

Chrysobalanaceae: traditional uses, phytochemistry and pharmacology

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Abstract: Chrysobalanaceae is a family composed of seventeen genera and about 525 species. In Africa and South America some species have popular indications for various diseases such as malaria, epilepsy, diarrhea, inflammations and diabetes. Despite presenting several indications of popular use, there are few studies confirming the activities of these species. In the course of evaluating the potential for future studies, the present work is a literature survey on databases of the botanical, chemical, biological and ethnopharmacological data on Chrysobalanaceae species published since the first studies that occurred in the 60's until the present day.

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Introduction

Chrysobalanaceae was first described by the botanist Robert Brown in his study "*Observations, systematical and geographical, on the herbarium collected by Professor Christian Smith, in the vicinity of the Congo, during the expedition to explore that river, under the command of Captain Tuckey, in the year 1816*" (Salisbury, 1818). It is a family composed of seventeen genera and about 525 species. These are woody plants, shrubs and trees found in tropical and subtropical regions, mainly in the New World tropics (Yakandawala et al., 2010). The wood is of little advantage due to high rate of silica, but several species have edible fruits (Prance, 1988).

Material and Methods

An extensive search through books and original articles was carried out in this work. The search was performed accessing SciFinder, ScienceDirect, Web of Science, Scielo and NAPRALERT databases, updated to February 2012. The keywords used for this review were Chrysobalanaceae, *Licania*, *Parinari* and the names of all other Chrysobalanaceae genus. More than 90% of the references obtained were later consulted.

Botany (morphology and microscopy)

The Chrysobalanaceae plants have entire leaves, hard, provision of alternate, distichous, with stipules.

Small flowers usually greenish-white, cyclic, zigomorphic, diclamides, with a developed receptacle, sepals and petals free, general pentamers, androecium consists of two stamens to many free or more or less welded together; superomedial ovary, bi to tricarpellate, unilocular, usually with only one ovule and fruit usually drupaceous. In the Brazilian Cerrado and in the Amazonian forests trees from the species of the genus *Licania* can be found. Some of them are known as "oitica", and they are oil-producing. The Cerrado species usually present a very twisted trunk. In Northeastern Brazil, species of *Licania* and *Moquilea* are known as "oiti". Other genera of the Amazon region produces the fruit called "pajurá" (*Parinari*). Also in the Amazon, species of *Couepia* produce a type of nut known as "castanha-de-cutia" (Joly, 1998). Again in Northeast Brazil, many are used as forage potential: *Chrysobalanus icaco*, *Couepia impressa*, *Couepia rufa*, *Couepia uiti*, *Licania parviflora*, *Licania salzmannii* and *Licania tomentosa*. In Pernambuco's Atlantic Jungle region, they are used as fodder: *Couepia impressa* and *Couepia rufa* and on the coast *Chrysobalanus icaco* and *Licania tomentosa* (Tabarelli & Silva, 2002).

Metcalf & Chalk (1988) describes anatomical features of some species of Chrysobalanaceae. The petiole has a closed cylinder of xylem and phloem, and two small adaxial vascular strands, with variations occurring among genera and species of a single genus. The leaves show paracytic stomata (sometimes only on the abaxial surface) and epidermis with mucilaginous walls, with papillose on abaxial surface; hypodermis

present in some species. It has a ramified, peltate, stellate or glandular hairs. Mesophyll has predominantly a dorsiventral traversed by lignified cells, like fiber. Veins with vascular bundles surrounded by sclerenchymatous fibers. Vessel cells with simple perforations without spiral thickening, uni-triseriate bands of apotracheal parenchyma in heterogeneous rays, and pits bordered in fibers. Silica crystal, isolated or clustered, is present into membranes, into epidermis cells, into idioblasts surrounding leaf veins and in the mesophyll. Secretory cavities are also found in some genera. A continuous or discontinuous ring of sclerenchyma encircles the vascular cylinder, characterizing the pericycle, and cells with U-thickening in transversal section. The main vascular bundle shows variations related to xylem and phloem arrangement.

Ethnopharmacology

In folk medicine, Chrysobalanaceae species are used for various purposes. Among those in popular use, the species of the genus *Licania* show the largest number of biological activities, and are vastly used in Venezuela as an anti-inflammatory (Pittier, 1978). Most of them are cultivated because of its edible fruits (Toledo et al., 1982).

In Northeastern Brazil, *Licania* species has its leaves used to treat diabetes (Agra et al., 2007), stomach aches (Albuquerque et al., 2007), diarrhea and dysentery (Cartaxo et al., 2010). The stem bark of *Parinari excelsa*, which is widespread in Senegal (Ndiaye et al., 2008), is also used to treat diabetes; and also leaves of *Hirtella racemosa*, that is commonly known in the northern Brazil as “ajirú-do-mato” (Coelho-Ferreira, 2009).

Chrysobalanus icaco, also known as “abajeru”, is a medium sized shrub native of the American coast. It is used in folk medicine for the treatment of leucorrhoea, bleeding and chronic diarrhea, and is also known for its diuretic, hypoglycemic and antiangiogenic effects (Costa, 1977; Paulo et al., 2000; Vargas-Simon et al., 1997). In Northern Brazil, its root is used to treat diabetes (Coelho-Ferreira, 2009).

Parinari species, like *P. curatellifolia* and *P. excelsa*, are traditionally used in Africa as a remedy for dysentery, epilepsy, malaria, toothache and venereal diseases (Uys et al., 2002; Arnold & Gulumian, 1984). The leave of *P. curatellifolia* is indicated to treat stomachaches in Southern Uganda (Ssegawa & Kasenene, 2007). The stem bark of *P. excelsa* is used in Guinea to treat infectious diseases (Magassouba et al., 2010). In West Africa, its stem bark is popularly known as anthelmintic, and its fruit is used to treat diarrhea (Diehl et al., 2004). In Tanzania it is used as an antiseptic and to treat malaria (Kamuhabwa et al., 2000). *P. polyandra* is also used to treat malaria in Ghana (Asase et al., 2005).

Maranthes floribunda bark is used in West Africa to treat diarrhea and dysentery (Koné et al., 2004), *Atuna racemosa* is used to treat pregnancy nausea in Polynesia (Ostraff et al., 2000), and in Latin America *Licania arborea* is used as an antifungal (Svetaz et al., 2010). In Senegal, a cigarette is prepared from the stem bark of *Neocarya macrophylla* used as a remedy for snake bite (Mohagheghzadeh et al., 2006).

The ethnopharmacological uses of these species reveal that they present a significant number of indications in South America and Africa, where they are distributed. Usually, the popular knowledge can guide the search for medicinal plants, which occasionally results in the discovery of molecules with biological activity (Maciel et al., 2002). Therefore, species of *Licania* and *Parinari* can be studied for anti-inflammatory activity, diabetes and malaria.

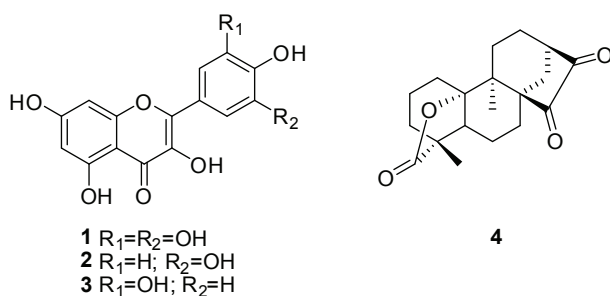
Phyto-constituents

There are few studies that address the chemical composition of species Chrysobalanaceae beyond genres *Licania* and *Parinari*. Note that there are no studies with other genera of the family as *Hirtella*, *Dactyladenia*, *Exellodendron* or *Grangeria*.

Early phytochemical studies occurred in the 60's and described the presence of aglycone flavonoids in species of Rosaceae, including two taxa of Chrysobalanaceae: *Chrysobalanus icaco* and *Licania rigida*, where was identified the myricetin (Chaffaud & Emberger, 1960).

Later, the investigation of 31 species of *Parinari* in 1985 presented that they showed a predominance of flavonoids glycosides based on myricetin (**1**), quercetin (**2**), and kaempferol (**3**) (Coradin et al., 1985). Other phytochemicals studies of *Parinari* species led to the isolation and identification of flavonoids with fatty acids and their glycosides (Chisholm & Hopkins, 1966; Coradin et al., 1985). The molecules identified in Chrysobalanaceae are shown in the Table 1.

Phytochemical studies with the genus *Licania* shown similarities with other Chrysobalanaceae, resulting in the isolation and characterization of two majority classes of compounds: flavonoids and triterpene metabolites (Castilho et al., 2005). Isocarthamidin and 4-hydroxybenzoic acid were isolated by the powdered stems of *P. anamense* (Werawattanachai & Kaewamatawong, 2010). Of *P. curatellifolia*, diterpenes with molecular core ent-kaurene derivative of 15-oxozoapatlin (**4**) were isolated and presented cytotoxic activity (Lee et al., 1996). In other species, *P. campestris*, six diterpenes kaurane were also isolated (Braca et al., 2005).



The study of the phytochemical composition of the other genera in the family can contribute to the characterization of the major constituents in Chrysobalanaceae.

Biological activities

There are studies that show the antihyperglycemic property of some species of Chrysobalanaceae, as *Chrysobalanus icaco* (Presta & Pereira, 1987) and *P. excelsa*, confirming its use in traditional medicine (Ndiaye et al., 2008).

Cytotoxic activity is observed in the pomolic acid of *Chrysobalanus icaco*. Betulinic and oleanolic acid of *Licania tomentosa*, show ability to inhibit the growth and induce apoptosis in the cell line erythroleukemia (K562), and also to prevent proliferation of Lucena 1, a derived vincristine-resistant from K562 (Fernandes et al., 2003). The root extract of *L. michauxii* has cytotoxicity against cultured human hepatoma (Hep G2) and colon

Table 1. Molecules identified in Chrysobalanaceae species.

Specie	Molecules	Reference
<i>Licania apetalá</i>	kaempferol-3-rutinoside, myricetin-3-rhamnoside, myricetin-4'-rhamnoside, quercetin-3-rhamnoside, quercetin-3-arabinoside, quercetin-3-galactoside, quercetin 3-glucoside, rutin, taxifolin-3-rhamnoside	(Braca et al., 2002)
<i>Licania arianeae</i>	acid 3- <i>O</i> -[6'- <i>O</i> -4-hydroxybenzoyl]- β -D-galactopyranosyl-ursa-12-en-28- δ ico, acid flavone-6-sulphonic, 4'- <i>O</i> -methyl-5,7-diidroxy-flavone-6-sulphonic.	(Carvalho & Da Costa, 2009)
<i>Licania densiflora</i>	myricetin (1), myricetin-3-rhamnoside, myricetin-3-glucoside, myricetin-3-galactoside, myricetin-4'-methoxy-3-rhamnoside, myricetin-3',5'-dimethylether-3-rhamnoside, myricetin-3'-methylether-3-galactoside, myricetin-3'-methylether-3-glucoside, myricetin-3',5'-dimethylether-3- <i>O</i> -glucoside, myricetin-3- <i>O</i> - α -L-(2''- <i>O</i> - α -L-rhamnopyranosyl)-rhamnopyranoside-3',4'-dimethylmyricetin-3- <i>O</i> - β -D-glucopyranoside, quercetin (2), quercetin-3-rhamnoside, quercetin-3-glucoside, narigenin-8-hydroxy-4'-methyl ether, catechin	(Braca et al., 1999a; Braca, 2001b)
<i>Licania heteromorpha</i>	myricetin-3-galactoside, myricetin-4'-methoxy-3-rhamnoside, myricetin-3,4'-di- <i>O</i> - α -L-rhamnopyranoside, myricetin-4'-methyl ether-3- <i>O</i> - β -D-galactopyranoside, myricetin-4'-methoxy-3-galactoside, myricetin-4'-methoxy-3-glucoside, myricetin-7-methyl ether-3,4'-di- <i>O</i> - α -L-rhamnopyranoside, betulinic acid, aliphitic acid	(Braca et al., 1999b; Braca et al., 1999c)
<i>Licania licaniaeflora</i>	kaempferol-3-(2''-xylosyl)-rhamnoside, kaempferol-3-rhamnoside, myricetin-3-arabinoside, myricetin-3-galactoside, dihidromyricetin-3-rhamnoside, quercetin-3-rhamnoside, quercetin-3-arabinoside, 8-hydroxy-narigenin, taxifolin-3-rhamnoside, oleanolic acid, maslinic acid, oleanolic acid 3- <i>O</i> -arabinoside, betulinic acid, arjunetin, tomentonic acid glucosyl ester, pomolic acid, olean-12-en-2 α ,3 β -diol	(Braca et al., 2002; Braca et al., 2001a; Bilia et al., 1996a)
<i>Licania pittieri</i>	quercetin (2), quercetin-3-rhamnoside, quercetin-3-arabinoside, quercetin-3-galactoside, quercetin 3-glucoside, catechin, epicathechin, ursolic acid, oleanolic acid	(Bilia et al., 1996a; Mendez et al., 1995)
<i>Licania pyrifolia</i>	kaempferol (3), kaempferol-3-rhamnoside, kaempferol-3-arabinoside, kaempferol-3-(2''-xylosil) rhamnoside, hypoletin, 8-hydroxy-eriodictyol, 8-hydroxy-narigenin, myricetin (1), myricetin-3-rhamnoside, myricetin-3-(2''-xylosyl)rhamnoside, quercetin (2), quercetin-3-rhamnoside, quercetin-3-arabinoside, quercetin-3-(2''-xylosyl)rhamnoside	(Bilia et al., 1996a)
<i>Licania tomentosa</i>	betulinic acid, licanolide, palmitoic acid, oleanolic acid, stigmasterol, sitosterol, lupeol, tomentonic acid, ursolic acid	(Castilho & Kaplan, 2008)
<i>Licania carii</i>	myricetin-3-rutinoside, myricetin-3-glucoside, myricetin-3-(2''-xylosyl)rhamnoside, quercetin-3-(2''-xylosyl)rhamnoside, quercetin-3-galactoside, quercetin 3-glucoside, rutin, 2 α -hydroxy ursolic acid, betulinic acid, maslinic acid.	(Bilia et al., 1996b)
<i>Parinari campestris</i>	kaempferol-3-rutinoside, 15-oxozoapatlin-13 α -yl-10' α ,16' α -dihydroxy-9' α -methyl-20' nor-kauran-19'-oic acid γ -lactone-17'-oate, 13-hydroxy-15-oxozoapatlin, 10 α ,13 α ,16 α ,17-tetrahydroxy-9 α -methyl-15-oxo-20-nor-kauran-19-oic acid γ -lactone, 2 α ,10 α ,13 α ,16 α ,17-pentahydroxy-9 α -methyl-15-oxo-20-nor-kauran-19-oic acid (19,10)-lactone, 3 α ,10 α ,13 α ,16 α ,17-pentahydroxy-9 α -methyl-15-oxo-20-nor-kauran-19-oic acid γ -lactone, 1 β ,16 α ,17-trihydroxy-ent-kaurane.	(Coradin et al., 1985; Braca et al., 2005)
<i>Parinari curatellifolia</i>	15-oxozoapatlin (4), 13-methoxy-15-oxozoapatlin, 13-hydroxy-15-oxozoapatlin.	(Lee et al., 1996)
<i>Chrysobalanus icaco</i>	pomolic acid.	(Fernandes et al., 2003)

carcinoma (Caco-2) (Badisa et al., 2000). *Ent*-kaurane diterpenes isolated from the root of *P. curatellifolia*, show cytotoxicity *in vitro* against several cancer cell lines (Lee et al., 1996). *P. capensis* has moderate cytotoxicity against cell lines of lung cancer, renal cancer and melanoma (Fouche et al., 2008).

The presence of cytotoxicity may be indicative of anticancer action of these compounds, further studies are needed to assess the mechanism of action responsible for cytotoxicity and *in vivo* evaluation of these molecules and extracts. The presence of cytotoxic activity of kaurane diterpenes is discussed in many studies in different species (He et al., 2009; Hueso-Falcón et al., 2010; Lin et al., 2012);

Diterpenes found in *P. capensis* have antifungal (Garo et al., 1997) and antimalarial activity, but have high toxicity (Uys et al., 2002). The hexane extract of *Couepia grandiflora* has antibacterial activity against *Pseudomonas aeruginosa* and the ethanolic extract against *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Zuque et al., 2004).

Diterpenes of *Chrysobalanus icaco* have anti-HIV activity (Gustafson et al., 1991), and aqueous extract of leaves have a potent genotoxic effect (Ferreira-Machado et al., 2004).

Other activities of the genus *Licania* are described. Quercetin flavonoids obtained from sheets of *L. licaniaeflora* and *L. heteromorpha* exhibit antioxidant activity (Braca et al., 2001a; Montoro et al., 2005). *Licania carii*, *L. pittieri* and *L. pyrifolia* are toxic against *Biomphalaria glabrata* Say, a mollusk involved in the reproductive cycle of *Schistosoma mansoni* Sambon (Bilia et al., 2000). The extract of *L. tomentosa* has the ability to inhibit herpes simplex virus type I acyclovir-resistant (ACVr-HSV1) and interfere with the initial process of infection in non-cytotoxic concentrations (Miranda et al., 2002).

The fruits of *Atuna racemosa* presents anti-inflammatory activity by inhibiting the biosynthesis of prostaglandins (Dunstan et al., 1997). Although *Licania* species have popular indication as anti-inflammatory, there are few studies to support this use.

Conclusion

Chrysobalanaceae species have indications in the traditional medicine and treatments for various diseases such as malaria, epilepsy, diarrhea, bleeding, venereal disease and diabetes. But there are few studies, both phytochemical and pharmacological, which express with larger therapeutic potential of these species and chemicals.

Chrysobalanus icaco and *Parinari excelsa* have results that express their potential on treating diabetes, but other species with popular indications such as *Hirtella*

racemosa, lack of pharmacological studies. *Licania tomentosa* and *Chrysobalanus icaco* have activity *in vitro* in the treatment of multidrug-resistant erythroleukemia, confirming the value of natural products in search of new active substances. We should also watch for the need of developing countries to research alternative therapies and substances candidates for drugs to fight diseases called "neglected". Species such as *Parinari excelsa* and *P. curatellifolia* present popular indication in the treatment of malaria, and there are no studies to prove this statement, while *Licania carii*, *L. pittieri* and *L. pyrifolia* need more studies to prove his action in the fight against schistosomiasis.

Moreover, it appears that the molecules isolated by Chrysobalanaceae, mostly, are flavonoids and terpenoids. In a particular way, flavonoids and terpenes being mentioned in most species of *Licania* and kaurane diterpene in species of *Parinari*.

Chrysobalanaceae still presents itself as an unexplored source for the isolation and characterization of new active substances. Thus, new researches can open new paths in the discovery of molecules with therapeutic action and drug discovery.

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