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ROLE OF *BOSWELLIA SERRATA* USING NANOTECHNOLOGY TO ENHANCE EFFECT AGAINST CHRONIC DISEASES (REVIEW ARTICLE)

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ABSTRACT

Boswellia serrata, sometimes known as Indian frankincense, is a resin herbal extract derived from the *Boswellia* tree that has been used in natural medicine for centuries. In this, we will look at the history of *Boswellia serrata*, its uses, and how it can benefit review the health. It is recognized to be good for a variety of conditions, including joint, gastrointestinal, and lung health. Furthermore, *Boswellia* and its active components, such as boswellic acid, seem to have a good anti-inflammatory effect on the body. It possesses anti-inflammatory properties that may benefit inflammatory disorders such as rheumatoid arthritis (RA), osteoarthritis (OA), inflammatory bowel disease (IBD), and asthma. It helps relieve pain and may prevent cartilage degeneration. *Boswellia* may cause nausea, diarrhea, and skin irritation. It is contraindicated pregnant woman because it may cause miscarriage in pregnant women. As a result, many more clinical trials with humans are required before therapeutic recommendation to uncover the magic effects and other side effects of *Boswellia,* as scientists do not know the effects of this chemical in humans and most research to far have employed cell or animal models.

Key Words: *Boswellia serrata*; inflammation; Nanotechnology

INTRODUCTION

Chronic disease can be defined as a physical or psychological state that leads to functional limitations or requires constant observation or treatment for a long period. Worldwide, chronic diseases have hampered the health and living conditions of many people **(Raghupathi and**

Raghupathi, 2018). Many of the universally used clinical drugs (especially the biologics) these days bear the shortcomings of side effects and high treatment cost **(Roy *et al.*, 2019)** . Thus, numerous natural compounds, which have identified as potent modulators of signaling and epigenetic pathways leading to cancer, are under development presently **(Dureja, 2014)** . Natural products have gained considerable attention as they are plentiful sources of diverse compounds, which can function as biologically active drugs against different chronic diseases **(Roy *et al.*, 2019)** .

Boswellia serrata is a branching tree which produces a gum resin commonly known as Indian frankincense or olibanum **(Suther *et al.*, 2022)**. The plant is native to the dry regions of India and the Middle East. The resin has a rich, centuries long history, being used in serval parts of the world for medicinal proposes. The active compounds of the resins are thought to be the boswellic acids (BAs) (pentacyclic triterpenic acids) **(Suther *et al.*, 2022)**. There are six different types of BAs are α and β-boswellic acids (BA), acetylated α and β-boswellic acids (ABA), 11-keto-β-boswellic acid (KBA), and 3-O-acetyl-11-keto-β-boswellic acid (AKBA), which are liable for inhibiting the enzymes involved in inflammation **(Iram *et al.*, 2017)**. The BAs target a variety of cancers, inflammatory and infectious diseases **(Roy *et al.*, 2019)**. BAs have been established as a multitargeting agent, modulating several targets, including enzymes (5-LOX), growth factors (Vascular endothelial growth factor), kinases (I-κB kinases), transcription factors (STAT3), receptors (DR4), and others related to the survival and proliferation of cells (Myeloid leukemia 1) **(Roy *et al.*, 2019)** .

To compile this review, an online search was conducted utilizing several databases, including PubMed, Google Scholar, Science Direct, and Scopus. This review focuses on the therapeutic/pharmaceutical effects of the genus *Boswellia* and its principal active ingredient, AKBA, on most autoimmune disorders, inflammation, and cancers.

Chemical constituents

Hydro distillation of *Boswellia serrata* bark was used to identify thirty-five components in its yellow volatile oil. *Boswellia serrata* peel oil primarily comprises monoterpenoids, including α-Pinene (73.28%)., the oil contained β-pinene (2.05%), cis-Verbenol (1.97%), transpinocarveol (1.80%), borneol (1.78%), myrcene (1.71%), verbenone (1.71%), limonene (1.42%), thuja-2,4(10)-diene (1.18%), and p-cymene (1.0%). The sole sesquiterpene found was α-copaene (0.13%) **(Kasali *et al.*, 2002)**.

Oleo-gum resin contains significant amounts of higher terpenoids (25-30%). In 1995, researchers validated the structure of a methyl ester of acetyle-β-boswellic acid. Boswellic acid is not the only triterpenoid extracted from gum resin. This molecule contains α-amyrins, 3-hydroxyl urs-9, 11-keto-α-boswellic acid, and 11-dien-24-oic acid **(Handa, 1995)**.

Gum production

Boswellia serrata, a gum-producing plant found in India's tropical dry deciduous forests, is known for its medicinal properties. The study compares the gum-producing potential of two plants based on their girth size. The plant demonstrated gum-producing capabilities, reaching a breast height of 38.1 cm. The gum production capacity stabilizes at a girth of 86 cm **(Mishra *et al.*, 2012)**.

Germination studies

A study on seed germination of *Boswellia serrata*, a threatened medical plant species, was done. The study was aimed to create a protocol for seed germination of *Boswellia serrata* and evaluate the impact of various pre-treatments on seed germination. Fruit of several kinds were obtained from natural trees in Pune and surrounding areas, with assistance from the Pune Forest Department Research Garden. The experiment included pre-treatments with hot water, GA3, IAA, KNO3, H2SO4, and thiourea. The hot water treatment was done for 15 and 30 minutes at 85°C, followed by multiple washings. For hormones, GA3 (500 ppm and 750 ppm) and IAA (500 ppm and 750 ppm) are administered for 36 hours. Pre-treatment with 1% KNO3 and Thiourea involves soaking seeds in a solution for 15-30 minutes. Similar treatment with H_2SO_4 solution for 15 and 30 minutes. According to the results, 63 per cent of the seeds germinated after being treated with hot water for 30 minutes. 68 per cent of the seeds germinated after mechanical scarification, compared to 20 percent of the control seeds.

When seeds are steeped in solution for 30 minutes, the pre-treatments of H_2SO_4, 1% thiourea, and 1% KNO_3 exhibit 75 per cent, 76 per cent, and 78 per cent of seed germination, respectively. The hormonal treatment of GA3 and IAA 750 ppm for 36 hours showed the highest rate of germination. In GA3, 88% of the seeds germinate, while in IAA, 83% do so **(Khan, 2015)**.

1. Pharmacological Activities of Boswellic Acid

The pharmacological activities of BA are attributed to its aptness to induce anti-inflammatory, expectorant, antiseptic, anxiolytic, anti-neurotic, analgesic, tranquilizing, and antibacterial effects **(Al-Yasiry**

and Kiczorowska, 2016) . It can modulate diverse targets such as enzymes, growth factors, kinases, and transcription factors, as well as receptors, which allow it to stimulate apoptosis, cell cycle arrest, etc. **(Roy *et al.*, 2016)** . It can also inhibit different signaling pathways **(Wang *et al.*, 2018)** related to cell survival , proliferation , and metastasis **(Roy *et al.*, 2019)** .

2. Molecular Targets of Boswellic Acids

It is now well established that BA is a multitargeting agent. It can modulate several molecular targets, including enzymes, growth factors, kinases, transcription factors, receptors, and others related to the survival and proliferation of cells **(Roy *et al.*, 2019)**. BAs act on a variety of targets specifically as enzyme on 5-lipoxygenase (5-LO), topoisomerases, angiogenesis, and cytochrome p450 enzymes.

2.1. 5-LO inhibition

In neutrophils, the 5-lipoxygenases enzyme is the predominant one to convert endogenous arachidonic acid to 5-hydroxyeicosatetraenoic acid (5-HETE) and leukotrienes. They cause vasoconstriction, bronchospasm increased permeability and chemotaxis. BA in dose dependent manner in rat peritoneal neutrophils inhibits the key enzyme for leukotriene synthesis i.e. lipoxygenase. BA is a novel specific non redox inhibitor of 5-lipoxygenase as neither it impair the cyclo-oxygenase and 12-lipoxygenase enzyme properties nor inhibit the peroxidation of arachidonic acid **(Roy *et al.*, 2016)** .

2.2. Leukocyte elastase inhibition

The human leukocyte elastase decreases the elasticity of lungs, constricts the lung passages, damages the secretion of mucous in lungs and decreases the removal of the mucus. BAs reduce the activity of elastase enzyme which is responsible for emphysema **(Roy *et al.*, 2019)**.

2.3. Topoisomerase inhibition

BAs have a dual catalytic inhibitory action on human topoisomerase (I and IIα). BAs not only inhibits DNA synthesis in human leukemia promyelocytic cells in a dose dependent manner but also inhibit the topoisomerase (I and IIα) through competition with DNA for binding the enzyme **(Roy *et al.*, 2019)**

2.4. Inhibition of C2 convertase

BA inhibits the C2 convertase enzyme, which has the most significant role in the classical compliment pathway for specific immunity. As only the antibody of specific classes formed irresponsive to

antigen stimulant and is able to stimulate the pathway, so the classical compliment pathway serves the specific immunity **(Roy *et al.*, 2019)**.

Furthermore, BAs were reported to have the ability to differentially-regulate the $Ca^{(2+/-)}$ and mitogen-activated protein kinases (MAPK) signaling cascades in blood cells, and also affect the functional cellular processes that are imperative for inflammatory reactions and tumor growth . Alterations of these inflammatory pathways can lead to serious diseases including ulcerative colitis, rheumatoid arthritis, bronchial asthma, chronic colitis, Crohn's disease, peritumoral brains edemas, etc., and BAs are known to target them through the above mentioned molecular mediators.

Several analogues of BA were also reported to target the key mediators involved in the pathogenesis of cancer including NF-κB, STAT3, peroxisome proliferator-activated receptor gamma (PPAR-γ), CCAAT enhancer-binding proteins alpha (C/EBP-α), cyclooxygenase-2COX-2, matrix metallopeptidase 9 (MMP-9), Caspase, Cyclin D, Cyclin E, p21, p53, Rb, Bcl-2, Bcl-xL,Mcl-1,inhibitor of apoptosis (IAP-1), survivin, vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), androgen receptor (AR), death receptor 5 (DR-5), CXCR4, PDGFR, Akt, ERK1/2, p38 MAPK, cyclin-dependent kinase (CDK) -2, CDK-4. These mediators are involved in different processes of cancer development, such as uncontrolled proliferation , unresponsiveness to inhibitory signals, resistance to apoptosis , angiogenesis , metastasis . Among these molecular targets, NF-κB and Akt play an important role in cancer progression regulating cancer cell proliferation, survival, invasion, metastasis, and high mortality of patients **(Akincilar *et al.*, 2016)**.

3. Bioavailability and Pharmacokinetics

Despite the valuable therapeutic effects of boswellic acids, the oral bioavailability of boswellic acids is poor **(Sharma and Jana, 2020)**. To overcome this problem and increase the water solubility of boswellic acids, several investigations have produced different types of boswellic acids nanoparticles (BA-NPs). This review summarizes the evaluation in preclinical and clinical trials of the therapeutic effects of boswellic acids nanoparticles and attempts to explain the best way to produce boswellic acids nano-formulation to enhance their bioavailability, water solubility, and therapeutic activity. Boswellic acids are lipophilic compounds which result in low gastric absorption and high half-life in human plasma **(Sharma and Jana, 2020)**. The mean elimination half-life time for

11-keto β-boswellic acid is about 6 h **(Sharma *et al.*, 2004).** Regarding the similar metabolic profle of 11-keto-β-boswellic acid in both in vitro and in vivo conditions, it is concluded that the administration step has a critical role in bioavailability enhancement **(Nakhaei *et al.*, 2023)**.

3.1. Nanoformulations

Strategies for preparation of nanoformulations different approaches have been used to improve boswellic acids bioavailability. Using the novel drug delivery systems, nanoparticles are particularly an important method for increasing bioavailability and pharmacokinetic properties of boswellic acids. Other strategies for increasing boswellic acids bioavailability have been used such as lecithin formulation **(Riva *et al.*, 2016)** and standardized meal administration. Based on pharmacodynamic/pharmacokinetic modelling, oral co-administration of Piper longum L., Piperaceae, and boswellic acids enhanced bioavailability and therapeutic effects of boswellic acid **(Vijayarani *et al.*, 2020)**. In 2018, Meins and coworkers **(Meins *et al.*, 2018)** demonstrated that Aquanova micellation technology increased the bioavailability of B. serrate extracts in rats through micellar solubilization for enhancing the solubility in water of poorly soluble boswellic acids **(Meins, *et al.*, 2018)**.

3.1.1. Metallic Nanoparticles

These formulations have an inorganic core made of metal (such as gold, silver, or iron, among others) or metal oxide (such as hydroxide, phosphates, and oxides) that is commonly enclosed with a shell of organic or inorganic material:

3.1.1.1. Zinc Oxide Nanoparticle

ZnO-NPs are the most common metal oxides for nanoparticle formation because they are biodegradable, inexpensive, and non-toxic, and have a high capacity to increase pharmacophore biological activity **(Mandal *et al.*, 2022)**.

3.1.1.2. Silver Nanoparticle

AgNPs are considered metallic nanoparticles with specific physicochemical properties and potential antimicrobial activity. The size and shape of AgNPs are highly affected by their thermal, optical, and catalytic properties **(Nakhaei *et al.*, 2023)**.

3.1.2. Polymeric Nanoparticles

This class of nanoparticles consists of polymeric cores that can be loaded with active biological compounds entrapped or surface adsorbed. The polymeric nanoparticles have an excellent drug loading capacity:

3.1.2.1. Chitosan Nanoparticles

Chitosan is a natural, non-toxic, biocompatible, and biodegradable polymer which is used as a carrier in human drug delivery. Chitosan

nanoparticle has a positive surface charge that increases cellular membrane adhesion and elevates sustained release drug delivery **(Mohammed *et al.*, 2017)**.

3.1.2.2. Poly (Lactic-co-Glycolic Acid) Nanoparticle

PLGA is an effective, biodegradable, and biocompatible polymer particularly used for nanoparticle drug delivery systems due to low toxicity and sustained drug release characteristics **(Bohrey *et al.*, 2016)** .

3.1.3. Polymeric Micelles

Polymeric micelles are nanosized amphiphilic selfassembled colloids formed in solution with polymers with a hydrophilic shell and a hydrophobic core (containing drugs) which elevate the pharmacokinetic properties of the active principle **(Ghezzi *et al.*, 2021)**. Polymeric micelles formation is a promising strategy to enhance pharmacokinetic properties. Different polymers such as poly ethylene glycol (PEG), poly vinyl pyrrolidone (PVP), and poly *N*-isopropyl acrylamide can produce polymeric micelle **(Agrawal *et al.*, 2020)**.

3.1.4. Dendrosome

This class of formulation is an inexpensive and straightforward synthetic method for polymeric micelle formation with desirable characteristics for drug delivery of hydrophobic compounds (*e.g.*, biocompatibility, safety, and stability). Encapsulation with dendrosome structures improved the aqueous solubility of lipophilic compounds **(Nakhaei *et al.*, 2023)**.

3.1.5. Nanogel

Three-dimensional polymer-based hydrogel materials in the nanoscale size with inner hydrophobic cores (containing drugs) and hydrophilic polymer chains with a great amount of water are promising nanocarriers for drug delivery with exciting properties such as high drug-loading capacity, acceptable permeability, high stability, and biocompatibility **(Suhail and Rosenholm, 2019)**. Carbomer 940 is a water-soluble, cross-linked polymer of polyacrylic acid with acceptable rheological, physical, and chemical properties for hydrogel preparation **(Jaworski *et al.*, 2022)**.

3.1.6. Phytosome

This lipid-based vesicular delivery system is a pure phospholipid complex containing biological compounds which can be used for natural products drug delivery systems. In phytosomes, the biologically active compounds, attached to the outer phosphatidyl-choline membrane (or any

hydrophilic polar head group), lead to higher solubility and enhancing pharmacokinetic properties **(Barani *et al.*, 2021)**.

3.1.7. Liposome

These small artificial vesicles are bilayer phospholipid vesicles that contain a hydrophilic head and lipophilic tail. Liposomes could encapsulate biological hydrophobic compounds in an aqueous medium which enhanced pharmacokinetics properties, efficacy, stability, and toxicity **(Nakhaei *et al.*, 2023)**.

4. Pharmacotherapeutic actions of Boswellic acids (BAs)

4.1. Anticancer or antitumor activity

Boswellia is a source of one of the most potent anticancerous agents occurring naturally. Methanolic extract of the gum resin exudates of *B. serrata* Boswellin (BE) showed presence of triterpenoids, β-Boswellic acid and its analogs. **Huang *et al*., (2020),** indicated that β-BA and its derivatives (the major constituents of Boswellin) have anticarcinogenic, anti-tumor and anti-hyperlipidemic activities **(Casapullo *et al.*, 2016)**. A number of researchers have also reported that pentacyclic triterpenes of *Boswellia* are one of the most promising anticancer agents . The BAs (AKBA, KBA) exerts their cytotoxic effects by inhibiting topoisomerase I & IIa leading to inhibition of cell growth and proliferation, by inducing apoptosis via a caspase-8 dependent pathway in human leukemia, colon, hepatoma and in various other cancer cell lines **(Casapullo *et al.*, 2016)**.

4.2. Anti-inflammatory and anti-arthritic activity

Boswellia species have been used a folkloric medicine since ancient time to treat the inflammatory diseases. The data of numerous scientific studies clearly support the claim that *B. serrata* possess potent anti-inflammatory and anti-atherosclerotic activity **(Iram *et al.*, 2017; Usapkar *et al.*, 2024)**,

Plenty of review articles published in the past have highlighted the potential biological actions and molecular targets of *Boswellia* plants especially anti-inflammatory and chemo preventive activities at cellular level. The useful therapeutic actions of BAs in experimental animal studies and clinical trials have also been documented in a systematic way. Inhibition of prostaglandin synthesis seems to play only a minor role as far as the anti-inflammatory effect of BAs is concerned. Contrary to this, inhibition of 5-LO by BAs that lead to a decreased production of leukotrienes has received high attention by the scientific community

since a variety of chronic inflammatory diseases are associated with increased leukotriene activity .

The anti-inflammatory actions of BAs are observed due to the inhibition of leukotriene synthesis via 5-LO, however, it has no effect on the activities of 12-lipoxygenase (12-LO) and the cyclooxygenase (COX) enzymes. In addition to this, peroxidation of arachidonic acid by iron and ascorbate was also not impaired by BAs. Authors have proposed that BAs inhibit leukotriene synthesis either by blocking the translocation or interacting directly with 5-LO and thus act as a potent anti-inflammatory agent. Oral administration of BAs changes the electrophoretic pattern of synovial fluid protein and reduces the number of leucocytes. *B. serrate* extract is also used in the treatment of chronic polyarthritis **(Notarnicola *et al.*, 2016)**.

4.3. Anti-inflammatory Bowel Diseases (IBDs)

IBDs can be defined as idiopathic chronic relapsing malfunctions of the gastrointestinal tract (GIT) with an unknown origin, is characterized by the heterogeneity and multifactorial nature of their pathogenesis **(Kolios, 2016)**. Ulcerative colitis affects the colon, where leukotrienes play a significant role. A study on effects of the BSE in patients with ulcerative colitis illustrated that administration of BSE for six weeks improved the stool properties, histopathology, and blood parameters, including Hb, serum iron, calcium, phosphorus, proteins, total leukocytes, and eosinophils . Further, in an attempt to study the effect of AKBA on experimental ileitis, it was observed that treatment with AKBA caused a significant decrease in rolling (up to 90%) and adherent (up to 98%) leukocytes **(Kolios, 2016)**. Also, high doses of *Boswellia* extract, as well as AKBA, significantly reduced tissue injury scores. Moreover, in an investigation on the effects of BSE in mouse models of chemically induced colitis, it was found that *BA* was incapable of ameliorating the symptoms of colitis and it exerted hepatotoxicity at higher doses. Contrary to this report, another study demonstrated the anti-inflammatory effect of the semisynthetic form of AKBA and showed that P-selectin-regulated recruitment of inflammatory cells may be a major site of action for this novel anti-inflammatory agent in dextran sodium sulfate (DSS)-induced experimental murine colitis **(Roy *et al.*, 2019)**.

4.4. Antioxidant Effects

Many studies show the antioxidant effect of boswellic acids in myocardial ischemia/reperfusion (I/R) injury, bowel disease, and

pulmonary fibrosis. Relating to myocardial I/R injury, a study by **Ding *et al.*, (2016)** reveals the neuroprotection effect of 3-acetyl-11-keto-β-boswellic acid by targeting Nrf2/HO-1 pathway and elevating the expression of Nrf2 and HO-1. An antioxidant study on Alzheimer's disease resulting from abnormal oxidative stress showed 3-acetyl-11-keto-β-boswellic acid-mediated neuroprotection in mice attributed to reduced oxidative damage through Nrf2/ HO-1 signaling pathways **(Wei *et al.*, 2020)**. To enhance the pharmacokinetic properties, 3-acetyl-11-keto-β-boswellic acid-loaded *O*-carboxymethyl chitosan nanoparticles were synthesized, which showed a higher plasma concentration–time, prolonged half-life, and better brain delivery in comparison with the free acid. Furthermore, chitosan boswellic acid nanoparticles revealed better neuroprotection effect as compared with 3-acetyl-11-keto-β-boswellic acid in an oxygen–glucose deprivation model and a middle cerebral artery occlusion model. The suggested mechanisms for anti-inflammatory effect of chitosan boswellic acid nanoparticles were related to an increment in erythroid 2-related factor 2 and heme oxygenase-1 expression and a reduction in NF-κB and 5-lipoxygenase expression. Overall, chitosan boswellic acid nanoparticles were a suitable candidate for treating stroke **(Ding *et al.*, 2016)**.

Furthermore, intramammary and intraperitoneal administration of boswellic acid silver nanoparticles in female albino mice demonstrated a powerful antioxidant activity through decreasing superoxide dismutase and catalase activities **(Ebrahimpour *et al.*, 2017)**. 3-Acetyl-11-keto-β-boswellic acid loaded ZnO-NPs exhibited great antioxidant effects with high intracellular ROS levels and could protect significantly from skin against UV radiation. Considering its good biocompatibility, this formulation has an excellent potential for the treatment and therapy in protein losing enteropathy (PLE) condition **(Huang *et al.*, 2020)**.

4.5. Immunomodulatory activity

Cell mediated and humoral components of the immune system and the immunotoxicological properties of BA, was a subject of investigation by many studies **(Iram *et al.*, 2017)**. Syrovets and Makare also reported the immunomodulatory activity of BAs . A detailed study on the structural requirements for BAs indicated that of all the six acids, AKBA shows most pronounced inhibitory activity against 5-LO. Studies also showed anti-anaphylactic and mast cell stabilizing or inhibiting mast cell degranulation activity in passive paws anaphylaxis and induced mast cell degranulation of BA **(Iram *et al.*, 2017)**.

Henkel *et al*., (2015), identified that functional target of BAs is the antimicrobial peptide LL-37.It is the only member of the human cathelicidin family that have immune system-modulating properties and believed to play an important role in autoimmune disease development. MALDI-TOF mass spectrometry technique was used to study the binding of BAs to the target source, LL-37 in human neutrophils. This binding lead to inhibition of the functionality of LL-37 and thus could be used for developing agents to LL-37 related disorders.

AKBA, KBA and *B. serrata* gum resin extracts exhibit variable actions in the immune system. A mixture of BAs at higher doses can reduce primary antibody titers in the humoral defence system while lower doses show enhanced secondary antibody titers after treatment with sheep erythrocytes. BAs appear to increase lymphocyte proliferation in the cellular defence but in higher concentration effects are inhibitory. The production or release of cytokines is affected by the BAs in addition to their increase activity of phagocytosis of macrophages.

Suppressions of the classic way of the complement system was found to be due to inhibition of the conversion of C3 into C3a and C3b **(Iram *et al.*, 2017)**.

4.6. Antidiarrhoeal activity

B. serrata extract is quite effective in controlling diarrhea, without causing constipation in the patients with inflammatory bowel syndrome. It inhibits contraction of intestinal smooth muscles and thereby controls acetylcholine and barium chloride induced diarrhea **(Iram *et al.*, 2017)** .

5. Toxicity

Toxicity studies have indicated that boswellic acids are safe for clinical studies. *In vivo* toxicity studies, including acute, subacute, and chronic tests on boswellic acids, have shown that oral and intraperitoneal administration of up to 2 g/kg did not result in any mortality in rats and mice. Additionally, rats that received *B. serrata* up to a dose of 500 mg/kg body weight for 90 days did not exhibit any adverse effects on their health factors (**(Nakhaei *et al.*, 2023)**.

REFERENCES

Agrawal, R.D.; A.A. Tatode ; N.R. Rarokar and M.J. Umekar (2020). Polymeric micelle as a nanocarrier for delivery of therapeutic agents: A comprehensive review. J. Drug Delivery and Therapeutics, 10(1-s): 191-195.

Akincilar, S.; E. Khattar; P. Boon; B. Unal; M. Fullwood and V. Tergaonkar (2016). Long-Range chromatin interactions drive mutant TERT promoter activation. Cancer Discovery, 6(11): 1276–1291.

Al-Yasiry, A.R.M. and B. Kiczorowska (2016). Frankincense–therapeutic properties. Advances in Hygiene and Experimental Medicine, 70: 380-391.

Barani, M.; E. Sangiovanni; M. Angarano; M. A. Rajizadeh; M. Mehrabani; S. Piazza and M. Dell'Agli (2021). Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of literature. Int. J. Nanomed., pp: 6983-7022.

Bohrey, S.; V. Chourasiya and A. Pandey (2016). Polymeric nanoparticles containing diazepam: Preparation, optimization, characterization, in-vitro drug release and release kinetic study. Nano Convergence, 3(1): 1-7.

Casapullo, A.; C. Cassiano; A. Capolupo; F. del Gaudio; R. Esposito; A. Tosco and M. C. Monti (2016). β-Boswellic acid, a bioactive substance used in food supplements, inhibits protein synthesis by targeting the ribosomal machinery. J. Mass Spectrometry, 51(9): 821-827.

Ding, Y.; Y. Qiao; M. Wang; H. Zhang; L. Li; Y. Zhang and A. Wen (2016). Enhanced neuroprotection of acetyl-11-keto-β-boswellic acid (AKBA)-loaded O-carboxymethyl chitosan nanoparticles through antioxidant and anti-inflammatory pathways. Molecular Neurobiol., 53: 3842-3853.

Dureja, H. (2014). Role of Boswellic acids in cancer treatment. J. Med. Sci., 14(6-8): 261.

Ebrahimpour, S.; M. Fazeli; S. Mehri; M. Taherianfard and H. Hosseinzadeh (2017). Boswellic acid improves cognitive function in a rat model through its antioxidant activity:-neuroprotective effect of boswellic acid. J. Pharmacopuncture, 20(1): 10.

Ghezzi, M.; S. Pescina; C. Padula; P. Santi; E. Del Favero; L. Cantù and S. Nicoli (2021). Polymeric micelles in drug delivery: An insight of the techniques for their characterization and assessment in biorelevant conditions. J. Controlled Release, 332: 312-336.

Handa, S. (1995). Herbal raw materials and traditional remedies. Eastern Pharmacist, 38: 23-23.

Henkel, A.; L. Tausch; M. Pillong; J. Jauch; M. Karas; G. Schneider and O. Werz (2015). Boswellic acids target the human immune

system-modulating antimicrobial peptide LL-37. Pharmacological Res., 102: 53-60.

Huang, X.; M. F. Nisar; M. Wang; W. Wang; L. Chen; M. Lin and J. L. Zhong (2020). UV-responsive AKBA@ ZnO nanoparticles potential for polymorphous light eruption protection and therapy. Materials Sci. and Eng.: C, 107: 110254.

Iram, F.; S. A. Khan. and A. Husain (2017). Phytochemistry and potential therapeutic actions of Boswellic acids: A mini-review. Asian Pacific J. Tropical Biomedicine, 7(6): 513-523.

Jaworski, Z.; T. Spychaj; A. Story and G. Story (2022). Carbomer microgels as model yield-stress fluids. Reviews in Chem. Eng., 38(7): 881-919.

Kasali, A. A.; A. M. Adio; A. O. Oyedeji; A. O. Eshilokun and M. Adefenwa (2002). Volatile constituents of *Boswellia serrata* Roxb.(Burseraceae) bark. Flavour and Fragrance J., 17(6): 462-464.

Khan, M. (2015). Studies on seed germination of a threatened, endangered medicinal plant species *Boswellia serrata* roxb. Weekly Sci., 2(39): 1-5.

Kolios, G. (2016). Animal models of inflammatory bowel disease: how useful are they really? Current Opinion in Gastroenterol., 32(4): 251-257.

Mandal, A. K.; S. Katuwal; F. Tettey; A. Gupta; S. Bhattarai; S. Jaisi and N. Parajuli (2022). Current research on zinc oxide nanoparticles: Synthesis, characterization, and biomedical applications. Nanomaterials, 12(17): 3066.

Meins, J.; D. Behnam. and M. Abdel-Tawab (2018). Enhanced absorption of boswellic acids by a micellar solubilized delivery form of *Boswellia* extract. NFS J., 11: 12-16.

Mishra, S.; N. Behera and T. Paramanik. (2012). Comparative assessment of gum yielding capacities of *Boswellia serrata* Roxb. and Sterculia urens Roxb. in relation to their girth sizes eds. Paper presented at the International Conference on Anthropogenic Impact on Environment & Conservation Strategy, Ranchi (India). pp:357-330.

Mohammed, M. A.; J. T. Syeda; K. M. Wasan and E. K. Wasan (2017). An overview of chitosan nanoparticles and its application in non-parenteral drug delivery. Pharmaceutics, 9(4): 53.

Nakhaei, K.; S. Bagheri-Hosseini; N. Sabbaghzade; J. Behmadi and M. Boozari (2023). Boswellic Acid Nanoparticles: Promising Strategies for Increasing Therapeutic Effects. Revista Brasileira de Farmacognosia: 1-11.

Notarnicola, A.; G. Maccagnano; L. Moretti; V. Pesce; S. Tafuri; A. Fiore and B. Moretti (2016). Methylsulfonylmethane and boswellic acids versus glucosamine sulfate in the treatment of knee arthritis: Randomized trial. Int. J. Immunopathol. and Pharmacol., 29(1): 140-146.

Raghupathi, W. and V. Raghupathi (2018). An empirical study of chronic diseases in the United States: A visual analytics approach to public health. Int. J. Environ. Res. and Public Health, 15(3): 431.

Riva, A.; P. Morazzoni; C. Artaria; P. Allegrini; J. Meins; D. Savio and M. Abdel-Tawab (2016). A single-dose, randomized, cross-over, two-way, open-label study for comparing the absorption of boswellic acids and its lecithin formulation. Phytomed., 23(12): 1375-1382.

Roy, N. K.; A. Deka; D. Bordoloi; S. Mishra; A. P. Kumar; G. Sethi and A. B. Kunnumakkara (2016). The potential role of boswellic acids in cancer prevention and treatment. Cancer Letters, 377(1): 74-86.

Roy, N. K.; D. Parama; K. Banik; D. Bordoloi; A. K. Devi; K. K. Thakur and G. Sethi (2019). An update on pharmacological potential of boswellic acids against chronic diseases. Int. J. Molecular Sci., 20(17): 4101.

Sharma, T. and S. Jana (2020). Investigation of molecular properties that influence the permeability and oral bioavailability of major β-boswellic acids. Eur. J. Drug Metabolism and Pharmacokinetics, 45: 243-255.

Suhail, M. and J. M. Rosenholm (2019). Nanogels as drug-delivery systems: A comprehensive overview. Therapeutic Delivery, 10(11): 697-717.

Suther, C.; L. Devon; L. Daddi; A. Matson; H. Panier; H. Yuan . . . and D. A. Sela (2022). Dietary Indian frankincense (*Boswellia serrata*) ameliorates murine allergic asthma through modulation of the gut microbiome. J. Functional Foods, 97: 105249.

Usapkar, P.; S. Saoji; P. Jagtap; M. Ayyanar; M. Kalaskar; N. Gurav and S. Gurav (2024). QbD-guided phospholipid-tagged nanonized boswellic acid naturosomal delivery for effective rheumatoid arthritis treatment. Int. J. Pharmaceutics, X, 7: 100257.

Vijayarani, K. R.; M. Govindarajulu; S. Ramesh; M. Alturki; M. Majrashi; A. Fujihashi and R. J. Babu (2020). Enhanced bioavailability of boswellic acid by Piper longum: A computational and pharmacokinetic study. Frontiers in Pharmacol., 11: 551911.

Wang, D.; S. Ge; J. Bai. and Y. Song (2018). Boswellic acid exerts potent anticancer effects in HCT-116 human colon cancer cells mediated via induction of apoptosis, cell cycle arrest, cell migration inhibition and inhibition of PI3K/AKT signalling pathway. J. BUON, 23(2): 340-345.

Wei, C.; J. Fan; X. Sun; J. Yao; Y. Guo; B. Zhou and Y. Shang (2020). Acetyl-11-keto-β-boswellic acid ameliorates cognitive deficits and reduces amyloid-β levels in APPswe/PS1dE9 mice through antioxidant and anti-inflammatory pathways. Free Radical Biol. and Med., 150: 96-108.

دور اللبان باستخدام تقنية النانو لتعزيز التأثير ضد الأمراض المزمنة (بحث مرجعي)

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يُعرف نبات اللبان المعروف علمياً بأسم البسويليا سيراتا او اللبان الهندي، وهو عبارة عن مستخلص عشبي راتنجي مشتق من شجرة اللبان التي استُخدمت في الطب الشعبي لقرون. وفي هذا البحث، سنلقي نظرة على تاريخ نبات اللبان واستخداماته وكيف يمكن أن يفيد الصحة. ومن المعروف أنه مفيد لمجموعة متنوعة من الحالات، بما في ذلك صحة المفاصل والجهاز الهضمي والرئة. علاوة على ذلك، يعرف أن نبات شجرة اللبان ومكوناته النشطة، مثل حمض البوزويليا، لها تأثير جيد مضاد للالتهابات على الجسم. كما يمتلك خصائص مضادة للالتهابات قد تفيد الاضطرابات الالتهابية مثل التهاب المفاصل الروماتويدي، وخشونة المفاصل، متلازمة القولون المتهيج ، والربو. كما يساعد في تخفيف الألم وقد يمنع تنكس الغضاريف. قد يسبب نبات اللبان الغثيان والإسهال وتهيج الجلد. ويُمنع استخدامه للناس لأنه قد يسبب الإجهاض عند النساء الحوامل. ونتيجة لذلك، هناك حاجة إلى إجراء المزيد من التجارب السريرية على البشر قبل التوصية بالعلاج للكشف عن التأثيرات السحرية والآثار الجانبية الأخرى للبوسويليا، حيث لا يعرف العلماء تأثير هذه المادة الكيميائية على البشر ومعظم الأبحاث حتى الآن استخدمت نماذج خلوية أو حيوانية .بالاضافة الى وقد كشفت العديد من الدراسات أن تكوين الجسيمات النانوية يمثل نهجًا مهمًا لتحسين التأثيرات العلاجية القيمة لأحماض البوسويليا.