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# Frankincense (Heaven's Gift) – Chemistry, Biology, and Clinical Applications

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Additional information is available at the end of the chapter

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## 1. Introduction

Frankincense, gold, and myrrh were the three gifts from the wise men (the Magi, or the three kings) brought from the East to celebrate the birth of baby Jesus Christ (Bible, Matthew 2:11) According to the Christian belief (Botros et.al. 2003). Nine compounds with immunostimulant and antiviral activity were isolated from the oleogum resin of frankincense (*Boswellia carterii* Birdwood). The frankincense essential oil (3%) found to contain monoterpenes (13.1 %), sesquiterpenes (1 %), and diterpenes (42.5 %). Both isolated oil and resins exhibited strong immunostimulant activity. Badria et al. (2003) proved that the of boswellia, curcumin, and glycyrrhizin exhibited the highest activity against *Herpes simplex* virus. However, boswellia extract retained a significant increase in both FEV1 and PEFr ( $P \leq 0.05$  and  $\leq 0.01$  respectively) with no significant change in FVC in the severe persistent bronchial asthma (Badria et. al. 2003). Boswellia-Curcumin preparation was investigated clinically for treatment of knee osteoarthritis (Badria et. al. 2002). Meanwhile, glycyrrhizin, curcumin and *Boswellia carterii* formula exhibited a hepatoprotective effect and used as endogenous interferon inducer, demonstrating that two phases of the induction of IFN in serum takes place; the induced IFN was regarded as IFN- $\gamma$ . This induction may be followed by activation of macrophages and augmentation of natural killer (NK) activity through the action of the induced IFN (Badria 2001). This combination was successfully tried in a clinical study as endogenous interferon inducer for treatment of hepatitis C (Badria 2001).

### 1.1. Historical Background and Folkloric use (Ryman, 1997)

The earliest recorded use of frankincense is found in an inscription on the tomb of a 15<sup>th</sup> century BC Egyptian queen named Hathsepsut who exported it from Punt's Land "Somalia" to prepare her cosmetics, skin care lotions, and perfumes. Ancient Egyptians burned frankincense as

incense in religious ceremonies and rituals. They used it also in embalming and mummification of dead bodies. As an evidence for incense burning, burners with a shape of long handle spoon from the old kingdom in ancient Egypt have been found in which the resin was burnt to provide aromatic warmth on the braziers of their homes in chilly weather. The ancient Egyptians used to grind the resin after charring to provide the black powder that called "Kohl" which used in manufacturing of distinctive eyeliner as seen in a lot of Egyptian art figures. This is the cause of employment of frankincense in the worship of the Egyptian sun God "Horus", a primordial symbol for who was the sacred "All-seeing" eye that burned with judgment.

The use of resin as incense was not confined to ancient Egyptians but extended to Babylonians, Greeks, Romans and Assyrians. It was Herodotus who reported that "in ancient Babylon, 1000 talents weight was offered every year during the feast of Bel, on the great altar of his temple". Nero burnt frankincense by the ton. Romans burnt large quantities of the resin along the routes of the Roman triumphs or victory parades.

The frankincense was a kings' gift, it is said that the queen of Sheba presented a large amount of frankincense, brought by her from Yemen, to the wise King Solomon in 950 B.C. The original use of the word "incense" was to describe the aromatic smoke that produced from a substance upon burning, the term has been gradually limited now to frankincense. Interestingly, several myths surrounded the harvest of frankincense; it was believed that valleys where frankincense is collected were guarded by huge horrible winged creatures and red poisonous snakes that attack any one trying to touch the frankincense tree. These mysterious stories tells also that the mythological bird Phoenix, when ready to die, makes its final nest from frankincense and *Cassia* and there; its spirit ascends to the heavens with the perfume of this sacred herb (Miller and Morris, 1988).

The use of camels in transport flourished frankincense trade in the 11<sup>th</sup> century BC. One of the oldest international trade routes, the frankincense route, runs parallel to the Red Sea outsetting from Yemen through a distance of almost 3,400 Km towards Palestine. Such huge trade made Pliny the Elder, the first century Greek Writer, to claim that "the control of the frankincense trade had made the South Arabians the richest people on earth".

Frankincense is one of the crude drugs that are heavily associated with religious rituals and cults; it was thought that incense smokes carried the prayers to the heaven. In Judaism, frankincense was one of the four sweet scents used in compounding the ceremonial incense of Jewish temples. As a part of the meet offering as well as the chew-bread on Sabbath day, pure frankincense was utilized. It was preserved with many other spices in great chamber of the GOD house at Jerusalem.

In Christianity, Frankincense occupied a distinguished place; it was mentioned 22 times in the Bible. According to the Christian belief; gold, frankincense, and myrrh were the three gifts from the wise men (the Magi, or the three kings) brought from the East to celebrate the birth of baby Jesus Christ (Bible, Matthew 2:11). Frankincense enters into the composition of incense now used in the Christian churches.

Frankincense was one of the most prized and costly substance in the ancient world, worth more than its weight in gold. Dioscorides and others mentioned the therapeutic use of the resin



**Figure 1.** *Boswellia carterii* Birdwood Tree; Frankincense

in the treatment of skin disorders, in ophthalmology, hemorrhages and pneumonia. Pliny the Elder (1<sup>st</sup> century) mentions it as antidote to hemlock (Encyclopedia Britannica web site). The Iranian physician Avicenna "Ibn Sina" (10<sup>th</sup> century) in his book "El-Kanon Fi El-Tibb" thought that frankincense was useful in many disorders and disease as fever, gastric disorders and tumors. *B. carterii* is used almost for everything in China.. In Ayurvedic medicine (Kapoor, 1990) the resin is prescribed in chronic lung diseases, diarrhea, dysentery, pulmonary diseases, menorrhoea, dysmenorrhoea, syphilis, piles, and liver disorders. The oil extracted from the gum resin is prescribed with a demulcent drink in gonorrhoea. A paste made of the gum resin with coconut oil or lemon juice is applied to ulcers, swellings, boils, and ringworm (Chopra *et al.*, 1956). The antiseptic action of the resin encourages healing so it is used to treat ulcers and wounds. The resin is used nowadays in manufacture of incense, and as ingredient in plasters and fumigating pastilles (Wallis, 1967). It is also important as a scent and a fixative in perfumery industry. The recommended dosage of frankincense in inflammatory or bronchoconstrictive conditions is 400 mg three times daily. The frankincense is one of the safest herbals. Toxicity studies of *Boswellia* in rats and primates showed that LD<sub>50</sub> was established at more than 2 g/kg (Murray, 1995).

Frankincense is an oleogum resin obtained through a deep longitudinal incision the trunk of the *Boswellia* tree. The milk-like juice which exudes is hardened by exposure to the air. In about three months, the resin attains the required degree of consistency, hardening into yellowish tears (Fig. 2). (Miller and Morris, 1988).

Even the frankincense collected from the wounds is graded into several grades (Singh and Atal, 1988) of which are, Grade I (Tears); which is the best and most carefully selected grade of white color; Grade II (Reddish) that is mixed white and reddish quality which contains some particles of the bark; and Grade III (Dust and Sifting). The latter grade, because of its low price and finer size, is the most suitable quality for distillation of volatile oil. The harvest lasts from May till the middle of September, when the first shower of monsoon rain puts a close to the gathering for that year. Once the collection season is completed, the raw frankincense is allowed to cure for three months before being sold. It is stored on the floor of dry caves during



**Figure 2.** Oleogum Resin Tears of *Boswellia carterii* Birdwood

that period of maturation. The resin occurs in small tears (Fig. 2) varying from 0.5 to 3 cm in length and usually ovoid, pear-shaped, or club-shaped. It is usually of pale yellowish color, frequently with a greenish, bluish or reddish tinge, semi-translucent and covered with a dull white dust, the surface of the tear being dull even after the dust has been removed. They are brittle and internally are opalescent and translucent, the fractured surface being dull and waxy. The drug has a fragrant, balsamic odor and an aromatic, slightly bitter taste, and softens to a plastic mass when chewed. The oleogum resin when triturated with water yields a whitish emulsion (Wallis, 1967).

After such presentation of the deep-rooted usage of frankincense, one can really understand how frankincense is a truly Kings' gift. The oleogum resin of different *Boswellia* species that has various vernacular names *viz.* Frankincense, Incense, or Olibanum in English; Luban Dakar, Bakhor, Kendar in Arabic; Salai guggal In Ayurveda, and H-15 in Germany and Switzerland; was subject to various phytochemical investigations. It is noteworthy that the word Frankincense comes from a 10<sup>th</sup> century French word meaning "luxuriant incense". The word olibanum is derived from the Hebrew word "Lebonah" and the Greek word "Libanos" meaning white.

The genus takes its name from Professor John Boswell (Miller and Morris, 1988) the uncle of the famous novelist James Boswell, the writer of the well-known Story of Samuel Johnson. The genus comprises several species; all of which are trees (Guenther, 1972 and Lawrence, 1969); of which the most reputed are:

### **1.2. *Boswellia carterii* Birdwood (Syn. *Boswellia sacra* Flüeckiger)**

A tree which is native to Somalia, Southern Yemen (in Hadra'mout valley), and Oman (in Dhofar region). Miller and Morris (Kapoor, 1990) stated that the only species of *Boswellia* present in the Arabian Peninsula is *Boswellia carterii*. This species was named after the English surgeon H.G. Carter who was the first to discover it in his expedition in Southern Arabia at 1846. In 1876, the Swiss chemist and botanist Flüeckiger re-examined the same plant describing it as new species and called it *Boswellia sacra*. Three years later, The English botanist Birdwood reviewed the whole genus and found that the specimens described earlier by Carter and

Flüeckiger are identical to those found in Somalia and Known as *Boswellia carterii* so that the two species should be considered synonymous (Miller and Morris, 1988).

### 1.3. *Boswellia frereana* Birdwood

A species which is grown in small scale in northern regions of Somalia.

### 1.4. *Boswellia serrata* Roxb. Ex Colebr.

A species which is grown in India and have been differentiated botanically into two varieties (var. *serrata* with serrated and pubescent leaves, and var. *glabra* with glabrous leaves). Both varieties yield Indian Olibanum.

### 1.5. *Boswellia papyrifera* (Delile ex Caill.) Hochst

A species which is grown in North Eastern tropical Africa, especially in Sudan (Benson, 1967). The Egyptians supply of the oleogum resin of Frankincense, Olibanum, or Luban dakar comes mainly from Somalia, and rarely from Sudan or Kenya, therefore it is considered to be originated from *Boswellia carterii* Birdwood.

## 2. Chemistry

A review of the chemistry of Frankincense is made by (Khalid, 1983).

### A-The Essential oil:

There has been considerable work done on the composition of olibanum oil from different species and commercial brands of *Boswellia* (Peyron *et al.*, 1980). The volatile oil was found to contain a variety of components *viz.*

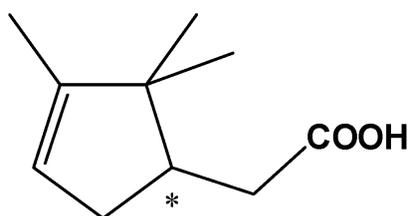
### Monoterpenes:

In 1978, Obermann investigated the essential oil derived from Aden and Eritrean frankincense and reported that  $\alpha$ -pinene is the main component in the Aden oil, whereas n-octyl acetate and n-octanol are the dominant compounds in the Eritrean oil.

In 1978, De Rijke *et al.* isolated traces of the monoterpene acid  $\alpha$ -campholytic acid [1] from olibanum oil. This acid was synthesized and showed a rather strong odor reminiscent of the oil. Thus in spite of being a trace constituent, it influences the olfactory character of the oil greatly.

In 1987, Abdel Wahab *et al.* examined the oil of Somali frankincense using GC/MS and found a variety of monoterpene hydrocarbons *viz.* sabinene, camphene, and myrcene; oxides *viz.* cineole; alcohols *viz.* decanol,  $\alpha$ -terpineol, and linalol; esters *viz.* bornyl acetate, neryl acetate, and geranyl acetate.

Olibanum oil is reported to contain several odorless cembranoid diterpenes *viz.* cembrene [2], isocembrene [3] (Khalid, 1983) that was initially identified in pine tree resins, whereas

 $\alpha$ -campholytic acid

[1]

incensole [4] and the 1-hydroxy derivative [5] occur only in olibanum. These cembranoid macromolecules may in part account for the reported fixative properties of frankincense oil (Ohloff, 1994); just like the macromolecules of Musk oil.

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 chemical profile of the oil is considered as a chemotaxonomical marker that confirmed the botanical and geographical source of the resin (Mikhaeil BR, 2003)

**B. The Gum:** In 1992, Sen *et al.* were able to isolate and elucidate the structure of 4-O-methyl-glucurono arabinogalactan from the oleogum resin of *Boswellia serrata* Roxb.

### C-The Resin:

Several authors reported the isolation and identification of various triterpenes of different skeletons from the resin of different species of the genus *Boswellia*.

#### 2.1. Pentacyclic Triterpenes

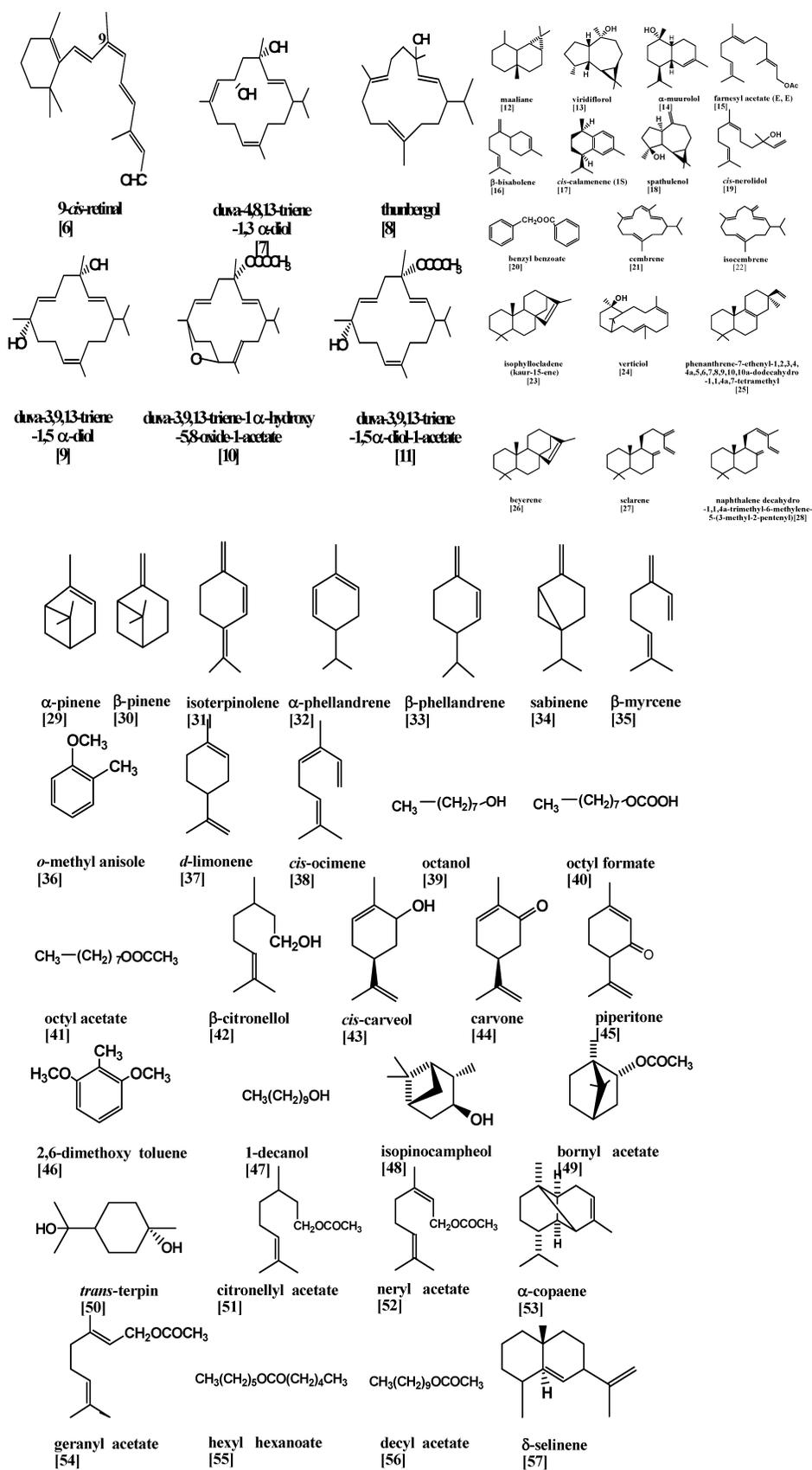
- Olean-12-ene ( $\beta$ -amyrin type) Triterpenoids:

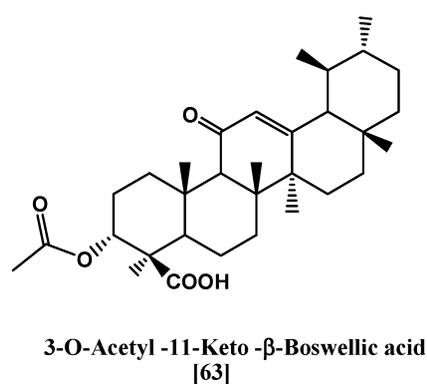
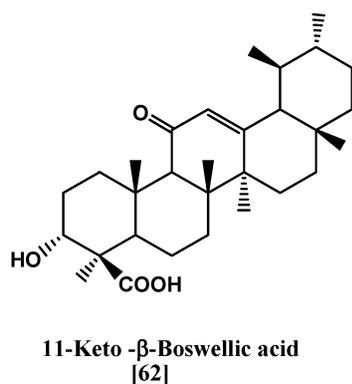
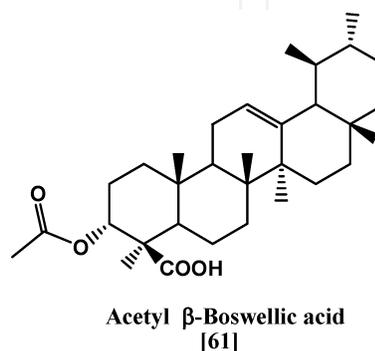
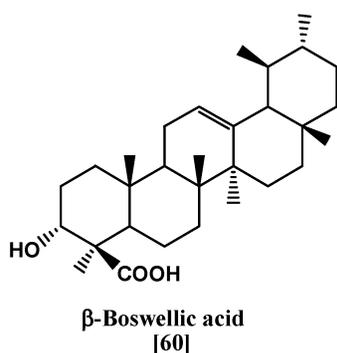
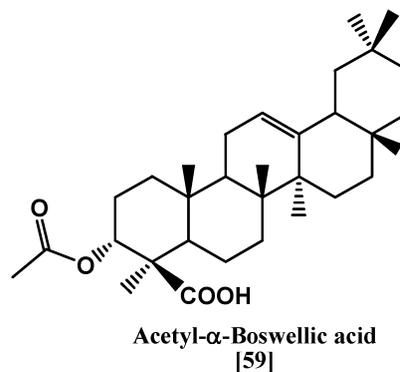
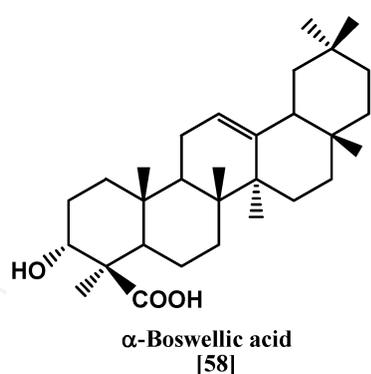
Classical acid-base extraction procedure led to isolation of  $\alpha$ -boswellic acid [58].

In 1972, Elkhadem *et al.* isolated the 3-acetoxy derivative [59] of  $\alpha$ -boswellic acid (acetyl  $\alpha$ -boswellic acid) by precipitation from ether extract of the resin of the Somaliland variety of olibanum by barium hydroxide followed by acetylation with acetic anhydride and hydrolysis.

Urs-12-ene ( $\alpha$ -amyrin type) Triterpenoids: Elkhadem *et al.* were able to eliminate that diene impurity completely by treatment of  $\beta$ -boswellic acid with maleic anhydride twice, followed by filtration of the adduct and crystallization. They were able also to prepare different synthetic derivatives of  $\alpha$ -, and  $\beta$ -boswellic *viz.* ethyl, ethyl acetyl, and methyl benzoyl esters.

The configurations of such groups and double bond position were later unveiled through progress in NMR spectroscopic techniques especially after 2D-NMR has emerged. Recent advances in crystallographic analysis confirmed the  $\alpha$ -configuration of 3-acetoxy group in



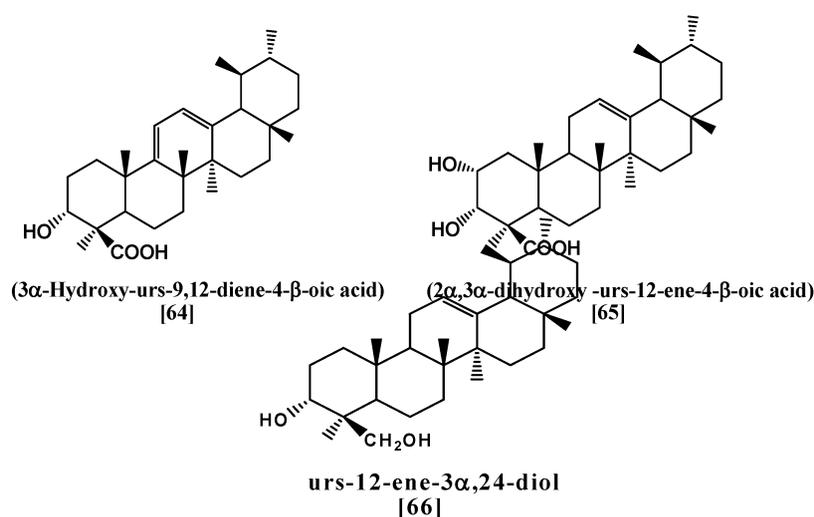


both acetyl- $\beta$ -boswellic acid, and 3-acetoxy-11-keto- $\beta$ -boswellic acid (AKBA) (Schweizer *et al.*, 2000).

In 1995, Mahajan *et al.* isolated 3 $\alpha$ -hydroxy-urs-9,12-diene-4 $\beta$ -oic acid [64] and 2 $\alpha$ , 3 $\alpha$ -dihydroxy-urs-12-ene-4 $\beta$ -oic acid [65] together with other known boswellic acid derivatives by repeated chromatography of the acidic fraction from the ethanolic extract of *Boswellia serrata* Roxb. oleogum resin. They separated also urs-12-ene-3 $\alpha$ ,24-diol [66] by chromatographic fractionation of the neutral fraction of the resin.

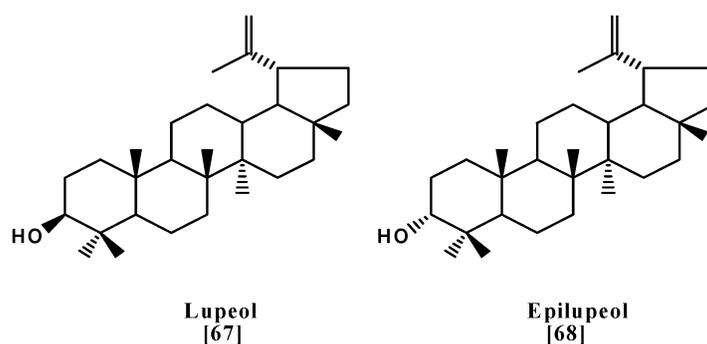
Lupane Triterpenoids:

Proietti *et al.*, 1981 managed to isolate 2 lupane-skeleton triterpenoids from resin exudate of *Boswellia frereana* distributed in the northern regions of Somalia namely, lupeol [67] and epilupeol [68].



## 2.2. Tetracyclic triterpenes

Tirucallane Triterpenoids:



Liang *et al.*, (22) reported the presence of a variety of tirucallane triterpenoids in family Burseraceae.

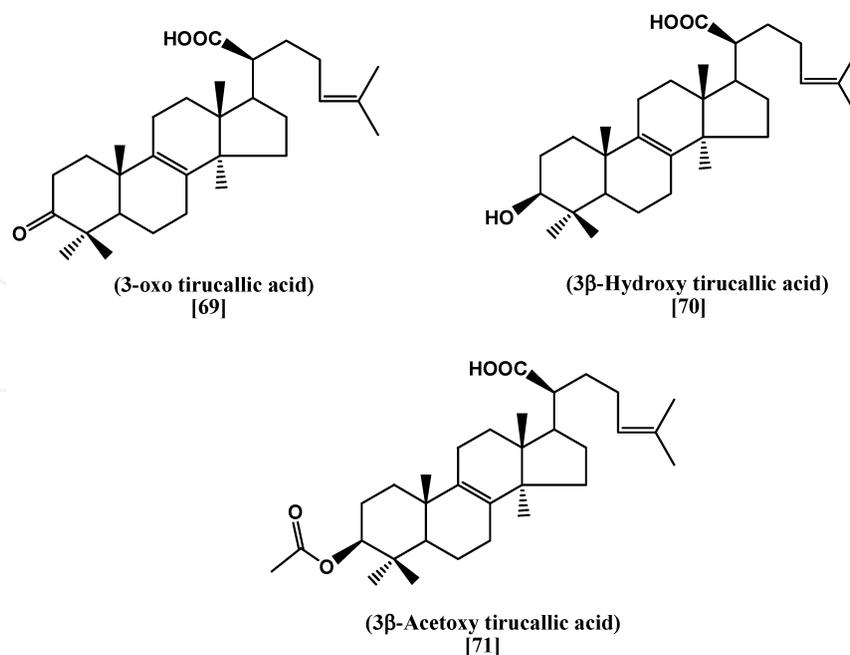
In 2001, Boden *et al.* reported isolation of three triterpenoids having tirucallane nucleus from the oleogum resin of *Boswellia serrata* Roxb. ; namely 3-keto-8,24-diene-21- $\beta$ -oic acid (3-oxo-tirucallic acid) [69], 3- $\beta$ -hydroxy-tirucall-8,24-diene-21- $\beta$ -oic acid (3-hydroxy-tirucallic acid) [70], and 3- $\beta$ -acetoxy-tirucall-8,24-diene-21- $\beta$ -oic acid (3-acetoxy-tirucallic acid) [71].

**Dammarane triterpenoids:**

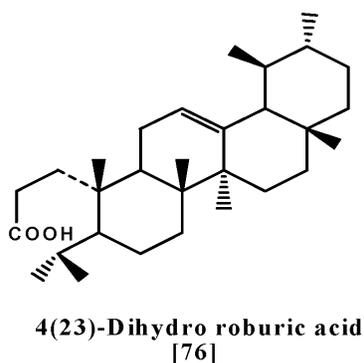
In 1985, Fattorusso *et al.* isolated four dammarane triterpenes from the most polar fractions of the chloroformic extract of the exudate of *Boswellia frereana*, namely 3 $\beta$ -acetoxy-16(S),20(R)-dihydroxy dammar-24-ene [72], 3 $\beta$ ,20(S)-dihydroxy dammar-24-ene [73], its 3-acetyl derivative [74], and 20(S)-protopanaxdiol [75].

- 3,4- Secotriterpenoids:

3,4-secotriterpenic acids carrying an isopropyl group at position 5 are very rare as naturally occurring compounds. They are considered to be degradation products originating through



geochemical process involving photochemical or photomimetic reactions. In 1983, Fattorusso *et al.* managed to isolate a member of such group of compounds, namely 4(23)-dihydro roburic acid [76] from the acidic fraction of incense *Boswellia carterii* Birdwood after methylation with diazomethane followed by catalytic hydrogenation of the produced methyl ester and column chromatography.



#### Analysis of the oleogum resin:

In 2001, Ganzera and Khan developed a reversed phase HPLC method for the separation of boswellic acids from *Boswellia serrata* oleogum resin. The first accurate determination of 6 individual acids was possible in the resin as well as in multi-component preparations. By using an acidic mobile phase, raised temperature, and a 4  $\mu\text{m}$  Synergi MAX-RP 80 A column, the acids could be detected at levels as low as 0.9  $\mu\text{g}/\text{ml}$ . The study of market products revealed significant variations in the content of these pharmacologically active compounds in commercial samples. (Ganzera & Khan, 2001)

Assignment of other atoms was made by referring to reported compilation data of a variety of similar compounds (Mahato *et al.*, 1994), and by using data from DEPT spectrum combined with  $^1\text{H}$ - $^1\text{H}$  COSY, HMQC correlations and long range C-H correlation data from HMBC spectrum which is illustrated by (Fig. 3). EI/MS fragments corroborated the aforementioned assignments showing a molecular ion peak  $[\text{M}]^+$  at  $m/z$  512.35 corresponding for the molecular formula  $\text{C}_{32}\text{H}_{48}\text{O}_5$ .

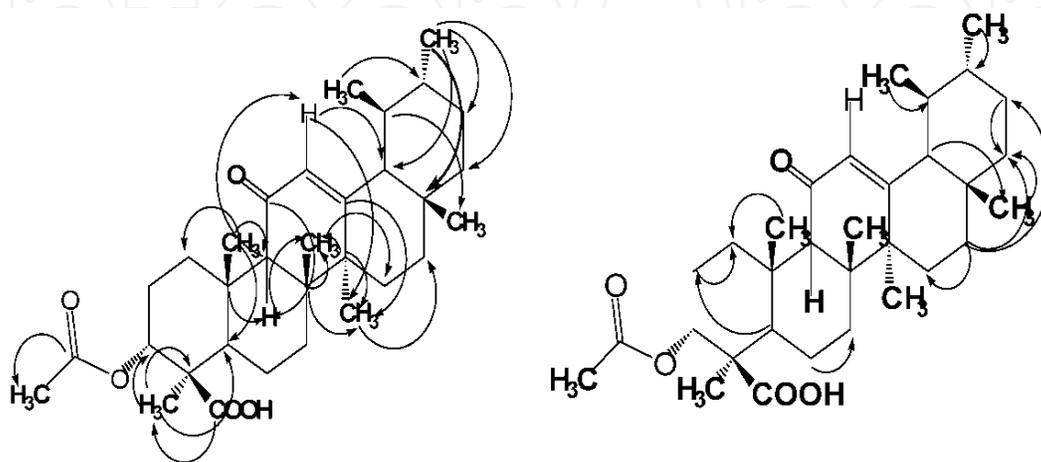


Figure 3. HMBC Correlation for 3-acetyl 11-keto  $\beta$ -Boswellic acid [63]

From the above mentioned data, and from literature data; one can conclude that compound A-6 is 3 $\alpha$ -acetoxy-urs-12-ene-11-Keto-24 $\beta$ -oic acid known as acetyl-11-Keto- $\beta$ -Boswellic acid (AKBA). A computer-generated model for that compound after energy minimization using

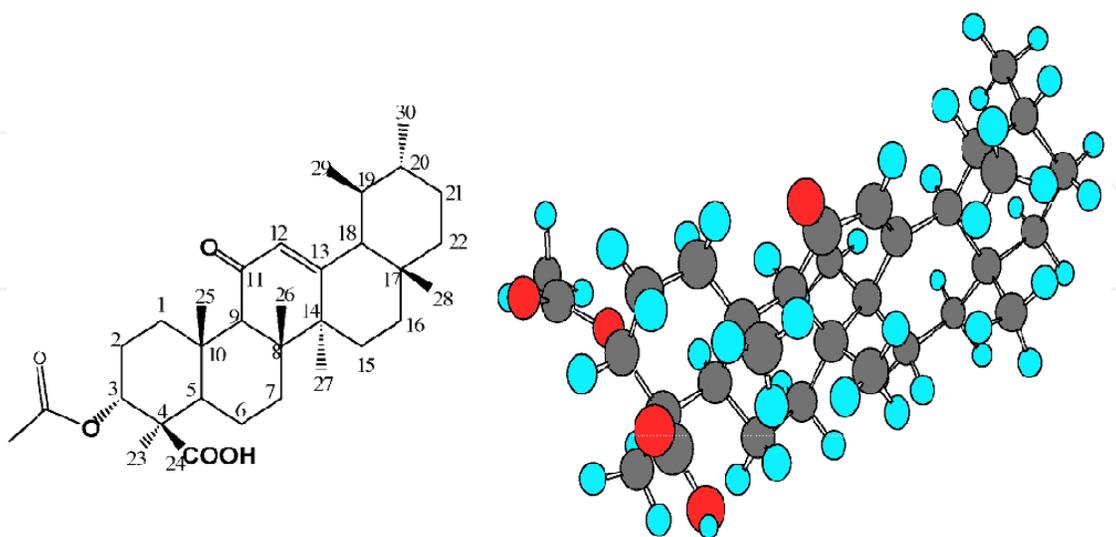


Figure 4. Computer-generated Model of 3-acetyl 11-keto  $\beta$ -Boswellic acid [63]

CSCChem3D program pro-version 4.0 (Cambridge Soft Corp.) is shown in Fig. 4.

The aforementioned data; it was suggested that  $3\alpha$ -hydroxy-urs-12-ene-11-keto-24 $\beta$ -oic acid known as 11-keto  $\beta$ -Boswellic acid (K $\beta$ -BA). A computer-generated model for that compound after energy minimization using CSChem3D program pro-version 4.0 (Cambridge Soft Corp.) is shown in (Fig. 5).

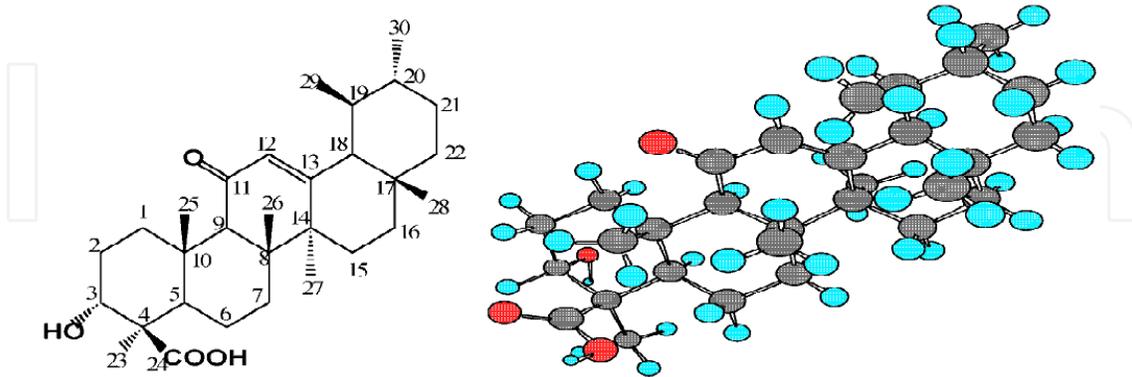


Figure 5. Computer-generated Model of 11-Keto- $\beta$ -Boswellic acid [62]

### 3. Biology

- Rough based Granular computing approach had been used to predict response to new medication from Boswellia and other components for treatment of HCV patients as presented in Fig. 6 (Badria et. Al al. 2013).

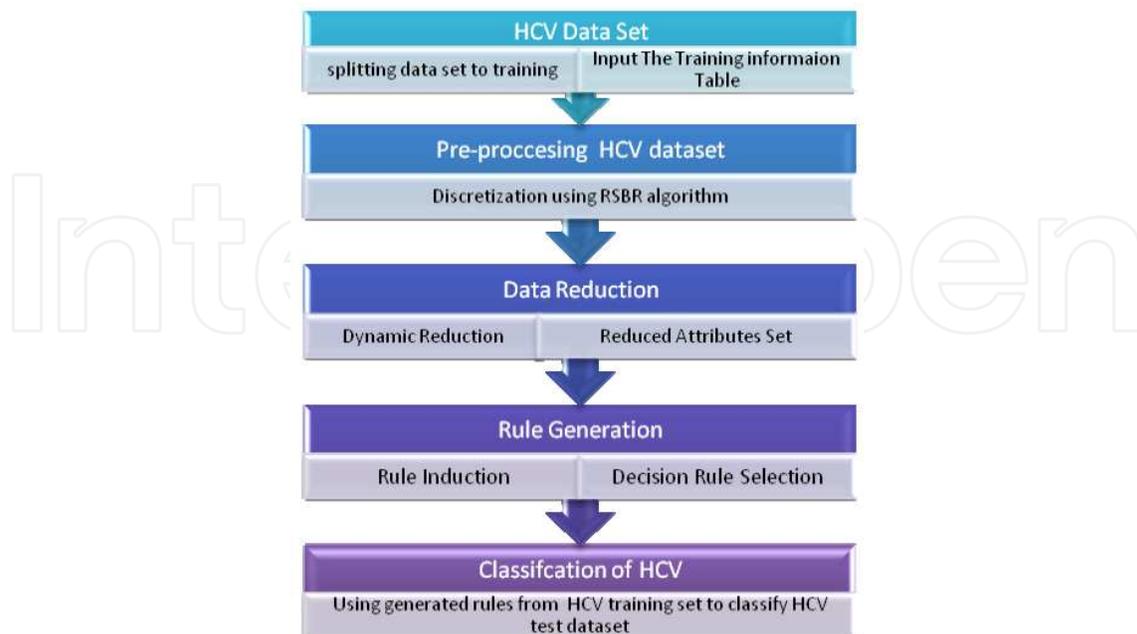
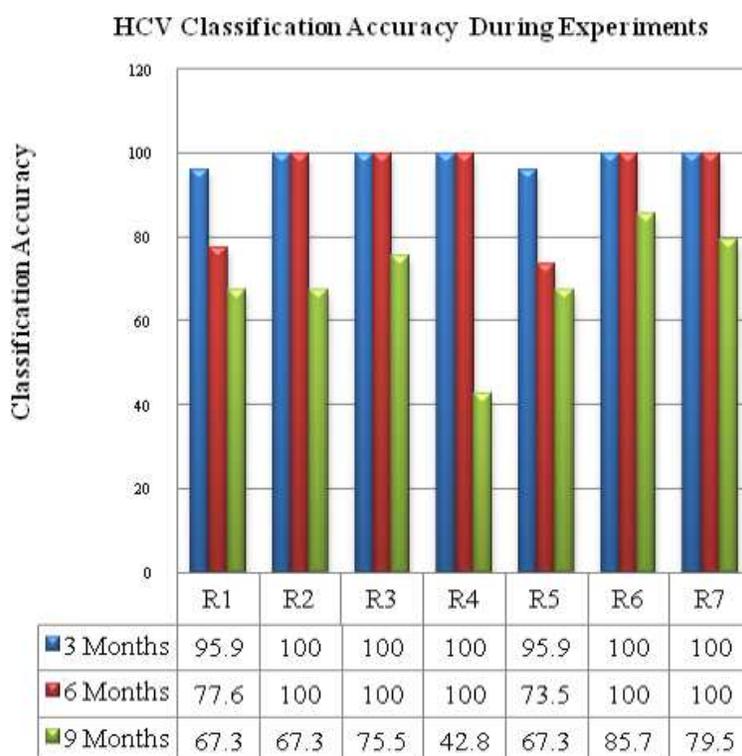


Figure 6. Rough based Granular Approach (RGA) Used in HCV Dataset Classification



**Figure 7.** Classifications Accuracy for Each Reduct During Experiment

- *Boswellia carterii* extract in combination with glycyrrhizin (Badria *et al.* 2003) showed a strong biochemical and histopathological hepatoprotective effect on rat Liver Injury.
- Frankincense triterpenoids showed Anti-Herpes activity (Badria *et al.* 2003) and Immunomodulatory effects (Badria *et al.* 2003 and Botros *et al.* 2003).
- Animal studies showed that the ingestion of a defatted alcoholic extract of *Boswellia* decreased polymorphonuclear leukocyte infiltration and migration, decreased primary antibody synthesis (Sharma and Singh, 1989) and caused almost total inhibition of the classical complement pathway (Wagner, 1989) and alternate complement system (Knaus and Wagner, 1996).
- The gum resin extract from *Boswellia* was recently shown to have positive therapeutic effects in inflammatory bowel disease. However, the mechanisms and constituents responsible for these effects are poorly understood (Krieglstein, 2001). Moreover, in a clinical study reported that *Boswellia* extract appears to be superior over mesalazine in terms of a benefit-risk-evaluation (Gehardt *et al.*, 2001).
- $\beta$ -boswellic acid and its derivatives have anti-tumor and antihyperlipidemic activities (Huan *et al.*, 2000).
- *Boswellia* has also been observed to inhibit human leukocyte elastase (Safayhi *et al.*, 1997 and Schweizer *et al.*, 2000): Boswellic acids are effective anti-inflammatory and anti-arthritis agents, they also help control high blood lipids and protect the liver against bacterial

galactosamine -endotoxin. The non acid part of the gum has pain relieving and sedative qualities, and in high doses can lower blood pressure, and reduce heart rate in dogs but increase in frogs observed benefits of *Boswellia* include reduction in joint swelling, increased mobility, steroid sparing action, less morning stiffness, improved grip strength, and general improvement in quality of life, for both osteoarthritis and rheumatoid arthritis. (Pachnanda et al. 1996).

- Boswellia gum has been used for the treatment of diabetes, skin and blood diseases, fever, cardiovascular disorders, neurological disorders, dysentery and diseases of the tests (Adrian, 1998).

### 3.1. Predicting the Effect of Boswellic Acid

If the boswellic acid was just another leukotriene inhibitor, then its effects probably could be predicted on the basis of these drugs: It probably works sometimes, it probably doesn't work for everyone, it probably is very effective for aspirin-induced asthma, it isn't going to be quite as strong as corticosteroids, and it isn't going to have as big an effect on the amount of air that can be expelled in one second as it does on other symptoms. These are, in fact, reasonable expectations (Safahyi *et al.*, 1992). However, the boswellic acids neutralize elastase (Safahyi *et al.*, 1997). It is not known how important this is. First, it is not known to what extent elastase contributes to the problem of asthma. Second, it is not known to what extent elastase is a problem when taking a leukotriene inhibitor (Safahyi *et al.*, 1997). Boswellic acid's ability to neutralize elastase is superfluous, or it might nicely complement the inhibition of leukotrienes. Also, we don't know how much the boswellic acids actually neutralize elastase.

### 3.2. Experimental Autoimmune Encephalomyelitis (Multiple Sclerosis)

Wildfeuer et al., 1998 administered a mixture of acetyl-boswellic acids to guinea pigs with experimental autoimmune encephalomyelitis. Multiple sclerosis occurs when the myelin insulating the neurons in the brain is destroyed. Researchers wishing to study this can't wait for rats to get multiple sclerosis. Instead, they create a problem that is much like multiple sclerosis, which is called experimental autoimmune encephalomyelitis (Wildfeuer et al., 1998). Two studies (Safayhi *et al.*, 1992) had previously found that leukotriene inhibitors reduced the development of experimental autoimmune encephalomyelitis. Of course, there is a jump from experimental autoimmune encephalomyelitis in a rodent to multiple sclerosis in a human. Curiously, the role of leukotrienes in multiple sclerosis seems to have garnered more attention. People with multiple sclerosis do have increased leukotrienes (Sailer *et al.* 1996).

## 4. Blocking the formation of leukotrienes

### 4.1. Leukotrienes Inhibitors

Safahyi *et al.*, 1992, observed the ability of the different boswellic acids to inhibit the formation of the leukotriene LTB<sub>4</sub>. As noted, the other leukotrienes are more important with regard to

asthma. However, the mode of action of the boswellic acids should be equally effective for all leukotrienes, because they inhibit 5-lipoxygenase, the key enzyme needed for starting the synthesis of all leukotrienes. Safahyi and his group (1992) measured the concentration needed to block the activity of LTB<sub>4</sub> by 50%. For AKBA, the needed concentration was 1.5 micromoles.

For the other boswellic acids, it was 4-7 micromoles, which means that 3 to 4 times greater a concentration was needed. A factor of 3 or 4 might not be that important as things go, but this finding singled out AKBA as being the most powerful boswellic acids (Safahyi *et al.*, 1992). Wildfeuer *et al.*, 1998, found that boswellic acids reduce leukotriene formation, and AKBA is the most effective.

## 5. Clinical applications

### 5.1. For treatment of knee osteoarthritis

After one month of treatment there was a significant reduction of pain on active movement, passive movement, tenderness, nocturnal pain and a significant improvement of pain free walking time. After two months of therapy, there was a highly significant reduction of pain on active movement, pain on passive movement, tenderness, nocturnal pain, and highly significant prolongation of pain free walking time. At the end of three months, there was a significant reduction of grade of knee effusion, with highly significant reduction of pain on passive movement, pain on active movement, tenderness, and significant prolongation of pain free walking time (Badria *et al.* 2004).

Efficacy and tolerability of *Boswellia* and turmeric in this work is superior to clinical trial of NSAIDs in treatment of active osteoarthritis. The efficacy of NSAIDs (diclofenace) were tested in a double blind clinical trail in 50 OA patients at dose of 50 mg bid for three weeks and follow up visit after seven weeks. At the end of the trial, there was a significant reduction in pain, joint tenderness ( $P < 0.05$ ) and swelling (Badria *et al.* 2002).

### 5.2. For treatment of bronchial asthma

Badria *et al.*, 2002 and Gupta *et al.*, 1998 performed the best type of research study in a double-blind, placebo-controlled study. Some subjects with bronchial asthma. During the 6 week treatment period, the subjects taking boswellic acid had an average of .3 asthmatic attacks and the subjects taking the placebo had an average of 1.2. despite worse starting signs, the subjects taking boswellic acid actually had fewer asthmatic attacks. Therefore, Gupta's study stands as good evidence that boswellic acid at least reduces the probability of an asthmatic attack (Gupta *et al.*, 1998).

After 2 weeks treatment with boswellia, there was a significant increase in both FEV<sub>1</sub> and PEF<sub>R</sub> ( $P \leq 0.05$  and  $\leq 0.01$  respectively) with no significant change in FVC in the severe persistent asthma subgroup (C1) when compared to those received placebo (C2). The potent inhibitory action of boswellia extract on blood eosinophils, can be explained by a potent anti-inflammatory action extends beyond the leukotriene inhibition (Badria *et al.* 2004).

### 5.2.1. *Ulcerative colitis*

Badria *et al.*, 2001 and Gupta *et. al.* 1997 compared boswellic acid to a typical therapy for ulcerative colitis, sulfasalazine. To roughly characterize the finding, there was no observable difference between the two treatments (Badria *et al.*, 2001)

### 5.3. For treatment of hepatitis C

Inclusion Criteria:

- positive PCR for HCV.
- Elevated liver enzymes within 6 months of the Entry, with no attribution to causes other than HCV
- Chronic HCV confirmed histologically with Liver biopsy within 2 years of entry
- Both genders were eligible within age of 18-70 years old.

Participants were enlisted from a group of HCV-infected patients currently enrolled in a large observational study in Egypt. Participants received the supplements daily for 18 months, with measures obtained every 6 months.

Measures to be assessed will include: compliance with assignment, retention in the study, Liver enzymes levels, serum collagen markers, self-described symptoms, viral load and clearance, abdominal ultrasound. It is hypothesized that the supplements led to clearance of HCV infections and/or at least prevent progression of liver disease in participants with chronic HCV hepatitis and, in some cases, reverse hepatic lesions that are already present, as well as improving the quality of life in individuals who use this dietary supplement. (Badria *et al.* 2002)

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