Behandlung rheumatischer Erkrankungen mit Weihrauch, Olibanum, Boswellia serrata (engl: Frankincense, Boswellic acid)

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Weihrauch ist das Harz des Boswellia-Strauches, vor allem der Boswellia serrata aber auch anderer Arten. Weihrauch wird traditionell zu religiösen Zwecken in vielen Kulturen verbrannt. Für medizinische Zwecke verwendeter Weihrauch wird oral eingenommen. Er wird auch Olibanum genannt. Weihrauch wurde bereits in den alten ägyptischen Kulturen medizinisch eingesetzt, später auch in der griechischen, römischen und mittelalterlichen Heilkunst. Er ist ein Bestandteil der ayurvedischen Medizin und wird hier in der Regel gemeinsam mit anderen Substanzen und Prozeduren angewandt. Eine Übersicht zur ayurvedischen Medizin ist bereits von der Kommission veröffentlicht worden. Diese Stellungnahmen bezieht sich daher auf Weihrauch als Einzelsubstanz.

1.) Möglicher Wirkmechanismus, wirksame Substanzen, vorhandene Präparate

Als ein über die Prostaglandin- und Leukotrien-Synthesehemmung potentiell entzündungshemmender Bestandteil des Weihrauchharzes wurden 11-keto-β-boswellic acid (KBA) und acetyl-11-keto-β-boswellic acid (AKBA) beschrieben [1, 10]. Weitere diskutierte Mechanismen sind eine Hemmung der Metalloproteinasen [4], TNF-α- und NF-κB-Hemmung [2, 14], Stabilisierung der (Lip-)Oxygenasen [11] sowie der extrazellulären Matrix [8].

Kombinationen von Weihrauchharzen mit MTX wurden in vitro [5] und Tiermodell [3] getestet, dabei wurden allerdings hohe Dosen von 2mg/kg MTX 2/Woche genutzt.

Zur Besserung der Bioverfügbarkeit wurden tierexperimentelle Untersuchungen mit Weihrauch-NSAR-Hybriden [13] und Nanopartikel [15] vorgestellt.

Im MMI sind zu Olibanum/Weihrauch 4 Wirkstoffe gelistet: Indischer Weihrauchbaumharz-Extrakt, Weihrauch, Weihrauch-Extrakt und Weihrauch-Öl. Diese werden vertrieben in 300 Präparaten (Stand 12/25), überwiegend als Nahrungsergänzungsmittel. Die Suche im MMI nach Apothekenpflichtigkeit liefert nur 1 Produkt (Aurum comp., Unguentum Wala Salbe, WALA Heilmittel GmbH). In der “Roten Liste” sind folgende Produkte als Homöopathika gelistet:

Olibanum, Boswellia serrata Bioxera, Weihrauch Indischer jeweils Kapsel D4 (a 400mg), über Diamant Natuur BV,

Olibanum Globuli und Tabletten in homöopathischen Konzentrationen C3-C100, D4-D30 über Dhu-Arzneimittel GmbH&CoKG,

Olibanum Lösung in homöopathischen Konzentrationen, LM1-LM500 über Dr. Sewerin GmbH&CoKG,

Olibanum RA Weihrauch Tropfen, Globuli und Tabletten über Fritz Zilly GmbH,

Olibanum Sacrum Globuli und Lösung C6-C1000 und Q1-Q3 über Gudjons GmbH,

Olibanum comp Kombination mit organischem Gold und Myrrhe über Weleda AG, MCM Klosterfrau Vertr. Ges, Wala Heilmittel GmbH,

Weihrauch 900mg Kapsel über Vitamaze GmbH,

Prosturol Zäpfchen in Wirkstoffkombination über Apogepha Arzneimittel GmbH, Als Creme (Thdcream, über Thd Spa; Dermalex Rosacea, über Perrigo Deutschland GmbH).

2.) Überblick über die wissenschaftliche Evidenz zur klinischen Wirksamkeit in der Literatur

Eine Pub-Med-Suche nach wissenschaftlichen Beiträgen zum Stichwort „Boswellic acid“ lieferte (Stand 19.5.2025) 640 Literaturstellen, davon 48 mit gleichzeitiger Nennung „Arthritis“.

Trotz zahlreicher Publikationen zur Besserung zahlreicher Surrogate wie Zytokinspiegel in vitro und im Tiermodell einer Adjuvans-induzierten Arthritis, welche von den Autoren als Hinweis auf eine Wirksamkeit von Weihrauchharzen bei Gelenkentzündungen im therapeutischen Einsatz am Menschen gewertet wurden, sind bislang nur sehr wenige Studien zur klinischen Wirksamkeit des Weihrauchharzes am erkrankten Menschen veröffentlicht worden

In Deutschland wurden zwei randomisierte doppelblinde Placebo-kontrollierte Studien mit dem Weihrauch-Präparat H15 (Boswellinsäure) bei ambulanten Patienten mit langjähriger RA in einer Dosis bis 3600mg/Tag durchgeführt und eine signifikant dem Placebo überlegene Wirkung der Testsubstanz als Abstract ohne Studiendetails und Berechnungsgrundlagen veröffentlicht [16][von Keudell C 1994]. Eine Neuberechnung der Rohdaten konnte einen Vorteil von Weihrauch gegenüber Placebo bei der add-on Therapie der RA nicht belegen [12].

Zur Behandlung der Gonarthrose wurden eine Reihe von Untersuchungen mitgeteilt. Jeweils 15 Patient:Innen mit Gonarthrose wurden mit 333mg Weihrauch oder Placebo für 8 Wochen behandelt. Dann wurden die Medikamente für 3 Wochen pausiert und die jeweils andere Gruppe für 8 Wochen behandelt. Wirksamkeitsparameter waren Schmerz, Schwellung und Funktionseinschränkung, beurteilt durch die Patient:Innen. Unter Verum werden Besserungen aller 3 Parameter um 80-90% benannt, unter Placebo um maximal 10%. Nach den 3 Wochen Therapiepause hatten die zuvor behandelten Patient:Innen aber bezüglich Schmerz wieder nahezu das Ausgangsniveau erreicht, auch Schwellung und Funktion waren wieder deutlich schlechter und hatten sich weiter verschlechtert. Die ausgeprägte Besserung konnte in der 2. Gruppe unter Verum erneut berichtet werden [6] bleibt aber dadurch nicht glaubhafter.

Bei einer Nachuntersuchung nach 6 Monaten zeigte eine Gonarthrose-Behandlung über 2 Monate mit 7,2mg Boswellinsäure /Tag einen tendenziellen Vorteil gegenüber Glucosaminen, eingeschlossen waren je Arm 60 Patient:Innen [9].

80 Patient:Innen mit Gonarthrose, die über 180 Tage randomisiert 100mg Weihrauch oder Placebo erhalten hatten, zeigten Besserungen sowohl funktioneller Scores (WOMAC, Lequesne's Functional Index scores, 6 Minuten Gehtest), metabolischer Surrogate (high-sensitivity C-reactives Protein, Matrix Metalloproteinase-3, Fibulin-3, Typ II Kollagen Degradationspeptid) sowie der Knorpeldicke und Gelenkspalt in der MRT, die das statistische Signifikanzniveau ($p < 0.001$; vs. Placebo) erreichten [7].

In einer Metaanalyse werden 7 Studien mit 545 Patienten und signifikanter Besserung von Schmerz und Funktion berichtet. [1]. Boswelliaharze wurden als effektiv und sicher bewertet. Eine Mindestbehandlung von 4 Wochen wird empfohlen.

3.) Mögliche Anwendungen in der Rheumatologie inclusive zu erwartender positiver Effekte

Daten aus der Anwendung am Menschen mit entzündlich rheumatischen Erkrankungen sind nur für die Rheumatoide Arthritis verfügbar. Ein Wirknachweis konnte nicht bestätigt werden.

Daten, die eine Äußerung über die Anwendung von Weihrauch bei anderen entzündlich rheumatischen Erkrankungen erlauben könnten, liegen nicht vor.

Daten aus Studien und einer Metaanalyse zur Einnahme von Weihrauch legen die Möglichkeit der Anwendung zur Schmerzlinderung und Besserung der Funktion bei Gonarthrose nahe. Dabei sind die

Studienpopulationen klein und ein starker Untersucherbias ist anzunehmen. Eine optimale Dosis ist aus der Studienlage nicht erkennbar. Beurteilbare Daten zur Wirkung bei anderen Arthrosen liegen nicht vor. Standardisierte Präparate sind hierfür verfügbar.

4.) Mögliche Nebenwirkungen und Limitationen

Die Ergebnisse, insbesondere die berichteten Besserungen (von z.B. 80% aller Parameter innerhalb von 3 Wochen, Zunahme der Knorpeldicke in der MRT), die sich in einem Teil der publizierten Studien finden, sind in ihrer massiven Ausprägung so wenig plausibel, dass sie für eine Beurteilung und Abschätzung der Wirksamkeit nicht genutzt werden können [6, 7].

Die Sicherheit der Anwendung von Weihrauch in den getesteten Dosierungen bis 3600mg/Tag ist in den publizierten Studien hoch und vergleichbar der Placebotherapie.

Aktuell bestehen Limitationen in der Verfügbarkeit der Substanzen aufgrund von Lieferschwierigkeiten für die Grundsubstanz.

5.) Abschließende Empfehlung der Kommission

Die wissenschaftliche Evidenz reicht nicht aus, um die Verschreibung und Anwendung von Weihrauchpräparaten für Patienten mit Symptomen aufgrund einer entzündlich-rheumatischen Krankheit zu empfehlen.

Die Effekte von Bestandteilen aus Weihrauchpräparaten auf Entzündungsmediatoren in vitro und in Tier-Arthritismodellen erlauben keine Rückschlüsse darauf, dass entzündungshemmende Bestandteile des Harzes in vivo beim Menschen so wirksam werden, dass eine messbare Besserung eintritt. Systematische kontrollierte klinische Studien an Fallkollektiven mit klar umrissenen rheumatologischen Krankheitsbildern konnten keinen Beleg einer Überlegenheit gegenüber Placebo zeigen.

Bei Behandlungswunsch der Gonarthrose auf Seiten der Patienten muss von einer von diesen initiierten Behandlung mit Weihrauch nicht abgeraten werden.

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Anhang

Literatur mit ausgewählten Abstracts

Ammon HP. Boswellic Acids and Their Role in Chronic Inflammatory Diseases. Adv Exp Med Biol. 2016;928:291-327. doi: 10.1007/978-3-319-41334-1_13. PMID: 27671822.

Boswellic acids, which are pentacyclic triterpenes belong to the active pharmacological compounds of the oleogum resin of different Boswellia species. In the resin, more than 12 different boswellic acids have been identified but only KBA and AKBA received significant pharmacological interest. Biological Activity: In an extract of the resin of Boswellia species multiple factors are responsible for the final outcome of a therapeutic effect, be it synergistic or antagonistic. Moreover, the anti-inflammatory actions of BAs are caused by different mechanisms of action. They include inhibition of leukotriene synthesis and to a less extend prostaglandin synthesis. Furthermore inhibition of the complement system at the level of conversion of C3 into C3a and C3b. A major target of BAs is the immune system. Here, BEs as well as BAs including KBA and AKBA, have been shown to decrease production of proinflammatory cytokines including IL-1, IL-2, IL-6, IFN-γ and TNF-α which finally are directed to destroy tissues such as cartilage, insulin producing cells, bronchial, intestinal and other tissues. NFκB is considered to be the target of AKBA. The complex actions of BEs and BAs in inflamed areas may be completed by some effects that are localized behind the inflammatory process as such tissue destruction. In this case, in vitro- and animal studies have shown that BAs and BEs suppress proteolytic activity of cathepsin G, human leucocyte elastase, formation of oxygen radicals and lysosomal enzymes.

Pharmacokinetics: Whereas KBA is absorbed reaching blood levels being close to in vitro IC50, AKBA which is more active in in vitro studies than KBA, but undergoes much less absorption than KBA. However, absorption of both is increased more than twice when taken together

with a high-fat meal.Clinical Studies There are a variety of chronic inflammatory diseases which respond to treatment with extracts from the resin of Boswellia species. Though, the number of cases is small in related clinical studies, their results are convincing and supported by the preclinical data. These studies include rheumatoid arthritis, osteoarthritis, chronic colitis, ulcerative colitis, collagenous colitis, Crohn's disease and bronchial asthma. It can not be expected that there is cure from these diseases but at least improvement of symptoms in about 60-70 % of the cases. Side Effects The number and severity of side effects is extremely low. The most reported complaints are gastrointestinal symptoms. Allergic reactions are rare. And most authors report, that treatment with BEs is well tolerated and the registered side effects in BE- and placebo groups are similar.

Choudhary R, Saroch D, Kumar D, Anjum S, Andrabi NI, Akram T, Shah BA, Shukla SK, Bhagat A, Kour G, Ahmed Z. Anti-inflammatory and anti-arthritic potential of methotrexate in combination with BA-25, an amino analogue of β-boswellic acid in the treatment of rheumatoid arthritis. Cytokine. 2023 Dec;172:156398. doi: 10.1016/j.cyto.2023.156398. Epub 2023 Oct 9. PMID: 37820446.

β- boswellic acid, a pentacyclic triterpene derived from Boswellia serrata is extensively known for its anti-inflammatory potential. BA-25 (3-α-o-acetoxy-4β-amino-11-oxo-24-norurs-12-ene) is an amino analogue of β-boswellic acid that has shown anti-inflammatory potential in LPS-induced macrophages and animal models. The present study aims at investigation of the combination of BA-25 with the conventional gold standard DMARD methotrexate (MTX) for its anti-inflammatory and anti-arthritic potential using in vitro and in vivo experimental models. The anti-inflammatory potential of MTX versus the combination (BA-25 + MTX) was investigated for inhibition of NO, ROS and pro-inflammatory cytokines including TNF-α and IL-6 using ELISA in LPS-stimulated RAW-264.7 cells. The results demonstrated significant reduction in NO, ROS, TNF- α and IL-6 production with the combination treatment in comparison to MTX alone. The cytokine inhibition potential of the combination was further validated in-vivo using balb/c wherein the combination restored LPS-induced increase in pro-inflammatory cytokines. The toxicological aspect of the in vivo doses of the combination was also investigated in mice after dosing for 28 days wherein the results suggested no significant change in the hematological parameters and serum biochemical parameters in the combination versus the vehicle group. The effect of BA-25 was also investigated on MTX-induced increase in liver function tests and the expression of Bax and blc2. The results demonstrated decrease in the production of liver enzymes with BA-25 administration along with downregulating the expression of apoptotic protein Bax while increasing the expression of anti-apoptotic protein Bcl2. Furthermore, pharmacokinetic studies of BA-25 were conducted in Balb/c mice wherein the compound showed rapid absorption, high volume of distribution and a t1/2 of 13.08. Finally the anti-arthritic effect of the combination of MTX + BA-25 vs MTX alone was investigated using CIA model in DBA/1 mice wherein the treatment with the combination resulted in significant reduction in paw inflammation, IL-6 and IL-1β levels. Furthermore, the western blot analysis demonstrated considerable decrease in the expression of p-NF-κB p65 and p-IκB in the ankle-joint tissue of the CIA mice treated with the combination therapy. The results insinuated increased anti-inflammatory and anti-arthritic potential of the combination of MTX with BA-25 as evident from in to vitro and in-vivo studies.

Notarnicola A, Maccagnano G, Moretti L, Pesce V, Tafuri S, Fiore A, Moretti B. Methylsulfonylmethane and boswellic acids versus glucosamine sulfate in the treatment of knee arthritis: Randomized trial. Int J Immunopathol Pharmacol. 2016 Mar;29(1):140-6. doi: 10.1177/0394632015622215. Epub 2015 Dec 18. PMID: 26684635; PMCID: PMC5806735.

Until now glucosamine sulfate (GS) has been the most widely used supplement and has been shown to be efficacious in the treatment of osteoarthritis (OA). Methylsulfonylmethane (MSM) and boswellic acids (BA) are new effective supplements for the management of inflammation and joint degeneration, according to previous experimental studies. The aim of our study is to test the effectiveness of association of MSM and BA in comparison with GS in knee arthritis.In this prospective randomized clinical trial, MEBAGA (Methylsulfonylmethane and Boswellic Acids versus Glucosamine sulfate in the treatment of knee Arthritis), 120 participants affected by arthritis of the knee were randomly assigned to an experimental group (MB group) or a control group (GS group) treated for 60 days with 5 g of MSM and 7.2 mg of BA or with 1500 mg of GS daily, respectively. At the 2-month (T1) and 6-months (T2) follow-up , the efficacy of these two nutraceuticals was assessed using the visual analog pain scale (VAS) and the Lequesne Index (LI) for joint function, along with the use of anti-inflammatory drugs (non-steroidal anti-inflammatory drugs and anti-cyclooxygenase-2).The repeated measures ANOVA analysis shows that for VAS, LI, and the use of anti-inflammatory drugs scores there are improvements due to the time in the two groups (respectively, F=26.0; P<0.0001; F=4.15; P=0.02; F=3.38; P=0.04), with a tendency to better values for the MB group at T2.On the basis of these preliminary data, we could support the efficacy of the MSM in association with BA in the treatment of OA. These results are consistent with the anti-inflammatory and chondroprotective effects previously occurred in experimental studies. This new combination of integration (MSM and BS) has presented good results and satisfactory in comparison with GS, until now the cornerstone of the treatment of arthritis in according to guidelines.

Shenvi S, Kiran KR, Kumar K, Diwakar L, Reddy GC. Synthesis and biological evaluation of boswellic acid-NSAID hybrid molecules as anti-inflammatory and anti-arthritic agents. Eur J Med Chem. 2015 Jun 15;98:170-8. doi: 10.1016/j.ejmech.2015.05.001. Epub 2015 May 5. PMID: 26010018.

Methyl esters of the β-boswellic acid (BA) and 11-keto-β-boswellic acid (KBA) obtained from Boswellia serrata resin were subjected to Steglich esterification with the different non-steroidal anti-inflammatory drugs (NSAID) viz., ibuprofen, naproxen, diclophenac and indomethacin. The novel hybrids of methyl boswellate (5-8) and that of methyl 11-keto boswellate (9-12) were evaluated for anti-inflammatory activity by carrageenan-induced rat hind paw edema model and anti-arthritic activity by Complete Freund's Adjuvant (CFA) induced arthritis in Wister albino rat. Significant inhibition on carrageenan-induced paw edema has been observed with 5, 6 and 10 where as in CFA induced rats, hybrids 5, 8, 9 and 12 exhibited pronounced antiarthritic activity. Hybrid molecules 5 and 9 have been found to be more effective in inhibiting in-vivo COX-2 than ibuprofen by itself, thus showing the synergistic effect. Hybrid 5 and 9 tested for in-vitro

lipoxygenase and cyclooxygenase-2 (LOX/COX-2) inhibitory activity. The studies revealed that both 5 and 9 inhibited COX-2 relatively better than LOX enzyme.

Usapkar P, Saoji S, Jagtap P, Ayyanar M, Kalaskar M, Gurav N, Nadaf S, Prasad S, Laloo D, Khan MS, Chikhale R, Gurav S. QbD-guided phospholipid-tagged nanonized boswellic acid naturosomal delivery for effective rheumatoid arthritis treatment. Int J Pharm X. 2024 May 19;7:100257. doi: 10.1016/j.ijpx.2024.100257. PMID: 39668885; PMCID: PMC11637072.

Studies have reported the potential role of Boswellic acids (BAs), bioactive pentacyclic triterpenes from Boswellia serrata (BS), in treating rheumatoid arthritis (RA). However, poor water solubility and limited oral absorption are restricting factors for its better therapeutic efficacy. Based on these assumptions, the current study aimed to develop naturosomal delivery of BAs to boost their extremely low bioavailability, colloidal stability, and water solubility. Nanonized naturosomes were developed and subsequently analyzed to show their physicochemical and functional features employing the quality-by-design approach. The solubility analysis of Boswellic acid naturosomes revealed a 16 times improvement in aqueous solubility compared to BS extract (BSE). The zeta potential and dynamic light scattering findings of BSE naturosomes (BSENs) have demonstrated their colloidal stability with regulated nano-size particles. Additionally, compared to BSE (≃ 31%), in-vitro dissolution experiments showed that >99% of pentacyclic triterpenes were released from BSENs. Studies on ex-vivo permeation showed that BSENs' permeation (>79%) significantly improved over BSE's (≃ 20%). In-vivo efficacy studies using CFA-prompted arthritis in rodents showed a critical expansion in body wt and an undeniable reduction in paw thickness, paw volume, and TNF-α treated with BSEN compared to the arthritis control and BSE-treated group. These findings suggest that BSENs can help treat RA drugs by demonstrating their efficacy in further clinical research to validate the significant improvements.

Majeed M, Nagabhushanam K, Lawrence L, Nallathambi R, Thiyagarajan V, Mundkur L. Boswellia serrata Extract Containing 30% 3-Acetyl-11-Keto-Boswellic Acid Attenuates Inflammatory Mediators and Preserves Extracellular Matrix in Collagen-Induced Arthritis. Front Physiol. 2021 Sep 28;12:735247. doi: 10.3389/fphys.2021.735247. PMID: 34650445; PMCID: PMC8506213.

Boswellia serrata extracts have been traditionally employed for the treatment of inflammatory diseases. In the present study, we have evaluated the mechanism of activity of Boswellin Super® FJ (BSE), a standardized extract of B. serrata containing not less than 30% 3-acetyl-11-keto-β-boswellic acid along with other β-boswellic acids. The in vitro anti-inflammatory activities were carried out in RAW 264.7 macrophages or human peripheral blood mononuclear cells stimulated with bacterial lipopolysaccharides (LPS) and treated with 1.25-5μg/ml BSE. The anti-arthritic activity of the extract was evaluated in a rat model of collagen-induced arthritis. BSE at 40 and 80mg/kg and celecoxib 10mg/kg were orally dosed for 21days. BSE showed significant ($p<0.05$) inhibition of inflammation (TNF-α, IL-6, nitric oxide, and COX-2 secretion) and downregulates the mRNA levels of TNF-α, IL-6, IL1-β, and inducible nitric oxide synthase in macrophages. BSE treatment reduced the levels of phosphorylated-NF-κB (P65), suggesting an anti-inflammatory activity mediated by blocking this key signal transduction pathway. In addition, BSE showed inhibition ($p<0.05$) of collagenase, elastase, hyaluronidase enzymes, and a reduction in reactive oxygen species and matrix-degrading proteins in RAW 264.7 macrophages stimulated with LPS. BSE treatment significantly ($p<0.05$) reduced the arthritic index, paw volume, and joint inflammation comparable to celecoxib in collagen-induced arthritis (CIA) in rats. The circulating anti-collagen antibodies were reduced in BSE and celecoxib-treated animals as compared to the CIA. In confirmation with in vitro data, BSE showed a significant ($p<0.05$) dose-dependent effect on C-reactive protein, prostaglandin E2, and erythrocyte sedimentation rate, which is widely used as a blood marker of inflammation. Further, BSE treatment suppressed the cartilage oligomeric matrix protein and significantly enhanced the hyaluronan levels in synovial fluid. As observed by collagen staining in joints, the loss of matrix proteins was lower in BSE-treated animals, suggesting that BSE could preserve the extracellular matrix in RA. The extract showed inhibition of collagenase enzyme activity in vitro, further strengthening this hypothesis. BSE treatment was found to be safe, and rats displayed no abnormal behavior or activities. The results suggest that Boswellin Super® mediates its activity by preserving matrix proteins, reducing pro-inflammatory mediators, and oxidative stress.

Banji D, Banji OJF, Rashida S, Alshahrani S, Alqahtani SS. Bioavailability, anti-inflammatory and anti-arthritic effect of Acetyl Keto Boswellic acid and its combination with methotrexate in an arthritic animal model. J Ethnopharmacol. 2022 Jun 28;292:115200. doi: 10.1016/j.jep.2022.115200. Epub 2022 Mar 17. PMID: 35306043.

Ethnopharmacological relevance: Rheumatoid arthritis is one of the most common disabling chronic progressive autoimmune diseases affecting the adult world population. Boswellia serrata has been a known anti-inflammatory agent since ancient times. Therefore, research on Boswellia extract based on Acetyl Keto Boswellic Acid (AKBA) content evaluating its efficacy and safety is necessary. The study aimed to find a suitable Boswellia extract rich in AKBA to evaluate its bioavailability, anti-inflammatory, and anti-arthritic effect. In addition, the synergistic action of AKBA extract with methotrexate (MTX) was also assessed on an animal model.

Materials and methods: Oral bioavailability of AKBA and the anti-inflammatory activity of 10% AKBA (5, 10, 20, 40 mg/kg b.w) was assessed and compared with 2% AKBA (40 mg/kg) and diclofenac (10 mg/kg). The effect of 10% AKBA at 20 mg/kg and 40 mg/kg was evaluated in the FCA induced arthritis animal model alone and combined with methotrexate (MTX) at 2 mg/kg b.w. Subplantar injection of FCA produced edema within a few hours with progressive arthritis by the 9th day after injection. All the treatments were initiated from the 10th day until the 45th day. Oral administration of 10% AKBA was done daily and MTX by intraperitoneal route once a week from day 10 to day 45. Paw volume, erythrocyte sedimentation rate (ESR), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP), total bilirubin, oxidative markers (superoxide dismutase (SOD) levels, malondialdehyde (MDA), total proteins and liver histopathology were examined.

Results: 10% AKBA provided 8.48-fold, 24.22-fold, 47.36-fold, and 110.53-fold higher AUC (0-α) of AKBA at 5 mg/kg, 10 mg/kg, 20 mg/kg and 40 mg/kg, respectively compared to 2% AKBA at 40 mg/kg. Percentage paw edema inhibition of 10% AKBA at 20 mg/kg and 40 mg/kg were significantly higher than 2% regular AKBA (40 mg/kg) and diclofenac (10 mg/kg). 10% AKBA at a dose of 20 and 40 mg/kg significantly reduced ESR compared with FCA treated group. A combination of methotrexate with 10% AKBA showed the highest reduction in ESR. 10% AKBA at both dose levels significantly reduced hepatic marker enzymes and total bilirubin levels. Treatment with 10% AKBA showed a significant increase in total proteins, antioxidant enzymes and a decrease in malondialdehyde levels. Similarly, 10% AKBA protected the hepatocytes compared with the FCA and FCA + MTX treated group. 10% AKBA was capable of significantly minimizing FCA and FCA + MTX induced changes.

Conclusion: Anti-inflammatory activity of AKBA due to inhibition of lipoxygenase (LOX) enzymes supports the use of AKBA in inflammatory disorders. Combination therapy of 10% AKBA with MTX is effective in inhibiting arthritis and circumventing hepatotoxicity produced by MTX in arthritic animals

Blain EJ, Ali AY, Duance VC. Boswellia frereana (frankincense) suppresses cytokine-induced matrix metalloproteinase expression and production of pro-inflammatory molecules in articular cartilage. Phytother Res. 2010 Jun;24(6):905-12. doi: 10.1002/ptr.3055. PMID: 19943332.

The aim of this study was to assess the anti-inflammatory efficacy of Boswellia frereana extracts in an in vitro model of cartilage degeneration and determine its potential as a therapy for treating osteoarthritis. Cartilage degradation was induced in vitro by treating explants with 5 ng/ml interleukin1alpha (IL-1alpha) and 10 ng/ml oncostatin M (OSM) over a 28-day period, in the presence or absence of 100 microg/ml B. frereana. Treatment of IL-1alpha/OSM stimulated cartilage explants with B. frereana inhibited the breakdown of the collagenous matrix. B. frereana reduced MMP9 and MMP13 mRNA levels, inhibited MMP9 expression and activation, and significantly reduced the production of nitrite (stable end product of nitric oxide), prostaglandin E2 and cycloxygenase-2. Epi-lupeol was identified as the principal constituent of B. frereana. This is the first report on the novel anti-inflammatory properties of Boswellia frereana in an in vitro model of cartilage degradation. We have demonstrated that B. frereana prevents collagen degradation, and inhibits the production of pro-inflammatory mediators and MMPs. Due to its efficacy we propose that B. frereana should be examined further as a potential therapeutic agent for treating inflammatory symptoms associated with arthritis.

Abdel-Tawab M, Werz O, Schubert-Zsilavecz M. Boswellia serrata: an overall assessment of in vitro, preclinical, pharmacokinetic and clinical data. Clin Pharmacokinet. 2011 Jun;50(6):349-69. doi: 10.2165/11586800-000000000-00000. PMID: 21553931.

Non-steroidal anti-inflammatory drug (NSAID) intake is associated with high prevalence of gastrointestinal or cardiovascular adverse effects. All efforts to develop NSAIDs that spare the gastrointestinal tract and the cardiovasculature are still far from achieving a breakthrough. In the last two decades, preparations of the gum resin of Boswellia serrata (a traditional ayurvedic medicine) and of other Boswellia species have experienced increasing popularity in Western countries. Animal studies and pilot clinical trials support the potential of B. serrata gum resin extract (BSE) for the treatment of a variety of inflammatory diseases like inflammatory bowel disease, rheumatoid arthritis, osteoarthritis and asthma. Moreover, in 2002 the European Medicines Agency classified BSE as an 'orphan drug' for the treatment of peritumoral brain oedema. Compared to NSAIDs, it is expected that the administration of BSE is associated with better tolerability, which needs to be confirmed in further clinical trials. Until recently, the pharmacological effects of BSE were mainly attributed to suppression of leukotriene formation via inhibition of 5-lipoxygenase (5-LO) by two boswellic acids, 11-keto-β-boswellic acid (KBA) and acetyl-11-keto-β-boswellic acid (AKBA). These two boswellic acids have also been chosen in the monograph of Indian frankincense in European Pharmacopoiea 6.0 as markers to ensure the quality of the air-dried gum resin exudate of B. serrata. Furthermore, several dietary supplements advertise the enriched content of KBA and AKBA. However, boswellic acids failed to inhibit leukotriene formation in human whole blood, and pharmacokinetic data revealed very low concentrations of AKBA and KBA in plasma, being far below the effective concentrations for bioactivity in vitro. Moreover, permeability studies suggest poor absorption of AKBA following oral administration. In view of these results, the previously assumed mode of action - that is, 5-LO inhibition - is questionable. On the other hand, 100-fold higher plasma concentrations have been determined for β-boswellic acid, which inhibits microsomal prostaglandin E synthase-1 and the serine protease cathepsin G. Thus, these two enzymes might be reasonable molecular targets related to the anti-inflammatory properties of BSE. In view of the results of clinical trials and the experimental data from in vitro studies of BSE, and the available pharmacokinetic and metabolic data on boswellic acids, this review presents different perspectives and gives a differentiated insight into the possible mechanisms of action of BSE in humans. It underlines BSE as a promising alternative to NSAIDs, which warrants investigation in further pharmacological studies and clinical trials.

Yu G, Xiang W, Zhang T, Zeng L, Yang K, Li J. Effectiveness of Boswellia and Boswellia extract for osteoarthritis patients: a systematic review and meta-analysis. BMC Complement Med Ther. 2020 Jul 17;20(1):225. doi: 10.1186/s12906-020-02985-6. PMID: 32680575; PMCID: PMC7368679.

Background: Osteoarthritis (OA) is the commonest form of inflammatory joint disease. Unfortunately, to date, there is no appropriate treatment for OA. Boswellia serrata was considered as a potent anti-inflammatory, anti-arthritic and analgesic agent that may be a drug for OA.

Methods: In this meta-analysis, data from randomized controlled trials were obtained to assess the effects of Boswellia or its extract versus placebo or western medicine in patients with OA. The primary outcomes included visual analogue score (VAS), WOMAC pain, WOMAC stiffness, WOMAC function and lequesne index.

Result: Seven trials involving 545 patients were included. Compared with the control group, Boswellia and its extract may relieve the pain [VAS: (WMD -8.33; 95% CI -11.19, - 5.46; P<0.00001); WOMAC pain: (WMD -14.22; 95% CI -22.34, - 6.09; P = 0. 0006)] and stiffness [WOMAC stiffness: (WMD -10.04; 95% CI -15.86, - 4.22; P = 0. 0007)], and improve the joint's function [WOMAC function: (WMD -10.75; 95% CI -15.06, - 6.43; P<0. 00001); lequesne index: (WMD -2.27; 95% CI -3.08, - 1.45; P<0. 00001)].

Conclusion: Based on current evidence, Boswellia and its extract may be an effective and safe treatment option for patient with OA, and the recommended duration of treatment with Boswellia and its extract is at least 4 weeks.

Kumar B, Ghaytidak AB, Pandey AK, Somepalli RR, Sarda P, Raychaudhuri SP, Rokkam MP. A Standardized Boswellia serrata Extract Improves Knee Joint Function and Cartilage Morphology in Human Volunteers with Mild to Moderate Osteoarthritis in a Randomized Placebo-Controlled Study. J Am Nutr Assoc. 2024 Dec 19:1-12. doi: 10.1080/27697061.2024.2438894. Epub ahead of print. PMID: 39700461.

Background and objective: Boswellia serrata Roxb. ex Colebr. (Family: Burseraceae; Genus: Boswellia) gum resin (Salai guggul) has profound therapeutic value in Ayurvedic and Unani medicines in alleviating several chronic inflammatory illnesses, including arthritis, asthma, skin and blood diseases, fever, etc. SN13108F (Aflapin®) is a proprietary, standardized Boswellia serrata gum resin extract. This 180-day randomized, placebo-controlled clinical study aimed to evaluate cartilage morphology using magnetic resonance imaging (MRI), pain and joint function and long-term safety in the SN13108F-supplemented volunteers with knee osteoarthritis (KOA).

Materials and methods: Eighty adult male and female subjects with the Kellgren-Lawrence grade II - III KOA were supplemented with SN13108F (100 mg/day) or a matched placebo for 180 consecutive days.

Results: SN13108F reduced ($p < 0.001$; vs. baseline and placebo) Western Ontario and McMaster Universities Osteoarthritis Index, Visual Analogue Scale, Lequesne's Functional Index scores, improved six-minute walk test, and stair climb test. Post-trial MRI assessments of the tibiofemoral joints revealed that the cartilage volume, thickness, and joint space width were increased ($p < 0.001$; vs. placebo), and levels of high-sensitivity C-reactive protein, matrix metalloproteinase-3, Fibulin-3, type II collagen degradation peptide in serum, and cross-linked C-terminal telopeptide of type II collagen in urine were significantly reduced ($p < 0.001$; vs. baseline and placebo) in the SN13108F-supplemented subjects. Hematology, complete serum biochemistry, urine analysis, and the participants' vital signs did not alter between the groups.

Conclusion: SN13108F supplementation is safe, and it mitigates joint pain and improves musculoskeletal function and cartilage morphology in KOA.

Kimmatkar N, Thawani V, Hingorani L, Khiyani R. Efficacy and tolerability of Boswellia serrata extract in treatment of osteoarthritis of knee--a randomized double blind placebo controlled trial. Phytomedicine. 2003 Jan;10(1):3-7. doi: 10.1078/094471103321648593. PMID: 12622457.

Osteoarthritis is a common, chronic, progressive, skeletal, degenerative disorder, which commonly affects the knee joint. Boswellia serrata tree is commonly found in India. The therapeutic value of its gum (guggulu) has been known. It posses good anti-inflammatory, anti-arthritic and analgesic activity. A randomized double blind placebo controlled crossover study was conducted to assess the efficacy, safety and tolerability of Boswellia serrata Extract (BSE) in 30 patients of osteoarthritis of knee, 15 each receiving active drug or placebo 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 distance. The frequency of swelling in the knee joint was decreased. Radiologically there was no change. The observed differences between drug treated and placebo being statistically significant, are clinically relevant. BSE was well tolerated by the subjects except for minor gastrointestinal ADRs. BSE is recommended in the patients of osteoarthritis of the knee with possible therapeutic use in other arthritis.