



Effects of a Traditional Iranian Remedy on Cutaneous Leishmaniasis

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Abstract

Background: Despite numerous studies aimed at finding a new treatment for cutaneous leishmaniasis (CL), glucantime remains the first-line approach. Side effects, drug resistance, and high cost are the challenges of glucantime treatment. A simple treatment method with the fewest side effects, minimum cost, and maximum efficacy is ideal. In Iranian traditional medicine (ITM), dry CL lesions are categorized as rashes, and for treatment, corrosive and keratolytic agents should be used, including garlic. The current study was conducted to assess the effects of an ITM treatment on CL.

Methods and Results: In this experimental study, 10 patients with 20 dry CL lesions received treatment based on ITM. For this purpose, some garlic poultices were used. The mean age of the patients was 36.2 years, and the average bout was nearly four months. Based on the findings, garlic poultices could treat all dry skin lesions completely during 14 days. Also, after 40, 70, 100, and 190 days of follow-up, 95% of cases were completely treated. On the 70-day follow-up, a nodule with negative direct smear and PCR results recurred in one patient. Overall, the applied treatment was cost-effective with no systemic side effects.

Conclusions: Garlic poultices can be used as an alternative for glucantime. Topical use, shorter course of treatment, and lower number of applications, side effects, and treatment cost are the main advantages of this regimen. We suggest similar multi-centered clinical trials with a larger sample size to further evaluate this treatment regimen.

Keywords: Dry Cutaneous Leishmaniasis, Treatment, Garlic, Iranian Traditional Medicine

1. Background

Cutaneous leishmaniasis (CL) is an infection caused by a protozoan parasite, called *Leishmania*. *Leishmania* generally involves a genus of sandflies as the vector and canines, rodents, and humans as the main reservoir host (1, 2). This infection is considered to be endemic in 88 countries. The World Health Organization (WHO) estimates that 700,000 to 1,200,000 people develop CL each year. The following countries account for 70 - 75% of total cases of the disease: Afghanistan, Algeria, Brazil, Colombia, Costa Rica, Ethiopia, Iran, Peru, Sudan, and Syria (3).

Generally, men and women of any age are susceptible to CL. Although this infection usually disappears on its own (4), failure to seek treatment can have adverse effects, such as disease transmission (5), growth of lesions, secondary infections, and aesthetic problems (6). Since 1929, pentava-

lent antimonials have been used in the treatment of diseases (7). Frequent side effects, parasite resistance to drugs (34.9% in some studies) (8), high cost, and injection pain are among the most important problems of these treatments. Other drugs, such as miltefosine, amphotericin B, paromomycin, ketoconazole, and fluconazole, have been also used as alternative remedies; however, application of these agents is limited due to variable efficacy rates and side effects (9).

To find a safer and less expensive medicine for CL, researchers have conducted various studies, a number of which are outlined here. Sharquie et al. in a clinical trial showed that 95% of patients were treated for CL through intralesional injection of 2% zinc sulfate (10), whereas Maleki et al. reported 33% (11). In addition, Haghighi et al. applied 20% *Berberis vulgaris* extract to eight CL lesions and found it to be majorly effective (12).

Treatment of ulcers and disappearance of induration are the clinical indicators of treatment progress. Reduction of side effects, treatment cost, and length of treatment is an important issue. On the one hand, reluctance of patients to receive glucantime injections, and on the other hand, their inclination towards traditional medicine and herbal treatments motivated us to use garlic cloves for therapeutic purposes. Iranian traditional medicine (ITM) references were the main sources of our study. In ITM, diseases (e.g., urban-type CL) involving pus-less rashes with a nodular form are termed “Bosreh”. These diseases should be treated with medicines, which can remove the node content using solvent and keratolytic agents.

Garlic (*Allium sativum*) has numerous therapeutic properties. Among the effective compounds of garlic, allicin, gamma glutamyl, sultosans, saponins, allysine, and ajoene can be mentioned. Garlic acts as a reducing agent of cholesterol, triglyceride, hypertension, and antiplatelet aggregation, with fibrinolytic (13), antineoplastic, and anti-allergic properties (14). The efficacy of garlic against *Salmonella*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella*, *Helicobacter*, *Candida albicans* (15), *Cryptosporidium* (16), *Entamoeba histolytica*, *Trypanosoma* (17), and *Histoplasma* (18) has been confirmed in various studies. Allysine in garlic controls the growth of *Leishmania major* (15). The antimicrobial effect of garlic is attributed to aldehyde allylic acid or acrolein (19). In addition, by stimulating some defense cells, such as macrophages, lymphocytes, NK cells, dendritic cells, and eosinophils, garlic improves the performance of the immune system (20).

ITM categorizes garlic into three types, i.e., garden garlic, garlic leek, and desert garlic. It also attributes various properties to garlic, such as treating inflammation, expelling flatus, and protecting the body against environmental changes (21). ITM argues that garlic has aesthetic and topical applications and suggests its use together with boiled oregano (or rubbing the mixture on the body) to destroy lice and nits. In addition, the mixture of garlic powder and honey is useful in the treatment of vitiligo and blood spots under eyelids.

Garlic is considered a remedy for Alopecia areata and abdominal abscess. In addition, a mixture of powdered garlic and honey is very helpful in treating impetigo and scabies; application of fresh desert garlic on malignant wounds is also helpful for treatment (22). However, garlic produces a burning sensation in the skin. In fact, if the skin is exposed to garlic for an extended period, it may be damaged. On the other hand, garlic is a strong dermal pore cleanser, and a mixture of garlic, salt, and olive oil or a mixture of garlic and honey can be helpful in treating exanthema (23).

Garlic exhibits anti-inflammatory properties and stim-

ulates the immune system. Various researchers have used garlic extracts, garlic gel, and garlic cream in CL treatment. However, after searching all valid scientific references and databases, we could not find any literature on the use of garlic poultice in CL treatment; therefore, use of garlic is quite novel in this context.

2. Objectives

In the present study, the effects of topical application of garlic bulb on 20 lesions were assessed in 10 patients with CL.

3. Methods

This experimental study with a before-after design was performed to determine the effects of an ITM treatment approach on CL lesions. The study population included 12 patients with 23 dry CL lesions, who were referred to Mashhad Health Center. The patients' disease was confirmed using direct smear and PCR assays. It should be noted that the patients were reluctant to receive glucantime injections. After recruiting eligible patients in the study, the research team conducted interviews and provided patients with comprehensive information, including the used medicine and its route of administration, possible side effects, duration of treatment, and potential responses. After agreeing to participate in the study, the patients signed the consent forms.

Images were acquired from the lesions, and size of induration was measured using a digital caliper (LASER® Digital Vernier Caliper, Manufacturer sku 4263) and recorded by two clinicians; following that, other proper measures were taken. Every participant was provided with some fresh raw garlic cloves and taught how to peel, wash, and crush garlic cloves in order to prepare poultices. In addition, the participants were instructed on how to protect the intact skin around the injured area. Furthermore, an adequate amount of garlic was given to each subject to prepare the poultices. The participants were also reminded of local infection symptoms and were advised to contact the researchers immediately if they found any symptoms. Finally, the participants were advised to take acetaminophen if they experienced severe pain in the injured areas where the poultices were applied.

The inclusion criteria were as follows: 1) reluctance to receive injections of glucantime; 2) age range of 18 - 60 years; and 3) detection of nodular lesion(s) ≤ 30 mm in diameter over the past six months. On the other hand, the exclusion criteria were: (1) secondary infections; (2) autoimmune disorders and immunodeficiency; (3) pregnancy; (4)

allergy to garlic; (5) failure to respond to treatment; and (6) receiving treatment for CL during the study or in the past three months.

The participants were asked to follow the instructions as described below:

1. Wash the lesion area with water and soap and dry it.
2. Demarcate the area affected by induration as ordered.
3. Cover the skin surface of the area outside the demarcated site with a thick layer of Vaseline (Hana Co.).
4. Crush cloves of garlic and place them on the affected area.
5. Complete a table containing information, such as the start time of poultice application, time of first burning sensation, time of maximum burning sensation, time of blister formation, and time of blister tear opening.
6. Continue the application of garlic poultice until blisters develop and tear open.
7. Apply a layer of honey on the wound, resulting from torn blisters on a daily basis (to cover the entire surface of the wound) and bandage them until the wound dries into crust.
8. Contact one of the researchers for visits at 3, 14, 40, 70, 100, and 190 days after the date of first honey dressing application. In the first follow-up, the lesions were examined for secondary infections, and in the subsequent visits, presence or absence of lesions and recovery or recurrence (via measurement of lesions) were determined.

4. Results

A total of 23 lesions were reported in 12 patients. However, two male participants left the study due to intolerance. Finally, 10 patients with 20 lesions completed the treatment process, including five males and five females. The mean age of the participants was 36.2 years (SD, \pm 14.53), and the mean number of lesions was two, with a life span of four months (\pm 1.33).

Based on the PCR assay, *Leishmania tropica* was detected in 100% of lesions. The average area of lesions was 191.26 mm (\pm 148.01), which significantly decreased to zero on the 14th day of the intervention ($P = 0.0001$). The mean onset time of burning sensation was about 17 minutes. The average time of blister formation following the application of poultice was 522 minutes (\pm 95.565). In seven lesions (35%), blisters tended to tear open within 10 hours of continuous poultice application. In nine other lesions (45%), blisters tore open within 10 - 12 hours after applying the poultices. In the other four lesions (20%), blisters tore open within 12 to 14 hours.

None of the wounds were infected up to the end of day 14 when use of honey dressing had started. In addition,

all the wounds had dried, and crusts were either fully removed or about to be removed; after the crusts were removed, no obvious scars remained. The red skin color in the original areas disappeared within 100 days and was hardly visible at the end of day 190. In one of the lesions with an original size of 7.6 mm, a nodule with the same size reappeared in the 70-day follow-up; the direct smear and PCR results were negative for *Leishmania*. On the other hand, on day 190 of the follow-up, no cases of recurrence were reported in 19 followed-up lesions, and no visible scars were found. The demographic data of the participants, as well as the results of treatment, are presented in [Table 1](#).

5. Discussion

The dominant agent causing CL in Mashhad, capital of Khorasan Razavi Province, Iran, is *Leishmania tropica* (nearly 94%) (24). The PCR assays in our population revealed that *Leishmania tropica* was responsible for CL in 100% of cases. Pentavalent antimonials are regarded as the first-line treatment, and some studies have reported an efficacy rate of 76.5% for glucantime injections (25).

Fatima et al. revealed the preventive effects of garlic methanol extract on promastigotes of *Leishmania major* in the culture media (26). Ghazanfari et al. (27), showed that garlic could prevent the spread of parasites by activating cellular immune responses, increasing the activity of macrophages, and improving the treatment of experimental leishmaniasis in BALB/c mice owing to its direct damaging effects on parasites (27). In another study, use of garlic extracts in BALB/c mice with experimental leishmaniasis, caused by *Leishmania major*, increased the activities of Th1 and its related cytokines. Glucantime also increased the activities of Th2 and its related cytokines, while using garlic extract and glucantime simultaneously improved the activities of both Th1 and Th2 (28).

Khoshzaban et al. (29), compared the results of treatment in two groups of mice with CL, caused by *Leishmania major*. One group was treated with an ointment made of garlic extract, while the other group received both garlic extract and glucantime. After three weeks, the researchers observed the remarkable effects of garlic ointment and its significant difference from glucantime (29). Additionally, Samdani et al. (30), used garlic gel to treat 70 CL patients and observed that 81.42% of cases positively responded to treatment. Khalid et al. (31), also observed that garlic methanol extract treated 100% of CL cases.

On the other hand, two studies suggest that garlic is not effective in treating CL. In a double-blind study, Gholami et al. compared the effects of garlic cream 5% with placebo and did not observe any significant differences

Table 1. Demographic Information and Treatment Results^a

Patient's No.	Gender	Age	Duration of Disease (Mo)	Size of Lesion (mm)	Site of Lesion	Time of Initial Burning Sensation (Minutes)	Time of Maximum Burning Sensation (Minutes)	Time of Blistering (Hours)	Tear Time of Blisters (Minutes)	Results of Observations During Visits on Days Following the Start Date of Honey Dressing Application					
										3	14	40	70	100	190
1	Female	28	4	10 × 10	Forearm	10	120	8	90	N	C	C	C	C	C
				9 × 12	Leg	15	150	7:30	150	N	C	C	C	C	C
				14 × 13	Leg	20	115	8	150	N	C	C	C	C	C
2	Male	19	3	20 × 20	Forearm	21	170	9	180	N	C	C	C	C	C
				17 × 15	Abdomen	6	100	7:30	90	N	C	C	C	C	C
3	Male	35	6	7 × 6	Posterior heel	23	190	6	150	N	C	C	R	-	-
4	Male	22	4	15 × 15	Forearm	16	163	11	150	N	C	C	C	C	C
				12 × 12	Forearm	10	116	9	180	N	C	C	C	C	C
				12 × 10	Forearm	6	139	8:30	90	N	C	C	C	C	C
5	Female	40	6	20 × 19	Forearm	35	255	9	150	N	C	C	C	C	C
6	Female	22	2	17 × 19	Posterior heel	13	192	6	150	N	C	C	C	C	C
				9 × 8	Posterior heel	9	70	6	90	N	C	C	C	C	C
7	Male	55	5	15 × 17	Forearm	30	200	10	100	N	C	C	C	C	C
8	Male	59	4	21 × 18	Leg	17	220	9	150	N	C	C	C	C	C
				13 × 15	Leg	21	170	9:30	90	N	C	C	C	C	C
				12 × 15	Leg	25	196	9	90	N	C	C	C	C	C
9	Female	31	3	20 × 17	Arm	14	105	9	150	N	C	C	C	C	C
				13 × 10	Arm	14	105	10	150	N	C	C	C	C	C
				12 × 12	Forearm	14	105	10	150	N	C	C	C	C	C
10	Female	51	3	30 × 30	Forearm	20	80	12	110	N	C	C	C	C	C

^a N, no secondary infection; C, cured (no induration, wound, or lesion); R, recurrence.

(32). Similarly, Babaee Khou et al. observed that garlic tinctures 50% and 100% were not effective in treating mice with experimental CL (33). In the study by Gholami et al. (32), an inadequate amount of effective compounds might have been used in the cream.

Duration of treatment with systemic glucantime injection is 20 days, and daily dosage is about 20 mg/kg, which is associated with some potential toxicity. On the other hand, in the national plan of Iran's healthcare system, duration of treatment with intralesionally injected glucantime is eight weeks, i.e., one injection per week. In some studies, the mean duration has been reported to be six weeks (34). In this regard, in a study by Samdani et al. on the use of garlic gel, 17.54% of patients were treated after six weeks, and 70.17% were treated during eight weeks (30). In most cases, patients with urban-type CL healed without any interventions (nearly 1% within three months, 68% within 12 months, and others within three years) (35).

The findings of the present study showed that 100% of lesions were completely treated at 14 days following the application of garlic poultices (for about 11 hours). However, on day 70 of the follow-up, a lesion recurred in one of the patients; therefore, the efficacy of treatment reduced to 95% within 190 days. Although the majority of dry CL lesions heal without any interventions, only 1% is cured by itself within three months after appearance, which is negligible. In this method, the required time for curing lesions is significantly less than the time required in other methods using glucantime and garlic gel or methanol extract.

In addition, the total cost of treating each case of CL with intralesional or intramuscular glucantime is estimated at 30 to 150 dollars in Iranian health centers. However, the total cost of treatment with garlic poultices is only six dollars. The findings of our study indicated that the prepared garlic poultice could compete with glucantime in terms of efficacy, treatment duration, treatment cost, and absence of systemic side effects; therefore, garlic poultices could be used as an alternative agent.

5.1. Conclusions and Suggestions

The present results indicated the positive and rapid effects of garlic on the treatment of dry CL at low cost. The effective substances of garlic by influencing the immune system components and infection-generating factors, besides exerting anti-inflammatory effects, can result in the treatment of lesions caused by *Leishmania tropica*. Considering the scarcity of related studies, we avoided the use of garlic poultices in sensitive areas of the body, such as the face. In order to confirm the efficacy of garlic in CL treatment, randomized controlled trials are recommended with an adequate sample size.

5.2. Limitations

The researchers' inability to directly supervise the patients during poultice application and some of the patients' failure to refer for follow-ups are the main limitations of this study. Also, lack of a control group is another limitation of this study, although disease progression in the absence of treatment reduces the necessity of a control group.

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Footnote

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