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BOSWELLIA SERRATA ROXB. A TRADITIONAL HERB WITH VERSATILE PHARMACOLOGICAL ACTIVITY: A REVIEW

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ABSTRACT: *Boswellia serrata* Roxb. is known as *kundur* in Unani medicine, belongs to the family Burseraceae. The plant is widely distributed in India, it occurs in dry hilly forests of Rajasthan, Madhya Pradesh, Gujarat, Bihar, Assam, Orissa, central peninsular regions of Andhra Pradesh etc. In ancient times Hindus, Babylonians, Persians, Romans, Chinese, Greeks and the people of old American civilization used its resin primarily for embalming and for its incense in cultural functions. This herb is mentioned in traditional Unani texts as an effective remedy for bronchitis, asthma, cough, cardiovascular diseases, diarrhea, dysentery, ringworm, boils, fevers (antipyretic), skin and blood diseases, mouth sores, vaginal discharges, etc. The qualitative phytochemical study of this plant extract indicates the presence of tannin, pentosans, lignin, holocellulose, β -sitosterol, and both volatile and non-volatile oils. The volatile oils of resin such as cadinene, eleanol, geraniol, linalool, β -pinene, phenols, terpenyl acetate, bornyl acetate etc and non-volatile oils like diterpene alcohol serratol, α - and β -amyrin and eight triterpenic acids, viz., Boswellic acid. It chiefly possesses anti-arthritis, anti-inflammatory, anti-hyperlipidemic, anti-cancer, hypoglycaemic, anti-asthmatic, analgesic, hepato-protective etc activities. This article is a comprehensive review to explore the correlation between the traditional uses proven by recent researches and furthermore, other researches are also highlighted, which are not reported in classical texts.

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INTRODUCTION: *Boswellia serrata* Roxb. (*Kundur*)^{1, 2, 3} is stem exudation of *B. Serrata*, oleo-gum resin belonging to the family, Burseraceae^{1, 2}.

In the plant kingdom, Burseraceae family is characterized with 17 genera and 600 species wide-spread in all tropical regions.

Genus *Boswellia* contains about 25 known species most of them occur in Arabia, north eastern coast of Africa and India⁴. *B. glabra* Roxb. is the synonym of *B. serrata*⁵.

The word *olibanum* (Indian frankincense tree) is derived from the Arabic *al-luban* and it means the milk (Arabic: لُبَّانٌ, *lubbān*; Hindi: *Dhoop*).

It has also been postulated that the name comes from the Arabic term for "Oil of Lebanon" since Lebanon was the place where the resin was sold and traded with Europeans. The English word is derived from old French "francencens" (i.e. high quality incense) and is used in incense and perfumes⁶.

The history reveals that for more than 5000 years, frankincense has been traded on the Arabian Peninsula and in North Africa. A mural depicting sacks of frankincense traded from the Land of Punt adorns the walls of the temple of ancient Egyptian Queen Hatshepsut, who died in circa 1458 BC. Hebrew and Talmus used frankincense in Ketoret ceremonies was an important component of the Temple service in Jerusalem and described it as one of the consecrated incenses. It is also mentioned in the Song of Solomon.

An especially "pure" kind, lebhonah zakkah, was presented with the showbread. Frankincense was reintroduced to Europe, although its name refers to its quality, not to the Franks themselves. It is better known as "frankincense" to westerners. The Greek historian, Herodotus was familiar with Frankincense and knew it was harvested from trees in southern Arabia. He reported that the gum was dangerous to harvest because of venomous snakes that lived in the trees. He goes on to describe the method used by the Arabians to get around this problem that being the burning of the gum of the stryax tree whose smoke would drive the snakes away. The resin is also mentioned by Theophrastus and by Pliny the Elder in his *Naturalis Historia*⁶. "Gajabhakshya" a Sanskrit name sometimes used for *Boswellia* suggests that elephants enjoy this herb as a part of their diet^{7,8}.

Botanical Description:

Taxonomical Classification

Kingdom	:	Plantae
Order	:	Sapindales
Family	:	Burseraceae
Genus	:	Boswellia
Species	:	<i>B. serrata</i>

Vernacular Names: *Kundur* (Unani, Arabic)⁹; *luban* (Arabic)¹⁰; Indian frankincense tree (English)⁹; Indian olibanum tree^{2,9}; *kundur, luban* (Hindi)^{1,2,11}; *salai* (Hindi)^{1,2,11,12}; *parangisambrani* (Tamil)^{1,12}; *phirangisambrani*¹; *parang*¹, *sambrani*,^{2,11} *anduga, kondagugi, tamu* (Telugu);¹¹ *kundur* (Persian)^{10,13}; *kundur* (Urdu)^{11,14}; *ashwamuthri, kunduru* (Sanskrit);^{1,11} *shallaki*,^{1,2,3,12} *Chitta*,¹ *gugula*,^{1,2} *dhupa*¹ *adimar, Chilakdhupa, Tallaki, Maddi* (Kannada)¹¹.

Morphological Description: *B. serrata* is medium to large-sized, deciduous, balsamiferous tree, up to 18 m height and 2.4m I girth (normally 1.5 m) commonly found in dry forests from Punjab to West Bengal, and in peninsular India^{1,11}. A balsimorous tree, bark frequently papyracious. Leaves alternate, imparipinnate, deciduous, with opposite, sessile, lanceolate or ovate, crenate, serrate, pubescent, leaflets. Flowers are in axillary racemes or panicles, small, and white. Drupes are trigonous, splitting into three valves, and subtended by the woody disk. Seeds are compressed, and pendulous. Flowers grow in March-April and fruits in the winter¹². Trees remain leafless during the entire period of flowering and fruiting.

The inflorescence is a terminal raceme and produces up to 90 bisexual, actinomorphic flowers. On average a flower produces 10 044, 1259 starch-filled pollen grains. About 85% of the fresh pollen grains are viable; the pollen to ovule ratio is 3348: 1. The stigma is of the wet papillate type. The style is hollow with three flattened stylar canals filled with a secretion product. The stylar canals are bordered by a layer of glandular canal cells. The inner tangential wall of the canal cells shows cellulose thickenings. The ovary is trilocular and bears three ovules, one in each locule. Flowers offer nectar and pollen as rewards to floral visitors¹⁵.

The tree, on injury, exudates a oleo-gum resin known as salai guggul. This is the only non-coniferous source of turpentine and rosin in India^{1,12}. The tree, olibanum is semitransparent tears, of a pinkish colour, brittle when cold, but becoming unctuous when heated. It burns with a clear steady flame, and diffuses an agreeable odor¹⁶. Tapping should start from November and should be stopped before the monsoon¹.

Generally four grades of gum-resin are known: Superfine grade is translucent, very light, yellow, in color, free from bark and other impurities; Quality 1 is brownish yellow, less translucent and free from bark and impurities; Quality II is brownish, semi-translucent and may have some impurities; and Quality III is dark brown, opaque and with impurities¹.

Pharmacognostical and Phytochemical Standardization of the Oleo-gum-resin:

Macroscopically the oleo-gum-resin occurs in transparent, brownish-yellow, up to 5 cm long, 2 cm thick, stalactitic, tears forming agglomerates of various shapes and sizes, fragrant, fracture brittle; fractured surface waxy and translucent; burns readily and emanates an agreeable characteristic, balsamic resinous odor, taste, aromatic and agreeable¹¹. Microscopically, debris of fibers, rectangular cork cells, very few yellowish oil globules and numerous small or large, oval to round or rhomboidal crystalline fragments present.

The Fluorescence test shows brownish yellow in color in day light; aqueous extract under UV light (366nm) light green and in (254nm) shows dark blue color; alcoholic extract under UV light (366nm) and in (254 nm) shows light green color. The TLC of alcoholic extract on Silica Gel G using Toluene: Ethylacetate (9:1) shows under UV (366 nm) four fluorescent zones of Rf. 0.23 (light blue), 0.79 (light blue), 0.91 (blue) and 0.96 (blue). On exposure to Iodine vapor nine spots appear at Rf. 0.08, 0.23, 0.29, 0.47, 0.55, 0.82, 0.91 and 0.96 (all yellow). On spraying with Vanillin- sulfuric acid reagent and heating the plate for ten minutes at 110¹¹.

Part used: Exudation of *B. Serrata*, bark, oleo-resin-gum³, Trunk and bark¹².

Taste: Oleo-resin-gum taste is bitterish, pungent, and slightly aromatic¹⁶.

Habitat: It is one of the commonest trees in some parts of Khandesh, Loonawara, and other neighboring territories¹⁷. It is a native of the mountainous parts of Coromandel, attaining a large size¹⁶. In India, it occurs in dry hilly forests of Rajasthan, Madhya Pradesh, Gujarat, Bihar, Assam, Orrisa as well as central peninsular regions of Andhra Pradesh etc^{1,7}.

Pharmacological Action Mentioned in Unani Literature and Ethnomedicine: The connotation of the actions of both Unani and ethnomedicine shows the accuracy of the data. This comparison provides a concise summary that the Unani medicine itself has abundant experienced evidences not a mere of chance.

Action Mentioned in Unani Medicine:

Muhallil riyah (dessicant)¹⁸; *Tanqiya roohe havani wa nafsani*¹⁸; *Muqawwie qalb wa hafiza* (Heart and memory tonic); *Kasire riyah* (carminative)¹⁰; *hazim*¹⁰; *Dafe bukhar* (antipyretic)¹⁰; *Dafe taffun* (antiseptic)¹⁴; *Munaffise balgham* (expectorant)¹⁴; *Amraze jashm* (diseases of eyes)¹³.

Therapeutic Uses mentioned in Unani Medicine:

- **Skin and Cosmetics:** Its application with honey removes whitlow, its bark is moderately effective in removing the scars¹⁹. Its local application is useful in septic wound¹⁸. With duck fat it is useful in *daad* (ringworm infection)^{18, 19}. It is useful in healing the wet wounds and ulcers¹⁰. Its use with *sirka* (vinegar) and *rogshan zaitoon* (olive oil) is useful in *daad*^{10, 19}.
- **Swelling:** It is incorporated in the plasters which are made to dissolve the inflammation of viscera. It is useful in hot inflammation of the breast in confined women. It is used with rose oil and camolian earth¹⁹.
- **Ulcers:** Particularly when it is fresh, it is a good wound healing drug and prevents the spread of malignant ulcers. It is applied with duck fat in ringworm infection. It is also beneficial in burn-wounds and cold fissures with swine fat. It is also helpful in healing burned ulcers¹⁹. It is useful in all types of septic ulcers and septic ulcers of anus and stops its spread. However it should be used dissolved in milk and used as *humool* (pessaries)^{10, 19}. Its use with honey is beneficial in wounds of burn¹⁰.
- **Head:** It strengthen memory when taken as infusion regularly in fasting. However, it excessive use causes headache. To remove the dandruff and drying the ulcer it is applied with sodium nitrate¹⁹. *Kundur* dissolved in alcohol is useful earache^{10, 18, 19}. It stops nasal hemorrhage.

It is useful drug for treating contusions of the ear. It dries *rutoobat dimaghi* and *balgham*^{10, 18}. It is useful to clear the voice and with gum of *babool* is useful in shortness of breath and halitosis¹⁸. It is useful in *nisyā'n*^{10, 18}.

- **Eye:** It heals and fills up ophthalmic ulcers and matures the associate chronic swellings. Its smoke is useful in hot swellings, stops the influx of ophthalmic fluid, heals serious ulcers and cleanses the underlying pus from the cornea. It is an important drug meant to be used in red and chronic pterygium and also for treating cancer of the eye¹⁹. It is useful in eye diseases such as *zakhm*, *jila basr*, *sartaan wa warm chashm*^{18, 19}. It is useful in night blindness¹⁰. According to Jalinoos, *surma* of *kundur* is useful in dissolving the blood, which is accumulated in the eye¹⁰.
- **Respiratory and cardiovascular system:** It is used as tonic as it is having *muqawwie qalb wa hafiza* (heart tonic) property. It is useful in *kafqan* (palpitation), chronic cough, and *dama* (asthma). *Kundur* with honey is useful in phlegmatic cough^{10, 18}. *Kundur* (1 g) with *luwab zamaq arabi* is used in *sual sho'abi* and *itsa' sho'abi*¹⁴. It is given along with other drugs in inflammation of organs and pneumonia. Its use with *teen qemuliya* and *roghan gul* (rose oil) is helpful in *warm har* (hot inflammation) of breast during puerperium¹⁰.
- **Gastrointestinal tract:** It stops vomiting and even hematemeses. It facilitates digestion¹⁹. It is useful in haemoptysis, hemorrhage and stomache¹⁰.
- **Genitourinary tract:** It stops diarrhea, sprue and bleeding from the anus and uterus. Its suppository stops the spread of malignant ulcers in the anal region^{10, 18, 19}. It is helpful to stop bleeding from any part of the body^{10, 18}. It is useful in *taqteerul boul* (dribbling of urine) cause by *zoafe quwate masika*¹⁸. *Kundur* and *sa'd* (in equal quantity), 4 g orally, is used in *taqteerul boul*. Locally, it is useful in chronic *sailanur rehm* (leucorrhoea). *Kundur*, half fried egg yolk, *jaiphal* and *javitri* is useful as *aphrodisiac* and *toleeda mani*¹⁸.
- **Fevers:** It is useful for treating phlegmatic fevers.

- **Toxicity:** Its excessive oral intake with wine may be fatal¹⁹.
- **Miscellaneous:** Its *duni* (fumigation) is useful in *waba*¹⁸.

Miqdar (Dosage): 1-3 g¹⁸

Muzir (Adverse effect): *Juzam* (leprosy), *junoos* (schizophrenia), headache^{10, 13}

Musleh (Corretive): *Barnaj farsi*, *sugar*¹³

Badal (Substitiutes): *Mastagi*, *post kundur*¹³

Actions Mentioned in Ethnomedicine:

Analgesic, anti-allergic, anti-alzheimeran, anti-arthritic, anti-asthmatic, anti-cancer, anti-complementary, anti-edemic, anti-inflammatory, antileukemic, antileukotriene, antipyretic^{2, 3, 5, 12}, anti-rheumatic, astringent, carminative, CNS depressant, collyrium, COX-2-inhibitor, demulcent, depurative,⁵ diaphoretic^{2, 5, 12, 16}, diuretic^{1, 2, 3, 5, 12}, emmenagogue^{2, 3, 5, 12}, expectorant^{5, 12}, hepatotonic, hypoglycemic, 5-lipoxygenase inhibitor, pectoral, propeptic, sedative, stomachic, tonic,⁵ antidysenteric, antiseptic¹², sedative and analgesic^{1, 3} stimulant^{1, 16}.

Indications and Uses Mentioned in Ethnomedicine:

- The bark is sweet, acrid, cooling, and tonic. It is good for pitta, asthma, dysentery, ulcers, hemorrhoids and skin diseases². Bark is useful in diarrhea, piles and skin diseases; mixed with butter applied as a poultice on bleeding or suppurating wounds¹².
- **Trunk:** The exuded oleo-gum-resin is beneficial in urinary disorders¹⁷ goiter, gout, piles, rheumatism, cutaneous and nervous diseases^{1, 12, 17}, chronic diarrhea and dysentery, cystic breast, chronic breast, tumors and ulcers; locally applied with benefit on buboes; gum-resin oil is useful in gonorrhoea; the main constituent of an ointment useful for sores is the gum-resin and is used with butter for syphilis^{1, 12}; it is useful in the form of ointment in chronic ulcers, diseased bones, buboes in which it promotes absorptions because of its astringent effect. Olibanum (one ounce) taken for longer period helps in reducing obesity.

The oil in 10-20 minim doses is useful as demulcent drinks²⁰.

- It is useful in fevers, diaphoresis, convulsions, dysentery, bronchitis, asthma, cough, stomatitis, syphilitic disease, chronic laryngitis, jaundice and arthritis².
- It is said to be demulcent, aperient, alterative, and a purifier of blood¹⁷.
- It is stimulant and diaphoretic and Indian physicians use it for the cure of gonorrhoea. It is also employed in rheumatism in the form of vapor¹⁶.
- It is useful in allergy, Alzheimer's, arthrosis, asthma, boil, bursitis, cancer, skin carbuncle, colitis, convulsion, cough, Crohn's disease, dermatosis, diabetes, diarrhea, dysentery, dysmenorrhoea, dyspepsia, edema, fever, hyperglycemia, inflammation, hemorrhoid, ulcerative colitis, vaginosis, wound, wrinkle⁵.

Contraindications and side effects: Diarrhea, nausea, and skin rash are the rare side effects may include¹².

Phyto-constituents:

Bark: The bark is reported to contain: tannin, 9.1; pentosans, 18.3; lignin, 28.8; holocellulose, 48.7% and β -sitosterol. It is reported to be used in diarrhea, piles and skin diseases^{1,12}.

Stem: The oil-gum-resin obtained from the stem yields both volatile and non-volatile oils furnishing cadinene, eleneol, geraniol, linalool, β -pinene, phenols, terpenyl acetate, bornyl acetate, α -thujene, 2,2,4-trimethyl-cyclopent-3-enyl acetic, α -camphelenic and α -campholytic acids (volatile oil); a new diterpene alcohol serratol, α - and β -amyryn and eight triterpenic acids, viz., β -Boswellic acid, its 11-Keto derivatives and their acetates, 24-dien-21-oic acid, 3 α - and 3 β -hydroxytirucall-8, 3 α -acetoxytirucall-8, and 3-ketotirucall-8 from non-volatile oil of resin¹².

Leaves: On steam distillation, the fresh leaves gave an essential oil having the following composition; Volatile oil: p-Cymene, 2.2; methylchavicol, 4.0; *d*-limonene, 3.9; α -terpineol, 13.6; α -pinene, 2.5;

bornyl acetate, 20.0; α -terpineolene, 1.9; α -phellandrene and *d*-thujone^{1,12}.

Flowers and seeds: The flowers and seeds are eaten. The seeds contain moisture, 9.0; crude protein, 8.0; pentosans, 29.3; and water sol mucilage, 1.2%. In folk medicines the dried, powdered flowers are used in colds and fevers^{1,12}.

Phytosterol: Chemical examination essential oil of its exudation showed presence of β -sitosterol²¹.

Mechanism of Action: Ingestion of a defatted alcoholic extract of *Boswellia* decreased polymorphonuclear leukocyte infiltration and migration, decreased primary antibody synthesis and almost totally inhibited the classical complement pathway in animal's studies proven in India²².

Boswellic acids, isolated from the gum resin of *Boswellia*, in a dose-dependent manner (*in vitro* testing) revealed that it blocks the synthesis of pro-inflammatory 5-lipoxygenase products, including 5-hydroxyeicosatetraenoic acid (5-HETE) and leukotriene B₄ (LTB₄), which cause chemotaxis, bronchoconstriction, and increased vascular permeability. Quercetin, other anti-inflammatory plant constituent also blocks this enzyme as an antioxidant in a more general fashion; whereas, boswellic acids seem to be specific inhibitors of 5-lipoxygenase.

In addition, 5- Boswellic acid, as a COX-2 inhibitory, might have anti-alzheimeran, anti-arthritic, certainly anti-inflammatory, and possibly anti-tumor activities⁵. Boswellic acid is different from other known non-steroidal anti-inflammatory drugs in its mode of action and relatively free from side effects as most NSAIDs act through the inhibition of prostaglandins produced by stimulated phagocytes⁷.

Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause a disruption of glycosaminoglycan synthesis, accelerating articular damage in arthritic conditions. *Boswellia* extract and ketoprofen for effects on glycosaminoglycan metabolism were examined in *in vivo* animal study. The study showed that *Boswellia* significantly reduced the degradation of glycosaminoglycans compared to controls; whereas, ketoprofen caused a decrease in total tissue glycosaminoglycan content.

In vitro studies by Ammon *et al.*, (1993) elucidated that boswellic acids inhibited leukotriene synthesis via 5-LO but did not affect the 12-lipoxygenase or cyclooxygenase activities, nor did they prevent peroxidation of arachidonic acid by iron or ascorbate. Therefore, Boswellic acids were shown to be specific, non-redox inhibitors of leukotriene synthesis, either interacting directly with 5-LO or blocking its translocation¹².

Human leucocyte elastase (HLE) is a serine protease, which initiates injury to the tissues which, in turn, triggers the inflammatory process. HLE may be involved in the pathogenesis of emphysema and it also stimulates mucus secretion and thus may play a role in chronic bronchitis, acute respiratory distress syndrome and cystic fibrosis. Boswellic acids inhibit the activity of (HLE), *in vitro*⁵. And this dual inhibitory action on the inflammatory process is unique. Of these four boswellic acids, 3-acetyl-11-keto- β -boswellic acid (AKBA) is the most potent inhibitor of 5-LO, an enzyme responsible for inflammation⁴.

The non-phenolic fraction of the resin possesses anti-tumour, sedative, and analgesic activity, and it's reported to produce a marked hypotensive effect in anaesthetized dog¹.

Mohammed and his co-workers observed reduction in the elevated levels of SGOT, SGPT, Alkaline phosphatase and bilirubin and increased membrane bound enzymes and total proteins with the treatment of *Boswellia serrata* aqueous bark extract 250 mg/kg, aqueous leaf extract 500mg/kg and aqueous gum extract 250mg/kg. *Boswellia serrata* extracts reduced the injurious effect of paracetamol on hepatocytes membrane. These biochemical restorations is probably because of inhibitory effect of *Boswellia serrata* extracts on the synthesis of 5 LOX (Lipo Oxygenase Enzyme), which is primarily responsible for injury and inflammation of hepatocytes.

Histopathological examination of the liver sections of rats treated with paracetamol showed severe focal necrosis, portal – portal bridging necrosis and intense inflammation. Minimal injury in rats treated with aqueous leaf extract of *Boswellia serrata* was seen and minimal necrosis and inflammation was noted in group of rats treated with aqueous gum extract of *Boswellia serrata*.

The group of rats treated with aqueous bark extract of *Boswellia serrata* showed mild swelling of liver cells with mild inflammation. This suggests the extracts reparative quality and maintenance of structural integrity of hepatocytic cell membrane of damaged liver cells.

The group of rats treated with LIV-52 shows minimum necrosis and swelling of hepatocytes. The ability of *Boswellia Serrata* to reduce the damaging effect or to preserve normal hepatic function disturbed by the hepatotoxin paracetamol is the index of its hepatoprotective effect²³.

It is recently established as an effective anti-hyperlipidaemic and anti-atherosclerotic agent^{1, 12}.

Pharmacological studies:

Anti-fungal Activity: The essential oil (0.6%) of the plant showed weak antifungal activity against human pathogens but was highly effective against plants pathogens^{1, 24}.

Anti-inflammatory Activity: A study observed that the mixture of boswellic acids inhibited 25-46% paw oedema in rats, proving its anti-inflammatory property⁴. The Boswellic acid from *B. serrata* showed significant activity of mean 35% inhibition of inflammation when tested in Papaya Latex Model (new model). Since the new model is reported to be sensitive to slowly acting, remission inducing drugs. Its mechanism of action seems to be unlike aspirin and steroidal drugs²⁵.

Another study showed that extract of salai guggal administered orally (p.o.) in dose ranges of 50-200 mg per kg -1 and interaperitoneal (i.p.) in does range of 50-100 mg per kg-1 caused inhibition of the Carrageenan induced rat hind paw oedema by 39.75% and 65-73% respectively compared to 47% inhibition seen with phenylbutazone (50mg/kg⁻¹ p.o.)²⁶.

Analgesic and Psychopharmacological Effects: The gum resin of *B. serrata* possesses sedative and marked analgesic effect in experimental animals. Researchers found that it produces reduction in the spontaneous motor activity and caused plosis in rats²⁷.

Anti-arthritic Effect: In the anti-arthritic study on the mycobacterium adjuvant-induced poly-arthritic in rats, salai guggal showed 34% and 49% inhibition of paw swelling with 50 and 100 mg per kg⁻¹ (p.o.) doses respectively as compared to controls.²⁶

Singh *et al.*,²⁸ showed that mixture of boswellic acid exhibited 45-67% anti-arthritic activity. The fraction was effective in both adjuvant arthritis (35-59%) as well as established arthritis (54-84%) It also showed antipyretic effect, with no ulcerogenic effect and well tolerated in as high a dose as 2 gm/kg p.o, mice.

Effects on Leucocytes Migration: Ammon *et al.*,²⁹ carried out studies on leukocytes migration into the inflammatory exudates caused by Carrageenan. It was found to exert marked inhibitory effect on both the volume and leucocytes population of pleural exudates. In acute test model of Carrageenan induced pleurisy in rats. Extract of salai guggal in a dose of 100 mg per kg orally showed significant reduction of pleural exudates volume (47.93%): P<0.001) and leucocytes population (26.42% P <0.001). The effects on these parameters were more pronounced when animals were treated with Extract of salai guggal in a dose of 100 mg per kg p.o. for 10 days before the test performance.

Anti-inflammatory and Analgesic Activity: Polyherbal formulations (MFT09 and MFG09) containing extracts of various plant constituents viz: *Boswellia serrata*, *Commiphora wightii*, *Withania somnifera*, *Curcuma longa*, *Tinospora cordifolia*, *Zingiber officinale*, *Alpinia galangal*, *Cyperus rotundus* and *Vitex negundo*, were evaluated for anti-inflammatory and analgesic activity. The effect of MFT09 produced significant analgesic activity against thermal induced pain stimuli in mice at various time intervals post treatment as indicating by increased latency to flick the tail which suggests that its activity might have resulted from its central action.

Treatment with MFT09 resulted in significant decrease in hind paw swelling as compared to MFG09. Meanwhile, the acute toxicity test results showed that for oral as well as topical preparation of MFT09 and MFG09 respectively indicate that it is relatively safe and/or non-toxic to rats. The findings of these experimental animal studies indicate that MFT09 possesses potential anti-inflammatory and analgesic activity as compared to MFG09³⁰.

Anti-anaphylactic and Mast Cell Stabilizing Activity: Extract of gum resin of *B. serrata* containing 60% acetyl 11-keto beta boswellic acid (AKBA) along with other constituents such as 11-keto beta-boswellic acid (KBA), acetyl beta-boswellic acid and beta-boswellic acid has been evaluated for anti-anaphylactic and mast cell stabilizing activity using passive paw anaphylaxis and compound 48/80 induced degranulation of mast cell methods. The extract inhibited the passive paw anaphylaxis reaction in rats in dose-dependent manner.

However, the standard dexamethasone (0.27 mg/kg, p.o) revealed maximum inhibition of edema as compared to the extract. A significant inhibition in the compound 48/80 induced degranulation of mast cells in dose-dependent manner was observed thus showing mast cell stabilizing activity. The standard disodium cromoglycate (50 mg/kg, ip) was found to demonstrate maximum per cent protection against degranulation as compared to the extract containing 60% AKBA³¹.

Another study investigated the effect of Boswellic acids, a mixture of pentacyclic triterpene acids (BA) obtained from *Boswellia serrata* Roxb. on cell mediated and humoral components of the immune system and the immunotoxicological potential. A single oral administration of BA (50–200 mg/kg) inhibited the expression of the 24 h delayed type hypersensitivity (DTH) reaction and primary humoral response to SRBC in mice. The secondary response was appreciably improved at lower doses. In a multiple oral dose schedule BA (25, 50 and 100 mg/kg) reduced the development of the 24 h DTH reaction and complement fixing antibody titers and slightly enhanced the humoral antibody synthesis.

In concentrations greater than 3.9 µg/mL BA produced almost similar and dose related inhibition of proliferative responsiveness of splenocytes to mitogens and alloantigen. Preincubation of macrophages with different concentrations of BA enhanced the phagocytic function of adherent macrophages. Prolonged oral administration of BA (25–100 mg/kg/d×21 days) increased the body weight, total leukocyte counts and humoral antibody titers in rats. It is not cytotoxic nor does it cause immunosuppression³².

Inflammatory Bowel Disease:

Ileitis: An animal study was conducted to determine the efficacy of *Boswellia* extract and one of its constituents, acetyl-11-keto- β -boswellic acid (AKBA), on leukocyte-endothelial cell interactions in inflammatory bowel disease³³. Ileitis was induced in Sprague-Dawley rats via subcutaneous injection of indomethacin. The animals were then given either *Boswellia* or AKBA at two different doses (low or high) or placebo. It was observed that *Boswellia* extract and both potencies of AKBA decreased rolling (up to 90%) and adherent leukocytes (up to 98%), attenuated tissue injury scores, and significantly reduced macroscopic and microscopic inflammation of the gut mucosa.

Anti-diarrheal Activity: The *Boswellia serrata* extract (BSE) inhibited gastrointestinal transit in croton and castor oil induced diarrhea in mice. However, intestinal motility remained unaffected in control mice by BSE³⁴.

Anticancer Activity: Inhibition of tumor growth by inhibiting cell proliferation and cell growth due to the interference with biosynthesis of DNA, RNA and proteins was observed with alcoholic extract of salai guggal (AESG) for anti-carcinogenicity in mice with ehrlic ascites carcinoma and S-180 tumour³⁵. Topical application of Boswellin with 5 nmol 12-Otetradecanoylphorbol-13-acetate (TPA) twice daily for 16 weeks to mice previously treated with dimethylbenz-anthracene caused 87- 99% inhibition in the number of tumor³⁶.

Anti-convulsant Activity: A study was conducted to evaluate the anti-convulsant activity and it was found that treatment with *Boswellia serrata* (10 and 200 mg/kg) delayed the onset of convulsion along with duration of tonic-clonic convulsions as well as it significantly reduced PTZ and STR-induced mortality in mice ($P < 0.05$ - $P < 0.001$). It also significantly ($P < 0.001$) reduced severity of electrically kindled seizures in rats and total number of rats seizure per group.

Mice treated with *Boswellia serrata* (10 and 200 mg/kg) significantly increased level of brain GABA, whereas it significantly decreased elevated level of brain NO and XO. In conclusion, the findings of present study provide pharmacological credence to anticonvulsant profile of *Boswellia serrata*.

The protection against the convulsions and restoration of endogenous enzyme level give an innuendo to its probable mechanism of action which may be mediated through the GABAergic pathway and inhibition of oxidative injury³⁷.

Anti-Depressant Activity: A polyherbal formulation (Trans-01) was investigated for its antidepressant properties. Trans-01 has the following composition: *Valeriana wallichii* (45%), *Convolvulus microphyllus* (30%), *Plumbago zeylanica* (7.5%), *Boswellia serrata* (15%), and *Acorus calamus* (3.5%). The effect of different doses of Trans-01 (25, 50, 75 and 100 mg/kg; PO) were studied and it was found to safe up to a dose of 5000 mg/kg as no mortality was observed within 48 h of administration.

Trans-01 showed a dose-dependent decrease in immobility time in TST, which is an indication of its antidepressant effect; this finding was further reinforced in the FST, where a significant effect on immobility was witnessed. Trans-01 significantly attenuated the elevated corticosteroid levels.

To ascertain whether the antidepressant effect of Trans-01 included general body stimulation, locomotor activity test was also done. These results indicate that Trans-01 can be a potential candidate for managing depression. However, further studies are required to substantiate the same³⁸.

Hypolipidemic Activity: A study proves that water soluble fraction of *B. serrata* extract showed Hypolipidemic potential in rats fed on atherogenic diet by decreasing total cholesterol (38-48%) and increasing HDL³⁹.

Hepatoprotective Activity: Gerlach observed that alcoholic extract of salai guggal (AESG) reduced titer of SGOT, SGPT, aminotransferase and serum enzymes in galactosamine/endotoxin induced liver damage in mice showing hepato-protection effect⁴⁰.

A study by Jyoti *et al.*, evaluated hepatoprotective effect of hexane extract of oleo-gum-resin of *Boswellia serrata* (BSHE) on liver injury induced by carbon tetrachloride, paracetamol or thioacetamide. The BSHE was given in two different doses (87.5mg/kg *p.o.* and 175mg/kg *p.o.*) and Silymarin (hepatoprotective agent) was used as standard.

The lower dose of BSHE (87.5mg/kg *p.o.*) significantly reduced the elevated levels of serum marker enzymes and prevented the increase in liver weight in all three models of liver injury, while the higher dose showed mild hepatoprotective activity. It was concluded that hexane extract of oleo-gum-resin of *Boswellia serrata* plant in lower doses possess hepatoprotective activity, which was supported by changes in histopathology⁴¹.

Hypoglycemic Activity: Herbal formulation containing *B. serrata* oleo-gum-resin as one of the ingredients has been reported to produce significant anti-diabetic activity on non-insulin dependent diabetes mellitus in streptozocin induced diabetic rat model where reduction in blood-glucose level was comparable to that of phenformin⁴².

Clinical Trials:

Anti-Asthmatic Activity: Gupta *et al.*, (1998) established anti-asthmatic potential of alcohol extract of salai guggal (AESG) in a double blind placebo control clinical study with 300 mg thrice daily dose for 6 weeks. He found that 70% of the patients with prolong history of asthma showed improvement in physical symptom and sign of dyspnea, bronchi, number of attacks, increase in stimulation of mitogen activated protein kinase (MAPK) and mobilization of intracellular Ca²⁺⁴³.

Anti-Cancer Activity: In glioblastoma patients, Boswellic acids showed induce concentration dependent inhibition of glioma cell proliferation and anti-edema effect⁴⁴. It was also revealed that Boswellic acids induced apoptosis is protein synthesis dependent and not associated with free radical scavenging activity.

Anti-Diarrhoeal Activity: Borrelli F *et al.*, found that *Boswellia serrata* extract (BSE) was effective in treating diarrhoea in patient with inflammatory bowel syndrome without causing constipation. Moreover, it was also effective against acetylcholine and barium chloride induced diarrhoea by inhibiting contraction of intestinal smooth muscles³⁴.

Anti-Arthritic Activity: A randomized double blind placebo controlled crossover study was conducted to assess the efficacy, safety and tolerability of *Boswellia serrata* extract (BSE) in patients (n=30) of knee osteoarthritis.

Patients were randomly allocated either to active drug (n= 15) or placebo (n=15) for eight weeks. After the first intervention, washout was given and then the groups were crossed over to receive the opposite intervention for eight weeks. All patients receiving drug treatment reported decrease in knee pain, increased knee flexion and increased walking distance⁴⁵.

Sontakke *et al.*, in their randomized, prospective, open-label, comparative trial studied the efficacy, safety, and tolerability of BSE was compared with valdecoxib in 66 patients of knee OA of for six months. The effect was assessed with WOMAC scale at baseline and monthly interval till one month after drug discontinuation. They concluded that BSE showed a slower onset of action but the effect persisted even after stopping therapy while the action of valdecoxib became evident faster but waned rapidly after stopping the treatment⁴⁶.

Ulcerative Colitis: *Boswellia* extract (350 mg three times daily) was compared to sulfasalazine (1 g three times daily) in ulcerative colitis patients. Patients on the *Boswellia* extract showed better improvements than patients on sulfasalazine; 82 percent of *Boswellia* patients went into remission compared with 75 percent on sulfasalazine. Leukotrienes are believed to play a role in the inflammatory process of ulcerative colitis⁴⁷.

A follow-up study of chronic colitis patients taking gum resin of *Boswellia* (900 mg daily in three divided doses for six weeks) and sulfasalazine (3 g daily in three divided doses for six weeks) again showed similar improvements. Furthermore, 14 of 20 patients (70%) treated with *Boswellia serrata* gum resin went into remission compared to 4 of 10 patients (40%) treated with sulfasalazine⁴⁸.

Crohn's Disease: Gerhardt *et al.*, studied the effect of *B. serrata* in Crohn's disease. Patients (n=44) were treated with *Boswellia* extract and patients (n=39) treated with mesalazine. The Crohn's Disease Activity Index decreased significantly with both *Boswellia* extract and mesalazine.

Although the difference between the two treatments was not statistically significant, the *Boswellia* extract proved to be as effective as the pharmaceutical⁴⁹.

Collagenous Colitis: Madisch *et al.*, in their randomized placebo controlled trial concluded that *B. serrata* extract (BSE) might be clinically effective in patients with collagenous colitis. Larger trials are clearly necessary to establish the clinical efficacy of BSE⁵⁰.

5-Loxin® is a novel *Boswellia serrata* extract enriched with 30% 3-O-acetyl-11-keto-beta-boswellic acid (AKBA), exhibited potential anti-inflammatory properties by inhibiting the 5-lipoxygenase enzyme⁵¹.

Other studies also prove that *Boswellia serrata* resin is effective in treating osteoarthritis^{45,52}.

Osteoarthrosis: Rumalaya forte is a polyherbal formulation containing extracts of *Boswellia serrata*, *Alpinia galanga*, *Commiphora wightii*, *Glycyrrhiza glabra*, *Tinospora cordifolia* and *Tribulus terrestris*, which are shown to have anti-inflammatory, anti-arthritic, immunomodulatory, muscle relaxant and analgesic activities. Rumalaya forte shows significant improvement of symptoms like pain, swelling, joint malfunction and mobility in patients of osteoarthrosis and does not produce any serious side effects⁵³.

Rumalaya gel is a polyherbal formulation and each gram contain extracts of *Mentha arvensis*, *Gaultheria fragrantissima*, *Pinus roxburghii*, *Cinnamomum zeylanicum*, *Cedrus deodara*, *Vitex negundo*, *Boswellia serrata* and *Zingiber officinalis*. This clinical trial was conducted to evaluate the efficacy and safety of Rumalaya gel in the symptomatic management of chronic inflammatory musculoskeletal disorders. This study observed a highly significant reduction in the mean score for muscular pain, joint swelling, joint tenderness, early morning joint stiffness, and joint pain from 1st month onwards, and the similar trend continued till the end of the study.

Also, there were no clinically significant adverse events and the overall compliance to the treatment was excellent. The researchers explained hypothesized mechanism of action of counterirritants and rubefacients include stimulation of the nociceptors, the “gate theory” and the release of endogenous opioids. Counterirritants inflame and irritate the skin, increase cutaneous blood flow, stimulate thermoreceptors and stimulate/depress pain

receptors. By activating the nociceptors with a peripheral noxious stimulus, counterirritants inhibit the response of central neurons that transmit pain or nociceptor desensitization. Some researchers suggest that a placebo effect is the most likely source of the analgesic effects acting through the power of autosuggestion. The power of autosuggestion psychologically stimulates the nervous system; alternatively the topical or subcutaneously applied analgesics could be depleting the nerve terminals of substance P, which is a nociceptive neurotransmitter. The principle constituents *Boswellia serrata* are acetyl 11-keto-beta boswellic acid, 11-keto beta-boswellic acid, acetyl beta-boswellic acid and beta-boswellic acid⁵⁴.

Cerebral Edema: A prospective, randomized, placebo-controlled, double-blind, pilot trial was conducted in patients (n=44) with primary or secondary malignant cerebral tumors were randomly assigned to radiotherapy plus either *Boswellia serrata* (BS) 4200 mg/day or placebo. A reduction of cerebral edema of >75% was found in 60% of patients receiving BS and in 26% of patients receiving placebo (P ¼ .023) compared with baseline and if measured immediately after the end of radiotherapy and BS/placebo treatment. These findings may be based on an additional anti-tumor effect and BS significantly reduced cerebral edema measured by MRI in the study population and it could potentially be steroid-sparing for patients receiving brain irradiation⁵⁵.

Chronic Toxicity Studies: A study was conducted to assess the chronic toxicity studies in 16 normal healthy monkeys divided in four groups. Haematological and biochemical estimations were done prior to drug administration and monthly intervals after drug administration. Biochemical hematological, histopathological, and other observations revealed no toxicity⁷.

CONCLUSION: This review enlightens that traditionally *B serrata* is useful in ailments such as diarrhea, asthma, arthritis, inflammation of viscera, skin diseases, ulcers, chronic bronchitis, depression, hematemesis or bleeding from any part of the body. In aforementioned disorders this herb has been pharmacologically and clinically proven as it has anti-arthritic, anti-diarrhoeal, anti-depressant, anti-asthmatic, anti-inflammatory, anti-convulsant properties and useful in inflammatory bowel

diseases. Moreover, recently the other pharmacological activities such as anti-cancer, hepato-protective, hypolipidemic, and hypoglycemic properties are also confirmed. These activities are credited to its phyto-chemical constituents such as boswellic acid, tannin, phenol, β -sitosterol, etc. Thus, this comprehensive review substantially acclaims that the traditional herb, *B. serrata* has versatile pharmacological properties.

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