The Pharmaceutical and Chemical Journal, 2017, 4(5):13-26

Available online www.tpcj.org

Review Article

ISSN: 2349-7092
CODEN(USA): PCJHBA

Genus *Deguelia*: Chemistry, Chemotaxonomy, Ethnopharmacology and Pharmacological Characteristics – A Review

Nerilson M. Lima[1], Vanessa N. C. Santos[2], Alessandra de Paula Carli[3], Christiane P. Soares[1]

[1]Department of Clinical Analysis of Paulista State University "Júlio de Mesquita Filho", Araraquara, SP, Zip Code 14801-970, Brazil
[2]Federal University of Amazonas, Manaus, AM, Zip Code 69067-005, Brazil.
[3]Instituto de Ciências, Engenharia e Tecnologia, Universidade Federal dos Vales do Jequitinhonha e Mucuri, Zip Code 39803-371, Brazil

Abstract The genus *Deguelia* comprises the American species previously included in *Derris* Lour. *Millettia* Wight & Arn. and *Lonchocarpus* subg. *Phacelanthus* Pittier. Considering the need of systematic definition to the genera *Derris*, *Deguelia* and *Lonchocarpus*, and also the economic importance presented by several species within these genera, which produces rotenone or deguelin (natural insecticides widely used in the past decades), this review is of great chemotaxonomic importance to corroborate studies of botanical systematics carried out with these genera, and guide the search for new therapeutic agents, since this bibliographic survey, approaches the biological and ethnopharmacological studies described for species of this genera.

Keywords Fabaceae, ethnopharmacology, flavonoids, chemotaxonomy

Introduction

The family Fabaceae has cosmopolitan distribution, including about 650 genera and approximately 18,000 species, representing one of the largest families of Angiosperms and one of the leading economically. In Brazil, there are about 200 genera and 1500 species. It was traditionally recognized as a single family with three subfamilies (Papilionoideae or Faboideae, Caesalpinioideae and Mimosoideae), except for Cronquist and other authors who preferred to recognize three distinct families (Fabaceae, Caesalpinaceae and Mimosaceae) [1-2]. Being the first classification the most accepted currently.

Papilionoideae is the largest of the three Fabaceae subfamilies, with approximately 500 genera and more than 10,000 species divided into 31 tribes. It has a wide distribution in the tropics, subtropical, extending to the temperate regions, but its greater diversity is in the American and African tropics. It consists of representatives of various types of habits, including herbs, lianas and trees. The roots, leaves, fruits and seeds of many species of this subfamily have several medicinal properties, of which we can mention *Dioclea*, which is an important source of non-protein amino acids, such as L-Dopa, used in the treatment of Parkinson's disease. The juice of species of the genus *Vatairea* is used to cure impinges, the seeds of *Dipteyx punctata* are used in the treatment of pneumonia, among others [3].

Hegnaueand Grayer-Barkmeijer emphasize that the flavonoids and the polysaccharides starch, galactomannans and amyloid commonly found in Fabaceae seeds are essential factors in the taxonomic characterization of this family[4]. In addition to the tribes of Phaseoleae, Vicieae, Cicereae and Swartzieae, in other tribes of the subfamily Papilionoideae, the occurrence of starch is irregular or absent, and in the storage of starch grains, Caesalpinioideae is an exception. While in the subfamily Mimosoideae, the situation is similar although the storage of starch grains in

seeds occurs a little more frequently. The presence of large amounts of amyloid is restricted to Detarieae and Amherstieae tribes of the Caesalpinioideae subfamily, and is therefore considered a key tool in distinguishing these tribes.

It has been suggested by many authors that flavonoid profiles may help to clarify the problematic distinction of the genera *Derris* and *Lonchocarpus*, Gottlieb and colleagues have presented an important chemosystematic study (Systematic Significance of Flavonoids in *Derris* and *Lonchocarpus* [5]) on flavonoids based on the standard of oxidation/methylation of these compounds. The authors further suggested that the dispersion of the original material from Asia to America and from the forest to habitats like Brazilian Cerrado was accompanied by the evolution of the necessary oxidative enzymes.

A particularity of the Fabaceae family is its high content of flavonoids and related compounds. About 28% of total flavonoids and 95% of all known isoflavonoid aglycones structures in the plant kingdom are produced by this family. Since 50% of the flavonoids and 66% of the described isoflavonoid structures present the 5-hydroxyl group. Another striking feature is the presence of the isoprenyl group and its varieties, such as the dimethylpyran group [4]. It should be mentioned that almost all classes of prenylated flavonoids are found in some genera of this family, such as *Derris, Flemingia, Glycyrrhiza, Lonchocarpus* and *Tephrosia* [6].

Other classes of secondary metabolites have been identified in species of Fabaceae, such as anthraquinones, piperidine, pyridine, pyridine[7], and pyrrolidine derivatives[8], coumarins[9], cyanogenic glycosides, terpenes (including essential oils, diterpenes, phytosterol, triterpenes and saponins), hydrolysable and condensed tannins [10], among others.

Within the family Fabaceae is the genus *Deguelia*, that is important from the therapeutic point of view, by the presence of its flavonoid compounds with recognized biological properties for the animal organism, and its contribution as a key tool in the chemosystematic of similar genera.

Plant profile

Taxonomic classification

Kingdom: Plantae;
Sub Kingdom: Viridaeplantae;
Phylum: Magnoliophyta;
Division: Tracheophyta;
Subdivision: Sparmatophytina;
Class: Equisetopsida;
Superorder: Rosanae;
Order: Fabales;
Family: Fabaceae (Leguminosae);
Subfamily: Faboideae (Papilonoideae)
Tribe: Millettieae
Genus: *Deguelia*

Flavonoids: Biological properties and contribution to the chemistry of Fabaceae family

Flavonoids are one of the most representative classes of secondary plant metabolism. They are divided into two main groups: the flavonoids and isoflavonoids. Flavonoids, mixed biosynthesis products, consist of a basic molecular skeleton with 15 carbon atoms ($C_6C_3C_6$). The isoflavones are structurally distinct from the other flavonoid classes because they contain a C_{15} skeleton based on 1,2-diphenylpropane, while the other classes have 1,3-diphenylpropane [11].

The isoflavonoid skeleton is established by an aryl migration enzyme known as isoflavone synthase. According to the mechanism of the reaction, the aryl migration appears to require a 4'- or 2'-hydroxyl group. Thus, almost all isoflavonoids are oxygenated at the C-4 'or C-2' positions of ring B of the corresponding isoflavanones and isoflavones [11].

The various enzymatic processes that occurs in the isoflavonoid skeleton as hydroxylation reactions, alkylation and formation of heterocyclic rings lead to the formation of numerous classes of isoflavonoids. As an example, pterocarpans, cumestans, rotenoids and isoflavans may be mentioned [12].

The abundance of isoflavonoid aglycones in species of Fabaceae can be attributed to:

a) The introduction of hydroxyl groups at the 6-, 8- and 2 'positions of the basic skeleton, which is usually found in the 5,7,4'-trihydroxy or 5,7,3,4'-tetrahydroxy form.

b) Loss of hydroxyl groups in the 5-position or the B-ring.

c) Methylation of hydroxyl groups or formation of methylenedioxides groups.

d) The presence of C-prenyl or C-geranyl groups, in addition to cyclization reactions for the formation of dimethylpyran and furan rings [4].

It is possible to affirmthat the structural diversity of flavonoids arises from a series of enzymatic reactions, such as oxidation, reduction, rearrangements, conjugation with sugar molecules. In this way, several categories of natural flavonoids arise.

The flavonoid biosynthesis reaction begins with the condensation of a unit of activated cinnamic acid (CoA) with three molecules of the malonic acid ester, which gives rise to chalcones that exist in chemical equilibrium with flavanones [5]. Chalcones are open chain flavonoids, in which two aromatic rings are linked by a three-carbon system of an α, β-unsaturated ketone, a 1,3-diphenyl-prop-2-en-1-one derivative [13].

Thus, from a chalcone, there are successive reactions catalyzed by specific enzymes giving rise to the various categories of flavonoids. The formation of flavonols, aurones, β-OH-chalcones, flavones and isoflavones occurs from oxidation reactions. The presence of a hydroxyl at the *p*- position of the B ring is essential for the rearrangement to the isoflavones and for the cyclization forming the aurones. Reduction reactions lead to the formation of pterocarpan and isoflavans [5].

Flavonoids play important properties in the plant organism, however, few generalizations about their function are possible. One of these implies that the different flavonoid structures work in the same way in a biological response, and that function of a specific flavonoid is a matter of chemical reactivity within a specific cell, and each type of tissue or cell possesses an appropriate system to accumulate and / or copy specific flavonoids [14].

Flavonoids are pigments known to be universally present in green leaves, which generally absorb in the region of 280-315 nm, and therefore can act in the absorption of the ultraviolet radiation, protecting the photosynthetic tissues from the damages caused by this type of radiation. Some classes of flavonoids, such as anthocyanins and flavones, act to stabilize the blue colors of angiosperm flowers, attract bees during the pollination process, and play an important role in the protection against antimicrobial and herbivory infection [15]. In addition to recognized antibacterial activity, they may act in inhibition of important viral enzymes, such as reverse transcriptase and protease. It is important to emphasize that its toxicity to animal cells is considered low [16].

Antimicrobial and fungicidal effects of flavonoids described are mainly due to the presence of phenolic hydroxyls, which have affinity for proteins and, therefore, act as inhibitors of microbial enzymes. On the other hand, prenyl groups favor its lipophilicity and, consequently, increase its capacity to permeate cell membranes favoring greater antimicrobial activity [11]. Similar conclusions were observed by Ávila and colleagues when they evaluated the inhibitory effect of chalcones on pathogenic microorganisms for humans. The influence of the substitution pattern involving hydroxyl, methoxyl, acetoxyl, methylenedioxy and isoprenoid groups were investigated [13]. However, a structure-activity relationship cannot yet be established, since the substitution pattern may change according to the nature of the flavonoid.

Flavonoids are a class of secondary metabolites with significant antioxidant properties, especially structures containing the *o*-dihydroxy group on the B ring (catechol) and the 2,3-double bond in conjunction with the carbonyl group. This balance between hydrophilicity and lipophilicity is of great importance for the antioxidant property of flavonoids [17].

The isoflavonoids phytoalexins found most frequently in species from subfamily Papilionoideae (Fabaceae) are pterocarpan and isoflavones, with the pterocarpan medicarpin being the most frequent [18].

More than half of the known isoflavonoid structures in Fabaceae are replaced by the 3,3-dimethylalila group (prenyl) or by lateral fixation of other groups derived from the prenyl substituent [11].

The structural diversity of the prenylated substituents generates groups with five membered, six membered rings and a variety of open chain structures.

Flavonoids: Chemotaxonomy, chemical composition and plant evolution

The existence of secondary metabolites in plants is an example of evolutionary response in each ecosystem, emphasizing the function of protection of these metabolites against other organisms and environmental factors. Thus, it is clear the relationship between chemical evolution of metabolites and ecology, culminating with the possibility that some of these compounds are good taxonomic markers. These biomarkers have complex biosynthetic pathways in common, and even a simple molecule implies the manifestation of many enzymes and cofactors, which are implicit manifestations of the species [19].

The detection and structural elucidation of the special metabolites in plants allows to perform a classification whose system is called chemotaxonomy, which consists in the classification of a taxon through its metabolites. So far, a good correlation has been observed between chemotaxonomy and botanical classification that is performed based on plant morphology [20].

It is evident that there is a positive correlation in the level of oxidation and the skeletal specialization of the secondary metabolites in angiosperms. For, the lower an organic molecule is, the less susceptible it is to an enzymatic transformation. However, to rationalize this positive correlation of the increase of the level of oxidation of the metabolites with the evolutionary advance of the vegetal species that produce them is still problematic [21].

According to Simmonds, the evolutionary order of the species within a class is evaluated by the complexity of the compounds from secondary metabolism [22]. Thus, it is assumed that a more derived species produces more elaborate metabolites, and therefore, its biosynthesis would have a greater number of stages. However, proving the biosynthetic route of a secondary metabolite is very difficult.

The methodology proposed by Gottlieb and colleagues dispenses any detailed knowledge of its biosynthesis [19]. It is necessary to know if the metabolite comes from the shikimic acid or acetate route, since an indication of evolution is the substitution of one route for the other. Gottlieb warns that the mere presence of a metabolite does not classify it as a taxonomic marker. What characterizes a marker is the presence of a variety of compounds coming from the same precursor and resulting from oxidation and methylation reactions.

According to Gottlieb and Borin, substitution of metabolites derived from the shikimic acid (CH) pathway by metabolites derived from the acetate (AC) route is an evolutionary trend [23].

Thus, the greater the value of AC% the more derivative the species is. This is, according to Gottlieb, the abandonment of the shikimic acid route (CH) and the predominance of the acetate (AC) route indicates a greater evolutionary character.

Flavonoids, according to Gottlieb, when used as chemical markers, can be evaluated through their degrees of oxidation and methylation. The arithmetic mean values of the oxidation index (O) and the methylation index (Me) of the compounds of each species are the evolutionary parameters based on oxidation (Ae_o) and methylation (AE_{Me}) of the species [19].

These results suggest that the micromolecular evolution depends on the oxygen content in the atmosphere. However, it does not act directly on the micromolecular evolution, but causes the evolution of the means of enzymatic protection, such as selective etherification, Schiff base formation or reduction for the orientation of the biosynthetic pathways of the metabolites. Oxygen also acts by establishing the conditions for the transformation of the molecular skeleton. These phenomena are essential in the diversification of secondary metabolites and, therefore, essential requirements for the adaptive flexibility of an organism in the environment [24].

The calculation of the value of the flavonoid oxidation index is made from the occurrences mentioned below and observed in the metabolite under analysis in relation to the precursor:

- Addition of an oxygenated group +1
- Absence of oxygenated group -1
- Methylenedioxy group +1

- Prenyl group 0
- Additional double bond +1

The oxidation reactions involved usually occur by increasing the number of oxygen in the molecule or the release of hydrogen atoms, such as the transformation of a pterocarpan into pterocarpen.

The first step in this methodology is to relate metabolites of the type required in analysis that occur in the genus and to compare with a precursor common to the metabolites found. Therefore, it is necessary to carry out a thorough bibliographical survey of the metabolites already isolated in the genus, starting from the fact that nearby species produce similar secondary metabolites, coming from the same biosynthetic pathway.

In view of the recognized flavonoid content of species of the Fabaceae family, several studies correlate the molecular structure of these metabolites with the taxonomic characterization of some genera such as *Deguelia* and *Lonchocarpus*. Especially when considering Gottlieb's proposal. Thus, the chemical study of chemically unexplored plant species contributes significantly to chemosystematics, allowing a more elaborate taxonomic classification of these species.

The genus *Deguelia* (Faboideae): Chemistry and Chemotaxonomy

The genus *Deguelia* was described in 1775 by AUBLET and in 1860 was considered synonymous of *Derris* by Bentham. Its story is closely related to the genera *Derris* Lour. and *Lonchocarpus* Kunt [25].

Although the *Derri*s and *Lonchocarpus* species showed a clear vegetative and floral similarity, it was observed that they presented some divergences in the taxonomic identification of their species, especially those known as Derris americana. Then, in 1942, Ducke transferred the "American Derris" to *Lonchocarpus* subg. Phacelanthus (= *Lonchocarpus* sect. Fasciculati). However, in 1943, MacBride, reunited them in unique genre, *Derris*. Such scientific divergences continued to persist, and thus these two genres continued to be recognized as distinct by several authors [25].

In 1989, Tozzi presented a review of the taxonomic studies of the *Lonchocarpus* and *Deguelia* species that occur in Brazil based on inflorescences. The author groups the species that were described for the genera *Lonchocarpus*, *Derris* and *Deguelia* exclusively in the genera *Lonchocarpus* and *Deguelia*. In this study, in addition to detecting the occurrence of 17 Brazilian species of *Deguelia*, three species had not yet been classified and were named: *D. hatschbachii* A. M. G Azevedo, *D. glaucifolia* A. M. G. Azevedo and *D. duckeana* A. M. G Azevedo [26].

Given the need for a systematic definition for the genera *Derris*, *Deguelia* and *Lonchocarpus* and the economic importance presented by several species within these genera, which produce rotenone or deguelin, natural insecticides widely used in the past decades, metabolic production studies of their Species becomes of great chemotaxonomic importance to corroborate the studies of botanical systematics performed with these genera and to elucidate chemosystematic problems.

Table 1: Species of genus *Deguelia* and their respective synonyms (Source: [25])

Deguelia* sect. *Multiovulis	
Species	**Synonym**
Degueliaspruceana	*Derrisspruceana* *Lonchocarpusspruceanus*
Degueliadensiflora	*Derrisglabrescens* *Lonchocarpusboliviensis* *Lonchocarpusdensiflorus* *Lonchocarpusglabrescens*
Degueliahatschbachii	-----
Deguelialongeracemosa	*Lonchocarpusneuroscapha*var. *Longeracemosa*
Degueliacostata	*Lonchocarpuscostatus*
Deguelia* sect. *Deguelia	
Species	**Synonym**
Degueliarufescens var. *urucu*	*Derris urucu* *Lonchocarpus nicou* var. *urucu* *Lonchocarpus urucu*

*Degueliarufescens*var.*rufescens*	*Derrisrufescens* *Lonchocarpusnitidulus* var. *sehomburgkii* *Lonchocarpusrufescens*
Deguelianitidula	*Derrisfloribunda* *Lonchocarpusfloribundus* *Lonchocarpusnitidulus*
Degueliarariflora	*Derrisrariflora* *Lonchocarpusrariflorus*
Deguelianegrensis	*Deguelia longifólia* *Derris longifólia* *Derrisnegrensis* *Lonchocarpuskillipii* *Lonchocarpuslongifolius*
Degueliaamazonica	*Derrisamazonica* *Lonchocarpusnegrensis*
Degueliautilis	*Lonchocarpusutilis* *Lonchocarpus nicou* var.*languidus* *Lonchocarpus nicou* var.*utilis* *Derrisutilis*
Degueliadasycalyx	*Lonchocarpusdasycalyx*
Degueliaangulata	*Derrisangulata* *Derrissilvestris* *Lonchocarpusangulatus* *Lonchocarpus sylvestris*
Degueliaduckeana	---
Degueliaoccidentalis	*Millettiaoccidentalis*
Degueliaglaucifolia	---

The largest scientific production found in the database (Scopus, PubMed, Science direct) are attributed for the genera *Lonchocarpus* and *Derris*, since the genus *Deguelia* is deeply related to these two genera and several synonymies of species from *Deguelia* are associated with *Lonchocarpus* and *Derris*. Most of the study in Chemistry is performed with flavonoids and chemically related compounds, as well as pharmacological studies with isolated compounds or fractions (figure 1).

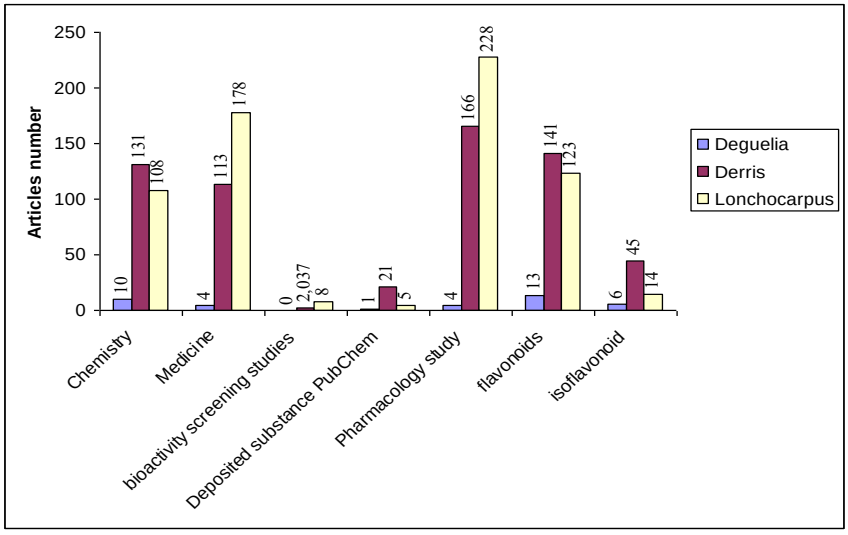


Figure 1: Production of articles about Chemistry, Medicine, Pharmacology and flavonoids from genera Derris, Deguelia and Lonchocarpus

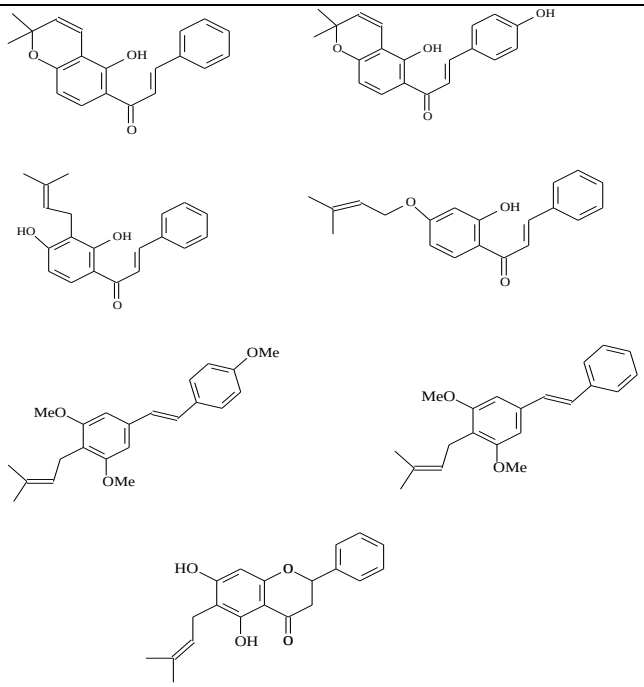
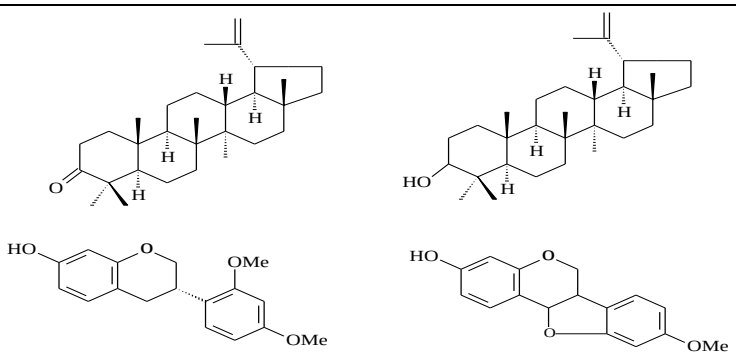
Chemically the genus *Deguelia* is a promising source of flavonoids and related compounds.

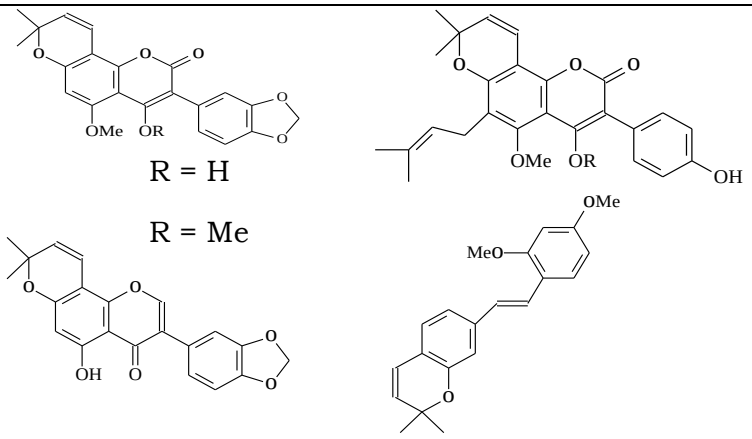
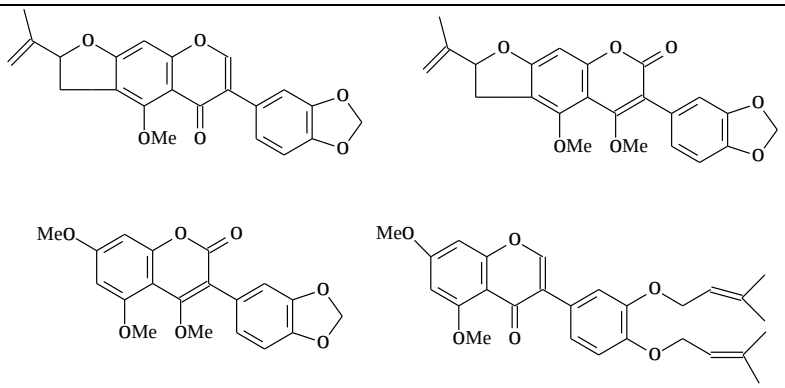
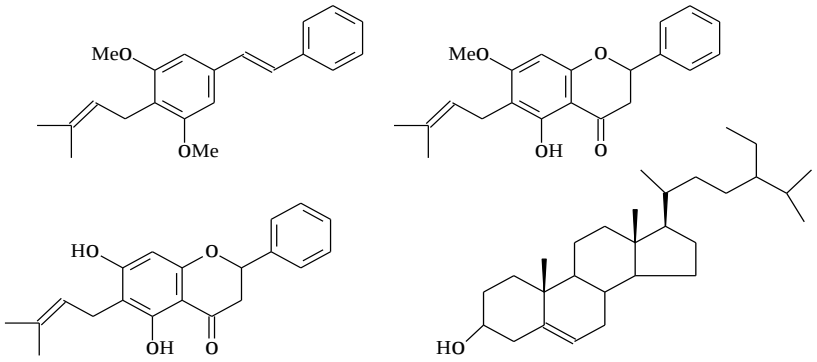
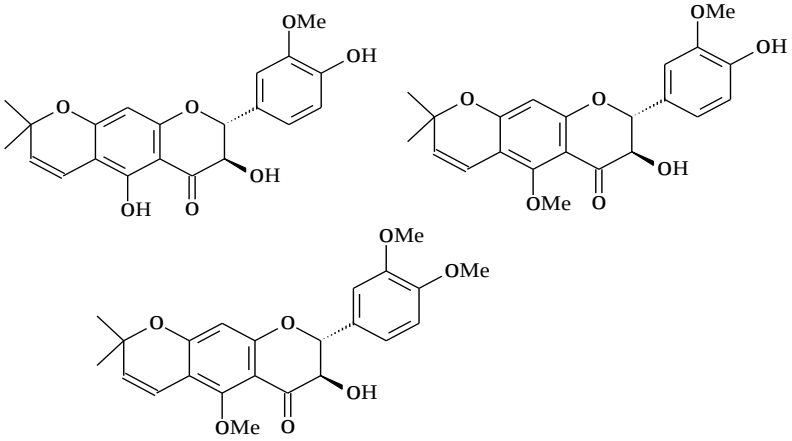
Moraes showed that the genus *Deguelia* is characterized by the presence of isoflavonoids, and in the section *Deguelia* sect. *Deguelia* predominate the rothenoids, whereas in the species of the section Deguelia sect. Multiovulis predominate the 4-hydroxy-3-phenylcoumarins [25]. The large amount of flavonoids found in the genus *Lonchocarpus* contributes significantly to Tozzi's proposal, according to which the genus *Deguelia* is more derivative than the genus *Lonchocarpus* [26]. The presence of 4-hydroxy-3-phenylcoumarins is conferred only on the species of Milletteae and Phaseoleae tribes of the subfamily Papilionoideae. This finding is of great chemotaxonomic importance, since it corroborates with the cladistic proximity between these two tribes [27].

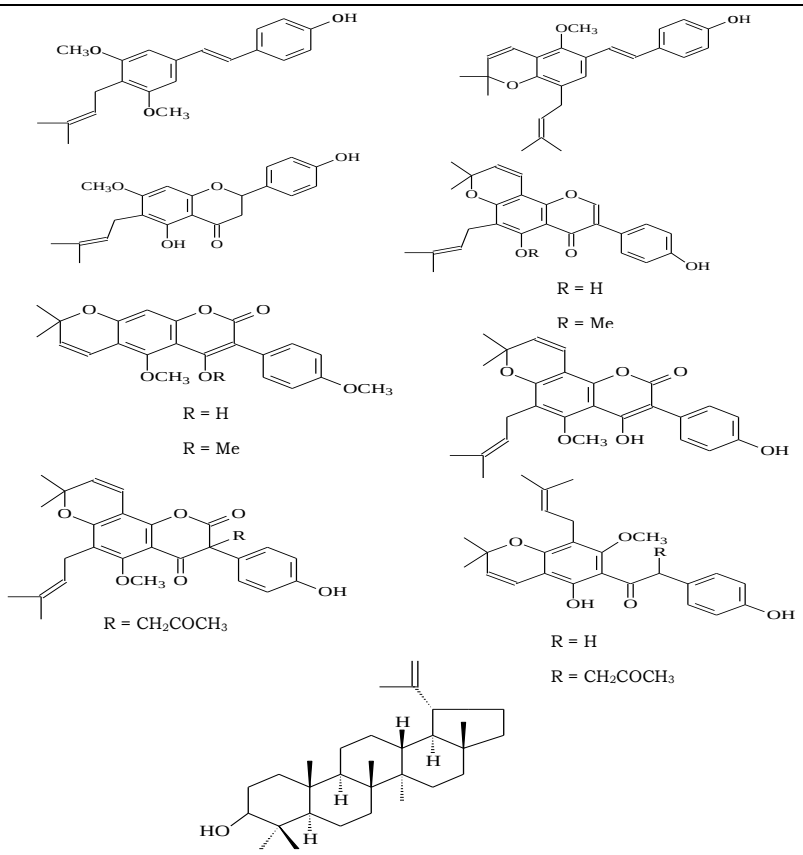
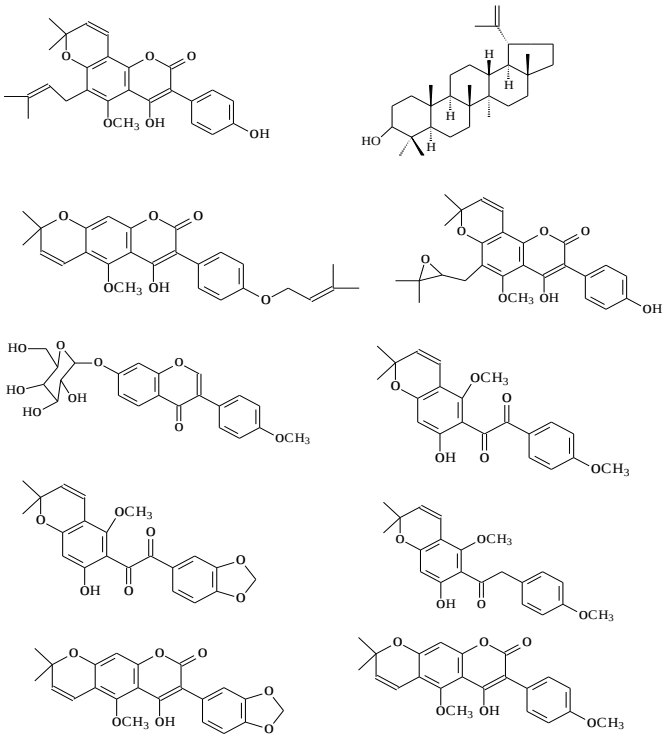
In this context, the phytochemical study of new species of the genus *Deguelia* becomes of great importance for the chemotaxonomy of the genus, especially when considering Gottlieb's proposal, according to which the degree of evolution of a species can be evaluated by the Its redox potential, which can be expressed through the mean oxidation/methylation (O/Me) values of its secondary metabolites [19].

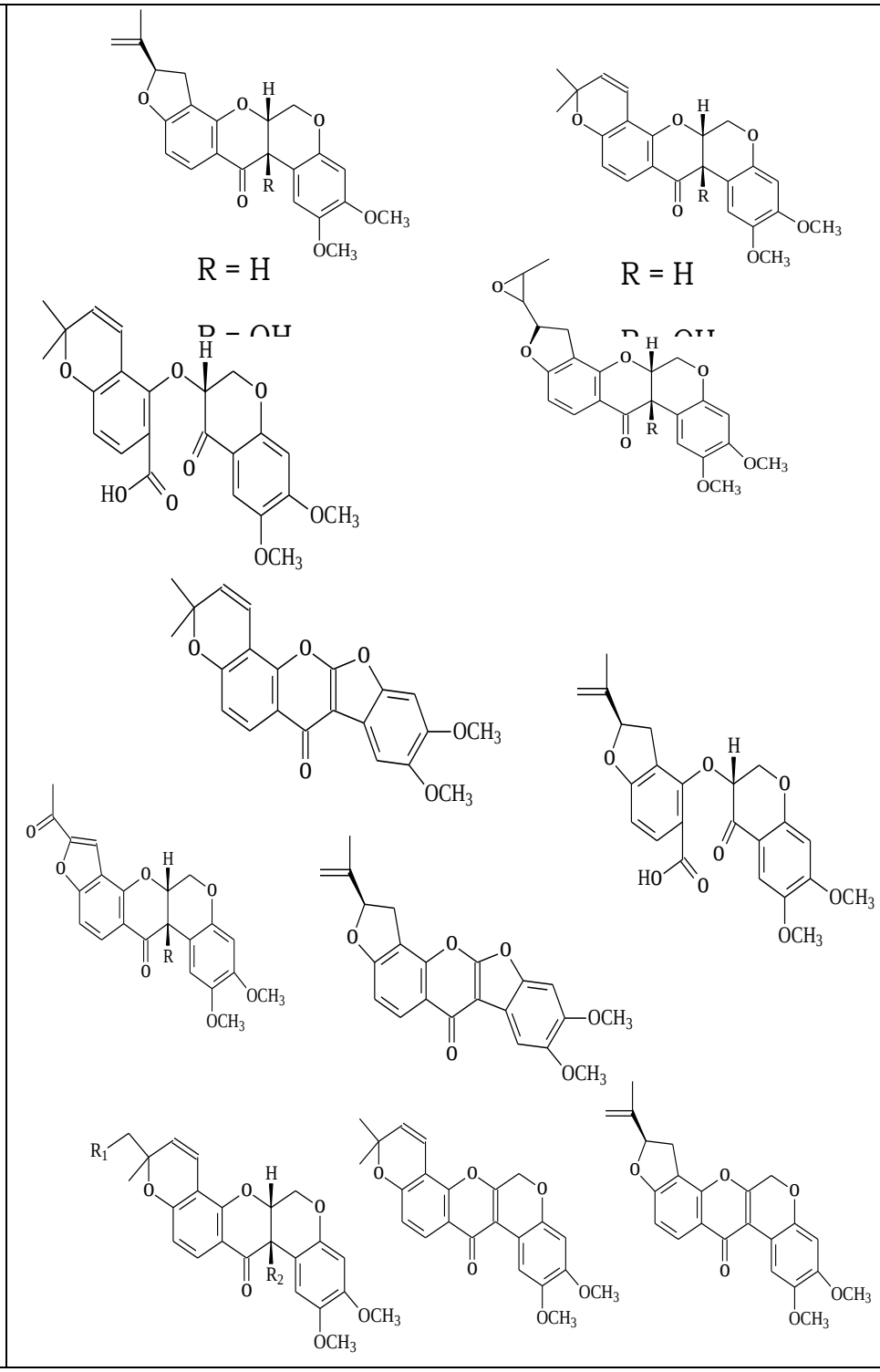
The expressive amount of flavonoids in the genus *Deguelia* can be observed in the survey of the metabolic production of this genus, which has been shown to be a good source of stilbenes, mainly with isoprenyl groups.

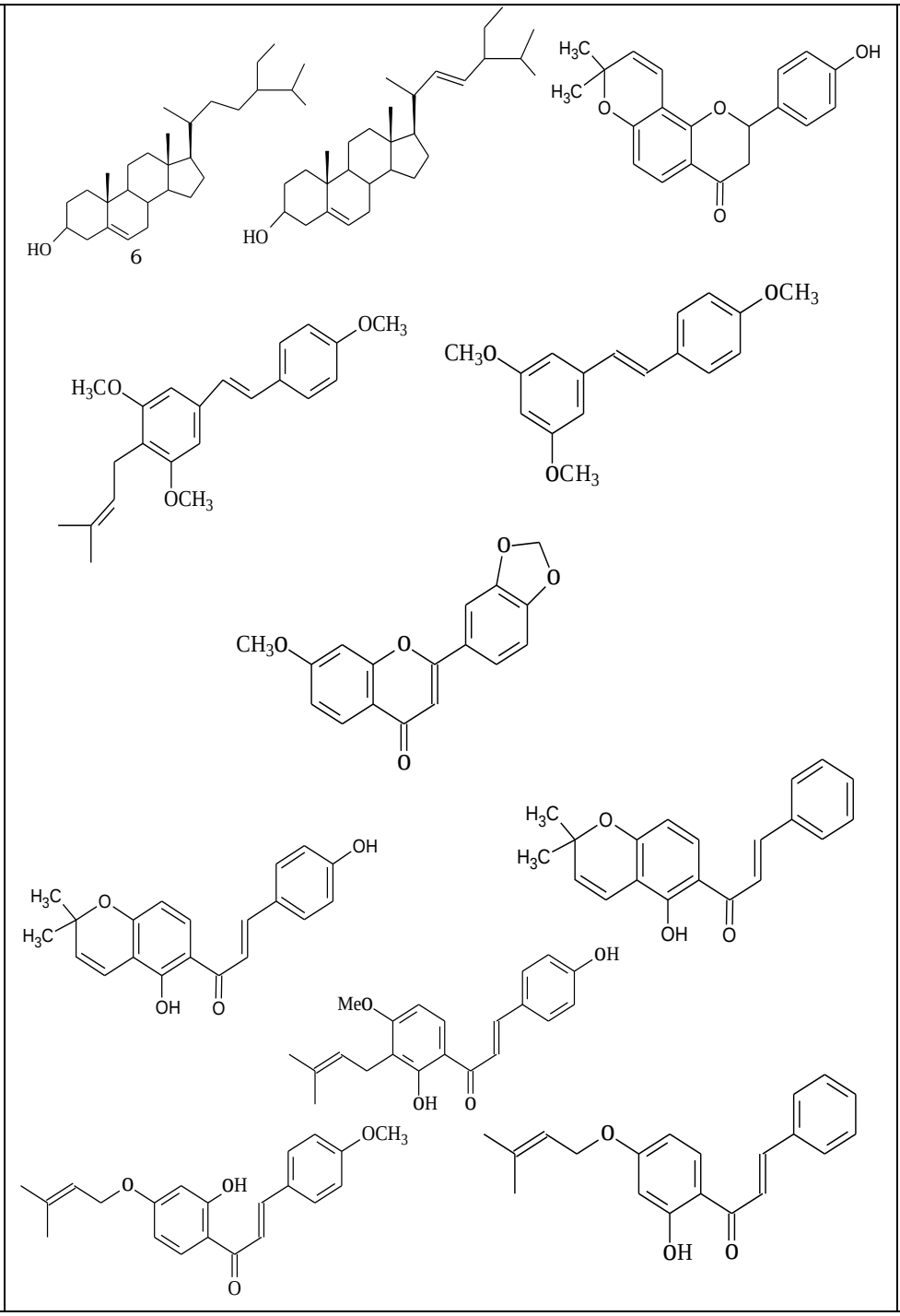
Table 1: Compounds isolated from *Deguelia* species

Species	Compounds	References
D. nitidula		[28]
D. amazonica		[28]

D. spruceana		[29]
D. densiflora		[30]
D. rariflora		[31]
D. rufescens		[32]

D. hatschbachii		[33]
D. longeracemosa		[27]

D. utilis		[34, 35, 36]

D. duckeana		[37, 38]

The genus *Deguelia* (Faboideae): Ethnopharmacology and pharmacological characteristics

Several classes of chemical compounds, such as flavonoids, stilbene, triterpenes and steroids, have been described in the various species of the genus *Deguelia* and their pharmacological potential. It has been reported in the literature that these species exhibit a wide range of pharmacological properties, including antitumor and antimicrobial activities that have proven to be efficacious in ethnomedicinal practices.

For many years, species of the genus *Deguelia* have been used by indigenous communities for the treatment of diseases and as ichthyotoxic.

Rotenone, a natural insecticide produced by species of this genus, has been widely used in past decades in agriculture, as it has more activity than other commercial insecticides (about 30 times greater than lead arsenate) and does not present toxicity to mammals, including man. Effects against animal parasites, such as sheep mange are also described [39].

Root powder of some species of this genus has been widely used in Southeast Asia, such as shampoo against lice and by South American natives as a fish poison [40].

Within the genus *Deguelia*, species that are used as antimalarial by indigenous populations of the Upper Rio Negro in Amazonas are included [41].

Deguelia duckeana isolated chalcones showed significant cytotoxic activity against the SK-N-SH neuron tumor cell line using the LDH assay. Other flavonoids of this species inhibited eukaryotic elongation factor 2 (eEF2) in SK-N-SH neural cells [38].

The crude extracts of leaves, branches and roots of *Deguelia duckeana* presented high cytotoxic potential in the lethality trial with *Artemia salina* at 5.0 μg / mL concentration and low antioxidant potential against DPPH and Fe_3 + / Phenantroline oxidants. The evaluation of the antibacterial potential of these extracts showed that the hexane extract of the branches was active against *Staphylococcus aureus* [42].

The extract of the species *Deguelia amazonica* presented promising antimalarial activity in in vitro assays.

3',4'-methylenedioxy-7-methoxyflavone flavone isolated from *Deguelia duckeana* reduced cell metabolism in the MTT assay without inducing cytotoxicity in the LDH assay. Other flavonoid compounds from this plant induced phosphorylation of AMP-activated protein kinase (AMPK) and eukaryotic elongation factor 2 (eEF2) [43].

Considering that the species of the genus *Deguelia* are closely related to the genera *Derris* and *Lonchocarpus*, few studies are found in the literature when searching for the terminology "Deguelia".

Conclusion

The literature review of the metabolic production and pharmacological properties of medicinal plants that are poorly studied from the scientific point of view becomes of crucial importance to guide future studies in the search of bioactive molecules and therapeutic products that may have innovation potential for clinical development. Within this scenario, we find plants of the genus *Deguelia*, whose species show a chemodiversity of biologically active compounds, especially belonging to the class of flavonoids, stilbenes and terpenoids. The survey of the metabolic production of its species and its flavonoid profile corroborates with its allocation in the genus *Deguelia* and with the chemosystematic studies presented until the present date. Ethnopharmacological and biological studies carried out with their species indicate great therapeutic potential for their phenolic molecules, especially as antineoplastic agents.

Acknowledgments

The authors are grateful to CAPES for financial support.

References

1. Cronquist A. (1988). *The Evolution and Classification of Flowering Plants*. 2nd Edition. The New York Botanical Garden, New York, 555p.
2. Souza VC, Lorenzi H. (2005). *Botânica sistemática: Guia ilustrado para identificação das famílias de Angiospermas da flora brasileira, baseado em APG II (Systematic botany:Illustrated guide for identification of Angiosperm families of the Brazilian flora, based on APG II).* Instituto Plantarum, Nova Odessa, 640p.
3. Ribeiro JELS, Hopkins MJG, Vicentini A, Sothers CA, Costa MAS, Brito JM, Souza MAD, Martins LHP, Lohmann LG, Assunção PACL, Pereira EC, Silva CF, Mesquita MR. (2002). *Flora da Reserva Ducke: Guia de identificacão das plantas vasculares de uma floresta de terra-firme na Amazônia Central (Flora of Ducke Reserve: Identification Guide to the vascular plants of upland forest in Central Amazon)*, 2nd Edition, INPA, Manaus, 799p.

4. Hegnauer R, Grayer-Barkmeijer RJ. (1993). Relevance of seed polysaccharides and flavonoids for the classification of the Leguminosae: a chemotaxonomic approach. *Phytochemistry*, 34(1): 3-16.
5. Gomes CMR, Gottlieb OR, Marini Bettolo GB, Delle Monache F, Polhill RM. (1981). Systematic significance of flavonoids in *Derris* and *Lonchocarpus*. *Biochemical Systematics and Ecology*, 9(2/3): 129-147.
6. Barron D, Ibrahim RK. (1996). Isoprenylated flavonoids – A survey. *Phytochemistry*, 43(5): 921-982.
7. Viegas JR. C, Rezende A, Silva DHS, Castro-Gambôa I, Bolzani VS, Barreiro EJ, Miranda ALP, Alexandre-Moreira MS, Young MCM. (2006). Aspectos químicos, biológicos e etnofarmacológicos do gênero *Cassia*. *Química Nova*, 29(6): 1279-1286.
8. Elbein AD, Michell M, Sanford BA, Fellows LE, Evans SV. (1984). The Pyrrolidine Alkaloid, 2, 5-Dihydroxymethyl-3, 4-dihydroxypyrrolidine, Inhibits Glycoprotein Processing. *Journal of Biological Chemistry*, 259(20): 12409-12413.
9. Cunha AP. (2005). *Farmacognosia e Fitoquímica (Pharmacognosy and Phytochemistry)*, 1st Edition, Fundação Caloust Gulbenkian, Lisbon.
10. Seigler DS. (2003). Phytochemistry of *Acacia* - sensu lato. *Biochemical Systematics and Ecology*, 31: 845–873.
11. Tahara R, Ibrahim RK. (1995). Prenylated isoflavonoids - An update. *Phytochemistry*, 38(5): 1073-1094.
12. Dewick PM. (2002). Medicinal Natural Products - A Biosynthetic Approach, 2nd Edition, Wiley, West Sussex, 2002: 507p.
13. Ávila HP, Smânia EFA, Monache FD, Smânia Júnior A. (2008). Structure - activity relationship of antibacterial chalcones. *Bioorganic & Medicinal Chemistry*, 16: 9790–9794.
14. Firmino CA. (1998). Estudo fitoquímico de *Lonchocarpus campestres* Tozzi, Unicamp, Campinas.
15. Harborne JB, Williams CA. (2000). Advances in flavonoid research since 1992. *Phytochemistry*, 55: 481-504.
16. Havsteen BH. (2002). The biochemistry and medical significance of the flavonoids. *Pharmacology & Therapeutics*, 96: 67–202.
17. Hendrich AB. (2006). Flavonoid-membrane interactions: possible consequences for biological effects of some polyphenolic compounds. *Acta Pharmacologica Sinica*, 27(1): 27–40.
18. Machado LMV. (2000). Estudo fitoquímico das raízes de *Platycyamus regnellii*, UNICAMP, Campinas, 2000.
19. Gottlieb OR. (1982). Micromolecular evolution, systematic and ecology – An essay into a novel botanical discipline, Spring Verlag, Berlin, 125p.
20. Santos CC. (2002). Estudo fitoquímico das raízes e dos frutos de *Swartzia langsdorffii*: Determinação estrutural de metabólitos e aplicacões. Detecção de alcaloides poliidroxilados nas raízes de *Lonchocarpus* spp. por CG/EM, UNICAMP, Campinas.
21. Gottlieb OR. (1992). Biodiversidade: Uma teoria molecular. *Química Nova*, 15(2): 167-172.
22. Simmonds MSJ. (1998). Chemoecology: The legacy left by Tony Swain. *Phytochemistry*, 1998, 49(5): 1183-1190.
23. Gottlieb OR, Borin MRMB. (1998). Natural products and evolutionary ecology. *Pure & Applied Chemistry*, 70(2): 299-302.
24. Gottlieb OR. (1989). The role of oxygen in phytochemical evolution towards diversity. *Phytochemistry*, 28(10): 2545-2558.
25. Moraes VRS. (2000). Estudo fitoquímico de *Deguelia hatschbachii* A.M.G. Azevedo, Isolamento, Determinação estrutural, Análise por CLAE e Testes biológicos, UNICAMP, Campinas.
26. Tozzi AMGA (1989). Estudos taxonômicos dos gêneros *Lonchocarpus* Kunth e *Deguelia* Aubl. no Brasil, UNICAMP, Campinas.
27. Souza Neta LC (2003). Estudo fitoquímico de *Deguelia longeracemosa* (Benth.) A. M. G. Azevedo, Isolamento, Determinação estrutural, Reações de Transformação da Escandenina e Testes Biológicos

(Leguminosae), UNICAMP, Campinas.

28. Braz-Filho R, Gottlieb OR, Mourão AP, Rocha AI, Oliveira FS (1975). Flavonoids from *Derris* species. *Phytochemistry*, 14: 1454-1456.
29. Garcia M, Kano MHC, Vieira DM, Do Nascimento MC, Mors WB. (1986). Isoflavonoids from *Derris spruceana*. *Phytochemistry*, 25(10): 2425-2427.
30. Delle-Monache F, Valera GC, Zapata DS and Marini-Bettolo GB. (1977). 3-Aryl-4-methoxycoumarins and isoflavones from *Derris glabrescens*. *Gazzetta Chimica Italiana*, 107(7-8): 403-407.
31. Mourão AP. (1975). Estudo químico de três timbós da Amazônia – *Derris amazonica*, *Derris floribunda* e *Derris laxiflora*, Universidade de São Paulo, São Paulo, 100p.
32. Lôbo LT, Silva GA, Ferreira M, Silva MN, Santos AS, Arruda AC, Guilhon GMSP, Santos LS, Borges RS, Arruda MSP. (2009). Dihydroflavonols from the leaves of *Derris urucu* (Leguminosae): Structural Elucidation and DPPH Radical-Scavenging Activity. *Journal of Brazilian Chemistry Society*, 20(6): 1082-1088.
33. Magalhães AF, Tozzi AMGA, Magalhães EG, Moraes VRS. (2001). Prenilated flavonoids from *Deguelia hatschbachii* and their systematic significance in *Deguelia*. *Phytochemistry*, 57: 77-89.
34. Lawson MA, Kaouadji M, Allais DP, Champavier Y and Chulia AJ. (2006). Substituted tubaic acids, new oxidative rotenoid metabolites from *Lonchocarpus nicou*. *Tetrahedron Letters*, 47: 451–454.
35. Lawson MA, Kaouadji M and Chulia AJ. (2008). Nor-dehydrodeguelin and nor-dehydrorotenone, C22 coumaronochromones from *Lonchocarpus nicou*. *Tetrahedron Letters*, 49: 2407–2409.
36. Lawson MA, Kaouadji M and Chulia AJ. (2010). A single chalcone and additional rotenoids from *Lonchocarpus nicou*. *Tetrahedron Letters*, 51: 6116–6119.
37. Lima NM, Martins D, Nunez CV. (2012). Determinação estrutural por RMN de 1H de flavonoides dos galhos e folhas de *Deguelia duckeana* (Fabaceae). In: XII Jornada Brasileira de Ressonância Magnética, São Carlos.
38. Cursino LMC, Lima NM, Murillo R, Merfort I, Humar M, Nunez CV. (2015). Flavonoids from *Deguelia duckeana* inhibit the eukaryotic elongation factor 2 (eEF2) in SK-N-SH neuronal cells. *Planta Medica*, 81: PM_149.
39. Wille JE, Ocmapo JA, Weberbauer A, Schofield D. (1939). El cube (*Lonchocarpus utilis*) y otros barbascos en el Peru. Peru, Dirección de Agricultura y Ganadería. Ministerio De Fomento. Boletin. 2nd Edition, Instituto de Alts Estudios Agricolas Del Peru, Lima, 129 p.
40. Purseglove JW. (1976). Tropical Crops – Dicotyledons, Longman, London.
41. Kffuri WC, Lopes MA, Minga LC, Odonnec G and Kinuppd VF. (2016). Antimalarial plants used by indigenous people of the Upper Rio Negro in Amazonas, Brazil. Journal of Ethnopharmacology, 178: 188–198.
42. Lima NM. (2011). Constituintes químicos e potencial biológico de *Deguelia duckeana*,Universidade Federal do Amazonas, Manaus.
43. Cursino LMC, Lima NM, Murillo R, Merfort I, Humar M and Nunez CV. (2016). Isolation of Flavonoids from *Deguelia duckeana* and Their Effect on Cellular Viability, AMPK, eEF2, eIF2 and eIF4E. *Molecules*, 2016, 21(2): 192.