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Effects of Medicinal Plants Extracts in Healing Split-Thickness Skin Graft Donor Site Wounds: A Systematic Review of Randomized Clinical Trials

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Abstract

The literature on Split-Thickness Skin Graft (STSG) donor site dressings has not yet identified an ideal dressing, and most products tested by researchers for wound dressing are prohibitively expensive in Low- and Middle-income settings. Clinical trials using biological dressings have offered an alternative option for managing STSG donor sites wound. The aim of this systematic review is to find evidences regarding the effectiveness of medicinal plants on STSG donor site wound healing. A total of 249 papers were identified in the initial search. After removing duplicates and applying the inclusion and exclusion criteria, 6 Randomized Clinical Trials were deemed relevant and included in the final review. Over twenty years four medicinal plants have entered clinical trial to enhance STSG donor site wound healing. The medicinal plants reviewed have large effect size regarding time to complete wound healing and wound score. However, the effect size of *Aloe vera* regarding time to complete wound healing and pain control vary from study to study. No patient quality of life was assessed neither cost-effectiveness of these products. Medicinal plants are potential cost effective antimicrobial and wound healing products for STSG donor site wound dressing. However, more clinical researches including patient quality of life among outcome measures are needed.

Keywords: Medicinal Plant, Split Skin Graft, Donor Site, Wound Healing.

INTRODUCTION

Split-thickness skin grafts (STSG) remain the standard of care in the treatment of significant cutaneous defects caused by burns, disease (e.g., tumor excision, diabetic foot ulcers, decubitus ulcers, venous leg ulcers), and traumatic injury [Osborne *et al*., 2016].The harvest of STSG consisting of epidermal and dermal tissue creates a partial-thickness wound that involves pain management, wound care, and healing time [Serebrakian *et al*., 2018]. Many patients report that their pain, pruritus, and discomfort levels are more significant at the donor site than at the graft-treated site [Rotatori *et al*., 2019]. Furthermore, healing at the donor site can be complicated by infection, depigmentation, and hypertrophic scarring [Osborne *et al*., 2016].

Although the principles of dressings applied to the recipient sites of skin grafts are standard and universally accepted, the ideal dressing material for manipulating the donor site is yet to be developed, and significant variability exists in managing the donor site [Demirtas *et al*., 2010; Rakel *et al*., 1998].

Due to their moisture properties, petroleum gauzes are often used as standard or traditional dressings. Some definite disadvantages of petrolatum ointment (Vaseline[R]) have been reported in previous studies, such as maceration of the wound surface during warm weather due to the water seal properties of the petrolatum ointment. The dressings become contaminated with the patient's sweat and exudate accumulation, making them suitable anaerobic medium for bacterial growth. When an infection is developed, it can rapidly spread to the entire wound surface. Vaseline has no antibacterial activity [Mahmoodi Nesheli *et al*., 2022].

The choice of dressing for the STSG donor site has been debated in the literature, with various materials having been adopted. Still, no conclusion has been drawn on the most effective option [*Jansen et al., 2018; Rahman et al*., 2020; Sood *et al*., 2014]. Furthermore, based on the literature review, it is not possible to identify the most suitable dressing for use in donor areas of STSG in terms of comfort, scarring, aesthetic, and protective aspects because although studies demonstrated promising results for different dressings, consensus is lacking about whether one is superior to the others [Ribeiro & Martuscelli, 2018]. Moreover, most products tested by researchers for wound dressing are prohibitively expensive in low-income settings [Benskin, 2013].

Clinical trials using biological dressings have offered an alternative option for managing STSG donor sites. Plant-derived extracts (phytochemicals) and naturally derived substances, such as Honey, amniotic membrane, keratinocytes and platelet-enriched dressings, among others, have been employed in clinical trials where they have been compared with standard non-biological dressings in practice. Biological dressings are indicated to be used for partial-thickness wounds such as burns, abrasions, donor sites, skin tears, etc [Gupta & Edwards, 2009; Rahman *et al*., 2020]. They increase the wound healing and epithelialization rate for STSG donor sites; however, they offer no additional advantage in reducing the incidence of infection or minimizing pain during dressing changes [Rahman *et al*., 2020].

Nevertheless, since ancient times, phytotherapy has efficiently treated cutaneous wounds, reduced the onset of infections, and minimized the usage of antibiotics that cause critical antibiotic resistance [Albahri *et al*., 2023]. Natural products have a long history of use in wound care, but there are only a few rigorous studies. Phytochemicals and naturally derived substances have gained an advantage due to their composition of many chemicals that may enhance wound healing in many ways. Using plants with medicinal properties to treat wounds has been found helpful in fighting against infection and speeding up wound healing [Monika *et al*., 2021].

With the growing interest in using natural products and the belief that they are safer than standard therapies, it is vital to understand the current knowledge of their efficacy and side effects [Sivamani *et al*., 2012]. The lack of consensus about the best dressing material for STSG donor site dressing, when many have shown promising results in trials, is an opportunity for each setting or hospital to find the cost-effective and available dressing material that responds better to local needs. We reviewed medicinal plants that have entered clinical trials over twenty years to the present to provide the best available evidence about their effectiveness in terms of time to wound healing, pain relief, the rate of infection, and patient quality of life following STSG donor site wound.

METHODS

Research Design

The PICOS approach (Patients, Interventions, Comparators, Outcomes, Study design) depicted in table 1 was used to develop and narrow the clinical question. A systematic manual and electronic search of literature was conducted to review medicinal plants that have entered clinical trials over last twenty years to provide the best available evidence about their effectiveness in terms of time to wound healing, pain relief, rate of infection, and patient quality of life following STSG donor site wound.

Table 1: PICOS design for RCTs of split-thickness skin graft donor site wounds healing with plant extracts

PICOS	***Endpoints***
Patients	Human participants, All age groups, Both genders
Intervention	Dressing with plant extracts
Comparators	All to be considered
Outcomes	Time to wound healing, Wound healing rate; Dressing removal pain score, Infection rate, Patient quality of life; Cost/effectiveness
Study design	All to be considered.

Literature Search

Electronic data were searched with PubMed, Cochrane, EMBASE and ICTRP databases using specific terms in the text, title and abstract. The keywords used were a combination of: "split-thickness skin graft, split skin graft, partial skin graft, biological dressing, medicinal plants, plants extracts, wound, donor site, donor area, healing, dressing, banana leaf (*Musa acuminata*), *Aloe vera*, *Alkanna tinctoria*, *Zataria multiflora*."

Selection Criteria

The articles were screened manually to ensure each met the inclusion and exclusion criteria. Only full papers published between January 1st, 2003 and June 30th, 2023, in English or French, concerning randomized clinical trials in human subjects of any country, any age whose STSG donor site wound was treated with medicinal plant extract as primary dressing. Animal studies, intervention using other dressing materials alone or combined with medicinal plant extracts for STSG donor site dressing were excluded.

Data Extraction

A data extraction form was used to ensure consistency in capturing the results, method, reliability, and validity of the studies reviewed. This form was developed using the Cochrane Collaboration data collection form as a guide. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards was used to conduct this study.

Quality Assessment

Reference lists and bibliographies of retrieved papers were hand-searched to identify further documents for consideration. Three individuals independently reviewed the content.

Statistical Analysis

The effect size was measured using the online effect size calculator from socscistatistics.com web site to understand the magnitude of differences found in the selected RCTs; Glass's delta test was applied since all RCTs' control and experimental groups had the same sample size but different standard deviations.

RESULTS

Selection of RCTs

As shown in Figure 1 overall 249 papers were identified in the initial search. After removal of duplicates and applying the inclusion and exclusion criteria, only 6 RCTs were deemed relevant and were included in the final review.

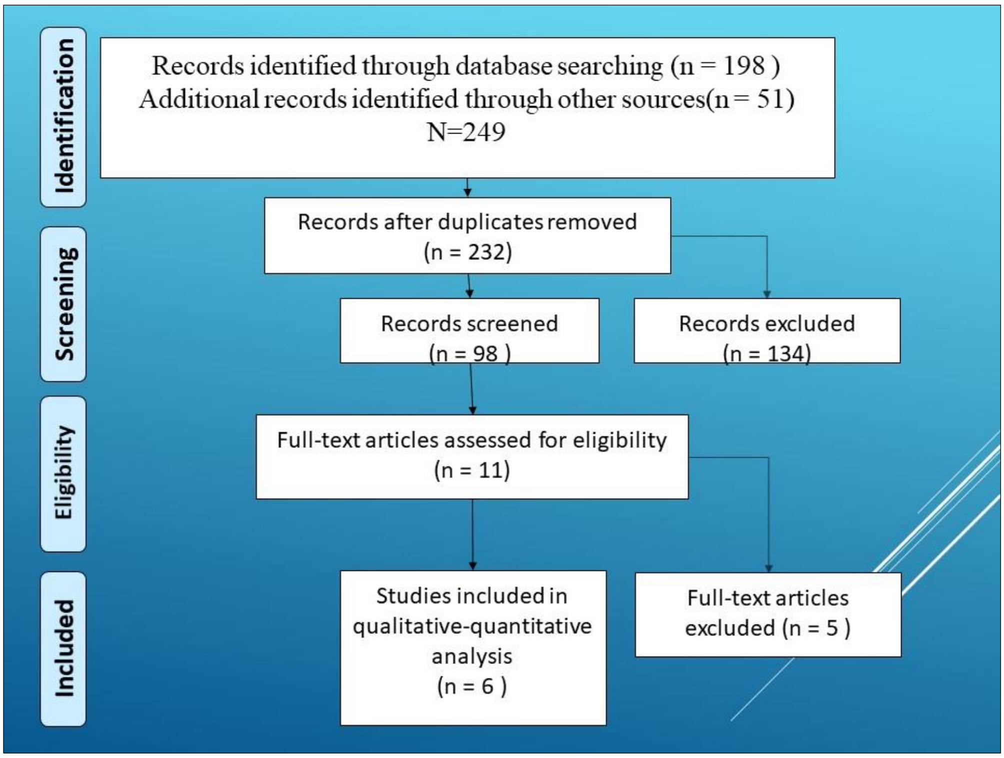

Figure 1: Flowchart of study selection according to PRISMA guidelines

Characteristics of Randomized Controlled Trial Retained

Only 4 plant extracts were studied in these 6 RCTs. Dressings used were *Alkanna tinctoria* tausch vs placebo (dressing with base ointment), *Zataria multiflora* impregnated gauze vs petrolatum gauze, *Aloe vera* gel vs Aquagel (sterilized glycerin), *Aloe vera* cream vs placebo and gauze dressing, Banana leaves vs Vaseline gauze, and Polyethylene surgical dressing (PSD) vs banana leaves. The evidences are summarized in table 2.

Table 2: Description of studies that evaluated the effects of plants extracts on the STSG donor site wounds

Study	Patients	interventions	Onset Time	Cure Rate	E.L	G.delta
Kheiri A. *et al*., (2017)	60	*Alkanna tinctoria* vs base ointment	4 weeks	96.66%, vs 50%	2a	1.58
Nesheli M.M *et al*., (2022)	30	*Zataria multiflora* vs petrolatum	4 weeks	96.7% vs 73.3%	2a	0.97
Burusapat C *et al*., (2018)	12	*Aloe vera* gel vs Aquagel	11.5 ± 1.45 vs 13.67 ± 1.61days	epithelialization	2a	1.34
Khorasani G *et al*., (2011)	45	*Aloe vera* cream vs gauze dressing	9.7 ± 2.9 vs 17 ± 8.6days	epithelialization	2a	0.84
Gore A.M, (2003)	30	Banana leaves vs vaseline gauze	8.67 vs 11.73 days	epithelialization	2a	2.91
Gore A.M *et al*., (2013)	50	Banana leaves vs polyethylene surgical dressing	7.6±1.087 vs 7.56±0.993 days	epithelialization	2a	0.03

E.L = Evidence Level

Kheiri A. *et al*., (2017) treated 60 patients with *Alkanna tinctoria* tausch extracts dressing and base ointment as a placebo. They observed 50% and 96.66% of patients with complete wound healing within 2 to 4 weeks respectively in treated group; 0% and 23.3% respectively in placebo groups, significantly different.

Nesheli M.M *et al*., (2022) treated 30 patients with *Zataria multiflora*-impregnated gauze vs petrolatum gauze. Wound reepithelialization occurred faster in the treatment group; 90% of patients in the *Zataria multiflora* group were entirely healed by the third week and 96.7% by the fourth week. In the control group 73.3% of patients' wounds were wholly healed by the fourth week. Wound healing and reepithelialization accelerated significantly in the first, second, third and fourth week after intervention in the *Zataria multiflora* treatment group due to modulating the inflammatory phase and improving the proliferative phase.

Burusapat C *et al*., (2018) treated 12 patients with *Aloe vera* gel vs Aquagel (sterilized glycerin). Times to complete reepithelization using *Aloe vera* were shorter than the placebo group (11.5 + 1.45 and 13.67 + 1.61 days (p<0.05). There is no statistical difference in the pain score across the two groups. Topical *Aloe vera* gel significantly demonstrated accelerated STSG donor site healing but did not significantly relieve pain.

Khorasani G *et al*., (2011) treated 45 patients with *Aloe vera* cream vs. placebo and gauze dressing. The mean time to complete re-epithelization was 17 ± 8.6, 9.7 ± 2.9 and 8.8 ± 2.8 days for the control/gauze dressing, *Aloe vera* and placebo groups respectively. The mean wound healing time in the control group was significantly different from the *Aloe vera* and placebo groups (p < 0.005). The healing rate was not statistically different between *Aloe vera* and placebo groups. This study showed a significantly shorter wound healing time for skin graft donor sites in patients treated with *Aloe vera* and placebo creams. The moist maintenance effect of these creams may contribute to wound healing.

Gore A.M (2003) treated 30 patients with banana leaves (BLD)vs Vaseline gauze. The mean time to complete epithelialization was 8.67 (BLD) and 11.73 (Vaseline gauze) (p<0.001). The average dressing removal pain score was 0.97 with BLD compared to 9.47 with Vaseline gauze (p<0.001). BLD is a completely non-adherent, cheapest and painless dressing. Authors strongly recommend using BLD for all skin graft donor areas.

Gore A. *et al*., (2013) treated 50 patients with BLD vs polyethylene surgical dressing (PSD). The average time to complete epithelialization of the donor area under BLD was 7.6±1.087 vs 7.56±0.993 under PSD (p=0.322). The background pain score under PSD was significantly less than that under BLD on days one and three post-harvest (day 1, p= 0.002; day 3, p=0.000). Dressing removal pain scores under PSD were significantly less than those under BLD on days 7 and 9 post-harvest. PSD is as effective as BLD for STSG donor site dressing and causes less background pain as well as dressing change pain as compared to BLD.

The effects of these 4 medicinal plants extracts on STSG wound healing are summarized in the forest plot chart shown in Figure 2.

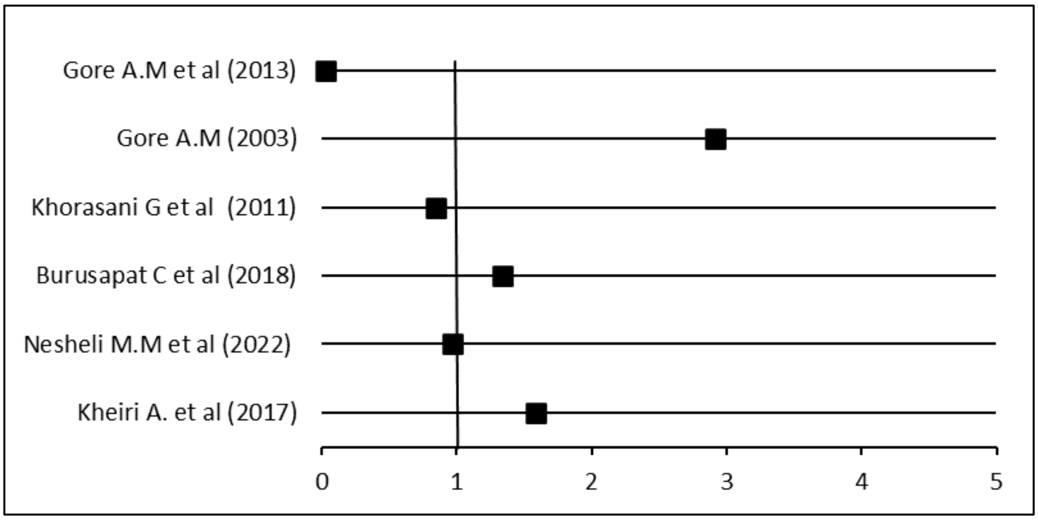

Figure 2: Effects of medicinal plants extracts on STSG wound healing.

DISCUSSION

In this review we have assessed effectiveness of medicinal plants in STSG donor site healing based on available published literature. Only four medicinal plants are documented to enhance STSG donor site wound healing especially banana leaves, *Aloe vera*, *Alkana tinctoria*, and *Zataria multiflora*. However, there is a wide variety of bioactive small molecules from natural sources available which possess beneficial bioactivities and are currently used worldwide [Moses *et al*., 2023].

We have assessed effectiveness in term of time to wound healing, pain control, rate of infection, patient quality of life and cost of the novel dressing material.

It comes out that *Alkanna tinctoria* and control product promote wound healing at day 14 with a significantly large effect size in the *Alkanna tinctoria* group compared to the control group (Glass's delta = 1.58); this is the same with *Zataria multiflora* which showed a large effect size compared to the control group regarding wound score (Glass's delta = 0.97) at day 14. In both study pain and time to wound healing were not assessed.

Aloe vera showed a large effect size regarding time to wound healing (Glass's delta =1.34) and small effect size regarding pain control associated with dressing (Glass's delta = 0.07) compared to control group. Mean time to complete epithelialization with *Aloe vera* is 9.7±2.9 days (d=0.84).

The effect size of Banana leaves to improve time to complete epithelialization and pain score is large compared to Vaseline gauze (d= 2.91 et 6.90 respectively) at day 8. No wound score was assessed for this study. However, compared to PSD *Aloe vera* has small effect size regarding time to complete wound healing (d= 0.03) and large effect size regarding pain control (d=8.31). Wound score was not assessed.

Gore *et al*., conducted an RCT using total extracts from banana leaves vs Vaseline gauze (control product) on STSG donor site wounds; first dressing change was planned for day eight post-harvest unless indicated earlier; interventional product and control were applied on the same patient either by dividing the donor site wound in two half or using different donor site on the same patient. Early epithelialization with BLD was statistically highly significant with $p < 0.001$; the difference in the mean days for healing (8.67 banana leaves and 11.73 vaseline gauze) was highly significant. Early epithelialization is vital for re-harvesting the donor site. Validated pain score showed that banana leaves is a non-adherent and pain free dressing compared to Vaseline gauze ($p<0.001$). There is no statistical difference regarding infection rate between Banana leaves and Vaseline gauze [M. A. Gore & Akolekar, 2003].

Wounds need to heal quickly, with minimal scaring, pain and infection, even in areas with limited resources. In low resource countries where access to contemporary wound care products is restricted or cost-prohibitive, healthcare workers frequently use botanical and other natural products as home remedies and promote wound healing [Haesler *et al*., 2016].

Ten years later, Gore *et al*., (2013) conducted another RCT using total extracts from banana leaves vs PSD. First dressing change was scheduled on day seven post-harvest. Average time to complete epithelialization of donor area under BLD and PSD is 7.6±1.087 and 7.56±0.993, respectively (p=0.322). The background pain score under PSD is significantly less than that under BLD on days one and three post-harvest (day 1, p= 0.002; days 3, p=0.000). The dressing removal pain scores under PSD were significantly less than that under BLD on days 7 and 9 post-harvest.

Under optimal conditions, the STSG donor site heals within 7 to 21 days [Karlsson *et al*., 2014]. A proper wound dressing may reduce the time to complete re-epithelialization and avoid conversion of the donor site to a full-thickness wound [Kheiri *et al*., 2017].

Although the two RCTs by Gore *et al*., reveal that BLD enhances wound healing with a good time to complete healing less than ten days, Study protocols vary from study to study, and outcome measures differ. In the study comparing banana leaves to Vaseline gauze pain was not assessed as either background or procedural; more background and dressing removal pain was seen with BLD compared to PSD. In both studies protocol of post-operative pain management is not described. We can't tell whether painkiller was given or not after surgery when the patient recovered from anesthesia. This consideration is essential for post-operative pain assessment. None of these studies assessed patient quality of life using validated tools. Banana leaves are presented as a cost effective dressing product for STSG donor site wounds in India, but this may not be true in other parts of the world.

Moreover, protocol for secondary dressing is not described. We hypothesis that the method of allocation of donor site wounds to interventional or control products for primary dressing can impair pain assessment: Separation of donor site wounds by a strip of normal skin and complete separation of their dressing materials instead of dividing the wound into two halves when using the same anatomical area should be ideal for pain assessment. The latter may bias pain assessment.

Banana leaves can become an alternative option of wound dressing material in contused, lacerated and sutured wounds over the head, neck and face region as they have demonstrated to cause less pain and trauma during dressing change and have other advantages such as cost and availability, comfort and ease of handling the dressing by health professionals [Chendake *et al*., 2021].

However, prepared BLD cannot be stored for more than 7-10 days. Fungal growth is seen on the leaves on prolonged storage, and they need to be discarded. Gamma irradiation increases the shelf life of banana leaves up to 2-3 months [M. A. Gore & Akolekar, 2003] and may affect the cost of the product.

The World Health Organization (WHO) has declared antibiotic resistance a global problem, as antibiotics are becoming less effective in treating many diseases. Therefore, the use of and search for plants with antimicrobial properties has accelerated in recent years [Sarma *et al*., 2021]. Gore *et al*., (2013) reported no evidence of infection with Banana leaves compared to Vaseline gauze or PSD.

The genetically closely related banana cultivars with genome ABB have better antimicrobial properties against food-borne and clinically significant pathogens. Moreover, the antibacterial activity is more potent in leaves and pseudostem than in the corm. This supports the traditional use of banana extracts for treating infections, including diarrhoea and dysentery. Additionally, selected cultivars showed anti-Candida biofilm activity, which is interesting in light of traditional use for treating sexually transmitted diseases [Jouneghani *et al*., 2020; Panda *et al*., 2020]. More study is needed to compare antimicrobial activity of banana leaves to other medicinal plants and commonly used antibiotics against microorganisms causing wound infection.

Evidence is lacking to support whether the effectiveness of banana leaves in STSG donor site healing is due to a synergistic effect of different components of the total extract or a particular bioactive compound of the section.

Aloe vera has been used to treat wounds since ancient times. However, data regarding the efficacy of *Aloe vera* for burns and split-thickness skin graft donor sites are inconclusive [Burusapat *et al*., 2018]. The Aloe species are typically found in dry climates, including Africa and India; the leaves present on *Aloe vera* contain a gel which is the component primarily used in wound-healing therapies [Liang *et al*., 2021; Salehi *et al*., 2018]. There are multiple active components within *Aloe vera* contributing to its wound-healing potential, including polysaccharides. Acemannan is a polysaccharide reported to be one of the active components contributing to fibroblast proliferation and type I collagen synthesis [Liang *et al*., 2021].

A double-blind, randomized controlled trial was conducted by Burusapat: Twelve patients with 24 donor sites have participated; STSG donor sites were divided into the *Aloe vera* and placebo groups. Times to complete epithelization for the *Aloe vera* and placebo groups were 11.5 ± 1.45 and 13.67 ± 1.61 days, respectively ($p < 0.05$). Topical *Aloe vera* gel significantly demonstrated accelerated split-thickness donor-site healing but did not show significant pain relief. Visual analogue scale scores after wound dressing for the *Aloe vera* and placebo groups were 17.18 ± 13.17 and 18.63 ± 11.20, respectively. No statistical significance was found between groups. No infection seroma, rash or itching of the donor site was detected in the groups. No allergy against *Aloe vera* was found [Burusapat *et al*., 2018].

An RCT by Khorasani revealed that the re-epithelization time in the control group was 17 ± 8.6 days (range, 8–37), while in the *Aloe vera* group and placebo group it was 9.7 ± 2.9 days (range, 5–18) and 8.8 ± 2.8 days (range, 4–14), respectively. Mean time to wound healing was significantly different in the control group compared to the *Aloe vera* and placebo groups ($P < 0.005$). There was no significant difference in mean re-epithelization time between *Aloe vera* and placebo (base) groups (p = 0.9): no allergic reactions or other adverse events (e.g., donor site infection) related to the dressings. No pain assessment using validated tools was done [Khorasani *et al*., 2011].

Regarding the in vivo study targeting wound healing properties, the *Aloe vera* sample size is small and there are few RCTs to support evidence [Burusapat *et al*., 2018]. Safia supported that *Aloe vera* gel at optimum concentration could be used as an antiseptic to prevent some microbial skin wound infections [Arbab *et al*., 2021].

There is a lack of human model studies targeting the effect of *Aloe vera* in STSG donor site wound healing. Many studies in the literature are focused on other types of wounds and are animal models.

An RCT by Kheiri evaluated wound healing properties of *Alkanna tinctoria* extracts; the grade and surface area of the STSG donor site were compared at days 14 and 28 after the intervention. There was no significant difference in wound scores of both groups at baseline. Still, the decrease in wound scores was significantly higher in the *Alkanna tinctoria* group compared to the placebo group on days 14 and 28 after the dressing was applied. In addition, the wound surface area was significantly reduced in the *Alkanna tinctoria* group compared to the control group following 28 days of intervention. No adverse effects were seen in either group treated with herbal and placebo ointments [Kheiri *et al*., 2017].

Aljanaby demonstrated that 300mg/ml of the hot-water extract from *Alkanna tinctoria* roots has perfect antibacterial activity against all drug-resistance bacteria isolated from patients with burn infections [Aljanaby, 2018].The main active ingredients of *Alkanna tinctoria* are Alkannin and shikonin. Alkannin derivatives show intense wound healing along with anti-inflammatory and antimicrobial properties [Kheiri *et al*., 2017].

To the best of our knowledge, there is no available evidence regarding effectiveness of *Alkanna tinctoria* on STSG donor site wound pain, rate of infection, patient quality of life, and cost-effectiveness of the dressing product.

Zataria multiflora is a historical plant from Lamiaceae family, also known as thyme. The main active ingredients of *Zataria multiflora* are p-cymene, ɤ-terpinene, carvacrol, and thymol, which lead to antioxidant, anti-inflammatory, antibacterial, and antifungal properties and accelerate wound healing. Thymol derivatives show intense wound healing along with anti-inflammatory and antimicrobial properties [Mahmoodi Nesheli *et al*., 2022].

A randomized, placebo-controlled clinical trial by Mahmoodi Nesheli showed that the wound size was significantly reduced in the *Zataria multiflora* group compared with the control group after the operation's first, second, third and fourth week. Wound reepithelialization occurs faster in the treatment group with *Zataria multiflora* than in the control group. The wounds of 90% of patients in the *Zataria multiflora* group were entirely healed by the third week and 96.7% by the fourth week. While in the control group, 73.3% of patients' wounds wholly healed by the fourth week. No adverse effects, such as erythema and pruritus, were seen in either group treated with *Zataria multiflora* and placebo creams [Mahmoodi Nesheli *et al*., 2022].

Several gram-positive and gram-negative bacteria are sensitive to *Zataria multiflora* antibacterial activity. It is helpful as antiseptic, analgesic and carminative agent [Zomorodian *et al*., 2011].

Some plant products used in wound care appear to have active components that contribute to wound care through antioxidant, antimicrobial, anti-inflammatory and tissue regeneration effects. In contrast, others are used primarily for their practical abilities to provide a protective covering for the wound. Despite the everyday use of many botanical products for wound care in low resource countries, formal research into their efficacy in promoting wound healing is in its infancy [Haesler *et al*., 2016].

The ideal dressing for STSG donor area should be painless when applied, non-adherent, non–toxic, non-antigenic, cheap, readily available, and achieve epithelization of STSG donor areas as early as possible. Non-adhesive dressings are ideal for these areas as they are pain free and minimize damage to the new epidermis during dressing removal, thus aiding the healing process [M. A. Gore *et al*., 2013].

Moisture properties of all medicinal plant dressings found in our literature review explain better why they can speed up wound healing process; however, the effects of the pharmacologic properties of these dressings on STSG donor site wounds are not well documented.

Moist wound-healing products are more effective than non-moist wound-healing products in reducing pain and promoting healing in STSG donor site wounds [Brown & Holloway, 2018]. Wet dressings provide an environment that prevents desiccation and is non-adherent to the wound bed. In contrast, non-moist dry dressing possesses no barrier to contain the extracellular fluid within the wound [Serebrakian *et al*., 2018].

Multiple challenges are involved in developing novel therapeutics, including safety and efficacy assessment, along with determining the optimal dosage range. Many in vitro and rodent in vivo studies on bioactive small molecules from natural sources exist. Still, there appears to be a gap in their progression to human clinical trials. Whilst these studies are of great interest and necessity to progress as a medicinal therapy, clinical trials are required to confirm the efficacy of novel therapies [Moses *et al*., 2023].

A systematic and meta-analysis review by Rahman reported that biological dressings have superior wound healing properties to non-biological dressings in managing STSG donor sites. The epithelialization rate was enhanced when using natural dressing products. However, this rate could not be quantified as the reporting criteria were not homogeneous among the study groups. Regardless, a qualitative assessment showed sufficient evidence to suggest that biological dressings enhance the epithelialization rate compared to non-biological dressing [Rahman *et al*., 2020].

Limitations

This review did not take into account animal model clinical trials and medicinal plants which have demonstrated their effectiveness on wounds other than split-thickness skin graft donor site. The current evidence base is limited by heterogeneous methodology, results reporting, and underpowered studies.

CONCLUSION

Our current knowledge about the effectiveness of medicinal plant extracts in STSG donor site healing is yet to be enough. The medicinal plants reviewed have large effect size regarding time to complete wound healing and wound score. However, the effect size of *Aloe vera* regarding time to complete wound healing and pain control vary from study to study. No patient quality of life was assessed neither cost effectiveness of these products.

Medicinal plants are potential cost effective antimicrobial and wound healing products for STSG donor site wound. However, more clinical researches including patient quality of life among outcome measures are needed.

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Author Contributions

Study conception, design and data collection by Tshimbila Kabangu JMV; draft manuscript preparation, analysis and interpretation of results by Tshimbila Kabangu JMV, Kadima Ntokamunda Justin, Mushagalusa Kasali Félicien, Lundimu Tugirimana Pierrot, Arung Kalau Willy. All authors reviewed the results and approved the final version of the manuscript.

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