



A New Strategy for Treatment of Chronic Wounds According to Persian Medicine: An Evidence-Based Review

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Abstract

Chronic wounds reduce patient's quality of life by complications such as pain, secretions, and reduction of movement and impose large costs to health system. Thus, looking for treatment methods with higher success and less complications seems to be necessary. In Iranian Traditional Medicine (ITM), a variety of specific nutrients and medicinal plants have been recommended for chronic wounds. The aim of present study was to scientifically evaluate the nutrients and medicinal plants claimed to be effective for chronic wounds in ITM. Nutrients and medicinal plants recommended for chronic wounds in ITM have been extracted from corresponding literature. The obtained items were individually searched in electronic databases to obtain any *in vitro*, animal, or clinical evidence of their efficacy and possible underlying mechanisms. treatment of chronic wounds in ITM consists of three steps. At first step some special foods like egg yolk and fig with special characteristics such as hematopoietic effect and antimicrobial activity are recommended. Administration of natural remedies in order to reduce internal inflammation and improve wound healing process such as *Crocus sativus* and *Aloe vera* consists of the second step. Finally, the third step includes the use of topical natural agents that affects various stages of wound healing and can complete the wound healing process. According to ITM, administration nutrients and medicinal plants is prior to topical treatments for management of chronic wounds. This strategy provides a new approach for management of chronic wounds and seems to be more useful than conventional treatment which is mostly focused on topical treatment.

Keywords: Iranian Traditional Medicine, Chronic wound, Medicinal plant, Nutrition, Homeostasis

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Introduction

Prevalence of chronic wounds with different etiologies including inflammatory, vascular, rheumatologic and decubitus is increasing with growing rate of age and diabetes in developed countries like the United States. The most common approaches for management include moisture retentive dressings plus other topical therapies [1]. The burden on patients, health care professionals and entire health care system is significant [2]. Wound healing is a complex process with various cellular and biochemical components which includes 4 temporarily overlapping phases: homeostasis, inflammation, proliferation, and maturation [3-5]. In normal acute wound healing process, wound contraction and clot formation occurs to stop bleeding in affected area. Then, blood cells such as polymorphonuclear cells, leukocytes and macrophage accumulate and release their enzymes in order to complete the process [5]. Chronic wounds are those wounds which will not be healed with physiological process in patients with underlying pathology, due to lack of adequate blood supply or neuropathy or disturbance in cell migration [6,7]. Every day, many people with underlying diseases lose their limbs and they need governmental aids for all day lives. Therefore, there is a crucial need for health care systems to find out new approaches for treatment [8, 9]. Iranian Traditional Medicine (ITM) suggest various natural remedies for treatment of chronic wounds. The aim of this study is to introduce nutrients and medicinal plants claimed to be effective for management of chronic wounds in ITM and bring forward

scientific evidence for this activity.

Methods

The authors searched the ITM literature for nutrients and medicinal plants with wound healing effect. According to ITM, systemic and topical herbal medicines both are required for treatments. The editors of the selected books were known as prestigious experienced physicians of ITM with well practical experiences, and expressed subject eloquently. Therefore medieval reports encompassing the profile of definition and terminology, classification and etiology, as well as sign and symptoms of chronic wounds collected and analyzed from selected medical textbooks of ITM [10-14]. Electronic databases including PubMed, Scopus, Web of Science, Google Scholar and the Cochrane library were searched for each of recommended nutrients and plants up to March 2016. All retrieved articles were evaluated for any in vitro, in vivo, animal or clinical evidence related to wound healing phases. Also, the pharmacological mechanisms of suggested nutrient and medicinal plants were registered completely. Any studies which exhibited apparent efficacy or any indirect effectiveness on wound healing process were included in this research. Only English published articles were included. The key words were all scientific name of each plant in the whole text and the terms “wound healing” or “chronic wounds” or “anti -oxidant” or “inflammation” in title and abstract. The publications without available full text, unpublished data, letters to the editor, case reports and experimental studies without proven

biological effects were excluded from the study. Duplications were also avoided by excluding multiple copies of the same article in different databases. Selected articles were checked for scientific names, part and extract of the plants, active components, type of experimental wound in animal model for in vivo, and type of cell line for in vitro studies. Results have been abstracted in tables 1-7.

Results

Wounds and wound healing process according to ITM

Wounds are divided into different types in ITM based on the quality of secretions, color, and apparent characteristics. The color of secretions can be yellow, white, black or bloody. Avicenna has divided the wounds into 2 types of simple and complex [14]. Simple wounds are superficial and without secretions and side effects and respond quickly to treatment. Complex wounds are deep with exudative secretions and associated with pain, swelling, systemic fever, and do not respond quickly to treatment [10,11,14]. According to ITM, the wound healing prognosis is dependent on 2 major factors: patient characteristics and wound properties (Table 1).

Wound care approach in ITM

According to ITM, the medication of wound is divided to 3 major parts: nutritional therapy, oral medicinal plants, and topical medicinal plants [11,12,14].

Table 1. Wound healing prognosis in Iranian Traditional Medicine

patient characteristics	Bad prognosis	Good prognosis
Age	> 60	< 60
Nutritional status	Malnutrition	Normal
Weight	Under weight (BMI < 18.5), obese(BMI > 30)	30 > BMI > 18.5
Coexisting illnesses	+	-
Fever	+	-
Anemia	+	-
Wound properties	Bad prognosis	Good prognosis
Duration of disease	> 40days	< 40days
Discharge	Exudative	Non-exudative
Edema	+	-
Pain	+	-
Osteomyelitis	+	-

A.Nutritional therapy

From the perspective of ITM, the healthy human body is a dynamic system that continually consumes required foods in order to prepare what is needed for being alive. The food components would be digested and absorbed properly through a healthy gastrointestinal system and would be consumed by all living parts of the body. At the end, the rest of additional material should be disposed from the body excretion routes completely. The above mentioned process is necessary for creation of hemostasis in the body. Hence, in order to treat chronic wounds, food with special characteristics should be consumed and also internal organs should be in optimum condition. The diet of patients with chronic wounds should contain hematopoietic components and also should have the ability

to strengthen the gastrointestinal system and liver. This kind of diet seems to be effective in reducing fever, internal inflammation and systemic infection. Table 2 shows different nutrients used in ITM for improving wound healing process along with their activities according to scientific evidence. By examining the components of foods, it is found that the diet of patients should contain a variety of ingredients to compensate anemia in the body, have anti-inflammatory and anti-bacterial properties and be effective in the wound healing process. Among animal products, the low-fat lamb meat and egg yolk are effective in hematopoiesis [15-

19]. In vitro and in vivo studies show, the fruits such as figs, pomegranates, grapes, lettuce, and barberry have shown strong anti-bacterial properties. Moreover, figs, pomegranate extract and pumpkin have demonstrated wound healing effect in several studies. The anti-inflammatory activity has been reported in egg yolk, lamb meat, figs, grapes and lettuce [16,18-21]. Additionally, the majority of mentioned food products including figs, pomegranates, lettuce and barberry have antioxidant properties and are also radical scavenging agents. Anti-wrinkle and anti-collagenase effects of fig and pomegranate have been proved by studies [21].

Table 2. Animal products and plant food recommended for chronic wound healing

Category	Name	Wound healing	Drug of anemia	Anti cancer	Radical scavenging	Anti-inflammatory	Anti-collagenase, anti-wrinkle	Anti-microbial	Antioxidant	References
Animal product	Egg yolk		*	*		*				[18,19]
	Lamb meat	*	*			*				[15-17, 22]
Plant food	Fig (<i>Ficus carica</i>)	*	*	*	*	*	*	*	*	[21,23- 34]
	Pomegranate (<i>Punicagranatum</i>)	*			*		*	*	*	[35-46]
	Grape (<i>Vitis Vinifera</i>)			*		*		*	*	[47-50]
	Pumpkin (<i>Cucurbitapepo</i>)	*		*						[51-53]
	Chickpea (<i>Cicer arietinum</i>)			*						[54]
	Green lettuce (<i>Lactuca sativa</i>)			*	*	*		*	*	[20, 55-57]
	Chicory (<i>Cichorium intybus</i>)			*	*	*		*	*	[58-64]
	Barberry (<i>Berberis vulgaris</i>)			*			*	*	*	[65-69]

B. Oral medicinal plants

Various medicinal plants have been prescribed orally for treatment of chronic wounds in ITM. According to ITM, the consumption of systemic medicinal plants leads to two different functions in the body. Firstly, cleansing the body from waste material and eliminating systemic infections, and secondly, creating an optimum environment inside the body in order to improve healing process. The human body is a dynamic system. All organs continually consume food products to survive and produce energy. As a result, due to consumption of food, waste material is generated in all part of the internal organs, which must be excreted from the body. As a result of this process, hemostasis appears inside the body. Several parts of the body including gastrointestinal tract, urogenital tract, respiratory system, hepatobiliary system and

sweat glands are involved in this process. Waste products should be removed through stool, urine, menstrual blood, semen, sweat and respiratory tract secretions (lung sputum). Medicinal plants used systemically for wound healing can help body to do this excretory function better. The whole body homeostasis and balance is important in chronic wound healing. From the perspective of ITM, The normal function of all internal organs such as gastrointestinal, hepatobiliary, cardiovascular, central nervous system, respiratory and urogenital systems is essential for wound healing process. Table 3 shows the effects of systemic administration of medicinal plants with wound healing activity on internal organs according to ITM.

Table 3. Effects of systemic administration of medicinal plants with wound healing activity on internal organs according to ITM

Table 3. Effects of systemic administration of medicinal plants with wound healing activity on internal organs according to ITM

Scientific name	Family	Name in ITM	Other use in ITM
<i>Aloe spp.</i>	Asphodelaceae	Sabr	Wound and injury, anti-inflammation, arthritis, hemorrhoid, fissure, urinary tract disorders
<i>Artemisia absinthium</i>	Asteraceae	Afsintin	Wounds and injury, headache, cerebrovascular accident
<i>Crocus sativus</i>	Iridaceae	Zaafaran	Wounds and injury, antidepressant, anti-inflammation, diuretic, cardiovascular disease, cerebrovascular accident
<i>Curcuma longa</i>	Zingiberaceae	Oruqosofr	Infected wounds and injury, dyspepsia
<i>Fiscus carica</i>	Moraceae	Tin , Anjir	Respiratory disorder, laxative, spleen and hepatobiliary system malfunction, dermatitis, anti-inflammation, scabies, eczema

<i>Fumaria officinalis</i>	Papaveraceae	Shahtaraj	Wounds and injury, urticaria, hepatobiliary system malfunction
<i>Glycyrrhiza glabra</i>	Leguminosae	Shirinbayan	Wounds and injury, dyspepsia, sore throat, cough
<i>Myrtus communis</i>	Myrtaceae	Aas ,Murd	Antidepressant, diarrhea, polymenorrhoea, bruise
<i>Pimpinella anisum</i>	Apiaceae	Anisun	Wounds and injury, cerebrovascular accident, diuretic, hepatobiliary system malfunction, respiratory disorder
<i>Pistacia lentiscus</i>	Anacardiaceae	Mastaki	Wounds and injury, peptic ulcer, inflammatory bowel disease, dyspepsia
<i>Rosa spp.</i>	Rosaceae	Gole sorkh ,Vard	Wounds and injury, antidepressant, dyspepsia, peptic ulcer,
<i>Senna alexandria</i>	Leguminaceae	Senna	Wounds and injury, dyspepsia, arthritis
<i>Sasamum indicum</i>	Pedaliaceae	Konjed	Wounds and injury, laxative, sexual dysfunction, hair loss, urinary tract malfunction
<i>Tamarindus indica</i>	Fabaceae	Tamre hendi	Wounds and injury, laxative, anti-inflammation, inflammatory bowel disease
<i>Terminalia chebula</i>	Combretaceae	Halilaj	wounds and injury, dyspepsia, headache
<i>Viola odorata</i>	Violaceae	Banafshaj	Wounds and injury, fever, common cold
<i>Zingiber officinale</i>	Zingiberaceae	Zanjabil	Wounds and injury, dyspepsia
<i>Ziziphus jujuba</i>	Rhamnaceae	Annab	Wounds and injury, cough, hepatic dysfunction, blurred vision

As shown in table 3, plants used in the treatment of chronic wounds have different impacts on other internal organs in addition to their direct effect on chronic wound healing process. For example Pimpinella anisum fruits affect nervous, genitourinary, hepatobiliary and respiratory system. Aloe spp, Crocus sativus, Ficus carica, Tamarindus indica and Viola odorata have anti-inflammatory effects. Various in vitro and in vivo studies were conducted to evaluate the effects of medicinal plants used orally for

treatment of wounds in ITM. Table 4 shows in vitro studies on medicinal plants with systemic wound healing activity used in ITM. Most of the plants including Aloe vera, Fumaria officinalis and Pimpinella anisum have anti-oxidants and broad spectrum antibacterial properties [70-72]. Some of them such as Artemisia absinthium, in addition to inhibitory effect on the growth of bacteria, have also inhibitory effect on the growth of yeast and dermatophytes [73]. Rest of other medicinal plants are noted in the tables.

Table 4: *In vitro* studies on plants with systemic wound healing activity used in ITM

plant	Part/extraction	Result	Active constituent	References
<i>Aloe vera ferox</i>	Gel /various extraction	Antioxidant activity	Polyphenols, indoles, and alkaloids	[71]
<i>Artemisia absinthium</i>	Aerial parts /oil	Antioxidant activity , inhibitory effects on the growth of bacteria (<i>E.coli</i> , <i>S. aureus</i> , and <i>S. epidermidis</i> , yeasts (<i>Candida albicans</i> , <i>Cryptococcus neoformans</i>), dermatophytes (<i>Trichophyton rubrum</i> , <i>Microsporum canis</i> , and <i>Microsporum gypseum</i>), <i>Fonsecaea pedrosoi</i> and <i>Aspergillus niger</i>	Myrcene tran-thujone trans-sabinyyl acetate	[73]
	Aerial parts/ethanol	Antioxidant activity and cytoprotective effect against oxidative damage in fibroblast-like cells	Phenolic compound	[74]
<i>Fumaria officinalis</i>	Aerial parts/ methanolic extract	Antioxidant activity, anti- microbial activity	–	[70]
<i>Pimpinella anisum</i>	Seed/water and ethanol extracts	Antioxidant activity and antimicrobial activities against <i>Proteus mirabilis</i> , <i>Citrobacter koseri</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumonia</i> , <i>Enterobacter aerogenes</i> <i>Micrococcus luteus</i> , <i>Staphylococcus epidermidis</i>	Phenolic compound	[72]
<i>Rosa gallica</i>	Flower / methanol	Antibacterial and antifungal activity	–	[75]
<i>Senna alexandrina</i>	Flower/ methanolic extract leaf/acetone extract	Antimicrobial activity against <i>Bacillus cereus</i> , <i>Aeromonas hydrophila</i> <i>Enterobacter aerogenes</i> , <i>Escherichia coli</i>	–	[76]
<i>Tamarindus indica</i>	Fruit/Methanolic extract	Antioxidant activity and antibacterial activity against <i>L. innocua</i> , <i>A. faecalis</i> , <i>E. amnigenus</i> , <i>E. gergoviae</i> , <i>A. hydrophila</i> , <i>S. marcescens</i> , <i>A. denitrificans</i> , <i>S.putrefaciens</i>	Phenolic compound	[77]
	Fruit / water and acetone and ethanol extract	Antibacterial activity against <i>Escherichia coli</i> , <i>Proteus mirabilis</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> , <i>Salmonella paratyphi</i> , <i>Shigella flexnerri</i> , <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i>	tannins, saponins, sesquiterpenes, alkaloids and phlobatamins	[78]
<i>Terminalia chebula</i>	Fruit /Water, chloroform, acetone and ethanol extract	Antioxidant activity and antibacterial activity against <i>Bacillus subtilis</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus aureus</i> , <i>Corynebacterium Salmonella typhi</i> , <i>Klebsiella pneumonia</i> , <i>Shigella boydii</i>	Phenolic compound	[79]
<i>Viola odorata</i>	Flower /petroleum ether, dichloromethane, ethyl acetate and the aqueous fractions	Antibacterial activity against <i>Escherichia coli</i> and <i>Klebsiella pneumoniae</i>	–	[80]
	Leaf /methanolic extract	Antioxidant activity	Phenolic compound	[81]
	Flower and twig /Aqueous extracts	Antibacterial activity against <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> , <i>Shigella flexneri</i> and <i>Staphylococcus aureus</i>	–	[82]

<i>Zingiber officinale</i>	Rhizomes/methanol extract	Antioxidant activity	Flavonoids, volatile oil and phenolic materials	[83]
	Rhizomes/oleoresin compound	Antioxidant activity and antimicrobial activity against <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> , <i>Aspergillus niger</i> , <i>Penicillium spp.</i>	Oleoresin	[84]
<i>Ziziphus jujuba</i>	Fruit / protein extract	Antioxidant activity	Proteins	[85]
	Fruit / ethanolic extract	Antioxidant activity	Total phenolics, flavonoid, and anthocyanins	[86]

Table 5 shows *in vivo* studies on plants claimed to have systemic wound healing activity in ITM. Systemic consumption of plants such as *Aloe vera* accelerates all phases of wound healing [87], and the use of some plants like

Terminalia chebula reduces the bacterial count and increases the rate of epithelizing time [88]. Systemic administration of some plants like *Ziziphus jujuba* reduces edema in the wound [89].

Table 5: *In vivo* studies on plants with systemic wound healing activity used in ITM

Plant name	Part used/solvent used for extraction	Method	Animal	Result	Active constituent	References
<i>Aloe ferox Mill.</i>	Whole-leaf juice/ Ascorbic acid	longitudinal incision wound, linear-incision and punch-incision model	Rat and rabbit	Facilitation of the healing process, selective inhibition of microbial growth		[90]
<i>Aloe vera</i>	Gel/ water	Single dose of 9 Gy soft x-rays	Male Wistar rats	Improvement of acute radiation delayed wound healing by increasing Tissue Growth Factor (TGF)beta-1 and Fibroblast Growth Factor (FGF) production	-	[91]
	Gel /water	Full-thickness excision/ incision wounds in diabetic rats	Male Wistar rats	Beneficial influence on the various phases of wound healing including inflammation, fibroplasia, collagen synthesis and maturation, and wound contraction	-	[87]
<i>Terminalia chebula</i>	Fruit/methanol	Full thickness wounds	Male Wister albino rats	Improving wound closure; reduction in bacterial count with significant level of collagen, hexosamine, uronic acid, and superoxide dismutase; Reduction of matrix metalloproteinase expression	-	[88]
	Fruit /hydro alcohol	Excision wound model and dead space wound model	Diabetic rats	↑The rate of epithelizing time, ↑ wet and dry granulation tissue weight content	-	[92]

<i>Ziziphus jojoba</i>	Fruit / hydro alcohol	Acute inflammation induced by sub plantar administration of carrageenan, Chronic inflammation induced by interscapular implantation of a sterile cotton pellet	Wister albino rats	Attenuation in edema; ↓ granuloma tissue formation; ↓ serum nitrite/nitrate level ↓	Jujubosides , flavonoids and terpenes	[89]
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C. Topical medicinal plants

Nutritional therapy and systemic consumption of herbal medicines help maintaining the internal homeostasis. After establishment of homeostasis, topical medicinal plants are required to complete the management of wounds treatment. Medicinal plants used in ITM for this purpose can be effective in various stages of wound healing. Table 6 shows *in vitro*

studies on medicinal plants used topically in ITM for wounds. These plants have antioxidant and antibacterial properties and are effective on gram-positive and gram-negative bacteria common in the skin such as *Ficus carica* and *Pistacia lentiscus* [93,94]. Some of them like *Glycyrrhiza glabra* have antifungal effects as well [95,96]. A list of plants with topical wound healing activity is mentioned in Table 6.

Table 6. *In vitro* studies on plants with topical wound healing activity used in ITM

plant	Part/solvent used for extraction	result	Active constituents	References
<i>Crocus sativus</i>	Stigma of flowers / methanol	Antioxidant activity	Crocin and safranal	[97]
<i>Curcuma longa</i>	Rhizomes / essential oil	Antioxidant activity	–	[98]
	Rhizome / water	Coagulant activity and fibrinolytic activity	Serine proteases	[99]
<i>Ficus carica</i>	Latex /Methanol, hexan, chloroform, and ethyl acetate	Antibacterial effect against <i>Enterococcus fecalis</i> , <i>Citrobacter freundei</i> , <i>Pseudomonas aeruginosa</i> , <i>Echerchia coli</i> and <i>Proteus mirabilis</i> , <i>Candida albicans</i>		[93]
<i>Glycyrrhiza glabra</i>	Root / water	Antioxidant activity		[95]
	Root / ethanol	Anti-microbial effect against <i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> <i>Escherichia coli</i> and on fungal spp. - <i>Candida albicans</i>	–	[96]
<i>Pistacia lentiscus</i>	Leaves/ Water , petroleum ether , ethanol	Anti-microbial effect against <i>Sarcina lutea</i> , <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> and <i>Candida albicans</i> , <i>Candida parapsilosis</i> , <i>Torulopsis glabrata</i> and <i>Cryptococcus neoformans</i>	–	[94]

<i>Sesamum indicum</i>	Sesame cake defatted with hexane / methanol	Antioxidant activity	Sesamol, sesamol dimer, sesamin, sesamol, sesaminol, sesaminol triglucoside, and sesaminol diglucoside, alpha tocopherol	[100]
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Table 7 shows the *in vivo* studies on medicinal plants used topically for wounds in ITM. Topical use of plants including *Crocus sativus*, *Curcuma longa* and *Pistacia lentiscus* shortens the speed of epithelialization. The use of plants

such as *Curcuma longa* causes faster closure of wound and increases the micro vessel density and leads to increased expressions of Vascular Endothelial Growth Factor (VEGF) and Transforming Growth Factor-beta1(TGF-b1).

Table7. *In vivo* studies on plants with topical wound healing activity used in ITM

Plant	Part / extraction	Method	Animal	Result	Active constituent	References
<i>Crocus sativus</i>	Pollen /ethanolic extract	Second-degree burn	Male Wistar rats	↑Re-epithelialization, anti-inflammatory and antioxidant effects	crocins, crocetin, picrocrocin, β-carotene and safranal	[101]
<i>Curcuma longa</i>	Curcumin (0.3%, SigmaAldrich) in PF-127 gel 25%	Open excisional diabetic wound	Wistar rats	Fast wound closure with well-formed granulation tissue dominated by fibroblast proliferation, collagen deposition, and complete early regenerated epithelial layer, well-formed blood vessels with ↑ micro vessel density, ↑ Expressions of Vascular Endothelial Growth Factor(VEGF) and Transforming Growth Factor – b1(TGF-b1), ↑ hypoxia inducible growth factor-1alpha, stromal cell-derived growth factor-1alpha, and heme oxygenase-1	–	[102]
	Curcumin cream (20%) from “Arjuna Natural Extracts Limited”, Cochin	Burn wounds created by pouring hot molten wax at 80°C	Wistar rats	Percentage of wound contraction, ↓ of the mean period of epithelization		[103]
	Nanoformulation based on MPEG-PCL co-polymer	Full thickness open excision wound	SD rats	Faster wound reduction and healing, reducing the period of re-epithelialization creating compact and well aligned collagen	Curcumin	[104]

<i>Glycyrrhiza glabra</i>	Root /hydroalcoholic extract	3rd degree burn wound infected to <i>P. aeruginosa</i>	Sprague - Dawley rats	↓ of erythema, edema and itching, anti inflammatory		[105]
<i>Pistacia lentiscus</i>	Resin / fatty oil	Burn wound	New zealan rabbit	Promoting wound contraction in different cicatrizing process	-	[106]
	Fruit /virgin fatty oil	Burn wound	New-Zealand rabbits	Promoting wound contraction and reduces epithelization period	Palmitic, oleic and linoleic acid	[107]
<i>Sesamum indicum</i>	Seed /sesamol	Incision, excision and dead space wounds	Albino rats	Increasing the tensile strength,rising in hydroxyproline levels	sesamol	[108]
	Seed /seed, oil	Incision, excision, dead space and burn wound	Albino wistar rat	Promoting the breaking strength, wound contraction and period epithelization in different models of wound		[109]

Discussion

Chronic wounds reduce the patient's quality of life due to complications such as pain, secretions, reduced motility, poor sleeping and social isolation. Moreover, this disorder imposes heavy costs on the health care systems. Conventional approach for treatment of wounds focus mainly on topical agents [110]. However, from the perspective of ITM, treatment should not be limited to topical medications and systemic medicinal plants are also needed for establishment of homeostasis in order to facilitate wound healing process [10,11,14]. Treatment of wounds consists of three steps. The first step is nutritional therapy. The recommended nutrients have shown hematopoietic, anti- microbial and anti -oxidant effect [18,21,22,37] as well as having different roles in wound healing process in studies [18,21,22,36,37,53]. The second step is the use of oral and systemic herbal medicines in order

to reduce internal infection and removal of the body waste materials. This process helps whole body to establish internal hemostasis which is the key point of an appropriate treatment according to ITM. Therefore, re-epithelialization could be improved properly [111]. The third step is the use of topical medicinal plants. Studies have shown that topical medicinal herbs like *Curcuma longa*, *Glycyrrhiza glabra* and *Pistacia lentiscus* are effective in various stages of wound healing including wound contraction, epithelization, fibroblast proliferation and collagen deposition [102,105,106].

Conclusion

From the perspective of ITM, the treatment of chronic wounds is based on removing the main cause of the disease, which includes three stages of nutritional therapy, systemic medication and topical therapy. Establishment of homeostasis and strengthening internal organs by using

systemic medicinal herbs is prior to topical treatment of the chronic ulcers. The eligibility of these medications has been confirmed by recent studies in conventional medicine and they could be used as complementary and/or alternative treatments for management of wounds especially chronic ones.

Conflict of interest

None.

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None.

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