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FRANKINCENSE STYRAX SPECIES OF ANTI-INFLAMMATORY IN WOUND

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Abstract

Styrax plants, belonging to the styraceae family, were extensively utilized in different ancient societies. The ancient Egyptians employed frankincense for addressing fever, colds, asthma, and hemostasis. It was also used for various purposes, such as treating urinary tract infections, respiratory issues, gynecological concerns, and skin ailments. There is much scientific research on its anti-inflammatory effects to support its ethnopharmacological use. In this review, the efficacy of four Styrax species, namely: S. Japonica A-E (1–5). S. Boswellia sacra, S. tonkinences;S. benzoin. This review article aims to provide a comprehensive view of the potential of the Frankincense Styrax species and its active compounds so that they can be used and developed further for wound treatment in the future. The method used is through literature searches first collected from searches using the Google Scholar, PubMed and Scopus sites. The keywords used in this search were "Styrax, pharmacological effects, anti-inflammatory, wounds, burns". The findings indicate that active components found in Frankincense Styrax Species are cinnamic acid, benzoic acid, benzaldehyde, benzyl benzoate, vanillin, styrene, styracin, coniferyl benzoate among others. This substance is recognized for its diverse pharmacological properties, which encompass antibacterial, anesthetic, anti-inflammatory, antispasmodic, antimutagenic, fungicide, herbicide effects. Additionally it acts as a tyrosinase inhibitor and inhibits LDL synthesis. Based on this research, it can be inferred that Frankincense Styrax Species shows promise for treating a variety of illnesses. The research extensively investigates the anti-inflammatory characteristics of styrax species and discusses potential future research paths and outlooks for utilizing plants as suppliers of anti-inflammatory substances. The majority of the pharmacological studies on assessing the anti-inflammatory impacts were conducted using extracts from styrax species in both laboratory and animal experiments. Among all the studied styrax species, S. boswellia stands out as the most thoroughly researched in terms of its anti-inflammatory effects.

Keywords: Frankincense, Styrax Species, Wound Healing, Inflammation, Infection, Burn.

INTRODUCTION

Wound healing is a complex process that involves the interaction of cells and molecules to restore tissue layer structures[52]. During the inflammatory phase of wound healing, various cells, such as neutrophils and macrophages, are recruited to the site of injury to remove debris and prevent infection. They release inflammatory mediators and growth factors that promote the migration of fibroblasts and endothelial cells, which are crucial for the next phase of proliferation [3].

Wound recovery is an intricate procedure that entails the interplay of cells and substances to repair tissue layers. In the inflammatory stage of wound healing, different cells, like neutrophils and macrophages, are called upon at the injury site to clear away debris and thwart infection [39, 18, 7]. Inflammatory mediators and growth factors they produce stimulate the movement of fibroblasts and endothelial cells, which

are essential for the succeeding proliferation phase[65, 8, 3]. This is then followed by the arrival of different types of inflammatory cells, beginning with the neutrophil. These cells release various mediators and cytokines to encourage angiogenesis, thrombosis, and reepithelialization. The fibroblasts go on to deposit extracellular components that will function as scaffolding [65, 8, 26, 57]. The inflammatory phase is characterized by hemostasis, chemotaxis, and increased vascular permeability, limiting further damage, closing the wound, removing cellular debris and bacteria, and fostering cellular migration. The duration of the inflammatory stage usually lasts several days. Frankincense, an aromatic resin, is obtained from trees in the genus Boswellia. It has been used for thousands of years in traditional medicine and religious ceremonies [44, 21, 9]. Boswellic acids, the active compounds in frankincense, have been widely studied for their anti-inflammatory effects. Frankincense has been used in the treatment of various inflammatory conditions, including as an anti-inflammatory agent in wound care. It is thought to reduce inflammation by inhibiting certain enzymes, like 5-lipoxygenase, and preventing the production of leukotrienes [9, 17, 21]. Frankincense, with its anti-inflammatory properties and ability to inhibit certain enzymes, has the potential to be an effective supplementary treatment for burn injuries [51].

Styrax belongs to a distinct group of trees that produces a resin known as benzoin. Certain species, such as Styrax benzoin, are utilized for the production of this resin with well-documented antiseptic and anti-inflammatory properties. The therapeutic effects of benzoin resin are attributed to compounds like cinnamic acid and benzoic acid present within it [22]. The use of Styrax benzoin resin, with its antiseptic and anti-inflammatory properties, may provide therapeutic benefits in the treatment of burn injuries.

In the context of wound healing, an anti-inflammatory agent like frankincense or Styrax resin can help to minimize inflammation, which is a natural part of the wound healing process [1, 61, 21, 19]. However, excessive inflammation can impede healing and lead to complications like scarring. By moderating the inflammatory response, these resins can support the healing process, reduce pain, and improve the overall outcome of wound care [45].

To conclude, Styrax have been used as anti-inflammatory agents, research into their use, particularly for wound healing [68], would involve investigating their effects on the inflammatory pathway and tissue repair both in vitro [25] (e.g., in cultured cells) and in vivo (e.g., in animal models), as well as through clinical trials to establish their safety and efficacy in human patients. [59, 51]

Historical Use: In the traditional Indian medicine, frankincense has been used to help with inflammation, arthritis, cell growth control, and pain relief in the treatment of connected illnesses [16, 54, 19]. Frankincense from Boswellia carterii is frequently utilized in traditional Chinese medicine to enhance blood flow and alleviate discomfort associated with conditions like leprosy, gonorrhea, and cancer. [19]. Frankincense has also been part of the cultural and religious customs of early societies such as the Egyptians, Greeks, Romans, and Babylonians. It was commonly used as incense in sacred ceremonies [16, 38, 19].

It has been noted that the use of frankincense in European countries has increased in the last decade, particularly for treating chronic inflammatory problems like arthritis, chronic bowel diseases, and asthma [1, 54, 19].

The review of Frankincense would explore its diverse roles in such traditional medical systems and how these historical uses have led to its consideration in modern phytotherapy [4, 38 54].

The text outlines the goal and extent of the examination of Frankincense, which is to explore its traditional medicinal roles and assess its potential for modern medical use. This includes a specific emphasis on its anti-inflammatory properties and its application in managing burn wounds [62, 18 4, 19].

Frankincense sap that comes out of the tree trunk

Figure 1: Frankincense Tree

Pathophysiology Wound

The pathophysiology of wound healing is a complex series of events that occurs in four stages: hemostasis, inflammation, proliferation, and remodeling to repair tissue after injury. [56, 48, 29]

Hemostasis: During hemostasis, immediately after an injury, the body works rapidly to halt bleeding through blood vessel constriction and clot formation, involving platelets and a coagulation cascade. Serotonin and prostacyclin A2 released by cell membranes signal vasoconstriction, while the coagulation cascade responds to collagen exposure by depositing thrombin and fibrin clots, creating a barrier against infection and a scaffold for future cytokine activity important for later healing stages. [23 31] Wound dressings have evolved through the years and have come a long way, 2021 [36 51, 60]. Different factors can affect this intricate process, including the type of wound (incisional, excisional, acute, or chronic), the presence of underlying conditions like diabetes or vascular disease, and the individual's overall health status [46]. In chronic wounds, the healing process is disrupted, leading to prolonged inflammation and improper tissue repair.

The inflammatory: response in wound healing starts concurrently with hemostasis, characterized by signs like swelling, pain, and edema. It's driven by inflammatory cells that infiltrate the wound within 24 hours, including leukocytes, neutrophils, and Langerhans cells. They release cytokines such as IL-1 β, TNF-α, and IFN-γ, which enable repair by breaking down fibrin and promoting angiogenesis and re-epithelialization. [15,14]. By 48 hours, monocytes join and aid in debris clearance, while macrophages secrete growth factors, fueling new tissue growth by stimulating fibroblasts and keratinocytes. [5, 42, 15, 47]. These cells are pivotal for the transition to the proliferative phase, fostering granulation tissue formation. As inflammation resolves, fibroblasts build an extracellular matrix, laying the groundwork for new tissue and epithelial cell replacement of damaged cells. [47].

Proliferation: During the proliferative phase, commencing 2–10 days post-injury [5], Fibroblasts synthesize collagen and extracellular matrix, while endothelial cells undertake angiogenesis to form new vessels, collectively contributing to granulation tissue and wound coverage [28, 10, 59]. This stage encompasses wound contraction, fibroplasia, neovascularization, and re-epithelialization, leading to wound closure. Endothelial cells, lymphocytes, and versatile pericytes, which can differentiate into various cell types, actively participate. Ultimately, keratinocytes rebuild the basal membrane, progressing to a stratified epidermis following successful reepithelialization. [51, 15, 2] .

Remodeling or Maturation: In the remodeling or maturation phase, the wound tissue strengthens as collagen realigns and the extracellular matrix is refined, improving tensile strength. [55, 35]. This phase, starting 2-3 weeks post-injury, can extend over a year, involving cellular and molecular dynamics with various growth factors and cytokines to restore tissue integrity. [15] Wound Healing and Scar Tissue Formation: New Mechanical Insights, 2023 [53, 32]. Scar tissue formation replaces the original tissue, with shorter healing times linked to reduced fibrosis. Full or partial-thickness wounds that do not regain functionality or show healed characteristics within 6 weeks may develop into chronic wounds. [52, 20]

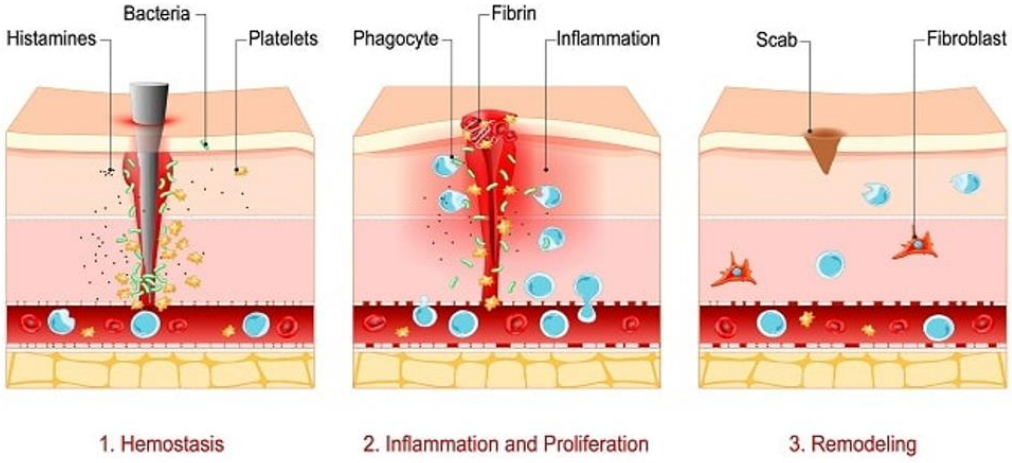

Figure 2: Proces Inflammation

Traditional Use of Frankincense in Medicine

Moreover, frankincense works through various mechanisms, including the suppression of leukotriene production and modulation of immune cells, which contribute to its anti-inflammatory effects. [9]. It has been shown to be effective in treating various conditions, such as osteoarthritis, multiple sclerosis, and asthma, without the typical side effects of traditional anti-inflammatory medications. It's important to mention that although frankincense is generally considered safe, there may still be potential for negative effects. Additional research could reveal more information about its toxicology, particularly with prolonged use or in specific groups like pregnant or breastfeeding women, children, and individuals with existing health issues.

Burn injuries can cause extensive effects on well-being, spanning from immediate physical outcomes to long-term physiological and psychological implications. The discussion of burns and their influence on health would involve the following elements [34, 49].

The Major Aspects of this Treatment are:

Initial management: inflammation is first addressed by providing ample fluids to counter the fluid loss from burn wounds and protect against shock. Wound Care: Burn injuries are often cleaned and treated with topical antimicrobial agents to prevent infection and promote a moist wound healing environment. Specialized dressings may also be used to administer medications or create ideal conditions for healing. Medications: Anti-inflammatory drugs like nonsteroidal anti-inflammatory medications are sometimes recommended for pain and inflammation management. Stronger pain relievers, such as opioids, may be necessary in certain situations to control pain.

Antibiotics: In cases of infection or high risk of infection, antibiotics are prescribed. Sepsis, a serious systemic reaction to infection, requires prompt treatment with intravenous antimicrobial therapy. Nutritional Support: Nutrition is essential for controlling inflammation and supporting the healing process. Burn patients typically require more calories because their bodies enter a hypermetabolic state due to the burn injury.

New treatments for inflammation caused by burns are comprehensive and varied, encompassing acute medical care, extended rehabilitation, and psychological assistance. Despite progress in burn care, ongoing research is focused on developing improved therapies and technologies to enhance results. This includes investigating the potential anti-inflammatory properties of natural products such as Frankincense.

Frankincense, scientifically called Boswellia species, has a long-standing tradition in traditional medicine in different societies. It is derived from the resin of Boswellia trees and is cherished for its fragrance as well as its healing properties.

Anti Inflamatory Effect Frankincense of Styrax Species

Styrax japonica

Belonging to the Styrax genus, Styrax japonicus Siebold & Zucc, is found in abundance across eastern Asia and China. Traditional Chinese medicine has utilized flower extracts of S. japonicus as a remedy for various discomforts, including toothaches and sore throats. Additionally, it is recognized for its potential as a source of high-quality honey due to the characteristics of its nectar [21]. Additionally, it has a decorative appeal with beautiful white flowers that are bell-shaped. Recent research on S. Japonicus has found that the primary chemical compounds are lignans, which include dibenzylbutane, furofuran, tetrahydrofuran, and benzofuran lignans. These lignans demonstrate diverse pharmacological effects like antioxidant, antifungal, and anti-inflammatory properties. Moreover, active compounds with biological properties are still being discovered in S. japonicus. Notable instances include jegosaponin A and B, which demonstrate the ability to break down red blood cells in prostate cancer cells. Additionally, jegosaponin A has calming, anxiety-reducing, and pain-relieving effects [21].

The new Lima lignan compounds from Styrax japonicas Siebold & Zucc. leaves, named Styraxjaponica A-E (1–5), together with eight known compounds (6–13), were isolated and characterized through extensive analysis including 1D and 2D NMR spectroscopy, UV, IR, HRESIMS, and comparison with literature. The absolute configuration of the new compounds was further determined using quantum chemistry electronic circular dichroism calculations supported by time-dependent density functional theory. Additionally, the anti-inflammatory effects of compounds 1–5 in LPS-induced RAW 264.7 cells were also assessed by measuring nitric oxide concentration. All the compounds demonstrated significant anti-inflammatory activity without affecting cell viability in vitro (May, 2021). Furthermore, compound 4 was determined to be the most potent candidate in its NO inhibitory effect at a concentration of 50 mM. Thus, this research can provide a fundamental basis for the development and utilization of S. japonicus for the treatment of inflammation.

Styrax Tonkinensis

Research on plant species such as Styrax continesis often includes the isolation and identification of active compounds found in the plant's extracts. These compounds are then tested for potential biological activity, including anti-inflammatory properties [6, 8]. The initial phase usually involves conducting in vitro assays to examine how these compounds affect cultured cells or enzymes related to inflammation (e.g., COX or LOX enzymes). If positive outcomes are detected, further studies may involve animal models to explore the effects on inflammation and wound healing through in vivo

experiments. Various research studies have investigated the anti-inflammatory properties of medicinal plants, such as Boswellia species and Styrax japonica.

Siam benzoin, also called Styrax tonkinensis or Vietnamese benzoin, is a tree native to Southeast Asia. It is primarily known for producing benzoin resin, which has long been used in medicine, incense, and perfumery [68, 57]. The tree's bark is tapped to extract the resin, which has a pleasant scent similar to vanilla and is highly valued in the perfume industry. It has been used for its potential antiseptic, anti-inflammatory, and expectorant properties in medical applications. In traditional medicine, it has also been employed to alleviate respiratory issues, skin problems, and wounds because of its calming and curative qualities [54, 24]. Styracin is a key component of the resin made by Styrax tonkinensis, along with benzoic acid, cinnamic acid, and benzyl cinnamate, potentially adding to its medicinal benefits. [68]

Research was conducted about nine previously undescribed pairs of enantiomers, (±)-styr axoids A−I, of Styrax tonkinensis resin, and their structures were fully characterized, including their absolute configurations, by spectroscopic and quantum chemical computational methods. Compound 7 was prepared with a 1,3-dioxane group, and compounds 8 and 9 contained a 1,3-dioxolane group. The results showed that both enantiomers of 1 could inhibit LPS-induced iNOS and COX-2 in RAW264.7 cells in a dose-dependent manner. This isolation provides previously undescribed insights into the chemical profile of S. tonkinensis resin beyond the well-investigated structural types, such as lignans and triterpene favonoids, and suggests their potential role in enhancing LPS-induced inflammation..

Styrax Boswellia

Boswellia: This plant family is famous for producing frankincense, a resin with strong anti-inflammatory effects. The key active compounds found in Boswellia resin are boswellic acids. Research has investigated the potential of Boswellia in reducing inflammation through both laboratory and animal studies [4, 26]. This has sparked interest in using it to potentially treat inflammatory conditions such as arthritis and certain inflammatory bowel diseases. Frankincense, a resin extract from trees of the Boswellia genus, has been utilized for centuries in cultural rituals, as a cosmetic ingredient and as a traditional remedy for various ailments, particularly inflammatory diseases including asthma, arthritis, cerebral edema, chronic pain syndrome, chronic bowel disease, cancer, and numerous other conditions. The active compound found in frankincense is boswellic acid, with AKBA (3-O-acetyl-11-keto-β-boswellic acid) being the most essential and potent among them [19]; [4, 24, 9]. According to certain research, frankincense has the potential to enhance learning and memory in both animals and humans. This suggests that it could serve as a natural alternative medicine for inflammatory conditions, chronic diseases, as well as brain and memory disorders [9, 54]. Burn injuries can have a significant impact on health by causing pain, tissue damage, and potential complications such as infections and scarring.

Research has mainly concentrated on the anti-inflammatory effects of boswellic acids found in Boswellia species, particularly their ability to inhibit 5-lipoxygenase [4, 50]. This enzyme is involved in the production of leukotrienes, which are known to contribute to inflammation [26] Additionally, they may prevent the infiltration of inflammatory cells into damaged tissue, reduce cytokine production, and protect against oxidative stress.

Clinical trials and drug research on Boswellia types have shown promising advantages for conditions like osteoarthritis, rheumatoid arthritis, asthma, and inflammatory bowel

disease [44]. For instance, certain studies have indicated decreased pain and enhanced movement in osteoarthritis patients who used boswellic acid supplements. Other areas of focus involve exploring the potential neuroprotective and anticancer properties of these substances. Frankincense and its ingredients have significant anti-inflammatory and analgesic effects in vitro and in vivo when different-induced models of inflammation and pain are used. Their effects are due to various mechanisms [9, 16]. For example, they can suppress pro-inflammatory cytokines such as interleukin (IL)− 1β and tumor necrosis factor (TNF)-α or inhibit the overexpression of cyclooxygenase-2 (COX-2) and prostaglandins, leading to suppression of leukotriene generation. Both Styrax and Boswellia resins' anti-inflammatory effects continue to be an area of active research.

Styrax Benzoin

The Frankincense tree, also known as Styrax Benzoin, belongs to the Styracaceae family and is commonly found in subtropical or tropical regions [68, 50, 21]. This tree has been grown for more than 200 years and is utilized for a range of uses, including religious rituals, raw materials for cosmetics, and traditional as well as modern medicinal treatments [6, 8]. Frankincense is frequently utilized as a preservative and scent in fragrance, soap, and cosmetics, as well as as an astringent flavoring in food, alcoholic beverages, and soft drinks. In Indonesia, the frankincense tree is widely found on the island of Sumatra and is also known by the name Sumatra Benzoin. Frankincense (Styrax benzoin) contains levels of phenolics and flavonoids that are a benchmark for its antioxidant activity. Styrax benzoin, which has a history of use in traditional medicine, Current scientific research on Styrax benzoin often examines its potential anti-inflammatory effects among other medicinal properties [21].

Research on Styrax benzoin typically involves the following steps: phytochemical analysis: identifying the compounds present in the resin. These often include benzoic acid, coniferyl benzoate, and cinnamic acid, known for their potential antimicrobial and anti-inflammatory effects. In vitro studies: testing extracted compounds or resins on cell cultures to observe their effects on inflammatory markers or pathways. For example, researchers might evaluate the impact of these compounds on enzymes like cyclooxygenase and lipoxygenase, which are critically involved in the inflammation process. In vivo Studies: Using animal models to study the efficacy and safety of the resin or specific compounds in reducing inflammation. Such studies might induce an inflammatory response in animals to then treat with the resin and observe the effects. Clinical Trials: If preclinical tests suggest both efficacy and safety, researchers might conduct clinical trials with human subjects to further explore the potential of Styrax benzoin resin for treating inflammatory conditions.

Pharmacological Effects of Styrax benzoin Frankincense Resin. Several studies have reported that cinnamic acid exhibits antioxidant, antimicrobial, anticancer [57], neuroprotective, anti-inflammatory and antidiabetic properties. The vanillin compound has a role as an anti-inflammatory, flavoring, antioxidant and anticonvulsant, in their research also stated that the synthesis of silver nanoparticles (AgNPs) of frankincense extract has antimicrobial, antibiofilm, antioxidant and anticancer activity.

Future Perspectives

The potential for additional investigation into the application of Frankincense in treating burn injuries is substantial, given its traditional use and some initial evidence pointing to its healing properties [24, 27, 37]

Further investigation could explore the distinct mechanisms through which Frankincense generates its anti-inflammatory and therapeutic effects, with the goal of improving its utilization in treating burns. [40, 13, 38] 5 Benefits and Uses of Frankincense — and 6 Myths, 2021). Rigorously planned randomized clinical trials are crucial to establish definitive proof of the effectiveness and safety of Frankincense in treating burns in humans. Research could center on creating consistent formulations of Frankincense that guarantee uniform quality and therapeutic impact. Directly comparing Frankincense with conventional burn treatments could help establish the position of Frankincense in the current treatment paradigm. [41, 54, 11, 43, 50, 4].

The unique bioactive compounds found in Frankincense, particularly boswellic acids, present the possibility of developing new treatments or products tailored for specific therapeutic uses. Here's a breakdown of this potentiality:Boswellic acids found in Frankincense have powerful anti-inflammatory properties, which could be utilized to develop topical treatments for alleviating inflammation in conditions such as burns, arthritis, and specific skin disorders. [44, 22, 26, 50] .

Additionally, evidence suggests that Frankincense's positive effects on brain tumor-related edema could inspire the creation of products aimed at managing cerebral edema or other neuroprotective needs. [9, 24]

Enhancing Drug Formulations: The compounds found in frankincense could be incorporated into current medication formulas to improve effectiveness or minimize adverse effects. For example, they could be used for their anti-inflammatory properties alongside other pain relievers or antiseptics for treating burns. There is potential to create dermatological products that make use of the therapeutic benefits of Frankincense, as there is evidence backing its effectiveness in conditions such as psoriasis, eczema, and plaque-induced gingivitis. gingivitis.[27, 16, 20 13, 54, 6]. Overall, there is great potential for the advancement of new treatments using compounds from Frankincense, driven by its long-standing medicinal use and the increasing scientific knowledge about its biological effects.

CONCLUSION

Frankincense contains active compounds like boswellic acids which showcase significant anti-inflammatory properties that may be beneficial in burn treatment. Its main actions include [13] Spiritual Centering with [13]; [12] reducing inflammation, inhibiting cell growth, managing cerebral edema, enhancing drug formulations, and potentially treating skin conditions [30] : Inhibiting enzymes that fuel inflammation, such as 5-lipoxygenase and cyclooxygenase, potentially reducing the inflammatory response in burn injuries. Modulating the immune system, which could decrease the production of pro-inflammatory cytokines and other inflammation-promoting agents. Offering antioxidant qualities that reduce oxidative stress, promoting wound healing and recovery from burns. Providing analgesic effects that may alleviate pain associated with burns by curbing the inflammation that contributes to pain sensation. Supporting the wound healing process by creating a more favorable environment for tissue repair, which is particularly useful for burn injuries.

Research highlights Frankincense’s potential in treating burns, but rigorous human clinical trials are necessary to verify its benefits and establish its role in burn treatment. Looking ahead, the efficacy of Frankincense could: Integrate natural products into conventional burn treatment regimens. Enhance personalized medicine with

alternative treatment options. Offer a cost-effective solution for burn care, especially in resource-limited settings. Serve in preventive care to reduce inflammation and pain severity at the start of burn treatment. Encourage a holistic approach to patient care by incorporating alternative treatments. Future exploration of Frankincense could lead to innovative burn care treatments, but it is essential that clinical evidence supports its safety and efficacy before it's integrated into clinical practice.

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References

1) Badria, F A. (2015, February 4). Frankincense (Heaven's Gift) — Chemistry, Biology, and Clinical Applications. https://doi.org/10.5772/59006

2) Banavar, S P., & Nelson, C M. (2023, November 24). Mechanical properties pattern the skin. https://www.science.org/doi/10.1126/science.adl2004

3) Bayani, A., Dunster, J L., Crofts, J J., & Nelson, M R. (2020, March 28). Mechanisms and Points of Control in the Spread of Inflammation: A Mathematical Investigation. Springer Science+Business Media, 82(4). https://doi.org/10.1007/s11538-020-00709-y

4) Börner, F., Werner, M., Ertelt, J., Meins, J L., Abdel-Tawab, M., & Werz, O. (2021, July 10). Analysis of Boswellic Acid Contents and Related Pharmacological Activities of Frankincense-Based Remedies That Modulate Inflammation. https://doi.org/10.3390/ph14070660

5) Budovsky, A., Yarmolinsky, L., Ben-Shabat, S., 2015. Effect of medicinal plants on wound healing. Wound Repair Regen. 23 (2), 171–183. https://doi.org/10.1111/wrr.12274

6) Burns - Knowledge @ AMBOSS. (2022, August 17). https://knowledge.manus.amboss.com/us/knowledge/Burns#Z15cc8b2f826f698033d18de14873b275

7) Chen, J., Lin, B., Hu, H., Lin, C., Jin, W., Zhang, F., Zhu, Y., Lu, C., Wei, X., & Chen, R. (2014, January 1). NGF Accelerates Cutaneous Wound Healing by Promoting the Migration of Dermal Fibroblasts via the PI3K/Akt-Rac1-JNK and ERK Pathways. https://doi.org/10.1155/2014/547187

8) Desmoulière, A., Darby, I A., Laverdet, B., & Bonté, F. (2014, November 1). Fibroblasts and myofibroblasts in wound healing. https://doi.org/10.2147/ccid.s50046

9) Efferth, T., & Oesch, F. (2022, May 1). Anti-inflammatory and anti-cancer activities of frankincense: Targets, treatments and toxicities. Elsevier BV, 80, 39-57. https://doi.org/10.1016/j.semcancer.2020.01.015

10) Ellis, S R., Lin, E J., & Tartar, D M. (2018, September 28). Immunology of Wound Healing. https://doi.org/10.1007/s13671-018-0234-9

11) El-Mancy, S S., El-Haddad, A E., Alshareef, W A., Saadeldeen, A M., El-Emam, S Z., & Elnahas, O S. (2021, August 2). Enhancement of Antimicrobial and Antiproliferative Activities of Standardized Frankincense Extract Using Optimized Self-Nanoemulsifying Delivery System. https://doi.org/10.3390/scipharm89030036

12) Essential Oils: Frankincense (Boswellia). (2018, October 5). https://www.drweil.com/health-wellness/balanced-living/healthy-living/frankincense/

13) Frankincense - the resin with healing power. (2021, May 27). https://dermaviduals.de/english/publications/special-actives/frankincense-the-resin-with-healing-power.html

14) Frangogiannis, N G. (2017, October 31). The Inflammatory Response in Tissue Repair. https://doi.org/10.1002/9783527692156.ch60

15) Gonzalez, A.C.O., Costa, T.F., Andrade, Z., Medrado, A.R.A.P., 2016. Wound healing - a literature review. An. Bras. Dermatol. 91 (5), 614–620. https://doi.org/10.1590/abd1806-4841.20164741

16) Hakkim, F L., Bakshi, H A., Khan, S S., Nasef, M., Farzand, R., Sam, S., Rashan, L., Al-Baloshi, M S., Hasson, S S., Jabri, A A A., McCarron, P A., & Tambuwala, M M. (2019, May 28). Frankincense essential oil suppresses melanoma cancer through down regulation of Bcl-2/Bax cascade signaling and ameliorates heptotoxicity via phase I and II drug metabolizing enzymes. https://doi.org/10.18632/oncotarget.26930

17) Habiboallah, G., Mahdi, Z., Majid, Z., Saghravanian, N., Taghavi, A M., Forouzanfar, A., & Arjmand, N. (2014, January 1). Enhancement of Gingival Wound Healing by Local Application of Silver Nanoparticles Periodontal Dressing Following Surgery: A Histological Assessment in Animal Model. https://doi.org/10.4236/mri.2014.33016

18) Halim, S A., Khan, A., Csük, R., Al-Rawahi, A., & Al-Harrasi, A. (2020, June 25). Diterpenoids and Triterpenoids From Frankincense Are Excellent Anti-psoriatic Agents: An in silico Approach. https://doi.org/10.3389/fchem.2020.00486

19) Hamidpour, R., Hamidpour, S., Hamidpour, M., & Shahlari, M. (2013, October 1). Frankincense (乳香 Rǔ Xiāng; Boswellia Species): From the Selection of Traditional Applications to the Novel Phytotherapy for the Prevention and Treatment of Serious Diseases. Elsevier BV, 3(4), 221-226. https://doi.org/10.4103/2225-4110.119723

20) Han, X., Rodriguez, D., & Parker, T L. (2017, June 1). Biological activities of frankincense essential oil in human dermal fibroblasts. https://doi.org/10.1016/j.biopen.2017.01.003

21) He, Q., Sun, Y., Chen, X., Feng, J., & Liu, Y. (2023, May 14). Benzoin Resin: An Overview on Its Production Process, Phytochemistry, Traditional Use and Quality Control. https://doi.org/10.3390/plants12101976

22) Henkel, A., Tausch, L., Pillong, M., Jauch, J., Karas, M., Schneider, G., & Werz, O. (2015, December 1). Boswellic acids target the human immune system-modulating antimicrobial peptide LL-37. https://doi.org/10.1016/j.phrs.2015.09.002

23) How Wounds Heal: The 4 Main Phases of Wound Healing. (2015, December 18). http://www.shieldhealthcare.com/community/news/2015/12/18/how-wounds-heal-the-4-main-phases-of-wound-healing/

24) Hu, D., Wang, C., Li, F., Su, S., Yang, N., Yang, Y., Zhu, C., Shi, H., Yu, L., Geng, X., Gu, L., Yuan, X., Wang, Z., Yu, G., & Tang, Z. (2017, January 1). A Combined Water Extract of Frankincense and Myrrh Alleviates Neuropathic Pain in Mice via Modulation of TRPV1. https://doi.org/10.1155/2017/3710821

25) Ibrahim, N '., Wong, S K., Mohamed, I N., Mohamed, N., Chin, K., Ima-Nirwana, S., & Shuid, A N. (2018, October 25). Wound Healing Properties of Selected Natural Products. https://doi.org/10.3390/ijerph15112360

26) Jamshidi-Adegani, F., Vakilian, S., Al-Kindi, J., Rehman, N U., Alkalbani, L., Al-Broumi, M., Alwahaibi, N., Shalaby, A., Al-Sabahi, J N., Al-Harrasi, A., & Al-Hashmi, S. (2022, July 1). Prevention of post-surgical adhesion bands by local administration of frankincense n-hexane extract. https://doi.org/10.1016/j.jtcme.2021.10.004

27) Jiang, X., Ma, J., Wei, Q., Feng, X., Qiao, L., Liu, L., Zhang, B., & Yu, W. (2016, January 1). Effect of Frankincense Extract on Nerve Recovery in the Rat Sciatic Nerve Damage Model. https://doi.org/10.1155/2016/3617216

28) Johnson, K E., & Wilgus, T A. (2014, October 1). Vascular Endothelial Growth Factor and Angiogenesis in the Regulation of Cutaneous Wound Repair. https://doi.org/10.1089/wound.2013.0517

29) Kangal, M K O., & Regan, J. (2022, May 8). Wound Healing. https://www.ncbi.nlm.nih.gov/books/NBK535406/

30) Kaneria, M J., Rakholiya, K., & Chanda, S. (2017, January 1). Role of Medicinal Plants and Bioactive Compounds Against Skin Disease–Causing Microbes, With Special Emphasis on Their Mechanisms of Action. Elsevier BV, 255-269. https://doi.org/10.1016/b978-0-12-811079-9.00015-x

31) Khoshmohabat, H., Paydar, S., Kazemi, H., & Dalfardi, B. (2016, February 6). Overview of Agents Used for Emergency Hemostasis. https://doi.org/10.5812/traumamon.26023

32) Leavitt, T., Hu, M S., Marshall, C D., Barnes, L A., Lorenz, H P., & Longaker, M T. (2016, June 2). Scarless wound healing: finding the right cells and signals. https://doi.org/10.1007/s00441-016-2424-8

33) Li, J., Tan, J L., Martino, M M., & Lui, K O. (2018, March 23). Regulatory T-Cells: Potential Regulator of Tissue Repair and Regeneration. https://doi.org/10.3389/fimmu.2018.00585

34) Mason, S A., Nathens, A B., Byrne, J P., Diong, C., Fowler, R A., Karanicolas, P J., Moineddin, R., & Jeschke, M G. (2019, June 5). Increased Rate of Long-term Mortality Among Burn Survivors: A Population-based Matched Cohort Study.. https://journals.lww.com/00000658-201906000-00028

35) Marshall, C D., Hu, M S., Leavitt, T., Barnes, L A., Lorenz, H P., & Longaker, M T. (2018, February 1). Cutaneous Scarring: Basic Science, Current Treatments, and Future Directions. https://doi.org/10.1089/wound.2016.0696

36) Medstock. (2015, December 18). https://medstock123.tumblr.com/tagged/woundcare

37) Mirshafiei, M., Yazdi, A., & Beheshti, S. (2023, January 1). Neuroprotective and anti-neuroinflammatory activity of frankincense in bile duct ligaion-induced hepatic encephalopathy.. https://doi.org/10.22038/ijbms.2023.68775.14991

38) Morikawa, T., Matsuda, H., & Yoshikawa, M. (2017, January 1). A Review of Anti-inflammatory Terpenoids from the Incense Gum Resins Frankincense and Myrrh. https://doi.org/10.5650/jos.ess1614

39) Neguț, I., Dorcioman, G., & Grumezescu, V. (2020, September 3). Scaffolds for Wound Healing Applications. https://doi.org/10.3390/polym12092010

40) New Study Finds How Frankincense Might Affect Inflammation. (2020, May 12). https://www.mindbodygreen.com/articles/how-and-why-frankincense-can-help-reduce-inflammation-according-to-new-research

41) Ning, Z., Wang, C., Liu, Y., Song, Z., Ma, X., Liang, D., Liu, Z., & Lü, A. (2018, December 18). Integrating Strategies of Herbal Metabolomics, Network Pharmacology, and Experiment Validation to Investigate Frankincense Processing Effects. https://doi.org/10.3389/fphar.2018.01482

42) Oishi, Y., & Manabe, I. (2018, August 25). Macrophages in inflammation, repair and regeneration. https://doi.org/10.1093/intimm/dxy054

43) Ojha, P K., Poudel, D K., Rokaya, A., Satyal, R., Setzer, W N., & Satyal, P. (2022, August 16). Comparison of Volatile Constituents Present in Commercial and Lab-Distilled Frankincense (Boswellia carteri) Essential Oils for Authentication. https://doi.org/10.3390/plants11162134

44) Oliver.werz@uni-tuebingen.de, D P O W. (n.d). Boswellic acids: biological actions and molecular targets.. https://www.eurekaselect.com/article/3226

45) Orhan, İ E., & Tümen, İ. (2015, January 1). Potential of Cupressus sempervirens (Mediterranean Cypress) in Health. Elsevier BV, 639-647. https://doi.org/10.1016/b978-0-12-407849-9.00057-9

46) Piraino, F., & Selimović, Š. (2015, January 1). Functional Biomaterials for Wound Care, Molecular and Cellular Therapies. http://downloads.hindawi.com/journals/bmri/2015/403801.pdf

47) Pereira, R.F., Bártolo, P.J., 2016. Traditional therapies for skin wound healing. Adv. Wound Care 5 (5), 208–229. https://doi.org/10.1089/wound.2013.0506

48) Przekora, A. (2020, July 6). A Concise Review on Tissue Engineered Artificial Skin Grafts for Chronic Wound Treatment: Can We Reconstruct Functional Skin Tissue In Vitro?. https://doi.org/10.3390/cells9071622

49) Randall, S M., Wood, F M., Rea, S., Boyd, J H., & Duke, J M. (2020, February 5). An Australian study of long-term hospital admissions and costs comparing patients with unintentional burns and uninjured people.. https://www.sciencedirect.com/science/article/pii/S0305417918308568

50) Schmiech, M., Lang, S J., Ulrich, J., Werner, K., Rashan, L., Syrovets, T., & Simmet, T. (2019, October 2). Comparative Investigation of Frankincense Nutraceuticals: Correlation of Boswellic and Lupeolic Acid Contents with Cytokine Release Inhibition and Toxicity against Triple-Negative Breast Cancer Cells. https://doi.org/10.3390/nu11102341

51) Serra, M.B., Barroso, W.A., da Silva, N.N., Silva, S., Borges, A., Abreu, I.C., Borges, M., 2017. From inflammation to current and alternative therapies involved in wound healing. Int. J. Inflamm. 3406215. https://doi.org/10.1155/2017/3406215. 2017

52) Shedoeva, A., Leavesley, D I., Upton, Z., & Fan, C. (2019, September 22). Wound Healing and the Use of Medicinal Plants. https://doi.org/10.1155/2019/2684108

53) Spielman, A., Griffin, M., Parker, J M R., Cotterell, A C., Wan, D C., & Longaker, M T. (2023, February 1). Beyond the Scar: A Basic Science Review of Wound Remodeling. https://doi.org/10.1089/wound.2022.0049

54) Su, S., Duan, J., Chen, T., Huang, X., Shang, E., Yu, L., Wei, K., Zhu, Y., Guo, J., Guo, S., Liu, P., Qian, D., & Tang, Y. (2015, September 2). Frankincense and myrrh suppress inflammation via regulation of the metabolic profiling and the MAPK signaling pathway. https://doi.org/10.1038/srep13668

55) Suzuki, S., & Ikada, Y. (2011, November 12). Biological Events Associated with Surgical Operation. Humana Press, 7-17. https://doi.org/10.1007/978-1-61779-570-1_2

56) Tito, A., Minale, M., Riccio, S., Grieco, F., Colucci, M., & Apone, F. (2020, January 1). A Triticum vulgare Extract Exhibits Regenerating Activity During the Wound Healing Process. https://www.dovepress.com/getfile.php

57) Wang, W., Zheng, B., Wu, J., Lv, W., Lin, P Y., & Gong, X. (2021, April 14). Determination of the Dissociation Constants of 16 Active Ingredients in Medicinal Herbs Using a Liquid–Liquid Equilibrium Method. Multidisciplinary Digital Publishing Institute, 8(4), 49-49. https://doi.org/10.3390/separations8040049

58) Wound dressings have evolved through the years and have come a long way. (2021, July 23). https://cmiblogging.blogspot.com/2021/07/wound-dressings-have-evolved-through.html

59) Wound Healing Phases. (2022, August 25). https://pubmed.ncbi.nlm.nih.gov/29262065/

60) Wound Physiology. (2022, May 21). https://www.ncbi.nlm.nih.gov/books/NBK518964/

61) Xia, D., Han, X., Yu, Z., & Zhang, N. (2023, July 22). Chemical Constituents and Their Biological Activities from Genus Styrax. https://doi.org/10.3390/ph16071043

62) Zhang, Y., Ning, Z., Lü, C., Zhao, S., Wang, J., Liu, B., Xu, X., & Liu, Y. (2013, September 12). Triterpenoid resinous metabolites from the genus Boswellia: pharmacological activities and potential species-identifying properties. https://doi.org/10.1186/1752-153x-7-153