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**THERAPEUTIC POTENTIAL OF *COMMIPHORA WIGHTII* IN THE
MANAGEMENT OF RHEUMATOID ARTHRITIS**

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ABSTRACT

Rheumatoid arthritis, or RA, is a chronic inflammatory and autoimmune illness caused by an imbalance in the immune system's control of the synovial joint membrane. Patients have shown tolerance to anti-RA drugs, and conventional dose forms—such as pills and tablets—are mostly used or readily accessible. Another name for the species *Commiphora wightii* is the Indian Bdellium-tree. This species is indigenous to Pakistan and India. Gujarat and Rajasthan are also native to it. It provides guggul gum, which is the most valuable resin in Indian medicine. Indian bdellium, a pale- yellow gum-resin with a fragrant scent released by the plant, is scraped and extracted into the Guggul of trade. Guggul's ability to lessen joint edema thickness suggests that it may be helpful in care of arthritis. It was just found out that Commiphora Mukul is beneficial against osteoarthritis of the knee. Guggul and ketoprofen have been combined to formulate guggulosomes, which have demonstrated a synergistic effect. Guggul has demonstrated that in studies, guggul a viable carrier for the making of sustained release medications.

Keywords: Rheumatoid arthritis, Inflammation; *Commiphora wightii*, Guggul, Guggulsterones.



1. INTRODUCTION

Rheumatoid arthritis, or RA, is a chronic inflammatory and autoimmune illness caused by an imbalance in the immune system's control of the synovial joint membrane.^{1,2} This leads to significant loss of cartilage and bone. The illness is marked by protracted synovial membrane inflammation, which usually results in the loss of articular cartilage and bone as well as irreversible deformity.³ Inflammatory arthritis of the joints is caused by activated pathogenic T cells migrating from the peripheral lymphoid tissues into the synovial tissue of the joints, mostly mediated by a chemotactic process. This produces an inflammatory milieu that draws additional cell types to the area, including fibroblasts, neutrophils, and macrophages. These cells work together to cause joint inflammation, bone destruction and cartilage, along with different effector molecules such as prostaglandins, proteolytic enzymes, cytokines, and other osteoclastogenic agents.⁴ The main objective of RA treatment is to decrease pro-inflammatory mediators such thrombin, TNF α , and IL-1 β . Failure to receive care in a timely manner might leave patients disabled or even dead. Studies has reported that preventing impairments and lowering the death and disability rates can be achieved with early sickness detection and management. To treat the rheumatoid arthritis there are various pharmacological classes (NSAID), and biologics and (DMARD). NSAIDs of the propionic acid class that has analgesic and antipyretic properties is ketoprofen. It works by preventing the body from producing prostaglandins (PGs), that are responsible for inflammatory symptoms associated with arthritis. Pain and inflammation can be relieved with ketoprofen. It is authorized for the treatment of fever, inflammation, menstrual pain, osteoarthritis, rheumatoid arthritis, and pain. By lowering levels of PGs, a hormone-like molecule that typically increases inflammation, it might aid in the reduction of edema. This medicine may make heart attacks and strokes more likely, which can be life-threatening cardiac events. If you take it frequently at large dosages, your risk may increase. It can also induce high BP or exacerbate pre-existing high blood pressure, and increase your chance of breathing difficulties, hives, or another significant allergic reaction and the adverse effects of anti-RA medications, including myelosuppression, stomatitis, depilation, respiratory symptoms such pneumonitis, liver dysfunction, kidney dysfunction, and digestive organ dysfunction. Additionally, patients have shown tolerance to anti-RA drugs, and



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conventional dose forms—such as pills and tablets—are mostly used or readily accessible. Other kinds of dosage forms include topical and parenteral. Parenteral preparations have the disadvantage of not offering control or adjustment of drug release and withdrawal, if necessary, despite their promise of 100% bioavailability. Similar to this, a solid dosage form exhibits a typical peak-valley effect that could cause a variation in the drug's plasma concentration. For medications with short therapeutic indices, maintaining the steady-state concentration can be challenging under certain situations. Furthermore, a patient's failure to comply with medication regimens, especially for medications with short half-lives that require frequent administration, poses a constraint.^{5,6,7} Overall, the difficulties with conventional dosage forms—such as dose variability, high dose requirements, and patient noncompliance—lead to decreased efficacy, toxicity, and adverse drug reactions, which renders modern medication therapy inappropriate.^{8,9} To overcome these problems Guggulosomes, which demonstrate a synergistic impact and lessen medication side effects, are made by combining guggul and ketoprofen. Each of these problems Guggulosomes have been created by combining guggul and ketoprofen, which has shown to have a synergistic impact and lessen medication adverse effects. According to studies, guggul can be employed as a carrier for developing medications with sustained release. There are numerous ways to apply topically, consume, or absorb Ayurvedic preparations.^{10,11} However, traditional methods of administering herbal medications to patients are not necessarily the most effective. Nonetheless, various drug delivery strategic created to improve drug release over time, reduce drug degradation, and maximize bioavailability.¹² Currently, drug molecules can be incorporated into carrier systems such liposomes, ethosomes, metal nanoparticles, and polymers to control drug release efficiently. Due to larger surface area, solubility, bioavailability, stability, and capacity to distribute drugs in a regulated and targeted manner, nanosized carriers are thought to be the most successful of the many drug delivery methods.



2. MEDICINAL HERBS FOR ARTHRITIS¹³⁻¹⁶

- *Withania somnifera*
- *Boswellia serrata*
- *Curcuma longa*
- *Commiphora wightii*
- *Zingiber officinale*
- *Pongamia pinnata*
- *Betula platyphylla*
- *Piper nigrum*

3. *COMMIPHORA WIGHTII*

Another name for the species *Commiphora wightii* is the Indian Bdellium-tree. This species is indigenous to Pakistan and India. Gujarat and Rajasthan are also native to it. Guggul is significant plant for medicine. Guggul is used for a wide range of disease conditions, including atherosclerosis, from ancient Indian medical system known as Ayurveda. These conditions include obesity, rheumatism, hypercholesterolemia, and atherosclerosis. This deciduous shrub can reach a height of 4 meters. The leaves are three to five centimeters long, with rounded tips and bases. The other vein is not as long as the main vein.^{17,18}

It provides guggul gum, which is the most valuable resin in Indian medicine. Indian bdellium, a pale- yellow gum-resin with a fragrant scent released by the plant, is scraped and extracted into the Guggul of trade.^{19,20}



Table 1: Brief information of guggul resin^{21,22}

Synonyms	Scented bdellium
Botanical name	Commiphora mukul
Plant family	Burceacea
Common name	Guggul, Gum guggul, Guggulu, Gugulipid, Mukul myrrh tree, Salautree u uli id.
Part used	Oleo gum resin
Colour	Brown to pale yellow
Odour	Agreeable, Aromatic and Balsamic
Solubility	When triturated with water, it forms milk emulsion

4. TRADITIONAL USE OF GUGGUL

Guggul lipid has a long history of use in Ayurveda medicine. In many Ayurvedic treatises, such as Charaka Samhita and Sushruta Samhita, guggul's action, applications, and indications, including its variants, are covered in detail. Furthermore, several medical lexicons were composed between the 12th and 14th centuries AD. It lowers fat and is recommended to treat everything from inflammation, arthritis, atherosclerosis, obesity, and hyperlipidemia to bone fractures.^{23,24}

Guggul is typically administered as a yog, which is a concoction of guggul, castor oil, and Indian clarified butter. Guggul is commonly found in the following popular Ayurvedic formulations: Triphla guggul, Kaishore gugguluvati, Yograj Gugguluvati, and PachPachamrit loh guggul.²⁵



5. PHARMACOLOGICAL ACTIVITIES

Studies have revealed that it possesses pharmacological properties, and ongoing investigations aim to uncover more potential uses for it in the oversight of other ailments.²⁶

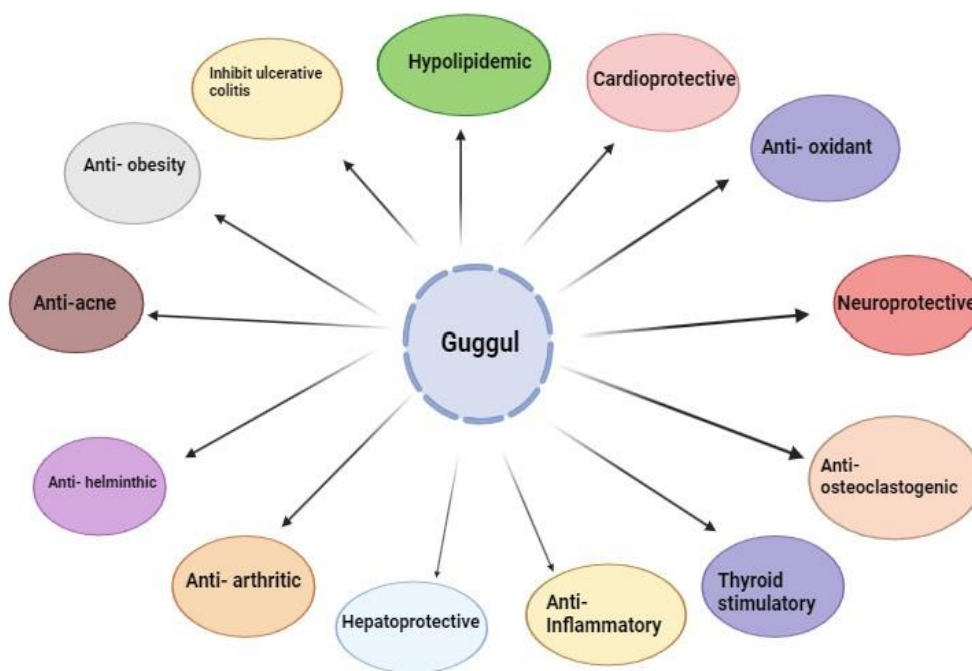


Fig.1: Pharmacological activities of guggul

5.1 Anti- Inflammatory effect

Guggul's ability to lessen joint edema thickness suggests that it may be helpful in care of arthritis. It was just found out that Commiphora Mukul is beneficial against osteoarthritis of the knee. Guggul and ketoprofen have been combined to formulate guggulosomes, which have demonstrated a synergistic effect. Guggul has demonstrated that in studies, guggul a viable carrier for the making of sustained release medications. Numerous inquiries have demonstrated that the triterpene myrrhanol A, which is derived from guggul, exhibits anti-inflammatory properties. Guggul



medication delivery methods that are novel. Guggulsterone is essential in suppressing inflammation because it activates NF-kappa B.²⁷

6. ACTIVE CONSTITUENT

The essential oil that makes up 0.37% of the oleoresin is mostly composed of myrcene, dimyrcene, and polymyrcene. Numerous methods, including solvent extraction, hydrolysis, and column chromatography, have become accustomed to guggul resin. In guggul lipid several active constituents are identified, including camphorene, cholesterol, sesamin, Z-guggulsterone, E-guggulsterone, Guggulsterone-1, Guggulsterone-2, and Guggulsterone-3. Guggul lipid also produced a diterpene alcohol. Using ethyl acetate as the solvent, the solvent extraction method separates the two fractions into a 45% soluble and a 55% insoluble fraction. Guggul-lipid, or the soluble component, has been demonstrated to contain bioactive chemicals, but the insoluble portion is devoid of any therapeutic benefits. As soluble guggul-lipid is further fractionated, two little acid-base fractions (4% and 1%, respectively) and a substantial neutral fraction (95%) with the highest concentration of bioactive chemicals are formed. The neutral component fractionates to yield a minor ketonic fraction of 12% and an isolated non-ketonic fraction of 88%. It is discovered that the non-ketonic neutral component lowers lipid levels because it forms two significant steroids, Z- and E-guggulsterones. The basic fraction is inert, while the acid portion exhibits anti-inflammatory properties.²⁸

7. GUGGULOSOMES

Guggulosome is a new carrier, first name reported by Dr. V. B. Gupta through his patent (Indian Patent application No. 1715/DEL/2004). The concept uses Guggul lipid as a raw material for preparing the vesicles termed "GUGGULOSOMES". In this patent investigations on these vesicles for entrapment of anti-inflammatory drug. Guggulosomes are a novel type of medicinal carrier that resemble lipid and biofilms in their bilayer structure. Guggulosomes mostly made up by phosphatides, either synthetic or naturally occurring. Guggulosomal encapsulated drugs can deliver different tissues and thins to the guggulosome, drug is released by destroying the guggulosome membrane, which is located in the target site. In guggulosomes, ketoprofen were



used as drug which has anti-inflammatory property which resembles with property of guggul lipid and causes synergistic effect also help in reducing drug dose in formulation and helps in minimizing side effect.²⁹

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