

Brief communication (Original)

A herbal cream consisting of *Aloe vera*, *Lavandula stoechas*, and *Pelargonium roseum* as an alternative for silver sulfadiazine in burn management

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Background: Silver sulfadiazine (SSD) is the most used topical agent for the treatment of burn wounds. However, it has some side effects such as delayed and incomplete epithelialization, generation of black scars, and limited penetration to the depth of a wound.

Objective: The present study investigated the efficacy of herbal combination cream containing *Aloe vera* gel and essential oils of *Lavandula stoechas* and *Pelargonium roseum* in the alleviation of symptoms in patients with superficial second-degree burns and comparison of its effects with those of SSD 1% cream.

Methods: One hundred eleven patients with second-degree burns (occurring in the preceding 48 hours and affecting <50% body area) were randomized to receive either herbal cream (n = 56) or SSD 1% cream (n = 55) applied once daily for 14 days. Prevalence of skin dryness and pain severity (assessed using a visual analogue scale) and evidence of infection was determined for patients at baseline as well days 2, 7, and 14.

Results: Both groups experienced a significant reduction in the pain severity at day 14 compared to baseline ($p < 0.001$). As for the magnitude of change in pain score, there was a significantly greater reduction from baseline to the seven ($p = 0.014$) and 14 ($p = 0.05$) day in the herbal cream compared to control group. The frequency of skin dryness was not significantly different between the groups at any of the assessed time points ($p > 0.05$). There was a single case of infection in the herbal cream group, which cleared with continuation of treatment.

Conclusion: Our findings suggested that the herbal cream used here is superior to SSD 1% cream in the alleviation of pain and may serve as a natural alternative for treatment of second-degree burns.

Keywords: *Aloe vera*, burn wound, *Lavandula stoechas*, *Pelargonium roseum*, silver sulfadiazine

Thermal burns are among the major causes of serious injury in the United States. About 1.1 million people are affected with burns annually, of which most are treated as outpatient. However, 45000 of these patients need hospital admission and another 4,500 die [1].

Because of burn injury to the skin, the first physiologic barrier against foreign microorganisms is impaired. Therefore, wound site infections are an important concern in the management of burn patients. Antibiotic therapy is among the main approaches for

the prevention and treatment of burn wounds and statistics indicate that there was an approximately 60% reduction in burn-related mortality following the introduction of topical antibiotics [1].

Based on the depth of injury, burns are classified into four degrees. First-degree burns affect only the epidermis. Second-degree burns extend into dermis but subcutaneous fat is not involved. In third-degree burns, necrosis extends through the entire dermis and affects the subcutaneous fat layer. In fourth-degree burns, injury extends through the entire skin into subcutaneous tissues and may involve underlying fascia, muscle, and bone. Second-degree burns are further classified into superficial and deep burns. The first-degree superficial form involves papillary dermis.

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It is characterized by formation of clear blisters and fluid accumulation between epidermis and dermis. In contrast, deep second-degree burns involve reticular dermis and lead to complete loss of the dermis layer and scar formation.

Silver sulfadiazine is the most used topical antibiotic for the treatment of burn wounds. However, it has drawbacks including delayed and incomplete epithelialization, generation of black scars, limited penetration to the depth of wound, hypersensitivity, neutropenia, and thrombocytopenia [2, 3]. Other topical antibiotics such as mafenide acetate and silver nitrate are also associated with side effects such as pain and hypersensitivity at the wound site, delayed wound healing, electrolytic imbalance, and hemoglobinemia [4, 5].

Therapeutic goals in burn management include prevention of infections and rapid healing with the least side effects. Given the adverse effects of currently used topical antibiotics, introduction of novel topical agents that could effectively and safely promote wound healing and relieve the associated pain are desirable. The previously reported healing, emollient, antimicrobial, and anti-inflammatory properties of *Aloe vera* gel [6-10] and the antimicrobial and anti-inflammatory effects of *Lavandula stoechas* and *Pelargonium roseum* essential oils [11-15], encouraged us to carry out a study on the efficacy of herbal combination cream containing the three aforementioned components in patients with superficial second-degree burns. Results were compared with those of silver sulfadiazine 1%.

Methods

This study was a randomized and double-blinded clinical trial among 120 patients (age range: 18 to 75 years) with superficial second-degree burns. Inclusion criteria were thermal second-degree burns affecting less than 5% of the body, occurrence of burn in the preceding 48 hours, presence of no other injuries and general physical and mental health. Exclusion criteria were the presence of any renal, hepatic, endocrine, cardiovascular or cerebrovascular disease, pregnancy, history of drug or alcohol abuse, and concurrent use (oral or topical) of antibiotics, steroids or immunosuppressive drugs. The study protocol was approved by the Ethics Committee of the relevant institute and written informed consent was obtained from participants.

Participants were randomized in a double-blind manner to receive herbal cream ($n = 60$) or SSD 1% ($n = 60$). The constituents of herbal cream were *A. vera* gel and essential oils from *L. stoechas* and *P. roseum*. Both creams were administered in identical tubes and were matched in their color and volume.

Following cleansing and debridement of burn wounds with antimicrobial solution, cream (5 g for each 10 cm² of burn area) was applied on wounds using a sterile spatula. After application of the creams, sterile gauze was applied and wounds bandaged. Treatment was continued once a day until recovery.

Patients were evaluated for the severity of pain, frequency of skin dryness, and infection at baseline as well as days 2, 7, and 14 following the initiation of treatment. Pain severity was assessed using a 10-score visual analogue scale (VAS). Patients were asked to mark their pain severity from 0 (reflecting no pain) to 10 (reflecting unbearable pain).

Statistical analysis

Statistical analyses were performed using SPSS software. Within-group comparisons were made using Wilcoxon signed ranks test or paired samples *t*-test. Between-group comparisons were performed by means of Mann-Whitney U test or Chi-square test. A two-sided *p*-value of <0.05 was considered as statistically significant.

Results

From the initial 120 patients with superficial second-degree burn that were recruited into the study, nine were excluded due to study protocol violation. Drop-out rate was not significantly different between the groups ($p > 0.05$). Data from 111 completers ($n = 56$ in the herbal cream and 55 in the SSD group) were included in the final analysis. There was no significant difference between the two groups regarding age, gender, percent burn area, and pain severity at baseline ($p > 0.05$). In the same manner, burn agents and consumption of analgesics were not significantly different between the groups ($p > 0.05$) as can be seen in **Table 1**.

The frequency of skin dryness on days 2, 7, and 14 post-burn were 12.5%, 12.5%, and 7.1% in the herbal cream group and 27.3%, 25.5%, and 10.9% in the SSD group, respectively. There was no significant difference in the frequency of skin dryness between the groups at any of the assessed time points ($p > 0.05$). In addition, the rate of change in the frequency of skin

dryness between days 2 and 7, 2 and 14, and 7 and 14 was not significantly different between herbal cream and SSD groups ($p > 0.05$) (Table 2).

Both groups experienced a significant reduction in pain severity at day 14 compared to baseline ($p < 0.001$) as shown in Figure 1. As for the magnitude of change in pain score, there was no significant difference between the groups from

baseline to the second day ($p = 0.059$). However, there was a significantly greater reduction from baseline to the seventh ($p = 0.014$) and fourteenth ($p = 0.05$) days in the herbal cream compared to control group (Table 3). Among the study population, there was only a single case of infection in the herbal cream group with recovered following continuation of treatment.

Table 1. Demographic characteristics of herbal cream and SSD groups.

	Herbal cream	SSD 1%	<i>p</i> -value
Age	33.6±13.4	37.4±12.7	>0.05
Gender (F/M)	21 (37.5)	25 (45.5)	>0.05
Burn %	2.48±1.45	2.38±1.42	>0.05
Burn agent			
Hot water/steam	24 (42.9)	23 (41.8)	
Fire	22 (39.3)	18 (32.7)	
Hot liquid	5 (8.9)	10 (18.2)	>0.05
Hot object	2 (3.6)	3 (5.5)	
Chemical substance	3 (5.4)	1 (1.8)	
Analgesic consumption	18 (32.1)	18 (32.7)	>0.05
Pain severity	5.68±3.2	4.56±4.87	>0.05

SSD: silver sulfadiazine

Table 2. Prevalence of skin dryness in different time points.

	Herbal cream	SSD 1%	<i>p</i> -value
Day 2	7 (12.5)	15 (27.3)	0.051
Day 7	7 (12.5)	14 (25.5)	0.081
Day 14	4 (7.1)	6 (10.9)	0.488

SSD: silver sulfadiazine.

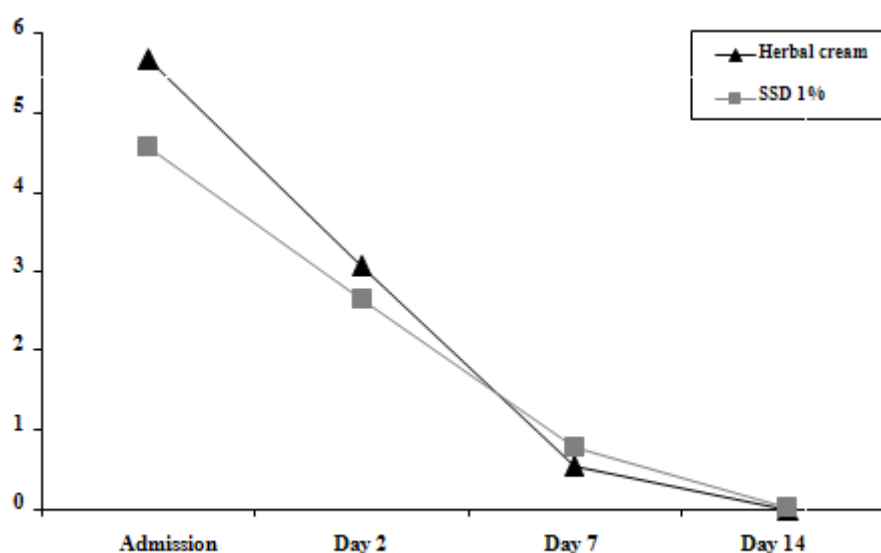


Figure 1. Severity of pain in the herbal cream and SSD groups at different time points.

Table 3. Changes in pain severity in the herbal cream and SSD groups.

	Herbal cream	SSD 1%	p-value
Baseline - day 2	2.61±1.55	1.91±2.25	0.059
Baseline - day 7	5.13±2.82	3.78±2.83	0.014
Baseline - day 14	5.68±3.2	4.54±2.83	0.05

SSD: silver sulfadiazine

Discussion

Herbal cream that was used in this study is a combination of *A. vera* gel and essential oils of *L. stoechas* and *P. roseum*. The clear jelly-like substance obtained from the inner layer of *A. vera* leaves, commonly referred to as *A. vera* gel, is the medicinal part of the plant that has been investigated in relation with a number of disorders [6, 7]. *A. vera* leaf gel has been reported to possess antibacterial and antiviral properties [16]. These properties could be attributed to the bioactive components present in the aloe gel such as aloe-emodin, for which inhibitory activity has been reported against strains of bacteria (including methicillin-resistant *Staphylococcus aureus*), fungi and viruses [17]. Aside from the antimicrobial effects, *A. vera* has documented anti-inflammatory activities such as inhibition of inflammatory cell migrations, inhibition of cyclooxygenase and blocking prostaglandin E2, bradykinin and histamine production. These effects could be attributed, at least in part, to the presence of salicylates and polysaccharides such as C-glucosyl and veracylgucans B and C in the *A. vera* gel [18-20]. Finally, there is evidence supporting the efficacy of *A. vera* in the healing of burn wounds, assessed in terms of healing success rate, healing time, and rate of epithelialization on post-skin grafting [21].

L. stoechas oil constituted another component of the herbal combination cream. The essential oil obtained from *L. stoechas* has medicinal properties including antimicrobial, anti-inflammatory, rubefacient, and analgesic actions. There is evidence indicating that *L. stoechas* oil has proper efficacy against Gram-negative bacteria and could partially affect *Pseudomonas* strains [11-13].

P. roseum oil was also included in the herbal cream. This oil has been reported to possess antiseptic, astringent, hemostatic, and wound healing properties [14]. In addition, this oil has been found to be effective against *E. coli*, *S. aureus*, *P. aeruginosa*, and *C. albicans* infection [15].

In spite of its painless topical application and efficacy against a broad spectrum of Gram-positive, Gram-negative (including most *Pseudomonas* species) bacteria, and fungal strains, SSD has some disadvantageous such as leaving black spots on skin, lack of enough penetration to the depth of the scar, and partial inhibition of epithelialization [2, 3].

Past animal and clinical studies have supported the efficacy of *A. vera* in the healing of first to second-degree burn wounds [21]. In a previous animal study, Muller et al. reported the efficacy of *A. vera* in shortening the healing time compared to SSD and reversing the inhibitory effect of SSD on wound healing [22]. In another investigation, Hosseini-mehr et al. reported a significant increase in reepithelialization by aloe cream compared to SSD [23]. Regarding clinical data, Visuthikosol and colleagues reported on 27 patients with partial thickness burn wounds where application of *A. vera* gel led to early epithelialization and a significantly faster healing compared to vaseline gauze [24]. There are also other consistent clinical reports on the positive impact of *A. vera* on the healing time and epithelialization rate of burn wounds [25-27].

In summary, the findings of the present trial indicated that the combination cream made of *A. vera* gel and essential oils of *L. stoechas* and *P. roseum* is superior to SSD 1% cream in alleviation of pain. Therefore, this cream may be used as a natural and effective alternative for SSD cream in superficial second-degree burns.

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Conflicts of interest

Hossein Akbari, Hossein Bekhradi, and Mohsen Taghizadeh are members of Barij Essence Pharmaceutical Co. (Kashan, Iran).

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