly in Rajasthan, Gujarat, Karnataka and Assam and used as a source of commercial gum guggul2.

Gum guggul has been used to treat various diseases including hypercholesterolemia, atherosclerosis, rheumatism, and obesity over several thousands of years. Guggulsterone is identified as bioactive constituents from gum guggul responsible for its therapeutic effects. Guggul was introduced to the medicine world in 1966 by G. V. Satyavati. Her studies of guggul on rabbits were directly inspired by Ayurvedic text, in which guggul was recommended for the treatment of atherosclerosis and in 1986, guggul was approved as Hypolipidemic drug in India3,4. In the middle 1990s, guggul was introduced as a remedy for hypercholesterolemia and other cardiovascular diseases into the western medical world. In the 1990’s, novel drugs from guggul were developed to treat and manage various cardiovascular disorders such as hypolipidemic, etc. To understand the mechanism at molecular level responsible for the hypolipidemic activity of guggul, substantial research has been made5. Looking upon wide prospects and potential of gum guggul for their novel use addressing the disease and health problems, it is worthwhile to cultivate this plant on large scale especially on unproductive and waste lands. The present review deals with the chemical profile including its pharmacological uses of gum guggul that largely support the therapeutic claims described in the ancient Ayurvedic text.

Botanical Characteristics of Commiphora species: Guggul is oleo-gum-resin obtained by making deep incisions at the basal part of stem bark of Commiphora plant belonging to family Burseraceae6. The common names for Commiphora species is ‘corkwood’ (an indication of the softness of the wood), ‘kanniedood’ (Afrikaans name, means cannot die) etc., an indication of the sustainability of the plant and also refers to the fact that the truncheons grow easily when planted. The characteristic features of the species are very diverse, and thus require a combination of morphological characters for identification. In early autumn, leaves become yellow and shred, and the plant become deciduous for most of the year, and having tendency to produce flowers prior to developing leaves, a very typical feature of Commiphora species7. The guggul tree is 4-6 feet tall, thorny, and free of foliage most of the year with ash-colored papery bark that flakes off into papery flakes, revealing a green bark underneath producing fragrant resins of economic, medicinal and
The under bark also comes off easily. It has also been described as a shrub. Branches are spirally ascending, spinescent and young parts are glandular and pubescent. The leaves are mostly compound, with only a few species bearing simple leaves. Compound leaves are 1-3 foliate whereas leaflets are sessile to sub-sessile, terminal ones the largest, rhomboid to ovate in shape, irregularly toothed margin, alternate phyllotaxy, lateral leaflets when present only less than half the size of the terminal ones (Figure 1). Flowers are small, brown to pink, unisexual, polygamous in fascicles. Glandular hairs are present on calyx, forming cylindrical cap. Petals are 4-5 times as long as sepal. Stamens are 8-10, alternately long and short. Stigmas are 8-10, inconspicuously bilobed. The fruit of Commiphora greatly enhances the identification of the species. Fruit is drupe, red, ovate or acuminate in shape, when ripe, the fruit splits into halves revealing a brightly colored pseudo-aril, the shape of the pseudo-aril differs from species to species. Cultivation and collection of oleo-gum-resin: The Guggul tree grows as a woody tree in sandy loam soil with more gypsum content, with pH 7.5-9. Guggul plant can be propagated both by seed and stem cutting in the arid or semi-arid zones, sloppy well drained lands are preferred for this purpose. The seeds are collected in July-September when the viability is more. The plants are raised through nursery beds and transplanted after 6 months. Oleo-gum-resin is collected from at least 5 years old plants. It is tapped from main stem with 7.5 cm diameter on which deep incisions are made. It should be noted that the resin ducts occur only in bark portions near cambial layer. Thick branches of tree give best grade of guggul. Each plant gives from 0.5-1 kg of guggul per year. Gum resin are secrete either in schizolysigenous ducts or secretion cells; in the former case they are

Table 1: A list of few of Commiphora species

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Table 2: Synonyms of Guggul of Indian Origin

| Synonyms | Indian b'dellium, aflatan, moqi, moqlearzaqi, mukeearahi, gugal, guggul, mukul, ranghanturb, guggala, gugal, goggle, gulag, boeajuhan, gugali, gugar, bhavvishtha, bhutahara, devadhupua, deveshta, dhurta, divya, kumbholu, kumbholukhalaka, kunti, mahishaksha, mahishakshaka, marudishta, nishadhaka, palankasha, pavandvishta, pura, puta, rakshohah, sarvasaha, shamhava, shiva, uddipta, ulukhalaka, usha, vayughna, ranghanturb, jatayu, javayu, ratadumma, mahishakshi etc |

Fig. 1: Leaves stem fruits and gum resin of Commiphora mukul
formed in the epithelial cells, and discharged into the ducts in the form of milky liquids which exude when the ducts are punctured\textsuperscript{10,16}.

Gum resin resides in the ducts of the soft bark of the tree; circular incisions are made on the main stem from which a pale yellow fluid exudates, which is aromatic in nature and quickly solidify to form agglomerates of tears of golden brown or reddish brown colour. The dried resin has bitter aromatic taste & balsamic odour. Application of ether to the incisions enhances guggul production 22 times, long term application of ether enhance the production but eventually kills the plant due to exhaustion\textsuperscript{11}.

Phytochemistry Profile: As the name indicates, guggul is oleo gum resin, chiefly contains resin and gum associated small quantities of volatile oils, bitter principle, enzyme, etc. The oleo gum resin of guggul contains gum (32%) and essential oils (1.45%). The drug also contains amino acid, camphorene, cembrene, allycembro, flavonoids and ellagic acid. Commercial product contains Merceryl alcohol and β-sitosterol were also present\textsuperscript{12}.

The oleo gum resin (Guggul) contains essential oils, containing mainly myrcene, dimycrene & polymycrene. Solvent extraction, hydrolysis and column chromatography over silica gel of guggul resin identifies a number of compounds such as diterpene hydrocarbon, a diterpene alcohol, Z-guggulsterone, E-guggulsterone, guggulsterol-I, guggulsterol-II and guggulsterol-III, cholesterol, sesamin and camphorene (Figure 2)\textsuperscript{13}. Saxena and Sharma reported that the components of the essential oil of C. mukul and their percentages by weight α-pinene, 4.75%; myrcene, 3.50%; eugenol, 14.70%, cadinene, 5.50%; geranial, 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-pinol, 4%; 1,8-cineole (eucalyptol), 3.5%; and unidentified compounds\textsuperscript{14,15}.

Extraction of resinous portion from Gum Guggul: Solvent extraction using ethyl acetate separates the oleo-gum-resin into two parts, i.e. gum and resin. The gum insoluble in ethyl acetate is chemically characterized as carbohydrate and the resinous portion dissolves in ethyl acetate. It was further separated into acidic, basic & neutral fraction that comprised approximately 4%, 0.3% & 95% of the ethyl acetate soluble and insoluble, respectively\textsuperscript{16}. The fractionation of gum guggul is described in figure-3. The crude gum guggul was found to contain 2% guggulsterones and its ethyl acetate extract having 4% - 4.5% guggulsterones. The neutral subfraction contains 4.2% - 4.7% guggulsterones. The ketonic subfraction of the neutral subfraction contains 35% - 40% guggulsterones, from which the 10% E- and Z-guggulsterones (C\textsubscript{21} and C\textsubscript{27} sterols) were present. Guggulsterol IV and guggulsterol V were isolated from the neutral fraction of gum guggul after saponification of the chloroform. Concentrations of guggulsterones in gum guggul may be determined by thin layer chromatography (TLC) and high performance liquid chromatography/mass spectrometry (HPLC/MS) and by a colorimetric method\textsuperscript{16}.

Ethnopharmacological Uses: Guggul means “wards off disease”, an Indian traditional Ayurvedic medication used to treat high cholesterol. Traditional uses are thyroid stimulant, anthelmintic, anti-inflammatory, antiseptic, antispasmodic, aperient, aperitif, astringent, carminative, demulcent, depurative, detergent, diaphoretic, diuretic, enrich blood, emmenagogue, expectorant, hypoglycemic alterative, lithontriptic, liver tonic, sedative, stomachic, stimulant, vulnerary. It is used as appetite stimulant, aphrodisiac, improves the general condition; reduce fever and secretion from diseased surfaces due to its anti-suppurative properties. The gum resin is used for indolent ulcers in lotion dosage form and in caries of the teeth, weak and spongy gums, pyorrhea alveolaries, chronic tonsilis and pharyngitis and ulcerated throat as a gargle. Inhalation of fumes from burning gum is recommended in hay fever, chronic bronchitis, nasal catarrh, laryngitis and phthisis. Smoke resin is mosquito repellent. Guggul is one of constitutes of several indigenous drugs. Guggulipid is useful in heart disease, spondylitis and gout. It is a constituent of Chinese medicine used in extradural haematomas. In India, Yogaraj guggulu (for detoxifying, treating obesity, joint pain, arthritic conditions, muscle aches, rheumatism, and gout), Punavadi guggulu (for detoxifying the kidneys, eliminating fluid, helping heart conditions, and inflammations), Triphala guggulu (for joint pain, arthritic conditions, muscle aches, rheumatism, and weight loss), etc are used\textsuperscript{14-17,20}.

Pharmacological activities: Research studies showed that guggul is effective against aspects of cardiovascular disease. More recently, Commiphora mukul was found to be a relatively safe and effective supplement for osteoarthritsis of the knee & hyperlipoproteinemia\textsuperscript{21-23}. The herb Inula racemosa, in combination with Commiphora mukul, is used to reduce chest pain and dyspnea of angina Guggulsterone may be of therapeutic benefit in diseases associated with oxidative stress, such as myocardial ischemia and neurodegenerative diseases (Figure 4)\textsuperscript{4}.

Hypolipidemic activity: To evaluate the effects of guggul on disorders of lipid metabolism, with special reference to atherosclerosis and obesity, Satyavati et al. conducted the first animal study on rabbits, from 1964-1966. It was demonstrated that administration of gum guggul significantly lowered the serum cholesterol levels of hyperlipidemic rabbits, prevented cholesterol-induced arteriosclerosis and decreased the body weight of the animals\textsuperscript{24}. The study by Satyavati et al. did not examine the effect of guggul on triglyceride levels; however, another study by Singh et al. examined the effect of guggulsterone on cholesterol and triglyceride levels in rats\textsuperscript{4,24}. Chander et al. examined the effect of guggulsterone on serum lipid levels in triton- and cholesterol fed rats, significantly reduced serum lipid levels\textsuperscript{25}.

With a view to understanding the mode of action of lipid lowering drugs, the effect of guggulsterone on lipid and lipoprotein metabolism was investigated in triton and cholesterol induced hyperlipidemic on rats by Burnstein.
Fig. 2: Chemical constituents of guggul gum resin

Fig. 3: Extraction of Guggulosterone from gum- guggul
in 1985. Animals that received guggulipid had significantly reduced serum cholesterol, triglyceride, and phospholipids levels and atherogenic index. Free fatty acid levels in serum, liver and heart were also significantly decreased, where as lipolytic activity was increased in liver and heart. Guggulipid inhibited liver cholesterol biosynthesis and increased excretion of bile acids and cholesterol in the feces. The crude gum guggul containing the E- and Z-guggulsterones have hypocholesteremic activity. The acidic fraction of gum guggul possesses significant anti-inflammatory activity; the neutral fraction possesses lipid lowering activity. The lipid lowering activity is found in ketonic fraction, which is a complex mixture of chemical compounds belonging to steroids. Numerous scientific studies have shown guggulipid effectively supports healthy levels of cholesterol and triglycerides. Guggulipid supports low levels of LDL ("bad") cholesterol and high levels of HDL ("good") cholesterol means hypolipidemic effect. The effect of dietary guggulipid on serum lipid levels was also evaluated in Fisher rats. Guggulpid decreases in serum levels of triglycerides, LDL, and VLDL and increases in serum levels of HDL were dose dependent. In the randomized controlled clinical trial of guggulipid failed to decrease the levels of LDL cholesterol in healthy adults with hyperlipidemia eating a typical western diet. Furthermore, there were no significant changes in total cholesterol, HDL, triglycerides, LDL. Administration of gum guggul partially reversed the atherosclerosis in the aorta that was induced by the high fat diet.

A standardized fraction from ethyl acetate extracts of guggul containing guggulsterone mixed with some other steroids, diterpine, esters & higher alcohols were effective in the treatment of hypercholesterolemia and atherosclerosis, provided the first experimental evidence to support claims in the Ayurvedic text as hypolipidemic drug. Several animal studies and clinical trials have been performed to evaluate the hypolipidemic effects of guggul. Guggul Markedly inhibits liver cholesterol synthesis by acting on HMG-CoA then decreased the LDL Level and increased the HDL Level.

Guggulsterones E and Z are responsible for the lipid lowering properties of guggul in human blood and at least four mechanisms have been proposed to explain their activity. First, guggulsterones-I might interfere with formation of lipoproteins by inhibiting biosynthesis of cholesterol in the liver. Guggulsterones-II has been shown to enhance the uptake of LDLs by the liver through stimulation of LDL receptor–binding activity in the membranes of hepatic cells. Guggulsterones-III increase fecal excretion of bile acids and cholesterol, substantially decreasing the rate of absorption of fat and cholesterol in the intestine.

Guggul-fed hypercholesterolemia induced male albino rabbits had significant decreases in the level of cholesterol and body weight. Whereas the lipid-lowering action of guggulipid was compared with that of S-methyl cysteine sulfoxide isolated from *Allium cepa* in Sprague-Dawley rats.

Cardio-protective effects: Several studies have reported the cardioprotective activity of guggulsterone that showed the reversal of isoproterenol-induced cardiac damage and the associated metabolic changes in rats. The cardioprotective activity of gum guggul in Combination with *Inula racemosa* was examined in 200 patients suffering from ischemic heart disease who had abnormal electrocardiogram (ECG) and chest pain. After treatment with guggul for 6 months, the levels of total cholesterol, triglyceride and total blood lipids were decreased. Moreover, normal ECG was restored in 26% of the patients and more than 50% of patients showed improvement in the ECG. Chest pain subsided in ¼ of the patients and decreased in the rest of the patients. The results suggest that guggul has cardioprotective benefits in patients with ischemia.

Neuroprotective effect: Guggulipid reversed streptozotocin induced neuronal damage and memory deficits. In parallel with these reversals, levels of glutathione in the brains of guggulipid-treated mice were significantly increased, suggesting that guggulipid inhibits oxidative stress in the brain. Guggulipid has an antioxidant and anti-acetylcholine esterase activities; showed protective effect against streptozotocin-induced memory deficits in the model of dementia. These observations suggest guggulipid as a potential anti-dementia drug and cognitive enhancer.

Antioxidant activity: In Indian system of medicine *Commiphora mukul* is an important medicinal plant its resinous part has been used in various ailments and as health tonic. To understand the mechanisms of pharmacological actions, the *in vitro* antioxidant activity of ethyl acetate extract of *Commiphora mukul* was investigated for reducing power activity and total antioxidant activity. The ethyl acetate extract of *Commiphora mukul* exhibited good reducing power and anti-lipid peroxidation activities were determined by thiocyanate method. *Commiphora mukul* extract increase the absorbance of the reaction mixture indicates stronger reducing power when studied according to the method of Oyaizu (1986).

Anti- Arthritis Activity, Analgesics and Anti-Inflammatory Activity: Guggul reduced the thickness of the joint swelling during the course of drug treatment, indicating that gum guggul has a beneficial role in experimental arthritis. Gum guggul appeared to be a relatively safe and effective supplement to reduce symptoms of osteoarthritis after 1 month treatment and significantly improve the WOMAC (Western Ontario and McMaster Osteoarthritis Index) total score and continued to further improvement on long term uses and after 2 months of treatment with no side effects were reported during the trial. A well documented ayurvedic literatures and variety of preparations is available on analgesic and anti-inflammatory actions of guggulipid.

Anticancer Activities: Guggulsterone has been shown to induce apoptosis and suppress proliferation, invasion, angiogenesis and metastasis of tumor cells. Various mechanisms have been suggested to explain the anti-carcinogenic effects of guggulsterone, including...
Table 4: Marketed formulation of guggul

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<th>S. No.</th>
<th>Name</th>
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<tr>
<td>1.</td>
<td>Triphala Guggul</td>
<td>Triphala Guggul is a compound extract (of triphala) to which guggul is added. It is for joint pain, arthritic conditions, muscle aches, rheumatism, and weight loss. (Ayurveda Bazar, India)</td>
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<td>2.</td>
<td>Yogaraja Guggul</td>
<td>It is an anti-arthritic herbal supplement useful for joint pain, genito urinary disorders, obesity. (Ayurveda Bazar, India)</td>
</tr>
<tr>
<td>3.</td>
<td>Kaishora Guggul</td>
<td>It is used as a blood purifier it is helpful in Athlete’s foot and helps in elimination of toxins from the joints. It supports healthy metabolism in the body and maintains healthy white blood cells and liver. (Herbs Forever, USA)</td>
</tr>
<tr>
<td>4.</td>
<td>Mahayograj Guggul</td>
<td>It is used in the Ayurvedic treatment of joint diseases, skin diseases, piles, sprue, diabetes, gout, fistula, bloating, emaciation, low digestion power, asthma, cold, cough, anorexia, male and female infertility. (<a href="http://ayurmedinfo.com/2012/02/17/mahayograj-guggul-benefits">http://ayurmedinfo.com/2012/02/17/mahayograj-guggul-benefits</a>)</td>
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<td>5.</td>
<td>Navaka Guggul</td>
<td>It is widely used in the Ayurvedic treatment of weight loss, it improves digestion. It is also used to relieve Rheumatoid arthritis. (<a href="http://ayurmedinfo.com/2012/05/13/navaka-guggulu-benefits-dosage-how-to-use-side-effects-ingredients/">http://ayurmedinfo.com/2012/05/13/navaka-guggulu-benefits-dosage-how-to-use-side-effects-ingredients/</a>)</td>
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<td>6.</td>
<td>Singhnad Guggulu</td>
<td>Useful for Lack of Appetite, Abdominal gas, Dysentery, Spasm digestion, gout. (Ayurveda Bazar, India)</td>
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<td>7.</td>
<td>Gokshuradi Guggulu</td>
<td>It is an outstanding remedy in urinogenousal problems, promoting urine flow, soothing the mucosa, and aiding in the excretion of stones and calculi. It supports kidney and bladder health, detoxification of the urinary tract and also support against enlarged prostate, urinary tract disorders, urinary Stones, inconsistent Urination. (Herbs Forever, USA)</td>
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<td>8.</td>
<td>Kanchanara Guggulu</td>
<td>It can be used to address deep-seated kapha imbalances. It supports healthy tissues including muscles, fat and bones as well as the thyroid and the lymphatic system. It is useful in Tumors and Goitre. (Banyan Botanicals, USA)</td>
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<td>9.</td>
<td>Trayodashanga Guggulu</td>
<td>Useful in Sciatica and nerve related pain, increase the number of red blood cells and used to promote appetite and digestion, increase the number of red blood cells, and aid in removal of undesirable fat in the body. (Ayurveda Bazar, India)</td>
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<td>10.</td>
<td>Laxadi Guggul</td>
<td>It is particularly helpful for healing broken bones, fractures, osteophytes removal. It is really an excellent natural formula to enhance calcium deposition on bones. (Ayurveda Bazar, India)</td>
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<tr>
<td>11.</td>
<td>Amrutadi Guggul</td>
<td>Useful in obesity, lowers cholesterol, also beneficial in other conditions like pimples, puss boils, hair follicle boil and buttock boils. (Ayurveda.com)</td>
</tr>
<tr>
<td>12.</td>
<td>Saptavinshati Guggulu</td>
<td>It is used for the treatment of any types of worm infestations in the body. And moreover this is beneficial in any age group of patients and is not specifically for a special age group. (Ayurveda Bazar, India)</td>
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Inhibition of ROI, suppression of inflammation and inhibition of nuclear receptors, transcription factors, and inflammatory cytokines, anti apoptotic proteins, cell survival pathways, COX- 2, MMP-9, iNOS and cell cycle-related proteins. Proliferation: Guggulsterone suppresses the growth and proliferation of a wide variety of tumor cells, including leukemia, head and neck carcinoma, multiple myeloma, lung carcinoma, melanoma, breast carcinoma and ovarian carcinoma. Besides suppressing proliferation, guggulsterone induces apoptosis in a wide variety of cells in a dose dependent manner. Guggulsterone suppresses the invasion, angiogenesis, metastasis through down-regulation of the expression of NF-κB-regulated gene products. Hepatoprotective effect: Pretreatment with the ethanolic extract prevented prolongation of the barbiturate sleeping time associated with carbon tetrachloride-induced liver damage in mice and replenished the low-level nonprotein sulphydryl concentration in the liver. The ethanolic extract of the gum of Commiphora opobalsamum, lowered the serum levels of transaminases, alkaline phosphatase and bilirubin in carbon tetrachloride-induced hepatotoxicity. Leaves and bark of Commiphora caudate & Commiphora berriy; gum extract of Commiphora mukul have significant hepatoprotective activities etc. Thyroid-stimulatory effect: Several studies have shown that guggulsterone stimulates the thyroid gland showed that administration of guggulsterone restored thyroid activity like an increase in iodine uptake by the thyroid and enhanced the activities of thyroid peroxidase and protease as well as oxygen consumption in hypothyroid rats.

Antihelminthic Activity: The antihelminthic effects of mirazid (from Commiphora molmol) have been extensively reported. Antibacterial Activities: It has been reported that the essential oil, chloroform extract and seven sesquiterpenoid compounds from the oleo-gum-resin of
**Conimphora mukul** showed the inhibitory action against both gram-positive and gram-negative bacteria\(^4\). Nodulocystic Acne Treatment: Guggulipid has been reported to be effective in the treatment of nodulocystic acne. Patients with nodulocystic acne had shown progressive reduction in lesions when received guggulipid for 3 months and patients with oily faces the acne responded better to guggulipid\(^5\). In the table 4 the ayurvedic preparations having gum guggul as one of the main ingredient are tabulated by market survey of various states of India.

**CONCLUSION**

From the ancient times, plants have been used for treatment of variety of disease. Guggul preparations are widely available and employed by practitioners traditionally in natural health for treatment of detoxifying, obesity, joint pain, arthritic conditions, muscle aches, rheumatism, and gout. Research studies showed that guggul is effective against aspects of cardiovascular disease. More recently, guggul was found to be a relatively safe and effective supplement for osteoarthritiss of the knee. To understand the molecular mechanisms responsible for the diverse pharmacological effects of guggul, vast research studies are going on. The present review describes the various updated research of guggul & novel use in the various disease and health problems.

**REFERENCES**


