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Review Article

Herbal, Animal and Mineral Remedies in Burn Wound: a review of Persian Traditional Medicine literature

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ABSTRACT

Background: Burn wound is one of the most common injuries worldwide. However, its management still remains a health concern and research is ongoing for more efficient therapies. Persian medicine has described different methods in this regard. Previous reviews have mostly focused on the herbal-based therapies for burn management. Hence, the current study aimed to review both non-herbal and herbal-based therapies used in Persian medicine for their burn healing properties, and to compare them with new evidence.

Method: The most important texts of Persian medicine were reviewed for burn wound classification, managements and treatment approaches. Moreover, herbal, minerals, and animal-based products claimed to possess burn wound healing activity, were extracted. In the next step, digital databases were searched to find new supporting data for the extracted-traditional remedies and their healing mechanisms.

Results: More than one hundred traditional medicinal herbs, minerals, and animal-based products have been recommended to treat burn wound in Persian medicine among them, the healing effect of thirty-five herbs and eight non-herbal treatments (mineral and animal-based compounds) were supported by new evidence. Otherwise, there was not new evidence reporting the healing effect of seventy-three herbs and sixteen non-herbal compounds extracted from Persian Medicine literature.

Conclusion: Although some managements of burn wounds in Persian medicine have been confirmed by new evidence, the efficacy of a plenty of materials needs to be methodically evaluated. Hence, it could introduce new clues for future research.

Keywords: Burn wound, Persian medicine, Medicinal herbs, Minerals, Animal-based products

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Introduction

Burning is the most devastating injury with a high potential for morbidity and mortality (1). It was estimated that, 6 million patients per year need medication for burns worldwide, but most of them are treated in outpatient clinics (2). However, burn shock, multi-organ failure, local and systemic resistant infections, hypertrophic scars and keloids, chronic wounds, cosmetic attentions, underlying disease and special conditions like pregnancy and childhood are serious challenges (3-6).

Rapid wound healing is considered the main aim of burn management to minimize infection and decrease functional and aesthetic complications. Essentially, topical medication has been used to diminish morbidity and mortality in patients with severe burns (7).

There are several topical medications in the market for the management of burn wounds. However, some of the most common drugs could have antimicrobial activity rather than wound healing effect with considerable side effects (8, 9). Although using tissue scaffolds, nanoparticles, reproductive stimulatory factors, stem cells, and gene therapy are relatively modern treatments, but more studies should be conducted for cost-effective methods (10).

Over the centuries, people have had to use the materials around them as medications and gradually, they have partially refined more effective subjects (11-17). The texts of traditional Persian medicine (TPM) possess a high investigational potential in introducing new methods and medications (18, 19). TPM literature has described some procedures for burn management and also introduced many compounds of plant, mineral and animal origin.

The current study has reviewed the perspective of TPM on burn wounds managing and introduces numerous herbal, animal, and mineral materials used from the 10^{th} to 19^{th} centuries, with their effects on wound healing that have been reported in the recent studies.

Material and Method

The most important texts of TPM, including the Canon of Medicine (20), Zakhire Kharazmshahi (21), Al-Hawi (22), Al-Mansouri fi al-Tibb (23) and Makhzan al-Advieh (24), were reviewed for burn wound classification, managements and treatment approaches. Moreover, medicinal herbs, minerals, and animal-based products, claimed to have burn wound healing activity, were extracted. Then, electronic databases, including Google Scholar, PubMed, and Scopus were searched for the related evidence from 2010 to 2019, using the search terms of "burn" or "wound", and the "scientific name" or "common name" of the materials in the title or abstract. All the collected articles were evaluated for inclusion of any *in-vivo*, animal, or clinical evidence of their efficacy related to burn and wound healing properties. Only articles in English language were included in the review. Review articles, case reports, and *in-vitro* studies were excluded. If a subject was not found in any study in the current time range, the search strategy was expanded to the previous years. If there had been many studies on the same topic, such as *Calendula officinalis*, some of them would have presented (researchers' discretion). The included articles were reviewed based on the used part of the component (only herbs), having single or combined formula, type of wound, and the type of the investigational model (i.e. animal or human). Also, the evidence was reviewed for histological (histopathology and immunohistochemistry tissue markers), molecular (oxidative and antioxidative markers and gene expressions), macroscopic (wound closure rate), mechanical (stretch test), physical (odor, scab, bed color and, exudate), and biological (antimicrobial or antifungal) parameters.

Results

1.1. Definitions and classification of wounds in TPM

In TPM, wound is defined as discontinuity of the skin, caused by external damage (hit, cut, burn, etc.), lesions under the skin (abscess, tumors, etc.), and skin rashes. Also, to determine the greatest treatment, wounds are described according to the following characteristics (Table 1).

Table 1. Defining Wound characteristics (20, 21, 25)

Characteristic	Classification
Cause	Hit/ burn/ abscess/ infection/ malignancy
Extent	Wide/ small
Location	Skin or mucus / involved area like face or organs
Depth (severity)	With or without blisters, along with damage to muscles or bones
Exudate	Color, odor, thickness, amount
Underlying health condition	Presence of underlying or associated illness, patient's tolerance against disease, age
Surrounding area	Swelling, torsion, inflammation, pain
Margins	Thickening, redness, inflammation, pain
Extension (conversion)	Infection, malignity
Weather considerations	Temperature, humidity, intensity and direction of wind

In TPM, burn is categorized as a separate group of injuries, and it is classified according to causative agents of fire, hot appliance, hot water, hot oil, chemicals, sunshine, and thunder.

1.2. Burned patient management in TPM

1. Early management of burn included cooling and cleaning the wound using cold water. Topical treatments were used to reduce pain and prevent blisters (Table 2) (20).

Lime salve, which is a combination of calcium hydroxide powder with herbal oils such as sesame or olive oils, is a common topical treatment used for burn wounds (26).

Table 2. Topical medications used to reduce pain and prevent blisters in TPM

Components
Red powdered Sandal wood (*Pterocarpus santalinus* L.), areal part of Betel nut (*Areca catechu* L.) and earthenware
The extract of Black nightshade (*Solanum nigrum*), rose flower (*Rosa Damascena*) distillate and powdered earthenware
Oily extract of rose flower and egg yolk
Oily extract of rose flower, egg yolk, washed barely flour and extract of aerial part of chicory (*Cichorium intybus*)
Baked lentils (*Lens culinaris* Medik.) and oily extract of rose flower
Armani* soil (a soil containing some heavy metals like Iron, Copper and Lead) and vinegar
Washed Lime (Calcium Hydroxide), egg white, Sefidab (a white-colored substance containing tin, silver or zinc components), opium, oily extract of rose flower, beeswax and milk
The extract of Malva (*Malva sylvestris*), black nightshade (*Solanum nigrum*) and coriander (*Coriandrum sativum* L.), Sefidab, Mordarseng (a soil containing heavy metals like Iron, Copper, and Lead) and the oily extract of rose flower

2. After burn injury, especially a large or severe one, a diet including light foods and nourishing fluids was being used (21-23, 26, 27):

- Oxymel (a syrup of vinegar and honey)
- Herbal extracts of Mallow (*Malva sylvestris*), Chicory (*Cichorium intybus*), and water lily (*Nymphaea odorata*)
- Juices of jujube (*Ziziphus jujuba* Mill.), cherry (*Prunus avium*), purslane (*Portulaca oleracea*), plum (*Prunus domestica*), and pomegranate (*Punica granatum*)
- Easy-to-digest foods; barley soup containing vegetables and little bird meat like partridge, soft-boiled eggs and sugar-almond syrup.
- After a few days and with the onset of congestion, it is recommended to eat heavier and nutritious foods, such as broth made with meats, beans and spices.

3. To relieve pain, two treatments were being used (20, 23):

- Topical supplements containing vegetable oils and egg white
- Oral drugs such as opium (*Opium poppy*), Mandrake (*Mandragora officinarum*) flower and poppy (*Papaver somniferous*) seeds

4. Other procedures of TPM in the management of burn wounds were Fasd (phlebotomy) and Hijamat (cupping) (28). Fasd is a special practice in TPM performed by fine cutting of a superficial vein and extracting some blood for therapeutic purposes (20). Usually, blood is taken from the veins away from inflamed site to control pain and inflammation; for example, phlebotomy of the left basilic vein in the right upper limb injury (29). Hijamat includes taking blood from the surface of the skin by cupping. TPM physicians believe that this practice helps to control inflammation (20, 29).

5. Surgery operations (21, 25):

- Excessive scarring (hypertrophic scar and keloid)
- Cutting the bed of wound to create a way out of the secretions
- Debridement, refreshment of the wound edges, and the removal of necrotic bones and other necrotic tissues

6. Compression bandage, wound drainage with oily wicks of cotton
7. Treating fever and other general complications
8. Treatment and prevention of injury-disability and rehabilitation with local softening agents, such as almond or olive oil with spices, massage and surgery (20, 22)

1.3. Materials used in burn wounds in TPM and new related evidences

Based on the TPM references mentioned in the method section, more than one hundred traditional medicinal herbs, minerals and animal-based products have been recommended to treat a burn wound. As shown in Table 3, most of the herbs that new evidences show their effects in burn wound healing are from Asteraceae, Boraginaceae, and Leguminosae family. Moreover, most of the results were related to fenugreek, marigold, arnebia, St John's wort, and sesame, in the order of their appearance. According to the 84 articles found on plants used for burn wound healing, the most used parts of herbs were leaf (26 cases), seed (21 cases), and flower (19 cases). Also, the other used parts of herbs were stem, root, bark, aerial part, fruit as well as resin. In the herbal studies on burn and wound healing, most of the *in-vivo* models were excision, incision, and burn wound models. Furthermore, among the 84 articles reviewed, the animals used in burn and wound healing models were rat (60 cases), mice (11 cases), human (6 cases), rabbit (4 cases), pig (2 cases), and dog (1 case). In non-human studies, the most studied parameters were included histological and macroscopic evaluations. Also, in human studies, macroscopic and physical parameters were often assessed.

As demonstrated in tables 4 and 5, fewer studies have been conducted on mineral and animal-based materials and most studies included silver, zinc, and honey. Despite the application of some materials in topical burn management in TPM, there was no new study in the databases (Tables 6 and 7). Therefore, new studies can be conducted on these materials such as medicinal herbs belonged to 47 families, particularly Asteraceae and Fabaceae families.

Table 3. Some new evidence of the topical medicinal herbs used in TPM for burn wound healing

Family name	Scientific name	Common name	Traditional name	Part used	Single/ combination	Study model	Animal type	Study parameters					
								Histological	Molecular	Macroscopic	Mechanical	Physical	Biological
Asphodelaceae	*Aloe vera* L.	Aloe vera	Sebr	Leaf	S	Chronic ulcer (30)	Human			*		*	
				Leaf	S	Burn wound (31)	Human						*
				Leaf	S	Burn wound (32)	Rat	*		*			
Asparagaceae	*Dracaena cochinchinensis* Lour.	Dragon's blood	Dam-ol-akhavain	Resin	S	Excision/ incision wound (33)	Rat			*	*		
Asteraceae	*Calendula officinalis* L.	Marigold	Hai-ol-aalam	Flower	S	Excision wound (34)	Rat	*	*	*			*
				Flower	C	Excision/ burn wound (35)	Mice			*			*
				Flower	S	Excision wound (36)	Rat	*	*	*		*	*
				Flower	C	Excision wound (37)	Rabbit	*	*	*		*	
				Flower	S	Excision wound (38)	Rat	*			*		
				Flower	S	Diabetic wound (39)	Human					*	*
				Flower	S	Excision wound (40)	Rat	*					*
	Cichorium intybus L.	Chicory	Hendeba	All organs	S	Incision/ excision wound (41)	Rat	*		*			

Table 3. Some new evidence of the topical medicinal herbs used in TPM for burn wound healing

	Tragopogon graminifolius DC.		Sheng	leaf and stem	S	Burn wound (42)	Rat	*		*			*
				Leaf & root	S	Burn wound (43)	Rat	*		*			
				Leaf	S	Burn wound (44)	Rat	*		*		*	*
Boraginaceae	*Arnebia euchroma* L.	Arnebia	Obukhalsa	Leaf	S	Burn wound (43)	Rat	*		*			
				Leaf	S	Excision wound (45)	Rat	*		*			
				Bark resin	S	Burn wound (46)	Rat			*		*	
				Leaf	C	Burn wound (47)	Rat	*		*			
				Flower	C	Excision wound (48)	Rat	*		*			
Brassicaceae	*Brassica oleracea* L.	Turnip	Shaljam	Flower	S	Excision wound (49)	Rat	*					
				Flower	C	Excision wound (50)	Rat	*		*			
Burseraceae	*Boswellia carteri* L.	Frankincense (olibanum)	Kondor	Resin	C	Excision wound (51)	Mice	*	*	*			
Fagaceae	*Quercus sp.*	Oak	Afes	Flower	S	Burn wound (52)	Pig			*			*
				Flower	S	Excision wound (53)	Dog	*	*	*			
				Aerial parts	S	Incision wound (54)	Rat	*	*		*		
Hypericaceae	*Hypericum perforatum* L.	St jhons wort	Hofarighon	All organs	S	Excision wound (55)	Rat	*		*			
				Flower	S	Burn wound (56)	Rat	*					
				Aerial parts	S	Excision/ incision/ burn wound (57)	Rat	*		*			
				Leaf	S	Excision wound (58)	Rat	*		*	*		
Iridaceae	*Crocus sativus* L.	Saffron	Zafaran	Flower	S	Burn wound (59)	Mice	*		*			
	Ocimum basilicum L.	Sweet basil	Shahasfarm bostani	Leaf	C	Excision wound (60)	Rat			*			
Lamiaceae				Leaf	S	Incision/ excision wound (61)	Rat	*	*	*	*		
	Ocimum sanctum L.	Holy basil	Shahasfarm jabali	Leaf	S	Excision wound (62)	Rat	*		*			
				Leaf	S	Incision/excision wound (63)	Rabbit		*	*			*
Lauraceae	*Cinnamomum comphora* L.	Camphor	Kafur	Bark resin	C	Burn wound (64)	Rat	*		*			
Leguminoseae	*Acacia auriculiformis* A.Cunn.	Ear leaf acacia	Aghagheia	Stem bark	S	Excision /incision wound (65)	Mice	*	*	*	*	*	
	Acacia leucophloea Roxb.	White bark acacia	Aghagheia	Bark	S	Excision/ incision wound (66)	Rat	*	*	*	*	*	
	Ceratonia siliqua L.	Locust bean (carob)	Kharnub	Bean	C	Excision wound (67)	Pig	*		*			
	Trigonella foenum graecum L.	Fenugreek	Holbeh	Seed	S	Excision/ incision/ dead space wound (68)	Rat		*	*	*		
				Seed	S	Excision wound (69)	Rat		*	*			*
				Seed	C	Excision wound (70)	Rat			*			*
				Seed	S	Excision wound (71)	Mice	*		*			
				Seed	C	Excision wound (72)	Rat	*		*	*	*	*

Table 3. Some new evidence of the topical medicinal herbs used in TPM for burn wound healing

				Seed	C	Excision wound (73)	Rat	*		*	*	
				Seed	S	Incision wound (74)	Rabbit	*				
				Seed	S	Incision/excision/dead space wound (75)	Rat/Mice	*		*	*	*
				Seed	C	Excision wound (76)	Rat	*		*		*
				Seed	S	Excision wound (77)	Rat	*				
Linaceae	*Linum usitatisimum* L.	Flax seed	Katan	Seed	S	Excision/ incision wound (78)	Rat	*		*	*	
				Seed	C	Excision/ incision wound (79)	Rat		*	*	*	
				Leaf	C	Excision wound (80)	Rat	*	*	*		
Lythraceae	*Lawsonia inermis* L.	Henna	Hana	Leaf	S	Incision wound (81)	Rat			*		
				Leaf	S	Excision/incision/ dead space wound (82)	Rat	*		*	*	
				Flower	S	Incision wound (83)	Mice	*				
Malvaceae	*Malva sylvestris* L.	Malva	Khobbazi	Flower	C	Excision wound (84)	Rat	*		*		
				Flower	C	Burn wound (85)	Rat	*	*			*
				Leaf	C	Excision/incision wound (86)	Rat	*		*	*	
Meliaceae	*Azadirachta indica* A.Juss.	Neem	Azad derakht	Seed	S	Non-healing chronic wound (87)	Human	*	*	*		
				Stem bark	S	Excision wound (88)	Mice			*	*	
Moraceae	*Morus alba* L.	Mulberry	Toot	Leaf	C	Excision/ dead space wound (89)	Rat	*	*	*		
Musaceae	*Musa paradisiaca* L.	Banana	Moze	Leaf	S	Burn wound (90)	Rat	*		*		*
Myrtaceae	*Myrtus communis* L.	Myrtle	Aas	Leaf	S	Burn wound (91)	Rat			*		*
				Leaf, stem and seed	S	Incision wound (92, 93)	Rat	*		*		
				Fruit	S	Burn wound (94)	Human			*		*
Oleaceae	*Olea europaea* L.	Olive	Zaitoon	Leaf	S	Incision wound (95)	Rat	*			*	
				Fruit	C	Burn wound (96)	Mice	*	*			*
				Fruit	C	Burn wound (97)	Mice	*	*			*
Pedaliaceae	*Cupressus sp.*	Cedar	Sarve	Barry and cone	S	Incision /excision wound (98)	Rat	*	*	*	*	*
	Sesamum indicum L.	Sesame	Semsem	Seed	S	Excision / incision / dead space burn wound (99)	Rat	*	*	*	*	
				Seed	S	Excision / incision/ dead space wound (100)	Rat		*	*	*	
				Seed	S	Incision wound (101)	Rat			*		
				Seed	S	Burn wound (102)	Rat	*		*		
Plantaginaceae	*Plantago major* L.	Broadleaf plantain	Bazr-e-ghatona	Seed	C	Burn wound (103)	Rat	*		*	*	
				Seed	S	Burn wound (104)	Rat	*			*	
				Leaf	S	Cutaneous incision wound (105)	Mice	*		*	*	

Table 3. Some new evidence of the topical medicinal herbs used in TPM for burn wound healing

Rosaceae	*Plantago ovate* L.	Psyllium	Bazr-e-ghatona	Seed husk	S	Excision wound (106)	Rat	*	*	*	*		
	Cydonia oblonga L.	Quince seed	Safarjal	Seed	S	Toxin-induced wound (107)	Rabbit	*				*	
				Seed	S	Biopsy punch (108)	Human			*			
	Rosa Damascena L.	Damask rose	Vard	Flower	C	Excision wound (109)	Rat	*		*			
				Flower	C	Burn wound (85)	Rat	*	*				*
Rutaceae	*Citrus limon* L.	Lemon	Limou	Fruit	S	Incision wound (110)	Mice	*		*			
Solanaceae	*Solanum nigrum* L.	Nightshade	Enab-ol-salab	Leaf	C	Burn wound (85)	Rat	*	*				*
Tamaricaceae	*Tamarix aphylla* L.	Saltcedar	Tarfa	Leaf	S	Excision wound (111)	Rat			*			

Table 4. Some new evidence of the topical minerals used in TPM for burn wound healing

Name	Molecular formula	Single/ combination	Study model	Animal type	Study parameters					
					Histological	Biochemical	Macroscopic	Mechanical	Physical	Biological
Silver	Ag	S	Burn wound (112)	Human			*		*	
		S	Pressure ulcers (113)	Human			*		*	
		S	Burn wound (114)	Rat						*
		S	Burn wound (115)	Human					*	*
		S	Donor site (116)	Human						
Zinc	Zn	S	Burn wound (117)	Rat		*	*			
		S	Burn wound (118)	Rat	*		*			*
		S	Burn wound (119)	Rabbit	*		*		*	
		S	Excision wound (120)	Human			*		*	
Lime	$Ca(OH)_2$	C	Burn wound (96)	Mice	*	*				*
		C	Burn wound (97)	Rat						
Copper	Cu	C	Diabetic wound (121)	Human			*		*	*
		S	Excision wound (122)	Mice	*	*	*			

Table 5. Some new evidence of the topical animal-based used in TPM for burn wound healing

Name	Single/ combination	Study model	Animal type	Study parameters					
				Histological	Biochemical	Macroscopic	Mechanical	Physical	Biological
Honey	S	Burn wound (123)	Human			*			
	S	Episiotomy wound (124)	Human			*			
	S	Incision wound (125)	Human			*			
	S	Burn wound (126)	Rat	*		*			
	S	Burn wound (127)	Human			*		*	*
	S	Cutaneous wound (128)	Rat	*		*			
	S	Incision/excision wound (129)	Rat	*			*		
	S	Intraoral wound (130)	Rat	*			*		
	S	Excision wound (131)	Mice	*			*		
	S	Incision/ excision/ burn wound (132)	Rat	*		*			
	S	Burn wound (133)	Human			*		*	*
Egg white	S	Incision wound (134)	Mice	*		*	*		*
Beeswax	S	Incision wound (135)	Rabbit		*	*			
Spider web	S	Excision/ incision wound (136)	Rat	*		*	*		

Table 6 Medicinal herbs used in the treatment of burn wounds in TPM, without new evidence

Family name	Traditional name	Scientific name	Common name	Used part
Amaranthaceae	Selgh	*Beta vulgaris* L.	Beet	Leaf/ root
Amaryllidaceae	Koras	*Allium schoenoprasum subsp. iranicum*	Chives	Leaf
Anacardiaceae	Somagh	*Rhus coriaria* L.	Sumac	Fruit
Apiaceae	Kozborah	*Coriandrum sativum* L.	Coriander	Leaf/ seed
	Javsheir	*Opopanax chironium* L.	Sweet myrrh	Resin
Araliaceae	Lablab	*Hedera helix* L.	Common ivy	Seed
Arecaceae	Fufal	*Areca catechu* L.	Betel nut	Aerial part
Aristolochiaceae	Zaravand	*Aristolochia rotunda* L.	Smearwort	Root
Asteraceae	Eshkheis	*Atractylis gummifera* L.	Stemless atractylis	Root
	Harshaf	*Cynara scolymus* L.	Artichokes	Root
	Lahiat-ol-tis	*Tragopogon pratensis* L.	Meadow salsify	Leaf/ root
	Argheitoun	*Arctium tomentosum* Mill.	Woolly burdock	Root/ seed
	Oghhovan	*Tanacetum parthenium* L.	Feverfew	Aerial part
Boraginaceae	Kornob	*Brassica oleracea* L.	Cabbage	Aerial part
	Fojl	*Raphanus sativus* L.	Radish	Leaf/ seed
Burseraceae	Morr	*Commiphora myrrha* Engl.	Myrrh	Resin
	Moghl	*Commiphora mukul* Engl.	Gugal	Resin
Capparaceae	Kabar	*Capparis spinosa* L.	Caper bush	Root
Cistaceae	Ladan	*Cistus ladanifer* L.	Labdanum	Resin
Colchicaceae	Surenjan	*Colchicum sp.*	Autumn crocus	Aerial part
Convolvulaceae	Habb-ol-nil	*Ipomoea hederaceae* Jacq.	Ivyleaf morningglory	Seed
	Torbod	*Silva manso* L.	Turpeth	Root
Cucurbitaceae	Ghesa	*Cucumis sativus* L.	Cucumber	Fruit
	Ghar	*Cucurbita pepo* L.	Squash	Fruit
Cupressaceae	Abhol	*Juniperus sabina* L.	Savin juniper	Fruit/ leaf
Dipsacaceae	Mamisa	*Scabiosa arvensis* L.	Scabiosa	Seed
Ebenaceae	Aabnus	*Diospyros ebenum* J. Koenig ex Retz.	Ebony	Bark
Fabaceae	Bagham	*Caesalpinia sappan* L.	Sappanwood	Leaf
	Adas	*Lens culinaris* Medik.	Lentil	Seed
	Nil	*Indigofera tinctoria* L.	True indigo	Aerial part
	Baghella	*Vicia faba* L.	Faba bean	Seed
	Kasira	*Astragalus gummifer* Labill.	Milkvetch	Leaf
	Sandal	*Pterocarpus santalinus* L.	Red sandalwood	Wood
	Termes	*Lupinus termis* Forssk.	White lupin	Seed
	Darshishaan	*Calicotome spinosa* L.	Spiny broom	Fruit
	Sana makki	*Senna acutifolia* L.	Alexandrian senna	Leaf
	Karasne	*Vicia ervilia* L.	Ervil	Seed
Gentianaceae	Jentiana	*Gentiana lutea* L.	Yellow gentian	Leaf/ root
Lamiaceae	Komazarius	*Teucrium chamaedrys* L.	Wall germander	Aerial part
Liliaceae	Susan	*Lilium candidum* L.	Madonna lily	Flower
Loranthaceae	Debgh	*Loranthus europaeus* Jacq.	Mistletoe	Seed
Malvaceae	Khatmi	*Alcea sp.*	Hollyhocks	Leaf
	Ghoton	*Gossypium herbaceum* L.	Levant cotton	Wool
Oxalidaceae	Hammaz	*Oxalis acetosella* L.	Wood sorrel	Leaf/ root
Palmaceae	Tamr	*Phoenix dactylifera* L.	Date	Fruit
	Narjil	*Cocos nucifera* L.	Coconut	Fruit

Table 6 Medicinal herbs used in the treatment of burn wounds in TPM, without new evidence

Papaveraceae	Khashkhash	*Papaver somniferum* L.	Opium poppy	Seed
Pinaceae	Sanoubar	*Pinus albicaulis* Engelm	Spruce	Leaf/ root
Platanaceae	Dolb	*Platanus orientalis* L.	Oriental plane	Bark/ fruit
Poaceae	Jow	*Hordeum vulgare* L.	Barley	Seed
	Hentah	*Triticum aestivum* L.	Wheat	Seed
	Oroz	*Oryza sativa* L.	Rice	Seed
Polygonaceae	Asioraie	*Polygonum aviculare* L.	Pigweed	Leaf
Portulacaceae	Baghlah-ol-hamgha	*Portulaca oleracea* L.	Pursley	Seed
Potamogetonaceae	Jaronahr	*Potamogeton natans* L.	Broad-leaved pondweed	Leaf
Primulaceae	Anaghalis	*Anagallis arvensis* L.	Pimpernel	Leaf
Pteridaceae	Barsiavashan	*Adiantum capillus-veneris* L.	Maidenhair	Aerial part
Punicaceae	Romman	*Punica granatum* L.	Pomegranate	Fruit
Ranunculaceae	Piaranga	*Thalictrum foliolism* DC.	Meadow-rue	Root
	Beesh	*Aconitum ferox* Wall. Ex Ser	Indian Aconite	Root
Rhamnaceae	Annab	*Ziziphus jujuba* Mill.	Jujube	Leaf
Rosaceae	Loz-ol-morre	*Prunus amygdalus var. amara*	Bitter almond	Seed
Rubiaceae	Ghalion	*Galium aparine* L.	Cleavers	Flower
Salicaceae	Gharab	*Salix babylonica* L.	Babylon willow	Leaf/ flower
Smilacaceae	Choob-e-chini	*Smilax china* L.	China root	Leaf/ root
	Oshbe maghrebie	*Smilax sarsaparilla* L.	Honduran	Leaf/ flower
Solanaceae	Osaj	*Lycium afrum* L.	Honey thorn	Root
	Kakanj	*Physalis alkekengi* L.	Chinese lantern	Fruit
Violaceae	Banafsaj	*Viola tricolor* L.	Pansy	Root
Vitaceae	Serkeh	*Vitis vinifera* L.	Vinegar	Fruit extract
Xanthorrhoeaceae	Ashraas	*Eremurus spectabilis* M.Bieb.	Eremurus	Root
Zingiberaceae	Jadvar	*Curcuma zedoaria* Rosc.	Zedoary	Root

Table 7. None-herbal materials used in the treatment of burn wounds in TPM, without new evidence

Traditional name	Formulation	Dosage forms
Salt	NaCl	Powder
Sangarf/ osranj/ mordasang	PbO	Powder
Wood ash	-	Powder
Shadanj	Fe_2O_3	Powder
Green zadj	$FeSo_4$	Powder
Lead cutting	Pb	Powder
Iron cutting	Fe	Powder
Earthenware	-	Powder
Tin whiter	SnO	Powder
Shell	-	Powder
Orpiment	As_2S_3	Powder
Spider's web	-	Dried powder
Animal feces	-	Dried powder/ ash
Animal skin	-	Dried powder/ ash/fresh skin as dressing
Animal hair	-	Dried powder/ ash
Elephant tusk	-	Dried powder

Discussion

Human beings have been familiar with the burn, wound injuries, and their management. Apart from the basics and methods of dealing with burn patients, the main difference between ancient and new therapies is the use of natural substances available in the living environment for treatments. These materials have usually been used in combination and gradually improved in quality and effectiveness. New evidence for traditional remedies is growing rapidly (137). Many of the herbal, mineral, and animal-based materials used for burn wound healing in TPM have been evaluated in recent years. Our results showed that the most common type of study for evaluating burn-healing materials were animal models, especially rats. Due to the availability, reasonable cost, easier

methods, and structural similarities of its skin with human skin, rats are the most suitable animals for burn and wound healing examinations (17, 138). Human models are not used for initial observations due to the large differences in the types of burns, ethical issues, and the difficulty of matching the samples. On the other hand, *in vitro* studies are limited in providing practical results to provide the basics of clinical studies. Therefore, it seems that using animal models is the best choice in most cases.

Our results showed that most of the herbs that have new evidence in burn wound healing were from the Asteraceae family. The efficacy of several plants from the Asteraceae family as wound healing agents has been indicated in ethnopharmacological studies. Due to distribution and ethnopharmacological importance of the plants, several plant products derived from this family have been studied, which some of their pharmacological activities have been already identified. These pharmacological activities include anti-inflammatory, antimicrobial, antioxidant, anti-protozoa, and healing activities. Also, their wound healing efficacy has been suggested to be due to their ability to promote the proliferation of keratinocytes and thus, the remodeling of the extracellular matrix (139). The Asteraceae species have been identified to produce numerous secondary metabolites, such as polyphenols, flavonoids, diterpenoids, and sesquiterpene lactones (140). *Cynara scolymus* L. and *Tanacetum parthenium* L. are from Asteraceae family used as components of topical remedy for burn wound in TPM. *Cynara scolymus* L. contains considerable amounts of minerals and polyphenolic compounds, along with antioxidant and cardioprotective effects (141-143). Also, numerous studies have argued the pharmacologic properties such as anti-inflammatory effect of *Tanacetum parthenium* L. (144). One member of this family, *Atractylis gummifera* L., has been used as a topical medication for burn healing in TPM. However, since the hepatotoxicity and nephrotoxicity effects of this drug has been reported in previous studies, its frequent topical administration, might lead to liver and renal injury (145).

The herbs of Boraginaceae family are well-known for their pharmacological properties. Arnebia species are rich in naphthoquinones, such as alkannins, shikonins, and their derivatives have different biological activities, including anti-inflammatory, antimicrobial, wound-healing, and anti-tumorous effects (43, 146). Borage seeds oil is rich in gamma-linoleic acid, a valuable component in wound healing owing to its anti-inflammatory effects (147, 148).

An oily amorphous resin obtained from the Burseraceae family chemically contains a mixture of triterpenes, sitostenonein, and mono and sesquiterpenes. Some of these compounds also present anti-inflammatory and antimicrobial activity (149). In TPM, the resins are widely used in topical treatments (150).

Isoflavonoids are the phytochemical characteristics of the Fabaceae, and have a limited distribution in non-leguminous plant families (151). Although there is limited evidence for the therapeutic use of Fabaceae family plants in modern medicine sources, they have been widely used in topical burn compounds in TPM, providing an appropriate research area.

The stool of animals, especially pigeons, has been reported in TPM as a material used for local therapy of burn wounds (21). The noteworthy point in this regard is whether the fecal microbial flora can affect wound healing processes. Several studies have investigated the effects of probiotics on skin disorders and their positive effects have been indicated (152, 153). In a clinical study, bacteria *Lactobacillus plantarum* had the same effect as silver sulfadiazine on the control of bacterial infection of burn wounds (154). In an *in-vitro* study, it was reported that this bacterium could inhibit the proliferation of *Pseudomonas aeruginosa* (155). In another study, *lactobacillus acidophilus* inhibited the bacteria isolated from burn wounds (156). However, there was no study on the effect of stool bacteria on wound pathogens. Other materials mentioned in TPM for the treatment of burn wounds include the skin of animals, such as sheep, goat, and horse, which are transient grafts (covering the surface of the burn with freshly squeezed animal skin), and ash or powdered skin (23). The use of pig xenografts in burn wounds has a successful history (157, 158). Animal collagen has been studied in the treatment of wound and currently is used to make new medications (159, 160). However, due to some issues such as health, environmental and ethical concerns, it is not possible to widely use animal products to produce medicine as has been common in ancient times. But, with the aid of new research, they can be promoted to be used

for developing of tissue scaffolds, hormone therapy, and isolation of microbial flora.

Also, the use of rocks and soils containing heavy metals (copper, lead, tin, silver, zinc and iron) in the combination of topical drugs was common in TPM (22, 23, 161). Among these compounds, silver still has had prominent position in wound treatment (162, 163). Zinc compounds are also used to treat various types of wounds (164, 165). However, in animal and human studies, copper-based coatings are effective in the treatment of wounds (121, 122). The use of tin and lead compounds has been obsolete, due to the side effects and systemic absorption. However, specific amounts of these ions play a role in the structure and function of the enzymes and bio-molecules inside or outside the cell. Iron ion increases the activity of some matrix metalloproteinase (MMPs). MMPs enzymes play a pivotal role in proliferation and remodeling processes of wound healing (166). Despite the reported negative effect of localized increase of Fe ion in chronic venous wounds (167, 168), the iron-chelating compounds accelerate the wound healing (169, 170). Lack of enough evidence for an appropriate range of these ions in the wound area requires more consideration in this field of research.

Many topical formulations recommended in TPM are a combination of several components. The composition and dose of ingredients have a great variety, preparing methods of traditional formulations do not match the current standards and criteria, and their preparation is time-consuming and difficult. Thus, the preparation method and dosing of formulations were not mentioned in the current study. However, new evidence for traditional combinations is increasingly available by different types of searches.

Conclusion

Although some managements of burn wounds in TPM resources have been confirmed by new evidence, the efficacy of a plenty of materials and procedures needs to be methodically evaluated. Hence, it could introduce new clues for future studies.

Conflict of interest

The authors declare that there are no conflicts of interest.

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