Effect of Aloe Cream *versus* Silver Sulfadiazine for Healing Burn Wounds in Rats

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SUMMARY The management of burn injury remains a problem and it is the major cause of death and disability. The aim of this study was to evaluate the efficacy of *Aloe vera* cream in the treatment of thermal burn wounds and to compare these results with silver sulfadiazine in rats. Animals were divided into four groups. Animals were administered topical cream (*Aloe vera* powdered gel 0.5% and silver sulfadiazine) at 24 h of burn injury induced by hot water. On special days, according to study protocol, wound size was determined and skin sample histopathology performed in animal groups administered topical therapies. On day 25, the mean wound size was 5.5, 4, 0.78 and 4.1 cm^2 in control, base, aloe and silver group, respectively. The wound size was significantly smaller in aloe group as compared with other groups. Histologic comparison showed aloe to increase reepithelialization in burn wounds significantly as compared with other cream-treated wounds. The results of this study showed aloe cream to significantly increase reepithelialization in burn wounds as compared with silver sulfadiazine.

KEY WORDS: burn, *aloe vera*, wound, silver sulfadiazine

INTRODUCTION

Thermal burn injury is a major cause of death and disability, with high health care cost. Healing of burn wounds remains a challenge to modern medicine, although many antiseptics have been discovered. Burn management entails significant length of hospital stay, expensive medication, multiple operative procedures and prolonged period of rehabilitation. This makes burn care an expensive proposition and every effort should be made to provide a shorter inpatient care for burn patients (1). We have recently shown that a significant number of patients exposed to thermal and boiling burn injury in northern Iran stay for long time at hospital for treatment. More than 60% stayed at

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hospital between 8 and 30 days (2). Silver sulfadiazine (SSD) cream 1% is the most widely used topical treatment for burn injury. The antimicrobial efficacy of SSD is probably the main reason for the widespread use of this agent (3). Delayed wound healing is the major clinical adverse effect of silver topical agent following treatment. The wound healing effects of SSD were studied with vaselinated tulle gras in burn patients. It was demonstrated that SSD delayed wound healing (4). Several adverse reactions and side effects have been reported, such as resistance to SSD, renal toxicity, and leukopenia, thus confirming that this topical cream should not be used for long periods on extensive wounds (4). Sloughing of dead tissue in partial thickness burns is retarded because SSD delays or prevents colonization by microorganisms. SSD might also slow down the healing of the wound (5). Prolonged application on partial-thickness burn wounds results in high patient care cost and complicates wound healing because inpatient follow up is needed. It is important to find more effective drugs with shorter time application.

Aloe vera (family Liliaceae) has been used in traditional medicine for a long time. It is one of the most recognizable herbs in the world. The medicinal parts are succulent leaves. Leaf gel, leaf juice, both fresh and dry aloe gel, obtained by breaking or slicing a leaf, is the principal part of the plant used in herbal medicine.

Topical skin gel provides excellent health support for the skin. *Aloe vera* contains many important nutrients for the body, including amino acids, B vitamins, and other nutrients that support general health. It has many pharmacological properties including antioxidant, wound healing, antibacterial, antifungal and immunomodulating effects (6-13). Although burn wound healing was one of the major indications for use of *Aloe vera* gel in several animal and clinical studies, there are few studies comparing the efficacy of this gel and SSD in the treatment of burns in animals (8,14).

Realizing the potential use of *Aloe vera* gel in wound healing, the present study was undertaken to study the effect of *Aloe vera* gel cream in comparison with SSD on the rate of burn wound healing, i.e. burn wound size and reepithelialization.

MATERIALS AND METHODS

Aloe vera

Pure spray-dried *Aloe vera* powder was obtained from Zarban Phyto-Pharmaceutical Company, Iran. These products consist of inner gel from plants; 150 g of *Aloe vera* powder were obtained from 30 L of gel filtered from the plant.

Preparation and formulation of aloe cream

Two grams of liquid white paraffin, 7.5 grams of sterile alcohol, 7.5 grams of acetyl alcohol, 3 grams of solid white paraffin, and propylene paraben (0.015 g) were mixed and heated to boiling point as aqueous phase. Half gram of pollen saffron with 70 mL deionized water was added to the mixture of 7 grams of propylene glycol, 3 grams of sodium luryl sulfate and 0.025 grams of methyl paraben. The mixture was heated as organic phase. Then, two separate phases were mixed continuously while being treated to lower temperature. Thus, a uniform cream was produced and filled in tube after cooling down. The cream contained 0.5% of *Aloe vera* gel powder. Our experimental study and formulations were carried out under sterile conditions. The final creams were tested for any probable microbial contamination.

Study animals

Male Wistar rats (n=48) weighing 180 to 200 grams were used and housed under standard conditions at room temperature and given laboratory food and water *ad libitum* throughout the study. The experimental protocol was approved by Ethics Committee of Mazandaran University of Medical Sciences prior to commencement of the study. The weights of the animals were measured. They were anesthetized intraperitoneally with thiopental (40 mg/kg body weight), while their backs were shaved. They were then placed in supine position inside the bottom of hot water (90 ^{O}C for 6 seconds). This heat exposure caused a uniform second-degree burn on the back of the skin. In this experiment, approximately 10% of total body surface (TBSA) was burned. The animals were resuscitated with an intraperitoneal injection of 5 mL of normal saline solution.

After 24 h, the animals were assigned at random to four groups of 12 animals. Group 1 served as control group and no topical agent was applied; group 2 were treated with base cream (base cream without effective agent); group 3 were treated with 1% SSD (Behvarzan Pharmaceutical Company, Rasht, Iran); and group 4 were treated with 0.5% powered *Aloe vera* cream. Treatment began 24 h after burn injury. Wounds were treated twice daily.

In order to quantify the rate of wound healing, the size of lesions was determined on days 1, 3, 7, 10, 14, 20 and 25 of burn injury. At this time, study

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Table 1. Mean wound size in control group and in base, aloe and silver sulfadiazine (SSD) cream treated groups of animals

Treatment group*	Days after burn				
	7	10	14	20	25
Control (cm^2)	28.9±2.9	26.7±5.6	21±8	7.5±4	5.5±3
Base (cm^2)	28.4±8.3	25.3±6	12.3±5.6	6.8±2.2	4±2.3
Aloe (cm^2)	30.34 ±5.8	17.4 ±3.2	5.3±5.7	1.8±1.5	0.78 ±1.3**
SSD (cm^2)	34±4.4	28±6	18.6±8.5	6.6±3.7	4.1±3.6

*Values are means ± SD for each group of animals; **P<0.05 comparison of aloe extract cream compared to other groups.

animals were kept in good position and wound margin was traced on a transparent plastic sheet using a fine-tipped pen. The lesion body area was displayed as mm^2 on each experimental day. The wound area on day 1 was considered as 100% and wound areas on subsequent days were compared with the initial wound area.

Histological study

Due to the wound healing of burn wounds, reepithelialization was evaluated after 25 days as the last day of treatment period. For this purpose, skin tissue samples were taken for histological studies with a small excision containing part of the wound area. Tissues were fixed in 10% formalin. Paraffin-embedded sections (5 µm thick) were prepared and stained with hematoxylin and eosin. Light microscopy was used to evaluate pathological changes, e.g., granulation tissue formation and reepithelialization in wounds and their comparison with normal tissue.

Statistical analysis

One-way analysis of variance (ANOVA) and Tukey post test were used on group comparison. Differences were considered significant at P<0.05.

RESULTS

Wound condition on day 7 after burn was assessed clinically in all groups to facilitate exact determination of wound size. Skin lesions were measured on days 7, 14, 20 and 25 of burn injury and the ratio to day 1 was evaluated. The mean wound size on day 25 was 5.5, 4, 0.78 and 4.1 cm^2 in the control, base, aloe and SSD group, respectively (Table 1). There were significant differences between aloe group and the other three groups (P<0.05). There was no statistically significant difference in wound size among the control, base and SSD groups on day 25 of treatment. The patterns of wound size ratios in the control and treatment groups are shown in Figure 1.

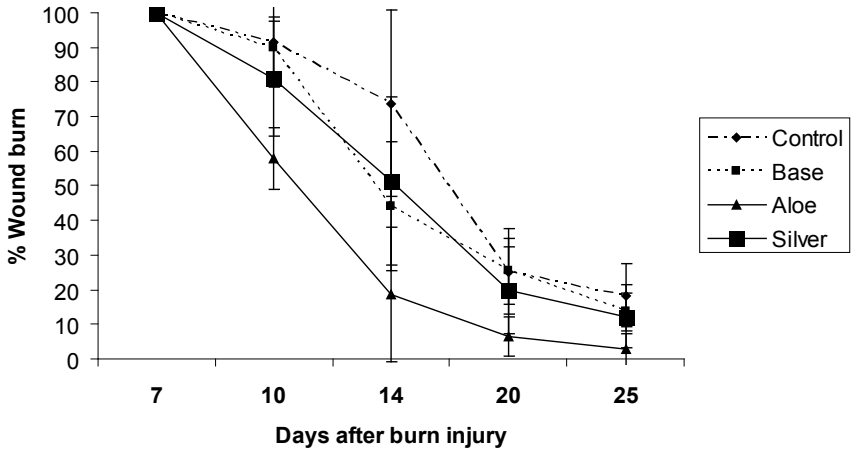

Figure 1. Comparison of wound burn size in control, base, *Aloe vera* and silver sulfadiazine treated groups. The wound size measured on day 7 was considered as initial and wound size on other days was calculated against this initial value.

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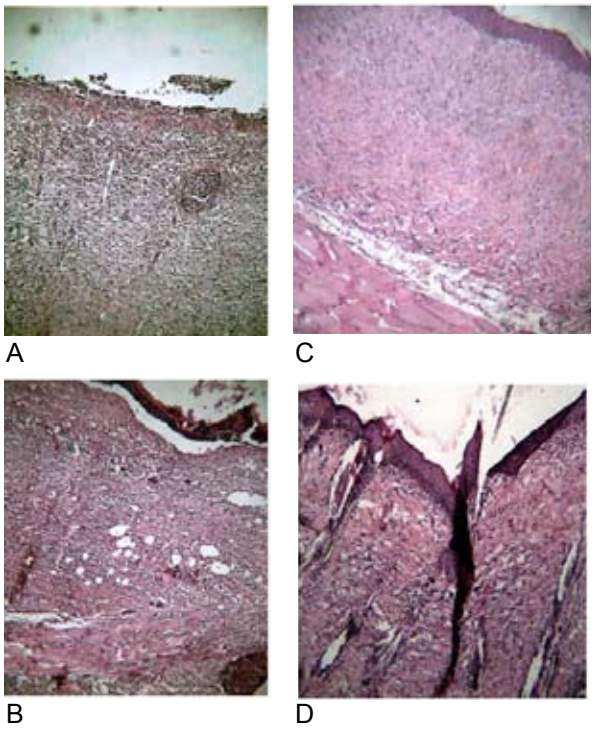

Figure 2. Photomicrograph of the rat skin wound section on day 25 day in control (A) and base treated (B), *Aloe vera* treated (C) and silver sulfadiazine treated (D) groups. Specimens were stained with hematoxylin and eosin.

Results of histological studies indicated an improvement in wound healing on day 25 of treatment. The slides from aloe treated burned skin biopsies showed significant wound healing by reepithelialization of the epidermis and fibrosis of the dermis. The inflammation and granulation tissue formation were minimal and bacteria were not found in this specimen (Fig. 2). The specimens of SSD treated wounds showed a lesser degree of wound healing as compared with aloe treated group according to reepithelialization of the dermis, fibrosis of the dermis with more ulceration, granulation of tissue formation and inflammation (Fig. 2). The slides of wounds treated with basic creams showed a lesser degree of wound healing compared to saffron and SSD treated groups. Bacteria were found in the wound treated with basic creams. Histological samples of non-treated control group showed negligible wound healing and many bacteria in the specimen. Macroscopic images of burned rats are shown in Figure 3.

DISCUSSION

Our findings demonstrated *Aloe vera* cream to have burn wound healing effects in rats. Healing parameters showed aloe to be very effective in healing of burn injury; these effects were observed in the size of wound healing and on histopathology. Although other studies showed aloe gel to be effective in wound healing in animal models (8,14), they did not compare it with SSD as a common topical cream for burn injury. Our studies showed aloe to be more effective than SSD in healing partial burn in rat. The antimicrobial effect is the major mechanism of SSD in wound healing. The silver ion binds to the organism DNA and consequently releases the sulfonamide that kills the microbes (15). However, topical administration of SSD may be associated with hepatic and renal toxicity. These side effects were observed in the treatment of extensive burns (16,17). Although silver-coated dressing acticoat has advantages over topical SSD, it also induced adverse reactions in patients (18).

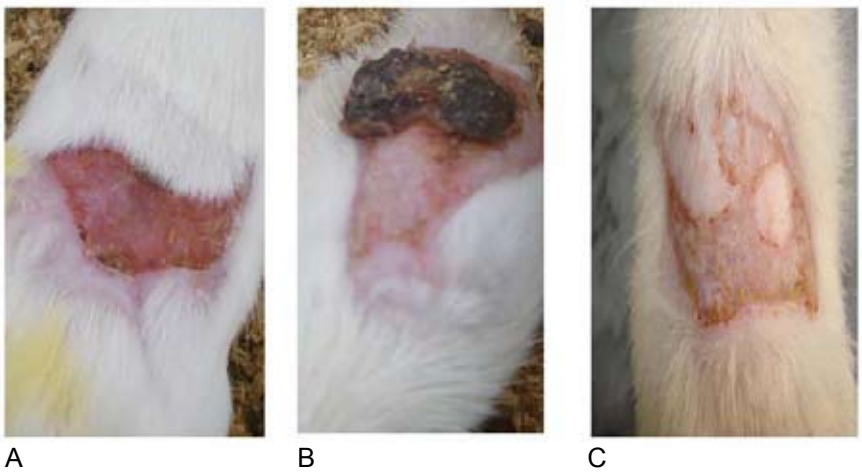

Figure 3. Visualization of burned rats from control (A), silver sulfadiazine treated (B) and aloe (C) cream treated groups on day 20.

Wound healing involves several biological processes such as inflammation and granulation tissue formation. Collagen is the major protein of the extracellular matrix and provides strength and integrity to the dermis and other supporting tissues (19-21). *Aloe vera* application has been indicated to increase the content of collagen (20). Glycoprotein fraction is the major component of aloe involved in its wound healing effect through cell proliferation and migration (22). Isolated glycoprotein fraction promoted growth of dermal fibroblasts, as compared with neutral polysaccharide fraction that exhibited no such effects (23). The anti-inflammatory effects of aloe can contribute to resolving the inflammatory process induced by burn injury (23). In this study, we observed that the aloe treated skin showed no bacteria in the biopsy specimen, while bacteria were found in the base cream treated skin. Infection is the main problem in the skin involved by burn injury; topical antimicrobial reduces burn compliance. SSD is effective in this mechanism. Aloe gel has antimicrobial effects (10,13) and can result in wound healing and reducing infection in burn injury. Muller *et al.* showed that wound contraction was delayed by SSD. *Aloe vera*, when added to SSD, reversed this effect and wound half-life, and healing times were shortest in the SSD/*Aloe vera* groups and longest in the 1% SSD group. These data showed *Aloe vera* to have synergistic effects in wound healing in comparison to SSD alone (14).

In this study, we showed that aloe cream was effective in wound healing in burn animals.

CONCLUSION

The size of skin lesion was smaller in saffron treatment as compared to SSD. The process of reepithelialization was more efficient in aloe treated animals than in SSD treated animals. The antimicrobial, cell proliferation and inflammatory effects may be the mechanism of aloe action in burn healing.

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Alga - known medicine against rheumatic as well as other kind of pain; year 1934.
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