A REVIEW ON PHYTOCONSTITUENTS AND THERAPEUTIC USES OF MUQIL (COMMIPHORA MUKUL)

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ABSTRACT

Muqil is one of the best drugs in traditional system of medicine since ancient. It belongs to Burseraceae family, has 540 species and is found in dry area of India known as Indian bdellium. It is bushy plant 1.2-1.8 m can provide yellowish gum resin also called as gugulipid. Most commonly gum of this plant used for therapeutic and medicinal purpose. According to Unani system of medicine (USM) it has two types: 1. Muqil-e-Saqalibi, 2. Muqil-e-Arabi. The plant Commiphora mukul is also known as Balsamodendron mukul Stock. Muqil has active constituents producing number of biological activities such as Anti-inflammatory effect (guggulsterones Z and E), Osteoprotective effect (guggulsterone), Anti-inflammatory, analgesic antiarthritic activities (Guglulsterone), Anti-diabetic effect (gum resin 900 mg daily), Antimicrobial, antibacterial, antiviral and antifungal activities (Eugenol, ellagic acid alpha-pinene, masumbinoic acid and masumbinone), Anti-hemorrhoid activity (Muqil resin), Anti-neoplastic activity (GS, gugulipid and Z-guggusterone), Cardioprotective effect (gugulipid and guggusterone), Nephroprotective effect, Nodulocystic Acne (Guggulipid), Neuroprotective effects (guggulipid), Immunomodulatory effect, Stimulate Thyroid gland activity (Commiphora mukul gum) Anti-asthmatic (300 mg of gum resin thrice daily), Inflammatory Bowel Disease (gum resin at a dose of 900 mg daily). It is also useful for systemic disease such as Osteoarthritis, Rheumatoid arthritis, Gout, Cadio-protective effect and thyro-protective effect, nervous diseases and urinarydiseases. Skin disorders are leprosy, pyorrhea, muscle spasm, demulcent, and depurative.

INTRODUCTION

Muqil (Commiphora mukul) is a gum traditionally used in Unani system of medicine since centuries to treat various disorders. It is also known as 'Indian bdellium' (Commiphora wightii, Balsamodendron mukul stock) belongs to Burseraceae family has about 540 species. It is found in dry area of India like Rajasthan, Gujarat, Assam, Madhya Pradesh and Karnataka. Also found in Pakistan and in Bangladesh. It is bushy plant 1.2-1.8 m can provide yellowish gum resin also called as gugulipid, comes through the bark after incision, the gum comes out through small ducts and collected before become harden mostly collect from November to January. Each tree provides 250-500 gm gum.¹²³ The extract has active constituents which are

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responsible for its medicinal values are Z-guggulsterone, E-guggulsterone, guggullignans I & II, guggulsterols; mukulol; allylcembrin; c-27 guggulsterols I, II, III; Z-guggulsterol mainly. These are responsible for their anti-hypelipidimic, anti-inflammatory, antimicrobial, anti-diabetic, antispasmodic, anti-suppurative, antiseptic, anti-helmintic. Also useful for systemic disease such as Osteoarthritis, Rheumatoid arthritis, Gout, Cardio-protective effect and thyro-protective effect, nervous diseases, urinarydiseases, skin disorders such as leprosy, pyorrhrea, muscle spasm, demulcent, depurative.

Morphology
Description of Muqil: It is bushy plant 1.2-1.8 m long having good fragrant, young plants are glandular branched, crooked and spread a part and ending at sharp spine.

Stem: The young stem is glandular and covered with small hair well branched, knotty, crooked and divaricated usually end in sharp spine. The old stem became brownish to pale yellow in color and covered with thin layer of the dead cells. Stem diameter is variable reaching up to 20 cm.

Leaves: Leaves are 1-3 foliolate, sub-sessile, rhomboid-ovate, serrated toothed in the upper part and lateral leaflets are smooth and shiny.

Flowers: Flowers present with 2-3 fascicles with very short pedicles, red-colored, and small in size, petals are brownish red in color, broadly linear with sepals are connate, glandular hairy. Stamens 8-10 in number in each flowers with alternately long and short, mostly half the length of petals and reflexed at the apex. Flowers are small, maroon-pinkish in color, it present in the form of male, female and polygamous. Disk 8-10 lobed, ovary oblong-ovoid attenuated into style and become drupes red when ripe.

Fruits: Fruits are small round shaped fleshy and green in color when ripe become red, 6-8 mm in diameter, ovoid, readily splitting into 2 parts. Epicarp, four valved pyrens ovate.

Bark: Bark is green-yellowish in color and wood is whitish in color.

Gum: Gum of plant is bitter, hot, acrid with bad odors and due to heat of sun it comes out from the trunk and large branches of plant. After incision on bark of plant and falls down on the earth some time present on plant in their spaces. It will be collected before harden, becomes reddish, thick, solid and changes into pieces of various sizes. When it broke they appear in rough wax with moist and sticky with agreeable fragrance and acrid in test used as medicine traditionally in USM. It has two type 1) Muqil-e-Saqalibi: it was darker black in color and softer than other type. 2) Muqil-e-Arabi: it is mujafif, and dry than first type and become bitterer with time.

Vernacular name:
- Arabic: Aflatan, Moql, Moqlearzaqi, Muqil-e-yahood
- Unani: Madiqoon, Aflatan, fadiloen
- Persian: Beojahudan, Gugal, Gugali, Gugar
- Sanskrit: Bhavabhishtha, Bhutahara, Devadhupa, Deveshta, Dhurta
- Hindi: Gogil, Gugal, Mukul, Ranghanturb
- Tamil: Gukkal, Gukkulu, Maishakshi
- Telgu: Gugul, Mahisaksh, Maisakshi.

Botanical name: Commiphora mukul Hook
English name: Indian Bedellium

Taxonomical Classification:

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Habitat: Mukul is distributed all over the world mostly in Italy, Oman, Arab countries, Bangladesh, Pakistan, in India Rajasthan, UP, Bengal, Mysore, Bihar, Assam, Deccan, Khandesh, M.P, Karnataka.7,10,11

Part used: Gum used for therapeutic purposes in different form such as paste, ointment, confection and plaster.

Temperament: Hot and Dry.

Dosage: In classical literature in different doses mention in different book
- Makhzanul-Mufradat: 1-1.5 gm.
- KhazainulAdvia: 3 gm.
- Quality standards of Indian medicinal plants: 2-4 gm.

Adverse effects: It is quit harmless but some time produces erythematos rashes like copaiba, headache, mild nausea, and, with very high doses, liver toxicity and kidney irritation and on the basis of clinical studies oral administration of GSE...
& Z causes some mild side effect are skin rashes, irregular period, and diarrhea.

**Correctives:** Kateera (Cochlospermum religiosum Linn), Zafran (Crocus Sativa Linn.) Substitute: Sibre-Zard (Aloe barbadensis Linn.), Mur Makki (Commiphora myrrha).

**Afaal (Actions)**

Munaffi-e-balgham (expectorant), Muquawi-e-bah (aphrodisiac), Muddir-e-haiz (emenogogue), Mulaili-e-waram (anti-inflammatory), kasir-e-riyah (carminative), Muddir-i-bowl (Diuretic), Dafe-e-sumoom (antidote), Jaali (Cleanser/ Detergent), Muddir-e-shir (Galactogogue), Mufatteh-e-sudad (deobstruent), Musakkin-e-Alam (alglescic), Mulattef, Mufatti-e-hasat (Lithotripthic), Mulaiyan (laxative), jazib (absorbefacient), Munaqqi-e-rahem, Qatil-e-kirm-e-shikam (Vernicidal), Musammin (adipogenous), Mujaffij (desiccant), Mane-e-sahej, Habis-ul-dam (Styptic).

**Medicinal uses:** As per the classical Unani literature, mukul is indicated in the following diseases such as Heals fractures, Ulcers, Fistula, Piles, Indigestion, Urinary discharges, Leucoderma, Tumours, Inflammation, Tubercular glands on the neck, Ascites, asthma, Remove bad discharges from ear, Expectorant, Muscular rheumatism, Dyspepsia, Skin diseases, Nervous diseases, Demulcent, Scrofulous affection, Abdominal pains, Acne, Boils, Incipient, Abscesses and bad ulcers, Kidney stone, Diuretic, Muscular pain and stiffness, Chronic endometritis, Menorrhagia, Amenorrhrea, Leucorrhoea, Wound, Throat pain, Chronic cough, Antidote, Warts, Fungal infections, Hysucels, Inflammation of rectum, Asthma, Falij, Waja-ul-mafasal, Sciatica, Gout, Plague, Mumps, Alopecia, Appetizer, Dental caries, Bleeding and spongy gum, Pyorrhea, Chronic tonsillitis, Pharyngitis, Chronic catarrh of bowels, Chronic colitis, Tubercular ulceration of bowel, Diarrhea, Pulmonary tuberculosis, Pleural effusion, Peritonitis, Marasmus, Anaemia, Neurasthenia debility, Laryngitis, Bronchitis, Pneumonia, Whooping cough, Gingivitis, Otitis media and Uveitis, Eczema and Psoriasis.

**Constituents**

Volatile oil (myrcene, dimyrcene, polymyrcene), gum-resin (Z-guggulsterone, E- guggulsterone, Z- guggulsterol, guggulsterol I-IV). Guggulu have steroids are diterpenoids, aliphatic esters, carbohydrates, amino acids, and triglyceride. Guggulsterone is a very important sterol.

**Scientific report**

Crude extract showed anti-inflammatory activity, guggul tablets showed anti-arthritic property. Ethanolic extract showed hypolipidemic effect in normal as well as in hyperlipidemic experimental animal. It also increases hypolipidemic activity, improved lipid profiles and also reduced body weight and thickness of subcutaneous tissue fold. In vivo and vitro study showed GSE & Z gum guggul inhibits cholesterol biosynthesis and inhibits platelet aggregation also pre-clinical study on monkey, rats, rabbit showed administration of GSE & Z gum guggul significantly reduced serum cholesterol and triglyceride. Its constituent Guggulipid gradually increase norepinephrine, dopamine and dopamine β-hydroxylase activity in brain as well as in heart tissue of Rhesus monkeys. Guggul and acid fraction were significantly reduced weight of rat uterus, ovaries and cervix and concomitantly increase their glycogen. Z-guggulsterone showed thyroid stimulatory action in albino rats also increase concentration of tri-iiodothyronine in mice. Steroid fraction, guggulsterone E and Z showed inhibition of ADP, adrenaline and serotonin induced platelet aggregation in vitro also block bile acid receptor and decrease blood cholesterol concentration.

**Pharmacological effect**

**Anti-oxidant effect**

There are various studies shows Muqil gum has active constituents guggulsterone which having H, CH3 and O bonds in the steroidal structure can helps in quenching free radicals they inhibits lipid peroxidation. They show antioxidant action of guggle also used in allergic dermatitis. In vitro, guggulsterone degraded lipid and liver microsomes in rats. Hence guggulsterone possess cardioprotective and antioxidant properties. Guggulipid and alcoholic fractions shows antioxidant, anti-aging and anti-sebum properties by controlling sebum and oil secretion, improved skin softening, shining and stickiness can reduces appearance of wrinkles, improve fairness, radiance, health and youthful appearance of skin.

**Antihyperlipidimic effect**

Hyperlipidimia also known as dyslipidimia in USM called as siman-e-mufrit (obesity) according to WHO obesity is define as a BMI greater than or equal to 30 is called as obesity. It is because of imbalance of intake of calories and its utilization. Globally there are mainly two reasons 1) increase intake of fatty foods and sweets but low in vitamins, macronutrients and micronutrients. 2) Sedentary life style and decrease in physical activity. Obesity also known as "New World Syndrome" was the 5th leading cause of death globally. Almost 2.8 million adults die every year due to obesity also increase the complication or incidence of diabetes (44%), ischemic heart disease (23%) and certain cancer (7% -41%), atherosclerosis. Moreover more than 1 in 10 of world’s adult population was obese. In vivo and vitro study showed GSE & Z gum guggul inhibits cholesterol biosynthesis and inhibits platelet aggregation.
aggregation also pre-clinical study on monkey, rats, rabbit in which administration of GSE&Z gum guggul significantly inhibits the proliferative activity of FLS significantly block the production of chemokines and inactivates MMPs.

**Anti-diabetic effect**

Diabetic Mellitus is metabolic disorder characterized by excessive thirst, excessive urination, increased blood glucose level (hyperglycemia), increased appetite, insulin resistance, excessive loss of body weight etc, and affecting large population all over the world. In USM known as *Ziabetus Sukkari*. In India DM was 40.9 million and may increase up to 69.6 million by 2025. In India in 2011 caused 4.6 million deaths. In T2DM insulin resistance developed by peripheral tissue (muscle, fat and liver) with β cell failure then insufficient production of insulin for glucose produced by liver. DM has multifactorial causes are physical inactivity, sedentary lifestyle, cigarette smoking and generous consumption of alcohol. In preclinical study administration of *Muqil* showed significant reduction in plasma insulin level, improve glucose tolerance and reduce weight gain capacity. A clinical study conducted by Ahangarpour et al., it revealed that oral administration of gum resin 900 mg daily for 6 weeks shows decreased risk factors associated with this disease. Further, the treatment also helped in maintaining fructosamine levels, hepatic enzyme activities, and to bring lipid profiles close to normal levels in the patients.

**Anti-helminthic activity**

There are various study revealed that *Muqil* showed Anti-helminthic activity, Eugenol, ellagic acid alpha -pinene, masumbinoic acid and masumbinone are responsible for its antimicrobial, antibacterial, antiviral and antifungal activities (against fungi candida albicane). masumbinoic acid and masumbinone showed antibacterial activity against staphylococcus strains, periodontopathic bacteria also inhibits gram +ve and gram -ve bacteria. In vitro study by singh B demonstrated that guggul gum extract (GGE) showed inhibition against *Staphylococcus intermedius* and *Streptococcus pyogenes* strain, *S. aureus, B. subtilis*. Guggul leaves extract showed inhibitory effect against minimum for B. cereus and maximum for S. aureus. Eugenol and ellagic acid showed antimicrobial activity. Muscanone also showed anti-fungal property against *Candida albicans*. Linalool and α-terpineol shows antimicrobial activity against cariogenic bacteria. The bicyclic monoterpane alpha- pinene also showed antifungal properties.

**Anti-hemorrhoid activity**

Hemorrhoid is one of most common problem through the world. It occurs in both sexes and at any age mostly patient about 50% over the age of 50 yrs it affect about 4.4% of general population. Mostly women are affecting during pregnancy and after delivery. Peak age of prevalence 45-65
and after 65 yrs its prevalence decreases and before 20 years its occurrence is unusual. Clinical feature are varying degree of bleeding, anal swelling, pain, painful defecation, discomfort, constipation, discharge and pruritus. Muqil has best monotherapy for piles locally and orally, because of laxative, antiseptic, analgesic, anti-septic, carminative properties. The study conducted by Yousefi M revealed that Muqil resin can significantly reduce the corresponding symptoms. 

**Anti-neoplastic activity**
Muqil has Myrrhanone C, a bycyclic tri-terpenoid these are showed significant anticancer activity against cancer cell lines namely A-549(lungs), Hela (cervical), MCF-7(breast), ACHN (renal), COLO-205(colon)and B-16 (mouse melanoma) by employing MTT assay. Oral cancer is the sixth most common cancer so there is urgent need to search anticancer drug. C. mukul and its constituents GS can suppress the growth of oral cancer cells by inducing apoptosis without any toxic effect on normal cell hence it is specially cytotoxic for cancerous cell only also suppressed the activity of nuclear factor-kappaB (NF-kB) are over expressed in all type of cancer as well as in oral cancer. C. mukul and its constituents GS are suppresses NF-kB activation which leading to suppression of tumor cell proliferation and apoptosis in both cell line study also decrease expression of anti-apoptotic gene, proliferation gene and metastatic gene in pancreatic and prostate cell and GS targeted smokeless tobacco-induced P13K/Akt in head and neck cancer cell. It is antagonist of farnesoid X receptor, which is essential for normal glucose and lipid metabolism. In vitro study GS induced apoptosis and inhibited the growth of PC-3, DU145 and LNCaP human prostate cancer cells. Ellagic acid has anti-cancer properties on cancer cells of breast, oesohagus, skin, colon, prostate and pancreas by preventing the destruction of P53 gene by cancer cells, also it bind to cancer causing molecule. Ellagic acid shows chemo-protective effect against to those chemicals has ability to induce cancer. β-sitosterol can reduce cell growth of prostate cancer and colon cancers cell. The study conducted by jiang G demonstrated that gugulipid its active constituents Z-guggusterone can significantly inhibit the growth and apoptosis of MCF-7 and MDA-MB-231 cells with an IC50 of GL ~30 μM can be detected by trypan blue dye exclusion assay.

**Cardio protective effect**
Various epidemiological studies revealed that heart diseases are major disease through the world at year of 2020. It is one of the most common cause of death all over the world involves heart and blood vessels. In which myocardial ischemia is the biggest problem of public health? In this state inadequate oxygenated blood supply according to metabolic demands of myocardium to that depressed myocardial contraction, infarction and arrhythmias. For that life threatening problems we have to give some very important Synthetic agents such as angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, angiotensin II receptor antagonists etc. These alternative medicine uses for long term to prevent of heart attack. Hence there is need to search novel pharmacotherapy from medicinal plants very effective for Ischemic heart diseases with few side effects. In preclinical study by K Ojha S demonstrated that the hydroalcoholic extract of Muqil can improve the cardiovascular function and prevent MI by increased heart rate, decrease systolic arterial pressure, diastolic arterial pressure (DAP) and mean arterial pressure, increase left ventricular end diastolic pressure (LVEDP), increased left ventricular function and also significant decrease in LDH in heart homogenates, gugulipid and guggusterone also inhibit platelet aggregation. Another study conducted by Singh and group shows that reduced levels of total cholesterol, triglyceride, and total blood lipids in the patients. It also restored the normal electrocardiogram (EKG) in 26% of the patients, showed improvement of ECG in 59% of the patients and lessened the chest pain in 25% of the patients. Another study conducted by Cheon et al., 2006 demonstrated that cardiac damage in mice produced by intraperitoneal injection of dl-isoproterenol hydrochloride (85 mg/kg) can significantly reversed cardiac damage after treatment with guggulsterone.

**Nephroprotective effect**

**Chronic Kidney Disease**
Chronic Kidney Disease (CKD) or Chronic Renal Failure (CRF) was one of the high mortality rate diseases all over the world due to excessive use of conventional medicine like NSAIDS and anti-tubercular drugs with unknown etiology. It is always associated with hypertension, Diabetes mellitus. In conventional system of medicine treatment is Renal Replacement Therapy (RRT) consist of dialysis and kidney transplantation which was unsatisfactory and too costly, so there is need to search some effective treatment with low cost. CKD nowadays spreading as well as increasing all over the world, in India death due to CKD was in 1990 it was 3.78 million on the basis of progression of CKD expect that it will be 7.63 million in 2020, 10% of population suffering from CKD and also becoming 8th leading cause of death in U.S. In India prevalence of CKD is 7852/ million and worldwide prevalence of CRF is 8-16% in 2013. When GFR less than 60ml/minute/1.73 m  over 3 month. In majority of population develop sign and symptoms in advance stages when treatment in conventional medicine is Renal Replacement Therapy (RRT) consist of dialysis and kidney transplantation. The study by Shelmadine et al revealed that reduced inflammation in patients with CKD which functioned via modulation of prostaglandin E2 (PGE2), also enhanced the levels of inflammatory cytokines in CKD patients.
Skin disorders

- **Eczema and Psoriasis:**
  Eczema is USM known as *Nar-farsi* and psoriasis are the skin inflammation. There are various studies revealed that that topical use of *Muqil* based cream can diminish the symptoms and erythema. In double blind study shows significant improvement in psoriasis, scales, and erythema was observed with Bosexil R compared to placebo. In addition, when eczema patients were administrated with Bosexil R formulation, it showed improvement in both erythema and itch of the patients without any case of waning. Guggulsterone having skin protective qualities like anti-sebum and antioxidant activity. Guggulipid can provide sebum control, oil control, improved skin feel, prevent shine and stickiness resulting reduced appearance of wrinkles and aged skin, improvement in skin color, radiance, health and youthful appearance of skin. Guggulsterone is as effective as tetracycline in treatment of nodulocystic acne in one study.21

- **Nodulocystic Acne:**
  The clinical study by Magin et al., 2006 demonstrated that patients with nodulocystic acne treated with Guggulipid topical as well as orally very effective. Another clinical study conducted by Thappa and Dogra, patients with nodulocystic acne were given guggulipid equivalent to 25 mg GS for 3 months orally can shows progressive reduction in lesions in majority of patients. However, patients with oily faces displayed better response to guggulipid.21

Neuroprotective effects:
The neuroprotective effects of *Muqil* (guggulipid) have been studied in rat’s with drug-induced memory deficit rat models. Dementia was induced in rats with streptozotocin (STZ). Antidementia activity can be measure by glutathione (GSH) and malondialdehyde (MDA) and activity of anticholinesterase enzyme (AChE). The administration of guggulipid shows that significant decrease in activity of AChE with a parallel rise in the concentration of glutathione in brains of STZ-treated mice. This antidementia activity can be attributed to antioxidant and anti-AChE activities of guggulipid. This suggests the use of guggulipid as a potential antidementia drug.30

Anti-fertility activity:
Guggul caused a reduction in the weight of rat uterus, ovaries and cervix with a concomitant increase in their glycogen and sialic acid levels thereby showing that it might be useful as an antifertility agent.29

Immunomodulatory effect:
Guggul have immune modulator properties. *Muqil* can improve the defense mechanism of body and also increases the production of white blood cells (WBC).20

ENT protective effect

- **Gingivitis:**
  Gingivitis is the inflammation of gum; the study revealed that Frankincense extract has been found to exhibit efficacy against gingivitis. Frankincense extract, 0.2 g of its powder might cause significant decrease in inflammatory indices in comparison to the groups without drug therapy and SRP.21

- **Otits media:**
  Otitis media is the inflammation of the middle ear. The study conducted by Song et al., 2010 can shows that Guggulsterone has anti-inflammatory effect can inhibits the lipopolysaccharide (LPS)-induced inflammation by down-regulation of tumor necrosis factor (TNF)-a and COX-2 in addition to degradation of IkBa in human middle ear epithelial cells.20

- **Uveitis:**
  Uveitis is the inflammation of the middle layer of the eye and guggul has anti-inflammatory effect (Guggulsterone) hence it prevents activation of NF-k B and suppresses inducible nitric oxide synthase to curb endotoxin-induced uveal inflammation in cultured human primary non-pigment ciliary epithelial cells also Ocular inflammation can thus be well treated with guggulsterone.30

Others effect

Thyroid gland:
In preclinical study on albino rats showed that isolated ketosteroid from *Commiphora mukul* gum can enhance the iodine uptake, activities of thyroid peroxidase, thyroxin (T4), tri-iodothyronine (T3), T3/T4 ratio, and protease and oxygen consumption by its effect on gland.33

Asthma:
Asthma is one of the major public health problems. It is chronic inflammatory disease of the respiratory tract. Most common clinical features are wheezing, coughing, chest tightness and shortness of breathing. In USM known as “Rabu-e-Revi”. The study conducted by Gupta et al., 1998 demonstrated that bronchial asthma with 300 mg of gum resin thrice daily for a period of 6 weeks. This led to improved prognosis in around 70% of the patients as various signs and symptoms of bronchial asthma like rhonchi, dyspnoea, and attacks disappeared upon treatment.21

Inflammatory Bowel Disease:
Inflammatory Bowel Disease is one of the major life style disorders include ulcerative colitis and Crohn’s disease. A clinical study conducted by Gupta et al. demonstrated that gum resin at a dose of 900 mg daily divided in three doses for 6 weeks shows significant improvement of stool properties, hemoglobin, serum iron, calcium, phosphorus, proteins, total leukocytes, and eosinophils in the patients. Also another
study conducted by Holtmeier et al., 2011 shows temporary reduction in symptoms of actively treated patients. Also Gupta et al demonstrated that Leukotrienes are mainly responsible for inflammation of the colon in ulcerative colitis for their biosynthesis 5-LOX enzyme was very crucial. Sallai guggul gum resin can inhibits 5-LOX enzyme hence Patients with grade II and III ulcerative colitis were treated with guggulipid at a dose of 350 mg thrice daily for 6 weeks can significantly improve stool properties, histopathology, and eosinophil. The study conducted by Cheon et al., 2006 demonstrated that significantly suppression of colitis in mice.  

REFERENCE


