

Leech therapy in skin conditions from the viewpoints of Avicenna and modern medicine: Historical review, current applications, and future recommendations

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Received: 24 March 2020
 Accepted: 19 May 2020

INTRODUCTION

Skin conditions cause considerable morbidity. Therefore, effective treatment with minimal side effects plays an important role in controlling

Background: Skin conditions are among the most common health problems worldwide and are associated with immense psychological, social, and financial burdens. Atopic dermatitis, alopecia, eczema, diabetic ulcers, and abscesses are common acute or chronic conditions, which are increasing dramatically in prevalence due to industrialization and unhealthy lifestyle habits. The use of complementary and alternative medicine to treat skin diseases has been increasing in recent years.

Methods: This review focuses on proposed skin conditions for leech therapy as mentioned by Avicenna, a great Iranian philosopher and physician (980-1037 AD) in the *Canon of Medicine*. Electronic databases including PubMed, Scopus, and Google Scholar were searched for clinical studies on treatment protocols in this book to compare them with recent clinical trials involving leech therapy.

Results: Investigation of traditional Iranian medicine literature can lead to the identification of natural medicines for the management of skin problems. Leech saliva contains anti-coagulative, anti-aggregative, and vasodilatory components.

Conclusions: In addition to the annelid's mechanical ability to extract blood, leeches can contribute to patients' health while posing minimal risks.

Keywords: skin disease, traditional medicine, eczema, alopecia, abscess

Iran J Dermatol 2020; 23: 168-175

DOI: [10.22034/ijd.2020.224195.1053](https://doi.org/10.22034/ijd.2020.224195.1053)

these conditions. For instance, topical steroids can ameliorate atopic dermatitis but can induce skin atrophy and secondary infection. These diseases are associated with dysfunction in the skin barrier. Although mild cases can be controlled

with antihistamines and topical corticosteroids, moderate-to-severe cases often require treatment with immunomodulatory drugs, which may give rise to adverse effects¹. Topical steroids and subcutaneous corticosteroids are very common in the treatment of alopecia areata, but continuous use causes skin thinning, telangiectasia, fungal infection, and skin atrophy². Diabetic ulcers are one of the complications of uncontrolled diabetes mellitus, which may lead to secondary infection and limb amputation³. Because of serious side effects, it seems logical to seek other available medicinal remedies with greater efficacy and fewer side effects. For this purpose, a valuable option is focusing on complementary and traditional medicine. Traditional remedies have been used by people in different regions for many centuries, which may be in favor of their effectiveness and safety. Avicenna (980-1037 AD), an illustrious Iranian philosopher and physician, depicted different kinds of skin conditions and focused on their treatment by leech therapy⁴. The present review aims to explain skin conditions claimed to be treated by leech therapy in Avicenna's *Canon of Medicine* and to find pieces of evidence regarding leech therapy for skin conditions in contemporary literature.

PARTICIPANTS AND METHODS

This article is a narrative review, based on examining Avicenna's *Canon of Medicine* for skin conditions treated by medicinal leech therapy. The whole process of collecting subjects was started by a thorough, line-by-line reading of the extracted materials and key sentences. The keywords used were as follows: "falaghmuñi", "namlah", "homrah", "irq ol-madaniil-masa'fah", "shara", "badishnam", "quba", "baras ol-aswad", "ghangharana", "ta'un", "waba", "saqirus" [scirrhus], "sara'an", "jodham" [leprosy], "da' olth-tha'lab" [fox's disease; alopecia areata], "hasaf", and "qarh." Then, the concepts were defined and coded. Signs, symptoms, etiologies, and treatments of the skin conditions were extracted and classified. In the next step, we defined equivalents in modern medicine based on the symptoms of skin diseases in Iranian traditional medicine. Then, electronic databases including PubMed, Scopus, and Google Scholar were searched for clinical and animal trials conducted from 1980 to 2020

with the following keywords: skin, leech, eczema, abscess, alopecia areata, frostbites, diabetic ulcers, or medicinal leech therapy. Finally, the data were classified and compared in the two groups of Iranian medicine and modern literature.

RESULTS

Skin conditions treated by medicinal leech therapy in the *Canon of Medicine*

Avicenna (980-1037 AD), an illustrious Iranian philosopher and physician, depicted different kinds of skin conditions using terms such as "falaghmuñi", "namlah", "homrah", "irq ol-madaniil-masa'fah", "shara", "badishnam", "quba", "baras ol-aswad", "ghangharana", "ta'un", "waba", "saqirus" [scirrhus], "sara'an", "jodham" [leprosy], "da' olth-tha'lab" [fox's disease; alopecia areata], "hasaf", and "qarh." He utilized leech therapy for the skin conditions described in Table 1⁴⁻⁶.

Pathology and common treatments of skin conditions in contemporary literature

Abscess

Skin and soft tissue infections are among the most common bacterial diseases and represent a significant disease burden⁷. Antibiotic stewardships have been called for across all sites of healthcare, including nursing homes⁸⁻¹⁵. Skin and soft tissue infections are the third most common indication for antibiotics in nursing homes, and should therefore be a focus of stewardship¹⁶. Considering the many side effects, the necessity of finding alternative treatments is evident.

Eczema

Atopic dermatitis comprises a group of chronic, relapsing, inflammatory conditions that involve the skin and are associated with decreased skin barrier function, resulting in periodic flare-ups of erythematous and pruritic lesions. Topical steroids ameliorate atopic dermatitis but may induce skin atrophy and secondary infections¹⁷. Atopic dermatitis is a familial disease, often coexisting with other atopic diseases; multiple risk factors are associated with atopic eczema.

Table 1. Skin diseases treated by medicinal leech therapy as mentioned in Avicenna's *Canon of Medicine*.

Disease name	Scientific description
<i>Falaghmūnī</i>	Absolute sanguine swelling, engorgement of tissue with blood, which leads to organ enlargement
<i>Namlah</i>	Progressive hot burning/swelling caused by acute yellow bile humor
<i>Bādishnām</i>	A skin condition characterized by the formation of red areas on the skin, especially in cold weather
<i>'Irq ol-madanī</i>	The Guinea worm, <i>Dracunculus medinensis</i> , which causes dracunculiasis
<i>Homrah</i>	Redness, erythema, hot yellow bile swelling of the skin, which is bright and red, and blanches when pressure is applied
<i>Sa'fah</i>	Ulcer or plaque, erythematous and scaly skin with or without oozing; may sometimes become purulent, occurs mostly on the head/face and manifests as two types: dry and wet
<i>Sharā</i>	A type of irritating urticaria with severe itching caused by yellow bile humor
<i>Qūbā, baraş ol-aswad</i>	Plaque caused by different humors (mostly by thick black bile humor), predominantly occurring in the skin; manifested by pruritus, tightness, and change of skin color to red or black
<i>Ghāngharānā</i>	An inflammation that putrefies the organ, though sensation is left intact
<i>Tā'ūn, wabā</i>	Any inflammation occurring in glandular, fleshy, or hollow organs
<i>Saqrūs [scirrhus]</i>	A firm type of inflammation that is caused by black bile, phlegm, or both, which may transform into cancer
<i>Waram saratānī</i>	A cancerous inflammation with erythema and pulsatile pain, caused by black bile humor; tumefaction generated from yellow bile or phlegm accompanied by a small amount of bile
<i>Jodhām</i>	Leprosy
<i>Dā' olth-tha'lab</i>	Fox's disease: loss of hair due to the accumulation of corrupt materials in the subcutaneous area, which blocks nutrients thus, causes hair roots to deteriorate [alopecia areata]
<i>Hasaf</i>	Dry scabies, heat rash, prickly heat, miliaria
<i>Qarh</i>	Ulcer

Eczema is one of the most common chronic inflammatory skin diseases, affecting about 20% of children. This disorder is characterized by itchy, dry, rough, and scaling skin. Patients suffering from atopic dermatitis are known to have a predisposition to colonization or infection by microbial organisms, including both *Staphylococcus aureus* and the herpes simplex virus (HSV). *S. aureus* infection leads to exacerbation of eczema and may induce flares in atopic skin by mediating inflammation¹⁸. The pathogenic mechanisms of eczema are still not fully understood, and current treatment of moderate-severe eczema is often difficult¹⁹⁻²¹. The disease is more frequent in urban areas compared with rural ones. Changes in nutrition and decrease in infant breastfeeding and respiratory allergies are contributory factors²².

Alopecia

Alopecia areata is a common cause of non-scarring alopecia that occurs in a patchy, confluent, or diffuse pattern. Alopecia areata is an immune-mediated disease that targets hair follicles in the anagen phase. Despite various therapeutic options, there is no cure for alopecia areata. Prostaglandin analogs have been recognized as being capable of inducing hypertrichosis²³. Another theory on the development of alopecia areata is related to an

autoimmune process involving T-cells. Apoptosis is one of the suspected culprits in the pathogenesis of alopecia areata. This disorder can be treated using contact sensitizers like diphencyprone (DPCP)²⁴.

Frostbite

In a study conducted in 2011, the efficiency of necrectomy methods for treating deep frostbites was analyzed according to the data of outcomes of surgical treatment of 272 patients. It was demonstrated that dissection of necrotic tissue in deep frostbites using modern physical techniques (electrosurgical, radiosurgical, and argon-plasma dissector) improved immediate results of surgical treatment due to decreased intraoperative blood loss, suppuration frequency, amputation, and hospitalization duration, and optimized the wound process by reducing microbial contamination and accelerating the proliferative phase of regeneration²⁵. In another study in 1989, the treatment of chilblains with nifedipine was evaluated. In this study, a 20 to 60 mg daily dose of nifedipine significantly reduced the clearance time of existing lesions and prevented the development of new chilblains. Nifedipine also reduced pain, soreness, and irritation of lesions²⁶. Considering the high risk of side effects for frostbite treatment, seeking alternative treatment is a necessity.

Diabetic ulcers

Diabetic foot ulcerations affect about a quarter of patients with diabetes mellitus during their lifetime. Increased local hypoxic conditions are the most important factor, causing delayed wound healing. Treatment of impaired wound healing is based on metformin and anti-glycemic agents including dipeptidyl peptidase 4 (DPP4) inhibitors²⁷. About 10-15% of diabetic patients suffer from foot ulcers and 15% of all limb amputations are performed in patients with diabetes²⁸.

Medicinal leech therapy for skin conditions

Eczema is managed with antibiotics, antihistamines, steroids, etc.; however, relapses, recurrences, and other complications are very common with these treatments. The efficacy of leech therapy in the management of eczema has been studied according to standard clinical parameters. According to the Eczema Area and Severity Index (EASI) score, Scoring of Atopic Dermatitis (SCORAD) Index, and Dermatology Life Quality Index (DLQI), significant relief of eczema symptoms have been achieved via leech therapy. Quality of life also improves significantly and no adverse reactions have been reported during the entire course of a study²⁹.

The management of alopecia areata, which is an autoimmune disease that affects hair follicles, usually involves prescribing corticosteroids, prostaglandin analogs (bimatoprost; latanoprost), apoptosis regulators (diphencyprone), sensitization agents (squaric acid dibutylester), T-regulatory cell promoters (recombinant interleukin 2), etc., but these treatments offer limited recovery rates. The efficacy of leech therapy in the management of alopecia areata was studied in 2014, with the results being indicative of significant visible effects in the form of hair growth³⁰. Management of diabetic foot and acute venous congestion by leech therapy is also considerable³¹. Some indications of leech therapy include tumors, hemorrhoids, abscesses, furuncles, skin disorders, ulcers, gout, eye diseases, headaches, herpes zoster, thrombosis, and wounds. Leech saliva consists of anesthetic agents, anticoagulants, an antiplatelet aggregation factor, antibiotics, anti-inflammatory compounds, and gelatinous substances. Leeches suck excess

blood, reduce tissue swelling, and promote healing by allowing fresh oxygenated blood to reach the area until normal circulation can be restored. Clinical studies have been conducted in different parts of the world to understand the mechanism of action in leech therapy. Studies with leeches have been carried out to investigate the healing of complicated varicose veins, pain reduction in osteoarthritis, and the treatment of other disorders Table 2³².

Mechanisms of action in leech therapy

a) Anti-inflammatory and analgesic substances

Antistasin: The analgesic effect of leech saliva is indirect. Leech saliva contains antistasin, a 15-kDa protein, which inhibits certain types of tissue kallikreins. Tissue kallikreins are proteases that cleave inactive forms of kininogens to generate biologically active kinins and mediate stressful conditions like tissue destruction and inflammation³³.

Eglin C: Eglin C effectively blocks the activity of neutrophil elastase and cathepsin G, which are secreted by activated neutrophils and cause severe tissue destruction. This 8.1-kDa protein maybe considered an anti-inflammatory agent that protects host tissues from the destructive impacts of endogenous neutrophils^{34,35}.

Tryptase inhibitor: Leech saliva contains a specific inhibitor of a 4.3–4.8 kDa mast cell enzyme called tryptase. Tryptase is a trypsin-like serine proteinase that is highly abundant in the extracellular space of tissues and acts as a marker for mast cell activation. The enzyme is active in plasma and the intestines and none of the usual protease inhibitors present in these compartments block its activity. Elevated levels of tryptase in the serum are associated with inflammatory conditions and anaphylactic reactions³⁵.

b) Inhibitors of C1 complement component

Inhibitors of the C1 complement component inhibit the classical pathway of complement activation and also offer anti-inflammatory effects³⁶.

c) Facilitation of diffusive distribution

Hyaluronidase: This 27.5-kDa protein cleaves hyaluronic acid in the host's extracellular matrix.

Table 2. Clinical and animal trials on the treatment of skin conditions using medicinal leech therapy.

Treatment protocol	Sample size	Group	Treatment duration	Results	Authors and year of the study	Reference No.
Evaluation of the efficacy of leech application in the management of eczema.	27	-	Leech application was carried out with a 7-day interval	Leech application gives significant relief for the symptoms of eczema. Quality of life also improved. No adverse reactions were reported.	Shankar KP, Rao SD, Umar SN, Gopalakrishnaiah V. 2014	[29]
Investigation of the effects of leech therapy (LT), in comparison with topical phenytoin (PHT) on incisional skin-wound healing in an animal model.	15 male rats (5 in each of 3 groups)	-	-	The process of wound healing was significantly faster in the LT group.	Darestani KD, Mirghazanfari SM, Moghaddam KG, Hejazi S. 2014	[47]
A study of leech therapy on a patient with a one-year history of alopecia areata.	-	-	1 to 2 fresh leeches were applied to affected areas for 30 minutes every 20 days with post leeching follow-ups for four months	The results of the study showed significant visible effects in the form of hair growth.	Bhat AI, Bhat AI, Habib A, Arjumand H, Mustafa KG, Afroza J, et al. 2014	[48]
Evaluation of the possible efficacy of medical leeches (<i>Hirudo medicinalis</i>) in the treatment of knee osteoarthritis versus transcutaneous electrical nerve stimulation (TENS).	72	-	Eight leeches (group 1: 27 patients) or TENS (group 2: 25 patients). 21 days	Single leech therapy showed significant, relevant, and sustained effects.	Stange R, Moser C, Hopfenmueller W, Mansmann U, Buehring M, Uehleke B. 2016	[30]
Effect of Taleeq (leech therapy) in Dawali (varicose veins).	50	-	30 in the intervention group and 20 in the control group. 2 months	Major improvement in all parameters was demonstrated in the intervention group: pain/leg discomfort, limb girth (calf, ankle, and feet), and pigmentation area and color.	Nigar Z, Alam MA. 2011	[49]
Treatment of diabetic foot ulcer with medicinal leech therapy and honey curcumin dressing: a case report.	Case report	-	12 weeks	Leech therapy in combination with honey and curcumin dressing is effective against disease progression in patients with diabetic foot ulcers.	ShirbeigiLaila, Eghbalian Fatemeh, Bakhtyari Lida, 2019	[50]
Leech therapy saved the diabetic foot of a patient from amputation.	1	A 60-year-old woman suffering from diabetic foot.	-	Pain score decreased within 20 days and no further pain-relieving medication was required. Necrotic areas disappeared and the wound healed over a time interval of 3.5 months.	Zaidi SA. 2016	[31]

The digestion of hyaluronic acids facilitates the diffusive distribution of other salivary peptides and proteins in the tissue around the feeding site³⁷.

d) Improvement of blood flow

Histamine: Histamine is a 111-Da protein that

increases vascular permeability in the host. It may induce partial permeabilization of blood vessels and smooth muscle cell relaxation in small arteries. This results in fluid release from the vessel lumen to the interstitium (edema) and, in prolonged cases, increases blood flow to the feeding site^{38,39}.

e) Inhibitors of platelet adherence and activation

Saratin: This 12-kDa molecule binds to exposed collagen I and II and inhibits binding of vWF (von Willebrand) in a competitive manner. Making use of this mechanism, recombinant saratin has been used topically to prevent thrombosis or arteriosclerosis in animal models^{40,41}.

Hirudin: An inhibitor of thrombin that prevents the formation of fibrin clots; it has a 7.1-kDa molecular mass³⁹.

Collagenase: A 100-kDa enzyme that cleaves and digests collagen in the extracellular matrix, which gets exposed to components of the blood plasma when the leech severs blood vessels in preparation for feeding. This may contribute to the leech's efforts to minimize host platelet adherence to vessel walls at the feeding site^{42,43}.

Apyrase: A 45-kDa protein that cleaves adenosine 5'-diphosphate (ADP), inhibiting platelet activation^{42,44}.

Destabilase: A 12-kDa protein, which contributes to cleavage of isopeptide bonds in stabilized fibrin, and thrombolysis⁴⁵.

Antimicrobial agents: Antimicrobial agents including destabilase have lysozyme-like activity (cleavage of cell wall components of bacteria) and defensin-like activity (inhibition of bacterial growth)^{45,46}.

DISCUSSION

Nowadays, medicinal leech therapy is drawing major publicity and immense scientific attention as novel indications are explored for this ancient treatment³². In this study, we focused on skin problems for which leech therapy has been recommended in Avicenna's *Canon of Medicine* and compared them with current treatment protocols. We came to the conclusion that some skin conditions maybe treated using medicinal leech therapy with no adverse effects as an alternative to common methods that have severe side effects, high failure rates, or low efficacy.

Pharmacological treatment of eczema, abscesses, and alopecia is achieved by immunosuppressive and anti-inflammatory agents such as corticosteroids as well as antibacterials in the case of secondary infections. In some instances, these treatments are only partially effective or merely reduce the

symptoms of the skin condition. A combination of proteins with anti-inflammatory (antistasin, eglins, trypsin inhibitor), antibacterial (destabilase), and anti-coagulation agents (hirudin, sarains, apyrase) are involved in medicinal leech therapy. According to clinical trials and case reports (Table 1), leech saliva is comprised of this combination of compounds and has no side effects; it can be prescribed for treating skin conditions. Medicinal leech therapy, as proposed by Avicenna, is not only indicated for the treatment of skin conditions but also other conditions such as renal and urinary tract disease, wound healing, headache, gastritis, vascular disease, joint pain, eye disease, leprosy, and bruises⁴.

Analysis of leech salivary secretions, comprising more than 100 proteins, has demonstrated beneficial properties including anti-inflammatory, antimicrobial, and anti-coagulant activities, as well as inhibition of platelet activation and thrombolysis. These factors seem to play important roles in the treatment of skin conditions. In conclusion, the pieces of evidence presented in this review are collectively in favor of focusing on the application of medicinal leech therapy as an alternative to other treatment protocols for diseases in the *Canon of Medicine*.

CONCLUSION

Due to the high rate of treatment failure in skin diseases, it seems necessary to find alternative methods. In this context it seems logical to use the resources of traditional medicine. In this review article, we not only witnessed the positive results of treating various skin diseases by directly application leeches, but also witnessed the treatment of diabetic foot by preparing a product from leeches. Of course, the need for further examination and clinical trial seems necessary.

Conflict of Interest: None declared.

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