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## Wound Healing Effect of Hydroalcoholic Extract of *Salvadora Persica* (Miswak) on Physically Induced Second-Degree Burn Wound in BALB/c Mice

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### Abstract

**Introduction:** Different Scholars have mentioned a lot of benefits for *Salvadora Persica*(SP) compounds. The Present study was conducted aiming at evaluating the effect of hydroalcoholic extract of SP on second-degree burn healing in Mice.**Materials and Methods:** The present study population was 60 mature mice (BALB/c). The mice were divided into 5 equal groups. Groups 1 and 2 were treated by means of the application of 5% hydroalcoholic extract of SP and 10% extract of it, respectively; regarding group 3 received silver sulfadiazine ointment. Group 4 was treated using Vaseline. Group 5 received no treatment. Then, samples from the injured sites was gathered, and wound healing was evaluated histopathologically.**Results:** Inflammation and infiltration of neutrophils and lymphocytes in the treatment groups, i.e. the groups to which 5% and 10% SP extract was applied, demonstrated a significant decrease, compared to the vaseline and sham groups ( $P<0.01$ ). Moreover, the number of fibroblasts increased followed by collagen production, epithelialization and new hair follicles formation at the wound margins on the 10<sup>th</sup> and 14<sup>th</sup> day in the 5% and 10% SP extract groups significantly increased compared to vaseline and sham groups ( $P<0.05$ ). The number of fibroblasts and the density of collagen tissues in the group treated with 10% SP extract even showed a significant increase compared to the groups treated with 5% SP extract and silver sulfadiazine on the 14<sup>th</sup> day.**Conclusion:** It was found that hydroalcoholic *salvadora Persica* extract accelerated the healing of second-degree burn injuries in BALB/c mice.

**Key Words:** *Salvadora Persica*, Wound, Burn, Skin, Mice

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## Introduction

The Skin is an important organ which acts as a physical barrier against the outer environment; and, as a natural immunity system prevents the entrance of microorganisms, pathogens, and harmful chemicals. It also has a role of dehydration prevention and keeping of the minerals of the body.<sup>[1]</sup> The skin consists of two layers of the epidermis with epithelial structure and the dermis that is made up of connective tissue. The hypodermis is a layer beneath the dermis with a fatty tissue structure. Burn injuries occur due to various factors such as heat, Chemicals, electricity, the sun, or nuclear radiation. In second-degree burns the epidermis is entirely and the dermis is either entirely or partially affected. Burns are divided into 4 types based on depth and penetration into the skin layers and lower parts. In second-degree burns, the epidermis and dermis are completely damaged. Burn injuries, whether local or systemic, decrease both the resistance of the skin, as a protective barrier against the environment and its capacity as a significant immunity organ. Following burns a collection of physiologic responses occur including changes in the cellular protective mechanisms, local and systemic inflammation.<sup>[2]</sup> The skin regeneration procedure is a fundamental and consecutive one having four main phases: homeostasis, inflammation, proliferation, and remodeling.<sup>[3-4]</sup>

The quality and speed of wound healing depends on a lot of factors such as type of the wound, the general condition of the patient, other relevant disease(s), the wound size, the infection (because of toxins and free radicals production), the existence of foreign bodies and microorganisms, the extent of local hemoperfusion, hypoxia; and also other factors such as age, health status, and nutrition of the patient.<sup>[5-6]</sup>

The favorable care and treatment of such injuries has always been taken into account by researchers to increase the rate of their healing, decrease scar formation and also prevent them from becoming chronic and infectious.<sup>[7]</sup>

Today, a lot of drugs having a natural origin. In Iranian Traditional Medicine medicinal herbs have a particular position and are used in treating a lot of disorders.<sup>[8-9]</sup> Medicinal herbs are less expensive and more appropriate for man's physiology and the occurrence of toxicosis and unfavorable side-effects due to their use is less Probable.<sup>[10-11]</sup>

*Salvadora Persica* is a plant which is called "Miswak" or "Arak" in Arabic and belongs to the Salvadoraceae family. Muslims have been using the twig of the plant as a toothbrush for the oral hygiene for centuries<sup>[12]</sup>. Among the most important extracted chemicals of the plant are: Salts (particularly chlorides), salvadoura, salvadorine, alkaloids, fluoride, silica, sulfur, vitamin C, resin, tannins, saponins, flavonoids, cyanogenic glycosides, and benzyl isothiocyanate. Due to having such chemicals SP has some pharmacological properties, including antibacterial and antifungal<sup>[13]</sup>, anti-inflammatory and sedative<sup>[14]</sup>, antioxidant<sup>[15]</sup>, anti-plaque, anti-hyperlipidemia, and hypoglycemia activities<sup>[16]</sup>. Among the studies on the healing process of gastrointestinal wounds in rats indicated that the extract of this plant has anti-inflammatory (by inhibiting the NF- $\kappa$ B pathway) and anti-ulcer properties.<sup>[17-18]</sup> Another study revealed that SP extract applied to the excisional wounds decreased the time of wound closure in rats.<sup>[19]</sup>

A cellular study showed that the aqueous extract of SP increased the number of fibroblasts in vitro.<sup>[20]</sup> With regard to the anti-inflammatory, antioxidant, and antimicrobial properties of SP, it seems that the extract of the herb could be effective in burn wound healing. Regarding that so limited studies have dealt with the healing effect of the herb on the burn wound, in the present study

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the effects of the hydroalcoholic extract of SP on the skin burn wound healing of BALB/c mice were assessed.

## Materials and Methods

### Experimental animals

The present study population was 60 male adult BALB/c mice (each 2.5 months old), each weighing  $25 \pm 5$  g. The mice were provided by the Experimental Medicine Research Center of BUMS. The rats were singly kept in clean cages so that food and water were freely available for each. Light and the dark cycles were equal to 12 hours a day, the temperature of the environment varied between 22-23 °C, and air humidity was 45%-50%.

Besides, the ethics measures regarding experimenting on lab animals according to the protocol of lab animals experimentation passed by BUMS with the code 45546 and the ethics code ir.bums.REC 139789 were all taken into account.

Mice were randomly divided into five equal groups; the first and the second group received 5% and 10% hydroalcoholic SP extract, respectively<sup>19</sup>. The third group, as the positive control group, received silver sulfadiazine; and the fourth group, as a negative control one, received vaseline dressing. The fifth group (sham) received no treatment.

First of all, mice were anesthetized through intra-peritoneal injection of 70 mg/kg ketamine and xylazine 2 mg/kg.<sup>[21-22]</sup> then, the hair in the back of each was shaved, and in sterile condition and considering all surgery measures a circular second-degree superficial burn whose diameter was 1 cm, including the thickness of the dermis was made by means of a flat round metal stamp. First, the flat head of the instrument was held over the flame of an alcohol lamp for 3 minutes. Then, the heated end was kept in touch with the back skin of each animal for 10 seconds.<sup>[7]</sup> The mice whose injuries had extended to hypodermis and muscles were excluded from the study. Finally, in order to macroscopically compare the wounds, a digital camera was used to take pictures of the burn sites. Then, the injuries of each group were dressed topically twice daily; at 8 a.m and 8 p.m for 14 consecutive days. In the end, 3 mice were randomly selected from each group on the 4<sup>th</sup>, 7<sup>th</sup>, 10<sup>th</sup>, and 14<sup>th</sup> day. After general anesthesia using ketamine and xylazine, samples were taken from their burn injuries.<sup>[23-24]</sup>

### Preparation of the herb extract

In order to prepare the hydroalcoholic extract of the herb, 60 g of it was mixed with 600 cc of 80% methanol for 48 hours at room temperature. Then, the obtained mixture was filtered via Whatman paper. The concentrated extract was dried in a freeze-dryer and kept at -20 C°. Finally, the yield of the extract was assessed. Besides, a herbarium sample of each result was provided as a document, which was approved by a skillful botanist and it was kept in the herbarium (code:2891) of National Resources and Living Environment of Birjand University. SP hydroalcoholic extract ointment whose concentration was 5% and 10% was obtained from the powder, with sterile vaseline base, taken from the freeze dryer. The ointment was kept in a refrigerator and each time a thick layer of it was put on the burn site; then, the injury was dressed.<sup>[7]</sup>

### Histology

First, the samples taken from the burn injuries on various days were fixed in 10% formalin. Then having histological processing done, i.e. dehydrating by excessive concentration of alcohol, and cleared in xylene. After being embedded in paraffin, the obtained moulds were cut into slices with 5 micron thickness using a rotary microtome. Then, the slices, after removing their paraffin, were first colored with hematoxylin and eosin aiming at examining the cells, epithelialization, and hair

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follicles. Specific staining of Masson's trichrome method was used to determine the general density of collagen fibers.<sup>[22]</sup> Several colored slices which covering the entire wound were specifically selected for examination. Every selected slide was randomly photographed by means of Olympus SZX Research Microscope equipped with Euromex-CMEX- 10 camera.

Finally, the enumeration of the cells, density of collagen fibers, epithelialization, and number of hair follicles was done using ImageJ Software.<sup>[24]</sup> The obtained results were compared by means of the statistical tests One-way ANOVA, followed by Post hoc Tukey; and analysed using SPSS (v:22) at the significant level 0.05. Data were presented as Mean  $\pm$  SD.

## Results

In the present study various parameters were assessed, including the number of neutrophils, lymphocytes, fibroblasts, the height of epithelialization, density of collagen fibers, and the number of hair follicles on different days. **The gathered results are presented in tables 1 below:**

Table 1. Neutrophils, lymphocytes, fibroblasts, collagen fiber density and epithelialization (all X 400x in 150 x 100  $\mu$ m) and hair follicles (X 100x in 1200 x 900  $\mu$ m) were examined



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Parameter	Day	SP 5% SD±mv	SP 10% SD±mv	Silver sulfadiazine SD±mv	Vaseline SD±mv	Sham SD±mv
Neutrophils	4	3.1±1.44	2.2±1.88	1.9±1.66 *	4.2±1.47	5.1±1.66
	7	37.7±7.86	31.3±5.75 *	32.5±5.75 *	42.8±6.35	44.7±4.54
	10	46.6±2.17	43.5±2.36 *_***	43.0±2.26 *	43.0±2.26	51.4±1.34
	14	43.4±6.41	38.7±4.21 *	39.0±7.83 *	51.9±7.72	53.0±8.78
Lymphocytes	7	3.4±2.11	2.3±1.25	2.5±1.77	4.3±1.88	5.3±1.94
	10	5.9±0.99 *	5.3±1.15 *	5.3±1.15 *	8.4±0.84	8.9±1.19
	14	4.6±1.17 *	4.00±1.05 *	3.8±1.31 *	6.7±0.94	7.7±1.25
Fibroblast cells	7	4.7±0.94 *	6.2±1.47 *_***	5.6±1.17 *	2.5±0.84	2.2±1.03
	10	22.8±3.99 *	29.7±3.83 *_***	25.6±3.13 *	17.2±2.93	16.5±4.88
	14	43.3±7.70 *	52.1±4.81 *_***_***	44.9±5.50 *	32.3±4.21	31.2±4.10
Density of collagen fibers	10	0.284±0.007 *	0.299±0.003 *_***_***	0.285±0.005 *	0.265±0.003	0.261±0.009
	14	0.361±0.008 *	0.373±0.009 *_***_***	0.359±0.005 *	0.339±0.007	0.337±0.009
Epithelialization in the margins	10	56.5±8.06	60.17±6.28	54.98±9.11	51.67±5.16	50.36±7.01
	14	86.96±6.89 *	88.01±10.00 *	78.88±5.76 *	71.0±3.13	65.36±4.21
Number of hair follicles in the margins	10	3.3±1.76	4.1±0.99 *	3.6±1.26	2.2±1.22	2.1±1.28
	14	4.4±1.07 *	5.1±1.10 *	5.0±0.94 *	2.7±1.33	2.2±1.39

\* Significant differences with Vaseline and Sham groups

\*\* Significant difference with silver sulfadiazine group

\*\*\* Significant difference between *Salvadora persica* group 10% to 5%

Nutrophils, lymphocytes, fibroblasts, collagen density and epithelialization have been examined under a magnification of 400 times in an area of 100×150 micrometer; and hair follicles under a magnification of 100 times in an area of 900×1200 micrometer.

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## Parameters analysis on the 4th day

On the 4<sup>th</sup> day mean number of neutrophils in the groups treated with 10% SP extract ( $P < 0.01$ ) and silver sulfadiazine ( $P < 0.01$ ) showed a significant decrease only compared to the sham group ( $p < 0.01$ ). Both margins coverings of the burn injuries were a lot apart from each other and the surface of the injuries was covered with fibrin. Thus, the other parameters were not detectable.

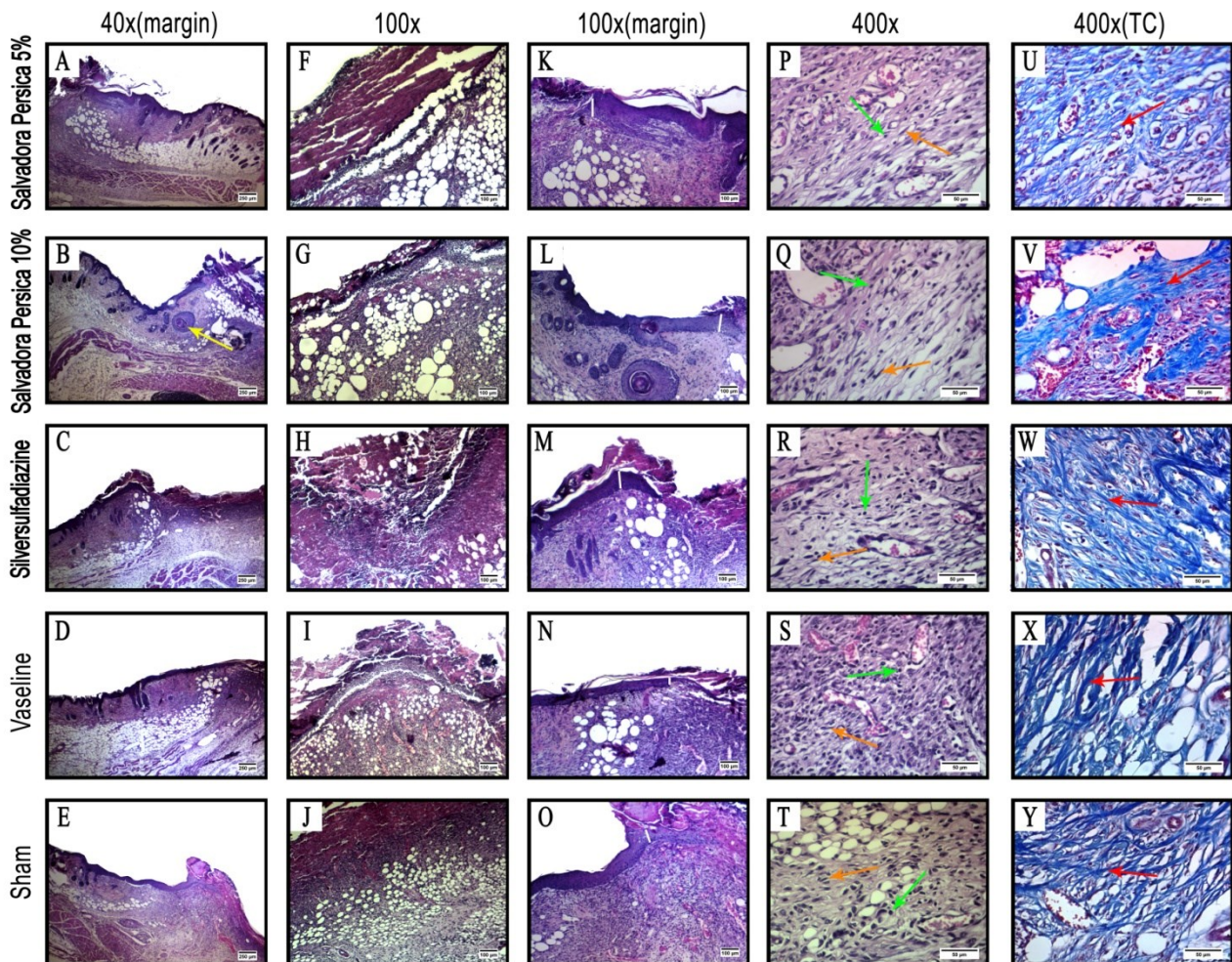
## Parameters analysis on the 7th day

The number of neutrophils and lymphocytes in the group treated with 10% SP extract ( $P < 0.01$ ) and silver sulfadiazine ( $p < 0.05$ ) reduced significantly compared to the sham group. Fibroblasts in both SP and silver sulfadiazine groups significantly increased in comparison with the sham group ( $p < 0.001$ ). The number of fibroblast cells in the group treated with 10% SP extract was significantly increased compared to the 5% SP extract group ( $p < 0.05$ ). Moreover, on the 7<sup>th</sup> day, no signs of collagen synthesis, formation of hair follicles, and start of epithelialization was observed.

## Parameters analysis on the 10th day

On the 10<sup>th</sup> day of the study, the number of neutrophils and lymphocytes in the both SP groups and the silver sulfadiazine group were significantly decreased in comparison with the sham ( $p < 0.001$ ). The number of neutrophil cells in the groups treated with 10% extract ( $P < 0.05$ ) and silver sulfadiazine ointment ( $P < 0.01$ ) had a significant reduction compared to the 5% extract group. Lymphocytes population in both groups treated with 5% ( $P < 0.01$ ) and 10% SP ( $P < 0.001$ ) extracts and silver sulfadiazine ( $P < 0.001$ ) was significantly increased compared to the sham group. The number of fibroblasts in the group treated with 10% extract had a significant increase compared to 5% ( $P < 0.01$ ). Besides, density of collagen fibers in both treatment and silver sulfadiazine groups was significantly increased compared with the sham ( $p < 0.001$ ). The 10% SP extract treatment manifested a significant increase of the collagen fibers density in comparison with the silver sulfadiazine group ( $P < 0.001$ ) and the 5% extract group ( $P < 0.01$ ). On the 10<sup>th</sup> day, epithelialization and hair follicles were not observed in the burn wound center. Thus, the height of the epithelium and the number of new hair follicles in the margins of the wounds were examined. The height of epithelium in the margins of the injuries was significantly higher in the 10% SP extract group compared to the sham group ( $p < 0.05$ ). Also, The number of hair follicles in the injuries' margins significantly higher only in 10% SP extract group contrasted with the sham group ( $p < 0.05$ ) (Figure 1).





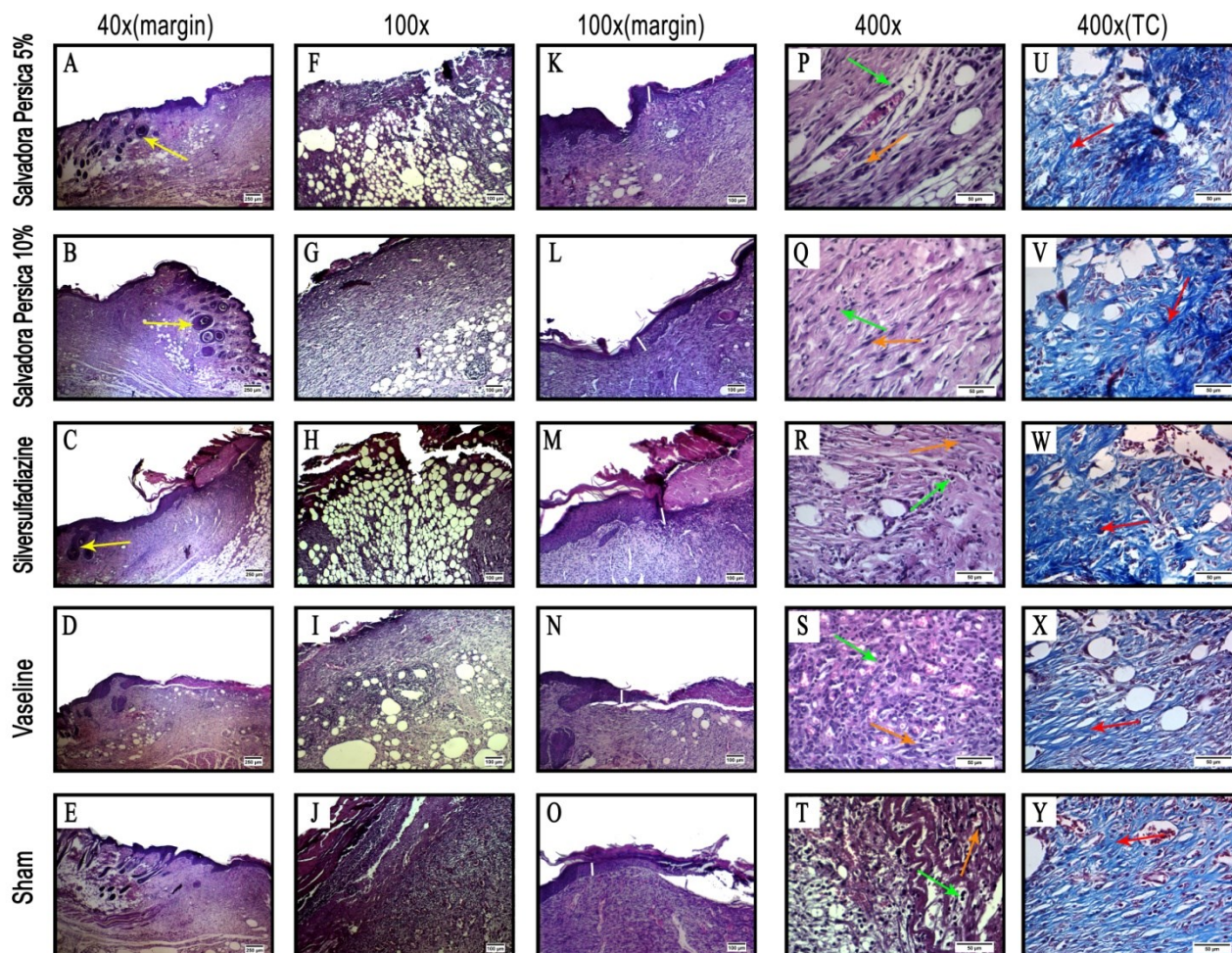
**Figure 1.** Representative photomicrographs of histopathological evaluation of wound healing processes in the study groups on day 10; A,B,C,D and E: Newly formed hair follicle (yellow arrow) in the margin of the wound on H&E staining,40x; F,G,H,I and J: Wound area on H&E staining,100x; K,L,M,N and O: Epithelialization in the margin of the wound (white lines) on H&E staining,100x; P,Q,R,S and T: Neutrophils (green arrows) and fibroblasts (orange arrows) on H&E staining,400x; U,V,W,X and Y: Collagen fibers(red arrows) on Masson's trichrome staining,400x

#### Parameters analysis on the 14th day

On the 14<sup>th</sup> day, the number of neutrophils and lymphocytes in both groups of 5% ( $P<0.05$ ) and 10% SP ( $P<0.001$ ) and silver sulfadiazine ( $P<0.01$ ) groups significantly decreased compared to the sham group; Fibroblast numbers and collagen fibers density in both treatment groups were significantly increased in comparison with the sham group ( $p<0.001$ ). In addition, the 10% SP extract group demonstrated a significant increase in both the number of fibroblasts and in collagen density compared to the silver sulfadiazine group ( $p<0.05$ ) and the 5% extract group ( $P<0.01$ ). On the 14<sup>th</sup> day of wound healing, epithelialization and hair follicles formation were not still observable in the wounds centers; thus, the thickness of epithelium and the newly formed hair follicles in the margins of the injuries were examined. These two parameters in both treatment groups of 5%



( $P < 0.01$ ) and 10% SP ( $P < 0.001$ ) extracts and silver sulfadiazine ( $P < 0.001$ ) showed a significant increase compared to the sham group (Figure 2).



**Figure 2.** Representative photomicrographs of histopathological evaluation of wound healing processes in the study groups on day 14; A,B,C,D and E: Newly formed hair follicles(yellow arrows) in the margin of the wound on H&E staining,40x; F,G,H,I and J:Wound area on H&E staining,100x; K,L,M,N and O: Epithelialization in the margin of the wound(white lines) on H&E staining,100x; P,Q,R,S and T: Neutrophils(green arrows) and fibroblasts(orange arrows) on H&E staining,400x; U,V,W,X and Y: Collagen fibers(red arrows) on Masson's trichrome staining,400x

### Discussion

Generally, the obtained results revealed that topical application of SP extract could have positive effects on the healing of second-degree skin burn injuries. Wound healing is a complex of sequential reactions; and it is the outcome of the interaction among various types of cells, molecules, and extracellular matrix. Wound healing process covers a collection of consecutive reactions that immediately start after the skin injury and may last a long time.<sup>[25]</sup> During the inflammatory phase, white blood cells, including neutrophils and lymphocytes migrate to the injury site, and their main role is the prevention of infection.<sup>[5]</sup> There is much evidence that pro-inflammatory cytokines such as IL-1 $\beta$ , IL-6, and TNF- $\alpha$  secreted by macrophages increase the inflammatory response and, if this continues, can delay wound healing and even create chronic



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wounds. Thus, if the wound healing process is accompanied by proper and temporary regulation of pro-inflammatory cytokine levels, it accelerates wound healing.<sup>[26]</sup> The results of the present study demonstrated that the inflammation and infiltration of neutrophils and lymphocytes on various days (i.e. the 4<sup>th</sup>, 7<sup>th</sup>, 10<sup>th</sup>, and 14<sup>th</sup>) in the 10% SP extract treatment group was totally lower than that in the 5% group; and it was somehow similar to the anti-inflammatory effect of the silver sulfadiazine group. Several studies have indicated that SP can prevent hyperinflammation. A study done by Lebda et al.<sup>[17]</sup>, (2018) to investigate the effect of SP aqueous extract on pro-inflammatory cytokines, nitric oxide synthesis, apoptosis pathways and oxidation and antioxidants pathways involved in gastric ulcer healing were performed on rats, showed that SP extract reduces the production of pro-inflammatory cytokines IL-1 $\beta$ , IL-6 and TNF- $\alpha$  by inhibiting the NF- $\kappa$ B signalling pathway due to its anti-inflammatory properties. due to having anti-inflammatory properties. Also, due to its antioxidant compounds such as furan, vitamin C, tannin, saponin, flavonoid and lycopene,  $\alpha$ -linolenic acid, oleic acid, lycopanthin and retinoic acid can also produce additional anti-inflammatory effects by reducing pro-apoptotic protein expression Bax, lipid peroxidation and TNF- $\alpha$  secretion. Another beneficial effect of this plant is the increase in NO production from eNOS, which leads to increased mucosal blood flow and mucus production and secretion, enhancing the gastric mucosa. Therefore, all these factors cause this plant to have positive effects in the prevention and treatment of gastric ulcers. Another research done by Ibrahim et al.<sup>[14]</sup>, (2011), assessed the anti-inflammatory effect of SP extract on the paw oedema in rats, induced by carrageenan. This study confirmed that ethyl-acetate extract of SP reduced inflammation and inflammatory mediators such as IL-1 $\beta$ , IL-6, TNF- $\alpha$  and TGF- $\beta$  and, in general, concluded that the extract of this plant has similar anti-inflammatory effects to indomethacin as a reference treatment, Which was probably due to its flavinoids.

On the other hand, SP is a rich source of sulfur<sup>16</sup>. Sulfur compounds have strong antioxidant, anti-inflammatory and anti-cancer effects. Studies have shown that sulfur-containing compounds inhibit the production of nitric-oxide, prostaglandin E2, and reduce the expression of pro-inflammatory cytokines including TNF- $\alpha$ , IL-1 $\beta$ , IL-6 by inhibiting the NF- $\kappa$ B pathway.<sup>[27]</sup>

Eleven flavonoid compounds have been known, all of which are flavonol glycerides, including apigenin rutin and quercetin extracted from *Salvadora Persica*.<sup>[14,16,28]</sup> Flavonoid compounds inhibit the degranulation of mast cells, releasing of inflammatory and pro-inflammatory mediators such as prostaglandins, histamine, IL-1 $\beta$ , TNF- $\alpha$  and TGF- $\beta$ , and reduction of inflammatory cells.<sup>[29-31]</sup> In our previous studies, we found the beneficial effects of quercetin in preventing the inflammatory process, ageing and the harmful effects of hyperglycemia on kidney tissue.<sup>[32]</sup>

Recent studies have shown that apigenin has significant anti-inflammatory, antioxidant and anti-cancer effects. It is also effective in treating the symptoms of gastritis, gastric ulcers and other mucosal inflammations. Some studies have also shown that apigenin can effectively treat skin inflammation arising from free radicals such as UV, X and  $\gamma$  and chemicals.<sup>[33-34]</sup> A study done by Shukla et al.<sup>[35]</sup>, (2016) evaluated the effect of apigenin on the healing of diabetic wounds in rats, and it was shown that the rate of wound closure and collagen production in the wounds of diabetic rats treated with apigenin was similar to the healthy rats who did not receive treatment.

In a study done by Chen et al.<sup>[36]</sup>, (2020) to evaluate the effectiveness of intraperitoneal injection of rutin in wound healing in hyperglycemic rats, it was found that rutin accelerates wound healing by its effects on controlling blood sugar, reducing the synthesis of inflammatory cytokines and growth factors, and promoting enzyme production with antioxidant properties.

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SP extract contains fatty acids such as linoleic acid (the main fatty acid of the epidermis), oleic acid and stearic acid.<sup>[37]</sup> Unsaturated fatty acid mitigates the inflammatory response.<sup>[38]</sup> The results of a study showed that consumption of both linoleic acid and oleic acid shortened the inflammatory phase, reduced the number of inflammatory cells and inflammatory mediators such as IL-6 and IL-1 in the first 24 hours and also shortened the closure of wound within 7 days after wound creation compared to control groups.<sup>[39]</sup> It was also found that the inflammatory response in wounds treated with oleic acid was modulated, and the wound size was smaller than the control group after 5 days.<sup>[38]</sup>

Oxidants and oxygen free radicals delay tissue regeneration and wound healing, so wounds treatment with antioxidants reduces tissue damage resulting from oxygen free radicals and improves skin regeneration.<sup>[40]</sup> Furan compounds derived from methanolic extract of SP have strong antioxidant activity. In addition, the antioxidant effect of this plant is closely related to the presence of compounds such as phenolic compounds, anthocyanin, carotenoids, Tocopherols, vitamin C and flavonoids. The peroxidase enzymes, catalase, superoxide dismutase and polyphenol oxidase also exist in the SP extract, which have antioxidant effects and have a synergistic effect with the antioxidant compounds of this plant.<sup>[15,30]</sup>

On the other hand, the repair of skin lesions is mostly related to the major role of fibroblast cells in the regeneration of the extracellular environment by producing large amounts of collagen.<sup>41</sup> In the current study, it was shown that *Salvadora Persica*, through increasing the number of fibroblasts, density of collagen fibers, regeneration of epithelium, and formation of new hair follicles in the margins of wounds accelerates the healing of burn injuries. Numerous studies have shown that the use of this plant can increase the growth of fibroblasts and collagen production and help the granulation tissue regeneration in ulcers treated with SP extract.<sup>[15,42]</sup>

Quantitative and qualitative analysis of *Salvadora Persica* plant extract has shown that this plant is a rich source of vitamin C and other chemicals, including silica, resin, sodium chloride and potassium chloride.<sup>[43]</sup> There are several reports based on the positive effects of vitamin C on the increase and proliferation of fibroblasts as well as increased expression of collagen genes type 1 and type 4 in these cells. Vitamin C is also a co-factor of lysyl and prolyl hydroxylase, which are required to stabilise of the third structure of collagen.<sup>[44]</sup>

A study conducted by Hina Imran et al. <sup>[19]</sup>, (2015) assessed the effect of *Salvadora Persica* ointment on the healing process of punch injuries in rats, and realized that in the 10% SP ointment treatment group the wound closure time was shorter than the other groups and the regeneration of epithelium was more. This finding, is in accord with the results of our study.

According to the compounds in *Salvadora Persica* and the presented report, it can be concluded that the hydroalcoholic extract of this plant has anti-inflammatory, antioxidant and antimicrobial effects and also increases the number of fibroblasts, collagen production and regeneration of the epidermis and hair follicle formation. Therefore, it positively affects on the phase of inflammation, proliferation and remodelling in wound healing



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## Conclusion

The current study showed that SP extract, through decreasing inflammation, accelerates the healing of burn injuries. Moreover, the extract has decisive effects leading to the increasing of fibroblasts which is followed by collagen generation; and also accelerating the epithelialization and formation of new hair follicles. Regarding the positive effects of the herb on the healing process of injuries it is recommended that, after clinical trials, the plant could be used in producing wound healing ointments.

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