

## Pharmaceutical properties of 'sucupira' (*Pterodon* spp.)

Daiane Hansen<sup>1,2,\*</sup>, Mitsue Haraguchi<sup>2</sup>, Antonio Alonso<sup>1</sup>

<sup>1</sup>Institute of Physics, University Federal of Goiás, <sup>2</sup>Center of Animal Health, Biological Institute of São Paulo

The plant of the genus *Pterodon* (*Fabaceae*, *Leguminosae*), commonly known as 'sucupira' or 'faveira', are disseminated throughout the central region of Brazil and has frequently been used in popular medicine for its anti-rheumatic, analgesic, and anti-inflammatory properties. In recent years, interest in these plants has increased considerably. The biological effects of different phytoextracts and pure metabolites have been investigated in several experimental models *in vivo* and *in vitro*. The literature describes flavonoids, triterpene and steroids, while one paper presented studies with proteins isolated from the genus. This review provides an overview of phytochemical and pharmacological research in *Pterodon*, showing the main chemical compounds studied to date, and focusing on the relationship between these molecules and their biological activity. Furthermore, this study paves the way for more in-depth investigation, isolation and characterization of the molecules of this plant genus.

**Uniterms:** Sucupira. *Pterodon*/phytochemistry. *Pterodon*/pharmacognosy. Diterpenes/biological activity. Isoflavones/biological activity. Medicinal plants.

As plantas do gênero *Pterodon* (*Fabaceae*/*Leguminosae*), conhecidas popularmente como "sucupira branca" ou "faveira", encontram-se distribuídas pela região central do Brasil e são frequentemente utilizadas na medicina popular por suas propriedades antirreumáticas, analgésicas e antiinflamatórias. Nos últimos anos, o interesse por estas plantas tem aumentado consideravelmente. Os efeitos biológicos dos diferentes fitoextratos e metabólitos puros têm sido investigados em vários modelos experimentais *in vivo* e *in vitro*. A literatura descreve flavonóides, triterpenos, esteróides e apenas um trabalho mostra estudos com proteínas isoladas do gênero. Esta revisão apresenta de maneira geral as investigações farmacológicas e fitoquímicas de *Pterodon*, mostrando os principais compostos já estudados, sua composição química, focando na relação entre estas moléculas e sua atividade biológica. Mais ainda, nós abrimos as portas para maior investigação, isolamento e caracterização de moléculas deste gênero de plantas.

**Unitermos:** Sucupira. *Pterodon*/fitoquímica. *Pterodon*/farmacognosia. Diterpenos/atividade biológica. Isoflavonas/atividade biológica. Plantas medicinais.

### INTRODUCTION

The broad biodiversity within Brazil's territory places the country in a strategic position to develop rational and sustained exploration of new metabolites with therapeutic value. Brazil's landmass covers a wide range of climates, soil types, and altitudes, providing a unique set of selective pressures for the adaptation of plant life in these habitats. The plant chemical diversity is also driven by these forces, in an attempt to best adapt the plant to suit the particular abiotic stresses, fauna, and microbes that

coexist in the environment. Certain areas of vegetation, such as the Amazonian Forest, Atlantic Forest, Cerrado (Brazilian Savanna), and Caatinga, are rich in biodiversity and are therefore of great interest for the discovery of natural compounds with biological activity against diseases (Basso *et al.*, 2005).

The vegetal genus *Pterodon* spp., belonging to the *Fabaceae* (= *Leguminosae*)/ *Faboideae* subfamily, is popularly known in Brazil as 'sucupira branca' or 'faveira' and comprises four native species: *Pterodon abruptus* Benth., *Pterodon apparicioi* Pedersoli., *Pterodon polygalaeiflorus* Benth. and, *Pterodon emarginatus* Vogel. (synonym *Pterodon pubescens* Benth.). Interestingly, the species *Pterodon emarginatus* and *Pterodon pubescens* are in fact the same plant species. In 1862 this plant was

\*Correspondence: D. Hansen. Centro de P&D de Sanidade Animal, Instituto Biológico. Av. Conselheiro Rodrigues Alves, 1252 - Vila Mariana - 04014-002 - São Paulo - SP, Brazil. E-mail: daianehansen31@hotmail.com

classified as *Pterodon pubescens* by Bentham, but Vogel subsequently demonstrated that it was in fact the same plant species as that of *Pterodon emarginatus*. The species now bears the official name of *Pterodon emarginatus* Vogel. Unfortunately, it is commonly misidentified as being two distinct species (Carvalho, 2004).

In general, these species are native aromatic trees reaching 5-10 m in height distributed throughout the central region of Brazil (Goiás, Minas Gerais and São Paulo) (Oliveira, Paiva, 2005; Dutra *et al.*, 2008a). These trees frequently grow in the Brazilian Cerrado and in transitional areas approaching the Paraná River basin's semi-deciduous forest. Despite their slow growth, these species are important in mixed reforestations designed to recover degraded areas (Oliveira, Paiva, 2005), due to their tolerance for direct sunlight and low soil fertility.

In mature seeds of some species, such as *Pterodon emarginatus* (Vogel), a distinguishing characteristic is the frequent presence of phenolic compounds in the integuments. Tests on these compounds have demonstrated their contribution to great hardness, low water permeability and high resistance to pathogen attack (Suárez, Engleman, 1980). Also, in mature seeds, the embryo show fleshy cotyledons, with accumulated lipid and protein reserves.

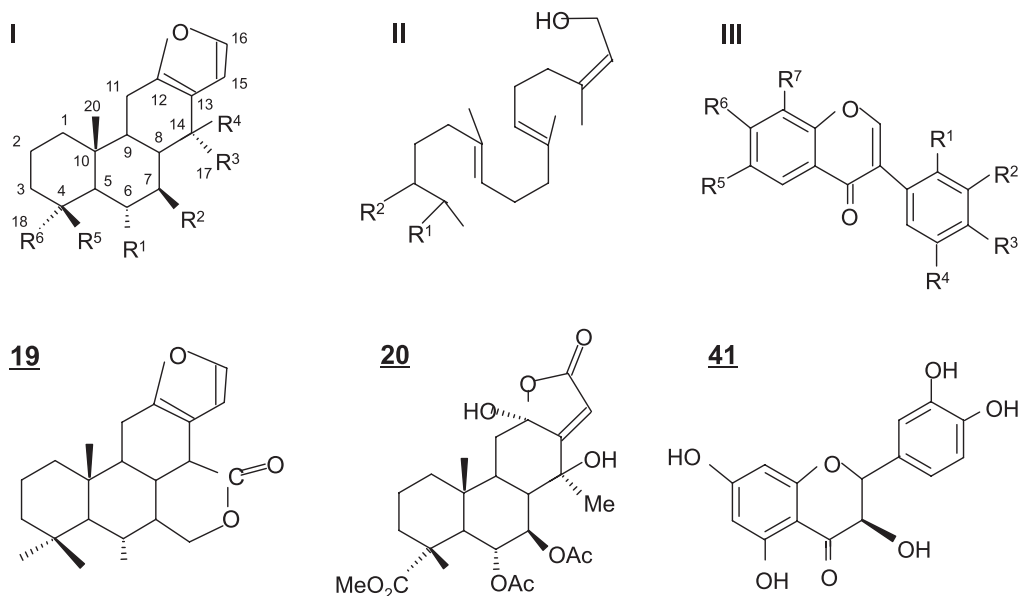
Although the 'sucupira' seeds are commercially available at the medicinal flora market and are widely used in domestic medicine for their anti-rheumatic (Sabino *et al.*, 1999b; Coelho *et al.*, 2004), analgesic (Coelho *et al.*, 2005) and anti-inflammatory (Carvalho *et al.*, 1999; Dutra *et al.*, 2009) properties, only a small number of papers have described the various flavonoids, amino-containing, triterpene, steroid, and others secondary compounds present in the *Pterodon* genus. In addition, to the best of

our knowledge, there is only one report available in the literature showing studies with proteins isolated from this genus, a 5 kDa  $\alpha$ -amylase inhibitor reported by Silva *et al.* (2007). In this review, we have described the main chemical compounds studied to date and focused on establishing a relationship between these molecules and their biological activity. The Tables I to V summarize the main molecules published in the literature.

## Chemistry

The interest in the *Pterodon* genus began in the sixties, when Mors *et al.* (1967) isolated the geranylgeraniol 21 (Table IV) and 14,15-epoxigeranylgeraniol 23 (Table IV) by extraction of *P. pubescens* fruit essential oil with hexane, followed by chromatography on silica gel. In 1970, diterpenoids (2, 13) were obtained from the fruits of *P. emarginatus* by extraction with petroleum ether by Mahajan and Monteiro. (Table III). Two years later, the same authors presented a new compound from the same fruit (19). All these molecules present a vouacapane skeleton in their structures. Yet in 1970, Fascio *et al.*, isolated new terpenes from *P. pubescens* fruit oil (7,14) (Table III). In 1975, diterpenoid 20 was isolated from the same species. This compound shows high biological activity against *S.mansoni* cercariae and inhibits *Crithidia fasciculata* in culture (Fascio *et al.*, 1975).

Braz Filho *et al.* (1971), based on a chemical study of Brazilian leguminosae, isolated isoflavones from trunk wood of *P. pubescens*. The IR, UV and NMR spectrum identified the compound  $C_{20}H_{20}O_7$ , and more specifically the molecules 3',4',6,7 tetramethoxyisoflavone (33), 2',6,7-trimethoxy-4',5' methylenedioxyisoflavone



(38), the isomeric 2',3',4',6,7-penta methoxyisoflavone and 2',4',5',6,7-pentamethoxyisoflavone (40), and 2',4',5',6,7-pentamethoxyisoflavone (39). All of these molecules are shown in Table V.

The seed of *P. emarginatus* was shown to contain sesquiterpenic essential oil such as *trans*- $\beta$ -caryophyllene (35.9%),  $\beta$ -elemene (15.3%), germacrene D (9.8%), spatulenol (5.9%),  $\alpha$ -humulene (6.8%) and, bicyclogermacrene (5.5%) (Dutra *et al.* 2008a, 2009).

From the *P. polygalaeiflorus* Benth. species, four fu-

ran diterpenes (12, 15, 17, 18) were described by Fascio *et al.* (1975). The 6 $\alpha$ -7 $\beta$ -dihydroxyvouacapan-17  $\beta$  oate (8) was demonstrated to have important biological activities (Nunan *et al.*, 1982; Duarte *et al.*, 1996). In addition to the phytochemical study of the above-referenced species, the diterpenes 6 $\alpha$ -hydroxyvouacapan (3), methyl 6 $\alpha$ , 7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate (8) and, vouacapan-6 $\alpha$ , 7  $\beta$ , 14  $\beta$ , 19-tetraol (5) were also isolated from seeds by Arriaga *et al.*, 2000. The same authors elucidated the structure of taxifolin (dihydroquercetin), the most com-

**TABLE I** - Biological activities *in vivo* of *Pterodon* spp. plant extracts/vouacapan derivative

Treatment	Dose	Activity	References
<i>P. pubescens</i> / <i>P. emarginatus</i>			
HAE	5 or 50 mg/kg	anti-rheumatic/anti-arthritic	Sabino <i>et al.</i> , 1999b
HE	500 mg/kg	anti-inflammatory; determination of ED <sub>50</sub>	Carvalho <i>et al.</i> , 1999
OEP	40 $\mu$ g; 200 $\mu$ g and 200 mg/kg (OEP).	anti-inflammatory	Silva <i>et al.</i> , 2004
Fractions PF1, PF2, PF3, PF4	2; 20 and 200 $\mu$ g/kg	anti-inflammatory	Silva <i>et al.</i> , 2004
Fractions PF1.1, PF1.2, PF1.3	0.1; 1.0 and 10 $\mu$ g/kg	anti-inflammatory	Silva <i>et al.</i> , 2004
OEP and fractions PF1, PF2, PF3 and PF4	0.0013 – 130 mg/kg	anti-nociceptive	Coelho <i>et al.</i> , 2004
EO, HE, BE and ME	100 – 500 mg/kg	anti-nociceptive	Dutra <i>et al.</i> , 2008a
EO	100, 300 and 500 mg/kg	anti-ulcerogenic and anti-inflammatory	Dutra <i>et al.</i> , 2009c
EE	0.1; 0.3 and 1 g/kg	anti-nociceptive and anti-inflammatory	Moraes <i>et al.</i> , 2009
<i>P. polygalaeiflorus</i>			
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate	200 $\mu$ mol/kg	anti-nociceptive	Nunan <i>et al.</i> , 1982
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate	125; 250 and 500 $\mu$ mol/kg	anti-nociceptive	Duarte <i>et al.</i> , 1992
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate	250; 375 and 500 $\mu$ mol/kg	anti-nociceptive	Duarte <i>et al.</i> , 1992
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate	250 and 500 $\mu$ mol/kg	anti-nociceptive	Duarte <i>et al.</i> , 1992
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate	125 and 500 $\mu$ mol/kg	anti-nociceptive	Duarte <i>et al.</i> , 1996
HAE	100, 200, 400 mg/kg	anti-nociceptive, anti-inflammatory and bronchodilator	Leal <i>et al.</i> , 2000
HE, ME, EO and 6 $\alpha$ -acetoxyvouacapan	12.5 - 500 $\mu$ g/mL	larvicidal on <i>Aedes aegypti</i>	Pimenta <i>et al.</i> , 2006
EO	100 - 1300 $\mu$ g/mL	effects on contractions	Evangelista <i>et al.</i> , 2007
EO	100 - 300 $\mu$ g/mL	antispasmodic	Leonhardt <i>et al.</i> , 2010

BE: buthanolic extract; EE: ethanolic extract; EO: essential oil; HAE: hydro-alcoholic extract; HE: hexanic extract; ME: methanolic extract; OEP: oleaginous extract

**TABLE II** - Biological activities *in vitro* of *Pterodon* spp. plant extracts/vouacapan derivative

Treatment	Dose	Activity	Reference
<i>P. pubescens</i> / <i>P. emarginatus</i>			
OEP and 14,15-epoxigeranylgeraniol diterpenoid	Pure or 5 % and 25 % diluted 8 µg/mL	chemoprophylactic on schistosomiasis chemoprophylactic on schistosomiasis and <i>Crithidia fasciculata</i> in culture	Mors <i>et al.</i> , 1966; 1967 Fascio <i>et al.</i> , 1975
EO	10, 25, 50 mg	antimicrobial	Neto, 1976; Dutra <i>et al.</i> , 2009a
OEP	100 ppm (soap)	chemoprophylactic on schistosomiasis	Dos Santos Filho <i>et al.</i> , 1987; Katz <i>et al.</i> , 1993
OEP geranylgeraniol	30, 300, 3000 µg/mL 1, 10, 100 nmol/mL	antiplatelet antiplatelet	Calixto <i>et al.</i> , 2007 Calixto <i>et al.</i> , 2007
geranylgeraniol	15-20 µg/mL (trypomastigotes) and 12.5-200 µg/mL (epimastigotes)	anti- <i>Trypanosoma cruzi</i> , effect on proliferation of epi- and trypomastigotes	Menna-Barreto <i>et al.</i> , 2008
subfraction A (HE derivative) and furan diterpene 1	10-100 µg/mL	antiproliferative on human melanoma cells	Vieira <i>et al.</i> , 2008
EO, BE, ME, EAE, HE	0.97-250 µg/mL	antioxidant activity	Dutra <i>et al.</i> , 2008b
6 $\alpha$ -acetoxi-7 $\beta$ -hydroxyvouacapan and four diterpenes furans	0.25-250 µg/mL	anticancer in prostate cell line	Spindola <i>et al.</i> , 2009
HE, BE, ME	6.25 – 100 µg/mL	leishmanicidal	Dutra <i>et al.</i> , 2009a
<i>P. polygalaeiflorus</i>			
furan diterpenes	100 e 1000 ppm	effect on plant growth	Demuner <i>et al.</i> , 1996
furan diterpenes	LC50 values of 50.08, 14.69, and 21.76 µg/mL	larvicidal against the <i>Aedes aegypti</i>	De Omena <i>et al.</i> , 2006
HE, ME, EO, 6 $\alpha$ -acetoxyvouacapan	12.5 - 500 µg/mL	larvicidal against the <i>Aedes aegypti</i>	Pimenta <i>et al.</i> , 2009
6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oic acid and its derivatives	0.25 – 250 µg/mL	antiproliferative on human cancer cells	Euzébio <i>et al.</i> , 2009

BE: buthanolic extract; EAE: ethyl acetate extract; EO: essential oil; HE: hexanic extract; ME: methanolic extract; OEP: oleaginous extract

mon member of the dihydroflavonol group (41). Details of these molecules are shown in Table III.

4-methoxybenzoic acid (*p*-anisic acid) and terpenes (lupeol and betulin) were isolated from the heartwood of *P. polygalaeiflorus* (Marques *et al.*, 1998). Sesquiterpenic essential oils were obtained from fruits and demonstrated to contain trans- $\beta$ -caryophyllene (20.6%) followed by spathulenol (16.6%),  $\alpha$ -capaene (10.4%),  $\gamma$ -muurolene (8.1%),  $\beta$ -elemene,  $\alpha$ -humulene, alloaromadendrene, bicyclogermacrene,  $\delta$ -cadinene,  $\alpha$ -cubenene,  $\gamma$ -cadinene,  $\beta$ -gurjunene, aromadendrene, germacrene D,  $\alpha$ -calacorene,  $\delta$ -elemene, and  $\alpha$ -gurjunene (Campos *et al.*, 1994; Evangelista *et al.*, 2007).

There are several papers referring to the isolation of alkaloid molecules of the *Pterodon* genus (Sabino *et*

*al.*, 1999a; Coelho *et al.*, 2005; Dutra *et al.*, 2008a,b; Menna-Barreto *et al.*, 2008; Vieira *et al.*, 2008; Dutra *et al.*, 2009b) but only one paper showed the structures of homoormosanine-type alkaloids from *Bowdichia virgiloides*, popularly called 'black sucupira' or 'sucupira preta' (Torrenegra *et al.*, 1989).

### Biological properties

The active metabolites were isolated at the same time that the medicinal properties were investigated. In folk medicine, wine infusions from *Pterodon* genus seeds are used in the treatment of rheumatoid arthritis, an autoimmune disease characterized by chronic inflamed joints and exacerbated functions of macrophages and T and B

**TABLE III** - Structure of the diterpenes based on **molecule I**, identified from the *Pterodon* genus

Diterpenes I	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R <sup>6</sup>	Species	References
1	H	H	( $\alpha$ ) Me	( $\beta$ )H	Me	Me	Ppo	Pimenta <i>et al.</i> 2006
2	H	OAc	( $\alpha$ ) Me	( $\beta$ ) H	Me	Me	Pe, Ppu	Mahajan, Monteiro, 1970, 1973; Spindola <i>et al.</i> , 2009
3	OH	H	( $\alpha$ ) Me	( $\beta$ ) H	Me	Me	Ppo	Arriaga <i>et al.</i> , 2000; Pimenta <i>et al.</i> , 2006
4	OH	OH	( $\alpha$ ) Me	( $\beta$ ) OH	Me	Me	Pe, Ppo	Mahajan, Monteiro, 1973; Fascio <i>et al.</i> , 1975; Demuner <i>et al.</i> , 1996
5	OH	OH	( $\alpha$ ) Me	( $\beta$ ) OH	CH <sub>2</sub> OH	Me	Ppo	Arriaga <i>et al.</i> , 2000; Demuner <i>et al.</i> , 1996
6	OH	OH	( $\alpha$ ) H	( $\beta$ ) CH <sub>2</sub> OH	Me	Me	Ppu	Spindola <i>et al.</i> , 2009
7	OH	OH	( $\alpha$ ) H	( $\beta$ ) COOH	Me	Me	Pe, Ppu, Ppo	Mahajan, Monteiro, 1972; 1973; Fascio <i>et al.</i> , 1975
8	OH	OH	( $\alpha$ ) H	( $\beta$ ) COOMe	Me	Me	Pe, Ppo, Ppu	Mahajan, Monteiro, 1972; 1973; Fascio <i>et al.</i> , 1975; Arriaga <i>et al.</i> , 2000; Spindola <i>et al.</i> 2009
9	OH	OAc	( $\alpha$ ) H	( $\beta$ ) COOMe	Me	Me	Pe, Ppo	Mahajan, Monteiro, 1972; 1973
10	OAc	H	( $\alpha$ )Me	( $\beta$ ) H	Me	Me	Ppo	Pimenta <i>et al.</i> , 2006
11	OAc	OH	( $\alpha$ ) Me	( $\beta$ ) H	Me	Me	Ppu	Spindola <i>et al.</i> 2009
12	OAc	OH	( $\alpha$ ) H	( $\beta$ ) COOMe	Me	Me	Ppo	Fascio <i>et al.</i> , 1975
13	OAc	OAc	( $\alpha$ ) Me	( $\beta$ ) H	Me	Me	Pe, Ppu	Mahajan, Monteiro, 1972; 1973; Spindola <i>et al.</i> , 2009
14	OAc	OAc	( $\alpha$ ) Me	( $\beta$ ) OH	COOMe	Me	Ppu	Fascio <i>et al.</i> , 1970
15	OAc	OAc	( $\alpha$ ) Me	( $\beta$ ) OH	Me	COOMe	Ppu	Fascio <i>et al.</i> , 1975
16	OAc	OAc	C=CH <sub>2</sub>		Me	Me	Pe	Mahajan, Monteiro, 1973
17	OAc	OAc	H	CHO	Me	Me	Ppu	Fascio <i>et al.</i> , 1975
18	OAc	OAc	H	COOMe	Me	Me	Ppu	Fascio <i>et al.</i> , 1975

Ppo: *Pterodon polygalaeiflorus*; Pe: *Pterodon emarginatus*; Ppu: *Pterodon pubescens*

**TABLE IV** - Structure of the diterpenes based on **molecule II**, identified from the *Pterodon* genus

Diterpenes II	R <sup>1</sup>	R <sup>2</sup>	References
21		H	Mors <i>et al.</i> , 1967
22		OH	Mors <i>et al.</i> , 1967
23		-O-	Mors <i>et al.</i> , 1967

lymphocytes (Cardoso *et al.*, 2008). Sabino *et al.* (1999b) and Coelho *et al.* (2004) have demonstrated the anti-arthritic effect of hydro-alcoholic extract of *P. pubescens* seeds using the collagen-induced arthritis model (Table I). Also, these researchers have presented studies *in vitro* and *in vivo* demonstrating that acute administration of even extremely high doses of the oil of *P. pubescens* seeds are

non-mutagenic, non-toxic, and non-cytotoxic to human peripheral blood mononuclear cells (PBMNCs) (Sabino *et al.*, 1999a). In subsequent work, sub-acute toxic effects were not observed with hydro-alcoholic extract in studies of hematological, histopathological, clinical, and biochemical parameters in arthritic mice, according to studies of Coelho *et al.* (2001). Further analysis revealed the anti-inflammatory (Silva *et al.*, 2004) and anti-nociceptive effects of ethanolic extracts of *P. pubescens* seeds, confirming the rationale behind the use of this plant in popular medicine to treat pain disorders (Coelho *et al.*, 2005) (Table I).

The investigations on the pharmacological properties of 'sucupira' surpass those of its anti-inflammatory and anti-rheumatic activities. Dutra *et al.* (2008b) studied the total phenolic content and antioxidant activity of seeds of *P. emarginatus* (Table II). The phenolic constituents found

**TABLE V** - Structure of the isoflavones based on **molecule III**, identified from the *Pterodon* genus

Isoflavones III	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R <sup>6</sup>	R <sup>7</sup>	Species	References
24	H	H	OH	H	H	OH	H	Pa	Galina, Gottlieb, 1974
25	H	H	OMe	H	H	OMe	H	Pa	Galina, Gottlieb, 1974
26	H	H	OMe	H	OMe	OH	H	Pa	Galina, Gottlieb, 1974
27	H	H	OMe	H	OMe	OH	H	Pa	Galina, Gottlieb, 1974
28	H	H	—O—CH <sub>2</sub> —O—	H	OMe	OMe	H	Pa	Galina, Gottlieb, 1974
29	H	OH	OMe	H	OMe	OH	H	Pa	Galina, Gottlieb, 1974
30	H	—O—CH <sub>2</sub> —O—	H	OMe	OMe	OH	H	Pa, Ppo	Galina, Gottlieb, 1974; Marques <i>et al.</i> , 1998
31	H	—O—CH <sub>2</sub> —O—	H	OMe	OMe	OMe	H	Ppo	Marques <i>et al.</i> , 1998
32	H	OMe	H	H	OMe	OMe	H	Ppo	Marques <i>et al.</i> , 1998
33	H	OMe	OMe	H	OMe	OMe	H	Pa, Ppu	Braz Filho <i>et al.</i> , 1971; Galina, Gottlieb, 1974; Marques <i>et al.</i> , 1998
34	H	OMe	OMe	OMe	OMe	OMe	H	Pa	Almeida, Gottlieb, 1975
35	OMe	H	OMe	OMe	OMe	OH	H	Pa	Galina, Gottlieb, 1974
36	OMe	H	—O—CH <sub>2</sub> —O—	H	OMe	OMe	H	Pa	Galina, Gottlieb, 1974
37	OMe	H	—O—CH <sub>2</sub> —O—	H	OMe	OMe	OMe	Pa	Galina, Gottlieb, 1974
38	OMe	H	—O—CH <sub>2</sub> —O—	OMe	OMe	OMe	H	Pa, Ppo, Ppu	Galina, Gottlieb, 1974; Braz Filho <i>et al.</i> , 1971; Marques <i>et al.</i> , 1998
39	OMe	H	OMe	OMe	OMe	OMe	H	Pa, Ppo, Ppu	Galina, Gottlieb, 1974; Marques <i>et al.</i> , 1998
40	OMe	OMe	OMe	H	OMe	OMe	H	Pa, Ppo, Ppu	Almeida, Gottlieb, 1975; Braz Filho <i>et al.</i> , 1971; Marques <i>et al.</i> , 1998

Pa: *Pterodon apparicioi*; Ppo: *Pterodon polygalaeflorus*; Ppu: *Pterodon pubescens*

in vegetables have attracted considerable attention because of their antioxidant activity. The antioxidant activities of phenolics are mainly due to their redox properties, which allow them to act as reducing agents, hydrogen donors, and singlet oxygen quenchers. They have a metal chelation potential and play an important role in the adsorption or neutralization of free radicals. Butanolic and methanolic fractions of the *P. emarginatus* seeds demonstrated a marked scavenging effect on DPPH radical (2,2-diphenyl-2-picrylhydrazyl hydrate).

Other studies have demonstrated the potential trypanocidal effect of the oleaginous ethanolic extract of *P. pubescens* seeds and its fractions (Menna-Barreto *et al.*, 2008) (Table II). *Trypanosoma cruzi* is the causative agent of Chagas' disease, the parasitic infection that remains one of the leading causes of heart diseases in Latin America. Current treatment options for this disease involve two nitroheterocyclic compounds that present

low efficacy and severe side effects. It is hoped that antiparasitic therapeutic agents can be identified from the plants through screening efforts aimed at discovering new molecules such as natural products, proteins and peptides with recognized biological activity (Araújo *et al.*, 2005; Hansen *et al.*, 2007).

Also in the area of parasitic diseases, a group of Brazilian researchers demonstrated that the *P. pubescens* fruit essential oil inhibited the penetration of the cercaries of *Schistosoma mansoni* (Dos Santos-Filho *et al.*, 1972, 1987; Katz *et al.*, 1993). One of the compounds identified as a component of this oil was the 14,15-epoxigeranylgeraniol (**3**), a molecule isolated by Mors *et al.* (1967), and shown to be effective as a chemoprophylactic agent in schistosomiasis. Mahajan and Monteiro (1973) also investigated the anti-cercaria action of *P. pubescens* while the other three species were studied by Fascio *et al.* (1975) (Table II).

Further biological activity data was presented by Neto (1973) during his doctoral research. He demonstrated that the oil obtained from *P. pubescens* seeds presented significant *in vitro* antimicrobial activity (Table II).

From the *P. polygalaeflorus* species, the diterpene 6 $\alpha$ -7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oate was demonstrated to have an anti-inflammatory activity in the paw edema produced by carrageenin (Nunan *et al.*, 1982) and, in subsequent studies, showed an important anti-nociceptive activity (Duarte *et al.*, 1996) (Table I). The ethanolic extract from seeds showed significant larvicidal activity against the *Aedes aegypti* mosquito (De Omena *et al.*, 2006) (Table II) and the hydro-alcoholic extract was the most active bronchodilator among those plants widely used in north-eastern Brazil for respiratory tract diseases (Leal *et al.*, 2000) (Table I).

### Toxicology

A paper written by Sabino *et al.* (1999a) presented a study in which the oil of *P. pubescens* seeds (PpSO) was tested for acute toxicity, mutagenic activity and cytotoxicity against human peripheral blood mononuclear cells (PBMNC). The study provided data to classify PpSO as non-cytotoxic to PBMNC, non-mutagenic and, non-toxic after acute administration, since the PpSO doses tested were significantly higher than those used by the population.

Also, the clastogenicity of 'sucupira oil' extracted from *P. pubescens* was tested *in vivo* on wistar rat bone marrow cells. Metaphase analysis showed that the compound did not induce a significant increase in the frequencies of chromosomal aberrations (Dias *et al.*, 1995).

### CONCLUSION

The broad biodiversity in Brazil places the country in a strategic position in the development and rational exploitation of new metabolites with therapeutic value. Areas of vegetation such as the Central Cerrado are rich in species of value in the search for natural compounds with activity against many diseases. The chemical characterization of these compounds, the determination of their mechanism of action and, the study of biological activities *in vitro* and *in vivo*, have yielded important information about the natural compounds and their derivatives.

The aim of this review was to present the studies involving the genus *Pterodon* and its natural compounds, with the goal of encouraging further investigation of these plants. The isolation and characterization of new molecules, and their correlation with new biological tests,

provides fertile ground for the development of drugs for a large number of diseases.

### ACKNOWLEDGMENTS

The authors would like to thank Dr. Kelly Boatright Sexton from North Carolina State University for reviewing the manuscript and are grateful to Mr. Randolph Carneiro Carvalho (Fazenda Eldorado, Urutaí, GO, Brazil) for incentive and popular information regarding the therapeutical properties of 'sucupira' seeds. CAPES/PNPd and CNPq provided financial support.

### REFERENCES

- ALMEIDA, M.E.L.; GOTTLIEB, O.R. Further isoflavones. *Pterodon apparicioi*. *Phytochemistry*, v.14, n.12, p.2716, 1975.
- ARAÚJO, A.P.U.; HANSEN, D.; VIEIRA, D.F.; OLIVEIRA, C.; SANTANA, L.A.; BELTRAMINI, L.M.; SAMPAIO, C.A.M.; SAMPAIO, M.U.; OLIVA, M.L.V. Kunitz type *Bauhinia bauhinioides* inhibitors devoid of disulfide bridges: isolation of the cDNAs, heterologous expression and structural studies. *Biol. Chem.*, v.386, n.6, p.561-568, 2005.
- ARRIAGA, A.M.C.; CASTRO, M.A.B.; SILVEIRA, E.R.; BRAZ-FILHO, R. Further diterpenoids isolated from *Pterodon polygalaeflorus*. *J. Braz. Chem. Soc.*, v.11, n.2, p.187-190, 2000.
- BASSO, L.A.; PEREIRA DA SILVA, L.H.; FETT-NETO, A.G.; AZEVEDO JR, W.F.; MOREIRA, I.S.; PALMA, M.S.; CALIXTO, J.B.; ASTOLFI FILHO, S.; DOS SANTOS, R.R.; SOARES, M.B.P.; SANTOS, D.S. The use of biodiversity as source of new chemical entities against defined molecular targets for treatment of malaria, tuberculosis, and T-cell mediated diseases- a review. *Mem. Inst. Oswaldo Cruz*, v.100, n.6, p.575-606, 2005.
- BRAZ FILHO, R.; GOTTLIEB, O.R.; ASSUMPÇÃO, R.M.V. Chemistry of Brazilian Leguminosae. XXXIV Isoflavones of *Pterodon pubescens*. *Phytochemistry*, v.10, n.11, p.2835-2836, 1971.
- CALIXTO, N.O.; COSTA E SILVA, M.C.; GAYER, C.R.; COELHO, M.G.; PAES, M.C.; TODESCHINI, A.R. Antiplatelet activity of geranylgeraniol isolated from *Pterodon pubescens* fruit oil is mediated by inhibition of cyclooxygenase-1. *Planta Med.*, v.73, n.5, p.480-483, 2007.

- CAMPOS, A.M.; SILVEIRA, E.R.; BRAZ-FILHO, R.; TEIXEIRA, T.C. Diterpenoids from *Pterodon polygalaeflorus*. *Phytochemistry*, v.36, n.2, p.403-406, 1994.
- CARDOSO, C.C.; PINTO, A.C.; MARQUES, P.R.; GAYER, C.R.M.; AFEL, M.I.R.; COELHO, M.G.P.; SABINO, K.C.C. Suppression of T and B cell responses by *Pterodon pubescens* seeds ethanolic extract. *Pak. J. Biol. Sci.*, v.11, n.19, p.2308-2313, 2008.
- CARVALHO, J.C.T.; SERTIÉ, J.A.A.; BARBOSA, M.V.J.; PATRÍCIO, K.C.M.; CAPUTO, L.R.G.; SARTI, S.J.; FERREIRA, L.P.; BASTOS, J.K. Anti-inflammatory activity of the crude extract from the fruits of *Pterodon emarginatus* Vog. *J. Ethnopharmacol.*, v.64, n.2, p.127-133, 1999.
- CARVALHO, J.C.T. Sucupira, *Pterodon emarginatus* Vog. In: CARVALHO, J.C.T. *Fitoterápicos anti-inflamatórios – aspectos químicos, farmacológicos e aplicações terapêuticas*. Ribeirão Preto: Tecmedd, 2004. p.383.
- COELHO, M.G.P.; MARQUES, P.R.; GAYER, C.R.M.; VAZ, L.C.A.; NETO, J.F.N.; SABINO, K.C.C. Subacute toxicity evaluation of a hydroalcoholic extract of *Pterodon pubescens* seeds in mice with collagen-induced arthritis. *J. Ethnopharmacol.*, v.77, n.2-3, p.159-164, 2001.
- COELHO, M.G.; SABINO, K.C.; DALMAU, S.R. Immunomodulatory effects of sucupira (*Pterodon pubescens*) seed infusion on collagen-induced arthritis. *Clin. Exp. Rheumatol.*, v.22, n.2, p.213-218, 2004.
- COELHO, L.P.; REIS, P.A.; CASTRO, F.L.; GAYER, C.R.M.; LOPES, C.S.; SILVA, M.C.C.; SABINO, K.C.C.; TODESCHINI, A.R.; COELHO, M.G.P. Anti-nociceptive properties of ethanolic extract and fractions of *Pterodon pubescens* Benth. seeds. *J. Ethnopharmacol.*, v.98, n.1-2, p.109-116, 2005.
- DE OMENA, M.C.; BENTO, E.S.; DE PAULA, J.E.; SANT'ANA, A.E. Larvicidal diterpenes from *Pterodon polygalaeflorus*. *Vector Borne Zoonotic Dis.*, v.6, n.2, p.216-222, 2006.
- DEMUNER, A.J.; BARBOSA, L.C.A.; VELOSO, D.P.; ALVES, D.L.F.; HOWARTH, O.W. Structure and plant growth regulatory activity of new diterpenes from *Pterodon polygalaeflorus*. *J.Nat.Prod.*, v.59, n.8, p.770-772, 1996.
- DIAS, F. D.; TAKAHASHI, C.S.; SAKAMOTO-HOJO, E.; VICHNEWSKI, W.; SARTI, S.J. Genotoxicity of the natural cercaricides “sucupira” oil and eremanthine in mammalian cells in vitro and in vivo. *Environ. Mol. Mutagen.*, v.26, n.4, p.338-344, 1995.
- DOS SANTOS FILHO, D.; SARTI, S.J.; KATZ, N.; ARAÚJO, N.; ROCHA FILHO, P.A.; ABREU, J.E.; BORTOLIN, M.E. Chemoprophylactic activity of soaps containing essential oil from the fruits of *Pterodon pubescens* in *Schistosomiasis mansoni*. *Mem. Inst. Oswaldo Cruz*, v.82, suppl.4, p.343-345, 1987.
- DOS SANTOS FILHO, D.; VICHNEWSKI, W.; BAKER, P.M.; GILBERT, B. Prophylaxis of Schistosomiasis. Diterpenes from *Pterodon pubescens*. *An. Acad. Bras. Ciênc.*, v.44, n.1, p.45-49, 1972.
- DUARTE, I.D.G.; NAKAMURA-CRAIG, M.; FERREIRA-ALVES, D.L. Possible participation of endogenous opioid peptides on the mechanism involved in analgesia induced by vouacapan. *Life Sci.*, v.50, p.891-897, 1992.
- DUARTE, I.D.; FERREIRA-ALVES, D.L.; VELOSO, D.P.; NAKAMURA-CRAIG, M. Evidence of the involvement of biogenic amines in the anti-nociceptive effect of a vouacapan extracted from *Pterodon polygalaeflorus* Benth. *J. Ethnopharmacol.*, v.55, n.1, p.13-18, 1996.
- DUTRA, R.C.; TREVIZANI, R.; PITTELLA, F.; BARBOSA, N.R. Anti-nociceptive activity of the essential oil and fractions of *Pterodon emarginatus* Vogel seeds. *Lat. Am. J. Pharm.*, v.27, n.6, p.865-870, 2008a.
- DUTRA, R.C.; LEITE, M.N.; BARBOSA, N.R. Quantification of Phenolic Constituents and Antioxidant Activity of *Pterodon emarginatus* Vogel seeds. *Int. J. Mol. Sci.*, v.9, n.4, p.606-614, 2008b.
- DUTRA, R.C.; BRAGA, F.G.; COIMBRA, E.C.; SILVA, A.D.; BARBOSA, N.R. Antimicrobial and leishmanicidal activities of seeds of *Pterodon emarginatus*. *Braz. J. Pharmacogn.*, v.19, n.2A, p.429-435, 2009a.
- DUTRA, R.C.; FAVA, M.B.; ALVES, C.C.; FERREIRA, A.P.; BARBOSA, N.R. Antiulcerogenic and anti-inflammatory activities of the essential oil from *Pterodon emarginatus* seeds. *J. Pharm. Pharmacol.*, v.61, n.2, p.243-250, 2009b.



- DUTRA, R.C.; PITTELLA, F.; FERREIRA, A.S.; LARCHER, P.; FARIAS, R.E.; BARBOSA, N.R. Healing effect of *Pterodon emarginatus* seeds in experimental models of cutaneous ulcers in rabbits. *Lat. Am. J. Pharm.*, v.28, n.3, p.375-382, 2009c.
- EUZEBIO, F.P.G.; DOS SANTOS, F.J.L.; PILÓ-VELOSO, D.; RUIZ, A.L.T.G.; CARVALHO, J.E.; FERREIRA-ALVES, D.L.; DE FATIMA, A. Effect of 6 $\alpha$ , 7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oic acid and its lactone derivatives on the growth of human cancer cells. *Bioorg. Chem.*, v.37, n.3, p.96-100, 2009.
- EVANGELISTA, G.L.; COELHO-DE-SOUZA, A.N.; SANTOS, C.F.; LEAL-CARDOSO, J.H.; LOPES, E.A.B.; DOS SANTOS, M.V.; LAHLOU, S.; MAGALHÃES, P.J.C. Essential oil of *Pterodon polygalaeflorus* inhibits electromechanical coupling on rat isolated trachea. *J. Ethnopharmacol.*, v.109, n.3, p.515-522, 2007.
- FASCIO, M.; GILBERT, B.; MORS, W.B.; NISHIDA, T. Two new diterpenes from *Pterodon pubescens*. *An. Acad. Bras. Ciênc.*, suppl.42, p.97-101, 1970.
- FASCIO, M.; MORS, W.; GILBERT, B.; MAHAJAN, M.B.; MONTEIRO, M.B.; SANTOS FILHO, D.; VICHNEWSKI, W. Diterpenoid furans from *Pterodon* species. *Phytochemistry*, v.15, n.1, p.201-203, 1975.
- GALINA, E.; GOTTLIEB, O.R. Chemistry of Brazilian Leguminosae. XLVI Isoflavones from *Pterodon appariciori*. *Phytochemistry*, v.13, n.11, p.2593-2595, 1974.
- HANSEN, D.; MACEDO-RIBEIRO, S.; VERÍSSIMO, P.; YOO-IM, S.; SAMPAIO, M.U.; OLIVA, M.L.V. Crystal structure of a novel cysteinless plant Kunitz-type protease inhibitor. *Biochem. Biophys. Res. Commun.*, v.360, n.4, p.735-740, 2007.
- KATZ, N.; DOS SANTOS FILHO, D.; SARTI, S.J.; MENDES, N.M.; ROCHA FILHO, P.A.; ARAÚJO, N. Chemoprophylactic activity on *Schistosomiasis mansoni* of soaps containing essential oil from the fruits of *Pterodon pubescens*. *Rev. Inst. Med. Trop.*, v.35, n.2, p.183-191, 1993.
- LEAL, L.K.; FERREIRA, A.A.; BEZERRA, G.A.; MATOS, F.J.; VIANA, G.S. Anti-nociceptive, anti-inflammatory and bronchodilator activities of Brazilian medicinal plants containing coumarin: a comparative study. *J. Ethnopharmacol.*, v.70, n.2, p.151-159, 2000.
- LEONHARDT, V.; LEAL-CARDOSO, J.H.; LAHLOU, S.; ALBUQUERQUE, A.A.C.; PORTO, R.S.; CELEDÔNIO, N.R.; OLIVEIRA, A.C.; PEREIRA, R.F.; SILVA, L.P.; GARCIA-TEÓFILO, T.M.N.; SILVA, A.P.F.S.; MAGALHÃES, P.J.C.; DUARTE, G.P.; COELHO-DE-SOUZA, A.N. Antispasmodic effects of essential oil of *Pterodon polygalaeflorus* and its main constituent  $\beta$ -caryophyllene on rat isolated ileum. *Fundam. Clin. Pharmacol.*, v.24, n.6, p.749-758, 2010.
- MAHAJAN, J.R.; MONTEIRO, M.B. New diterpenoids from *Pterodon emarginatus*. *An. Acad. Bras. Ciênc.*, v.42, (Supplement), p.103-107, 1970.
- MAHAJAN, J.R.; MONTEIRO, M.B. New diterpenoids from *Pterodon emarginatus*. *An. Acad. Bras. Ciênc.*, v.44, n.1, p.51-53, 1972.
- MAHAJAN, J.R.; MONTEIRO, M.B. New diterpenoids from *Pterodon emarginatus*. *J. Chem. Soc. Perkin Trans. I*, p.520-525, 1973.
- MARQUES, D.D.; MACHADO, M.I.L.; CARVALHO, M.G.; MELEIRA, L.A. DA C.; BRAZ-FILHO, R. Isoflavonoids and triterpenoids isolated from *Pterodon polygalaeflorus*. *J. Braz. Chem. Soc.*, v.9, n.3, p.295-301, 1998.
- MENNA-BARRETO, R.F.S.; LARANJA, G.A.T.; SILVA, M.C.C.; COELHO, M.G.P.; PAES, M.C.; OLIVEIRA, M.M.; CASTRO, S.L. Anti-*Trypanosoma cruzi* activity of *Pterodon pubescens* seed oil: geranylgeraniol as the major bioactive component. *Parasitol. Res.*, v.103, n.1, p.111-117, 2008.
- MORAES, W.F.; MATOS, L.G.; NASCIMENTO, M.V.M.; PAULA, J.R.; BARA, M.T.F.; CUNHA, L.C.; VALADARES, M.C.; COSTA, E.A. Anti-inflammatory and anti-nociceptive effects of *Pterodon emarginatus* stem bark alcohol extract. *Pharm. Biol.*, v.47, n.2, p.146-150, 2009.
- MORS, W.B.; PELLEGRINO, J.; DOS SANTOS FILHO, M.F. Ação profilática do óleo dos frutos de Sucupira-Branca, *Pterodon pubescens* Benth, contra a infecção pelo *Schistosoma mansoni*. *An. Acad. Bras. Ciênc.*, suppl.38, p.325-330, 1966.
- MORS, W.B.; SANTOS, M.F.; MONTEIRO, H.B. Chemoprophylactic agent in schistosomiasis: 14,15-epoxygeranylgeraniol. *Science*, v.157, n.3791, p.950-951, 1967.

- NETO, J.J. Contribuição ao Estudo Farmacognóstico dos frutos de *Pterodon pubescens* Benth. Parte III- Identificação cromatográfica em fase gasosa, química e ação microbiológica do óleo do fruto. *Rev. Fac. Farm. Odontol., Araraquara*, v.10, n.2, p.317-327, 1976.
- NUNAN, E.A.; CARVALHO, M.G.; PILÓ-VELOSO, D.; TURCHETTI-MAIA, R.M.M.; FERREIRA-ALVES, D.L. Furane diterpenes with anti- and pro-inflammatory activity. *Rev. Bras. Pesq. Med. Biol.*, v.15, n.6, p.450-451, 1982.
- OLIVEIRA, D.M.T.; PAIVA, E.A.S. (2005) Anatomy and Ontogeny of *Pterodon emarginatus* (FABACEAE: FABOIDEAE) Seed. *Braz. J. Biol.*, v.65, n.3, p.483-494, 2005.
- PIMENTA, A.T.A.; SANTIAGO, G.M.P.; ARRIAGA, A.M.C.; MENEZES, G.H.A.; BEZERRA, S.B. Estudo fitoquímico e avaliação da atividade larvicida de *Pterodon polygalaeiflorus* Benth (*Leguminosae*) sobre *Aedes aegypti*. *Rev. Bras. Farm.*, v.16, n.4, p.501-505, 2006.
- SABINO, K.C.; GAYER, C.R.; VAZ, L.C.; SANTOS, L.R.; FELZENSZWALB, I.; COELHO, M.G. In vitro and in vivo toxicological study of the *Pterodon pubescens* seed oil. *Toxicol. Lett.*, v.108, n.1, p.27-35, 1999a.
- SABINO, K.C.; CASTRO, F.A.; OLIVEIRA, J.C.; DALMAU, S.R.; COELHO, M.G. Successful treatment of collagen-induced arthritis in mice with a hydroalcohol extract of seeds of *Pterodon pubescens*. *Phytother. Res.*, v.13, n.7, p.613-615, 1999b.
- SANTOS FILHO, D.; GILBERT, B. Prophylaxis of Schistosoma by the fruit oil of *Pterodon pubescens* Benth. [Profilaxia de esquistossomose pelo óleo de *Pterodon pubescens* Benth: Dois novos diterpenos]. *Bol. Fac. Farm. Odontol. Ribeirão Preto*, v.6, n.1, p.142-149, 1969.
- SILVA, M.C.; GAYER, C.R.; LOPES, C.S.; CALIXTO, N.O.; REIS, P.A.; PASSAES, C.P.; PAES, M.C.; DALMAU, S.R.; SABINO, K.C.; TODESCHINI, A.R.; COELHO, M.G. Acute and topic anti-edematogenic fractions isolated from the seeds of *Pterodon pubescens*. *J. Pharm. Pharmacol.*, v.56, n.1, p.135-141, 2004.
- SILVA, D.P.; CASADO-FILHO, E.L.; CORRÊA, A.S.R.; FARIAS, L.R.; BLOCH, JR., C.; GROSSI DE SÁ, M.F.; MENDES, P.A.M.; QUIRINO, B.F.; NORONHA, E.F.; FRANCO, O.L. Identification of an  $\alpha$ -Amylase Inhibitor from *Pterodon pubescens* with Ability To Inhibit Cowpea Weevil Digestive Enzymes. *J. Agric. Food Chem.*, v.55, n.11, p.4382-4387, 2007.
- SPINDOLA, H.M.; CARVALHO, J.E.; RUIZ, A.L.T.G.; RODRIGUES, R.A.F.; DENNY, C.; SOUSA, I.M.O.; TAMASHIRO, J.Y.; FOGGIO, M.A. Furanoditerpenes from *Pterodon pubescens* Benth with selective in vitro anticancer activity for prostate cell line. *J. Braz. Chem. Soc.*, v.20, n.3, p.569-575, 2009.
- SUÁREZ, G.R.; ENGLEMAN, E.M. Depósito de taninos en la testa de *Amaranthus hypochondriacus* L. (alegria). *Agrociencia*, v.42, p.35-50, 1980.
- TORRENEGRA, R.; BAUEREIB, P.; ACHENBACH, H. Homormosanine-Type Alkaloids from *Bowdichia Virgiloides*. *Phytochemistry*, v.28, n.8, p.2219-2221, 1989.
- VIEIRA, C.R.; MARQUES, M.F.; SOARES, P.R.; MATUDA, L.; DE OLIVEIRA, C.M.A.; KATO, L.; DA SILVA, C.C.; GUILLO, L.A. Antiproliferative activity of *Pterodon pubescens* Benth. seed oil and its active principle on human melanoma cells. *Phytomedicine*, v.15, n.6-7, p.528-532, 2008.

Received for publication on 06<sup>th</sup> Jan 2010.

Accepted for publication on 16<sup>th</sup> April 2010.