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Medicinal plants in burns treatment – a systematic review

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ABSTRACT

Introduction and aim. The World Health Organization (WHO) reports that around 11 million people experience burn injuries each year.^{1,2} Burn injuries occur when tissue damage is caused by various factors such as UV radiation, heat, chemicals, or electric current.^{3,4} While burns primarily affect the skin, they can also extend to deeper tissues like bones or muscles. When the skin is burned, its vital functions, including protection against the external environment, pathogens, and evaporation, are compromised.¹ The appropriate treatment method must be chosen based on the burn stage, the patient's condition, and the cause. The aim of this paper is to provide a comprehensive review based on literature, concerning superficial burns and sunburns treatment, with a focus on nature-derived topical treatment methods.

Material and methods. PubMed database was searched for the following terms: “burns”, “burn treatment”, “aloe vera”, “sunburn”, “centella asiatica”, “climate change”, “wound healing” for the articles published between 2005-2023 and written in the English language.

Conclusion. Herbal-derived compounds, with their diverse mechanisms of action, antibacterial activity, and safety profiles present a competitive alternative to conventional treatment of burns and sunburns, however, there are still not enough clinical trials to assess the effectiveness and safety profiles of nature-derived compounds.

Keywords. burn; burn treatment; sunburn; Aloe vera; Centella asiatica, medicinal plants

Introduction

The skin is the largest organ in the human body and can sustain severe and excruciating injuries known as burns.⁵ Burns occur as a result of injuries caused by agents capable of generating excessive heat, leading to damage to body tissues and cell death.⁶ These injuries commonly affect children, the elderly, and individuals with disabilities. Moreover, because of climate change and escalating temperatures, we may anticipate a higher incidence of sunburns, which are the predominant form of burn injuries. The increasing vulnerability of

people on Earth to UV radiation is a direct consequence of the depletion of the ozone layer, which serves as a protective stratospheric barrier that absorbs the majority of the sun's ultraviolet radiation.^{7,8}

The aging population also contributes to the susceptibility to burns, with elderly individuals being among the most vulnerable groups. The greatest number of burns take place in low-income and developing countries, where poorly designed healthcare systems contribute to an increased risk of post-injury complications, which can result in long-term disability.^{4,9,10} Consequently, the treatment of burn wounds remains a significant challenge, particularly in terms of finding cost-effective therapeutic approaches.^{1,10,11}

Researchers are actively engaged in the search for the optimal approach to burn treatment, aiming to improve and expedite the healing process while minimizing the risk of infection.

This review will specifically concentrate on superficial and superficial partial-thickness burns, providing valuable insights into the management of these types of burn injuries with the help of cost-friendly nature-derived products, as they seem to be equally efficient as the conventional treatment.

Aim

The aim of this paper is to provide a comprehensive review based on literature, concerning superficial burns and sunburn treatment, with a focus on nature-derived topical treatment methods and dressings.

Material and methods

PubMed database was searched for the following terms: “burns”, “burn treatment”, “aloe vera”, “sunburn”, “centella asiatica”, “climate change”, “wound healing” for the articles published between 2005-2023 and written in the English language.

Skin morphology and functions

Skin covers the entire surface of the human body, accounting for about 8% of total body mass. Moreover, it is the fastest-growing tissue in the human body. The layers of the skin include the epidermis, the dermis, and the hypodermis (Figure 1).¹²

The skin has many functions. A few of them are:¹²

1. protection – creating barrier between the external and internal environment of a body
2. thermoregulation – overheating prevention
3. perception – gives us the sensation of touch, pain, and pressure
4. regeneration – skin layers constantly migrate and skin regenerates

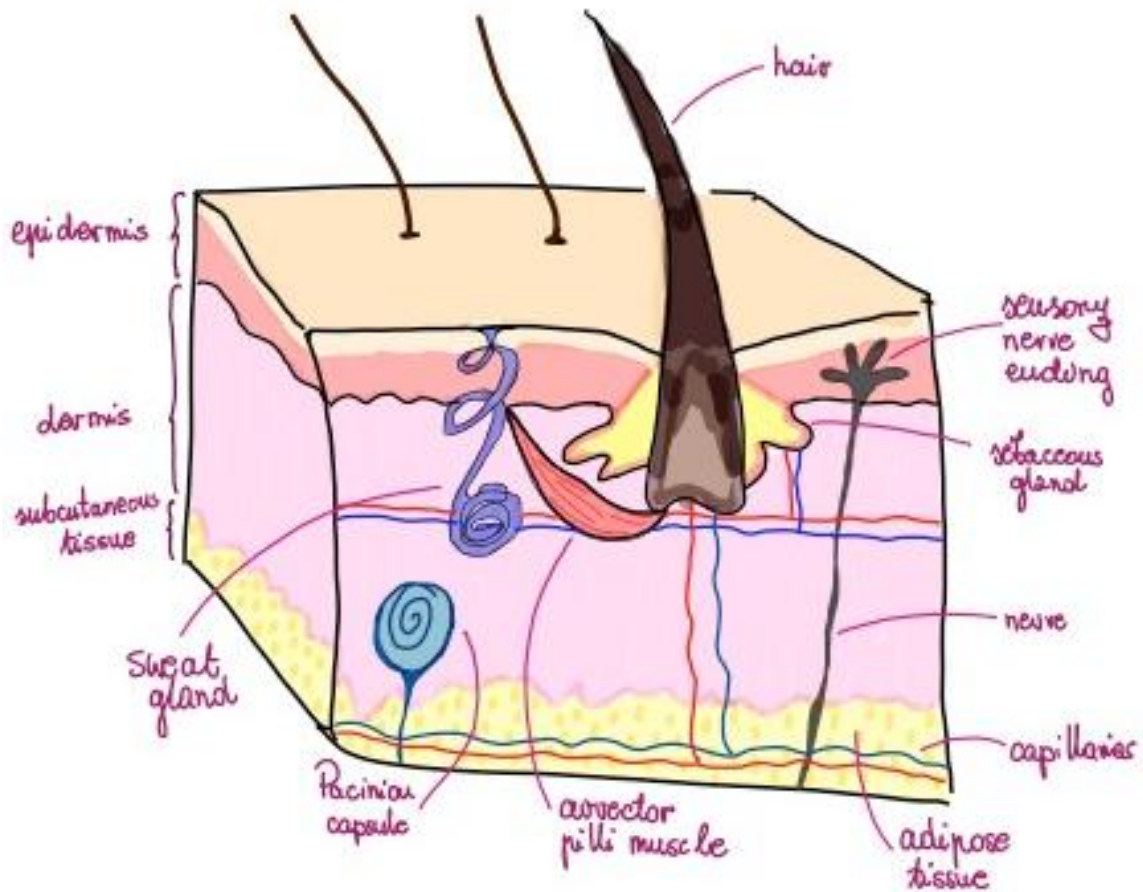


Figure 1. Skin morphology, scheme.¹²

Burns classification

When the skin is damaged - it loses its functions, leading to dehydration, infections, and more severe consequences. Normally it regenerates quickly, however, when the burns are deep it creates cicatrices when healing.

Burns can be categorized into four stages based on depth, determined by factors such as temperature, contact time, source, and skin thickness. Classification of burns consists of four main stages based on depth^{3,4,13}:

I - only epidermis is affected, painful, cause: sunburn, heals with no scars

IIA - epidermis and upper dermis are affected, painful, cause: scald, usually heals with no scars

IIB - epidermis and dermis are affected, painful or not, cause: scald, hot oil, heals with scars

III - epidermis, dermis and hypodermis are affected, insensate, cause: scald, hot oil, flame, heals with scars

IV - epidermis, dermis, hypodermis and organs below (like muscles) are affected, insensate, cause: scald, hot oil, flame, heals with scars

To assess the surface area of a burn, the "9% rule" (also known as Wallace rule) is used, where each arm and leg represents 9%, the trunk is 36%, the head is 9%, and the genitals are 1% in adults.¹³

Healing process

The process of wound healing is complex and continuous, influenced by multiple factors, and requires an optimal environment to facilitate faster healing. Wound healing consists of three distinct phases^{4,6,11,14,15}:

Inflammation: This initial phase involves coagulation, the release of cytokines, and cell movement in response to chemical signals. Inflammation is crucial for initiating the healing process.

Proliferation: During this phase, dermal resurfacing occurs through processes such as formation of new blood vessels and production of new fibrous tissue. This phase contributes to the reconstruction of the damaged tissue.

Maturation: In the final phase, the extracellular matrix is remodeled, and scar tissue is formed. The wound gradually closes.

With advancements in medical technology and the recognition of various types of wounds, specialized products have been developed to address and treat specific skin lesions, providing targeted healing approaches.

Debridement, ointment, and dressing

The debridement process begins by cleaning the surrounding skin with soap, detergent, or antiseptic. In the case of superficial partial-thickness burns, large blisters can be drained, and small blisters can be left.

Dressing is typically unnecessary for first-degree wounds, which involve minimal impairment of the skin's protective function. Instead, pain relief and moisture maintenance are achieved through the application of topical balms, and Aloe vera gels. Pain can also be alleviated by taking cool showers, using cold moist compresses, or oral administration of painkillers such as paracetamol or ibuprofen. Additionally, it is essential to maintain oral hydration.

Second-degree superficial wounds can be effectively managed by performing daily dressing changes using topical antibacterial agents, cotton gauze, and elastic wraps.

An appropriate dressing plays a crucial role in the treatment of wounds, serving multiple purposes as it provides protection for the damaged epithelium, and minimizes the risk of bacterial and fungal colonization.¹⁶ The dressing should have an occlusive nature to minimize heat loss and evaporation. Furthermore, it should prioritize the comfort of the patient by offering pain relief and should be non-toxic and cost-effective.^{1,12}

Burn wounds are often contaminated with the usual skin bacterial flora – *Staphylococci* and *Streptococci*.¹⁷ Conventional topical synthetic antibacterial agents used in burns include:

Silver sulphadiazine (SSD), Silver nitrate, nystatin, bacitracin, neomycin, and polymyxin B or mupirocin.¹⁸ Nevertheless, they exhibit side effects such as delayed wound healing, leukopenia, cytotoxicity,^{1,19} auditory nerve toxicity, hyperchloremic metabolic acidosis, hyperventilation,⁹ and renal toxicity.⁴ Moreover, they are not affordable for all the world's population.

Medicinal plants

Certain herbal preparations exhibit superior effectiveness in the treatment of burn wounds compared to conventional treatments previously mentioned. With their diverse mechanisms of action, antibacterial properties, safety profiles, and cost-effectiveness, herbal preparations can provide competition to conventional treatments. The growing interest in alternative medicine and herbal remedies serves as encouragement for further research in this field.¹

Aloe vera

Aloe vera gel, derived from the *Asphodelaceae* plant, has a long history of medicinal use dating back to ancient cultures. Over the years, numerous studies have been conducted to investigate its pharmacological properties, which include antibacterial⁶, antiviral, anticancer, antioxidant, and anti-inflammatory effects.²⁰ *Aloe vera* has gained popularity as a remedy for minor wounds and burns, although its precise mechanism of action in wound healing remains unknown.^{20,21}

Aloe vera is widely recognized for its beneficial effects on the skin, particularly in the context of wound healing,²¹ and is commonly used as an ingredient in cosmetic and pharmaceutical products.^{1,3} It has gained popularity in society as a remedy for skin issues like acne, burns, and itching.⁶ Clinical trials and reviews have demonstrated that the application of aloe vera cream can fasten the healing process of second-degree burns, leading to reduced wound size and faster recovery time.²² Additionally, it has been observed to provide pain relief and prove cost-effective when compared to the use of 1% silver sulfadiazine cream.

Research carried out by Tadihoedoho et al. (2019), showed that topical administration of *Aloe vera* gel extract increased the number of macrophages and epithelialization in sunburn mice, with the greatest aloe vera concentration being the most effective. Macrophages are cells that play an important role in wound healing, promoting debridement, proliferation, angiogenesis, and re-epithelialization, therefore it can be concluded that *Aloe vera* is efficient in promoting wound healing. Moreover, in comparison to SSD cream, *Aloe vera* shows faster epithelialization.²³

In a clinical experiment carried out by Teplicki et al. (2018), they demonstrated that Aloe vera accelerates wound healing with a positive effect on the proliferation and migration of human skin fibroblasts and keratinocytes, along with a protective effect against keratinocyte death.¹⁴ Khorasani et al. (2009) showed in a clinical study that the rate of re-epithelialization and healing was significantly faster in the wound treated with *Aloe vera* than SSD cream in second-degree burnt patients.²² Shahzad et al. (2013) as well demonstrated better healing properties of aloe vera than SSD cream. Moreover, they observed that *Aloe vera* is better in alleviating pain and showed no difference in wound infection.⁹ In another study, Muangman et al. (2016) examined patients with second-degree burns. Half of the participants were treated with dressings containing 0.5% chlorhexidine acetate, while the other half received dressings infused with extracts of medicinal plants, predominantly Aloe vera. Positive outcomes were observed, including faster healing rates and shorter hospital stays compared to the control group. However, no significant differences were noted in terms of pain levels. It is

worth mentioning that one complication related to *Pseudomonas aeruginosa* infection occurred in the group receiving the treatment with *Aloe vera* extracts.⁶

Existing evidence indicates the effectiveness of *Aloe vera* extracts in treating burns. However, there is limited research on the antioxidant properties of *Aloe vera* plants during different growth stages, and only a few clinical trials and in vitro studies have explored their bioactive potential. Therefore, it is recommended to conduct further trials with larger sample sizes to gather more conclusive evidence on the use of *Aloe vera* dressings for medium burns.^{6,21}

Centella asiatica

Centella asiatica (also known as Gotu Kola) belongs to the *Apiaceae* family. This plant holds significant traditional value, particularly in Southeast Asia, due to its nutritional and therapeutic properties. It has been recommended for the treatment of various skin conditions and dermatoses²⁴ including lupus, eczema, psoriasis, leprosy, and varicose ulcers. The wide utilization of *Centella asiatica* is attributed to its antimicrobial, antioxidant, anti-inflammatory, neuroprotective, and wound healing properties.²⁵

Studies have shown that extracts of *Centella asiatica* promote wound healing by enhancing collagen synthesis and influencing microcirculatory function. The stimulation of wound healing, particularly in angiogenesis, may be attributed to the activation of collagen I, Fibroblast Growth Factor (FGF), and Vascular Endothelial Growth Factor (VEGF) production. VEGF also stimulates vasodilation and the formation of the extracellular matrix. *Centella asiatica* exhibits anti-inflammatory effects by reducing the levels of pro-inflammatory mediators, such as Interleukin-1 β (IL-1 β), Interleukin-6 (IL-6), Tumour Necrosis Factor α (TNF α), prostaglandin E2 (PGE2), and cyclooxygenase-2 (COX-2).²⁵

In the study by Saeidinia et al. (2017), patients with second-degree burns were topically treated once a day with either *Centella* ointment or 1% SSD cream, which served as the control. The group treated with *Centella asiatica* showed faster healing, and a shorter time of re-epithelialization.²⁶

Moreover, oral supplementation of *C. asiatica* has shown to enhance collagen synthesis, cellular proliferation, and promote re-epithelialization and wound contraction.²⁵ When applied in recommended amounts *C. asiatica* doesn't exhibit any toxicity, however, an allergic reaction when used topically, such as burning may happen. When overdosed *per os*, it may result in dizziness.²⁴

Albizia julibrissin

Albizia julibrissin is a plant belonging to the *Fabaceae* family and is native to south-eastern Asia. In traditional medicine, *Albizia* species have been used to treat a range of conditions, such as abdominal pain, diabetes, rheumatism, wounds, snake bites, hemorrhoids, abscesses, erysipelas, and leprosy.¹ In some studies, the plant showed anti-platelet effects and anticancer activity. The main compounds that are isolated are triterpene saponins, with the presence of flavonoids, lignans, alkaloids, and phenolic glycosides. In the study by Asgarirad et al. (2017) where they compared *Albizia julibrissin* with 1% SSD cream, they showed that the use of *Albizia julibrissin* results in significant relief of pain, inflammation, and discharge. Furthermore, there was a reduction in healing time for both second-degree burns and third-degree burns with *Albizia julibrissin* treatment. No significant adverse reactions were observed.²⁷ These findings suggest that *Albizia julibrissin* holds promise as a new herbal remedy for wound healing and the treatment of burn injuries.

Arnebia euchroma

Arnebia euchroma, belonging to the Boraginaceae family, is naturally found in high mountain regions such as the Himalayas. It contains compounds such as naphthoquinones like shikonin, alkannin, and isohexenylnaphthazarin, with potential medicinal properties such as wound healing, antibacterial, antiviral, antifungal, anti-inflammatory, and anticancer effects.^{1,19}

Nasiri et al. (2015) in a study carried out on rats, demonstrated that the healing rate of *A. euchroma* group was faster compared to the standard SSD ointment. In the *Arnebia euchroma* ointment (AEO) group, fewer complications were observed. The histopathological assessment showed significantly improved re-epithelialization in animals treated with 10% AEO. Treatment with *A. euchroma* resulted in increased neovascularization, faster epithelialization, and absence of infection. Re-epithelialization was significantly increased in the 10% AEO group compared to other groups.¹⁹

One year later, in a clinical study also carried out by Nasiri et al. (2016) where he compared the efficacy of *Arnebia euchroma* ointment to 1% silver sulfadiazine (SSD) cream, he confirmed the superiority of the plant. The average healing time was significantly shorter for *Arnebia euchroma* ointment compared to 1% SSD cream. Moreover, patients reported lower burning sensation and pain but higher warmth in the area treated with natural compound.²⁸

On the other hand study carried out by Ashkani-Esfahani et al. (2012) shows that *Arnebia euchroma* treatment was relatively comparable to SSD cream, however also had limitations.¹⁸

Other medicinal plants

Betula pendula,²⁹ *Hippophaë rhamnoides*,³⁰ *Juglans regia*,³¹ *Hypericum perforatum*,³² *calendula officinalis*¹⁵ - these are a few of the medicinal plants that also exhibit great potential for treating burn wounds. Multiple studies have highlighted the advantages of using these plants over silver sulfadiazine cream, including quicker healing time, reduced pain and burning sensation, and a higher percentage of wound epithelialization.¹ Moreover some of these plants exhibit properties such as stimulation of fibroblast motility and keratinocytes differentiation or collagen production. Increasing interest in alternative therapies and therefore increased demand, may help to create more valuable trials, as there is still not enough high-quality evidence concerning and limited number of trials concerning plant-based medications.¹⁵

Other nature-derived compounds

Marine-derived compounds, honey,^{12,33,34} and curcumin should also be mentioned, as they show a great range of anti-inflammatory, antioxidant, and regenerative properties and are the objects of many studies.¹²

Conclusion

According to the United Nations estimation, developing countries account for 83% of the world's total population, which is equal to around 6.6 billion inhabitants.³⁵ These people are the most frequently affected by burns, which globally rank as the fourth most frequent injuries.² Considering the fact, that the economic situation and health system in developing countries are not stable, we should look for more accessible and affordable means to treat burn wounds. This review suggests that the use of affordable medicinal plants can successfully replace the more expensive chemical treatment for burns. Herbal-derived compounds, with their diverse mechanisms, antibacterial activity, and safety profiles present a competitive alternative to conventional treatment. However, there are still not enough clinical trials to assess the effectiveness and safety profiles of nature-derived compounds.¹

The development of an ideal dressing for burn wounds remains a challenge in modern medicine. Nevertheless, the research presented in this review indicates that herbal products could become a strong competitor to synthetic compounds.

Supplementary materials

Figure 1. Skin morphology, scheme.

Author's contribution

Conceptualization, IŁ, PR; methodology, IŁ, AW, DA; check, PR, DP, AC; resources, IŁ, AJ, KK; writing - rough preparation, IŁ, DA; writing - review and editing, IŁ, AM, KK, AW.

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The authors declare no conflicts of interest.

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