Chapter 2

Ethno-Pharmacological Relevance/ Features of Some Latin American Wild Medicinal Plants

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Introduction

The traditional herbal healers, along with wild medicinal plants and the knowledge they have about them, in certain regions of Latin America, are the prevalent alternatives for some people/communities to cover any primary health care requirements (e.g., treatment to prevent/improve/release pain/symptoms/ disorders/diseases). traditional (plant-based) medicine has gained worldwide acceptance because the plants used for this purpose have been apparently efficacious and safe for a long time (decades/centuries), these being some reasons why the WHO created the traditional, complementary and integrative unit. (WHO 2019).

Despite this, it is important to remember (i) what "ethnopharmacology" studies are about, which are, shortly, the uses, possible action modes, and bioproperties of plant-based preparations; and (ii) the contribution made by phytochemistry and pharmacology along with other related sciences (botany, pharmacy, microbiology, virology, parasitology, etc.) to find/check any biologically active drugs (molecules/fractions/extracts). In that sense, traditional medicine systems need more evidence-based studies that allow establishing the pharmacological potential together with the validation of therapeutic uses of medicinal plants and its chemical constituents [isolated or mixtures (fractions/extracts)] in such a way that safety and effectiveness are verified, as well as to reveal/understand their preventive and/or therapeutic mechanisms (Mukherjee et al. 2010, Schmidt and Klaser-Cheng 2017).

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The 18 wild medicinal plants of interest were selected in agreement with the science literature revision and the know-how of the co-authors taking into account (i) the importance of these plants for the ethnic/afrodescendant/mestizo groups in Bolivia, Brazil, Colombia, Ecuador, Mexico and Peru; (ii) the therapeutic benefits (as treatment for different disorders/diseases); (iii) the pharmacological potential validated/determined (*in vitro*/*in vivo*); (iv) the active extracts/fractions and molecules obtained/isolated; and, (v) the useful parts of plants. Accordingly, the present chapter comprises the text mining of the subject, the general aspects of selected plants from Latin America, and pharmacological properties recognized of extracts/molecules from these plants.

Text Mining for the Topic "*Ethnopharmacology related to Latin American Wild Medicinal Plants*"

For the establishment of the research trend correlated with ethnopharmacological studies of some Latin American wild medicinal plants, a scientometric measurement was performed by using Scopus database (Elsevier 2019), whose data obtained were analyzed through the specialized Vantage Point software for text mining (Search Technology, http://www.thevantagepoint.com/). For this, the following search equation was structured: (*title-abs-key* (*ethnopharmacolog **) *and title-abs-key* (*"medicinal plant *" and wild*)) *and doctype* (*ar*), with which 180 documents indexed in the database were obtained (Figure 2.1), and 2014 and 2015 being the years of greatest scientific activity (20 and 23 articles, respectively). Based on De Solla Price's Law (De Solla Price 1963), the annual growth rate of the articles published since 2000 related to this topic was calculated, which was ca. 23%/year (R^2 0.956); despite that, in the last four years (2016–2019) there was a decrease in the dynamic of publication.

In accordance with the mining analysis, the most important research/application areas were associated with toxicology and pharmacy, medicine, agriculture and biological sciences; these research areas are related to each other due to the interdisciplinary studies. Similarly, anti-inflammatory (25 articles), antioxidant (18), antiparasitic [malaria (10), protozoa (4), helminth (4)], and antimicrobial [bacteria (7), fungi (5)] were the most studied biological properties. On the other hand, Italy (24), Turkey (24), Pakistan (15), India (12) and USA (11) stood out for being the countries with the largest number of records, while in the top five of Latin America were Mexico (6), Brazil (4), Colombia and Peru (3), and Argentina (2).

When the plants of interest in the search equation were considered, *Guazuma ulmifolia* (198), *Calophyllum brasiliense* (130), *Amburana cearensi* (98), *Casimiroa edulis* (54), *Montanoa tomentosa* (46) had the highest number of records, while *Renealmia thyrsoidea* (3), *Huperzia compacta* (2),

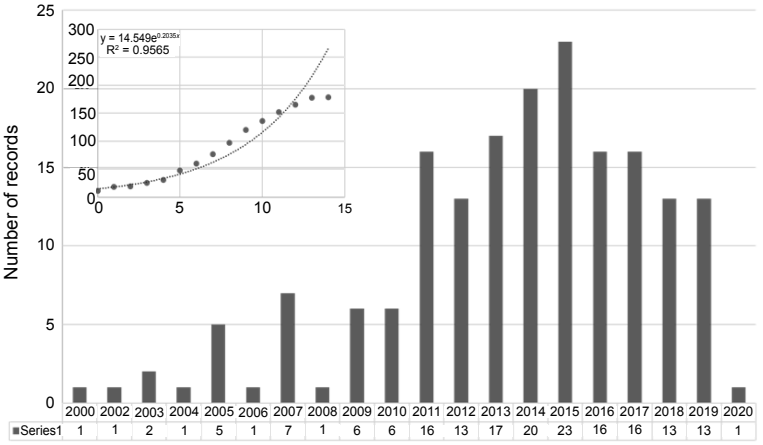

Figure 2.1. Distribution of publication by the number of registers per year (timeline 2000–2020), related to ethno-pharmacological studies of Latin American wild medicinal plants. Furthermore, it is included the trend of the growth rate by De Solla Price law. Source: Bibliometry Unit – CRAI-Library, Universidad Santo Tomas (Bucaramanga). Calculations base on Scopus information (Elsevir, B.V. 2019), processed with VantagePoint software (Search Technology).

H. espinosana (2), *H. tetragona* (1) and *Salacia impressifolia* (1) were the ones with the lowest number of records. Subsequently, Brazil and Mexico were the countries with the highest number of registers that involved the first three plants (*G. ulmifolia*, *Cal. brasiliense* and *Am. cearensis*), and the primary biological effects established for these plants were antioxidant, antibacterial and anti-inflammatory, each one with 36, 32 and 29 registers.

Selected Plants from Some Latin American Countries

Based on the review of the scientific literature and in the know-how of the co-authors, 18 plants (among herbs, shrubs and trees) from Bolivia, Brazil, Colombia, Ecuador, Mexico, and Peru were selected (three for each country), which have different/interesting ethnobotanical uses and some pharmacological results validated. These plants are *Adiantum cf. latifolium* Lam. (Pteridaceae), *Renealmia thyrsoidea* Poepp. (Zingiberaceae), *Salacia impressifolia* A.C. Sm (Hippocrateaceae), *Amburana cearensi* A.C. (Fabaceae), *Caesalpinia ferrea* (Mart. ex Tul.) L.P. Queiroz (Fabaceae), *Echinodorus macrophyllus* (Kunth) Micheli (Alismataceae), *Brosimum utile* Kunth. (Moraceae), *Guazuma ulmifolia* L. (Malvaceae), *Calophyllum brasiliense* Cambess. (Calophyllaceae), *Huperzia compacta* (Hook.) Trevis., *H. espinosana* B. Øllg., *H. tetragona* (Hook. & Grev.) Trevis. (Lycopodiaceae), *Agastache mexicana* (Kunth) Lint. & Epling. (Lamiaceae), *Casimiroa edulis* La Llave & Lex. (Rutaceae), *Montanoa tomentosa* Cerv. (Asteraceae), *Campsiandra angustifolia* Spruce ex Benth. (Fabaceae), *Copaifera paupera* (Herzog) Dwyer (Fabaceae) and *Sambucus peruviana* Kunth (Adoxaceae)—Figure 2.2. In other countries (from Latin America and/or Asia) different from those mentioned above, some of these plants have been found and certain indigenous/mestizo/afro-descendant communities have used them. In Table 2.1, each species has been described briefly in a general way.

Referring to Table 2.1, the plants under study are mainly (~ 56%) evergreen flowering trees (with fruits) with heights between 2–60 m, while the other species (~ 44%) are shrubs/fern up to 3 m. These plant species are mostly distributed in Latin American (tropical forest) although some of them (e.g., *Ad. latifolium*, *S. impressifolia*, *Cae. ferrea*, *B. utile*, *G. ulmifolia*) have been found in other regions of the world (e.g., India, Zimbabwe, China, Malaysia, Vietnam, Sri Lanka), where they were introduced. The different parts (flowers, leaves, fruits, seeds, barks, roots, oleoresins/exudates) of the trees/shrubs have some important ethnobotanical uses as medicine, food or source of ink by indigenous/mestizo/afro-descendant groups (e.g., Tacana, Bororos, Quilombolas, Witotos, Tikunas, Conibo, Saraguro, Otomi, Nahuatl, Totonaco, Quiché) from Amazon countries (Bolivia, Brazil, Colombia, Ecuador, Peru) and Mexico. The wide range of medicinal uses which these plants present should be noted, such as *antidote*, antiseptic, antipyretic, antifungal, antiherpetic, antiparasitic (leishmania and malaria), vermifuge, antiproliferative/cytotoxic/antitumor, hypotensor, diuretic, emollient, cleanser (against skin conditions), *purgative*, astringent, for treatment of respiratory (asthma, flu, expectorant), neuralgic and digestive (gastritis, diarrhea), circulatory, metabolic disorders, as well as for disorders of reproductive and muscle-bone (arthritis, rheumatism, osteoporosis) systems, against inflammation, diabetes, anemia, contusions, alopecia, *amoebiasis* and hemorrhoids, ulcers, for prevention of *tissue necrosis* (bite of the bushmaster snake), wound healing, among others.

Apart from this, some indigenous/afro-descendant healers (Tacana, Quilombolas, Saraguro) use certain plants for magical-religious healing rituals, for instance, *Ad. latifolium*, *E. macropyllus* and *Hurpezia* spp. ("wamingas/trencillas") have been applied to treat *susto* (folk illness in Bolivia), as protector (healer women in Brazil) and to cure "supernatural" ailments (*shuka*/*vaho* water/negative energy in Ecuador), respectively (Dixit et al. 1995, Bourbonnais-Spear et al. 2007, Maciel and Neto 2006, Armijos et al. 2012, 2014); other plants have been used by indigenous/peasant communities (Ingano, Coreguaje, Witotos, Huasteca (teenek), Bora-Miraña, Tikunas and Cocamas) as an important source of food, e.g., *B. utile* (exudate/resin) as a lactagogue (substitute milk), *G. ulmifolia* (fruit/seed/sap) to prepare flour/beverage/candy, and *S. impressifolia* and *Cas. edulis* (fruits) as edible fruit (Standley and Steyermark 1946, Bernal and Correa 1989, García-Barriga 1992, Argueta and Cano 1994, Castaño-Arboleda et al. 2007, Quattrocci 2012, Grandtner and Chevrette 2014, Texeira et al. 2019). For particular plants such as *B. utile*, *G. ulmifolia*, *Cal. brasiliense* and *Cop. paupera*, its exudates/oleoresins resulted to be the parts with the main ethnobotanical uses due to greater pharmacological effects.

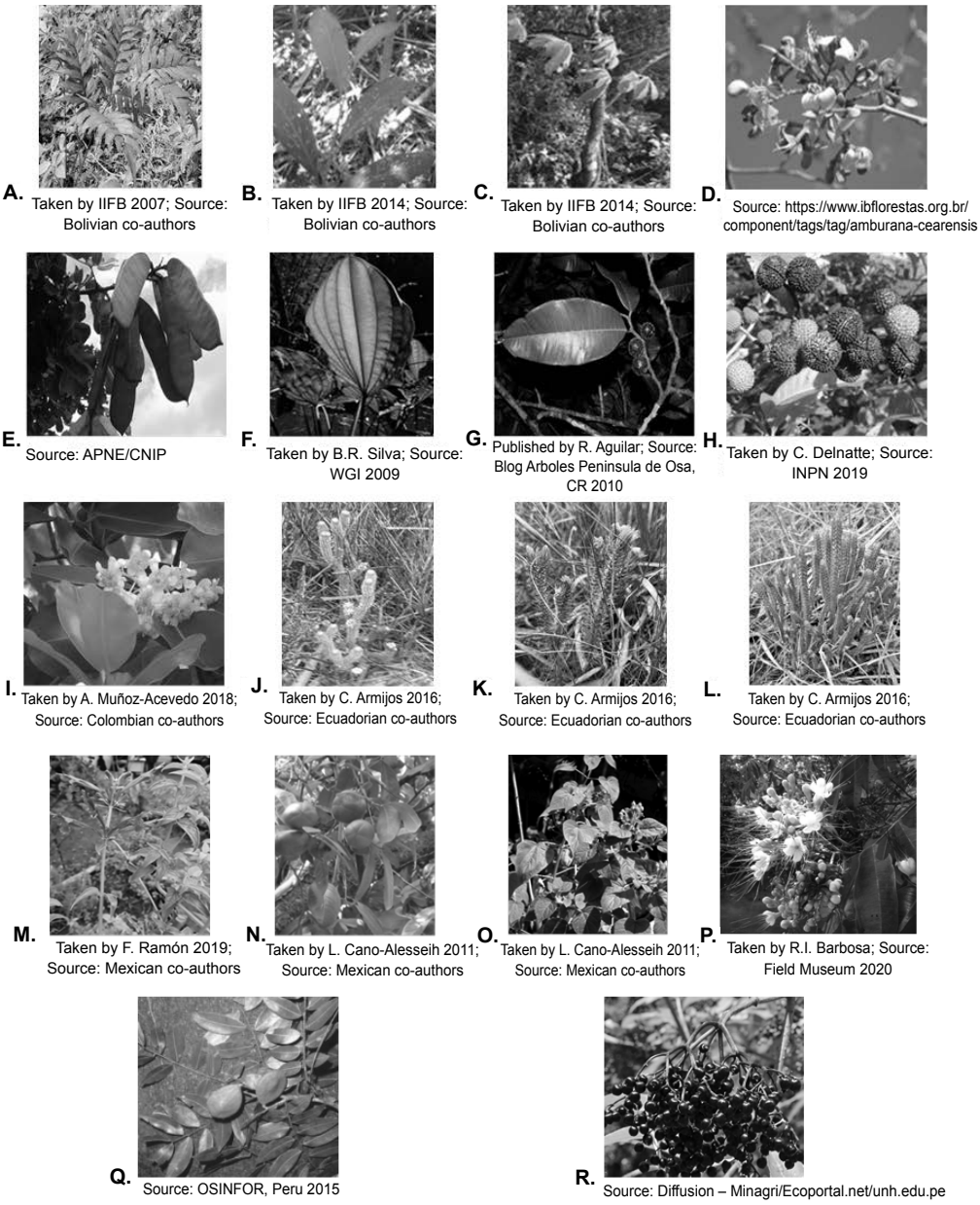

Figure 2.2. Images of the 18 interesting plants from Latin American countries. **A.** *Ad. latifolium*; **B.** *R. thyrsoidea*; **C.** *S. impressifolia*; **D.** *Am. cearenst*; **E.** *L. ferrea*; **F.** *E. macrophyllus*; **G.** *B. utile*; **H.** *G. ulmifolia*, **I.** *Cal. brasiliense*; **J.** *H. compacta*; **K.** *H. espinosana*, **L.** *H. tetragona*; **M.** *Ag. mexicana*; **N.** *Cas. edulis*; **O.** *M. tomentosa*; **P.** *Cam. angustifolia*; **Q.** *Cop. paupera*; **R.** *S. peruviana*.

Pharmacological Properties Recognized from Selected Plants from Latin America

The pharmacological properties (including *in vitro*/*in vivo* assessments) determined from extracts/isolated compounds obtained from the useful parts, according to the traditional uses reported for each plant and by indigenous/peasant/afro-descendant communities are included in Table 2.2.

Table 2.1. General information (including synonyms, common names, etc.) along with the ethnobotanical uses for some communities related to the 18 selected plants from Latin America.

Countries	Plants	Synonyms	Common names	Morphological characteristics	Communities	Ethnobotanical uses	References
Bolivia	*Adiantum latifolium*	*A. fovearum*, *A. humile*, *A. lucidum* var. *bipinnatum*	Atarisi huachidhi (Bolivian Tacana language), sorrapilla (Peru), shebebe (Shipibo/Conibo), shakushia (Amahuaca), montañero, cermanar (Colombia), avenca (Brazil)	Fern, 25–60 cm (height)	Ethnic groups from Bolivia, Brazil, Peru and Colombia	For skin infections, wounds, necrosis; as anxiolityc, analgesic, and antiinflammatory.	Dixit et al. 1995, Lopez et al. 2001, Bourbonnais Spear et al. 2007, Nonato et al. 2011, Arévalo-López et al. 2018
	Renealmia thyrsoidea	*R. cardenassi*, *Alpinia silvicola*, *Ethanium thyrsoideum*, *Amomum thyrsoideum*	Shiguango (Kichwa), nhaca nhaca (Bolivia), gönequemö, tëtemö (Huao, Ecuador), vira-cirindanga (Colombia), u´yume (Peru)	Flowering herb with fruits, 2–6 m	Ethnic groups from Bolivia, Ecuador	Against snakebites, leishmaniasis ulcers diarrhea; as healing and antipyretic	Davis et al. 1983, Muñoz et al. 2000, Odonne et al. 2013, Gómez-Betancur and Benjumea 2014, Cabanillas et al. 2014, Félix-Silva et al. 2017, Arevalo-López et al. 2018
	Salacia impressifolia	*Anthodon grandiflorum*, *S. grandiflora*, *Raddia impressifolia*	Panu/guapomó (Bolivia), miraruíra (Brazil), yuu pot (Colombia), chuchuhuasa (Perú), guoguo (Mexico), cachete viejo (Venezuela)	Flowering tree/liana with fruits, 5–10 m	Ethnic groups from Bolivia, Brazil and Peru	To treat diabetes, inflammation, general pain, rheumatism, cancer, dengue and renal affections	Bourdy et al. 2000, Grandtner and Chevrette 2014, Paz et al. 2018, Vásquez-Ocmín et al. 2018, Rodrigues et al. 2019
Brazil	*Amburana cearensis*	*Torresea cearensis*, *A. claudii*, *T. acreana*	Umburana-de-cheira, imburana (Brazil), cumaré (Paraguay), sorioco/tumi (Bolivia), caschoú (French Guiana), tsaik/tsantimatiqui (aguaruna/asháninca, Peru)	Perennial flowering tree, 4–10 m	Ethnic and afrodescendant groups from Brazil	As treatment for rheumatism, as well as for respiratory, neuralgic and digestive disorders	Lorenzi 1992, Cunha and Ferreira 2003, Almeida et al. 2005, Da Conceição et al. 2011, Quattrocci 2012, Silva et al. 2013a, Grandtner and Chevrette 2014, Braga 2015, Lima 2015
	Caesalpinia ferrea	*Libidibia ferrea*, *C. leiostachya*, *Apuleia ferrea*	Jucá, pau-ferro, ibirá-obi, imira-itá	Perennial flowering tree, 4–10 m	Ethnic groups from Brazil	Against respiratory and digestive disorders; to treat anemia, tuberculosis, diabetes and as healing and antiseptic, etc.	Di Stasi and Hiruma-Lima 2002, Maia et al. 2004, Queiroz 2009, Oliveira et al. 2010, Quattrocci 2012, Farias 2013, Grandtner and Chevrette 2014, Lewis 2015, De Souza 2015
	Echinodorus macrophyllus	*Alisma macrophyllum*, *E. scaber*, *Aquarius macrophyllus*	Chapéu-de-couro, chá-de-campanha, erva-do-pântano, erva-do-brejo, congonha-do-brejo	Flowering cryptophyte herb, with rhizome and fruit, 0.5–1.1 m	Ethnic and afro-descendant groups from Brazil	To release renal, respiratory, liver and skin disorders, as well as hypertension, diabetes, rheumatism	Stalcup 2000, Maciel and Neto 2006, De La Cruz 2008, Alonso 2016, Cajaiba et al. 2016, Nunes et al. 2016, Canalli and Bove 2017, Teixeira et al. 2017, Dos Santos et al. 2019, Pasa et al. 2019

Colombia	*Brosimum utile*	*B. allenii, B. foetidum, B. krukovii, B. humboldtii, Alicastrum utile, Galactodendron utile, Piratinera utilis*	Árbol de leche, sande (negro), yanchama colorada, Nw´wiri, noeme (Ticuna), avichuri, b(v)aco, amapa-murure, frutipán de monte, lechero, jihuigene/panguana, palo de hule	Perennial flowering tree (with milky exudate and fruits), up to 50 m	Ethnic and peasant groups from Colombia, Peru, Brazil	Against digestive, skin, respiratory and reproductive disorders; as food (latex is lactagogue)	Bernal and Correa 1989, García-Barriga 1992, Castaño-Arboleda et al. 2007, Quattrocchi 2012, Grandtner and Chevrette 2014
	Guazuma ulmifolia	*G. bubroma, Theobroma guazuma, Bubroma guazuma, Diuroglossum rufescens*	Aquiché, bolaina, cabeza de negrito, caulote, gua(á)c(s)imo(a), iumanasi, guasmo, jacocalalu, jenumara, tzuyui, ajya, cambaaca, chico-magro, pixoy, jumú, ya ana, yaga yana, mutamba	Perennial flowering and many-branched tree (with fruits), 5–15 m	Ethnic/peasant groups from Brazil, Panama, Peru, Colombia, Ecuador	As emollient, analgesic, diuretic; to treat malaria, skin conditions and gastrointestinal/respiratory disorders; also, as food	Bernal and Correa 1989, García-Barriga 1992, Roth and Lindorf 2002, Quattrocchi 2012, Grandtner and Chevrette 2014, UEIA 2014, Al Muqarrabun and Ahmat 2015, IUCN 2019, Pereira et al. 2020
	Calophyllum brasiliense	*C. antillanum*, *C. calaba*, *C. jacquinii*, *C. lucidum*, *C. piaroanum*, *C. chiapense*	Árbol de aceite, lagarto (Colombia), jacareuba, guanandi (Brazil), balsamaría (Bolivia), lagarto caspi (Peru), Santa María (Mexico), ocuje (Cuba), Barí, dame Marie (Haiti)	Perennial flowering tree (yellowish milky exudate and fruits), up to 50 m	Ethnic/peasant groups from Brazil, Peru, Colombia	As wound healing, vermifuge, diuretic, antifungal/antidysenteric; to treat skin conditions and relieve pain for lepra	Roth and Lindorf 2002, Quattrocchi 2012, García-Zebadúa et al. 2014, Grandtner and Chevrette 2014, Gómez-Verjan et al. 2015
Ecuador	*Huperzia compacta*	*Phlegmariurus compactus*, *Lycopodium compactum*, *L. jamesonii, Urostachys compactus*	Waminga verde	Perennial shrub, 10–20 cm	Ethnic groups from Ecuador	As purgative agents and for curing supernatural diseases (shuka, water vaho); to treat fractures	Lozano 2009, Bussman and Sharon 2015, Armijos et al. 2016a, Plant List 2019, Tropicos 2019
	Huperzia espinosana	*Phlegmariurus espinosanus*	Waminga oso hembra or musgo				
	Huperzia tetragona	*Lycopodium tetragonum, L. rubrum, Urostachys tetragonus, Phlegmariurus tetragona*	Trencilla roja				

Table 2.1 Contd. .

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Countries	Plants	Synonyms	Common names	Morphological characteristics	Communities	Ethnobotanical uses	References
Mexico	*Agastache mexicana*	*Brittonastrum mexicanum*, *Cedronella mexicana*, *Dracocephalum mexicanum*, *Dekinia coccinea*, *Gordoquia betonicoides*	Toronjil morado, olotillo, abejera, cidronela, melisa, toronjil morado/rojo/colorado, hisopo	Flowering and fragrant erect herb, 50–60 cm	Ethnic/peasant groups from Mexico	As sedative, relaxant, antipyretic; to treat epilepsy, earache, high blood pressure, CNS disorder	Lint and Epling 1945, Santillán-Ramírez et al. 2008, Hernández-Abreu 2009, Ávila-Rosas 2013, Zielińska-Matkowski 2014, Tropicos 2019
	Casimiroa edulis	*C. pringlei*, *C. sapota*, *C. tetrameria*, *Fagara bombacifolia*, *Zanthoxylum araliaceum*	Matasano, tapaculo, zapote blanco, pera mejicana, ajachel, ahache, chapote, cacchique, cochitzapotl	Evergreen flowering tree (fruits), 2–18 m	Ethnic/peasant groups from Mexico	To relieve the symptoms related to metabolic, circulatory and central nervous system disorders, as well as food	Standley and Steyermark 1946, Argueta and Cano 1994, Grijalva 2006, Chízmar 2009, Quattrocchi 2012, Orellana 2014
	Montanoa tomentosa	*M. floribunda*, *M. pilosipalea*, *Eriocoma floribunda*, *E. fragrans*, *Montagnaea tomentosa*	Zoapatle, cihuapatli, náhuatl, nocuana-titete-xini-ni, cuana-xuana, ciguapactli, pirimo blanco, too, hierba de la perida	Flowering, branches-prominent shrub (fruits), up to 3 m	Ethnic groups from Mexico	To help childbirth and other disease of women (puerperium, uterotonic, antihemorrhage)	Gallegos 1983, Bejar et al. 2000, Tropicos 2019
Peru	*Campsiandra angustifolia*	*C. rosea*	Huacapurana, acapurana (Peru), acapu-do-igapo, caacapoc, pimakaru'ywa (Brazil), amanagüe, duíra, lavallaga (Colombia), chingo	Perennial flowering tree (fruits), 5–20 m	Ethnic groups from Colombia, Peru, Brazil	As treatment for rheumatism/joint pain, diarrhea, malarial, ulcers, cure sores, female reproductive disorders and as tonic	López-Camacho et al. 2006, Rengifo 2007, Quattrocchi 2012, Grandtner and Chevrette 2014, Lagos-Castillo 2015, Vásquez-Ocmín et al. 2018
	Copaifera paupera	*Copaiba paupera*, *C. langsdorffii* var. *peruviana*, *C. reticulata* var. *peruviana*	Copaiba, copaiba blanca, Bolivia copaifera, copal, copaiba balsam, copaiba resin, nanpiwara	Evergreen flowering tree-shrub (with fruits), up to 35 m	Ethnic groups from Peru, Bolivia, Brazil	As antimicrobial, blood purifier, expectorant, wound, healing, leishmanicidal; to treat bronchitis, dermatitis, herpes, malaria	Pérez 2002, Estevez et al. 2007, Duke 2008, Quattrocchi 2012, Odonne et al. 2013, Grandtner and Chevrette 2014, Vásquez-Ocmín et al. 2018
	Sambucus peruviana	*S. nigra* var. *peruviana*, *S. graveolens*, *S. laciniata*	Sauco (Colombia, Peru, Bolivia, Ecuador), kiola (Argentina), r'ayan (Quechua), sambuco, tilo, saucotillo, cinta de novia	Perennial flowering tree-shrub with fruits, 3–12 m	Ethnic groups from Peru	As febrifuge, diuretic, emetic, diaphoretic, disinfectant, purgative, analgesic; to treat rheumatism, malaria	Brack 1999, Quattrocchi 2012, Grandtner and Chevrette 2014, Bussman and Sharon 2015

Table 2.2. Pharmacological properties (including *in vitro*/*in vivo* assessments) reported for 18 interesting plants in the reviewed scientific literature.

Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
Ad. latifolium	Whole plant, leaves (poultice/decoction/infusion/ compresses)	Fraction 3 (F3) and EtOH extract (EE) (whole plant)	Cytotoxic (LD_{50}, µg/mL)	HeLa line; F3: 36 ± 15; EE: 74 ± 2	Lopez et al. 2001, Nonato et al. 2011, Jhonson et al. 2017, Thomas 2017, Arévalo-López et al. 2018, Pradeep-Kumar et al. 2018, 2019
			Antiparasitic	*Leishmania* spp. (5 strains), IC_{50} (µg/mL), EE: 25 ± 2–78 ± 3; F3: 15 ± 8 - 49 ± 15	
		Acetone (AE) and EtOH extracts (EE) (whole plant)	Antibacterial (ϕ inh. mm)	5 Strains; 1 mg/each extract, AE: 7.1 ± 0.5–9.1 ± 0.4, EE: 6.8 ± 0.3–14.4 ± 0.4	
		Acetone (AE) and MeOH extracts (ME) (whole plant)		3 Strains; 30 µg/each extract, AE: 8.7 ± 0.5–13.9 ± 0.4; ME: 13.4 ± 0.4–16.2 ± 0.5	
		MeOH extract (aerial part)	Antiviral	DNA HSV-1–MIC 12 µg/mL	
			Antiinflammatory	Dose 100–200 mg/kg/IP, 4 h	
			Antinociceptive	Writhing test, 1–100 mg/kg/IP, 200–400 mg/kg/OP	
		MeOH extract (ME) and ethyl acetate fraction (EAF) (aerial part)	Larvicidal	%Mortal.; LD_{50} (mg/kg) on *O. rhinoceros*, ME (1%): 93 ± 2, 5018; EAF (0.1%): 88 ± 2, 583	
		Adiantobischrysene (**1**) isolated of EAF		1–5 mg–~ 55–95% mort., LD_{50} 8.4 mg/kg	
		22-Hydroxyhopane (**2**) isolated of ME		50 mg/kg–93 ± 5% mort., LC_{50} 29 mg/kg	
R. thyrsoidea	Stem, leaves, rhizomes, roots, fruits (infusion/decoction/poultice)	EtOH extracts (rhizomes, leaves, roots)	Antiparasitic (µg/mL)	IC_{50}, *P. falciparum* chloroquine resistant: 7 ± 2; *L. amazonensis* (ax. amast.): 10.0 ± 0.8	Valadeau et al. 2009, Cabanillas et al. 2014, Noriega et al. 2016, 2017
		3–9 isolated from leaves/rhizomes		*L. amazonensis*, EC_{50}, **3**: 20 ± 2, **4**: 23 ± 5, **5**: 36 ± 10, **6–8**: 119 ± 35–166 ± 47, **9**: 68	
		Essential oils (L-leaves/R-rhizomes)	Antioxidant IC_{50} (mg/mL)	L-$ABTS^{+\cdot}$: 1.4 ± 0.1; DPPH·: 20.9 ± 0.4; R-DPPH·: 17.1 ± 0.3; $ABTS^{+\cdot}$: 52.4 ± 0.4	
			Antimicrobial (MIC mg/mL)	4 Bacteria and 2 fungi; L: 0.4–1.4; R: 0.3–11	

Table 2.2 Contd. ...

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Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
Sal. impressifolia	Bark (decoction/maceration/syrup-powder)	EtOH extract (peels)	Antifungal	*C. albicans* - MIC 10 µg/mL	Soares et al. 2018, Rodriguez et al. 2019
		EtOAc extract and fraction 3 from EAE	Anticancer/cytotoxic	Inh. tumor (HL-60) mice; 20 mg/kg, F3: 82%, EAE: 40%	
		EtOAc extract (stem bark)		8 Cell lines; IC_{50}: 8–30 µg/mL; 2 non-cancer cells; IC_{50}: 8–>50 µg/mL	
		Fraction 3 from EtOAc extract Fraction 1 from MeOH extract		8 Cell lines; IC_{50} (µg/mL) - F1: 0.5–1.0, F3: 0.1–0.8; 2 non-cancer cells - F1: 0–0.6, F3: 0.1–0.9	
		10-12 isolated from F3		8 Cell lines; IC_{50} (µM) - **10**: 0.8–2.2, **11**: 0.1–0.6, **12**: 2.9–13.6; 2 non-cancer cells - **10**: 0.8–8.6, **11**: 0.1–38.5, **12**: 0.6–3.5	
Am. cearensis	Bark, seeds, leaves (decoction/tea/infusion)	H_2O/EtOH extract (stem bark)	Antimicrobial	*S. aureus* - MIC: 512 µg/mL	Marinho et al. 2003, Silveira and Pessoa 2005, Oliveira et al. 2009, Figueredo et al. 2013, Lima et al. 2013, Gouveia et al. 2015, Dantas et al. 2016
			Antinociceptive	400 mg/kg, 41% red. contract (writhing test)	
			Immunomodulatory	400 mg/kg/v.o., 81% inh. (OVA-antibodies in asthma model)	
		H_2O/EtOH extract (leaves)	Ovarian follicle protection	Caprine ovarian tissue preantral follicles protection with 0.2 mg/mL	
		H_2O/EtOH:H_2O extracts (stem bark/seeds)	Anti-inflammatory	200 mg/kg, 42% inh. (carrageenan-induced cell migration)	
		H_2O extract (seeds)	Antiedematogenic	500 mg/kg, 50% inh. (carrageenan-induced paw edema)	
		Hexane extract (leaves)	Acaricidal	25 mg/mL on *R. microplus*, 67% efficacy	

Cae. ferrea	Stem, barks, leaves, fruits, seeds, flowers (decoction/macerate/powder/ointment)	H_2O extract (fruits)	Analgesic Anti-inflammatory	50 mg/kg, 67% inh. ear edema (ind. acetic acid); 74% inh. contortions number	Carvalho et al. 1996, Nakamura et al. 2002, Gonzalez 2005, Menezes et al. 2007, Nozaki et al. 2007, Cavalheiro et al. 2009, Sampaio et al. 2009, Oliveira et al. 2010, Vasconcelos et al. 2011, Lopes et al. 2013, Sawada et al. 2014, Nascimento et al. 2015, Biasi-Garbin et al. 2016
		EtOH extract (core stem/leaves)	Antiulcerogenic	10 mg/kg i.v., 15% oral, 37% red. (acute gastric lesion induced by EtOH/HCl test)	
		EtOH extract (core stem/fruits/leaves)	Antioxidant	0.8 µg/mL, 84–94% antioxidant effect (inh. autooxidation homogenate rat brain)	
		MeOH extract (fruits)	Antibacterial	MIC (µg/mL); *S. mutans*: 40, *S. salivarius*: 66, *S. oralis*: 100, *L. casei*: 66	
			Antifungal	*C. albicans*, MIC: 25 µg/mL	
		H_2O extract (bark)		*T. mentagrophytes* and *T. rubrum* MIC/MFC: 31–62 µg/mL	
			Hypotension	10 mg/kg/i.v., –9% $P_{arterial}$ reduction (measurement mean $P_{arterial}$. in rats)	
			Hypoglycaemic	300 mg/kg/day (streptozotocin-induced diabetics Wistar rats model)	
		Powder (bark)	Wound healing	Complete epithel. 1 mL ointment on goats	
		EtOAc extract (fruits)	Antimutagenic	100 µg/mL, 100% inh. Epstein-Barr antigen induced cells	
		H_2O extract (seeds)	Antinociceptive	1 mg/kg, 30% inh. contract (writhing test)	
			Larvicidal	16 % (v/v), *Aedes aegypti* 85% mortality	
			Enzimatic inhibition	10 % (w/v), 5% residual action on tripsine	
		SO_4^{-2} polysacch. of H_2O extract (seed)	Antiviral	IC_{50} (µg/mL), HSV: 405, Poliovirus: 2	

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Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
E. macrophyllus	Leaves (infusion/macerate)	H_2O extract (leaves)	Immunosuppressive	0.5-5 mg/kg/b.w., 29-41% red. (hind paw edema mice model)	Pinto et al. 2007, Tanus-Rangel et al. 2010, Fernandes et al. 2012, Portella et al. 2012, Nascimento et al. 2014, Da Silva et al. 2016b
		Flavonoid-rich fraction from H_2O extract (leaves)/EtOH extract (leaves)	Antiinflammatory	F-RF: 2.5 mg/kg, red. 30% leukocytes and 90% leukotriene B4; EE: 75% leukotr. B4	
		Hexane extract (leaves)	Antiinflammatory Antinociceptive	25 mg/kg, 52% inh. # writh. (ind. acetic acid); 50 mg/kg, 60-90 min, antinociception	
		EtOH extract (leaves)	Diuretic	300 mg/kg, 30% urine decr. (rats)	
		NaCl 0.9 % solution (crude leaves)	Renoprotection	2 mg/kg, 65% red. urinary peroxides (CP-ind. acute renal lesions in rats)	
		Essential oil (leaves)	Antinociceptive	50 mg/kg, 65% inh. (writhing test)	
B. utile	Latex, fruits (decoction)	Latex suspension in $CHCl_3$/EtOAc	Cytotoxicity	*Artemia salina*, IC_{50}: 48-895 mg/L	Ferrari et al. 2005, Padilla et al. 2008, Rivera-Parada 2012, Chindoy 2013, Jiménez 2015, Acosta et al. 2017
		Alkaloid-rich fraction (**32**) from latex suspension in MeOH	Antimicrobial	4 Bacterial/1 fungal strains, MIC 1.6 mg/mL; 2 fungal strains, 2 mg/mL (ϕ inh. mm) - *T. rubrum*: 19.5±0.5, *E. floccosum*: 17.4±0.5	
		H_2O suspension from latex	Anticancer (IC_{50}, µg/mL)	K-562: 1.5	
		33 isolated from root bark		MCF-7: 26; PC-3: 28; HF: 130	
		$MeOH_{acid}$/Me_2CO:H_2O (7:3) extract (bark)	Antioxidant	Red. power: 59.7±0.4 AsAE/g, AA: 61%, DPPH· - EC_{50}: 1.3; inh: 83%	

G. ulmifolia	Bark, mucilage, leaves, branches (decoction/infusion/poultice)	H_2O suspension from EtOH extract (leaves/flowers)	Gastroprotective	Wistar Rats - 125 mg/kg	Caballero-George et al. 2002, Navarro et al. 2003, Felipe et al. 2006, Lima et al. 2006, Berenguer et al. 2007, Funk et al. 2007, Alonso-Castro and Salazar-Olivo 2008, Hokche 2008, Magos et al. 2008, Kaneria et al. 2009, Jacobo-Salcedo et al. 2011, Boligon et al. 2013, Maldini et al. 2013, Lukman et al. 2014, Calixto Júnior et al. 2016, Da´i et al. 2016, Morais et al. 2017, Kumar and Gurunani 2019
		Proanthocyanidins isolated (BuOH fraction from bark extract)	Angiotensine II type 1 inhibition	CHO-K_1 cell line, IC_{50}: 13–286 µM	
		Procyanidin-rich fraction from acetone extract (bark)	Hypotensive Vasorelaxant	10 mg/kg, vasorelaxant on rats, IC_{50} (ng/mL) 35 ± 12, 101 ± 57	
		H_2O extract (bark)	Antidiabetic (T2-D)	Preadipocites, IC_{50} 1–70 µg/mL	
		MeOH extract (leaves)	Antioxidant	IC_{50} (µg/mL), $DPPH^{\cdot}$: 50.2 ± 0.2, $OH^{\cdot}$: 250 ± 11; $O_2^{-\cdot}$: 72.8 ± 0.4	
		EtOH extract (leaves)		$DPPH^{\cdot}$ - EC_{50}: 120 ± 2 µg/mL	
			AChE inhibition	Inhibition zone, 1 cm	
		Me_2CO:H_2O extract EtOAc fraction (branch bark)	Antiviral	P-1 and BHV-1 viruses, 10–40 µg/mL	
		Three flavanocoumarins isolated (MeOH extract of bark)	Anti-STAT1 activity on THP-1 line	**43**,**44** K_D (M) 1–2 × 10^{-6}	
		Tiliroside (**46**) isolated (leaves)	Antiproliferative	IC_{50} (µg/mL) - T47-D: 68, MCF-7: 113	
		EtOH extract (leaves)	Antitumoral	HeLa line, IC_{50} 175 ± 1 µg/mL	
			Cytotoxicity	NCTC929 fibroblasts, LC_{50}: 413 µg/mL	
			Antiparasitic (500 µg/mL)	Promast. inh. *L. infantum*: 95.2 ± 0.4%, *L. brasiliensis*: 92.20 ± 0.04%; epimast. inh. *T. cruzi*: 61 ± 1%	
		EtOH extract (stem bark)	Antibacterial	*S. aureus* NORA and MSRA strains - susceptible	
		Essential oil (leaves)		4 Bacterial strains, MIC 62–750 µg/mL	
		H_2O lyophilized extract (bark)	Antifungal	*C. albicans*; 75 µg extr., ϕ inh.: 26 ± 2 mm	

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Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
Cal. brasiliense	Bark (infusion)	Hexane/CH_2Cl_2 fraction/extract and mammea A/BB (**53**) from EtOH extract (leaves)	Antiparasitic	$IC_{50\text{-}90}$ (µg/mL); *L. amazonensis*, $DE_{promast.}$: 40–73, $DE_{amast.}$: 4–20, $HF_{promast.}$: 17–35, $HF_{amast.}$: 3–17, $\mathbf{53}_{promast.}$: 3–5, $\mathbf{53}_{amast.}$: 0.9–2	García-Barriga 1992, Da Silva et al. 2001, Mesía-Vela et al. 2001, Ito et al. 2002,2003, Cottiglia et al. 2004, Huertas-Reyes et al. 2004a,b, Isaias et al. 2004, Pretto et al. 2004, Reyes-Chilpa et al. 2004,2006,2008, Kimura et al. 2005, Yasunaka et al. 2005, Braga et al. 2007, Brenzan et al. 2007,2008a,b, Ruiz-Marcial et al. 2007, Suffredini et al. 2007,2014, Mesquita et al. 2009, Souza et al. 2009, Albernaz et al. 2010, Honda et al. 2010, García-Zebadúa et al. 2011, Lemos et al. 2012, Tiuman et al. 2012, Blanco-Ayala et al. 2013, Gonçalves et al. 2013, Kudo et al. 2013, Rea et al. 2013, Oliveira et al. 2014, Matsuda et al. 2015, Pires et al.
				LD_{50} (µg/mL); *L. braziliensis*, $DE_{promast.}$: 65, $\mathbf{53}_{promast.}$: 23	
		Mammeas mixture (**52–54**) and **52** from hexane extract (leaves)		3 Strains of *T. cruzi*; IC_{50} (µM), MM: 11–22, **52**: 18; growth inh. $MM_{epim.}$: 17–54, $\mathbf{52}_{epim.}$: 10–18;	
		53 isolated from CH_2Cl_2 extract **58** isolated from hexane fraction		IC_{50} (µM); *L. amazonensis*, $\mathbf{53}_{promast.}$: 7.4 ± 0.3, $\mathbf{53}_{amast.}$: 14 ± 2, $\mathbf{58}_{promast.}$: 30 ± 4	
		Coumarin (**53**) from CH_2Cl_2 extract (leaves)		*L. amazonensis*, red. lesion mice, 18 mg/kg/d (i.m.): 60%; 0.2% (topical): 68%	
		Hexane fraction and CH_2Cl_2 extract from leaves		LD_{50} (µg/mL); promast. *L. amazonensis*, HF: 40, DE: 20	
		CH_2Cl_2 extracts from root wood (RW)/bark (RB)		IC_{50} (µg/mL); *P. falciparum* - RWE: 6.7 ± 0.9, RBE: 9.50 ± 0.02; *L. chagasi* - $RWE_{promat.}$: 27.6 ± 0.8; *T. cruzi* - $RBE_{epimast.}$: 97.1 ± 0.4	
		CH_2Cl_2 extract and **67** isolated from leaves/stems		IC_{50} (µg/mL); *P. falciparum* - DE: 8 ± 2, **67**: 55 ± 14	
		Different extracts from leaves/stems		IC_{50} (µg/mL); *P. falciparum* - EAE: 9 ± 1, DE/EAE: 8 ± 1	
		69 isolated of hexane/MeOH extract from stem bark		*T. cruzi*; IC_{50} (µM), $\mathbf{69}_{trypomast.}$: 220, $\mathbf{69}_{amast.}$: 210	

		73/**76** isolated from MeOH extract (heartwood)	Antioxidant	**73**/**76** scavenged to ROS ($O_2^{\cdot-}$, $HO^{\cdot}$, $ONOO^{-}$), IC_{50}: 0.070 ± 0.03–336 ± 9 μM	2016, García-Niño et al. 2017, Klein-Júnior et al. 2017, Mesa-Vanegas et al. 2019a,b, Rodríguez-Hernández et al. 2019
		Soxhlet (hexane/CH_2Cl_2)/SFE-CO_2 extracts (leaves)		$DPPH^{\cdot}$, IC_{50} (μg/mL) - HE: 243, DE: 207, SFE: 132–149	
		EtOH extracts (leaves/stems)	Angiotensine converting enzyme inhibition	100 μg/mL, ACE inh., LE: 34 ± 2%, SE: 55 ± 16%	
		CH_2Cl_2 extracts from root wood/bark	Antifungal	MIC (μg/mL), *C. neoformans* RWE/RBE: 2; *C. albicans* RWE: 8, RBE: 16	
		PCA isolated from MeOH extract		2 Strains, MIC-PCA: 400–500 μg/mL	
		Different extracts and molecules from flowers/leaves/stems/fruits/roots	Antibacterial	9 Strains, $MIC_{Fl/L/S/Fr/RE}$: 100–900; PCA: 200–800, **70**: 200–800.	
		Soxhlet/maceration/SFE-CO_2 extracts (leaves) and isolated coumarin **61**		*M. tuberculosis*; MIC 62.5 μg/mL, for all extracts; MIC 125 μg/mL, for **61**	
		CH_2Cl_2:MeOH and H_2O extracts from leaves/stems/fruits		4 Strains, MIC/MBC (μg/mL), DME: 190–510/250–810, WLE: 280–600/300–840	
		Chromanones acids (**88**–**91**) isolated of hexane/EtOAc extract (bark)		MIC (μg/mL), *S. epidermis*: 16, *B. cereus*: 1–16	
		Hexane/$(CH_3)_2CO$/MeOH extracts and **52**/**72**/**73**/**76**/mammea A/AA isolated from leaves/heartwood		MIC (μg/mL), HE/AE/ME - *S. aureus*: 2–32, *E. coli*: 128–512, MSSA/MRSA: 8–32; **73**/**76** - *E. coli*: 128, **52**/**72**/**73**/**76**/mammea A/AA - MSSA: 1–256	
		CH_2Cl_2 fraction and hydroethanol extract from stem bark		*H. pylori*; 125–1000 μg/disk (ϕ inh. mm), WEE: 8–14, DF: 10–16	
		Hexane extract and chromanone acid-rich fraction from stem bark		*H. pylori*; 25–400 μg/disk (ϕ inh. mm) - HE: 7–14, CARF: 10–12; MIC 31 μg/mL, growth inh. CARF: 17–44%	

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Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
			Antiulcer	Gastric ulcer red., 5–100 mg/kg HE: 63–97%; 20–100 mg/kg CARF: 67–95%	
		Xanthones and coumarins isolated of $(CH_3)_2CO$/MeOH extracts (heartwood)		H^+/K^+-ATPase inh., IC_{50} (µM), xanthones: 47 ± 8–173 ± 9, coumarins: 110 ± 8–638 ± 149	
		$CHCl_3$ fraction and **68**/**71** from MeOH extract (roots)	Antinociceptive	CF (mg/kg), ID_{50} 9–48 i.p. (132 p.o.), 41–94% inh. const. (≠ tests); **68:** ID_{50} 7 µmol/kg, **71:** ID_{50} 28 µmol/kg	
		Polar/non polar fractions, **50**/**70** and MeOH extracts, (flowers/fruits/roots)		ME (3–10 mg/kg i.p.), 70 ± 6–80 ± 4% inh. constr. (writhing test); PF - 81 ± 8%; NPF - 98 ± 6%; ID_{50} (µmol/kg) **50**: 12 (84 ± 4%), **70**: 30 (94 ± 2%)	
		62/**63** isolated from stem bark	Cytotoxicity/antitumoral-anticancer	6 Human cell lines, IC_{50} (µM), $\mathbf{62}_{\mathbf{BV173}}$: 3, $\mathbf{63}_{\mathbf{BV173}}$: 9; **62** on 5 cell lines: 2–5	
		CH_2Cl_2 extract (root)		4 Human cell lines, IC_{50}: 3–18 µg/mL	
		CH_2Cl_2: MeOH extract (wood) H_2O extract (leaves)		100 µg/mL, inh. cell lines; KM-12 - DME: 100%, WE: 34%; RPMI8226 - WE: 84%	
		CH_2Cl_2 extract from root bark		NIH-3T3 line, IC_{50}; RBE: 137 µg/mL	
		Hexane extract from stem bark		CHO-k1 line, IC_{50} (µg/mL), HE: 120 ± 4 (24 h) - 8 ± 2 (72 h)	
		73 isolated from heartwood		Normal human PBMC, IC_{50}: 86 ± 12 µM	
		CH_2Cl_2: MeOH and H_2O extracts from leaves/stems		5 Cell lines, GI_{50} (µg/mL) - DME: 2-95, WLE: 0.6–49	
		52/**53** mixture from CH_2Cl_2 extract (leaves)		BMK cells, 24 µg/mL - Inh.: 52 ± 5%	
		50,**52**,**53**,**55–60** isolated from hexane-$(CH_3)_2CO$/MeOH extracts (leaves)		3 Cell lines, growth inh. (31 µM), $\mathbf{50}_{\mathbf{PC3}}$:62%, remaining: 47–100%; IC_{50}: **52**, **53**/**55–60**: 0.04 ± 0.02–11 ± 1.	

		Calanolides/mammea/brasixanthones-brasimarins isolated of $(CH_3)_2CO$ ext. (stem bark)	Cancer chemopreventive	TPA-ind. EBV-EA activ. Raji cells, IC_{50} (mole ratio), **56**, **62**,**64**, **66**, **71**, **72/77–87**: 120–525	
		Hexane/Me_2CO extract (leaves)	Antiviral	HIV-1 RT, IC_{50} (µg/mL), HE: 30, AE: 31	
				HIV-1 RT, inh. (50 µg/mL), HE: 77.9 ± 0.5% (IC_{50} 30 µg/mL), AE: 81 ± 2%	
		62 isolated from stem bark		Inh. HIV-1 replication on infected cells (PMA/TNF-α), IC_{50}: 8.4 µM	
				Inh. HIV-1 entry, 25–65% (10–100 µM)	
		Fractions from hexane/Me_2CO/MeOH extracts and **64–67** isolated from leaves		HIV-1 RT, inh. (50 µg/mL) fract. 18/19 (HE): 75 ± 4%, fract. 2 (AE): 60 ± 4%, EtOAc ins. fract. (ME): 74 ± 2%; IC_{50} (mM), **64**: 0.3, **65**: 0.5, **66**: 1, **67**: 0.7	
H. compacta	Whole plant (decoction/macerate)	Alkaloid-rich fraction from MeOH:H_2O extract (9:1)	Enzymatic inhibition	AChE inh., IC_{50}: 62 ± 17 µg/mL	Wu et al. 2009, Ham et al. 2012, Bishayee et al. 2013, Armijo et al. 2016b, Li et al. 2016
			Antitumoral	PC-3 cell line (dose: 148 µM at 12 h)	
		Tricin	Antioxidant	DPPH·, EC_{50}: 90 µg/mL	
			Antiinflammatory	2 mg/kg induced paw edema (50%)	
H. espinosana		Selgin (**97**)	Enzymatic inhibition	α-Glucosidase inh.: 34–36 µM	
H. tetragona		Alkaloid-rich fraction from MeOH:H_2O extract (9:1)		50 µg/mL, inhibition AChE – 87%, 68%	
			Anti-inflammatory	45 mg/kg, on rats (24% inh.)	
Ag. mexicana	Stems and leaves (decoction)	CH_2Cl_2/MeOH extracts and tilianin (**98**) isolated from leaves	Vasorelaxant Antihypertensive Toxicity	Relax. effect (%) aorta rings (rat); DE: 76%, ME: 62%, **98**: 75-85%; IC_{50} (µg/mL) DE: 189, ME: 232, **98**: 240-276; 50 mg/kg, **98** dec. 38%/35% $P_{syst/diast}$, incr. heart rate 5%; mice, LD_{50}: 6624 mg/kg	Molina-Hernández et al. 2000, Hernández-Abreu 2009, 2013, Ibarra-Alvarado et al. 2010, Ávila-Rosas 2013, Verano et al. 2013, Estrada-Reyes et al. 2014,
		MeOH extract and **98** (whole plant)	Anxiolitic-like effect	Effect at 30 mg/kg p.i. for extract and **98**	

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Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
		H_2O extract (aerial parts)	Anxiolitic-like effect Sedative	AEBT (< 10 mg/kg), BBT (10 mg/kg), HBT (> 10 mg/kg), FST (1–100 mg/kg) on mices; LD_{50} > 5 g/kg	González-Trujano et al. 2015, Flores-Flores et al. 2016, Esquivel-Gutiérrez et al. 2017, Navarrete et al. 2017, Ventura-Martínez et al. 2017, Cruz-Torres 2019
		98 isolated from whole plant (MeOH)	Antihypertensive	ED_{50}: 54 mg/kg, LD_{50}: 6.6 g/kg	
		CH_2Cl_2 extract and **99**–**101** isolated/mixture (aerial parts)	Vasorelaxant	Relax. effect aorta ring (rat), EC_{50} (µg/mL), DE: 174 ± 6, **99**: 211 ± 6, **100**: 40 ± 9, **99**/**101**: 33 ± 6, **99**/**100**/**101**: 34 ± 11	
		H_2O extract (whole plant)	Vasoactive	Rat aortic segment, EC_{50}: 234 ± 46 µg/mL, $E_{max.}$: 25 ± 7% on ACh	
			Antioxidant	$DPPH^{\cdot}$, IC_{50}: 502 ± 1 µg/mL; TEAC: 927 µmol Trolox®/g	
		MeOH extract (aerial parts)		100 µg/mL, inhition $DPPH^{\cdot}$: 93%, $ABTS^{+\cdot}$: 99%, TBARS: 94%	
		MeOH extract from flowers	Spasmogenic	Guinea pig ileum contr. resp. 62 % (316 µg/mL)	
		Essential oil (aerial parts)	Vasorelaxant	Guinea pig trachea ring, 5–50 µg/mL relax. effect 100%; EC_{50}: 18 ± 1 µg/mL	
		Solid (precipitate) from whole plant		Relax. effect (%) aorta rings/smooth muscle (rat); solid: 100% (1 mg/mL), CE_{50}: 4.5 ± 0.7–157 ± 9 µg/mL	
			Hypoglycaemic	Rats, 100 mg/kg solid red. 50% sugar level	
			Antihypertensive	Rats, 100 mg/kg solid dec. 20%/40% $P_{syst/diast}$, incr. heart rate 5%	
		EtOAc extract and **100** isolated (aerial parts)	Antinociceptive	ED_{50} (mg/kg) i.p., EAE: 34, **100**: 2; FT: **100**, ED_{50}: 44; LD_{50}: 2828 mg/kg	
		H_2O extract (leaves)	Anxiogenic	Male rats (EPMT/OFT/FST), 3–12 mg/kg i.p., no change in OFT/FST; at 32 mg/kg incr. mobility in FST	

Cas. edulis	Leaves and seeds (Infusion/ drunk)	H_2O extract (leaves)	Hypotensive (angiotensin II)	Hypertensive rats decr. 17–33% SBP (100–600 mg/kg)	Magos and Vidrio 1991, Magos et al. 1995,1999, Navarro-Ruíz et al. 1995, Ito et al. 1998, Garzón-De-La-Mora et al. 1999, Molina-Hernández et al. 2004, Awaad et al. 2006, 2007, 2012, Vázquez-Cruz et al. 2009, Bertin et al. 2011,2014, Esposito et al. 2011, Froldi et al. 2011, Nagai et al. 2014
			Anxiolitic-like effect	Rats (EPMT/OFT), 25–35 mg/kg incr. exploration	
			Anticonvulsive (MES and METsc)	Rats (OD 100 mg/kg), dec. 50%/70% MES/METsc	
		H_2O and EtOH extracts (seed)		Rats, MES - WE: 70%, 10 mg/kg (2 h); EE: 70%, 100 mg/kg (4 h)	
		H_2O extract (kernel)	Relaxant/contractile effects	Inh. aorta vein constrict. on rats, 0.01–1 mg/mL increased 5HT > NA > $F_{2\alpha}$	
		Hexane and MeOH extracts (seed)	Vasorelaxation (20 µg/mL)	Red. constrict. arterial ring, HE: 86 ± 2%, ME: 95.4 ± 0.9%	
				Relax. arterial tissues of young/older rats, ME: 95 ± 2% (young), 54 ± 5% (older)	
		MeOH extract and molecules isolated (seed)	Vasodilation Antioxidant	Rat art. tissues, ME: 40 ± 2% dilat. (20 µg/mL); EC_{50} - **107**: 4 µM - **114** > **107**; DPPH, ME: 72 ± 3% inh. (600 µg/mL); IC_{50} - **107**: 2 mM - **107** > **114**	
			Hypotensive	Rats, extract induced hypotension	
		Imidazole/synephrine derivatives isolated from MeOH extract (kernel)		Rats, H, MMH and DMH showed hypotensive response lasting 3 min.	
		H_2O:EtOH extract (seed)	Antiviral Antiproliferative	HIV-1 RT (RDDP/RNase H), IC_{50} (µg/mL), RDDP: 0.3, RNase H: 2; K562, CC_{50}: 3×10^{-4} µg/mL	
		EO, EtOH extract/different fractions and coumarins isolated (leaves)	Toxicity Anticoagulant Antimicrobial	LD_{50}, EM > 5000 mg/kg; anticoagulant (s), EM/coumarins (60–400 mg/kg), PT: 22.6 ± 0.7–25.0 ± 0.5, APTT: 35.3 ± 0.8–40 ± 1; 8 bacterial and 3 fungi strains, 60 µg/ each sample (ϕ inh. mm), EO: 13–30; EE: 0–19, EIF: 0–10, EIIF: 0–15; MIC (µg/mL), EO: 12–135; EE: 0–321, EIF: 0–321, EIIF: 0–252	

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		Extracts/isolated compounds	**Tests**	**Results**	
		EtOAc fraction and **103-106/110/111** isolated from MeOH extract (seeds)	Chemopreventive against mutagen DMBA	*S. typhimorium*, IC_{50} (µg/mL) **110**: 2, **103**: 4, **106**: 8, **111**/**104**: 10, **105**: 11; red. lesion mice mamma gland, 10 µg/mL EAF: 80%	
		Different extracts and flavonoids isolated (leaves)	Antioxidant Toxicity	$ABTS^{+}$ (µmol TE/g), ME: 842, EAF: 712, flavonoids: 452–772; LD_{50}: 6.0 ± 0.4 g/kg	
		Coumarins (**108**/**109**) isolated from MeOH extract (leaves)	Adipogenesis	3T3-L1 adipocyte, **108** and **109** (5 µM) incr. (1.5-fold) synthesis of palmitic acid	
		EtOH extract, alkaloid-rich fraction and alkaloids isolated (fruits)	Antihypertensive	Dog, dose (mg/kg), dec. hypert. 10–60 min. - EE: 500 (18%), ARF: 200 (30%), **118**: 50 (45%), **119**: 100 (36%), **120**: 200 (45%), **121**: 300 (33%)	
M. tomentosa	Leaves and flowers (infusión)	H_2O extract (leaves)	Aphrodisiac	Male rats incr. $\#_{eyac.}$ 100%, at 75 mg/kg	Senties and Amayo 1864, Landgren et al. 1979, Lozoya et al. 1983, Bejar et al. 1984, Campos-Bedolla et al. 1997, Carro-Juárez et al. 2004,2006, Sollozo-Dupont et al. 2015, Estrada-Camarena et al. 2019, Lagunes-Merino et al. 2019
			Oxytocinergic-like	Women ing. dose 2–15% causing vaginal dilation/uterine contr./ expulsion dead fetus	
			Abortifacient	Women ing. dose 1.1–1.3 g/kg p-o.a. causing cervix dilation, uterotonic effect	
			Anxiolytic/anxiogenic-like	Female rats, beneficial actions under low hormone conditions (PW challenge)	
			Anxiolytic-like	Male rats, 3 mg/kg ind. effect in EPMT, HBT, BBT,	
				Male rats, OFT, FST related OXT, 50 mg/kg incr. latency immobil., #Fos/ OXT	

		H_2O extract (whole plant)	Anxiolytic	Male rats, incr. oxytocin prod. at 50 mg/kg	
				Hypothal. OXT act. in male rats (HLT/OFT/FST), 50 mg/kg, decr. 32% non-mobility time.	
			Pro-ejaculatoy	Spinal system male rats, 25 mg/kg incr. $\#_{des}$: 13.3 ± 0.3, penile erection/ movement	
		H_2O extract and **136** isolated (leaves)	Uterine motility	Mot. uterine tubes (rats), 20 µL/mL (WE) incr. SAI: 40–290%; 12 µg/mL (**136**) incr. SAI: 87–357%	
		135/**136** isolated from leaves (hexane)	Uterine contraction	10–20 µg/mg, %inh. uter. contr. ind. ACh/OXT/ST, ACh: 53–80, OXT: 68–72, ST: 69–100	
		H_2O and hexane extracts, HE suspension and **136** isolated (leaves)		Uter. strips (rat/dog/guinea pig), WE (20 µL/mL), HE_{susp} (40 µg/mL), **136** (20 µg/mL) inhited contractions	
Cam. angustifolia	Bark (decoction)	MeOH extract (bark)	Enzymatic inhibition	PDE-5, 100–200 µg/mL: 81–89%	Kvist et al. 2006, Ravarocci-Quiroz and Carrasco-Huamán 2010, Ruiz et al. 2011, Vásquez-Ocmín et al. 2018, Schmeda-Hirschmann et al. 2019, Roumy et al. 2020
			Antimicrobial	15 Strains, IC_{50}: 0.3 ± 0.1–1.2 ± 0.4 mg/mL	
			Antioxidant	$DPPH^{\cdot}$, %inh. 94.5 ± 0.3 (2.5 mg/ mL), IC_{50}: 0.069 ± 0.003 mg/mL	
		EtOH:H_2O extract (bark)	Antiparasitic (IC_{50} µg/mL)	IC_{50} (µg/mL), *P. falciparum*: 9, FBIT: 7	
		EtOH extract (bark)		*P. falciparum*, < 10	
				P. falciparum: >10, *L.. donovani*: > 20, *T. brucei gambiense*: > 10	
				L. amazonensis, amast./prom.: > 100	
Cop. paupera	Oleoresin (direct use/topical application)	Oleoresin/kaurene-rich fraction/**137** and nanoemulsions containing to them		*L. amazonensis* - Norm: 17 ± 3–168 ± 7; Nanot.: 2 ± 1–35 ± 10; *L. infantum* - Norm: 11 ± 1–203 ± 18, Nanot.: 2.2 ± 0.8–55 ± 6	Ticunsi et al. 2002, Estevez et al. 2007, Dos Santos et al. 2008, Santos et al. 2008, Izumi et al. 2012, Amorim et al.

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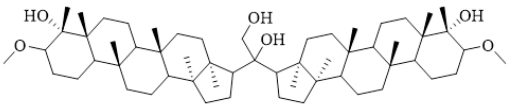
Species	Plant useful parts/types of preparation based on ethnomedicine	Pharmacological effects - *in vitro*/*in vivo* evaluations			References
		Extracts/isolated compounds	**Tests**	**Results**	
		135/**140**-**142** isolated (oleoresin)		*T. cruzi*, epim.: 43 ± 6–168 ± 6 µM, amast.: 1.30 ± 0.06-28 ± 6 µM, $EC_{50\text{-}tryp.}$: 377 ± 88–965 ± 66 µM	2017, Furtado et al. 2018, Rodrigues et al. 2018, Vásquez-Ocmín et al. 2018, Liviac et al. 2019, Ribeiro et al. 2019, Roumy et al. 2020
		Oleoresin		*L. amazonensis*, 11.0 ± 0.4	
			Wound healing	Mice, 200 mg/kg, decr. wounds, NDM: 70%, DM: 43 ± 7%	
			Antimicrobial	5 Strains, IC_{50}: 0.15 ± 0.05–1.2 ± 0.4 mg/mL	
				5 Bacteria, MIC/MBC (µg/mL), MIC/MBC: 62–1000	
		135/**140**,**141** isolated (oleoresin)		3 Bacteria, MIC (µg/mL), *B. subtilis*: 3.1–30, *S. aureus*: 6–50, *S. epidermidis*: 4–40	
		Volatile oil from oleoresin		6 Strains, MIC: 125–2000 µg/mL	
		EtOH extract (oleoresin)	Antioxidant Toxicity	FRAP: 2.43 ± 0.08 µmol/g, TBARS: 14.2 ± 0.4 mg/g; oral tox. rats, LD_{50} > 5 g/kg	
		Oleoresin/leaf EtOH:H_2O extract	Genotoxic/cytotoxic	Mice, OR/EWE: no genotoxic; V-79 line, IC_{50} (µg/mL), OR: 41 ± 8, EWE: 412 ± 66; OR/EWE: no cytotoxic *in vivo*	
		135/**140**-**142** isolated (oleoresin)	Cytotoxic	$LLCMK_2$ and erythrocytes, CC_{50}: 39 ± 5–76 ± 5 µM, HC_{50}: 65.7 ± 0.2– > 1582 µM	
		142 isolated (oleoresin)		4 Cell lines, IC_{50}: 2.5–10 µg/mL	

Sam. peruviana	Leaves, flowers and fruits (infusion/decoction)	EtOH extract (leaves)	Antibacterial	7 Strains, ϕ inh. > 7 mm for all strains at 100 mg/mL	Hernández et al. 2000, Neto et al. 2002, Schmeda-Hirschmann et al. 2005, Bussman et al. 2011, Chirinos et al. 2013, Román-Farje et al. 2017
		Flavonoid-rich fraction from MeOH:H_2O extract (aerial parts)		3 Strains, CAEC (μg/mL): 38–61	
		MeOH:H_2O:HCl extract from dried fruits	Antioxidant	AOC (μmol TE/g), $DPPH^{\cdot}$: 155 ± 6, $ABTS^{+\cdot}$: 303 ± 7, ORAC: 361 ± 23.	
		MeOH extract from fruits		$DPPH^{\cdot}$, inh. 49 ± 4% at 100 μg/mL	
		H_2O and EtOH extracts (leaves)	Toxicity	*Artemia* sp., LC_{50} (μg/mL), WE: 168–10000, EE: 26–124	
		H_2O and EtOH extracts (leaf/bark/root)		*D. magna* (LC_{50}, g/L), *S. zeamais*/*C. koehleri* (mortality, %), LC_{50}: 0.4–23, %Mortal. (160 mg/g): 0–28 (120 h), %Mortal. (160 mg/g): 0–25 (48 h)	

In agreement to Table 2.2, a good antiparasitic effect on promastigotes of five strains of *Leishmania* spp. (*L. amazonensis*, *L. aethiopica*, *L. braziliensis* native, *L. lainsoni*, and *L. braziliensis*), with IC_{50} (μg/mL) values of 78 ± 3, 74 ± 22, 35 ± 5, 28 ± 9, and 25 ± 2, respectively, was exhibited for the total EtOH extract from *Ad. latifolium* (whole plant); even so, a remarkable pharmacological result was found for fraction three (F3) against the same strains whose IC_{50} (μg/mL) values were 37 ± 4, 49 ± 15, 32 ± 11, 19 ± 1, and 15 ± 8, severally. However, F3 turned out to be more cytotoxic on HeLa cells than the total extract (EE), according to the LD_{50} values (Arévalo-López et al. 2018). In consideration to the antibacterial potential for this plant, Thomas (2017) reported that the acetone and EtOH extracts (1 mg for each) from entire plant, tested on five bacterial strains (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli* and *Serratia marcescens*), presented acceptable diameters of inhibition zone (mm) as follows: *P. aeruginosa*: 9.1 ± 0.4–14.4 ± 0.4, *S. aureus*: 0–8.5 ± 0.6, *K. pneumoniae*: 0–6.8 ± 0.3, *E. coli*: 7.2 ± 0.7–10.1 ± 0.4, and *S. marcescens*: 7.1 ± 0.5–8.1 ± 0.3; *P. aeruginosa* being the most susceptible strain for both extracts. The values of minimum inhibitory and bactericidal concentrations (MIC/MBC) on *P. aeruginosa* were ~ 18 mg/mL and ~ 38 mg/mL, in that order, for EtOH extract. In contrast to above statement, Johnson et al. (2017) evaluated the acetone and MeOH extracts (30 μg for each) from whole plant against *E. coli*, *K. pneumoniae*, and *S. aureus*; these authors reported that the two extracts were highly effective on the most bacterial strains (*S. aureus* was the least susceptible strain to the acetone extract), with diameters of inhibition zone (mm) just like that: *E. coli*: 13.9 ± 0.4–16.2 ± 0.5, *K. pneumoniae*: 12.4 ± 0.3–13.4 ± 0.4, and *S. aureus*: 8.7 ± 0.5–13.6 ± 0.5. Furthermore, the MeOH extracts showed a notable antiviral (MIC 12 μg/mL), antinociceptive and anti-inflammatory (inhibition interleukin-1β production), larvicidal (0.1–1 mg extract/fraction, 88 ± 2–93 ± 2% mortality, LD_{50} 583–5018 mg/kg)/antibacterial (5–25 mg/mL extract/fraction, ϕ inh. 15–25 mm) effects using DNA herpes simplex virus type 1 (HSV-1), writhing/formalin/tail-flick tests (1–100 mg/kg/I.P., 200–400 mg/kg/O.P.), and carrageenan-induced/arachidonic acid-induced paw/ear edemas, and *Orycites rhinoceros* and eight bacterial strains, as reported by Lopez et al. (2001), Nonato et al. (2001), and Pradeep-Kumar et al. (2018). The last authors [Pradeep-Kumar et al. (2018, 2019)] isolated two triterpene: a type ecdysteroid [adiantobischrysene (**1**)] and other type hopanoid [22-hydroxihopane (**2**)] from ethyl acetate fraction or methanol extract which presented larvicidal (*O. rhinoceros*) and antibacterial activities.



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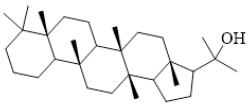

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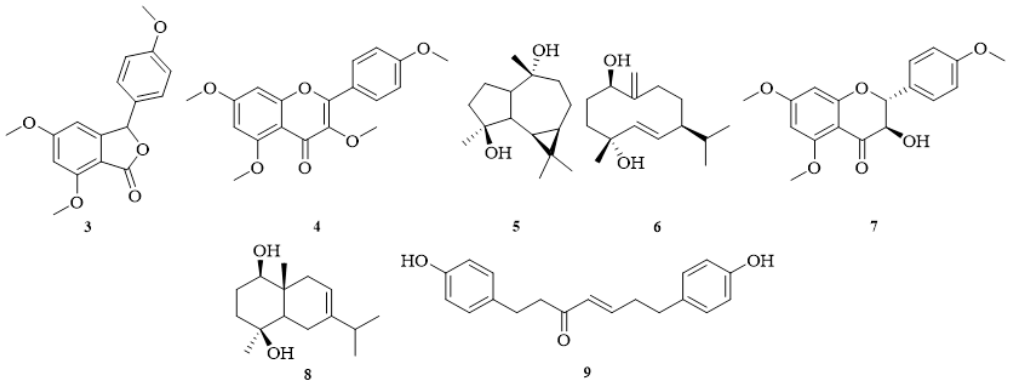
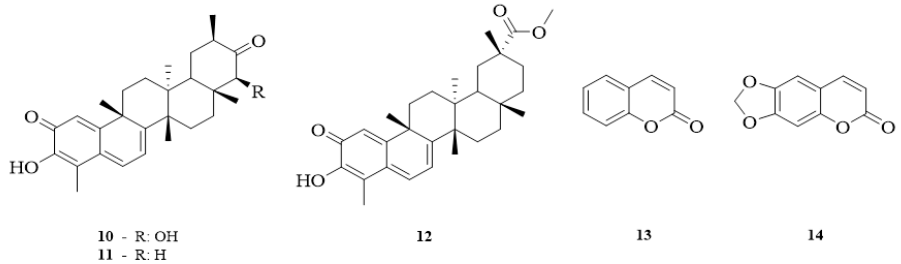
As to *R. thyrsoidea*, some indigenous communities (Yanesha/Chayahuita, Peru; Kichwa, Ecuador) have used this plant against malaria and leishmaniasis (Valadeau et al. 2009, Odonne et al. 2013, Noriega et al. 2017). Valadeau et al. (2009) validated the traditional use when they proved that the EtOH extract from rhizomes was active against *Plasmodium falciparum* chloroquine resistant and *L. amazonensis* amastigotes. Moreover, Cabanillas et al. (2014) isolated 11 and seven constituents (type sesquiterpenes, dihydrobenzofuranone, flavonoids, diarylheptanoids) from leaves and rhizomes, respectively, of which seven (**3–9**) were active (IC_{50}: 20 ± 2–166 ± 47 μg/mL) on *L. amazonensis* axenic amastigote form; the molecules **3–5** had the best IC_{50} values (20 ± 2–36 ± 10 μg/mL). Noriega et al. (2016, 2017) divulged the chemical composition of the essential oil (0.05% yield) from plant leaves/rhizomes and the radical-scavenging ($ABTS^{+\cdot}$ and $DPPH^{\cdot}$) and antimicrobial (*P. aeruginosa*, *E. coli, S. aureus* subsp. *aureus*, *Streptococcus mutans*, *Candida albicans*, *C. tropicalis*) capabilities; scilicet, terpinolene (~ 26%)/α-phellandrene (~ 17%), and β-pinene (~ 41%) were the main constituents for leaves and rhizomes, individually, while the IC_{50} values for radical-scavenging were among 1.4 ± 0.1–52.4 ± 0.4 mg/mL and MIC (mg/mL) values were: *P. aeruginosa*: 0–0.4, *E. coli*: 0–0.4*, S. aureus*: 1.4–10.8, *S. mutans*: 1.4–5.6, *C. albicans*: 0.4–0.7, and *C. tropicalis*: 0.3–1.4.

In another way, *Salacia* genus has been characterized by containing α-glucosidase inhibitors such as salacinol and kotalanol (1-deoxy-4-thioarabinofuranosyl cation derivatives) along with kotalagenin



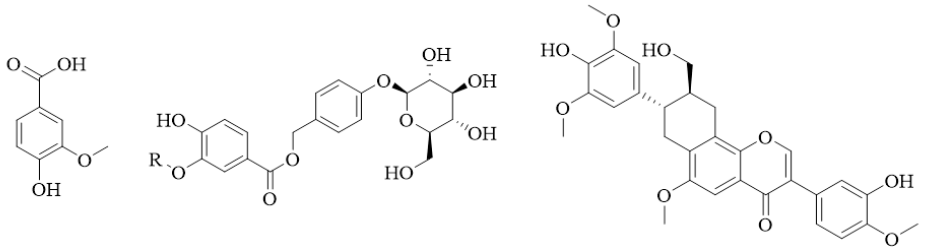
16-acetate (triterpenoid) as active principles (Deepak et al. 2014, Ripardo et al. 2015), as well as other triterpenoids belonging to series type ursanes, oleananes, friedelanes, lupanes, and quinonemethides (Ramakrishna et al. 2015, 2016, Da Silva et al. 2016a), all of them possibly responsible for the traditional use of *Salacia* spp. for the treatment of diabetes. Recently, *in vivo* and *in vitro* antileukemia and cytotoxic activities of extract (ethyl acetate, EAE)/fractions (F1 and F3)/isolated compounds (**10–12**, quinonemethide triterpenes) from stem bark were reported by Rodrigues et al. (2019). The IC_{50} values [μg/mL—extract/fractions, μM—isolated compounds] determined on cancer and non-cancer cells were: EAE—MCF-7: 8, HCT116: 13, HepG2: 27, SCC-4: 10, HSC-3: 10, HL-60: 29, K-562: 30, B16-F10: 18, and MRC-5: 8; F3 (from EAE)—MCF-7: 0.4, HCT116: 0.4, HepG2: 0.1, SCC-4: 0.2, HSC-3: 0.8, HL-60: 0.4, K-562: 0.6, B16-F10: 0.4, MRC-5: 0.1, and PBMC: 0.9; F1 (from ME)—HepG2: 0.5, HL-60: 0.6, K-562: 1.0, B16-F10: 0.5, and PBMC: 0.6; **10** (22-hydroxytingenone)—MCF-7: 2, HCT116: 2, HepG2: 1, SCC-4: 2, HSC-3: 0.8, HL-60: 1, K-562: 2, B16-F10: 1, MRC-5: 0.8, and PBMC: 9; **11** (tingenone)—MCF-7: 0.5, HCT116: 0.6, HepG2: 0.4, SCC-4: 0.6, HSC-3: 0.1, HL-60: 0.4, K-562: 0.5, B16-F10: 0.5, MRC-5: 0.1, and PBMC: 38; and **12** (pristimerin)—MCF-7: 8, HCT116: 9, HepG2: 8, SCC-4: 13, HSC-3: 3, HL-60: 9, K-562: 14, B16-F10: 6, MRC-5: 4, and PBMC: 0.6.

Based on the revised phytochemical studies (Bravo et al. 1999, Costa-Lotufo et al. 2003, Negri et al. 2004, Silveira and Pessoa 2005, Canuto et al. 2006, 2010) on *Am. cearensis*, it was found that alcohol/aqueous extracts from bark/leaves contained constituents type coumarins [e.g., coumarin (**13**), scopoletin, ayapin (**14**)], phenolic derivatives and flavonoids [e.g., 3,4-dihydroxybenzoic acid, protocatechuic acid, vanillic acid (**15**), quercetin, kaempferol, isokaempferide, afrormosine, catechol, guaiacol, 4-methoxy-physetin, amburosides A and B (**16**/**17**)], as well as anthraquinones (crysophanol), sterols (e.g., β-sitosterol, γ-sitosterol, stigmasterol, lupeol) and fatty acid derivatives (e.g., methyl/ethyl palmitate). Due to this diversity of secondary metabolites, the pharmacological effects related to the ethnomedicinal uses could be explained, among them: antibacterial (against *S. aureus*; MIC: 512 μg/mL), antinociceptive, antiinflammatory, analgesic, antispasmodic and bronchodilator activities of the hydroalcoholic extract from the stem bark, without any evidence of toxicity in usual doses (Silveira and Pessoa 2005, Oliveira et al. 2009, Figueredo et al. 2013), as well as immunomodulatory activity on OVA-antibodies in asthma model (400 mg/kg oral; 81% inhibition) (Marinho et al. 2004). An interesting



isolated compound from those mentioned above is the phenolic glycoside amburoside A (**16**), which would be responsible for the *in vitro* bioactivities such as anti-malarial (50 mg/kg; 24% inhibition on *P. berghei*), neuroprotective (0.1–100 µg/mL; 24–64% inhibition) and hepatoprotective activities (25–50 mg/kg) (Bravo et al. 1999, Leal et al. 2005).

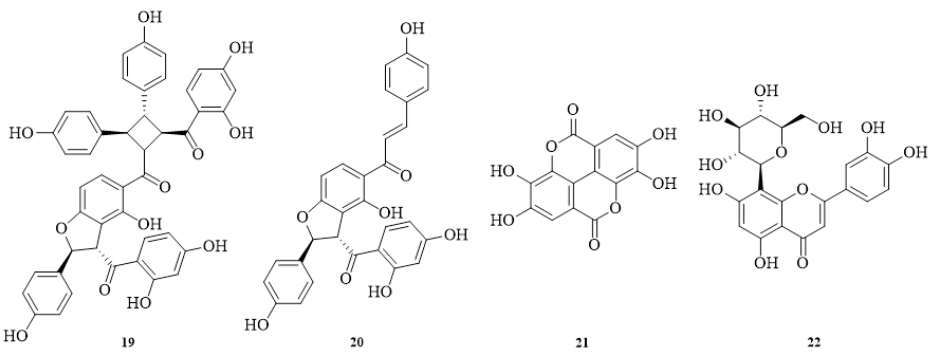
Four other interesting manuscripts by Leal et al. (2003, 2011), Oliveira et al. (2017) and Nunes et al. (2018) reported, respectively, that: (i) the standardized ethanol extracts and vanillic acid (**15**) obtained from trunk barks from cultivated (4–9 month)/wild plants showed similar antiinflammatory activities on different models; (ii) 15 phenolic compounds were isolated including two novel molecules [dilmin (**18**) and lulin] of the 32 constituents (isoflavones, flavanonols, chalcones, isoflavonolignan and isoflavoquinone) characterized by HLPC/MS from resin; the principal compounds were evaluated against human DNA topoisomerase II-α which exhibited a good activity; and (iii) EtOH extract from *Am. cearenses* leaves showed a good solar protection factor (18) due to its content in the phenolic



15 **16** A - R: H; **17** B - R: CH_3 **18**

compounds. In addition, the aqueous extract from seeds presented antiedematogenic activity (Lima et al. 2013); the leaf hexane partition (at 2.5%) also demonstrated acaricidal activity on *R. microplus* (Dantas et al. 2016) and protective activity on the ovarian follicle of goats (Gouveia et al. 2015). Likewise the EtOH extract and the hexane/CH_2Cl_2/ethyl acetate fractions from previous extract [containing coumarin, C_{16}–C_{18} fatty acids (saturated and unsaturated), sitosterol] were able to increase the viability for PC12 cells (despite the toxicity induced by glutamate), as a measurement of neuroprotective effects, without evidencing any toxicity (Pereira et al. 2017).

The chemical diversity, e.g., pauferrols A (**19**)/B (**20**)/C (stem), catechin/epicatechin (bark), gallic (stem/bark, fruits and leaves)/ellagic (**21**) acids (bark and fruits), lectin (fruits and leaves), lupeol, α-amyrin, quercetin/vitexin/orientin (**22**)/isoorientin (leaves) and galactomannans (seeds), of the *Cae. ferrea* organs would be related to its wide medicinal uses (Port's 2011, Lopes et al. 2013, Ohira et al. 2013, De Souza 2015). Several scientific studies have demonstrated the notable pharmacological potential of isolated compounds and plant extracts; for instance, Gonzalez (2005) reported the antiulcerogenic (37% reduction of lesion in treated rats with 1 mL 15% orally) and antioxidant (protector effect 84–94%) activities of the crude EtOH extract from core stem; like the stem, the leaf extract also showed antiulcerogenic property (81% reduction of affected area). In turn, Lima (2012, 2013) stated that the fruit



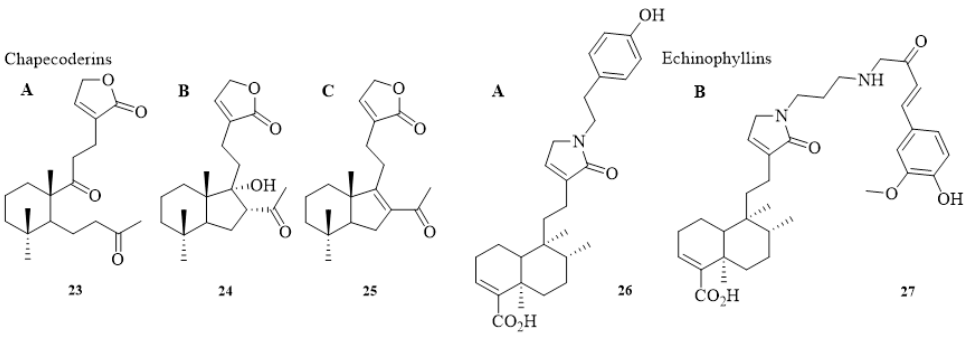
19 **20** **21** **22**

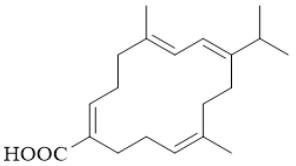
extract (ethanol, 50 mg/kg) showed anti-inflammatory/edematogenic (67% inhibition of ear edema by writhing test) and analgesic (74% reduction of the contortion number) activities. Nascimento et al. (2015) observed the antioxidant effects of ethanol extract by DPPH· (EC_{50}: 4.40 ± 0.05), $ABTS^{+\cdot}$ (EC_{50}: 2.50 ± 0.06) and β-carotene (47% inhibition) methods.

By comparison, Menezes et al. (2007) indicated that H_2O extract (bark) caused hypotension (in non-anesthetized rats) along with vasodilation in the mesenteric arteries; it also demonstrated hypoglycaemic activity in Wistar rats model (dose administered for seven days), reducing and improving their glucose levels in blood and the metabolic state. Likewise, Vasconcelos et al. (2011) found that protein kinase B in the liver/skeletal muscle of rats was increased, whereas acetyl-CoA carboxylase and AMP-activated protein kinase were reduced for both and only in the skeletal muscle, respectively. Still, the H_2O extract of the fruits showed anti-inflammatory activity (10–20 mg/kg, 88–92% reduction in number of writhing), i.e., the paw edema in rat induced by carrageenan was significantly inhibited (23–36% for 1–2 h) by oral administration of 300 mg/kg of the extract (Carvalho et al. 1996). In addition, the aqueous seed extract was active as an antinociceptive agent at 1 mg/kg, probably inhibiting the opioid and cholinergic receptors (Sawada et al. 2014); this extract also displayed larvicide activity against *Aedes aegypti* with 85% mortality (Cavalheiro et al. 2009).

According to Biasi-Garbin et al. (2016), the H_2O, EtOH and acetone extracts from barks presented antifungal activity on *Trichophyton rubrum* (MIC/MFC: 62 μg/mL) and *T. mentagrophytes* (MIC/MFC: 31 μg/mL); moreover, the MeOH extract exhibited antimicrobial activity (MIC: 25–100 μg/mL) against *C. albicans, S. mutans, S. salivarius, S. oralis* and *Lactobacillus casei* (Sampaio et al. 2009). Under other conditions, the ethyl acetate extract (fruits) had a prominent antitumor activity against Epstein-Barr virus early antigen (total inhibition of cell viability, at 100 μg/mL) (Nakamura et al. 2002). Among the isolated and pharmacologically active molecules could be mentioned, e.g., **19** (from acetone stem extract) which revealed a high inhibition (IC_{50}: 2.1 μM) on DNA topoisomerase II as described by Nozaki et al. (2007), and the sulphate polysaccharides (from H_2O seed extract) that disclosed the antiviral activity against herpes simplex virus (HSV, IC_{50}: 405 μg/mL) and poliovirus (IC_{50}: 2 μg/mL) (Lopes et al. 2013).

The Brazilian plant, *E. macrophyllus*, has been constituted by non-volatile [diterpenoids (chapecoderins A/B/C (**23**–**25**, labdanes), echinophyllins A (**26**)/B (**27**) (nitrogen-containing clerodanes), echinoic acid (**28**), echinodolides A/B (**29**, **30**) (cembranes) and flavonoids] (Kobayashi et al. 2000a, b, Shigemori et al. 2002) and volatile (essential oils—EO) secondary metabolites. All of them, both as individual components and in mixtures (extracts/essential oil), could be responsible for some pharmacological properties. For the case of the EO, they had different compositions according to the place of collection, i.e., from Nova Friburgo, the main constituents of EO were dillapiole (24%) and 2-tridecanone (15%) (Coelho et al. 2012), while from Belo Horizonte, the EO was constituted by methyl-palmitate (44%) and dihydroedulan (3%) (Silva et al. 2013b). With regard to the flavonoid content, they are also present in high concentrations (Da Silva et al. 2016b), and a new flavonoid [6-C-hexa-hydroxy-apigenin (**31**)] has been isolated for the species (Silva 2010). Moreover, other chemical groups are present in the plant, such as alkaloids, saponins, xanthones, triterpenoids and steroids (Silva 2010, Tanus-Rangel et al. 2010).





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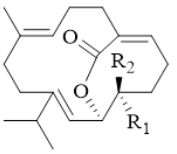
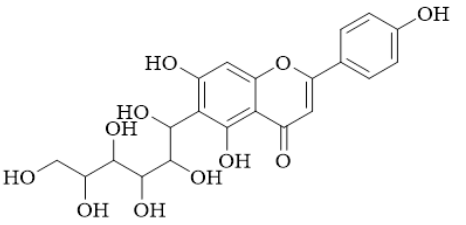


29 A - R_1:CH_3, R_2:OH
30 B - R_1:OH, R_2:CH_3



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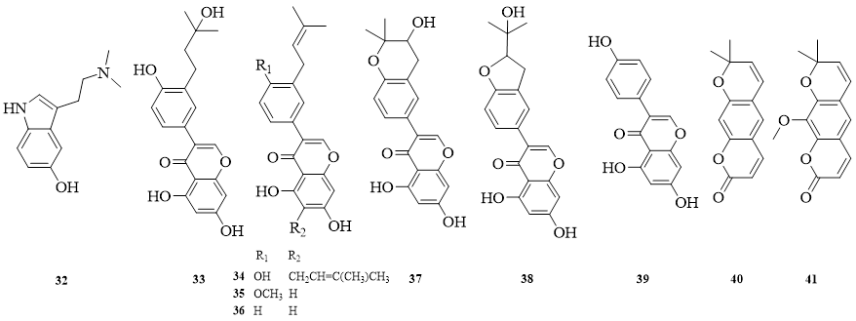
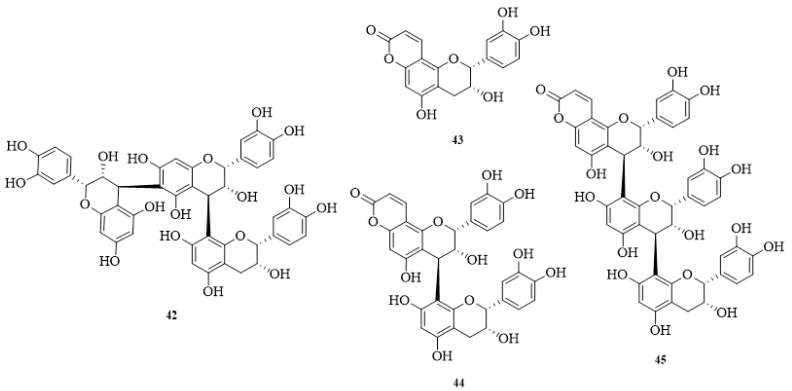
Concerning the pharmacological potential based on scientific studies, the species has presented a wide variety of effects; the aqueous extract showed immunosuppressive activity (on the antibody production by B cells, 0.5 mg/kg b.w.) on mice during seven days and delayed type hypersensitivity (on T cells, 0.5–5 mg/kg b.w.), by reducing the subcutaneous tissue infiltration. The extract also inhibited *in vitro* production of NO· (by stimulating J774 cells) (Pinto et al. 2007). Still, the flavonoid-rich fraction from H_2O extract exhibited antiinflammatory activity (*in vivo*/*in vitro*); at 2.5 mg/kg, it reduced total mice leucocytes (30%), showed inhibition of LTB4 (90%) and proteins (42%), as well as it caused *in vitro* inhibition of neutrophil migration and NO· production (Da Silva et al. 2016b). The EtOH extract (leaves) demonstrated significant and potent topical and systemic anti-inflammatory effect in rats by causing inhibition of paw edema and decreases in the leukocyte migration, as well as reduced the vascular permeability and ear edema in mice (Tanus-Rangel et al. 2010). Also, it presented diuretic action (10–300 mg/kg, reduction in urine elimination) and throwback of polyuria and glomerular filtration rate (reduction) (Portella et al. 2012). Interestingly, a renoprotective effect was also observed on rats treated with a leaf solution (2 mg/kg) (Nascimento et al. 2014). Finally, the plant EO from Nova Friburgo evidenced antinociceptive capability on mice treated orally (contortion inhibition of 65%, 50 mg/kg) (Coelho et al. 2012).

The reviewed scientific literature on *B. utile* showed that latex and bark were the most useful parts of plant from a pharmacological point of view due to its promising cytotoxic/antitumor properties [on *A. salina* (IC_{50} 48 μg/mL) and cancers of breast (IC_{50} 26 μg/mL), prostate (IC_{50} 28 μg/mL) and leukemia] (Ferrari et al. 2005, Chindoy 2013, Rivera-Parada 2013). Nonetheless, the antioxidant power (using different tests) of the bark extract from Venezuelan plant was determined by Padilla et al. (2008), who found that the extract was moderately active (reducing power: 59.7 ± 0.4 AsAE (ascorbic acid equivalent mg)/g, antioxidant activity: 61% (β-carotene bleaching), DPPH·—EC_{50} 1.3; %inh: 83); also, they measured the total phenolic [62 ± 4 GAE (galic acid equivalent mg)/g), flavonoid (8.9 ± 0.3 RTE (rutin equivalent mg)/g), and tannin (3.9 ± 0.4 CTE (catechin equivalent mg)/g] contents present in the extract. It is worth highlighting that an alkaloid-rich fraction [possibly containing bufotenin (**32**)] from latex suspension in MeOH of the Ecuadorian plant was obtained/reported by Jiménez (2015) and Acosta et al. (2017), which found it an antimicrobial potential based on the MIC values (1.6 mg/mL, for *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *E. coli*, and *C. albicans*) and the diameters of inhibition zone (2 mg/mL, *T. rubrum*: 19.5 ± 0.5 mm, *Epidermophyton floccosum*: 17.4 ± 0.5 mm). A particular chemistry has been associated to some isolated molecules (e.g., coumarins and isoflavones) from *B. utile*. Thus, Ferrari et al. (2005) purified seven isoflavones (**33**–**39**) from root bark; six of them were known molecules [lupalbigenin (**34**), alkenyl derivative of biochanin A (**35**), isowigtheone (**36**), ficuisoflavone (**37**), lupinisoflavone C (**38**), genistein (**39**)] and the last one was a new isoflavone [isowigtheone hydrate (**33**)], which was active on MCF7 and PC3 cell lines by *in vitro* cytotoxicity assays. In addition to isoflavones, the trunk bark was constituted by the coumarins xanthyletin (**40**) and luvangetin (**41**), according to the report by INPA (1972) on the chemical composition of Amazon plants.

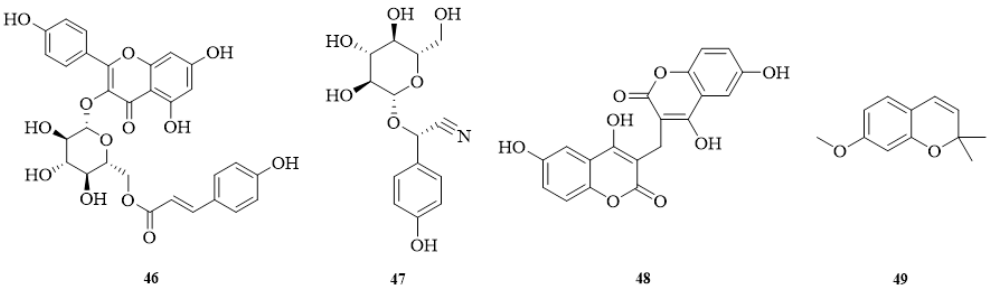
The analysis of the consulted scientific literature on bioactive extracts from *G. ulmifolia* indicated that it is one of the wild medicinal plants with higher pharmacological evidences according to the *in vitro*/*in vivo* biological tries (Table 2.2). Among the remarkable bioactivities can be mentioned angiotensine II type 1 and acetylcholinesterase inhibitions, gastroprotective and vasorelaxing effects, antidiabetic, anti-



STAT1, antiproliferative/antitumoral, antimicrobial, antiparasitic and antiviral. Nevertheless, promising bioproperties were vasorelaxing effect (IC_{50} 35 ng/mL), angiotensine II inhibition (IC_{50} 13-286 µM), antidiabetes (IC_{50} 1–70 µg/mL on T2-D), antiviral (IC_{50} 10 µg/mL on P-1 virus), anti-STAT1 (K_D 1–2 × 10^{-6} M), antiparasitic (500 µg/mL, strain inhibition epimastigotes of *L. infantum*: 95.2 ± 0.4%, *L. brasiliensis*: 92.20 ± 0.04%; epimastigotes *Trypanosoma cruzi*: 61 ± 1%) and antifungal (75 µg extract, ϕ inh.: 26 ± 2 mm for *C. albicans*). Regarding the chemical constituents from *G. ulmifolia* some important groups of secondary metabolites (proanthocyanidin, coumarins, terpenes, and flavonoids) have been identified (Pereira et al. 2019). Between them, proanthocyanidin oligomers and polymers [containing 1–15 units of epicatechin and catechin, e.g., **42** (three units)] from EtOH extract of bark were isolated by Hör et al. (1996) and these compounds inhibited the secretion of cholera toxin on rabbit distal colon set in an Using chamber. Additionally, specific flavanocoumarins (**43**–**45**) were isolated by Maldini et al. (2013) from plant bark and two of them (**43**, **44**) showed affinity for STAT1 (signal transducer and activator of inhibition of STAT1-DNA binding) which could be related to the anti-inflammatory properties attributed to *G. ulmifolia*.

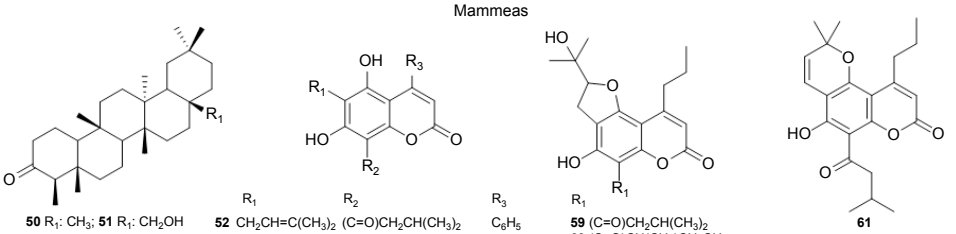


A glycoside flavonoid coumaroyl ester derivative, tiliroside (**46**), was also isolated from leaves as reported by Da´i et al. (2016); this ester derivative resulted to be a moderate antiproliferative agent against T47D and MCF lines via apoptosis mechanism by extrinsic pathways (caspases 8/9, p53, Bcl2 protein). Into the bargain, unusual molecules -2R-taxiphyllin (**47**) and dicoumarol (**48**)-insulated from leaves and roots were reported by Seigler et al. (2005) and Agarwal et al. (2010), respectively, which are a nitrile glucoside compound and a biscoumarin. Eventually, the leaf EO presented different main constituents: precocene I (**49**) (56%) and β-caryophyllene (14%) (Arriaga et al. 1997); citronellol (13%) and β-caryophyllene (12%) (Matulevich-Peláez and García-Rodríguez 2016); and thymol (21%), carvacrol (14%) and eugenol (10%) (Boligon et al. 2013). Particularly, the above mentioned EO presented a good radical-scavenging capacity ($DPPH^{\cdot}$, IC_{50} 7.61 ± 0.09 µg/mL) as well as favorable antibacterial effects against *P. aeruginosa* (MIC 62 µg/mL), *S. aureus* (MIC 125 µg/mL), *E. coli* (MIC 500 µg/mL) and *S. epidermidis* (MIC 750 µg/mL).



An astonishing Latin American plant is *Cal. brasiliense*: the extracts of the different parts (bark, leaves, resin) and the isolated/identified/tested chemical constituents (**50**–**91**, triterpenoids, coumarin, xanthones, chromanones, biflavonoids, etc.) were powerful biologically active substances as anti-HIV, anti-leishmaniasis/malarial/chagas, antinociceptive, anti-*Mycobacterium*, antibacterial, antifungal, cytotoxic, and antitumoral agents. Hence, hexane fraction and CH_2Cl_2 extract along with mammea A/BB (**53**) from EtOH extract (leaves) were active against *L. amazonensis* for promastigote (IC_{50} 3–40 µg/mL/IC_{90} 5–73 µg/mL) and axenic amastigote (IC_{50} 0.9–4 µg/mL/IC_{90} 2–20 µg/mL) forms (Brenzan et al. 2007). Furthermore, the selectivity index (SI) determined for **53** (on J774G8 macrophages) was highest for amastigote (SI: 29) form. In addition, **53** was able to reduce (60% and 68%) the lesion induced by infection subcutaneous with *L. amazonensis* on Balb/c mice (Tiuman et al. 2012); the CH_2Cl_2 extract and **53** were also active against promastigote form of *L. braziliensis* (Brenzan et al. 2008a), and coumarins **53**/**58** (mammea B/BB) were effective (IC_{50} 7.4 ± 0.3 µg/mL –30 ± 4 µg/mL) on *L. amazonensis* (intracellular amastigotes and promastigotes) (Brenzan et al. 2008b). Moreover, different extracts [ethyl acetate, CH_2Cl_2, CH_2Cl_2/MeOH (1:1), CH_2Cl_2/ethyl acetate (1:1)] and **67** isolated from leaves/stems restricted the growth of *P. falciparum* with IC_{50} values ranged amongst 8 ± 1 µg/mL and 55 ± 14 µg/mL (Mesa-Vanegas et al. 2019a, b). Other coumarins type mammea as **52** and **69** together with specific mixture (**52**–**54**) isolated of leaves and stem bark inhibited the growth of *T. cruzi* strains in some of its forms (epimastigotes, amastigotes and trypomastigotes) with IC_{50} values among 10–220 µM (Rea et al. 2013, Rodríguez-Hernández et al. 2019). Albernaz et al. (2010) determined the antimalarial (*P. falciparum*), antiChagas (*T. cruzi*) and antileishmanial (*L. chagasi*) power of CH_2Cl_2 extracts from root, wood and bark; the IC_{50} values were between 6.7 ± 0.9 µg/mL –97.1 ± 0.4 µg/mL.

An amazing pharmacological action determined for some fractions/extracts and isolated molecules from *Cal. brasiliense* has been the antiviral effectiveness on human immunodeficiency virus type 1 reverse transcriptase (HIV-1 RT). Accordingly, Huerta-Reyes et al. (2004a, b), García-Zebadúa et al. (2011), Kudo et al. (2013) and Matsuda et al. (2015) reported (i) the percentage inhibition (77.9 ± 0.5%–81 ± 2%) and IC_{50} value of hexane (30 µg/mL) and acetone (50 µg/mL) extracts on viral enzyme; (ii) the IC_{50} values (0.3–1 mM) for calanolides A-C (**64**–**66**) and soulattrolide (**67**), and the inhibition (60 ± 4%–75 ± 4%) for some fractions [18/19 (hexane extract), 2 (acetone extract) and ethyl acetate insoluble (MeOH

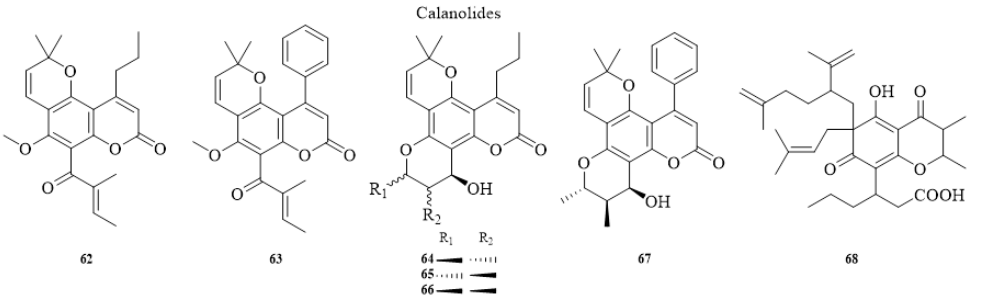


	R_1	R_2	R_3
52	$CH_2CH=C(CH_3)_2$	$(C=O)CH_2CH(CH_3)_2$	C_6H_5
53	$CH_2CH=C(CH_3)_2$	$(C=O)CH(CH_3)CH_2CH_3$	C_6H_5
54	$CH_2CH=C(CH_3)_2$	$(C=O)CH(CH_3)_2$	C_6H_5
55	$CH_2CH=C(CH_3)_2$	$(C=O)CH_2CH(CH_3)_2$	$(CH_2)_2CH_3$
56	$CH_2CH=C(CH_3)_2$	$(C=O)CH(CH_3)CH_2CH_3$	$(CH_2)_2CH_3$
57	H	$(C=O)CH_2CH(CH_3)_2$	$(CH_2)_4CH_3$
58	H	$(C=O)CH(CH_3)CH_2CH_3$	$(CH_2)_4CH_3$

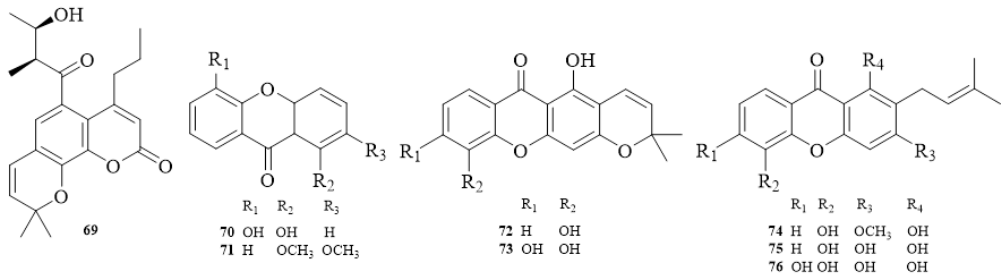
	R_1
59	$(C=O)CH_2CH(CH_3)_2$
60	$(C=O)CH(CH_3)CH_2CH_3$

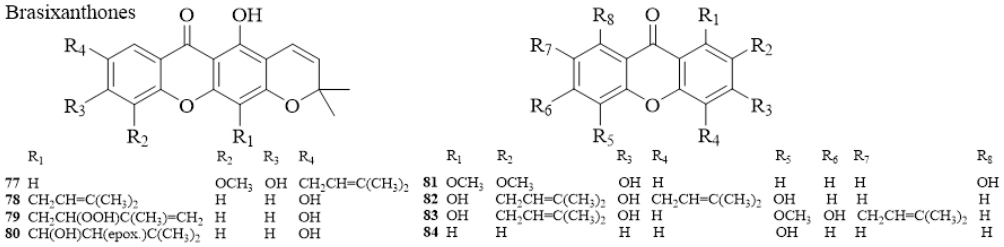
extract)] at 50 µg/mL on HIV-1 RT; (iii) the IC_{50} values for hexane (30–48 µg/mL) and acetone (31 µg/mL) extracts from leaves against the same enzyme; (iv) the inhibition (IC_{50} 8.4 µM) by **62** (isolated from stem bark) on HIV-1 replication of infected cells (U1 and Molt-4, in the presence of PMA and TNF-α); and, (v) the inhibition (25–65%) of HIV-1 entry (fusion cell) by **62** (10–100 µM) via decrease of cell membrane fluidity.

The validation of the use of "guanandi" as an analgesic in the ethnomedicine from Brazil, by means of *in vivo* antinociceptive evaluation, has been carried out by Da Silva et al. (2001), Isaias et al. (2004) and Klein-Júnior et al. (2017). These authors found that hexane/ethyl acetate/$CHCl_3$ fractions and MeOH extracts from leaves/flowers/fruits/roots, as well as some isolated molecules [friedelin (**50**), brasiliensic acid (**68**), 1,5-dihydroxanthone (**70**) and 1,2-dimethoxyxanthone (**71**)] were competent to inhibit the muscular constriction on mice measured by different methods [acetic acid-induced writhing, formalin-induced paw licking (phases I/II and edema), capsaicin-induced and glutamate-induced nociception] with the percentage inhibition values of 70 ± 6%–80 ± 4% at 3–10 mg/kg (i.p.) for MeOH extracts (flowers/fruits/roots), 41–94% at 60 mg/kg (i.p.) for $CHCl_3$ fraction (roots), 81 ± 8% for polar fractions (roots), 98 ± 6% for non polar fractions (roots), while the ID_{50} values were 9–48 mg/kg i.p. (132 p.o.) for $CHCl_3$ fraction (roots), 12 µmol/kg for **50**, 7 µmol/kg for **68**, 30 µmol/kg for **70** and 28 µmol/kg for **71**.



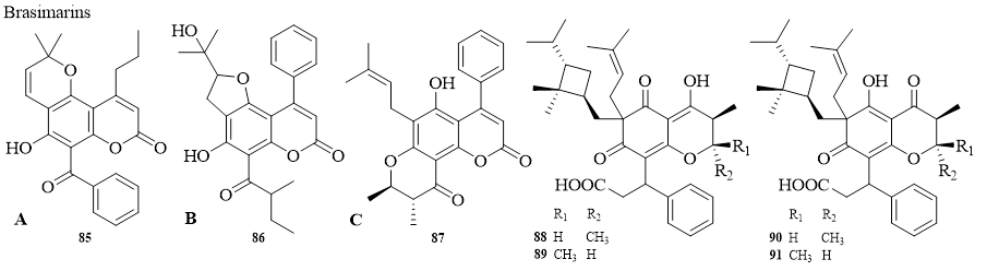
Some extracts/isolated molecules turned out to be moderate/good antimicrobials. For instance, certain extracts (Soxhlet, maceration and SFE-CO_2) and **61** (mammea B/BB cyclo D) isolated from leaves were useful against *Mycobacterium tuberculosis* with MIC values of 62.5 µg/mL and 125 µg/mL, respectively (Pires et al. 2016). Also, hexane, CH_2Cl_2, acetone, MeOH and H_2O extracts obtained from flowers/leaves/stems/fruits/roots and **52**/**70**/**72**/**73**/**76**, mammea A/AA, PCA (protocatechuic acid), chromanone acids (**80**–**83**) isolated from the leaves/bark/heartwood showed a good bacterial/fungi inhibition against 13 bacterial [*B. cereus* (MIC 1–900 µg/mL), *Enterobacter cloacae* (MIC 400 µg/mL), *E. faecalis* (MIC 300–510 µg/mL), *E. coli* (MIC 128–512 µg/mL), *Proteus mirabilis* (MIC 500 µg/mL), *P. aeruginosa* (MIC 190–800 µg/mL), *Salmonella typhimurium* (MIC 700 µg/mL), *S. aureus* (MIC 2–600 µg/mL), MSSA (MIC 1–256 µg/mL), MRSA (MIC 8–32 µg/mL), *S. saprophyticus* (MIC 400–900 µg/mL), *S. epidermis* (MIC 16 µg/mL), and *S. agalactiae* (MIC 100–700 µg/mL)] and three fungi [*C. albicans* (MIC 8–500 µg/mL), *C. tropicalis* (MIC 400 µg/mL), *Cryptococcus neoformans* (MIC 2 µg/mL)] strains (Cottiglia et al. 2004, Pretto et al. 2004, Albernaz et al. 2010, Suffredini et al. 2014). An important infectious bacterial agent causing gastric lesions is *Helicobacter pylori*, over which the CH_2Cl_2/chromanone acid-





rich fractions and hydroethanol/hexane extracts from stem bark have shown a potential; these extracts and fractions produced inhibition halos (ϕ inh.) between 8–16 mm (at 125–1000 µg/disk) or 7–14 mm (at 25–400 µg/disk, percentage inhibition 17–44%—MIC 31 µg/mL). Similarly, the extracts and fractions diminished gastric ulcer induced on rats with percentage inhibition of 63–97% (at 5–100 mg/kg) and 67–95% (at 20–100 mg/kg) (Souza et al. 2009, Lemos et al. 2012). Further, xanthones (**73**) and coumarins (**52**, **57**) isolated from acetone/MeOH extracts (heartwood) inhibited the H^+/K^+-ATPase enzyme as a measurement of its gastroprotective capacity; the IC_{50} values were (i) xanthones: 47 ± 8 µM–173 ± 9 µM, (ii) coumarins: 110 ± 8 µM–638 ± 149 µM (Reyes-Chilpa et al. 2006).

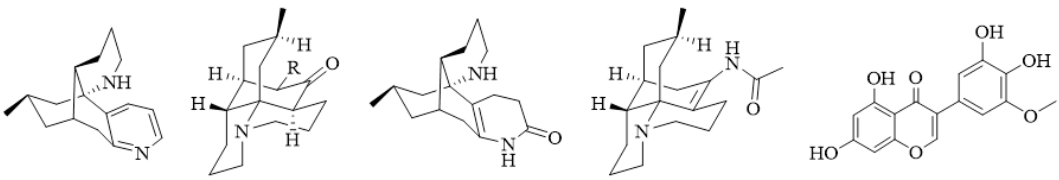
Besides, the antineoplastic/anticancer/antitumoral potential of extracts/molecules from "Bari" has been proved; thus, CH_2Cl_2 extract from root suppressed the growth of MDA-MB-435, HCT-8, HL-60 and SF-295 cell lines with IC_{50} values of 3 µg/mL, ~ 5 µg/mL, ~ 6 µg/mL, ~ 18 µg/mL, individually (Mesquita et al. 2009), whilst CH_2Cl_2:MeOH and H_2O extracts (100 µg/mL) inhibited the KM-12 and RPMI-8226 cancer cells with percentage values of 100% and 34–84%, one-to-one (Suffredini et al. 2007). The hexane extract obtained by Oliveira et al. (2014) from stem bark was effective against CHO-k1 line; similarly, the CH_2Cl_2:MeOH and H_2O extracts from leaves and stems were able to inhibit the growth of some cell lines (MCF7, PC3, NCIH460, KM12 and RPMI8226). Thus, the most active extract (aqueous of stem) inhited four lines (except RPMI8226) with GI_{50} values of 0.6 µg/mL, 49 µg/mL, 12 µg/mL and 1.2 µg/mL, respectively, followed by the H_2O extract from leaves, which inhibited three cell lines (except MCF7 and PC3) and with GI_{50} values of 16 µg/mL, 4 µg/mL, and 0.6 µg/mL, respectively (Suffredini et al. 2014). On the other hand, **50**, **52**, **53**, **55–60** isolated from hexane/acetone/MeOH extracts (leaves) inhibited three cancer lines (PC3, K562 and U251). Among all molecules tested on cell lines, coumarin 52 resulted the most active with IC_{50} values between 0.04 ± 0.02 µM–0.6 ± 0.2 µM, followed by a mixture **55**/**56** with IC_{50} values between 0.65 ± 0.09 µM–1.5 ± 0.1 µM (Reyes-Chilpa et al. 2004). Likewise, xanthones **62** and **63** from stem bark were evaluated on BV173, K562, NALM6, HL60, SEM and HCT116 cell lines; **62** (IC_{50} 2–5 µM) and **63** (IC_{50} 9 µM) inhibited the six lines and BV173 cell, in that order (Kimura et al. 2005). Also, calanolides (**62**, **64**, **66**), brasixanthones (**77**–**80**), xanthones (**81**–**84**), brasimarins (**85**–**87**), and mammeas (**56**) isolated from stem bark could be categorized as chemopreventive agents when assessed on TPA-EBV-EA (12-*O*-tetradecanoylphorbol-13-acetate induced Epstein-Barr virus early antigen activation) in Raji cells; the most active molecules were **78**, **56**, **79**, **80**, **62** and **64** with IC_{50} (mol ratio/32 pmol TPA) values of 120, 170, 200, 210, 268 and 290 (Ito et al. 2002, 2003). Moreover, a mixture of mammeas **52** and **53** (24 µg/mL) from leaves inhibited ca. 52% of BMK cell growth (Ruiz-Marcial et al. 2007), and **73** isolated from heartwood was cytotoxic,



genotoxic and cytostatic by different tests (MTT, trypan blue cell cycle and proliferation, micronucleus, alkaline SCGE, aneuploidy, lethal dose 50) (García-Niño et al. 2017).

Lastly, Blanco-Ayala et al. (2013) determined the antioxidant potential (measuring the scavenging capability of $O_2^{-\cdot}$, $HO^{\cdot}$ and $ONOO^-$) of two xanthones [jacareubin (**73**) and **76**] isolated from heartwood; the IC_{50} values were 336 ± 9 μM ($O_2^{-\cdot}$), 1.82 ± 0.06 μM ($HO^{\cdot}$) and 64 ± 12 μM ($ONOO^-$) for **73**, and 262 ± 8 μM ($O_2^{-\cdot}$), 0.070 ± 0.003 μM ($HO^{\cdot}$) and 30 ± 7 μM ($ONOO^-$) for **76**. In addition, Gonçalves et al. (2013) measured the antioxidant capacity of different extracts from leaves, which were effective against $DPPH^{\cdot}$ radical with IC_{50} values of 243 μg/mL, 207 μg/mL, 132–149 μg/mL for hexane, CH_2Cl_2 and SFE extracts. According to the authors, the mammea A/BB (**53**) could be the responsible compound for this activity. Carvalho et al. (2016) reported that dry and granulated hydroethanol extract (500 mg/kg) orally administered to diabetic rats significantly reduced the glycemia levels as well as other clinical parameters (triacylglycerides, cholesterol, LDL, transaminases, urea and creatinine); Braga et al. (2007) found that EtOH extracts from leaves and stems (at 100 μg/mL) inhibited the angiotensine converting enzyme with values of 34 ± 2% and 55 ± 16%, respectively.

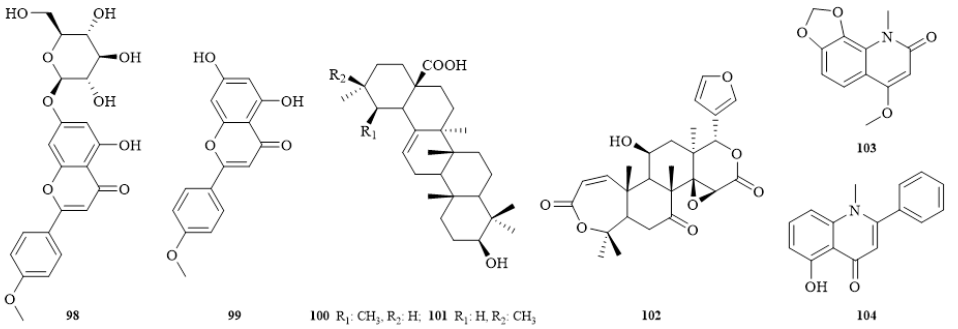
In consideration of medicinal species from Ecuador, Saraguros have used them in the health care systems (Armijos et al. 2012). Among the studies developed in 2016 by Armijos et al., they recorded the uses of *Huperzia* species into the magical-religious practices for the Saraguros; the healers use these plants as purgative agents, and to prepare psychotropic products, for ritual ceremonies. In the phytochemical analysis, a MeOH extract produced two fractions: (i) an alkaloid solution and (ii) a flavonoid/triterpene-rich precipitate. From the chemical analysis by GC-MS of the alkaloid-rich fractions from *Huperzia* spp., some constituents were presumably identified: lycodine (**92**), lycopodine (**93**), 6-hydroxy-lycopodine (**94**), des-N-methyl-α-obscurine (**95**) and flabelline (**96**) in *H. tetragona*; whilst **93** and **94** in *H. compacta*. Moreover, Gilardoni et al. (2014) and Malagon et al. (2016) identified/reported new hydroquinolinic alkaloids from *H. espinosana*. A non-common flavonoid [selgin (**97**)], previously isolated from *H. selago* (Voirin and Jay 1978), was positively identified in the non-alkaloid fraction from *H. espinosana*, as well as the flavonoid tricin in *H. tetragona* and *H. compacta*; this last compound was found in a high content in the extracts (Armijos et al. 2016b). The traditional use of species belonging to the genus *Huperzia* has been mainly to treat ailments possibly related to nervous disorders and this feature determined its potential as inhibitors of enzymes involved in central nervous system illness, e.g., Alzheimer´s disease and the associated enzyme [acetylcholinesterase (AChE)]; evidently, the alkaloid-fractions from *Huperzia* spp. inhibited AChE with percentage values between 24–87%.



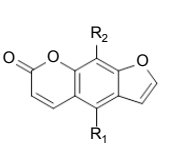
92 **93** R: H; **94** R: OH **95** **96** **97**

In Mexico, the ethnomedical use of *Ag. mexicana* is diverse. It is mainly used for "susto or nervios" and "espanto", a health condition known as cultural affiliation syndrome, dealing with fear and terror (Guzmán-Gutiérrez et al. 2014). It is not attended by modern allopathic doctors, but it is a well known illness among traditional medicine therapist, mainly in rural and indigenous communities. Different preparations (containing flavonoids and/or terpenoids) along with EO from this plant would be related to hypotensive, vasorelaxing, hypoglycaemic, depressant/anxiogenic, antioxidant, anti-inflammatory/antinociceptive, spasmogenic and relaxing effects based on the reports by Molina-Hernández et al. (2000), Hernández-Abreu et al. (2009, 2013), Ibarra-Alvarado et al. (2010), Ávila-Rosas (2013), Verano et al. (2013), Estrada-Reyes et al. (2014), González-Trujano et al. (2015), Flores-Flores et al. (2016), Esquivel-Gutiérrez et al. (2017), Navarrete et al. (2017), Ventura-Martínez et al. (2017) and Cruz-Torres (2019). In accordance with these authors, the CH_2Cl_2, MeOH and H_2O extracts resulted in antihypertensive, vasorelaxing/vasoactive, anxiogenic, anti-inflammatory/antinociceptive and antioxidant properties.

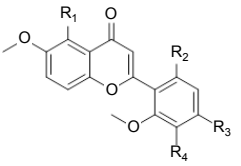
Thus, CH_2Cl_2 extracts showed a good relaxatory effect on contraction of aortic rings (with/without endothelium), and the H_2O extracts were from moderate to good anxiogenic, vasoactive and antioxidant agents. In the case of the antioxidant, MeOH extract (100 μg/mL, > 93% inh.) was partly (mainly) constituted by limonene, linalool, mentone, α-terpineol, pulegone and eugenol, whereas the EO (0.7% yield) with relaxing effect contained estragole (80%) and limonene (18%). The last chemical composition and yield differed in the amounts [estragole (87%)/limonene (11%) and yield (1.2%)] as described by Estrada-Reyes et al. (2004). An important flavonoid is tilianin (**98**) isolated from plant, which had an antihypertensive, vasorelaxant, depressant power, and acacetin (**99**) and ursolic acid (**100**) as vasorelaxant and antinociceptive, respectively.



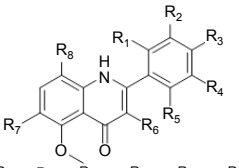
Another Mexican species of great potential is *Cas. edulis* due to its widely demonstrated pharmacological effects as hypotensive/vasorelaxant, anticonvulsive, antiviral, antioxidant, anticoagulant, antimicrobial, antiproliferative, chemopreventive (antimutagenic), non-toxic and relaxant, etc., from the extracts/fractions/isolated compounds of their leaves/seeds/kernel/fruits (Table 2.2). For instance, extracts (H_2O/hexane/MeOH/EtOH), fractions (ethyl acetate and alkaloid-rich) and isolated constituents [furocoumarin (**107**), flavonoid (**114**), alkaloids (quinolinones **118**–**121**) and imidazolic derivatives] from different parts (leaves/seeds/kernel/fruits) acted as effective hypotensors (Magos et al. 1995, 1999, Awaad et al. 2007, Froldi et al. 2011, Bertin et al. 2014). In a like manner, H_2O and EtOH extracts from leaves and seeds, respectively, showed satisfactory anticonvulsive action based on MES (maximal electroshock seizure) and METsc (subcutaneously injected metrazole) on rats (Navarro-Ruíz et al. 1995, Garzón-De La Mora et al. 1999). Four other interesting pharmacological properties [antiHIV-1 RT (on DNA polimerase and ribonuclease H activities), anticoagulant (based on prothrombin/activated parcial prothrombin times, PT/APTT), antimicrobial (against *B. subtilis*, *Micrococcus kristinae*, *S. aureus*, *Sarcina maxima*, *E. coli*, *S. typhi*, *Moraxella lacunata*, *Proteus vulgaris*, *C. albicans*, *Aspergillus niger* and *A. flavus*) and adipogenesis (on 3T3-L1 adipocyte)] revealed the EO, the hydroalcohol and EtOH extracts, and some fractions (EIF: ether:$CHCl_3$ and EIIF: ethyl acetate:butanol) and isolated coumarins (**107**–**109**) from seeds and leaves (Esposito et al. 2011, Awaad et al. 2012, Nagai et al. 2014). Considering the EO (leaves), it was constituted by *trans*-caryophyllene (28%) and benzyl-2-cyanoethyl ether (10%), which differed from the composition [germacrene D (16–22%) and (*E*)-caryophyllene (16–17%)] reported by Miller et al. (2009). Nonetheless, EO was effective against all microbial strains evaluated, while EtOH extract distinctively was not active against *A. flavus* and *S. typhi*. On the other hand, furocoumarins **108**/**109** were able to increase the glucose uptake, palmitic acid synthesis, and lipid accumulation in adypocites. By last, some extracts (MeOH), fractions (ethyl acetate) and isolated compounds [furocoumarins (**105**–**107**/**110**)/ flavonoids (**111**/**114**/quercetin/rutin)/alkaloids (**103**/**104**)] were chemopreventive and antioxidant agents (Ito et al. 1998, Awaad et al. 2006), and the mucilage presented hypoglycemic effect (Ibrahim et al. 2019). It is worth noting that *Cas. edulis* has been a source of molecules with a widespread structural diversity, i.e., limonoid (**102**), furocoumarins (**105**–**110**), flavonoids (**111**–**115**) and alkaloids (**103**/**104**, **116**–**122**, γ-fagarine) such as zapoterin (**102**), casimiroin (**103**)/casimiroedine, isopimpinellin (**105**)/phellopterine (**106**)/imperatorin (**107**) and zapotinin/zapotin (**112**). This last molecule has been able to suppress *in*



	R_1	R_2
105	OCH_3	OCH_3
106	OCH_3	$OCH_2CH=C(CH_3)_2$
107	H	$OCH_2CH=C(CH_3)_2$
108	H	$OCH_2CH=C(CH_3)CH_2O(C=O)CH_3$
109	OCH_3	$OCH_2CH=C(CH_3)CH_2O(C=O)CH_3$
110	OCH_3	$OCH_2CH=C(CH_3)(CH_2)_2CH(OH)C(OH)(CH_3)_2$



	R_1	R_2	R_3	R_4
111	OCH_3	H	H	H
112	OCH_3	OCH_3	H	H
113	OH	OCH_3	H	H
114	OCH_3	H	OCH_3	OCH_3
115	OCH_3	OCH_3	OCH_3	OCH_3

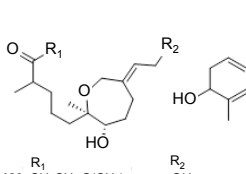


	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
116	H	OCH_3	H	H	H	H	OCH_3	H
117	H	OCH_3	OCH_3	H	H	H	OCH_3	H
118	OCH_3	H	H	OCH_3	OCH_3	H	OCH_3	H
119	OH	H	OCH_3	H	H	Propyl	H	OCH_3
120	H	OCH_3	H	H	H	Propyl	H	OCH_3
121	H	OCH_3	OCH_3	H	H	Propyl	H	OCH_3
122	H	OCH_3	H	OCH_3	OCH_3	H	OCH_3	H

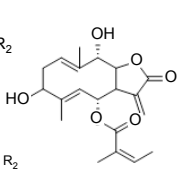
vitro cell proliferation on the HT-29 (IC_{50} 192–212 ng/mL/2.7 × 10^{-1} μM), SW480 (IC_{50} 2.3 × 10^{-1} μM), and SW620 (IC_{50} 5.3 × 10^{-1} μM) lines, as well as autophagy and apoptosis on HeLaPKCεA/E sub-line (Sondheimer and Meisels 1960, Dreyer and Bertelli 1967, García-Argáez et al. 2000, Khaleel 2002, Murillo et al. 2007, Toton et al. 2016).

The last Mexican plant considered in this chapter is *M. tomentosa* (zoapatles or cihuapatli), which has been used in the traditional medicine since prehispanic times, mainly to help women to speed up labor (oxytocic property/uterotonic), and as an antifertility (anticonceptive) agent; in addition, it is also used as an "aphrodisiac" for men. The aforementioned properties have been validated along with anxiolityc-like/anxiogenic-like effects of the H_2O extracts from leaves/aerial parts (Table 2.2). Possibly, the molecules responsible for the oxytocic effect were the oxepane diterpenoids zoapatanol (**123**), montanol (**124**), and tomentol (**125**); other oxepane derivatives [tomexanthol (**126**) and tomexanthin (**127**)] were also isolated. Moreover, other purified molecules were sesquiterpene lactones (heliangolides/guaianolides) as tomentosin (**128**), zoapatanolides A-E (**129**–**133**)/pumilin (**134**) (Levine et al. 1979, Cotter 1981, Hahn et al. 1981, Smith et al. 1981, Kanojia et al. 1982, Quijano et al. 1982, 1984, 1985, Seaman et al. 1984, Oshima et al. 1986). Particular non-polar diterpenes as kaurenoic (**135**) and grandiflorenic (**136**) acids were also identified/isolated from plant, and the hexane or H_2O extracts along with diterpenes acted by increasing both uterine contraction/motility and anxiolytic/anxiogenic properties, which would be contradictory. Nonetheless, some studies (reports) have shown that the above mentioned properties depend on hormonal stage (endocrine conditions) and that nonpolar-factions/molecules would favor spontaneous contraction, whereas polar fractions/molecules would favor uterine stimulation. Lastly, in addition to finding diterpenic acids, some sesquiterpenoids [valencene (25–45%) and β-eudesmol (27–56%)] were identified in the glandular trichomes of plant leaves (Lozoya et al. 1983, Waller et al. 1987, Campos-Bedolla et al. 1997, Robles-Zepeda et al. 2009, Estrada-Camarena et al. 2019).

To conclude, the final group of plants dealt with in this chapter was of Peruvian origin. Based on the scientific review carried out, the first of them, *Cam. angustifolia*, has validated four pharmacological effects: antimicrobial, antioxidant, antiparasitic and enzymatic inhibition. Recently, Roumy et al. (2020) established the antimicrobial potential of the bark MeOH extract against 36 strains (some of them isolated from human infections); of these strains, 20 (e.g., *K. pneumoniae*, *Yersinia pseudotuberculosis*, *P. aeruginosa*, *Stenotrophomas maltophilia*, *Enterococcus* sp., *E. faecalis*, *S. aureus*, *S. epidermidis*, *S. lugdunensis*, *S. warneri*, *S. agalactiae*, *S. dysgalactiae*, *Corynebacterium striatum*, *M. smegmatis*, and *C. albicans*) showed various susceptibility to the extract, with MIC values between 0.3 ± 0.1 mg/mL and 1.2 ± 0.4 mg/mL. The majority of strains had MIC values of 0.6 ± 0.2 mg/mL and the most



	R_1	R_2
123	$CH_2CH=C(CH_3)_2$	OH
124	$CH=C(CH_3)CH(CH_3)_2$	OH
125	$CH_2C(=CH_2)CH(CH_3)_2$	OH
126	$CH=CHC(OH)(CH_3)_2$	OH
127	$CH=CHC(OH)(CH_3)_2$	$O(CO)CH_3$



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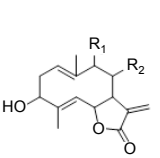
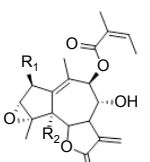
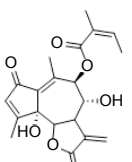


129 R_1: OH, R_2: $O(C=O)C(CH_3)=CHCH_3$
130 R_1: $O(C=O)C(CH_3)=CHCH_3$, R_2: OH



131 R_1: $O(C=O)CH_3$, R_2: OH
132 R_1: $O(C=O)CH_3$, R_2: H
133 R_1=R_2: OH



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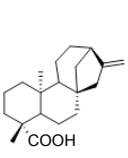

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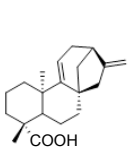

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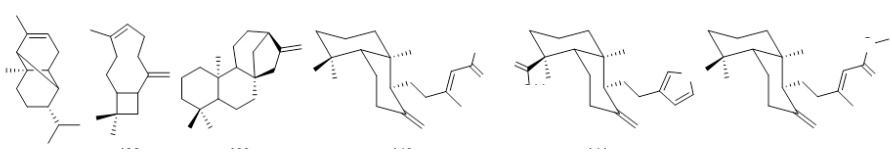
susceptible strain was *S. epidermidis* with a MIC value of 0.3 ± 0.1 mg/mL. In addition, Ravarocci-Quiroz and Carrasco-Huamán (2010), who studied the DPPH· radical-scavenging capacity (IC_{50} 69 ± 3 µg/mL) of the same type of extract, found through the phytochemical screening that it contained saponins, flavonoids, and phenols/tannins. For its part, Schmeda-Hirschmann et al. (2019) described the probable chemical composition of a polar extract (MeOH) by HPLC-DAD-ESI-MS/MS and the inhibitory effect (81–89% at 100–200 µg/mL) on the phosphodiesterase-5 enzyme (PDE-5), which would represent one of the mechanisms involved in the adequate male erectile function (*Cam. angustifolia* is an ingredient of the most commercialized beverages as traditional male sexual enhancers of the Peruvian Amazon). The chemical analysis allowed the tentative identification of 31 constituents including mainly proanthocyanidins and gallotannins, flavonoids and caffeoylquinic acid. Vásquez-Ocmín et al. (2018), Ruiz et al. (2011) and Kvist et al. (2006) determined the effectivity of the EtOH and EtOH:H_2O extracts against *P. falciparum*, *L. donovani* axenic amastigotes and *T. brucei gambiense* trypomastigotes strains with IC_{50} values < 10 µg/mL and > 20 µg/mL. A last revised document (patent) on *Cam. angustifolia* mentioned the ability of an extract (ethyl acetate/MeOH) to inhibit COX-2 (30–60%) as a mechanism to treat inflammation or cancer (Koepke et al. 2009). To date, no bioactive compound has been isolated/structurally characterized for this plant.

Another Amazon plant with interesting and verified pharmacological properties is *Cop. paupera*, and particularly its oleoresin; some authors (Ticunsi et al. 2002, Estevez et al. 2007, Dos Santos et al. 2008, Santos et al. 2008, Izumi et al. 2012, Amorim et al. 2017, Furtado et al. 2018, Rodrigues et al. 2018, Vásquez-Ocmín et al. 2018, Liviac et al. 2019, Roumy et al. 2020) have examined the antiparasitic (*P. falciparum*, *L. amazonensis*, *L. donovani*, *L. infantum*, *T. cruzi* and *T. brucei gambiense*), antimicrobial (*S. aureus*, methicillin resistant *S. aureus*, *S. epidermidis*, *S. lugdunensis*, *B. subtilis*, *E. faecalis*, *S. agalactiae*, *S. dysgalactiae* and *C. striatum*), antioxidant (FRAP and TBARS), cytotoxic/genotoxic/toxic (P-388, A-549, HT-29, MEL-28, V79, $LLCMK_2$ cell lines and erythrocites) and wound healing potential of pure oleoresin, certain oleoresin fraction (kaurene-rich), oleoresin/leaves/bark extracts, and isolated molecules (**135**, **137**–**142**). Thus, oleoresins (OR_1/OR_2), kaurene (**139**)-rich fraction (KRF) and isolated α-copaene (**137**) were able to inhibit the parasitic infection of the *L. amazonensis* and *L. infantum* promastigotes forms according to Rodrigues et al. (2018); these authors reported the IC_{50} values (µg/mL) which were OR_1/OR_2: 62 ± 8–104 ± 6, KRF: 168 ± 7 and **137**: 17 ± 3 against *L. amazonensis*; OR_1/OR_2: 66 ± 9–203 ± 18, KRF: 176 ± 4 and **137**: 11 ± 1 on *L. infantum*. Surprisingly, the nanoemulsions prepared by the same authors with the OR_1/OR_2/KRF/**137** increased the antiparasitic effectiveness between two-fold and seven-fold; viz., the IC_{50} values (µg/mL) were OR_1/OR_2: 17 ± 2–35 ± 10, KRF: 29 ± 4 and **137**: 2 ± 1 for *L. amazonensis*; OR_1/OR_2: 39.8 ± 0.3–47 ± 9, KRF: 55 ± 6 and **137**: 2.2 ± 0.8 for *L. infantum*. The oleoresins were constituted by OR_1: kaurene (33%), α-copaene (22%) and caryophyllene oxide (12%), and OR_2: α-copaene (39%) and β-caryophyllene (21%), whilst the fraction contained 65% of kaurene. Other oleoresin (Acre, Brazil), with promising antileishmaniasis effect (IC_{50} 11.0 ± 0.4 µg/mL), presented as main constituents to β-bisabolene (20%), α-zingiberene (19%) and kaurenoic acid (13%) (Santos et al. 2008). Besides, the OR with wound healing property was composed by α-copaene (23%), hardwickiic acid (8%) and δ-cadinene (7%) (Amorim et al. 2017). Otherwise, Dos Santos et al. (2008) and Roumy et al. (2020) also determined the antimicrobial efficacy on nine strains (*S. aureus*, methicillin resistant *S. aureus*, *S. epidermidis*, *S. lugdunensis*, *S. agalactiae*, *S. dysgalactiae*, *B. subtilis*, *E. faecalis* and *C. striatum*) by oleoresins, which had MIC values (in mg/mL) as follows: *S. epidermidis*: 0.6 ± 0.2–1.2 ± 0.4, *S. lugdunensis*: 0.6 ± 0.2, *S. agalactiae*: 0.3 ± 0.1–0.6 ± 0.2, *S. dysgalactiae*: 0.15 ± 0.05 and *C. striatum*: 0.3 ± 0.1 mg/mL, while MIC/MBC values (in µg/mL) were: *S. aureus*: 250/1000, methicillin resistant *S. aureus*: 250/500, *S. epidermidis*: 1000/1000, *B. subtilis*: 62/62 and *E. faecalis*: 62/500. While Ribeiro et al. (2019) measured the antimicrobial capacity of the volatile oil (43% yield) from oleoresin



against six strains (*S. aureus*, *P. aeruginosa*, *Salmonella choleraesuis*, *C. albicans*, *C. tropicalis* and *C. krusei*), the most significant MIC values (μg/mL) were 125 and 500 on *S. choleraesuis* and *S. aureus*, in that order. The volatile oil was mainly constituted by α-copaene (35%), δ-cadinene (14%) and α-cubebene (10%). Last but not the least, an OR and hydroalcohol extract from leaves inhibited (*in vitro*) V79 cells with IC_{50} values individually of 41 ± 7 μg/mL and 412 ± 66 μg/mL, but they were not cytotoxic and genotoxic (*in vivo*) (Furtado et al. 2018).

Alternatively, some isolated sesquiterpenes (**137**)/kaurene type diterpenoids (**135**, **139**–**142**) inhibited the growth of microorganisms, replication of cancer cells and/or parasitic infection (*T. cruzi*) (Ticunsi et al. 2002, Isumi et al. 2012, Rodrigues et al. 2018). For example, IC_{50} values (96 h - μg/mL) of **135**, **140**–**142** on *T. cruzi* amastigote form were 16 ± 3, 1.30 ± 0.06, 28 ± 6 and 2.50 ± 0.06, respectively, while CC_{50}/HC_{50} values (96 h/3 h - μg/mL) against $LLCMK_2$ and erythrocyte cells were 76 ± 5/464 ± 56, 39 ± 5/65.7 ± 0.2, 60 ± 9/> 1582 and 69 ± 4/1597 ± 9, one-to-one. Other IC_{50} values for **142** as a measure of the anticancer potential were on P-388 (2.5 μg/mL), A-549 (5 μg/mL), HT-29 (5 μg/mL) and MEL-28 (10 μg/mL) lines. Meanwhile, the MIC values (μg/mL) calculated for **135**, **140** and **141** against *B. subtilis*, *S. aureus* and *S. epidermidis* were in turn: **135**: 5–2, 8–6 and 6–4; **140**: 6–3, 10–8 and 5–4; and **141**: 30–20, 50–40 and 40.

To sum up, the H_2O/MeOH/EtOH/hydroalcohol extracts or fractions from sauco (*Sam. peruviana*) were active as antimicrobial, antioxidant and toxic/insecticidal agents as described by Hernández et al. (2000), Neto et al. (2002), Schmeda-Hirschmann et al. (2005), Bussman et al. (2011), Chirinos et al. (2013) and Román-Farje et al. (2017). In this fashion, the EtOH extract or flavonoid-rich fraction (from H_2O:MeOH extract) were capable of inhibiting the growth of bacterial strains; that is, the EtOH extract (100 mg/mL) produced diameters of the inhibition zone > 7 mm on *Streptococcus bovis*, *S. pneumoniae*, *S. agalactiae*, *Clostridium histolyticum*, *C. diphtheria*, *Bacteroides fragilis* and *B. megaterium*, and the flavonoid-rich fraction (at 200 μg/mL) inhibited the growth of *S. epidermidis*, *B. subtilis* and *S. aureus* with equivalent concentrations of chloramphenicol (CAEC) of 38 μg/mL, 53 μg/mL and 61 μg/mL. Besides, the total extracts (MeOH or H_2O:MeOH:HCl) of fruits exhibited promising radical-scavenging/antioxidant capacities by $DPPH^{\cdot}$, $ABTS^{+\cdot}$ and ORAC methods: the total antioxidant capacity values (AOC), expressed as μmol TE/g, were between 155 ± 6 and 361 ± 23, and the percentage inhibition of 49 ± 4% on radical $DPPH^{\cdot}$ by MeOH extract, at 100 μg/mL. The preliminary phytochemical analysis of fruits from *Sambucus* spp. indicated the presence of anthocyanins such as cyanidin 3-*O*-sambubioside as principal constituent (Anton et al. 2013), but other secondary metabolites were also presumably identified in its leaves (e.g., flavonoids, lactones, triterpenes/steroids, saponins) (Ruiz-Reyes et al. 2013). Lastly, the extracts (H_2O and EtOH) from *Sam. peruviana* (leaf/bark/root) evidenced intermediate toxicity (2–28% of mortality) on *Sitophilus zeamais* and *Copidosoma koehleri*, whilst those extracts on crustaceans *Daphnia magna* and *A. salina* were moderate to highly lethal (LC_{50} 0.4–23 g/mL, 26–168 μg/mL).

Conclusion

The plants (tree/shrub/herb) selected/analyzed have been important as sources of medicine or food, and some of them with special purposes to cure "supernatural" diseases for the communities Tacana, Quilombolas, Saraguro, Ingano, Coreguaje, Witotos, Huasteca (teenek), Bora-Miraña, Tikunas and Cocamas, inter alia, from Bolivia, Brazil, Colombia, Ecuador, Mexico, and Peru. Among the relevant ethnobotanical uses, related to the therapeutic benefits of the 18 plants, could be mentioned: as treatment for disorders of the central nervous, circulatory, digestive, respiratory, reproductive and nervous systems, as well as treatment for diseases caused by microorganisms (bacteria/fungi/virus)/parasites (leishmania/Chagas/malaria)/tumors. Some benefits according to the traditional uses have been validated (others determined) through the establishment of the pharmacological effects (*in vitro*/*in vivo*), for instance, anti-leishmania/Chagas/malaria, anti-HIV/HSV/BHV, anti-tumoral/cancer/cytotoxic, anti-bacterial/fungal, anxiolytic/angiogenic/uterotonic/aphrodisiac and wound healing, from the EO/oleoresins and extracts/fractions (SFE-CO_2/hexane/ethyl acetate/$CHCl_3$/CH_2Cl_2/acetone/EtOH/MeOH/H_2O) obtained from the plant's useful parts (e.g., flowers/leaves/stems/barks/wood/heartwood/fruits/seeds/roots/rhizomes/latex/oleoresin). As a final point, specific/particular constituents (e.g., tingenones, amburosides, pauferrols,

chapecoderins, echinophyllins, echinodolides, mammeas, calanolides, brasixanthones, brasimarins, furocoumarins, quinolinones, zoapatanolides, sesquiterpenes, diterpenes, among other), responsible for the pharmacological actions, were isolated and structurally characterized.

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