NPC Natural Product Communications

2016
Vol. 11
No. 3
297 - 314

Phytochemistry and Ethnopharmacology of the Ecuadorian Flora. A Review

Omar Malagón[a], Jorge Ramírez[a,c], José Miguel Andrade[a], Vladimir Morocho[a], Chabaco Armijos[a] and Gianluca Gilardoni[b,*]

[a]*Departamento de Química, Universidad Técnica Particular de Loja, San Cayetano Alto s/n, Loja – Ecuador*
[b]*Prometeo Project Researcher, Departamento de Química, Universidad Técnica Particular de Loja, San Cayetano Alto s/n, Loja – Ecuador*
[c]*Chemistry Department, Università degli Studi di Pavia, Viale Taramelli 10, 27100, Pavia, Italy*

gianluca.gilardoni@gmail.com

Received: March 30th, 2015; Accepted: February 10th, 2016

Ecuador owns many high quantity and wealthy ecosystems that contain an elevated biodiversity in flora and fauna. The use of native medicinal plants has been maintained by at least 18 different indigenous cultures; furthermore, this country has been the witness of the discovery of important medicinal plants, such as Cinchona, and is an understudied resource of new natural products. The objective of this review is to update the ethnopharmacological and phytochemical studies accomplished on the Ecuadorian flora, pointing to the 253 native families and more than 15,000 species registered at present.

Keywords: Ecuador, Phytochemistry, Metabolites, Ethnopharmacology, Ethnomedicine.

Ecuador is a country with an area of 283.560 Km^2, extending between +1° N and -5° S, on the Pacific coast of South America. As its name describes, Ecuador is crossed by the equatorial line and is therefore characterized by only two climatic seasons during the year: the dry one and the humid one. From the climatic and ecological viewpoint, Ecuador is divided into four main regions: the coast (la Costa), the highlands (la Sierra), the forest (la Selva or Amazonía or el Oriente) and the Island region (Islas Galapagos).

The coast, the western part of the country, is exposed to the Pacific Ocean and extends in altitude between 0 and about 500 m.a.s.l.; it is characterized by a constantly hot climate, with the humid season ranging between December and May and with temperatures fluctuating between 20°C and 33°C. The highlands are the central part of the country, corresponding to the Andes; they range between 500 and 6268 m.a.s.l., the volcano Chimborazo being the highest point of Ecuador. Due to the oblate spheroid shape of the earth and its proximity to the equator, the Chimborazo summit is the farthest point from the center of the planet. In this region the temperature ranges from -20°C (perpetual snow) and 26°C, with the humid season extending from November to April. The Andean region is the higher place in the world located at the equatorial line, and in consequence it is also among the regions with the most intense ultraviolet irradiation on the planet. The forest is the eastern region of Ecuador, extending from about 1000 to 200 m.a.s.l.; it is the western limit of the Amazonian forest and is characterized by temperatures ranging between 20°C and 33°C, with a humid season extending from January to September. The Galapagos islands, Ecuador island region, constitute an archipelago emerging from the Pacific Ocean at about 1000 Km from the coast, with a temperature ranging between 22°C and 32°C.

All these features make Ecuador one of the countries characterized by the highest biodiversity in the world; in particular it has been defined as *megadiverse*, being one of the 17 countries with the highest number of vegetal and animal species on the planet. For this reason, Ecuador attracted some of the major naturalists in the history of science such as Alexander von Humboldt, who reached Ecuador in 1802, and Charles Darwin, who reached the Galapagos islands in 1835. The biodiversity of Ecuador makes this country the ideal place not only to discover new living species but also to discover new secondary metabolites, as a result of the chemical investigation of living organisms, belonging to the different kingdoms.

In this review we are interested in the chemical characterization of secondary metabolites isolated until now from the native flora of Ecuador; we are also interested in their biological activity, both from an ecological perspective and for preliminary pharmacological information, orientated to the development of new drugs. For this reason, we are going also to consider in this article an ethnographic discipline, traditionally closely related to drug discovery and phytochemistry: ethnopharmacology.

In fact, before the Spanish conquest of the Andean region, this was inhabited by native civilizations, mainly the Incan empire, whose ancestral knowledge was also related to ritual and medical applications of plants.

After the conquest, this knowledge was transmitted partly to the rural populations but mainly it was preserved by the indigenous communities, some of them living nowadays in Ecuador. This ethnopharmacological knowledge constitutes an important and privileged way to select new plants as sources for new bioactive secondary metabolites, since it developed during many centuries of application. In fact the properties of many native botanicals are unknown to modern medicine and pharmacology, mainly evolved in Europe and North America with different botanical models. Furthermore, the study of ethnopharmacology is particularly urgent since much of this knowledge, generally transmitted orally inside the same communities, is probably destined to be lost as a consequence of urbanization [1].

According to the Catalogue of the Vascular Plants of Ecuador (http://www.tropicos.org/Project/CE), in this country 15,901 botanical species have been recorded and 186 are not recorded but are expected to be present. Of all these species 15,306 are native, of which 4,173 are endemic of Ecuador. The native species, the main object of this review, belong to 254 families (Table 1).

An exhaustive bibliographic research performed on these 245 families about their recollection or use in Ecuador, reveals that only 402 scientific articles have been published in the major international journals in all the fields of science. Of these studies 53 are related to the family Arecaceae, 33 to the Poaceae, 22 to the Asteraceae, 21 to the Fabaceae, 20 to the Cucurbitaceae, 19 to the Solanaceae, 15 to the Orchidaceae and 13 to the Euphorbiaceae, for a total of 196 publications. This means that about 50% of all the scientific publications on the botanical native species are related to only 8 families, the remaining 246 being scarcely studied, with few or no publications on either phytochemistry or ethnopharmacology for the major part of the Ecuadorian flora (Table 1).

In Ecuador not only biodiversity but also cultural heritage is superlative. More than 20 indigenous cultures subsist in different ecosystems and most of them maintain a traditional use of plants in food, health and construction (Figure 1). One of the most interesting native cultures of Ecuador is the Saraguro, living in the southern region of the country, at about 60 Km from the town of Loja. In a recent publication [2] Armijos *et al.* reported, from an ethnobotanical viewpoint, the use of plants, with the treatment of supernatural diseases among them. These applications refer mainly to psychosomatic, behavioral and "magical" illnesses; consequently, the plants are often applied to a ritual context and belong to species, genera or families notoriously containing alkaloids, some time with psychotropic activity.

Table 1: Botanical families according to the native species of Ecuador.

Family	Number of native botanical species of Ecuador	Number of bibliographic references according to SciFinder ®	Family	Number of native botanical species of Ecuador	Number of bibliographic references according to SciFinder ®
Orchidaceae	2999	15	Dilleniaceae	14	0
Asteraceae	863	22	Anacardiaceae	13	4
Melastomataceae	553	9	Brunelliaceae	13	0
Rubiaceae	493	4	Erythroxylaceae	13	0
Poaceae	451	33	Olacaceae	13	1
Bromeliaceae	440	4	Theophrastaceae	13	0
Piperaceae	438	7	Alismataceae	12	0
Araceae	397	1	Burmanniaceae	12	0
Solanaceae	338	19	Eriocaulaceae	12	0
Dryopteridaceae	309	0	Lemnaceae	12	1
Fabaceae	259	21	Portulacaceae	12	0
Gesneriaceae	239	3	Quiinaceae	12	0
Euphorbiaceae	225	13	Cuscutaceae	11	2
Ericaceae	224	7	Lentibulariaceae	11	0
Cyperaceae	211	1	Ochnaceae	11	0
Polypodiaceae	199	0	Clethraceae	10	2
Mimosaceae	178	0	Grossulariaceae	10	0
Lauraceae	167	5	Marattiaceae	10	0
Campanulaceae	155	3	Mendonciaceae	10	0
Acanthaceae	144	1	Pontederiaceae	10	0
Verbenaceae	133	1	Smilacaceae	10	0
Pteridaceae	130	0	Thymelaeaceae	10	0
Sapindaceae	130	1	Ulmaceae	10	0
Schrophulariaceae	127	0	Connaraceae	9	0
Clusiaceae	124	4	Icacinaceae	9	0
Arecaceae	123	53	Vochysiaceae	9	0
Moraceae	120	6	Balanophoraceae	8	0
Lamiaceae	119	6	Ophioglossaceae	8	0
Thelypteridaceae	108	0	Polemoniaceae	8	0
Annonaceae	105	3	Styracaceae	8	1
Bignoniaceae	98	1	Basellaceae	7	0
Hymenophyllaceae	98	0	Davalliaceae	7	0
Caesalpiniaceae	97	0	Gunneraceae	7	0
Malvaceae	95	9	Isoetaceae	7	0
Marantaceae	92	0	Molluginaceae	7	0
Apocynaceae	91	1	Podocarpaceae	7	0
Malpighiaceae	90	1	Plantaginaceae	7	0
Passifloraceae	90	1	Potamogetonaceae	7	0
Convolvulaceae	86	2	Agavaceae	6	0
Asclepiadaceae	85	0	Caryocaraceae	6	0
Urticaceae	84	2	Hydrangeaceae	6	0
Myrtaceae	83	1	Magnoliaceae	6	0
Boraginaceae	82	0	Nymphaeaceae	6	0
Lycopodiaceae	78	2	Primulaceae	6	1
Aspleniaceae	70	0	Salviniaceae	6	0
Cucurbitaceae	70	20	Bixaceae	5	0
Rosaceae	70	4	Chenopodiaceae	5	2
Amaranthaceae	69	1	Cannaceae	5	0
Myrsinaceae	69	1	Ebenaceae	5	1
Gentianaceae	65	1	Humiriaceae	5	0
Cyclanthaceae	61	0	Lacistemataceae	5	1

Cyatheaceae	60	0	Turneraceae	5	0
Meliaceae	59	3	Anthericaceae	4	0
Begoniaceae	58	1	Crassulaceae	4	1
Cecropiaceae	57	0	Equisetaceae	4	0
Flacourtiaceae	57	1	Hydrocharitaceae	4	0
Heliconiaceae	57	0	Hernandiaceae	4	0
Selaginellaceae	56	0	Hydrophyllaceae	4	0
Chrysobalanaceae	55	2	Linaceae	4	0
Apiaceae	54	5	Najadaceae	4	0
Araliaceae	54	2	Zamiaceae	4	0
Onagraceae	53	0	Aizoaceae	3	0
Polygalaceae	53	0	Buxaceae	3	0
Oxalidaceae	50	1	Columelliaceae	3	0
Sterculiaceae	49	6	Limnocharitaceae	3	0
Viscaceae	49	0	Marsileaceae	3	0
Sapotaceae	48	2	Oleaceae	3	1
Bombacaceae	47	4	Rhizophoraceae	3	1
Cactaceae	47	9	Rapateaceae	3	0
Dennstaedtiaceae	47	0	Salicaceae	3	0
Myristicaceae	47	7	Santalaceae	3	0
Menispermaceae	45	0	Staphyleaceae	3	1
Brassicaceae	44	5	Xyridaceae	3	0
Caryophyllaceae	44	0	Achatocarpaceae	2	0
Burseraceae	40	2	Cabombaceae	2	0
Violaceae	40	1	Callitrichaceae	2	0
Blechnaceae	39	0	Ceratophyllaceae	2	0
Lecythidaceae	39	0	Cupressaceae	2	0
Monimiaceae	39	3	Dicksoniaceae	2	0
Alstroemeriaceae	37	0	Elatinaceae	2	0
Capparaceae	35	0	Ephedraceae	2	0
Valerianaceae	35	0	Eremolepidaceae	2	0
Dioscoreaceae	33	1	Haloragaceae	2	0
Rutaceae	33	2	Hypoxidaceae	2	1
Aquifoliaceae	32	1	Hugoniaceae	2	0
Loranthaceae	32	1	Mayacaceae	2	0
Polygonaceae	31	2	Melanthiaceae	2	0
Amaryllidaceae	30	3	Myricaceae	2	1
Berberidaceae	30	0	Opiliaceae	2	0
Hippocrateaceae	30	0	Osmundaceae	2	0
Commelinaceae	28	0	Papaveraceae	2	0
Nyctaginaceae	27	3	Plagiogyriaceae	2	0
Symplocaceae	27	0	Plumbaginaceae	2	0
Cunoniaceae	26	2	Saxifragaceae	2	0
Loasaceae	26	1	Typhaceae	2	0
Loganiaceae	26	1	Zygophyllaceae	2	1
Marcgraviaceae	26	0	Alliaceae	1	0
Zingiberaceae	25	1	Aspodelaceae	1	0
Geraniaceae	24	1	Bataceae	1	0
Tropaeolaceae	23	0	Betulaceae	1	0
Actinidiaceae	22	2	Coriariaceae	1	0
Juncaceae	22	1	Cornaceae	1	0
Combretaceae	21	2	Cyrillaceae	1	0
Tiliaceae	21	1	Dracaenaceae	1	0
Vitaceae	21	0	Droseraceae	1	0
Elaeocarpaceae	20	1	Gnetaceae	1	0
Ranunculaceae	20	1	Goodeniaceae	1	0
Caprifoliaceae	18	1	Haemodoraceae	1	0
Celastraceae	18	0	Hippocastanaceae	1	0
Costaceae	18	0	Juglandaceae	1	0
Sabiaceae	18	0	Juncaginaceae	1	0
Vittariaceae	18	0	Krameriaceae	1	0
Phytolaccaceae	17	1	Lophosoriaceae	1	0
Proteaceae	17	1	Loxsomataceae	1	0
Rhamnaceae	17	0	Menyanthaceae	1	0
Theaceae	17	0	Metaxyaceae	1	0
Aristolochiaceae	16	0	Nolanaceae	1	0
Chloranthaceae	16	1	Podostemaceae	1	0
Dichapetalaceae	16	0	Pellicieraceae	1	0
Gleicheniaceae	16	0	Phormiaceae	1	0
Iridaceae	16	1	Psilotaceae	1	0
Lythraceae	16	0	Rafflesiaceae	1	0
Caricaceae	15	4	Strelitziaceae	1	0
Schizaeaceae	15	0	Tovariaceae	1	0
Simaroubaceae	15	0	Triuridaceae	1	0
Buddlejaceae	14	0	Taxodiaceae	1	0
Cypripediaceae	14	0	Winteraceae	1	0

Figure 1: Indigenous cultures in Ecuador.

Another very interesting native people of Ecuador are the Shuar [3]. They live in the eastern part of the country and, differently from the Saraguro, they are not a Kichwa speaking people as they were not incorporated into the context of the Inca empire. Diversely from the Saraguro knowledge, based on the Andean flora, the Shuar traditional medicine is based on the Amazonian biodiversity; in this regard a statistical study has been performed by Bennet and Husby [4], in order to describe the pattern of the Shuar medicinal flora through a contingency table and binomial analysis, as an alternative to a regression approach.

In this article we can learn that the Shuar tradition knows the use of 210 species belonging to 119 families, which are listed in the article. Of these families, only nine comprise about 40% of all the species: Lamiaceae, Solanaceae, Fabaceae, Malvaceae, Asteraceae, Piperaceae, Rubiaceae, Cyperaceae and Euphorbiaceae.

Outside of the native peoples, the highlands region of Ecuador shows a traditional use of plants for the treatment of diseases; a description of this phenomenon has been reported by Cavender and Albán [5], which includes the use of 17 "magical" species, based on interviews with 116 curanderos (healers) from all the highland provinces of Ecuador.

An interesting series of articles have been provided by Bussmann *et al.* [6–9], who described the use of many botanical species, in particular in the region between the south of Ecuador and the north of Perú. This region, equivalent in Ecuador to the provinces of Loja and Zamora-Chinchipe, shows a rich ethnobotanical tradition, also described by Tene *et al*. [10] who report a detailed list of 275 species with their use and applications.

A very interesting and comprehensive review of the phytochemistry of many plants of Ecuador, based on their anticancer activity, has been recently published by Bailón *et al.* [11]. The authors reported 16 ethnomedical species with informed antitumor activity and 12 indigenous plants of Ecuador with anticancer potential, whose phytochemical composition is described. Secondary metabolites such as isopteropodine (**1**), isomitraphylline (**2**), pteropodine (**3**), uncarine (**4**), mitraphylline (**5**), tapsine (**6**), condurango glycoside A (**7**), quercetin (**8**), emodin (**9**), physcion (**10**), bryophyllin A (**11**), bryophyllin B (**12**), taraxerol (**13**), minquartynoic acid (**14**), quinine (**15**), chloroquine (**16**), quinidine (**17**), 3-hydroxyquinine (**18**), squamocin (**19**), bullatacin (**20**), montecristin (**21**), cohibin A (**22**), murihexocin (**23**), arianacin (**24**), intrapetacin A (**25**), intrapetacin B (**26**), cucurbitacin B (**27**), casearvestrin A (**28**), casearvestrin B (**29**), casearvestrin C (**30**), casearin X (**31**), IGDE (**32**), and MGDE (**33**) are described (Figure 2).

In this review we report 263 molecules isolated from 58 plant families. The traditional medical uses of the species reported are very diverse, and in general there are no systematic studies that validate their employment. This point is demonstrated through this review by different plant species that present only ethnobotanical, pharmacological or phytochemical studies, but not together.

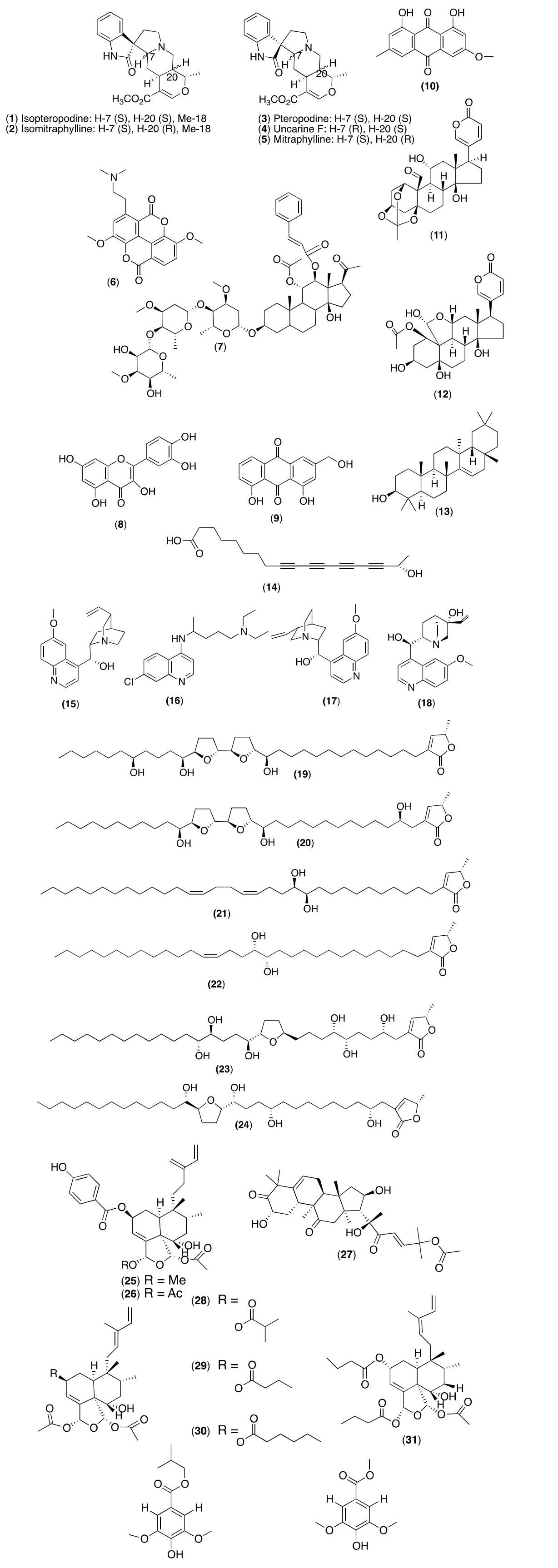


Figure 2: Secondary metabolites discovered in plant species with informed antitumor activity and indigenous plants of Ecuador with anticancer potential.

The review presents updated information on the ethnobotanical and phytochemical studies performed in Ecuador. For example, even though the Orchidaceae family is the most common in Ecuador, the Asteraceae is the most studied family with 69 compounds reported. Solanaceae is another important botanical family from the ethnobotanical point of view, often used in traditional medicine to treat diseases such as *mal de aire* and headache, or for psychotropic purposes; furthermore, scarce phytochemical research has been found in the literature on the native species of Ecuador. The family Lamiaceae that includes the genera *Clinopodium*, *Lepechinia* and *Scutellaria*, contain species widely used in traditional medicine. In general these species are very rich in essential oil and the different components of the volatile fraction are often involved in their biological activities. Another plant abundant in essential oil is *Ocotea quixos* (Lauraceae) that contains *trans*-cinnamaldehyde, involved in the significant reduction of the normal production of NO in the inflammation process. It has also been demonstrated that this oil can reduce the chance of blood clot formation by preventing platelet aggregation.

A mention of *Ayahuasca*, a psychotropic traditional drink, is noteworthy. The potion is the result of the combination of *Banisteriopsis* spp. (Malpighiaceae), containing harmaline, and *Psychotria viridia* (leaves), that contain dimethyltryptamine (DMT); the combination of the two natural ingredients produces the effect. Harmaline is a well-known MAO inhibitor alkaloid that increases the bio-availability of endogenous and exogenous phenylethylamines, such as DMT contained in *Psychotria viridia*.

Phytochemistry and ethnopharmacology of the botanical families

Acanthaceae, Acrobolaceae* and *Adelanthaceae: *Fittonia albivenis* (Acanthaceae) is used by two Amazonian indigenous cultures: the Cofán (or Kofán) use it for urinary pain and the Siona–Secoya for headache or muscle pains [12]. Furthermore, a series of prenylated bibenzyl derivatives (**34-38**) [13,14], shown in Figure 3, was isolated from *Lethocolea glossophylla* (Acrobolaceae), collected in Pichincha province.

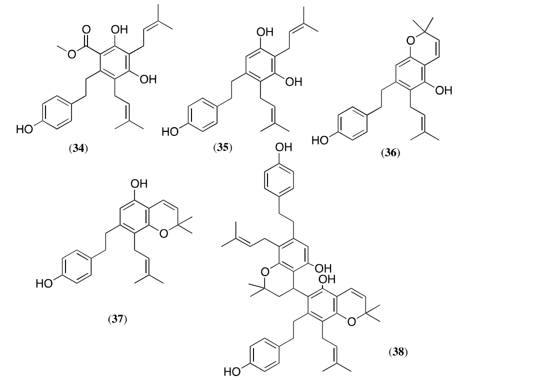


Figure 3: Prenylated bibenzyl derivatives from *L. glossophylla*.

Some Ecuadorian and foreign samples of the liverwort *Adelanthus decipiens* (Adelanthaceae) were studied and highly oxygenated naphthalenes and acetophenones were discovered [15]. From the Ecuadorian samples were isolated: wettsteins A (**39**) and B (**40**), 1,2,3,4,5-pentamethoxyacetophenone (**41**), 2-hydroxy-tetramethoxyacetophenone (**42**), 2-hydroxy-3,4,6-trimethoxy-acetophenone (**43**), 1,2,3-trimethoxynaphtalene (**44**) and 1,2,3,4-tetramethoxynaphtalene (**45**). Compound **41** was the major component found in the Ecuadorian liverwort (Figure 4).

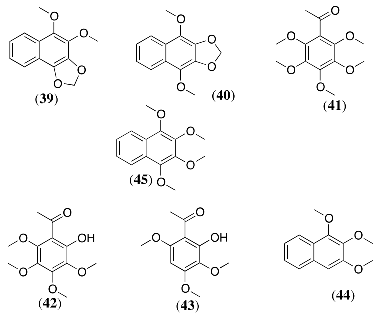


Figure 4: Naphthalene and acetophenones from *Adelanthus decipiens*.

Amaranthaceae, Anacardiaceae* and *Annonaceae: The use of *Cyathula achyranthoides* (Amaranthaceae) was described by Russo *et al.* [12]. Among the Kichwa speaking people, flowers and shredded leaves of *allcupanga* (local common name) are used in the case of dog bite. Moreover, the Shuar family eats raw young leaves of *yajauch isma* (local common name) to relieve headaches and to treat fever. Additionally, the supercritical fluid extract oil of the seeds of *Amaranthus caudatus* (Amaranthaceae) was characterized and its content of tocopherols determined: fatty acids, sterols and tocopherols were in a higher amount in Ecuadorian than in Italian samples [16].

In a study performed in 1954 [17] the fatty acid composition of the oil of *Anacardium excelsum* (Anacardiaceae) was analyzed and resulted in a content of 11% of oleic acid and 7.7% of lauric acid. The melting point of the fat is between 47 and 48°C.

For the Annonaceae family, Davis, Yost and Schultes [18,19] reported that the crushed bark aqueous extract of *Guatteria cf. schunkevigoi* is used in treating fever by the Waorani indigenous culture.

Apocynaceae* and *Aquifoliaceae: *Himatanthus sucuuba* (Apocynaceae) releases a white latex that is used by Waorani to treat warble fly (*Dermatobius hominis*) [18]. Moreover, *Bonafousia sanano* and *B. longituba* (Apocynaceae) ethanolic extracts showed a significant anti-inflammatory activity *in vivo*, by reducing the edematous response induced by carrageenan [20].

Ilex guayusa (Aquifoliaceae) is used for different medicinal purposes and in traditional rituals of the Shuar culture. The content of methylxanthines was evaluated in a study performed by Lewis *et al.* [21], showing that the principal component is caffeine in a range of 1.73 – 3.48% and traces of theobromine and other methylxanthines. Russo [12] reported different uses of *I. guayusa* by Kichwa and Shuar indigenous cultures: as a stimulant drink, a tonic, a calmative, a stomachic, to 'kill the bitter taste' of ayahuasca and for the prevention of hangover.

***Araceae*:** Two fractions from the flowers of *Anthurium versicolor* (Araceae) showed significant radical-scavenging effect [22]. Additionally, four flavone glycosides were isolated: acacetin 6-*C*-[α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranoside] (**46**), acacetin 6-C-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside] (**47**), acacetin 6-C-[β-D-apiofuranosyl-(1→3)-β-D-glucopyranoside] (**48**), and acacetin 8-C-[α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranoside] (**49**), as well as vitexin and rosmarinic acid (Figure 5). Patil *et al*. studied the metabolites present in the stem of wood and bark of *Chamaedorea linearis* (Araceae), an inhibitor of DNA recombination [23]. Five spirostane glycosides (**50-54**) were isolated, including two sulfonic acid glycosides (Figure 6). Finally, the Waorani use *Philodendron* sp. (Araceae) to treat snake bite [18] and *Anthurium* sp. (Araceae) leaves in bot fly infestation [19]; the Secoya use *Anthurium cf. uleanum* roots in headache treatment [12].

***Arecaceae* and *Aristolochiaceae*:** Some Arecaceae palms are reported for their fixed oil composition: some unidentified palms were studied by Oilar [17]; Blicher-Mathiesen *et al.* studied *Attalea colenda* (Arecaceae) as a potential lauric acid source, showing a composition in the oil of more than 45% [24]. Cámara-Leret *et al*. wrote about the under documentation existing on the traditional use of Arecaceae in Northwestern South America, including Ecuador [1]. *Bactris gasipaes* (Arecaceae) is a widespread used palm, whose fatty oil composition was studied by Radice *et al*. [25]. Lauric, myristic and oleic acids were the major compounds.

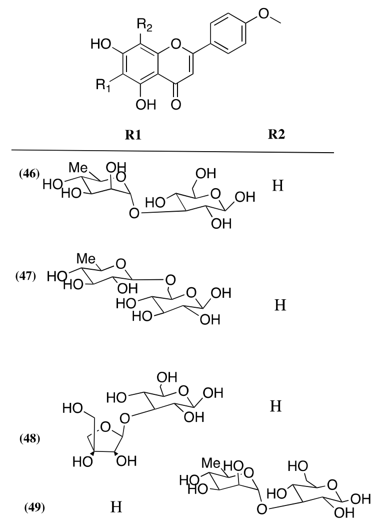
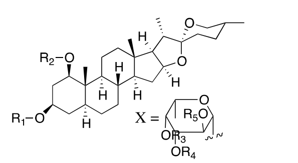


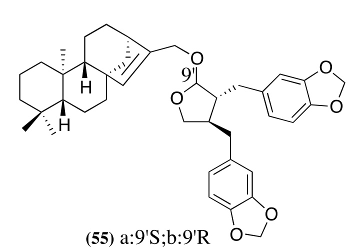
Figure 5: *Anthurium versicolor* flavone glycosides.



(**50**) R1= R4 = R5 = H, R2=X, R3=SO_3
(**51**) R1= R4 = R5 = Ac, R2=X, R3=SO_3H
(**52**) R1 = R2 = H
(**53**) R1 = R3 = R4 = R5 = H, R2 = X
(**54**) R1 = R3 = R4 = R5 = Ac, R2 = X

Figure 6: *Chamaedorea linearis* spirostane glycosides

The aerial parts of *Aristolochia constricta* (Aristolochiaceae) are used as antispasmodic, anticancer, antimalarial, and anti-inflammatory agents, as an emmenagogue and for the treatment of snakebites. Twenty compounds were isolated, including the diterpene-lignan 9-*O*-[(-)-kaur-15-en-17-oxyl]cubebin (**55**) (Figure 7) [26].



(**55**) a:9'S;b:9'R

Figure 7: *Aristolochia constricta* diterpene-lignan 9-*O*-[(-)-kaur-15-en-17-oxyl]cubebin.

***Asteraceae*:** Quercetagetin, patulatin and their respective glycosides were identified in the aerial parts of *Tagetes zipaquirensis*, collected in the Chimborazo region of Ecuador [27]. *T. pusilla*, used traditionally in popular medicine, showed a significant anti-inflammatory activity *in vivo* [20]. *T. filifolia* and *Artemisia sodiroi* contain essential oils, whose compositions have been described [28].

The crude methanolic extract of *Erigeron apiculatus* showed an interesting activity against *Cladosporium cucumerinum* and *Pylicularia oryzae*, two fungal plant pathogens. According to bioautographic assays, the metabolites responsible for the biological activity were identified as known polyacetylene esters [29].

Some furanoeremophilanes and cacalohastine derivatives (Figure 8) were isolated from the aerial parts of *Senecio canescens* (**56-66**), used against infections and rheumatism [30]. Similar compounds were isolated from *Lasiocephalus ovatus* [31] (**67-75**), together with some common compounds such as α-amyrin and its acetate, α-amyrenone, β-sitosterol and stigmasterol.

From *Ayapana ecuadorensis* pentaynene (**76**), euparin (**77**), *trans*-3-hydroxy-2,3-dihydroeuparin-[α-acetoxymethyl-*trans*-crotonate] (**78**), *cis*-3-hydroxy-2,3-dihydroeuparin-[α-acetoxymethyl-*trans*-crotonate] (**79**), *trans*-3-hydroxy-2,3-dihydroeuparin-angelicate (**80**) and germacrene-D (**81**) were isolated [32] (Figure 9).

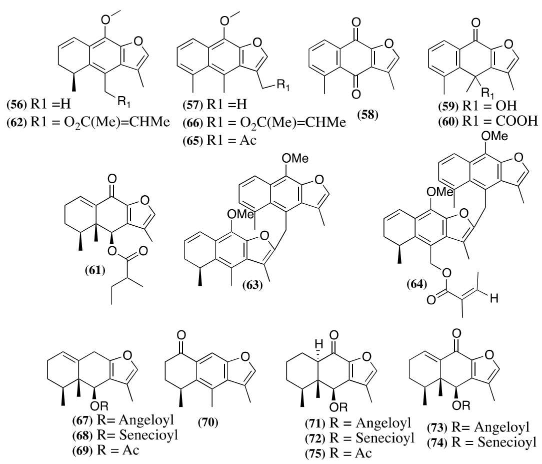


Figure 8: Furanoeremophilanes and cacalohastine derivatives from *Senecio canescens*.

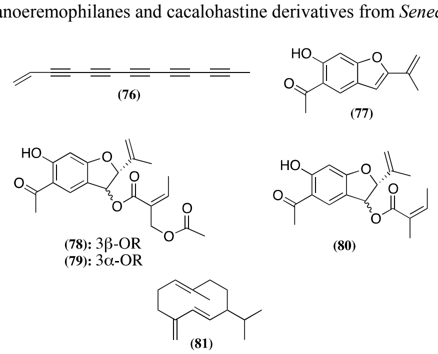


Figure 9: Compounds isolated from *Ayapana ecuadorensis*.

A series of kaurene diterpenoids (**82-84**), and austrofolin and its derivatives (**85-89**) were isolated from *Austroepatorium inulaefolium* [32] (Figure 10).

Eupatorium glutinosum has been used in the traditional medicine of Ecuador as an astringent, antirheumatic, and antimicrobial and to cure stomach ulcers, diarrhea and headaches. In addition, two

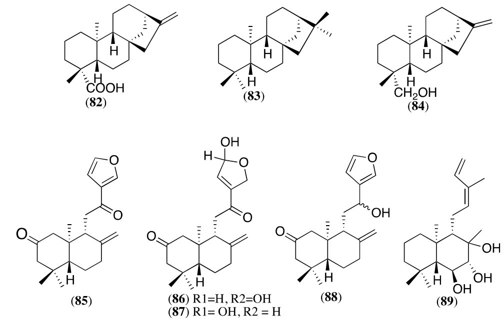


Figure 10. Diterpenes from *Austroepatorium inulaefolium*.

Labdane-type diterpenes (**90-91**) were isolated from this plant (Figure 11) [33]. The Shuar use *Eupatorium macrophyllum* leaves to treat headache [12].

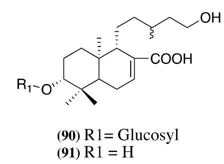


Figure 11: Diterpenes from *Eupatorium glutinosum*.

From *Perymenium ecuadoricum* some kaurene diterpenes and some kaurene isovalerian esters (**92-96**) were isolated (Figure 12) [34].

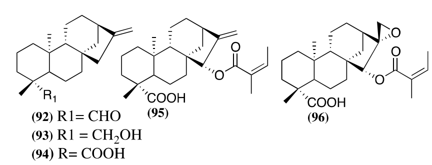


Figure 12: Diterpenes from *Perymenium ecuadoricum*.

Schistoscarpha eupatorioides, an Asteraceae from the Heliantheae tribe, is used to cure internal ulcers and diarrhea and to heal wounds. β-Sitosterol and stigmasterol were isolated, together with some fatty acid esters and glycosyl derivatives of the same compounds. Fatty acid phytyl esters were also found (**97-99**). Moreover, some terpene hydrocarbons were identified in the volatile fraction (**100-107**) [35]. (Figure 13).

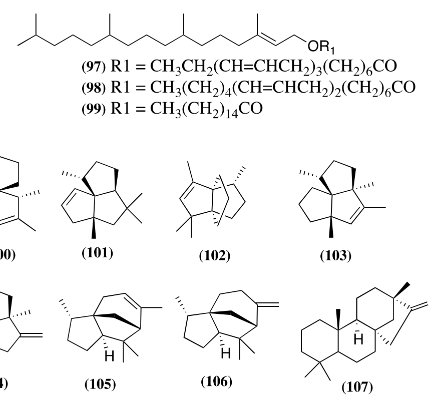


Figure 13: Fatty acid derivative and terpene hydrocarbons from *Schistoscarpha eupatorioides*.

Xanthium catharticum is known in Ecuador as *Cashamarusha* (*spiny chrysalis*) and is used by Kichwa speaking people as a diuretic, emetic, purgative and for prostate diseases. The methanol extract of the roots and the chloroform extract of the aerial parts demonstrated weak antibacterial and antifungal activity [36]. The sesquiterpenlactone ziniolide and the sesquiterpene laisidiol *p*-methoxybenzoate were discovered in the root methanol extract (**108,109**). In the chloroform soluble fraction of the methanol extract obtained from the aerial parts of *X. catharticum,* three sesquiterpene lactone xanthanolides were isolated. The most abundant was 11α,13–dihydro-8-*ep*i-xanthatin (**110**), accompanied by the two corresponding 1,5 epoxides (**111,112**) (Figure 14).

Oligosaccharides from Ecuadorian, Bolivian and Peruvian *Smallanthus sonchifolius* (*yacon*), a traditional Andean tuber, were studied by Lachman *et al.* [38]. The Ecuadorian ecotype showed the highest content of inulin and glucose. Moreover, a study of sesquiterpene lactones (**113,114**) from leaves of an Ecuadorian *yacon* is reported (Figure 15) [38].

Gynoxys verrucosa is used in the traditional medicine of Ecuador for healing wounds. Ordoñez *et al*. found interesting anti-MRSA activity in the sesquiterpene lactones leucodine (**115**) and dehydroleucodine (**116**), isolated from this plant [39] (Figure 16).

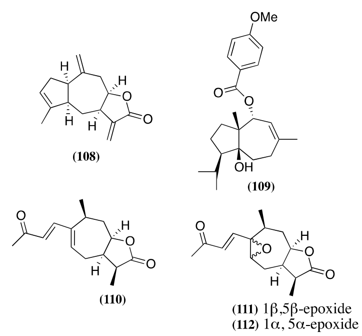


Figure 14: Sesquiterpenes isolated from *Xanthium catharticum*.

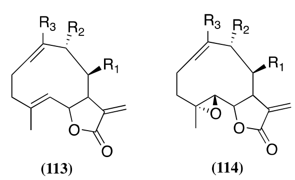


Figure 15: Sesquiterpenlactone skeletons from leaves of *Smallanthus sonchifolius*.

Baccharis latifolia is used in Ecuador to treat stomach pain, hepatic pain, fractures, gangrene, rheumatism, liver and kidney problems and as an anti-inflammatory agent. The essential oil analysis revealed the presence of the monoterpenes limonene, β-phellandrene, sabinene and β-pinene as main constituents [40].

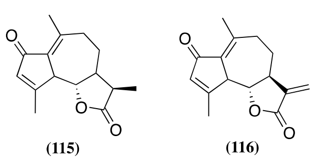


Figure 16: Leucodine and dehydroleucodine from *Gynoxys verrucosa*.

Baccharis teindalensis is used in the traditional medicine of Ecuador as an anti-inflammatory, analgesic and antimicrobial remedy. The ethanol extract showed antidiarrheic activity against castor oil induced diarrhea. Higher doses of the ethanol extract reduced considerably ethanol-induced gastric ulcers and inhibited the myeloperoxidase activity as an index of the neutrophilic infiltration. Many flavonoids were isolated from this extract (Figure 17) (**117-121**), together with oleanolic acid (**122**), spathulenol (**123**), scopoletin (**124**) and the infrequently found bacchotricuneatin B (**125**) [41].

Baccharis obtusifolia essential oil was analyzed by GC-MS. The major constituents were (+/-)limonene, germacrene D, α-pinene, β-pinene, bicyclogermacrene and δ-cadinene. The essential oil showed antibacterial and antifungal activity [42].

Bignoniaceae: The Waorani use *Mansoa standleyi* to treat fever, sore muscles and arthritic ailments [18].

Jacaranda glabra showed promising activity against *Plasmodium falciparum*. An activity-guided isolation led to the discovery of four phenylethanoid glucosides, named jacaglabrosides A–D (**126-129**) (Figure 18) [43].

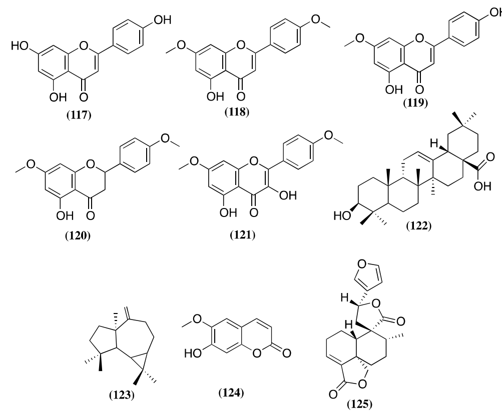


Figure 17: Compounds isolated from the ethanol extract of *Baccharis latifolia*.

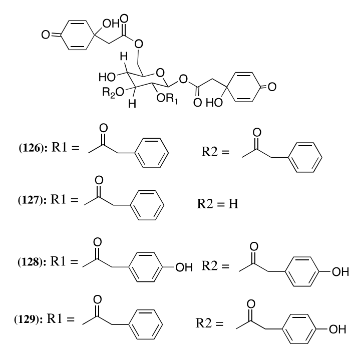


Figure 18: Phenylethanoid glucosides from *Jacaranda glabra*.

Burseraceae **and** ***Cactaceae:*** The essential oil obtained from the stem of *Bursera graveolens* (Burseraceae), called *Palo Santo* and collected from the eastern slopes of Puerto Lopez (midwestern lowland of Ecuador), was analyzed. The oil was found to consist of monoterpenes (78.2%) and sesquiterpenes (9.6%); the major constituents were limonene (58.6%), and α- terpineol (10.9%) [44].

Echinopsis pachanoi (Cactaceae) is a medicinal plant employed in the Saraguro community. The main applications of this cactus, named "*San Pedro",* are to induce visions (oral or inhaled), as a purgative, to cure supernatural diseases, to treat anxiety, nervous system alterations and as an anti-inflammatory or wound disinfectant [2].

Celastraceae**:** *Maytenus laevis*, locally named *chuchuhuasha* or *chuchuaso,* is used in the folk medicine of the sub-Andean regions of the Amazonian basin (Peru, Ecuador, Colombia). The powdered red root bark is used as an alcoholic infusion, generally in *aguardiente,* as a general tonic, for the treatment of rheumatism and even as an aphrodisiac. In topical use it is employed as an antitumor agent in skin cancer and also for the treatment of sores. González *et* *al.* [45] established the presence of 22-hydroxytingenone (**130**), tingenone (**131**), 4'-methyl-(-)-epigallocatechin (**132**) and two proanthocyanidins (ouratea-proanthocyanidins A and B) (**133**). The biological activities (antitumor and anti-inflammatory) of these compounds support the properties claimed by the traditional medicine [46]. According to Schultes [19], the bark is believed to be a strong stimulant when taken in infusion. The principal molecules are indicated in Figure 19.

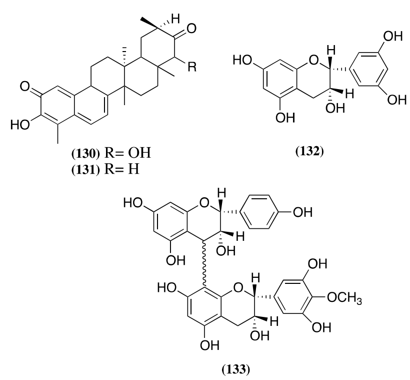
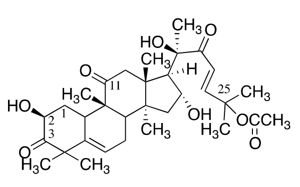


Figure 19: Compounds isolated from *Maytenus laevis*.

***Commelinaceae* and *Cucurbitaceae*:** The Kichwa name of *Geogenanthus ciliates* (Commelinaceae) is *supi-panga*. According to the collectors, the leaf is patted on the bottom of a person suffering from flatulence [19]. The Shuar give the name *sanchu* to *Commelina diffusa* (Commelinaceae), and the Spanish name is *suelda con suelda*. Among the Shuar, a tea is prepared from the flowers, which is employed as an emollient. It is also used internally to treat headache and, for toothache, it is used as an oral irrigation. The Siona use it similarly for headache and toothache, and for ant stings [46].

The chloroform extracts of *Cucurbita ecuadorensis* (Cucurbitaceae), obtained from leaves, fruits and roots, contain cucurbitacins active as kairomones in Diabroticide beetles [47]. The main cucurbitacins (**134-139**) studied are indicated in Figure 20.

***Cyatheaceae*:** The Waorani people have given the name "*toyaba"* to the fern *Sphaeropteris* sp. and its sap is employed topically for toothache. The latex is harvested and, when it thickens, it is applied to the exposed nerves [19]. Wade validated this use to soothe toothache with a similar procedure [48].



(134)	Cucurbitacin B	
(135)	E	1,2 C=C
(136)	D	25=OH
(137)	I	1,2 C=C; 25=OH
(138)	L	1,2 C=C; 25=OH, 23, 24, H,H
(139)	R	23, 24 H; 25 = OH

Figure 20: Chemical structures of cucurbitacins active as kairomones for diabroticite beetles.

***Ericaceae* and *Erythroxylaceae*:** The phenolic compounds were studied of *mortiño berries* (*Vaccinium floribundum,* Ericaceae), collected in the *paramos* of Ecuador. (-)-Epicatechin, one dimer and one trimer were found at a total concentration of 18 mg/100 g fresh weight. Among the flavonol glycosides (38 mg/100 g of fresh weight), quercetin and myricetin were found as 3-*O*-hexosides, 3-*O*-pentosides and 3-*O*-deoxyhexosides. Chlorogenic and neochlorogenic acids, together with caffeic and ferulic acid derivatives, were found as predominant components among the hydroxycinnamic acids in the berry. Anthocyanins, including cyanidin and delphinidin derivatives, were the major phenolic compounds (345 mg cyanidin-3-*O*-glucoside/100 g fresh weight) [49]. The main compounds (**140-154**) are indicated in Figure 21.

The existence of a distinct variety of *Erythroxylum coca* (var. Ipadu) and the deep magic-religious role played by this plant and its products in the northwest Amazonia was analyzed by Schultes [50]. Moreover, *Erythroxylum* spp. (Erythroxylaceae) leaves, collected in Manabí province, were analyzed by GC-MS [51]. Coca leaves from Bolivia, Perú, Ecuador and Colombia were subjected to the determination of cocaine, *cis*- and *trans*-cinnamoylcocaine, tropacocaine, hygrine, cuscohygrine and the isomeric truxillines. In another study, Moore [52] performed chromatographic analyses of alkaloids of wild and greenhouse-cultivated coca. All chromatographic profiles displayed a similar tropane alkaloid pattern: hygrine (**160**), anhydro-ecgonine methyl ester (**157**), ecgonine methyl ester (**156**), cocaine (**155**), and two characteristic cinnamoylcocaines (**158-159**). The structure of cocaine and the detected tropane alkaloids, together with the biosynthetic precursor hygrine, present in *E. laetevirens* are indicated in Figure 22.

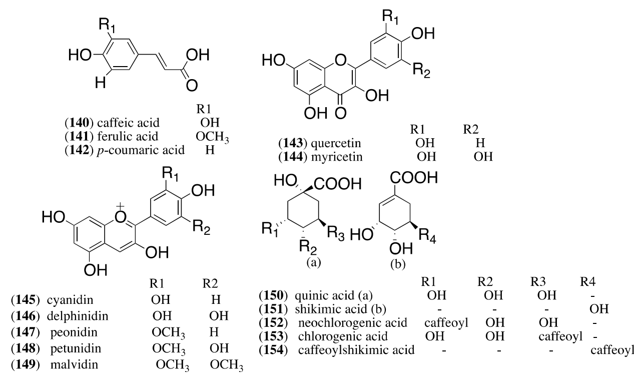


Figure 21: Shikimate derivatives isolated in Ecuadorian *Vaccinium floribundum*.

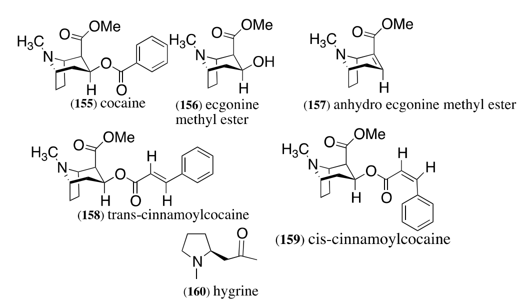


Figure 22: Structure of cocaine and other tropane alkaloids present in *Erythroxylum laetevirens* and in cultivated *Erythroxylum* species.

E. ulei is a plant used in the Amazonia of Ecuador, named by the Kofan as *awi-iti-fasi* and *iti-fasi*. The Rio Eno Siona call it *suara-iko* and the Shushulindi Siona *na-nyame-iko*. The Kofan people use it for itching, sore throat, stomachache, bloody diarrhea, amebiasis and headache. The Rio Eno Siona use this species for sore throat and stomachache, the Shushufindi Siona use it for similar indications and in addition in case of headache [46].

Euphorbiaceae: According to Bussmann and Sharon [7], 11 medicinal species of *Euphorbiaceae* are used by the indigenous people of Southern Ecuador, with special focus on Loja province and with a development since the early colonial period. In Ecuador species of *Caryodendron, Jatropha*, *Hevea, Croton* and *Euphorbia* have been studied.

Caryodendron orinocense was studied for its oil and metabolic composition [53,54]. In one of the studies the fatty acids and unsaponifiable fraction were analyzed by chromatographic methods. For *C. orinocence*, linoleic acid (85.59%) was the main component. The unsaponifiable fraction (8.06%) evidenced a remarkable content of β–sitosterol, campesterol, stigmasterol, squalene and vitamin E (816 ppm). In addition, the antioxidant activity was measured by the DPPH test [25].

Jatropha curcas is known in Ecuador as *piñón*, and its nut is more toxic than castor bean. This plant is an abundant bush in Ecuador and is used for fences. The oil yield is about 38% with a low percentage of free fatty acids (2-3% as oleic acid) [17].

The latex of *Hevea guianensis* is used to treat warble fly infestation. It is placed over the wound where it hardens into rubber, and suffocates the larva. The latex is also drunk as a tonic to make people stronger. The plant is used also for treating tooth decay [18].

Croton mentodorum is used in the traditional medicine of Ecuador and was evaluated for its anti-inflammatory and antioxidant activities [20].

C. lechleri essential oil, distilled from the fresh stem bark of Amazonian adult plants, was analyzed and seventy-four compounds were detected and identified; the most abundant in descending order were the sesquiterpenes sesquicineole (17.29%), α-calacorene (11.29%), 1,10-di-*epi*-cubenol (4.75%), β-calacorene (4.34%) and *epi*-cedrol (4.09%). The monoterpenes present in a greater proportion than 2.0% were α-pinene (2.01%), *p*-cymene (2.61%), limonene (4.20%) and borneol (2.67%). Spectrophotometric 1,1-diphenyl-2-picrylhydrazyl (DPPH) and bioautographic assays showed a lower radical scavenging capacity (IC_{50}) with respect to commercial thyme essential oil and BHA (butylated hydroxyl anisole), pointing out, however, that the *C. lechleri* essential oil fraction, characterized by α-calacorene, β-calacorene and δ-cadalene, was the most involved in the bioactivity. A bioautographic assay performed with Gram-positive and Gram-negative bacteria revealed minimum inhibitory concentration (MIC) values between 0.10 mg/mL (*Escherichia coli*) and 10.10 mg/mL (e.g. *Pseudomonas aeruginosa*); the fraction characterized by the presence of sesquicineole (97.4%) was the most involved in the antibacterial activity. The Ames test employing *Salmonella typhimurium* TA98 and TA100, with and without a metabolic activation mixture (S9 mix), demonstrated the absence of mutagenicity of the *C. lechleri* essential oil between a concentration range of 10^{-2} and 100 mg/plate [55]. Moreover, three known alkaloids: norisoboldine (**161**), isoboldine (**162**) and magnoflorine (**168**), have been isolated from *Croton lechleri*, a source of the wound healing latex *sangre de drago*. A large number of latex and leaf samples of *C. lechleri* from 22 sites in northern Peru and Ecuador were analyzed, to gain an understanding of the natural variation in alkaloid content for the species. Up to six alkaloids were found to occur in the leaves including, in addition to those listed above, thaliporphine (**163**), glaucine (**166**) and taspine (**169**), whereas the latex contained only **169**. Taspine (**169**) has been previously found to be responsible for the wound healing activity of *C. lechleri* latex, and the mean concentration throughout the range examined is about 9% of the latex dry weight [56]. The alkaloids contained in leaves and latex of *Croton lechleri* are indicated in Figure 23**.**

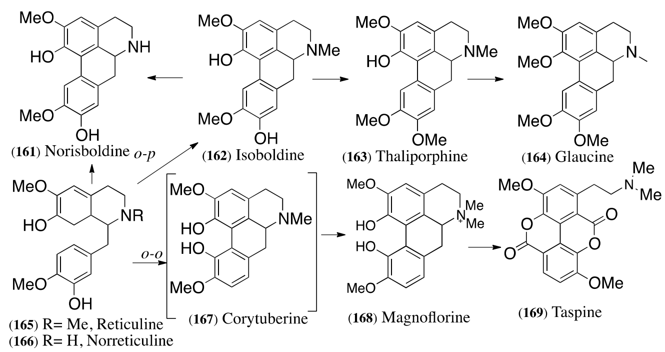


Figure 23: Alkaloids present and probable biosynthetic relationship of alkaloids isolated from *C. lechleri*.

From *Croton eluteria,* collected near Guayaquil on the Pacific coast of Ecuador, five new neoclerodane diterpenoids [58], named cascarillins E-I (**170-174**), were isolated; these compounds are indicated in Figure 24.

Euphorbia cotinifolia is a tree named *lechero* in the Amazonian region of Ecuador. The latex of this plant is applied to ingrown toenails and nail infections. *Euphorbia prostrata* is used for infected pustules; the entire plant is boiled and the affected area washed with the decoction. For ulcers, the infusion is drunk before breakfast and during the day [59].

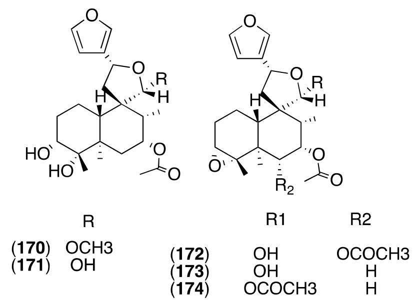


Figure 24: Neoclerodane diterpenoid derivatives from *Croton eluteria*.

***Fabaceae*, *Flacourtiaceae*, *Frullaniaceae*, and *Gesneriaceae*:** *Bauhinia tarapotensis* (Fabaceae) is a small tree that is native to Ecuador, where it is commonly called *Pongacarachupaju*, *Corazon panga* or *pata de vaca* [59]. It is used to stop bleeding from dental extractions, the leaves are ground and applied to the affected site; the leaves and flowers are also cooked and the decoction is drunk for heart pain. Leaves of this plant collected from the Pastaza region yielded a new cyclohexenone (**175**) and a new caffeoyl ester derivative (**176**), together with the known compounds (-)-isolariciresinol-3-α-*O*-β-D-glucopyranoside (**177**), (+)-1-hydroxypinoresinol-1-*O*-β-D-glucopyranoside (**178**), isoacteoside (**179**), luteolin-4´-*O*-β-D-glucopyranoside (**180**) and indole-3-carboxylic acid (**181**) [59]. These compounds (**175-181**) are shown in Figure 25.

Casearia sylvestris (Flacourtiaceae) is named *pisang* and it is used for snakebite. From the leaves and twigs, collected in a tropical rain forest of Ecuador in the Pastaza region, three bioactive clerodane diterpenoids were isolated: casearvestrins A (**182**), B (**183**) and C (**184**) (Figure 26) [60].

Two sesquiterpenoids, (+)-arbusculin B (**185**) and (-)-α-bisabolol (**186**)**,** have been obtained from *Frullania brasiliensis* (Jubulaceae, ex Frullaniaceae)*,* collected in Ecuador [61] (Figure 27).

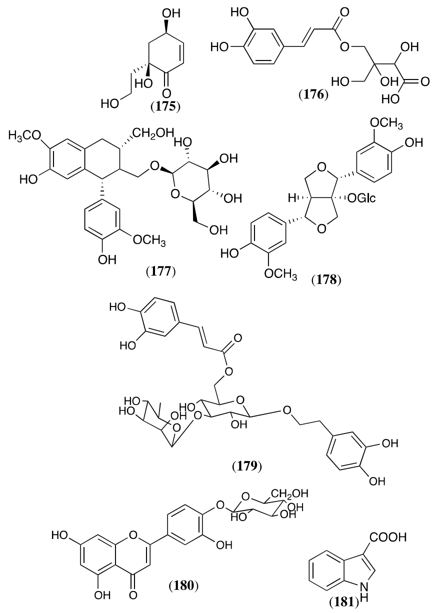


Figure 25: Compounds isolated from *B. tarapotensis*

Codonanthopsis dissimulata (Gesneriaceae) is named by the Kofan as *kugi-kisi* and *hugi kisi*; and by the Siona as *huku-iko* and *kuku iko*. The Kofan use the leaves, pounded with a rock and boiled, for headache, by snorting the liquid with a spoon. The Siona use it similarly for headache and toothache and for ant stings [12].

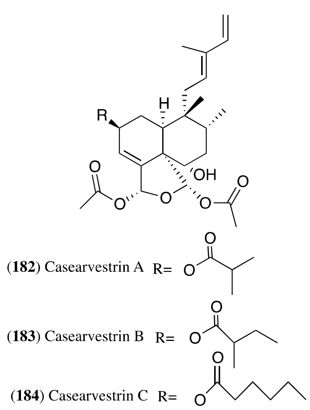


Figure 26: Clerodane diterpenoids (casearvestrin) derivatives from *Casearia sylvestris.*

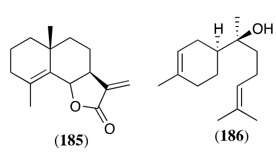


Figure 27: Sesquiterpenoid derivatives from *Frullania brasiliensis*

Gramineae, Herbertaceae, and Hymenophyllaceae: *Cymbopogon citratus* (Gramineae), known in Ecuador as *hierba luisa*, is cultivated and recommended as a drink to calm abdominal pain, rheumatism and ulcers. The Kichwa people utilize it for headache and stomach pain, by infusing its leaves and roots in water. The Siona use the infusion of the leaves with sugar to treat stomachache. From *Paspalum conjugatum* (Gramineae), local name *turvara*, some cyanogenic heterosides were found. The Shuar use this plant in infusion for headache [12]. *Herbertus acanthelius* and *H. subdentatus* (Herbertaceae) produce isocuparene-type sesquiterpenoids as major components [60]. From *H. subdentatus,* collected in Ecuador, (-)-α-herbertenol (**187**), (-)-herbertenediol (**188**) and (-)-β-herbertenol (**189**) were isolated; while from *H. acanthelius* only (-)-α-herbertenol (**187**) has been isolated; these compounds are showed in Figure 28.

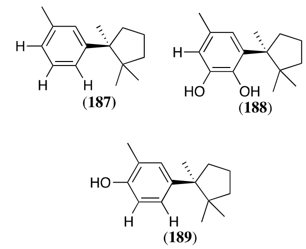


Figure 28: Isocuparene-type sesquiterpenoids from *Herbertus subdentatus* and *H. acanthelius.*

Trichomanes membranaceum (Hymenophyllaceae) is known as *tusana-si-sehe-pa* by the Kofan; the plant is boiled and the liquid is used to bathe the head to treat headache [12].

Lamiaceae: The essential oil of *Clinopodium nubigenum* [28, 62] and *C. tomentosum* [63], the second one analyzed also through gas chromatography-olfactometry (GC-O), are composed of many monoterpenes, among which the main constituents are menthane derivatives. In the essential oil of *Lepechinia paniculata* 34 components have been determined, the major one being aromadendrene. *L. paniculata* is used to treat headache by direct application of its buds to the head; the flowers are used for the treatment of nervous system affection and for the treatment of *mal de aire*, a traditional ailment in Kichwa towns [64]. *Lepechinia mutica* is an endemic Ecuadorian plant known as *casa casa*. The plants of this genus are used against headache, toothache and muscle pain. In the essential oil of *L. mutica* [64] 54 components were identified, constituting 94% of the total oil; monoterpene hydrocarbons were the main group of constituents. The essential oils of *Satureja glabrata* and *Minthostachys mollis* were characterized by a high percentage of oxygenated monoterpenes [63–65].

Satureja glabrata is known as *sacha romero*, and the leaves of *Satureja* spp. in general are used in body washes by the Saraguro. *Minthostachys mollis* (*poleo*) leaves are prepared as a tea and used as a digestive, carminative and antispasmodic, whereas a decoction is employed against muscle pain and rheumatism. In the essential oil of *Scutellaria volubilis* 37 compounds, which represent 93.8 % of the total sample, have been determined; sesquiterpene hydrocarbons were the main group of constituents. *S. volubilis* is used traditionally also in the treatment of the nervous system, as well as for heart and kidney infections [64].

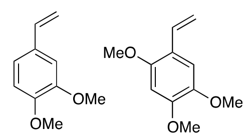
Salvia scutellaroides, *S. macrophylla* and *S. pichinchensis* are used for liver and kidney problem; the leaves of this species are stuck on the head for treating headache [66]. The seed oil fatty acid composition of *S. hispanica*, known as *chia*, was determined by gas chromatographic analysis. The oil composition showed the presence of linolenic, linoleic, oleic, stearic and palmitic acids [67].

Oreocallis grandiflora is used by the Saraguro to treat many different diseases, including diabetes. The extracts were assessed through hypoglycemic and antioxidant tests, and showed interesting activity [68].

Lauraceae: *Ocotea quixos* is an endemic plant of the rainforest of Ecuador. It has been traditionally esteemed for its aromatic properties since Incaic times and appreciated as an appetizer, eupeptic, disinfectant and as a local anesthetic. Its leaves are also used to prepare an anti-diarrheic infusion. Its essential oil was shown to possess significant inhibitory effects on platelet aggregation and clot retraction in rodent plasma, antioxidant and antimicrobial activities, and antibacterial and antifungal properties. Chemical analysis of the essential oil led to the identification of 61 compounds, with β-cariophyllene, *trans*-cinnamaldehyde and methyl cinnamate being the most abundant, reaching values up to 15.1%, 27.8% and 21.6%, respectively [69-71].

Leguminosae and Lejeuneaceae: *Cassia macrophylla* and *C. ruiziana* (Leguminosae) are known by the Kofan as *kongee-hee-te-ta* and *konghi-hi-se-he-pa*; they are used to treat headache and earache. *Myroxylon balsamum* (Leguminosae) is known as *corteza de balsam* and the Kichwa people extract the bark and scrape off its interior, then mix it with a little lukewarm water and drink it to treat headache. *Enterolobium* sp. (Leguminosae) and another undetermined species of Leguminosae are used to treat fungal infections and infestations of mites; the Waorani wash their clothes in a bath prepared with this bark to eliminate scabies [12,18,19].

Two aromatic compounds have been isolated from Ecuadorian *Marchesinia brachiata* (Lejeuneaceae): 3,4-dimethoxy-1-vinylbenzene (**190**) and 2,4,5-trimethoxy-1-vinylbenzene (**191**) (Figure 29). This result confirms that species of *Marchesinia* are chemically very different from the other subfamilies of the Lejeuneaceae, because of the presence of styrene derivatives as major components [72].



(**190**) (**191**)

Figure 29: Compounds isolated from *Marchesinia brachiate*.

Loganiaceae and Lycopodiaceae: *Buddleja incana* (Loganiaceae) is a large shrub which grows in the central Andean region from Ecuador to Bolivia and Chile; in Ecuador it is known as *quisuar* and the leaves are used to treat infected wounds [73].

The traditional use of the Lycopodiaceae family is widely known by native Andean inhabitants of Ecuador. For example, a mixture of *trencillas* (Lycopodiaceae spp.), *cararango* (*Lobelia* sp.), *Santa Maria* (*Tanacetum parthenium*), *Palo santo* (*Bursera graveolens*) and *San Pedrillo* (*Echinopsis pachanoi*), are prepared by maceration in water or *aguardiente* (a liquor distilled from fermented sugar cane) to treat *susto* (a disease that is produced by unpleasant experiences, accidents, violent episodes, or moments of distress, producing an emotional impact on the patient). They are used also in purgative preparations [2].

Some of us recently discovered in two Ecuadorian *Huperzia* species the presence of new hydroquinolinic alkaloids, whose data are still unpublished [74], due to partial structural characterization. In fact, *H. crassa* and *H. espinosana*, used by the Saraguro for the preparation of psychotropic beverages, showed the presence of at least eight alkaloids, isolated through liquid chromatography and studied by NMR spectroscopy and MS. All these compounds present a similar structure and a molecular weight of about 600 amu; in particular, one alkaloid, shows a structure related to the known *Lycopodium* alkaloid cryptadine B [75], but with a higher molecular weight; this result is different from all the alkaloids present in the literature. The exact structural characterization of this alkaloid requires X-ray diffraction analysis. Finally, the phenolic metabolites present in the leaves of 170 Ecuadorian *Lycopodium* specimens, representing 49 species and varieties, have been examined by EPR spectroscopy [76].

Malpighiaceae and Malvaceae: *Urena lobata* (Malvaceae) shows anti-inflammatory and antioxidant activity and is used in the traditional medicine of Ecuador [20].

The famous plant "*ayahuasca"* actually represents several species of the genus *Banisteriopsis* (Malpighiaceae); it is known as *yagué*, *caapi*, *pinole* and *nepi* and is a natural hallucinogenic drug used in healing rituals. After the interpretation of Ecuadorian archaeological remains, there is evidence of a prehistoric *ayahuasca* use and also the evidence of a belief system connected to the use of major hallucinogenic plants between the Jibaro Indians and other tribal groups. The main alkaloid responsible for the hallucinogenic activity of *ayahuasca* was first called yageine or telepathine. In 1929 Lewin extracted an alkaloid that he called banisterine and used it successfully in the treatment of different kinds of paralysis; in 1975 the alkaloids harmine, harmaline and tetrahydroharmine were identified as the main psychoactive substances [77,78]. In Ecuador, *ayahuasca* is used by the aborigines of the coastal lowlands and of the Amazon Basin, though to a much lesser extent than before [77].

Marchantiales and Meliaceae: *Melia azedarach* (Meliaceae) is known by the Kichwa as *copapanga*; the cooked leaves are eaten to relieve headache [12]. In 1992 ecuadorin (**192**), a novel tetranortriterpenoid, was isolated from *Guarea kunthiana* (Meliaceae). This compound was also reduced to the dihydro and tetrahydro derivatives (**193**,**194**) (Figure 30) [79]. The major component of *Marchantia plicata* (Marchantiales) is marcantin A (**195**) (Figure 30), a chemical taxonomic marker for this family. *Marchantia* species are spread worldwide and represent a rich source of cyclic bis-bibenzyls [61].

Menispermaceae and Monimiaceae (Siparunaceae): *Curarea tecunarum* (Menispermaceae) is the principal source of an especially strong arrow and dart poison, prepared in the northwestern Amazon. It is the most important source of poison for the Waorani and the preparation of curare from it is a highly esteemed skill [18]. *Abuta grandiflora* (Menispermaceae) is used for hemorrhage and pain and has been employed to treat colic in nervous children [12].

Fruits from *Siparuna* sp. (Siparunaceae) are used to treat fever and headache. When crushed, the leaves and fruits are very pungent and are rubbed directly onto the face and head [18]. A monoterpene glycoside (**196**) has been extracted from the leaves of *Siparuna thecaphora*, collected in Puerto Napo. Moreover, some sesquiterpenes of the cadinane group (**197-203**) [80,81], shown in Figure 31, were isolated from *S. macrotepala*, collected in Napo province. *S. eggersii* provided an essential oil, whose composition has been described by Ruiz *et al*. [28].

***Moraceae and Myristicaceae*:** The Cayapá and Chocó indigenous people of Ecuador use the dried latex of some species from the family Moraceae, mixed to a paste obtained from some lemon or lime juice, and apply it to the tips of the darts. The poison is used mainly against birds and small mammals. The Colorado people, from northwestern Ecuador, may have taken *Naucleopsis chiguila* as a resource for hunting, and the Coaiquer Indians still hunt with the latex of *Naucleopsis naga* [82].

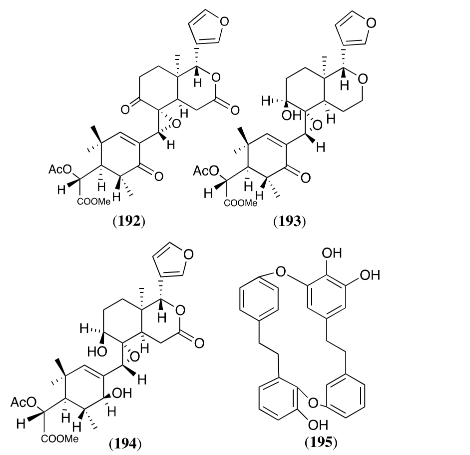


Figure 30: Compounds isolated from *Guarea kunthiana* and *Marchantia plicata*

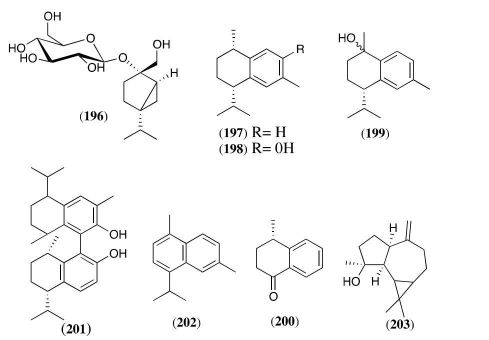


Figure 31: Compounds isolated from *Siparuna* species

Waorani people use some species of Myristicaceae, in particular the resin of *Iryanthera* cf. *elliptica*, *I. juruensis and I.* cf. *paraensis* as antifungal agents. It is also used to kill mites and scabies. Also the bark and bright red resin of *Otoba parviflora* are crushed and rubbed on the skin as a treatment for the bites of mites and for fungal infections. The inner bark of *Virola calophylla* is squeezed and the copious red resin directly applied to fungal infections and scabies infestations [18].

Myrtaceae: The chemical composition was studied of the essential oil obtained from *Myrcianthes rhopaloides*, collected in Cerro el Villonaco (Loja, Ecuador). Forty constituents, representing 92% of the total sample, were identified in the essential oil of *M. rhopaloides*, mainly geranial (34%) and neral (25%), followed by α- and β-pinene in a proportion of 7% and 9% respectively [65].

***Olacaceae*:** Decoctions of leaves of *Heisteria* spp. are used to wash or preparing compresses for headache and for epistaxis (nosebleed). The leaves are also steeped in cold water and the infusion used to bathe the head [12]. From *H. nitida*, collected at the Reserva Biologica Jatun Sacha, Napo Province, two cyclopeptide alkaloids (**204-205**) (Figure 32) were isolated [83]. From *H. acuminata*, collected at the Reserva Biologica Jatun Sacha, Napo province, five linear acetylenic compounds (**206-210**) were isolated [84]. Chemical structures are shown in Figure 32.

Minquartia guianensis is extracted in water to prepare a fish poison [19]. From *M. guianensis*, collected in the Napo River, a polyacetylene acid was isolated. The aqueous extract of the stem bark gave, in a brine shrimp bioassay, a LC_{50} of 25.1 μg/mL and a P-388 ED_{50} of 3.2 μg/mL. The $CHCl_3$ extract gave in a brine shrimp bioassay a LC_{50} of 20.4 μg/mL and a P-388 ED_{50} of 2.16 μg/mL [85].

Palmae (Arecaceae): The palms are very important for the Amazonian indigenous peoples. The Waorani use the leaves of *Jessenia bataua* to provide thatch, while the adventitious roots are employed to treat worms, diarrhea, headaches and stomach ailments. The Siona Secoya use the oil from the mesocarp in cooking and as a hair tonic; the petiole from *Maximiliana* aff. *maripa* is cut into short lengths for making darts for blowguns. The fruits are eaten as food and used as an infusion to treat colds [12,18].

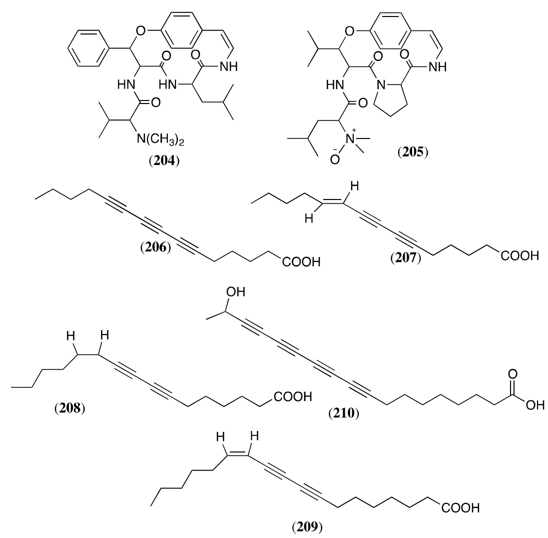


Figure 32: Chemical compounds from Olacaceae species.

Piperaceae: Ecuadorian native communities use different species of *Piper*. The stems of *P. augustum* and *P. conejosense* are broken off and used as toothbrushes. The ancestors are said to have used this plant to turn teeth black, as this was thought to prevent tooth decay [18,19].

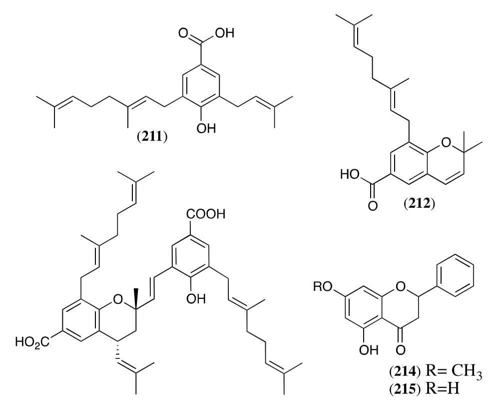


Figure 33: Chemical structure of compounds isolated from *Piper kelleyi* and *P. ecuadorense*

From the essential oils distilled from the aerial parts of *P. aduncum* and *P. obliquum*, collected in Macas, Morona Santiago Province, 46 and 33 compounds were identified, respectively. Safrole (45.8%) was the major compound in *P. obliquum* essential oil and dillapiol (45.9%) the main constituent in *P. aduncum* [86]. From *P. kelleyi,* collected in Napo province, one prenylated benzoic acid derivative and two chromane structures were isolated (**211-213**) [87].

P. ecuadorense, known as *matico de monte*, is a plant used by many indigenous communities in Loja and Zamora provinces to treat hangover, as a disinfectant and in wound healing. The Saraguro use it for the treatment of *mal de aire*, a supernatural disease. The methanol extract showed an important anti-fungal activity, while from the dichloromethane extract two known flavonoids, pinostrobin (**214**) and pinocembrin (**215**), have been isolated [88]. All the metabolites are shown in Figure 33.

Plagiochilaceae and Rosaceae: From *Plagiochila micropteryx* (Plagiochilaceae) three sesquiterpene type compounds were isolated (**216-218**)[59] (Figure 34).

A series of phenolic compounds were isolated from fruits of four species of Rosaceae that were purchased in three markets in Quito: *Fragaria ananasa*, *Rubus glaucus*, *Prunus salicina* and *P. serotina* (**219-230**) [89] (Figure 34).

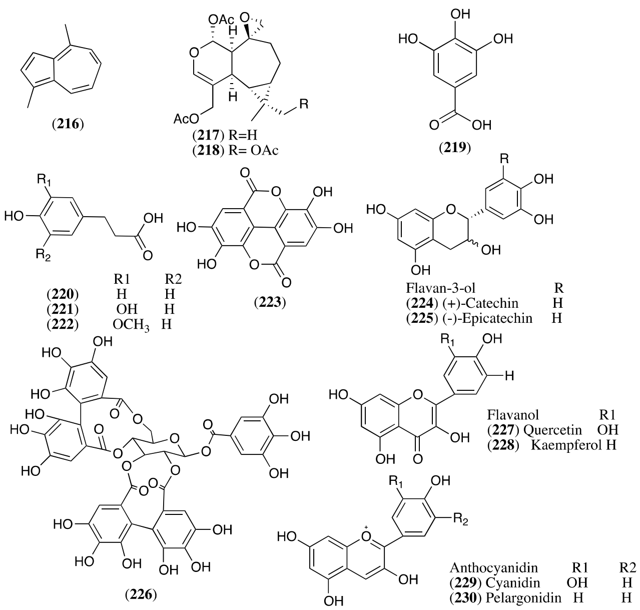


Figure 34: Chemical structure of phenolic compound of Rosaceae family.

Rubiaceae: *Duroia hirsuta*, known as *owecawe*, is an abundant myrmecophyte tree of the primary rain forest. The Waorani open the swollen stems that house the ants and apply the tissue and the concentrated pheromones directly to the inside of the cheek. It is said to relieve the pain that results from excessive use of the blowgun, or when ulcerated gums or cheeks prevent normal blowgunning [18]. An investigation of the roots of *D. hirsuta* from Ecuador yielded the iridoid lactone duroin, together with 3,7,3′,5′-tetramethoxy-4′-hydroxyflavone, 3,7,3′-trimethoxy-4′,5′-dihydroxyflavone and 7,3′,5′-trimethoxy-3,4′-dihydroxyflavone as novel constituents (**231-234**) [90], shown in Figure 35**.**

Coussarea macrophylla (Rubiaceae) is a woody plant, occurring in the tropical swamp forests of Ecuador. Five naturally occurring anthracene derivatives: 1,4,10-trimethoxyanthracene-2-carbaldehyde (**235**), 1,4,10-trimethoxy-2-anthracen-2-yl methanol (**236**), 1,4,8,10-tetramethoxyanthracene-2-carbaldehyde (**237**), 1,4,10-trimethoxyanthracene-2-carboxylic acid (**238**), methyl 1,4,10-trimethoxyanthracene-2-carboxylate (**239**) and 1,3-dimethoxy-2-methoxymethylanthraquinone (**240**), were isolated from *C. macrophylla,* along with three known compounds: 3-hydroxy-1-methoxy-2-methoxymethylanthraquinone (**241**), scopoletin, and 3-*epi*-pomolic acid [91]. Some of us have also isolated eight triterpene acid derivatives [92], with seco-cycloartane and seco-dammarane type structure; six of these compounds, called macrocoussaric acid A-F, are novel (**243-245, 247-249**) and two, (24*E*)-3,4-secodammara-4(28),20,24-triene-3,26-dioic acid (**242**) and secaubryenol (**246**), are known. All these molecules are shown in Figure 36**.**

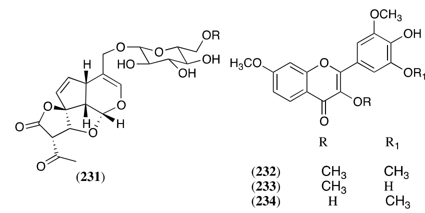


Figure 35: Chemical constituents from *Duroia hirsuta*

The bark of *Calycophyllum acreanum* is used by the Waorani natives to prepare a decoction to treat fungal infections [18, 19]. *Pentagonia spathicalyx* is known as *boyomo* by the Waorani, i.e. "the stingray leaf" because the broad leaf looks like a stingray. This forest tree gives an edible fruit used to treat stingray wounds, the most painful of jungle injuries [18].

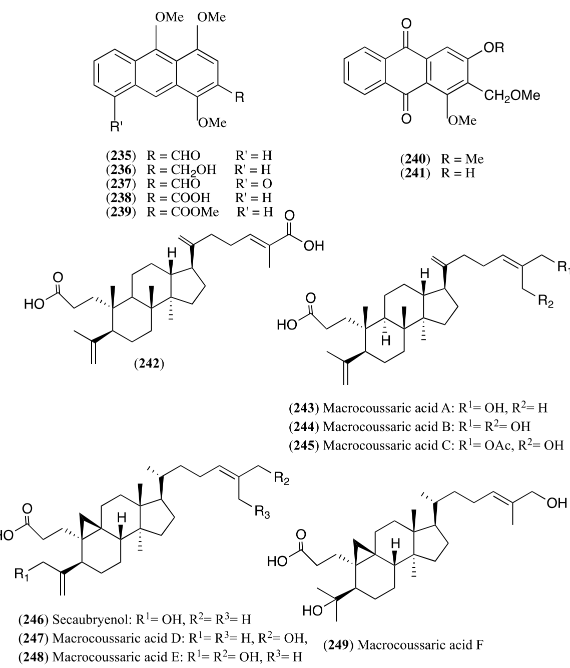


Figure 36: Anthracene and triterpene derivatives from *Coussarea macrophylla*.

Rutaceae, Sapindaceae, and Simaroubaceae: The essential oils distilled from *Citrus* spp. (Rutaceae) were chemically characterized. *C. aurantium* petitgrain exhibited as major components sabinene (38.3 %), *trans-E*-ocimene (6.7 %), and linalool (8.8 %); other minor components were 3-carene (8.9 %), *D*-limonene (7.9 %), β-myrcene (3.4 %), 4-terpinenol (2.5 %), α-pinene (1.9 %), geranial (1.9 %) and β-pinene (1.8 %). *C. limon* (CL1) essential oil evidenced a high abundance of limonene (52.7 %) and linalool (15.1 %) and, as minor compounds, citronellal (3.1 %), sabinene (2.7 %) and carvone (2.6 %). In *C. limon* (CL2) petitgrain sabinene (36.1 %) predominated, followed by limonene (24.1 %), linalool (4.7 %), 4-terpinenol (3.9 %), γ-terpinene (3.9 %), citronellal (3.6 %), *trans*-β-ocimene (3.2 %), α- terpinene (2.8 %) and β-myrcene (2.6 %). *C. nobilis* petitgrain evidenced high abundance of linalool (41.6 %) and appreciable contents of γ-terpinene (14.3 %) and thymol (9.0 %), followed by *trans-E*-ocimene (10.9 %), *p*-cymene (4.1 %), α-pinene (3.6 %), β-pinene (3.1 %) and limonene (2.8 %) as minor compounds [93].

From *Cupania cinerea* (Sapindaceae) two diterpene glycosides (**250, 251**), named cupacinoside and 6-de-*O*-acetylcupacinoside, a lactonized triterpene bearing an oxepin moiety and named cupacinoxepin (**252**), together with the known compounds scopoletin (**253**), caryophyllene oxide (**254**), two bisabolane sesquiterpenes (**255, 256**), lichexanthone (**257**), gustastatin (**258**), lupenone (**259**), betulone (**260**), 17β,21β-epoxyhopan-3-one (**261**), taraxerol (**262**) and taraxerone (**263**) were isolated [94]. The compounds are shown in Figure 37. The stem cortex of *Paullinia yoco* (Sapindaceae) is traditionally used by the natives of Ecuador to prepare a caffeine rich beverage [95].

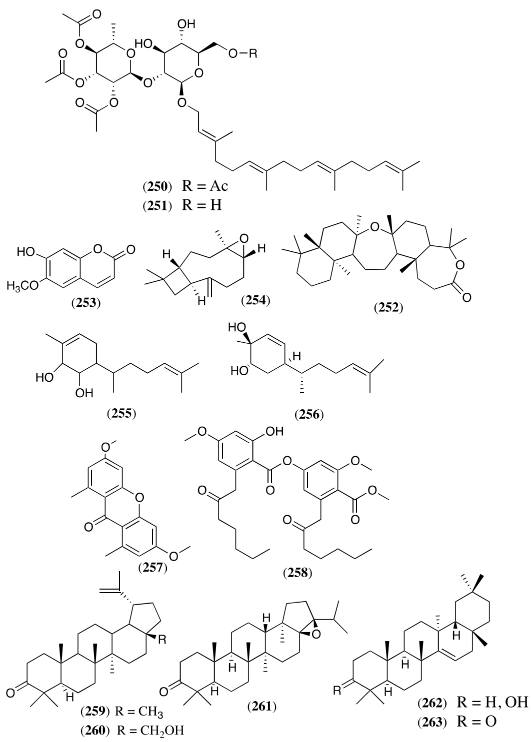


Figure 37: Chemical constituents from *Cupania. cinerea*

Picramnia sp. (Simaroubaceae) was collected in Napo, at the confluence of Rios Quiwado and Tiwaeno. The crushed flowers provide a purple dye. The Waorani name of the plant is *degin tai-gip-enii* [19].

Solanaceae: The traditional use of medicinal plants in Southern Ecuador include 11 species of Solanaceae. The fresh plants, often collected in the wild state, are commonly applied by ingestion as herb decoction or by application of the plant material as poultices [7].

The aqueous extract of the dried roots of *Solanum dulcamara*, is marketed as a greenish brown suspension with a mild bittersweet smell. The commercial plant extract, called BIRM, contains antitumor compounds, with a relevant antiproliferative activity *in vitro* and *in vivo* against prostate cancer cells. Three active ingredients in BIRM with a relative molecular mass of 3500 were identified [96].

Solanum pectinatum and *S. sessiliflorum* are used by the Waorani people. The fruits of this cultivated shrub are eaten or sucked to relieve thirst; moreover, they are rubbed into the scalp to make the hair shine. The pulp of the fruit is imbibed after scorpion stings and spider bites to prevent vomiting and the fruits are rubbed onto any type of sting. The Cofan people use the pulp of *S. mammosum*, to keep cockroaches out of their houses [18].

The fruits of the cultivated pepper *Capsicum chinense* are used to treat stomachache. It is not eaten as food, but is often used by the shaman's wife to induce their husband out of the intoxication caused by *Banisteriopsis muricata* [18].

Brugmansia arborea (Syn. *Datura arborea*) has the Kichwa name of *huanduc* or *lumucha guantu*, in Spanish *floripondio*. This is one of a few related species of small trees commonly employed as hallucinogens and found also as a cultivated plant. Indigenous cultures of Amazonia make longitudinal cuts in the stems and branches and apply them to the head or other painful body parts. The strip is bandaged in place for 15 minutes. If employed longer, a soporific or temporary anesthetic effect may be produced. A preparation of this plant is also given to dogs to make them better hunters [12].

The leaves of *Brunfelsia grandiflora* are added to the hallucinogenic drink *ayahuasca* or *yaje,* prepared from the bark of *Bunisteriopsis caapi* or *B. inebrians.* This additive greatly increases the effects of the drink and prolongs the intoxication. Another medicinal use of this plant is as an anti-rheumatic: an infusion is ingested for several days to allay the effects of what is commonly described as rheumatism [19].

Sterculiaceae: The lipid fraction from seeds of the wild Ecuadorian plant *Theobroma subincanum* was compared with that of *T. cacao*. The results revealed that in *T. subincanum* the triglycerides contain fatty acids with longer chains. The melting point, peroxide and saponifiable numbers were determined for each *Theobroma* sample. The results led to the conclusion that *T. subincanum* would produce poorer quality butter than *T. cacao*. Nevertheless, the results do point toward a significant commercial use of *T. subincanum* for low-profile products [97]. In addition, *T. subincanum* seeds were analyzed to determine quali-quantitative tocopherol distribution. Fatty acids and sterols in the embryos, teguments and endosperm were also evaluated with an aim to better characterization. Tocopherols were particularly abundant in the embryo, with quali-quantitative data similar to wheat germ oil whereas, in the teguments and endosperm, the concentrations of tocopherols were lower. The fatty acid profile and phytosterol characterization of the seed parts showed qualitative homogeneous data. In the endosperm, 80% of the entire FAP consisted of oleic and stearic acid while, among sterols, cycloartenol was more abundant in the endosperm than in the embryos and teguments. *T. subincanum* seeds can be proposed as possible substitutes in the cocoa processing industry and as a potential source of vitamin E [98].

Theophrastaceae and Urticaceae: *Clatija* sp. (Theophrastaceae) was collected in Pastaza province, Rio Chico. The seeds and roots are employed in the village of Rio Chico for treating diarrhea [19]. *Urera baccifera* (Urticaceae) is used by the Waorani natives either to punish children or as a way to pass on their own adult strength to the children. An elder may return from the fields and beat his children in order to instill his ability to work hard. Also this plant is used to relieve all types of pain, including aching muscles, pulled muscles, arthritis, fainting, snake bite, sting ray stings and stings of various insects such as the conga ant, azteca ants and fire ants [18]. The fruit is used for all pain of aching muscles, arthritis, ant strings, azteca ants, fire ants and conga ants [19].

Verbenaceae and Zingiberaceae: *Lantana armata* (Verbenaceae) belongs to a genus of shrubs and herbs, often prickly, which contains alkaloids and camphor. Among the Shuar, the cooked leaves are eaten to relieve headache, as well as for general body pains [12].

Renealmia asplundii and *R. thyrsoidea* (Zingiberaceae) are used by Waorani indigenous people to treat snakebite [18]. The Waorani call *R. asplundii teentemo* ("snake leaf"). The stem is pounded fresh, and the pulp is mixed with water and drunk once a day to prevent swelling from snakebite; it may be taken twice daily for internal bleeding and to prevent swelling [19]. *R. thyrsoidea* is also collected in Napo province. Amongst the Waorani, the stem is crushed fresh, mixed with water and drunk once a day to prevent swelling from the bite of the *fer-de-lance*. The plant is called *teentekage* ("snake's hair") [19].

The Kofan, Kichwa, Secoya and Shuar natives employ a decoction of the rhizome of *Zingiber officinale* (Zingiberaceae) to relieve stomachache and diarrhea. The Shuar additionally apply a beaten egg with the plant on hematomas. Among some Spanish speaking people (mestizos), crushed leaves are made into a compress to relieve pain, while the macerated rhizome is employed to relieve headaches and stomach pain. When one's eyes exhibit excrescence, a drop of sap is applied once; excessive use is said to burn the eye [12].

Conclusions: This review shows the high potential of Ecuador as a source of novel secondary metabolites and biologically active plant extracts. In particular, it is evident how great is the biodiversity of this country with respect to the number of phytochemical and pharmacological publications. Furthermore, the ethnobotanical knowledge of the Ecuadorian native people is also a very rich resource for the discovery of new pharmacologically active molecules. All these considerations suggest that scientific institutions should take into account Ecuador as a destination for stronger investments in the chemical and pharmacological research on natural products.

Acknowledgments - This work was supported by *Proyecto Prometeo, Secretaría de Educación Superior, Ciencia, Tecnología e Innovación (SENESCYT), República del Ecuador*.

References

[1] Cámara LR, Paniagua ZN, Balslev H, Macía MJ. (**2014**) Ethnobotanical knowledge is vastly under-documented in northwestern South America. *PLoS ONE*, ***9***, e85794.

[2] Armijos C, Cota I, González S. (**2014**) Traditional medicine applied by the Saraguro yachakkuna: a preliminary approach to the use of sacred and psychoactive plant species in the southern region of Ecuador. *Journal of Ethnobiology and Ethnomedicine*, ***10***, 26.

[3] Giovannini P. (**2015**) Medicinal plants of the Achuar (Jivaro) of Amazonian Ecuador: Ethnobotanical survey and comparison with other Amazonian pharmacopoeias. *Journal of Ethnopharmacology*, ***164***, 78–88.

[4] Bennett BC, Husby CE. (**2008**) Patterns of medicinal plant use: An examination of the Ecuadorian Shuar medicinal flora using contingency table and binomial analyses. *Journal of Ethnopharmacology*, ***116***, 422–430.

[5] Cavender AP, Albán M. (**2009**) The use of magical plants by curanderos in the Ecuador highlands. *Journal of Ethnobiology and Ethnomedicine*, ***5***, 3.

[6] Bussmann RW, Sharon D. (**2006**) Traditional medicinal plant use in Northern Peru: tracking two thousand years of healing culture. *Journal of Ethnobiology and Ethnomedicine*, ***2***, 47.

[7] Bussmann RW, Sharon D. (**2009**) Shadows of the colonial past-diverging plant use in Northern Peru and Southern Ecuador. *Journal of Ethnobiology and Ethnomedicine*, ***5***, 4.

[8] Bussmann RW, Sharon D. (**2006**) Traditional medicinal plant use in Loja province, Southern Ecuador. *Journal of Ethnobiology and Ethnomedicine*, ***2***, 44.

[9] Bussmann RW, Sharon D, Vandebroek I, Jones A, Revene Z. (**2007**) Health for sale: the medicinal plant markets in Trujillo and Chiclayo, Northern Peru. *Journal of Ethnobiology and Ethnomedicine*, ***3***, 37.

[10] Tene V, Malagón O, Vita Finzi P, Vidari G, Armijos C, Zaragoza T. (**2007**) An ethnobotanical survey of medicinal plants used in Loja and Zamora-Chinchipe, Ecuador. *Journal of Ethnopharmacology*, ***111***, 63–81.

[11] Bailón NC, Romero JC, Tinitana F, Ostrosky WP. (**2015**) Medicinal plants of Ecuador: a review of plants with anticancer potential and their chemical composition. *Medicinal Chemistry Research*, ***24***, 2283–2296.

[12] Russo EB. (**1992**) Headache treatments by native peoples of the Ecuadorian Amazon: A preliminary cross-disciplinary assessment. *Journal of Ethnopharmacology*, ***36***, 193–206.

[13] Kraut L, Mues R, Zinsmeister HD. (**1997**) Prenylated bibenzyl derivatives from *Lethocolea glossophylla* and *Radula voluta*. *Phytochemistry*, ***45***, 1249–1255.

[14] Kraut L, Mues R, Zinsmeister HD. (**2006**) Corrigendum to "Prenylated bibenzyl derivatives from *Lethocolea glossophylla* and *Radula voluta*." *Phytochemistry*, ***67***, 1297.

[15] Rycroft DS, Cole WJ, Rong S. (**1998**) Highly oxygenated naphthalenes and acetophenones from the liverwort *Adelanthus decipiens* from the British Isles and South America. *Phytochemistry*, ***48***, 1351–1356.

[16] Bruni R, Medici A, Guerrini A, Scalia S, Muzzoli M, Sacchetti G. (**2001**) Wild *Amaranthus caudatus* seed oil, a nutraceutical resource from Ecuadorian flora. *Journal of Agricultural and Food Chemistry*, ***49***, 5455–5460.

[17] Oilar RD. (**1954**) Several rare and uncatalogued oils of Ecuador. *The Journal of The American Oil Chemists' Society*, ***31***, 142–143.

[18] Davis EW, Yost JA. (**1983**) The ethnomedicine of the Waorani of Amazonian Ecuador. *Journal of Ethnopharmacology*, ***9***, 273–297.

[19] Schultes RE. (**1985**) De plantis toxicariis e mundo novo tropicale commentationes XXXV: Miscellaneous notes on biodynamic plants of the northwest Amazon. *Journal of Ethnopharmacology*, ***14***, 125–128.

[20] De Las Heras B, Slowing K, Benedí J, Carretero E, Ortega T, Toledo C. (**1998**) Antiinflammatory and antioxidant activity of plants used in traditional medicine in Ecuador. *Journal of Ethnopharmacology*, ***61***, 161–166.

[21] Lewis WH, Kennelly EJ, Bass GN, Wedner HJ, Lewis MP, Fast D. (**1991**) Ritualistic use of the holly *Ilex guayusa* by Amazonian Jívaro Indians. *Journal of Ethnopharmacology*, ***33***, 25–30.

[22] Aquino R, Morelli S, Lauro MR, Abdo S, Saija A. Tomaino A. (**2001**) Phenolic constituents and antioxidant activity of an extract of *Anthurium versicolor* leaves. *Journal of Natural Products*, ***64***, 1019–1023.

[23] Patil AD, Baures PW, Eggleston DS, Faucette L, Hemling ME, Westley JW. (**1993**) A screen for inhibitors of DNA recombination: Identification of two new spirostanol glycosides from *Chamaedorea linearis*. *Journal of Natural Products*, ***56***, 1451–1458.

[24] Blicher MU, Balslev H. (**1990**) *Attalea colenda* (Arecaceae), a potential lauric oil resource. *Economic Botany*, ***44***, 360–368.

[25] Radice M, Viafara D, Neill D, Asanza M, Sacchetti G, Guerrini A. (**2014**) Chemical characterization and antioxidant activity of Amazonian (Ecuador) *Caryodendron orinocense* Karst and *Bactris gasipaes* Kunth seed oils. ***1250***, 1243–1250.

[26] Zhang G, Shimokawa S, Mochizuki M, Kumamoto T, Nakanishi W, Watanabe T. (**2008**) Chemical constituents of *Aristolochia constricta*: Antispasmodic effects of its constituents in Guinea-pig ileum and isolation of a diterpeno-lignan hybrid. *Journal of Natural Products*, ***71***, 1167–1172.

[27] Abdala LR, Seeligmann P. (**1995**) Flavonoids in *Tagetes zipaquirensis* and their chemosystematic significance. *Biochemical Systematics and Ecology*, ***23***, 871–872.

[28] Ruiz S, Malagón O, Zaragoza T, Valarezo E. (**2010**) Composition of the essential oils of *Artemisia sodiroi* Hieron., *Siparuna eggersii* Hieron., *Tagetes filifolia* Lag. and *Clinopodium nubigenum* (Kunth) Kuntze from Loja Ecuador. *Journal of Essential Oil Bearing Plants*, ***13***, 676–691.

[29] Vidari G, Abdo S, Gilardoni G, Ciapessoni A, Gusmeroli M, Zanoni G. (**2006**) Fungitoxic metabolites from *Erigeron apiculatus*. *Fitoterapia*, ***77***, 318–320.

[30] Abdo S, De Bernardi M, Marinoni G, Mellerio G, Samaniego S, Vidari G. (**1992**) Furanoeremophilanes and other constituents from *Senecio canescens*. *Phytochemistry*, ***31***, 3937–3941.

[31] De Bernardi M, Vidari G, Vita Finzi P, Abdo S, Marinoni G, Mellerio G. (**1988**) Metabolites of medicinal plants II. Furanoeremophilanes from *Lasiocephalus ovatus*. *Gazzetta Chimica Italiana*, ***118***, 565–568.

[32] Bohlmann F, Zdero C. (**1977**) Weitere Inhaltsstoffe aus Vertretern der Eupatorium-Gruppe. *Chemische Berichte*, ***110***, 1034–1041.

[33] El-Seedi H, Sata N, Torssell KBG, Nishiyama S. (**2002)** New labdene diterpenes from *Eupatorium glutinosum*. *Journal of Natural Products*, *6****5***, 728-729.

[34] Bohlmann F, Zdero C. (**1977**) Eine Neue Diterpensäure aus *Perymenium ecuadoricum*. *Phytochemistry*, ***16***, 786–787.

[35] Gilardoni G, Tosi S, Mellerio G, Maldonado ME, Chiriboga X, Vidari G (**2011**) Lipophilic components from the Ecuadorian plant *Schistoscarpha eupatorioides*. *Natural Product Communications*, ***6***, 767–772.

[36] Jativa C, Marinoni G, Bernardi MDE, Vidari G, Vita Finzi P. (**1991**) New sesquiterpenes from *Xanthium catharticum*. *Journal of Natural Products*, ***54***, 460–465.

[37] Lachman J, Havrland B, Fernández EC, Dudjak J. (**2004**) Saccharides of yacon [*Smallanthus sonchifolius* (Poepp. Et. Endl.) H. Robinson] tubers and rhizomes and factors affecting their content. *Plant, Soil and Environment,* ***50***, 383-390.

[38] Mercado MI, Coll MV, Manrique I, Grau A, Catalán C. (**2014**) Variability in sesquiterpene lactones from the leaves of yacon (*Smallanthus sonchifolius*) accessions of different geographic origin. *Genetic Resources and Crop Evolution*, ***61***, 1209–1217.

[39] Ordóñez PE, Quave CL, Reynolds WF, Varughese KI, Berry B, Breen PJ. (**2011**) Sesquiterpene lactones from *Gynoxys verrucosa* and their anti-MRSA activity. *Journal of Ethnopharmacology*, ***137***, 1055–1059.

[40] Valarezo E, Rosillo M, Cartuche L, Malagón O, Meneses M, Morocho V. (**2013**) Chemical composition, antifungal and antibacterial activity of the essential oil from *Baccharis latifolia* (Ruiz & Pav.) Pers. (Asteraceae) from Loja, Ecuador. *Journal of Essential Oil Research*, ***25***, 233–238.

[41] Vidari G, Vita Finzi P, Zarzuelo A, Gálvez J, Zafra C, Chiriboga X. (**2003**) Antiulcer and antidiarrhoeic effect of *Baccharis teindalensis*. *Pharmaceutical Biology*, ***41***, 405–411.

[42] Valarezo E, Rosales J, Morocho V, Cartuche L, Guaya D, Ojeda-Riascos S, Armijos C, Gonzalez S. (**2015)**. Chemical composition and biological activity of the essential oil of *Baccharis obtusifolia* Kunth from Loja, Ecuador. *Journal of Essential Oil Research*, ***27***, 212-216.

[43] Gachet MS, Kunert O, Kaiser M, Brun R, Muñoz RA, Bauer R. (**2010**) Jacaranone-derived glucosidic esters from *Jacaranda glabra* and their activity against *Plasmodium falciparum*. *Journal of Natural Products*, ***73***, 553–556.

[44] Young DG, Chao S, Casablanca H, Bertrand MC, Minga D. (**2007**) Essential oil of *Bursera graveolens* (Kunth) Triana et Planch from Ecuador. *Journal of Essential Oil Research*, ***19***, 525–526.

[45] Gonzalez J, Delle Monache G, Delle Monache F, Marini BG. (**1982**) Chuchuhuasa -a drug used in folk medicine in the Amazonian and Andean areas. a chemical study of *Maytenus laevis*. *Journal of Ethnopharmacology*, ***5***, 73–77.

[46] Ethan BR. (**1992**) Headache treatments by native peoples of the Ecuadorian Amazon: a preliminary cross-disciplinary assessment. *Journal of Ethnopharmacology*, ***36***, 193–206.

[47] Metcalf RL, Metcalf RA, Rhodes AM. (**1980**) Cucurbitacins as kairomones for diabroticite beetles. *Proceedings of the National Academy of Sciences of the United States of America*, ***77***, 3769–3772.

[48] Wade E. (**1983**) The ethnomedicine of the Waorani of Amazonian Ecuador. *Journal of Ethnopharmacology*, ***9***, 273–297.

[49] Vasco C, Riihinen K, Ruales J, Kamal EA. (**2009**) Chemical composition and phenolic compound profile of mortiño (*Vaccinium floribundum* Kunth). *Journal of Agricultural and Food Chemistry*, ***57***, 8274–8281.

[50] Schultes RE. (**1981**) Coca in the northwest Amazon. *Journal of Ethnopharmacology*, ***3***, 173–194.

[51] Bieri S, Brachet A, Veuthey JL, Christen P. (**2006**) Cocaine distribution in wild *Erythroxylum* species. *Journal of Ethnopharmacology*, ***103***, 439–447.

[52] Moore JM, Casale JF, Klein RFX, Cooper DA, Lydon J. (**1994**) Determination and in-depth chromatographic analyses af alkaloids in South American and greenhouse-cultivated coca leaves. *Journal of Chromatography A*, ***659***, 163–175.

[53] Padilla FC, Alfaro MJ, Chavez JF. (**1998**) Note. Chemical composition of the nogal de Barquisimeto (*Caryodendron orinocense*, Euphorbiaceae) seeds: Nota. Composicion quimica de las semillas del nogal de Barquisimeto (*Caryodendron orinocense*, Euphorbiaceae). *Food Science and Technology International*, ***4***, 285–289.

[54] Alfaro MJ, Padilla FC, Perez RMN. (**2000**) *Caryodendron orinocense* ('nuez de Barinas') oil: Tocopherol content and use in cosmetics. *International Journal of Cosmetic Science*, ***22***, 335–340.

[55] Rossi D, Guerrini A, Maietti S, Bruni R, Paganetto G, Poli F. (**2011**) Chemical fingerprinting and bioactivity of Amazonian Ecuador *Croton lechleri* Müll. Arg. (Euphorbiaceae) stem bark essential oil: A new functional food ingredient? *Food Chemistry*, ***126***, 837–848.

[56] Milanowski DJ, Winter REK, Elvin-Lewis MPF, Lewis WH. (**2002**) Geographic distribution of three alkaloid chemotypes of *Croton lechleri*. *Journal of Natural Products*, ***65***, 814–819.

[57] Vigor C, Fabre N, Fouraste I, Moulis C. (**2002**) Neoclerodane diterpenoids from *Croton eluteria*. *Journal of Natural Products,* ***65,*** 1180–1182.

[58] Ríos M, Koziol MJ, Borgtoft Pedersen H, Granda G. (**2007**) *Useful plants of Ecuador: Applications, challenges, and perspectives*. Abya-Yala, Quito. p. 652.

[59] Braca A, De Tommasi N, Di Bari L, Pizza C, Politi M, Morelli I. (**2001**) Antioxidant principles from *Bauhinia tarapotensis*. *Journal of Natural Products*, ***64***, 892–895.

[60] Oberlies NH, Burgess JP, Navarro HA, Pinos RE, Fairchild CR, Peterson RW. (**2002**) Novel bioactive clerodane diterpenoids from the leaves and twigs of *Casearia sylvestris*. *Journal of Natural Products*, ***65***, 1–3.

[61] Nagashima F, Nishioma E, Kameo K, Nakagawa C, Asakawa Y. (**1991**) Terpenoids and aromatic compounds from selected Ecuadorian liverworts. *Phytochemistry*, ***30***, 215–217.

[62] Gilardoni G, Malagon O, Morocho V, Negri R, Tosi S, Guglielminetti M. (**2011**) Phytochemical researches and antimicrobial activity of *Clinopodium nubigenum* Kunth (Kuntze) raw extracts. *Brazilian Journal of Pharmaconosy*, ***21***, 850–855.

[63] Benzo M, Gilardoni G, Gandini C, Caccialanza G, Vita Finzi P, Vidari G. (**2007**) Determination of the threshold odor concentration of main odorants in essential oils using gas chromatography-olfactometry incremental dilution technique. *Journal of Chromatography A*, ***1150***, 131–135.

[64] Valarezo E, Castillo A, Guaya D, Morocho V, Malagón O. (**2012**) Chemical composition of essential oils of two species of the Lamiaceae family: *Scutellaria volubilis* and *Lepechinia paniculata* from Loja, Ecuador. *Journal of Essential Oil Research*, ***24***, 37–41.

[65] Malagón O, Vila R, Iglesias J, Zaragoza T, Cañigueral S. (**2003**) Composition of the essential oils of four medicinal plants from Ecuador. *Flavour and Fragrance Journal*, ***18***, 527–531.
[66] Jenks AA, Kim S. (**2013**) Medicinal plant complexes of *Salvia* subgenus *Calosphace*: An ethnobotanical study of new world sages. *Journal of Ethnopharmacology****146***, 214–124.
[67] Ayerza R. (**2009**) The seed's protein and oil content, fatty acid composition, and growing cycle length of a single genotype of chia (*Salvia hispanica* L.) as affected by environmental factors. *Journal of Oleo Science*, ***58***, 347–354.
[68] Espinosa M, Jaramillo X, Ojeda S, Malagón O, Ramírez J. (**2013**) Actividad antioxidante y antihiperglucemiante de la especie medicinal *Oreocallis grandiflora* (Lam.) R. Br., al sur del Ecuador. *Boletin Latinoamericano y del Caribe de Plantas Medicinales y Aromaticas*, ***12***, 59–68.
[69] Ballabeni V, Tognolini M, Bertoni S, Bruni R, Guerrini A, Moreno G. (**2007**) Antiplatelet and antithrombotic activities of essential oil from wild *Ocotea quixos* (Lam.) Kosterm. (Lauraceae) calices from Amazonian Ecuador. *Pharmacological Research*, ***55***, 23–30.
[70] Bruni R, Medici A, Andreotti E, Fantin C, Muzzoli M, Dehesa M. (**2004**) Chemical composition and biological activities of Ishpingo essential oil, a traditional Ecuadorian spice from *Ocotea quixos* (Lam.). *Food Chemistry*, ***85***, 415–421.
[71] Sacchetti G, Guerrini A, Noriega P, Bianchi A, Bruni R, Naturali R. (**2006**) Essential oil of wild *Ocotea quixos* (Lam.) Kosterm. (Lauraceae) leaves from Amazonian Ecuador. *Flavour and Fragrance Journal, **21**,* 674–676.
[72] Nagashima F, Murakami Y, Asakawa Y. (**1999**) Aromatic compounds from the Ecuadorian liverwort *Marchesinia brachiata*: a revision. *Phytochemistry*, ***51***, 1101–1104.
[73] Houghton P. (**1984**) Ethnopharmacology of some *Buddleja* species. *Journal of Ethnopharmacology*, ***11***, 293–308.
[74] Gilardoni G, Armijos C, Malagón O, Lozano MA, Fronza G, Vidari G. (**2014**) Isolation of novel hydroquinolinic alkaloids from Ecuadorian plants of the genus *Huperzia*, employed in the traditional medicine of Saraguro people. *XXIII Italo-Latinoamerican Congress of Ethnomedicine*, Marsala. p. OR7.
[75] Koyama K, Hirasawa Y, Kobayashi J, Morita H. (**2007**) Cryptadines A and B, novel C27N3-type pentacyclic alkaloids from *Lycopodium cryptomerinum*. *Bioorganic and Medicinal Chemistry*, ***15***, 7803–7808.
[76] Pedersen JA, Llgaard B. (**1982**) Phenolic acids in the genus *Lycopodium*. *Biochemical Systematics and Ecology*, ***10***, 3–9.
[77] Naranjo P. (**1979**) Hallucinogenic plant use and related indigenous belief sytems in the Ecuadorian Amazon. *Journal of Ethnopharmacology*, ***1***, 121–145.
[78] Andritzky W. (**1989**) Sociopsychotherapeutic functions of Ayahuasca healing in Amazonia. *Journal of Psychoactive Drugs*, ***21***, 77–89.
[79] Mootoo B, Jativa C, Tinto WF, Reynolds WF, McLean S. (**1992**) Ecuadorin, a novel tetranortriterpenoid of *Guarea kunthiana*: structure elucidation by 2-D NMR spectroscopy. *Canadian Journal of Chemistry*, ***70***, 1260–1264.
[80] Vera MB, Naranjo BF, Malafronte N, Braca A. (**2014**) A new monoterpene glycoside from *Siparuna thecaphora*. *Natural Product Research: Formerly Natural Product Letters*, ***28***, 57–60.
[81] El-Seedi H, Ghia F, Torssell KBG. (**1994**) Cadinane sesquiterpenes from *Siparuna macrotepala*. *Phytochemistry*, ***35***, 1495–1497.
[82] Shrestha T, Kopp B, Bisset NG. (**1992**) The Moraceae-based dart poisons of South America. Cardiac glycosides of *Maquira* and *Naucleopsis* species. *Journal of Ethnopharmacology*, ***37***, 129–143.
[83] El-Seedi HR, Gohil S, Perera P, Torssell KBG, Bohlin L. (**1999**) Cyclopeptide alkaloids from *Heisteria nitida*. *Phytochemistry*, ***52***, 1739–1744.
[84] Kraus CM, Neszmélyi A, Holly S, Wiedemann B, Nenninger A, Torssell KBG. (**1998**) New acetylenes isolated from the bark of *Heisteria acuminata*. *Journal of Natural Products*, ***61***, 422–427.
[85] Marles RJ, Farnsworth NR, Neill DA. (**1989**) Isolation of a novel cytotoxic polyacetylene from a traditional anthelmintic medicinal plant, *Minquartia guianensis*. *Journal of Natural Products*, ***52***, 261–6.
[86] Guerrini A, Sacchetti G, Rossi D, Paganetto G, Muzzoli M, Andreotti E. (**2009**) Bioactivities of *Piper aduncum* L. and *Piper obliquum* Ruiz & Pavon (Piperaceae) essential oils from Eastern Ecuador. *Environmental Toxicology and Pharmacology*, ***27***, 39–48.
[87] Jeffrey CS, Leonard MD, Glassmire AE, Dodson CD, Richards LA, Kato MJ. (**2014**) Antiherbivore prenylated benzoic acid derivatives from *Piper kelleyi*. *Journal of Natural Products*, ***77***, 148–153.
[88] Ramirez J, Cartuche L, Morocho V, Aguilar S, Malagon O. (**2013**) Antifungal activity of raw extract and flavanons isolated from *Piper ecuadorense* from Ecuador. *Brazilian Journal of Pharmacognosy*, ***23***, 370–373.
[89] Vasco C, Riihinen K, Ruales J, Kamal EA. (**2009**) Phenolic compounds in Rosaceae fruits from Ecuador. *Journal of Agricultural and Food Chemistry*, ***57***, 1204–1212.
[90] Aquino R, De Tommasi N, Tapia M, Lauro MR, Rastrelli L. (**1999**) New 3-methyoxyflavones, an iridoid lactone and a flavonol from *Duroia hirsuta*. *Journal of Natural Products*, ***62***, 560–562.
[91] Chiriboga X, Gilardoni G, Magnaghi I, Vita Finzi P, Zanoni G, Vidari G. (**2003**) New anthracene derivatives from *Coussarea macrophylla*. *Journal of Natural Products*, ***66***, 905–909.
[92] Gilardoni G, Chiriboga X, Vita Finzi P, Vidari G. (**2015**) New 3,4-secocycloartane and 3,4-secodammarane triterpenes from the Ecuadorian plant *Coussarea macrophylla*. *Chemistry & Biodiversity, **12***, 946- 954.
[93] Guerrini A, Rossi D, Grandini A, Scalvenzi L, Rivera P, Andreotti E. (**2014**) Biological and chemo-diverse characterization of Amazonian (Ecuador) *Citrus* petitgrains. *Journal of Applied Botany and Food Quality*, ***87***, 108–116.
[94] Gachet MS, Kunert O, Kaiser M, Brun R, Zehl M, Keller W. (**2011**) Antiparasitic compounds from *Cupania cinerea* with activities against *Plasmodium falciparum* and *Trypanosoma brucei rhodesiense*. *Journal of Natural Products*, ***74***, 559–566.
[95] Weckerle CS, Stutz M, Baumann TW. (**2003**) Purine alkaloids in *Paullinia*. *Phytochemistry*, ***64***, 735–742.
[96] Dandekar DS, Lokeshwar VB, Cevallos-Arellano E, Soloway MS, Lokeshwar BL. (**2003**) An orally active Amazonian plant extract (BIRM) inhibits prostate cancer growth and metastasis. *Cancer Chemotherapy and Pharmacology*, ***52***, 59–66.
[97] Bruni R, Bianchini E, Bettarello L, Sacchetti G. (**2000**) Lipid composition of wild Ecuadorian *Theobroma subincanum* Mart. seeds and comparison with two varieties of *Theobroma cacao* L. *Journal of Agricultural and Food Chemistry*, ***48***, 691–694.
[98] Bruni R, Medici A, Guerrini A, Scalia S, Poli F, Romagnoli C. (**2002**) Tocopherol, fatty acids and sterol distributions in wild Ecuadorian *Theobroma subincanum* (Sterculiaceae) seeds. *Food Chemistry*, ***77***, 337–341.