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Phytochemical Studies in Pteridophytes Growing in Brazil: A Review

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ABSTRACT

Some 13,600 species of pteridophytes are known all around the world. Brazil, with about 1,300 species is considered as one of the centers of endemism and speciation of the South American continent. Notwithstanding this amazing biodiversity, very few phytochemical studies have been reported. The present study intends to review phytochemical investigations in pteridophytes growing in Brazil. We found 78 phytochemical studies carried out on 60 species and two varieties. Biological activity was the principal focus of published works (56 papers), the second most studied theme was molecular identification (with 21 publications) and then chemical ecology with 12 papers. The most addressed species was *Pteridium arachnoideum* (Kaulf.) Maxon (42 papers).

Keywords: ferns, Lycophyta, monilophytes, special metabolites

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INTRODUCTION

Pteridophytes comprise a group of plants formed by two lineages, Lycophyta and monilophytes (Pryer *et al.* 2001, 2004; Smith *et al.* 2006). Both produce spores, not seeds; the former has fronds with no leaf gap in the stem stele (lycophylls) and the latter fronds with a leaf gap in the stem stele (euphylls). Lycophytes include three clades: the homosporous species (Lycopodiales) and the heterosporous species (Isoetales and Selaginellales). Monilophytes in turn, includes the species traditionally termed "ferns". These two lineages have been treated together under various terms such as "pteridophytes" or "ferns and allied plant". According to Smith *et al.* (2006), there are nomenclature problems involving the term Monilophyta. They claim that this name was not validly published. In the light of modern classification, but taking into account that "pteridophytes" is still a term broadly used in scientific literature, we decided to use it throughout this paper.

Some 13600 species of pteridophytes are known all around the world (Moran 2008). Prado (1998) estimates that 1200 to 1300 species of pteridophytes occur in Brazil and, following Tryon (1986), the south-southeast region of Brazil possesses about 600 species, being one of the centers of endemism and speciation of pteridophytes in the South–American continent.

The present work intends to review phytochemical investigations on the special metabolites of pteridophytes carried out in Brazil, on Brazilian species, or on worldwide distributed species also found in Brazil during the period extending from 1966 until 2010.

PHYTOCHEMICAL STUDIES IN BRAZILIAN PTERIDOPHYTES

Soeder (1985) reported a large inventory of papers that appeared between 1966 and 1984 on the chemical constituents of pteridophytes. This author lists a total of 671 references, but only one work had been carried out in Brazil (Miraglia *et al.* 1985). In the present review, about 78 publications have been found describing phytochemical studies carried out in Brazil on pteridophytes, covering the period from 1966 to 2010. The most addressed species was *Pteridium arachnoideum* (Kaulf.) Maxon with one reference on chemical ecology (Santos *et al.* 2005) and 41 on biological activity (**Table 1**). There is great interest in this species since it is eaten in some regions of Brazil (Corrêa 1984; Zurlo and Brandão 1989) and also for its medicinal properties as astringent, diuretic, cough medicine, expectorant and rheumatism (Lima 1940; Corrêa 1984; Barros and Andrade

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Invited Review

Table 1 Species of pteridophytes that are the object of phytochemical studies realized in Brazil, scope of the studies and respective references. CE: Chemical Ecology, BA: Biological Activity, MI: Molecular Identification.

Species	Focus	Articles
Adiantopsis radiata (L.) Fée	CE	Peres *et al.* 2004; Santos *et al.* 2005
Adiantum cappilus-veneris L.	CE	Meinerz *et al*. 2008
Adiantum raddianum C.Presl	CE	Santos *et al*. 2005
	BA	Bresciani *et al*. 2003
	MI	Bresciani *et al*. 2003
Adiantum serratodentatum Willd.	CE	Peres *et al.* 2004
Adiantum tetraphyllum Humb. and Bonpl. ex Willd.	CE	Peres *et al.* 2004; Melos *et al.* 2007
	MI	Melos *et al.* 2007
Anemia hirsuta (L.) Sw.	CE	Santos *et al*. 2005
Anemia tomentosa (Sav.) Sw. var. *anthriscifolia* (Schrad.) Mickel	CE	Moraes *et al.* 2003; Santos *et al.* 2005
	MI	Santos *et al*. 2003, 2006; Pinto *et al.* 2007, 2009a, 2009b; Joseph-Nathan *et al*. 2010
	BA	Pinto *et al.* 2009a
Anemia villosa Humb. and Bonpl. Ex Willd.	CE	Moraes *et al.* 2003; Santos *et al.* 2005
Antigramma plantaginea (Schrad.) C. Presl	CE	Santos *et al.* 2005
Blechnum occidentale L.	BA	Nonato *et al.* 2009
Blechnum regnellianum (Kunze) C. Chr.	MI	Miraglia *et al.* 1985
Blechnum serrulatum Rich.	CE	Santos *et al.* 2005
Cheilanthes flexuosa Kunze	MI	Salatino and Prado 1998
Cheilanthes goyazensis (Taub.) Domin	MI	Salatino and Prado 1998
Cyathea phalerata Mart.	BA	Brighente *et al.* 2007; Pizzolatti *et al*. 2007; Hort *et al.* 2008
	MI	Brighente *et al.* 2007; Pizzolatti *et al*. 2007; Hort *et al.* 2008
Dicksonia sellowiana (Presl.) Hook	BA	Bora *et al*. 2005
Dicranopteris flexuosa (Schrad.) Underw.	CE	Soares and Vieira 2000; Müller *et al*. 2007; Campos *et al*. 2008
Doryopteris collina (Raddi) J.Sm.	CE	Santos *et al*. 2005
Doryopteris concolor (Langsd. and Fisch.) Kuhn	MI	Salatino and Prado 1998
Doryopteris ornithopus (Hook. and Baker) J. Sm.	MI	Salatino and Prado 1998
Doryopteris varians (Raddi) J. Sm.	CE	Santos *et al*. 2005
Equisetum arvense L.	BA	Do Monte *et al.* 2004; Santos Jr. *et al.* 2005a, 2005b
Equisetum giganteum L.	MI	Michelin *et al.* 2005; Danielski *et al.* 2007
Equisetum hyemale L.	BA	Oliskovicz *et al.* 2006
Gleichenella pectinata (Willd.) Ching	CE	Peres *et al.* 1998; Soares and Vieira 2000; Müller *et al.* 2007; Campos *et al*. 2008
Hemionitis tomentosa (Lam.) Raddi	CE	Santos *et al.* 2005
Lycopodiella cernua (L.) Pic.Serm.	CE	Santos *et al*. 2005
Macrothelypteris torresiana (Gaudich.) Ching	CE	Santos *et al*. 2005
Microgramma squamulosa (Kaulf.) de la Sota	BA	Suffredini *et al.* 1999
Microgramma vacciniifolia (Langsd. and Fisch.) Copel.	CE	Santos *et al.* 2005; Peres *et al.* 2009
	MI	Patitucci *et al.* 1995; Peres *et al.* 2009
	BA	Peres *et al.* 2009
Pellaea cymbiformis Prado	MI	Salatino and Prado 1998
Pellaea gleichenioides (Gardner) Christ	MI	Salatino and Prado 1998
Pellaea pinnata (Kaulf.) Prantl	MI	Salatino and Prado 1998
Pellaea riedelii Baker	MI	Salatino and Prado 1998
Phlebodium aureum L.	MI	Patitucci *et al.* 1995
Pityrogramma calomelanos (L.) Link	CE	Peres *et al.* 2004
Pityrogramma ebenea (L.) Proctor	MI	Miraglia *et al.* 1985
Pleopeltis pleopeltifolia (Raddi) Alston	MI	Patitucci *et al.* 1995
Pteridium arachnoideum (Kaulf.) Maxon	CE	Santos *et al*. 2005
	BA	Döbereiner *et al.* 1966; Tokarnia *et al.* 2002; Andrade *et al.* 1977; Barros *et al.* 1987; Basile *et al.*1981; Santos *et al.* 1986; Santos *et al.* 1987; Moura *et al.* 1988; Fernandes *et al.* 1990; Santos *et al.* 1990; Gerenutti *et al.* 1992; Ribeiro *et al.* 1992, 1995; Santos *et al.* 1992; Gerenutti *et al.* 1993; Souza and Graça 1993; Gerenutti *et al.* 1994; Marliére *et al.* 1994; Oliveira *et al.* 1995; Ribeiro *et al.* 1995; Brasileiro-Filho *et al.* 1996; Marçal and Campos Neto 1996; Marliére *et al.* 1998; Freitas *et al.* 2000a; Silva *et al.* 2000; Freitas *et al.* 2002; França *et al.* 2002; Gava *et al.* 2002; Marçal *et al.* 2002; Marliére *et al.* 2002; Tokarnia *et al.* 2002; Cruz *et al.* 2003; Lindsey 2003; Recouso *et al.* 2003; Cruz and Bracarense 2004; Cruz *et al.* 2005; Falbo *et al.* 2005; Santos *et al.* 2006; Souto *et al.* 2006; Rissi *et al.* 2007; Campos-da-Paz *et al*. 2008; Oliveira-Pereira *et al.* 2008
Pteridium caudatum (L.) Maxon	BA	Freitas *et al.* 2000b
Pteris altissima Poir.	MI	Salatino and Prado 1998
Pteris angustata (Feé) C.V. Morton	MI	Salatino and Prado 1998
Pteris decurrens C. Presl	MI	Salatino and Prado 1998
Pteris deflexa Link.	MI	Salatino and Prado 1998
Pteris denticulata Sw.	CE	Peres *et al.* 2004
Pteris denticulata Sw. var. *tristicula* (Raddi) Prado	MI	Salatino and Prado 1998
Pteris plumula Desv.	MI	Salatino and Prado 1998
Pteris podophylla Sw.	MI	Salatino and Prado 1998
Pteris propinqua J. Agardh	MI	Salatino and Prado 1998
Pteris splendens Kaulf.	MI	Salatino and Prado 1998

Table 1 (Cont.)

Species	Focus	Articles
Pteris vittata L.	MI	Salatino and Prado 1998
Selaginella muscosa Spring	CE	Santos *et al.* 2005
Selaginella sellowii Hieron.	CE	Santos *et al.* 2005
Selaginella sulcata (Desv. ex Poir.) Spring ex Mart.	CE	Santos *et al.* 2005
Serpocaulon latipes (Langsd. and Fisch.) A.R.Sm.	CE	Esteves and Felippe 1990
	MI	Esteves and Felippe 1990
Serpocaulon catharinae (Langsd. and Fisch.) A.R. Sm.	CE	Santos *et al.* 2005
Serpocaulon meniscifolium (Langsd. and Fisch.) A.R. Sm.	MI	Patitucci *et al.* 1995
Serpocaulon triseriale (Sw.) A.R. Sm.	BA	Barros *et al.* 1989
	CE	Santos *et al.* 2005
Sticherus bifidus (Willd.) Ching	CE	Soares and Vieira 2000
Sticherus lanuginosus (Fée) Nakai	CE	Moraes and Garcia 2007
Sticherus nigropaleaceus (Sturm) J. Prado	CE	Soares and Vieira 2000
Sticherus pruinosus (Mart.) Ching	CE	Soares and Vieira 2000; Müller *et al.* 2007

1997; Santos and Sylvestre 2000). In addition, *P. arachnoideum* is a species that invades crops and pastures (Lima 1940), being reported as toxic, by the presence of the cyanogenic glycosides and a norsesquiterpene called ptaquiloside (Santos *et al.* 1987; Marliére *et al.* 2002; Santos *et al.* 2005; Yamada *et al.* 2007). Accidental ingestion of this plant by livestock can poison them (Döbereiner *et al.* 1966; Barros *et al.* 1987; Marçal *et al.* 2001; Souza and Graça 1993; Gava *et al.* 2002).

Biological activity was the principal focus of most (56) published works, the second most studied theme was molecular identification (with 21 publications) and then chemical ecology with 12 papers (**Table 2**). Of note, some studies related to biological activity also discuss the production of special metabolites. All together, these studies covered only 60 species and two varieties. Two of those species, *Adiantum cappilus-veneris* L. and *Equisetum arvense* L., are not natives of Brazil, but cultivated, mainly as medicinal plants. Thus, this review presents the studies carried out on 58 species and two varieties of Brazilian pteridophytes, which represents 4.7% of the pteridoflora estimated in Brazil.

Another point that should be emphasized is that most of the analyses were carried out on sporophytes (stems, fronds or whole plant), but only two on spores (Patitucci *et al.* 1995; Freitas *et al.* 2000a). So far there have been no publications on gametophytes.

Table 2 Phytochemical references of studies on Brazilian pteridophytes, organized by their scope.

Biological activity
Döbereiner *et al.* 1966; Tokarnia *et al.* 1967; Andrade *et al.* 1977; Basile *et al.* 1981; Santos *et al.* 1986; Barros *et al.* 1987; Santos *et al.* 1987; Moura *et al.* 1988; Barros *et al.* 1989; Fernandes *et al.* 1990; Santos *et al.* 1990; Gerenutti *et al.* 1992; Ribeiro *et al.* 1992; Santos *et al.* 1992; Gerenutti *et al.* 1993; Souza and Graça 1993; Gerenutti *et al.* 1994; Marliére *et al.* 1994; Oliveira *et al.* 1995; Ribeiro *et al.* 1995; Brasileiro-Filho *et al.* 1996; Marçal and Campos Neto 1996; Marliére *et al.* 1998; Suffredini *et al.* 1999; Freitas *et al.* 2000a, 2000b; Silva *et al.* 2000; Freitas *et al.* 2002; França *et al.* 2002; Gava *et al.* 2002; Marçal *et al.* 2002; Marliére *et al.* 2002; Tokarniaa *et al.* 2002; Bresciani *et al.* 2003; Cruz *et al.* 2003; Lindsey 2003; Recouso *et al.* 2003; Cruz and Bracarense 2004; Do Monte *et al.* 2004; Bora *et al.* 2005; Cruz *et al.* 2005; Falbo *et al.* 2005; Santos Jr. *et al.* 2005a, 2005b; Oliskovicz *et al.* 2006; Santos *et al.* 2006; Souto *et al.* 2006; Brighente *et al.* 2007; Pizzolatti *et al.* 2007; Rissi *et al.* 2007; Campos-da-Paz *et al.* 2008; Hort *et al.* 2008; Oliveira-Pereira *et al.* 2008; Nonato *et al.* 2009; Peres *et al.* 2009; Pinto *et al.* 2009a
Chemical ecology
Esteves and Felippe 1990; Peres *et al.* 1998; Soares and Vieira 2000; Moraes *et al.* 2003; Peres *et al.* 2004; Santos *et al.* 2005; Melos *et al.* 2007; Moraes and Garcia 2007; Müller *et al.* 2007; Campos *et al.* 2008; Meinerz *et al.* 2008; Peres *et al.* 2009
Molecular identification
Miraglia *et al.* 1985; Esteves and Felippe 1990; Patitucci *et al.* 1995; Salatino and Prado 1998; Suffredini *et al.* 1999; Bresciani *et al.* 2003; Santos *et al.* 2003; Do Monte *et al.* 2004; Bora *et al.* 2005; Michelin *et al.* 2005; Santos *et al.* 2006; Brighente *et al.* 2007; Danielski *et al.* 2007; Melos *et al.* 2007; Pinto *et al.* 2007; Pizzolatti *et al.* 2007; Hort *et al.* 2008; Peres *et al.* 2009; Pinto *et al.* 2009a, 2009b; Joseph-Nathan *et al.* 2010

BIOLOGICAL ACTIVITY

Many studies showed that Brazilian pteridophytes are responsible for a number of biological activities. Several species are shown to be endowed with antibiotic, anti ulcer, antioxidant, analgesic, antinociceptive, anti-inflammatory, sedative and even anticonvulsant activities. Studies have also shown poisoning of livestock that feeds on some kinds of pteridophytes and even carcinogenic properties.

Extracts prepared from fronds and rhizomes of the species *Polypodium brasiliense* Poiret (=*Serpocaulon triseriale* (Sw.) A.R.Sm.), collected by Barros *et al.* (1989) in a remaining area from the Atlantic Forest (Mata de Dois Irmãos, Recife, PE, Brazil) have been tested against seven different microorganisms, four Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus faecalis* and *Mycobacterium smegmatis*), one Gram-negative bacteria (*Escherichia coli*), one yeast (*Candida albicans*) and one filamentous fungus (*Monilia silophila*). During the microbiological test, we observed as result that the *M. silophila* was the only that did not suffer growing inhibition in exposure to the extracts of *Serpocaulon triseriale*.

In the region of São Paulo, Brazil, the population makes use of a tea prepared from rhizomes of a plant known popularly as "erva-silvina" or "polipódio-escamoso", for the treatment of ulcers. This plant was identified as *Micrograma squamulosa* (Kaulf.) Sota. Suffredini *et al.* (1999) evaluated the action of a crude extract of this species, collected in São Paulo, against acute ulcers caused by ethanol and hydrochloric acid, using misoprostol and cimetidine as reference substances in both tests. The same extract and the control cimetidine were tested also against sub-chronic ulcers induced by acetic acid. The extracts showed significant activity against sub-chronic ulcers, but not against acute ulcers. The authors conclude that the mechanism of action must be related to the presence of tannins in the extracts, which would induce a stringent action, or to the presence of flavonoids, through a systemic action, perhaps similarly to the cimetidine action. The authors also evaluated the toxicological sub-chronic action of the crude extract, using a dose of 800 mg/kg for 30 days. After this time, the animals did not show any significant variation in the consumption of food and water, and neither variation of weight, thus not presenting any evidence of toxicological action.

The species *Adiantum cuneatum* Langsd. & Fish, (=*Adiantum raddianum* C. Presl) is used as an ornamental plant, and is popularly known as "avença" ("maidenhair ferns"). This species is found in several regions of South America, mainly in Brazil, and is famous for its medicinal properties, mainly in the treatment of pain. Bresciani *et al.* (2003) collected this species in Caxambu do Sul, State of Santa

Catarina, Brazil, performing crude extracts from the fronds. The hexane extract proved to be responsible for a strong dose-dependent analgesic action in rats, demonstrating to be equipotent to acetyl salicylic acid and to acetaminofen. Phytochemical examination of this extract showed it to be rich in triterpenes. Fractionation of this extract led to the isolation of the triterpenes filicene [**1**], filicenal [**2**], adiantol [**3**] and isoadiantone [**4**]. The analgesic activity of filicene and filicenal was tested; it was shown that these metabolites are responsible, at least in part, for the activity presented by the hexane crude extract. Hence, these results confirm and justify the popular use of this species in the treatment of pain.

The results described by Nonato *et al.* (2009) also support the folk medicine use of another fern species, *Blechnum occidentale* L. This species has been used to treat inflammatory and pulmonary diseases, urinary infections and liver diseases (Barros and Andrade 1997). Nonato *et al.* (2009) evaluated the antinociceptive and anti-inflammatory action of the methanolic crude extract of blades of this species. The antinociceptive effect was observed by acetic acid-induced writhing and formalin tests, but not in the tail flick test. The extract produced anti-inflammatory effect on carrageenan-induced paw oedema and neutrophil migration. The study also demonstred that systematic administration of the methanolic extract of *B. occidentale* did not produce any motor performance alteration.

Stems of the species *Equisetum arvense* L., a plant popularly known as "cavalinha" ("horsetail ferns"), collected in Santa Catarina, Brazil, furnished a hydro-alcoholic extract that has shown analgesic effect against chemical models of pain perception (acetic acid induced writhing syndrome), but not in thermal models (hot plate), with central and peripheral action (do Monte *et al.* 2004). The same extract also showed anti-inflammatory activity. Santos Jr. *et al.* (2005a, 2005b) studied the hydro-alcoholic extract of the same species, collected in an undefined locality of the State of Santa Catarina, Brazil, and evaluated its antioxidant activity and the action on the central nervous system (CNS). The authors have shown that this extract presents sedative and anticonvulsant activities, and improves cognitive deficits in aged rats. Phytochemical analysis detected the presence of tannins, saponins, sterols and flavonoids, whose structures were not investigated.

Similarly to *E. arvense*, the species *Equisetum hyemale* L. is also popularly known as "cavalinha" ("horsetail ferns"). This species is native to Brazil and has proven healing properties in experimental models. It is a plant toxic to horses and other domestic animals due to the antitiaminic substances it contains. Oliskovicz *et al.* (2006) conducted a comparative study, in rats, of the healing action on skin wounds treated with an ointment containing the ethanolic extract of *E. hyemale*, obtained from two different cultures made in the region of Mato Grosso do Sul. It should be stressed that the author reports the name *Equisetum pyramidale*, without any reference either to a plant voucher or to the taxonomist who identified the material. Looking at the picture of the plant provided in the paper, we concluded that this species must be *E. hyemale* L.

The authors noted that, after 14 days of treatment, the so called "control" ointment containing the extract was the most active, being even more efficient for healing purposes than the commercial Fribrase®.

Cyathea phalerata Mart. is a species that grows in tropical and subtropical areas of Brazil. It is popularly known as "xaxim", being used to treat various diseases associated with inflammatory processes. Phytochemical investigations of this plant showed the presence of an active flavonoid (kaempferol-3-neohesperidoside) with hypoglycaemic activity (Pizzolatti *et al.* 2007), besides the presence of cyathenosin A, a spiropyranosil derivative of protocatechuic acid, from the stem pith of *C. phalerata*. Hort *et al.* (2008) studied the antioxidant and hepatoprotector potential of the crude hydroalcoholic extract and of fractions obtained by treatment with organic solvents of increasing polarity. The authors noted that the ethyl acetate fraction of the crude extract displayed the best antioxidant and hepatoprotector activities, and concluded that the flavonoids contained in this fraction could be responsible for these activities.

Peres *et al.* (2009) evaluated the antioxidant activity of an etanolic crude extract and fractions of *Microgramma vacciniifolia* (Langsd. & Fich.) Copel. fronds using 2,2-diphenyl-1-picrylhydrazyl (DPPH). The ethyl acetate fraction showed good activity in DPPH assay. These authors also studied the antimicrobial effects of the same species. The hexan fraction from ethanolic crude extract was most effective against the *Sacharomices cerevisae* and *Candida albicans* fungi.

The species *Dicksonia sellowiana* (Presl.) Hook is a typical plant of the Brazilian Atlantic Forest. Also popularly known as "xaxim" it is characterized by its tree size. Fronds were collected by Bora *et al.* (2005) and extracted with solvents of increasing polarity. These extracts were tested for antioxidant potential and to assess the concentration in phenolic substances. The authors observed that the extracts that contained a higher concentration of polyphenols also showed more potent antioxidant activity, concluding that the antioxidant activity of *D. sellowiana* must be related to the presence of this class of substances.

The species *Pteridium aquilinum* (L.) Kuhn. [=*Pteridium arachnoideum* (Kaulf.) Maxon], know by the popular name "samambaia-das-roças" ("bracken fern"), has been the subject of studies to test its potential toxicity in several animals, mainly on the cattle and horses (Andrade *et al.* 1977; Basile *et al.* 1981; Fernandes *et al.* 1990; Gerenutti *et al.* 1992, 1993; Ribeiro *et al.* 1995; Marçal and Campos-Neto 1996; Marçal 2002). Another papers approach the clastogenic (Ribeiro *et al.* 1992; Lindsey 2003) and apoptosis proprieties (Oliveira-Pereira *et al*. 2008) induced by this species. Rats treated with another species of "bracken fern", *Pteridium caudatum* (L.) Maxon, also shows DNA damage (Freitas *et al.* 2000b). Studies reported that *P. arachnoideum* can induce tumors and cancers (Santos *et al.* 1992; Gerenutti *et al.* 1994; Brasileiro-Filho *et al.*1996; Silva *et al.* 2000; Cruz *et al.* 2003). This is a problem, mainly in the Ouro Preto region, Minas Gerais state, when this crozier is consumed by humans (Santos *et al.* 1986; Marliére *et al.* 1994; Marliére 1998).

Gava *et al.* (2002) conducted an epidemiologic investigation on cattle poisoning in the State of Santa Catarina, Brazil, in the period from 1987 to 2001. These authors showed that this species is a major cause of poisoning in cattle in this state. These data were further confirmed by Rissi *et al* (2007). Several papers describe the intoxication and the incidence of neoplasias in cows associated with the spontaneous consumption of bracken fern (Tokarnia *et al.* 1967; Souza and Graça 1993; Marçal *et al.* 2002; Tokarnia *et al.* 2002; Souto *et al.* 2006). Falbo *et al.* (2005) showed hematological, biochemical, urinary and histopathologic changes by clinical and laboratorial exams in bovine intoxicated by bracken fern. Data concerning epidemiological, toxicological, clinical and pathological features observed in animals poisoned by *Pteridium arachnoideum* were described by França *et al.* (2002). The same species is consumed as food by the population of the city of Ouro Preto, State of Minas Gerais, Brazil, where it is known as "broto de samambaia" ("crozier"). This fact led Santos *et al.* (1987) to assess the carcinogenic potential in Wistar rats fed with this species over 70 weeks. The animals were then sacrificed and carefully examined for verification of the presence of tumors. All animals subjected to this diet had tumors in the gastrointestinal tract, mainly in the ileum, most of which were characterized as malignant lesions (sarcomas and carcinomas), but benign adenomas were also found. There were no tumors in animals of the control group. These data clearly demonstrate the carcinogenic potential of this species to rats. Moura *et al*. (1988) observed chromosome aberrations in cattle raised on bracken fern pasture. The frequency of structural chromosome aberrations detected in peripheral blood cells was significantly

higher when compared to that detected in animals raised on pasture containing no bracken fern. Recouso *et al*. (2003) showed that significant increased levels of chromosomal abnormalities, such as chromatid breaks in cultured peripheral lymphocytes, could be verified, by cytogenetic analysis, in human consumers of bracken fern. Santos *et al.* (1990) showed the induction of tumors in rats and the oncogenicity of bracken fern (*P. arachnoideum*) from Ouro Preto, Brazil. The clastogenic and aneugenic properties of bracken fern were investigated by Santos *et al.* (2006).

Oliveira *et al.* (1995) concluded that low-dose crude bracken fern in the diet does not promote rat urinary bladder carcinogenesis after a 32-week period of exposure. Freitas *et al*. (2002) investigated possible genomic alterations in some malignant bracken fern-induced tumors of rats for mutations in the genes associated with the colorectal cancer, however, no mutations were found in any of the tumors.

Cruz *et al.* (2005) also noted the induction of tumors in the ileum of rats treated with shoots of *P. arachnoideum* collected in the state of Paraná. The norsesquiterpene ptaquiloside [**5**], a glycoside intermediary of the biosynthesis of pterosides, is currently considered to be the major responsible for the bracken toxicity, being mutagenic, and also for the onset of cancer (Yamada *et al.* 2007). In humans, there are three ways to be poisoned: direct ingestion of the plant, physical contact by ingestion or inhalation of spores from contaminated water, and ingestion of raw milk from animals that ate the plant (Cruz and Bracarense 2004; Campos-da-Paz *et al.* 2008).

CHEMICAL ECOLOGY

Peres *et al.* (1998) investigated the allelopathic activity of aqueous extracts and *n*-butanol fractions obtained from rhizomes, young fronds, green and dried fronds of *Gleichenia pectinata* (Willd.) C. Presl [=*Gleichenella pectinata* (Willd.) Ching] in bioassays to assess the germination of seeds of *Lactuca sativa* L. (Asteraceae) and *Clidenia hirta* (L.) D. Don (Melastomataceae), a species that occurs in the same area as populations of *G. pectinata*. These authors noted the occurrence of allelopathic effects in extracts obtained at different times of the year, especially in spring and autumn. The aqueous extracts delayed the time of germination of *C. hirta*, but the germination rate increased in relation to the control. On the contrary, the *n*-butanolic fractions anticipated and increased the germination rate of *C. hirta* but inhibited the germination of *L. sativa*. The authors suggested that the active principles of *G. pectinata* may significantly alter the strategies of germination of *C. hirta*, and this may have consequences on the population dynamics during different seasons of the year.

G. pectinata and other species of the family Gleicheniaceae, collected in the Zona da Mata, State of Minas Gerais, were tested by Soares and Vieira (2000). Green and senescent fronds of *Dicranopteris flexuosa*, *G. pectinata*, *Sticherus bifidus*, *Sticherus penniger* [=*Sticherus pruinosus* (Mart.) Ching] and *Sticherus nigropaleaceus* furnished aqueous extracts that were tested on the germination and development of lettuce radicles (*L. sativa* L. cv. 'Grand rapids'). The authors reported that inhibition of germination was caused by the extracts of green fronds of all the species and by the extracts of senescent fronds of *D. flexuosa*, *S. bifidus* and *S. nigropaleaceus*. All the extracts also inhibited the growth of the radicle and induced the development of necrosis. They suggested the possibility of production and release, by these species, of allelopathic metabolites, mainly by the living tissues. Aqueous extracts of *Sticherus lanuginosus* (Fée) Nakai, another species of Gleicheniaceae also induced alterations in the germination, speed of germination, dry mass and development of lettuce radicles and hypocotyls (*L. sativa* L. cv. 'Grand rapids') (Moraes and Garcia 2007).

Further studies showed the cytotoxic effect of extracts from *G. pectinata* and *D. flexuosa* on root meristems of *Zea mays* L. (Poaceae) and *L. sativa* (Campos *et al*. 2008). The authors noted that the reduction of root growth was due to inhibition of the mitotic process and induction of aberration of chromosomes and cell death. They also observed typical toxic effects. This stronger answer was induced by extracts made with plants collected during the wet season, suggesting a possible effect of rain on the release of active substances.

Polypodium latipes Langsd. and Fisch. [=*Serpocaulon latipes* (Langsd. and Fisch.) A.R. Sm.], collected in the State of São Paulo, was studied by Esteves and Felippe (1990). The water and ethanol crude extracts of leaflets inhibited the germination of lettuce seeds. More interestingly, the methanol: water (1: 1) crude extract of leaflets inhibited germination of spores from the plant itself. This activity was attributed to the presence of coumarin [**6**] and may explain, following the authors, why *Serpocaulon latipes* is often found in almost monospecific vegetation islands. Total phenols and coumarin content were determined in the latter extract. They amount respectively to 61.4 and 15.4 $mg.mg^{-1}$ leaflets.

Peres *et al.* (2004) studied the species *Adiantopsis radiata*, *Adiantum serratodentatum*, *Pteris denticulata*, *Adiantum tetraphyllum* and *Pityrogramma calomelanos*. Ethanolic extracts of green fronds were tested on the germination of *Allium cepa* L. (Liliaceae) and *L. sativa* and on the growth of the radicles and hypocotyls. The authors did not observe any effects of the extracts of the five species on the germination of *L. sativa* and *A. cepa*; however, they observed a differential response on the growth inhibition, characterized by inhibition of radicle growth with oxidation of the apex and the absence of root hairs. The authors discuss the possible difference of allelochemical compositions of the analyzed pteridophyte species. They also call the attention for the target-specific answer, as observed from the different behaviors between tested monocotyledon and the dicotyledon. Peres *et al.* (2009) assayed the allelopathic effects of the ethanolic crude extract and hexane, ethylacetate and hydroethanolic fractions of *Microgramma vacciniifolia* fronds. In the bioassay was tested the germination and development of lettuce radicles and hypocotyls (*L. sativa* cv. 'Grand rapids') and onion radicles and coleoptiles (*A. cepa* cv. 'Baia Periforme') The extract and fractions delayed the time of germination, reduced the percentage of germinated seeds, inhibited the growth of the radicle and promoted morphological alterations. This result suggests allelopathic activity of this species, probably attributed to the higher contents of the total phenols.

Another example of this target-specific answer may be reinforced by the analysis of the results obtained by Müller *et al*. (2007). These authors assayed *D. flexuosa*, *G. pectinata* and *S. penniger* [=*Sticherus pruinosus* (Mart.) Ching] extracts with onion seeds and verified accelerated germination and stimulation of the radicle and coleoptile, which differs from the results with lettuce assays obtained by Soares and Vieira (2000). This clearly points out the potential for the development of new products for the protection against harmful plants using substances from pteridophytes.

Melos *et al.* (2007) observed the allelopathic effect of *A. tetraphylum* Humb. and Bonpl. ex Willd, collected in the State of Mato Grosso do Sul. They reported the presence of a mixture containing fatty acids ethyl esters, and isolated flavonoids, diterpenes, triterpenes and one sterol, described in the appropriated section of this paper. No bioassays were carried out with purified compounds.

Aqueous extracts obtained from fresh or dried fronds of *Anemia tomentosa* var. *anthriscifolia* and *Anemia villosa*, two species of the family Schizaeaceae, collected in a rocky substrate, were examined by Moraes *et al.* (2003). This study reported the inhibition of germination and of the development of seedlings of lettuce by extracts obtained from dry plant material. This differed from other studies in which the extracts obtained from fresh material were more effective to induce changes in the development of bioassayed species. These authors suggest, based on histochemical studies, that phenolic substances may be responsible for the observed effects.

Santos *et al.* (2005) screened, monthly along one year, species collected from a rocky substrate to check for the occurrence of cyanogenesis. The study analyzed 19 species, distributed in 13 genera and 9 families. The results showed that 9.9% of the samples were cyanogenic, principally the species of the family Polypodiaceae, in which all examined species displayed cyanogenesis. *Microgramma vacciniifolia* and *Pteridium arachnoideum* were cyanogenic throughout the period of analysis. Variability in cyanogen production and intrapopulation polymorphism in the ability of release of cyanhydric acid were also observed.

Another study related to plant defense observed the production of phytoalexins in sorghum mesocotyls and in soybean cotyledons, induced by dry frond extracts of *Adiantum cappilus-veneris* L., suggesting promising potential for exploration of pteridohytes' bioactive substances in a number of extracts, mainly those containing polar compounds (Meinerz *et al*. 2008). Due to differences in the patterns of response from the application of the extracts, substances appear to be distinct and to display a specific-species response.

MOLECULAR IDENTIFICATION

The few Brazilian studies concerning the chemistry of pteridophytes indicate the ubiquitous presence of flavonoids and terpenoids. There are also reports of the presence of tannins, saponins and steroids. However, it is important to note that only a part of the studies that indicated the presence of these metabolites were prospective, and were not concerned with the isolation and structural elucidation of the chemicals. Thus, the work of Suffredini *et al.* (1999) reports the positive reaction to tannins and flavonoids of the hydroalcoholic crude extract of *Microgramma squamulosa* and its partitions in ethanol and ethanol: water (1: 1). The same kind of study was conducted by do Monte *et al.* (2004), with the hydroalcoholic extract of stems from *Equisetum arvense*, resulting in a positive response to the presence of tannins, saponins, flavonoids and steroids. Besides these studies of chemical prospection, there are also studies aimed at determining the concentration of substances, without previous isolation, such as the work of Bora *et al.* (2005), which determines the amount of phenolic substances, by the colorimetric method of Folin-Cicaulteau, related to the antioxidant activity of the plant. As expected, this activity was directly proportional to the concentration of polyphenols in the sample, and the ethyl acetate fraction resulting from the partition of the crude extract of *D. sellowiana* appeared to be the most active and therefore, contained a greater concentration of these substances.

Similarly, Esteves and Felippe (1990) collected *Polypodium latipes* Langsd. and Fisch. [=*Serpocaulon latipes* (Langsd. and Fisch.) A.R.Sm.], in the cerrado of the State of São Paulo and quantified, without previous isolation, phenols and coumarin [**6**] in the methanol: water (1: 1) extract from the leaflets. Identification resulted from its Rf in thin layer chromatography comparing with standards, and from its UV spectrum.

One of the most representative works aiming to characterize the chemical profile assesses the presence of flavonoids in Pteridaceae and was published by Salatino and Prado in 1998. The study focused the flavonoid distribution in epicuticular waxes, although one of the characteristics observed in most of the Brazilian species of Pteridaceae was exactly the absence of the material covering the farinose leaf. The species studied by Salatino and Prado (1998) belong to the family Pteridaceae and are divided into two of its six subfamilies, Cheilanthoideae and Pteridoideae. Cheilanthoideae have seven genera distributed in Brazil; they are adapted to xeric or semi-xeric environments, being of common occurrence in campos rupestres (*Doryopteris*, *Hemionitis* and *Argyrochoma*) and some species of the genera *Cheilanthes* and *Pellaea* are endemic of habitats of southeastern Brazil. In contrast, only two genera of Pteridoideae have representatives in Brazil: *Pteris* and *Acrostichum*. The distribution of flavonoids observed indicated their possible use as taxonomic markers of these two subfamilies, since the species belonging to Cheilanthoideae presented exclusively the production of flavonols, and the representatives of Pteridoideae produced predominantly flavones (**Fig. 1**). Hence, the Brazilian species belonging to these two subfamilies can be separated according to their flavonoid patterns, based on the aglycones. Thus, Cheilanthoideae seem to show more derived characters, which is supported by a more restricted and more homogeneous chemical profile, being characterized by the exclusive production of flavonols, while Pteridoideae is characterized by the production of flavones and flavonols. The study by Salatino and Prado (1998) also suggests correlations between the flavonoid profile and the venation patterns in *Pteris*, besides intraspecific variation based on protection patterns of the flavonoid hydroxyl groups.

Studies by Bresciani *et al.* (2003) demonstrated the presence of terpenoids as predominant metabolites in *Adiantum cuneatum* Langsd. and Fisch. (=*Adiantum raddianum* C. Presl), or "avenca" ("maidenhair ferns"). This had already been observed for species cultivated in Japan and other countries. Phytochemical analysis of the partition in hexane of the methanol crude extract from fronds of *A. raddianum* led to the isolation of four known triterpenoids: filicene (**1**), filicenal (**2**), adiantol (**3**) and isoadiantone (**4**). Other terpenes were also detected but could not be isolated due to their low concentrations.

Melos *et al.* (2007) isolated from the ethanol crude extract of *Adiantum tetraphylum* a mixture of long-chain carboxylic acids esters, identified by CG, as the ethyl esters of palmitic, petroselenic, oleic, (*Z*)-vacenic, stearic, linoleic, decosahexenoic, a-linolenic, margaric, arachidic and behenic acids. Further purifications led to the isolation of β-sitosterol, two triterpenes: 30-normethyl-lupan-20-one [**12**] and hopan-22-ol [**13**], two diterpenes: phytol [**14**] and phyten-3(20)-1,2-diol [**15**], two flavonoids: quercetin [**7**] and quercetin-3-*O*-β-D-glucoside, and a mixture of ferulic acid, caffeic acid and *p*-hydroxybenzaldehyde.

According to Miraglia *et al.* (1985), a new substance isolated from the fronds of *Pityrogramma ebenea* was identified as 2',6'-dihydroxy-4,3'-dimethoxy-4',5'-methylenedioxydihydrochalcone [**16**]. The same work also reports the identification of the flavonoid (2S)-5,-dihydroxy-4'-methoxy-6,8-dimethylflavanone [**17**] in another pteridophyte, *Blechnum regnellianum*.

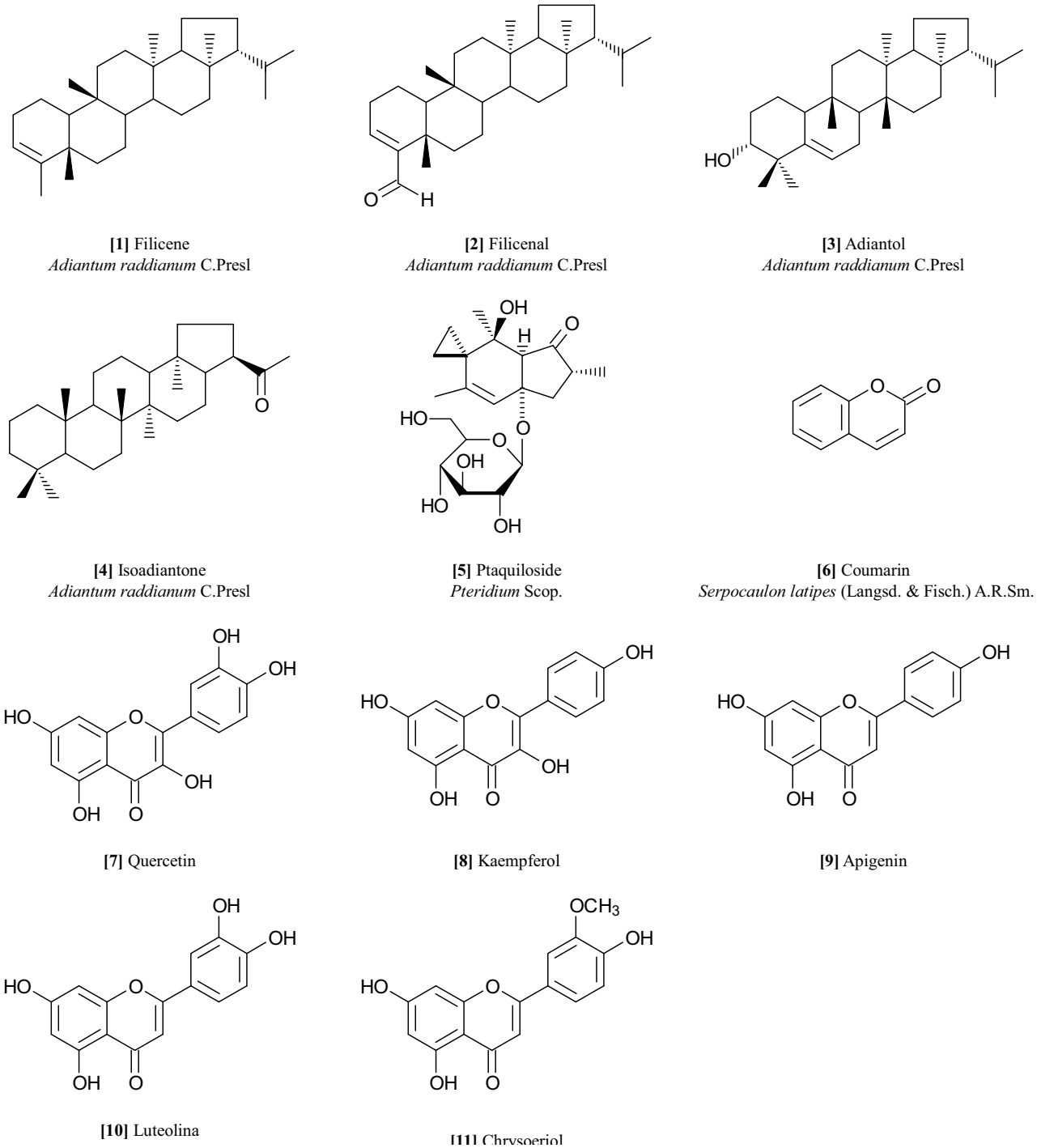
Although some species of pteridophytes possess a quite typical smell, there is only one work in Brazil aimed to characterize the chemical composition of their essential oil. Thus, Santos *et al.* (2003, 2006) reported the presence of isoafricanol [**18**], a highly uncommon sesquiterpene, found in the essential oil of *Anemia tomentosa* var. *anthriscifolia*. This was the first report of the African skeleton in a pteridophyte.

Pinto *et al.* (2007) studied the chemical composition of the essential oil from that species and detected the presence of sesquiterpenes of the silfiperfolane, pre-silfiperfolane, isocumene, cariophyllene, pre-nopsane and nopsane types. These authors reported the occurrence of two major components, pre-silfiperfolane-1-ol [**19**] and silfiperfol-6-ene [**20**]. In additional studies with *Anemia tomentosa* var. *anthriscifolia*, Pinto *et al.* (2009a) detected thirty one substances and Pinto *et al.* (2009b) isolated a new triquinane sesquiterpene (-)-epi-presilfiperfolan-1-ol, reevaluated by Joseph-Nathan *et al.* (2010) to 9-epi-presilfiperfolan-1-ol.

Regarding the presence of oleoresins in pteridophytes, two studies were performed with *Equisetum giganteum*. According to Danielski *et al.* (2007) this species is able to concentrate great amounts of vitamins and minerals and, moreover, contains large quantities of alkaloids, saponins and flavonoids (flavones, isoflavones, flavonols and flavanols). The chemical composition of the oleoresins of that species, obtained by extraction with supercritical fluid, was described by Michelin *et al.* (2005). Hydrocarbons and phytosteroids were observed. This study assessed the composition of the oleoresin obtained using supercritical fluid in dif-

ferent operating conditions. The chemical profile and the yield of the procedure were compared with classical extractions made with organic solvent such as *n*-hexane and dichloromethane. The yield of the extraction with supercritical fluid was *ca.* 85% higher when compared to the extraction with organic solvent. According to Michelin *et al.* (2005), the oleoresin of *E. giganteum* is a dark green viscous material that consists basically of substances of high molecular weight. This study thus indicated the ability of the process in extracting such substances. The following metabolites were identified: dodecanoic acid; 3-nonynoic acid methyl ester; 3,6-dimethyl decane; *n*-heneicosane; 26-hydroxycholesterol [**21**]; ergosta-4,7,22-trien-3-one [**22**]; 8,12-dimethyl-4Z,8E,12E-octadecanoic acid; gorgost-5-en-3b-ol [**23**]; methenolone; 2,6,10,14-hexadecatetraen-1-ol-3,7,11,15-tetramethyl-acetate; *Z*-13-octadecenal and bufa-20,22-dienolide-3,14-dihydroxy [**24**]. Further experiments have been carried out by the same group in order to evaluate other parameters related to obtaining the oleoresin of *E. giganteum* in supercritical CO_2 (Danielski *et al.* 2007).

The genus *Cyathea* has some records of phytochemical studies related to the production of triterpenes, phenolic acids and flavonoids, whose aglicone is frequently kaempferol [**8**]. Thus, Brighente *et al.* (2007) reported the isolation, from the hydroalcoholic extract of fresh wood samples of *Cyathea phalerata*, of kaempferol, kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside and 4-*O*-β-D-glucopyranosylcaffeic acid. In the same study, the determination of flavonoids and total phenols contents were also performed. Further studies by Hort *et al*. (2008) using fresh material from *C. phalerata* resulted in the isolation and identification of 9 substances: kaempferol-3-neohesperidoside (major component of the extract), 4-*O*-β-D-glucopyranosyl caffeic acid, 4-*O*-β-D-glucopyranosyl *p*-coumaric acid, 3,4-spyroglucopyranosyl protocatechuic acid, sitosterol β-D-glucoside, β-sitosterol, kaempferol, vitexin [**25**]



[1] Filicene
Adiantum raddianum C.Presl

[2] Filicenal
Adiantum raddianum C.Presl

[3] Adiantol
Adiantum raddianum C.Presl

[4] Isoadiantone
Adiantum raddianum C.Presl

[5] Ptaquiloside
Pteridium Scop.

[6] Coumarin
Serpocaulon latipes (Langsd. & Fisch.) A.R.Sm.

[7] Quercetin

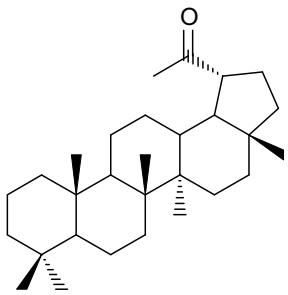
[8] Kaempferol

[9] Apigenin

[10] Luteolina

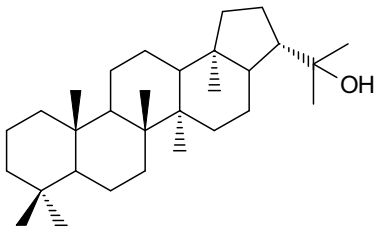
[11] Chrysoeriol

Fig. 1 Major pteridophyte flavones, encountered free or as glycosides.



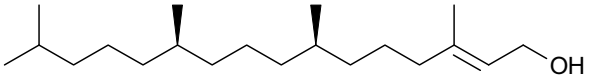
[12] 30-normethyl-lupan-20-one

Adiantum tetraphylum Humb. & Bonpl. ex Willd.

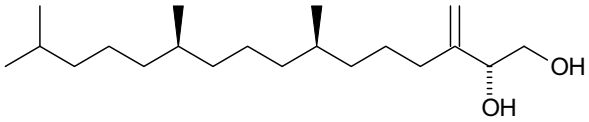


[13] hopan-22-ol

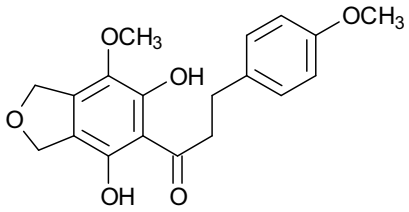
Adiantum tetraphylum Humb. & Bonpl. ex Willd.



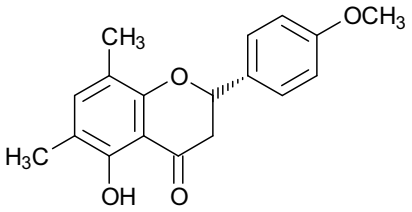
[14] phytol
Adiantum tetraphylum Humb. & Bonpl. ex Willd.



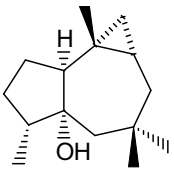
[15] phyten-3(20)-1,2-diol
Adiantum tetraphylum Humb. & Bonpl. ex Willd.



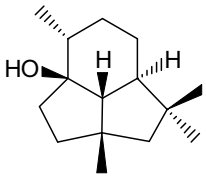
[16] 2',6'-dihydroxy-4,3'-dimethoxy-4',5'-methylenedioxydihydrochalcone
Pityrogramma ebenea (L.) Proctor



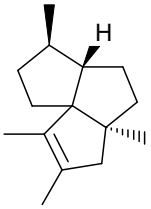
[17] (2S)-5,-dihydroxy-4'-methoxy-6,8-dimethylflavanone
Blechnum regnellianum (Kunze) C. Chr.



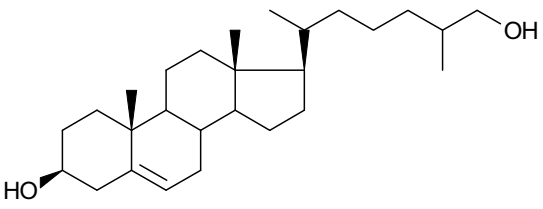
[18] Isoafricanol
Anemia tomentosa (Sav.) Sw. var. *anthriscifolia* (Schrad.) Mickel



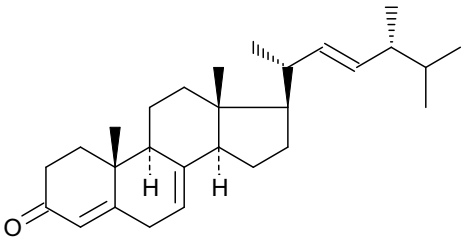
[19] pre-silfiperfolane-1-ol
Anemia tomentosa (Sav.) Sw. var. *anthriscifolia* (Schrad.) Mickel



[20] silfiperfol-6-ene
Anemia tomentosa (Sav.) Sw. var. *anthriscifolia* (Schrad.) Mickel



[21] 26-hydroxycholesterol
Equisetum giganteum L.

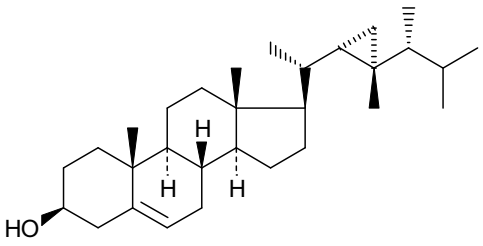


[22] ergosta-4,7,22-trien-3-one
Equisetum giganteum L.

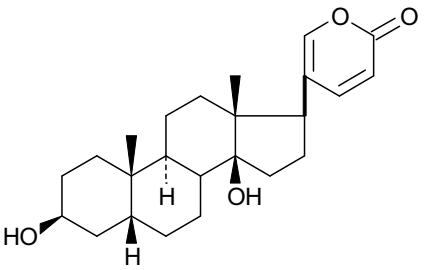
and ethylgalactoside.

Studies by Pizzolatti *et al.* (2007) also with *C. phalerata*, collected at Palhoça, State of Santa Catarina, again showed the presence of 4-*O*-β-D-glucopyranosyl caffeic acid, 4-*O*-β-D-glucopyranosyl *p*-coumaric acid, besides cyathenosin A [**26**]. This work represented the first description of the occurrence of a spiro-orthoester glucoside in the plant kingdom.

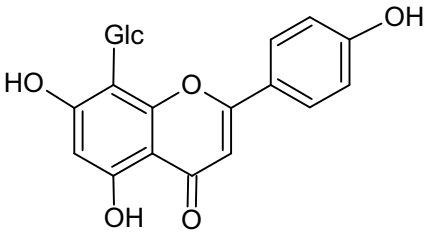
Patitucci *et al.* (1995) used high-resolution gas chromatography coupled to computerized mass spectrometry to perform direct analysis of crude extracts and of pre-fractioned extracts of low and medium polarity. In this study were evaluated seven apolar crude extracts of four species of Polypodiaceae: *Pleopeltis angustum* [=*Pleopeltis pleopeltifolia* (Raddi) Alston] (spore and rhizome), *Polypodium meniscifolium* [=*Serpocaulon meniscifolium* (Langsd. and



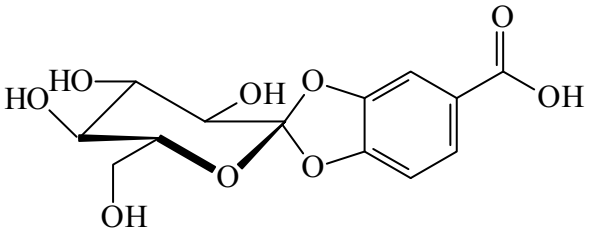
[23] gorgost-5-en-3β-ol
Equisetum giganteum L.



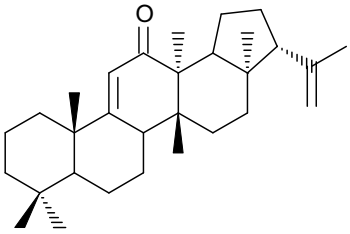
[24] bufa-20,22-dienolide-3,14-dihydroxy
Equisetum giganteum L.



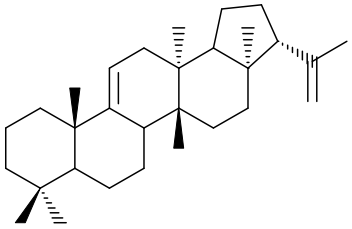
[**25**] Vitexin
Cyathea phalerata Mart.



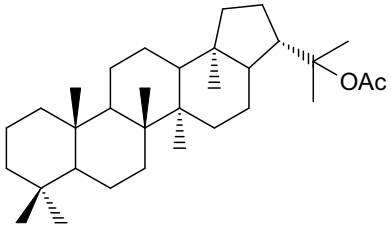
[**26**] Cyathenosin A
Cyathea phalerata Mart.



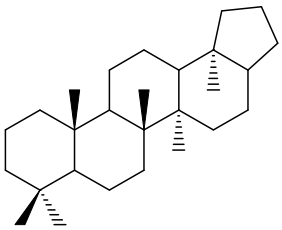
[27] fern-9(11)-en-12-one



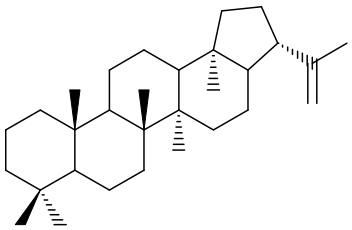
[28] fern-9(11)-ene



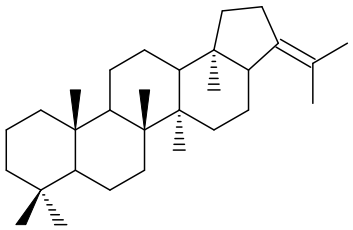
[29] 22-acetoxy-hopane



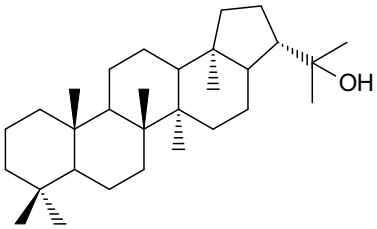
[30] 17βH-22,29,30-tris-nor-hopane



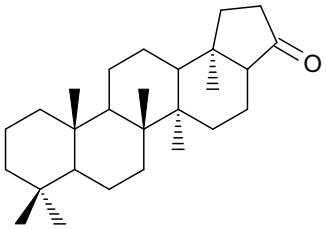
[31] hop-22(29)-ene



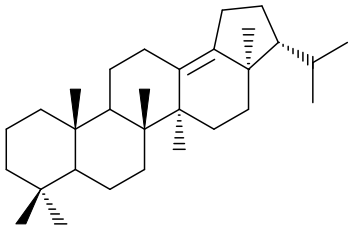
[32] hop-21-ene



[33] 22-hydroxy-hopane



[**34**] 22,29,30-tris-nor-hopan-21-one



[35] neo-hop-13(18)-ene

Fig. 2 Triterpenes identified in Polypodiaceae species, following Patitucci *et al.* (1995).

Fisch.) A.R. Sm.] (spore and rhizome), and rhizome of *Polypodium aureum* [=*Phlebodium aureum* L.] (two varieties) and *Microgramma vacciniifolia*. The advantage of the technique, according to the authors, comes mainly from the amount of information that can be obtained saving time, botanic material, amount of extracts, organic solvents, reagents and adsorbents. Thus, the substances were detected in extracts and confirmed by co-injection with certified standards, which can be obtained through isolation or prior synthesis. The following substances were isolated: fern-9(11)-en-12-in-one [**27**] – as a colorless solid obtained from the hexane: benzene (1:1) fraction from the hexane crude extract of *S. meniscifolium*; *fe*rn-9(11)-ene [**28**] and 22-acetoxy-hopane [**29**] – both obtained from the hexane crude extract of *P. aureum* by precipitation with acetone and further purification by successive crystallizations and flash column chromatography; two homologous series of alkanes (C_nH_{2n+2}, n=15 to 31) and carboxylic acids ($C_nH_{2n}O_2$, n=5 to 22) – obtained by flash column chromatography fractionation of the rhizome extract of *M. vacciniifolia*. In the alkane series, traces of 22,29,30-trisnorhopane [**30**] were detected. This is the first record of this hydrocarbon in Polypodiaceae. **Table 3** and **Fig. 2**, respectively show the distribution and the structures of the triterpenes identified by Patitucci *et al*.

Table 3 Triterpenes evidenced (not isolated) in the extracts analyzed by Patitucci *et al.* 1995.

Compound	Plant
Hop-22(29)-ene **[31]**	*Serpocaulon meniscifolium*
	Phlebodium aureum
	Microgramma vacciniifolia
Hop-21-ene **[32]**	*Pleopeltis pleopeltifolia*
	Serpocaulon meniscifolium
	Phlebodium aureum
	Microgramma vacciniifolia
22-hydroxy-hopane **[33]**	*Phlebodium aureum*
22-acetoxy-hopane **[29]**	*Microgramma vacciniifolia*
22,29,30-tris-nor-hopan-21-one **[34]**	*Pleopeltis pleopeltifolia*
	Serpocaulon meniscifolium
	Phlebodium aureum
	Microgramma vacciniifolia
Neo-hop-13(18)-ene **[35]**	*Phlebodium aureum*
Fern-9(11)-ene **[28]**	*Pleopeltis pleopeltifolia*
	Serpocaulon meniscifolium
	Phlebodium aureum
	Microgramma vacciniifolia
17(β-H)-22,29,30-tris-nor-hopane **[30]**	*Microgramma vacciniifolia*

(1995). Peres *et al.* (2009) isolated and identified from the hexane and ethylacetate fractions from ethanolic crude extract of *Microgramma vacciniifolia* fronds, the steroid β-sitosterol, the triterpene and hopan-22-ol; one flavone glycoside 6-metoxiapinenin-7-*O*-β-D-allopyranoside and a mixture containing the ethyl esters of hexadecanoic, oleic, 15-methyl-heptadecanoic and linoleic acids.

Table 4 reports all substances isolated from pteridophytes growing in Brazil.

CONCLUDING REMARKS

Despite the megabiodiversity of the Brazilian flora, very little is known about the chemistry of pteridophytes. Only 4.7% of the pteridophyte flora that grows in Brazil has received chemical attention. Almost all the studies were conducted on sporophytes and there are no analyses on gametophytes. If taken into account only the plant group comprising pteridophytes, things are even worse and one may state that many species may be disappearing without even having been described or studied.

A considerable number of papers (53.8%) is concentrated on one single species, *Pteridium arachnoideum*, with emphasis on its biological activity. Beside this species only 11 other species have been assessed regarding their biological activity, i.e., 0.8% of pteridophytes estimated in Brazil. There is therefore an enormous potential for investigations on biological activity, especially when combined with ethnobotanical information, such as in Barros and Andrade (1997) and Santos and Sylvestre (2000).

Incipient is also the investment in the identification of molecules, with only 2.3% of the species investigated. There are very promising approaches such as on essential oils and cyanogenic compounds. Indeed, Soeder (1985) already alerted to the importance of studies on the volatile constituents in pteridophytes. The genus *Anemia* (Anemiaceae), for example, possesses many aromatic species, and Brazil is one of the centers of diversity of the genus. As for cyanogenic compounds, Santos *et al.* (2006) only detected cyanogenesis, but until now, no study of molecular identification of these compounds has been performed.

Chemical ecology investigations on Brazilian species are scarce. Most of the research examines allelopathic effects of extracts obtained from fronds, at different stages of development, in seeds germination bioassays and on the development of seedlings. Studies aiming at the chemical identification of active substances were not undertaken. Only one study used a different approach, analyzing the cyanogenesis in sporophytes.

From the small number of species and groups analyzed in comparison with the occurring biodiversity, it may be stated that there is great potential for studies on the Brazilian pteridoflora, and an enormous potential for the detection of a plethora of new chemicals.

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Table 4 Substances isolated from pteridophytes growing in Brazil.

Species	Plant organ	Extract	Compounds	Reference
Adiantum raddianum	Fronds	Hexane fraction of the methanolic crude extract	Filicene, filicenal, adiantol, isoadiantone	Bresciani *et al*. 2003
Adiantum tetraphyllum	Leaves	Hexane fraction from ethanolic crude extract	Palmitic, petroselinic, oleic, stearic, linoleic, α-linolenic, (*Z*)-vacenic, decosahexenoic, margaric, arachídic and behenic acids esters; 30-normetil-lupan-20-one; hopan-22-ol; phytol ; phyten-3(20)-1,2-diol; β-sitosterol	Melos *et al*. 2007
	Leaves	Ethyl acetate fraction from ethanolic crude extract	Mixture of ferulic and caffeic acid with ρ-hydroxibenzaldehyde Quercetin; quercetin-3-*O*-β-D-glycoside	Melos *et al*. 2007
Anemia tomentosa	Fronds	Aqueous (essential oil)	Isoafricanol	Santos *et al*. 2006
var. *anthriscifolia*	Fronds	Aqueous (essential oil)	α-Pinene, *trans*-sabinol, *trans*-2-caren-4-ol, pinocarvone, p-menta-1,5-dien-8-ol, *cis*-pinocamphone, thymol, silfiperfol- -5-ene, presilfiperfol-7-ene, 7-epi-silfiperfol-5-ene, α-cubebene, silfiperfol-4,7(14)-diene, longicyclene, silfiperfol-6-ene, α-isocomene, β-elemene, (*E*)-caryophyllene, α-guaiene, α-muurolene, cameroonan-7-α-ol, (-)-epi-presilfiperfolan-1-ol, silfiperfolan-7-β-ol, nopsan-4-ol, silfiperfolan-6-β-ol, prenopsan-8-ol, presilfiperfolan-8-ol, di-epi-α-cedrene epoxide, β-atlantol, caryophylla-4(14),8(15)-dien-5-α-ol, ishwarone, α-bisabolol, pre-silfiperfolane-1-ol, 9-epi-presilfiperfolan-1-ol	Pinto *et al.* 2007, 2009a, 2009b; Joseph-Nathan *et al*. 2010
Blechnum regnellianum			(2S)-5,7-Dihydroxy-4'-methoxy-6,8-dimethylflavanone	Miraglia *et al.* 1985
Cheilanthes flexuosa	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Quercetin diglycoside Quercetin triglycoside Kaempferol diglycoside	Salatino and Prado 1998
Cheilanthes goyazensis	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Kaempferol diglycoside Quercetin monoglycoside Quercetin diglycoside	Salatino and Prado 1998
Cyathea phalerata	Caudex	Ethyl acetate fraction from the aqueous residue of the hydroalcoholic crude extract	Kaempferol Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside 4-*O*-β-D-glucopyranosylcaffeic acid	Brighente *et al*. 2007
	Caudex	Ethanolic extract	4-*O*-β-D-glucopyranosyl caffeic acid 4-*O*-β-D-glucopyranosyl coumaric acid Cyathenosin	Pizzolatti *et al*. 2007
Cyathea phalerata	Caudex	Hydroalcoholic extract	Kaempferol-3-neohesperidoside 4-*O*-β-D-glucopyranosyl caffeic acid 4-*O*-β-D-glucopyranosyl coumaric acid 3,4-spyroglucopyranosyl protocatechuic acid β-sitosterol, sitosterol-β-D-glucoside kaempferol, vitexin, ethylgalactoside	Hort *et al.* 2008
Doryopteris concolor	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Kaempferol diglycoside Quercetin diglycoside	Salatino and Prado 1998
Doryopteris ornithopus	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Quercetin monoglycoside Quercetin diglycoside	Salatino and Prado 1998
Equisetum arvense	Stems	Hydroalcoholic extract	Positive reactions for tannins, saponins, flavonoids and sterols	Santos Jr. *et al*. 2005
	Stems	Hydroalcoholic extract	Positive reactions for pirrogalic tannins, sterols, saponins and flavonoids	Do Monte *et al*. 2004
Equisetum giganteum	Aerial parts	Oleoresin (supercritical CO_2 extraction)	Dodecanoic acid, *n*-heneicosane; 3-nonynoic acid methyl ester; 3,6-dimethyldecane; 26-hydroxicholesterol; ergosta-4,7,22-trien-3-one; 8,12-dimethyl-4Z,8E,12E-octadecatriene; mehtenolone, gorgost-5-ene-3-ol; 2,6,10,14-hexadecatetraen-1-ol,3,7,11,15-tetramethyl-acetat (*E,E,E*); *Z*-13-octadecenal; bufa-20,22-dienolide,3,14-dihydroxy	Michielin *et al*. 2005
Microgramma squamulosa	Rhizome	Ethanolic extract (70%) Chloroforme partition Ethanol partition Ethanol:Water (1:1) partition	Positive reaction for tannins and flavonoids	Suffredini *et al*. 1999
Microgramma vacciniifolia	Fronds	Hexane and ethyl acetate fractions from ethanolic crude extract	β-sitosterol; hopan-22-ol; 6-metoxiapinenin-7-*O*-β-D-allopyranoside and a mixture containing ethyl esters of carboxylic acids	Peres *et al.* 2009
Pellaea cymbiformis	Fronds	Methanolic extract after immersion in chloroform	Quercetin monoglycoside Quercetin diglycoside	Salatino and Prado 1998
Pellaea gleichenioides	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Quercetin monoglycoside Quercetin diglycoside Quercetin triglycoside Kaempferol diglycoside	Salatino and Prado 1998
Pellaea pinnata	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Quercetin monoglycoside Quercetin diglycoside	Salatino and Prado 1998
Pellaea riedelii	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Quercetin monoglycoside Quercetin diglycoside	Salatino and Prado 1998
Phlebodium aureum	Rhizome	Precipitation after treatment of the crude hexane extract with acetone	Fern-9(11)-ene **(13)** 22-acetoxy-hopane **(10)**	Patitucci *et al.* 1995

Table 4 (Cont.)

Species	Plant organ	Extract	Compounds	Reference
Pityrogramma ebenea	Fronds		2',6'-dihydroxy-4,3'-dimethoxy-4',5'-methylenedioxydihydrochalcone	Miraglia *et al*. 1985
Pteris altissima	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Apigenin diglycoside; Luteolin monoglycoside; Luteolin diglycoside	Salatino and Prado 1998
Pteris angustata	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Chrysoeriol monoglycoside	Salatino and Prado 1998
Pteris decurrens	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Luteolin; Luteolin monoglycoside	Salatino and Prado 1998
Pteris deflexa	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Kaempferol diglycoside Quercetin diglycoside	Salatino and Prado 1998
Pteris denticulata var. *tristicula*	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Apigenin monoglycoside; Luteolin monoglycoside; Luteolin diglycoside	Salatino and Prado 1998
Pteris plumula	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Apigenin monoglycoside; Luteolin monoglycoside; Luteolin diglycoside; Kaempferol monoglycoside; Quercetin monoglycoside	Salatino and Prado 1998
Pteris podophylla	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Luteolin monoglycoside	Salatino and Prado 1998
Pteris propinqua	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Apigenin monoglycoside; Luteolin diglycoside	Salatino and Prado 1998
Pteris splendens	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Apigenin monoglycoside	Salatino and Prado 1998
Pteris vittata	Fronds	Methanolic extract (80%) after immersion in $CHCl_3$	Kaempferol monoglycoside; Kaempferol diglycoside; Quercetin monoglycoside; Quercetin diglycoside	Salatino and Prado 1998
Serpocaulon latipes	Leaflets	MeOH-water (1:1)	Coumarin	Esteves and Felippe 1990
Serpocaulon meniscifolium	Rhizome	Hexane:Benzene fraction (1:1) from hexane crude extract	Fern-9(11)-en-12-one **(15)**	Patitucci *et al.* 1995

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