Figure 2. *Boswellia serrata* from the trunk of a tree (Siddiqui, 2011).

Figure 3. Burseraceae tree ("*Boswellia Serrata*," 2015)

Boswellia Serrata is known as *Boswellia carterii* (figure 4) in some places. It exudes the resin of the Boswelia tree from the tree bark which is cut to allow a white, milky resin to flow. Researchers such as Wang et al. (2011) found out that the most studied oils of olibanum is the *Boswellia carterii* essential oil. Octyl acetate is the main component of the oil resin, with 60% predominance in the oil. The pale yellow oil is the hydrodistillate of *Boswellia craterii* with its major constituents made up of α-thujene (1.7%), α-pinene (10.9%), camphene (1.0%), sabinene (0.7%), β-pinene (0.7%), myrcene (0.5%), hexyl-acetate (0.3%), p-cymene (1.4%), Z-β-ocimene (0.4%), E-β-ocimene (1.7%), limonene (1.5%), 8-cineole (1.2%), 1-octanol (11.9%), linalool (2.1%), α-pinene epox-ide (0.5%), trans-verbenol (0.4%), terpinene-4-ol (0.4%), octyl acetate (39.3%), bornylacetate (2.2%), geranylacetate (0.4%), *E*-nerolidol (0.2%), cembrene A (2.1%), cembrene C (0.1%), verticilla-4(20),7,11-triene (6.0%), incensole (1.0%) and incensole acetate (2.3%). Diterpenoid constituents and octyl acetate were found to be present in the extract called with a little amount monoterpenoid constituents.

Figure 4 *Boswellia carterii* (Frankincense, 2019)

2.2 Boswellia resin

The frankincense product has four different types of proteoglycans and glyco-. Major components of the water-soluble poly-meric substances from the resins of *Boswellia carterii* and *Boswellia serrata* are classical arabinogalactan proteins. These proteoglycans are basically made up of D-galactose units in the core chains, which are highly branched at positions 3 and 6. Uronic acids, glucuron-ic acid, terminal 4-O-methyl-glucuronic acid and the arabinose are in the side chains. In the polymer group, there are high contents of fructose, mannose and glucosamine are in the polymer group showing that glycoproteins occurs. This contains L-arabinose and D-galactose. The protein parts are made of two hydroxyproline and serine which are amino acids. *Boswellia serrata* has a higher protein content than *Boswellia carterii* (Camarda et al. 2007).

2.3 Essential Oils

Frankincense essential oils are used in aromatherapy (also called essential oil theraphy). Aromatherapy uses plant extracts for therapeutic purposes. The oils are sourced from the frankincense species. Their natural ingredients include pinen, sclarene, thunbergol, octanol, octy formate, decyl acetate, O-methylanisole, verticiol, and 9-cis-retinal (figure 5).

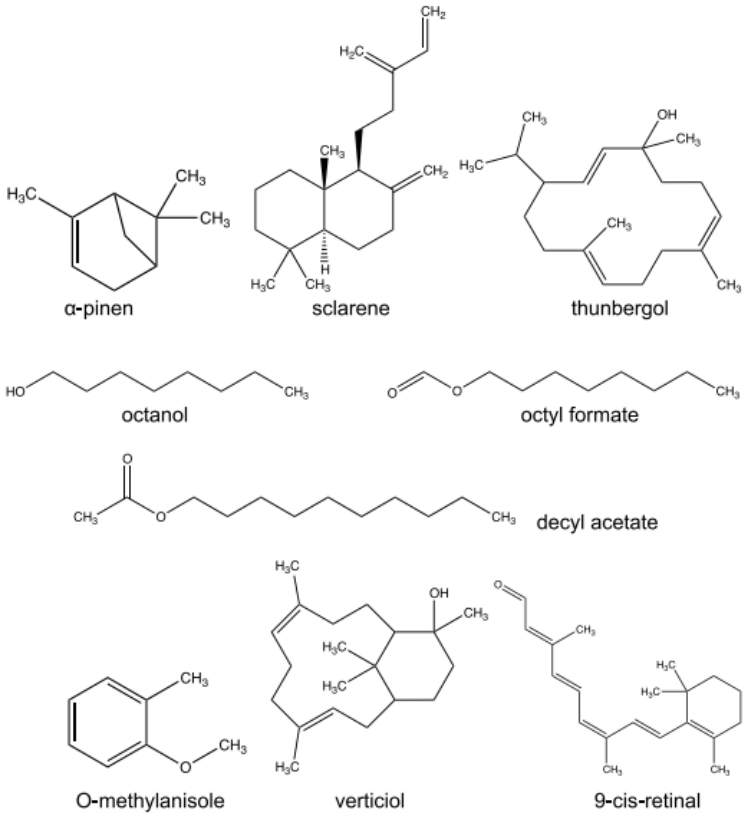

Figure 5. Chemical structures of Boswellia essential oil ingredients (Ben-Yehoshua et al. 2012)

2.4 Frankincense Extracts and Gums

Extracts and gums from the stem bark of frankincense species from India are applied in the treatment of various diseases. The gums exude from the stem bark of *Boswellia serrata*. The other constituent called Boswellic acid has anticancerous, anti-inflammatory, and, anti-ulcerous activities. The inflammation pathway contains kinases, toposiomerase I and II, 5-lipoxygenase, leukotriene (inflammatory chemical messengers), and human leukocyte elastase, (Poeckel and Werz 2006). Studies focusing on finding out if a cardio protective effect can be offered by gum resin extract interrupting complex interactions. Based on information gathered, antithrombotic properties have never been in *Boswellia serrata's* gum resin. The initiation of thrombocytes function means there is a

chance for stopping thrombosis. Anticoagulant and antithrombotic drugs such as heparin have been used. With the long-term effects that come with the use of heparin, drugs used as its alternative drugs are on high demand. In India, Ayurvedic medicinal plant is a system used with *Boswellia serrata*. Pentacyclic triterpenic acids are in the Ayurvedic plant and possess the several pharmacological activities. In spite of the medicinal compound of the BAs their activities are restricted because of the low aqueous solubility following its nature which results in a poor bioavailability (Shen and Lou 2008).

2.5 Health and Benefits of Frankincense

Anti-inflammatory effects are revealed in frankincense and its ingredients act against immunological diseases. Data are provided and are meant give a firm reason to trust the clinical trials conducted. There has been an isolation of numerous phytochemicals which includes the boswellic acid type, triterpenoids, and non-terpenoids. The development of pharmaceutical drugs has been drawn from semisynthetic derivatives. The outcome of anti-inflammatory have not only been carried out in vitro, it has also been in several in vivo studies, showing this can be transferred. Frankincense and its phytochemicals have shown favorable results towards inflammation-related diseases through using animal models (Governa et al. 2018).

One of the physical changes seen was the reduction of oxidative stress. The production of reactive oxygen species and membrane lipid peroxidation were reduced by a reactive nitrogen species (RNS) (Mbiantcha et al. 2018). The immune system decreased in some regard. Some of which involved mast cell, T-effector cells, T-regulatory cells, and granulocytes. Hepatic symptoms, serum lipids, blood glucose, and atherosclerotic plaques were also affected (Henkel et al. 2012).

2.5.1 Anti-bacterial activity

Boswellia carterii and *Boswellia serrata* acid fractions are characterized by high antibacterial activity. *Boswellia serrata* showed a higher activity. A large inhabitation zone against *Proteus vulgaris* was shown by the *Boswellia serrata* aqueous extract. Phenolic acid in Boswellic acid is thought to have resulted in its anti-bacterial resin properties. The effectiveness of energy and protein is enhanced by phenolic compounds (Patel et al. (2012).

This occurs through the reduction of competition for microbes with the host for nutrients. Antibacterial activities of Boswellic acids from *Boswellia serrata* tested in vitro on a clinically significant panel of oral bacteria. Of all four Bosewllic acids acting against all bacterial pathogens, the most effective was Acetyl-keto-boswellic acid (AKBA) (Akihisa et al. 2006).

2.5.2 Anti-arthritic activity

Traditional medicine has been used to treat arthritis. Some of the drugs are steroids and no steroidal anti-inflammatory drugs (NSAIDs). Others are interleukin-1 beta antagonists (IL-1β), and tumor necrosis factor alpha (TNF-α-). Extract of *Boswellia carterii* gum resin mixed with acetone reduced arthritis. It TNF-α- and IL-1β in rats (Fan et al. 2005). Another study involving 30 osteoarthritis patients decreased knee pain and allowed them walk. The swell in the joints also reduced. Prescriptions of Boswellia extract is offered to such patients (Kimmatkara et al. 2003).

2.5.3 Anti-cancer activity

The activities of Boswellic acid and its derivatives include antitumour, anticarcinogenic, and antihyperlipidemic. These constitute the methanol extract of *Boswellic serrata*. The trepertinoid acids are isolated and characterized using anti-proliferative effects (Van Vuuren el al. 2010).

Isolated compounds and oleogum resin extracts have been used in such studies. Extracts and phytochemicals from frankincense species showed their cytotoxicity in cancer cell lines both in vivo and in vitro. This gave a possibility of beginning to explore these extracts as potential agents in drugs fighting cancer just like synthetic ones.

The phytochemicals work in opposition in a wide array of strong carcinoma and sarcoma including those of fibers, breast, prostate, liver, cervix, lung, pancreas, and liver. Others are in hematopoietic tumors (myeloma and leukemia), meningioma as well as glioblastoma. The inhibition of tumour growth remains a very unique in vivo quality of frankincense (Xia et al. 2017).

The gum resin of *Boswellia sacra* has a chemotherapeutic quality. This is derived from its hydro-distillate. It functions to prevent attacks on urothelial cell carcinoma. Results from experiments show that this is potent in human leukemia cells. It decreased cell growth, proliferation, and angiogenesis. (Ranjbarnejad et al. 2017).

2.5.4 Anti-microbial activity

Essential oil gotten from resins of *Boswellia carterii* has been effective in microorganisms of fungi, bacteria (gram-positive and gram-negative). An activity test was conducted in vitro with AKBA, although limited to gram-positive, proving to be the most effective inhibiting agent against pathogens. Also, the outside membrane of lipophilic acid with its lipopolysaccharides and hydrophilic barrier serves as a potent guard against hydrophobic compounds. It is suggested that gram-negative bacteria's resistance against AKBA is important (Rahimi et al. 2010).

Biofilms are multilayered cells made up of *Staphylococci* making them difficult to be altered. Biofilms are resistant against antibiotics which makes them infectious. Conversely, AKBA inhibits staphylococcal biofilm by reducing its performance. Thus, AKBA can cause a reduction in the production *Staphylococcus aureus* and *Staphylococcus epidermidis*. This makes AKBA the most effective compound against pathogens gram-positive bacteria (Raja et al. 2011).

Boswellic acid was also found to have antimicrobial activity in oral cavities. In this, AKBA was also the most effective antibacterial and thus has been adapted as a component of mouthwash products to prevent and treat oral infections (Raja et al. 2011).

2.6 Inflammatory Diseases

The body tissues respond to pain, swelling, redness and loss of function in several ways (figure 6). These result from infections, immune disorders, injuries, and irritations. These changes may be in form of oxidative stress or inflammation (Ammon 2006).

Inflammation is as a result of small chemicals called mediators produced by body cells. They cause migration of cells to Leukotriene. They also promote free radicals, cell adhesion, and autoimmune reactions (Birkner 2006).

Leukotrienes cause inflammations leading to psoriasis, arthritis, asthma, rheumatism, and colitis. Boswellia inhibits leukotriene by blocking its synthesis and shrinking inflamed tissues resulting in pain and discomfort (Siemoneit et al. 2011).

Frankincense has shown therapeutic characteristics against diseases. Studies conducted both in vitro and in vivo, showed pharmacological activity against inflammation and tumors. It was also observed that gingivitis was effective against inflammation of periodontium. Extracts and powders of frankincense resulted in reduction of these effects (Khosravi Samani et al. 2011).

2.7 Controlled Release of Drugs

Drugs are channeled to required tissues by a system known as controlled drug delivery. In experiments involving frankincense a drug embedded matrix was applied to direct tablets. There was a need for safety and efficiency. This was in spite of various matrix and polymers used. The goal was to control and improve bioavailability of the drugs (Chowdary and Reddy 2012).

The controlled release of natural resins, nifedipine, and colophony were used and resulted in gradual and spread of drugs in 24 hours. Olibanum, used for microencapsulation, was the most suitable resin (Chowdary et al. 2009).

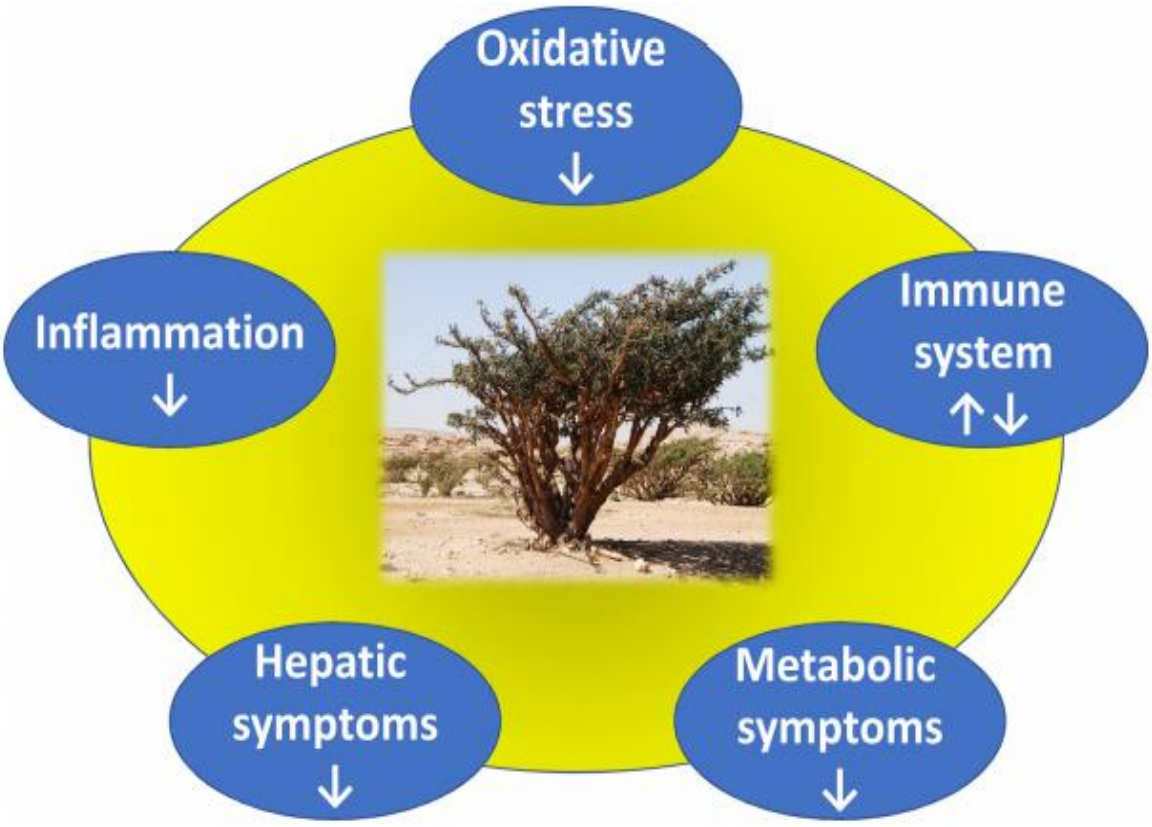

Figure 6. Anti-inflammatory changes elicited by Frankincense (Efferth and Oesch 2020)

Olibanum was also used as an agent in natural lipophilic polymer. Its resins were also used for other drugs such as carbamazepine and diclofenac. Drug release decreased as the concentration of the resin increased (Rao et al. 2009).

2.7.1 Preparation and dosages

There are various methods for drug administration including rectal, oral, and parenteral. For frankincense studies, the oral method was preferred. Drugs in form of capsules or tablets were prepared using diluents such as lubricants, binding, disintegration, and wetting agents.

Injections are administered intramuscularly, intravenously, intra-arterially or subcutaneously. Preparations in single or multiple doses can be in form of suspensions, emulsions or solutions. The dosage of Boswellia is difficult to ascertain but a 300-400mg to be taken thrice a day is generally recommended. (Siddiqul 2011).

2.7.2 Safety

Frankincense continues to be used as a remedy for diseases. The anti-inflammatory effects of Boswellia appears to have the least negative effects when compared to other anti-inflammatory chemical drugs. It does not adversely affect respiration, heart rate, or blood pressure. Its resin is also of low toxicity. It has been endorsed as a food additive by the United States Food and Drug Administration (USFDA).

It is sold in the market where oral preparations of *Boswellia serrata* extract containing AKBA can be bought over the counter. Clinical examinations show that it has high tolerance and minimum side effects of rheumatoid arthritis and CD. When taken in the right dosages, it is very safe (Siddiqul 2011).

2.8 Psychoactivity of Frankincense

Many plants have been used in mythological, religious, and cultural customs. Some of them have essential roles. A few are *Salvia divinorum*, *Nicotiana tabacum, Aryan soma*, *Cannabis sativa, Ipomoea violacea.*

The psychoactivity of frankincense has not been a recent study. It was recognized in the first century C.E. by Dioscorides who said it causes insanity. Also, it was given to prisoners in Jewish Talmud to make their senses numb and in Ethiopia for its calming effect. (Moore 2006).

Assays were used in experimental studies to examine the physiological, behavioral, and pharmacological examination of Incensole acetate (IA). Mice models were used to examine the anti-depressive and anxiolytic quality of frankincense (Moussaieff et al. 2008).

Transient receptor potential (TRP) channels which has a sub-family called TRP vanilloid (TRPV) is made up of six groups: TRPV1-TRPV4. It produces varying temperatures that measure the psyoactivity of frankincense (Petit-Demouliere et al. 2005).

A range of 31–39°C was used for TRPV3 causing warmth feeling resulting in the activation of chemical agents that are found to be agonists (Moqrich et al. 2005).

3. MATERIALS AND METHOD

3.1 Systematic Search

The first step was to conduct a literature search. This was done over the course of one week using the following databases: Science, PLOS One, TOPNET, Google Scholar, and Elsevier. The search process was organized and performed in a structured and pre-planned way by considering search terms, selection of resources (including databases), choice of search methods, and reflecting on the search results obtained during the process. Advanced researched works spanning the 21st century from 2001 to 2020 were considered. The search language was English. This was applied across board.

The layers of keywords focused on were: (1) frankincense species and essential oils (2) keywords for frankincense in disease therapy such as cancer, diabetes, anti-inflammatory disease (3) side effects of frankincense.

In applying this systematic way, there was a greater chance of avoiding disparities and selection bias. It also allowed the identification of gaps in existing research and minimizing the reproduction of already existing research.

The search for the primary indicator (frankincense essential oils) was performed on the search bar. The second indicator was searched in title, abstract, keywords, and introduction. The “press” checklist was used as it is the most prominent and it aims to develop evidence-based guidelines to peer review of electronic search strategies.

Key texts were identified based on the research objective and their accessibility and prominence within the Near East University systematic reviewing practice. Several guidance documents were identified. These documents provide guidance for different types of reviews including interventions, technologies, qualitative research studies, and therapeutic topics.

3.2 Inclusion Criteria

Publications that met the criteria of search strategy were downloaded in pdf format, studied, and reviewed by the student. The primary sources were are identified based on the question, related keywords and appropriate range of publication years. The summary of studies was presented in a logical flow using themes. This was succinct and adequately represents the reviewed literature/knowledge based on the topic.

Summaries/paraphrasing of material (direct quotes of content used only for specific purposes and referenced appropriately) was done. After that critical review of study methods, outcomes and applicability was done.

To form a coherent study, there was an assessment of study quality, using accepted review 'criteria' to analyze strengths, weaknesses or limitations and conflicts or gaps in information. This helped to link studies together and form a new and logical whole.

4. DISCUSSION

The application of frankincense in inflammatory diseases has gained recent traction especially in chronic cases. In Atherosclerosis, which occurs when plaques build up in blood vessels and hardens the arteries, inhibition of nuclear transcription factor-kappa B (NF-κB) by AKBA has been of therapeutic use. This method could be further developed. (Cuaz-Perolin 2008).

In non-modern medicine, frankincense has its importance as an agent for respiratory improvement. It has been applied in stem inhalations and baths. In this regard, it has been used to treat and manage catarrh, cough, asthma, and bronchitis. In asthma, leukotriene biosynthesis is inhibited by Boswellic acids. This reduces and prevents inflammation. In some cases, 70% improvement was recorded in patients. Physical symptoms like breathing difficulty and rhonchi was seen to have either reduced or completely disappeared. This research used the gum resin of *Boswellia serrata* to treat bronchial asthma (Nusier et al. 2007).

Extract of *Boswellia serrata* has also been used to reduce skin diseases such as redness, irritation, and skin tone. In China, it has been used to treat bruises and sores. The pentacyclic triterpene structure provides a delicate effect on irritated skins. *Boswellia serrata* extract is dissolved needs to be dissolved or dispersed in either fatty acids or alcohols. It is then added with other derivatives. These include those that enhance skin or hair protection and ensure the product is stabilized. This is needed to prevent side effects (Qurishi et al. 2010).

Inflammatory bowel diseases result from chronic diseases of the intestine such as UC and CD. In many cases, the actual cause of IBD remains elusive. However, two factors seem to contribute. First is a genetic or environmental factor. The second is an abnormal gastrointestinal (GI) tract luminal factor. Some are microorganisms, oxidative stress elements, and defects in the intestine. The role of leukotriene cannot be ignored in chronic inflammatory diseases. This is enhanced by Boswellic acids. They are gum resins have a

characteristically specific, and non-competitive inhibitors of the important enzyme of leukotriene called 5-lipoxygenase (Rahimi et al. 2010).

In chronic colitis, which affects the inner lining of the colon, the gum resin of *Boswellia serrata* has been of therapeutic value especially in Traditional Iranian medicine (TIM). The oleogum resin of *Boswellia serrata* and *Boswellia carterii* reduces inflammation to a significant level. The effect has shown to possess other qualities against ulcer, wound, and diarrheal. A dosage of 350 mg of *Boswellia serrata*, which was administered for three times a day for 6 weeks, showed an 80% remission in patients with ulcer colitis (Shehata et al. 2011).

Brain tumor is a disease in which cancerous tumors take over the brain. As they grow fast and malignant, they surround the brain's tissues. Surgical procedures are used to remove the tumor. However, different factors such as the type, location, and size of the tumor makes this process difficult and mostly impossible. Even a surgical and radio-therapeutic treatment only gives the patient 9 months to live. Very active leukotriene and other inflammatory mediators are formed in the brain and surrounding tumors in these patients. Thus frankincense can be used to attack the leukotriene. (Simmet et al. 2001).

In some patients, the resin of *Boswellia serrata* has been used to treat brain tumor. Or 7 days, there was a 22-48% reduction in peritumoral brain edema. Patients who were not treated showed an increase in 2 weeks (Estrada et al. 2010).

Diabetes mellitus, which shows high blood sugar level over a prolonged period of time, has also been studied with frankincense. Oral administration of aqueous extracts from leaves and roots reduced the blood glucose level. Furthermore, over 28 days there was a reduction in levels of cholesterol, triglyceride, creatinine, and urea. (Kavitha et al. 2007).

Type I diabetes causes beta cell death and insulin problems. *Boswellia serrata* has been used to target mediators relating to this disease. The anti-diabetic effects of the extract can be a defense against diabetes organ complications (Ahmadpour et al. 2012).

Triterpenoids is gotten from Oleogum resins. Synthesis of DNA, RNA, and protein were inhibited in human leukemia (HL-60) using gum resin of *Boswellia serrata*. The most inhibition was caused AKBA. DNA synthesis was observed to be irreversible. There was no influence on cell viability (Alam et al. 2012).

According to studies, boswellic acids are potent apoptotic agents to cancer cells. In six human myeloid leukemia cell lines the boswellic acid acetate through a mediated pathway seems to induce apoptosis which is through the induction of the death receptors 4 and 5 is activated (Xia et al. 2005). AKBA anticancer activity to the inhibitory effect on the lipoxygenases which leads to the inhibition of cell proliferation and induction of apoptosis in tumor cells (Raja et al. 2011).

Boswellia serrate inhibits the proliferation of prostate cancer cells. This is largely due to the presence of pentacyclic triterpenoids. AKBA also prevents the growth of factors such as vascular endothelial. This inhibits cancer growth. Tirucallic acid, extracted from oleogum resin of *Boswellia carterii*, is also an effective inhibitor. It applies its cytotoxic effect on human prostate cancer cell lines in vitro and in vivo. Akt, a serine/threonine protein kinase, plays a vital role in several cell processes. These include proliferation, transcription, apoptosis, and migration. (Siddiqul et al. 2011).

It has been thought overtime that frankincense improves both learning and memory especially in the elderly and pregnant women for their offspring (Hosseini et al. 2010). During gestation period, aqueous extract of *Boswellia serrata* was administered. It showed a significant increase in learning at post-learning stage (Sharifabad et al. 2004)

A part of the brain called Hippocampus is important in learning and memory. In rats whose mothers were treated with *Boswellia serrata* extracts, there was an expansion of their terminal dendritic branches. This is important as it serves as a means for information transfer. The control group did not show this expansion. The increase of hippocampal neurons in cornu ammonis is due to improved learning and memory performance in these offspring. This opens an avenue for studying the neurophysiology and future of frankincense in brain diseases (Sharifabad and Esfandiari 2007).

5. CONCLUSION

The use of frankincense for therapeutic purposes continues from ancient times and now in modern medicine. The traditional use gives vital information for its bioactivity. However, modern medicine needs scientific evidence to establish this. This would help move its discussion from an experienced-based medicine to a more durable evidence-based one.

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