Fruit-Bearing Plant Ethnopharmaceuticals for the Treatment of Old World Cutaneous Leishmaniasis: A Systematic Review



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Introduction

- Old World Cutaneous Leishmaniasis (OWCL): a neglected parasitic disease caused by members of the genus Leishmania, passed onto humans by the bite of sandflies¹
- · Better drugs are needed due to the toxicity, accessibility limits, and expense of first-line treatment options
- **Ethnopharmaceuticals:** plant-based compounds with potential anti-leishmanial effects found in and around local endemic communities²
- Potential to overcome the aforementioned therapeutic challenges using ethnopharmaceuticals is supported by anecdotal evidence of efficacy

Objective: Aim to synthesize existing evidence around available fruit-bearing ethnopharmaceuticals to promote drug discovery for the prevention and treatment of OWCL.

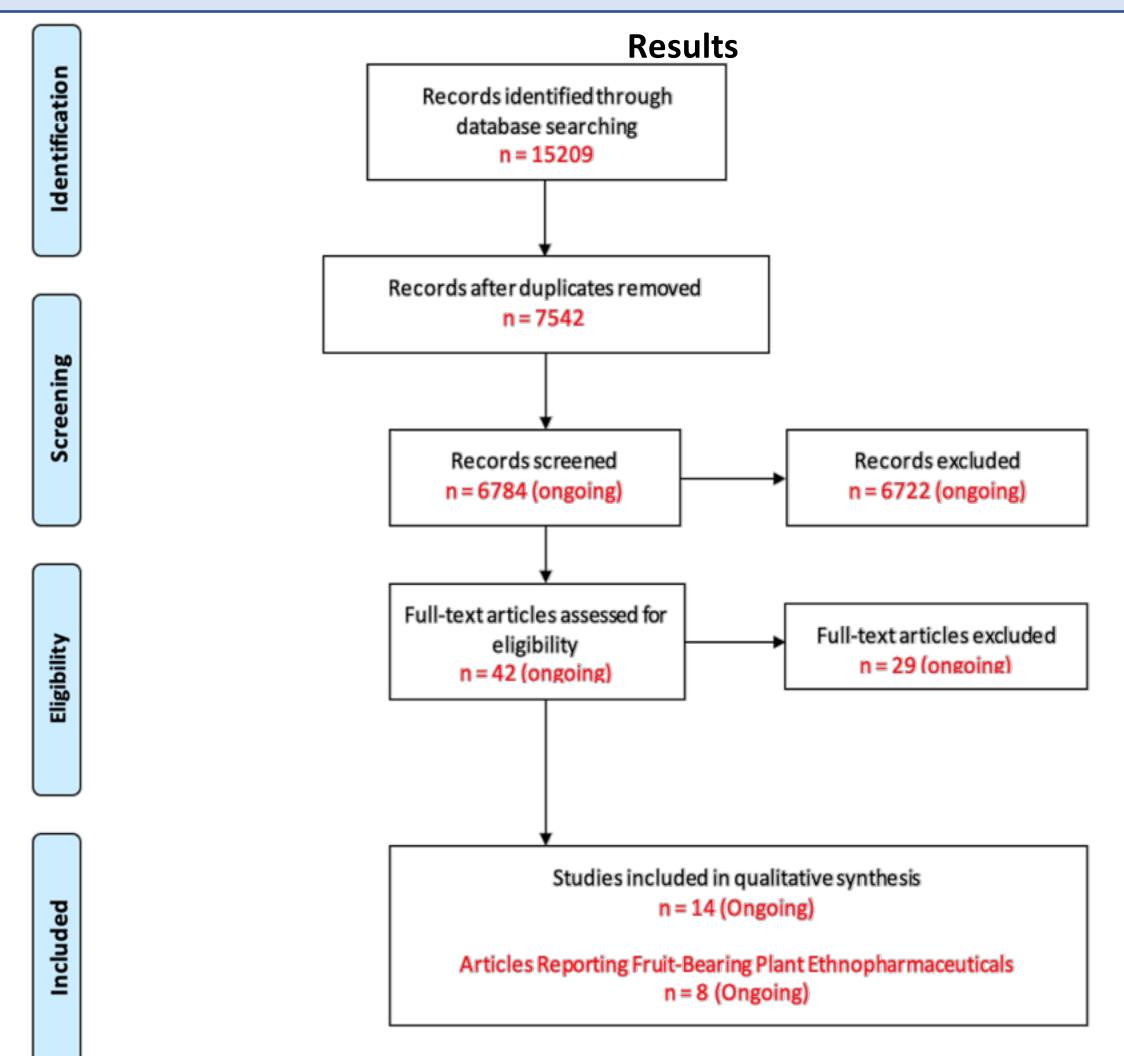


Figure 1. PRISMA Flow Diagram for studies captured in the search strategy.

Methods

- PubMed (NCBI), Medline (OVID), Embase (OVID), and Web of Science (BioSIS) were searched using combinations of the search terms and related concepts of "cutaneous leishmaniasis" and "ethnopharmaceuticals"
- Inclusion criteria: CL patient from the Old World (Africa, Asia, Europe), treated with an ethnopharmaceutical, patient outcome(s) reported after treatment
- GRADE approach used to assess the quality of studies reporting therapeutic interventions⁴
- Data were grouped and summarized by *Leishmania* spp. and plant species

Discussion & Conclusions

- 14 studies were included evaluating a number of topical applications of ethnopharmaceuticals including: *Cassia fistula*, garlic, and pepper. 8 out of the 14 pertained to fruit-bearing ethnopharmaceuticals.
- Most trials tested interventions in combination with standard therapies (e.g., Glucantime), not as stand-alone treatments.
- · Some agents (e.g., Cassia fistula, Juniperus excelsa) have shown cure rates comparable to or superior to those of conventional drugs.
- · Variability in study design, small sample sizes, and inconsistent reporting limit the certainty of evidence.
- · Adverse events were generally mild and tolerable, supporting feasibility in clinical use.
- · Highlights the potential of ethnopharmaceuticals to inform drug discovery pipelines, particularly in resource-limited settings.
- Future work requires rigorous, well-designed RCTs and testing of novel compounds identified in preclinical models.

Author, Year	Setting	Population	Design/Sample Size	Study Period	Species	Type of Fruit-Bearing Plant	Treatment/Intervention	Outcomes
Jaffary 2009	Iran	Inclusion: Confirmed CL on smears, lesions (<5 in quantity, <3cm). Exclusion: Lesions close to the eyelids, pregnant or breastfeeding mothers.	RCT; 140 Patients. Group A: 70. Group B: 70.	Not reported	Not reported	Cassia Fistula	Group A: 70% topical gel containing 2% DMSO from C. fistula 1x/day for 1-4 weeks + Glucantime (1- 2.5mL) 2x/week up to 4 weeks. Group B: placebo gel 1x/day for 1-4 weeks + Glucantime (1-2.5mL) 2x/week up to 4 weeks.	Complete recovery at week 4: Group A (28/70) Group B (25/70) (p=0.0945). Relative recovery at week 4: Group A (28/70) Group B (22/70). Complete recovery at week 12: Group A (47/70) Group B (29/70) (p<0.001. Relative recovery at week 12: Group A (20/70) Group B (21/70). Mean complete recovery time: Group A (7.9+/-0.5) Group B (8.2+/-0.4) (p=0.005). Adverse events: Group A (9), Group B (9) - Erythema and itchiness (p=0.25).
Jaffary 2014C F	Iran	Inclusion: Confirmed CL on smears, age 6-60 years old, lesions (<5 in quantity, <3cm, <12 weeks old, not near eye)	RCT; 165 Patients. Group A: 55. Group B: 55. Group C: 55.	16 weeks	Not reported	Cassia fistula	Group A: boiled extract- soaked gauze applied 1x/day up to 4 weeks. Group B: hydroalcoholic extract soaked gauze applied 1x/day up to 4 weeks. Group C: intralesional Glucantime (0.5-2mL) 2x/week up to 4 weeks.	Complete cure at 16 weeks: Group A - 22 (40%), Group B - 20 (36.4%), Group C - 36 (65.5%) (p=0.02). Adverse Events: Group A - 3 (5.5%), Group B - 2 (3.6%), Group C - 2 (3.6%) due to allergic reaction.
Jaffary 2014AM	Iran	Inclusion: Severe CL for >5 years, lesions (<5 in quantity, <5cm²)	RCT; 60 Patients. Group A: 60 Group B: 60	January 2009- Feburary 2010	Not reported	Achillea millefolium	Group A: IV Glucantime 20mg/kg/day x4 weeks + topical gel of 5% yarrow 2x/day. Group B: IV Glucantime 20mg/kg/day x4 weeks + placebo gel of 5% chlorophyll 2x/day	Complete or partial cure at 12 weeks: Group A (21/30) Group B (18/30) (p=0.0351). Adverse Event at 6 weeks: Group A (10/30) Group B (12/30) (p>0.05). Mild to moderate itching at 12 weeks: Group A (8/30) Group B (2/30) (p=0.014). Increased wound discharge: Group A (1/30).
Mozafari 2019	Iran	Inclusion: Confirmed CL on smears, lesions (>14 days old). Exclusion: Pregnant women, known adverse reactions to treatment, treatment within the last month, lesions (>3 months old, near the eyelids, nose, mouth, and eyes).	RCT; 110 Patients. Group A: 55. Group B: 55.	December 2017- June 2018	Not reported	Samacucus ebulus	Group A: 5% <i>S.ebulus</i> gel + Glucantime 2x/day up to 12 weeks. Group B: placebo gel + Glucantime 2x/day up to 12 weeks.	Duration of recovery: Group A (mean 26.64(16.24) days) Group B (mean 30.05(18.54) days) (p=0.31). Complete recovery (total epithelialization): Group A (30) Group B (29) (p=0.87). Medium recovery (>50% decrease in lesion size): Group A (8) Group B (10). Mild recovery (<50% decrease in lesion size): Group A (9) Group B (9). Failure: Group A (5) Group B (7).
Parvizi 2017	Iran	Inclusion: Confirmed CL on	Group B: 29	Not reported	Leishmania major and Leishmania infantum	Juniperus excelsa	Group A: Topical cream of 5% hydroalcoholic leaf extract 3x/day + Cryotherapy. Group B: Placebo cream 3x/daily + Cryotherapy.	Complete cure: Group A (82%) Group B (34%). Partial cure: Group A (9%) Group B (14%). Treatment failure: Group A (9%) Group B (52%). Adverse events: Group A (85%) Group B (100%).
Sattar 2012	Pakistan	Inclusion: Patients with CL, age 6-70 years old	Cohort; 40 (30M 10F)	6 weeks	Leishmania donovani	Morinda citrifolia	1% dry methanol leaf extract gel 3x/day then weekly up to 6 weeks	Excellent response: 20/40 (50%). Good response: 12/40 (30%. No response: 8/40 (20%). Adverse events: none.
Rahman 2012	Iran	Patients with CL	Cohort; 100 Patients (35 at 2 week follow- up)	Not reported	Not reported	Physalis minima	25% methanolic extract with white soft parrafin-based petroleum gel	Cure: 23/35 (65.71%) of patients showed excellent response and recovery by topical application
Zerehs az 1999	Iran	Inclusion: Confirmed CL on smears for <4 months. Exclusion: Severe CL and pregnancy.	RCT; 171 patients. Group A: 86. Group B: 85.	Not reported	Not reported	Z-HE herbal extract (Althaea rosa, Althaea officinalis, Leguminosae, Faliaceae, Malvaceae, and Lythrace)	Group A: topical Z-HE x5 days + 0.5mL saline injection x20 days. Group B: topical placebo x5 days + 15- 20mL/kg/day Glucantime x20 days.	Complete cure: Group A (74.4%) Group B (24.1%). Partial cure: Group A (11.6%) Group B (14.1%). Failure: Group A (14%) Group B (58.8%). Adverse Events: Group B had urticaria and generalize pruritis.

Table 1. Summary of findings tables for studies included in this study.

