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Introduction

- Toxicity, expense, and accessibility limit treatment success in cutaneous leishmaniasis (CL), a neglected parasitic disease caused by members of the genus *Leishmania*.¹
- Old World Cutaneous Leishmaniasis (OWCL) is widespread in the Middle East, the Mediterranean, Arabian Peninsula, Africa and the Indian Subcontinent.
- OWCL is caused due to *L. major*, *L. tropica*, *L. aethiopicus*, *L. infantum*, and *L. donovani*.
- High toxicity and ineffective treatment management of current drugs warrants the development of novel medications with better health and risk ratio
- Ethnopharmaceuticals are plant-based compounds with potential anti-leishmanial effects found in and around local endemic communities²

Objective

We aim to synthesize existing evidence around available ethnopharmaceuticals to promote drug discovery for the treatment of OWCL

Methods

- PubMed (NCBI), Medline (OVID), Embase (OVID), Web of Science (BioSIS) and LILACS (VHL) were searched from inception to October 31, 2019 using combinations of the search terms "cutaneous leishmaniasis" "ethnopharmaceuticals", "botanical", "plant derived", "curcumin", and "turmeric"
- Systematic review includes molecular, mechanistic, and observational studies, case reports, case series, cohort studies, as well as clinical trials reporting therapeutic outcomes, if possible

Results

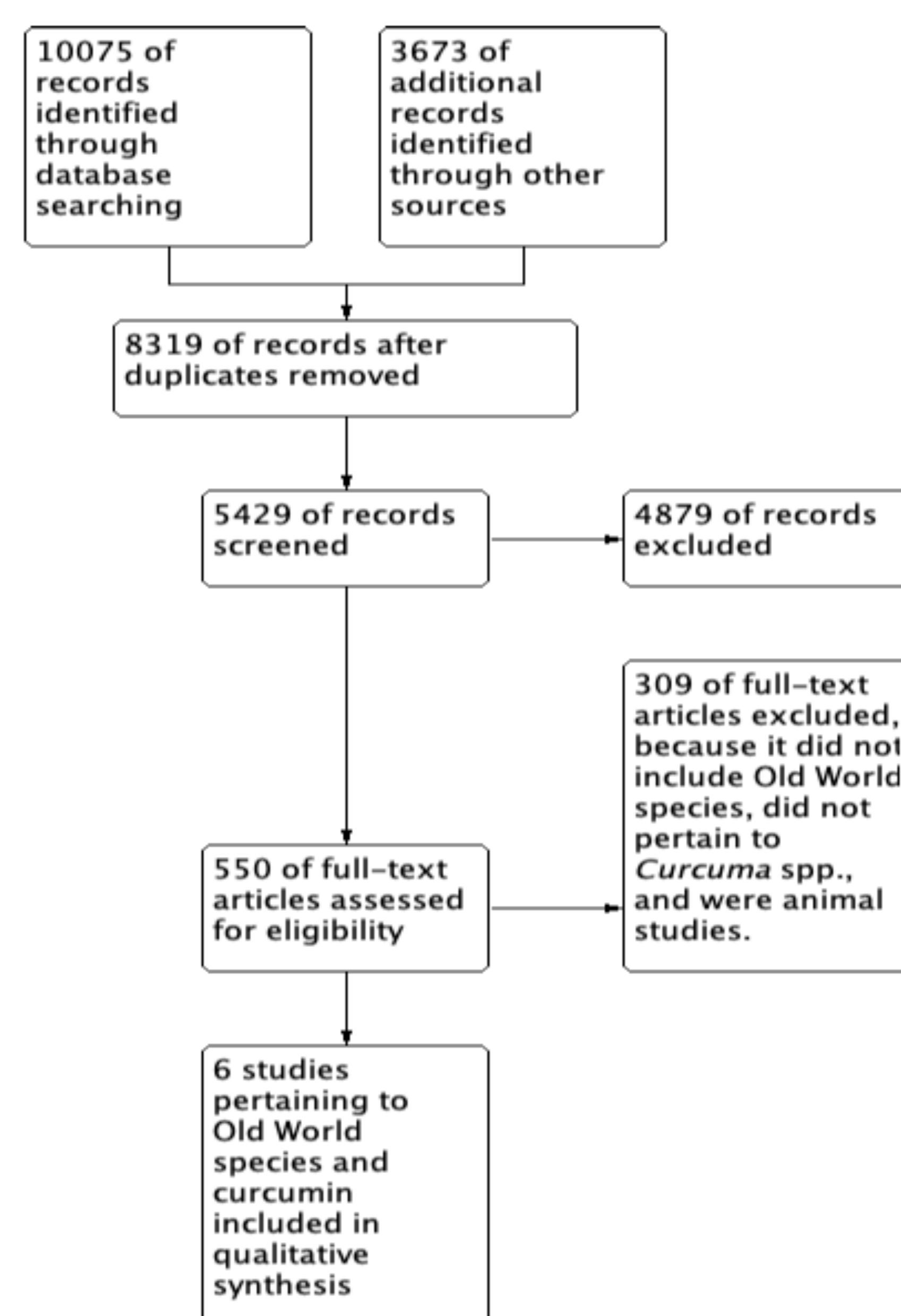


Figure 1: Workflow highlighting abstract and full-text inclusion and exclusion criteria

Old World CL species distribution in abstracts

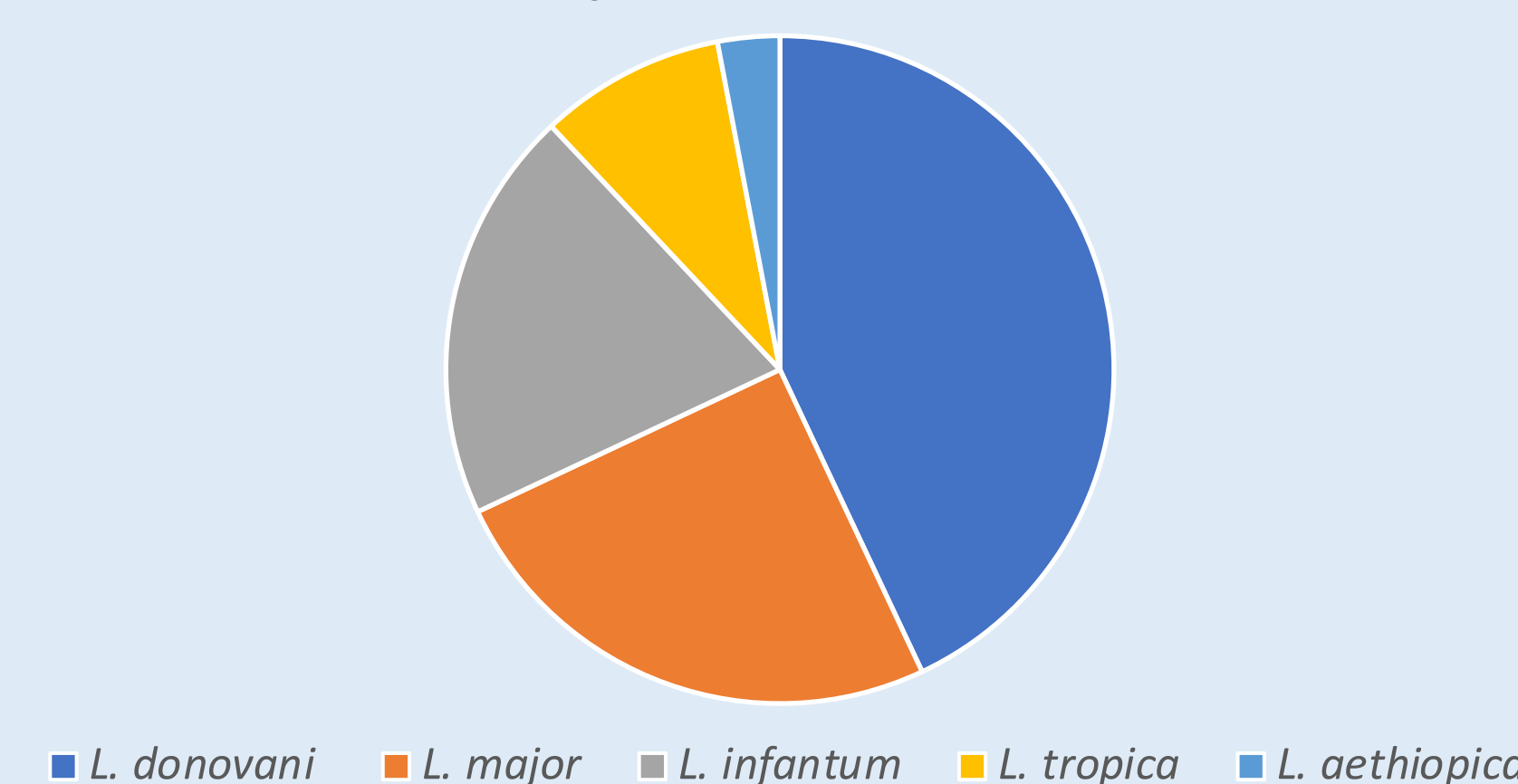


Figure 2: OWCL species distribution prevalent in abstracts

Old World CL species distribution in full-text articles

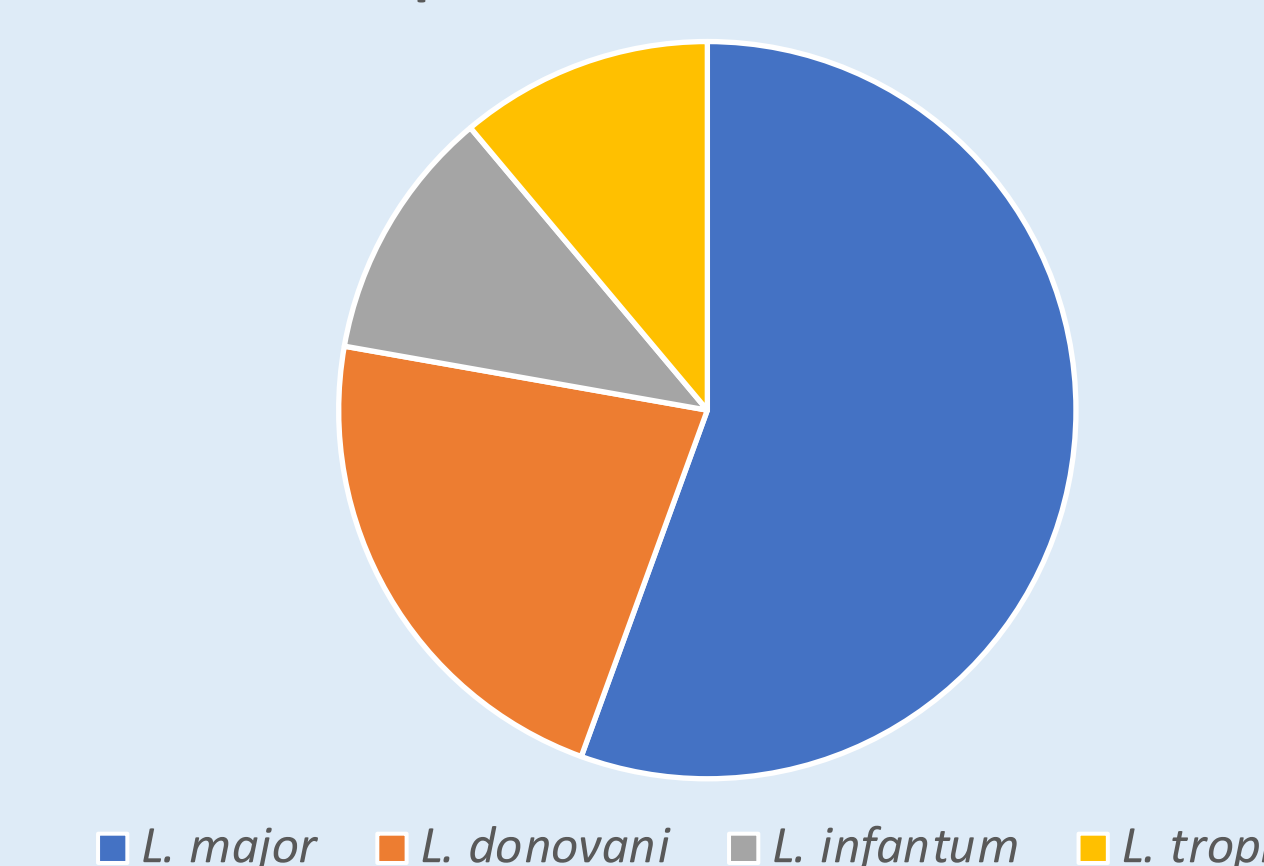


Figure 3: OWCL species distribution prevalent in full-text articles pertaining to "curcumin" or "turmeric"

Table 1: Antileishmanial activity of Curcumin compounds against OWCL in vitro

Study reference	Preparation/ concentration	OWCL species	Main outcome
Salheen et al., 2002	Serial dilutions of drugs (curcumin and pentamidine) in culture medium of <i>L. major</i> (100ml/well)	Promastigotes: <i>L. tropica</i> , <i>L. infantum</i> , <i>L. major</i>	The leishmanicidal effects of curcumin compared with pentamidine show curcumin has a higher potency in vitro at 13.5 mM
Koide et al., 2002	Various concentrations of curcumin dissolved in dimethyl sulfoxide (DMSO) was added in each well and incubated at 27°C. The leishmanicidal activity of curcumin was shown as 50% growth inhibitory (GI ₅₀), 100% growth inhibitory concentration (TGI) and LD ₅₀ after incubation with leishmania for 24h.	Promastigotes: <i>L. major</i>	Curcumin demonstrated leishmanicidal activity in a concentration dependent manner
Man-Ying Chan et al., 2005	20mM (stock solution) added at different concentrations to the cultures	Promastigotes: <i>L. major</i> , <i>L. donovani</i>	At a range from 5 mM to 15 mM, curcumin did not affect the growth of promastigotes of <i>L. major</i> Curcumin concentrations at up to 15 mM also did not affect the growth of <i>L. donovani</i>
Changtam et al., 2010	Curcumin, demethoxycurcumin, and bisdemethoxycurcumin were chemically modified to 46 analogs and 8 pairs of 1:1 mixture of curcuminoid analogs	Promastigotes: <i>L. major</i>	Parent and analog curcuminoids were assessed against Leishmania Among the active analogs, 4 compounds demonstrated EC50 values of less than 5mm against <i>L. major</i> promastigotes
Fouladvand et al., 2013	Curcumin, gallium curcumin, indium curcumin, and diacetylcurcumin vs. amphotericin B	Promastigotes: <i>L. major</i>	Indium curcumin was the most effective than others, followed by gallium curcumin, and lastly diacetylcurcumin 5µg/ml for all, IC50: 38,32,52, and 20 µg/ml respectively
Cheikh-Ali et al., 2015	squalenoyl conjugates + curcumin (squalenoylcurcumins) vs. only curcumin	Promastigotes: <i>L. donovani</i>	Squalenoylcurcumins was more effective than only curcumin in <i>L. donovani</i> promastigotes

Results

- 2320 abstracts were found using the GRADE approach from 1957-present. Of the 260 abstracts pertaining to Old World, *Curcuma* spp. "Turmeric" was identified in 6 articles (2%), to date (Figure 1)
- 551 abstracts met inclusion criteria for full-text review, of which, 260 (47%) abstracts pertained to Old World species, and 113/ 260 (21%) were specific to *L. donovani*, followed by *L. major* (66, 25%), *L. infantum* (53, 20%), *L. tropica* (24, 9%), and *L. aethiopicus* (4, 2%) (Figure 1 & 2).
- In the 6 full-text articles, 4 Old World CL species were prevalent: *L. major* (5, 83%), *L. donovani* (2, 33%), *L. tropica* (1, 17%), and *L. infantum* (1, 17%) (Figure 3)
- Two, in-vitro studies to date have compared the effects of curcumin against standardized treatments (pentamidine and amphotericin B) in which, curcumin, in higher concentrations, yielded greater potency than the control (Table 1)

Conclusion

- Synthesizing the current evidence surrounding ethnopharmaceuticals for the treatment of OWCL may contribute to drug discovery pipelines and potentially lead to novel therapeutics in a field that has not seen any new drug development for over half a century.

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