



## The evaluation of herbal medicine efficacy on cutaneous leishmaniasis

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ARTICLE INFO	ABSTRACT
<p><b>Article type</b> Review article</p> <p><b>Article history</b> Received: 22 Dec 2013 Revised: 8 Jan 2014 Accepted: 15 Jan 2014</p> <p><b>Keywords</b> Cutaneous leishmaniasis Herbal medicine</p>	<p>Leishmaniasis including Cutaneous, mucocutaneous and Visceral forms of clinical syndromes is one of the important health care problem in the world specially in developing countries. Because of long time duration of treatment, being expensive, many associated side effects and eventually resisted cases to conventional therapy, enormous efforts have been performed to replace herbal and new therapeutic strategies as alternative choices.</p> <p>This review argue about reported studies have conducted by many researchers around the world since 1990 that the subject of all of them were about herbal medicine in treatment of leishmaniasis with emphasis on cutaneous leishmaniasis.</p>

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### Introduction

Leishmaniasis refers to a variety of several clinical syndromes including cutaneous, the commonest type that limited only to the skin mucocutaneous and visceral or diffuse form so called Kala-azar each disease has its typical picture in clinical manifestation (1,2).

Leishmaniasis is caused by Leishmania a protozoan intracellular parasite belonging to Trypanosomatidae family, There are

many species of leishmania that each one cause a specific type of disease. Leishmaniasis genuses are scattered in more than 80 endemic foci-countries in all seven continent (except for Australia and Antarctica remained spared area) belonging namely to old and new world. Old world refer to parts of Asia including Iran, Afghanistan, Saudi Arabia, Syria and many countries in Africa and new world

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refer to parts of South and central America like Mexico and Brazil (1,3). Cutaneous leishmaniasis affects about 1.5 million people annually around the world, Put it the 7th important health care human challenge by WHO (4).

As natural ecosystem undergoes many man-made harmful and destructive changes, the contacts between human as an accidental host and sandflies as vectors, will increase, lead to worldwide enhancement of disease rates (5). Cutaneous Leishmaniasis has a wide spectrum clinical presentation ranging from small and localized involvement as skin nodules to widespread skin and mucosal damages (3).

Visceral form of Leishmanin is a catastrophic and fatal disorder (if untreated) which impact many important organs like spleen, Liver and bone marrow and manifest as a long time fever (a cause for FUO), huge hepatosplenomegaly and pancytopenia that make the patient susceptible for additional opportunistic infections (4-6).

Leishmanin is broadcasted by phlebotomine sandflies. This female bite accumulated by promastigote form of protozoa, plays as a vector for leishmania and transmits the parasite to the man (accidental victim) or other mammalian host, in which the protozoa transform to amastigote form that arrive and live in mononuclear phagocytic cells (6).

#### ***Current therapy; advantage and disadvantages***

Pentavalent antimonials are presently first-line available treatment administered for both visceral and cutaneous Leishmaniasis since 1945. The second choice agents are amphotericin B and Pentamidine, solely apply for visceral form of course (7). Spontaneous cure almost always occur in cutaneous leishmaniasis but based its causative agent relapse frequently occur

also. Most causative agents of cutaneous leishmanin in the old world are *L. major* and *L. tropica*. The responsible organisms in new world are *L. braziliensis* and *L. mexicana* (8). Drug selection is related to the causative leishmania species. The major problems associated with conventional therapies such as high toxicity, growing rate of parasite resistance to current drugs and in some cases long time duration of treatment and resulted unwanted side effects and expensive cost of medications as well as, make them poor tolerated drugs. Thus conventional treatment of leishmania faced with many serious problems, leading in enormous efforts to develop new therapeutic strategies among them are phytotherapy, synthetic and or semisynthetic medication with botanical basis and improved pharmacological approaches including cochleates preparation which transfer drug directly into the cells through a particle-based delivery system, nanoparticles as well as transfer leishmanicidal agents that invade to intracellular parasites with least toxicity and high efficacy (9,10).

#### ***Herbal products as antileishmania agents***

To candidate a plant as a source for antileishmania medicine several different categories should be researched, among them the traditional application of that plant by native people (11) chemical constituent existing in the herb, easy availability and low toxicity are considered criteria (12). To manufacture a herbal medicine from a wild plant many processing pathways should be performed including extract preparing from different parts of a plant (leaves, bark, roots) by various solvents and then isolation and purification of the active compounds followed by fractioning of huge inactive molecules to small bioactive agents and finally assessment of bioactivity and toxicity of each fractional compound. This multi-

step approach, named bioactivity-guided fractionation is a low cost, easy and repeatable test (13,14). The yielded active component should be used against promastigote, axenic mastigote and intracellular amastigotes forms of leishmania. In vitro screening of retrieved substances against various species of *Leishmania* is preferred in primary steps rather than in vivo evaluation (15).

### **Literature review**

Leishmaniasis is a hyperendemic tropical disease for which no vaccine has been approved yet however many practical vaccines have been used in high risk persons successfully. Although cutaneous leishmaniasis cure spontaneously without any intervention but it takes a long time for complete wound healing, of course with remaining whole life scars. High universal prevalence of leishmaniasis make it a high priority For WHO as the tropical disorders programme of WHO emphasizes on investigation about traditionally used medicine for leishmaniasis as an alternative treatment (16).

Almost in all endemic foci of leishmaniasis, affected people had adopted themselves with localized available herbs and following them many researcher have conducted many studies to approve the traditionally used herbs for treating leishmaniasis and results of their investigates have reflected in published related literature in a review article published in phytomedicine in 2005, authors have investigated about 101 plants and 288 chemical compound isolated from the plants. This review summarized all published articles between years 1992-2001 (17) followed by our review in which 20 articles are explored and among them 30 plants are produced, almost all of them have therapeutic effect on cutaneous leishmaniasis. These studies are performed

around the world especially in 2 polar endemic area of leishmania, Asia, Africa (old world) and south and central America (new world). According to declare of their conductors, all of applied plants have been strongly effective against leishmania spp and surely could be candidate for more investigation as an alternative choice. A summary of the results are gathered in Table 1.

### **Conclusion**

The present study shows a range of published articles from 2003-2013 available in PubMed. Almost all of the authors claimed successful results about their investigated plants, but really, their studies were suffering many limitations which could influence on the accuracy of their obtained results. Some of included defects of these studies are described in detail as lacking of double blind cohort in all of human study, some of investigations performed in vitro only and have not in vivo performance (18-22), duration of trying drugs seems not to be enough in some of studies (19) and at last in one study the toxicity level of investigated plant was too high to apply that plant with a safe border in involved patients (25), many of published data obtained from only animal experimental model without confirming of related results on human (19,23,26).

One paper was only a case report (18) and the other one was an editorial note as if expert opinion presentation (28) which both have a low worthy. According to all documented data, Phytomedicine has provided a large and hopeful view to find new, safe and effective leishmaniacidal agents, waiting for discovering by future investigators.

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### Conflict of Interest

The authors declare no conflict of interest.

**Table 1.** Summary of plants which was used for leishmaniasis treatment

Reference number	Description	Leishmania species	Extract/Chemical compound	Family/Plant
18	Case study	ND	Leaf extract	Kalanchoe pinata
17	Stimulate parasite engulfment	L.Major	Derivative protein fraction	Allium sativum/garlic
19	Effective for both visceral and cutaneous leishmaniasis	L.Amazonensis	Essential oil	Chenopodium ambrosioides
20	Simultaneous invitro and invivo evaluation	L.Tropica	Acidified and alcoholic extract	Autaceae/haplophyllum myrtifolium
21	Native plants of Yucatan and peninsula	L.Mexicana promastigote	Leaves Bark Bark Leaves Bark Leaves Whole plant Root Whole plant Root	Aphelandra scabra Byrsonima bucidaefolin Byrsonima carassifolin Clusia flava Cupania deatata Diphysa cartagenensis Dorstenia contrajerva Millerin quinqueflava Tridax procumbens Vitex gaumeri
22	Apply for cutaneous L.	L.Donovani	Leaf extract	Alo vera
23	Apply for cutaneous L.	ND	Propolis hydroalcoholic extract	Thymus vulgaris/achillea millefolium
24	Apply for cutaneous L.	L.amazonensis	Leaf extract	Choopodium ambrosioides
25	Apply for cutaneous L.	ND	Whole plant extract	Genus jacaranda
26		L.Major	Extract	Warburgia ugandensis
27		L.Amazonensis	Essential oil	Chnopodium ambrosioides
28	Adopted from a scientific letter to edditor	All species of L.	Leaf extract	Green tea
29	Apply for cutaneous L.	L. Mexicana promastigote	Extract	Tridax prucumbens
30	Apply for cutaneous L.	L.Amazonensis	Fluroquinolines and coumarins in extract	Hellieta apiculata
31	Apply for cutaneous L.	L.Amazonensis	Synthetic analogue derivatives	Piperine
32	Apply for cutaneous L.	L.Major	Root extract	Plumbago capensis
33	Apply for cutaneous L.	L.Amazonensis	Coumarine(-)mammas A/BB isolated from leaves	Calluphyllum braziliensis
34	Apply for cutaneous L.	ND	Herbal mixture	Z-HE fresh preparation
35	Apply for cutaneous L.	L.Major	Extract	Garlic
36	Apply for cutaneous L.	L.Amazonensis	Argentilacton isolated	Annona haematantha

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