Tamanu Oil in Acne Management: Potential Anti-Inflammatory and Wound-Healing Properties for Scar Reduction

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Keywords: Tamanu Oil, Calophyllum inophyllum, Acne Management, Anti-Inflammatory Properties, WoundHealing, Acne Scars, Erythema Reduction, Inflammation Reduction, Scar Reduction, Alternative Acne Therapies,Natural Acne Treatments, Dermatological Applications of Tamanu OilReceived: September 27, 2024Accepted: October 28, 2024Published: October 31, 2024

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ABSTRACT

Tamanu oil, derived from the nuts of *Calophyllum inophyllum*, has gained increasing attention for its potential in acne management due to its purported anti-inflammatory and wound-healing properties. This analysis evaluates the efficacy of tamanu oil in acne treatment with a specific focus on its impact on inflammation and scar reduction. The novelty of this research lies in its comprehensive analysis of tamanu oil's dual mechanism of action: reducing acne-related inflammation and promoting the healing of acne scars. Clinical trials and laboratory analyses were conducted to assess the oil's effectiveness in diminishing erythema, swelling, and postacne scarring compared to conventional treatments. Preliminary findings demonstrate that tamanu oil significantly reduces inflammation and accelerates wound healing, potentially offering a promising adjunct or alternative to standard acne therapies. Future research should aim to optimize formulation and application protocols, long-term effects, and comparative therapeutic efficacy with other anti-inflammatory agents. Tamanu oil offers a novel and effective approach to acne management, with potential advantages that go beyond inflammation reduction to include enhanced scar reduction, making it a subject that warrants further investigation.

1. INTRODUCTION

Acne vulgaris is the most common chronic skin condition in the United States, affecting nearly 50 million individuals annually, predominantly during adolescence and young adulthood [1]. The condition primarily affects the pilosebaceous follicles and emerges from a combination of factors, including excess sebum production, abnormal keratinization, colonization by *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*), and inflammation. This multifactorial etiology often leads to the development of various types of lesions, ranging from comedones (whiteheads and blackheads) to inflammatory papules, pustules, and more severe nodular or cystic lesions [2]. Acne can cause permanent scarring and exert profound psychosocial consequences, such as lowered self-esteem and increased risk of anxiety and depression [1]. Conventional treatments for acne include topical retinoids, benzoyl peroxide, antibiotics, and, in severe or refractory cases, oral isotretinoin. While these treatments are effective, they are often associated with significant side effects, including skin irritation, antibiotic resistance, and teratogenicity [1]. Given these limitations, there is a growing demand for alternative therapies that offer effective acne treatment with fewer and safer adverse effects.

Tamanu oil has been used for centuries in traditional medicine for the treatment of skin conditions like acne, eczema, and wounds [3]. The oil is rich in fatty acids, including oleic and linoleic acids, which are known to play a role in restoring the skin's barrier function and aiding in wound healing [4]. Moreover, tamanu oil contains bioactive compounds like calophyllolide, which has demonstrated potent anti-inflammatory effects by reducing pro-inflammatory cytokines, including IL-1 β , IL-6, and TNF-a, while promoting the release of IL-10, an anti-inflammatory cytokine [5]. These effects are particularly relevant in the context of acne, where inflammation plays a central role in lesion development. Additionally, tamanu oil has demonstrated antimicrobial activity, specifically against *C. acnes*, the bacterium implicated in acne pathogenesis [6]. This antimicrobial action can help prevent the proliferation of acne-causing bacteria, reducing the like-lihood of future breakouts and complementing tamanu oil's anti-inflammatory benefits to enhance skin healing.

Recent studies on tamanu oil have highlighted its potential in reducing acne-related inflammation as well as in promoting wound healing and reducing scar formation. These effects can be largely attributed to its antioxidant properties, which combat oxidative stress in the skin, stimulate collagen production, and enhance tissue regeneration [3]. These findings suggest that tamanu oil's broad antimicrobial and anti-inflammatory properties could offer a dual-action mechanism, addressing both active acne and post-inflammatory scarring by controlling acne symptoms and promoting healthier skin regeneration. This dual mechanism makes tamanu oil a promising alternative or adjunctive therapy for acne management. Given these promising properties and the gaps in current acne treatment methods, this review seeks to evaluate the efficacy of tamanu oil in reducing acne-related inflammation and promoting scar healing. In addition, the review will compare the effects of tamanu oil with conventional acne treatments to determine its potential as a safer, more natural option for acne management. We hypothesize that tamanu oil will significantly reduce acne inflammation, accelerate wound healing, and improve scar outcomes, offering a novel and effective solution for acne treatment.

2. LITERATURE REVIEW

Tamanu oil, derived from the nuts of the *Calophyllum inophyllum* tree, has a long history of use in traditional medicine, particularly in Southeast Asia and the Pacific Islands. Historically, it has been valued for its ability to heal wounds, soothe skin irritations, and treat various skin conditions [5]. The oil is rich in fatty acids, specifically oleic and linoleic acids, which are essential for maintaining skin hydration, supporting the skin's natural barrier function, and facilitating skin-repairing processes. Oleic acid, a monounsaturated fatty acid, enhances skin permeability, enabling deeper penetration of moisturizing agents. It also helps maintain skin softness and elasticity and supports wound healing by promoting cell regeneration. Linoleic acid, an essential polyunsaturated fatty acid, is a key component of the skin's lipid barrier. It helps retain moisture, reduces transepidermal water loss, and strengthens the skin's barrier function, which is vital for

preventing dryness and promoting overall skin health [4]. Together, these fatty acids contribute to tamanu oil's moisturizing and skin-repairing properties, making it an effective treatment for dry and damaged skin.

Beyond its moisturizing benefits, tamanu oil possesses potent antibacterial and anti-inflammatory properties. One of its key bioactive components is calophyllolide, a molecule with significant anti-inflammatory effects. It inhibits the production of pro-inflammatory cytokines and mediators, such as IL-1 β , IL-6, and TNF- α , which play a role in the inflammatory response. Additionally, calophyllolide has been shown to upregulate the activity of IL-10, an anti-inflammatory cytokine [5]. By modulating these pathways, calophyllolide, along with other constituents, enables tamanu oil to effectively combat inflammation, making it a potential treatment for inflammatory skin conditions like acne or dermatitis. Tamanu oil has also been found effective against *Propionibacterium acnes* and *Propionibacterium granulosum*, bacteria linked to acne formation [6]. By reducing bacterial presence and inflammation, tamanu oil offers a potential natural alternative to conventional acne treatments, providing an effective approach for managing and preventing acne breakouts.

Tamanu oil has garnered attention for its potent anti-inflammatory properties, particularly its ability to inhibit two key enzymes involved in inflammation: proteinase K (PTA) and lipid oxygenase (15-LOX). 15-LOX plays a role in the oxidation of arachidonic acids, leading to leukotriene production, while proteinase K is a serine protease enzyme, both of which are associated with inflammatory disorders of the skin [7]. Calophyllolide, the compound found in tamanu oil, has been shown to be involved in capillary permeability reduction in mice when induced by the inflammatory mediators histamine and bradykinin [8]. This reduction in permeability helps to limit fluid leakage and the swelling commonly associated with inflammation. Furthermore, calophyllolide causes a significant reduction in myeloperoxidase activity, which decreases the creation of reactive oxygen intermediates that further contribute to inflammation [3]. As ongoing research reveals the many anti-inflammatory properties of tamanu oil, it is essential to explore and further investigate its potential as a natural method for reducing inflammation.

Among tamanu oil's numerous benefits is its ability to accelerate wound healing. Due to high contents of tannins, flavonoids, saponins, alkaloids, naphthoquinones, and triterpenes, medicinal plants such as *Calophyllum inophyllum* have been widely studied in the improvement of wound healing [9]. Although the efficacies of various extraction methods have not been widely studied, the tamanu oil specifically extracted from the plant has shown considerable healing benefits. In experimental rat studies, those treated with tamanu oil exhibited significantly lower wound contraction compared to other groups [10]. Calophyllolide, calophyllic acid, and inophyllum have been shown to be responsible for this impressive impact on wound healing [11]. This is attributed to these components being correlated with a higher intensity of macrophage infiltration and mature granulation tissue formation [10]. These findings highlight tamanu oil's potential as a natural therapeutic agent for enhancing wound repair and tissue regeneration.

In addition to its numerous benefits for inflammation and wound healing, tamanu oil also supports the healing process by helping to reduce scarring. Although existing research studies are limited to the use of tamanu oil on scarring, tamanu oil is frequently used as an herbal aid to scar reduction [12]. The exact method of scar improvement is hypothesized to follow the same biochemical basis as wound healing. Topical application of tamanu oil may facilitate scar reduction by promoting wound closure in fibroblast and keratinocyte monolayers. Enhanced cell proliferation, along with increased collagen and glycosaminoglycan production, supports effective wound healing and helps minimize scarring [13]. Studies have shown that tamanu oil enhances cellular regeneration, which is critical in scar healing. Compared to controls, tamanu oil resulted in increased fibrosis and higher collagen density within the wound, further supporting its effectiveness in scar treatment [10]. Continued studies are necessary to fully understand its mechanisms, but current evidence points to tamanu oil as an effective natural treatment for both wound healing and scar minimization.

3. ACNE PATHOPHYSIOLOGY AND TREATMENT

Acne vulgaris is a prevalent chronic inflammatory skin condition that typically arises during adolescence

and can persist into adulthood. During puberty, elevated androgen levels, including dehydroepiandrosterone (DHEA) and dihydrotestosterone (DHT), stimulate increased sebum production [1]. Additionally, insulin-like growth factor 1 (IGF-1) suppresses Forkhead Box protein O1 (FoXO1), a transcription factor that typically downregulates androgen receptor transduction [14]. Excess sebum can hinder the natural shedding of dead keratinocytes, resulting in the accumulation of debris that clogs the hair follicle pores. This accumulation creates an environment that promotes the proliferation and overgrowth of acne-causing bacteria, such as *Cutibacterium acnes* [1]. Thus, a microcomedone is formed. If the blockage is superficial within the pore, melanin within the skin is exposed to air and oxidized, resulting in a dark-colored, open comedone (blackhead). If the microcomedone occurs deeper within the pore, a light-colored, closed comedone (whitehead) forms.

Inflammation plays a central role in the progression and severity of acne. Initially, comedones are primarily non-inflammatory. However, the subsequent involvement of *C. acnes* and the immune response lead to various inflammatory lesions. The transition from non-inflammatory comedones to inflammatory lesions, such as pustules and nodules, occurs when the follicular wall ruptures. This rupture allows keratin, sebum, and bacteria to enter the dermis, inciting a more pronounced inflammatory response. *C. acnes* promotes inflammation through Toll-like receptors 2 and 4 (TLR2 & TLR4) and Nod-like receptor 3 (NLRP3), causing the release of various inflammatory interleukins [14]. *C. acnes* also activates adaptive immunity using CD4+ T-cells, which release more inflammatory interleukins and interferons [14]. The degree of inflammation determines the likelihood of scarring.

Acne scarring arises from the body's attempt to repair damage caused by inflammation. Matrix metalloproteinases, which are upregulated by *C. acnes* and fibroblasts, determine the type of scarring [15]. Atrophic (depressed) scars, such as icepick, boxcar, and rolling scars, are the most common. They are caused by excess matrix metalloproteinases that remodel the extracellular matrix and degrade collagen during the healing process [15]. Conversely, hypertrophic (raised) scars occur when excess collagen is produced due to a lack of matrix metalloproteinase activity. The risk of scarring is higher in people of color and those with severe, inflammatory acne. Additionally, scarring can be exacerbated by behaviors that disrupt the healing process, such as picking or squeezing lesions. Early intervention to address inflammation and minimize these habit-forming behaviors is crucial in reducing the likelihood and severity of both atrophic and hypertrophic scars.

4. DISCUSSION

The therapeutic success of tamanu oil in treating various skin conditions in traditional Polynesian medicine can be explained by its potent anti-inflammatory, antioxidant, and antimicrobial properties. An analysis of tamanu oil found that linoleic acid and its derivatives account for over a quarter of its composition [16]. Linoleic acids contribute to the maturation and maintenance of the stratum corneum's permeability barrier [17], which can mitigate the risk of acne caused by toxins, debris, or compromised skin. This barrier function also helps ensure that the skin retains the proper amount of moisture, which can provide relief for patients whose acne presents alongside excessive dryness or oiliness. Tamanu oil also contains a high percentage of oleic and palmitic acid, both of which accelerate the production and release of β -defensin 2 from macrophages [6]. β -Defensin 2 acts as the immune system's natural antibiotic, disrupting the membranes of harmful gram-negative bacteria and inhibiting mitosis of gram-positive bacteria. Because of this, tamanu oil can enhance the skin's innate ability to identify and respond to bacterial infections, making it a possible treatment option for individuals who cannot tolerate topical or oral antibiotics like erythromycin.

Both *in vivo* and *in vitro* studies have observed tamanu oil's ability to decrease inflammation and neutralize free radicals. *In vivo* studies conducted on mice indicate that tamanu oil downregulates pro-inflammatory cytokines IL-6, TNF- α , and IL-1 β while upregulating the anti-inflammatory cytokine IL-10, which is essential for preventing and repairing immune-mediated tissue damage. In mouse models, these mechanisms resulted in reduced fibrosis and quick wound closure [5]. Because of this, patients with a history of slow wound healing or excessive scar formation may find tamanu oil effective in treating and preventing

inflammation associated with acne. *In vitro* studies on human cancer cells have shown that tamanu oil also exhibits significant antioxidant activity and modulates reactive oxygen species (ROS) levels [18]. Acne and many other skin conditions are associated with an imbalance in free radicals and the exogenous and endogenous systems that neutralize them [19]. Antioxidants play a crucial role in protecting skin cells from damage by helping them remain in a tissue-repairing state. By reducing oxidative stress and restoring this equilibrium, antioxidants can prevent the recurrence of acne breakouts. Thus, studies have found that administering small doses of topical antioxidants, when administered in concentrations that resemble physiological ones, reduces the risk of further aggravating the skin and proves most effective in the treatment of inflammatory skin conditions [19]. Given the role of antioxidants in inflamed skin, tamanu oil's antioxidative mechanisms demonstrate the potential to work synergistically with the endogenous anti-inflammatory pathways of skin cells while maintaining the delicate balance between free radical activity and antioxidant defense systems.

Flavonoids are phytochemicals that have shown pharmacological effects on cell signaling pathways [20]. Tamanu oil contains flavonoids, particularly bioactive neoflavonoids, that increase cell proliferation and the amount of collagen III in cells *in vitro* [21]. These neoflavonoids are also thought to influence tamanu oil's ability to modulate gene expression involved in M2-related macrophage skewing and O-glycan biosynthesis [5, 13]. The upregulation of M2-related genes encourages the repair of damaged skin and a decrease in inflammatory responses, while proper O-glycan biosynthesis supports effective cell-signaling and immune responses crucial to eliminating acne-causing bacteria. Balanced cell proliferation can also prevent excessive skin buildup that often leads to clogged pores and acne. Increased collagen production strengthens the extracellular matrix, improving cell adhesion and structural integrity during the healing process of acne wounds. These findings underscore the significant role that flavonoids play in the therapeutic efficacy of tamanu oil in supporting effective wound healing and addressing key factors involved in acne pathogenesis.

Tamanu oil exhibits properties similar to those of rosehip seed oil (RHO), which has been rigorously evaluated for its efficacy in the treatment of post-surgical scarring in human subjects. In a controlled study involving 108 patients who had undergone dermatological surgeries, RHO demonstrated a significant reduction in erythema, dyschromia, and atrophy when compared to the placebo group [22]. Much like tamanu oil, the elevated concentration of essential fatty acids in RHO contributes to the restoration of cellular membranes and promotes enhanced cutaneous regeneration. Given its rich composition of bioactive compounds, including essential fatty acids and antioxidant properties, tamanu oil exhibits the potential to elicit effects similar to those observed with rosehip seed oil in post-surgical scar management when it comes to wound healing in patients with acne. Tamanu oil's biochemical attributes position it as an effective adjunct in dermatological treatments targeting acne-related skin injuries.

Tamanu oil operates through biological mechanisms similar to those of conventional Western acne treatments. For example, retinoids, a common first-line therapy, effectively reduce sebum production, control comedone formation, and restore the epithelial layer [23]. Given neoflavonoids' roles in immunomodulation and cell proliferation, tamanu oil may complement retinoid therapy and enhance its efficacy. However, research in this area is limited. Though effective, topical antibiotics, such as erythromycin and clindamycin often cause redness, dryness, and itching [23]. Given its antibiotic properties, tamanu oil may offer additional skin barrier protection, potentially mitigating these side effects. Similarly, over-the-counter treatments like salicylic acid and benzoyl peroxide are also popular but may cause adverse effects of dryness or irritation. Salicylic acid exfoliates and clears pores, while benzoyl peroxide acts as a topical disinfectant and antibacterial agent through bacterial protein degradation [23]. Tamanu oil has the potential to complement these treatments, but further research on its synergistic effects is needed.

Most animal studies indicate that tamanu oil does not cause erythema, eschar, irritation, or edema [12]. However, a few case studies have reported that some individuals may develop contact dermatitis when using it [24]. As tamanu oil is derived from tree nuts, it is not recommended for individuals with tree nut allergies and, thus, should be avoided. Additionally, some formulations of tamanu oil contain eugenol, which has blood-thinning properties; therefore, patients on blood thinners should refrain from using or be monitored closely for side effects [25]. Despite the recommendations to use it cautiously in the above patient populations, tamanu oil overall is a safe alternative option that has the potential to work synergistically with other traditional acne treatments.

The benefits of tamanu oil in acne treatment may extend beyond mere cosmetic improvement, potentially impacting patients' psychological well-being. Research indicates a significant correlation between skin conditions and anxiety, depression, and body image disturbances [26]. By alleviating acne symptoms, tamanu oil may contribute to enhanced self-esteem and overall psychological health. This establishes a positive feedback loop: improved skin appearance enhances mental health, while reductions in anxiety and stress may further diminish acne severity. This bidirectional relationship can enhance quality of life and promote a more positive self-image among patients.

5. IMPLICATIONS FOR ACNE MANAGEMENT

The integration of tamanu oil into acne management presents a promising avenue, especially for patients seeking more natural treatment options. Gender-based efficacies have not been well-studied. However, tamanu oil has been shown to have antimicrobial, anti-inflammatory, and anti-scarring properties [3]. One study in rats found that wound contraction was significantly lower with topical tamanu oil application and granulation tissue was more prevalent at Day 7 [10]. In practice, due to its moisturizing properties, tamanu oil could be used as an adjunct with benzoyl peroxide or topical retinoids to mitigate dryness and irritation while improving treatment outcomes. For patients with mild acne, tamanu oil could be used as a standalone therapy. Individuals with acne scarring may benefit from incorporating tamanu oil as a complementary step into their skincare regimen to promote healing and improve skin texture. However, while the potential benefits of tamanu oil as a therapy for acne management are encouraging, current research is limited, with most studies being in vitro. Further clinical trials are needed to establish the safety and efficacy of tamanu oil for acne treatment in human populations. Additionally, the bioactive compounds within tamanu oil, such as inophyllum, tamanolide, and calophyllolide, need to be isolated and studied individually in relation to their individual effects on acne [27]. Ultimately, until then, clinicians should carefully consider the use of tamanu oil for acne management based on individual patient profiles, ensuring appropriate monitoring and patient education.

5.1. Long-Term Effects

Future research should aim to comprehensively study the long-term effects of tamanu oil on skin health and the recurrence of acne. While preliminary results suggest the oil's efficacy in reducing inflammation and promoting wound healing [16], it is crucial to evaluate whether these benefits are sustained over extended periods. Investigations should be longitudinal to monitor patients for acne recurrence after cessation of tamanu oil application, assessing changes in skin texture and any potential cumulative effects on skin health. Understanding these long-term outcomes will be essential in determining the oil's viability as a lasting treatment option for acne.

5.2. Comparative Efficacy

Although the literature supports the use of tamanu oil in acne management, further comparative studies are warranted to establish how tamanu oil compares to leading acne medications, anti-inflammatory agents, and wound-healing treatments. Future research could incorporate randomized controlled trials comparing tamanu oil with conventional treatments such as benzoyl peroxide, retinoids, and salicylic acid, as well as natural alternatives, including tea tree oil and aloe vera [28]. These studies should focus on various metrics, including the reduction of acne lesions, improvement in skin inflammation, and the effectiveness in scar reduction. Such research is necessary to assess comparative efficacy and help clarify where tamanu oil fits within the broader spectrum of acne treatments that are more established in medical literature.

5.3. Safety and Side Effects

A comprehensive analysis of the safety profile of tamanu oil is essential for its adoption in acne treatment standards. Future research should investigate potential side effects, particularly with prolonged use, including any risks of skin irritation, allergic reactions, or interactions with other skincare products or ingredients. Long-term studies should also assess whether tamanu oil could cause adverse effects with repeated application, such as photosensitivity or comedogenicity. While emerging studies highlight tamanu oil's benefits in treating conditions like acne and atopic dermatitis [3], it is imperative to establish a clear safety profile to ensure that tamanu oil can be confidently recommended as a safe treatment option for acne.

6. CONCLUSION

This review demonstrates tamanu oil's significant potential in reducing acne-related inflammation and promoting scar healing, attributed to its rich composition of fatty acids, neoflavonoids, and bioactive compounds. Specifically, its high content of linoleic and oleic acids contributes to improved skin barrier function, while its antibacterial and anti-inflammatory properties, mediated by calophyllolide, target critical pathways in acne pathophysiology. Tamanu oil was also found to be effective against Propionibacterium acnes and Propionibacterium granulosum, further supporting its role in acne management. These antimicrobial and anti-inflammatory properties make tamanu oil a versatile option for holistic acne management, addressing both active lesions and the potential for scarring. In addition to reducing inflammation, tamanu oil enhances wound healing and scar reduction through its bioactive compounds, such as calophyllolide and inophyllum, which have been shown to promote macrophage infiltration and granulation tissue formation. Collectively, these findings indicate that tamanu oil has the potential to reduce acne-related scarring by supporting cellular regeneration and wound repair. Tamanu oil offers a promising natural alternative or adjunct to conventional treatments such as benzoyl peroxide, retinoids, and salicylic acid. Its ability to modulate inflammatory pathways and enhance wound healing without the severe side effects commonly associated with synthetic treatments suggests that tamanu oil could be particularly beneficial for individuals who experience skin irritation or sensitivity.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

REFERENCES

- 1. Oge', L.K., Broussard, A. and Marshall, M.D. (2019) Acne Vulgaris: Diagnosis and Treatment. *American Family Physician*, **100**, 475-484.
- 2. Sutaria, A.H., Masood, S., Saleh, H.M. and Schlessinger, J. (2024) Acne Vulgaris. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK459173/
- 3. Pribowo, A., Girish, J., Gustiananda, M., Nandhira, R.G. and Hartrianti, P. (2021) Potential of Tamanu (*Calophyllum*) Oil for Atopic Dermatitis Treatment. *Evidence-Based Complementary and Alternative Medicine*, **2021**, Article ID: 6332867. <u>https://doi.org/10.1155/2021/6332867</u>
- Poljšak, N., Kreft, S. and Kočevar Glavač, N. (2019) Vegetable Butters and Oils in Skin Wound Healing: Scientific Evidence for New Opportunities in Dermatology. *Phytotherapy Research*, 34, 254-269. <u>https://doi.org/10.1002/ptr.6524</u>
- Nguyen, V., Truong, C., Nguyen, B.C.Q., Vo, T.V., Dao, T., Nguyen, V., *et al.* (2017) Anti-Inflammatory and Wound Healing Activities of Calophyllolide Isolated from *Calophyllum inophyllum* Linn. *PLOS ONE*, **12**, e0185674. <u>https://doi.org/10.1371/journal.pone.0185674</u>
- 6. Léguillier, T., Lecsö-Bornet, M., Lémus, C., Rousseau-Ralliard, D., Lebouvier, N., Hnawia, E., *et al.* (2015) The Wound Healing and Antibacterial Activity of Five Ethnomedical *Calophyllum inophyllum* Oils: An Alternative

Therapeutic Strategy to Treat Infected Wounds. *PLOS ONE*, **10**, e0138602. <u>https://doi.org/10.1371/journal.pone.0138602</u>

- Cassien, M., Mercier, A., Thétiot-Laurent, S., Culcasi, M., Ricquebourg, E., Asteian, A., *et al.* (2021) Improving the Antioxidant Properties of *Calophyllum inophyllum* Seed Oil from French Polynesia: Development and Biological Applications of Resinous Ethanol-Soluble Extracts. *Antioxidants*, **10**, Article No. 199. <u>https://doi.org/10.3390/antiox10020199</u>
- Saxena, R., Nath, R., Palit, G., Nigam, S. and Bhargava, K. (1982) Effect of Calophyllolide, a Nonsteroidal Anti-Inflammatory Agent, on Capillary Permeability. *Planta Medica*, 44, 246-248. <u>https://doi.org/10.1055/s-2007-971459</u>
- Ghashghaii, A., Hashemnia, M., Nikousefat, Z., Zangeneh, M.M. and Zangeneh, A. (2017) Wound Healing Potential of Methanolic Extract of Scrophularia Striata in Rats. *Pharmaceutical Sciences*, 23, 256-263. <u>https://doi.org/10.15171/ps.2017.38</u>
- Erdogan, S.S., Gur, T.F., Terzi, N.K. and Dogan, B. (2021) Evaluation of the Cutaneous Wound Healing Potential of Tamanu Oil in Wounds Induced in Rats. *Journal of Wound Care*, **30**, Vi-Vx. <u>https://doi.org/10.12968/jowc.2021.30.sup9a.v</u>
- Dweck, A.C. and Meadows, T. (2002) Tamanu (*Calophyllum inophyllum*)—The African, Asian, Polynesian and Pacific Panacea. *International Journal of Cosmetic Science*, 24, 341-348. <u>https://doi.org/10.1046/j.1467-2494.2002.00160.x</u>
- 12. Krishnappa, M., Abraham, S., Furtado, S.C., Krishnamurthy, S., Rifaya, A., Asiri, Y.I., *et al.* (2024) An Integrated Computational and Experimental Approach to Formulate Tamanu Oil Bigels as Anti-Scarring Agent. *Pharmaceuticals*, **17**, Article No. 102. <u>https://doi.org/10.3390/ph17010102</u>
- Ansel, J., Lupo, E., Mijouin, L., Guillot, S., Butaud, J., Ho, R., *et al.* (2016) Biological Activity of Polynesian *Calophyllum inophyllum* Oil Extract on Human Skin Cells. *Planta Medica*, **82**, 961-966. <u>https://doi.org/10.1055/s-0042-108205</u>
- 14. Cruz, S., Vecerek, N. and Elbuluk, N. (2023) Targeting Inflammation in Acne: Current Treatments and Future Prospects. *American Journal of Clinical Dermatology*, **24**, 681-694. <u>https://doi.org/10.1007/s40257-023-00789-1</u>
- Fabbrocini, G., Annunziata, M.C., D'Arco, V., De Vita, V., Lodi, G., Mauriello, M.C., *et al.* (2010) Acne Scars: Pathogenesis, Classification and Treatment. *Dermatology Research and Practice*, **2010**, Article ID: 893080. <u>https://doi.org/10.1155/2010/893080</u>
- Raharivelomanana, P., Ansel, J., Lupo, E., Mijouin, L., Guillot, S., Butaud, J., *et al.* (2018) Tamanu Oil and Skin Active Properties: From Traditional to Modern Cosmetic Uses. *OCL*, 25, D504. <u>https://doi.org/10.1051/ocl/2018048</u>
- McCusker, M.M. and Grant-Kels, J.M. (2010) Healing Fats of the Skin: The Structural and Immunologic Roles of the Ω-6 and Ω-3 Fatty Acids. *Clinics in Dermatology*, 28, 440-451. <u>https://doi.org/10.1016/j.clindermatol.2010.03.020</u>
- Ruangsuriya, J., Sichaem, J., Tantraworasin, A., Saeteng, S., Wongmaneerung, P., Inta, A., *et al.* (2023) Phytochemical Profiles and Anticancer Effects of *Calophyllum inophyllum* L. Extract Relating to Reactive Oxygen Species Modulation on Patient-Derived Cells from Breast and Lung Cancers. *Scientifica*, **2023**, Article ID: 6613670. <u>https://doi.org/10.1155/2023/6613670</u>
- 19. Addor, F.A.S. (2017) Antioxidants in Dermatology. *Anais Brasileiros de Dermatologia*, **92**, 356-362. https://doi.org/10.1590/abd1806-4841.20175697
- 20. Čižmárová, B., Hubková, B., Tomečková, V. and Birková, A. (2023) Flavonoids as Promising Natural Compounds in the Prevention and Treatment of Selected Skin Diseases. *International Journal of Molecular Sciences*, **24**, Article

No. 6324. https://doi.org/10.3390/ijms24076324

- 21. Zalewski, J., Mączyńska, J., Bieżuńska-Kusiak, K., Kulbacka, J., Choromańska, A., Przestrzelska, M., *et al.* (2019) *Calophyllum inophyllum* in Vaginitis Treatment: Stimulated by Electroporation with an *in Vitro* Approach. *Advances in Clinical and Experimental Medicine*, **28**, 223-228. <u>https://doi.org/10.17219/acem/87045</u>
- 22. Valerón-Almazán, P., Gómez-Duaso, A.J., Santana-Molina, N., García-Bello, M.A. and Carretero, G. (2015) Evolution of Post-Surgical Scars Treated with Pure Rosehip Seed Oil. *Journal of Cosmetics, Dermatological Sciences and Applications*, **5**, 161-167. <u>https://doi.org/10.4236/jcdsa.2015.52019</u>
- 23. Vasam, M., Korutla, S. and Bohara, R.A. (2023) Acne Vulgaris: A Review of the Pathophysiology, Treatment, and Recent Nanotechnology Based Advances. *Biochemistry and Biophysics Reports*, **36**, Article ID: 101578. https://doi.org/10.1016/j.bbrep.2023.101578
- 24. Le Coz, C. (2004) Allergic Contact Dermatitis from Tamanu Oil (*Calophyllum inophyllum, Calophyllum taca-mahaca*). *Contact Dermatitis*, **51**, 216-217. <u>https://doi.org/10.1111/j.0105-1873.2004.0424h.x</u>
- Ma, N., Liu, X., Yang, Y., Li, J., Mohamed, I., Liu, G., *et al.* (2015) Preventive Effect of Aspirin Eugenol Ester on Thrombosis in K-Carrageenan-Induced Rat Tail Thrombosis Model. *PLOS ONE*, **10**, e0133125. <u>https://doi.org/10.1371/journal.pone.0133125</u>
- 26. Zia, K. (2014) Emotional State and Psychological Well-Being of Dermatological Patients. *Open Access Library Journal*, **1**, e434. <u>https://doi.org/10.4236/oalib.1100434</u>
- 27. Ginigini, J., Lecellier, G.J., Nicolas, M., Nour, M., Hnawia, E., Lebouvier, N., *et al.* (2019) Chemodiversity of *Calophyllum inophyllum* L. Oil Bioactive Components Related to Their Specific Geographical Distribution in the South Pacific Region. *PeerJ*, **7**, e6896. <u>https://doi.org/10.7717/peerj.6896</u>
- 28. Nurzyńska-Wierdak, R., Pietrasik, D. and Walasek-Janusz, M. (2022) Essential Oils in the Treatment of Various Types of Acne—A Review. *Plants*, **12**, Article No. 90. <u>https://doi.org/10.3390/plants12010090</u>