TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 3, Issue 3, Summer 2018

Review

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

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Received: 2 May 2018 **Accepted:** 12 May 2018

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

Citation: Shirbeigi L, karami S, Mohebbi M, Nejatbakhsh F, Rahimi R. **A New Strategy for Treatment of Chronic Wounds according to Persian Medicine: An Evidence-Based Review.** Trad Integr Med 2018; 3(3): 162-176.

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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 (*Ficuscarica*)	*	*	*	*	*	*	*	*	[21,23- 34]
	Pomegranate (*Punicagranatum*)	*			*		*	*	*	[35-46]
	Grape (*Vitis Vinifera)*			*		*		*	*	[47-50]
	Pumpkin (*Cucurbitapepo*)	*		*						[51-53]
	Chickpea *(Cicer arietinum)*			*						[54]
	Green lettuce (*Lactuca sativa)*			*	*	*		*	*	[20, 55-57]
	Chicory (*Cichorium intybus)*			*	*	*		*	*	[58-64]
	Barberry (*Berberis vulgari*)			*		*		*	*	[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
***Aloe* spp.**	Asphodelaceae	Sabr	Wound and injury, anti-inflammation, arthritis, hemorrhoid, fissure, urinary tract disorders
Artemisia absinthium	Asteraceae	Afsintin	Wounds and injury, headache, cerebrovascular accident
Crocus sativus	Iridaceae	Zaafaran	Wounds and injury, antidepressant, anti-inflammation, diuretic, cardiovascular disease, cerebrovascular accident
Curcuma longa	Zingiberaceae	Oruqosofr	Infected wounds and injury, dyspepsia
Fiscus carica	Moraceae	Tin , Anjir	Respiratory disorder, laxative, spleen and hepatobiliary system malfunction, dermatitis, anti-inflammation, scabies, eczema

Fumaria officinalis	Papaveraceae	Shahtaraj	Wounds and injury, urticaria, hepatobiliary system malfunction
Glycyrrhiza glabra	Leguminosae	Shirinbayan	Wounds and injury, dyspepsia, sore throat, cough
Myrtus communis	Myrtaceae	Aas ,Murd	Antidepressant, diarrhea, polymenorrhera, bruise
Pimpinella anisum	Apiaceae	Anisun	Wounds and injury, cerebrovascular accident, diuretic, hepatobiliary system malfunction, respiratory disorder
Pistacia lentiscus	Anacardiaceae	Mastaki	Wounds and injury, peptic ulcer, inflammatory bowel disease, dyspepsia
***Rosa* spp.**	Rosaceae	Gole sorkh ,Vard	Wounds and injury, antidepressant, dyspepsia, peptic ulcer,
Senna alexandria	Leguminaceae	Senna	Wounds and injury, dyspepsia, arthritis
Sasamum indicum	Pedaliaceae	Konjed	Wounds and injury, laxative, sexual dysfunction, hair loss, urinary tract malfunction
Tamarindus indica	Fabaceae	Tamre hendi	Wounds and injury, laxative, anti-inflammation, inflammatory bowel disease
Terminalia chebula	Combretaceae	Halilaj	wounds and injury, dyspepsia, headache
Viola odorata	Violaceae	Banafshaj	Wounds and injury, fever, common cold
Zingiber officinale	Zingiberaceae	Zanjabil	Wounds and injury, dyspepsia
Ziziphus jujuba	Rhamnaceae	Annab	Wwounds 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, Fiscus 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
Aloe vera ferox	Gel /various extraction	Antioxidant activity	Polyphenols, indoles, and alkaloids	[71]
Artemisia absinthium	Aerial parts /oil	Antioxidant activity , inhibitory effects on the growth of bacteria (*E.coli*, *S. aureus*, and *S. epidermidis*, yeasts (*Candida albicans, Cryptococcus neoformans*),dermatophytes (*Trichophyton rubrum, Microsporum canis*, and *Microsporum gypseum*), *Fonsecaea pedrosoi* and *Aspergillus niger*	Myrcene tran-thujone trans-sabinyl acetate	[73]
	Aerial parts/ethanol	Antioxidant activity and cytoprotective effect against oxidative damage in fibroblast-like cells	Phenolic compound	[74]
Fumaria officinalis	Aerial parts/ methanolic extract	Antioxidant activity, anti- microbial activity	–	[70]
Pimpinella anisum	Seed/water and ethanol extracts	Antioxidant activity and antimicrobial activities against *Proteus mirabilis*, *Citrobacter koseri ,Staphylococcus aureus, Streptococcus pneumonia, Enterobacter aerogenes Micrococcus luteus, Staphylococcus epidermidis*	Phenolic compound	[72]
Rosa gallica	Flower / methanol	Antibacterial and antifungal activity	_	[75]
Senna alexandrina	Flower/ methanolic extract leaf/acetone extract	Antimicrobial activity against *Bacillus cereus, Aeromonas hydrophila Enterobacter aerogenes, Escherichia coli*	_	[76]
Tamarindus indica	Fruit/Methanolic extract	Antioxidant activity and antibacterial activity against *L. innocua, A. faecalis, E. amnigenus, E. gergoviae, A. hydrophila, S. marcescens, A. denitrificans, S.putrefaciens*	Phenolic compound	[77]
	Fruit / water and acetone and ethanol extract	Antibacterial activity against *Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Salmonella paratyphi, Shigella flexnerri, Staphylococcus aureus, Bacillus subtilis*	tannins, saponins, sesquiterpenes, alkaloids and phlobatamins	[78]
Terminalia chebula	Fruit /Water, chloroform, acetone and ethanol extract	Antioxidant activity and antibacterial activity against *Bacillus subtillis, Enterococcus faedalis , Staphylococcus aureus , Corynebacterium Salmonella typhi, Klebsiella pneumonia, Shigella boydii*	Phenolic compound	[79]
Viola odorata	Flower /petroleum ether, dichloromethane, ethyl acetate and the aqueous fractions	Antibacterial activity against *Escherichia coli* and *Klebsiella pneumoniae*	–	[80]
	Leaf /methanolic extract	Antioxidant activity	Phenolic compound	[81]
	Flower and twig /Aqueous extracts	Antibacterial activity against *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi, Shigella flexneri* and *Staphylococcus aureus*	–	[82]

Zingiber officinale	Rhizomes/methanol extract	Antioxidant activity	Flavonoids, volatile oil and phenolic materials	[83]
	Rhizomes/oleoresin compound	Antioxidant activity and antimicrobial activity against *Escherichia coli, Bacillus subtillis , Staphylococcus aureus, Bacillus cereus, Aspergillus niger, Penicillium spp.*	Oleoresin	[84]
Ziziphus jujuba	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 jojoba* 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
Aloe ferox Mill.	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]
Aloe vera	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-1and 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]
Terminalia chebula	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]

Ziziphus jojoba	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]

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

Sesamum indicum	Sesame cake defatted with hexane / methanol	Antioxidant activity	Sesamol, sesamol dimer, sesamin, sesamolin, sesaminol triglucoside, and sesaminol diglucoside, alpha tocopherol	[100]

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
Crocus sativus	Pollen /ethanolic extract	Second-degree burn	Male Wistar rats	↑Re-pithelialization, anti-inflammatory and antioxidant effects	crocins, crocetin, picrocrocin, β-carotene and safranal	[101]
Curcuma longa	Curcumin (0.3%, SigmaeAldric) h 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 80ºC	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]

Glycyrrhiza glabra	Root /hydroalcoholic extract	3rd degree burn wound infected to P. aeruginosa	Sprague - Dawley rats	↓of erythema, edema and itching, anti inflammatory		[105]
Pistacia lentiscus	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]
Sesamum indicum	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.

Acknowledgments

None.

References

[1]Powers JG, Higham C, Broussard K, Phillips TJ. Wound healing and treating wounds: Chronic wound care and management. J Am Acad Dermatol 2016;74:607-625.

[2]Situm M, Kolic M, Redzepi G, Antolic S. Chronic wounds as a public health problem. Acta Med 2014;68:5-7.

[3]Bellavia G, Fasanaro P, Melchionna R, Capogrossi MC, Napolitano M. Transcriptional control of skin reepithelialization. J Dermatol Sci 2014;73:3-9.

[4]Shaw TJ, Martin P. Wound repair at a glance. J Cell SCI 2009;122:3209-3213.

[5]Kondo T, Ishida Y. Molecular pathology of wound healing. Forensic Sci Int. 2010;203:93-98.

[6]Li G, Gustafson-Brown C, Hanks SK, Nason K, Arbeit JM, Pogliano K, et al. c-Jun is essential for organization of the epidermal leading edge. Dev Cell 2003;4:865-877.

[7]Atiyeh BS, Ioannovich J, Al-Amm CA, El-Musa KA. Management of acute and chronic open wounds: the importance of moist environment in optimal wound healing. Curr Pharm Biotechno. 2002;3:179-195.

[8]Fonder MA, Lazarus GS, Cowan DA, Aronson-Cook B, Kohli AR, Mamelak AJ. Treating the chronic wound: A practical approach to the care of nonhealing wounds and wound care dressings. J Am Acad Dermatol 2008;58:185-206.

[9]Guest JF, Gerrish A, Ayoub N, Vowden K, Vowden P. Clinical outcomes and cost-effectiveness of three alternative compression systems used in the management of venous leg ulcers. J Wound Care 2015;24:300.

[10]Kermani N. Sharhe Asbaab-o-Alaamaat. Ehyae-Tebe-Tabiee Publications. Tehran 2008.

[11]Azam Khan M. Exir-E-Azam. Tehran. Institute of Historical Studies, Islamic and Complementary Medicine. Tehran 2008.

[12]Arzani M. Teb-E-Akbari. Ehyae-Tebe-Tabiee Publications. Tehran 2008.

[13]Jorjani S. Al-Aghraz al- Tibbva val Mabahess al- Alaiia. Tehran University. Tehran 2006.

[14]Avicenna H. Al-Qanun-Fi-Teb. Beirut: Al-Ama Lelmatbuaat Publications. 2005.

[15]Kouvari M, Tyrovolas S, Panagiotakos DB. Red meat consumption and healthy ageing: A review. Maturitas. 2016;84:17-24.

[16]Wright JA, Richards T, Srai SK. The role of iron in the skin and cutaneous wound healing. Front Pharmacol. 2014;5:156.

[17]Tung YT, Tang TY, Chen HL, Yang SH, Chong KY, Cheng WT, et al. Lactoferrin protects against chemical-induced rat liver fibrosis by inhibiting stellate cell activation. J DAIRY SCI. 2014;97:3281-3291.

[18]Hambraeus L. Animal- and plant-food-based diets and iron status: benefits and costs. P Nutr Soc. 1999;58:235-242.

[19]Miller J, McNeal LS. Bioavailability of egg yolk iron measured by hemoglobin regeneration in anemic rats. The J Nutr. 1983;113:115-123.

[20]Pepe G, Sommella E, Manfra M, De Nisco M, Tenore GC, Scopa A, et al. Evaluation of anti-inflammatory activity and fast UHPLC-DAD-IT-TOF profiling of polyphenolic compounds extracted from green lettuce (Lactuca sativa L.; var. Maravilla de Verano). Food Chem. 2015;167:153-361.

[21]Ghimeray AK, Jung US, Lee HY, Kim YH, Ryu EK, Chang MS. In vitro antioxidant, collagenase inhibition, and in vivo anti-wrinkle effects of combined formulation containing Punica granatum, Ginkgo biloba, Ficus carica, and Morus alba fruits extract. Clin Cosmet Investig 2015;8:389-396.

[22]Hooda J, Shah A, Zhang L. Heme, an essential nutrient from dietary proteins, critically impacts diverse physiological and pathological processes. Nutrients 2014;6:1080-1082.

[23]Di Pierro G, O'Keeffe MB, Poyarkov A, Lomolino G, FitzGerald RJ. Antioxidant activity of bovine casein hydrolysates produced by Ficus carica L.-derived proteinase. Food Chem 2014;156:305-311.

[24]Lee HY, Kim JH, Jeung HW, Lee CU, Kim DS, Li B, et al. Effects of Ficus carica paste on loperamide-induced constipation in rats. Food Chem Toxicol 2012;50:895-902.

[25]Ali B, Mujeeb M, Aeri V, Mir SR, Faiyazuddin M, Shakeel F. Anti-inflammatory and antioxidant activity of Ficus carica Linn. leaves. Nat Prod Res 2012;460:25-26.

[26]Viuda-Martos M, Sendra E, Sayas E, Perez-Alvarez JA, Fernandez-Lopez J. Fig (Ficus carica) Liquid Co-Products as New Potential Functional Ingredient: Physico-Chemical and In Vitro Antioxidant Properties. Nat Prod Commun 2015;10:1219-1223.

[27]Abbasi AM, Shah MH, Li T, Fu X, Guo X, Liu RH. Ethnomedicinal values, phenolic contents and antioxidant

properties of wild culinary vegetables. J Ethnopharmacol 2015;162:333-345.
[28]Jing L, Zhang YM, Luo JG, Kong LY. Tirucallane-type triterpenoids from the fruit of Ficus carica and their cytotoxic activity. Chem Pharm Bull 2015;63:237-243.
[29]Camero M, Marinaro M, Lovero A, Elia G, Losurdo M, Buonavoglia C, et al. In vitro antiviral activity of Ficus carica latex against caprine herpesviru. Nat Prod Res. 2014;28:2031-2035.
[30]Allahyari S, Delazar A, Najafi M. Evaluation of general toxicity, anti-oxidant activity and effects of ficus carica leaves extract on ischemia/reperfusion injuries in isolated heart of rat. Adv Pharm Bull. 2014;4:577-582.
[31]Badgujar SB, Patel VV, Bandivdekar AH, Mahajan RT. Traditional uses, phytochemistry and pharmacology of Ficus carica: a review. Pharm Biol 2014;52:1487.
[32]Saoudi M, El Feki A. Protective Role of Ficus carica Stem Extract against Hepatic Oxidative Damage Induced by Methanol in Male Wistar Rats. Evid-Based Compl Alt 2012;2012:150458.
[33]Mawa S, Husain K, Jantan I. Ficus carica L. (Moraceae): Phytochemistry, Traditional Uses and Biological Activities. Evid-Based Compl Alt. 2013;2013:974256.
[34]Tian J, Zhang Y, Yang X, Rui K, Tang X, Ma J, et al. Ficus carica polysaccharides promote the maturation and function of dendritic cells. Int J Mol Sci 2014;15:12469-12479.
[35]Hayouni EA, Miled K, Boubaker S, Bellasfar Z, Abedrabba M, Iwaski H. Hydroalcoholic extract based-ointment from Punica granatum L. peels with enhanced in vivo healing potential on dermal wounds. Phytomedicine : Phytomedicine 2011;18:976-984.
[36]Mo J, Panichayupakaranant P, Kaewnopparat N, Nitiruangjaras A, Reanmongkol W. Wound healing activities of standardized pomegranate rind extract and its major antioxidant ellagic acid in rat dermal wounds. J Nat Med 2014;68:377-386.
[37]Finegold SM, Summanen PH, Corbett K, Downes J, Henning SM, Li Z. Pomegranate extract exhibits in vitro activity against Clostridium difficile. Nutrition 2014;30:1210-1212.
[38]Li G, Xu Y, Wang X, Zhang B, Shi C, Zhang W. Tannin-rich fraction from pomegranate rind damages membrane of Listeria monocytogenes. Foodborne Pathog Dis. 2014;11:313-319.
[39]Haghayeghi K, Shetty K, Labbe R. Inhibition of foodborne pathogens by pomegranate juice. J Med Food 2013;16:467-470.
[40]Israr F, Hassan F, Naqvi BS, Azhar I, Jabeen S, Hasan SM. Report: Studies on antibacterial activity of some traditional medicinal plants used in folk medicine. Pak J Pharm Sci 2012;25:669-674.
[41]Su X, Howell AB, D'Souza DH. Antibacterial effects of plant-derived extracts on methicillin-resistant Staphylococcus aureus. Foodborne Pathog Dis 2012;9:573-578.
[42]Turkyilmaz M, Tagi S, Dereli U, Ozkan M. Effects of various pressing programs and yields on the antioxidant activity, antimicrobial activity, phenolic content and colour of pomegranate juices. Food Chem 2013;138:1810-1818.
[43]Fawole OA, Makunga NP, Opara UL. Antibacterial, antioxidant and tyrosinase-inhibition activities of pomegranate fruit peel methanolic extract. BMC Complem Altern M 2012;12:200.
[44]Nayak SB, Rodrigues V, Maharaj S, Bhogadi VS. Wound healing activity of the fruit skin of Punica granatum. J Med Food. 2013;16:857-861.
[45]Jadoon S, Karim S, Bin Asad MH, Akram MR, Khan AK, Malik A, et al. Anti-Aging Potential of Phytoextract Loaded-Pharmaceutical Creams for Human Skin Cell Longetivity. Oxid Med Cell Longev. 2015;2015:709628.
[46] Amal B, Veena B, Jayachandran VP, Shilpa J. Preparation and characterisation of Punica granatum pericarp aqueous extract loaded chitosan-collagen-starch membrane: role in wound healing process. J Mater Sci-Mater M. 2015;26:181.
[47]da Silva JK, Cazarin CB, Correa LC, Batista AG, Furlan CP, Biasoto AC, et al. Bioactive compounds of juices from two Brazilian grape cultivars. J Sci Food Agr. 201;16:23-27.
[48]Perez C, Ruiz del Castillo ML, Gil C, Blanch GP, Flores G. Supercritical fluid extraction of grape seeds: extract chemical composition, antioxidant activity and inhibition of nitrite production in LPS-stimulated Raw 264.7 cells. Food Funct 2015;6:2607-2613.
[49]Nile SH, Park SW. Determination of polyphenols and antioxidant activity of Vitis labrusca cv. baile berries. Indian J Exp Biol 2015;53:671-675.
[50]Campanholo VM, Silva RM, Silva TD, Neto RA, Paiotti AP, Ribeiro DA, et al. Oral concentrated grape juice suppresses expression of NF-kappa B, TNF-alpha and iNOS in experimentally induced colorectal carcinogenesis in Wistar rats. Asian Pac J Cancer P 2015;16:947-952.
[51]Burri BJ, La Frano MR, Zhu C. Absorption, metabolism, and functions of beta-cryptoxanthin. Nutr Rev 2016;74:69-82.
[52]Attard E, Martinoli MG. Cucurbitacin E, An Experimental Lead Triterpenoid with Anticancer, Immunomodulatory and Novel Effects Against Degenerative Diseases. A Mini-Review. Curr Top Med Chem 2015;15:1708-1713.
[53]Bardaa S, Moalla D, Ben Khedir S, Rebai T, Sahnoun Z. The evaluation of the healing proprieties of pumpkin and linseed oils on deep second-degree burns in rats. Pharm Biol 2015:1-7.
[54]Xue Z, Gao J, Zhang Z, Yu W, Wang H, Kou X. Antihyperlipidemic and antitumor effects of chickpea albumin hydrolysate. Plant Food Hum Nutr 2012;67:393-400.
[55]Ferrari CK, Percario S, Silva JC, da Silva Torres EA. An

apple plus a nut a day keepS the doctors away: antioxidant capacity of foods and their health benefits. Curr Pharm Design 2015;22:189-190.
[56] Aires A, Marques E, Carvalho R, Rosa EA, Saavedra MJ. Evaluation of biological value and appraisal of polyphenols and glucosinolates from organic baby-leaf salads as antioxidants and antimicrobials against important human pathogenic bacteria. Molecules 2013;18:4651-4668.
[57]Gridling M, Popescu R, Kopp B, Wagner KH, Krenn L, Krupitza G. Anti-leukaemic effects of two extract types of Lactuca sativa correlate with the activation of Chk2, induction of p21, downregulation of cyclin D1 and acetylation of alpha-tubulin. Oncol Rep 2010;23:1145-1151.
[58]Zhang HL, Dai LH, Wu YH, Yu XP, Zhang YY, Guan RF, et al. Evaluation of hepatocyteprotective and anti-hepatitis B virus properties of Cichoric acid from Cichorium intybus leaves in cell culture. Biol Pharm Bull 2014;37:1214-1220.
[59]Esmaeilbeig M, Kouhpayeh SA, Amirghofran Z. An Investigation of the Growth Inhibitory Capacity of Several Medicinal Plants From Iran on Tumor Cell Lines. Iran J Cancer Prev 2015;8:e4032.
[60]Zhu D, Wang Y, Du Q, Liu Z, Liu X. Cichoric Acid Reverses Insulin Resistance and Suppresses Inflammatory Responses in the Glucosamine-Induced HepG2 Cells. J Agric Food Chem 2015;63:10903-10913.
[61]Lee NY, Chung KS, Jin JS, Bang KS, Eom YJ, Hong CH, et al. Effect of Chicoric Acid on Mast Cell-Mediated Allergic Inflammation in Vitro and in Vivo. J Nat Prod 2015;78:2956-2962.
[62]Abbas ZK, Saggu S, Sakeran MI, Zidan N, Rehman H, Ansari AA. Phytochemical, antioxidant and mineral composition of hydroalcoholic extract of chicory (Cichorium intybus L.) leaves. Saudi J Biol Sci 2015;22:322-326.
[63]El-Sayed YS, Lebda MA, Hassinin M, Neoman SA. Chicory (Cichorium intybus L.) root extract regulates the oxidative status and antioxidant gene transcripts in CCl4-induced hepatotoxicity. PloS one. 2015;10:e0121549.
[64]Rizvi W, Fayazuddin M, Shariq S, Singh O, Moin S, Akhtar K, et al. Anti-inflammatory activity of roots of Cichorium intybus due to its inhibitory effect on various cytokines and antioxidant activity. Ancient science of life 2014;34:44-49.
[65]Jyothilakshmi V, Thellamudhu G, Chinta R, Alok K, Anil K, Debadatta N, et al. Beneficial antioxidative effect of the homeopathic preparation of Berberis vulgaris in alleviating oxidative stress in experimental urolithiasis. Forsch Komplementmed (2006). 2014;21:7-12.
[66]Snowden R, Harrington H, Morrill K, Jeane L, Garrity J, Orian M, et al. A comparison of the anti-Staphylococcus aureus activity of extracts from commonly used medicinal plants. J Altern Complem Med 2014;20:375-382.
[67]Zarei A, Changizi-Ashtiyani S, Taheri S, Ramezani M. A quick overview on some aspects of endocrinological and therapeutic effects of Berberis vulgaris L. Avicenna J Phytomed. 2015;5:485-497.
[68]Hoshyar R, Mahboob Z, Zarban A. The antioxidant and chemical properties of Berberis vulgaris and its cytotoxic effect on human breast carcinoma cells. Cytotechnology 2015.
[69]Saedi TA, Ghafourian S, Jafarlou M, Sabariah MN, Ismail P, Eusni RM. berberis vulgaris fruit crude extract as a novel anti-leukaemic agent. J Biol Reg Homeos Ag. 2019;395:31-37.
[70]Sengul M, Yildiz H, Gungor N, Cetin B, Eser Z, Ercisli S. Total phenolic content, antioxidant and antimicrobial activities of some medicinal plants. Pak J Pharm Sci 2009;22:102-106.
[71]Loots DT, van der Westhuizen FH, Botes L. Aloe ferox leaf gel phytochemical content, antioxidant capacity, and possible health benefits. J Agr Food Chem. 2007;55:6891-6896.
[72]Gülçın İ, Oktay M, Kıreçcı E, Küfrevıoğlu Öİ. Screening of antioxidant and antimicrobial activities of anise (Pimpinella anisum L.) seed extracts. Food Chem 2003;83:371-382.
[73]Lopes-Lutz D, Alviano DS, Alviano CS, Kolodziejczyk PP. Screening of chemical composition, antimicrobial and antioxidant activities of Artemisia essential oils. Phytochemistry 2008;69:1732-1738.
[74]Craciunescu O, Constantin D, Gaspar A, Toma L, Utoiu E, Moldovan L. Evaluation of antioxidant and cytoprotective activities of Arnica montana L. and Artemisia absinthium L. ethanolic extracts. Chem Cent J 2012;6:97.
[75]Shahidi Bonjar G, Aghighi S, Karimi Nik A. Antibacterial and antifungal survey in plants used in indigenous herbal-medicine of south east regions of Iran. J Biol Chem. 2004;4:405-412.
[76]Kamaraj C, Rahuman AA, Siva C, Iyappan M, Kirthi AV. Evaluation of antibacterial activity of selected medicinal plant extracts from south India against human pathogens. Asian Pac J Trop Med. 2012;2:S296-S301.
[77]Tril U, Fernández-López J, Álvarez JÁP, Viuda-Martos M. Chemical, physicochemical, technological, antibacterial and antioxidant properties of rich-fibre powder extract obtained from tamarind (Tamarindus indica L.) Ind Crop Prod 2014;55:155-162.
[78]Doughari J. Antimicrobial activity of Tamarindus indica Linn. Trop J Pharm Res 2007;5:597-603.
[79]Kathirvel A, Sujatha V. In vitro assessment of antioxidant and antibacterial properties of Terminalia chebula Retz. Leaves. Asian Pac J Trop Med 2012;2:S788-S795.
[80]Ziad D, Elias A, Roula A-M. Antibacterial activity of Rheum rhaponticum, Olea europaea and Viola odorata on ESBL producing clinical isolates of Escherichia coli and Klebsiella pneumoniae. Int J Pharm Sci Res 2011;2:1669-1678.
[82]Ebrahimzadeh MA, Nabavi SM, Nabavi SF, Bahramian F, Bekhradnia AR. Antioxidant and free radical scavenging activity of H. officinalis L. var. angustifolius, V. odorata, B.

hyrcana and C. speciosum. Pak J Pharm Sci 2010;23:29-34.
[83]Amir M, Khan A, Mujeeb M, Ahmad A, Usmani S, Akhtar M. Phytochemical analysis and in vitro antioxidant activity of Zingiber officinale. Biochem Soc Symp 2011;1:75-81.
[84]Bellik Y. Total antioxidant activity and antimicrobial potency of the essential oil and oleoresin of Zingiber officinale Roscoe. Asian Pac J Trop Med 2014;4:40-44.
[85]Memarpoor-Yazdi M, Mahaki H, Zare-Zardini H. Antioxidant activity of protein hydrolysates and purified peptides from Zizyphus jujuba fruits. J Funct Foods. 2013;5:62-70.
[86]Zhang H, Jiang L, Ye S, Ye Y, Ren F. Systematic evaluation of antioxidant capacities of the ethanolic extract of different tissues of jujube (Ziziphus jujuba Mill.) from China. Food Chem Toxicol 2010;48:1461-1465.
[87]Chithra P, Sajithlal G, Chandrakasan G. Influence of Aloe vera on the healing of dermal wounds in diabetic rats. J Ethnopharmacol 1998;59:195-201.
[88]Kumar MS, Kirubanandan S, Sripriya R, Sehgal PK. Triphala promotes healing of infected full-thickness dermal wound. J Surg Res 2008;144:94-101.
[89]Goyal R, Sharma PL, Singh M. Possible attenuation of nitric oxide expression in anti-inflammatory effect of Ziziphus jujuba in rat. J Nat Med. 2011;65:514-518.
[90]Jia Y, Zhao G, Jia J. Preliminary evaluation: the effects of Aloe ferox Miller and Aloe arborescens Miller on wound healing. J Ethnopharmacol 2008;120:181-189.
[91]Atiba A, Nishimura M, Kakinuma S, Hiraoka T, Goryo M, Shimada Y. Aloe vera oral administration accelerates acute radiation-delayed wound healing by stimulating transforming growth factor-β and fibroblast growth factor production. Am J Surg 2011;201:809-818.
[92]Singh MP, Sharma CS. Wound healing activity of Terminalia chebula in experimentally induced diabetic rats. Int J Pharm 2009;1:1267-1270.
[93]Aref HL, Salah K, Chaumont JP, Fekih A, Aouni M, Said K. In vitro antimicrobial activity of four Ficus carica latex fractions against resistant human pathogens (antimicrobial activity of Ficus carica latex). Pak J Pharm Sci 2010;23:53-58.
[94]Iauk L, Ragusa S, Rapisarda A, Franco S, Nicolosi V. In vitro antimicrobial activity of Pistacia lentiscus L. extracts: preliminary report. J Chemotherapy. 1996;8:207-209.
[95]Tohma HS, Gulçin I. Antioxidant and radical scavenging activity of aerial parts and roots of Turkish liquorice (Glycyrrhiza glabra L.). Int J Food Prop 2010;13:657-671.
[96]Patil S, Patil M, Sapkale G. Antimicrobial activity of Glycyrrhiza glabra Linn. roots. Int J Chem Sci 2009;7:585-91.
[97]Assimopoulou A, Sinakos Z, Papageorgiou V. Radical scavenging activity of Crocus sativus L. extract and its bioactive constituents. Phytother Res. 2005;19:997-1000.
[98]Shahwar D, Raza MA, Bukhari S, Bukhari G. Ferric reducing antioxidant power of essential oils extracted from Eucalyptus and Curcuma species. Asian Pac J Trop Med 2012;2:S1633-S1636.
[99]Shivalingu BR, Vivek HK, Nafeesa Z, Priya BS, Swamy SN. Comparative analysis of procoagulant and fibrinogenolytic activity of crude protease fractions of turmeric species. J Ethnopharmacol. 2015;172:261-4.
[100]Suja KP, Jayalekshmy A , Arumughan C. Free radical scavenging behavior of antioxidant compounds of sesame (Sesamum indicum L.) in DPPH system). J Agr Food Chem. 2004;52:912-915.
[101]Khorasani G, Jalal Hosseinimehr S, Zamani P, Ghasemi M, Ahmadi A. The effect of saffron (Crocus sativus) extract for healing of second-degree burn wounds in rats. Keio J Med 2008;57:190-195.
[102]Kant V, Gopal A, Kumar D, Pathak NN, Ram M, Jangir BL. Curcumin-induced angiogenesis hastens wound healing in diabetic rats. J Surg Res. 2015;193:978-988.
[103]Durgaprasad S, Reetesh R, Hareesh K, Rajput R. Effect of a topical curcumin preparation (BIOCURCUMAX) on burn wound healing in rats. J Pharmaceut Biomed 2011;8:20-26.
[104]Li X, Nan K, Li L, Zhang Z, Chen H. In vivo evaluation of curcumin nanoformulation loaded methoxy poly(ethylene glycol)-graft-chitosan composite film for wound healing application. Carbohyd Polym 2012;88:84-90.
[105]Tanideh N, Rokhsari P, Mehrabani D, Samani SM, Sarvestani FS, Ashraf MJ. The healing effect of licorice on Pseudomonas aeruginosa infected burn wounds in experimental rat model. World Journal of Plastic Surgery 2014;3(2):99.
[106]Maameri Z, Beroual K, Djerrou Z, Habibatni S, Benlaksira B, Serakta M, et al. Preliminary study to assess cicatrizing activity of honey and Pistacia lentiscus fatty oil mixture on experimental burns in rabbits. J Appl Res Med Aromat Plants. 2012;2:476-480.
[107] Djerrou J, Maameri Z, Hamdo-Pacha Y, Serakta M, Riachi F, Djaalab H, et al. Effect of virgin fatty oil of Pistacia lentiscus on experimental burn wound's healing in rabbits. Afr J Tradit Complem 2010;7:13-15.
[108]Shenoy RR, Sudheendra AT, Nayak PG, Paul P, Kutty NG, Rao CM. Normal and delayed wound healing is improved by sesamol, an active constituent of Sesamum indicum (L.) in albino rats. J Ethnopharmacol. 2011;133:608-12.
[109]Kiran K, Asad M. Wound healing activity of Sesamum indicum L seed and oil in rats. Indian J Exp Biol. 2008;46:777.
[110]Posnett J, Franks P. The burden of chronic wounds in the UK. Diabetic Med. 2008;14:S7-S85.
[111]Leoni G, Neumann PA, Sumagin R, Denning TL, Nusrat A. Wound repair: role of immune-epithelial interactions. Mucosal Immunol 2015;8:959-968.