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Leishmanicidal and trypanocidal activities of Bolivian medicinal plants

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Abstract

Cutaneous and mucocutaneous leishmaniasis are endemic diseases in South America, especially in the subandean areas of the humid lowlands of Bolivia. Fourteen plants used topically in folk medicine to treat cutaneous leishmaniasis were collected in the tropical regions of colonization and in the rain forest occupied by Chimane Indians. Three of four plants used by the Chimane Indians exhibited an in vitro activity against three species of *Leishmania*. Two of ten plants used by the colonists showed an in vitro activity. We have also included results obtained with extracts from 53 Bolivian medicinal plants used for other diseases and from 43 plants collected with basis of chemotaxonomic criteria from all parts of Bolivia. All extracts were also screened in vitro against three strains of *Trypanosoma cruzi* (Trypanosomatidae), the causative agent of Chagas' disease.

Key words: Chimane Indians; Colonists; Folk medicine; Cutaneous leishmaniasis; Chagas' disease; Medicinal plants; Bolivia

1. Introduction

For Latin American countries comprising Amazonian areas, development of their vast wilderness regions has become a national priority. The process of colonization of Eastern Bolivia or 'Oriente' began in earnest in the late 1950s, following the Social Revolution of 1952 and the Agrarian Reform law. Nationalisation of mines and expropriation of hacienda lands resulted in unexpected negative effects. In a project to decrease demographic pressures in the highlands, which represent 70% of the country's population, the Bolivian government began an expansion program in the Oriente, including the Departments of Beni, Cochabamba, Santa Cruz, Pando and the tropical areas of the Department of La Paz (Stearman, 1982). Roads were opened and ambitious projects initiated for farming the tropical rain forest and

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for providing settlements for the Quechua or Aymara migrating from the Andean areas of 'Altiplano'.

Upon migrating to these tropical regions, the people become exposed to tropical diseases such as malaria, Chagas' disease, yellow fever and cutaneous and mucocutaneous leishmaniasis popularly known as 'espundia'. They are infected when they prepare their allotments by the bite of the vectors of tegumentary leishmaniasis, namely the phlebotomine sand flies. In Bolivia, the agent causing cutaneous and mucocutaneous leishmaniasis is the protozoan, *Leishmania braziliensis*, which sometime cause disfiguring lesions of the mouth and nose. The colonists or the natives of the endemic regions of cutaneous leishmaniasis recognise this disease that represents a canker which they attempt to burn with natural or chemical products. For example, they may use gasoline, fuel oil, kerosene, sulphuric acid from electric battery, lemon juice, black powder from a battery, caustic latex from trees (*Ficus* sp. (Moraceae) or *Hura crepitans* L. (Euphorbiaceae)) directly on the lesions or sometimes they may burn the canker by direct contact with a candle flame.

The Instituto Boliviano de Biologia de Altura (IBBA) and ORSTOM (French Institute of Scientific Research for the Development in Cooperation) have undertaken investigations in the endemic areas of cutaneous leishmaniasis on the use of medicinal plants as local treatment for this disease. This paper presents the results obtained in the field, the ethnopharmacological and botanical investigations, and the results of a biological study using in vitro bioassays to confirm the parasitological activity. We have tested the extracts on *Trypanosoma cruzi*, an other Trypanosomatidae responsible for Chagas' disease, in spite of the lack of information on any traditional use of plants to treat this disease. The results have been tabulated and we have added the bibliographic data about the use of the described material and chemical references.

2. Materials and methods

2.1. Ethnopharmacological and botanical studies

Ethnopharmacological and botanical researches have been carried out in two endemic areas of cutaneous leishmaniasis in the Departments of La Paz and Beni.

The first is a subtropical region of the Yungas (Department of La Paz), an old area of colonization, essentially inhabited by the highlanders from Altiplano and a minority of black people. The Yungas culminate at 2500–3000 m and are incised by deep valleys between 1300 and 800 m; they have a subtropical climate with pronounced seasons. The flora differ with the altitude among tropical, subtropical, tempered or mountain species. The forest in Yungas has been largely replaced with coffee, fruits and coca cultures. In this part of Bolivia, a number of human cases of visceral leishmaniasis have been described (Desjeux et al., 1986). In the Yungas, transmission takes place in houses, mainly at night on sleeping people, and the evolutive mucocutaneous forms of leishmaniasis are observed in 7% of infected people (Le Pont et al., 1992).

The second is a tropical region of the foothills of the Andes called Alto-Beni (Departments of La Paz and Beni), a new area of colonization by highlanders. Alto-Beni is occupied by a primary forest and by the ultimate mountains of Andes called 'serranias'. The serranias are composed of relieves and valleys oriented SE/NW, their summits reach a height at a contact with the Yungas and do not top 1200 m in their eastern part. The valleys reach a height between 900 and 250 m. This region is inhabited by the colonists and also by native people, Mozetenes, Tacanas or Chimanes. In Alto-Beni we have collected ethnopharmacological and botanical information from the migrant people as well as the natives, especially the Chimane Indians.

Besides selecting plants on the basis of ethnopharmacological criteria, we have collected others on the basis of chemotaxonomic criteria. These plants were harvested in the tropics (Yungas, Alto-Beni), the mountains (Altiplano) and in the Bolivian Chaco (South of Bolivia near the borders of Argentina, Department of Tarija). Many of these plants are used in traditional medicine by other ethnic groups (Aymara, Quechua).

Herbarium samples were identified by numerous botanists of the following institutions: Polygon-

aceae, Pr. R.A. Howard (The Arnold Arboretum of Harvard University, USA); Euphorbiaceae, Dr. M. Huft (Field Museum of Natural History, USA); Bignoniaceae, Dr. A.H. Gentry (Missouri Botanical Garden, USA); Asteraceae, Dr. H. Robinson; Ericaceae, Dr. J. Luteyn; Leguminosae, Dr. R.S. Cowan; Menispermaceae, Dr. R. Barneby; Rutaceae, Dr. J. Kallunki; Sapindaceae, Dr. P. Acevedo and Dr. H. Beck; Solanaceae, Dr. M. Nee (New York Botanical Garden, USA); Piperaceae, Dr. H.A. Valdebenito (Ohio State University, USA); Labiatae, Dr. R.M. Harley (Royal Botanic Garden, Kew, UK); Annonaceae, Pr. P.J.M. Maas (State University of Utrecht, Netherlands); Ulmaceae, Dr. C.A. Todzia (University of Texas, USA); Apocynaceae, Loganiaceae, Dr. A.J.M. Leeuwenberg (University of Wageningen, Netherlands). The remainder of the plants were identified by Dr. S. Beck (National Herbarium of Bolivia) and Dr. J. Solomon (Missouri Botanical Garden, USA). Voucher specimens have been deposited at the National Herbarium of Bolivia, La Paz.

2.2. Preparation of extracts

For each plant part, extracts were prepared by macerating 5 g of powdered dry material in stoppered flasks containing 50 ml of solvent (petroleum ether, chloroform, ethyl acetate or 50% ethanol) for 5 days. When the presence of alkaloids or quinones was detected, we prepared alkaloidal or quinonic extracts. After filtration, the solvent was evaporated under reduced pressure.

2.3. Biological assays

Parasites. Cultures of *Leishmania* spp. and *Trypanosoma cruzi* were obtained from IBBA (Instituto Boliviano de Biologia de Altura, La Paz) and identified by isoenzyme analysis.

Strains of *Leishmania* used during these investigations were as follows: *L. amazonensis* IFLA/BR/67/PH8 — MHOM/GF/84/CAY H-142, *L. braziliensis* MHOM/BR/75/M 2904 — MHOM/BR/75/M2903, and *L. donovani* MHOM/IN/83/HS-70 — MHOM/BR/74/M 2682.

Strains of *Trypanosoma cruzi* used were as follows: C8 CL1 (Brazilian strain), Tehuentepec (Mexican strain) and Tulahuen (isolated from *Triatoma infestans* in Brazil).

Culture and maintenance of Leishmania. Promastigote forms of *Leishmania* were grown at 28°C in USMARU medium (Evans, 1987) containing 10% heat-inactivated (56°C for 30 min) foetal bovine serum. Promastigote cultures in the logarithmic phase of growth were maintained by transferring 10^6 cells/ml. The extracts and fractions (4 mg) were dissolved in 50 μl of DMSO (dimethyl sulfoxide), filtered through a Millipore 0.22 μm filter and then diluted to the appropriate concentration (100–5 μg/ml) with complete culture mediums. Parasites were counted after 48 h of contact with extracts in a haemocytometer and the results were compared with those of controls grown without drug. The 90% inhibitory concentrations (IC_{90}) were chosen for comparing susceptibilities of the strains with tested drugs. Pentamidine® (Aldrich Chemical and May and Baker, UK) and ketoconazole (Janssen Pharmaceutica Co, Belgium) were used as reference drugs in order to evaluate the efficacy of the extracts. Each assay was performed in triplicate.

Culture and maintenance of Trypanosoma cruzi. Epimastigotes of *T. cruzi* were maintained in continuous exponential growth in liver infusion tryptose medium (LIT, Bacto) supplemented with 10% foetal calf serum at 28°C with an inoculum of 10^6 cells/ml. The extracts and fractions (4 mg) were dissolved in 50 μl of DMSO (dimethyl sulfoxide), filtered through a Millipore 0.22 μm filter and then diluted to appropriate concentration (100–5 μg/ml) with complete culture mediums. Parasites were counted after 48 h of contact with extracts in a haemocytometer and the results were compared with those of controls grown without drug. Nifurtimox (Bayer, Germany) and benznidazole (Roche, USA) were used for comparison.

3. Results and discussion

In the present study fourteen plants, used topically to treat cutaneous leishmaniasis in areas where this disease is endemic, have been tested in vitro for toxicity against *Leishmania* spp. and *T. cruzi* (see Table 1). Ten plants are used by colonists and four plants by Chimane Indians. Only

Table 1
Bolivian plants used for the treatment of cutaneous leishmaniasis

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Therapeutic properties	Plant part used[b]
	REFERENCE DRUGS				
	ASTERACEAE				
402	*Baccharis genistelloides* (Lam.) Pers.	Charara (K)	topical poultice	cutaneous leishmaniasis, tropical fever	WP,L
	BIGNONIACEAE				
761	*Jacaranda cuspidifolia* Martius	arabisco (S)	topical poultice	cutaneous leishmaniasis	L
	EUPHORBIACEAE				
851	*Hura crepitans* L.	soliman (C)	topical poultice	cutaneous leishmaniasis	Lat.
781 and *846*	*Pera benensis* Rusby	apaïñiki (C)	topical poultice	cutaneous leishmaniasis	SB
					RB
	LEGUMINOSAE				
696	*Acacia* sp.	wikamallki (K)	topical poultice	cutaneous leishmaniasis	L
577	*Erythrima* sp.	flor de mayo (S)	topical poultice	cutaneous leishmaniasis	SB
	MORACEAE				
581	*Ficus* sp.	matapalo (S)	topical poultice	cutaneous leishmaniasis	Lat.
	OXALIDACEAE				
427	*oxalis* sp.	'sebastian' (Col.)	topical poultice	cutaneous leishmaniasis	L
	PAPAVERACEAE				
568	*Bocconia integrifolia* H and B	palo amarillo (S) amakari (K)	topical poultice	cutaneous leishmaniasis	L,Lat.
					SB
379 and *555*	*Bocconia pearcei* Hutch.	amakari (K)	topical poultice	cutaneous leishmaniasis	L,Lat.
					SB

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
Pentamidine	2.5	2.5	2.5				
Ketoconazole	50	50	100				
Benznidazole				25	50	50	
Nifurtimox				25	25	100	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Kuroyanagi et al., 1985; Fournet et al., 1990
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.,AQ	—	—	—	—	—	—	
PE,	25	25	25	25	25	25	Fournet et al., 1992a
Qui.	10	10	10	10	10	10	
Et.	50	50	50	50	50	50	
PE	5	10	10	5	5	5	
Qui.	5	10	5	5	5	5	
Et.	100	100	100	100	100	100	
plumbagin	5	5	5	5	5	5	Fournet et al., 1992b
3,3′-biplumbagin	50	50	50	50	50	50	
8,8′-biplumbagin	5	5	5	5	5	5	
Lupeol	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
AQ	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
PE	—	—	—	—	—	—	Oechslin et al., 1991
Alk.	10	10	10	10	10	10	
Et.	25	25	25	25	25	25	
PE	—	—	—	—	—	—	
Alk.	25	25	25	25	25	25	
Et.	50	50	50	50	50	50	
PE	—	—	—	—	—	—	Manske, 1953
Alk.	25	25	25	25	25	25	
Et.	100	100	100	100	100	100	
PE	—	—	—	—	—	—	
Alk.	10	10	10	25	25	25	
Et.	100	100	100	100	100	100	

Table 1 (continued)

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Therapeutic properties	Plant part used[b]
	PIPERACEAE				
570	*Piper elongatum* Wahl	matico chico (S)	topical poultice	cutaneous leishmaniasis	L
583	*Potomorphe peltata* (L.) Miqu.	sipu-sipu (K)	topical poultice	cutaneous leishmaniasis	L
	RUTACEAE				
790 and *850*	*Galipea longiflora* Kr	evanta (C)	topical poultice	cutaneous leishmaniasis	L SB RB
	ULMACEAE				
884	*Ampelocera edentula* Kulm	sou'sou' (C)			SB,RB

[a]C, Chimane; Col., colonist; K, Kechua; S, Spanish.
[b]B, bark; F, flowers; L, leaves; Lat., latex; RB, root bark; SB, stem bark; WP, whole plant.
[c]Alk., alkaloidal extract; AQ, aqueous extract; Et., ethanol extract; EA, ethyl acetate extract; PE, petroleum ether extract; Qui., quinonic extract.
[d]*L.a.*, *Leishmania amazonensis* (PH8 or H-142); *L.b.*, *L. braziliensis* (2903 or 2904); *L.d.*, *L. donovani* (H-70 or M 2632); *T.c.*, *Trypanosoma cruzi*.; — , inactive at 100 μg/ml.

two plants employed by colonists showed an in vitro antileishmanial activity: *Bocconia integrifolia* H. and B. and *B. pearcei* Hutch (Papaveraceae). These two botanically similar species, called 'palo amarillo' or 'amakari' due to their brown yellow latex, are often mistaken for each other by their users. In earlier phytochemical studies, benzophenanthridine alkaloids such as sanguinarine and chelerythrine, had been isolated from these plants (Maccio, 1946; Manske, 1953); such constituents might explain their activity (Oechslin et al., 1991).

Three other active plants, *Ampelocera edentula* Kuhlm. (Ulmaceae), *Galipea longiflora* Kr. (Rutaceae) and *Pera benensis* Rusby (Euphorbiaceae) employed by Chimane Indians had earlier been shown to be effective in mice infected with *Leishmania amazonensis* or *L. venezuelensis* (Fournet, 1991), cutaneous leishmaniasis New World species. From these plants we have isolated by activity-guided fractionation, the active compounds, 4-hydroxy-1-tetralone from *A. edentula* Kuhlm. (Fournet, 1991), three naphthoquinones (Fournet et al., 1992a,b) from *P. benensis* and

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
PE	50	50	50	100	100	100	Fournet et al., 1993
Alk., Et.	100	100	100	100	100	100	
PE,EA,ET.Alk.	100	100	100	100	100	100	Fournet et al., 1989
PE,	50	50	50	50	50	50	
Alk., Et.	100	100	100	100	100	100	
PE	—	—	—	—	—	—	Fournet, 1991
Quin.	50	50	50	50	50	50	
Et.	100	100	100	100	100	100	
4-hydroxyl-1-tetralone	10	10	10	10	10	10	

various quinoline alkaloids from *G. longiflora*. (Fournet et al., 1989, 1993a). The choice of these plants by the Chimane Indians is probably the result of numerous empirical applications on the cutaneous lesions of bark, latex or leaves they can find in their environment.

Table 2 shows the results obtained with 53 medicinal Bolivian plants and bibliographical data on these plants. A number of plants were active in vitro against *Leishmania* spp. and *T. cruzi* at 100 μl/ml. From *Oxandra espintana* (Annonaceae), we have previously isolated and identified the new active monoterperne espintanol (Hocquemiller et al., 1991). From the stems and the roots of Bolivian *Berberis* spp. some bisbenzylisoquinoline have been isolated alkaloids (Weber et al., 1989); these compounds (berbamine, obaberine and isotetrandrine) are known to exhibit antiprotozoal activities (Fournet et al., 1988, 1993b). Of 26 medicinal species of the Asteraceae that have been screened, 10 extracts (38%) showed activity at 100 μl/ml, but no extract from the Solanaceae and Leguminosae that were tested showed any activity. For *Aniba canellila* H.B.K. (Lauraceae), a medicinal plant

Table 2
Bolivian medicinal plants not used for the treatment of cutaneous leishmaniasis

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Uses	Plant part used[b]
	ANNONACEAE				
510 and *791*	*Duguetia spixiana* Mart.	pisara (C)	maté	scabies and fungus infections	SB,RB Fr.
777	*Guatteria* aff. *schomburgkiana* Mart.	sañakasa (C)		wood used to build habitation	RB,SB RB,SB
481	*Oxandra espintana* (Spruce) Baillon	rimo (C)	topical	repellent, insecticide	SB
779	*Xylopia aromatica* (Lam.) Mart.	tiki (C)		wood used to build habitation	L SB
	ARALIACEAE				
760	*Oreopanax* sp.	maki maki (K)	massage	to treat rheumatism	L
	ASTERACEAE				
629	*Acanthospermum hispidum* DC.	guajerilla (S)	maté	antidiarrhea, sudorific, eczema, abortifacient	WP
600	*Achyroclina alata* DC.	kkaja wira wira (K)	maté	pneumonia, expectorant	L,AP
693	*Achyrocline flaccida* (Weinm.) DC.	marcela hembra (S)	maté	antispasmodic, anti-helmintic, febrifuge	WP
386	*Achyrocline polycephala* Rusby	china wira wira (K)	maté	expectorant, antidiarrhea	WP
634	*Achyrocline ramosissimosa* (Sch. Bip.) Britt.	uchuj wira wira (K)	maté	expectorant, pneumonia	L
603	*Ageratina pentlandiana* (DC.) K. & R.	pitichilka (K)	maté	sudorific, pneumonia, bronchitis	L
701	*Baccharis dracunculifolia* DC.	chilca (K)	massage, maté	antiseptic, bronchitis	WP,L,S
605	*Baccharis incarum* Wedd.	chajhura (K)		used as combustible	L,S
765	*Baccharis pentlandii* DC.	mayu chilka (K)	massage, maté	expectorant, anti-rheumatism, wounds	L,S
638	*Baccharis salicifolia* (R. & P.) Pers.	chilca marga (K)	massage, maté	antirheumatism, eczema, ichthyotoxic	L,S

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
Alk.	100	100	100	100	100	100	Debourges et al., 1985
PE,Ch.,	—	—	—	—	—	—	Debourges et al., 1987a,b
Et.	100	100	100	100	100	100	Rasamizafy et al., 1987
PE,EA,Et.	—	—	—	—	—	—	
Alk.	100	100	100	100	100	100	Cortes et al., 1985; De Carvalho et al., 1988
PE	25	50	25	100	100	100	
Alk.	100	100	100	100	100	100	
Et.	—	—	—	—	—	—	
Espintanol	1	1	1	1	1	1	Hocquemiller et al., 1991
Isoespintanol	25	25	25	25	25	25	
PE,EA,Et.	—	—	—	—	—	—	Moraes and Roque, 1988
PE,Alk.,	100	100	100	100	100	100	
EA,Et.	—	—	—	—	—	—	
PE	100	100	100	100	100	100	Girault, 1984
EA, Et.	100	100	100	—	—	—	
PE,EA	—	—	—	—	—	—	Zardini 1984a; Schmeda-Hirschmann and
Et.	100	100	100	100	100	100	Bordas, 1990
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Schmeda-Hirschmann and Bordas, 1990
PE,EA	—	—	—	—	—	—	Gutkind et al., 1984; Zardinai, 1984a
Et.	—	100	100	—	—	—	
PE,EA,Et.,AQ	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE	50	100	100	50	50	50	Bastien, 1983
EA	50	50	50	50	50	50	
Et.	100	100	100	50	50	50	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Zardini, 1984a; Givovich et al., 1986
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,Et.	—	—	—	—	—	—	Zardini, 1984a
EA	100	100	100	—	—	—	

Table 2 (continued)

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Therapeutic properties	Plant part used[b]
548	*Baccharis tricuneata* (L.f.) Pers.	china thula (K)	maté	expectorant, anaemia	L,S
660	*Barnadesia odorata* Griseb.	clavel, clavillo (S)		used as combustible	L,S
732	*Chersodoma jodoppapa* (Sch. Bip.) Cabrera	chichi chichi (K) salvia de al puna (S)	massage, maté	expectorant, bronchitis, antirheumatism, febrifuge	L,S
630	*Cnicothamnus lorentzii* Griseb.	azafrán (S)		used as combustible	L,S
657	*Conyza bonariensis* (L.) Cronq.	carnizera (S)	maté	hepatic infections	WP
737	*Diplostephium haenkei* (DC.) Wedd.	yunka piti chilka del monte (K,S)	cough mixture, maté	expectorant, sudorific	L,S
364	*Gamochaeta spicata* (Lam.) Cabrera	chiñi kketo kketo (K)	cataplams, maceration	expectorant, pectoral, antiseptic	L,S
678	*Mutisia acuminata* R. & P.	chinchirkuma (K)	maté, masticate	cardiotonic, diuretic, antispasmodic, used to prepare the 'llipta' for alkalinize the chewing of coca leaves	L,S
672	*Ophryosporus piquerioides* (DC.) Benth.	china wari chilka (K)	maté, poultice	expectorant, migraine	WP
755	*Perezia multiflora* (H. & B.) Less.	escornozera (S), sutuma (K)	maté, poultice	bronchitis, expectorant, anti-inflammatory, anti-pyretic	WP
673	*Pterocaulon alopecuroides* (Lam.) DC.	frezadilla negra (S)	maté poultice	aromatic, astringent, expectorant, insecticide, anti-inflammatory	WP
602	*Senecio adenophylliodes* Sch. Bip.	lechugilla (S)	poultice, maté	antiseptic, antipyretic	L,S
712	*Senecio clivicola* Wedd.	maicha (K)	maté	antidiarrhea	L,S EA,
640	*Tagetes minuta* L.	wacatay (K) wakataya (A)	maté	aromatic, bronchitis, repellent, vermifuge, insecticide	L,S
635	*Tessaria integrifolia* R. & P.	kkallakaśa (K)	poultice, maté	bronchitis, antirheumatism, expectorant, uses against asthma and altitude sickness (soroche)	L,S
756	*Werneria nubigena* H.B.K.	condor cebolla (S) china pupusa (K)	maté	antihelmintic, digestif	WP

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
PE,EA,ET.	—	—	—	—	—	—	Zardini, 1984a; Bohlmann et al., 1979
PE,EA,Et.	—	—	—	—	—	—	Zardini, 1984a
PE,EA,Et.	100	100	100	100	100	100	Girault, 1984; Zardini, 1984b; Morales et al., 1986
PE	—	—	—	—	—	—	Zardini, 1984b
EA,Et.	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	Zardini, 1984a
PE,EA,ET.	—	—	—	—	—	—	Girault, 1984
PE,ET.,AQ	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Bastien, 1983; Zardini, 1984b; Daily et al., 1988
PE,Et.	100	100	100	100	—	100	Girault, 1984
EA	100	100	100	100	100	100	Sigstad et al., 1992
PE,EA	100	100	100	100	100	—	Girault, 1984
Et.	100	100	100	50	100	—	Zdero et al., 1988b
PE	—	—	—	—	—	—	Zardini, 1984a
EA,Et.	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE	—	—	—	—	—	—	Zardini, 1984b
Et.	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Zardini, 1984b
PE,EA,Et.	—	—	—	—	—	—	Scarpa and Aimi, 1981; Girault, 1984; Senatore et al., 1991
PE	—	—	—	—	—	—	Girault, 1984
EA,EA	50	50	50	100	100	—	
Et.	100	100	100	—	—	—	

Table 2 (continued)

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Therapeutic properties	Plant part used[b]
625	*Xanthium catharticum* L.	alkko kichka (K)	poultice, maté	febrifuge, depuratif, anti-inflammatory, anti-septic, jaundice	R S
	BERBERIDACEAE				
624	*Berberis* aff. *paucidentata* Rusby	charoli (K)	maté	antidiarrhoeas	SB
	ERICACEAE				
381	*Pernettya prostrata* (Cav.) D.C.	orkko thorluchi (K)	maté	emetic, sudorific	L,S
	LABIATAE				
636	*Hyptis mutabilis* (Rich.) Briq.	tuknay (K)	maté	carminative	L,S
556	*Marrubium vulgaris* L.	marubio (S), taya (K)	maté	antiseptic, bronchitis, febrifuge	WP
599	*Minthostachys andina* (Britt.)	muña (K)	maté, essential oils	antirheumatism, stomachic insecticide	L
559	*Salvia haenkei* Benth	salvia grande (S)	maté	antipyretic, diuretic	WP
547	*Satureja boliviana* (Benth) Briq	muña (K)	poultice, maté	antirheumatism, migraine, insecticide, sudorific, stomachic	L S
	LAURACEAE				
786 and *855*	*Aniba canelilla* H.B.K.	canelon (S) churéchu (C)	maté	fever, migraine, anti-diarrhoeas and wood used to build the pirogues	SB
856	*Aniba* sp.	cheréchosom (C)		wood used to build the priogues	SB
	LEGUMINOSAE				
874	*Senna reticulata* (Willd) Irwin	sésamé (C)	massage	antihistaminic	L,S
784	*Tephrosia vogelii* J.D. Hooker	tito (C)		ichthyotoxic	L
	LOGANIACEAE				
611	*Buddleja incana* R & P	jatin kiswara (K)	maté	antiseptic, analgesic	L
746	*Buddleja montana* Britton	chiñi kiswara (K)	maté	disinflammatory	L,S
	MYRISTICACEAE				
870	*Iryanthera* sp.	mey'an (C)	topical	fungus infections	Lat., SB

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
PE,EA	100	100	100	100	100	100	Bastien, 1983; Girault, 1984; Cumanda et al., 1991
Et.	75	100	75	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
Alk.	50	100	100	100	100	100	Weber et al., 1989
Et.	50	50	50	50	50	50	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Pereda-Miranda and Gascón-Figueroa, 1988; Barbosa and Ramos, 1992
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Bastien, 1983; Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA	—	—	—	—	—	—	
Et.	100	100	100	100	100	100	
PE,EA	100	100	100	100	100	100	Naranjo et al., 1981; Oger et al., 1992
Et.	—	—	—	—	—	—	
PE,EA,Et.	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	Oblitas-Poblete, 1969; Houghton, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	

Table 2 (continued)

Vouchers A.F.	Botanical name	Vernacular name[a]	Medicinal preparation	Therapeutic properties	Plant part used[b]
	POLYGALACEAE				
601	*Monnima macrolada* Chodat.	suwila (K)	maté	antidiarrhoeas, dysentery	Fl.,L
	POLYGONACEAE				
508	*Triplaris setosa* Rusby	palo santo (S) (especie without ants)	maté	dysentery, migraine	Fl.,L,SB
	ROSACEAE				
563	*Acaena ovalifolia* R & P	pimpinella del monte (S)	maté	antispasmodic	WP
	SAPINDACEAE				
702	*Dodonea viscosa* N.V.	chamana (K)	maté	bronchitis	WP
780	*Serjania tenuifolia* Radlk	wasi (C), barbasco (E)		ichthyotoxic	L,S S
	SOLANACEAE				
685	*Nicandra physaloides* (L.) Gaertn.	capuli cimarrón (E)	maté or topical	antiseptic	L,S
677	*Nicotiana glauca* Grahm.	jatun sairi (K)	poultice, maté	antiasthmatic, intestinal parasitism	L,S
549	*Solanum nitidum* R & P	chinchi chinchi (K, A)	poultice	antirheumatism, emetic	L,S

[a]A, Aymara; C, Chimane; K, Kechua; S, Spanish.
[b]Fl., flowers; Fr., fruits; L, leaves; Lat., latex; R, root; RB, root bark; S, stem; SB, stem bark; WP, whole plant.
[c]Alk., alkaloidal extract; AQ, aqueous extract; Ch., chloroformic extract; Et., ethanolic extract; EA, ethyl acetate extract; PE, petroleum ether extract.
[d]*L.a.*, *Leishmania amazonensis*; *L.b.*, *L. braziliensis*; *L.d.*, *L. donovani*; *T.c.*, *Trypanosoma cruzi*; — , inactive at 100 μg/ml.

used in folk medicine by the Chimane Indians and the people of Beni against fever and diarrhoea, we found an in vitro activity at 100 μg/ml, but this activity was not confirmed in vivo in mice infected with *L. amazonensis* (unpublished results).

In Table 3, we present the results obtained with 43 plants collected on the basis of chemotaxonomic criteria. Extracts of 14 (32.5%) were active in vitro at 100 μg/ml. Various plants contain isoquinoline alkaloids: *Cardiopetalum calophyllum* Schldl. (Annonaceae) (Seguineau et al., 1991), *Abuta rufescens* Aublet (Menispermaceae) (Cava et al., 1972) and *Abuta pahni* Mart. (Dute et al., 1987). From the leaves of *Munnozia maronii* André

Extract/ principle[c]	Antiprotozoal activity (μg/ml)[d]						References
	L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Mata et al., 1991
PE,EA	—	—	—	—	—	—	
Et.	100	100	100	100	100	100	
PE	25	25	25	25	25	25	
EA	50	50	25	25	25	25	
Et.	100	100	100	100	100	100	
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984; Saitoh et al., 1985
PE,EA,Et.	—	—	—	—	—	—	Girault, 1984

(Asteraceae), we have isolated by activity-guided fractionation a sesquiterpene lactone and we have identified it as dehydrozaluzanin C, responsible for antileishmanial activity against *Leishmania* spp. (Fournet et al., 1993c).

These ethnopharmacological studies on Bolivian plants used in folk medicine to treat the lesions of cutaneous leishmaniasis show that various plants have an antileishmanial activity. We observe that the medicinal plants harvested by the Chimane Indians are potentially more effective than the medicinal plants collected in the tropical areas occupied by colonists. The natural knowledge of the rain forest and its flora by Chimane

Table 3
Bolivian plants collected on the basis of chemotaxonomic criteria

Vouchers A.F.	Botanical name	Plant part[a]	Extract/ principle[b]	Antiprotozoal activity (μg/ml)[c]						References
				L.a.	*L.b.*	*L.d.*	*T.c.* Tula.	*T.c.* Teh.	*T.c.* C8 CL1	
	ANNONACEAE									
775	*Cardiopetalum calophyllum* Schldl.	L,S	PE,EA,Et.	—	—	—	—	—	—	Seguineau et al., 1991
		L,S	Alk.	100	100	100	100	100	100	
	APOCYNACEAE									
578	*Mandevilla antennacea* (A.D.C.) K. Schum.	L,S	PE,EA	—	—	—	—	—	—	
			Et.	100	100	100	—	—	—	
	ASTERACEAE									
766	*Ageratina azangaroensis* (Sch. Bip. ex. Wedd.) K. & R.	WP	PE,EA,Et.	—	—	—	—	—	—	Bohlmann et al., 1985
633	*Mikania urticifolia* Hook. & Arn.	L,S	PE,EA,Et.	—	—	—	—	—	—	Guttierez et al., 1988
616	*Munnozia fournetii* H. Robinson	L,S	PE	—	—	—	—	—	—	Robinson, 1987
			EA,ET.	100	100	100	100	100	100	
434	*Munnozia maronii* (André) H. Robinson	L	PE	10	25	25	25	25	25	
			EA	25	25	50	50	50	25	
			Et.	25	50	25	25	50	25	
		S	PE,EA,Et.	—	—	—	—	—	—	Bohlmann and Grenz, 1979
	Dehydrozaluzanin C (sesquiterpene lactone)			2.5	2.5	2.5	5	5	10	Fournet et al., 1993
667	*Stevia yaconensis* Hieron.	WP	PE	100	100	100	100	100	100	Zdero et al., 1988a
			EA	50	50	50	100	100	—	
			Et.	50	50	50	100	—	—	
429	*Vernonia fournetii* H. Robinson & B. Kahn	WP	PE,EA,Et.	—	—	—	—	—	—	Robinson and Kahn, 1985
783	*Vernonia patens* H.B.K.	L,S	PE,EA,Et.	—	—	—	—	—	—	Jakupovic et al., 1986
682	*Vernonia squamulosa* Hook. & Arn.	L	PE,EA,Et.	—	—	—	—	—	—	Catalán et al., 1986
		S	PE,EA	100	100	100	100	100	100	
			Et.	—	—	—	—	—	—	
	BERBERIDACEAE									
584	*Berberis boliviana* Lechl.	B,S	PE,EA	—	—	—	—	—	—	
		B	Et.	50	50	50	50	50	50	Weber et al., 1989
		B	Alk.	50	25	25	75	75	75	
		S	Alk.	50	50	50	100	100	100	
718	*Berberis bumeliaefolia* Schum	B	PE,EA,Et.	—	—	—	—	—	—	
586	*Berberis cf. laurina* Epl.	S	PE	—	—	—	—	—	—	Weber et al., 1989
			Alk.,Et.	100	100	100	100	100	100	Weber et al., 1989
	BIGNONIACEAE									
713	*Macfadyena unguis-cati* (L.) A. Gentry	WP	PE,EA,Et.	—	—	—	—	—	—	
716	*Tecoma stans* (L.) Juss. ex HBK	WP	PE,EA,Et.	—	—	—	—	—	—	
	EUPHORBIACEAE									
503 and *506*	*Acalypha benensis* Britton	L,S	—	—	—	—	—	—		

527	*Acalypha stricta* Poeppig	L	—	—	—	—	—			
	LEGUMINOSAE									
614	*Amicia lobliana* Benth ex Rusby	WP	PE,EA,Et.	—	—	—	—	—	—	
709	*Galactia speciosa* (DC) Britton	L	PE,EA,Et.	—	—	—	—	—	—	
764	*Lupinus altiplani* C.P. Smith	L,S	PE,EA,Et.	—	—	—	—	—	—	
350	*Lupinus bogotensis* Benth	S	PE,EA,Et.	—	—	—	—	—	—	
782	*Rynchosia pyramidalis* (Lamk.) Urban	L	PE,EA,Et.	—	—	—	—	—	—	
	LOGANIACEAE									
664	*Buddleja australis* Vell.	L,S	PE,EA,Et.	—	—	—	—	—	—	
698	*Buddleja tucumanensis* Griseb.	L,S	PE,EA,Et.	—	—	—	—	—	—	Houghton, 1984
	MENISPERMACEAE									
531	*Abuta pahni* Mart.	S	PE,EA	—	—	—	—	—	—	Dute et al., 1987
			Alk.	100	100	100	100	100	100	
787	*Abuta rufescens* Aublet	B,S	PE,EA	—	—	—	—	—	—	Bisset, 1992
			Alk.,Et.	100	100	100	100	100	100	
878	*Anomospermum bolivianum* Kruk. & Mold	B	PE,Et.	—	—	—	—	—	—	
			Alk.	100	100	100	100	100	100	
479	*Odontocarya rusbyi* Barneby	S	PE,EA,Et.	—	—	—	—	—	—	
	ONAGRACEAE									
365	*Epilobium denticulatum* Ruiz & Pavon	WP	PE,EA,Et.	—	—	—	—	—	—	
545	*Fuchsia boliviana* Carr	L,S	PE,EA,Et.	—	—	—	—	—	—	
	PIPERACEAE									
492	*Peperomia apodostachia* Yuncker	L	PE,EA,Et.	—	—	—	—	—	—	
725	*Piper acutifolium* Ruiz & Pavon	L	PE,EA,Et.	—	—	—	—	—	—	
580	*Piper bolivianum* C. DC	L	PE,EA,Et.	—	—	—	—	—	—	
507	*Piper coriaceilimbum* C. DC	L	PE,EA,Et.	—	—	—	—	—	—	
666	*Piper rusbyi* C. DC	WP	PE,EA	100	100	100	100	100	100	
			Et.	—	—	—	—	—	—	
474	*Piper semimetrale* C. DC	L	PE,EA,Et.	—	—	—	—	—	—	
	RUTACEAE									
875	*Metrodonea flavida* Krause	L,S	PE,EA,Et.	—	—	—	—	—	—	
	SOLANACEAE									
405 and *421*	*Solanum actaeabotrys* Rusby	L	PE,EA	—	—	—	—	—	—	
			Et.	100	100	100	100	100	100	
495	*Solanum albidum* Dunal	L	PE,EA,Et.	—	—	—	—	—	—	
686	*Solanum aphyodendron* S. Knapp	L,S	PE,EA,Et.	—	—	—	—	—	—	
727	*Solanum consimile* Morton	L,S	PE,EA,Et.	—	—	—	—	—	—	
408	*Solanum pearcei* Britton & Rusby	L	PE,EA,Et.	—	—	—	—	—	—	
517	*Solanum wrightii* Benth	L,S	PE,EA,Et.	—	—	—	—	—	—	

[a]B, bark; L, leaves; R, root; S, stem; WP, whole plant.

[b]Alk., alkaloidal extract; Et., ethanolic extract; EA, ethyl acetate extract; PE, petroleum ether extract.

[d]*L.a.*, *Leishmania amazonensis*; *L.b.*, *L. braziliensis*; *L.d.*, *L. donovani*; *T.c.*, *Trypanosoma cruzi*.; — , inactive at 100 μg/ml.

Indians explains these interesting results. The present study shows that the ethnopharmacological investigations are a way to find new active compounds against the leishmaniasis or other protozoan diseases.

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