The Potential of Traditional Knowledge to Develop Effective Medicines for the Treatment of Leishmaniasis

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Leishmaniasis is a neglected tropical disease that affects people living in tropical and subtropical areas of the world. There are few therapeutic options for treating this infectious disease, and available drugs induce severe side effects in patients. Different communities have limited access to hospital facilities, as well as classical treatment of leishmaniasis; therefore, they use local natural products as alternative medicines to treat this infectious disease. The present work performed a bibliographic survey worldwide to record plants used by traditional communities to treat leishmaniasis, as well as the uses and peculiarities associated with each plant, which can guide future studies regarding the characterization of new drugs to treat leishmaniasis. A bibliographic survey performed in the PubMed and Scopus databases retrieved 294 articles related to traditional knowledge, medicinal plants and leishmaniasis; however, only 20 were selected based on the traditional use of plants to treat leishmaniasis. Considering such studies, 378 quotes referring to 292 plants (216 species and 76 genera) that have been used to treat leishmaniasis were recorded, which could be grouped into 89 different families. A broad discussion has been presented regarding the most frequent families, including Fabaceae (27 quotes), Araceae (23), Solanaceae and Asteraceae (22 each). Among the available data in the 378 quotes, it was observed that the parts of the plants most frequently used in local medicine were leaves (42.3% of recipes), applied topically (74.6%) and fresh poultices (17.2%). The contribution of Latin America to studies enrolling ethnopharmacological indications to treat leishmaniasis was evident. Of the 292 plants registered, 79 were tested against Leishmania sp. Future studies on leishmanicidal activity could be guided by the 292 plants presented in this study, mainly the five species Carica papaya L. (Caricaceae), Cedrela odorata L. (Meliaceae), Copaíba paupera (Herzog) Dwyer (Fabaceae), Musa × paradisiaca L. (Muscaceae), and Nicotiana tabacum L. (Solanaceae), since they are the most frequently cited in articles and by traditional communities.

Keywords: ethnopharmacology, traditional knowledge, natural drugs, leishmaniasis, medicinal plants, neglected disease

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INTRODUCTION

The use of plants based on existing empirical knowledge, consecrated by continuous use in traditional communities, directs research, saves time and money in pharmacological and phytochemical studies (Mukherjee et al., 2017). The selection of plants for research and production of drugs, based on claims made by traditional communities regarding a given therapeutic effect in humans, can be a valuable shortcut for the discovery of new active molecules (Súntar, 2020) and to provide, from the academic point of view, evidence for the use of plants as medicines.

Some interesting examples of drugs extracted from plants used in traditional knowledge are (i) alpha humulene from Varronia curassavica (Jacq.), which has been used as a topical anti-inflammatory agent (Marques et al., 2019); (ii) quinine, which was purified from Cinchona sp. and has antimalarial activity (Boratyński et al., 2019); (iii) galegine from Galega officinalis L., which was used as a molecular prototype to synthesize the antidiabetic drug metformin (Bailey, 2017); (iv) morphine and codeine, as hypnoanalgesics, both extracted from Papaver somniferum (Stefano et al., 2017); (v) taxol, an antitumour agent extracted from Taxus brevifolia Nutt. (Yang and Horwitz, 2017); (vi) vimblastine, an antineoplastic agent, from Catharanthus roseus (L.) G. Don (Haque et al., 2018); and (vii) digoxin, purified from Digitalis lanata Ehrl. that displays cardiotonic effect (Patocka et al., 2020), among other examples.

Considering that ethnopharmacological studies have guided the characterization of biologically active molecules and drugs for different diseases, it is evident that this science can contribute to the search for active substances to treat neglected diseases, such as leishmaniasis, an infectious disease caused by parasitic protozoa of the genus Leishmania, endemic in tropical and subtropical countries. This neglected infectious disease is transmitted during the blood meal of sandflies of the genera Lutzomyia and Phlebotomus (Francesquini et al., 2014; Courtenay et al., 2017).

Leishmaniasis has a wide variety of clinical manifestations, from cutaneous to visceral forms (Burza et al., 2018). In cutaneous leishmaniasis (CL), the parasite infects phagocytic cells (mainly macrophages) in the skin tissue. This clinical form is characterized by skin lesions that can be single, multiple or diffuse throughout the body (Gabriel et al., 2019). Some patients have lesions in the mucous membranes, mainly in the upper airways; such injuries can occur years after the resolution of skin lesions (Kevric et al., 2015). Visceral leishmaniasis (VL) is a zoonosis of chronic evolution with systemic involvement. In this clinical form, the parasite migrates to the viscera and infects macrophages in the spleen, liver, lymph nodes, and bone marrow. Typical manifestations are chronic fever, weight loss and hepatosplenomegaly, which can lead to patient death if not properly treated (Hermida et al., 2018). These clinical changes progress along with physiological and histological modifications mainly in the spleen, liver, and bone marrow (Faleiro et al., 2014).

According to the World Health Organization, it is estimated that 50,000 to 90,000 new cases of VL and between 600,000 and one million new cases of CL occur annually. The growth in the number of cases in recent decades has been associated with environmental changes, such as deforestation, irrigation schemes, building dams and urbanization (World Health Organization, 2019). Despite these epidemiological data and the fact that there are different species of parasites occurring in 98 countries, the treatment of this important infectious disease has serious limitations and is based on few drugs, such as pentavalent antimonials, amphotericin B and miltefosine (Passero et al., 2018). Additionally, these drugs induce severe side effects in humans, and in some situations, as is the case of liposomal amphotericin B, high costs limit their use in low-income countries. Furthermore, some species of parasites have become resistant to drugs (Ghorbani and Farhoudi, 2017; Ponte-Sucre et al., 2017).

Considering the epidemiology of leishmaniasis, the scarcity of treatment and the severe side effects of drugs currently used it becomes urgent to find new molecules with leishmanicidal activity. The secondary metabolism of plants offers a panel of molecules with important pharmacological activity, and in leishmaniasis, a series of molecules has already been described with leishmanicidal potential (Passero et al., 2014; Jesus et al., 2017). In this regard, it has been observed that some studies have used the information available in published works about traditional knowledge to select plants, purify bioactive molecules and perform in vitro studies; however, only a few works have investigated the natural resources that traditional communities use to treat leishmaniasis and molecules in vitro and in vivo models.

Thus, this review intends to investigate, through a bibliographic survey, information about medicinal plants indicated by traditional communities that are employed in the treatment of leishmaniasis, as well as their uses and peculiarities, guiding future studies on the characterization of new compounds with leishmanicidal activity.

BIBLIOGRAPHIC SURVEY

To verify the existence of scientific studies about plants used by traditional communities to treat leishmaniasis, a bibliographic survey was carried out. For this purpose, a Boolean search was performed in the Scopus and PubMed databases. It was performed from May to June 2020, and the combination of words was used to expand the possibility of finding data that would meet the expectations of the present study: "(ethnomedicine OR ethnopharmac* OR ethnobotanic* OR "traditional knowledge") AND (plant OR vegetal) AND (leishmani* OR antileishmiani*)".

The searches in the PubMed and Scopus databases retrieved a total of 238 and 161 articles, respectively. Additionally, it was observed that 105 articles were common to both databases; therefore, a total of 294 articles were analysed herein. The following exclusion criteria were used in this review: 1) review articles; 2) articles that did not clearly mention the genera or species of studied plants; and 3) articles that demonstrated leishmanicidal activity of plants without having carried out an
ethnopharmacological study. The following inclusion criteria were used: 1) original articles from any year, referring to any country; 2) articles that contained clear information about the collection of ethnopharmacological data, except for the literature review; and 3) articles in English, Spanish, Portuguese and French. By considering all of these items, 20 articles were selected and analysed.

Plants with identification up to the genus level were included in the present survey, as they represent approximately 20.4% of the total indications. Species indicated with "cf"—whose taxonomic identification could not be confirmed—were also included in the present survey. In addition, all species underwent a review of their correct spelling and current taxonomic classification on the website Plants of the World online: http://www.plantsoftheworldonline.org. The following species: Anthurium myyemense Croat, Trema integerrima (Beurl.) Standl., Inga bourgionii (Aubl.) DC., Meteoridion sp., and Citrus aurantiaca (L.) Swingle, were not found in this website, but data about them were available in the website of TROPICOS: https://www.tropicos.org/home. Species with divergent scientific names in articles and on the website were synonymous, and thus, they were recorded only once. Considering the data found in the selected articles, Tables 1 and 2 and Figures 1 and 2 were included.

Table 1 summarizes the findings observed in the ethnopharmacological surveys and contains the following data: family, scientific and vernacular names, traditional recipe (part of plant used and route), country (traditional community involved in the knowledge), traditional use (emic term, the one used by the communities), and whether the study included laboratory assays to determine the efficacy of plant extracts on Leishmania sp.

The map (Figure 2) was prepared using the software QGIS (available at www.qgis.org) using a collection of spatial data from the Brazilian Institute of Geography and Statistics (available at https://mapas.ibge.gov.br/bases-e-referencial/bases-cartograficas/digital meshes) and using the geographic coordinates reference system “sirgas 200” (Geocentric Reference System for the Americas).

PLANTS RECOMMENDED FOR THE TREATMENT OF LEISHMANIASIS BY TRADITIONAL COMMUNITIES WORLDWIDE

Plants (species, families and vernacular names)

From the 20 selected articles, 378 quotes were obtained referring to 292 plants indicated by several traditional communities around the world to treat leishmaniasis. These plants belong to 89 taxonomic families (Table 1). To record the number of plants, each species and genus was counted as a single citation; for example, in the case of the genus Gurania sp. Although it was cited two times in the articles, it was considered one species because it was not possible to classify Gurania sp. as one or two species. Additionally, it is not possible to know if these two examples of the genus Gurania belong to Gurania lobate (L.) Pruski—as illustrated in Table 1 - because taxonomic elements were not available in the articles. Thus, the 292 plants presented herein refer to 216 species (identified until the species level) and 76 genera (the ones counted only once) (Table 1). Only 74% of the plants available in the articles could be identified to the species level, pointing out the need for more adequate ethnopharmacology methods during fieldwork.

Considering those 378 plant quotes, the most frequent families used by traditional communities were Fabaceae (27 quotes); Araceae (23); Asteraceae and Solanaceae (22 each), Euphorbiaceae (21) and Rubiaceae (20) (Figure 1).

Moreover, 207 out 292 plants had their vernacular names (Table 1) described in the publications. The absence of these data makes ethnopharmacological analysis precarious, since recording the vernacular name of a certain plant can provide valuable information about its potential pharmacological effects. An example discussed by us in a previous work is the plant caprankohireho (Euphorbiaceae), which has been used by the Brazilian Krahó Indians as a tranquilizer, and the literal translation of caprankohireho is the ‘leaf of turtle spine’. This translation describes the pharmacological effect of this plant—which induces ‘slowness’ (Rodrigues and Barnes, 2013). This and many other examples demonstrate that the careful recording of vernacular names of plants during ethnopharmacological studies is extremely relevant to increase the probability of finding bioactive molecules according to the knowledge of traditional communities.

In addition, from the 216 plants described up to the species level, only 29 were present in at least two articles; six out 29 species were described in three articles: Brunfelsia grandi flora D. Don (Solanaceae), Capirona decorticans Spruce (Rubiaceae), Chelonanthus alatus (Aubl.) Pulle (Gentianaceae), Hura crepitans L. (Euphorbiaceae), Nicotiana tabacum L. (Solanaceae), Tabernaemontana sananho Ruiz & Pav. (Apocynaceae), while the following four species were cited in four articles: Carica papaya L. (Caricaceae), Cedrela odorata L. (Meliaceae), Copaifera paupera (Herzog) Dwyer (Fabaceae), and Musa × paradisiaca L. (Musaceae) (Table 1).

In Table 1, it was also observed that most of the species were cited by traditional communities from only one country, 26 species were cited by at least two countries. Three of them belonged to the traditional communities of Peru, Ecuador, and French Guiana simultaneously: Carica papaya L. (Caricaceae), Musa × paradisiaca L. (Musaceae), and Nicotiana tabacum L. (Solanaceae).

Recipes (parts of the plants used, method of preparation, route of administration)

As registered in Table 1, not all ethnopharmacological studies gave information on the parts of the plants used, the form of preparation, route of administration, dose, and/or duration of the treatment. Considering the 378 quotes, only 138 (36.5%) specified the recipes, 351 (92.9%) mentioned the plant parts used in the recipe, and 300 (79.4%) detailed the routes of administration of the recipes. The absence of these data offers two possible justifications. The first possible explanation may be the lack of adequate methods during ethnopharmacological fieldwork;
although this may be less likely, such works may reflect the lack of knowledge of these data on the part of the communities under study. The absence of these data can impact further studies on phytochemistry and pharmacology and, as a consequence, the discovery of new bioactive molecules of medicinal plants. On the other hand, several ethnopharmacological studies described in great detail the recipes used in the treatment of leishmaniasis. An example is the study conducted by Vásquez-Ocmín and collaborators (Vásquez-Ocmín et al., 2018), which described the use of the plant *Virola surinamensis* (Rol. ex Rottb.) Warb. (Myristicaceae), whose popular name is Cumula Colorada (Table 1). The bark was used as described by the interviewee during the field work “... Boiled 5 g of the bark in 1 L of water. Drink one cup every morning for three days ...”. In other words, all necessary information was offered in detail, except for possible contraindications and adverse events of the plant.

Among the available data in the 378 quotes, it was observed that the parts of the plants most frequently used in local medicine were leaves (42.3% of recipes), followed by bark (15%), stems (11.6%), and roots (5.6%). On the other hand, the fruits, aerial parts, flowers, oleoresins, seeds, tubers, whole plants, stalks, shoots, saps, resin, rhizomes, apical meristems, bulbs, cloves, exudates and latex were used at minor frequencies. The most suitable route of administration for plants was the topical route (74.6% of the recipes), followed by the oral route (5%) and inhalation/nasal route (1.3%); for a large number of plants, no route of administration was indicated (20.6%).

In addition, as shown in Table 1, 17.2% of the methods used to prepare the recipes refer to fresh poliches (lotion juice in natura, crushed, crude parts, paste) applied on the affected area, named fresh-po in Table 1, followed by pow-po (6.3%), which are powered plants that are also applied on the wounds. Finally, with minor frequencies, other methods were mentioned, such as decoction and infusion that can be ingested and/or used to wash the affected area. In these last cases, they were presented in Table 1 as inf-po (infusion used as a poltice) and dec-po (decoction used as a poltice).

In the selected studies, a predominance of leaves (42.3%) used topically (74.6%) for the treatment of leishmaniasis was observed. Several studies, including those carried out by some members of our team, point out the use of leaves and the topical route in traditional treatments for leishmaniasis. Thus, the quilombolas in the Pantanal from Poconé, Brazil, use a decoction-type tea with the leaf/bark of mangava-brava—*Lafoensia pacari* A. St.-Hil. (Lythraceae), combined twice a day; the juice from the leaves of mastruz, *Disphania ambrosiodes* (L.) Mosyakin & Clemants (Amaranthaceae), is used as a compress to treat leishmaniasis; finally, the river dwellers from Amazon, Brazil, use the bark of mango, *Mangifera indica* L. (Anacardiaceae), as a compress directly on the cutaneous lesions (Rodrigues, 2006).

### Knowledge of traditional communities in the world

The analysed works showed that traditional communities spread across seven countries use plants for the treatment of leishmaniasis. The majority of these communities are located in Latin America. Ecuador is the most representative of the range of plants indicated in the treatment of leishmaniasis (59 botanical families; 145 plant species; seven traditional communities; two articles), followed by Peru (39; 80; 8; 7), French Guiana (22; 34; 2; 1), Bolivia (15; 20; 7; 4) and Colombia (14; 16; 2; 2). In addition to these countries, studies developed in Saudi Arabia (8; 8; 1; 1) and Ethiopia (6; 6; 2; 3) (Figure 2) also highlighted the use of medicinal plants in the treatment of leishmaniasis.

Brazil and Colombia are countries with a high occurrence of cases of cutaneous leishmaniasis, above five thousand. However, the data collected show few or no published studies involving the use of traditional knowledge for the treatment of this infectious disease, with only two studies found in Colombia and none in Brazil. Although during this review it was not possible to obtain Brazilian studies focusing on “ethnopharmacology x leishmaniasis”, some studies within the scope of ethnopharmacology have offered information on the use of natural resources for the treatment of leishmaniasis (França et al., 1996; Rodrigues, 2006; Santos et al., 2019), but they were not included in this review, as they were not found during the Boolean search.

Figure 2 (a) highlights in yellow the endemic countries that had more than five thousand cases of cutaneous leishmaniasis until 2018 (World Health Organization, 2019). In part (b) of Figure 2, emphasis was given to the numbers of botanical families and species, articles, and traditional communities that contributed to ethnopharmacological research in each of the countries of Latin America, since these were the most expressive when considering the data on traditional knowledge vs. leishmaniasis.

The data on the traditional communities that participated in the studies analyzed herein exhibited the relevant contribution of traditional knowledge from South America in the treatment of leishmaniasis, and this is correlated with the continent that displays the highest number of cases of cutaneous leishmaniasis in the world, suggesting that in some areas, alternative medicines are not available, and people need to use alternative medicines. Figure 2 shows the amount of data associated with the traditional treatment of leishmaniasis generated by traditional communities in countries with a high incidence of leishmaniasis. Of all countries with cases of cutaneous leishmaniasis, only 40% also presented ethnopharmacological studies on the disease. Among them, the country that presented the most studies was Peru (7 studies), followed by Bolivia (4). Both are low-income countries, with deficiencies in their economic and educational systems. The main traditional communities cited among the analyzed articles belong to the following ethnic groups from Ecuador: Kichwa of Amazonia, Kichwa of the Andes, Chachi, Mestizo, Afroecuadorian, Awa and Êpera (contributeing 38.3% of the citations of plants to treat leishmaniasis), followed by Peruvian ethnic groups Chayahuita (22.7%), Wayápi of French Guiana (7.6%) and Yanesha of Peru (5.5%). In addition, 12.9% of the citations did not mention the community that provided traditional knowledge, and some of the authors referred to them as local people or ethnic groups. In relation to the total number of studies analyzed, two out seven countries (Ethiopia and Saudi Arabia) had no record of the occurrence of cutaneous...
TABLE 1 | The 378 plant quotes obtained from the 20 publications, their families, species/genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|----------------------------------------|---------|----------------|----------------------------------------|---------------------------------|---------------------------|-----------------------------------|------------|
| Acanthaceae (4 quotes and 4 species)   | Fittonia sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Hygrophila costata Nees | Chupador | (ae, to) | Colombia (Afro-Colombian and indigenous groups) | $$^r_La +$$ | $$^r_Lb +$$ $$^r_Li +$$ $$^a_Lp +$$ | Weniger et al. (2001) |
| Amaranthaceae (6 quotes and 5 species) | Hygrophila sp. | - | (wp, to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Alternanthera sp | Sangorache | (le) | Ecuador # | - | - | Gachet et al. (2010) |
|                                       | Amaranthus caudatus L. | Sangorache | (le) | Ecuador | Outaneous leishmaniasis | - | Weigel et al. (1994) |
|                                       | Chenopodium murale (L.) S. Fuentes, Uotila & Borsch | A’Tra | Fresh-po (ap, to) | Saudi Arabia | - | - | Ali et al. (2017) |
|                                       | Dysphania ambrosioides (L.) Mosyakin & Clemants (2 quotes) | Paico | (sho) | Peru # | Uta | $$^f_{Lm}$$ IC_{50} > 100 μg/ml | Kwist et al. (2006) |
|                                       | Iresine diffusa Humb. & Bonpl. ex Willd. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Anamalidaceae (4 quotes and 4 species) | Allium cepa L. | Cebolla Paitena | (le/sta) | Ecuador | Outaneous leishmaniasis | - | Weigel et al. (1994) |
|                                       | Allium sativum L. | Ajo | (c) | Ecuador | Outaneous leishmaniasis | - | Weigel et al. (1994) |
|                                       | Crinum sp. | - | (ro, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Scadoxus multiflorus (Martyn) Raf. | Dem Astefi | po (ro, to) | - | Ethiopia | ‘Gurtb’ leishmaniasis | - | de la Torre et al. (2021) |
| Anacardiaceae (6 quotes and 3 species) | Mangifera indica L. (2 quotes) | Mango | (c) | Peru# | Uta | $$^f_{Lm}$$ IC_{50} > 100 μg/ml | Kwist et al. (2006) |
|                                       | Spondias mombin L. (2 quotes) | Ubos | dec (ba, to/or) | Peru (Chayahuita) | Uta | $$^f_{Ls}$$ > 100 μg/ml | Esteevez et al. (2007) |
|                                       | Spondias purpurea L. | - | (c) | Peru# | Uta | $$^f_{Lm}$$ - NA | Kwist et al. (2006) |
|                                       | Annona obtata Aubl. | Iwitay | po (ba, to) | Peru | Uta | $$^f_{Lm}$$ - NA | Gachet et al. (2010) |
| Annonaceae (2 quotes and 2 species)    | Cremastosperma longicuspe R.E.Fr. | Maya Schult | Pow-po (ba, to) | Peru (Chayahuita) | - | $$^a_La$$ > 100 μg/ml | Odone et al. (2011a) |
| Apocynaceae (9 quotes and 7 species)   | Aspidosperma excelsum Benth. | Remo Caspi (De Baja) | po (st/ba, to) | Peru (Chayahuita) | - | $$^a_La$$ > 100 μg/ml | Odone et al. (2009) |
|                                       | Aspidosperma rigidiun Rusby | Gabetillo | (co) | Peru | Uta | $$^f_{Lm}$$ - NA | Kwait et al. (2006) |
|                                       | Himanthus articulatus (Vahl) Woodson | Compunhuan | po (ba, to) | Peru (Chayahuita) | - | - | Hajdu and Hohmann, (2012) |
|                                       | Tabernaemontana flavicans Roem. & Schult. | Shinanpi | Pow-po (ba, to) | Peru (Chayahuita) | - | - | Odone et al. (2009) |
|                                       | Tabernaemontana sananho Ruiz & Pav. (3 quotes) | Shinambik | Fresh-po (ro, to) | Peru (Chayahuita) | Uta | $$^f_{Lm}$$ = 9 μg/ml | Esteevez et al. (2007) |
|                                       | - | - | (ba, to) | Ecuador# | - | - | Gachet et al. (2010) |

(Continued on following page)
The 378 plant quotes obtained from the 20 publications, their families, species/genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|-------------------------------|-----------------------------|-----------------------------------|-------------|
| Araceae (23 quotes and 16 species)    | Anthurium muyunense Croat. | Shinanp | pow-po (ba, to) | Peru (Chayahuita) | - | - | Gachet et al. (2010) |
|                                       | Anthurium sp. | Radie Capiaye | po (lt, to) | French Guiana | Leishmaniasis | - | Odonne et al. (2009) |
|                                       | Tabernaemontana sp. | Lobo sanango | (Ro) | Peru | - | - | Odonne et al. (2011a) |
|                                       | Caladium bicolor (Alton) Vent. | Ahtata’Ta | po, (ro, to) | Peru (Chayahuita) | Uta | - | Odonne et al. (2009) |
|                                       | Caladium pictatum K.Koch & C.D.Bouché. | Io Ata’ | po, (tu, to) | Ta’Ta’ | - | - | Odonne et al. (2009) |
|                                       | Colocasia esculenta (L.) Schott. | Patiquina, Hoja Blanca | Inf-po (st, to) | Peru | Uta | - | Gachet et al. (2010) |
|                                       | Dieffenbachia seguine (Jacq.) Schott | Corech | dec-po (wp/le, to) | Peru (Yanesha) | Uta De Agua, Marenets | - | Vásquez-Ocmín et al. (2018) |
|                                       | Dieffenbachia seguine (Jacq.) Schott | Mata Boro | po (st/ba, to) | - | - | - | Hajdu and Hohmann, (2012) |
|                                       | Dieffenbachia seguine (Jacq.) Schott | Pataquina | (le) | Peru (Chayahuata) | Uta | - | Odonne et al. (2009) |
|                                       | Dracontium spruceanum (Schott) G.H.Zhu. | Jergón Sacha, Hierba Del Jergón, Fer De Lance | pow-po (tu, to) | Peru | Uta | - | Vásquez-Ocmín et al. (2018) |
|                                       | Philodendron surinamense (Miq.) Engl. | Huambe | "Drunk In Small Quantities Three Times Daily" dec (ro, or) (le, to) | Peru (Chayahuita) | Uta | - | Estvez et al. (2007) |
|                                       | Philodendron sp. (3 quotes) | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
|                                       | Pistia stratiotes L. | Puto puto | (le) | Peru | Uta | - | Kivist et al. (2006) |
|                                       | Rhodospatha sp. | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
|                                       | Stenospermation sp. (2 quotes) | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
|                                       | Thaumatophyllum solimoensesense (A.C.Sm.) Sakur., Caizan & Mayo. | Huambe | "Drunk In Small Quantities Three Times Daily" dec (ro, or) (le, to) | Peru (Chayahuata) | Uta | - | Estvez et al. (2007) |
|                                       | Xanthosoma sp. | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|-------------------------------------|---------|----------------|--------------------------------------|--------------------------------|---------------------------|-----------------------------------|------------|
| Arecaceae (1 quote and 1 species)   | Euterpe oleracea Mart. | Wasey | fresh-po (am/vr, to) | French Guiana | Leishmaniasis | - | Gachet et al. (2010) |
| Aspleniaceae – Pteridophyta (1 quote and 1 species) | Thelypteris sp. | - | fresh-po (le, to) | Ecuador # | - | - | Gachet et al. (2010) |
| Asteraceae (22 quotes and 20 species) | Achillea arabica Kotschyi. | Aldefera | fresh-po (ap, to) | Saudi Arabia | Leishmania | - | Gachet et al. (2010) |
| | Acmeilia brachyglossa Cass. | - | fresh-po (le, to) | Ecuador # | - | - | Alì et al. (2017) |
| | Adenostemma brasiliannum Cass. | - | fresh-po (lt, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Baccharis sagittalis (less.) DC. | Charara | (wp/le, to) | Bolivia (Kecha) | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | Fournet et al. (1994) |
| | Bidens pilosa L. | - | (se, to) | Ecuador # | - | - | Gachet et al. (2010) |
| | Cibaedium cf. microcephalum S.F.Blake. | - | (le/st, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Egeron sp. | - | (wp, to) | Peru (Yanesha) | Lita De Agua, Marefets | - | Weigel et al. (1994) |
| | Elefantoptus mollis Kunth. | - | fresh-po (le, to) | Peru (Yanesha) | - | - | Gachet et al. (2010) |
| | Egeron bonanensis L. | - | (le, to) | Ecuador | Cutaneous leishmaniasis | - | Gachet et al. (2010) |
| | Eupatorium sp. | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Matricaria chamomilla L. | Manzanilla | (fl.) | Ecuador | - | - | Gachet et al. (2010) |
| | Mikania sp. | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Murraya hastifolia (Poepp.) H. Rob. & Brettell. (2 quotes) | Hualipanren | fresh-po (le, to) | Peru | - | - | Gachet et al. (2010) |
| | Pipitocoma discolor (Kunth) Pruski. | - | fresh-po (lt, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Porphyllyum ruderale (Jacq.) Cass. | Ebus’ A Ina, | pov-po, (le, to) | Bolivia (Takana indians) | Leishmaniasis | - | AREVALO-LÓPEZ et al. (2018) |
| | Pseudolephantopus spicatus (Juss. ex Aubl.) C.F.Baker. (2 quotes) | Huapato, Pato, Chahuirro Pacatro | - | Chile (Chayahuatta) | Ta’Ta’ | - | Ordonez et al. (2010) |
| | Taraxacum cymphyloides G.E.Haglund | - | (le, to) | Ecuador | - | - | Gachet et al. (2010) |
| | Tessaria integrifolia Ruiz & Pav. | Cawara | fresh-po (le, to) | Bolivia (Takana indians) | Leishmaniasis | - | AREVALO-LÓPEZ et al. (2018) |
| | Vernonanthura patens (Kunth) H.Rob. | - | (le/st, to) | Ecuador | - | - | Gachet et al. (2010) |

*Continued on following page*
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|----------------------------------------|---------|----------------|----------------------------------------|---------------------------------|-----------------------------|-----------------------------------|------------|
| Begoniaceae (1 quote and 1 species)    | Begonia sp. | -              | (st, to)                                | Ecuador#                        | -                           | -                                 | Gachet et al. (2010) |
| Bignoniaceae (13 quotes and 10 species)|         |                |                                        |                                 |                             |                                   | Odonne et al. (2011a) |
|                                        | Callichlamys latifolia (rich.) K. Schum. | Kalasapau Poã Ipo Pînd | fresh-po (ba, to)                     | French Guiana (Wayãpi)          | Leishmaniasis                | -                                 | Odonne et al. (2011a) |
|                                        | Crescenda cujete L. (2 quotes)          | Kwí1 po (ba, to) (le, or)              | Ecuador#                        | -                              |                             |                                   | Gachet et al. (2010) |
|                                        | Friesia nigrescens (Sandwith) L.G.Lohmann. | Kalasapau Poã Ipo Pînd | fresh-po (ba, to)                     | French Guiana (Wayãpi)          | Leishmaniasis                | -                                 | Odonne et al. (2011a) |
|                                        | Handroanthus impetiginosus (mart. ex DC.) Mattos. | Tahuari | "Boil 200 G of the bark in 1 L. Of Water. Wash The Affected Area And Apply As A Compress Until Cicatrization Of The Ulcers" | Peru                      | Uta                          |                                   | Odonne et al. (2011a) |
|                                        | Jacaranda copaí (Aubl.) D.Don. (2 quotes) | Charapachpan dec-po (le, to)          | Peru (Yanesha)                   | Uta De Agua, Marehets           | ^La IC<sub>50</sub> = 16.5 μg/ml | Valadeau et al. (2009) |
|                                        | Jacaranda cuspidifolia mart. Arabisco (le, to) | |                                     |                                 |                             |                                   | Valadeau et al. (2010) |
|                                        | Jacaranda gletba (DC) Bureau & K. Schum. (2 quotes) | Chepere Qui dec-po (ba/le/fr, to)     | Bolivia (Takana indians)         | Leishmaniasis                  |                             |                                    | Fournet et al. (1994) |
|                                        | Mansoa alliacea (Lam.) A.H. Gentry. | Ananan pow-po (le, to)                 | Peru (Chayahuita)               | Ta’Ta’                         |                                   |                                    | Achiote (1994) |
|                                        | Mansoa standleyi (Steyerm.) A.H. Gentry. | Ajo sacha (macho) (ro)                | Peru#                          | Uta                            | F<sup>La</sup>; F<sup>Lb</sup>; F<sup>Ld</sup> IC<sub>50</sub> = 45.4 μg/ml | Valadeau et al. (2009) |
|                                        | Mansoa sp. | Ajo Silvestre, De Monte, Sacha, Kofan: Cumanapataema, Palobre | |                                 |                             |                                    | Kvist et al. (2006) |
|                                        | Bixaceae (2 quotes and 1 species)       | Bixa orellana L. (2 quotes)           | Uluku fresh-po (se, to)          | French Guiana (Wayãpi)          | Leishmaniasis                | -                                 | Odonne et al. (2011a) |
|                                        | Bromeliaceae (1 quote and 1 species)    | Billbergia decorata Poepp. & Endl.   | Nara Shimpanantê fresh-po (st, to) | Peru (Chayahuita)               | -                            |                                    | Wieg et al. (1994) |
|                                        | Burseraceae (1 quote and 1 species)     | Commiphora geltensis (L.) C.Chr.      | Al-Bisham fresh-po (or, to)      | Saudi Arabia                    | Leishmaniasis                | -                                 | Odonne et al. (2009) |
|                                        | Cactaceae (1 quote and 1 species)       | Cereus hexagonus (L.) Mill.           | Kau Kau fresh-po (ba, to)        | French Guiana (Wayãpi)          | Leishmaniasis                | -                                 | Ali et al. (2017) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|-------------------------------|--------------------------|----------------------------------|------------|
| Cannabaceae (2 quotes and 2 species)  | Trema integerrima (Beurl.) Standl. | - | (le/st, to) | Ecuador* | - | - | Gachet et al. (2010) |
| Caricaceae (4 quotes and 1 species)   | Trema micrantha (L.) Blume. | Surumumbo, Veraquillo | - | Colombia (Kofan) | - | - | Gachet et al. (2014) |
| Celastraceae (4 quotes and 3 species) | Maytenus macrocarpa (Ruiz & Pav.) Briq. (2 quotes) | Shoshohuasha | pow-po (ba, to) | Peru (Chayahuita) | Ta'Ta' | - | Odonne et al. (2009) |
| | Maytenus sp. | Chuchuhuasi, Chuchuhuasha (Del Bajo) | (co) | Peru# | Uta | | Odonne et al. (2009) |
| Combretaceae (1 quote and 1 species)  | cf Combretum sp. | Ipoyu | (le/st/wp, to) | Ecuador* | - | - | Gachet et al. (2010) |
| Commelinaceae (2 quotes and 2 species) | Dichorisandra hexandra (Aubl.) C.B.Clarke. | - | (le/st/wp, to) | Ecuador* | - | - | Gachet et al. (2010) |
| Convolvulaceae (1 quote and 1 species) | Ipomoea sp. | - | (st, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Costaceae (1 quote and 1 species)     | Costus sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Crassulaceae (2 quotes and 2 species) | Kalanchoe gastonis-bonnieri Raym.- Hamet & H. Perrier. | Hoja Ancha (Kofan, Putumayo, Colombia) | - | Colombia (Kofan) | - | - | Gachet et al. (2014) |
| Cucurbitaceae (4 quotes and 3 species) | cyclanthus sp. | - | (le, on/to) | Ecuador# | - | - | Gachet et al. (2010) |
| Cyclanthaceae (1 quote and 1 species) | Cyclanthus sp. | - | - | Colombia (Kofan) | - | - | Gachet et al. (2014) |
| Dilleniaceae (1 quote and 1 species)  | Diplolarus sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Equisetaceae (1 quote and 1 species)  | Equisetum bogotense Kunth. | - | (st, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Euphorbiaceae (21 quotes and 15 species) | Acalypha alopecuroidea Jacq. | - | (wp, to) | Colombia (Kofan) | - | - | Gachet et al. (2014) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|----------------------------------------|---------|----------------|----------------------------------------|-------------------------------|----------------------------|---------------------------------|------------|
| Fabaceae (27 quotes and 23 species)    | Acacia sp. | Wikamallki | (le, to) | Bolivia (Kechara) | Espundia (cutaneous and mucocutaneous leishmaniasis) | La IC50 > 100 μg/ml | Fournet et al. (1994) |
|                                       | Bauhinia tarapotensis Benth. | - | (le/st, or/to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Cajanus cajan (L.) Huth. | Huacapurana | (co) | Perú# | Uta | Lm IC50 > 100 μg/ml | Kvet et al. (2006) |
|                                       | Campsis arborescens cv. spruce ex Benth. | - | (le/st, to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Cassia sp. | - | (le/st, or/to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Copaifera officinalis L. | Bálásmo, copalba | - | Colombia (Kofan) | Cutaneous leishmaniasis | - | Gutiérrez et al. (2014) |
|                                       | Copaifera paupera (Herzog) Dwyer. | Namphuora | fresh-po (sa, to) | Perú (Chayahuita) | Uta | La IC50 > 100 μg/ml | Estévez et al. (2007) |
|                                       | Copaifera paupera (Herzog) Dwyer. | Namphuora | fresh-po (st, to) | Perú (Chayahuita) | Uta | La IC50 > 100 μg/ml | Estévez et al. (2007) |

(Continued on following page)
### TABLE 1 | (Continued) The 378 plant quotes obtained from the 20 publications, their families, species/genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|----------------------------------------|---------|----------------|---------------------------------------|---------------------------------|---------------------------|-----------------------------------|------------|
| Gentianaceae (4 quotes and 2 species)   | Copaiba | (re)           | (re, or/to)                           | Peru                            | Uta                       | \(^{1,1,1}\)Lm - NA               | Kvist et al. (2006) Odonne et al. (2009) Vásquez-Ocmín et al. (2018) |
|                                        | Nanpinha | fresh           | (re, or/to)                           | Peru                            | Ta‘Ta’                     | -                                 | Odonne et al. (2009) Fournet et al. (1994) |
|                                        | Copaiba | *Take Five Drops Of Oil (Exsudate) Diluted In A Tablespoon Of Warm Water, On An Empty Stomach, For Seven Days* fresh (sa, or) | Peru                            | Uta                            |                           | Odonne et al. (2011a) |
|                                        | Degueilia chrysophylla (Kleinhoonte) R.A.Camargo & A.M.G.Azevedo. | Imeku | po                                      | French Guiana                   | Ta‘Ta’                     | \(^{1,1,1}\)La IC\(_{50} = 17\) μg/ml \(^{1,1,2}\)La; \(^{1,1,3}\)Lb; \(^{1,1,4}\)Ld Leishmaniasis | Gachet et al. (2013) Odonne et al. (2011a) |
|                                        | Desmodium axillare (Sw.) DC. | Së‘È | pow-po (le, to)                         | Peru                            | Ta‘Ta’                     | -                                 | Odonne et al. (2009) Fournet et al. (1994) |
|                                        | Erythrina sp. | Flor De Mayo | (st, to)                               | Bolivia                          | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | - |
|                                        | Gronia adscendens (Sw.) H.Chashi & Ohashi. | - | (le/st/wp/fr, or/to)                   | Ecuador                          | -                           | -                                 | Gachet et al. (2010) |
|                                        | Hydrochoera corymbosa (Rich.) Barneby & J.W.Grimes. | Kalai Pei | po (ba, to)                            | French Guiana                   | (Teko)                      | Leishmaniasis                     | Odonne et al. (2011a) |
|                                        | Inga bourgoni (Aubl.) DC. | Inga Sisi, Bougourni |                                      | French Guiana                   | (Wayapi, Teko)              | *                    | |
|                                        | Inga edulis Mart. (2 quotes) | Inga Wasa |                                      | French Guiana                   | (Wayapi)                    | -                                 | |
|                                        | Inga oerstediana Benth. | - | (le, to)                               | Ecuador                          | -                           | -                                 | |
|                                        | Inga sp. | Inga U | po (ba, to)                            | French Guiana                   | (Mixed Wayapi/Teko)          | Leishmaniasis                   | Gachet et al. (2010) |
|                                        | Lonchocarpus seorsus (J.F. Macbr.) M. Sousa ex D.A. Niell, Kltg. & G.P. Lewis. | - | (ba, to)                               | Ecuador                          | -                           | -                                 | Weigel et al. (1994) |
|                                        | Lupinus taufis Benth. | Tauri | (le)                                   | Ecuador                          | Cutaneous leishmaniasis     | -                                 | |
|                                        | Mucuna sp. | - | (ba, or/to) (ba, to) (le/st, to) (le, to) | Ecuador                          | -                           | -                                 | |
|                                        | Myrocyton balansum (L.) Harms. Phaseolus sp. | Pole | Inf-po (le)                            | french Guiana                   | (Wayapi)                    | Leishmaniasis                   | Odonne et al. (2011a) |
|                                        | Piptadenia sp. | | | French Guiana                   | (Teko)                      | Leishmaniasis                   | Odonne et al. (2011a) |
|                                        | Senna reticulata (Willd.) H.S.Inwr & Barneby. | Couboubea ramosa Aubl. | Marianwà Puà fresh-po (le, to) | Peru                            | Yanesha                      | Leishmaniasis                   | Valadeau et al. (2010) Vásquez-Ocmín et al. (2018) |
|                                        | Helia alata (Aubl.) Kuntze. (3 quotes) | Pole | Puepa‘ –Tpau fresh-po (le, to) | Peru                            | Uta                       | Leishmaniasis                   | Odonne et al. (2011a) |

(Continued on following page)
TABLE 1 | (Continued) The 378 plant quotes obtained from the 20 publications, their families, species/genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species) | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|--------------------------------|-----------------------------|-------------------------------------|------------|
| Gesneriaceae (2 quotes and 2 species)  | Drymonia tumulatae Hanst. | Puepa'TPan | fresh-po (le, to) | Peru (Yanesha) | Uta De Agua, Mareñets | ¹La IC₅₀ = 37.4 µg/ml | Valadeau et al. (2009) |
| Haemodoraceae (1 quote and 1 species)  | Xiphodium caeruleum Aubl. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Heliconiaceae (1 quote and 1 species)  | Heliconia stricta Huber. | Taran Tancomé | fresh-po (ro, to) | Peru (Chayahuita) | - | - | Odonne et al. (2009) |
| Hypericaceae (2 quotes and 1 species)  | Vismia sp. (2 quotes) | Mareñetsorech | fresh-po (ft, to) | Peru (Yanesha) | Leishmaniasis | - | Valadeau et al. (2010) |
| Gesneriaceae (2 quotes and 2 species)  | Drymonia tumulatae Hanst. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Haemodoraceae (1 quote and 1 species)  | Xiphodium caeruleum Aubl. | - | (le, to) | Ecuador# | - | - | Odonne et al. (2009) |
| Heliconiaceae (1 quote and 1 species)  | Heliconia stricta Huber. | Taran Tancomé | fresh-po (ro, to) | Peru (Chayahuita) | - | - | Odonne et al. (2009) |
| Hypericaceae (2 quotes and 1 species)  | Vismia sp. (2 quotes) | Mareñetsorech | fresh-po (ft, to) | Peru (Yanesha) | Leishmaniasis | - | Valadeau et al. (2010) |
| Iridaceae (1 quote and 1 species)      | Euchidaeae bulbosa (Mill.) Urb. | Wasey Lainga | fresh-po, (bu, to) | French Guiana (Wayãpi) | Leishmaniasis | - | Odonne et al. (2011a) |
| Lamiaceae (9 quotes and 7 species)     | Cantinoa mutabilis (rich.) Harley & J.F.B. Pastore. (2 quotes) | Tapacha Ina | pow-po (le/ro, to) | Bolivia (Takana indians) | Leishmaniasis | ¹La IC₅₀ = 29.7 µg/ml ¹b IC₅₀ = 9.8 µg/ml | Arévalo-López et al. (2018) |
| Lamiaceae (9 quotes and 7 species)     | Hyptis capitata Jacq. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Hyptis jacustris A.St.-Hil. ex Benth. (2 quotes) | Olampepan | fresh-po (st/le, to) | Peru (Yanesha) | Uta De Agua, Mareñets | ¹La IC₅₀ = 10 µg/ml | Valadeau et al. (2009) |
| Lamiaceae (9 quotes and 7 species)     | Costus pinnatus H.B.K. (2 quotes) | - | (le/wp, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Couroupita guianensis Aubl. (2 quotes) | - | (Fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Lamiaceae (9 quotes and 7 species)     | Grias neuberthii J.F.Macbr. | Aya huma | (co) | Peru# | Uta | ¹La IC₅₀ > 100 µg/ml | Kirst et al. (2006) |
| Lamiaceae (9 quotes and 7 species)     | Grias peruviana Miers. | Anpi | fresh-po (fr/ba, to) | Peru (Chayahuita) | Ta’Ta’, Huayaní | - | Gachet et al. (2010) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|--------------------------------|---------------------------|-------------------------------|------------|
| Malpighiaceae (1 quote 1 species)     | Banisteriopsis caapi (Spruce ex Griseb.) Morton. | - | (le/st, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Malvaceae (11 quotes and 11 species)  | Abutilon sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Ceiba pentandra (L.) Gaertn. | Kumaka | fresh-po (ba, to) | French Guiana (Wayãpi) | Leishmaniasis | - | - | Odonne et al. (2011a) |
| | Gossypium barbadense L. | Coton Violet | fresh-po (flle, to) | French Guiana (Brazilian and mixed Wayãpi/Teo) | Leishmaniasis | - | - | Odonne et al. (2011a) |
| | Gossypium sp. | Jirbi (O) Tit (A) | "The Seed Is Powdered And Pasted With Butter" pow-po (se, to) | Ethiopia (Oromo) | Outaneous leishmaniasis | - | - | Suleman and Aemnu (2012) |
| | Hibiscus rosa-sinensis L. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Hibiscus sabdariffa L. | - | (le/st, to) | French Guiana (Wayãpi) | Leishmaniasis | - | - | Odonne et al. (2011a) |
| | Hibiscus sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Matisia cordata Bonpl. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Pavonia fruticosa (Mill.) Fawc. and Rendle. | - | (le) | Ecuador | Outaneous leishmaniasis | - | - | Gachet et al. (2010) |
| | Sida rhombifolia L. | - | Escobilia | - | - | - | - | Gachet et al. (2010) |
| | Theobroma cacao L. | - | (se, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Marantaceae (2 quotes and 2 species) | Calathea sp. | Tumbaje (Kofan, Putumayo Colombia) | - | Colombia (Kofan) | Outaneous leishmaniasis | - | Gutiérrez et al. (2014) |
| | | Ischnosiphon sp. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Melastomataceae (6 quotes and 5 species) | Adelobotrys sp. | - | (wp, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | | Antherotoma senegambiensis (Gill. & Perr.) Jacq.-Fél. | - | (le, na) | Ethiopia (Ment) | Outaneous leishmaniasis | - | Gachet et al. (2010) |
| | | Clidemia allardii Wurdack. Miconia sp. (2 quotes) | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | | Yococa guianensis Aubl. | - | - | - | - | - | Gachet et al. (2010) |
| | Meliaceae (5 quotes and 2 species) | Carapa guianensis Aubl. | Yani | fresh-po (ba/le, to) | French Guiana (Wayãpi) | Leishmaniasis | - | Odonne et al. (2011a) |
| | | Cedrela odorata L. (4 quotes) | Cedro | dec-bath (ba, to) | Peru | Uta | - | Vásquez-Ocmin et al. (2018) |
| | | | - | (ba/le, or/to) | Ecuador# | - | - | Gachet et al. (2010) |
| | | | Cedro | (co) | Peru# | Uta | - | Kvist et al. (2006) |
| | | Nonara | pow-po (ba, to) | Peru (Chayahuita) | Ta’Ta’ | - | Odonne et al. (2009) | (Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|---------------------------------|-----------------------------|----------------------------------|------------|
| Menispermaceae (2 quotes and 1 species)| Curarea tecunumaru Barneby and Krukoff. (2 quotes) | Abuta | (st) | Peru# | Uta | \(IC_{50} > 100 \mu g/ml\) | Kvist et al. (2006) |
| | | Capari Nonintê | pow-po (ba, to) | Peru (Chayahuita) | Ta’Ta’ | - | Odonne et al. (2009) |
| Meteoriaeae (1 quote and 1 species) | Meteoridium sp. | - | (wp, to) | Ecuador# | - | - | Gachet et al. (2010) |
| Meteoriaeae (1 quote and 1 species) | Poraqueiba sericea Tul. | Umari | (co) | Peru# | Uta | \(IC_{50} > 100 \mu g/ml\) | Kvist et al. (2006) |
| Moraceae (7 quotes and 6 species) | Artocarpus altîs (Parkinson) Fosberg. Castilla elasticâ Cerv. | Cauchî Négrô | | Colombia (Afro-Colombian and indigenous groups) | | - | |
| | Dorsteria foetïda Schweinf. | Orm -Lakef | bath (to) | Saudi Arabia | | - | |
| | Ficus dendrocîda Kunth. | Matapalo | (as) | Ecuador | | - | |
| | Ficus insïpida Wild. (2 quotes) | Ojé | (re) | Peru# | Uta | \(IC_{50} > 100 \mu g/ml\) | Kvist et al. (2006) |
| | Ojé, Doctor Ojé | fresh-po (lt, to) | Peru | Uta | - | Vásquez-Ocmín et al. (2018) |
| | Ficus sp. | Matapalo | (lt, to) | Bolivia | Espundia (cutaneous and mucocutaneous leishmaniasis) | \(IC_{50} > 100 \mu g/ml\) | Fournet et al. (1994) |
| Musaceae (5 quotes and 2 species) | Musa acumínata Colla. | - | (le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | Musa x paradisiaca L. (4 quotes) | Paîko | po (to) | French Guiana (Wayãpi) | Leishmaniasis | - | Odonne et al. (2011a) |
| | | - | (fr, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | | Plâtano | (sa/lt) | Ecuador | Cutaneous leishmaniasis | - | Weigel et al. (1994) |
| | | Pantapi | pow-po (fr, to) | Peru (Chayahuita) | Ta’Ta’ | - | Odonne et al. (2009) |
| | Myristicæae (3 quotes and 3 species) | Otoba novogranatensis Moldenke. Otoba parvîfola (Markgr.) A.H.Gentry. Virola surinâmensis (Rol. ex Rottb.) Warb. | Otobo | (re, to) | Colombia (Afro-Colombian and indigenous groups) | - | \(IC_{50} > 100 \mu g/ml\) | Weniger et al. (2001) |
| | | | fresh-po (re, to) | - | | \(IC_{50} > 100 \mu g/ml\) | |
| | Myrticæae (4 quotes and 3 species) | Myrtus communis L. Psidium acutângulum DC. Psidium guajava L. (2 quotes) | Ali-A’S | fresh-po (le, to) | Saudi Arabia | - | - | Alî et al. (2017) |
| | | Alali (Goyave Saut) | fresh-po (ba, to) | French Guiana (Wayãpi) | Leishmaniasis | - | Odonne et al. (2011a) |
| | | - | (ba/le, to) | Ecuador# | - | - | Gachet et al. (2010) |
| | | Guayaba | - | Ecuador | - | - | Weigel et al. (1994) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|--------------------------------------|---------|----------------|---------------------------------------|---------------------------------|---------------------------|----------------------------------|------------|
| Olacaceae (2 quotes and 1 species)    | Minquartia guianensis Aubl. (2 quotes) | Huacapú | (co) | Peru# | - | - | Kvist et al. (2006) |
| Oleaceae (1 quote and 1 species)     | Olea europaea L. | Al-aotem | inf-po (st, to) | Saudi Arabia | - | - | Gachet et al. (2010) |
| Onagraceae (1 quote and 1 species)   | Ludwigia sp. | ‘Sebastian’ | (le, to) | Bolivia | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | - | Gachet et al. (2010) |
| Oxalidaceae (1 quote and 1 species)  | Oxalis sp. | - | - | - | - | - | - |
| Papaveraceae (1 quote and 1 species) | Bocconia integrifolia Bonpl. | Palo Amarillo/Amakari | (le/fr/st, to) | Bolivia (Kechua) | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | - | Fournet et al. (1994) |
| Peraceae (2 quotes and 1 species)    | Per a benensis Rusby. (2 quotes) | Apalíiki | (st/ro/ba, to) | Bolivia (Chimane indians) | - | - | Fournet et al. (1994) |
| Polypodiaceae (2 quotes and 2 species) | Campylosternum angustifolium Fée. | Calaguaça | (ss) | Ecuador | Cutaneous leishmaniasis | - | - | Weigel et al. (1994) |
| Phyloctaceae (1 quote and 1 species) | Physollanthus attenuatus Miq. | Coto Chupe | (rh) | Ecuador# | - | - | Kvist et al. (2006) |
| Phytolaccaceae (1 quote and 1 species) | Phytolacca dodocketa L’Hér. | Endode (O,A) | “The Root Is Powdered And Pasted With Butter” pow-po (ro, to) | Ethiopia (Oromo) | Cutaneous leishmaniasis | - | - | Gachet et al. (2010) |
| Picramniaceae (1 quote and 1 species) | Picramnia sp. | - | - | Colombia (Kofan) | Cutaneous leishmaniasis | - | - | Cuberé et al. (2014) |
| Pinaceae (1 quote and 1 species)     | Pinus sp. | Píñon | (ss) | Ecuador | Cutaneous leishmaniasis | - | - | Weigel et al. (1994) |
| Piperaceae (13 quotes and 10 species) | Piper aduncum L. | Matico Chico | (le, to) | Bolivia | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | - | Fournet et al. (1994) |
| Piper barbatum Kunth. | - | (le, to) | Ecuador# | Cutaneous leishmaniasis | - | - | Gachet et al. (2010) |
| Piper consanguineum (Kunth) Steud. | Matico | (le) | Ecuador | Cutaneous leishmaniasis | - | - | Gachet et al. (2010) |
| Piper hispidum Sw. (2 quotes)        | Atukan | fresh-po (le, to) | Peru (Chayahuita) | - | - | - | Estévez et al. (2007) |
| Piper lorecanum Trel.                | Atocan | pow-po (le, to) | Peru (Chayahuita) | - | - | - | Gachet et al. (2010) |
| Piper mediocre CDC.                  | - | - | - | - | - | - | Odonne et al. (2009) |

(Continued on following page)
The 378 plant quotes obtained from the 20 publications, their families, species/genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|--------------------------------------|---------|-----------------|----------------------------------------|---------------------------------|---------------------------|----------------------------------|------------|
| Piper musteum Trel.                  | -       | (le, to)        | Ecuador                               |                                 |                           |                                  | Gachet et al. (2010)             |
| Piper peltatum L. (2 quotes)         | Sipu-sipu | (to)           | Bolivia (Kechua)                       | Espundia (cutaneous and mucocutaneous leishmaniasis) |                           |                                  | Fournet et al. (1994)            |
| Piper umbellatum L.                  | Ariniê Huëron | fresh-po (le, to) | Peru (Chayahuita)                     | Ta’Ta’                          |                           |                                  | Gachet et al. (2010)             |
| Piper sp. (2 quotes)                 | -       | (le, to)        | Ecuador                               |                                 |                           |                                  | Odonne et al. (2009)             |
| Plantaginaceae (3 quotes and 3 species) | Conobea scopariaoides (Cham. & Schltdl.) Benth | Hierba De Sapo | Colombia (Afro-Colombian and indigenous groups) | -                              |                           |                                  | Odonne et al. (2009)             |
| Plantago major L.                   | Lantén  | (le)            | Ecuador                               | Cutaneous leishmaniasis        |                           |                                  | Weigel et al. (1994)             |
| Scoparia dulcis L.                  | -       | (le/wp, to)     | Ecuador                               |                                 |                           |                                  | Gachet et al. (2010)             |
| Poaceae (3 quotes and 3 species)     | Panicum trichoides Sw | Lapakunga | Peru                                  | Uta or Chagas                   | F^Lm - NA                 |                                  | Kivist (2006)                   |
| Pharus sp.                           | -       | (le, in)        | Ecuador                               |                                 |                           |                                  | Gachet et al. (2010)             |
| Zea mays L.                          | -       | (f/le/fr, to)    | Ethiopia                              | ‘Gurtb’ leishmaniasis           |                           |                                  | Tekdehaymanot (2009)            |
| Polygonaceae (3 quotes and 3 species) | Rumex nepalis Spreng. | Tult    | Ethiopia                              |                                 |                           |                                  | Gachet et al. (2010)             |
| Rumex pulcher L.                    | -       | (le, to)        | Ecuador                               |                                 |                           |                                  | Kivist (2006)                   |
| Triplaris weigeltiana (Rchb.) Kuntze. | Tangarana | (co)            | Peru                                  | Uta or Chagas                   | F^Lm                    |                                  | Odonne et al. (2011a)           |
| Portulacaceae (1 quote and 1 species) | Portulaca pilosa L. | Tui | French Guiana                        | Leishmaniasis                   | -                         |                                  | Gachet et al. (2010)             |
| Primulaceae (1 quote and 1 species)  | Clavija weberbaueri Mez. | -         | Ecuador                               |                                 |                           |                                  | Valadeau et al. (2009)          |
| Pteridaceae (1 quote and 1 species)  | Pityrogramma calomelanos (L.) Link. | Seseropan | Peru (Yanesha)                       | Uta De Agua, Marehefs           | F^La                   |                                  | Gachet et al. (2010)             |
| Rhamnaceae (1 quote and 1 species)   | Gouania luteoloides (L.) Urb. | -         | Ecuador                               |                                 |                           |                                  | Gachet et al. (2010)             |
| Rosaceae (1 quote and 1 species)     | Prunus sp. | -            | Ecuador                               |                                 |                           |                                  |                                     | (Continued on following page)   |
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|--------------------------------------|---------|----------------|----------------------------------------|---------------------------------|-----------------------------|---------------------------------|------------|
| Rubiaceae (20 quotes and 15 species) | Calycophyllum multiflorum Griseb. (2 quotes) | Capirona | fresh-po (ba, to) | Peru | Uta | Na | Vásquez-Ocmín et al. (2018) |
|                                      | Químanan | pow-po (ba, to) | Peru (Chayahuita) | Ta‘Ta‘ | IC_{50} < 100 μg/ml | | Odonne et al. (2009) |
|                                      | Capirona | (co) | Perú | Uta | | IC_{50} > 100 μg/ml | | Kvist et al. (2006) |
|                                      | C. spruceanum (Berth.) Hook.f. ex K.Schum. | Capirona | inf-bath (ba, to) | Peru | Uta | - | Vásquez-Ocmín et al. (2018) |
|                                      | Capirona decorticans Spruce (2 quotes) | Yoquinan | | Peru (Chayahuita) | Ta‘Ta‘ | | Odonne et al. (2009) |
|                                      | Llukina | “The Bark Is Boiled And Watery Preparation Is Drunk Twice Daily Until Cicatrisation” dec (ba, or) | Peru | Uta | IC_{50} > 100 μg/ml | | Estevez et al. (2007) |
|                                      | Coussarea sp. | - | (ba, to) | Ecuador | - | - | Gachet et al. (2010) |
| Kutchubaea cf. oocarpa (Standl.) C.H.Pers. | Genipa americana L. | Isa | fresh-po (fr, to) | Peru (Chayahuita) | Ta‘Ta‘ | | Odonne et al. (2009) |
| Hamelia sp. | - | (le, to) | Ecuador | - | | | Gachet et al. (2010) |
| Ladenbergia sp. | Kutchubaea cf. oocarpa (Standl.) C.H.Pers. | Guayabochi | po (st/ba, to) | Bolivia | Cutaneous leishmaniasis | | Hajdu and Hohmann, (2012) |
| Luqina | Quina, Miraña, Guayabate, Resbalomono, Sicornue (Col.) | - | Colombia (Kofan) | Cutaneous leishmaniasis | | | Gutierrez et al. (2014) |
| Pascourea sp. | Pascoa sp. (4 quotes) | Psychotria sp. | (le, to) (le/st, to) (le, to) | Ecuador | - | | Gachet et al. (2010) |
| Rudges brevemegkoppiana Steyerm. | Beso Rojo | - | Colombia (Kofan) | Outaneous leishmaniasis | | | Gutierrez et al. (2014) |
| Rudges lorentesi Standl. | Spermacoce laevis Lam. | Nahuénara | fresh-po (ba, to) | Peru (Chayahuita) | Ta‘Ta‘ | IC_{50} = 34–39.6 μg/ml | Gachet et al. (2010) |
| Spermacoce laevis Lam. | - | (le/st, to) | Ecuador | - | | IC_{50} = 34–39.6 μg/ml | Odonne et al. (2009) |
| Uhnaria guianensis (Aubl.) J.F.Gmel. | Uhnaria tormentosa (Wild. ex Schult.) DC. | Ochara | (or/to) | Peru (Chayahuita) | Ta‘Ta‘ | Cutaneous leishmaniasis | Odonne et al. (2009) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|----------------------------------------|---------------------------------|---------------------------|-----------------------------------|------------|
| Rutaceae (12 quotes and 7 species)    | Angostura longiflora (K.Krause) Kallunki. | Evanta | (le/st/ro, to) | Chimane indians (Bolivia) | Espundia (cutaneous and mucocutaneous leishmaniasis) | IR; IRb; IRd | Fournet et al. (1994) |
|                                       | Citrus aurantiaca (L.) Swingle. | Limón | - | Ecuador | Cutaneous leishmaniasis | - | Weigel et al. (1994) |
|                                       | Citrus × aurantifolia (Christm.) Swingle (2 quotes) | Nino | fresh-po (fr/ba, to/n) | Peru (Chayahuita) | Ta’Ta’, Huayani | - | Odonne et al. (2009) |
|                                       | Citrus × aurantium L. (3 quote) | Naranja | - | Ecuador | Cutaneous leishmaniasis | - | Odonne et al. (2011a) |
|                                       | Toronja | (ro) | | Peru# | Uta | - | Weigel et al. (1994) |
|                                       | Mandarin | - | | Ecuador | Cutaneous leishmaniasis | - | Odonne et al. (2011a) |
|                                       | Citrus × limon (L.) Osbeck. | Limón | (ro) | Peru# | Uta | - | Kvik et al., (2006) |
|                                       | Citrus sp. (2 quotes) | - | (se, to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Ruta graveolens L. (2 quotes) | Ruda | (le) | Ecuador | Cutaneous leishmaniasis | - | Weigel et al. (1994) |
| Sapindaceae (1 quote and 1 species)   | Dodonaea viscosa Jacq. | Shath | po (le, to) | Saudi Arabia | Leishmaniasis | - | Ali et al. (2017) |
| Sapotaceae (7 quotes and 6 species)    | Chrysophyllum prieuni ADC. | Cotoquinilla | fresh-po (le, to) | Peru | Uta | - | Vásquez-Ocmín et al. (2018) |
|                                       | Chrysophyllum sp. | - | (se, to) | Ecuador# | - | - | Gachet et al. (2010) |
|                                       | Manilkara sp. | Baytakini | inf-bath, lt, to | French Guiana (Teko) | Leishmaniasis | - | Odonne et al. (2011a) |
|                                       | Pouteria caimito (Ruiz & Pav.) Radlk. (2 quotes) | Caimito | (le) | Peru# | Uta | - | Kvit et al. (2006) |
|                                       | Pouteria guianensis Aubl. | Caimito | - | Peru | Uta | - | Weigel et al. (1994) |
|                                       | Pouteria torta subsp. tuberculata (Skeuemer) T.D.Penn. | - | (le, to) | Ecuador# | - | - | Odonne et al. (2009) |
| Siparunaceae (3 quotes and 1 species) | Siparuna sp. (3 quotes) | Huaya Muuktuna | “The Woody Stem Grated Ad Boiled. This Preparation Is Drunk Three Times A Day For 8 Days” dec (lt, or) | Peru (Chayahuita) | Uta | IRa | Vásquez-Ocmín et al. (2018) |
|                                       | | Huayan Motonan | fresh-po (le, to) | | | - | Odonne et al. (2010) |
| Smilacaceae (4 quotes and 2 species)  | Smilax salicifolia Griseb. | Sankarín | “Roots Are Bold, And This Preparation Is Drunk Many” | Peru (Chayahuita) | - | IRa - NA | Estvez et al. (2007) |

(Continued on following page)
| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|----------------|---------------------------------------|-------------------------------|---------------------------|----------------------------------|------------|
| Solanaceae (22 quotes and 14 species)  | Smilax sp. (3 quotes) | - | (wp, to) Ecuador# | - | - | | Weigel et al. (1994) |
| Brugmansia sp. (2 quotes)              | Zarzaparilla | (ro) | Peru# | Uta or Chagas | \(f^Lm\) | \(IC_{50} > 100 \mu g/ml\) | Gachet et al. (2010) |
| Brunfelsia grandiflora D.Don. (3 quotes) | Chuanishqui pow-po (le, to/in) | Peru (Chayahuita) Ta‘Ta’, Huayani | - | - | - | Gachet et al. (2010) |
| Brugmansia sp. (2 quotes)              | Chiric Sanango (ro) | Perú# | Uta | \(f^Lm\) | \(IC_{50} = 53 \mu g/ml\) | Gachet et al. (2010) |
| Capsicum sp. (2 quotes)                | No’Ca | (le, to) | Ecuador# | - | - | - | Odonne et al. (2009) |
| Cestrum lindenii Dunal.                | - | (le, to) | Ecuador# | - | - | - | Gachet et al. (2010) |
| Cestrum sp.                            | Markea sp. | (le, to) | Ecuador# | - | - | - | Gachet et al. (2010) |
| Nicotiana tabacum L. (3 quotes)        | Pinchi pow-po (le, to/in) | Peru (Chayahuita) Ta‘Ta’, Huayani | - | - | - | Odonne et al. (2009) |
| Solanum americanum Mill. (2 quotes)    | Tabaco | fresh-po (le fermented, to) | French Guiana | Leishmaniasis | - | Weigel et al. (1994) |
| Solanum crinitum Lam.                  | Yerba Mora (Mortino) | (fr/le) | Ecuador# | - | - | - | Odonne et al. (2011a) |
| Solanum incanum L.                     | Y’U ñisí po (ba, to) | French Guiana (Wayãpi) | - | - | - | Odonne et al. (2011a) |
| Solanum mammosum L.                    | Al-hadiak po (le, to) | Saudi Arabia | | | | Ali et al. (2017) |
| Solanum suberme Jacq.                  | Y’U Sowú po (ba, to) | French Guiana (Wayãpi) | | | | Gachet et al. (2010) |
| Solanum sp. (2 quotes)                 | - | (le, to) | Ecuador# | - | - | - | Odonne et al. (2011a) |
| Witheringia solanacea L’Hérit. Talinum paniculatum (Jacq.) Gaertn. | Yoro Qui’Sha fresh-po (ro, to) | Peru (Chayahuita) Ta‘Ta’ | | | | Gachet et al. (2010) |

(Continued on following page)
### TABLE 1
(Continued) The 378 plant quotes obtained from the 20 publications, their families, species genera, vernacular names, traditional recipes, countries (traditional community), traditional uses, and plants tested for leishmaniasis (in vitro).

| Family (Number of quotes and species)* | Species | Vernacular name | Traditional recipe (plant part, route) | Country (traditional community) | Traditional use (emic term) | Tested for leishmaniasis (results) | References |
|---------------------------------------|---------|-----------------|----------------------------------------|---------------------------------|---------------------------|----------------------------------|-----------|
| Thurniaceae (1 quote and 1 species)   | Thurnia sphaerocephala (Rudge) Hook.f. | Kwayiti (fr, to) | French Guiana (Teko) | Leishmaniasis | - | Odonne et al. (2011a) | |
| Ulmaceae (1 quote and 1 species)      | Ampelocera edentula Kuhl. | Sou’Sou’ (st/ro, to) | Bolivia (Chimane indiana) | Espundia (cutaneous and mucocutaneous leishmaniasis) | - | Odonne et al. (1994) | |
| Urticaceae (3 quotes and 3 species)   | Cecropia obtusa Tréc. | Ama’i fresh-po (ba, to) | French guiana (wayápi) | Leishmaniasis | - | Odonne et al. (2011a) | |
| | Urena laciniiata Wedd. | - (le/st, to) | Ecuador# | - | - | Gachet et al. (2010) | |
| | Urtica dioica L. | - (le, to) | Ecuador# | - | - | Gachet et al. (2010) | |
| | Duraíta sp. | - (le, to) | Ecuador# | - | - | Gachet et al. (2010) | |
| Verbenaceae (8 quotes and 6 species)  | Lantana camara L. | Thurniaceae (1 quote and 1 species) | Kwayiti (fr, to) | French Guiana (Teko) | Leishmaniasis | - | Odonne et al. (2011a) | |
| | Lantana trifolia L. | Yahua’Tan Huíron pow-po (le, to) | Peru (Chayahuita) | Leishmaniasis | - | Odonne et al. (2009) | |
| | Lantana sp. (3 quotes) | T Epeshpan | Peru (Yanesha) | Uta De Agua, Mareñets | L. | Weigel et al. (1994) | |
| | Lantana sp. (3 quotes) | T Epeshpan | Peru (Yanesha) | Uta De Agua, Mareñets | L. | Weigel et al. (1994) | |
| | Verbena ilíforis Kunth. | Berbena/Verbena | Ecuador | Outaneous leishmaniasis | - | Gachet et al. (2010) | |
| | Verbena microphylla Kunth. | Berbena/Verbena | Ecuador | Outaneous leishmaniasis | - | Gachet et al. (2010) | |
| Viburnaceae (1 quote and 1 species)   | Sambucus nigra L. | - (le/st, to) | Ecuador# | - | - | Gachet et al. (2010) | |
| Violaceae (1 quote and 1 species)     | Leonia sp. | - (le, or/to) | Ecuador# | - | - | Gachet et al. (2010) | |
| Zamiaceae (3 quotes and 3 species)    | Zamia amazonum D.W.Stev. | Oreja De Perro fresh-po (ro, or/to) | Peru (Chayahuita) | Uta | La & La= 10 μg/ml | Odonne et al. (2009) | |
| | Zamia pospígiana Mart. & Eichler. | Ukupampa | Peru (Chayahuita) | Uta | La & La= 81 μg/ml | Odonne et al. (2009) | |
| | Zamia sp. | Coocha Panp | Peru (Chayahuita) | Ta’Ta’, Huayani | - | Odonne et al. (2009) | |
| | Zingiber officinale Roscoe. (2 quotes) | Nato | Peru (Chayahuita) | Ta’Ta’, Huayani | - | Odonne et al. (2009) | |
| | Zingiber officinale Roscoe. (2 quotes) | Nato | Peru (Chayahuita) | Ta’Ta’, Huayani | - | Odonne et al. (2009) | |

**Traditional recipe:** Decoction — dec; Decoction used as a poultice — dec-po; Decoction used as a bath — dec-bath; Fresh plant used as a poultice — fresh-po; Infusion — inf; Infusion used as a bath — inf-bath; Infusion used as a poultice — inf-po; Poultice — po; Powder plant used as a poultice — pow-po; Plant Part: Aerial Part – ae; Apical meristem – am; Blanks – ba; Bulb – bu; Cloves – cl; Cortex – co; Exudate – ex; Flower – fl; Fruit – fr; Leaf – le; Látex – lt; Oleogum Resin – or; Resin – re; Rhizome – rh; Root – ro; Sap – sa; Seed – se; Shoot – sho; Stalk – sta; Stem – st; Tuber – tu; Whole Plant – wp; Route: Inhalation — in; Nasal — na; Oral – or; Topical – to. Countries and Communities: Ecuador# - Kichwa of Amazonia, Kichwa of the Andes, Chachi, Mestizo, Afroecuadorian, Awa, Épera; Bolivia# - Guarasug’we indigenous and Chiquitano mestizos; Perú# - Mestizo, Chayahuito, Cocama, Quechua, Ticuna. *promastigote; **amastigote; La — L. amazonensis; Li — L. infantum; IC50 — Inhibitory concentration 50%; NA — Not active.

*In the above citations we counted each species and genus as a single citation, for example, in the case of the genus Gurania sp. although it was cited two times in the articles, it was accounted as one species, because it was not possible to classify Gurania sp. as one or two species. Additionally, it is not possible to know if these two quotes of the genus Gurania in this table belong to Gurania lobata (L.) Pruski, because taxonomic elements are lacking in the published articles. Thus, the 292 plants here presented refer to 216 species (identified until species level) and 76 genera (the ones counted only once).
leishmaniasis above 5,000 cases. According to World Health Organization (2019), both Ethiopia and Saudi Arabia had a record of 100–999 cases of cutaneous leishmaniasis.

It is important to note that leishmaniasis exhibits different clinical forms that can be recognized and named in different ways depending on the specificity of each country and ethnic group. In ethnopharmacological studies, the correlation between the emic terms (the ones used by the traditional communities) and their corresponding etic terms (the ones used in biomedicine) may provide insights to guide further pharmacological studies since they are the bases for suggesting the potential bioactivity of these resources (Pagani et al., 2017). Approximately half of the articles present records of emic terms to leishmaniasis, such as “Gurtb”, in Ethiopia (Teklehaimanot, 2009); “Espundia” for the Chimane Indians, in Bolivia (Fournet et al., 1992b, 1994); “Ta’Ta’”, for the Chayahuitas in Peru (Odonne et al., 2009); ”Uta” and “Uta De Agua” for some communities in Peru, such as Chayahuitas or Yaneshas (Estevez et al., 2007; Valadeau et al., 2009; Vásquez-Ocmín et al., 2018).

Plants tested for leishmaniasis

From the 292 plants registered, 79 described in nine of the twenty selected articles were tested against Leishmania sp. Among the Leishmania species investigated in these studies, L. (L.) amazonensis predominated, followed by L. (L.) major and L. (V.) braziliensis. The results of the tests with some of these plants are available in more than one publication, including the resins and saps of Copaifera paupera (Herzog) Dwyer and the bark and cortex of Spondias mombin L. (Kvist et al., 2006; Estevez et al., 2007), the latex and resin of Hura crepitans L. (Fournet et al., 1994; Kvist et al., 2006), the stem bark and root bark of Pera benensis Rusby (Fournet et al., 1992a, 1994), and the leaves of Pseudoelephantopus spicatus (B. Juss. ex Aubl.) Rohr ex C.F. Baker (Odonne et al., 2009; 2011b). Below, descriptions of the in vitro activity of extracts or purified molecules from the plants used in traditional communities will be provided.

Estevez and colleagues (Estevez et al., 2007) investigated the leishmanicidal activity of nineteen plants indicated by the Chayahuite community to treat cutaneous leishmaniasis. Among them, only the ethanolic extracts produced with the leaves of Piper hispidum Sw. and P. strigoso Trel (Piperaceae) showed expressive activity against intracellular forms of L. (L.) amazonensis. Odonne and collaborators (Odonne et al., 2009) observed that different plants have been used by the Chayahuites in the treatment of leishmaniasis, probably because they live in an endemic area of the disease and have limited access to medical centers. The leishmanicidal activities of ethanolic extracts produced with the selected plants were evaluated in axenic amastigote forms of L. (L.) amazonensis. Ethanolic extracts produced with the aerial parts of Desmodium axillare, Pseudoelephantopus spicatus and Piper loreteanum were the most active extracts at eliminating amastigote forms (IC50 between 13.6 and 27 μg/ml). Ethanolic extracts produced with the bark and/or leaves of Rudgea loreteana Standl and Salacia juruana Loes showed moderate leishmanicidal activity (IC50 between 10 and 15.7 μg/ml). In addition, all these plants were clearly indicated to treat leishmaniasis. On the other hand, it was also demonstrated that ethanolic extracts produced with plants that have not been used to treat leishmaniasis showed significant leishmanicidal activity (IC50 between 10 and 15.7 μg/ml), as is the case for ethanolic extracts produced with the leaves, roots and aerial parts of Piper sanguineispicum Trel., Cybianthus anthuriophyllus Pipoly, (Myrsinaceae), Clibadium sylvestre (Aubl.) Baill. (Asteraceae), respectively.

Further studies characterize the major components in the ethanolic extract produced with the leaves of Pseudoelephantopus spicatus. The purified molecules 1) 8,13-diacetyl-piptocarfol, 2) 8-acetyl-13-O-ethyl-piptocarfol [also

FIGURE 1 | Frequency of the most cited families referring to the 378 quotes of species extracted from the 20 articles, only those species quoted at least 7 times.
isolated from other species: *Vernonia mollissima* (D. Don ex Hook. & Arn.), *Eirmocephala megaphylla* (Hieron.) H. Rob., *Chrysolaena verbascifolia*, *Lepidaploa remotiflora*, and *Vernonia scorpioides* and 3) ursolic acid (Odonne et al., 2011b) were assayed on axenic amastigote forms of *L. (L.) amazonensis*. Molecules 1 (IC$_{50}$ = 0.2 μM) and 2 (IC$_{50}$ = 0.37 μM) showed leishmanicidal activity (in vitro) comparable with amphotericin B (IC$_{50}$ = 0.41 μM), which is used in the treatment of human leishmanial infections. Molecule 3 also eliminated amastigote forms with high activity (IC$_{50}$ = 0.99 μM). Although leishmanicidal action has been observed, the authors considered that the second compound originated from the chemical reaction resulting from the extraction of the ethanolic extract and not from the plant in natura. This work corroborated the leishmanicidal effects observed during traditional treatment (Odonne et al., 2009; 2011b); in addition, it showed for the first time the production and accumulation of such classes of secondary metabolites in *P. spicatus* and supported further preclinical works with molecule 3 in the context of cutaneous and visceral leishmaniasis (Jesus et al., 2020; de Jesus et al., 2021), which in fact reinforces the occurrence of important bioactive molecules in plants traditionally used to treat leishmaniasis.

In the community of Buena Vista, Bolivia, thirty-eight plants have been used to treat skin problems, and eight of them were recommended by Tacana medicine for the treatment of leishmaniasis (Arévalo-Lopéz et al., 2018). Extracts were produced with all these plants, and the leishmanicidal activity assayed on promastigote forms of *L. (L.) amazonensis* and *L. (V.) braziliensis*. It was observed that 42.1% of them were inactive and 23.7% highly active, and the leishmanicidal activity of 34.2% of them was dependent on the part of plant used to produce the extracts. With respect to the plants that were specifically indicated to treat leishmaniasis, extracts produced with the leaves of *Hyptis mutabilis* (Lamiaceae) and the bark of *Jacaranda glabra* (Bignoniaceae) and *Tessaria integrifolia* (Asteraceae) were active on *L. (L.) amazonensis* and *L. (V.) braziliensis*. Further studies showed that fractions purified from the crude ethanolic
extracts of *J. glabra* and *T. integrifolia* were also active toward promastigote forms of *L. (L.) amazonensis*, *L. (L.) aethiopica*, *L. (V.) braziliensis* and *L. (V.) lainsoni*. Although extracts and fractions produced with these plants displayed multispecies action, it was noted that the selective indexes of these natural medicines were low when compared with amphotericin B. On the other hand, it is relevant to observe that in the field, the production of these natural medicines is completely different from those produced in the laboratory, and it can account for the extraction of cytotoxic molecules. Furthermore, this study showed the leishmanicidal activity of five species of Tacana medicinal plants for the first time, showing the relevance of ethnopharmacology to characterize leishmanicidal molecules.

An ethnopharmacological study conducted among Chimane Indians from Amazonian Bolivia showed that stem bark *Pera benensis* Rusby has been used to treat cutaneous leishmaniasis caused by *L. (V.) braziliensis*. In the laboratory, it was verified that chloroform extracts containing quinones were active on promastigote forms of *L. (V.) braziliensis* (Fournet et al., 1992a). Further fractionation of the extract led to the identification of plumbagin, 3,3′-biplumbagin, 8,8′-biplumbagin and lupeol. Promastigote forms of *L. (L.) amazonensis*, *L. (V.) braziliensis* and *L. (L.) donovani* were eliminated when incubated with plumbagin; 3,3′-biplumbagin; 8,8′-biplumbagin; and intracellular amastigotes of *L. (L.) amazonensis* were highly sensitive to plumbagin and 3,3′-biplumbagin, which were able to eliminate 100 and 85% of intracellular parasites at 50 μg/ml.

Subsequently, an ethnopharmacological study conducted in Bolivia among settlers and Chimane Indians recorded that 14 plants were used to treat leishmaniasis as a topical poultice. Ten plants were indicated by the colonists and four by the indigenous people (Fournet et al., 1994). Extracts were prepared with different plant parts using petroleum ether, chloroform, and ethyl acetate of ethanol 50%; additionally, alkaloidal and quinonic fractions were also produced. Extracts were tested *in vitro* against *L. (L.) amazonensis*, *L. (V.) braziliensis*, and *L. (L.) donovani*; and from 10 plants indicated by the colonists, only *Bocconia integrifolia* Bonpl. and *B. pearcei* (Papaveraceae) were active. However, according to *Plants of the World online*, these plants are currently classified as synonyms, and the accepted name is *Bocconia integrifolia* Bonpl. Considering the four plants indicated by the Chimane Indians, extracts produced with the leaves, stem bark or root bark of the following three species were active on *Leishmania sp.: Galipea longiflora* K. Krause, *Ampelocera edentula* Kulm. and *Pera benensis* Rusby. In previous studies, it was demonstrated that 4-hydroxy-1-tetralone from *A. edentula*, three naphthoquinones from *P. benensis*, and quinoline alkaloids from *G. longiflora* displayed leishmanicidal activity (Fournet et al., 1989; 1992a; 1992b; 1993a). These studies reinforce that medicinal plants indicated by the Chimane Indians are potentially more effective than those indicated by the group of colonists, and extracts, fractions or purified molecules may be used as prototype drugs to treat human leishmaniasis according to the traditional knowledge of native people from Colombia.

An ethnopharmacological survey performed in northeastern Peru recorded 289 uses of plants for the treatment of leishmaniasis (Kvist et al., 2006). Twenty-eight plants were selected, and ethanolic extracts were produced and tested toward promastigote forms of *L. (L.) major*. It was observed that crude ethanolic extracts produced with the cortex of *Maytenus sp.*, *Minquartia guianensis*, *Aspidosperma rigidum*, with the roots of *Mansoa standleyii*, *Rauwolfia sp.*, *Tabernaemontana sp.*, with the bulb of *Curcuma longa* and with the resin of *Copaifera pauperi* displayed significant IC_{50} values against promastigote forms (between 10 and 20 μg/ml). In addition, 62 citations of the genus *Maytenus* were recorded in the treatment of leishmaniasis, suggesting that in addition to the high bioactivity of this plant on *L. (L.) major* (IC_{50} < 10 μg/ml), it has been used by different people living in traditional communities.

In the Yanesha community, Peru, ninety-four plants have been used to treat symptoms related to malaria and cutaneous leishmaniasis. In this community, twelve plants have been employed in the treatment of leishmaniasis (Valadeau et al., 2009); however, only eleven plants were tested in a laboratory context. In this case, ethanolic extracts of the plant parts were produced and assayed in axenic amastigote forms of *L. (L.) amazonensis*. Among plants used by the Yanesha group, ethanolic extracts produced from the leaves of *Carica papaya* L. (Caricaceae), *Hyptis lacustris* A. St.-Hil. ex Benth. (Lamiaceae) and *Lantana sp.* (Verbenaceae) were highly active plants for the elimination of parasites (IC_{50} = 10 μg/ml). However, it is important to note that the community uses the latex of *C. papaya*, the exudate of the bark or leaves from the stem from *Hyptis lacustris* and finally uses concentrated infusion of *Lantana sp.* This was the first study to record the leishmanicidal activity of latex from *papaya* (*C. papaya*). In addition, it was found that the treatment widely used in the fight against leishmaniasis by the community consists of the application of whitish latex, recently dripped from *Acalypha macrostachya* Jacq. (Euphorbiaceae) in the entire affected area for three consecutive days. This recipe is used for both cutaneous and mucocutaneous leishmaniasis. On the other hand, other plants used as traditional medicinal, such as *Vismia sp.* (Clusiaceae) and *Pityrogramma calomelanos* (L.) Link (Pteridaceae) showed low/moderate activity in the laboratory, possibly because the authors were unable to legitimately reproduce the mode of use, that is, testing the latex recently extracted from these plants, as indicated by the healers in the Yanesha community. On the other hand, some plants not employed in the traditional treatment of leishmaniasis also displayed significant leishmanicidal activity, as is the case for *Hyptis lacustris* Jacq. (Lamiaceae) and *Renealmia thyrsoidea* (Rottb.) Maas (IC_{50} = 9 μg/ml) and *Renealmia nig* (IC_{50} = 10 μg/ml) and *Renealmia* *alpinia* (IC_{50} = 9 μg/ml) and *Renealmia thyrsoidea* (Rottb.) Maas (IC_{50} = 9 μg/ml) and *Renealmia thyrsoidea* (Rottb.) Maas (IC_{50} = 9 μg/ml).

In Colombia, an ethnopharmacological survey was carried out among Afro-Colombians and indigenous people to record plants traditionally used to treat malaria, Chagas disease and leishmaniasis. Based on ethnopharmacological and chemotaxonomy, the antiprotozoal activity of methylene
chloride and methanolic extracts produced with 44 plants were analyzed. Among these plants, five have been used to treat leishmaniasis (Weniger et al., 2001). In this case, it was verified that the aerial parts of Conobea scoparioides (Scrophulariaceae) and Hygrophila guianensis (Acanthaceae), the bark exudate of Otoba novogranatensis and O. parviflora (Myristicaceae), and Castilla elastica (Moraceae) have been used as traditional medicines to treat leishmaniasis. In vitro experiments showed that methylene chloride extract produced with the leaves of C. scoparioides was highly active at eliminating promastigote forms of L. (L.) amazonensis, L. (L.) infantum and L. (V.) braziliensis; additionally, macrophages infected with L. (V.) panamensis and incubated with this extract for 96 h eliminated 50% of parasites at 6.7 μg/ml. Methylene chloride and methanolic extracts produced with the fruits of O. novogranatensis were also active against the same species, and on amastigote forms, both eliminated intracellular L. (V.) panamensis (IC50 = 6.5 and 10.6 μg/ml, respectively). Apolar and polar extracts produced with the leaves of this plant also killed promastigote forms; however, they displayed only low or moderate activity on intracellular amastigotes (IC50 = 177 and >40 μg/ml, respectively); similar findings were observed with the apolar extract produced with the bark of O. parvifolia. Although some extracts displayed moderate or low activity on amastigote forms, once more, it becomes important to highlight the fundamental differences in the production of the natural medicines used by healers in communities and the way that researchers produce extracts in laboratories and use them in biological systems, which obviously minimizes the complexity of human physiology and the interactions between molecules, cells and parasites.

Table 1 summarizes the leishmanicidal activity of plants described above, displaying the 50% inhibitory concentrations (IC50) if available, parasite species and form (amastigote or promastigote) used and described in the selected articles.

**Contributions of some botanical families and species in the experimental treatment of leishmaniasis**

In the present review, it was verified that at least 292 plants may be employed in the traditional treatment of leishmaniasis in different communities around the world, and it was verified that some families of plants have been widely used by communities, such as Apocynaceae, Araceae, Bignonieae, Asteraceae, Euphorbiaceae, Lamieae, Fabaceae, Malvaceae, Piperaceae, Rubiaceae, Rutaceae, Solanaceae and Verbenaceae. Below are described mainly in vivo studies about the efficacy of extracts and/or purified molecules from the botanical families used by traditional communities. Furthermore, details about the treatment, route of administration, parasite species, clinical form and efficacy of treatment are shown in Table 2.

Plants from the Apocynaceae family are rich in bioactive secondary metabolites (Siddiqui et al., 1986; Arambewela and Ranatunge, 1991; Muruganandam et al., 2000; Bhaskar and Natarajan, 2015; Kaunda and Zhang, 2017), and such molecules may have activity on tissue amastigote forms. In this regard, it was found that the genus Tabernanontana has been cited several times in different communities as healing symptoms related to leishmaniasis, but few scientific advances have been made with this genus. Despite few works about the species traditionally used, it has been verified that the leishmanicidal effect of molecules purified from a related species, T. catharinensis A. DC., may be linked to the immunomodulatory activity of this genus (Soares et al., 2007). In addition, it was verified that the leishmanicidal molecule voacamine, an indole alkaloid purified from T. divaricata (L.) R.Br. ex Roem. & Schult, altered the mitochondria, kinetoplast and nucleus of L. (L.) amazonensis and L. (L.) donovani promastigotes, and such morphological changes correlated with the relaxation activity of topoisomerase IB. Additionally, it was verified that BALB/c mice infected with wild-type or drug-resistant L. donovani treated with 2.5 and 5 mg/kg voacamine by the intraperitoneal route twice a week for three weeks displayed fewer parasites in the spleen and liver than the untreated control (Chowdhury et al., 2017), reinforcing that this genus contains important classes of antileishmanial molecules. Although these species were not cited by traditional communities, it is possible that plants belonging to the same genus share similar compounds. Hexanic extract produced with the roots of the less cited species from this family, Pentalinon andrieuxii (Müll. Arg.) B.F. Hansen & Wunderlin, was active on promastigote forms of L. (L.) mexicana in vitro (Lezama-Dávila et al., 2007) and BALB/c mice infected with L. (L.) mexicana treated with 10 μg of this extract by the topical route, once a day for six weeks, presented fewer parasites in the skin; in addition, treated animals produced high levels of IL-12 cytokine along with the expression of the costimulatory molecules CD40, CD80, and CD86 (Lezama-Dávila et al., 2007; Reina et al., 2014), suggesting that, at least in part, the leishmanicidal activity in vivo may be associated with stimulation of innate immune cells. Further studies led to the identification of sterols from the roots of this plant that were active on intracellular amastigote forms of L. (L.) mexicana with an IC50 between 0.03 and 14.5 μM (Pan et al., 2012), and the steryl pentalinonsterol encapsulated in liposomes, given by the intravenous route at 2.5 mg/kg, significantly reduced the number of viable parasites in the liver, spleen and bone marrow of BALB/c mice infected with L. (L.) donovani; additionally, this molecule activated the Th1 immune response in treated animals (Gupta et al., 2015). The genus Aspidospernum has been cited as a source of natural medicine against leishmaniasis, and bioactive alkaloids purified from different species of this genus may be responsible for the efficacy of plants observed in traditional communities (Tanaka et al., 2007; Reina et al., 2014); however, studies involving experimental models of leishmaniasis (in vivo) have not been performed thus far.

Different species of plants from the family Bignonieae were cited 13 times to treat symptoms associated with leishmaniasis in communities. Among these plants, it was demonstrated that the naphthoquinone lapachol, purified from Handroanthus serratifolius (Vahl) S.O. Grose, was active (in vitro) on amastigote forms of L. (L.) amazonensis (Costa et al., 2017), and the possible mechanism of action of...
**TABLE 2** | *In vivo* activity of medicinal plants. Families, plant species, clinical form of leishmaniasis, parasite species, extract or purified molecules employed in experimental treatment, doses, route of administration, scheme of treatment and efficacy of the treatments in experimental leishmaniasis.

| Family             | Plant species                  | Clinical form and parasite species | Treatment                          | Route of administration | Efficacy                                      | Ref                  |
|--------------------|--------------------------------|-----------------------------------|-----------------------------------|-------------------------|----------------------------------------------|----------------------|
| Amaranthaceae      | Dysphania ambrosioides (L.) M. Monzote et al. (2006) | CL – L.a                          | Essential oil (30 mg/kg)          | Intraperitoneal, once a day for 15 days | Reduced by ∼68% the number of parasites       | Patrício et al. (2008) |
|                    | Mosyakin & Clemants            | Leaves - hydroalcoholic crude extract (5 mg/kg) | Intraperitoneal, 5 injection at every 4 days | Oral, once a day for 15 days | Oral: No effect                              |                      |
|                    |                                |                                    |                                   |                         |                                              |                      |
|                    |                                |                                    |                                   |                         |                                              |                      |
| Amaryllidaceae     | Allium sativum L.              | CL–L.m                            | Fresh garlic bulb—aqueous extract (20 mg/kg) | Intraperitoneal, daily for 15 days | Reduced by ∼65% the size of cutaneous lesions | Ghazanfari et al. (2000) |
|                    |                                |                                      | Fresh and dried garlic bulb—aqueous extract (20 mg/kg) | Intraperitoneal, daily for 15 days | Dried extract—Inhibited lesion progression and parasite multiplication | Gamboa-León et al. (2007) |
|                    |                                |                                    |                                   |                         | Fresh extract—No effect                       |                      |
|                    |                                |                                    |                                   |                         | CL—oral and intraperitoneal treatment reduced by ∼90 and 80% the size of skin lesion, respectively | Wabwoba et al. (2019) |
|                    |                                |                                    |                                   |                         |                                              |                      |
| Apocynaceae        | Pentalinon andrieuxii (Mull.Arg.) B.F. Hansen & Wunderin | CL–L.me                          | Root hexanic extract (10 μg)      | Topical; once a day for 6 weeks | Reduced in 2 times the number of parasites in the skin | Lezama-Dávila et al. (2014) |
|                    |                                |                                    |                                   |                         |                                              |                      |
|                    |                                |                                    |                                   |                         |                                              |                      |
|                    |                                |                                    |                                   |                         |                                              |                      |
| Bignoniaceae       | Tabernaemontana divaricata (L.) R.Br. ex Poem. & Schlitt. | VL–L.d                           | Liposome-encapsulated pentalinonsterol (2.5 mg/kg) | Intravenous             | Reduction of 64, 83 and 57% of parasites in the liver, spleen and bone marrow, respectively | Gupta et al. (2015) |
|                    |                                |                                    |                                   |                         |                                              |                      |
|                    |                                |                                    |                                   |                         |                                               |                      |
| Euphorbiaceae      | Croton caudatus Geiseler       | LV–L.d                            | Dehydrozaluzanin C (100 mg/kg)    | Oral, once a day for 14 days | Reduced the severity of cutaneous lesions     | Fournet et al. (1993b) |
|                    |                                |                                    | Lapachol (25 mg/kg)              |                         |                                              | Araújo et al. (2019) |
|                    |                                |                                    |                                   |                         |                                              |                      |
| Fabaceae           | Pleurolobus gangeticus (L.) J.S. Hil. ex H.Ohashi & K.Ohashi | VL–L.d                           | Whole plant - ethanolic extract; hexane; n-butanol and aqueous fractions (100 mg/day) | Oral route, once a day for 5 consecutive days | Reduced by 64.4 and 5.3 the number of parasites in the spleen and liver, respectively | Singh et al. (2005) |
|                    | Copaifera martil Hayne         | CL–L.a                            | Copaiba oil (100 mg/kg)           |                         |                                              | dos Santos et al. (2011) |

(Continued on following page)
**TABLE 2** (Continued) In vivo activity of medicinal plants. Families, plant species, clinical form of leishmaniasis, parasite species, extract or purified molecules employed in experimental treatment, doses, route of administration, scheme of treatment and efficacy of the treatments in experimental leishmaniasis.

| Family | Plant species | Clinical form and parasite species | Treatment | Route of administration | Efficacy | Ref |
|--------|---------------|-----------------------------------|-----------|-------------------------|----------|-----|
| **Piperaceae** | *Piper rusbyi* C. DC. | CL—L.a | Flavokavain B (1–5 mg/kg) | Subcutaneous; oral; topical; oral + topical; for 4 weeks | Oral, oral plus topical treatments decreased the lesion size by ~ 4 times | Flores et al. (2007) |
| | *Piper pseudoarboreum* Yunck | CL—L.a | (E)-pipiplartine (25 mg/kg) | Subcutaneous, alternative days for 28 days | Animals treated with 5 mg/kg displayed reduction in the size of lesions by 32.2% | Ticona et al. (2020) |
| **Rutaceae** | *Angostura longiflora* (K.Krause) Kallunki | CL—L.a | Root and stem bark- total alkaloid extract (50 mg/kg) | Intraperitoneal, once a day until the week 14 | Stem extract: Intraperitoneal and oral treatments decreased the parasite loads by 99 and 49%, respectively | Fournet et al. (1996) |
| | | | | | | |
| **Solanaceae** | *Solanum lycocarpum* A.St.-Hil | CL—L.me | Solamargine plus solasonine (10 μg) | Topical, once a day for 6 weeks | Reduced in 3 times the number of parasites | Lezama-Dávila et al. (2016) |
| | *Solanum havanense* Jacq., *Solanum myriacanthum* Dunal, *Solanum nudum* Humb. & Bonpl. ex Dunal, *Solanum seaforthianum* Andrews | CL—L.a | Leaves—hydroalcoholic extracts (30 mg/kg) | Intraperitoneal, every 4 days, 5 doses | Reduction of parasites in animals treated with *S. havanense* (93.6%), *S. nudum* (80%) *S. myriacanthum* (56.8%) and *S. seaforthianum* (49.9%) | Cos et al. (2018) |
| | | | | | | |
| **Urticaceae** | *Urtica thumbergiana* Siebold & Zucc. | CL—L.m | Plant aqueous extract (150; 200, and 250 mg/kg) | Intramuscular and intraperitoneal, three times/week for 30 days | All treatments inhibited lesion development and suppressed parasite dissemination, with special activity to the intraperitoneal treatment | Badriadeh et al. (2020) |

CL—Cutaneous leishmaniasis; VL—visceral leishmaniasis; L.a—Leishmania (Leishmania) amazonensis; L.d—Leishmania (Leishmania) donovani; L.i—Leishmania (Leishmania) infantum; L.m—Leishmania (Leishmania) major; L.me—Leishmania (Leishmania) mexicana; L.b—Leishmania (Viannia) braziliensis.

This molecule involves programmed cell death (Araújo et al., 2019). In addition to the *in vitro* studies, it was demonstrated that lapachol, given orally for 10 days, decreased the number of amastigote forms of *L. (L.) amazonensis* in experimental cutaneous leishmaniasis, and a significant reduction in splenic and hepatic parasites was observed in visceral leishmaniasis caused by *L. (L.) infantum* (Araújo et al., 2019). In the same way, it was verified that *Jacaranda* species have also been traditionally used to treat leishmaniasis; however, only *in vitro* studies were carried out (Passero et al., 2007).

With respect to the family Asteraceae, 22 citations of plants that have been used in the context of skin diseases by traditional communities were observed. However, few works have been developed thus far with the most frequently cited genera. The genus *Munnizia*, cited as a healing agent, was studied with respect to leishmanicidal and trypanocidal activities. In this regard, the petroleum ether extract produced with the leaves of *Munnizia maronii* (André) H.Rob and the isolated compound dehydrozaluzanin C showed *in vitro* activity against *L. (L.) amazonensis*; additionally, it was demonstrated that dehydrozaluzanin C, given once a day for 14 days at 100 mg/kg, reduced the severity of cutaneous lesions in the experimental model of cutaneous leishmaniasis caused by *L. (L.) amazonensis* (Fournet et al., 1993b). Sesquiterpene lactones have also been isolated from *Pseudelephantopus spicatus* (Juss. ex Aubl.) C.F.Baker, a species used by traditional communities, and the leishmanicidal activity of such molecules (IC\textsubscript{50} = 0.2–0.99 μM) was similar to the activity of amphotericin B (IC\textsubscript{50} = 0.41 μM), a second-line drug used in the treatment of patients with leishmaniasis (Odonne et al., 2011b). The thiophene derivative 5-methyl-2,2′,5′-2″-tertiophene purified from *Porophyllum ruderale* (Jacq.) Cass. was also active on axenic amastigote forms of *L. (L.) amazonensis* (Takahashi et al., 2011), and such activity was associated with physiological and morphological alterations in parasite mitochondria (Takahashi et al., 2013). Despite these interesting *in vitro* data described with plants from the...
Asteraceae family that have been used by traditional communities, it was observed that experiments confirming the efficacy *in vivo* of molecules purified from plants used in traditional medicine are missing; however, *in vitro* data obtained with bioactive molecules suggest that plants produce and accumulate leishmanicidal compounds.

In the present review, 21 citations related to the traditional uses of plants from the Euphorbiaceae family were observed. Among them, the genus *Croton* has been used to treat skin diseases, and the medicinal activity can be related to the molecule linalool present in the essential oil of *Croton cajucara* Benth., which displayed a strong leishmanicidal potential against amastigote forms of *L. (L.) amazonensis* (IC$_{50}$ = 8.7 ng/ml) and immunomodulatory effects on peritoneal macrophages that, once treated, were able to produce elevated amounts of nitric oxide, an important microbicidal molecule (Rosado et al., 2003). In addition, other compounds, such as 7-hydroxycalamenene, trans-dehydrocrotonin, trans-crotonin, and acetylatediuritolic acid, from *C. cajucara* Benth. also inhibited the proliferation of intracellular amastigote forms of *L. (L.) amazonensis* or *L. (L.) chagasi* (Rosado et al., 2003; Rodrigues et al., 2013; Lima et al., 2015). Despite these phytochemical studies revealing the molecular diversity of the *Croton* genus as well as the leishmanicidal potential of molecules, only one study showed that a fraction purified from the hexanic extract from the leaves of *C. caudatus* Geiseler, given by oral route for five consecutive days at 5 mg/kg, reduced the number of viable parasites by 65 and 69% in the spleen and liver of experimental animals infected with *L. (L.) donovani*, respectively (Dey et al., 2015), and this therapeutic activity was associated with the restoration of IFN-$\gamma$ levels in CD4 T lymphocytes. In addition to *Croton* species, several molecules purified from *Euphorbia* genus showed leishmanicidal activity *in vitro* on intracellular amastigotes, such as piceatannol, simiarenoi, 1-hexacosanol, $\beta$-sitosterol, and $\beta$-sitosterol-3-O-glucoside (Duarte et al., 2008; Amin et al., 2017). Tannin- and saponin-rich fractions from the root of *E. wallichii* Hook.f. eliminated extra and intracellular forms of *L. tropica* with similar activities as the standard treatment; additionally, these fractions permeabilized the parasite's cell membrane and triggered apoptosis in *L. tropica* (Ahmad et al., 2019), but to the best of our knowledge, no *in vivo* studies were performed with all of these purified molecules.

Traditional communities have used plants from the Fabaceae family to treat symptoms related to leishmaniasis. The genera *Copaifera*, *Desmodium*, *Lonchocarpus*, and *Senna* have been cited and recorded in different studies. The copaiba oil extracted from different species of *Copaifera* showed activity against promastigote and amastigote forms of *L. (L.) amazonensis* (Santos et al., 2008); additionally, it was observed that BALB/c mice infected with *L. (L.) amazonensis* and treated with the essential oil of *Copaifera martii* Hayne at 100 mg/kg by the oral, subcutaneous and topical routes displayed smaller skin lesions than untreated BALB/c mice (dos Santos et al., 2011). Further studies suggested that pinifolic and kaurenoic acids (dos Santos et al., 2011) or $\beta$-caryophyllene may be responsible, at least in part, for the *in vitro* and *in vivo* activities observed in such studies. The species *Desmodium adscendens* and *D. axillare* have also been used as traditional remedies. Although scientific records about the leishmanicidal activity of such species do not exist, studies have already shown that the n-butanol fraction produced with whole *Pleurolobus gangeticus* (L.) J.St.-Hil. ex H. Ohashi & K. Ohashi plants given orally once a day for five consecutive days inhibited the multiplication of amastigote forms in the spleen of experimental animals with visceral leishmaniasis caused by *L. (L.) donovani* (Singh et al., 2005); on the other hand, the ethanolic extract and hexanic and aqueous fractions displayed moderate and weak leishmanicidal activity *in vivo*. Furthermore, the therapeutic activity of *D. gangeticum* may be associated with the occurrence of glycolipids, aminoglucoyl glycerolipids and cerebrosides in extracts (Mishra et al., 2005). Similarly, *Senna reticulata* is used by traditional communities, but pharmacological studies with respect to leishmanicidal activity have been performed only with *S. spectabilis* (DC) H.S.Irwin & Barneby, and its activity was related to the presence of alkaloïds (Melo et al., 2014), which can possibly interact with leishmanial arginase (Lacerda et al., 2018), inducing cell death; however, no proof of concept exists concerning the *in vivo* properties of such molecules.

Plants from the Piperaceae family have also been used by traditional communities, and there are many works addressing advances with the genus *Piper*. These works describe the molecular diversity of the genus as well as the leishmanicidal activity of the purified molecules. In this regard, it was observed that chalcones, phenolic compounds, lignans, and terpenes, among other molecules, display leishmanicidal properties (Torres-Santos et al., 1999; Hermoso et al., 2003; Cabanillas et al., 2010; Vendrametto et al., 2010; García et al., 2013; Dal Picolo et al., 2014; Capello et al., 2015; Ceole et al., 2017). Additionally, it was observed that the possible cellular targets of such molecules were the mitochondria and plasma membrane of *Leishmania sp.* (Misra et al., 2009; de Oliveira et al., 2012), in addition, these molecules can stimulate immune responses, facilitating the destruction of intracellular parasites (Chouhan et al., 2015). Despite knowledge about the molecular diversity of the *Piper* genus and the bioactivity of such molecules on *Leishmania sp.*, only a few works have shown the *in vivo* relevance of this genus. Chalcone flavokavain B purified from the leaves of *Piper rusbyi* C. DC. given by the subcutaneous route to BALB/c mice infected with *L. (L.) amazonensis* at 5 mg/kg was able to reduce the size of lesions by 32% (Flores et al., 2007), and (E)-pipiltartine isolated from the leaves of *Piper pseudoarboresum* Yunck, given once a day for 4 days by the intrasional route at 25 mg/kg, reduced the size of cutaneous lesions by 35% and inhibited the visceralization of *L. (L.) amazonensis* in BALB/c mice (Ticona et al., 2020).

Plants from the Solanaceae family have been cited by traditional communities to treat symptoms related to leishmaniasis; however, only a few scientific advances have been made with plants of this family. Recently, it was demonstrated that hydroalcoholic extracts produced with the leaves of *Solanum havanense* Jacq., *S. myriaeanthum* Dunal,
S. nudum Humb. & Bonpl. ex Dunal, and S. sefoorthianum Andrews showed high selective indexes on L. (L.) amazonensis (in vitro) and in experimental leishmaniasis caused by L. (L.) amazonensis. It was observed that the hydroalcoholic extract produced with S. havanense, given every 4 days (5 doses) by the intraslesional route at 30 mg/kg, decreased the number of parasites by 93.6%. Hydroalcoholic extracts produced with the leaves of S. nudum, S. myricanthum and S. sefoorthianum reduced the number of amastigotes in the skin of experimental animals by 80, 56.8 and 49.9%, respectively (Cos et al., 2018). In addition, it was demonstrated that the combination of the alkaloids solamargine and solasonine purified from S. lyocarpum A.St.-Hil. topically applied at 10 μg in the skin of C57BL/6 mice infected with L. (L.) mexicana reduced the size of cutaneous lesions and the number of tissue parasites (Lezama-Dávila et al., 2016), emphasizing the presence of potent bioactive molecules in the family Solanaceae.

Plants from the families Rubiaceae and Rutaceae have been used by traditional communities in the treatment of leishmaniasis; however, few works have characterized and tested the bioactive molecules of these plants (Muhammad et al., 2003; Quintin et al., 2009). Despite this, studies have shown that quinolines and alkaloids from Angostura longiflora (K.Krause) Kallunki (Rutaceae) exhibit leishmanicidal activity (in vitro), and in vivo, it was demonstrated that quinolin alkaloids from the bark or root of this plant given by oral or intraslesional routes to experimental animals infected with L. (L.) amazonensis or L. (V.) braziliensis controlled the experimental infection, reducing the number of parasites in the skin (Fournet et al., 1996; Calla-Magariños et al., 2013); additionally, these studies suggested that animals treated by the intraperitoneal route displayed a significant reduction in parasites.

Some families were less cited by healers in communities; however, interesting results have been observed in the scientific literature, as is the case for Dysphania ambrosioides (Amaranthaceae) (L.) Mosyakin & Clemenst. This plant has been used by a rural population in a coastal area of Bahia state, Brazil, in cases of cutaneous leishmaniasis (França et al., 1996). Experimentally, it was verified that the essential oil given by the intraperitoneal route once a day for 15 days at 30 mg/kg reduced the number of amastigote forms in the skin of BALB/c mice by 68% (Monzote et al., 2006). In addition, it was demonstrated that hydroalcoholic extract produced with the leaves of this plant given by the intraslesional route reduced the number of amastigote forms of L. (L.) amazonensis in the skin, lymph nodes and spleen of BALB/c mice. However, the treatment given by the oral route did not alter the course of infection. The essential oil of D. ambrosioides (L.) Mosyakin & Clemenst given by the oral route also reduced the number of amastigote forms in experimental cutaneous leishmaniasis caused by L. (L.) amazonensis (Patrício et al., 2008). Furthermore, it was demonstrated that the essential oil of this plant and its components can affect the mitochondria of parasites (Monzote et al., 2006, 2007; Pastor et al., 2015). Allium sativum L. (Amaryllidaceae), garlic, was cited only once as a traditional remedy for the treatment of leishmaniasis; however, advances concerning leishmanicidal activity in vitro and in vivo have been demonstrated. In the experimental model of cutaneous leishmaniasis caused by L. (L.) major, it was demonstrated that aqueous extract produced with dried bulbs of garlic, given by intraperitoneal route daily for 15 days at 20 mg/kg, inhibited the progression of cutaneous lesions as well as parasite multiplication. However, it was demonstrated that aqueous extract produced with fresh bulbs given at the same dose and route was inactive (Gamboa-León et al., 2007), but interestingly, it was verified that the aqueous extract produced with fresh bulbs of garlic collected in Hamadan (Iran), given by the intraperitoneal route at 20 mg/kg daily for 15 days to BALB/c mice infected with L. (L.) major, was able to reduce the size of lesions by 65% (Ghazanfari et al., 2000). These data suggest that the origin of garlic may impact the pharmacological activity of this plant. Methanolic extract produced with fresh bulbs and given daily by oral or intraperitoneal routes for 4 weeks also inhibited the size of cutaneous lesions in experimental animals infected with L. (L.) major by approximately 90 and 80%, respectively; and in experimental visceral leishmaniasis caused by L. (L.) donovani, the same treatment reduced the rate of parasitism in the spleen by 65 and 55% when it was given by oral or intraperitoneal routes, respectively (Wabwoba et al., 2010). Furthermore, the efficacy of A. sativum L. in leishmaniasis may be associated with the immunomodulatory activity of molecules produced by this plant (Ghazanfari et al., 2000; Gamboa-León et al., 2007). Unfortunately, no biomolecules were purified and assayed in vivo in an attempt to produce a standardized medicine.

Maytenus sp. (Celastraceae) has also been cited as a natural medicine used in leishmaniasis. It has been demonstrated that different species have leishmanicidal activity, and such activity can be mainly related to terpenes and sesquiterpenes synthesized by this genus (Alvarenga et al., 2008). Although only in vitro studies have been carried out so far, the most important finding is related to the potential of molecules against multidrug resistant parasites (Pérez-Victoria et al., 1999; Kennedy et al., 2001, 2011). The plant Juniperus excelsa M. Bieb (Cupressaceae) was cited only once by traditional communities, and few studies have been conducted on this species. The first published work showed that different extracts of the aforementioned species were able to eliminate L. major promastigotes (Moein et al., 2017). A further triple-blind randomized controlled clinical trial showed that 82% of patients with cutaneous leishmaniasis treated with a topical formulation produced with the leaves of J. excelsa M. Bieb hydroalcoholic extract plus cryotherapy healed the cutaneous lesions compared to the placebo control; additionally, they healed the lesions shorter than placebo control (Parvizi et al., 2017), suggesting that this plant species has bioactive molecules that can be further explored to develop new leishmanicidal drugs.

In this study, Curcuma longa L. (Zingiberaceae) was cited as a natural remedy for leishmaniasis only once. However, the leishmanicidal activity of curcumin has been recorded since 2000 (Rasmussen et al., 2000; Saleheen et al., 2002), and further works demonstrated that synthetic derivatives also present high
activity at eliminating extra- and intracellular parasites (Gomes et al., 2002; Chauhan et al., 2018; Teles et al., 2019), and such activity may be related to programmed cell death in L. donovani (Chauhan et al., 2018). Despite these advances, in vivo studies with Curcuma longa L. or curcumin are scarce in the literature.

In addition, it was verified that the species Urtica dioica L. (Urticaceae) was cited only once, and just one work was published characterizing the leishmanicidal activity of this plant. In this regard, BALB/c mice infected with L. major and treated with the aqueous extract of E. dioica L. at 150, 200 or 250 mg/kg by intramuscular routes three times per week for 30 days significantly decreased the size of cutaneous lesions and suppressed the dissemination of parasites to the spleen; furthermore, the in vivo activity was related to the reduction of arginase levels (Badirzadeh et al., 2020). This enzyme is able to inhibit nitric oxide production, and therefore, low levels of this circulating enzyme may be essential to achieve cure in leishmaniasis.

Details about families, plant species, clinical form of leishmaniasis, parasite species, extract or purified molecules employed in the treatment, doses, route of administration, scheme of treatment and efficacy of the treatments in experimental leishmaniasis are shown in Table 2.

LIMITATIONS

In the present review, it was observed that only 20 articles addressed the traditional treatment of leishmaniasis using medicinal plants. Despite the few articles published to date, a substantial diversity of plants (89 plant families referring to 292 plants) has been cited by 29 traditional communities from different nationalities, which in fact supports the local treatment of symptoms related to leishmaniasis. On the other hand, this potential is far from reflecting reality, and there is still considerable work from an ethnopharmacological point of view to be conducted, which will certainly expand our knowledge about medicinal plants with antileishmanial properties. In this review, the authors emphasize that future ethnopharmacological studies must follow methodological rigor, consistent with the data to be collected. This should be carefully considered because in this review, several limits were found in terms of analysis due to the unavailability of some ethnopharmacological data in the articles consulted. As examples, only 74% of the plants were identified to the species level, 36.5% specified the recipes, 20.6% detailed the route of administration, and only 55.5% mentioned the vernacular names of the plants. Furthermore, 12.9% of the articles did not mention the community that provided traditional knowledge, and some of the authors referred to them as local people or ethnic groups. This is a critical point in the field of ethnopharmacology, as it weakens the right to intellectual property of the traditional communities involved. Furthermore, it was observed that practically no article mentioned the contraindications and possible adverse reactions to these plants, although it is well known that traditional communities often obtain this knowledge from their therapeutic practices. These specific data would be relevant in the case of the development of drugs to treat leishmaniasis, since it is necessary to find drugs with fewer adverse reactions in comparison with those currently in use.

In addition, although a plethora of plants have been described in the traditional treatment of leishmaniasis, only a few works were capable of describing them from a chemical or pharmacological point of view. Furthermore, only a minority of them analysed, in experimental models of cutaneous or visceral leishmaniasis, the efficacy of such plants or purified molecules. Finally, it would be promising to perform bioprospective studies on such plants, since in fieldwork, researchers have already observed their curative properties, which in fact could shorten the time of development of an effective medicine.

FUTURE PERSPECTIVES AND PRIORITIES

This review opens up a huge range of research possibilities in the field of leishmaniasis from a chemical and pharmacological point of view. Table 1 presents 292 plants (216 species and 76 genera) to be investigated as extracts and/or as drugs aimed at developing antileishmanial medicines. Some of these possible “hint plants” are presented in Contributions of Some Botanical Families and Species in the Experimental Treatment of Leishmaniasis. The botanical families and genera that had a higher frequency of citations during this survey are presented and compared with data from other studies in this section.

In addition, the species most frequently mentioned in articles and by the traditional communities in certain countries were highlighted throughout the text. In this context, four species are noteworthy since they were mentioned in four articles: Carica papaya L. (Caricaceae), Cedrela odorata L. (Meliaceae), Copaifera paupera (Herzog) Dwyer (Fabaceae), and Musa × paradisiaca L. (Musaceae), while Nicotiana tabacum L. (Solanaceae), Carica papaya L. (Caricaceae), and Musa × paradisiaca L. (Musaceae) were cited simultaneously by traditional communities from Peru, Ecuador, and French Guiana. Thus, these last two species are among the most cited in articles and by traditional communities.

On the other hand, it becomes important to note that the majority of articles dealing with extracts or purified molecules from plants with ethnopharmacology relevance presented only an inhibitory concentration of 50% against promastigote and/or amastigote forms. Although such data shed light on this scenario, articles should investigate the leishmanicidal properties of plant extracts or molecules against the intracellular amastigote form, which is the form of the parasite that persists and causes disease in the host. Furthermore, it was observed that preclinical studies with medicinal plants traditionally used to treat leishmaniasis are surprisingly rare, but they should be encouraged, since the proof of concept—that a given plant has therapeutic activity in humans—was already provided by healers, and in these specific cases, scientists should standardize mandatory steps related to phytochemistry, pharmacology and parasitology to produce effective medicines.

Finally, this review suggests that future investigations should be guided but not limited to the five species cited above, expanding the chance of discovering new medicines for this disease since, according to the survey presented herein, few or no studies have been performed with plants traditionally used to treat leishmaniasis.
AUTHOR CONTRIBUTIONS
Conceptualization and Supervision: LP and ER. Data acquisition: EB, TS, TP, JJ, LP, and ER. Data curation: EB, LP, and ER. Formal analysis: EB, LP, and ER. Software: TS and TP. Writing: EB, LP, and ER. Writing, review; editing: EB, TS, TP, JJ, LP, and ER.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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