

# Effects of Frankincense Compounds

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*Boswellia* trees, found throughout the Middle East and parts of Africa and Asia, are the source of frankincense oil. Since antiquity, frankincense has been traded as a precious commodity, but it has also been used for the treatment of chronic disease, inflammation, oral health, and microbial infection.

Keywords: inflammation ; oral health ; frankincense ; infection ; microbiology

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## 1. Introduction

The increasing rate of antibiotics drug resistance, the cost of drugs, and the lack of access to healthcare systems for many people <sup>[1][2]</sup>, especially in less developed countries, support the need for studying traditional medicines for sustainable, cost-effective therapeutic purposes. Frankincense is one of the common sources for traditional medicine <sup>[3]</sup>. The word “frankincense” is derived from an old French term “franc encens” and means “pure incense” or “pure and noble high-quality incense”. <sup>[4]</sup> Traditionally, frankincense gum has been burned for the pleasant fragrance it produces. It can be produced as a hardened resin or gum-like material discharged by the *Boswellia sacra* Flück. tree through cuts made in the trunk. **Figure 1** shows the *B. sacra* tree, a member of the *Boswellia* genus. Frankincense has been traded and used as one of the most valuable materials since the beginning of written history <sup>[5]</sup>.



**Figure 1.** *Boswellia sacra* in Wadi Dawkah, a natural park of frankincense-producing trees in Oman. *Boswellia sacra* photo from Wikimedia.org.

The *Boswellia* genus includes around thirty species and is usually found in the arid regions of tropical Africa, the Arabian Peninsula, and South Asia <sup>[6]</sup>, where moisture is supplied by morning mist. For example, *Boswellia serrata* Roxb. is found in India, *Boswellia sacra* in the Arabian Peninsula, *Boswellia papyrifera* (Caill. ex Delile) Hochst. and *Boswellia rivae* Engl. in Ethiopia, *Boswellia neglecta* S.Moore in Eritrea, and *Boswellia carterii* and *Boswellia frereana* Birdw. in North Africa and Somalia <sup>[7]</sup>. However, frankincense is obtained mostly from *B. frereana*, *B. sacra*, *B. papyrifera*, and *B. serrata*, which grow in Somalia, Yemen, Oman, India, and Pakistan <sup>[8]</sup>. Although many *Boswellia* species are known to produce frankincense, *B. serrata* (India), *B. sacra* (Oman), and *B. carterii* (Somalia) are the major sources of commercial frankincense <sup>[9]</sup>.

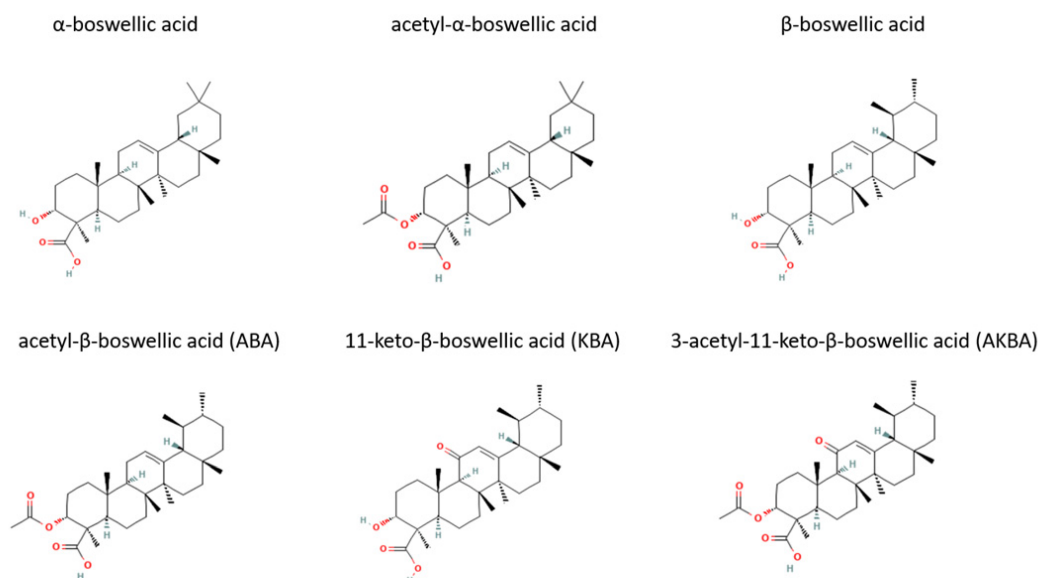
The oleoresin from the *Boswellia* trees has been considered as a treasure for more than a millennium due to its aromatic and medicinal applications [4]. Frankincense resin is secreted as a milky-white, sticky liquid when the plant is injured, and it is also known as olibanum [10]. Olibanum is produced mainly by four different species of *Boswellia*, which are *B. serrata*, *B. carterii*, *B. frereana*, and *B. sacra* [10][11]. The oleo gum resin produced by members of the genus *Boswellia* helps the plant defend against various infections and pests [12] and has been used in religious ceremonies, perfume production, and as a phytomedicine since antiquity [13]. Recently, the essential oils derived from frankincense are gaining high economic importance internationally for aromatherapy and perfumery [14].

## 2. Description of Frankincense Resins, Oils, and Boswellic Acids

The resin is available in yellowish, bluish, and greenish shades, and is composed of 3–8% volatile oils containing various terpenes and sesquiterpenes, 60–70% resin, and 27–35% gum [15]. In the mid-twentieth century, it was found that the gum contains two types of polysaccharides [16]. More recently, the composition showed that the monosaccharides present were predominantly galactose, arabinose, and glucuronic acid, along with small amounts of rhamnose and glucose [17]. However, recent scientific advancements allow researchers to identify the molecular content of diverse frankincense products such as incense mixtures, components of conventional medicines, and archaeological specimens.

The concentrated volatile, aromatic liquid obtained from different parts of the plant such as roots, seeds, leaves, flowers, and resins is called an essential oil. Mostly, a distillation process is used to extract the essential oil from *Boswellia* plants [18]. The main chemical constituents of frankincense oil are pentacyclic triterpenoids [19], tetracyclic triterpenoids [20], and a variety of other oils [21]. The most common characteristic and intensely studied component in frankincense are the pentacyclic triterpenoids [7][22].

The major active components of frankincense are the boswellic acids (BA), which are extracted from the woody parts of different *Boswellia* trees. The representative phytochemicals are  $\beta$ -boswellic acid, acetyl- $\beta$ -boswellic acid (ABA), 11-keto- $\beta$ -boswellic acid (KBA), 3-acetyl-11-keto- $\beta$ -boswellic acid (AKBA),  $\alpha$ -boswellic acid, and acetyl- $\alpha$ -boswellic acid. **Figure 2** shows the chemical structure of the main BA.



**Figure 2.** Chemical structure of common boswellic acids found in frankincense. Two-dimensional chemical structures were obtained from Pub Chem. Pub Chem CIDs are as follows:  $\alpha$ -boswellic acid, 637234; acetyl- $\alpha$ -boswellic acid, 15181201;  $\beta$ -boswellic acid, 168928; acetyl- $\beta$ -boswellic acid (ABA), 11386458; 11-keto- $\beta$ -boswellic acid (KBA), 9847548; 3-acetyl-11-keto- $\beta$ -boswellic acid (AKBA), 11168203.

The chemical composition and yield vary according to different factors such as the geographical region of the tree, the wood surface area, the collection season, the collection method, the age of the tree, and the storage conditions [23]. For instance, the gum resin from *B. serrata* has relatively similar quantities of 11-keto- $\beta$ -boswellic acid (3–4.7%) and acetyl-11-keto- $\beta$ -boswellic acid (2.2–2.9%) [7]. However, the resin from *B. carterii* contains 0.5% 11-keto- $\beta$ -boswellic acid and 3.3% acetyl-11-keto- $\beta$ -boswellic acid [7].

The gum resin of *B. carterii* reported from Somalia has  $\alpha$ -thujene (19.2%), sabinene (9.4%), limonene (7.8%), and  $\alpha$ -pinene (7.2%) as the main constituents [24]. This is a native plant of the Red Sea region of North-East Africa, where it is abundant in Somalia and Ethiopia. Other studies on the composition of the oleo resin reported different components in

different concentrations. For instance, Wahab reported that the oil contains 62.1% esters, 15.4% alcohols, 9.9% monoterpene hydrocarbons, and 7.1% diterpenes [25], and Wang et al. reported octyl acetate (60.0%), octanol (12.7%), and *p*-cymene (8.7%) [26]. The gas chromatography–mass spectrometry (GC/MS) analysis of the hydro-distillate of *B. carterii* resin showed the presence of 40 different constituents. The major constituents were verticilol (14.48%), isobutylcyclopentane (12.25%), *n*-octyl acetate (9.20%), and 9-oxabicyclo-[6.1.0]-non-3-yne (9.12%) [27]. However, the composition of the resin differs due to different factors such as climate, geography, season of the year, and the extraction conditions. This notion is corroborated by a report from Chen et al. (2013) which observed low concentrations of the above components [28], while other studies reported higher concentrations of *n*-octyl acetate [28][29].

*Boswellia dalzielii*, which grows in West Africa, is an understudied species. However, a study conducted using essential oil from 21 oleoresin samples from northern Nigeria and two samples from Ghana revealed that  $\alpha$ -pinene was the dominant component (21.7–76.6%), followed by  $\alpha$ -thujene (2.0–17.6%), myrcene (up to 35.2%), *p*-cymene (0.3–15.6%), and limonene (1.1–32.9%) [30]. It was reported that out of the 29 compounds obtained from the essential oil from leaves,  $\alpha$ -pinene was the dominant component (45.7%) [31]. On the other hand, it was also reported that out of 50 compounds isolated,  $\delta$ -3-carene (27.7%) was the dominant one [32].

### 3. Modern Medicinal Uses of Frankincense

Many plant components from *Boswellia* are used to treat chronic diseases with comparatively few side effects [33][34]. Indian traditional medicine practice narrates that *Boswellia* decoctions were used to treat various gastrointestinal tract conditions such as diarrhea, flatulence, alimentary stoppage, and vomiting [35][36][37][38]. It was believed that the decoctions contain active ingredients from *Boswellia*, which are useful in treating the above-mentioned diseases. Furthermore, the extract was used to treat bronchitis, asthma, hoarseness, dyspnea, cough, and cold [39][40].

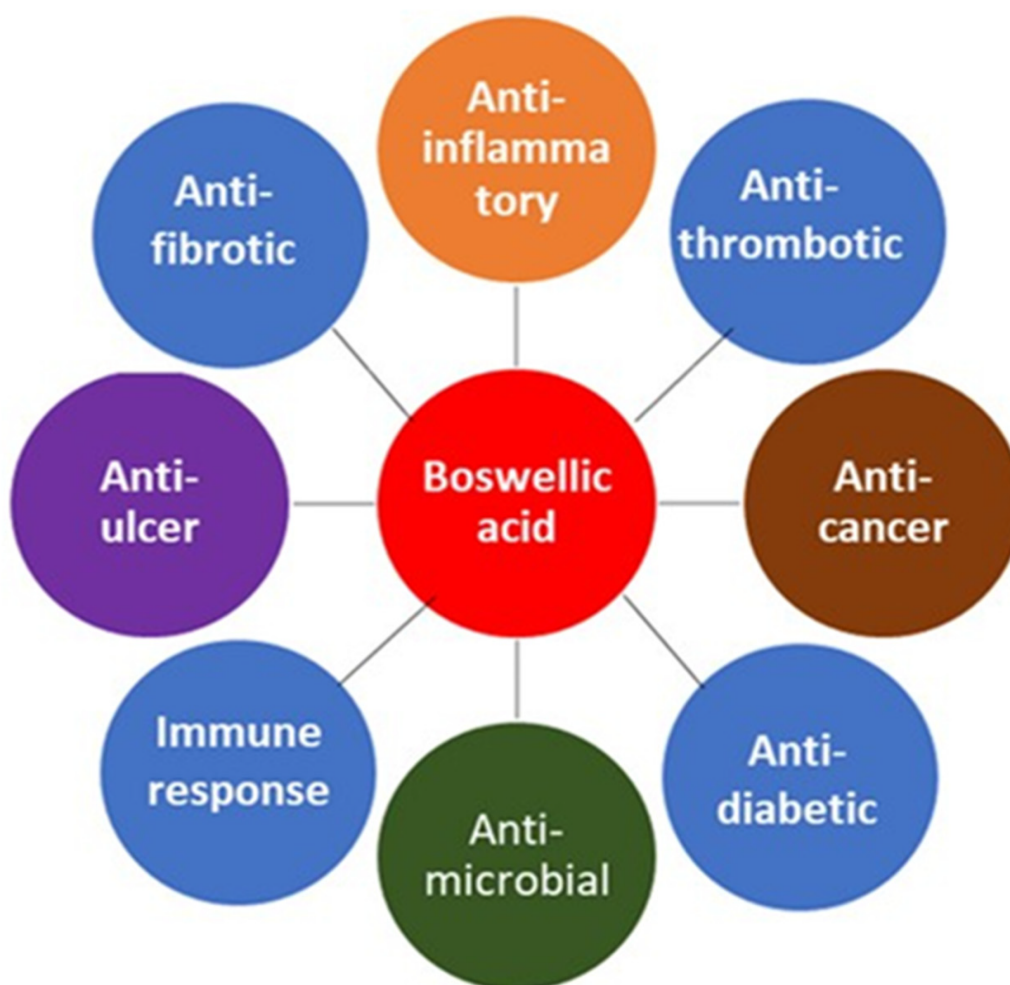
The gum extracts or resins from *Boswellia* sp. and their triterpenes, especially BA, have attracted the attention of pharmacologists, medicinal chemists, and biochemists as therapeutic agents due to their efficacy in treating rheumatoid arthritis and chronic inflammation without side effects and toxicity. The gum exudate obtained from the bark of the tree *B. serrata*, also called Indian olibanum, has been extensively used in the treatment of arthritis, asthma, ulcers, and skin diseases by practitioners of Indian traditional medicine [15][25]. It has also been widely used in various formulations for the treatment of inflammation related disorders in the past decade [15][41]. One study analyzed the effects of gum resins of *B. serrata* (900 mg daily divided in three doses for 6 weeks) on human patients suffering from chronic colitis [33][42]. The authors found that out of 20 patients treated with *Boswellia* gum resin, 18 patients showed an improvement in one or more parameters, including stool properties, histopathology and scanning electron microscopy characterization, hemoglobin, serum ion, calcium, phosphorus, proteins, total leukocytes, and eosinophils [33][42]. The control group (10 patients) was given sulfasalazine at a dose of 1 g three times a day for 6 weeks. The authors reported that 6 out of 10 patients in the control group showed similar improvements with the same parameters tested in the *B. serrata* group. Researchers demonstrate that a gum resin preparation from *B. serrata* might be effective in the treatment of chronic colitis, with minimal side effects [33][42]. The same research group evaluated the effects of *B. serrata* gum resin on the treatment of patients with bronchial asthma [40]. Their data demonstrated that 70% of patients treated with 300 mg thrice daily for 6 weeks showed improvement of disease, evident by the disappearance of physical symptoms and signs such as dyspnea, rhonchi, number of attacks, as well as a decrease in eosinophilic counts. The control group (treated with placebo) only showed 27% of improvements in symptoms [40]. These data imply that gum resin from *B. serrata* could serve as a pharmacological agent in the treatment of bronchial asthma.

Gum resin from *B. serrata* was reported to be a potential remedy for inflammation, and it has been used as a folk medicine for topical and systemic inflammatory diseases for centuries [15]. The oleo gum resin of *B. carterii* has been used in folk medicine to treat cough and asthma and as an embalming fluid for human corpses. In addition, it has been used as an incense, respiratory antiseptic, and diuretic stimulant [25].

The oleo gum resin of *B. serrata* and *B. carterii* were also used in traditional medicine in different countries to treat rheumatic and other inflammatory diseases, including Crohn's disease and ulcerative colitis [42][43][44]. However, *B. serrata* was reported to be the least effective in recurrent infections [45]. In addition, frankincense extracts and oils were used as antiseptic agents in mouthwash and also used to treat cough and asthma [43]. Furthermore, recent studies on animals and humans have demonstrated the efficacy of resin gum of *B. serrata* to treat inflammatory bowel disease, asthma, osteoarthritis, and rheumatoid arthritis [42][46][47].

Though frankincense has been known for its medicinal properties since antiquity, it is still widely used in modern medical treatment. In 2010, Moussaieff and Mechoulam reviewed *Boswellia* resin constituents in vitro, in vivo, and in clinical trials

studies [48]. Indeed, in Ayurvedic medicine, different parts of the *Boswellia* tree and derived extracts are used for the treatment of respiratory, gastrointestinal, immune system, and skin conditions. Most of the published work focuses on the pharmacological activities of boswellic acids, specifically on their anti-inflammatory, analgesic, and anti-arthritic properties. As an example, there is growing evidence to support the clinical efficacy of *Boswellia* in osteoarthritis patients. However, there is inadequate evidence to demonstrate the clinical efficacy in rheumatoid arthritis patients [49]. The application of frankincense to treat different diseases of recent times is discussed below and summarized in **Figure 3**. Frankincense has been used to treat both infections and chronic diseases.



**Figure 3.** Modern medicinal uses of *Boswellia*.

#### **4. Antimicrobial Activity of Frankincense**

In general, the bioactive natural compounds produced by different plants are considered better alternatives to synthetic antimicrobial and antioxidant agents. Different compounds obtained from *Boswellia* resins, particularly BA and their derivatives, exhibited diverse biological activities. The antimicrobial effects can vary depending on the study and the amount of bioactive compounds present in the frankincense extracts.

The oleo gum resin essential oils from *B. carterii* (Somalia), *B. papyrifera* (Ethiopia), *B. serrata* (India), and *B. rivae* (Ethiopia) were individually tested against different fungi and Gram-positive and Gram-negative bacteria. The essential oils exhibited significant antifungal activity against both *C. albicans* and *C. tropicalis*, with the essential oils from *B. carterii* and *B. papyrifera* showing the best activity [50]. The MIC values for *C. albicans* and *C. tropicalis* were 12.86 and 12.86 µg/mL (*B. serrata*), 6.16 and 6.16 µg/mL (*B. carterii*), 6.09 and 6.09 µg/mL (*B. papyrifera*), and 2.65 and 27.38 µg/mL (*B. rivae*), respectively, compared with the MIC of 0.15 µg/mL for amphoterecin B. The essential oil of *B. rivae* resin exhibited the best activity against *C. albicans* [50]. Limonene present in the essential oils is thought to be responsible for the antifungal activity [51], since oleo gum resin essential oils without limonene lack antifungal activity. The oleo gum resins also showed significant antibacterial effects against Gram-positive *S. aureus* and *S. epidermidis*, with MIC values ranging from 3.52 to 107.20 µg/mL. These values can be compared with the MIC of 1 µg/mL for vancomycin and 2 µg/mL for amikacin used as controls in the experiments [50]. The frankincense compounds against Gram-negative *E. coli* and *P. aeruginosa* showed MIC ranging from 6.60 to 107.18 µg/mL, compared to the vancomycin MIC of 10 and 5 µg/mL for *E.*



coli and *P. aeruginosa*, respectively. It is noteworthy that some of the frankincense compounds had antimicrobial effects at concentrations that were comparable or very close to concentrations of the standard antibiotics used in the in vitro experiments. Future studies might confirm and expand the results to in vivo and clinical models.

Dental caries and periodontitis remain two of the major oral diseases that affect more than half of the global population [52]. Periodontitis is often referred as a common inflammatory disease in humans. The etiology of these diseases has been linked to certain bacterial species, plaque and biofilm formation, and the resultant inflammatory states. Current therapies for treating periodontal disease place an emphasis on biofilm removal. This is exercised via a combination of mechanical (such as scaling and root planing) and antibiotic treatments. However, these treatment modalities are still unable to fully remove biofilms. This has led to an interest in incorporating herbal extracts into current treatment regimens.

Many studies have been performed using the resin of *B. serrata*. As noted above, this resin contains boswellic acid, which are the active components in its anti-inflammatory effects. In addition, both the boswellic acid and the essential oils of *B. serrata* exhibit antimicrobial properties. Of the four major boswellic acids, acetyl-11-keto- $\beta$ -boswellic acid (AKBA), has consistently demonstrated the greatest antibacterial effects. In fact, several studies have determined that AKBA is the most active component in the resin of *B. serrata* and other *Boswellia* species [53].

In terms of antibacterial effectiveness, AKBA isolated from *B. serrata* demonstrated activity against *Streptococcus mutans*, *Enterococcus faecalis*, *Enterococcus faecium*, *Actinomyces viscosus*, *Streptococcus sanguinis*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Porphyromonas gingivalis*. Furthermore, the post-antibiotic effects of AKBA were determined to be greater than those of ciprofloxacin, and AKBA was also shown to inhibit biofilms of the cariogenic bacteria *S. mutans* [53].

In a double-blinded, randomized clinical trial, the effectiveness of traditional scaling and root planing methods were compared to the use of *B. serrata* extract or powder [54]. The results indicated that the addition of *B. serrata* extract or powder to traditional scaling and root planing treatments leads to better gingival health as measured by gingival, plaque, and bleeding indices, as well as probed pocket depths [54]. The authors concluded that the anti-inflammatory properties of *B. serrata* extract had results comparable or even superior to traditional scaling and root planing treatments. Given its antibacterial, antifungal, and antioxidant properties, it is not surprising that frankincense also has promising beneficial effects on oral health.

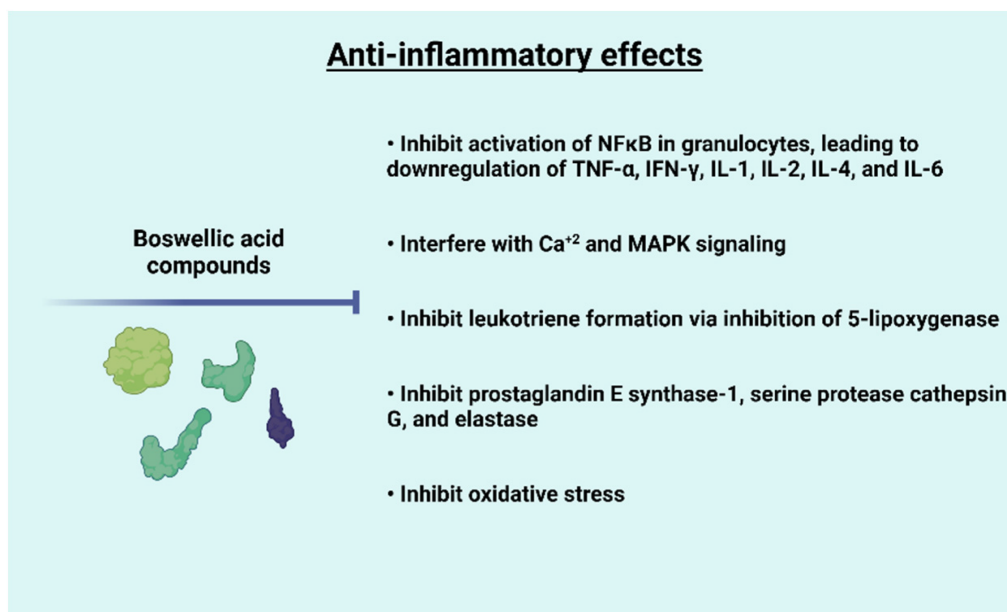
## 5. Anti-Inflammatory Effects of Frankincense

Many patients consuming non-steroidal anti-inflammatory drugs (NSAID) suffer from adverse effects of the drugs on the gastrointestinal or cardiovascular systems. Many efforts have been made to develop drugs that avoid these complications, but the goal is still far from being achieved. Hence, it is necessary to search for novel, alternative drugs. In this context, *B. serrata* and other *Boswellia* species have gained prominence as potential alternatives as anti-inflammatory herbal remedies. The anti-inflammatory properties of boswellic acids have been well-established by several studies with cells in vitro, and preclinical, and clinical trials [4][7].

Studies on animals and humans have shown the anti-inflammatory potential of *B. serrata* gum resin to treat different inflammatory disorders such as inflammatory bowel disease, rheumatoid arthritis, osteoarthritis, and asthma [46]. Corticosteroids are essential to control cerebral edema but they also cause severe negative impacts. In contrast, the gum resin of *B. serrata* was found to control the peritumoral brain edema associated with glioma [55].

The anti-inflammatory activity of *B. serrata* is due to the presence of  $\alpha$ - and  $\beta$ -boswellic acid and other pentacyclic triterpenic acids. These compounds inhibit pro-inflammatory processes by acting on 5-lipoxygenase and cyclooxygenase and on the complement system [39][56][57]. Inhibition of prostaglandin synthesis plays only a minimal role in the anti-inflammatory effect of BAs. However, inhibition of 5-lipoxygenase by BA decreases production of leukotrienes, whereas chronic inflammatory diseases are associated with increased leukotriene activity [56].

BA is involved in the inhibition of inflammation induced by factors such as histamine, prostaglandins, leukotriene, 5-lipoxygenase, human leukocyte elastase, cytokines, tumor necrosis factor, and free oxygen radicals. **Figure 4** summarizes the inhibitory effects induced by BAs. To demonstrate the anti-inflammatory activity of the gum resin of *Boswellia* species, experiments were conducted in animal models. Carrageenan-induced mouse paw edema and rat pleurisy models were employed to test the effectiveness of defined BAs in vivo. Researchers also demonstrated the suppression of PGE<sub>2</sub> formation by BAs via interference with mPGES1, which may represent a biochemical basis for the anti-inflammatory effectiveness of BAs [58].



**Figure 4.** Schematic diagram showing anti-inflammatory effects of boswellic acids and *Boswellia* extracts.

Some limitations must be considered. First, more studies are required to elucidate the antimicrobial and anti-inflammatory mechanisms exerted by frankincense extracts and compounds. Secondly, more studies, including pre-clinical and randomized clinical trials, are needed to better understand the beneficial effects of frankincense extracts and compounds on human health.

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