www.cropwatch.org

THE FIRST TRULY INDEPENDENT WATCHDOG FOR THOSE WORKING WITH NATURAL AROMATIC MATERIALS

E: info@cropwatch.org T: ++44 (0)7771 872 521

Frankincense – A Cropwatch Bibliography.

Compiled by Cropwatch v1.11 July 2010.
[to be progressively extended].

Contents.

Cropwatch Notes. Frankincense gum (syn. Olibanum) (syn. Incense) is the dried exudation obtained from the schizogenous gum-oleoresin pockets in the bark of various *Boswellia* trees, appearing as whitish-yellow or yellow-orange tears or lumps. The *Boswellia* group within the *Burseraceae* family constitutes some 25 species of shrubs or small trees found in the dry tropical areas of N.E. Africa and India (including N.E. Tanzania and Madagascar) at a height of 1000 to 1800 m.

Hedberg I. & Edwards S. (1989) present 6 spp. of *Boswellia* in Ethiopia:
B. papyrifera (Del) Hochst
B. pirottae Chiv
B. rivae Engl.
B. microphylla Chiov
B neglecta S. Morre
B. ogadensis Vollesen

Thulin M. (1999) lists the *Boswellia* spp. in Somalia as constituting:
B. rivae Engl.
B. sacra Flück
B. frereana Birdw.
B. neglecta S. Moore.

In the same article Thulin states that only *B. frereana* and *B. sacra* are of major economic importance, with gum from *B. sacra* being the most exported species. In addition this comment from Wood (1997)* is of interest: "Contrary to popular belief, frankincense does not come from Yemen but Dhofar or Somalia".

For more information on the status of individual *Boswellia* spp., see Cropwatch's *Updated List of Threatened Aromatic Plants Used in the Aroma & Cosmetic Industries* v1.19 Jan 2010.

* Wood J.R.I. (1997) *Handbook of Yemen Flora* publ. Royal Botanic Gardens Kew 1997 p197.

General Articles.

Anon (2008) "*Boswellia serrata*. Monograph." *Altern Med Rev.* **13**(2),16

Author to be established (2008) "Weihrauch (*Boswellia sacra*, *Boswellia carteri*; Burseraceae)." *Komplementäre und Integrative Medizin* **49**(11-12), 64-65.

Chikamai B.N (2002) *On the State of Knowledge of* Boswellia *Species and Commercialization of Frankincense in the Drylands*. FAO/EU/FORNESSA AFREA (Forestry Research Network for Sub-Saharan Africa

Dorr A. (1973) "Frankincense, Myrrh & Opoponax." *Dragoco Report* **5**, 100-102,

Ertelt J. & Ertelt W. (2008) "Topical use of Frankincense." *Phytomedicine* **15**(6-7),542 June 2008. Abstract. The idea of topical use of frankincense has a long history. The use of pastes, bandages and patches containing frankincense has already been mentioned in several sources of ancient world. Efforts in developing chemical drugs and associated alterations in pharmacopoeias are possible reasons of the disappearance of frankincense. Following scientific reports of Prof. H.P.T. Ammon with highest interest and in search of new herbal and effective, therapeutical alternatives, we attempted to match consumer needs having diversified discomfort with published results of frankincense research. We first developed and tested several preparations including complete resin of frankincense in our pharmacy over years using various galenic basis material. We finally obtained an extract by using a process (patent pending) including a special mixture of solvents. This allowed us to provide frankincense for topical use. Monitored success extending over several years in the use of these products by customers of our drug store suffering from chronic diseases like arthrosis, psoriasis and atopic dermatitis led to foundation of AureliaSan GmbH, Tubingen. Our intention is to analyse and to prove experiences gathered in pharmaceutical practise, that is, scientifically and clinically. In planned future cooperation with the Universities of Tubingen and of the Saarland, we want to investigate and explore the research on frankincense for topical use.

Farah A.Y., Ornäs T.R.H. af- (1994) *The Milk of the Boswellia Forests: Frankincense Production Among the Pastoral Somali.* EPOS - 1994 - EPOS, Research Programme on Environmental Policy and Society

Ghazanfar S.A. (1994) *Handbook of Arabian Medicinal Plants* CRC Press Florida 1994.

Groom N. (1981) *Frankincense and myrrh. A study of the Arabian incense trade*. Longman: London & New York.

Hedberg I. & Edwards S. (1989) *Flora of Ethiopia* Vol 3 publ. The National Herbarium, Biol. Dept., Science Faculty Addis Ababa University Ethiopia and Dept. of Systematic Botany Uppsala University Sweden 1989,

Hepper FN. (1969) "Arabian and African Frankincense trees." *Journal of Egyptian Archaeology* **55.** 66-72.

Kerr, J. (1997) "Essential Oil Profile: Frankincense" *Aromatherapy Today* **2**, 13-16

Krishna-Murthy T. & Shiva, M.P. (1977) "Salai guggul from *Boswellia serrata*. Roxb. Its exploitation and utilization." *Indian Forester* **103**, 466–474.

Kustrak D. (2001) "Tamian-okibanum. *Boswellia sacra*." *Farmaceutski Glasnik* **57**, 465-76.

Lemenih M., Abebea T. & Olsson M. (2003) "Gum and resin resources from some *Acacia*, *Boswellia* and *Commiphora* species and their economic contributions in Liban, south-east Ethiopia." *J of Arid Environments* **553**, 465-482. Abstract. Oleo-gum resins, hardened resinous plant exudates obtained from some *Acacia*, *Boswellia* and *Commiphora* species in the lowlands of Ethiopia, have been traded for centuries both on the international and domestic markets. However, their economic contribution to the rural households is little documented. A reconnaissance survey was carried out in Liban, one of the administrative zones in the Ethiopian Somali National Regional State, to investigate major oleo-gum-resins collected for commerce and their economic contributions to rural households. The results showed that five types of oleo-gum-resins are collected for commerce in Liban. These are gum arabic obtained from *Acacia Senegal*, gum talha obtained from *A. seyal*, frankincense obtained from *Boswellia neglecta* and *B. ogadensis*, myrrh obtained from *Commiphora myrrha* (syn. *C. molmol*), *C. truncata* and *C. borensis* and hagar obtained from *C. africana*. The average annual cash income generated per household was estimated to be US$ 80.00. This income contributes to 32.6% of annual household subsistence, and ranks second after livestock in the overall household livelihood. The contribution from crop farming was estimated to be 12%, which is about one-third of the contribution from oleo-gum resins. These results show that oleo-gum resins obtained from the vegetation resources play a significant role in the economy of rural households in Liban. The vegetation resources and their oleo-gum resins also provide various goods and services for the rural households in Liban. Fodder for livestock, traditional medicines for human and livestock disease treatments, incense for fumigation, cultural and religious rituals, and emergency foods during droughts are among the most common. Opportunities and constraints for oleo-gum-resin-based development in Liban and other similar areas in Ethiopia are discussed. The results could be used as baseline information for evaluating the potential of the arid and semi-arid land vegetation resources of the country, to plan for extensive studies of their management, conservation and proper utilization. **
-see also Retraction notice to 'Gum and resin resources from some *Acacia*, *Boswellia* and *Commiphora* species and their economic contributions in Liban, Southeast Ethiopia': [*J. Arid Environ.* 2004 (56)149–166] *Journal of Arid Environments*, **58(4), 611 by Lemenith M. Abebe T. & Olsson M.

Lemenith M. & Taketay D. (2003) "Frankincense and myrrh resources of Ethiopia: II. Medicinal and industrial uses" *SINET: Ethiopian Journal of Science* 2003. Abstract. Oleo-gum resins such as frankincense and myrrh are some of the economically and culturally valuable products obtained from trees and shrubs of the genera *Boswellia* and *Commiphora*, respectively. They are important natural plant products used in several industries that include pharmacology, food, flavour, liqueur and beverage, cosmetics, perfumery and others. Moreover, frankincense and myrrh have several local applications in medicinal, hygienic, and insecticide areas that could be developed through research. They are widely used in traditional medicines of several countries for treatments of a wide variety of ailments from embalming to cancer, leprosy, bronchitis, diarrhea, dysentery, typhoid, mouth ulcers, inflammatory complaints, viral hepatitis, female disorders, infections/wounds, coughs, tumour, and others. Although Ethiopia is one of the few countries that are endowed with large frankincense and myrrh resources, little proper exploitation

of these resources has been made so far. In this paper a review is presented on pharmacological and industrial applications of these valuable resources. The information is expected to prompt the enormous economic opportunity that these resources could provide both at national and local levels. Concurrently, this opportunity, if properly exploited, will contribute significantly towards the conservation and management of the vegetation resources that yield frankincense and myrrh as well as their ecosystems.

Mandaville J.P. Jr. (1980). “Frankincense in Dhofar”. In: Shaw-Reade S.N., Sale J.B., Gallagher M.D., Daly R.H. (eds.), The scientific results of The Oman Flora and Fauna Survey 1977 Dhofar). *Journal of Oman Studies*, Special Report 2: 87-89.

Marshall S. (2003) “Frankincense: festive: pharmocognosy.” *Pharm. J.* **271**, 862-4.

Menon M, *et al*. (1971) “Analgesic and psychopharmacological effects of the gum resin of *Boswellia serrata*.” . *Planta Med* . **19**(4):333-41.

Miiller W. (date?) "Notes on the use of Frankincense in South Arabia.” *Proceedings of the Ninth Seminar for Arabian Studies.*

Thulin M. & Warfa A.M. (1987) “The frankincense trees (*Boswellia* spp., Burseraceae) of Northern Somalia and Southern Arabia”. *Kew Bulletin* **42**(3), 487-500.

Thulin M. (2001) "Two new species of frankincense trees (*Boswellia*, Burseraceae) from Socotra." *Kew Bulletin* **56**(4), 983-988. Abstract. The two new species *Boswellia bullata* and *B. dioscoridis* from Socotra (Yemen) are described and illustrated.

Verghese J. (1988). “Olibanum in focus.” *Perf. & Flav*. **13**, 2-11.

Verhoff M., Muller C. & Werz O. (2008) "*Boswellia* preparations: current market situation and clinical trials.(Brief article]." *Phytomedicine* **15**(6-7) Abstract. The anti-inflammatory properties of frankincense, the gum resin derived from *Boswellia* species, are well-recognized, and frankincense extracts are frequently and increasingly used in folk medicine to cure chronic inflammatory diseases all over the world. Animal studies and clinical trials confirmed the anti-inflammatory efficacy of such preparations. In this presentation we will give an overview about the current market situation regarding the variety of preparations based on frankincense. Today, frankincense preparations are not approved as drugs, but are at least available as dietary supplement. We summarized published clinical trials that had been performed with respect to the treatment of various chronic inflammatory diseases including arthritis, colitis, Crohn's Disease, asthma as well as of cancer.

Wagner H. & Knaus U (2008) “*Boswellia* and the complement system: A multiherbal drug for multitarget therapy.” *Phytomedicine* **15**(6-7) June 2008. Abstract. Because a pathologically prolonged and sustained activation of the complement system is implicated in a variety of inflammatory disorders, from rheumatoid arthritis and glomerulonephritis to systemic lupus erythematodes, we have investigated the influence of [beta]-boswellic acid from *Boswellia carteri* on the classical and alternative complement pathways. Significant reduction of immunohemolysis in vitro was observed at [beta]-boswellic acid concentrations between 0.05 and 0.1 mM with an [IC.sub.50] value of about 10 [micro]M (Knaus and Wagner, 1996). All other pharmacological activities reported for the Boswellia extract, the -boswellic acid, the four other boswellic acid derivatives and the essential oil of the resin, allow us to suggest that *Boswellia* can be considered a promising example of a multiherbal drug for multitarget synergy therapy (Wagner, 2006).

Biocidal Activity.

Gangwal M. L. & Vardhan D. K. (1995). “Antifungal studies of volatile constituents of *Boswellia serrata*.” *Asian J. Chem*. **7**, 675-678.

Khater H.F. & Shalaby A.A. (2008) "Potential of biologically active plant oils to control mosquito larvae (*Culex pipiens*, Diptera: Culicidae) from an Egyptian locality." *Rev Inst Med Trop* Sao

Paulo. **50**(2),107-12. Abstract. The insecticidal effect of six commercially available plant oils was tested against 4th larval instars of *Culex pipiens*. Larvae were originally collected from Meit El-Attar, Qalyubia Governorate, Egypt, and then reared in the laboratory until F1 generation. The LC50 values were 32.42, 47.17, 71.37, 83.36, 86.06, and 152.94 ppm for fenugreek (*Trigonella* foenum-grecum), earth almond (*Cyperus esculentus*), mustard (*Brassica compestris*), olibanum (*Boswellia serrata*), rocket (*Eruca sativa*), and parsley (*Carum petroselinum*), respectively. The tested oils altered some biological aspects of *C. pipiens*, for instance, developmental periods, pupation rates, and adult emergences. The lowest concentrations of olibanum and fenugreek oils caused remarkable prolongation of larval and pupal durations. Data also showed that the increase of concentrations was directly proportional to reduction in pupation rates and adult emergences. Remarkable decrease in pupation rate was achieved by mustard oil at 1000 ppm. Adult emergence was suppressed by earth almond and fenugreek oils at 25 ppm. In addition, the tested plant oils exhibited various morphological abnormalities on larvae, pupae, and adult stages. Consequently, fenugreek was the most potent oil and the major cause of malformation of both larval and pupal stages. Potency of the applied plant oils provided an excellent potential for controlling *C. pipiens*.

Krüger P., Daneshfar R., Eckert G.P., Klein J., Volmer D.A., Bahr U., Müller W.E., Karas M., Schubert-Zsilavecz M. & Abdel-Tawab M. (2008) "Metabolism of boswellic acids *in vitro* and *in vivo*." *Drug Metab Dispos*. **36**(6),1135-42. Abstract. *Boswellia serrata* resin dry extract is among the few herbal remedies designated with an orphan drug status for the treatment of peritumoral brain edema. In addition, boswellic acids (BAs), the main active ingredients of *B. serrata* extracts, have potent anti-inflammatory properties, and may represent promising agents for the treatment of inflammatory diseases. Pharmacokinetic studies, however, revealed poor bioavailability, especially of 11-keto-beta-boswellic acid (KBA) and 3-acetyl-11-keto-beta-boswellic acid (AKBA), the most potent BAs. To address the question of whether BAs are extensively metabolized, we determined the metabolic stability of KBA and AKBA in vitro, investigated the in vitro metabolism of BAs, and compared the metabolic profiles of KBA and AKBA with those obtained in rats in vivo. In rat liver microsomes and hepatocytes as well as in human liver microsomes, we found that KBA but not AKBA undergoes extensive phase I metabolism. Oxidation to hydroxylated metabolites is the principal metabolic route. In vitro, KBA yielded metabolic profiles similar to those obtained in vivo in rat plasma and liver, whereas no metabolites of AKBA could be identified in vivo. Furthermore, AKBA is not deacetylated to KBA. This study indicates that the efficacy of *B. serrata* extract may be enhanced by increasing the bioavailability of AKBA.

Magesa S.M. & Kamugisha M.L. (2006) "Evaluation of the bio-efficacy of three brands of repellents against wild populations of anthropophilic mosquitoes." *Tanzan Health Res Bull*. **8**(3), 145-8 Abstract. Three commercial repellents marketed in Tanzania: Zero Bite (a blend of microcrystalline waxes, mineral oils, natural flavours, Olibanum oil, Eucalyptus oil, Geranium oil, Citronella oil and Isopropyl myristrate); X-pel (a petroleum jelly formulation containing diethyl toluamide (DEET) and dimethyl phthalate); No Bite (a spray formulation with diethyl toluamide, 2 methyl 2,4 pentondiol and phthalic ester acids) were tested and compared for their repellency effect against wild anthropophilic mosquito populations. Human forearms, feet and legs were treated with the repellent products. All repellents provided protection against wild populations of biting mosquitoes (mainly *Culex quinquefasciatus* and *Aedes scatophagoides*) with varying levels of efficacy. No Bite provided the best overall protection (98%) followed by X-pel (87%). Zero Bite gave the least protection (48%) against the two mosquito species. All products except No Bite displayed reduced efficacy after four hours of application. The results indicate that the two best products give satisfactory levels of personal protection against biting mosquitoes at least for the first five hours, following application, thus could provide complementary protection against mosquito bites particularly during the period when most people have not retired to bed where they may be protected by treated bednets.

Schillaci D., Arizza V,. Dayton T., Camarda L. & Di Stefano V. (2008) "In vitro anti-biofilm activity of *Boswellia* spp. oleogum resin essential oils." *Lett Appl Microbiol*. **47**(5), 433-8. Abstract. AIMS: To evaluate the anti-biofilm activity of the commercially available essential oils from two *Boswellia*

species. METHODS AND RESULTS: The susceptibility of staphylococcal and *Candida albicans* biofilms was determined by methyltiazotetrazolium (MTT) staining. At concentrations ranging from 217.3 microg ml(-1) (25% v/v) to 6.8 microg ml(-1) (0.75% v/v), the essential oil of *Boswellia papyrifera* showed considerable activity against both Staphylococcus epidermidis DSM 3269 and *Staphylococcus aureus* ATCC 29213 biofilms. The anti-microbial efficacy of this oil against *S. epidermidis* RP62A biofilms was also tested using live/dead staining in combination with fluorescence microscopy, and we observed that the essential oil of *B. papyrifera* showed an evident anti-biofilm effect and a prevention of adhesion at sub-MIC concentrations. *Boswellia* rivae essential oil was very active against preformed *C. albicans* ATCC 10231 biofilms and inhibited the formation of C. albicans biofilms at a sub-MIC concentration. CONCLUSIONS: Essential oils of *Boswellia* spp. could effectively inhibit the growth of biofilms of medical relevance. SIGNIFICANCE AND IMPACT OF THE STUDY: Boswellia spp. essential oils represent an interesting source of anti-microbial agents in the development of new strategies to prevent and treat biofilms.

Weckesser S., Engel K., Simon-Haarhaus B., Wittmer A., Pelz K. & Schempp C.M. (2007) "Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance." *Phytomedicine.* **14**(7-8), 508-16. Abstract. There is cumulative resistance against antibiotics of many bacteria. Therefore, the development of new antiseptics and antimicrobial agents for the treatment of skin infections is of increasing interest. We have screened six plant extracts and isolated compounds for antimicrobial effects on bacteria and yeasts with dermatological relevance. The following plant extracts have been tested: *Gentiana lutea*, *Harpagophytum procumbens*, *Boswellia serrata* (dry extracts), *Usnea barbata*, Rosmarinus *officinalis* and *Salvia officinalis* (supercritical carbon dioxide [CO2] extracts). Additionally, the following characteristic plant substances were tested: usnic acid, carnosol, carnosic acid, ursolic acid, oleanolic acid, harpagoside, boswellic acid and gentiopicroside. The extracts and compounds were tested against 29 aerobic and anaerobic bacteria and yeasts in the agar dilution test. *U. barbata*-extract and usnic acid were the most active compounds, especially in anaerobic bacteria. Usnea CO2-extract effectively inhibited the growth of several Gram-positive bacteria like *Staphylococcus aureus* (including methicillin-resistant strains - MRSA), *Propionibacterium* acnes and *Corynebacterium* species. Growth of the dimorphic yeast *Malassezia furfur* was also inhibited by *Usnea*-extract. Besides the *Usnea*-extract, *Rosmarinus*-, *Salvia*-, *Boswellia*- and *Harpagophytum*-extracts proved to be effective against a panel of bacteria. It is concluded that due to their antimicrobial effects some of the plant extracts may be used for the topical treatment of skin disorders like acne vulgaris and seborrhoic eczema.

Chemistry

Caution should be exercised here, since many researchers have apparently obtained their frankincense material from local markets, without expert botanical verification of the source - see Hamm *et al*. (2005).

Abdel Wahab S. M., Aboutabl E. A., Elzalabani S. M. Fouad H. A., De Pooter H. L., & El Fallaha B. (1987). “The essential oil of olibanum.” *Planta Med*. **53**,382-384.

Al-Harrasi A. & Al-Saidi S.. (2008) "Phytochemical analysis of the essential oil from botanically certified oleogum resin of *Boswellia sacra* (Omani Luban)." *Molecules* **13**(9), 2181-9. Abstract. The yield of hydrodistillation of a botanically certified Oleogum Resin of *Boswellia sacra* essential oil (5.5%); and its chemical constituents were determined. The GC/MS technique was used for the analysis of the oil. Several oil components were identified based upon comparison of their mass spectral data with those of reference compounds published in literature or stored in a computer library. The oil was characterized by the high content of the monoterpenes (34) which constituted 97.3% in which *E*-beta-ocimene and limonene were the major constituents. The remaining 2.7% was accounted for the sesquiterpenes (16) in which the *E*-caryophyllene was the major constituent. The analysis proved the complete absence of the diterpenes.

Ammar N., Founier G. & El-Deeb S. (1994). “The volatile constituents of *Boswellia sacra*: Frankincense.” *J. Drug Res. Egypt.* **21**, 55-58.

Ammon H. (1996) “Salai guggal *Boswellia serrata* : from a herbal medicine to a non-redox inhibitor of leukotriene biosynthesis.” *Eur J Med Res* .**1**(8),369-70.

Ammon H.P.T., Mack T., Singh G.B., Safayhi H. (1991) “Inhibition of leukotriene B_4 formation in rat peritoneal neutrophils by an ethanolic extract of the gum resin exudate of *Boswellia serrata” Planta Med.* **57**, 203-207.

Anderson, D.M.W., Cree G.M., Marshall J.J. & Rahman, S. (1965) “Studies on uronic acid materials. XI. The carbohydrate component of the oleoresin from *Boswellia papyrifera* (Del.) Hochst.” *Carbohydrate Research* **1**, 320–323.

Atta-ur-Rahman, Naz H., Fadimatou., Makhmoor T., Yasin A., Fatima N., Ngounou F.N., Kimbu S.F., Sondengam B.L. & Choudhary M.I. (2005) *J Nat Prod.* **68**(2), 189-93. Abstract. Phytochemical investigation of the stem bark extract of *Boswellia papyrifera* afforded two new stilbene glycosides, trans-4',5-dihydroxy-3-methoxystilbene-5-O-{alpha-L-rhamnopyranosyl-(1-->2)-[alpha-L-rhamnopyranosyl-(1-->6)]-beta-D-glucopyranoside (1), trans-4',5-dihydroxy-3-methoxystilbene-5-O-[alpha-L-rhamnopyranosyl-(1-->6)]-beta-D-glucopyranoside (2), and a new triterpene, 3alpha-acetoxy-27-hydroxylup-20(29)-en-24-oic acid (3), along with five known compounds, 11-keto-beta-boswellic acid (4), beta-elemonic acid (7), 3alpha-acetoxy-11-keto-beta-boswellic acid (8), beta-boswellic acid (9), and beta-sitosterol (10). The stilbene glycosides exhibited significant inhibition of phosphodiesterase I and xanthine oxidase. The triterpenes (3-9) exhibited prolyl endopeptidase inhibitory activities.

Awadh Ali N.A., Wurster M., Arnold N., Teichert A., Schmidt J., Lindequist U. & Wessjohann L. (2008) "Chemical composition and biological activities of essential oils from the oleogum resins of three endemic Socotraen *Boswellia* species." *Rec. Nat. Prod.* **2**(1), 6-12 Abstract. The chemical composition, antioxidant and anticholinesterase activity of three essential oils (EOs) obtained from the oleogum resin of three endemic Socotraen *Boswellia* species, *Boswellia socotrana* Balf. f, *Boswellia ameero* Balf. f, and *Boswellia elongata* Balf. f were determined. GC-MS technique was used for the analysis of the oils. Oils of *B. socotrana* and *B. ameero* were characterized by a high content of monoterpenes. The main constituens of *B. socotrana* and *B. ameero* were (E)-2,3-epoxycarene (51.8%), 1,5-isopropyl-2-methylbicyclo[3.1.0]hex-3-en-2-ol (31.3%), and a-cymene (7.1%); (3E,5E)-2,6-dimethyl-1,3,5,7-octatetraene (34.9%), 1-(2,4-Dimethylphenyl)ethanol (20.3%), 3,4-dimethylstyrene (17.3%), a-campholenal (13.4%) and a-terpineol (12.4%) respectively. The composition of *B. elongata* oil was dominated by the diterpene verticiol (52.4%), the sesquiterpene caryophellene (39.1%) and methylcycloundecanecarboxylate (7.8%). The oils were screened for their antioxidant activity by using the DPPH free radical scavenger assay and their anticholinesterase activity on acetylcholinesterase enzyme by using in vitro Ellman method. The antioxidant activity of EOs from *B. socotrana* (IC50 =121.4 µg/mL) appeared to be more potent than that of *B. elongata* (IC50 =211.2 µg/mL) and *B. ameero* (IC50 =175.2 µg/mL). EO of *B. socotrana* showed the higher AChE inhibitory activity with 59.3% at concentration of 200 µg/mL in comparison to EOs of B. elongata and B. ameero (29.6, 41.6 enzyme inhibition) respectively.

Baser K.H.C., Demirci B., Dekebo A. & Dagne E (2003) “Essential oils of some *Boswellia* spp, Myrrh and Oppoponax” *Flav & Frag J* **18**, 153-6.

Basar S., Koch A., König W.A. (2001) “A verticillane-type diterpene from *Boswellia carterii* essential oil” *Flav. Frag. J.* **16**, 315-318.

Basar S. (2005) *Phytochemical investigations on* Boswellia *species: Comparative studies on the essential Oils, pyrolysates and boswellic Acids of* Boswellia carterii *Birdw.,* Boswellia serrata *Roxb.,* Boswellia frereana *Birdw.,* Boswellia neglecta *S. Moore and* Boswellia rivae *Engl.* PhD Thesis, Universität Hamburg 2005.

van Bergen P.F., Peakman T.M., Leigh-Firbank E.C., Evershed R.P. (1997) “Chemical evidence for archaeological frankincense: Boswellic Acids and their derivatives in solvent soluble and insoluble fractions of resin-like materials.” *Tetrahedron Lett.,* **38**, 8409-8412.

Büchele B. & Simmet T. (2003) "Analysis of 12 different pentacyclic triterpenic acids from frankincense in human plasma by high-performance liquid chromatography and photodiode array detection." *Journal of Chromatography B* **795**(2),355-362. Abstract. For the determination of pentacyclic triterpenes of the boswellic acid family in human plasma a novel sensitive method was developed combining serial extraction on diatomaceous earth and graphitized carbon black followed by reversed phase high-performance liquid chromatography (HPLC) and photodiode array detection. The overall average extraction yield of 12 different pentacyclic triterpenic acids was approximately 66%. The calibration graphs were linear with coefficients of correlation for all compounds greater than 0.999. The overall within-day and between-day coefficients of variation (CV) for the 12 pentacyclic triterpenic acids were 5.6 and 6.8%, respectively. This HPLC procedure delivers the analytical sensitivity, precision and accuracy required for clinical pharmacokinetic and therapeutic studies.

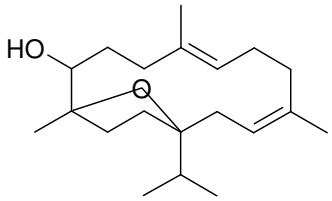
Büchele B., Zugmaier W. & Simmet T. (2003) "Analysis of pentacyclic triterpenic acids from frankincense gum resins and related phytopharmaceuticals by high-performance liquid chromatography. Identification of lupeolic acid, a novel pentacyclic triterpene." *Journal of Chromatography B* **791**(1-2), 21-30. Abstract. An HPLC gradient method with photodiode array detection was developed for the simultaneous analysis of 12 different pentacyclic triterpenic acids in Indian and African frankincense gum resins as well as in related phytopharmaceuticals. The triterpenic acids were obtained by an exhaustive extraction procedure. Identification of the compounds was based on retention times, UV-spectra and add on technique with standards isolated from African frankincense. The method allows differentiation of frankincense of different origin and standardization of frankincense-based phytopharmaceuticals. Further, this is the first report identifying a novel pentacyclic triterpene, lupeolic acid, as a constituent of frankincense gum resins.

Buchele B., Zugmaier W.& Simmer T. (2003) "Analysis of pentacyclic triterpenic acids from frankincense gum resins and related phytopharmaceuticals by high performance liquid chromatography. Identification of lupeolic acid, a novel pentacyclic triterpene.” *Journal of Chjromatography B*, **791**, 21-30.

Camarda L., Dayton T., Di Stefano V., Pitonzo R. & Schillaci D. (2007) “Chemical composition and antimicrobial activity of some oleogum resin essential oils from *Boswellia* spp. (Burseraceae).” *Ann Chim*. **97**(9), 837-44. Abstract. The chemical composition of *Boswellia carteri* (Somalia), *B. papyrifera* (Ethiopia), *B. serrata* (India) and *B. rivae* (Ethiopia) oleogum resin essential oils was investigated using GC-MS to identify chemotaxonomy marker components. Total ion current peak areas gave good approximations to relative concentrations based on GC-MS peak areas. *B. carteri* and *B. serrata* oleogum resin oils showed similar chemical profiles, with isoincensole and isoincensole acetate as the main diterpenic components. Both n-octanol and n-octyl acetate, along with the diterpenic components incensole and incensole acetate, were the characteristic compounds of *B. papyrifera* oleogum resin oil. Hydrocarbon and oxygenated monoterpenes were the most abundant classes of compounds identified in the *B. rivae* oleogum resin oil. The antimicrobial activities of the essential oils were individually evaluated against different microorganisms including fungi, Gram-positive and Gram-negative bacteria strains. The essential oils with the best activity against fungal strains were those obtained from *B. carteri* and *B. papyrifera* with MIC values as low as 6.20 microg/ml. The essential oil of *B. rivae* resin showed the best activity against *C. albicans* with a MIC value of 2.65 microg/ml.

Chiavari G., Galletti G.C., Piccagali R. & Mohammed M.A. (1991). "Differential between resins of *Boswellia carteri* and *Boswellia frereana* (Frankincense) of Somali origin.” *J. Ess. Oil Res*. **3**, 185-186.

Corsano S. & Nicoletti R. (1967) "The structure of incensole" *Tetrahedron* **23**(4), 1977-1984. Abstract. A new diterpene alcohol, incensole (I) isolated from frankincense is related to cembrane. Chemical and physico-chemical data support the structure 12-isopropyl-1,5,9-trimethyl-1,12-oxido-5,9-cyclotetradecadien-2-ol.



incensole

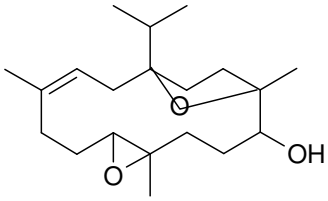
Culioli G., Mathe C., Archier P. & Vieillescazes C. (2001) "A lupane triterpene from frankincense (*Boswellia* sp., Burseraceae)." *Phytochemistry* **62**(4), 537-41. Abstract. A new lupane-type triterpene, 3alpha-hydroxy-lup-20(29)-en-24-oic acid, was isolated from the methanolic extract of "Erytrean-type" resin of commercial frankincense together with the known 3alpha-hydroxy-olean-12-en-24-oic acid (alpha-boswellic acid) and 3alpha-hydroxy-urs-12-en-24-oic acid (beta-boswellic acid). Their structures were characterized on the basis of chemical and spectral evidence including two dimensional NMR experiments and mass spectrometric techniques.

Dagne E., Dekebo A., Desalegn E., Bekele T., Tesso H. &, Bisrat D. (1998) "Preliminary report on essential oils from frankincense, myrrh and other plants of Ethiopia." Regional Conference for Africa on Conservation, Management and Utilisation of Plant Gums, Resins and Essential Oils, Nairobi (Kenya), 6-10 Oct 1997 in *Conservation, management and utilisation of plant gums, resins and essential oils. Proceedings:* Mugah, J.O. (ed.) Chikamai B.N. (ed.) Mbiru S.S. (ed.) Casadei E. (ed.).- Rome (Italy), pub. WAICENT Rome 1998.

Dekebo A., Dagne E., Gautun O.R. & Aasen A.J. (2002) "Triterpenes fom the resin of *Boswellia negelecta*." *Bulletin of Chem Soc. of Ethiopia* **16**(1), 87-90(4). ***Cropwatch comments***: Triterpenes found to be canaric acid, α-amyrin, α-amyrone and *epi*-α -amyrin

Fattorusso E., Santacroce C. & Xaasan C.F.(1983) "4(23)-Dihydroroburic acid from the resin (Incense) of *Boswellia carterii" Phytochem* **22**, 2868-2869.

Forcellese M.L. Nicoletti R. & Santarelli C. "The Revised Structure of Isoincensole-oxide" *Tetrahedron Lett.*, **39**(1973), 3783-3786.



isoincensole oxide

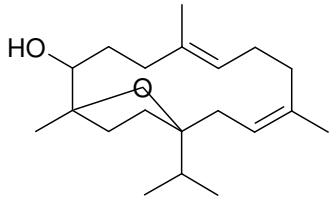
Forcellese M.L., Nicoletti R. & Petrossi1 U. (1972) "The structure of isoincensole-oxide" *Tetrahedron* **28**(2), 325-331. Abstract. A new macrocyclic diterpene, Isoincensole-oxide (I), has been isolated from Frankincense in very small amount. Isoincensole-oxide (I) can be obtained synthetically from Incensole; chemical and physico chemical data support the structure 12-isopropyl-1,5,9-trimethyl-1,12-oxido-5,6-epoxy cyclotetradec-9en-2ol.

Hairfield E.M. & Hairfield H.H. (1989) "GC, GC/MS, and TLC of β-boswellic acid and O-acetyl-β-boswellic acid from *B. serrata, B. carterii and B. papyrifera* ," *J. Chrom. Sci.*, 27(**1989**), 127-133.

Hamm S., Bleton J., Connan J. & Tchapla A. (2005) "A chemical investigation by headspace SPME and GC-MS of volatile and semi-volatile terpenes in various olibanum samples." *Phytochemistry.* **66**(12), 1499-514. Abstract. Six different olibanum samples with certified

botanical origin were analyzed by headspace SPME-GC/MS in order to define their mono-, sesqui- and diterpenic composition, as pertinent criteria of identification. *Boswellia carteri* and *Boswellia sacra* olibanum have quite similar chemical composition, with isoincensole acetate as the main diterpenic biomarker. Although *Boswellia serrata* olibanum also exhibits this biomarker, the presence of methylchavicol, methyleugenol and an unidentified oxygenated sesquiterpene distinguishes *B. serrata* olibanum from the two other species. The characteristic chemical compounds of *Boswellia papyrifera* are the diterpenic biomarkers incensole and its oxide and acetate derivatives, n-octanol and n-octyl acetate. *Boswellia frereana* olibanum is devoid of diterpenes of the incensole family but contains a high amount of many dimers of alpha-phellandrene. The chemical composition of olibanum, which is demonstrated to be different for each *Boswellia* species allowed the determination of the taxonomic origin of frankincense samples purchased on various markets in East Africa, in the Near East and in Yemen. Moreover, terpenic fingerprints allowed the botanical origin of olibanum used in traditional incense mixtures to be identified. Furthermore, this study gave us the opportunity to assign a botanical origin to an archaeological frankincense sample.

Hamm S., Lesellier E, Bleton J. & Tchapla A. (2003) "Optimization of headspace solid phase microextraction for gas chromatography/mass spectrometry analysis of widely different volatility and polarity terpenoids in olibanum." *J Chromatogr A.* **1018**(1), 73-83. Abstract. The aim of this study was the optimization of headspace SPME conditions for trapping diterpenes present in frankincense (olibanum). Diterpenes like cembrenes or incensole and its derivatives are characteristic of olibanum. So in order to detect by SPME the occurrence of olibanum in archeological objects, it appears essential to have the best extraction conditions for these diterpenes that will be in very small quantities. Both sampling time and extraction temperature were studied and five fiber coatings were tested: polydimethylsiloxane (PDMS), polydimethylsiloxane/divinylbenzene (PDMS/DVB), carboxen/polydimethylsiloxane (CAR/PDMS), divinylbenzene/carboxen/polydimethylsiloxane (DVB/CAR/PDMS) and carbowax/divinylbenzene (CW/DVB). The PDMS/DVB fiber was found to be the most efficient for trapping olibanum characteristic diterpenes, with a sampling time of 1 h and a sampling temperature of 80 degrees C.



incensole

Hans-Ulrich J. & Ilan E. "Extract of Olibanum (Frankincense gum) in the form of nanoparticles, and use thereof." Patent No: WO2006128634 (A1). Abstract. The invention relates to a novel and improved nanoparticulate form of a frankincense gum extract, containing, inter alia, Boswellic acids and/or their derivatives. The nanoparticles have advantageous properties for use in the treatment of inflammatory diseases. Surprisingly, these advantages are obtained both in topical application and oral administration. When used in topical formulations, the nanoparticles are better absorbed by the skin than are known, tacky extracts, and they are thus suitable for the treatment, for example, of neurodermatitis and/or actinic keratosis and/or basal cell carcinoma and/or epithlioma and/or squamous cell carcinoma of the skin. For example, in soft gel capsules that dissolve in the small intestine, the nanoparticles have much improved bioavailability, which also considerably improves oral administration for treatment of inflammatory conditions. Finally, the nanoparticles can also be used for coating stents and implants.

Hayashi S., Amemori H., Kameoka H., & Hanafusa M. (1998) "Comparison of volatile components from olibanum from various countries." *J. Ess. Oil Res.* **10**, 25-30.

Higazy S.A. Abel Akher M.A.O., El-Wakell F.A. & Loutfy (1974) “Fractionation and identification of the components of olibanum resinoid extracted by ethyl alcohol from Arabic olibanum gum.” *Egypt. J. Food Science* **2**(1), 29-40.

Jauch J. (2008) "Chemistry & Incense." *Phytomedicine* **15**(6-7), 542-543. June 2008 Abstract. We became interested in incense and boswellic acids in 1996 through an article in "Schwabisches Tagblatt" where the research of Prof. Ammon was highlighted. At that time, I started independent scientific work at TU Munchen in the field of antiviral natural products. Our own research on boswellic acids had to wait until the antiviral project was almost finished. Up to this point, all researchers around the world isolated boswellic acids from incense according to a laborious procedure from Winterstein and Stein which dates back to 1932 and leads only to mg-amounts of AKBA. For elucidation of all the fascinating pharmacological activities, above all the anti-inflammatory effect, first a method had to be developed to prepare boswellic acids in large quantities. Thus, we developed our so-called "focussing synthesis" which makes use of all boswellic acids found in incense extracts. We simply convert all boswellic acids through well-known reactions into AKBA or any other boswellic acid and thus obtain e.g. 35 40% of AKBA, in comparison to the natural content of ca. 1%. With large quantities of AKBA in hand, we were able to chemically modify the parent molecule to find others with improved inflammatory activities. In cooperation with Prof. Dr. O. Werz, we elucidated other cellular targets for boswellic acids and synthesized new derivatives with exciting pharmacological activities. Parallel to our synthetic endeavours, we isolated new compounds from incense extracts, which also show interesting pharmacological effects.

Kala CP (2009) "Aboriginal uses and management of ethnobotanical species in deciduous forests of Chhattisgarh state in India." *J Ethnobiol Ethnomed.* **5**,20. Abstract. A study on the native uses of ethnobotanical species was carried out in the south Surguja district of Chhattisgarh state in India with the major objective of identifying different food and medicinal plant species and also to understand their ongoing management and conservation. Through questionnaire and personal interviews, a total of 73 ethnobotanical species used by tribal and non-tribal communities were documented, of these 36 species were used in curing different types of diseases and 22 were used as edible food plants. This rich traditional knowledge of local people has an immense potential for pharmacological studies. The outside forces, at present, were mainly blamed to change the traditional system of harvesting and management of ethnobotanical species. The destructive harvesting practices have damaged the existing populations of many ethnobotanical species viz., *Asparagus racemosus*, *Dioscorea bulbifera*, *Boswellia serrata*, *Buchnania lanzan*, Sterculia urens and *Anogeissus latifolia*. The sustainable harvesting and management issues of ethnobotanical species are discussed in view of their conservation and management.

Kasali A.K., Adio A.M., Oyedeji A.O., Eshilokun A.O. & Adeferwa M. (2002). "Volatile constituents of *Boswellia serrata* Roxb (Bursearaceae) bark." *Flavour Frag. J.* **17**, 462-464.

Kato T.,Yen C.C., Uyehara T., Kitahara Y. (1977) “Cyclization of polyenes XXIII, Synthesis and stereochemistry of isoincensole-oxide” *Chem. Lett.*, **1977**, 565-568.

Klein E. & Obermann H. (1978) ”(S)-1-Isopropyl-4,8,12-trimethyl-cyclotetradeca-3E,7E,11E-trien-1-ol, ein neues cembrenol aus dem ol von Olibanum” *Tetrahedron Lett.*, 4(**1978**), 349-352.

Klein E. & Obermann H. (1979) “The chemistry of frankincense.” *Proceedings of VIIth International Congress of Essential Oils Kyoto Japan pp400-402 (1979).*

Koch A.J. (2002) “Stability testing of *Boswellia* species and Its preparations by HPLC” *50th Annual Congress of the Society for Medicinal Plant Research*, Barcelona, Spain, **2002**.

Kubmarawa D., Ogunwande I.A., Okorie D.A., Olawore N.O. & Kasali A.A., (2006). "Constituents of the essential oils of *Boswellia dalzielii* Hutch. from Nigeria. *J. Ess. Oil Res*. **18**, 19-120.

Lawrence B.M. (1982) “Olibanum; Progress in essential oils” *Perf & Flav* **7**, 48,50.

Lawrence B.M. (1992) “Olibanum; Progress in essential oils” *Perf & Flav*, **17**, 61-66.

Mertens M., Buettner A. & Kirchhoff E. (2009) "The volatile constituents of frankincense - a review." *Flav & Frag J* **24**(6), 279-300. Abstract. The smell of frankincense resin & powder, as` well as burned frankincense, has been linked to a series of health effects since ancient times. Additionally, frankincense and its fumes are used as a eans to induce positive psychophysical effects and well-being, not only in an ecclesiastical setting but also in traditional medical applications. This review aims to provide an overview of current knowledge of the volatile constituents of frankincense, with explicit consideration concerning the diverse Boswellia varieties. Altogether, more rthan 300 volatiles in frankincense have been reported in the literature. In particular, a broad diversity has been found in the qualitative & quantitative composition of the volatiles with respect to different varieties of Boswellia. A detailed discussion of the various analytrical approaches to isolating and analysing the volatile fractions of frankincense is also presented.

Mathe C., Culioli G., Archier P., Vieillescazes C. (2004) "High-performance liquid chromatographic analysis of triterpenoids in commercial Frankincense." *Chromatographia* 60, (No. 9/10). Abstract. A reversed-phase high-performance liquid chromatographic procedure has been developed: it is a simple and specific method for the determination of fifteen pentacyclic triterpenic compounds (a-boswellic acid, 3-O-acetyl-a-boswellic acid, b-boswellic acid, 3-O-acetyl-b-boswellic acid, a-amyrin, b-amyrin, lupeol, 3-epi-a-amyrin, 3-epi-b-amyrin, 3-epi-lupeol, a-amyrenone, b-amyrenone, lupenone, lupeolic acid and 3-O-acetyl-lupeolic acid) found in the most commonly traded frankincense, usually called ‘‘Eritrean-type’’ olibanum. In addition, the chromatographic comparison between fresh commercial resins and botanically certified ones was described in order to determine the geographical and/or the botanical origins of commercial frankincense. According to previous botanical studies, it appears difficult to make an unequivocal distinction between *Boswellia carteri* and *B. sacra*. On the other hand, *Boswellia frereana* (considered as a source of high-grade frankincense) shows a characteristic chromatogram and could be unambiguously distinguished from the other producing species of commercial frankincense. In a chemical point of view, *Boswellia carteri* and *B. sacra* were more especially characterized by the presence of lupeolic acid, boswellic acids and their respective O-acetyl derivatives, whereas 3-epi-lupeol was the major compound in *B. frereana* methanolic extracts.

Maupetit P. (1984/1985) “New constituents in olibanum resinoid and essential oils.” *Perf & Flav* **9**(6),19-37. ***Cropwatch comments***: Maupetit analyses the ‘Aden’ type of olibanum, finding 47 new constituents and confirming the presence of 169 previously identified materials.

Mikhaeil B.R., Maatooq G.T., Badria F.A. & Amer MM.A. (2003) "Chemistry and immunomodulatory cctivity of Frankincense oil." *Z. Naturforsch*. **58c,** 230-238 (2003). Abstract. The yield of steam distillation of frankincense essential oil (3%); and its physicochemical constants were determined. Capillary GC/MS technique was used for the analysis of the oil. Several oil components were identified based upon comparison of their mass spectral data with those of reference compounds published in literature or stored in a computer library. The oil was found to contain monoterpenes (13.1%), sesquiterpenes (1%), and diterpenes (42.5%). The major components of the oil were duva-3,9,13-trien-1,5α-diol-1-acetate (21.4%), octyl acetate (13.4%), o-methyl anisole (7.6%), naphthalene decahydro-1,1,4a-trimethyl-6-methylene-5-(3-methyl-2-pentenyl) (5.7%), thunbergol (4.1%), phenanthrene-7-ethenyl-1,2,3,4,4a,5,6,7,8,9,10,10a-dodecahydro-1,1,4a,7-tetramethyl (4.1%), α-pinene (3.1%),sclarene (2.9%), 9-cis-retinal (2.8%), octyl formate (1.4%), verticiol (1.2%) decyl acetate(1.2%), n-octanol (1.1%). The chemical profile of the oil is considered as a chemotaxonomical marker that confirmed the botanical and geographical source of the resin. Biologically, the oil exhibited a strong immunostimulant activity (90% lymphocyte transformation) when assessed by a lymphocyte proliferation assay.

Nicoletti R., Forcellese M.L. (1968), *The Structure of Incensole-oxide Tetrahedron.*, **24**(1968), 6519-6525.

Obermann H. (1978) “Monoterpensäuren als Spuren komponenten in Olibanumöl (Monoterpene acids as trace components in olibanum oil).” *Dragoco Rep*. (Germ. Edn.) 25 (**3)**, 55-60.

Obermann H. (1977) "Die chemischen und geruchlichen Unterschiede von Weihrauchharzen (Differences in the chemistry & odour of incense resins)" *Dragoco Rep*, 11/12, **24,** 260-265. Also presented at *VII International Congress of Essential Oils, Kyoto 1977*, pp400-402.

Pailer M., Scheidl O., Gutwillinger H., Klein E. & Obermann H. (1981) "Über die Zusammensetzung des Pyrolysates von Weihrauch "Aden“, dem Gummiharz von *Boswellia carteri* Birdw..” *Monatsh. Chem.*, **112,** 341-358.

Pailer M., Scheidl O., Gutwillinger H., Klein E., Obermann H. (1981) "Über die Zusammensetzung des Pyrolysates von Weihrauch "Aden“, dem Gummiharz von *Boswellia carteri* Birdw. 2.” *Monatsh. Chem.*, **112,** 595-603.

Pailer M., Scheidl O., Gutwillinger H., Klein E., Obermann H. (1981) "Über die Zusammensetzung des Pyrolysates von Weihrauch "Aden“, dem Gummiharz von *Boswellia carteri* Birdw. 3.” *Monatsh. Chem.*, **112,** 987-1006.

Pardhy R.S. & Bhattacharyya S.C. (1978) Tetracyclic triterpene acids from the resin of *Boswellia serrata* Roxb.” *Ind. J. Chem.*, **16B**, 174-175.

Pardhy R.S. & S. C. Bhattacharyya S.C, (1978) "β-Boswellic acid, acetyl-β-boswellic acid, acetyl-11-keto-β-boswellic acid and 11-keto-β-boswellic acid. four pentacyclic triterpene acids from the resin of *Boswellia serrata* Roxb., *Ind. J. Chem.,* **16B**, 176-178

Pardhy R.S. &. Bhattacharyya S.C. (1978) “Structure of serratol, a new diterpene cebranoid alcohol from *Boswellia serrata* Roxb.” *Ind. J. Chem.*, **16B**, 171-173.

Peyron L., Acchiardi J., Bigmotti D. & Pellerin (1980) “Comparaison des extraits d’encens obtenus par des technologies diverses a partin de gommes d’origines geographiques differentes,” *Paper No 95. International Congress of Essential Oils, Cannes, Oct. 1980*.

Pozharitskaya O.N., Ivanova S.A., Shikov A.N., Makarov V.G.. (2006) "Separation and quantification of terpenoids of *Boswellia serrata* Roxb. extract by planar chromatography techniques (TLC and AMD)." *J Sep Sci.* **29**(14), 2245-50. Abstract. An high-performance TLC (HPTLC) method for the separation of boswellic acids, the active constituents in *Boswellia serrata* extract, has been developed and TLC of these compounds on silica by automated multiple development (AMD) using solvent gradients was performed. Enhancement of the separation of boswellic acids on HPTLC plates was carried out by AMD chromatography. Densitometric analysis of the developed plate was carried out to quantify the four boswellic acids. 11-Keto-beta-boswellic acid (KBA) and acetyl-11-keto-beta-boswellic acid (AKBA) were quantified by densitometric scanning of the developed plate at 254 nm. beta-Boswellic acid (BA) and acetyl-beta-boswellic acid (ABA) were quantified after derivatization with anisaldehyde sulfuric acid reagent at 560 nm. The AMD system provided a clean separation according to polarity for each of the four groups studied and good results were obtained. The proposed HPTLC method for the simultaneous quantification of the major boswellic acids BA, ABA, KBA, and AKBA was found to be simple, precise, specific, sensitive, and accurate and can be used for routine quality control and for the quantification of these compounds in plant materials. The study of market products revealed significant variations in the content of these pharmacologically active compounds in commercial samples.

Provan G.J., Gray A.I. & Waterman P.G. (1987) *Fl. & Frag J.* **2**, 115-118 ***Cropwatch comments:*** Authors provide details of composition of essential oil of *Boswellia neglecta.* .

De Rijke D., Traas P.C., ter Heide R., Boelens H. & Takken H.J. (1978) “Acidic components in essential oils of costus root, patchouli and olibanum.” *Phytochemistry* **17**, 1664-1666.

Ruzicka L. & W. Wirz W. (1939) "Zur Kenntnis der Triterpene. Umwandlung der α-Boswellinsäure in β-Amyrin" *Helv. Chim. Acta*, **22**, 132-135.

Safayhi H. & Ammon H.P.T. (1997) “Pharmakologische Aspekte von Weihrauch und Boswelliasäuren “ *Pharm. Z.*, **142** (39), 11-20.

Sen A. *et al.*(1992) “Isolation and structure of a 4-O-methyl-glucuronoarabinogalactan from *Boswellia serrata*.” *Carbohydr Res* . **223**, 321-27.

Shah S.A., Rathod I.S., Suhagia B.N., Pandya S.S. & Parmar VK.(2008) "A simple high-performance liquid chromatographic method for the estimation of boswellic acids from the market formulations containing *Boswellia serrata* extract." *J Chromatogr Sci.* **46**(8), 735-8. Abstract. A simple, rapid, and reproducible reverse-phase high-performance liquid chromatographic method is developed for the estimation of boswellic acids, the active constituents in *Boswellia serrata* oleo-gum resin. The chromatographic separation is performed using a mobile phase consisting of acetonitrile-water (90:10, % v/v) adjusted to pH 4 with glacial acetic acid on a Kromasil 100 C18 analytical column with flow rate of 2.0 mL/min and detection at 260 nm. The elution times are 4.30 and 7.11 min for 11-keto beta-boswellic acid (11-KBA) and 3-acetyl 11-keto beta-boswellic acid (A-11-KBA), respectively. The calibration curve is linear in the 11.66-58.30 microg/mL and 6.50-32.50 microg/mL range for 11-KBA and A-11-KBA, respectively. The limits of detection are 2.33 microg/mL and 1.30 microg/mL for 11-KBA and A-11-KBA, respectively. The mean recoveries are 98.24% to 104.17% and 94.12% to 105.92% for 11-KBA and A-11-KBA, respectively. The inter- and intra-day variation coefficients are less than 5%. The present method is successfully applied for the estimation of boswellic acids from the market formulations containing *Boswellia serrata* extract.

Shi S.M, Tian J.G. & Wang B.Q.. (2002) "[Study on the detecting methods of the imported materia medica--olibanum]" *Zhongguo Zhong Yao Za Zhi*. **27**(3), 170-3. Abstract. OBJECTIVE: To analyse the chemical components of the essential oil of Gum olibanum somalilnds and Gum olibanum Ethiopia, and to set up determination methods of their main components. METHOD: Two kinds of essential oil are identified by GC-MS, and assayed by Gas chromatography, using SE-54 as the packing material (column 2.1 m x 3.2 mm), with column temperature starting from 80 degrees C, holding for 1 min, and then rising at the rate of 15 degrees C per minute to 170 degrees C. RESULT: 40 kinds of chemical compounds in the essential oil of Gum olibanum somalilnds and 22 kinds of those of Gum olibanum Ethiopia were identified by GC-MS, the main component in the essential oil of Gum olibanum somalilnds being alpha-pinene, and the main one of Gum olibanum Ethiopia being Octyl acetate 17 batches of samples were determined with the linear range of alpha-pinene being 0-10.80 micrograms, the correlation coefficient being 0.9995, the recovery being 98.16%, RSD being 1.83%; the linear range of Octyl acetate being 0-10.32 micrograms, the correlation coefficient being 0.9996, the recovery being 99.56%, and RSD being 1.36%. CONCLUSION: This study can be used for the setting up of the specification of Olibanum.

Singh B., Kumar R., Bhandari S., Pathania S. & Lal J. (2007) “Volatile constituents of natural *Boswellia serrata* oleo-gum-resin & commercial samples.” *Flavour & Fragrance J.* **22**, 145-147

Snatzke G. & Vértesy L. (1967) "Über die Neutralen Sesqui- und Triterpene des Weihrauchs" *Monatsh. Chem*. **98**(1967), 121-132.

Stenhouse J. "Zusammensetzung des Elemi- und Olibanumöls" *Lieb. Ann. Chem.*, **35**(1840), 304-306.

Strappaghetti G., Corsano S., Craveiro A. & Proietti G. (1982). “Constituents of essential oil of *Boswellia frereana*.” *Phytochemistry* **21**, 2114-2115.

Tschirch A. & O. Halbey O. (1898) "Untersuchungen über die Sekrete. 28: Über das Olibanum." *Arch. Pharm*. **236**, 487-502.

Verghese J. *et al.* (1987) "A fresh look at the constituents of Indian olibanum oil." *Flav. & Frag. J.* **2**(3), 99-102.

Vernin G. Boniface C., Metzger J., MaireY., Rakotorijaona A., Fraisse D., Parkanyi C. (1989) "GC-MS Data Bank Analysis of the essential oils from *Boswellia frereana* Bidw. and *Boswellia carterii* Birdw." *Proceedings of the 6th International Flavor Conference, Flavors and Off-Flavors, 1989*. ***Cropwatch comments:*** Same article appears in *Flavours & Off-Flavours* ed. G. Charalambous Elsevire Publ.BV Amsterdam pp511-542 (1989).

Wang F,, Li Z,, Liu T, & Hua H. (2009) "[Cembrane diterpenes in olibanum]." *Zhongguo Zhong Yao Za Zhi*. **34**(19), 2477-80. Abstract. OBJECTIVE: To study the constituents in the chloroform extract of olibanum and their antitumor activities. METHOD: The compounds were isolated by chromatographic methods and their structures were identified on the basis of spectroscopic methods and X-ray diffraction. The antiproliferative effect of the compounds in human leukemia HL-60 cells was tested by viable cell counting. RESULT: Four cembrane diterpenes were isolated and identified as incensole-oxide (1), acetyl incensole-oxide (2), incensole (3), and acetyl incensole (4). CONCLUSION: Compounds 2 and 4 were isolated from the genus Boswellia for the first time. Compound 4 showed growth inhibitory effect against human leukemia HL-60 cell lines with IG50 value of (16.3 +/- 3.4) micromol x L(-1).

Wang W., Zhu Y.X., Liy L.Z., Link D.K., Qin X.L. & Tian J.G. (1993)."Analysis of the chemical constituents of essential oil of *Boswellia carteri* Birdwood from Somali origin." *Yaowu Fenxi Zazhi*, **13**, 170-173

Yates R.L. & Wenninger J. A. (1970). "Constituents of olibanum oil: Sesquiterpene hydrocarbons." *J. Assoc. Anal. Chem*. **53**, 941-948.

Yoshikawa M, Morikawa T, Oominami H. & Matsuda H. (2009) "Absolute stereostructures of olibanumols A, B, C, H, I, and J from olibanum, gum-resin of *Boswellia carterii*, and inhibitors of nitric oxide production in ipopolysaccharide-activated mouse peritoneal macrophages." *Chem Pharm Bull (Tokyo)*. **57**(9), 957-64. Abstract. Three new monoterpenes, olibanumols A (1), B (2), and C (3), and three new triterpenes, olibanumols H (4), I (5), and J (6), were isolated from olibanum, the exuded gum-resin from *Boswellia carterii* BIRDW. Their structures including the absolute configuration were determined by chemical and physicochemical evidence. Among the constituents, olibanumols A (1), H (4), and I (5), and isofouquierol (12) exhibited nitric oxide production inhibitory activity in lipopolysaccharide-activated mouse peritoneal macrophages.

Zhou J.Y. & Cui R. (2002) "[Chemical components of *Boswellia carterii*]" *Yao Xue Xue Bao*. **37**(8), 633-5. Abstract. AIM: To investigate the chemical components of *Boswellia carterii.* METHODS: Chromatographic technologies were used for separation and purification, while spectral analysis was used for structure elucidation. RESULTS: Six compounds were isolated and their structures were identified as acetyl-alpha-boswellic acid (1), acetyl-beta-boswellic acid (2), lup-20(29)-ene-3 alpha-acetoxy-24-oic acid (3), alpha-boswellic acid (4), beta-boswellic acid (5) and acetyl-11-keto-beta-boswellic acid (6). CONCLUSION: Compound 3 is a new constituent.

Ecology – *Boswellia* spp.

Cropwatch notes: Several *Boswellia* spp. are listed in the IUCN Red List of Threatened Species 2008, including: several from Socotra, Yemen.

Boswellia aff. ameero Vulnerable D2 - native to Socotrana
Boswellia ameero Vulnerable B2ab(ii,iii) - native to Socotrana
Boswellia bullata Vulnerable D2 - native to Socotrana
Boswellia dioscorides Vulnerable D2 - native to Socotrana
Boswelia elongata Vulnerable B2ab(iii) - native to Socotrana
Boswellia nana Vulnerable D2 - native to Socotrana
Boswellia ogadensis Vulnerable D2 - only from 1 river location in Ethiopia.
Boswellia pirottae LR/nt - only from 3 river locations in Ethiopia

Boswellia popoviana Vulnerable D2	- native to Socotrana
Boswellia sacra LR/nt	- native to Oman, Somalia & S. Yemen.
Boswellia socotrana Vulnerable D2	- native to Socotrana

However the status of other *Boswellia* spp. is also causing concern to environmentalists e.g. *Boswellia papyrifera* - see Cropwatch's *Updated List of Threatened Aromatic Plants Used in the Aroma & Cosmetic Industries* v1.08 Dec 2008 for more detailed information.

Chikamay B.N. (Ed.) (2002) *Review and synthesis on the state of knowledge of* Boswellia *species and commercialization of frankincense in the drylands of Eastern Africa*. FAO/EU/FORNESSA.

Moore P.D. (2006) "Conservation biology: unkind cuts for incense." *Nature* **444**(7121),829.. Abstract. Gold, frankincense and myrrh — the three royal gifts of the Christmas story — remain valuable commodities. But as Toon Rijkers *et al.Journal of Applied Ecology* (**43,** 1188–1195; 2006) say, the latter-day story of frankincense is also a tale for our times.

Tucker A.O. (1986) "Frankincense and Myrrh." *Economic Botany* **40**, 425-433. Abstract. While frankincense and myrrh have been harvested from a multitude of species, certain species have predominated in history. *Boswellia carteri* and *B. frereana* are the main sources of frankincense today, while *B. papyrifera* was the principal source of antiquity and *B. sacra* was the principal species of classical times.*Commiphora myrrha* is the chief source of myrrh today, but *C. erythraea* was the principal source of ancient and classical times. Each of these oleo-gum-resins has a characteristic odor that is predominately due to a mixture of complex sesquiterpenes.

Ecology - *Boswellia papyrifera* (Del.) Hochst.

Abiyu A., Vacik H. & Glatzel (2005) "Population viability risk management applied to *Boswellia papyrifera* (Del.) Hochst in North-eastern Ethiopia." *Journal of the Drylands* **1**(2), 98-107. Abstract. *Boswellia papyrifera* (Del.) Hochst, is an ecologically and economically important tree species found in the arid lowlands of Ethiopia. As Ethiopia is one of the world's largest producers of Frankincense (olibanum), the exploitation of olibanum is one of the top employment generating activities in the remotest parts of Ethiopia and therefore a very important source of income for the rural people residing there. Due to this exploitation the potential range of forest communities with B. papyrifera is greatly reduced and the species itself is classified as endangered. In Amhara region, there is a large reserve of approximately 604,000 ha of this forest in Tekeze and Abay (Blue Nile) catchments, where the species is cohabiting the same niche with Acacia and Commiphora species. Based on this background the framework of a Population viability risk management (PVRM) is used for the design and evaluation of in-situ conservation strategies for B. papyrifera population in Amhara region. As part of the PVRM the Analytical Hierarchy Process (AHP) is used to evaluate the conservation strategies with regard to the viability of Boswellia. The viability of B. papyrifera is described based on the results of an analysis of the current environmental, social and economical state and a characterization of the ecological parameters of its population. The significant risk factors such as successful regeneration, pressures like grazing and tapping or the kind of ownership are compared and prioritized against their impact on the viability of *B. papyrifera* population. Effects of different conservation strategies (e.g. change of tapping frequency, grazing regime) are determined through a qualitative assessment of the probability of a decrease of B. papyrifera population along with scenarios under different environmental conditions. In this context strategies combining silvicultural measures that increase regeneration and growth of Boswellia and measures that consider ownership and benefit sharing seem to be the most effective. The rational and pitfalls using the concept of population viability risk management is discussed along with the results of the scenario analysis.

Eshete A. (2002): *Regeneration status, soil seed banks and socio-economic importance of* Boswellia papyrifera *in two Woredas of North Gonder Zone, Northern Ethiopia.* MSc. thesis, Swedish University of Agricultural Sciences, Skinnskattenberg.

Gebrehiwot K. (2003) *Ecology and management of Boswellia papyrifera (Del.) Hochst. dry forests in Tigray, Northern Ethiopia*. PhD thesis Georg-August-University of Göttingen, Germany.

Gebrehiwot K., Muys B, Haile M. & Mitloehner R. (2003) “Introducing *Boswellia papyrifera* (Del.) Hochst and its non-timber forest product, Frankincense.” *International Forestry Review* **5**, 348-353. Abstract. *Boswellia papyrifera* has been an important multipurpose tree species in central and eastern Africa since ancient times. The species is best known for its non-timber forest product, frankincense. In addition, it has numerous environmental, socio-economic, traditional and industrial uses. However, the species is declining at an alarming rate and thus needs priority in conservation. Populations are facing degradation due to agricultural expansion, overgrazing, fire, poor incense harvesting practices, shifting cultivation, termite and other infestations and urgent conservation measures are required to save the species. Conservation strategies could include promotion of natural regeneration through closed areas and enrichment planting. Nevertheless, more ecological and silvicultural studies are required in order to streamline specific interventions.

Gebrehiwot K *et al* (date?) "The importance of closed areas for the natural regeneration of *Boswellia papyrifera* (Del.) Hochst in Ethiopia" In: S.A. Ghazanfar & H.J. Beentje (eds) *Taxonomy & ecology of African plants, their conservation & sustainable use*. pp147-156 Royal Botanic Gardens Kew. Abstract The population of *Boswellia papyrifera* (Burseraceae), a dryland tree species known for production of frankincense, is declining. This paper attempts to evaluate the effectiveness of closed areas on the natural regeneration of the species in N Ethiopia. The distribution of seedlings with respect to mature trees at four sites is analysed. the sites were closed for livestock grazing since 1994, whereas open grazing is practicised at the other two sites. Cutting down trees is not allowed at any of the four sites. Data were collected from sixteen plots (each 20m x 20m) at the four sites. The results show that there is a significant improvement of natural regeneration in closed sites and that regeneration is mainly concentrated within a radius of two metres from mature trees. Higher mortality rate >90% of seedling was recorded at the sites where open grazing is practised. The study shows that protection from livestock grazing is essential for the growth & survival of seedlings of *B. papyrifera*. The use of closed areas is an effective way of promoting natural regeneration of this important but declining species.

Gebremedhin T. (1997) *Boswellia papyrifera (Del.) Hochst. from Western Tigray: opportunities, constrains and seed germination responses*. MSc. thesis No. 12. Swedish University of Agricultural Sciences, Skinnskatteberg. Abstract. Studies on *Boswellia papyrifera* were carried out both in the field and in a laboratory. A survey study was done in the Western Zone of Tigray to learn about gum olibanum production methods (such as timing and methods of tapping, resin collection, as well as methods of resin processing and grading), socio-economic significance of the species, potential gum production, and problems and constraints causing deterioration of the stock of the species. Potential of the species as an agro-industrial crop was also reviewed. Thr field survey was done by preparing a checklist of the information needed and a transect walk along the contour was done together with key informants for discussion on the issues under list. Laboratory experiments were also performed to see the germination responses of the seeds of the species under different treatment conditions. The treatments used were concentrated sulphuric acid (seeds immersed in sulphuric acid for 1, 2, 5, 10, 20, 30, and 60 minutes), hot water (seeds immersed in hot water for 1, 2, 5, 10, 20, 30, and 60 minutes), pricking, nicking, presoaking (5, 10, 15, 20 days soaking), and treatments with GA3 (10 minus cubic, 10 minus fourth, 10 minus fifith, 10 minus sixth, 10 minus seventh, 10 minus eighth, and 10 minus nineth M solutions). treatment with distilled water was used as a control. Percentage germination and germination value for each treatment were calculated and compared. The survey study revealed that tapping commences during the second half of September and ends early June before rain starts to fall. Tapping is done by scrapping of a thin layer of the bark by using an instrument called mengaff. A tree is tapped 8-12 times per annum. Collection of resin is done concurrently with tapping. The raw gum is cleaned and selected and finally sorted into five grades based on the size and color of the pieces. Collection of gum olibanum from the species was also found very important in that it generates income for the government and creates job opportunities for thousands of Ethiopians. The growth of the species on wastelands is also of paramount importance since it is making an economic use of the wastelands in addition to the protection of

the soil from erosion. The estimated potential gum production in the zone (average 177,538 quintals per year) was found to be very high as compared to the average exploitation so far (less than 25 percent) and the annual demand at a national level (ca. 60,000 quintals). A review on the use of gum olibanum in the production of various industrial outputs in perfumery, pharmacceutical, plastic, etc. industries revealed that there is a high potential for use of the gum. In spite of the various goods and services obtained from the species, its stock has been deteriorating and natural regeneration has been impeded by human and livestock interferences, forest fire, termite and insect infestation, lack of systematic tapping and lack of knowledge about its propagation methods. A high incidence of insect attack (17.5 percent) and a high proportion of "embryolessness" (greater than 28 percent) were also observed on B. payrifera seeds. Gibberellic acid-3 (except at 10 minus cubic M), nicking and distilled water treatments resulted in a significantly high percentage germination and germination value, i.e. (88-98 percent, 52.80-64.02, (89 percent, 57.16), and (91 percent, 66.88), respectively. A complete inhibition of germination was observed on seeds treated with sulphuric acid, hot water and presoaking (except for the 5 and 10 days soaking). Generaly, little or no dormancy problem has been observed on the seeds.

Gebremedhin T. & Negash L. (1999) “The effect of different pre-sowing seed treatments on the germination of *Boswellia papyrifera*, a key dryland tree.” *Ethiopian Journal of Natural Resources* **1**, 37-55.

Negussie A. Aerts R., Gebrehiwota K. & Muys B. (2007) "Seedling mortality causes recruitment limitation of *Boswellia papyrifera* in northern Ethiopia." *Journal of Arid Environments* **72**(4),378-383. Abstract. The Frankincense tree *Boswellia papyrifera* is an important resource in the semiarid lower highlands of eastern Africa but its populations are declining due to human pressure and environmental degradation. To assess the perspectives of (assisted) natural regeneration for *Boswellia* woodland restoration, we examined *Boswellia* stand structure and seedling densities in a grazed woodland and in a livestock grazing exclosure. We also tested topsoil scarification as a means to increase seedling survival. *Boswellia* populations lacked small diameters, indicating recruitment limitation. During the rainy season, seedling densities were 8331 ha−1 in the exclosure and 3325 ha−1 in the grazed woodland. Respectively, 19% and 11% of these seedlings survived the first dry season. However, the lack of saplings suggests a lack of surviving seedlings over successive dry seasons and thus a cumulative seedling mortality approximating 100% within each generation. Topsoil scarification had an adverse effect on seedling survival. Dry season seedling mortality seriously limits the potential of natural *Boswellia* woodland recovery. To restore a healthy population structure in exclosures, additional management interventions such as shading to support early seedling survival or planting of large rooted cuttings need to be tested.

Ogbazghi W. (2001) *The distribution and regeneration of Boswellia papyrifera (Del.) Hochst. in Eritrea*. PhD thesis, Wageningen University, The Netherlands. Abstract. *Boswellia papyrifera* (Del.) Hochst. is a deciduous gum-producing multipurpose perennial tree species growing in Sudanian and Sahelian regions. The tree is tapped on the stem for oleo-gum called olibanum (true frankincense). Land clearing for agriculture and un-regulated grazing are threatening the future of the natural *Boswellia* woodlands in Eritrea. Against this background, a study was carried out to investigate the distribution of the species and the factors determining its distribution in Eritrea, to study the structure and dynamics of *Boswellia* populations, including the natural regeneration, and to identify the factors causing the decline of *Boswellia* woodlands and measures which can reverse this situation. At macro-level, the distribution of the species was found to be limited to the southwestern and southern parts of the country between 800-1850 m altitude receiving a mean annual rainfall of 375-700 mm with a dependable length of growing period of 45-100 days. At micro-level, the abundance and distribution of the species was found to be affected in order of importance by altitude, land use intensity, soil organic matter, and to a lesser extent by silt and pH. Tree development studies showed that trees in the lowlands were twice as high as those in the highlands. The most important outcome of the population structure study is the lack of regeneration. Out of five areas investigated regeneration was only found at

two sites where trees were not tapped and which were not accessible to livestock. Further research showed that the present system of intensive annual tapping throughout the dry season leads to low production of non-viable seeds and that where viable seeds are produced, seedlings and saplings are usually destroyed by livestock. Establishment of enclosures in which tapping and grazing is not allowed were found to be an effective measure to promote natural regeneration. Further research is needed to refine this system and to investigate the feasibility of replanting former *Boswellia* areas.***Cropwatch comments***: Ogbazghi notes that the export of frankincense has decreased from c. 1700 t/y in the 1960s &1970s to ox. 450 t/y approx. in 1996–98.

Ogbazghi W., Bongers F., Rijkers T. & Wessel M. (2006) "Population structure and morphology of the frankincense tree *Boswellia papyrifera* along an altitude gradient in Eritrea." *J of the Drylands* **1**(1), 85-94. Abstract. In Eritrea, the frankincense tree *Boswellia papyrifera* is a multipurpose plant. Human induced factors such as land clearing for agriculture, overgrazing by livestock and overtapping of resin are threatening its distribution. Against this background, a study was carried out to investigate the species current population structure and tree morphology in five *Boswellia* areas along an altitude gradient (range 800 - 2000 m a.s.l.). In each area sample plots of 20 by 20 m were inventoried; a total of 144 plots were studied. The population structure analysis showed that there was an overall absence of juvenile trees between 1 and 8 cm DBH. Natural regeneration was found only in two areas in which trees were not tapped for resin and inaccessible to livestock. Tree height, DBH, crown depth and crown diameter decreased with increasing altitude. In the lowland area trees were about two times taller (10 to 12 m) with deeper crowns than those growing in the highland areas. This indicates that the species grows better in the warm moist lowlands than in the moist and dry highlands. To promote natural regeneration and seedling establishment in existing Boswellia woodlands control measures are needed including proper tapping procedures and controlled grazing.

Ogbazghi W., Rijkers T, Wessel M. & Bongers F (2006) “The distribution of the frankincense tree *Boswellia papyrifera* in Eritrea the role of environment and land use.” *Journal of Biogeography* **33**, 524-535. Abstract. Aim We determined the present and past distribution, and the abundance, of *Boswellia papyrifera* in Eritrea, and the environmental and land-use factors determining its distribution limits. Location Eritrea, in the Horn of Africa. Methods In 1997 a *Boswellia* field survey was conducted in 113 village areas covering four administrative regions. Species occurrence was related to rainfall, air temperature and length of growing period. Additionally, the relationship between the abundance of *Boswellia* trees and selected physical and chemical soil factors, topography and land-use types was determined for five study areas (with a total of 144 plots) situated along an altitude gradient of 800–2000 m a.s.l. Results The geographical distribution of *B. papyrifera* was limited to the south-western and southern parts of the country between 800 and 1850 m altitude receiving a mean annual rainfall of 375–700 mm, with a growing period of 45–100 days. Species abundance was affected by, in order of importance: altitude, land-use intensity and soil organic matter. Most trees were found in hilly areas; tree density increased from the foot slope to the hill summit; no trees occurred in valleys. Land-use intensity, especially agriculture, fallow and grazed areas, had a profound negative effect on tree abundance. Natural regeneration of the species was promoted in areas where grazing by livestock was not allowed or regulated.
Main conclusions The distribution of *B. papyrifera* in Eritrea has decreased during past decades, mainly due to an increasing human population, resulting in the conversion of woodlands into agricultural fields and increasing livestock pressure hindering natural regeneration. Consequently, Boswellia trees are found mainly in hilly areas on steep slopes with shallow soils of low fertility. The species appears to be able to adapt to these harsh growing conditions: in adjacent countries it was also found in comparable growth habitats.

Rijkers T., Ogbazghi W., Wessel M. & Bongers F. (2006) "The effect of tapping for frankincense on sexual reproduction in *Boswellia papyrifera*." *Journal of Applied Ecology* **43**, 1188–1195. Abstract.

1. In the Horn of Africa, frankincense (an aromatic hardened wood resin) is obtained by tapping *Boswellia papyrifera.* World-wide, frankincense is of great economic and social importance as an important element of incense and perfumes. The production is declining as a result of poor natural regeneration of the *Boswellia* woodlands, possibly as a result of the low production of viable seeds. We hypothesize that this is because of the current intensive tapping regime, which might favour allocation of carbohydrates for synthesis of resin at the expense of allocation for generative growth.
2. Investigations were carried out at sites in different agro-ecological zones with annually tapped trees and with trees that had not been tapped for several years. Seed viability and germination success were determined for 200 randomly collected seeds in each site. For three stands, the sexual reproduction (number of flowers, fruits and seeds) was determined for different sized trees subjected to three experimental tapping intensities (no, normal and heavy tapping).
3. At the stand level, non-tapped trees produced three times as many healthy and filled seeds as tapped trees. Germination success was highest in stands with non-tapped trees (> 80%) and lowest for those with tapped trees (< 16%).
4. At the tree level, sexual reproduction decreased with increasing tapping regime irrespective of tree size. Overall, large trees tended to produce slightly heavier seeds than small trees, and seeds from non-tapped trees were heavier than those from tapped trees. In the stands where tapping was prohibited changes in tapping regimes had the greatest effect on sexual reproduction. Trees subjected to annual tapping always showed the lowest sexual reproduction.
5. Synthesis and applications. Tapping for frankincense results in limited flower and fruit production, and low production of mainly non-viable seeds in *B. papyrifera*. We argue that tapping causes competition for carbohydrates between frankincense production, and fruit and seed setting. Consequently, the current tapping regimes will cause tree exhaustion and eventually a decline in vitality. Tapping may potentially reduce natural regeneration of the species. New tapping regimes are suggested that include periods of time in which tapping is prohibited in order for trees to recover and replenish theirstored carbon pool, and a reduction in the number of tapping points per tree. This is important in view of the long-term sustainability of frankincense production, an internationally highly valued resource.

Tilahun M.. Olschewskib R., Klein C, & Gebrehiwotd K. (2007) "Economic analysis of closing degraded *Boswellia papyrifera* dry forest from human interventions — A study from Tigray, Northern Ethiopia " *Forest Policy and Economics* **9**(8), 996-1005. Abstract. In Ethiopia, environmental degradation leads to a reduction of forest areas with economically important tree species like *Boswellia papyrifera.* In an attempt to reverse this development and assist natural rehabilitation, closing degraded forest from free grazing, fuel wood collection and other interference is practiced in Tigray. Sustainability of this management will, among other things, depend on the resources' tangible benefits. This study aimed to determine and compare net benefits (in Ethiopian Birr (ETB) per ha) from the closed and open *Boswellia papyrifera* forestlands. Production and household surveys were carried out in Jijike and Siye tabias of Abergelle woreda in northern Ethiopia. Data on costs and benefits of frankincense production were collected from firms trading the product. Net benefits from forestlands and croplands were determined using the Net Present Value criterion. The estimated mean frankincense productions were 127 kg/ha/yr for closed forest land and 84.54 kg/ha/yr for open forest land. A significant difference ($p < 0.05$) was observed between per tree mean frankincense yield of closed and open sites. The average grass harvest from closed area was 2851 kg/ha/yr. The financial Net Present Values were 8622 ETB/ha for closed and 6468 ETB/ha for open forestlands. These values were by 4574 ETB and 2005 ETB higher than the sum of NPV from crop and crop residuals of a hectare of cropland in the study area of the two sites, respectively. Exporting frankincense could generate foreign exchange of 53.28 and 39.05 USD/ha/yr from closed and open sites, respectively. Rural households earn about 74% of the annual total revenue (ETB/ha) from closed and open area as wage for tapping and collecting frankincense and using of grass. Sensitivity analysis showed that managing degraded *Boswellia papyrifera* forestland as closed area always generates a higher NPV than the open one in case of changes in discount rate and prices of inputs and outputs. Thus, managing the forest through closed areas is a competitive land-use alternative and provides higher net benefits than both open forestland and agricultural croplands.

Ecology- *Boswellia sacra* (Flück).

Monod T. (1979). "Les arbres à encens (Boswellia sacra Flückiger, 1867) dans le Hadramaout (Yemen du Sud)." *Bull. Mus. Hist. nat. Paris* B1: 131-169.

Raffaelli M., Mosti S., Tardelli M. (2003). "The Frankincense tree (*Boswellia sacra* Flueck, Burseraceae) in Dhofar, southern Oman field investigations on the natural populations. *Webbia* **58**: 133-149.

Strumia F., Dapporto L., Dellacasa M. & Scaramozzino P.L. (2007) "Notes on so.e insects asociated to Frankincense Tree (*Boswelia sacra* Flückiger, 1867, Burseraceae) in Dhofar (Sultanate of Oman)". *Atti Soc. tosc. Sci. nat., Mem., Serie B*, 114 (2007), 35-139, figg. 9. Abstract. We report on preliminary observations made in Dhofar (Sultanate of Oman) in order to identify insects dangerous to the frankincense tree (*Boswellia sacra* Flueckiger1867) The purpose was to identify the web of insects connected to this species and therefore, could damage the Frankincense tree, since nothing was previously published about this subject. We observed two species of long-horned beetles (Coleoptera Cerambycidae) and one of Buprestidae beetle (Coleoptera Buprestidae), whose larvae develops under the bark and in the into the trunk of living Frankincense trees The Cerambycidae are identified as Neoplocaederus atlanticus (Rungs, 1952) and Derolus martini ssp. hayekae Villiers, 1968, and the Buprestidae beetle as *Sphenoptera chalcichroa* Obenberger, 1914. This last is known as a possible allochthonous species, very dangerous for the *Acacia nilotica* in Sudan.

Ecology- *Boswellia serrata* Roxb. ex Colebr.

Sunnichan, V.G., Mohan Ram, H.Y. & Shivanna, K.R. (2005) “Reproductive biology of *Boswellia serrata*, the source of salai guggul, an important gum-resin.” *Botanical Journal of the Linnean Society* **147**, 73–82.

Sagar R., Raghubanshi A.S. & Singh J.S. (2003) "Tree species composition, dispersion and diversity along a disturbance gradient in a dry tropical forest region of India." *Forest Ecology and Management* **186**(1-3),61-71. Abstract. Forest inventory data were collected in 1998–2000 from fifteen 1 ha permanent plots along a disturbance gradient in a dry tropical forest region of India. A total of 4033 stems, 49 species, 44 genera and 24 families of adult trees (≥30 cm CBH), occurred in the 15 ha of forest area. The study indicated that the dry tropical forest is characterised by a patchy distribution of species and individuals with mixed species composition, and the sites are represented by different combinations of the dominants and co-dominant species. A PCA ordination indicated that the variation in species composition of the sites is explained by the variation in soil nitrogen as well as the degree of disturbance. About half the analysed species showed changing nature in dispersion along the disturbance gradient. The distribution of *Boswellia serrata*, *Holarrhena antidysenterica* and *Lannea coromandelica* changed from clumped to uniform and the distribution of *Butea monosperma*, *Cassia fistula* and *Elaeodendron glaucum* changed from uniform to clumped as the degree of disturbance increased. The mean stem density was highest (419 stems ha−1) at the least disturbed site and lowest (35 stems ha−1) at the highly disturbed site, and for basal area, the highest value (13.78 m2 ha−1) was for the second least disturbed forest site and the lowest value (1.30 m2 ha−1) was for the most disturbed site. The total number of stems, indices of species richness, evenness and α-diversity decreased with disturbance. A strong influence of number of species per individual on β-diversity suggests that for resisting change in floristics due to disturbance, a site must have low species-individual ratio.

Frankincense - Ethnic Medicine

El Fortia M., Badi H., Elalem Kh., Kadiki O. & Topov Y. (2006) "Olibanum bezoar: complication of a traditional popular medicine." *East Mediterr Health J.* **12**(6):927-9.

Frankincese – Therapeutics General.

Bishnoi M., Patil C.S., Kumar A., SK Kulkarni S.K. (2005) "Analgesic activity of acetyl-11-keto-beta-boswellic acid, a 5-lipoxygenase-enzyme inhibitor." *Research Letter* **37**(5), 255-256.

Choi O.B., Park J.H., Lee Y.J., Lee C.K., Won K.J., Kim J., Lee H.M. & Kim B. (2009) "Olibanum extract inhibits vascular smooth muscle cell migration and proliferation in response to platelet-derived growth factor." *Korean J Physiol Pharmacol*. **13**(2), 107-13. Abstract. Olibanum (Boswellia serrata) has been shown to have anti-inflammatory, anti-arthritic and anti-cancer effects. This study determined the role of a water extract of olibanum in platelet-derived growth factor (PDGF)-stimulated proliferation and migration of rat aortic smooth muscle cells (RASMCs). PDGF-BB induced the migration and proliferation of RASMCs that were inhibited by olibanum extract in a dose-dependent manner. The PDGF-BB-increased phosphorylation of p38 mitogen-activated protein kinase (MAPK); the heat shock protein (Hsp) 27 was significantly inhibited by the olibanum extract. The effects of PDGF-BB-induced extracellular signal-regulated kinase1/2 was not altered by the olibanum extract. Treatment with olibanum extract inhibited PDGF-BB-stimulated sprout out growth of aortic rings. These results suggest that the water extract of olibanum inhibits PDGF-BB-stimulated migration and proliferation in RASMCs as well as sprout out growth, which may be mediated by the inhibition of the p38 MAPK and Hsp27 pathways.

Ernst E. (2008) "Frankincense: systematic review." *BMJ* Dec 2008. Abstract. OBJECTIVE: To assess evidence from randomised clinical trials about the effectiveness of extracts of Boswellia serrata (frankincense). DESIGN: Systematic review. DATA SOURCES: Electronic searches on Medline, Embase, Cinahl, Amed, and Cochrane Library. Hand searches of conference proceedings, bibliographies, and departmental files. REVIEW METHODS: All randomised clinical trials of *B serrata* extract as a treatment for any human medical condition were included and studies of *B serrata* preparations combined with other ingredients were excluded. Titles and abstracts of all retrieved articles were read and hard copies of all relevant articles were obtained. Selection of studies, data extraction and validation were done by the author. The Jadad score was used to evaluate the methodological quality of all included trials. RESULTS: Of 47 potentially relevant studies, seven met all inclusion criteria (five placebo controlled, two with active controls). The included trials related to asthma, rheumatoid arthritis, Crohn's disease, osteoarthritis, and collagenous colitis. Results of all trials indicated that *B serrata* extracts were clinically effective. Three studies were of good methodological quality. No serious safety issues were noted. CONCLUSIONS: The evidence for the effectiveness of *B serrata* extracts is encouraging but not compelling

Frank A & Unger T. (2006) "Analysis of frankincense from various *Boswellia* species with inhibitory activity on human drug metabolising cytochrome P450 enzymes using liquid chromatography mass spectrometry after automated on-line extraction " *Journal of Chromatography A* **1112**(1-2), 255-262. Abstract. In our search for herbal remedies with inhibitory activity on cytochrome P450 (CYP) enzymes, we identified extracts of the gum-resin of *Boswellia carteri*, *Boswellia frereana*, *Boswellia sacra* and *Boswellia serrata* as equally potent, non-selective inhibitors of the major drug metabolising CYP enzymes 1A2/2C8/2C9/2C19/2D6 and 3A4. LC/LC/ESI-MS fingerprint analyses of the boswellic acids 11-keto-β-boswellic acid, α-boswellic acid, β-boswellic acid and their 3-O-acylated derivatives were used for the authentication of the commercially obtained frankincense samples. Although the boswellic acids could be identified as moderate to potent inhibitors of the applied CYP enzymes, they are not the major CYP inhibitory principle of frankincense.

Holmes P. (1999) “Frnkincense Oil” *International J. Aromatherapy* **9**(4), 156-161.

Michie C.A. & E Cooper E. (1991) "Frankincense and myrrh as remedies in children." *J R Soc Med* **84**, 602-605. Abstract. Two cases of therapy with frankincense and myrrh in children are presented. The long history of this unusual treatment is outlined, demonstrating that for several millenia such agents have been employed in a number of medical contexts, as well as in the perfume and incense industries. Myrrh has found recent pharmacological application in the reduction of cholesterol and triglycerides, as predicted by several traditional therapies.

Krieglstein C.F, Anthoni C., Rijcken E.J.M., Laukötter M., Spiegel H-U, Boden S.E., Schweizer S., Safayhi H., Senninger N., Schürmann G. (2004) "Acetyl-11-keto-ß-boswellic acid, a constituent of a herbal medicine from *Boswellia serrata* resin, attenuates experimental ileitis." *International Journal of Colorectal Disease* **16**(7), 1432-1262. Abstract. The gum resin extract from *Boswellia serrata* (H15), an herbal product, was recently shown to have positive therapeutic effects in inflammatory bowel disease (IBD). However, the mechanisms and constituents responsible for these effects are poorly understood. This study examined the effect of the *Boswellia* extract and its single constituent acetyl-11-keto-#-boswellic acid (AKBA) on leukocyte-endothelial cell interactions in an experimental model of IBD. Ileitis was induced by two subcutaneous injections of indomethacin (7.5 mg/kg) in Sprague-Dawley rats 24 h apart. Rats also received oral treatment with the *Boswellia* extract (H15) or AKBA at two different doses (low and high) equivalent to recommendations in human disease over 2 days. Controls received only the carriers NaHCO3 (subcutaneously) and tylose (orally). Effects of treatment were assessed by intravital microscopy in ileal submucosal venules for changes in the number of rolling and adherent leukocytes and by macroscopic and histological scoring. Increased leukocyte-endothelial cell adhesive interactions and severe tissue injury accompanied indomethacin-induced ileitis. Treatment with the *Boswellia* extract or AKBA resulted in a dose-dependent decrease in rolling (up to 90%) and adherent (up to 98%) leukocytes. High-dose *Boswellia* extract as well as both low- and high-dose AKBA significantly attenuated tissue injury scores. Oral therapy with the *Boswellia* extract or AKBA significantly reduces macroscopic and microcirculatory inflammatory features normally associated with indomethacin administration, indicating that the anti-inflammatory actions of the *Boswellia* extract in IBD may be due in part to boswellic acids such as AKBA.

Shah B.A., Qazi G.N., Taneja S.C.(2009) "Boswellic acids: a group of medicinally important compounds" *Nat. Prod. Rep.* **26**, 72 - 89.

Sharma M. L., Khajuria A., Kaul A., Singh S., Singh G. B. & Atal C. K. (1988), “Effect of salai guggal ex-*Boswellia serrata* on cellular and humoral immune responses and leucocyte migration.” *Agents Actions* **24**, 161-164.

Anti-colitis Uses.

The use of *Boswellia* preparations to treat another inflammatory disease, ulcerative colitis, may also owe its beneficial action to 5-lipoxygenase inhibition (Gupta *et al.* 1997).

Anthoni C., Laukoetter M.G., Rijcken E., Vowinkel T., Mennigen R., Muller S., Senninger N., Russell J., Jauch J., Bergmann J. *et al* (2006) “Mechanisms underlying the anti-inflammatory actions of boswellic acid derivatives in experimental colitis.” *Am J Physiol Gastrointest Liver Physiol* **290.** G1131-1137.

Chande N., McDonald J.W. & MacDonald J.K. (2006) "Interventions for treating collagenous colitis." *Cochrane Database Syst Rev.* 2006 Oct **18**;(4):CD003575. Abstract. BACKGROUND: Collagenous colitis is a disorder that is recognized as a cause of chronic diarrhea. Treatment has been based mainly on anecdotal evidence. This review was performed to identify therapies for collagenous colitis that have been proven in randomized trials. OBJECTIVES: To determine effective treatments for patients with clinically active collagenous colitis. SEARCH STRATEGY: Relevant papers published between 1970 and June 2006 were identified via the MEDLINE and PUBMED databases. Manual searches from the references of identified papers, as well as review papers on collagenous or microscopic colitis were performed to identify additional studies. Abstracts from major gastroenterological meetings were searched to identify research submitted in abstract form only. Finally, the Cochrane Controlled Trials Register and the Cochrane Inflammatory Bowel Disease and Functional Bowel Disorders Group Specialized Trials Register were searched for other studies. SELECTION CRITERIA: Seven randomized trials were identified. One trial studied bismuth subsalicylate (published in abstract form only), one trial studied *Boswellia serrata* extract (published in abstract form only), one trial studied probiotics, one trial studied prednisolone, and 3 trials studied budesonide for the therapy of collagenous

colitis. DATA COLLECTION AND ANALYSIS: Data were extracted independently by each author onto 2x2 tables (treatment versus placebo and response versus no response). For therapies assessed in one trial only, p-values were derived using the chi-square test. For therapies assessed in more than one trial, summary test statistics were derived using the Peto odds ratio and 95% confidence intervals. Data were combined for analysis only if the outcomes were sufficiently similar in definition. MAIN RESULTS: There were 9 patients with collagenous colitis in the trial studying bismuth subsalicylate (nine 262 mg tablets daily for 8 weeks). Those randomized to active drug were more likely to have clinical (p = 0.003) and histological (p = 0.003) improvement than those assigned to placebo. Eleven patients were enrolled in the trial studying prednisolone (50 mg daily for 2 weeks). There was a trend towards clinical response in patients on active medication compared to placebo (p = 0.064). The effect of prednisolone on histologic improvement was not studied. Thirty-one patients were enrolled in the *Boswellia serrata* extract trial. Clinical improvement was noted in 44% of patients who received active treatment compared to 27% of patients who received placebo (p = 0.32). Twenty-nine patients were enrolled in the probiotics trial. Clinical improvement was noted in 29% of patients who received probiotics compared to 13% of patients who received placebo (p = 0.635). A total of 94 patients were enrolled in 3 trials studying budesonide (9 mg daily or in a tapering schedule for 6 to 8 weeks). The pooled odds ratio for clinical response to treatment with budesonide was 12.32 (95% CI 5.53-27.46), with a number needed to treat of 2 patients. There was significant histological improvement with treatment in all 3 trials studying budesonide therapy. Budesonide also appears to improve patients' quality of life. AUTHORS' CONCLUSIONS: Budesonide is effective for the treatment of collagenous colitis. The evidence for benefit with bismuth subsalicylate is weaker. The effectiveness of prednisolone, *Boswellia serrata* extract, probiotics and other therapies for induction or maintenance of remission of collagenous colitis is unknown and requires further study.

Gupta I., Parihar A., Malhotra P., Singh G. B., Ludtke R., Safayhi H. & Ammon H.P. (1997). “Effects of *Boswellia serrata* gum resin in patients with ulcerative colitis.” *Eur. J. Med. Res.* **2**, 37-43. Abstract. Ulcerative colitis is a chronic inflammatory disease of the colon where leukotrienes are suggested to play an important role for keeping inflammation active. Boswellic acids, the biologically active ingredients of the gum resin of *Boswellia serrata* (Sallai guggal), have been shown to be specific, nonredox and noncompetitive inhibitors of 5-lipoxygenase, the key enzyme of leukotriene biosynthesis. In patients suffering from ulcerative colitis grade II and III the effect of Boswellia serrata gum resin preparation (350 mg thrice daily for 6 weeks) on stool properties, histolopathology and scan microscopy of rectal biopsies, blood parameters including Hb, serum iron, calcium, phosphorus, proteins, total leukocytes and eosinophils was studied. Patients receiving sulfasalazine (1 g thrice daily) served as controls. All parameters tested improved after treatment with *Boswellia serrata* gum resin, the results being similar compared to controls: 82% out of treated patients went into remission; in case of sulfasalazine remission rate was 75%.

Gupta I., Parihar A., Malhotra P., Gupta S., Ludtke R., Safayhi H. *et al*. (2001) "Effects of gum resin of *Boswellia serrata* in patients with chronic colitis." *Planta Med* **67**, 391-5. Abstract. Patients studied here suffered from chronic colitis characterized by vague lower abdominal pain, bleeding per rectum with diarrhoea and palpable tender descending and sigmoid colon. The inflammatory process in colitis is associated with increased formation of leukotrienes causing chemotaxis, chemokinesis, synthesis of superoxide radicals and release of lysosomal enzymes by phagocytes. The key enzyme for leukotriene biosynthesis is 5-lipoxygenase. Boswellic acids were found to be non-redox, non-competitive specific inhibitors of the enzyme 5-lipoxygenase. We studied the gum resin of *Boswellia serrata* for the treatment of this disease. Thirty patients, 17 males and 13 females in the age range of 18 to 48 years with chronic colitis were included in this study. Twenty patients were given a preparation of the gum resin of *Boswellia serrata* (900 mg daily divided in three doses for 6 weeks) and ten patients were given sulfasalazine (3 gm daily divided in three doses for 6 weeks) and served as controls. Out of 20 patients treated with Boswellia gum resin 18 patients showed an improvement in one or more of the parameters: including stool properties, histopathology as well as scanning electron microscopy, besides haemoglobin, serum iron, calcium, phosphorus, proteins, total leukocytes and eosinophils. In the

control group 6 out of 10 patients showed similar results with the same parameters. Out of 20 patients treated with *Boswellia* gum resin 14 went into remission while in case of sulfasalazine remission rate was 4 out of 10. In conclusion, this study shows that a gum resin preparation from *Boswellia serrata* could be effective in the treatment of chronic colitis with minimal side effects.

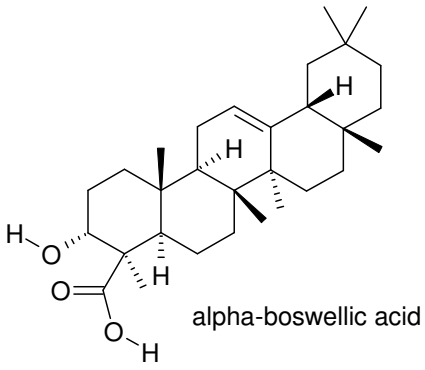
Kiela P.R., Midura A.J., Kuscuoglu N., Jolad S.D., Sólyom A.M. , Besselsen D.G., Timmermann B.. & Ghishan F.K. (2005) "Effects of *Boswellia serrata* in mouse models of chemically induced colitis." *Am J Physiol Gastrointest Liver Physiol*. **288**(4), 798-808. Abstract. Extracts from *Boswellia serrata* have been reported to have anti-inflammatory activity, primarily via boswellic acid-mediated inhibition of leukotriene synthesis. In three small clinical trials, *boswellia* was shown to improve symptoms of ulcerative colitis and Crohn's disease, and because of its alleged safety, *boswellia* was considered superior over mesalazine in terms of a benefit-risk evaluation. The goal of this study was to evaluate the effectiveness of boswellia extracts in controlled settings of dextran sulfate- or trinitrobenzene sulfonic acid-induced colitis in mice. Our results suggest that boswellia is ineffective in ameliorating colitis in these models. Moreover, individual boswellic acids were demonstrated to increase the basal and IL-1beta-stimulated NF-kappaB activity in intestinal epithelial cells in vitro as well as reverse proliferative effects of IL-1beta. We also observed hepatotoxic effect of *boswellia* with pronounced hepatomegaly and steatosis. Hepatotoxity and increased lipid accumulation in response to *boswellia* were further confirmed in vitro in HepG2 cells with fluorescent Nile red binding/resazurin reduction assay and by confocal microscopy. Microarray analyses of hepatic gene expression demonstrated dysregulation of a number of genes, including a large group of lipid metabolism-related genes, and detoxifying enzymes, a response consistent with that to hepatotoxic xenobiotics. In summary, *boswellia* does not ameliorate symptoms of colitis in chemically induced murine models and, in higher doses, may become hepatotoxic. Potential implications of prolonged and uncontrolled intake of *boswellia* as an herbal supplement in inflammatory bowel disease and other inflammatory conditions should be considered in future clinical trials with this botanical.

Latella G., Sferra R., Vetuschi A., Zanninelli G., D'Angelo A., Catitti V., Caprilli R. & Gaudio E. (2008) "Prevention of colonic fibrosis by *Boswellia* and *Scutellaria* extracts in rats with colitis induced by 2,4,5-trinitrobenzene sulphonic acid." *Eur J Clin Invest*. **38**(6),410-20. Abstract. BACKGROUND: Currently, no effective preventive measures or medical therapies are available for intestinal fibrosis and, thus, surgery remains the only available strategy in the management of fibrostenotic enteropathies, especially Crohn's disease. The aim of this study was to evaluate the efficacy of a combined therapy of anti-inflammatory *Boswellia* and antifibrotic *Scutellaria* extracts on the development of colonic fibrosis in rats. MATERIALS AND METHODS: Chronic colonic inflammation-associated fibrosis was induced in rats by intracolonic administration of 2,4,5-trinitrobenzene sulphonic acid (TNBS). Sixty-four healthy male Sprague-Dawley rats were assigned to five groups: 8 controls, 14 TNBS, 14 TNBS orally treated with *Boswellia* extracts (50 mg kg(-1) day(-1)), 14 TNBS orally treated with *Scutellaria* extracts (150 mg kg(-1) day(-1)), and 14 TNBS orally treated with both Boswellia (50 mg kg(-1) day(-1)) and *Scutellaria* extracts (150 mg kg(-1) day(-1)). The colon was removed after 21 days of treatment and assessed by macroscopic, histological, morphometric and immunohistochemical analyses. For immunohistochemical analysis, alpha-smooth muscle actin (alpha-SMA), collagen types I-III, connective tissue growth factor (CTGF), transforming growth factor-beta1 (TGF-beta1), Smad3, Smad7 and CD3 antibodies were used. RESULTS: Combined oral administration of *Boswellia* and *Scutellaria* significantly improved the course and macroscopic findings of TNBS-induced chronic colitis assessed by disease activity index, colon weight, length, adhesions, strictures, dilatation, thickness, oedema, ulcerations and extension of damage. The histological severity of the colonic fibrosis was also notably improved by the treatment and associated with a significant reduction in the colonic expression of alpha-SMA, collagen I-III, CTGF, TGF-beta1, Smad3, and Smad7. CONCLUSIONS: These data demonstrate that the prophylactic administration of anti-inflammatory *Boswellia* and antifibrotic *Scutellaria* extracts is effective in preventing colonic fibrosis in TNBS-induced colitis. Their antifibrotic mechanism of action seems to be mediated by the inhibition of TGF-beta1/Smad3 pathway.

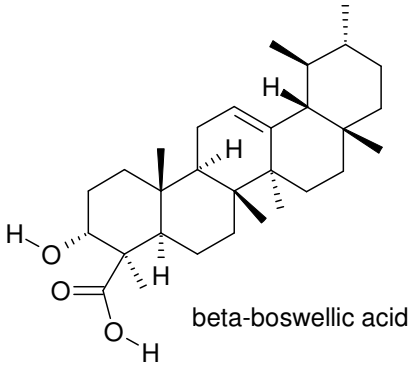
Madisch A., Miehlke S., Eichele O., Mrwa J., Bethke B., Kuhlisch E., Bastlein E., Wilhelms G., Morgner A., Wigginghaus B. & M. Stolte M. (2008) "*Boswellia serrata* extract for the treatment of collagenous colitis a double-blind randomized, placebo-controlled, multicenter trial." *Phytomedicine* **15**(6-7) June 200-8. Abstract. Background & Aims: To investigate the effect of *Boswellia serrata* extract (BSE) on symptoms, quality of life and histology in patients with collagenous colitis. Methods: Patients with chronic diarrhoea and histologically proven collagenous colitis were randomized to receive either oral BSE 400 mg three times daily for 6 weeks or placebo. Complete colonoscopy and histology were performed before and after treatment. Clinical symptoms and quality of life were assessed by standardized questionnaires and SF-36. The primary endpoint was the percentage of patients with clinical remission after 6 weeks (stool frequency [less then or equal to] 3 soft/solid stools per day on average during the last week). Patients of the placebo group with persistent diarrhea received open-label cross-over BSE therapy for a further 6 weeks. Results: Thirty-one patients were randomized, 26 patients were available for per-protocol-analysis. After 6 weeks the proportion of patients in clinical remission was higher in the BSE group than in the placebo group (per protocol 63.6%; 95%CI: 30.8-89.1 versus 26.7%, 95%CI: 7.7-55.1; p = 0.04; intention-to-treat 43.8% versus 26.7%, p = 0.25). Compared to placebo, BSE treatment had no effect on histology and quality of life. Five patients discontinued BSE treatment prematurely. Discontinuation was due to: adverse events (n = 1), unwillingness to continue (n = 3), or loss to follow-up for unknown reasons (n = 1). Seven patients received cross-over BSE therapy, five of whom achieved complete remission. Conclusions: Our study suggests that BSE might be clinically effective in patients with collagenous colitis. Larger trials are clearly necessary to establish the clinical efficacy of *Boswellia serrata* extract.

Anti-inflammatory effects.

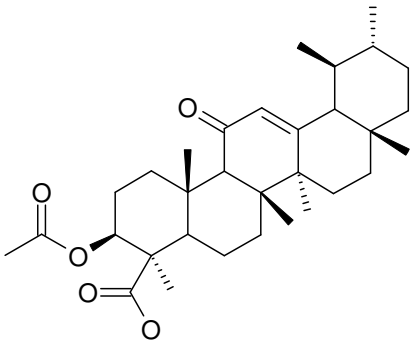
Cropwatch comments: Given the use of *B. serrata* extracts in treating inflammatory disease in Arabian & Ayervedic medicine, a number of researchers have investigated the anti-inflammatory & anti-arthritic effects of the contained boswellic acids. Frankincense contains the *Boswellia* resins - the α- and β-boswellic acids from 3α-hydroxy-olean-12-en-24-oic acid and 3α-hydroxy-urs-12-en-24-oic acid respectively. Boswellic acid & pentacyclic triterpene acids are marketed as anti-inflammatory & anti-arthritic drugs in India (Handa S.S. (1992) *Fitoterapia* **63**(10), 3). The mechanism of action may cccur via the inhibition of 5-lipoxygenase, together with inhibition of human leukocyte elasase, since both of these enzymes play key roles in inflammatory & hypersensitivity-based diseases. The most active inhibitor of 5-lipoxygenase seems to be acetyl-11-keto-beta-boswellic acid which is cyctotoxic to meningioma cultures. N.B. Commercialised products containing boswellic acids include 'Boswellin' (patented product of Sabinsa Corporation) described as the standardized ethanol extract of *Boswellia serrata* gum resin, containing 60% to 65% boswellic acids.



alpha-boswellic acid



beta-boswellic acid



acetyl-11-ketoboswellic acid

Ammon H.P. (2008) “Salai guggul & boswellic acids: their effects on the arachidonic acid cascade.” *Phytomedicine* **15**(6-7), 546. Abstract. Salai guggal is the gum resin from the tree *Boswellia serrata*. Based on studies by G.B. Singh and C.K. Atal showing anti-inflammatory activity of extracts, we studied the effect of an extract of *B. serrata* and a variety of boswellic acids on the formation of products of the arachidonic acid cascade. Prostaglandins: In human platelets, which produce only prostaglandins, salai guggal inhibited formation of 6-keto-PGF l[alpha] only at very high concentrations being around 100 [micro]g/ml. When a mixture of acetyl boswellic acids was employed, no inhibition was found up to 60 [micro]g/rnl. On the other hand, acetyl-keto-beta-boswellic acid produced inhibition in concentrations above 10 [micro]M. Leukotrienes: Using polymorphnuclear leukocytes which can produce only leukotrienes, salai guggal in a sigmoid concentration-dependent manner inhibited production of LT[B.sub.4] and other 5-LO products. Employing acetyl-boswellic acids, again an inhibition of LT[B.sub.4] and other 5-LO product formation was observed. Among several boswellic acids, acety1-11-keto-[beta]-boswellic acid (AKBA) was the most effective, the [IC.sub.50] was 1.5 [micro]M. As far as ll-keto-j3-boswellic acid (KBA) is concerned [IC.sub.50] was 4.5 [micro]M. Other boswellic acids have been found to be less or not effective at all. There was a close structure-activity relationship. Inhibition of leukotriene synthesis occurred in a nonredox and noncompetitive manner. In photo-labeling studies with [125]-azido-boswellic acid, it was found that this compound binds to the enzyme 5-lipoxygenase and could be removed in the presence of unlabeled AKBA or other boswellic acids. It is concluded that certain boswellic acids including AKBA and KBA preferentially inhibit 5-lipoxygenase and with far less activity cyclooxygenase. This leads to the hypothesis that chronic inflammatory diseases with increased leukotriene formation may be a target for the treatment with salai guggal or certain boswellic acids. Pilot studies so far suggest therapeutic benefit in chronic bowel diseases, rheumatoid arthritis and bronchial asthma.

Ammon H.P. (2006) "Boswellic acids in chronic inflammatory diseases." *Planta Med.* **72**(12),1100-16. Abstract. Oleogum resins from *Boswellia* species are used in traditional medicine in India and African countries for the treatment of a variety of diseases. Animal experiments showed anti-inflammatory activity of the extract. The mechanism of this action is due to some boswellic acids. It is different from that of NSAID and is related to components of the immune system. The most evident action is the inhibition of 5-lipoxygenase. However, other factors such as cytokines (interleukins and TNF-alpha) and the complement system are also candidates. Moreover, leukocyte elastase and oxygen radicals are targets. Clinical studies, so far with pilot character, suggest efficacy in some autoimmune diseases including rheumatoid arthritis, Crohn's disease, ulcerative colitis and bronchial asthma. Side effects are not severe when compared to modern drugs used for the treatment of these diseases.

Ammon H.P. (2002) "[Boswellic acids (components of frankincense) as the active principle in treatment of chronic inflammatory diseases]" *Wien Med Wochenschr.* **152**(15-16),373-8. Abstract. Preparations from the gum resin of *Boswellia serrata* have been used as a traditional remedy in Ayurvedic medicine in India for the treatment of inflammatory diseases. Compounds from the gum with genuine antiinflammatory effects are pentacyclic triterpenes of the boswellic acid type. Boswellic acids inhibit the leukotriene biosynthesis in neutrophilic granulocytes by a non-redox,

noncompetitive inhibition of 5-lipoxygenase. The effect is triggered by boswellic acids binding to the enzyme. Moreover certain boswellic acids have been described to inhibit elastase in leukocytes, to inhibit proliferation, induce apoptosis and to inhibit topoisomerases of leukoma- and glioma cell lines. A series of chronic inflammatory diseases are thought to be perpetuated by leukotrienes. In clinical trials promising results were observed in patients with rheumatoid arthritis, chronic colitis, ulcerative colitis, Crohn's disease, bronchial asthma und peritumoral brains edemas.

Ammon H.P. (1996) “Salai Guggal - *Boswellia serrata*: from a herbal medicine to a non-redox inhibitor of leukotriene biosynthesis.” *Eur J. Med Res* **1**(8):369-70.

Ammon H. *et al* (1993). “Mechanism of antiinflammatory actions of curcumine and boswellic acids.” *J. Ethnopharmacol* . **38**(2-3):113-19.

Ammon, H. P. T., Singh T. & Safayhi H. (1991). “Inhibition of leukotriene B4 formation in rat peritoneal neutrophils by an ethanolic extract of the gum resin exudate of *Boswellia serrata*.” *Planta Med*. **57**, 203-207.

Banno N., Akihisa T., Yasukawa K., Tokuda H., Tabata K., Nakamura Y., Nishimura R., Kimura Y & Suzuki T. (2006) "Anti-inflammatory activities of the triterpene acids from the resin of *Boswellia carteri*." *J Ethnopharmacol*. **107**(2), 249-53. Abstract. Boswellic acids are the main well-known active components of the resin of *Boswellia carteri* (Burseraceae) and these are still dealing with the ethnomedicinal use for the treatment of rheumatoid arthritis and other inflammatory diseases. Although several studies have already been reported on the pharmacological properties, especially on the anti-inflammatory activity, of *Boswellia carteri* resin and boswellic acids, the ethnomedicinal importance of *Boswellia carteri* and its components, boswellic acids, prompted us to undertake detailed investigation on the constituents of the resin and their anti-inflammatory activity. Fifteen triterpene acids, viz., seven of the beta-boswellic acids (ursane-type) (1-7), two of the alpha-boswellic acids (oleanane-type) (8, 9), two of the lupeolic acids (lupane-type) (10, 11), and four of the tirucallane-type (12-14, 16), along with two cembrane-type diterpenes (17, 18), were isolated and identified from the methanol extract of the resin of *Boswellia carteri*. Upon evaluation of 17 compounds, 1-14 and 16-18, and compound 15, semi-synthesized from 14 by acetylation, for their inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation (1 microg/ear) in mice, all of the compounds, except for 18, exhibited marked anti-inflammatory activity with a 50% inhibitory dose (ID(50)) of 0.05-0.49 mg/ear.

Blain E.J., Ali A.Y. & Duance V.C. (2009) "Boswellia frereana (frankincense) suppresses cytokine-induced matrix metalloproteinase expression and production of pro-inflammatory molecules in articular cartilage." *Phytother Res*. 2009 Nov. Abstract. 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 mug/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.

Chevrier M.R., Ryan A.E., Lee D.Y., Zhongze M., Wu-Yan Z. & Via C.S. (2005): “*Boswellia carterii* extract inhibits TH1 cytokines and promotes TH2 cytokines in vitro.” *Clin Diag Lab Immunol* 2005 **12**, 575-580.

Dahmen U., Gu Y.L., Dirsch O. *et al.* (2001) *Transplant Proceed* **33**, 539-541

Dohling C. (2008) "*Boswellia serrata* - from traditional Indian medicine to evidence-based medicine." *Phytomedicine* **15(**6-7), 540.. Abstract. For thousands of years, frankincense has been used for medical purposes. In traditional Indian medicine, frankincense is an ingredient of medicine applied by diseases of the nervous system; frankincense was furthermore used for the therapy of different diseases of the gastro intestinal tract, and for gynecological purposes. In the spotlight of research are the anti-inflammatory effects of the boswellic acids, the most important properties of frankincense, which show the mentioned anti-inflammatory effects in different pharmacological target systems. The inhibition of various enzymes of the arachidonic acid cascade, among these the lipoxygenases and the cyclooxygenases, might be a possible target. Lyosomal proteases and other mediators of human organism like tumor cells or like leukocytes are also influenced by frankincense. In vitro, apoptosis of tumor cells could be successfully realized.Clinical trials, partly pilot studies, showed the effectiveness of frankincense against diseases like rheumatism. inflammatory diseases of the gastro intestinal tract, asthma and even the treatment of edema in the case of brain tumors. Presently, the attention is also drawn to the external use of frankincense, e.g. in the case of inflammatory diseases of the skin like atopic dermatitis or psoriasis. Further clinical trials and research is needed to give solid proof of its effectiveness. The following abstracts overview the latest results concerning oral and topical use of frankincense.

Gayathri B., Manjula N., Vinaykumar K.S., Lakshmi B.S. & Balakrishnan A.(2007) "Pure compound from *Boswellia serrata* extract exhibits anti-inflammatory property in human PBMCs and mouse macrophages through inhibition of TNFalpha, IL-1beta, NO and MAP kinases." *Int Immunopharmacol*. **7**(4),473-82. Abstract. The aim of the present study is to probe the anti-inflammatory potential of the plant *Boswellia serrata* by studying the effect of the crude extract and the pure compound isolated from it on key inflammatory mediators like TNFalpha, IL-1beta, and NO thus enabling the understanding of the key signaling events involved. The crude methanolic extract and the pure compound were analysed for their inhibitory effect on TNFalpha, IL-1beta and IL-6. The results demonstrated that all three cytokines are down regulated when PBMCs are cultured in the presence of crude extract or the pure compound at various time points. Observations on Th1/Th2 cytokines revealed marked down regulation of Th1 cytokines IFNgamma and IL-12 while the Th2 cytokines IL-4 and IL-10 were up regulated upon treatment with crude extract and pure compound. The extract and the pure compound isolated also showed considerable inhibition of NO production in activated RAW 264.7 cells, possibly via suppression of inducible NO synthase mRNA expression. Further to elucidate the underlying mechanism of action the effect of 12-ursene 2-diketone on LPS-induced activation of MAPK has also been examined. Our results demonstrated that 12-ursene 2-diketone inhibits the expression of pro-inflammatory cytokines and mediators via inhibition of phosphorylation of the MAP kinases JNK and p38 while no inhibition was seen in ERK phosphorylation in LPS-stimulated PBMCs. The above study therefore indicates that the crude methanolic extract and the isolated pure compound are capable of carrying out a natural anti-inflammatory activity at sites where chronic inflammation is present by switching off the pro-inflammatory cytokines and mediators, which initiate the process.

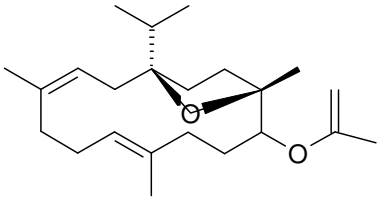
Kulkarni R. *et al.* (1991) "Treatment of osteoarthritis with a herbomineral formulation: a double-blind, placebo-controlled, cross-over study." *J Ethnopharmacol* . **33(**1-2):91-95.

Krüger P, Kanzer J, Hummel J, Fricker G, Schubert-Zsilavecz M. & Abdel-Tawab M. (2008) "Permeation of *Boswellia* extract in the Caco-2 model and possible interactions of its constituents KBA and AKBA with OATP1B3 and MRP2." *Eur J Pharm Sci* Oct 2008. Abstract. Traditionally *Boswellia serrata* extract is used in the Indian Ayurvedic medicine for the treatment of inflammatory diseases. In 2002 the EMEA designated *Boswellia* an orphan drug status for the treatment of peritumoral oedema. Pharmacokinetic studies yielded low plasma concentrations of the active ingredients 11-keto-beta-boswellic acid (KBA) and 3-acetyl-11-keto-beta-boswellic acid (AKBA). In continuation of the tests investigating the factors limiting bioavailability of boswellic

acids, the present study examined the permeability of KBA and AKBA in human Caco-2 cell lines. In addition, the interaction of KBA and AKBA with the organic anion transporter OATP1B3 and the multi drug resistant proteins P-glycoprotein and MRP2 was evaluated using partly fluorescent-based assays. The permeability studies revealed poor permeability of AKBA and moderate absorption of KBA with a P(app) value of 1.69x10(-6)cm/s. Most of KBA and AKBA were found to be retained by the Caco-2 monolayer. Neither KBA nor AKBA could be identified as substrates of P-glycoprotein. However, both KBA and AKBA modulated the activity of OATP1B3 and MRP2, indicating that therapeutic relevant interactions with other anionic drugs may be expected. The results of the present study provide the first explanation for the pharmacokinetic properties of KBA and AKBA.

Moussaieff A, & Mechoulam R. (2009) "Boswellia resin: from religious ceremonies to medical uses; a review of in-vitro, in-vivo and clinical trials." *J Pharm Pharmacol*. **61**(10), 1281-93. Abstract. OBJECTIVES: Despite its historical-religious, cultural and medical importance, Boswellia has not been thoroughly studied, and gaps still exist between our knowledge of the traditional uses of the resin and the scientific data available. Here we review the pharmacology of Boswellia resin and of the small molecules identified as the active ingredients of the resin. KEY FINDINGS: The resin of Boswellia species ('frankincense', 'olibanum') has been used as incense in religious and cultural ceremonies since the beginning of written history. Its medicinal properties are also widely recognized, mainly in the treatment of inflammatory conditions, as well as in some cancerous diseases, wound healing and for its antimicrobial activity. Until recently, work on Boswellia focused on the immunomodulatory properties of the resin and boswellic acids were considered to be the main, if not the only, active ingredients of the resin. Hence, this family of triterpenoids was investigated by numerous groups, both in vitro and in vivo. These compounds were shown to exert significant anti-inflammatory and pro-apoptotic activity in many assays: in vitro, in vivo and in clinical trials. We recently found incensole acetate and its derivatives, which are major components of Boswellia resin, to be nuclear factor-kappaB inhibitors, thus suggesting that they are, at least in part, responsible for its anti-inflammatory effects. Incensole acetate also exerts a robust neuroprotective effect after brain trauma in mice. Furthermore, it causes behavioural as well as anti-depressive and anxiolytic effects in mice. It is also a potent agonist of the transient receptor potential (TRP)V3 channel. It thus seems that incensole acetate and its derivatives play a significant role in the effects that Boswellia resin exerts on biological systems. CONCLUSIONS: Altogether, studies on Boswellia resin have provided an arsenal of bio-active small molecules with a considerable therapeutic potential that is far from being utilized.

Moussaieff A., Shein N.A., Tsenter J., Grigoriadis S., Simeonidou C., Alexandrovich A.G., Trembovler V., Ben-Neriah Y., Schmitz M.L., Fiebich B.L., Munoz E., Mechoulam R. & Shohami E. (2008) "Incensole acetate: a novel neuroprotective agent isolated from *Boswellia carterii*." *J Cereb Blood Flow Metab.* **28**(7),1341-52. Abstract. *Boswellia* resin has been used as a major anti-inflammatory agent and for the healing of wounds for centuries. Incensole acetate (IA), isolated from this resin, was shown to inhibit the activation of nuclear factor-kappaB, a key transcription factor in the inflammatory response. We now show that IA inhibits the production of inflammatory mediators in an in vitro model system of C6 glioma and human peripheral monocytes. Given the involvement of postinjury inflammation in the pathophysiology and outcome of traumatic brain injury, we examined the effect of IA on the inflammatory process and on the recovery of neurobehavioral and cognitive functions in a mouse model of closed head injury (CHI). In the brains of post-CHI mice, IA reduced glial activation, inhibited the expression of interleukin-1beta, and tumor necrosis factor-alpha mRNAs, and induced cell death in macrophages at the area of trauma. A mild hypothermic effect was also noted. Subsequently, IA inhibited hippocampal neurodegeneration and exerted a beneficial effect on functional outcome after CHI, indicated by reduced neurological severity scores and improved cognitive ability in an object recognition test. This study attributes the anti-inflammatory activity of *Boswellia* resin to IA and related cembranoid diterpenes and suggests that they may serve as novel neuroprotective agents



incensole acetate

Poeckel D. & Werz O. (2006) "Boswellic acids: biological actions and molecular targets." *Curr Med Chem.* **13**(28), 3359-69. Abstract. Gum resin extracts of *Boswellia* species have been traditionally applied in folk medicine for centuries to treat various chronic inflammatory diseases, and experimental data from animal models and studies with human subjects confirmed the potential of B. spec extracts for the treatment of not only inflammation but also of cancer. Analysis of the ingredients of these extracts revealed that the pentacyclic triterpenes boswellic acids (BAs) possess biological activities and appear to be responsible for the respective pharmacological actions. Approaches in order to elucidate the molecular mechanisms underlying the biological effects of BAs identified 5-lipoxygenase, human leukocyte elastase, toposiomerase I and II, as well as IkappaB kinases as molecular targets of BAs. Moreover, it was shown that depending on the cell type and the structure of the BAs, the compounds differentially interfere with signal transduction pathways including Ca(2+/-) and MAPK signaling in various blood cells, related to functional cellular processes important for inflammatory reactions and tumor growth. This review summarizes the biological actions of BAs on the cellular and molecular level and attempts to put the data into perspective of the beneficial effects manifested in animal studies and trials with human subjects related to inflammation and cancer.

Pedretti A,, Capezzera R., Zane C., Facchinetti E. & Calzavara-Pinton P. (2009) "Effects of topical Boswellic Acid on photo and age-damaged skin: clinical, biophysical, and echographic evaluations in a double-blind, randomized, split-face study." *Planta Med*. Nov, 2009. Abstract. Boswellic acids (BAs) are pentacyclic triterpenes with strong anti-inflammatory activity; their most important source is the extract of the gum resin of BOSWELLIA SERRATA, a tropical tree that grows in India and Africa. In the present randomized, double-blind, split-face, comparative study we have assessed efficacy, tolerability, and safety of a base cream containing 0.5 % BAs as compared to the same cream without these active ingredients in the treatment of clinical manifestations of photoaging of facial skin. Fifteen female volunteers were enrolled; they applied creams once daily for 30 days. At baseline, at the end of the treatment, and after a 2-month follow-up, clinical findings were assessed according to the Dover classification scale for photoaging and by biophysical and ecographic measurements. We registered a significant improvement of tactile roughness and fine lines in the half side of the face treated with BAs; noninvasive instrumental diagnostic investigations showed an improvement of elasticity, a decrease of sebum excretion, and a change of echographic parameters suggesting a reshaping of dermal tissue. The treatment was always well tolerated without adverse effects. The present findings seem to indicate that the topical application of BAs may represent a suitable treatment option for selected features of skin photoaging.

Roy S., Khanna S., Shah H., Rink C., Phillips C., Preuss H., Subbaraju G.V., Trimurtulu G., Krishnaraju A.V., Bagchi M., Bagchi D., Sen C.K. (2005) "Genome screen to identify the genetic basis of the anti-inflammatory effects of *Boswellia* in microvascular endothelial cells." *DNA and Cell Biology*. **24**(4), 244-255.

Roy S., Khanna S., Krishnaraju A.V., Subbaraju G.V., Yasmin T., Bagchi D. & Sen C..K.. (2006) "Regulation of vascular responses to inflammation: inducible matrix metalloproteinase-3 expression in human microvascular endothelial cells is sensitive to antiinflammatory *Boswellia*." *Antioxid Redox Signal*. **8**(3-4):653-60. Abstract. Endothelial cells are critical elements in the pathophysiology of inflammation. Tumor necrosis factor (TNF) alpha potently induces inflammatory responses in endothelial cells. Recently we have examined the genetic basis of the antiinflammatory effects of *Boswellia* extract (BE) in a system of TNFalpha-induced gene

expression in human microvascular endothelial cells (HMECs). Of the 522 genes induced by TNFalpha in HMECs, 113 genes were sensitive to BE. BE prevented the TNFalpha-induced expression of matrix metalloproteinases (MMPs). In the current work, we sought to test the effects of BE on TNFalpha-inducible MMP expression in HMECs. Acetyl-11-ketobeta- boswellic acid (AKBA) is known to be an active principle in BE. To evaluate the significance of AKBA in the antiinflammatory properties of BE, effects of BE containing either 3% (BE3%) or 30% (BE30%, 5-Loxin) were compared. Pretreatment of HMECs for 2 days with BE potently prevented TNFalpha-induced expression and activity of MMP-3, MMP-10, and MMP-12. In vivo, BE protected against experimental arthritis. In all experiments, both in vitro and in vivo, BE30% was more effective than BE3%. In sum, this work lends support to our previous report that BE has potent antiinflammatory properties both in vitro as well as in vivo.

Safayhi H., Sailer E.R. & Ammon H.P. (2009) “Mechanism of 5-lipoxygenase inhibition by acetyl-11-keto-beta-boswellic acid." *Molecular Pharmacology* **47**(6), 1212-1215. Abstract. The formation of 5-lipoxygenase (EC 1.13.11.34) products from endogenous substrate by intact rat neutrophilic granulocytes and from exogenous arachidonic acid by rat granulocyte 105,000 x g supernatants and affinity chromatography-purified human leukocyte 5-lipoxygenase was inhibited by acetyl-11-keto-beta-boswellic acid (IC50 values of 1.5 microM, 8 microM, and 16 microM, respectively). With other pentacyclic triterpenes lacking the 11-keto function and/or the carboxyl function on ring A (e.g., amyrin and ursolic acid), no 5-lipoxygenase inhibition was observed. The presence of the noninhibitory pentacyclic triterpenes both in intact cells and in the cell-free system caused a concentration- dependent reversal of the 5-lipoxygenase inhibition by acetyl-11-keto- beta-boswellic acid, whereas the inhibitory actions of 5-lipoxygenase inhibitors from different chemical classes (MK-886, L-739,010, ZM- 230,487, and nordihydroguaiaretic acid) were not modified. The inhibition by acetyl-11-keto-beta-boswellic acid and the antagonism by noninhibitory pentacyclic triterpenes were not due to nonspecific lipophilic interactions, because lipophilic four-ring compounds (cholesterol, cortisone, and testosterone) neither inhibited the activity of the 5-lipoxygenase nor antagonized the inhibitory action of acetyl-11-keto-beta-boswellic acid. Therefore, we conclude that acetyl- 11-keto-beta-boswellic acid acts directly on the 5-lipoxygenase enzyme at a selective site for pentacyclic triterpenes that is different from the arachidonate substrate binding site.

Safayhi H., Boden S.E., Schweizer S. & Ammon H.P.. (2000) "Concentration-dependent potentiating and inhibitory effects of *Boswellia* extracts on 5-lipoxygenase product formation in stimulated PMNL." *Planta Med* .**66**(2), 110-3. Abstract. Preparations from the gum of *Boswellia* spec. have been used in the traditional medicine for the treatment of inflammatory diseases. Extracts from *B. serrata* gum were shown to inhibit leukotriene biosynthesis by impairing the 5-lipoxygenase (5-LO) activity. In order to identify the minimal effective concentrations of extracts in vitro we studied the effects of ethanolic extracts from commercially available resins from two regions (B. serrata gum from India and Olibanum in granis from Arabia) on the 5-LO product formation from endogenous substrate in calcium and ionophore stimulated neutrophils in a defined concentration range. Both extracts inhibited 5-LO product formation in vitro in concentrations greater than 10 to 15 micrograms/ml as reported previously for an ethanolic B. serrata extract. In contrast, lower concentrations of extracts (1 to 10 micrograms/ml) even potentiated 5-LO product formation, especially the biosynthesis of 5(S)-HETE. The in vitro data underline the major importance of drug standardization when Boswellia resin containing preparations are used for the treatment of diseases.

Safayhi H., Rall B., Sailer E-R. & Ammon H.P.T. (1997) "Inhibition by boswellic acids of human leukocyte elastase." *Pharmacology* **281**(1), 460-463. Abstract. Frankincense extracts and boswellic acids, biologically active pentacyclic triterpenes of frankincense, block leukotriene biosynthesis and exert potent anti-inflammatory effects. Screening for additional effects of boswellic acids on further proinflammatory pathways, we observed that acetyl-11-keto--boswellic acid, an established direct, nonredox and noncompetitive 5-lipoxygenase inhibitor, decreased the activity of human leukocyte elastase (HLE) in vitro with an IC50 value of about 15 µM. Among the pentacyclic triterpenes tested in concentrations up to 20 µM, we also observed substantial

inhibition by -boswellic acid, amyrin and ursolic acid, but not by 18-glycyrrhetinic acid. The data show that the dual inhibition of 5-lipoxygenase and HLE is unique to boswellic acids: other pentacyclic triterpenes with HLE inhibitory activities (e.g., ursolic acid and amyrin) do not inhibit 5-lipoxygenase, and leukotriene biosynthesis inhibitors from different chemical classes (e.g., NDGA, MK-886 and ZM-230,487) do not impair HLE activity. Because leukotriene formation and HLE release are increased simultaneously by neutrophil stimulation in a variety of inflammation- and hypersensitivity-based human diseases, the reported blockade of two proinflammatory enzymes by boswellic acids might be the rationale for the putative antiphlogistic activity of acetyl-11-keto--boswellic acid and derivatives.

Safayhi H., Sailer E. R. & Ammon H. P. T. (1995). "Mechanism of 5-lipoxygenase inhibition by acetyl-11-keto-Boswellic acid." *Mol. Pharmacol*. **47**, 1212-1216. Abstract. The formation of 5-lipoxygenase (EC 1.13.11.34) products from endogenous substrate by intact rat neutrophilic granulocytes and from exogenous arachidonic acid by rat granulocyte 105,000 x g supernatants and affinity chromatography-purified human leukocyte 5-lipoxygenase was inhibited by acetyl-11-keto-beta-boswellic acid (IC50 values of 1.5 microM, 8 microM, and 16 microM, respectively). With other pentacyclic triterpenes lacking the 11-keto function and/or the carboxyl function on ring A (e.g., amyrin and ursolic acid), no 5-lipoxygenase inhibition was observed. The presence of the noninhibitory pentacyclic triterpenes both in intact cells and in the cell-free system caused a concentration-dependent reversal of the 5-lipoxygenase inhibition by acetyl-11-keto-beta-boswellic acid, whereas the inhibitory actions of 5-lipoxygenase inhibitors from different chemical classes (MK-886, L-739,010, ZM-230,487, and nordihydroguaiaretic acid) were not modified. The inhibition by acetyl-11-keto-beta-boswellic acid and the antagonism by noninhibitory pentacyclic triterpenes were not due to nonspecific lipophilic interactions, because lipophilic four-ring compounds (cholesterol, cortisone, and testosterone) neither inhibited the activity of the 5-lipoxygenase nor antagonized the inhibitory action of acetyl-11-keto-beta-boswellic acid. Therefore, we conclude that acetyl-11-keto-beta-boswellic acid acts directly on the 5-lipoxygenase enzyme at a selective site for pentacyclic triterpenes that is different from the arachidonate substrate binding site.

Safayhi H., Mack T., Sabieraj J., Anazodo M. I., Subramanian L. R. & Ammon H. P. T. (1992). “Boswellic acids: Novel, specific, nonredox inhibitors of 5-lipoxygenase.” *J. Pharmacol. Exp. Therap*. **261**, 1143-1146.

Sander O, Herborn G, Rau R (1998). “Is H15 (resin extract of *Boswellia serrata*, “incense”) a useful supplement to established drug therapy of chronic polyarthritis? Results of a double-blind pilot study [in German]. *Z Rheumatol* . **57**(1):11-16.

Schweizer S., von Brocke A.F.W., Boden S.E., Bayer E., Ammon H.P.T. & Safayhi H. (2000) "Workup-dependent formation of 5-lipoxygenase inhibitory boswellic acid analogues.” *J. Nat. Prod.* **63**(8),1058-1061 Abstract. Pentacyclic triterpenes from the 11-keto-boswellic acid series were identified as the active principal ingredients of *Boswellia* resin, inhibiting the key enzyme of leukotriene biosynthesis, 5-lipoxygenase (5-LO). Of the genuine boswellic acids hitherto characterized, 3-O-acetyl-11-keto-â-boswellic acid, AKBA (1), proved to be the most potent inhibitor of 5-LO. In the course of purification of further boswellic acid derivatives from Boswellia resin, we observed the degradation of the natural compound 3-O-acetyl-11-hydroxy-â-boswellic acid (2) to the thermodynamically more stable product 3-O-acetyl-9,11-dehydro-â-boswellic acid (4). The metastable intermediate of this conversion, under moderate conditions of workup in methanolic solutions, was identified as 3-O-acetyl-11-methoxy-â-boswellic acid (3). The novel artifactual boswellic acid derivatives inhibited 5-LO product formation in intact cells with different characteristics: 4 almost totally abolished 5-LO activity, with an IC50 of 0.75 íM, whereas 3 and 9,11-dehydro-â-boswellic acid (5), the deacetylated analogue of 4, were incomplete inhibitors. The data suggest that the conditions chosen for the workup of *Boswellia* extracts could significantly influence the potency of their biological actions and their potential therapeutic effectiveness.

Singh G. B. & Atal C. K. (1986). “Pharmacology of an extract of salai guggal ex-*Boswellia serrata*, a new non-steroidal anti-inflammatory agent.” *Agents Actions* **18**, 407-412.

Singh G.B., Singh S. & Bani S. (1996) “Anti inflammatory actions of boswellic acids.” *Phytomedicine* **3**, 81-5.

Singh T., Bhakuni R.S. (2007) "A new euphane triterpene and a lipid constituent from the bark of *Boswellia serrata*." *Cheminform* **36**(19).

Singh T. & BhakuniR.S. (2008) "A New Euphane Triterpene (I) and a Lipid Diester (II) from Oleo-gum Resin of *Boswellia serrata*." *ChemInform* **37(**34).

Singh S., Khajuria A., Taneja S.C., Johri R.K., Singh J. & Qazi G.N. (2008) "Boswellic acids: A leukotriene inhibitor also effective through topical application in inflammatory disorders" *Phytomedicine* **15**(9),400-407. Abstract. Boswellic acids (BA), a natural mixture isolated from oleo gum resin of *Boswellia serrata* comprised of four major pentacyclic triterpene acids: β-boswellic acid (the most abundant), 3-acteyl-β-boswellic acid, 11-keto-β-boswellic acid, and 3-acetyl-11-keto-β-boswellic acid, is reported to be effective as anti-inflammatory, immunomodulatory, anti-tumor, anti-asthmatic and in Chron's disease. It inhibits pro-inflammatory mediators in the body, specifically leukotrienes via inhibition of 5-lipoxygenase, the key enzyme of leukotriene synthesis, is the scientifically proved mechanism for its anti-inflammatory/anti-arthritic activity. All previous work on BA for its biological activity has been done through the systemic application but no pre-clinical data reported for its anti-inflammatory activity by topical application. We here by report anti-inflammatory activity of BA through this route by applying different acute and chronic models of inflammation i.e., arachidonic acid and croton oil-induced mouse ear edema, carrageenan-induced rats paw edema and adjuvant-induced developing arthritis in rats. The results of the study revealed that the effect observed through this route is in accordance to the study conducted with the systemic route, thus establishing that BA when used through topical application is as effective as through the systemic route.

Singh G.B. (2008) “Pharmacological profile of boswellic acids obtained from *Boswellia serrata* as a new type of non-steroidal anti-inflammatory drug." *Phytomedicine* **15** (6-7) Abstract. Over last three decades, we have been actively engaged in research and development of safe and effective anti-inflammatory drugs particularly from natural sources (Singh et al., 1986, 1993, 1994a, b, 1996a-c) with selective inhibitory action on LTB4. Based on our research work alcoholic extract of salai guggal ex-*Boswellia serrata* was marketed in India in 1982 as SALLAKI with no reports of adverse effects (H-15 in Switzerland). Further study on this resulted in isolation of boswellic acids. Anti-inflammatory activity (AIA) of boswellic acids (BA) was evaluated in a variety of test models. BA in a dose range of 50-200 mg/kg orally showed statistically significant dose-related inhibitory action. In acute tests of carrageenan, histamine and dextran-induced edema, BA produced 26-48% inhibitory action. It showed 42-60% inhibitory effect in acetic acid-induced vascular permeability in mice. In chronic test of formaldehyde, developing and established adjuvant polyarthritis, BA elicited anti-arthritic action by 32-62% and decreased secondary lesions. In sodium urate gouty arthritis in dogs and bovine serum albumin (BSA) arthritis in rabbits, BA demonstrated inhibitory action of the knee joints swelling and leucocytes count of aspirated synovial fluid (21-58%). In carragenan- and dextran-induced pleurisy in rats, BA decreased the exudate volume and migration of lucocytes. It showed weak anti-pyretic action in pyretic rats and rabbits but no analgesic effect. It failed to show any ulcerogenic potential. On biochemical investigations, BA decreased the arthritis elevated levels of SGOT & SGPT and alkaline phosphatase levels. It failed to exhibit cytotoxic action on PMNL as revealed by the dye exclusion test or irritant effect on rabbit cornea. Unlike other NSAID's orally administered, BA failed to prolong gestation period, parturition time in pregnant rats and did not affect the of castor oil-induced diarrhea effects attributed to inhibition of PG's. BA inhibited the formation LT[B.sub.4] from endogenous arachidonic acid in rat peritoneal neutrophils (Ammon et al., 1991; Safahyi et al., 1992). In acute toxicity, BA (2g/Kg) produced no mortality in rats and mice over 72 h. In subacute toxicity (4 weeks) and chronic toxicity (6 months) in rats and monkeys, BA produced no undesirable effects. Clinical, haematological and biochemical parameters were found to be within

the limits and histopathology showed no changes in cell structure. Clinical studies carried on 60 volunteers patients of arthritis over 8 weeks revealed no untoward symptoms. Hence, BA is a new class of anti-inflammatory and anti-arthritic drug with a novel mode of inhibitory action on LT[B.sub.4]

Tausch L., Siemoneit U., Poeckel D., Kather N., Franke L., Schneider G., Holtmeier W., Beckhaus T., Karas M., Jauch J. & Werz O. (2008) "Identification of targets and molecular modes of action of boswellic acids." *Phytomedicine* **15** (6-7). June 2008 Abstract. The anti-inflammatory properties of frankincense, the gum resin derived from *Boswellia* species, are generally well-recognized, and frankincense extracts are frequently and increasingly used in folk medicine to cure chronic inflammatory diseases. The pentacyclic triterpenes boswellic acids are assumed to be the active principles of frankincense. Numerous animal studies and clinical trials confirmed the anti-inflammatory efficacy of frankincense preparations, and various scientific studies had been performed aiming to reveal the respective underlying molecular basis. However, until today, the pharmacological relevance of the suggested targets e.g. lipoxygenases, cyclooxygenases, topoisomerases, human leucocyte elastase and I[kappa]B kinases are a matter of debate. Here, we describe a methodology for the identification of molecular targets for boswellic acids. Thus, we introduce a target-fishing strategy using immobilized boswellic acids as bait and neutrophil or monocyte lysates as protein sources. The selectively precipitated proteins can be separated by SDS-PAGE and analyzed by mass spectrometry (MALDI-TOF) as well as by immunological detection (Western blot). Functional analysis may reveal an interference of boswellic acids with the respective protein, and investigations in blood ex vivo of patients treated with frankincense may support the pharmacological relevance.

Tawab M.A., Kruger P. & Schubert-Zsilavecz M. (2008) "Systemic availability of boswellic acids following oral administration." *Phytomedicine* **15**(6-7). Abstract. In vitro studies revealed, that boswellic acids (BAs), the active ingredients of *Boswellia serrata* extract, may represent promising alternative/adjuvant agents for the treatment of inflammatory diseases and cerebral oedema. 11-Keto-[beta] boswellic acid (KBA) and 3-acetyl-11-keto-[beta]-boswellic acid (AKBA) are the most potent inhibitors of 5-lipoxygenase with IC values of 2.8 and 1.5 [micro]M respectively, in intact rat polymorphonuclear leucocytes (PMNLs) (Sailer et al., 1996). In the frame of a preliminary pharmacokinetic study the concentration of KBA was determined to be 1.6 [micro]M in human plasma following single-dose administration of 1600 mg B. serrata extract, whereas AKBA could not be detected (Tawab et al., 2001).zIn rats, dosed with 240 mg/kg B. serrata extract, KBA and AKBA were determined in plasma at 0.4 and 0.2 [micro]M, respectively, and at 0.3 [micro]M in brain. The rat brain-to-plasma ratios were 0.5 for KBA and 0.8 for AKBA, indicating a higher brain penetration of AKBA (Reising et al, 2005).Studies on the metabolic stability of KBA and AKBA revealed that KBA undergoes an extensive phase I metabolism yielding hydroxylated derivatives. AKBA is metabolically stable and is not deacetylated to KBA. Permeability studies using CaCo-2 cells suggest poor absorption of KBA and AKBA from the gastrointest inal tract. Any attempts to enhance the bioavailability of BAs should focus on the metabolically more stable AKBA (Kruger et al., 2008).

Wildfeuer A., Neu I.S., Safayhi H., Metzger G., Wehrmann M., Vogel U. & Ammon H.P. (1998) "Effects of boswellic acids extracted from a herbal medicine on the biosynthesis of leukotrienes and the course of experimental autoimmune encephalomyelitis." *Arzneimittelforschung*.**48**(6), 668-74. Abstract. Mixed acetylboswellic acids, pentacyclic triterpenes extracted from the gum resin of *Boswellia serrata* Roxb., significantly inhibited the ionophore-stimulated release of the leukotrienes (LT) B4 and C4 from intact human polymorphonuclear neutrophil leukocytes (PMNLs), with IC50 values of 8.48 micrograms/ml and 8.43 micrograms/ml, respectively. Purified acetyl-11-keto-beta-boswellic acid was about three times more potent as inhibitor of the formation of both LTB4 (IC50 = 2.53 micrograms/ml) and LTC4 (IC50 = 2.26 micrograms/ml) from human PMNLs in the same assay. The comparative agent MK 886 (3-[1-(4-chlorobenzyl)-3-t-butyl-thio-5-isopropylindol-2-yl]- 2,2-dimethylpropanoic acid, L-663,536, CAS 118, 414-82-7) was about 10 to 100-fold more active than the boswellic acids in inhibiting the formation of 5-lipoxygenase products in human PMNLs, with IC50 values of 0.0068 microgram/ml (LTB4) and 0.49

microgram/ml (LTC4). After daily intraperitoneal dosage the extract of mixed acetylboswellic acids (20 mg/kg) significantly reduced the clinical symptoms in guinea pigs with experimental autoimmune encephalomyelitis (EAE) between days 11 and 21. However, the inflammatory infiltrates in the brain and the spinal cord were not significantly less extensive in the treated animals than in the respective control group. The multiple intraperitoneal application of boswellic acids did not inhibit the ionophore-challenged ex vivo release of leukotrienes B4 and C4 from PMNLs separated from the blood of guinea pigs with EAE. The boswellic acids have thus been characterized as selective, non-redox and potent inhibitors of the biosynthesis of leukotrienes in vitro.

Anti-carcinogenic / Anti-tumorigenic Properties.

Cropwatch Comments: Extracts of *B. serrata* & boswellic acids & their derivatives have been investigated for anti-carcinogenic/anti-tumorigenic effects via cytotoxic & apoptosis effects in various *in vitro* cell lines.

Akihisa T., Tabata K., Banno N., Tokuda H., Nishimura R., Nakamura Y., Kimura Y., Yasukawa K. & Suzuki T. (2006) "Cancer chemopreventive effects and cytotoxic activities of the triterpene acids from the resin of *Boswellia carteri*." *Biol Pharm Bull.* **29**(9), 1976-9. Abstract. Fifteen triterpene acids, viz., seven of the beta-boswellic acids (ursane-type) (1-7), two of the alpha-boswellic acids (oleanane-type) (8, 9), two of the lupeolic acids (lupane-type) (10, 11), and four of the tirucallane-type (12-14, 16), and two cembrane-type diterpenes (17, 18), isolated from the MeOH extract of the resin of *Boswellia carteri* (Burseraceae), together with a triterpene acid 15 (the acetyl derivative of 14), were examined for their inhibitory effects on the induction of Epstein-Barr virus early antigen (EBV-EA) by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells and on activation of (+/-)-(E)-methyl-2[(E)-hydroxyimino]-5-nitro-6-methoxy-3-hexemide (NOR 1), a nitrogen oxide (NO) donor, and cytotoxic activities against three human neuroblastoma cell lines, IMR-32, NB-39, and SK-N-SH in vitro. On evaluation against the EBV-EA activation induced by TPA, seven compounds, 2, 10, 11, and 13-16, showed potent inhibitory effects on EBV-EA induction. Upon evaluation against activation of NOR 1, five compounds, 7, 13, and 14-16, showed potent inhibitory effects. Further, fifteen compounds, 1-7, 9-11, 13-15, 17, and 18, exhibited potent cytotoxic activities with IC(50) values of 4.1-82.4 muM against all of the three human neuroblastoma cells tested.

Anon (2010) "Frankincense: Could it be a cure for cancer?" downloaded 9th Feb 2010: see: http://news.bbc.co.uk/1/hi/world/middle_east/8505251.stm

Cassileth B. (2009) "Complementary therapies, herbs, and other OTC agents: Boswellia (Boswellia serrata)." *Oncology* **23**(12), 1108.

Flavin D.F. (2007) "A lipoxygenase inhibitor in breast cancer brain metastases." *J Neurooncol.* **82**(1),91-3. Abstract. The complication of multiple brain metastases in breast cancer patients is a life threatening condition with limited success following standard therapies. The arachidonate lipoxygenase pathway appears to play a role in brain tumor growth as well as inhibition of apoptosis in in-vitro studies. The down regulation of these arachidonate lipoxygenase growth stimulating products therefore appeared to be a worthwhile consideration for testing in brain metastases not responding to standard therapy. *Boswellia serrata*, a lipoxygenase inhibitor was applied for this inhibition. Multiple brain metastases were successfully reversed using this method in a breast cancer patient who had not shown improvement after standard therapy. The results suggest a potential new area of therapy for breast cancer patients with brain metastases that may be useful as an adjuvant to our standard therapy.

Frank B.M., Qing Yang, Osban J. Azzarello J.T., Saban M.R., Saban R., Ashley R.A., Welter J.C., Fung K.-M. & Lin H-K. (2009) "Frankincense oil derived from *Boswellia carteri* induces tumor cell specific cytotoxicity." *BMC Complementary and Alternative Medicine* **9**(6). Abstract. Background: Originating from Africa, India, and the Middle East, frankincense oil has been important both socially and economically as an ingredient in incense and perfumes for thousands of years.

Frankincense oil is prepared from aromatic hardened gum resins obtained by tapping *Boswellia* trees. One of the main components of frankincense oil is boswellic acid, a component known to have anti-neoplastic properties. The goal of this study was to evaluate frankincense oil for its anti-tumor activity and signaling pathways in bladder cancer cells. Method: Frankincense oil-induced cell viability was investigated in human bladder cancer J82 cells and immortalized normal bladder urothelial UROtsa cells. Temporal regulation of frankincense oil-activated gene expression in bladder cancer cells was identified by microarray and bioinformatics analysis. Results: Within a range of concentration, frankincense oil suppressed cell viability in bladder transitional carcinoma J82 cells but not in UROtsa cells. Comprehensive gene expression analysis confirmed that frankincense oil activates genes that are responsible for cell cycle arrest, cell growth suppression, and apoptosis in J82 cells. However, frankincense oil-induced cell death in J82 cells did not result in DNA fragmentation, a hallmark of apoptosis. Conclusion: Frankincense oil appears to distinguish cancerous from normal bladder cells and suppress cancer cell viability. Microarray and bioinformatics analysis proposed multiple pathways that can be activated by frankincense oil to induce bladder cancer cell death. Frankincense oil might represent an alternative intravesical agent for bladder cancer treatment.

Huang M.T., Badmaev V., Ding Y., Liu Y., Xie J.G. & Ho C.T. (2000) "Anti-tumor and anti-carcinogenic activities of triterpenoid, β-boswellic acid." *BioFactors* **13**, 225-230.

Hostanska K., Daum G. & Saller R. (2002) "Cytostatic and apoptosis inducing activity of boswellic acid towards malignant cells in vitro." *Anticancer Research* **22**, 2853-62.

Liu J-J., Nilsson A., Oredsson S., Badmaev V., Zhao W-Z. & Duan R-D (2002) "Boswellic acids trigger apoptosis via a pathway dependent on caspase-8 activation but independent on Fas/Fas ligand interaction in colon cancer HT-29 cells*." Carcinogen.* **23**, 2087-2093.

Liu J.J., Nilsson A., Oredsson S., Badmaev V.& Duan R.D. (2002) "Keto- and acetyl-keto-boswellic acids inhibit proliferation and induce apoptosis in Hep G2 cells via a caspase-8 dependent pathway. *Int J Mol Med* **10**, 501-505.

Mazzio E.A. & Soliman K.F. (2008) "In vitro screening for the tumoricidal properties of international medicinal herbs." *Phytother Res*. 2008 Oct 9. Abstract. There is growing use of anticancer complementary and alternative medicines (CAMs) worldwide. The purpose of the current study is to assess a sizeable variety of natural and plant sources of diverse origin, to ascertain prospective research directives for cancer treatment and potential new chemotherapy drug sources. In this study, 374 natural extracts (10 microg/mL-5 mg/mL) were evaluated for dose-dependent tumoricidal effects using immortal neuroblastoma of spontaneous malignant origin. The findings indicate no pattern of tumoricidal effects by diverse plants with similar families/genus under the classes Pinopsida, Equisetopsida, Lycopodiosida, Filicosida, Liliopsida Monocotyledons or Magnoliopsida Dicotyledons. The results indicate that many of the most commonly used CAMs exhibited relatively weak tumoricidal effects including cats claw, astragalus, ginseng, echinacea, mistletoe, milk thistle, slippery elm, cayenne, chamomile, don quai, meadowsweet, motherwort and shepherd's purse. The data demonstrate that the most potent plant extracts were randomly dispersed within the plantae kingdom (LC(50) = 31-490 microg/mL) in order of the lowest LC(50) *Dioscorea villosa* (Dioscoreaceae) > *Sanguinaria canadensis* (Papaveraceae) > *Dipsacus asper* (Dipsacaceae) > *Populus balsamifera* (Salicaceae) > *Boswellia carteri* (Burseraceae) > *Cyamopsis psoralioides* (Fabaceae) > *Rhamnus cathartica* (Rhamnaceae) > *Larrea tridentate* (Zygophyllaceae) > *Dichroa febrifuga* (Hydrangeaceae) > *Batschia canescens* (Boraginaceae) > *Kochia scoparia* (Chenopodiaceae) > *Solanum xanthocarpum* (Solanaceae) > *Opoponax chironium* (Umbelliferae) > *Caulophyllum thalictroides* (Berberidaceae) > *Dryopteris crassirhizoma* (Dryopteridaceae) > *Garcinia cambogia* (Clusiaceae) > *Vitex agnus-castus* (Verbenaceae) > *Calamus draco* (Arecaceae). These findings show tumoricidal effect by extracts of wild yam root, bloodroot, teasel root, bakuchi seed, dichroa root, kanta kari, garcinia fruit, mace, dragons blood and the biblically referenced herbs: balm of gilead bud, frankincense and myrrh gum.

Park Y.S., Lee J.H., Bondar J., Harwalakr J.A., Safayhi H. & Golubic M. (2000) “Cytotoxic action of acetyl-11-keto-β-boswellic Acid (AKBA) on meningioma cells.” *Planta Med.* **68**, 397-401.

Shao Y., Ho C.T., Chin C.V., Badmaev V., Ma W. & Haung M.Y. (1997). "Inhibitory activity of boswellic acids from *Boswellia serrata* against human leukemia HL-60 Cells in culture. *Planta Med* **64**, 328–331.

Winking M., Sarikaya S., Rahmanian A., Jodicke A. & Boker D.K. (2000 "Boswellic acids inhibit glioma growth: a new treatment option?" *J Neurooncol* **46**, 97-103.

Winking M. (2008) "Effects of boswellic acids on malignant glioma." *Phytomedicine* June 2008. Abstract. Conventional malignant glioma therapy regarding to surgery, radiation therapy and chemotherapy is not satisfying. The prognosis of the glioma patient depends more on the histological grading of the tumor and patients age than on the therapy. Especially the adjuvant chemotherapy failed to significantly influence survival time in glioma patients. For a prolongation of the survival time in those patients additional therapeutic regimes are necessary. In glioma patients the release of cysteinyl-leukotrienes (cys-LT), measured by their metabolites in patients' urine correlates significantly with the tumor malignancy. Correlating the perifocal edema volume in those patients with the amounts of cys-LT metabolites in the urin, a significance was detected indicating that increasing cys-LT release is accompanied by increasing edema volume. Knowing about the inhibiting effects of boswellic acids on the key-enzyme 5-lipoxygenase, an alcoholic extract from olibanum was used for edema treatment. Boswellic acids were able to reduce the perifocal edema in a concentration dependent manner. Using the highest dose (3 x 1200 mg) the edema showed significant reduction in those patients. Also the clinical condition improved slightly In an animal experiment, Wistar rats were treated with a Boswellia extract 14 days after inoculation of C6 tumor cells into their right caudate nucleus. In the group with the highest dosage (3 x 240 mg/kg BW) the survival time of the rats was more than double of the control group ($p < 0.01$) (Winking et al., 2000). These data demonstrate an influence of boswellic acids on glioma growth and may give an opportunity for a new therapeutic regimen on glioma treatment in man. Ref: Winking, M. *et al*. 2000. *J. Neurooncol.* **46**, 97-103.

Yuan H.Q., Kong F, Wang X.L., Young C.Y., Hu X.Y. & Lou H.X.. (2008) "Inhibitory effect of acetyl-11-keto-beta-boswellic acid on androgen receptor by interference of Sp1 binding activity in prostate cancer cells." *Biochem Pharmacol.* **75**(11), 2112-21. Abstract. Androgen receptor (AR)-mediated signaling is crucial for the development and progression of prostate cancer (PCa). Naturally occurring phytochemicals that target the AR signaling offer significant protection against this disease. Acetyl-11-keto-beta-boswellic acid (AKBA), a compound isolated from the gum-resin of Boswellia carterii, caused G1-phase cell cycle arrest with an induction of p21(WAF1/CIP1), and a reduction of cyclin D1 as well in prostate cancer cells. AKBA-mediated cellular proliferation inhibition was associated with a decrease of AR expression at mRNA and protein levels. Furthermore, the functional biomarkers used in evaluation of AR transactivity showed suppressions of prostate-specific antigen promoter-dependent and androgen responsive element-dependent luciferase activities. Additionally, down-regulation of an AR short promoter mainly containing a Sp1 binding site suggested the essential role of Sp1 for the reduction of AR expression in cells exposed to AKBA. Interruption effect of AKBA on Sp1 binding activity but not Sp1 protein levels was further confirmed by EMSA and transient transfection with a luciferase reporter driven by three copies of the Sp1 binding site of the AR promoter. Therefore, anti-AR properties ascribed to AKBA suggested that AKBA-containing drugs could be used for the development of novel therapeutic chemicals.

Zhao W., Entschladen F., Liu H., Niggemann B., Fang Q., Zaenker K.S.& Han R. (2003) "Boswellic acid acetate induces differentiation and apoptosis in highly metastatic melanoma and fibrosarcoma cells." *Cancer Detec Prev* **27**, 67-75.

Frankincense – Use in Treating Crohn’s Disease

Schwarz J.A., Holtmeier W.H. & Skarke C. (2008) "Development steps of the herbal medicinal product Boswelan[C] for maintaining remission of Crohn's disease." *Phytomedicine* **15**(6-7) June

2008. Abstract. *Boswellia serrata* gum resin was formulated into soft gelatine capsules as semifluid mass from its ethanol extract mixed with a polyethylene as inert carrier. The scientific advice by the competent Higher Federal Authority in Germany (BfArM) triggered two clinical trials: The Phase II trial "A multicenter, randomized, double-blind, placebo-controlled study of an orally administered Boswellia serrata Extract PSO201 Bo for maintaining remission of Crohn's Disease" (Co-ordinating Investigator: PD Dr. med. Wolfgang Holtmeier, Vorlage-Nr.: 4021191) was started in 6 investigational sites in Germany but was soon increased to 25 sites due to poor patient recruitment. The Phase I trial addressed the "Safety, tolerability and pharmacokinetics of a single dose application of two Boswellia serrata extract capsules in healthy male volunteers. Part I: Double blind, randomized, placebo controlled, sensory crossover discrimination test, Part II: Open, randomized, cross-over pharmacokinetics (ll-keto-[beta]-boswellic acid-KBA and acetyl-11 -keto-[beta]-boswellic acid - AKBA) after fasting or an standardized light breakfast" (Principal Investigator: Dr. med. Carsten Skarke, EudraCT No: 2006-002939-24, Vorlage-Nr.: 4031905). The regulatory requirements and hurdles as well as the present status of the Crohn's Disease trial and the results of the Phase I trial will be presented.

Frankincense – Use in Treating Respiratory Diseases,

Gupta I., Gupta V., Parihar A., Gupta S., Ludtke R., Safayhi H. & Ammon H. P. (1998). “Effects of *Boswellia serrata* gum resin in patients with bronchial asthma: results of a double-blind, placebo-controlled, 6-week clinical study.” *Eur. J. Med. Res*. **3**, 511-514. Abstract. The gum resin of *Boswellia serrata*, known in Indian Ayurvedic system of medicine as Salai guggal, contains boswellic acids, which have been shown to inhibit leukotriene biosynthesis. In a double-blind, placebo-controlled study forty patients, 23 males and 17 females in the age range of 18 - 75 years having mean duration of illness, bronchial asthma, of 9.58 +/- 6.07 years were treated with a preparation of gum resin of 300 mg thrice daily for a period of 6 weeks. 70% of patients showed improvement of disease as evident by disappearance of physical symptoms and signs such as dyspnoea, rhonchi, number of attacks, increase in FEV subset1, FVC and PEFR as well as decrease in eosinophilic count and ESR. In the control group of 40 patients 16 males and 24 females in the age range of 14-58 years with mean of 32.95 +/- 12.68 were treated with lactose 300 mg thrice daily for 6 weeks. Only 27% of patients in the control group showed improvement. The data show a definite role of gum resin of *Boswellia serrata* in the treatment of bronchial asthma.

Krüger P., Kanzer J., Hummel J., Fricker G., Schubert-Zsilavecz M. & Abdel-Tawab M. (2008) "Permeation of *Boswellia* extract in the Caco-2 model and possible interactions of its constituents KBA and AKBA with OATP1B3 and MRP2." *Eur J Pharm Sci.* 2008 Oct 25. Abstract. Traditionally *Boswellia serrata* extract is used in the Indian Ayurvedic medicine for the treatment of inflammatory diseases. In 2002 the EMEA designated *Boswellia* an orphan drug status for the treatment of peritumoral oedema. Pharmacokinetic studies yielded low plasma concentrations of the active ingredients 11-keto-beta-boswellic acid (KBA) and 3-acetyl-11-keto-beta-boswellic acid (AKBA). In continuation of the tests investigating the factors limiting bioavailability of boswellic acids, the present study examined the permeability of KBA and AKBA in human Caco-2 cell lines. In addition, the interaction of KBA and AKBA with the organic anion transporter OATP1B3 and the multi drug resistant proteins P-glycoprotein and MRP2 was evaluated using partly fluorescent-based assays. The permeability studies revealed poor permeability of AKBA and moderate absorption of KBA with a P(app) value of 1.69x10(-6)cm/s. Most of KBA and AKBA were found to be retained by the Caco-2 monolayer. Neither KBA nor AKBA could be identified as substrates of P-glycoprotein. However, both KBA and AKBA modulated the activity of OATP1B3 and MRP2, indicating that therapeutic relevant interactions with other anionic drugs may be expected. The results of the present study provide the first explanation for the pharmacokinetic properties of KBA and AKBA.

Other Properties.

Borrelli F., Capasso1 F., Capasso1 R., Ascione1 V., Aviello1 G., Longo R. & Izzo1 A.A. (2006) *British Journal of Pharmacology* **148**, 553–56. Abstract.

1. Clinical studies suggest that the Ayurvedic plant *Boswellia serrata* may be effective in reducing diarrhoea in patients with inflammatory bowel disease. In the present study, we evaluated the effect of a *Boswellia serrata* gum resin extract (BSE) on intestinal motility and diarrhoea in rodents.
2. BSE depressed electrically-, acetylcholine-, and barium chloride-induced contractions in the isolated guinea-pig ileum, being more potent in inhibiting the contractions induced by acetylcholine and barium chloride.
3. The inhibitory effect of BSE on acetylcholine-induced contractions was reduced by the L-type Ca2+ channel blockers verapamil and nifedipine, but not by the sarcoplasmic reticulum Ca2+-ATPase inhibitor cyclopiazonic acid, by the phosphodiesterase type IV inhibitor rolipram or by the lipoxygenase inhibitor zileuton.
4. 3-acetyl-11-keto--boswellic acid, one of the main active ingredients of B. serrata, inhibited acetylcholine-induced contractions.
5. BSE inhibited upper gastrointestinal transit in croton oil-treated mice as well as castor oil-induced diarrhoea. However, BSE did not affect intestinal motility in control mice, both in the small and in the large intestine.
6. It is concluded that BSE directly inhibits intestinal motility with a mechanism involving L-type Ca2+ channels. BSE prevents diarrhoea and normalizes intestinal motility in pathophysiological states without slowing the rate of transit in control animals. These results could explain, at least in part, the clinical efficacy of this Ayurvedic remedy in reducing diarrhoea in patients with inflammatory bowel disease.

Chowdary K.P.R., Mohapatra P. & Murali Krishna M.N (2006) "Evaluation of olibanum and its resin as rate controlling matrix for controlled release of diclofenac." *Indian J Pharm Sciences* **68**(4), 497-500. Abstract. Olibanum and its resin and carbohydrate fractions were evaluated as rate controlling matrix materials in tablets for controlled release of diclofenac. Diclofenac matrix tablets were formulated employing olibanum and its resin and carbohydrate fractions in different concentrations and the tablets were evaluated for various tablet characters including drug release kinetics and mechanism. Olibanum and its resin component exhibited excellent retarding effect on drug release from the matrix tablets even at very low concentrations, 1 and 2% w/w in the formula. Diclofenac matrix tablets formulated employing olibanum and its resin component provided slow and controlled release of diclofenac over more than 24 h. Drug release from the matrix tablets was by Fickian diffusion and followed first order kinetics. Diclofenac release from some of the formulated tablets was comparable to that of Voveran SR tablets.

Fan A.Y., Lao L, Zhang R.X., Zhou A.N., Wang L.B., Moudgil K.D., Lee D.Y., Ma Z.Z., Zhang W.Y. & Berman B.M. (2005) "Effects of an acetone extract of *Boswellia carterii* Birdw. (Burseraceae) gum resin on adjuvant-induced arthritis in lewis rats." *J Ethnopharmacol*. **101**(1-3), 104-9. Abstract. Ruxiang (Gummi olibanum), the dried gum resin of *Boswellia carterii* (BC), has been used in traditional Chinese medicine to alleviate pain and inflammation for thousands of years. In this random, blinded study, the anti-arthritic effects of a BC extract were observed and compared to vehicle control in a Lewis rat adjuvant arthritis model (n=8/group). Arthritis was induced by injecting CFA subcutaneously into the base of the tail, and the extract was administered orally (i.g.) for 10 consecutive days beginning on day 16 after the injection. Arthritic scores, paw edema, and the local tissue pro-inflammatory cytokines tumor necrosis factor alpha (TNF-alpha) and interleukin-1 beta (IL-1beta) were assessed. Toxicity and adverse effects of the extract were evaluated. At 0.90 g/kg per day, BC significantly decreased arthritic scores between days 20 and 25 ($p<0.05$) and reduced paw edema on days 18, 20 and 22 compared to control ($p<0.05$). It also significantly suppressed local tissue TNF-alpha and IL-1beta ($p<0.05$). No major adverse effects were observed in animals during the repeated-dose treatment profile although mild fur discoloration was noted. The data show that BC extract has significant anti-arthritic and anti-inflammation effects and suggest that these effects may be mediated via the suppression of pro-inflammatory cytokines.

Kim H.R., Kim M.S., Kwon D.Y., Chae S.W. & Chae H.J. (2008) "*Boswellia serrata*-induced apoptosis is related with ER stress and calcium release." *Genes Nutr*. **2**(4),371-4. Abstract. It has

been reported that the gum resin of *Boswellia serrata* (BS), which has been shown to have anti-inflammatory properties, might also have anticancer effects. This study examined the potential of BS as an anticancer agent. The BS extract induces apoptosis in HeLa human cervical carcinoma cells, as confirmed by two apoptosis analyses, Hoechst staining and Annexin V/PI assay. Among the apoptosis pathways, the ER stress-associated mechanism was examined to determine its role in BS-induced apoptosis. The expression of GRP78 and CHOP, which are representatives of the ER stress proteins, and the calcium-binding protein-calpain were determined. The results showed significantly higher levels of both GRP78 and CHOP, and stronger calpain activity in the BS-treated cells than in the control cells. This shows that there is a correlation between ER stress signaling and apoptosis, which suggests the possibility of the BS-ER stress initiator as an anticancer therapeutic agent in human cervical carcinoma.

Krüger P, Daneshfar R, Eckert GP, Klein J, Volmer DA, Bahr U, Müller WE, Karas M, Schubert-Zsilavecz M, Abdel-Tawab M.(2008) "Metabolism of boswellic acids *in vitro* and *in vivo*." *Drug Metab Dispos.* **36**(6), 1135-42. Abstract. *Boswellia serrata* resin dry extract is among the few herbal remedies designated with an orphan drug status for the treatment of peritumoral brain edema. In addition, boswellic acids (BAs), the main active ingredients of *B. serrata* extracts, have potent anti-inflammatory properties, and may represent promising agents for the treatment of inflammatory diseases. Pharmacokinetic studies, however, revealed poor bioavailability, especially of 11-keto-beta-boswellic acid (KBA) and 3-acetyl-11-keto-beta-boswellic acid (AKBA), the most potent BAs. To address the question of whether BAs are extensively metabolized, we determined the metabolic stability of KBA and AKBA in vitro, investigated the in vitro metabolism of BAs, and compared the metabolic profiles of KBA and AKBA with those obtained in rats in vivo. In rat liver microsomes and hepatocytes as well as in human liver microsomes, we found that KBA but not AKBA undergoes extensive phase I metabolism. Oxidation to hydroxylated metabolites is the principal metabolic route. In vitro, KBA yielded metabolic profiles similar to those obtained in vivo in rat plasma and liver, whereas no metabolites of AKBA could be identified in vivo. Furthermore, AKBA is not deacetylated to KBA. This study indicates that the efficacy of *B. serrata* extract may be enhanced by increasing the bioavailability of AKBA.

Moussaieff A., Rimmerman N., Bregman T., Straiker A., Felder C.C., Shoham S., Kashman Y., Huang S.M., Lee H., Shohami E., Mackie K., Caterina M.J., Walker J.M., Fride E. & Mechoulam R.(2008) "Incensole acetate, an incense component, elicits psychoactivity by activating TRPV3 channels in the brain." *FASEB J.* **22**(8), 3024-34. Abstract. Burning of *Boswellia* resin as incense has been part of religious and cultural ceremonies for millennia and is believed to contribute to the spiritual exaltation associated with such events. Transient receptor potential vanilloid (TRPV) 3 is an ion channel implicated in the perception of warmth in the skin. TRPV3 mRNA has also been found in neurons throughout the brain; however, the role of TRPV3 channels there remains unknown. Here we show that incensole acetate (IA), a *Boswellia* resin constituent, is a potent TRPV3 agonist that causes anxiolytic-like and antidepressive-like behavioral effects in wild-type (WT) mice with concomitant changes in c-Fos activation in the brain. These behavioral effects were not noted in TRPV3(-/-) mice, suggesting that they are mediated via TRPV3 channels. IA activated TRPV3 channels stably expressed in HEK293 cells and in keratinocytes from TRPV3(+/+) mice. It had no effect on keratinocytes from TRPV3(-/-) mice and showed modest or no effect on TRPV1, TRPV2, and TRPV4, as well as on 24 other receptors, ion channels, and transport proteins. Our results imply that TRPV3 channels in the brain may play a role in emotional regulation. Furthermore, the biochemical and pharmacological effects of IA may provide a biological basis for deeply rooted cultural and religious traditions.

Ota M. &. Houghton P.J. (2005). “Boswellic acid with acetylcholinesterase inhibitory properties from frankincense.” *53rd Annual Congress of Society of Medicinal Plants, Societa Italiana di Fitochimica Florence , Italy 21st-25th (Book of abstracts, p. 339.*

Singh S., Khajuria A., Taneja S.C., Khajuria R.K., Singh J., Johri R.K. & Qazi G.N. (2008) “The gastric ulcer protective effect of boswellic acids, a leukotriene inhibitor from *Boswellia serrata*, in rats.” *Phytomedicine*. **15**(6-7), 408-15. Abstract. Aim of the study is to evaluate the anti-ulcer efficacy of the boswellic acids (BA), a triterpenoid known as anti-inflammatory/anti-arthritic agent,

which is in clinical use. The reason for the study is that, the known non-steroidal anti-inflammatory drugs (NSAIDs) are full of side effects especially ulceration which is at the top. BA, although, used as an anti-arthritic agent yet it is not only devoid of ulcer production but protective also. The activity evaluation was done by the following universally accepted animal models viz., pyloric ligation, ethanol-HCl, acetylsalicylic acid, indomethacin and cold restrained stress-induced ulceration in rats. Results of the present study revealed that BA possess a dose dependent antiulcer effect against different experimental models. It showed different degree of inhibition of the ulcer score towards different ulcerogenic agents. The ulcer score against various ulcer inducing agents viz., pyloric ligation, ethanol/HCl, (acute and chronic) acetylsalicylic acid, indomethacin and cold restraint stress, was inhibited by 39%, 38%, 51%, 31%, 37% and 42% respectively at 250mg/kg. From the data it is concluded that BA inhibited ulcer production non-specifically in all the experimental models, whereby, it is not possible to propose a single specific mechanism. Nevertheless it is possible that BA might be acting by increasing the gastric mucosal resistance and local synthesis of cytoprotective prostaglandins and inhibiting the leukotriene synthesis.

Sharma R, Singh S, Singh GD, Khajuria A, Sidiq T, Singh SK, Chashoo G, Pagoch SS, Kaul A, Saxena AK, Johri RK, Taneja SC (2009) "In vivo genotoxicity evaluation of a plant based antiarthritic and anticancer therapeutic agent Boswelic acids in rodents." In press *Phytomedicine*. (2009 Aug 12). Abstract. The genotoxic potential of anti-inflammatory/anti-arthritic and anticancer plant based drug molecule Boswelic acids (BA) was studied by in vivo system. Systematic literature survey revealed that studies on the genotoxicity of BA are not available. Although reports on genotoxicity of Boswellia serrata dry extract and modified 3-O-acetyl-11-keto-beta-boswelic acid are available and these studies were conducted in in vitro systems. The earlier general toxicity study of BA has been conducted by us, revealed it to be non toxic. The genotoxicity was carried out in Wistar rats using different cytogenetic assay system-abnormalities viz. chromosomal aberrations; sperm morphology, micronuclei and comet assays. Six groups of animals, each comprised of five rats, were taken for each study. Group1-4 received BA at 125, 250, 500 and 1000mg/kg p.o., respectively prepared as 2% gum acacia suspension, fifth group received a positive control cyclophosphamide (CP) 40mg/kg p.o. or metronedazole (MTZ) 130mg/kg p.o. or mercuric chloride (HgCl(2)) 0.864mg/kg p.o. (as per the experiment requirement) whereas the sixth group kept as vehicle control. The results on the bases of the data obtained revealed that BA is quite safe as it did not show any genotoxicity at any dose level up to 1000mg/kg. The positive controls used in different experiments showed highly significant abnormal cytogenetic changes in comparison to the control group.

Shen T. & Lou H.X.. (2008) "Bioactive constituents of myrrh and frankincense, two simultaneously prescribed gum resins in Chinese traditional medicine." *Chem Biodivers*. **5**(4),540-53.

Weber C.C., Reising K., Müller W.E., Schubert-Zsilavecz M. & Abdel-Tawab M. (2006) "Modulation of Pgp function by boswellic acids." *Planta Med.* **72**(6), 507-13. Abstract. Boswellic acids, the main active ingredients of *Boswellia serrata*, are gaining more and more importance in the treatment of peritumoural oedema and chronic inflammatory diseases. They may be even considered as alternative drugs to corticosteroids in reducing cerebral peritumoural oedema. An important focus for drugs acting in the central nervous system is achieving a high extent of brain penetration. Today there is increasing evidence for the importance of transporters, especially P-glycoprotein (Pgp), for drug disposition and resulting clinical response. Pharmacokinetic studies revealed that the concentrations of the potent keto derivatives, the 11-keto-beta-boswellic acid (KBA) and the acetyl-11-keto-beta-boswellic acid (AKBA), in proportion to boswellic acids lacking a keto group, like the beta-boswellic acid, are much lower in plasma than in the orally administered extract. Moreover the brain/plasma ratio for KBA and AKBA determined in preliminary experiments on rats was only about 0.51 and 0.81, respectively, in spite of their lipophilicity. Until now little is known about the cerebral pharmacokinetics of boswellic acids and how it may be influenced. Since many drugs are known to interact with Pgp at the level of the intestine and the blood-brain barrier the modulatory potencies of the *Boswellia serrata* extract of

H15(R) and the major boswellic acids on the transport activity of Pgp have been determined in two in vitro assays. A human lymphocytic leukaemia cell line (VLB cells) expressing Pgp was chosen as model for human Pgp, and porcine brain capillary endothelial cells (PBCEC cells) were taken as model for the blood-brain barrier using calcein acetoxymethyl ester (calcein-AM) as Pgp substrate. It was found that the *Boswellia* extract, as well as the keto-boswellic acids inhibit the transport activity of Pgp in the micromolecular range in both cell types. No modulation was observed using those boswellic acids which have no keto group in their structure. The inhibition of Pgp at the blood-brain barrier by Boswellia extract is probably not relevant for the brain availability of other Pgp substrates, because of the low plasma levels determined for KBA and AKBA. However the presented data could not exclude the possibility of drug interactions caused by modulation of Pgp by extracts of *Boswellia serrata* on the gastrointestinal level.

Kamath J.V. & Asad M.(2006) "Effect of hexane extract of *Boswellia serrata* oleo-gum resin on chemically induced liver damage." *Pak J Pharm Sci.* **19**(2), 129-33. Abstract The hexane extract of oleo-gum-resin of *Boswellia serrata* (BSHE) was evaluated for its effect on liver injury induced by carbon tetrachloride, paracetamol or thioacetamide. The BSHE was given in two different doses (87.5 mg/kg p.o. and 175 mg/kg p.o.). Silymarin, a known hepatoprotective agent was used as standard. The lower dose of BSHE (87.5 mg/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. The hepatoprotective effect of lower dose of BSHE was supported by changes in histopathology. It was concluded that hexane extract of oleo-gum-resin of *Boswellia serrata* plant in lower doses possess hepatoprotective activity.

Safety.

Etuk E.U., Agaie B.M., Onyeyili P.A. & Ottah C.U.. “Toxicological studies of aqueous stem bark extract of *Boswellia dalzielii* in albino rats.”. *Indian J Pharmacol* [serial online] 2006 [cited 2008 Dec 26];**38**:359-60.

Gerhardt H., Bouhmidi-Boumariz Z., Buvari P.G. & Seifert F.C**.** (2008) “Efficacy & safety of *Boswellia serrata* extract H15.” *Phytomedicine* **15**(6-7), 543. Abstract. Our study therapy of active Crohn's disease with *Boswellia serrata* extract H15 [Z. Gastrenterol. 2001; 39: 11-17] aimed at comparing the efficacy and safety of H15 with mesalazine. As primary outcome, changes of the CDAI values between the status of enrolment and end of therapy were chosen. H15 was tested on non-inferiority compared to standard treatment with mesalazine. The study confirmed that therapy with H15 is not inferior to mesalazine. Significant quality-of-life improvement in all eight parameters of the SF-36 test were found in H15-treated Crohn patients by Seifert, F.C. [Dissertations of Faculty for Medicine-Mannheim of the Heidelberg University], whereas the control group ameliorated in only three of them. Regarding safety, blood tests for clinical parameters in 2057 patients treated with H15 over a period of 6 years, comparing values before therapy onset with those at the end of treatment, are not significantly different from normal values. There were not any indications for organotoxic effects (Buvari, P.G. [Dissertations of Faculty for Medicine Mannheim of the Heidelberg University]). Fifty patients treated with H15 over 4 years displayed increased bone density, as measured by Q-CT and significantly diminished motility pain after having stopped corticoid treatment (Bouhmidi-Boumaris, Z. [Dissertations of Faculty for Medicine-Mannheim of the Heidelberg University]). These results provide strong evidence for the efficacy of the *Boswellia serrata* extract H15 in comparison to mesalazine, which is the proven state-of-the-art treatment for active Crohn's disease.

Opdyke D.L.J. (1978a) “Monographs on fragrance raw materials. Olibanum.” *Food and Cosmetics Toxicology* **16**, 837.

Opdyke D.L.J. (1978b) “Monographs on fragrance raw materials. Olibanum absolute.” *Food and Cosmetics Toxicology* **16**, 835.