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The Effect of Aloe Vera Hydrogel on the Process of Burn Healing: A Systematic Review and Meta-Analysis

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Abstract
Background: Heat, chemicals, radiation, electricity, and fire can burn skin. Aloevera, among other treatments, helps speed up burn healing, especially first- and second-degree burns. This article examines if aloe vera speeds burn recovery.
Purpose: In this investigation, the effect of aloe vera on the progression of first- and second-degree burns was evaluated
Methods: This systematic review and meta-analysis examined ProQuest, PubMed, Scopus, Web of Science, ScienceDirect, and CINAHL studies from January 2016 to March 2021. RevMan 5.4.1 and R-Studio meta-analysis risk of bias 2.0
Results: An examination of residual heterogeneity in 278 people over 4 trials revealed significant variations in wound healing, with an I2 value of 0%. The healing of burn wounds using aloe vera showed a Standard Mean Difference (SMD) of 0.00, with a 95% Confidence Interval (CI) ranging from -0.46 to 0.47, indicating a strong level of significance
Conclusion: Aloe vera's effect on the progression of first- and second-degree burns was the purpose of this research

Keywords: aloe vera; wound burn; wound healing; wound care

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Introduction

Wound Burns is a type of injury or destruction of tissue resulting from exposure to heat sources such as fire, scalding water, chemicals, electricity, and radiation. The extent of tissue damage resulting from fire is greater than that generated by hot water (Jeschke et al., 2020). Furthermore, the duration of tissue exposure to the heat source directly influences the magnitude and penetration of tissue injury, ultimately impacting the duration of the recovery process (Żwierełło et al., 2023). Tissue damage becomes more extensive and severe as the duration of contact increases. Burns are a significant health issue that health personnel frequently encounter nowadays (Jeschke et al., 2020). There is a significant number of burn patients in Indonesia, particularly in densely populated and slum areas (Wardhana et al., 2017).

According to the World Health Organization's media center on burn injuries, burns pose a significant global public health concern (Jeschke et al., 2020). Annually, around 180,000 fatalities are attributed to burns, primarily resulting from scalding water, electrical incidents, chemical exposure, and other various causes (Burhan et al., 2022). Most burn cases are reported in poor and medium-income countries (Smolle et al., 2017). The fatality rate in Indonesia resulting from burns remains high, approximately 40%, primarily owing to severe burns produced by fire and electric shock (Wardhana et al., 2017). The Basic Health Research (Ministry of Health RI, 2018), revealed that the prevalence of burn injuries varied across different provinces in Indonesia. Papua had the largest proportion of burn injuries at 2.1%, while North Sulawesi had the lowest at 0.5%. South Sumatra had a frequency of 1.4% burn cases. According to the statistics provided, the occurrence of burns in Indonesia is still very high. As a result, the involvement of nurses is necessary in the healing process. It is important to note that numerous variables might hinder the natural healing process at each stage, leading to poor healing.

Keywords: aloe vera; wound burn; wound healing; wound care

Impaired wound healing can result from various medical states, including diabetes, immunological diseases, ischemia, venous stasis, and injuries such as burns, wounds caused by overcooling, and gunshot wounds (Mulatu et al., 2022). Epithelialization is the last stage of the proliferative phase, characterized by the migration, proliferation, and differentiation of epithelial cells from the borders of the wound to regenerate and repair the damaged tissue (Burhan & Sebayang, 2022). Epithelialization in burn wounds is postponed until the formation of a layer of granulation tissue, which facilitates the migration of epithelial cells (Rousselle et al., 2019).

Presently, the utilization of conventional medicine and herbal components for treatment remains prevalent as an option in society. Consequently, there is a need for complementary therapy to enhance the effectiveness of primary topical antimicrobials in the healing of burns (Monika et al., 2022). Aloe vera, a semi-tropical plant with thick, tapering leaves and short stalks, has a long history and is highly regarded as a versatile herbal remedy for burns. Aloe vera is classified as a member of the aloe barbadense species, which is part of the lily tree family. It is important to note that aloe vera is not a cactus (Hekmatpou et al., 2019).

Aloe vera possesses anti-inflammatory, anti-arthritis, antibacterial, antifungal, and hypoglycaemic properties. Aloe vera's antibacterial and antifungal qualities help reduce the occurrence of dandruff on the scalp. Aloe vera plants can effectively manage fungal infections, including those associated with alopecia illness. Additionally, aloe vera possesses the ability to promote wound healing and alleviate skin damage. Furthermore, the application of this therapy has been seen to alleviate pain at the site of injury. The hydrating properties of aloe vera have been effectively showcased using topical treatments (Hashemi et al., 2015). levels regarding the best way to wash wounds, leading to variations in the healing process (Monika et al., 2022). Therefore, this study aimed to see how different wound-washing methods affect chronic and acute wounds.

Aloe vera has numerous advantageous properties for the human body. These include promoting faster wound healing, reducing inflammation, acting as a laxative, moisturizing the skin, and possessing antidiabetic, antibacterial, and antimicrobial qualities. Wound healing is facilitated by the interaction between glucomannan and gibberellin with growth factor receptors on fibroblasts (Sánchez et al., 2020). This interaction stimulates activity and proliferation, leading to an increase in collagen synthesis. Additionally, it promotes the synthesis of hyaluronic acid and dermatan sulfate, which accelerates the process of granulation for wound healing. Aloe vera has a positive impact on burn wounds by promoting the activity of fibroblasts and macrophages, enhancing the production of collagen and proteoglycans, improving the function of growth factor hormones and granulation, and exhibiting antibacterial and anti-inflammatory properties. As a result, it accelerates the healing process of burn wounds (Pereira & Bártolo, 2016).

Method

Eligibility Requirements for Systematic Reviews

Table 1 shows the agreed-upon elements that make up the PRISMA guideline, which this systematic review followed. These elements include population, intervention, center, and study design (Shamseer et al., 2015).

Search Strategy

The following online databases were searched by the authors to locate every PICOS-compliant study: PubMed/Medline (2019–2024), EBSCOhost (2019–2024), ProQuest (2019–2024), and ScienceDirect (2019–2024). Search phrases in two categories (i) aloe vera gel OR aloe vera hydrogel and wound burn OR wound burns OR burn wound and combine them based on various attributes and databases should be combined with several subjects. The sole sources of study materials are journals with DOIs that are written in English.

Criteria for inclusion

The search criteria for reviewing articles in the database are as follows: articles published between 2009 and 2024, written in English, focusing on negative pressure wound therapy intervention in wound burn, examining the association between aloe vera gel and the healing process, conducted in the home, public health center, or hospital settings, utilizing a quantitative design such as a clinical trial or a randomized controlled trial (RCT), and excluding research protocols and systematic reviews.

Study selection.

The initial four reviewers performed a first screening by separately reading the title and recognizing the abstract. During the subsequent screening, we thoroughly examined the complete text of the literature that satisfied the specified criteria for inclusion. When disagreements arose among the three researchers, we engaged in

discussions and sought the input of the fourth researcher to reach a conclusive decision. All relevant information is taken from the text, including the author, study type, subject characteristics, participant details, country, number of respondents, intervention, instrument used, and outcome. In a published study, data were selectively collected based on relevance and only the most recent or thorough data were included.

Evaluation of the Studies' Quality

The study's quality was assessed using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Page et al., 2021; Shamseer et al., 2015), as well as the methodology for a systematic review of quantitative research Randomized Control Trial (RCT) and Clinical Trial (CT) from the Joanna Briggs Institute (JBI) (Lockwood et al., 2011). Risk of Bias 2.0 employs Revman 5.4.1 (Cochrane, 2020).

Data extraction refers to the process of retrieving specific information or data from a larger dataset or source.

Fifteen papers were selected according to the PRISMA standards (Shamseer et al., 2015). The articles included information such as author, study type, subject characteristics, participant details, country, number of respondents, intervention, instrument used, and outcome. All things will be documented in the data extraction (Table 2).

Bias Assessment

To evaluate the potential for bias, we employed a RoB 2.0 evaluation consisting of five domains. We utilized free software Review Manager version 5.4.1 (Cochrane, 2020), to conduct the bias assessment. High risk refers to the situation when the allocation of population and the implementation of interventions are concealed from the participants and personnel, leading to potential bias in performance assessment. Nevertheless, the likelihood of partiality in our writing was consistent and minimal in the extensive investigation. The outcomes of our bias evaluation are displayed in Figure 2 and Figure 3.

Meta-analysis

The R-Studio software was utilized to do meta-analyses. The subgroups were categorized based on the patients' type of wounds and the type of outcome variable. The effect measure for the categorical data was determined as the relative risk (RR), whereas the combined effect sizes for the measurement data were assessed using the weighted mean difference. The effect sizes are displayed alongside their corresponding 95% confidence intervals. Outcome The study's heterogeneity was assessed using the Fixed and Random Effects models, with the Omnibus test yielding a value of less than 0.001. After observing homogeneity in the study, the next step was to apply the random effects model to examine the impact when the p-value is less than 0.001 and the confidence interval is 95%. Publication bias in meta-studies was analyzed using Egger's test, Fail-safe N, and Funnel Plot, with a significance threshold of $p>0.05$. The effect size of the study was analyzed using a random effect model test, and the results were presented using a forest plot.

Results

Following validation and analysis using six worldwide databases, we reported n=1173. We also discovered numerous publications (n=30), but four reviewers eliminated 1084 based on title and abstract, and we recorded a number (n=12) for those missing data. Studies were also omitted due to inadequate population size (n=2), inappropriate intervention (n=1), and irrelevant and incomplete analysis (n=5). As a result, four randomized controlled trials were eligible for inclusion in this analysis. So, four randomized controlled trials (RCTs) made it to the next round of the study since they fulfilled the inclusion criteria. The PRISMA flow diagram (Figure 1), shows the steps taken to find studies in the database, through screening, eligibility, and inclusion (Figure 1).

Published between 2009 and 2022 were four randomized controlled trials (Khorasani et al., 2009; Molazem et al., 2014; Sabaghzadeh Irani et al., 2021; Yaghoubi et al., 2015). The sample size varied from 30 to 45 respondents, with an average age ranging from 18 to 65 years, and there were 278 male and female respondents overall. Burn patients, both male and female, were treated in hospitals and clinics with aloe vera gel. The size of wounds was reduced, and healing times were shortened in four separate experiments (Table 1). Burn wound healing was reported in four out of the twelve investigations. According to (Burhan et al, 2022), the results demonstrated that the application of aloe vera as an intervention accelerated the healing process of burns (Effect Size SMD: 0.00 95%). Figure 2a shows that there is a high level of heterogeneity in the studies included in this investigation, as indicated by the CI: -0.46, 0.47, and the analysis of the I^2 value of 0% with $p<0.00$ (Figure 2).

Evaluation of the studies' quality.

The evaluation of prejudice is demonstrated during the risk analysis phase, as depicted in Figure 2. All four investigations on Random Sequence Generation demonstrated a little risk of bias across the board. However, two research that employed allocation concealment exhibited a significant risk of bias (Khorasani et al., 2009; Molazem et al., 2014), while two studies (Sabaghzadeh Irani et al., 2021; Yaghoubi et al., 2015), demonstrated minimal risk values (Figure 3).

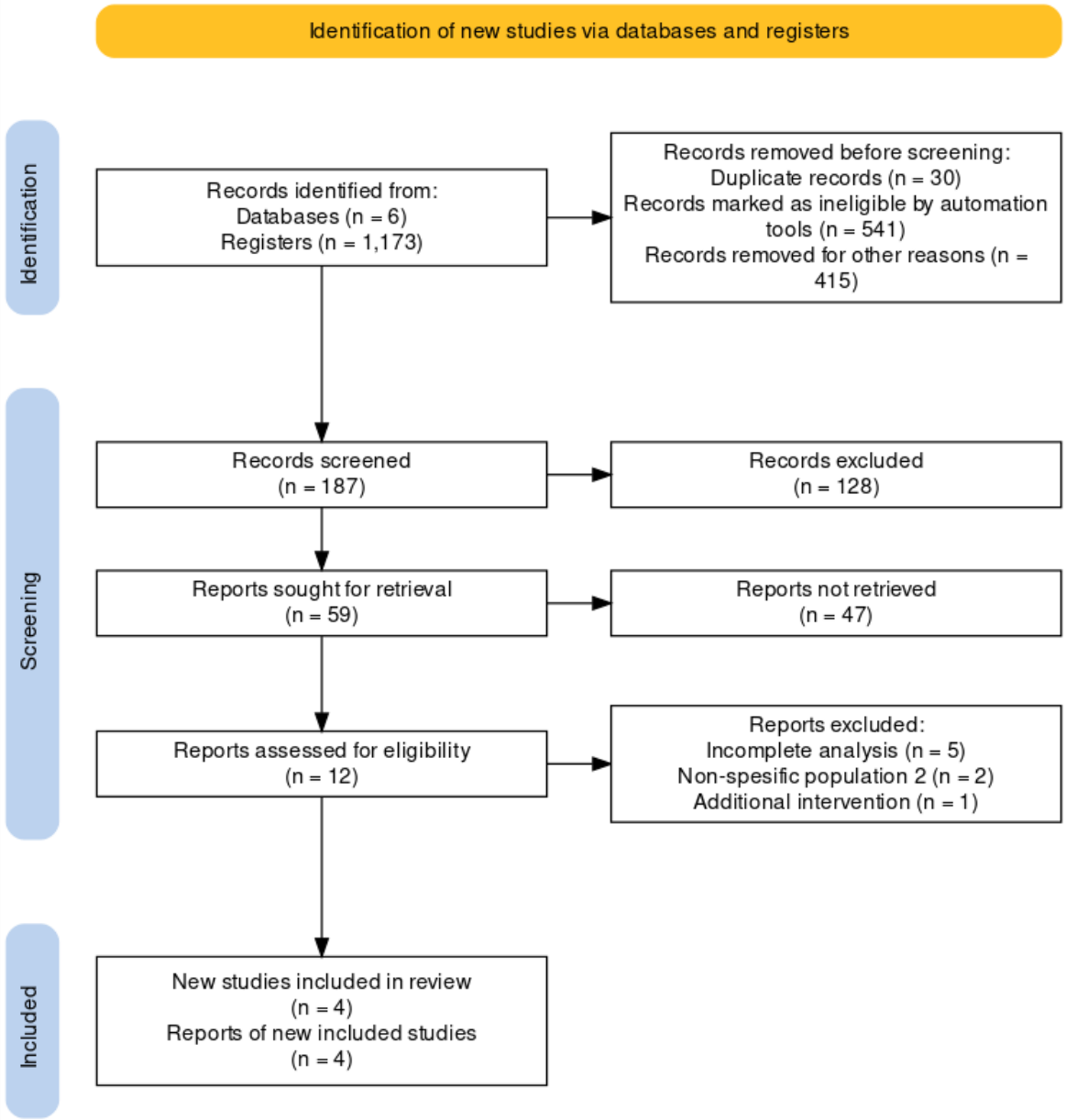

Figure 1. PRISMA Flow Chart (Haddaway et al., 2020).

Publication Bias

We used the correlation test as the analysis of this study based on Begg and Mazumdar's ranking guidelines, with the Kendall tau statistical method, which is a continuity correction, to see and analyze the publication bias of the study. The Kendall tau statistical values were .01, z = 0.001, p -0.034 on wound burn healing, .000, z = .002, p = .021. Thus, these findings showed a high publication rate, so we used random effects analysis to see the significance of the intervention (Figure 3).

Discussion

Aloe vera gel on burn wound healing.

The results of the article analysis indicate that four (Khorasani et al., 2009; Molazem et al., 2014; Sabaghzadeh Irani et al., 2021; Yaghoubi et al., 2015), articles utilize aloe vera gel to demonstrate that its antimicrobial and cell proliferation properties accelerate the burn epithelialization process. The saponin content of aloe vera has the potential to promote the healing of second-degree burns in group II, specifically when applied as a spread (Hekmatpou et al., 2019). Saponin, which is present in aloe vera, has the potential to speed up wound healing by acting as a bacterial component and causing injury to the bacterial wall. This results in bacterial lysis and ultimately diminishes the risk of infection in the affected area (Sánchez et al., 2020). In addition to promoting cellular proliferation, saponins possess the capability of penetrating the epidermal layer and retaining bodily fluids,

thereby contributing to the regulation of fluid homeostasis. Aloe vera's saponin content has been found to facilitate an increase in TGF-β activity, consequently leading to indirect stimulation of nascent cell proliferation (Hekmatpou et al., 2019). Additionally, aloe vera contains compounds that alleviate wound pain.

Table 1. Characteristic of studies employing Aloe Vera and Placebo

Reference	Study Design	Country	Sample Size	Outcome	Quality Power (JBI)
(Khorasani et al., 2009)	A randomized controlled clinical trial (RC-CT)	Iran	30 patients Aloe vera: 22 SSD: 54	The rate of re-epithelialization and healing of the partial thickness burns was significantly faster in the site treated with aloe than in the site treated with SSD (15.9 ± 2 vs 18.73 ± 2.65 days, respectively; P < 0.0001).	A
(Molazem et al., 2014)	A randomized controlled clinical trial (RCT)	Iran	90 patients Aloe vera: 45 Placebo: 45	Overall, 45 participants in the aloe vera group and 35 in the control group had obtained a zero score 24 hours after the operation. These measures were respectively obtained 42 and 41eight days after the operation.	A
(Yaghoubi et al., 2015)	A Randomized Control Trial	Iran	68 patients Aloevera: 34 SSD: 34	The wound itching significantly reduced half an hour after being dressed in Aloe vera gel. The wound pain in the experimental group was less than the control group during the study period. Moreover, there was no pain in either the experimental or control group on day 14.	A
(Sabaghzadeh Irani et al., 2021)	A Randomized Control Trial	Iran	60 Patients Aloe vera 30 2% Nitrofurazone: 30	The repeated measure ANOVA showed that there was a significant change in the score of BWAT in all areas during the intervention period (p=0.001), but the trend of healing in the two groups during the intervention period was not significantly different (p=0.098).	A

According to a study conducted (Akhoondinasab et al., 2014), aloe vera has been found to expedite the healing of burn wounds compared to a group that was treated with silver sulfadiazine. This is because aloe vera contains antibacterial substances and promotes the growth of cells, which speeds up the process of forming new skin tissue. (Wang et al., 2023), shown that the coadministration of aloe vera gel and adipose-derived stem cells (ASCs) effectively mitigated the inflammatory response by downregulating the expression of TGF- b 1 and IL-1 b genes on the seventh day after treatment. Additionally, they observed a greater rate of angiogenesis and re-epithelialization on day 14 in comparison to the other groups. (Meza-Valle et al., 2021), conducted research demonstrating that the application of aloe vera gel can enhance wound closure. The study found that by Day 28, the wound had fully healed with little scarring. Furthermore, according to the pathology assessment, the group treated with Aloe vera and BMSCs had a greater rate of angiogenesis and re-epithelialization compared to the other groups. The administration of Aloe vera resulted in a higher rate of angiogenesis and reepithelialization compared to the control group. Angiogenesis in granulation tissue enhances perfusion at the wound site, hence delivering vital oxygen and nutrients that are crucial for the wound healing process (Sánchez et al., 2020).

Effect of Aloe vera gel extract on the healing of burn wounds

The examination of papers reveals that two specific articles (2,4) have examined the effects of aloe vera gel extract. These articles demonstrate that the application of aloe vera gel extract with concentrations of 10% and 20% leads to the most rapid healing of burn wounds, surpassing the effectiveness of other treatment groups. According to (Hekmatpou et al., 2019), aloe vera with concentrations of 10% and 20% creates a moist wound texture. Suggest that a moist environment in the wound can accelerate the formation of new blood vessels, leading to increased tissue oxygenation. Enhancing tissue oxygenation and nutrition delivery to injured tissues will expedite tissue epithelialization, hence accelerating wound contraction (Rousselle et al., 2019).

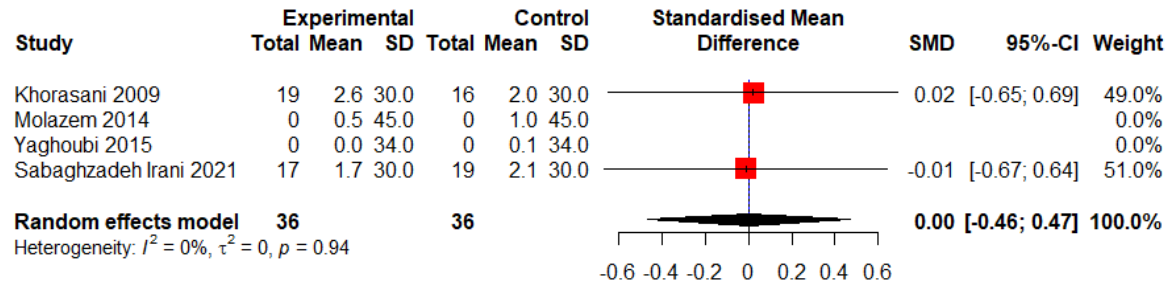

Figure 2. Forest plot standards mean different.

The method of making additional aloe vera typically involves maceration, which refers to immersing the finely prepared plant material until it permeates and softens the cellular structure, allowing soluble components to dissolve. The benefit of employing maceration for filtration is that it requires straightforward and easily maintainable craftsmanship and equipment. A drawback of maceration is its lengthy duration and the somewhat imperfect filtration process (Ministry of Health RI, 2018).

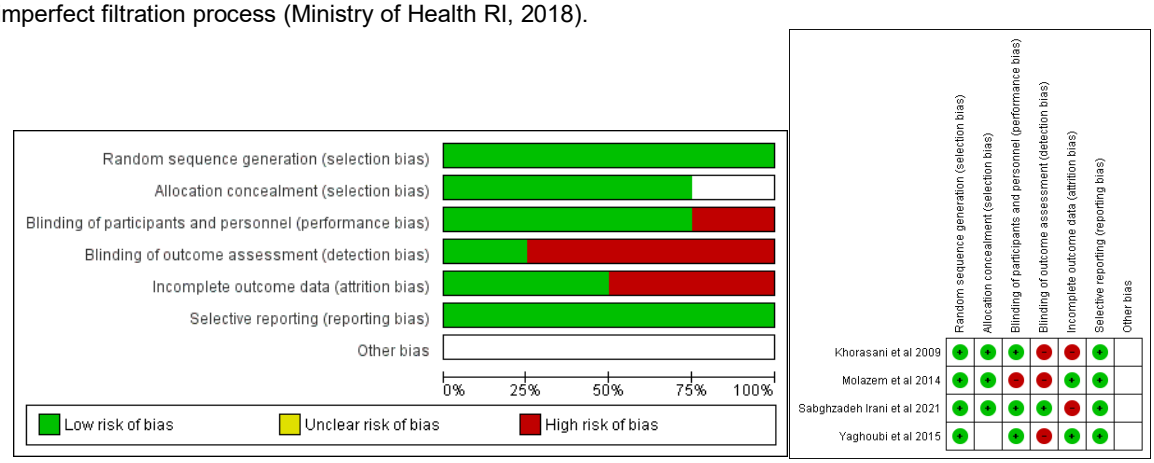

Figure 3. Risk of bias of the included studies using Rev-Man 5.4.1

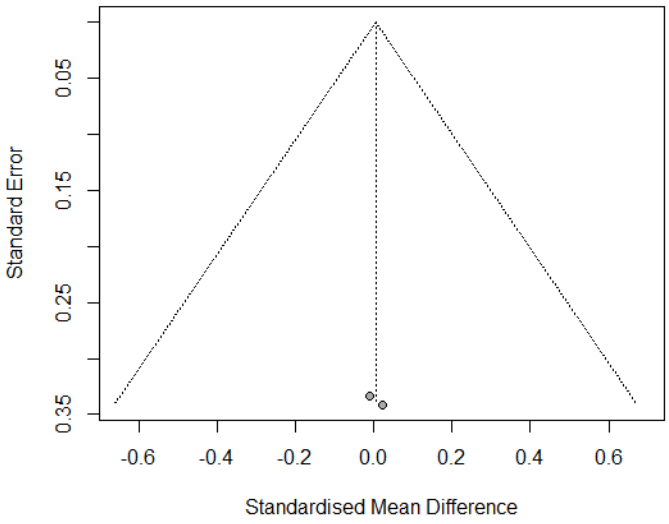

Figure 4. Funnel plot publication bias.

The research of the authors demonstrated that the administration of aloe vera gel extract resulted in significant healing of burns. This was evidenced by a decrease in burn area across all groups, because of the anti-inflammatory properties present in aloe vera skin. The application of aloe vera skin extract gel at concentrations of 10% and 20% resulted in the most rapid healing of burns compared to other treatment groups (Hekmatpou et al., 2019). Additional use of aloe vera gel can aid in the healing of dry burn wounds by promoting the

production of collagen. This, in turn, stimulates cell growth and enhances the development of dermal fibroblasts, which play a crucial role in the drying process of burn wounds

Strengths And Limitations of The Study

This study investigated the effectiveness of using aloe vera gel to enhance the healing process of burn wounds. While this review presents compelling evidence and employs a targeted research approach, it does have a few potential shortcomings. These factors encompass the inclusion of research conducted on a small scale, insufficient sample sizes, a restricted number of articles, and the utilization of varied outcome measures. Furthermore, certain research revealed the presence of heterogeneity, albeit at a modest level. Additional study on aloe vera using a randomized control trial technique is necessary to enhance the empirical foundation for the application of aloe vera in treating burns

implications on patient care and the profession.

Considerations for those working in the field and those providing treatment to patients with first- and second-degree burns: This study's findings provide vital information for burn nurses, particularly when deciding how to utilize enzymatic aloe vera. Everyone involved in burn care, including nurses, doctors, and academics, will profit from the results.

Conclusion

Based on the analysis of eight articles, it can be concluded that aloe vera administration in the form of gel or aloe vera extract can significantly accelerate burn wound healing due to the anti-inflammatory, antibacterial, and antimicrobial proteins, carbohydrates, saponins, minerals, amino acids, and various other anti-inflammatory agents present in aloe vera, as well as reduce the reduction in burn wound healing.

Author contribution

Significantly contributed to the conception, design, data collecting, analysis, and interpretation: Rahmat Effan Fahri Mahendra prepared the manuscript and critically revised important intellectual material. Asmat Burhan; Finished edition before publishing. Each author must contribute enough to be held accountable for a reasonable amount of the content: Asmat Burhan; Take responsibility for every aspect of the project to permit full investigations and resolutions of inquiries about the work's precision or integrity: Rahmat Effan Fahri Mahendra and Asmat Burhan

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None

Conflict of Interest Statement

The authors declare that they have no competing interests.

Data Availability

On a proper request, the owner of the dataset that has either developed or analyzed it in the current study can be contacted directly.

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