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Revisão

Genus *Pouteria*: Chemistry and biological activity

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RESUMO: "Gênero *Pouteria*: Química e atividade biológica". O gênero *Pouteria* pertence à família Sapotaceae e pode ser encontrado em muitos continentes. As plantas desse gênero têm sido utilizadas na construção civil, na alimentação e também na medicina popular. Algumas atividades biológicas são reportadas às espécies desse gênero, tais como, antioxidante, anti-inflamatória, antibacteriana e antifúngica, mas seu real potencial como fonte de novos fármacos ainda é pouco conhecido. Assim, uma revisão sobre a composição química e as atividades biológicas de *Pouteria* é apresentada, com o intuito de estimular a continuação dos estudos das espécies aqui citadas, e a investigação de outras espécies para as quais não foram encontrados relatos.

Unitermos: *Pouteria*, Sapotaceae, triterpenos, flavonoides, plantas medicinais.

ABSTRACT: The genus *Pouteria* belongs to the family Sapotaceae and can be widely found around the World. These plants have been used as building material, as food, because the eatable fruits, as well as remedies in folk medicine. Some biological activities have been reported to species of this genus such as antioxidant, anti-inflammatory, antibacterial and antifungal. However, the real potential of this genus as source of new drugs or phytomedicines remains unknown. Therefore, a review of the so far known chemical composition and biological activities of this genus is presented to stimulate new studies about the species already reported moreover that species have no reference about chemistry or biological activities could be found until now.

Keywords: *Pouteria*, Sapotaceae, triterpene, flavonoid, medicinal plants.

INTRODUCTION

The Sapotaceae family is subdivided into five tribes with 53 genera and about 1,250 species, with a worldwide distribution, mainly in the tropical and subtropical regions of Asia and South America (Swenson & Anderberg, 2005). The genus *Pouteria* Aublet is a pan tropical group consisting in 9 sections and 325 species (Triono et al., 2007). Many of them produce high-quality timber and edible fruit, representing a great economic value. Besides their commercial significance, several species have been used in folk medicine for several purposes. So far, however, few species were studied about chemistry composition or biological properties. Therefore, this report covers the chemical and biological activity studies of the species belonging to this genus until now.

Chemical composition of *Pouteria* species

Triterpenes and flavonoids are the main constituents of this genus. Some of them have been found in regular basis in all here considered species. Usually, triterpenes has been isolated as long chain or acetate esters. Besides, long chain hydrocarbons, alcohols, acids and esters also are found mainly in species occurring in dry regions, for example, Brazilian savannah (David, 1993; Lopez, 2005; Silva, 2007). In addition, *Pouteria* species have been evaluated as enzymes sources to be used as synthesis reagent as well as biological activity purposes (Lott & Jackes, 2001; Solis et al., 2004; Hernandez et al., 2006). The mainly compounds isolated from each species are showed at Figure 1 and Table 1.

Pouteria torta (Mart.) Radlk is one of the most studied species. From hexane and dichloromethane extract of flowers and fruits (David, 1993) were isolated α- and β-amyrin **(1, 2)**, also isolated from the leaves (Lopez, 2005), besides lupeol **(3)**, taraxasterol **(4)**, pseudotaraxasterol **(5)**, cycloartenol **(6)**, lanosterol **(7)**, lanosta-7,24-dien **(8)** and erythrodiol palmitate **(9a)**. Fatty acids, triglycerides and normal and branched hydrocarbons also were isolated from these extracts (David, 1993).

Pouteria torta branches presented α-amyrin acetate **(1a)**, β-amyrin acetate **(2a)**, betulinic acid **(10)** and ursolic acid **(11)**, isolated from methanol extract (Che et al., 1980). Hexane extract from leaves gave lupeol acetate **(3a)** (Perfeito et al., 2005) and from ethanol extract was isolated a mixture of α- and β-friedelinol **(13, 14)** (Lopez, 2005).

Betulinic **(10)** and ursolic acids **(11)**, as well as α- and β-amyrin acetate **(1a, 2a)** also were isolated from cortex of *Pouteria tomentosa* (Roxb.) Baehni (Anjaneyulu, 1965).

The phytochemical study of the benzene extract from *Pouteria caimito* (Ruiz & Pav.) Radlk. fruits showed the presence of α-amyrin **(1)**, lupeol **(3)**, erythrodiol **(9)**, and dammarenediol **(15)**; and from the barks extract, taraxerol **(16)** and its acetate **(16a)**,

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Table 1. *Pouteria* species chemically researched until 2008.

Species	Compound	References
Pouteria caimito (Ruiz & Pav.) Radlk.	**1**, **3**, **9**, **15**, **16**, **16a, 16b**, **17**, **18, 26**	(Pellicciari et al., 1972; Maia et al., 2003)
Pouteria cambodiana (Pierre ex Dubard) Baehni	**24**	(Manosroi et al., 2005; 2006)
Pouteria campechiana (Kunth) Baehni	**20, 21**, **21a**, **21b**, **21c**, **22**, **23, 24**	(Ma et al., 2004)
Pouteria gardnerii (Mart. & Miq.) Baehni	**1**, **2**, **1a**, **3a**, **10, 11**, **12**	(Silva, 2007)
Pouteria mammosa (L.) Cronquist (sin. Achras mammosa L. and Calocarpum mammosum Pierre)	**9, 42**	(Bondioli & Folegatti, 1996; Takeda et al., 1997; Miller et al., 2006)
Pouteria pariry (Ducke) Baehni	**26**	(Maia et al., 2003)
Pouteria sapota (Jacq.) H. E. Moore et Stern (Calocarpum sapota (Jacq.) Merr. and Sideroxylon sapota Jacq.)	**20**, **21**, **21a**, **21b**, **21c**, **23**, **42, 43, 43a**	(Takeda et al., 1997; Ma et al., 2004; Miller et al., 2006; Pino et al., 2006)
Pouteria splendens (A. DC.) Kuntze	**27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**, **40**, **41**	(Sotes et al., 2006)
outeria subrotata Cronquist	**42**	(Miller et al., 2006)
Pouteria venosa (Mart.) Baehni	**4**, **11**, **16, 18**, **19**, **19a**	(Montenegro et al., 2006)
Pouteria viridis (Pittier) Cronquist (sin. Calocarpum viride Pittier)	**20**, **21**, **21a**, **21b**, **21c**, **22**, **23**	(Ma et al., 2004)
Pouteria vitiensis (Gillespie) O.Deg.	**18**, **24a**, **25**	(Cambie et al., 1997)
Pouteria tomentosa (Roxb.) Baehni	**1a**, **2a**, **10**, **11**	(Anjaneyulu, 1965)
Pouteria torta (Mart.) Radlk.	**1**, **1a**, **2**, **2a, 3**, **3a**, **4, 5, 6**, **7**, **8**, **9a, 10**, **11**, **13**, **14**, **22**, **23**, **24**, **25**	(Che et al., 1980; David, 1993; Lopez, 2005; Perfeito et al., 2005)

taraxenona **(16b)** and β-sitosterol **(17)** (Pellicciari et al., 1972). From hexane extract of the leaves was extracted spinasterol (18) (forthcoming paper), also present in *Pouteria venosa* (Mart.) Baehni leaves and stem barks and in the *Pouteria vitiensis* (Gillespie) O.Deg. heartwood (Cambie et al., 1997). Erythrodiol (9) also was isolated from Pouteria mammosa (L.) Cronquist (Bondioli & Folegatti, 1996).

Pouteria venosa leaves and stem bark ethanol extracts gave ursolic acid (11) and taraxerol (16), respectively. From ethanol extract of stems were isolated miriantic acid (19) and 19α,23-dihydroxyursolic acid (19a) (Montenegro et al., 2006).

Hexane extract from *Pouteria gardnerii* (Mart. & Miq.) Baehni leaves gave α- and β-amyrin (1, 2), α-amyrin acetate (1a), ursolic acid (11) lupeol acetate (3a), and oleanolic acid (10) (Silva, 2007).

The methanol extracts of fruits from *Pouteria campechiana* (Kunth) Baehni, *Pouteria sapota* (Jacq.) H. E. Moore & Stern and *Pouteria viridis* (Pittier) Cronquist gave gallic acid (20), (+)-gallocatechin (21), (+)-catechin (21a), (-)-epicatechin (21b), (+)-catechin-3-O-gallate (21c), dihydromyricetin (22) and myricitrin (23) (Ma et al., 2004). Myricitrin (23) was also isolated from *P. torta* (forthcoming paper). *Pouteria vitiensis* gave vanilloyl sucrose (24a) besides myo-inositol (25) and sucrose (Cambie et al., 1997). *Pouteria cambodiana* (Pierre ex Dubard) Baehni contains protocatechuic acid (24) (Manosroi et al., 2005; 2006), carotenoids (Lanerolle et al., 2008) and stylbenes (Hernandez et al., 2008).

As several *Pouteria* species furnish eatable fruits, the composition of the essential oil is valuable information for food sciences, and can be used to develop new flavors and brands. But as far we know, only four species were analyzed about essential oil content: *Pouteria* (Ducke) Baehni, *P. caimito* (Maia et al., 2003), *P. sapota* and *Pouteria splendens* (A. DC.) Kuntze (Sotes et al., 2006). The mainly component of volatil e oil from fruits of *P*. *pariry* is methyl butanoate; and the analysis of oil from *P. caimito* fruits showed that palmitic acid**,** hexadecil acetate and α-copaen **(26)** were the most abundant constituents (Maia et al., 2003). Analysis of oil from fruits of *P. sapota* revealed the presence, besides others, of benzaldehyde, hexanal, and palmitic acid that were the major ones (Pino et al., 2006). From the almonds of these three species were isolated palmitic, estearic, oleic and linoleic acids (Solis-Fuentes et al., 2001; Solis-Fuentes & Duran-de-Bazua, 2003).

By GC-MS analysis of the essential oil from *P. splendens* leaves, were identified: *cis*,*trans*-α-farnesol **(27)**, *trans*-nerolidol **(28)**, *cis*-β-elemene **(29)**, germacrene D **(30)**, β-selinene **(31)**, eremophilene **(32)**, δ-cadinene **(33)**, 10-*epi*-α-cadinol **(34)**, 10-*epi*-α-muurolol **(35)**, *epi*-globulol **(36)**, globulol **(37)**, ledene **(38)**, palustrol **(39)**, isophytol **(40)**, *trans*-phytol **(41)**. Also were identified: 1-octanol, 2,5-dimethylcyclohexanol, 3,5-dimethylcyclohexanol, dodecanal, tridecanal, tetradecanal, hexadecanal,

2-decyl-oxirane, perhydrofarnesylacetone, tetradecanoic acid, hexadecanoic acid, and 9,12,15-octadecatrienoic acid (α-linolenic acid) (Sotes et al., 2006).

Cyanogenic compounds were detected on leaves, fruits and seeds of the *Pouteria subrotata* Cronquist and *P. torta* (Miller et al., 2006), and in leaves of *P. amygdalicarpa* and *P. campechiana* (Thomsen & Brimer, 1997). Lucumin **(42)** was isolated from seeds of *P. sapota*, *P. mammosa* and was found in leaves extracts from *P. subrotata* (Takeda et al., 1997; Miller et al., 2006). Additionally, lucuminic acid **(43)** and lucuminamide **(43a)** were isolated from *P. sapota* (Takeda et al., 1997).

Other interesting compound, pouterin, a protein with lectin-like activity, was isolated from the seeds of *P. torta* (Boleti et al., 2007).

Biological activities of *Pouteria* species

Several *Pouteria* species have been used in folk medicine to treat fever, inflammation, skin eruptions, ulcers, diabetes (Ma et al., 2004; Montenegro et al., 2006) diarrhea (Perfeito et al., 2005), nausea, vomiting, back pain, and to promote lactation on milk feeding mothers (Manosroi et al., 2006). However, there is a lack of scientific evidence for most of these claimed biological activities.

On the other hand, the secondary metabolites present in this genus can explain some of the already proved biological activities as well as the claimed ones. The presence of phenolic compounds in the *Pouteria* extracts can explain, at least in part, the antioxidant and radical scavenging activities presented by the more polar extracts and fractions (Rice-Evans et al., 1996). In addition, lupeol, ursolic acid and others triterpenes also have demonstrated capacity to intercept free radicals (Bracco et al., 1981; Saleem et al., 2001).

In fact, compounds belonging to both class of

Table 2. Biological activity from *Pouteria* species investigated until 2008.

Species	Parts	Biological activity	References
Pouteria caimito	leaves	Antioxidant	(Castro et al., 2006)
Pouteria cambodiana	stem bark	Imunomodulatory, antioxidant; cell antiproliferative	(Manosroi et al., 2006)
Pouteria campechiana	fruits juice	Antioxidant and antinitrosative, anti-mitotic	(Franco, 2006; Hernandez et al., 2008)
Pouteria grandiflora	leaves	antimicrobial and DNA-damaging	(Agripino et al., 2004)
Pouteria guianensis	wood	subchronic embryotoxicity to *Crassostrea gigas*	(Libralato et al., 2007)
Pouteria pallida	-	antimicrobial	(Humason, 2005)
Pouteria psamophila	leaves	antimicrobial and DNA-damaging	(Agripino et al., 2004)
	wood	fungicidal	(Costa et al., 2003)
Pouteria ramiflora	leaves	Antioxidant; anti-inflammatory and antinociceptive activity; toxicity to *Artemia salina* larvae	(Fontes-Junior, 2004; Nunes, 2004; Castro et al., 2006)
Pouteria reticulata	barks	antimycobacterial	(Graham et al., 2003)
Pouteria sapota	fruits juice	Antioxidant	(Franco, 2006; Palomino et al., 2006)
	stems	trypanocidal activity *in vitro*	(Abe et al., 2002)
Pouteria splendens	leaves	germination inhibition	(Bustamante et al., 2007)
Pouteria torta	leaves	Antioxidant, toxicity to *Artemia salina* larvae, antibacterial and antifungal, germination and growth inhibition, estrogen antagonism	(Alves et al., 2000; Franzotti, 2004; Lopez, 2005; Perfeito et al., 2005; Castro et al., 2006; Nascimento et al., 2007)
	seeds	antifungal and induction of human, rabbits and rats erythrocyte agglutination ability	(Boleti et al., 2007)
Pouteria venosa	leaves	Antioxidant, antimalarial activity *in vivo*	(Montenegro et al., 2006)
	leaves	anti-HIV	(Bedoya et al., 2008)
Pouteria viridis	fruits juice	Antioxidant	(Franco, 2006; Palomino et al., 2006)
	Stem, stem bark	antitermite	(Barbosa et al., 2007)

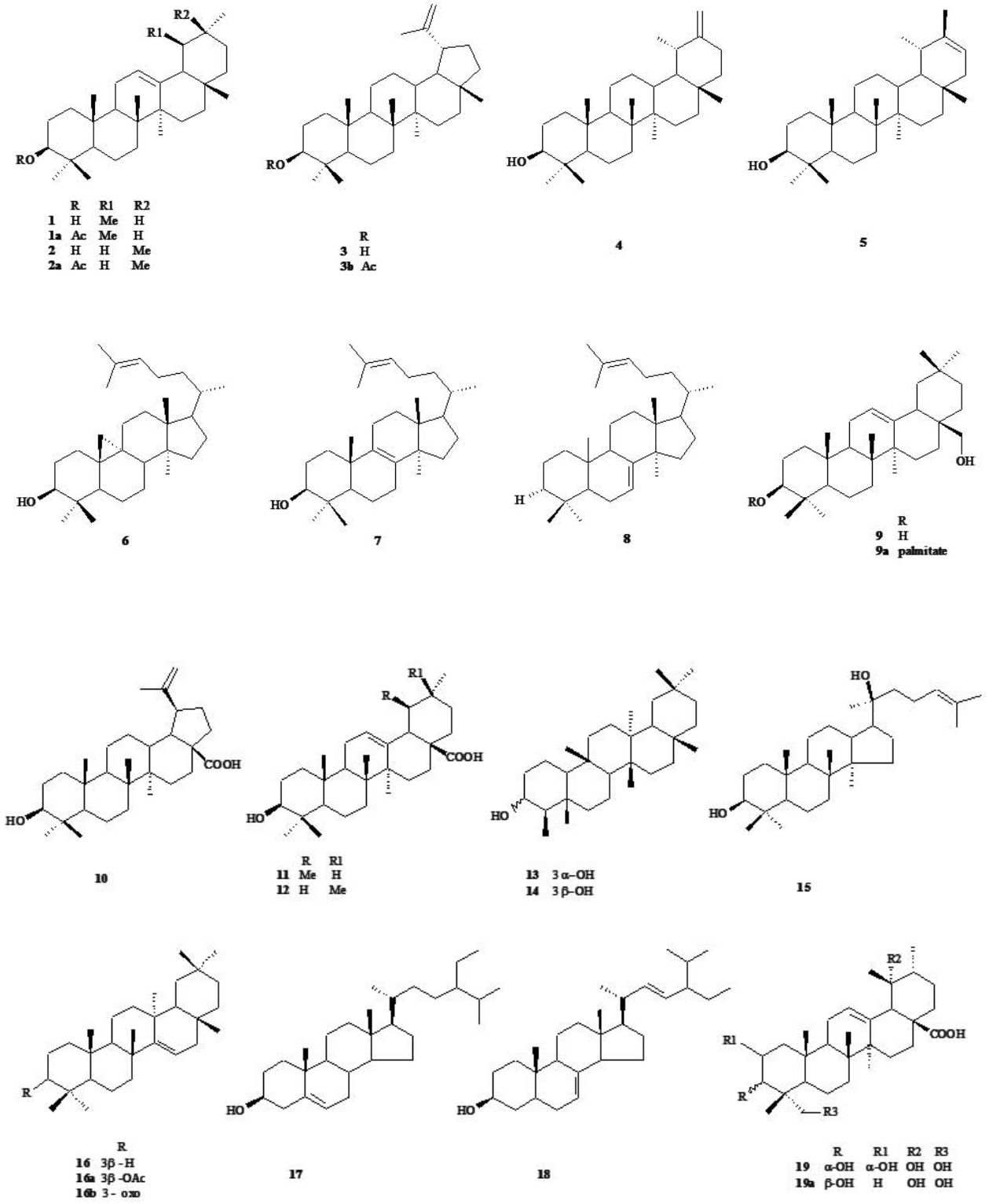

Figure 1. Isolated substances from species of genus *Pouteria* (Sapotaceae).

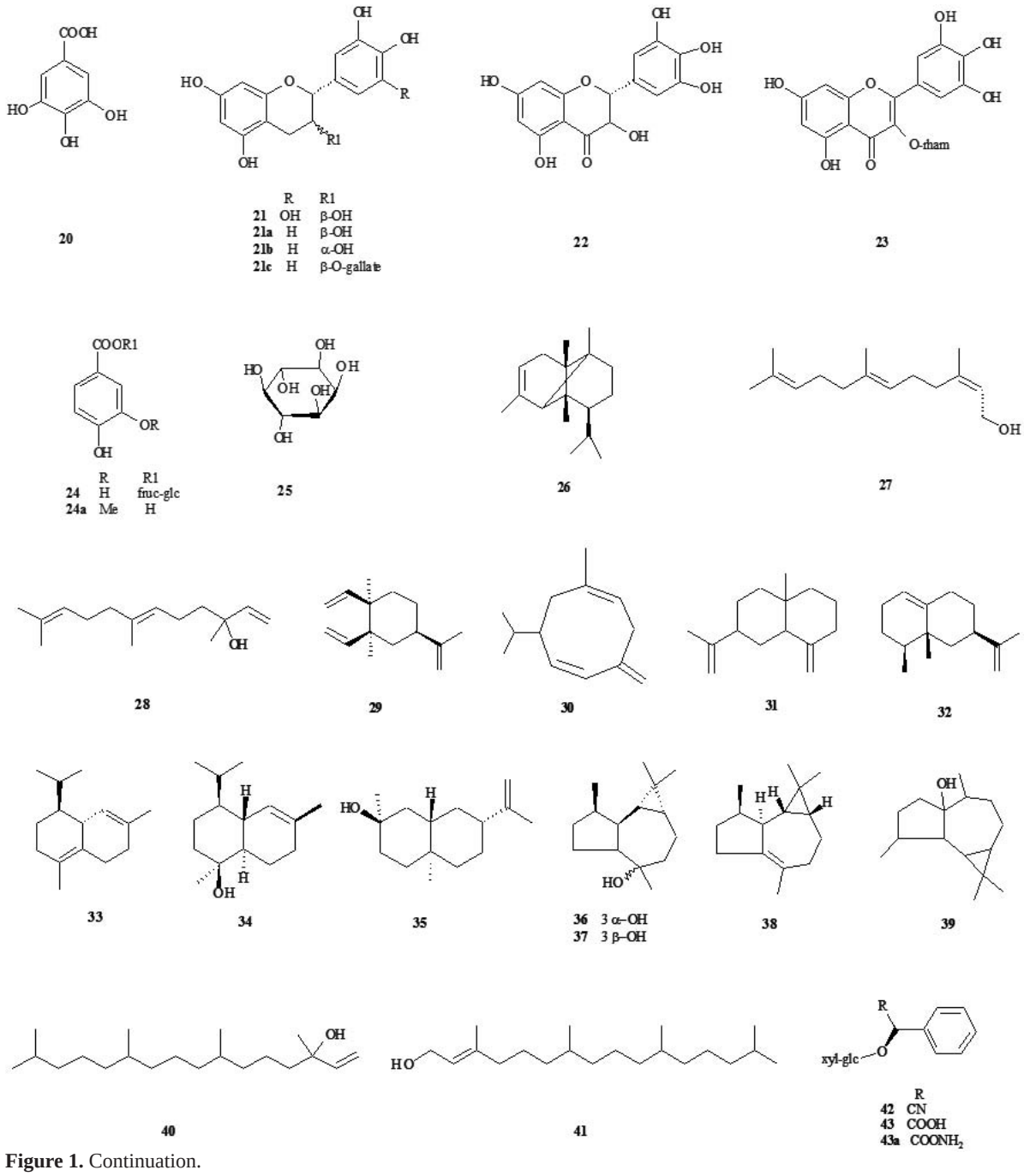

Figure 1. Continuation.

substances, phenolics and triterpenes, present several biological activities, since antimicrobial, cytotoxicity to anti-inflamatory and others (Ying et al., 1991; Pelzer et al., 1998; Nijveldt et al., 2001; Hodges et al., 2003; Cushnie & Lamb, 2005; Fontanay et al., 2008).

The biological activity of the species of *Pouteria* is summarized in Table 2.

Radical scavenging and antioxidant activities

The acetone and hydroethanol extracts from *P. campechiana* fruits (Suda et al., 2005), aqueous extract from *P. caimito* fruits (Oliveira et al., 2007) and *P. torta* leaves and also ethanol extracts from *P. caimito, Pouteria ramiflora* (Mart.) Radlk and *P. torta* leaves (Castro et al., 2006) presented 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activity.

This activity was also noted at ethanol extract and some fractions from leaves, stem and stem bark of *P. venosa* (Montenegro et al., 2006), in the ethyl acetate fraction of methanol extracts from *P. sapota* and from *P. viridis* fruits (Ma et al., 2004; Mahattanatawee et al., 2006), and also in the methanol and acetone extracts from *P. campechiana* fruit and *P. sapota* juice (Franco, 2006).

The methanol extract of *P. campechiana* stem

bark showed free radical scavenging activity in the DPPH radical assay (IC_{50} 0.24 mg/mL), but it was less active than ascorbic acid, butylated hydroxytoluene (BHT) and α-tocopherol (IC_{50} 0.08, 0.10 and 0.11 mg/mL, respectively). In addition, this extract at doses up to 0.073 mg/mL had no effect on lipid peroxidation (Manosroi et al., 2005).

Chloroform extract from *P. campechiana* fruits presented antioxidative and antinitrosative activities by employing two cellular experimental systems: phorbol ester-induced O_2^- generation from differentiated HL-60 human promyelocytic leukemia cells; and lipopolysaccharide (LPS)-induced NO generation in RAW264.7 murine macrophages (Murakami et al., 2005). The ethyl acetate extract presented anti-mitotic activity *ex vivo* (Hernandez et al., 2008).

The fruits of *P. viridis* also presented antioxidant activity in the deoxyribose degradation and Fenton reaction models (Palomino et al., 2006). Six antioxidant compounds **(20, 21, 21a-c, 22)** were isolated and identified from the fruits of *P. sapota*; **20**, **21, 21a-b** and **23**, from *P. viridis* fruits; and **20** and **21b**, from the fruits of *P. campechiana* (Ma et al., 2004).

Immunomodulatory activity and citoxicity

The methanol extract from *Pouteria cambodiana* stem bark presented *in vitro* immunomodulatory activity of mouse immune system for both macrophage phagocytosis (EC_{50} 0.02mg/mL) and splenocyte proliferation (EC_{50} 0.01 mg/mL) (Manosroi et al., 2005; 2006).

By the *in vitro* phagocytic assay on nitroblue tetrazolium (NBT) dye reduction and on cellular lysosomal enzyme activity, different concentrations of aqueous and acetone extracts from *P. cambodiana* stem bark gave phagocytic modulation without dose response relationship, being acetone the more active extract (Manosroi et al., 2006). On the other hand, using 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, the same extracts did not show reduction of proliferation on bone marrow cells and splenocytes (Manosroi et al., 2006). Also, the aqueous extract did not affect male body and testicular weights as well as cauda epididymal sperm counts, after 8 days treatment (Chanda et al., 2008), showing no toxicity at the tested conditions.

Hexane, ethanol and aqueous extracts from *P. ramiflora* (forthcoming paper) and *P. torta* leaves (Perfeito et al., 2005) as well as the obtained fractions from these extracts; and methanol extract from *P. torta* leaves (Alves et al., 2000) were evaluated about toxicity to *Artemia salina* larvae (Brine Shrimp Toxicity method) (Meyer et al., 1982). The aqueous fraction from ethanol extract of *P. ramiflora* and the aqueous extract from *P. torta* were toxic to *A. salina* (Perfeito et al., 2005). On the other hand, methanol and aqueous extracts from *P. caimito* bark and *P. guianensis* roots and wood did not presented toxicity against *A. franciscana* larvae (Quignard et al., 2003; Libralato et al., 2007).

Hexane and ethanol extracts from *P. ramiflora* did not inhibit NO production on LPS/IFN-γ-activated J774 macrophages model and did not present cytotoxicity by MTT cell viability test (Napolitano et al., 2005).

Pouterin, from *P. torta* showed the ability to induce agglutination of human, rabbits and rats erythrocytes (Boleti et al., 2007). Also presented a remarkable activity inducing apoptosis in mammalian cells (Boleti et al., 2008).

Antibacterial and antifungal activities

The hexane and ethanol extracts from *P. torta* leaves showed antimicrobial activity against Staphylococcus aureus and Pseudomonas aeruginosa. Pseudomonas aeruginosa growth also was inhibited by the aqueous extract. Further, this extract showed activity against Escherichia coli (Lopez, 2005) and the methanol extract was active against Cladosporium sphaerospermum, E. coli, S. aureus, Bacillus cereus and P. aeruginosa (Alves et al., 2000). Pouteria pallida (C.F.Gaertn.) Baehni inhibited multidrug resistant S. aureus (Humason, 2005).

Pouterin, from *P. torta* seeds, showed antifungal activity against *Fusarium oxysporum*, *Colletotrichum lindemuthianum* and *Saccharomyces cerevisiae* (Boleti et al., 2007).

The pyroligeneous liquor from *P. ramiflora* wood presented fungicidal activity against *Aspergillus niger* and *Trichoderma* sp. (Costa et al., 2003).

The hydroethanol extracts from *Pouteria psamophila* (Mart.) Radlk. and *Pouteria grandiflora* (A.DC.) Radlk. leaves were evaluated for antimicrobial and DNA-damaging activities. *Pouteria psamophila* was active against *Cladosporium cladosporioides*, but inactive against *C. sphaerospermum*, *E. coli*, *S. aureus* and *Candida albicans*. On the other hand, *P. grandiflora* presented a weak activity against *C. sphaerospermum*, and was inactive against *C. cladosporioides*, *E. coli*, *S. aureus* and *C. albicans* (Agripino et al., 2004). The dichloromethane extract from *Pouteria reticulata* (Engler) Eyma barks presented a weak activity against *Mycobacterium tuberculosis* (Graham et al., 2003)

Allelopathy activity

Aqueous extract from *P. torta* leaves presented germination and growth inhibition of lettuce in a dose-dependent way (Nascimento et al., 2007) and extract from *P. splendens* leaves promoted germination inhibition of *Triticum* spp. (Bustamante et al., 2007).

Trypanocidal and antimalarial activities

The methanol extract from *P. sapota* stems presented trypanocidal activity in vitro (2 mg/mL) against epimastigote form of *Trypanossoma cruzi* (Abe et al., 2002). The ethanol extract from *P. venosa* leaves (250 mg/mL), as well as the hydroethanol fraction (500 mg/mL), presented antimalarial (against Plasmodium berghei) activity *in vivo* reducing the induced infection in rats (Montenegro et al., 2006).

Insecticidal and antitermite activities

Pouteria venosa also was evaluated about larvicidal activity. The ethanol extract did not presented activity on *Aedes aegypti* larvae. However, the hexane-ethyl acetate (1:1) fraction killed 100% from the larvae after 24h exposure (Montenegro et al., 2006).

Extracts from *P. gardnerii*, *P. ramiflora* and *P. torta* also did not present larvicidal activity against *A. aegypti*, *Rhodnius milesi* and *Dipetalogaster maxi* (Coelho, 2006). On the other hand, pouterin, from *P. torta*, presented insecticidal activity on *Callosobruchus maculatus* F. larvae (Boleti et al., 2007).

The hydroethanol extracts from *P. guianensis* stem and stem bark presented antitermite activity in repelling *Nasutitermes* sp. (Barbosa et al., 2007).

Others

- Several others biological activities were reported to *Pouteria* extracts, such as:

- Anti-inflammatory and antinociceptive activities *in vivo* by the ethanol extract from *P. ramiflora* leaves(Fontes-Junior, 2004; Nunes, 2004).

- Estrogen antagonist activity by hexane *P. torta* leaves when tested about agonism and antagonism on estrogen receptor beta (ER_{β}) (Franzotti, 2004).

- Anti-HIV activity by the methanol extract of *P. viridis* leaves when tested using MTT and recombinant viruses (RV) assays (Bedoya et al., 2008).

- Subchronic embryotoxicity to the oyster *Crassostrea gigas* by *P. guianensis* wood (Libralato et al., 2007).

Although the *Pouteria* genus has wide ethnobotanical tradition as food, remedies or wood to general uses, most of the available scientific information is limited to few species with economical potential as source of eatable fruits, while several other species remain without information about their pharmacological and economical potential. Indeed, most of them grow in areas suffering accelerated degradation, such as Brazilian savannah and rain forests. Therefore, considering the already isolated compounds, and the potential of *Pouteria* species as a resource of triterpene- and flavonoid-based material, further investigations should be carried out as part of the effort for a correct exploitation of wild species to be used as cosmetic and pharmaceutical actives.

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