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Anti-inflammatory and Anti-oxidant Activity of Oleo-Gum Resin of *Commiphora mukul* Hook. ex Stocks, a Herbal Drug used in the Management Rheumatoid Arthritis

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ABSTRACT

Commiphora mukul Hook. ex Stocks is a well-known medicinal plant and its gum is commonly known as *Muqil* or *Guggul*, which is an important herbal drug, widely used in the treatment of many clinical conditions, such as rheumatoid arthritis, hyperlipidemia, and obesity. Out of 165 species, 5 species of the plant are found in India. *Muqil* has been used either single or in combination with other drugs in Unani as well as Ayurvedic system of medicine for centuries. It is an oleo-gum resin obtained by making deep incision at the basal part of stem bark of *Commiphora mukul* belonging to the family Burseraceae. *Muqil* contains special group of steroidal compounds called guggulsterone, which are responsible for its therapeutic activity. E and Z guggulsterone are major constituents, which account for its use in arthritis. Other bio-active alkaloids present in *Muqil* include Naringenin, Cembranoids, Myrrhanol-A, Ellagic-acid, L-arabinose, Myrrhanol B, Muscanone, Diayamgambin, Quercitin,1-8 cineole, Mansumbinoic acid and Mansumbinone. Various preclinical and clinical studies have been conducted to evaluate its pharmacological activities. In this review paper, an attempt has been made to explore anti-inflammatory and anti-oxidant activity of *Muqil*, a herbal drug, used in the management of Rheumatoid-Arthritis.

Keywords: *Commiphora mukul*, *Muqil*, Anti-inflammatory, Anti-oxidant, Rheumatoid Arthritis, Unani Medicine

INTRODUCTION

Rheumatoid arthritis is an autoimmune inflammatory disease that causes pain, swelling and morning stiffness. Commonly involved joints are PIP joints of the fingers, MCP joints, wrists, knees, ankles and MTP joints(Tierney Lawrence M, Mcphee Stephen J, 2005). Usually peripheral joints are involved in this disease(Subramoniam, Madhavachandran and Gangaprasad, 2013). RA affects approximately 0.5-1% of the population worldwide. In India, the prevalence of RA is 0.5% to 0.75%. It is more commonly seen in females than in males, with a ratio of 3:1. The peak age of onset is between 30 and 50 years(Walker BR, Colledge NR, Ralston SH, 2014). The characteristic feature of RA is persistent inflammatory synovitis which usually involves peripheral joints in a symmetric manner(Jameson JL, Kasper DL, Hauser SL, 2015). In severe cases, the synovial inflammation leads to articular cartilage damage, bone erosion and subsequently it leads to changes in joint integrity(Subramoniam, Madhavachandran and Gangaprasad, 2013). RA is characterized not only by local inflammation, but also by systemic inflammation. Different autoimmune and inflammatory processes are variably active in RA, making the entire disease entity clinically and patho-biologically heterogeneous(Kadhim, Kaizal and Hameed, 2017). Extra articular manifestations are subcutaneous nodules, interstitial lung diseases, pleural effusion, pericarditis, splenomegaly with leukopenia and vasculitis are also seen in RA(Tierney Lawrence M, Mcphee Stephen J, 2005).

PATHOGENESIS OF RHEUMATOID ARTHRITIS

The inflammatory immune process exacerbates the activation of immune cells by enduring production of pro-inflammatory cytokines and chemical mediators in the synovial membrane(Benito, 2018), leading to synovial membrane inflammation, accumulation of excess synovial fluid, hyperplasia of synovial cells, and the development of pannus in the synovium(Wadekar, Sawant and Patel, 2015). Chemical mediators such as prostaglandins, leukotrienes, vasoactive amines, kinins, endothelins, reactive oxygens, neutral proteinases and cytokines such as,interleukin-1 (IL-1), IL-6, IL-8, TNF, platelet derived growth factor (PDGF), GM-CSF and M-CSF are constantly produced by the rheumatoid synovium resulting in joint destruction. Macrophages are also responsible for the development of inflammation, but activation of different subtypes of T-cells has a key role in the progression and perpetuation of the process. TNFα, via its receptors TRNR-I and TNFR-II, contributes to the pathologic state of RA by activating T-cells(Benito, 2018). In addition, free radicals are indirectly responsible for the joint damage, and they play an important role as secondary messengers in inflammatory and immunological cellular response in Rheumatoid Arthritis and they can directly affect joint cartilage by attacking its proteoglycan and inhibiting its synthesis. In a study done by Moncada *et al*., 1991, it was concluded that overproduction of nitric oxide is associated with oxidative stress, which is involved in the pathogenesis of cardiovascular diseases, diabetes, rheumatoid arthritis, neurodegenerative diseases, or chronic inflammation. The pathology of the disease process often leads to the destruction of articular cartilage(Wadekar, Sawant and Patel, 2015).

UNANI CONCEPT OF RHEUMATOID ARTHRITIS (Munshi Y, Huma R et al 2013, Samarqandi 2009)

In the classical Unani texts, *Waja'al-Mafāṣil* is broadly explained, and it is correlated with a chronic inflammatory joint disease, rheumatoid arthritis(Munshi *et al.*, 2016). *Waja 'al-Mafāṣil* is an Arabic term, where *Waja* 'means 'pain' and *Mafāṣil* means 'joints. *Waja 'al-Mafāṣil* is also known as *Gathiya*. When all the joints of the body are painful, it is called *Waja 'al-Mafāṣil* Aam (Majūsī, 1889), and when pain and inflammation is in smaller joints of hands and feet, it is known as *Waja 'al-Mafāṣil* khas (Rheumatoid Arthritis). *Waja 'al-Mafāṣil* is a painful or inflammatory condition, which occurs in joints and the structure surrounding the joints like muscle and ligaments. It may involve any joint, including knee, hips, wrists, hands etc. Sometimes due to inflammatory condition other vital organs like heart and lung are also involved in *Waja'al-Mafāṣil*(Samarqandi, 2010). Many scholars believe that it is having a strong relation with temperament of individual, *Balghami* temperament individuals are more prone to this disease, and *Damawī, Safrāwī* and *Sawdawi* temperament individuals get least affected by this disease.

OPINIONS OF UNANI SCHOLARS

Some of the Unani scholars stated that this disease occurs due to accumulation of vitiated matter in the joints, which is a main cause for pain and inflammation (Azam, 2011).

Ibn Sīnā: Ibn Sīnā stated that *Waja 'al-Mafāṣil* is the pain of joints which includes the pain in great toe, in the disease Gout (*Niqris)*, Sciatica ('*Irq al-Nasā*) and various other types of joint pain. He also mentioned that *Waja'al-Mafāṣil* is caused by phlegm, blood, yellow bile and black bile in the decreasing order (Mohammad, 2014).

Zakariyya Rāzī: *Zakariyya Rāzī* stated that "*Waja'al-Mafāṣil* is a disorder of joints which occurs in the form of attacks, which are paraoxysmal and recurrent in nature; he also adds that this disease is caused by the accumulation of excessive fluids (Arzāni, 2010).

'Allamā Najīb al-Dīn Samarqandī: *'Allamā Najīb al-Dīn Samarqandī* believed that *Waja'al-Mafāṣil* is that pain and inflammation ,which occurs in the joints of the organs(Chandpuri, 1984).

'Allamā Nafīs: *'Allamā Nafīs* elaborated the above definition and stated that this condition occurs in the adjoining structures of joints like synovial membrane, cartilage, ligaments, tendons and muscles (Razi, 2004).

Ismāī'l Jurjānī: *Ismāī'l Jurjānī* explained in the 12th century that when the vitiated material (*Mawād-i Fuzūnī*) get accumulated inside the joints of organs, it results in inflammation and pain, and the condition is called *Waja 'al-Mafāṣil*.

According to Samarqandi, the substance which is responsible for the cause of *Waja 'al-Mafāṣil* is of a very thick consistency and white in colour, whereas *Ibn Sīnā* stated that this substance almost resembles to pus (*Rīm*). Humours responsible for the development of *Waja'al-Mafāṣil* may be of four types based on the humours involved: *Waja 'al-Mafāṣil Balghamī, Waja 'al-Mafāṣil Damawī, Waja 'al-Mafāṣil Safrāwī* and *Waja 'al-Mafāṣil Sawdāwī* (Sina).

HISTORY(Razi, 2004)(Tabri,2010)(Majūsī,1889)

Waja'al-Mafāṣil is a disease whose history is as old as the history of human beings; this disease is thoroughly elaborated in Unani classical literature. Some evidences reveal the presence of disease in the era of dinosaurs. This malady did not even spare historical personalities like Alexander 'The Great' (356-323 BC). This disorder was well described in the old Egyptian, Greek and Roman medical classics and thoroughly elaborated in Unani Classical literatures. Hippocrates presented the first compendium on the disease in the book known as *Kitāb al-Mafāṣil*, and Dioscorides (70 AD) described the disease in details in his book *Kitāb al-Hashāi'sh*. Rufus (117 AD) prepared the next compendium on the disease having title *KitābAuja al-Mafāṣil*, and Galen (129-217 AD) discussed the disorder in his book *Kitāb al-Elal-wal-Amrāḍ*. It is very common problem of old age, but may start in earlier stage of life, especially when there is predominance of *Balgham* along with obesity, indigestion, poverty, exposure to cold and humid climates. According to Samarqandi, *madda* (substance) responsible for the development of *Waja'al-Mafāṣil* is of a very thick consistency and white in colour, whereas Ibn Sīnā states that this *madda* almost resembles to pus (Reem). Ibn Sīnā also mentioned that *Waja'al-Mafāṣil* is caused by phlegm, blood, yellow bile and black bile in the decreasing order of frequency, i.e. *Waja'al-Mafāṣil Balghami* is more common, *Waja'al-Mafāṣil Damawī* is common, *Waja'al-Mafāṣil Safrāwī* is less common and *Waja'al-Mafāṣil Sawdāwī* is rare.

TREATMENT(Walker BR, Colledge NR, Ralston SH,2014, Jameson JL, Kasper DL, Hauser SL 2015)

Although NSAIDs and analgesics may provide pain relief, they are largely palliative and associated with serious side effects, including gastritis, peptic ulcer disease as well as impairment of renal function. DMARDs are not so effective and they are also associated with side effects such as irreversible retinal damage and cardio-toxicity by hydroxychloroquine; myelosuppression, hepatotoxicity, and alopecia by methotrexate; and reactivation of latent TB and increased risk of bacterial and fungal infections by TNF-α antagonists. Failure to achieve adequate improvement with DMARD therapy and its significant side effects call for consideration of new alternative therapies with superior efficacy and safety to maximize response and minimize side effects, which can bring the disease under control and nearer to remission.

There are so many single and compound drugs mentioned in Unani system of medicine for the treatment of *Waja'al-Mafāṣil*.

Single drugs (Mufradat)(kabeeruddin)(Usmani, 2008)

Suranjan *(Colchicum luteum Baker),* Bozidan *(Tanacetum umbelliferum),* Asgandh *(Withania somnifera),* Filfil Siyah *(Piper nigrum),* Turbud *(Operculina terpethum),* Khardal *(Brassica nigra Linn),* Zanjabeel *(Zingiber officinale),* Sana Maki *(Cassia augustifolia),* Mako (*Solanum nigrum),* Halela Siyah *(Terminalia chebula),* Kasni *(Chicorium intybus Linn),* Badiyan *(Foeniculum vulgare),* Baboona *(Matricaria chamomilla),* Sibr *(Aloe barbadensis)*

Lufah *(Atropa belladona),* Marzanjosh *(Origanum majorana),* Muqil *(Commiphora mukul)*

Nakhoona *(Astragalus hamosus),* Qunturyoon *(Centauria centaurium),* Qust *(Saussurea lappa),* Saqmonia *(Convolvulus scammonia)*

Compound Unani Formulations (Murakkabat)

Habb-e-Suranjan, Habb-e-Asgandh, Habb-e-Azaraqi, Habb-e-Mafasil, Habb-e-Kuchla, Majoon Azaraqi, Majoon Chobchini, Majoon Suranjan, Qurs Mafasil

Herbal remedies plays a significant role in curing many ailments andthis review attempts to highlight the role of Muqil (Commiphora mukul) in the disease Rheumatoid arthritis with respect to its chemical constituents, mechanism of action, pharmacological activities,pre- clinical and clinical studies.

MUQIL (*Commiphora mukul* Hook. ex Stocks)

INTRODUCTION

Commiphora mukul is a flowering plant (Anurekha and Gupta, 2006). It is commonly known as *Muqil* or *Guggul*. It is an oleo-gum resin obtained by making deep incision at the basal part of stem bark of *Commiphora mukul* and it belongs to the family Burseraceae(Ragavi and Surendran, 2018)·(Anonymous., 2007). The plants leaves are 1-3 foliate, and it bears small brown to pink flowers(Bhagyasree *et al.*, 2019). It is one of the most important Unani drug used since centuries in many disease conditions, like atherosclerosis, hypercholesterolaemia, rheumatism and obesity(Khan, Chavan and Sathe, 2015). It is mainly found in India, Bangladesh and Pakistan.

VERNACULAR NAMES(Khan, Chavan and Sathe, 2015)(KM., 2007)

Bengali, Gujarati: Guggul

Hindi: Guggulu, Guggal

Marathi: Guggul

Kashmiri: Guggul Dhoop, Kanth Gan

Malayalam: Gulgulu, Guggulu, Mahishaksh

Oriya: Guggulu

Punjabi: Guggal

Telugu: Makishakshi Guggulu, Guggipannu

Arabic: Moql, Moqle-arzaqi, Aflatan

Urdu: Muqil (Shihappu)

Bengali: Guggulu, Mukul

Assamese: Guggul

Unani: Muqil, Muqallal Yahood, Bu-e-Jahudaan

FAMILY

Burseraceae

TEMPERAMENT(Ibn Hubal., 2007)

Hot 2° and Dry 3°

ACTIONS(Anonymous., 2007)

Moḥallil-i Waram (Anti-inflammatory), *Muqawwī-i Aasab* (Nerve Tonic), *Mufattiḥ Sudad* (Deobstruent), *Kasir-ī Riyāḥ* (Carminative)

PART USED(Khan, Chavan and Sathe, 2015)

Oleo gum resin

CHEMICALCONSTITUENTS(Jasuja,Nakuleshwar,2012)(Kokate,CK.Purohit, A.P.Gokhale, 2007)

Carbohydrates, Steroids, Guggulsterone E-Z, Essential Oil, Naringenin, Myrrhanol,1-8 cineole, phenolics

PHARMACOLOGICAL ACTIVITIES(Ragavi and Surendran, 2018)(Bhagyasree *et al.*, 2019)(Khan, Chavan and Sathe, 2015)(Khare C.P,2004)

Anti-inflammatory

Anti-Rheumatic

Anti-Hyper-cholesterol emic

Anti-Hyperlipidaemic

Cardioprotective

Nephroprotective

Antibacterial

Anti-acne

Antifertility

Hepatoprotective

Antihelminthic

Anti-oxidant

CHEMICAL CONSTITUENTS (Jain A and Gupta VB,2006) (Bhagyasree *et al.*, 2019)

Carbohydrate

The resinous portion of this plant, dissolves in ethyl acetate and possesses both anti-inflammatory and lipid lowering properties, while acidic fraction possesses significant anti-inflammatory activity.

Steroids

It contains special group of steroids called guggulsterone (E-Z) and these are active principle of plant. A major compound of the resin which comes in the lipid soluble fraction of the drug is also called guggulipid. Guggulsterone occurs as a white crystalline powder and have aromatic odour.

Naringenin

It prevents the accumulation of lipoproteins and also possesses anti-bacterial, anti-inflammatory, anti-viral properties.

Myrrhanol

It is tri-terpenoid of *Muqil* which acts as anti-inflammatory.

Eugenol

It is a mono-terpenoid and has anti-oxidant property.

Mansumbionic Acid

It has anti-inflammatory property.

1,8-Cineole

It acts as anti-inflammatory and antinociceptive agent.

Diayangambin

It possesses immunomodulatory and anti-inflammatory activity.

Ellagic Acid

It has anti-mutagen, anti-inflammatory and anti-cancer activity

Phenolics

It possesses substantial anti-oxidant and anti-inflammatory activity.

Quercetin

The major flavonoids contents of the flowers are identified as quercetin. It exerts anti-inflammatory action.

1,8-Cineole

It exerts anti-inflammatory, analgesic action.

Guggulosome

It exerts significant anti-inflammatory activity

MECHANISM OF ACTION(Deng, 2007)

Guggulsterone

Guggulsterone together with transcription factor plays an inhibitory role for pro inflammatory signals, (Sharma and Sharma 1999). A number of NF-κB target genes have a primarily inflammatory function, such as monocyte chemotactic protein (MCP)-1, and secreted protein (RANTES), interleukin-1 (IL-8), C-X-C motif ligands (CXCLs), and C-C motif ligand 20 (CCL20). Guggulsterone inhibits NF-κB and such repression of NFκB activation is mediated through a direct inhibition of IKK activation by guggulsterone. NFκB is a critical regulator for inflammatory responses. Under the resting condition, NF-κB is associated with an inhibitory subunit of NF-κB (IκB) in cytoplasm. Upon stimulation by various agents, IκB is phosphorylated by IκB kinase (IKK) for ubiquitin-dependent degradation, leading to nuclear translocation of NF-κB and activation of NF-κB

target genes. In another study, it was proposed that repression of NF-κB activation through inhibition of IKK activity represents a mechanism of the anti-inflammatory effect of guggulsterone.

Quercetin

It has an inhibitory action on various cytokines including tumour necrosis factor.

1,8-cineole

It acts by inhibiting increased capillary permeability and the chemical nociception.

Myrrhanol B /Myrrhanones A, Myrrhanones B

It acts by inhibiting nitric oxide production.

Diayangambin

It acts by inhibiting human mono nuclear cell proliferation and also by reduction of (40.8%) prostaglandin E2 generation.

ANTI-OXIDANT AND ANTI-INFLAMMATORY ACTIVITIES (Jain A and Gupta VB,2006, Jasuja, Nakuleshwar CJ 2012, Deng R.2007, Patel SS, Jignasha K, Savjani.2015, Azam R, Mushtaq S, Nisar S. 2015**)**

PRE- CLINICAL STUDY ON ANTI-INFLAMMATORY ACTIVITY

- In a study done by Sharma and Sharma (1977), an arthritic condition was induced in albino rabbits by intra-articular injection and noticed that Fraction "A" of guggul extract at 500 mg/kg p.o. decreased the joint swelling within 5 months of treatment.
- In another study, aqueous extract of guggal was used and inhibited both the maximal oedema response and total oedema response during 6 hrs of carrageenan-induced rat paw oedema.
- Jain and Gupta carried out a study, in which acidic fraction of ethyl acetate extract of guggal was used in experimental arthritis, which decreased the thickness of joint swelling.
- In a study carried out by Duwiejva *et al*, 1993, it was found that mansumbinone exhibited significant anti-inflammatory activity as it reduced joint swelling.
- Formica and Regelson, 1995 found that quercetin has anti-inflammatory activity, as it influences the production of eicosanoids including leukotrienes and prostaglandins.
- In another study done by Santos and Rao, 2002, it was observed that 1-8 cineole a terpenoid oxide displays an inhibitory effect on experimental inflammation in rats and also inhibits the increase in peritoneal capillary permeability and chemical nociception induced by intraplantar formalin and intraperitoneal acetic acid.
- A study carried out by De Leon et al, 2002 showed that diayangambin significantly suppressed inflamed paw volume and prostaglandin E-2 levels.
- A study done by Manjeet and Ghosh, 1999; Nair *et al*, 2006 reported that in-vitro quercetin can inhibit various cytokines including TNF β.
- The aqueous extract significantly inhibited both the maximal oedema response and the total oedema response during 6 hrs of carrageenan-induced rat paw oedema. Fraction containing gum-guggul (acidic fraction of ethyl acetate extract) in experimental arthritis decreased the thickness of the joint swelling during the course of drug treatment.

- In a study, arthritis induced rats (both formaldehyde and Complete Freund's Adjuvant) guggul showed a significant reduction in joint swelling as well as in WBC count, Rheumatoid factor, Erythrocyte Sedimentation Rate, Cholesterol, Triglycerides and LDL.
- In a study done by Shishodia and Aggarwal 2004, Guggulsterone appears to reduce circulating levels of pro-inflammatory cytokines and markers such as IL-2 and TNF-α, Guggulsterone are also able to reduce (COX-2) mRNA levels and suppress its TNF-α mediated induction.
- Guggulosome prepared using guggul serve as a carrier were loaded with Ibuprofen, sustained release of the drug was observed. Guggulosome prepared exerts significant anti-inflammatory activity at 5 hrs against carrageenan injection suggesting that it may have a sustained and synergistic action. Several studies have demonstrated that guggulsterone produces its effect through suppression of cytokines. The crude ethyl acetate extract of gum guggul suppressed inflammatory mediators such as IL-2, TNF-α, IL-β. No inhibition was observed in the case of anti-inflammatory cytokine IL-10.
- In a study, steroidal compound isolated from *Commiphora mukul* showed dose- dependent anti-inflammatory activity. Steroid fraction had a pronounced effect on primary and secondary inflammation induced by Freund's adjuvant; it was less effective than hydrocortisone acetate in the primary phase, but more effective in reducing the severity of secondary lesions.

PRE-CLINICAL STUDY ON ANTI-OXIDANT ACTIVITY(Deng, 2007)

- In a study done by Moncada *et al*,1991 revealed that overproduction of nitric oxide is associated with oxidative stress, which is involved in the pathogenesis of cardiovascular diseases, diabetes, rheumatoid arthritis, neurodegenerative diseases, or chronic inflammation.
- In a study done by Meselhy, 2003, guggulsterone isomers (E- and Z- forms) exhibited potent inhibitory activity against the production of nitric oxide induced by bacterial lipopolysaccharides (LPSs) in macrophages with IC50 values of 1.1 and 3.3 μM, respectively which shows its anti-oxidant activity.
- Chander *et al*, 2002 found that guggulsterone inhibits the generation of oxygen free radical.
- Matsuda *et al*, 2004 studied on guggal gum resin constituents, which showed inhibitory effect on nitric oxide production.

CLINICAL STUDY ON ANTI-INFLAMMATORY ACTIVITY (Khan MB, Chavan R, Sathe N.2015, Priyanka P, Mittal KS, Gupta VK, Singh J, Sweety.2014)

- In a study carried out by Singh *et al*, 2003, the anti-inflammatory activity of guggul was evaluated in 30 patients with arthritis in at least one knee. Gum guggul at 500 mg three times daily for one month significantly improved the WOMAC (Western Ontario and McMaster Osteoarthritis Index) total score and continued to improve it at the 2-month marker and follow-up. With the secondary measures of pain in the visual analogue scales, patients exhibited significant improvement after 2 months of treatment. Thus, the results suggest the anti-inflammatory effect of guggul therapy.
- A clinical study undertaken on the effect of tablet Arthnex Forte on rheumatoid arthritis and osteo arthritis. Arthnex Forte was tried in 80 patients in the dose of 2 tablets, t.i.d for 1 month, 2 tablets b.i.d

for 1month and 1tablet daily from then onwards, with warm water. Arthnex Forte contains *Pluchea lanceolata, Tinospora cordifolia, Ricinus Communis, Cedus Deodara, Zingiber officinale, Sida cordifolia, Vitex negundo* and *Commiphora myrrh*. Out of 80 patients, 74 patients (92.5%) improved remarkably and 6 patients (5-7%) showed moderate improvement.

- In a study conducted by Szapary *et al*, 2003, in the United States, it was found that the median serum hs-CRP level was decreased by 29% in the group receiving guggulipid at a dose of 2000 mg daily, while the hs-CRP level was increased by 25% in the group receiving placebo during the trial period and it indicates the anti-inflammatory activity of guggulipid.

CLINICAL STUDY ON ANTI-OXIDANT ACTIVITY(Deng, 2007)

- In a study done by Kaul and Kapoor, 1989, the anti-oxidant effect of guggul and guggulsterone has been demonstrated in-vitro and in-vivo, the underlying mechanism remains largely to be determined. Guggulsterone was found to reverse both isoproterenol-induced production of xanthine oxidase and isoproterenol-mediated decrease of superoxide dismutase.
- In one study, done by Singh *et al*, 1993 and by Miller, 1998, the cardioprotective activity of gum guggul in combination with *Inula racemosa*, was examined in 200 patients suffering from ischemic heart disease with 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 by 39%, 51%, and 32%, respectively, and at the end of the study, in 26% of the patients the normal ECG was restored and 59% of subjects showed improvement in the ECG. In addition, after treatment with guggul, 25% of the patients experienced no more chest pain with the rest having less pain. The results suggest cardioprotective benefits of guggul in ischemic patients, presumably through its antioxidant activity.

CONCLUSION

Commiphora mukul Hook. ex Stocks has displayed a variant role in different diseases and extensively used now a days but it plays a remarkable role in management of rheumatoid arthritis and in this review attempt is made to highlight the anti-oxidant and anti-inflammatory activity of *Commiphora mukul* .It is mentioned in our classical literature that it is having *Moḥallil-i Waram* (Anti-inflammatory) property and many pre-clinical and clinical studies conducted also revealed its anti-inflammatory and anti-oxidant activity. Therefore, it can be concluded that *Commiphora mukul* Hook. ex Stocks is effective in the management of rheumatoid arthritis but more research need to be conducted in order to strengthen the fact.

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AUTHOR'S CONTRIBUTIONS

Each author contributed in data collection, analysis of the data, writing and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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