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REVIEW ARTICLE

Phytotherapy in Burn Wound Healing: A Review of Native Iranian Medicinal Plants

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KEYWORDS

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ABSTRACT: Studies have shown that burn wounds are one of the most severe forms of trauma which may cause disability, morbidity and mortality, stupendous hospital costs, and emotional disturbance. In spite of the therapeutic effects of synthetic drugs, due to their unwanted side effects, the tendency of people to use these drugs has been decreasing, contrary to the use of natural origin drugs. Medicinal plants that can be formulated to treat and repair the wound should be identified. Therefore, in this article a number of native Iranian medicinal plants that have been studied and their healing effects on burn wounds have been reported are discussed. In this review article, the keywords medicinal plants, burn, burn wound repair, burn wound and Iran were used to search for relevant articles indexed in databases such as *IranMedex*, *Scientific Information Database*, *Google Scholar*, *Scopus*, *Institute for Scientific Information*, *Web of Science* and *PubMed*. Based on the results, the medicinal plants *Aloe vera* (L.) Burm.f., *Matricaria chamomilla* L, *Quercus brantii* Lindl., *Cydonia oblonga* Mill., *Scrophularia striata*, *Camellia sinensis* (L.) Kuntze, *Portulaca oleracea* L, *Cinnamomum zeylanicum* Blume, *Achillea talagonica* Boiss., *Olea europaea* L., *Hypericum perforatum* L., *Cucurbita pepo* L., *Teucrium polium* L., *Myrtus communis*, *Brassica oleracea* L., *Plantago major* L., *Malva sylvestris* L., *Arnebia euchroma* (Royle) I.M.Johnst., *Cucurbita moschata* Duchesne, *Achillea millefolium* L., *Lythrum salicaria* L., *Crocus sativus* L. and *Allium sativum* L. are some of the most important herbal remedies to repair burn wounds. According to the various researches on the medicinal plants, the anti-inflammatory, antimicrobial and antimicrobial effects of these plants have been scientifically demonstrated, which has led to information that can be used to produce antimicrobial drugs for infectious and burn wounds.

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INTRODUCTION

Burning is the fourth leading accident in the world following road crash, falling and violence between people [1, 2]. Burn is a risk that threatens people in different ways. Studies show that more than 95% of burns occur in developing and underdeveloped countries [3]. Burn and associated injuries are the most common causes of mortality and morbidity [4]. Studies show that burn injuries are one of the most severe forms of trauma that cause disability, morbidity and mortality, stupendous hospital and treatment costs, and emotional disturbance [5]. Burn affects all aspects of life. Clinical experience of burn patients show that this accident is associated with a devastating tension and can lead to permanent psychological and physical changes [6]. Minor burns remain a major health issue in developing countries in terms of long-term discomfort and disability [7]. The statistics show that the mortality rate from burn is about 2.1 per 100,000 people [8]. Studies show that 1.1 million people in the United States experience burn, with a total of 4,500 deaths [9]. In Iran, burn is also a cause of death [10, 11]. According to Iran Ministry of Health and Medical Education, 5% of all accidents in the country are due to burns [12]. In acute and severe burns, physiological changes, especially those related to hematologic factors, occur that can interfere with the treatment of patients. Changes in the amount of granulocytes due to burn depends on the severity of thermal injury, the presence or absence of infection and the characteristics of the patients [13-15]. Treatment of pain is always associated with pain, and care for burn wounds requires administration of an analgesic such as an opioid at a high dose [16,17]. Complications of burn include pain, inflammation, scar, deformity, and organ dysfunction (18-20). After a burn injury, a series of physiological responses occur, which includes changes in cellular protection mechanisms, systemic and topical inflammation, and reperfusion injury, all of which are due to injuries and sudden loss of cellular energy [21-23]. Burns are taken into account due to damage to the skin and its appendices, and development of deep scars. Wound healing is a process of healing that occurs after damage to the skin and soft tissues.

After the damage occurs, inflammatory response is developed and the cells under the derma begin to increase the production of collagen, and then the epithelial tissue is gradually restored [24]. Skin is normally composed of epidermis, dermis and hypodermis. In burns, various layers of the skin are affected. For example, in second-degree burns, the epidermis and some parts of the dermis are damaged. In second- and third-degree burns, the burn extends through the epidermis and into the dermis. In second-degree burns, reversible epithelial components from which epithelial regeneration may originate may remain, but in third-degree burns, the entire thickness of the skin and epithelial components are completely and irreversibly destroyed, and therefore spontaneous regeneration is unlikely [25]. The healing of skin wounds is a process that is accomplished by coordination of tissues, cells and various agents [26].

For treatment, standard topical antibiotics (silver nitrate, mafenide acetate and silver sulfadiazine) are also used to treat wounds but they usually cause certain complications [27, 28]. Besides, antiseptic solutions such as betadine, acetic acid, normal saline and antibiotic ointments are also used for the treatment of skin lesions. In spite of the therapeutic effects of synthetic drugs, due to their unwanted side effects, the tendency of people to use these drugs has been decreasing day, and their tendency to use drugs of natural origin has increased. Due to the widespread use of antimicrobial agents, microorganisms have acquired drug resistance [29, 30]. In traditional medicine, medicinal plants are commonly used as remedies for the treatment of severe thermal injuries [31].

Natural compounds and medicinal plants have been studied for the treatment of burns, while burn treatment continues to be a challenge despite the use of normal saline, antimicrobial drugs and systemic treatments [32]. There are many antioxidants in plants that protect the cell against peroxidation damage. Due to the lack of definitive drugs to increase the rate of wound healing, studies on medicinal plants and herbal drugs that are effective in the process of wound healing are being

conducted [33]. Plants or their bioactive and antioxidant compounds must be identified and formulated for the treatment and healing of the wound. Therefore, in this regard, a number of native Iranian medicinal plants that have so far been studied and their healing effects on burn wounds have been demonstrated will be discussed in this review article.

MATERIALS AND METHODS

In this review article, the keywords medicinal plants, burn, burn wound repair, burn wound and Iran were used to search for relevant articles indexed in databases such as *IranMedex*, *Scientific Information Database*, *Google Scholar*, *Scopus*, *Institute for Scientific Information*, *Web of Science* and *PubMed*..

RESULTS

Based on the results, the medicinal plants *Aloe vera* (L.) Burm.f., *Matricaria chamomilla* L, *Quercus brantii* Lindl., *Cydonia oblonga* Mill., *Scrophularia striata*, *Camellia sinensis* (L.) Kuntze, *Portulaca oleracea* L, *Cinnamomum zeylanicum* Blume, *Achillea talagonica* Boiss., *Olea europaea* L., *Hypericum perforatum* L., *Cucurbita pepo* L., *Teucrium polium* L., *Myrtus communis*, *Brassica oleracea* L., *Plantago major* L., *Malva sylvestris* L., *Arnebia euchroma* (Royle) I.M.Johnst., *Cucurbita moschata* Duchesne, *Achillea millefolium* L., *Lythrum salicaria* L., *Crocus sativus* L. and *Allium sativum* L. are some of the most important herbal remedies to repair burn wounds.

Additional information on native herbal drugs that are effective on burns is presentes below:

Aloe vera (Asphodelaceae)

Aloe vera has been grown in many parts of the world over the centuries, including the Middle East, Africa, the Caribbean, the United States, Latin America, Europe, and East Asia and Iran, and today is found in many hot and dry regions around the world. The results of a study showed that the combination of gon honey *Aloe vera* in one-to-one ratio in adult male rats with second-degree burns for 21 days resulted in improved burn wounds, so that the area of the ulcers ranged from 250 mm to 34.024 ± 125 mm square [34].

Matricaria chamomilla L (Asteraceae)

Based on the results of a study in rats, it was found that topical use of hydroalcoholic extract of chamomile increased the rate of burn wound healing in rat. Accordingly, the hydroalcoholic extract of chamomile in olive oil at a dose of 8 g/kg twice daily for 67 days resulted in a wound healing of 74.77 ± 5.2% [35].

Quercus brantti (Fagaceae)

Based on the results of the study of the effect of oak blue oat extract on Wistar rats, the epithelial thickness in the groups receiving the extract (oak) with concentrations of 1%, 4% and 7% and silver sulfadiazine was increased significantly compared to the control group Had you Epithelial thickness increased in the pairs extracting group as compared to the sulfadiazine group. Also, the dermal thickness in the groups receiving the pair extract and silver sulfathiazine increased significantly compared to the control group [36].

Cydonia oblonga (Rosaceae)

The results of a study showed that grains extract accelerates the healing of burn wounds in Balb/C mice. Accordingly, daily 1 g ointment of 1% seed extract for 21 days resulted in an improvement in the percentage of burn wounds of 99.50% in Balb/C mice, while the silver sulfadiazine ointment recovered 92.26% of burn wounds [37].

Scrophularia striata (Scrophulariace)

The results of the test of hydroalcoholic extract of thirsty plant with 2.5% and 5% doses for 21 days on Wistar rats showed that the area of burn wounds decreased. This decrease in burn area for hydroalcoholic extract of 5% on day 21 was 58.06 ± 293.12 [38].

Camellia sinensis (Theaceae)

Alcoholic extract of green tea on the process of burn wound healing in Wistar rats showed that the extract

containing 0.06% of green tea during 21 days resulted in an average recovery time of 18 ± 0.62 in burn wounds. Also, there was a significant decrease in burn wound area in the third week in the group treated with green tea [39].

***Portulaca oleracea* L. (Portulacaceae)**

Peppermint extract with a dose of 10% accelerates the healing process of burn wounds in Balb / C mice. Based on the results of the study, the effects of purple hydroalcoholic extract on second-degree burn wounds on Balb/C rats revealed that the purple hydroalcoholic extract (10%) for 21 days resulted in a recovery of 89.24% (5.26%) of wound healing (daily wounds per day Zero at the area of 16.46 ± 74.38 mm 2, which decreased to 5.45 ± 10.6 mm^2 after 21 days of treatment [40].

***Cinnamomum zeylanicum* (Lauraceae)**

The results of a study evaluating the effects of cinnamon hydroalcoholic extract at a dose of 75 mg/kg body weight of diabetic and non-diabetic rats showed that in the diabetic group, topical control and topical treatment on day 14 produced a significant decrease in the level of diabetic Wistar wound burns. Based on the results, hydroalcoholic extract of cinnamon accelerates the healing of burn wounds. This accelerates wound healing in a non-diabetic group than diabetic. The peritoneal injection method was more effective than the topical method. The recovery rates of cinnamon extract in the anti-and injectable group on day 21 were 100% and 100%, respectively. Also, the rates of recovery on the 21st day were 96.5% and 95% for cystic ointment and ointment groups respectively [41].

***Achillea talagonica* (Asteraceae)**

The results of this study evaluating the effects of alcoholic extract of 5% *Achillea talagonica* mixed with vaseline gel twice daily until complete wound healing in New Zealand rabbits of second grade burn wounds showed that complete epidermis reconstruction with superficial creatinization and complete filling of wound area with strings thick collagen occurred in the group treated with Bronsafe alcoholic extract [42].

***Olea europaea* (Oleaceae)**

The results of the study evaluating the effect of olive oil combined with lime water on the healing of second grade burn wounds in Wistar rats showed that, by the end of the fourth week, the number of blood vessels had risen over time and the meat bud was regular and the epidermis was complete [43].

***Hypericum perforatum* (Hypericaceae)**

The results of the study of the effect of hydroalcoholic extract of weed extract on Wistar rat wound healing showed that daily germination of 4 mg/kg of grass extract increased the burning surface, epidermis thickness and malondialdehyde level in the grass treated group compared with the sulfadiazine group of silver and the control group was close to normal. Comparison of mean and standard deviation of skin tissue variables with second degree burns in male rats showed that grass could improve the surface of burn, thickness of epidermis and the level of malondialdehyde [44].

***Cucurbita pepo* (Cucurbitaceae)**

The results of a study which evaluated the effect of silver nanoparticles and hydrotagonal extract of pods on restoration of burns in albino hair show that nano-particles of 70% hydrochloric acid extracts after 28 days of treatment caused an average burn diameter of 0.46 ± 1.16 cm to Zero centimeters [45].

***Teucrium polium* (Lamiaceae)**

The results of one study showed that the percentage of burn wound healing with haplaceous peppermint at 1 g twice daily resulted in wound healing in rats, which was 39% and 78% on days 12 and 18, respectively [46].

***Myrtus communis* (Myrtaceae)**

The results of the effect of methanolic extract of the plant on second-degree burn wound healing in mice showed that 30-day treatment with extract of the case caused an increase in the number of blood vessels (1.48 ± 9.87) and fibroblast (2.2 ± 23.62) in the burn area and recovery [47].

***Brassica oleracea* (Brassicaceae)**

The results of a study showed that simultaneous administration of cabbage extract and sucralfate compared to silver sulfadiazine in female rats showed significant differences after the second week. Epithelization and blindness accelerated in sacral and cabbage groups. The percentage of health and well-being (Welfare percentage) in the Sucrallet and Cabbage groups was about 100%, while other groups did not fully heal. As a result, it can be concluded that Sucrallept and Brassica oleracea have positive effects on burn wound healing [48].

***Plantago major* (Plantaginaceae)**

The results of a study in the rat model showed that 50% solution of plantachia extract was effective in comparison with silver sulfadiazine, and 50% solution of plantago might be a suitable alternative to silver sulfadiazine [49].

***Malva sylvestris* (Malvaceae)**

The results of a study showed that ethereal diethyl ether extract of Red Peppermint Plant at a dose of 200 mg/kg/day in male Wistar rats resulted in skin regeneration in edema, monocellular, and cellular necrosis. The ratio of the injured area at the end of the 16th day was 0.09 ± 0.23 cm^2 for the red squamous juice extract and 0.05 ± 0.52 cm^2 for silver sulfadiazine group (50).

***Arnebia euchroma* (Boraginaceae)**

The results of a study showed that Diethyl ether extract of *Arnebia euchroma* plant with a dose of 200 mg/kg/day in male Wistar rats showed that skin regeneration in the burn wounds of edema, single cell and cellular necrosis cells in Treatment of herbal ointments and medications was not observed. The ratio of the injured area at the end of the 16th day was 0.02 ± 0.08 cm^2 for the Abu Khlasa extract (with the fat base of the goat), 0.06 ± 0.08 cm^2 for Abuhlasa extract (with cold cream base), 0.02 ± 0.41 cm^2 for the control group and 0.05 ± 0.52 cm^2 for silver sulfadiazine equal [50].

***Cucurbita moschata* (Cucurbitaceae)**

The results of a study evaluating the effect of squash extract on Wistar rat showed that the ethanolic extract of this plant with a concentration of 20% for 14 days resulted in wound healing and skin lesions of 90.80% ulcers and a significant decrease in oxidative stress biomarkers. Histological analysis confirmed the effect of burn wound healing on the pumpkin skin extract [51].

***Achillea millefolium* (Asteraceae)**

The results of a study in New Zealand White Rabbit showed that the wound treated with Yarrow's alcoholic extract had better burn wound healing than the control group. Local use of yolk alcohol extract in this study not only improved the quality of wound healing, but also reduced the microbial load of these wounds in rabbits [52].

***Lythrum salicaria* (Lythraceae)**

The results of a study showed positive effect of Hydromethanol extract of *Litteram salicarya* on second degree burns in rats. The results of this study clearly demonstrated the effectiveness of topical ointment of *L. salicaria* as a wound healing agent, probably due to polyphenolic content and antioxidant properties. The epidermal layer was also well organized and the normal appearance of the dermal layer was found more frequently in the Hydromethanolic extract of *Litteram salicaria* [53].

***Crocus sativus* (Iridaceae)**

The results of a study that investigated the effect of saffron extract cream in treating heat-induced burn wounds and compared its results with silver sulfadiazine in rats revealed that for twenty-five days, rats treated with different groups, ultimately in the control group, the base, saffron and silver had an average thickness of 5.5, 4, 0.9 and 4.1 cm^2. The size of the wound group of Saffron was significantly lower than that of the other groups. Also histological studies showed that saffron again increased epithelialization in burn wounds [54].

***Allium sativum* (Amaryllidaceae)**

The results of this study showed that garlic blue extract was effective on infected wounds in dog wounds, so that 1% extract of garlic extract reduced microbial load and wound healing in dogs [55].

A summary of Iranian medicinal plants effective in healing burn wounds is given in Table 1.

Table 1. Scientific name of medicinal plants, herbal family and type of extract affecting burn wound healing for native medicinal plants of Iran

Medicinal plants	Herbal family	Description	Ref.
Aloe vera	Asphodelaceae	Gel	[34]
***Matricaria chamomilla* L**	Asteraceae	Hydroalcoholic extract	[35]
Quercus brantti	Fagaceae	Extract	[36]
Cydonia oblonga	Rosaceae	Grains extract	[37]
Scrophularia striata	Scrophulariace	Hydroalcoholic extract	[38]
Camellia sinensis	Theaceae	Alcoholic extract	[39]
***Portulaca oleracea* L**	Portulacaceae	Hydroalcoholic extract	[40]
Cinnamomum zeylanicum	Lauraceae	Hydroalcoholic extract	[41]
Achillea talagonica	Asteraceae	Alcoholic extract	[42]
Olea europaea	Oleaceae	Oil	[43]
Hypericum perforatum	Hypericaceae	Hydroalcoholic extract	[44]
Cucurbita pepo	Cucurbitaceae	Hydroalcoholic extract	[45]
Teucrium polium	Lamiaceae	Hydroalcoholic extract	[46]
Myrtus communis	Myrtaceae	Methanolic extract	[47]
Brassica oleracea	Brassicaceae	Aqueous extract	[48]
Plantago major	Plantaginaceae	Hydroalcoholic extract	[49]
Malva sylvestris	Malvaceae	Diethyl ether extract	[50]
Arnebia euchroma	Boraginaceae	Diethyl ether extract	[51]
Cucurbita moschata	Cucurbitaceae	Ethanolic extract	[52]
Achillea millefolium	Asteraceae	Alcoholic extract	[53]
Lythrum salicaria	Lythraceae	Hydromethanol extract	[54]
Crocus sativus	Iridaceae	Aqueous extract	[55]
Allium sativum	Amaryllidaceae	Aqueous extract	[56]

DISCUSSION

The use of plant products in the treatment of various types of ulcers, such as cuts, burns, etc., has a long history in many countries, including Iran. *Aloe vera* is topically used to treat skin diseases [56]. *A. vera* has bacteriostatic and bactericidal properties [57, 58]. *M. chamomilla* has a moisturizing and gentling property [59, 60]. The antibacterial properties of *M. chamomilla* have also been demonstrated [61]. *Q. brantii* has a healing property for the stomach ulcer [62]. Antimicrobial effects of *Q. brantii* on *Escherichia coli*, *Klebsiella pneumoniae*, *Shigella dysenteriae*, *Brucella melitensis*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Bordetella bronchiseptica* and *Proteus mirabilis* have been proven [63]. Tannins are one class of the compounds that are responsible for antimicrobial activity. The antimicrobial activities and properties of tannins are related to their ability to inactivate microbial adhesion, enzymes and cell membrane transport proteins [64]. *S. striata* is traditionally used as an anti-inflammatory and antimicrobial agent, and for healing wounds [65]. *S. striata* species contain the components aucubin and catalopol [66, 67]. *C. sinensis* has antioxidant property due to its compounds [68]. *C. sinensis* has therapeutic effects on skin disorders [69]. *P. oleracea* has antioxidant properties [70,71]. *P. oleracea* contains alpha-tocopherol, glutathione, carotene, polysaccharides,

saponins, cerebrosides, coumarins and proanthocyanidins [72,73]. Cinnamon contains cinnamaldehyde, eugenl, caryopyllene, linalool, alpha terpineol, coumarin and cineol [74]. Cinnamon exhibits antioxidant properties [75]. *O. europaea* contains oleuropein, squalene and beta-carotene [76, 77]. *O. europaea* is typically applied on the skin to relieve pain [78]. *Hypericum perforatum* has analgesic, anti-ulcer, antioxidant, and anti-inflammatory effects [79]. Its main compounds include hypericin, pseudohypericin, hyperin, quercetin, and phloroglucinol [80, 81]. The Cucurbitaceae family contains triterpenes, pectin and phenolic compounds [82-84]. *C. pepo* has antioxidant properties [85, 86]. *T. polium* contains tannin, tropenoid, saponin, flavonoid, glycoside-alpha, sterol, leucoanthocyanidin, beta-caryophyllene, hemolin, caryophyllene oxide, diterpenoid and asparagine [87, 88], with proven wound-healing, anti-inflammatory and antimicrobial effects [89-91]. *M. communis* is used in as a wound healing, antiseptic and antimicrobial agent [92-94]. Having active ingredients phenolic compounds, flavonoids, and alkaloids, *P. major* is a common medicinal plant that has antioxidant effects. In traditional medicine, it is a refrigerant agent and is used to treat skin lesions and infections [95,96]. *Arnebia euchroma* contains naphthoquinone, alkannin and shikonin [97]. *Arnebia euchroma* produces wound-healing, antimicrobial and anti-inflammatory effects [98-100]. Yarrow contains compounds such as flavonoid, sesquiterpene, lactone, betaine, acetylene, resin, tannin and achillin [101, 102]. Saffron contains crocin, picrocrocin, safranal, quercetin and delphinidin [103]. Allicin is the most important antimicrobial constituent of garlic [104,105]. Burn is associated with increased oxidative stress due to increase in free radicals. These plants, other than having effective components against burn injury, have antioxidant activities. Antioxidants by counteracting oxidative stress have beneficial effective in various diseases [106-122]. Therefore, the plants presented in this article may induce their positive effects, partly by their antioxidant properties. Furthermore, they also should have beneficial effects in other conditions

CONCLUSIONS

Wound healing is a complex process through which the wounds (burns or cuts) are healed by the same process. Since temporary or permanent body dysfunction is one of the most important complications of burn, one of the most important treatments that can be used for burn patients is to speed up the process of burn wound healing, which can reduce the risk of developing burn complications including infections [123]. Throughout the process of skin healing, several factors can also be involved. Hyaluronic acid is a compound that the skin absorbs to accelerate its healing process. Hyaluronic acid is one of the main members of the amino acid glucose chain in the skin. It is possible that the active ingredients of the plants stimulate collagen production and faster contraction of the wound, angiogenesis, and vascular dilatation, and also decrease inflammation, hemorrhage and edema [124]. Many of the medicinal plants also have anti-inflammatory, antimicrobial and wound healing properties. By having the active ingredients and probably through antioxidant, antimicrobial, and wound healing-accelerating processes, the plants reduce inflammation and the microbial burden of the wound, leading to repair of burn wounds. The effects of medicinal plants on skin disorders and diseases are undeniable. These plants are commonly used either traditionally or for the preparation of natural processed products to preserve skin, and prevent and treat skin diseases. According to numerous studies on numerous plants, the effects of a number of them have been scientifically demonstrated, which has led to information that can be used to produce pharmaceutical products.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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