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Revisión | Review

Genus Nectandra: "Phytochemistry and Biological Activity"

[Género Nectandra: "Fitoquímica y Actividad Biológica"]

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Abstract: The genus Nectandra belongs to the Ocotea complex and these species (Nectandra) are generally trees. It is considered endemic in the Neotropics. This genus has been reported uses in folk medicine as antifungal, anti-inflammatory, antimalarial, analgesic, treatment of ulcers, and febrifuge, among others; have also been reported some biological activity assays including: antitumor and antimalarial activity, activity against cardiovascular disease, among others. The genus Nectandra contains different secondary metabolites and they have been reported: Alkaloids; such as aporfinic, proaporfin, benzylisoquinoline, bisbenzylisoquinoline, and morfinandienone-type; lignans and neolignans, furofuran, benzofuran, tetrahydrofuran and dihydrofuran, and 3,3-neolignans-type; terpenes and sesquiterpenoid (monocyclic and bicyclic); Phytosterols and derived from those (3-hydroxy and the 3-ketone pentacyclic compounds); flavonoids, particularly O-glycosylated; xanthones, phenolic acids, polyalcohol, and alkene-alkyne, especially rubrenolide and rubrynolide.

Keywords: Nectandra, phytochemistry, biological activity, Lauraceae

Resumen: El género Nectandra pertenece al complejo Ocotea y estas especies (Nectandra) son por lo general árboles. Se considera endémica en el Neotrópico. Este género se ha informado de usos en medicina popular como antifúngico, anti-inflamatorio, antimalárico, analgésico, el tratamiento de las úlceras, y febrífugo, entre otros; También se han informado de algunos ensayos de actividad biológica, incluyendo: antitumoral y actividad antipalúdica, actividad contra las enfermedades cardiovasculares, entre otros. El género Nectandra contiene diferentes metabolitos secundarios y se han reportado alcaloides; tales como aporfinas, proaporfina, benzylisoquinolina, y del tipo morfinandienona; lignanos y neolignanos, furofuran, benzofurano, tetrahidrofurano y dihidrofurano, y del tipo 3,3-neolignanos; terpenos y sesquiterpenoide (monocíclicos y bicíclicos); Los fitoesteroles se derivan de aquellos (3-hidroxi y los compuestos pentacíclicos 3-cetona); flavonoides, particularmente O-glicosilada; xantonas, ácidos fenólicos, polialcohol, y alqueno-alquino, especialmente rubrenolide y rubrynolida.

Palabras clave: Nectandra, fitoquimica, actividad biologica, Lauraceae

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INTRODUCTION

The word 'biodiversity' is on nearly everyone's lips these days, but 'chemodiversity' is just as much a characteristic of life on Earth as biodiversity. The importance of natural products in medicine, agriculture and industry has led to numerous studies on the synthesis, biosynthesis and biological activities of these substances. Yet we still know comparatively little about their actual roles in nature (Gershenzon & Dudareva, 2007). Inside the biodiversity have been studied different plant families, among which are various genus of the Lauraceae family.

The Lauraceae family, which includes the genus *Nectandra*, is composed of 2500-3000 species distributed in 49-50 genera. The family is widely distributed in tropical and subtropical regions of the world, predominantly in Southeast Asia and Brazil (Cronquist, 1992). Ethnobotanical research has determined different uses of these species, including as an antifungal, antidiarrheal, analgesic, antirheumatic, anti-inflammatory, antipyretic, energizing and hypotensive agent (da Silva Filho et al., 2004; (Moreno *et al*., 2007; Oliveira De Melo *et al*., 2006). In addition, bioassays in the genus *Nectandra* have been reported to determine their biological activity, which includes the antitumor activity of *Nectandra rigida*, antimalarial activity of *N. cuspidate* and *N. salicifolia*, anti-cardiovascular disease activity of *N. salicifolia* (Oliveira De Melo *et al*., 2006), and even antimalarial activity associated with the presence of alkaloids in bark extract (*N. salicifolia*) (Böhlke *et al*., 1996). A more extensive description of the uses in folk medicine and the biological activity of these species will be provided in this paper.

In the genus *Nectandra*, the presence of certain types of secondary metabolites has been determined, including sesquiterpenes, phytosterols, polyalcohols, arylpropionic acid derivatives, flavonols, arylpropanoids, furofuran lignans, dihydrobenzofuran neolignans (Barbosa-Filho *et al*. 1989), and certain norlignans (Chérigo *et al*., 2005). Other studies have reported the presence of indole alkaloids (da Silva Filho *et al*., 2004), tannins (Moreno *et al*., 2007), diterpenes (Moro *et al*., 1987), and components of essential oils (Agius *et al*., 2007). However, despite the variety of metabolites in the genus, the chemotaxonomic characteristics are determined by the presence of lignan-type compounds, some of which possess chemotherapeutic biological activity (da Silva Filho *et al*., 2004).

According to information from the Scopus Database, the first publication was generated in 1960 (Figure 1); and showed the following statistical result:

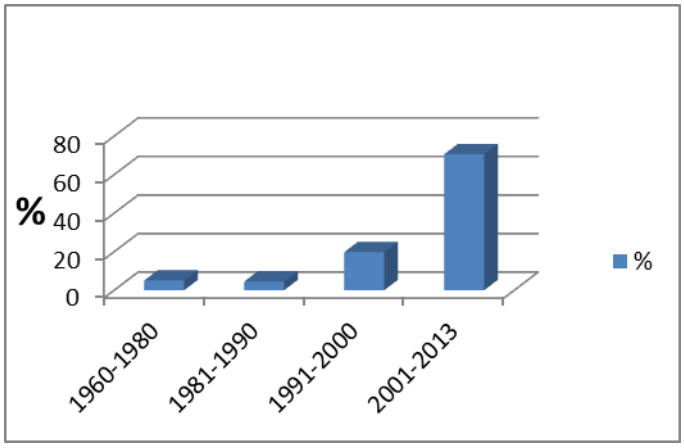


Figure Nº 1
Number of article or documents published per year

Knowledge areas in which they have been distributed publications on genus *Nectandra* are: (number and percentage): agricultural and biological sciences (132, 44%); pharmacology, toxicology and pharmaceutics (47, 16%), chemistry (30, 10%), biochemistry, genetics and molecular biology (29, 9.7%), environmental science (26, 8.7%), medicine (18, 6%), chemical engineering (3, 1%), earth and planetary sciences (3, 1%), immunology and microbiology (2, 0.7%), materials science (2, 0.7%),

undefined (2, 0.7%), engineering (1, 0.3%), health professions (1, 0.3%), multidisciplinary (1, 0.3%), physics and astronomy (1, 0.3%) and veterinary (1, 0.3%).

Knowledge about *Nectandra* genus is interesting to many researchers because of the variety of different secondary metabolites and possible chemical and / or biological potential in the species reported. The objective of this review is to provide updated and comprehensive information on different aspects of phytochemical, such as biological activity, secondary metabolites isolated or characterized, ethnobotanical uses, which have been reported in different database [Science Direct, EBSCO, WILLEY, PubMed, Electronic Library Online (SciELO), Springer, among others].

OVERVIEW OF THE GENUS *NECTANDRA*

Phylogeny, morphology, taxonomy and distribution

Based on the phylogeny of the family *Lauraceae*, the genus *Nectandra* belongs to the *Ocotea* complex and is related to the genera *Endlicheria*, *Rhodostemonodaphne*, *Ocotea*, *Licaria*, *Umbellularia*, *Pleurothyrium*, etc. All of these species belong to the *Perseeae-Laureae* clade, based on Matrix I (tmL-tmF, psbA-tmH cpDNA) (Chanderbali *et al*., 2001).

The genus *Nectandra* is considered endemic in the Neotropics (Chanderbali *et al*., 2001) and has the second highest number of specific entities of the Lauraceae family in South America (114 of entities of plants), with 30 species described at the end of the last century (Rohwer, 1993). These species are generally trees with subglabrous or minutely tomentulous branches. Leaves that have a slightly canaliculated petiole. The inflorescences are characterized by small flowers and in some cases small amounts of these (flowers), with pedicels 4-7 mm long. Flowers are hermaphrodite, puberulent at the base, glabrous towards the apex, and 7-9 mm in diameter. The anthers are sessile papillose with an apex that is somewhat obtuse. The ovaries are glabrous and globose with a well-developed style and obtuse stigma. The fruits are globose and 7-8 mm long, with an initial green color that subsequently becomes blackish (Bernardi, 1962). Additionally it is the second major evolutionary line is characterized by a separation of sexes, retention of nectar production and wide opening of the flowers (mainly *Ocotea* and *Nectandra* species) (Kubitzki & Kurz, 1984).

The pollen wall of all species of the *Laurales* (i.e. *Persea americana, Nectandra* sp), consists of a thin, spinulous exine and a thick, channelled intine. Besides striking similarities in pollen wall ultrastructure, some differences, especially in *Gomortega,* can be found (Hesse & Kubitzki, 1983).

According to the current listing reported in the taxonomical internet database lead by the Royal Botanical Gardens at Kew and the Missouri Botanical Garden (www.theplantlist.org— accessed 22 October 2014), the genus *Nectandra* encompasses the following 117 accepted (32.8%) taxons (Table 1):

Table 1
Classification taxonomy

Nº	Name
1	*Nectandra acuminata* (Nees & C. Mart.) J.F. Macbr.
2	*Nectandra acutifolia* (Ruiz & Pav.) Mez
3	*Nectandra amazonum* Nees
4	*Nectandra ambigens* (S.F.Blake) C.K.Allen
5	*Nectandra angusta* Rohwer
6	*Nectandra angustifolia* (Schrad.) Nees & Mart.
7	*Nectandra apiculata* Rohwer
8	*Nectandra astyla* Rohwer
9	*Nectandra aurea* Rohwer
10	*Nectandra baccans* (Klotzsch & H.Karst. ex Meisn.) Mez
11	*Nectandra barbellata* Coe-Teix.
12	*Nectandra bartlettiana* Lasser
13	*Nectandra belizensis* (Lundell) C.K. Allen

14	*Nectandra bicolor* Rohwer
15	*Nectandra brittonii* Mez
16	*Nectandra brochidodroma* Rohwer
17	*Nectandra canaliculata* Rohwer
18	*Nectandra canescens* Nees & Mart.
19	*Nectandra caudato-acuminata* O.C. Schmidt
20	*Nectandra cerifolia* Rohwer
21	*Nectandra cissiflora* Nees
22	*Nectandra citrifolia* Mez & Rusby
23	*Nectandra coeloclada* Rohwer
24	*Nectandra cordata* Rohwer
25	*Nectandra coriacea* (Sw.) Griseb.
26	*Nectandra crassiloba* Rohwer
27	*Nectandra cufodontisii* (O.C.Schmidt) C.K.Allen
28	*Nectandra cuneatocordata* Mez
29	*Nectandra cuspidata* Nees & Mart.
30	*Nectandra dasystyla* Rohwer
31	*Nectandra debilis* Mez
32	*Nectandra discolor* (Kunth) Nees
33	*Nectandra egensis* Rohwer
34	*Nectandra embirensis* Coe-Teix.
35	*Nectandra filiflora* Rohwer
36	*Nectandra fragrans* Rohwer
37	*Nectandra fulva* Rohwer
38	*Nectandra furcata* (Ruiz & Pav.) Nees
39	*Nectandra gardneri* Meisn.
40	*Nectandra globosa* (Aubl.) Mez
41	*Nectandra gracilis* Rohwer
42	*Nectandra grandiflora* Nees & Mart.
43	*Nectandra grisea* Rohwer
44	*Nectandra guadaripo* Rohwer
45	*Nectandra herrerae* O.C. Schmidt
46	*Nectandra heterotricha* Rohwer
47	*Nectandra hihua* (Ruiz & Pav.) Rohwer
48	*Nectandra hirtella* Rohwer
49	*Nectandra hypoleuca* Hammel
50	*Nectandra impressa* Mez
51	*Nectandra japurensis* Nees & C. Mart.
52	*Nectandra krugii* Mez
53	*Nectandra lanceolata* Nees & Mart.
54	*Nectandra latissima* Rohwer
55	*Nectandra laurel* Klotzsch ex Nees
56	*Nectandra leucantha* Nees & Mart.
57	*Nectandra leucocome* Rohwer
58	*Nectandra lineata* (Kunth) Rohwer
59	*Nectandra lineatifolia* (Ruiz & Pav.) Mez
60	*Nectandra longicaudata* (Lundell) C.K.Allen

61	*Nectandra longifolia* (Ruiz & Pav.) Nees
62	*Nectandra longipetiolata* van der Werff
63	*Nectandra lundellii* C.K.Allen
64	*Nectandra martinicensis* Mez
65	*Nectandra matogrossensis* Coe-Teix.
66	*Nectandra matthewsii* Meisn.
67	*Nectandra matudae* Lundell
68	*Nectandra maynensis* Mez
69	*Nectandra megapotamica* (Spreng.) Mez
70	*Nectandra membranacea* (Sw.) Griseb.
71	*Nectandra micranthera* Rohwer
72	*Nectandra microcarpa* Meisn.
73	*Nectandra minima* Rohwer
74	*Nectandra mirafloris* van der Werff
75	*Nectandra nitida* Mez
76	*Nectandra nitidula* Nees & Mart.
77	*Nectandra obtusata* Rohwer
78	*Nectandra olida* Rohwer
79	*Nectandra oppositifolia* Nees & Mart.
80	*Nectandra paranaensis* Coe-Teix.
81	*Nectandra parviflora* Rohwer
82	*Nectandra patens* (Sw.) Griseb.
83	*Nectandra paucinervia* Coe-Teix.
84	*Nectandra pearcei* Mez
85	*Nectandra pichurim* (Kunth) Mez
86	*Nectandra psammophila* Nees & C. Mart.
87	*Nectandra pseudocotea* C.K.Allen & Barneby ex Rohwer
88	*Nectandra puberula* (Schott) Nees
89	*Nectandra pulchra* Ekman & O.C. Schmidt
90	*Nectandra pulverulenta* Nees
91	*Nectandra purpurea* (Ruiz & Pav.) Mez
92	*Nectandra ramonensis* Standl.
93	*Nectandra reflexa* Rohwer
94	*Nectandra reticularis* Britton & P. Wilson
95	*Nectandra reticulata* Mez
96	*Nectandra riparia* Rohwer
97	*Nectandra roberto-andinoi* (C.Nelson) C.Nelson
98	*Nectandra rudis* C.K.Allen
99	*Nectandra ruforamula* Rohwer
100	*Nectandra salicifolia* (Kunth) Nees
101	*Nectandra salicina* C.K.Allen
102	*Nectandra sanguinea* Rol. ex Rottb.
103	*Nectandra smithii* C.K.Allen
104	*Nectandra sordida* Rohwer
105	*Nectandra spicata* Meisn.
106	*Nectandra subbullata* Rohwer
107	*Nectandra tomentosa* van der Werff

108	*Nectandra truxillensis* Mez
109	*Nectandra turbacensis* (Kunth) Nees
110	*Nectandra umbrosa* (Kunth) Mez
111	*Nectandra utilis* Rohwer
112	*Nectandra venulosa* Meisn.
113	*Nectandra viburnoides* Meisn.
114	*Nectandra warmingii* Meisn.
115	*Nectandra weddellii* Meisn.
116	*Nectandra wurdackii* C.K. Allen & Barneby ex Rohwer
117	*Nectandra yarinensis* O.C. Schmidt

However, despite the extensive list of species reported, there are other significant numbers (37 species) in the category of unresolved (names for which the contributing data sources did not contain sufficient evidence to decide whether they were accepted or synonyms, or where there were conflicting opinions that could not be readily resolved).

The plant list includes 357 scientific plant names of species rank for the genus *Nectandra*, of these 117 are accepted species names and 184 synonyms (51.5%) [a synonym is an alternative name which has been used to refer to a species (or to a subspecies, variety or forma) but which *the plant list* does not consider to be the currently accepted name]. The decision to assign the Status of Synonym to a name record is based upon a taxonomic opinion recorded in the cited data source (**www.theplantlist.org** accessed 22 October 2014). This is largely due to the fact that it has been almost impossible to get reliable determinations for the plant material. Probably many of the names used in the publication of compounds are incorrect. Unfortunately, some authors still fail to cite voucher specimens, so that there is no way to check their identifications. In other cases species have since been excluded from *Nectandra* (Rohwer, 1993).

Ethnobotany

Plants have always been available to people and have therefore been a constant part of our diet and healing practices (Young, 2007). Considerable benefits for developing countries are possible when the local medicinal plants are subjected to scientific methods of validation of traditional use and quality control. This approach has met with success in some parts of the world but is not always appreciated by national governments and international agencies (Houghton, 1995). The interest of many biological assays are based on the use of the plant in the folk medicine. In fact, in reviews some biological activity tested in plants, for example, *N. megapotamica*; was used in malaria treatment and then tested against the same antimalarial activity; perhaps as a way of validating their pharmacological action (Bero *et al.*, 2009).

Table 2
Uses in folk medicine

Species	Uses in folk medicine	References
N. mollis (Kunth) Nees and *N. puberula* (Scott.) Nees	Diuretic, carminative and emmenagogue disorders.	(Brandãoa *et al.*, 2008)
N. salicifolia	Antifungal, antidiarrheal, analgesic activity and antirheumatic properties.	(Oliveira de Melo *et al.*, 2006)
N. membranacea (Sw.) Griseb and *N. globosa* (Aubl) Mez	Astringent, antidiarrheal, antipyretic, and tonic properties.	(Berdonces, 2010).
N. oleifera Pos	Provides effective bronchitis, insect bite, gonorrhea,	(Berdonces, 2010)

	leucorrhea, wound and ulcer treatment.	
N. rodioei Schomb	Serves as a nervous and digestive system tonic and stimulant, provides anorexia and dyspepsia treatment, and exhibits spasmolytic and antineuralgic properties	(Berdonces, 2010).
N. megapotamica	Antifungal, antidiarrheal, analgesic and antirheumatic.	(da Silva Filho *et al*., 2004; Oliveira de Melo *et al*., 2006)
N. elaiophora	Treatment for parasitic diseases of the scalp	(Fenner *et al*. 2006).
N. cinnamomoides	Local anaesthetic.	(Ballabeni *et al*., 2007)
N. angustifolia	Snake venom treatment.	(Torres *et al*., 2014)
N. cuspidata	Stomachache.	(Muñoz *et al*., 2000)
N. coto	The beverage is an integral part of the religious and social life and has tranquilizing and sleep-inducing properties.	(Seigler, 1998)
N. coriacea	Diuretic and to treat kidney disease.	(Pérez Machín *et al*., 2011)
N. grandiflora	Antirheumatic, digestive and diuretic properties.	(Ribeiro *et al*., 2002)
Nectandra sp	Anti-inflammatory, febrifuge, energizing, hypotensive agent, treatment of nervous disorders, fevers, snakebite, toothache, infections of the genitourinary, gastrointestinal and bronchopulmonary systems, remedy for syphilis.	(da Silva-Filho *et al*., 2004 ; da Silva Filho *et al*., 2008; Moreno *et al*., 1993; Morton, 1975)

Secondary metabolites isolated from the genus Nectandra and their evaluated biological activity

The wide variety of secondary metabolites is usually linked to interest in the development of bioassays for therapeutic purposes; therefore it must be noted that the goals of using plants as sources of therapeutic agents are: *a*) to isolate bioactive compounds for direct use as drugs, *b*) to produce bioactive compounds of novel or known structures as lead compounds for semisynthesis to produce patentable entities of higher activity and/or lower toxicity, *c*) to use agents as pharmacologic tools, and *d*) to use the whole plant or part of it as a herbal remedy (Fabricant & Farnsworth, 2001).

Alkaloids

The most common alkaloid types of the genus *Nectandra* are aporphines, proaporphines, benzylisoquinolines, bisbenzylisoquinolines, and morphinandienones (Gottlieb, 1972).

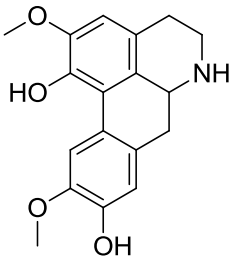
Lauraceae species have been recognized for a long time as a source of alkaloids. Benzyltetrahydroisoquinolines and aporphins are probably present in most of their members (Gottlieb, 1972). Relatively few amino acid precursors are actually involved in alkaloid biosynthesis and building blocks from the acetate, shikimate, or methylerythritol phosphate pathways are also frequently incorporated into the alkaloid structures (Dewick, 2002).

Aporphine

All the aporphine alkaloids are based on the 4*H*-dibenzo[*d*,*g*]quinoline structure or its *N*-methyl derivative, commonly known as the aporphine nucleus. The aporphine alkaloids can be divided into three groups depending upon the degree of methylation at the nitrogen atom (Shamma & Slusarchyk, 1964).

Among the species of the genus *Nectandra* of which these metabolites have been isolated, *Nectandra rigida* Nees is prominent, and from wood has been isolated laurelliptine (**1**) (Le Quesne *et al*. 1980). In *N. salicifolia*, from trunk bark extract were isolated (+)-laurolitsine [known as (+)-norboldine] (**2**), (+)-laurotetanine (**6**) (In *N. salicifolia* and *N. grandiflora*), (+)-*N*-methyllaurotetanine (**7**), (6a*S*)-glaziovine (**3**), (+)-norpurpureine (**4**), isocorydine (**5**),

(+)-norisocorydine (**8**), (+)-boldine (**9**) (In *N. salicifolia* and *N. ramonensis*), and (+)-isoboldine (**10**) (In *N. salicifolia* and *N. pichurim*) (Böhlke *et al*., 1996; Ferrari, *et al*., 1971; López-Vargas *et al*., 1995; Moreno *et al*., 1993). In *N. sinuata*, from trunk bark extract were isolated (*S*)-3-methoxy-nordomesticine (**11**), nordomesticine (**12**), and norlirioferine (**13**) (Castro-Castillo *et al*., 1991); ocoteine (**14**) and dehydro-ocoteine (**15**) from *N. saligna* (Barralle *et al*., 1972). The most frequently detected alkaloids in Lauraceae belong to the aporphinic group, with only one benzyltetrahydroisoquinoline, with methoxyls and only a few hydroxyl groups (Custódio & da Veiga Junior, 2014).



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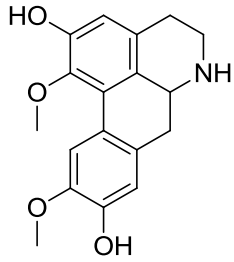

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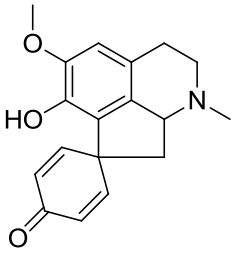

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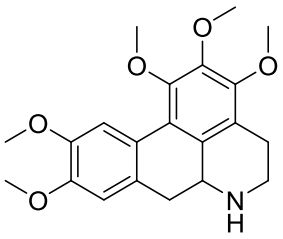

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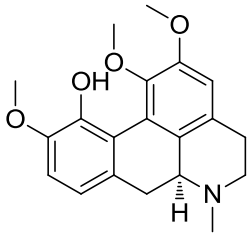

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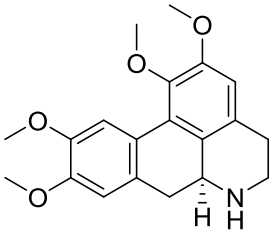

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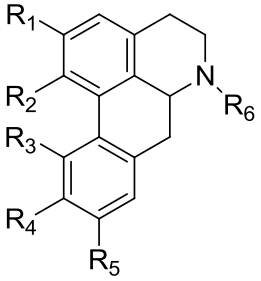

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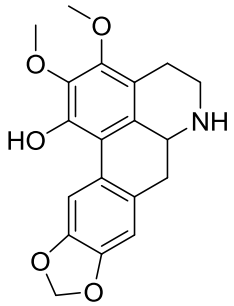
8	OMe	OMe	H	OMe	OH	H
9	OH	OMe	H	OMe	OH	Me
10	OMe	OH	H	OMe	OH	Me



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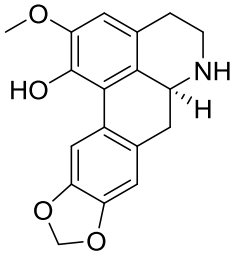

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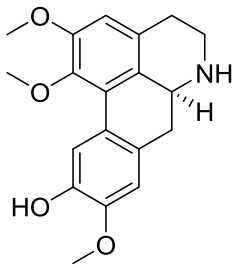
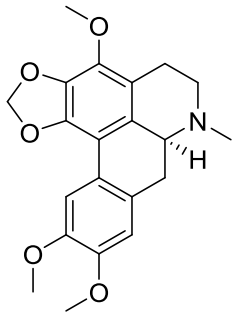
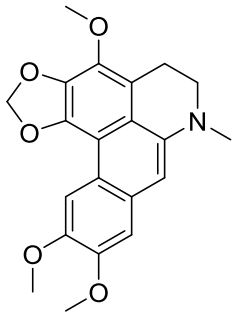


(**13**)



(**14**)



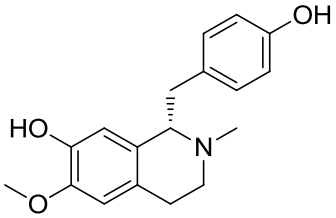
(**15**)

Many of these secondary metabolites, especially those isolated from *N. salicifolia*, were tested as antiplasmodial agents, and they presented the following IC_{50} values (in ng/mL): 1240 (for compound (**2**); 3900 (**6**); 1510 (**4**); 7150 (**7**); 1990 (**8**); 2130 (**9**); and 668 (**10**). In addition, the aqueous extract (decoction) presented vasoactive activity as a potent muscle relaxant, with a percentage of relaxation of 68% (Böhlke *et al*., 1996; Slish *et al*., 1999).

Benzyltetrahydroisoquinolines

The isoquinoline alkaloids are formed from the amino acid tyrosine by consecutive reactions forming the tetrahydroisoquinoline core and have a great importance due several pharmacological activities described (Lauraceae family) to the benzyltetrahydroisoquinoline, aporphine, among other (Custódio & da Veiga Junior, 2014).

The phytochemical study of the bark of *N. salicifolia* according to the literature, reports the isolation of benzyl tetrahydroisoquinoline metabolites: (1*R*)-coclaurine (**11**), (1*S*)-*N*-methylcoclaurine (**12**), (1*S*)-reticuline (**13**), (1*S*)-juziphine (**14**) and (1*S*)-norjuziphine (**15**) (+)-costaricine (**16**), (9*S*)-sebiferine [(9*S*)-*O*-methylflavinantine] (**17**) (Böhlke *et al*., 1996). In *N. ramonensis* (±)-norarmepavine (**18**) was isolated (López-Vargas *et al*., 1995); while bebeerine (biberine) (**19**) from *N. rodioei* (Hultin, 1961; Humphrey, 1915; McKennis Jr *et al*., 1956).



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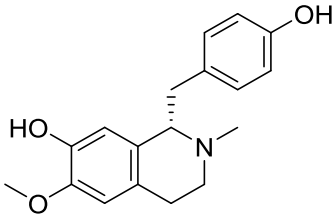

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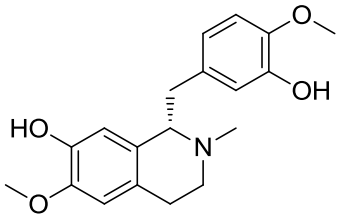

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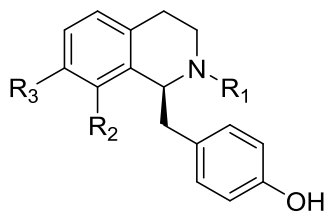
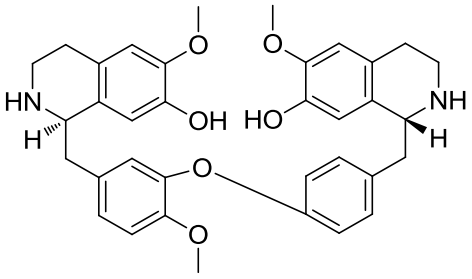
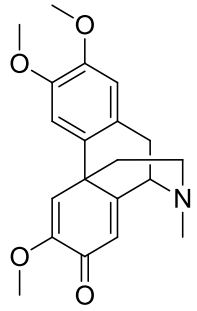


No	R_1	R_2	R_3
14	Me	OH	OMe
15	H	OMe	OH



(16)



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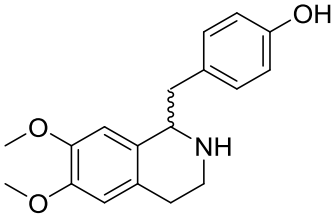
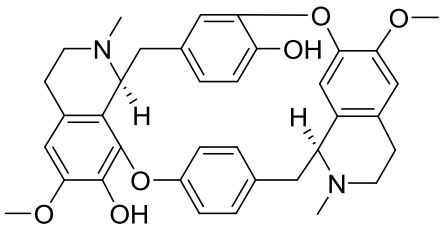


(**18**)



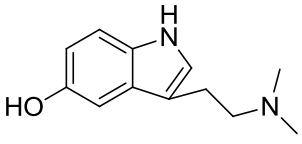
(**19**)

The study of the antiplasmodial biological activity of certain metabolites (benzyl-tetrahydroisoquinoline-type) isolated from the bark and trunk of the species mentioned above (*N. salicifolia*) allowed for the observation of the following IC_{50} values (in ng/mL): 50 (**16**); 7100 (**17**), 5800 (**13**); 2730 (**12**); 4100 (**15**); 4090 (**14**) (Böhlke *et al*., 1996). The diversity of pharmacological effects observed within this group of molecules is obviously a function of differences in chemical structures; however, convincing structure-activity relationships had not been developed for the bisbenzylisoquinoline alkaloids (Angerhofer *et al*., 1999). The effects of biological activity reflect differences stereoisomeric, as also, the presence of quaternary nitrogen atoms leads to a lack of activity against *Plasmodium* clones (Angerhofer *et al*., 1999). In other bioassays with these types of alkaloids show that the only significant trend that was observed was the decrease in activity (and toxicity) on quaternization or *N*-oxidation, which may be explained by diminished membrane permeability brought about by these changes (Go, 2003).

Simple Indole

This class of secondary metabolites includes different types of alkaloids, such as: Non-tryptamines (indole phytoalexins, and carbazoles), tryptamines (piperazinediones, pyrroloindoles, β-carbolines), bisindole alkaloids and peptide alkaloids (Ishikura *et al*., 2013). The indole alkaloids have been reported in some species of the Lauraceae family (obtained from *Ocotea minarum* fruits, *Litsea petiolata* bark and *Neolitsea daibuensis* roots) (Custódio & da Veiga Junior, 2014). However for genus *Nectandra*, indole alkaloids have been reported in only one species (Pech & Bruneton, 1983)**.**

From the trunk of *N. megapotamica*, the presence of bufotenine was determined (**20**) (Pech & Bruneton, 1983).



(**20**)

For the genus *Nectandra* there are no reports of biological activity of these secondary metabolites (simple indole). However, the indole alkaloids have been reported results of biological activity, such as: moderate anti-inflammatory activity for indole alkaloids (daibucarboline A, IC_{50} of 18.41 mM) (Custódio & da Veiga Junior, 2014), significant activity in reversing multidrug resistance in vincristine-resistant KB (VJ300) cells, strong inhibitory activity against *Mycobacterium tuberculosis*, protein kinase inhibition activity, anti-Saprolegnia parasitica activity, antitumor activity against three cancer cell lines (KB, MCF7, NCI-H187), and antimicrobial activity (Ishikura *et al*., 2013).

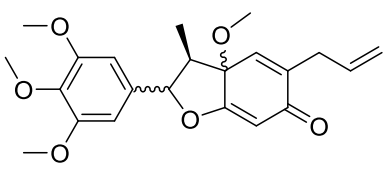
Lignoids

The presence of phenylpropanoids and dimerization products (lignans and neolignans) correspond to the most common secondary metabolites in the genus (Rohwer, 1993). Although there are a variety of lignans, their biological activity in some cases is selective in certain types of biological assays, for example, benzofuran neolignans were found to be selective COX-2 inhibitors, whereas bicyclooctane neolignans inhibit selectively the platelet-activating factor action as well as COX-1 and 5-LOX. The neolignan 9-*nor*-7,8-dehydro-isolicarin B and cinerin C were found to be the most potent COX-2 inhibitor and PAF-antagonist, respectively (Coy *et al*., 2009b). These findings suggest (perhaps) that the mechanism of action in the inhibition of PGE2 production is the direct inhibition of COX enzymatic activity (Saleem *et al*., 2005).

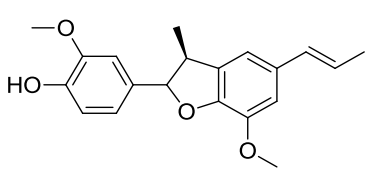
Dihydrobenzofuran lignans

The genus *Nectandra* have dihydrobenzofuran-type lignans, such as mirandin A (**21**) and mirandin B (**22**) isolated from *N. miranda* (wood) (Aiba et al., 1977); dehydrodiisoeugenol (**23**) isolated from *N. rigida* Nees (wood); licarin A (**24**) and licarin B (**25**) isolated from *N. grandiflora* (leaves) (Le Quesne *et al*., 1980); and burchellin (**26**) isolated from *N. grandiflora* (fruits and fruit calyx) (Ribeiro *et al*., 2005).

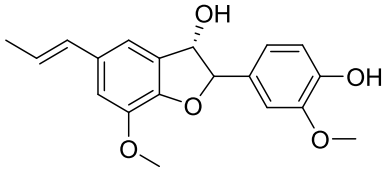
The toluene extract of the stem bark of *N. purpurascens* (R&P) Mez. contained methyl 7-methoxy-2-(3,4-methylenedioxyphenyl)benzofuran-5-carboxylate (**27**), 5-(2-propenyl)-7-methoxy-2-(3,4-methylenedioxyphenyl)benzofuran (**28**), and egonoic acid (**29**) (Rios-Motta & Avella, 2010).



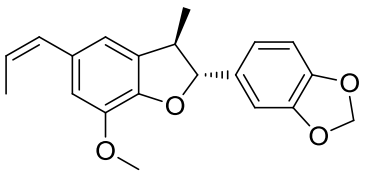
	Ar	MeO
21	α	α
22	β	β



(**23**)



(**24**)



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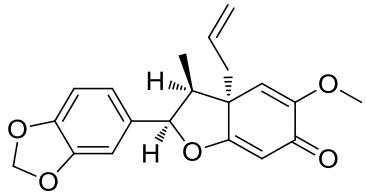

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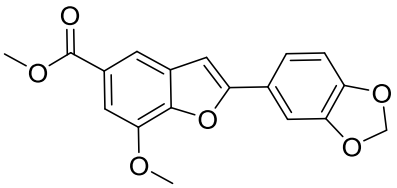
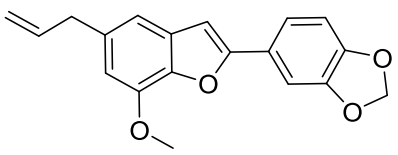
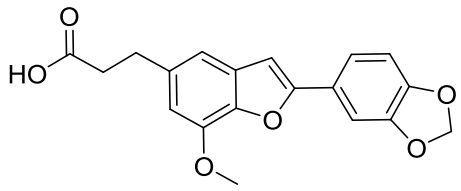


(**27**)



(**28**)



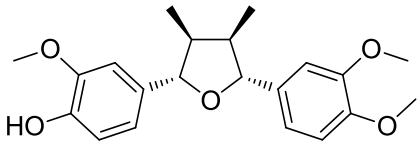
(**29**)

Of these compounds, licarin A (**24**) (isolated from *N. amazonum*) was tested, and 1 µl was applied to larvae in groups of 30 specimens. At this dose, the compound inhibited the post-embryonic development of *Chrysomya megacephala* larvae, establishing its larvicidal activity (Cabral *et al*., 2007), although several lignans with larvicidal activity have been isolated from other species (Xiao *et al*., 2012). Some reports (lignans) indicate that the biological activity may vary with respect to the hydrophobicity which depends on the number of hydroxyl groups on the compound (probably an important factor for their insecticidal activity) (Nishiwaki *et al*., 2011).

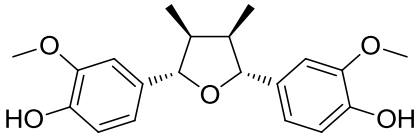
Tetrahydrofuran lignans

3,4-Dimethyl-2,5-bis(3,4-dimethoxyphenyl)tetrahydrofurans belong to a well-recognized subgroup of natural products known as lignans and may exist in *six* stereoisomeric forms (Biftu *et al*., 1986).

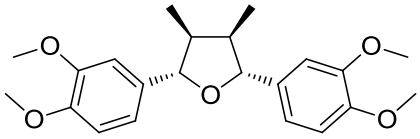
Tetrahydrofuran lignans, such as nectandrin A (**30**), nectandrin B (**31**) and galgravin (**32**), have been isolated from *N. rigida* Nees (wood) (Le Quesne *et al*., 1980), and veraguensin (**33**); from *N. puberula* (wood) (Moro *et al*., 1987), machilin G (**34**), calopiptin (**35**), aristolignin (**36**), nectandrin C (**37**), ganschisandrine (**38**), nectandrin D (**39**), nectandrin E (**40**), nectandrin A (**30**), nectandrin B (**31**), and galgravin (**32**), from *N. megapotamica* (da Silva Filho *et al*., 2008).



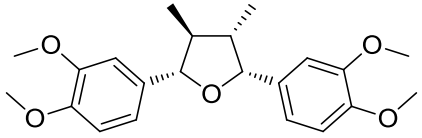
(**30**)



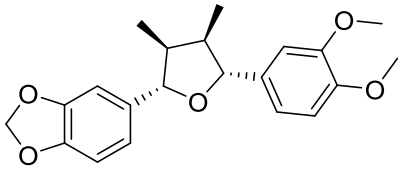
(**31**)



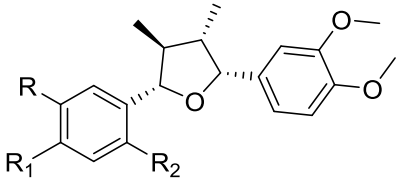
(**32**)



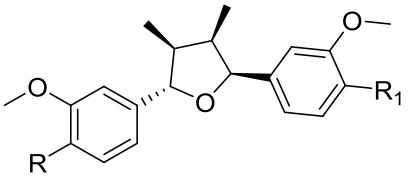
(**33**)



(**34**)



No	R	R_1	R_2
35	OCH_2O		H
36	OCH_3	OH	H
37	OCH_3	OCH_3	OH



No	R	R_1
38	OCH_3	OCH_3
39	OCH_3	OH
40	OH	OCH_3

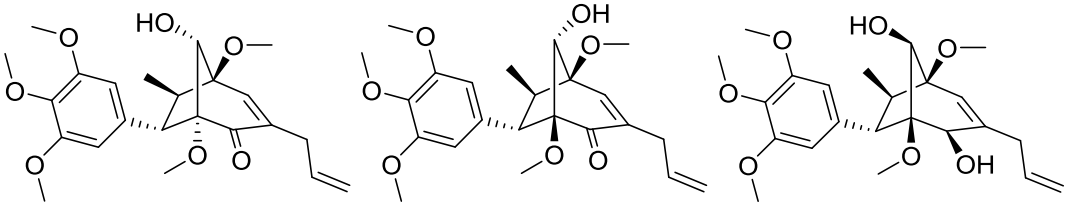
For this type of secondary metabolites there are not many reports about biological activity, but, if has been reported for the *Nectandra megapotamica* on tripanocidal activity (da Silva Filho *et al*., 2004) and *in vitro* antileishmanial and antimalarial activities (da Silva Filho *et al*., 2008). Additionally, there are many reports of biological activity of tetrahydrofuran lignans in other genus and from synthetic origin, such as: trypanocidal activity (Martins *et al*., 2003), platelet activating factor antagonists (Biftu *et al*., 1986), inhibition of nitric oxide production, and antifungal activity (Akiyama *et al*., 2007), among other. It is difficult to compare the biological activity (tripanocidal) of the compounds, due to the diversity of parasite strains, stage of the life cycle and experimental conditions applied (da Silva Filho *et al*., 2008).

The structure- activity relationship for this type of secondary metabolites has been reported for lignans with methylenedioxy group present in the molecule, wherein the biological activity is related to the number or presence of this group (Felippe *et al*., 2008).

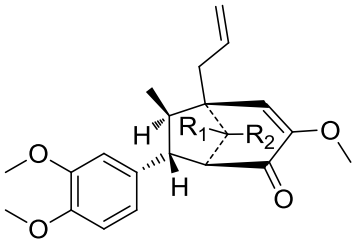
Bicyclo [3.2.1] octane lignans

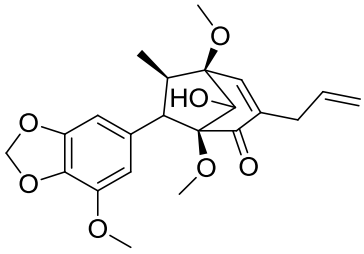
The Lauraceae plants (preferably the genera including the *Ocotea* complex) are known to contain bicyclo[3.2.1]octanoid neolignans, an important class of natural products, which are further subdivided into the guianin and the macrophyllin classes (Coy *et al*., 2009c). Among the known bicyclo[3.2.1]octanoid neolignans, macrophyllin-type neolignans are less common than guianin-type neolignans. Most of the isolated macrophyllin-type neolignans, however, have excellent PAF (platelet-activating factor) antagonistic activities (Wang *et al*., 2002).

Bicyclo-octane type lignans are present in *N. amazonum* (fruits and fruit calyx), which is consistent with the phytochemical study of nectamazin A-C (**41-43**) (Coy *et al*., 2009a). Other species studied with this type of metabolites is *N. grandiflora*, whose leaves revealed the presence of (7*S**,8*R**,1'*R**,3'*R**)-3,4,5'-trimethoxy-3,7'-cyclo-8,1'-neolig-8'-ene-2,4'(3'*H*)-dione (**44**) and bicyclo[3.2.1]octane neolignan 2'-*oxo*-piperol B (**45**) (Ribeiro *et al*., 2005), whereas in *Nectandra sp*, its wood revealed the presence of macrophyllin-B (46) (Filho *et al*., 1980).



(**41**) (**42**) (**43**)





(**46**)

44	R_1,R_2=O
45	R_1=OH, R_2=H

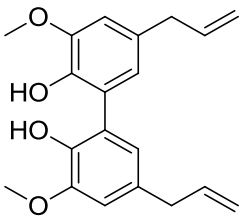
Platelet-activating factor (PAF) is a potent lipid mediator in inflammation and asthma (Kuroyanagi *et al*., 2000). Numerous cells and tissues synthesize PAF (1-*O*-alkyl-2-acetyl-sn-glycero-3-phosphocholine) upon suitable stimulation, which was discovered to be a lipid mediator of hypersensitivity and inflammation (Coy *et al*., 2009).

In that sense, in the genus *Nectandra* have been evaluated some lignans of this type, such as the compounds (**41-43**) which have respectively an IC_{50} (in µM) for COX-1 of 72.2, 152 and 74.6; for COX-2 of 255, 569 and 6.83; and for 5-LOX of 156, 42.4 and 12.8; in addition, bioassays show that they present

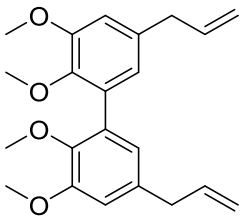
inhibitory activity for COX, LOX, and platelet aggregation (Coy *et al*., 2009b).

[3, 3'-neolignan]

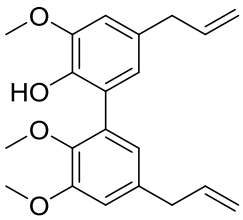
3,3'-neolignan-type compounds are present in *N. polita* wood, and analysis allowed the isolation of compounds: dehydrodieugenol (**47**), di-*O*-methyldehydrodieugenol (**48**), and *O*-methyldehydrodieugenol (**49**) (Suarez *et al*., 1983). However, this type of compounds also was isolated from the species of *Ocotea* (de Diaz *et al*., 1980). It has not been reported biological activity for these secondary metabolite found in the genus *Nectandra*.



(**47**)



(**48**)

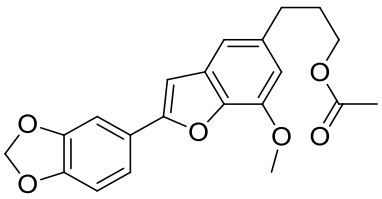


(**49**)

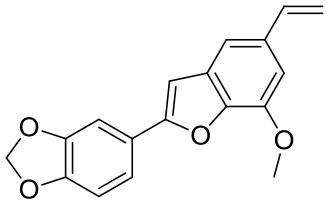
Norlignans

Norlignans have two aromatic rings and a side chain with five carbons. It has been hypothesized that the norlignan biosynthesis is partly related to lignan biosynthesis. However, several hypothetical biosynthetic pathways were proposed in line with the above restrictions and norlignan chemical structures (Suzuki & Umezawa, 2007).

Norlignans have been found in the leaves of *N. lineata*: 3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-*nor*-8,5'-neolignan-9'-acetoxy (**50**); and 3'-methoxy-3,4-methylenedioxy-4'-7-epoxy-9-*nor*-8,5'-neolignan-7,8'-diene (**51**) (Chérigo *et al*., 2005).



(**50**)

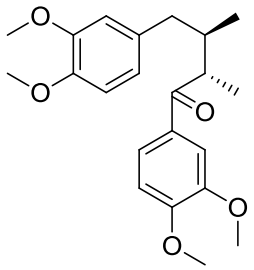


(**51**)

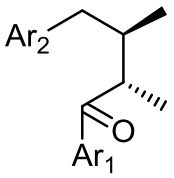
The antitrypanosomal activity of this class of compounds has been studied; such activity causes growth inhibition of *Trypanosoma cruzi* epimastigotes with IC_{50} values (in µM) of 111 and 70 for (**50**) and (**51**), respectively (Chérigo *et al*., 2005). Additionally, it has been evaluated the *in vitro* cytotoxic activity [cytotoxic activity against the two cancer cell lines HL-60 (human leukemia) and K562 (human leukemia) by the MTT-assay method] (Lee *et al*., 2010) and it has been found moderate inhibition of COX-1 and COX-2 (Bertanha *et al*., 2012).

Diarylbutanone lignans

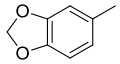
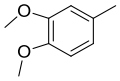
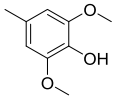
Diarylbutanone lignans are a type of secondary metabolite that have been found in *N. puberula* (wood) and are represented by the compounds 7-*oxo*-3,4,3',4'-tetraoxy-8.8´-neolignan (**52**) and a group of aryl ketones (**53-56**) (Moro *et al*., 1987; Whiting, 1990). It has not been reported biological activity for these secondary metabolite found in the genus *Nectandra*.



(52)

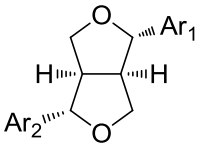


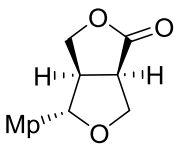
53	Ar_1=Pi; Ar_2=Gu
54	Ar_1=Ar_2=Pi
55	Ar_1=Pi; Ar_2=Ve
56	Ar_1=Ve; Ar_2=Pi

Ar		
P_i	**Ve**	**Gu**
		

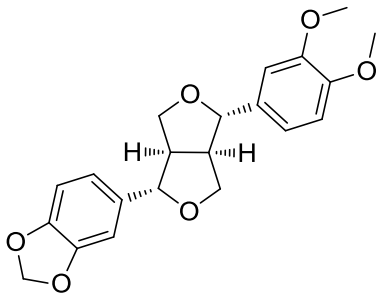
Furofuran lignans

Furofuran lignans have been reported in the bark of *N. turbacensis*, where they are represented by the following: (+)-sesamin (**57**), (+)-demethoxyexcelsin (**58**), (+)-piperitol (**59**), (+)-methoxypiperitol (**60**) and (1***R***, 2***S***, 5***R***)-2-(3'-methoxy-4',5'-methylenedioxy-phenyl)-3,7-dioxa-6-oxobicycle[3.3.0]octane (**61**) (De Carvalho *et al*., 1986), and in *N. glabrescens*, where (+)-*O*-methylpiperitol (**62**) was isolated from fruit calyces (Barbosa-Filho *et al*., 1989).



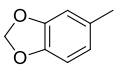
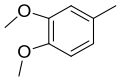
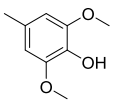


(**61**)



(**62**)

	Ar_1	**Ar_2**
57	P_i	P_i
58	P_i	Mp
59	P_i	Gu
60	Gu	Gu

Ar		
P_i	**Mp**	**Gu**
		

In the genus have not been reported bioassays for these secondary metabolites. However, the biological activity of these compounds has been reported, such as: inhibition of cholesterol absorption (Hirose *et al*., 1991), antihypertensive effect (Matsumura *et al*., 1998), protective effects (Hou *et al*., 2004), and antioxidant activity (Kato, *et al*., 1998).

Essential oils

Essential oils are very complex natural mixtures which can contain about 20–60 components at quite different concentrations and they are composed of terpenes and terpenoids (aromatic and aliphatic), all characterized by low molecular weight (Bakkali *et al*., 2008). The terpenoids constitute the largest family of natural products; over 22,000 individual compounds of this class have been described, and the number of defined structures has doubled every decade since the 1970s. The terpenoids play diverse functional roles in plants (McGarvey & Croteau, 1995).

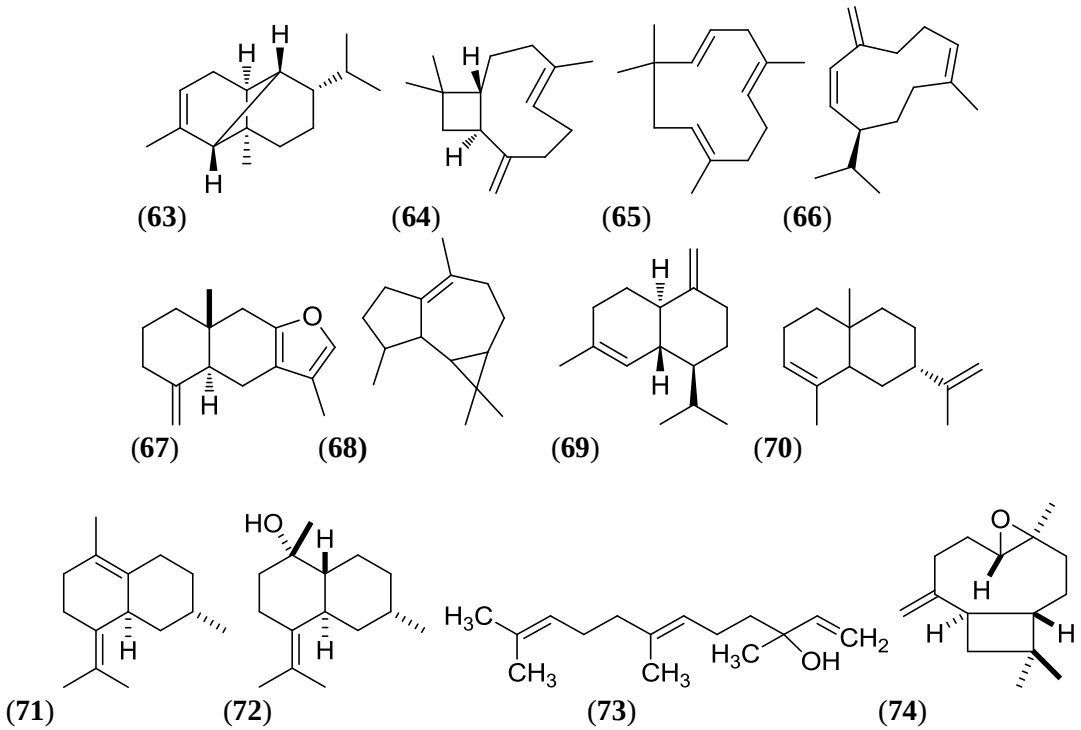
The chemical components of the oils extracted from the genus *Nectandra* are represented

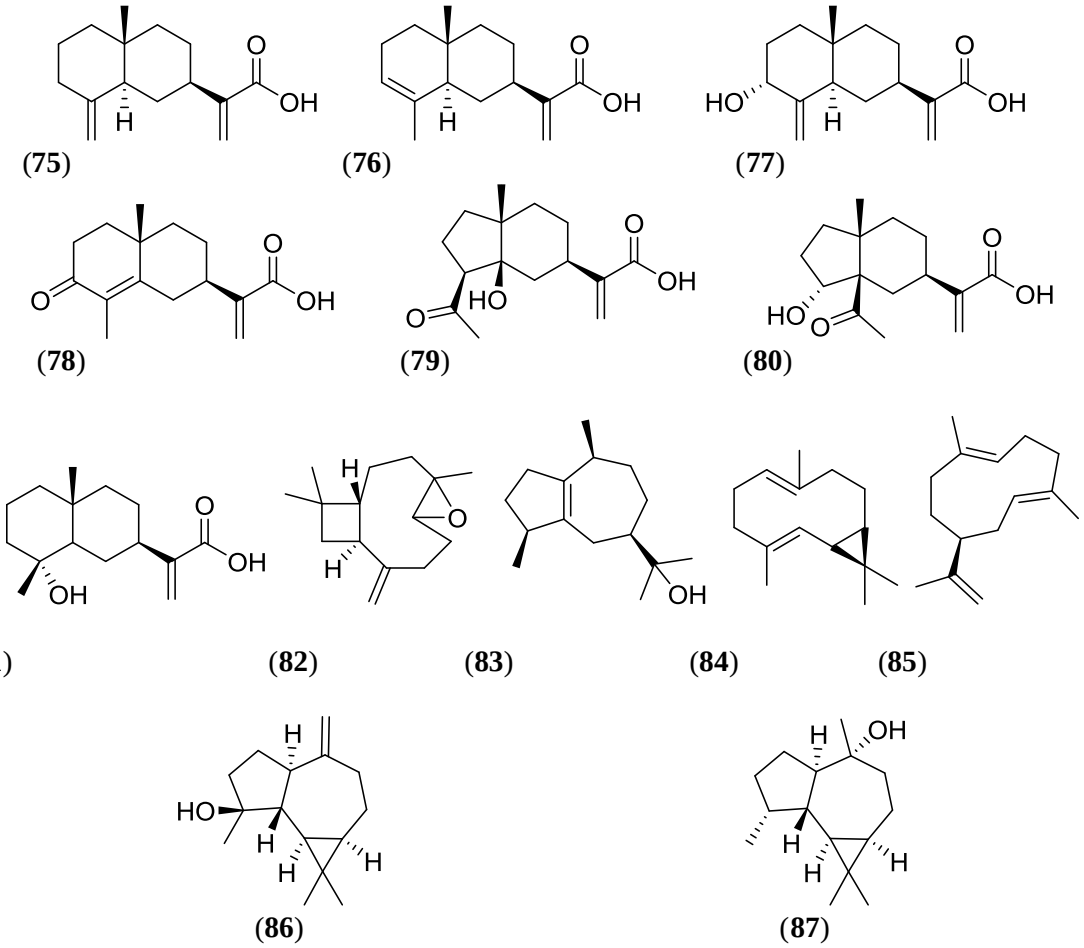
(in particular) by sesquiterpenes (monocyclic and bicyclic), which includes oxygenated, hydrocarbonated, and/or phenylpropanoid compounds. However, the methods of extraction of essential oils from plants significantly affect the chemical constituents and composition of the essential oil.

Sesquiterpenes

N. membranacea is a species from which the following sesquiterpenes were isolated from the wood: α-copaene (**63**), β-caryophyllene (**64**), α-humulene (**65**) and germacrene D (**66**) (Setzer *et al*., 2007). In *N. salicina*, atractylone (**67**), viridiflorene (**68**), δ-cadinene (**69**), 7-epi-α-selinene (**70**) and germacrene D (**66**) were isolated from the branches (Cicció *et al*., 2009), whereas β-caryophyllene (**64**), α-humulene (**65**) and δ-cadinene (**69**), were also isolated from the leaves (Cicció *et al*., 2009). From these types of metabolites (sesquiterpenes), and specifically from the cadinane-type, have been reported the isolation of the following compounds: *rel*-(4*S*,6*S*)-cadina-1(10),7(11)-diene (**71**), and *rel*-(1*R*,4*S*,6*S*,10*S*)-cadin-7(11)-en-10-ol (**72**) in the species *N. amazonum* (Cuca *et al*., 2013). In *N. amazonum* and *N. glabrescens*, nerolidol (**73**) was isolated (Barbosa-Filho *et al*., 1989). From the trunk bark of *N. megapotamica* has been isolated *trans*-1(10)-epoxy-4(15)-caryophyllene (**74**) (Romoff *et al*., 2010) and four eudesmane-type sesquiterpenes, costic acid (75), 12-carboxyeudesman-3,11(13)-diene (3-isocostic acid) (76), viscic acid (77), 3-oxo-γ-costic acid (78) and two rearranged eudesmane derivatives, 3α-hydroxyisoiphion-11(13)-en-12-oic acid (79) and 5β-hydroxy-4-oxo-11(13)-dehydroiphionan-12-oic acid (80), have been isolated from the trunk bark of *N. cissiflora* (Garcez *et al*., 2010). Phytochemical investigation of the bark extract has yielded three eudesmane sesquiterpenes, ilicic acid (**81**), costic acid (**75**), and 3-isocostic acid (**76**) (Wu *et al*., 2006).

The essential oil from leaves of *N. antillana* was isolated by hydrodistillation and the major constituents of the essential oil were caryophyllene oxide (16.0%) (**82**), β-caryophyllene (9.9%) (**64**) and guaiol (8.7%) (**83**) (Pino *et al*., 2014). Moreover, in *N. leucantha* were identified several sesquiterpenes, including: bicyclogermacrene (28.44%) (**84**), germacrene A (7.34%) (**85**), spathulenol (5.82%) (**86**), and globulol (5.25%) (**87**) (Grecco *et al*., 2014).





(**75**) (**76**) (**77**)

(**78**) (**79**) (**80**)

(**81**) (**82**) (**83**) (**84**) (**85**)

(**86**) (**87**)

An analysis of the essential oil components in the leaves and branches in *N. salicina* showed the following percentage composition: in the leaves, (**67**) (14.6%), (**68**) (10.1%), (**64**) (7.2%), (**65**) (7.0%), (**69**) (6.1%), (**66**), (5.8%), (**98**) (9.4%) and (**99**) (6.0%) (monoterpenoids); and in the branches, (**66**) (10.7%), (**67**) (21.1%), (**68**) (7.9%), and (**70**) (5.0%). In addition, bioassays of the total oil were performed and showed LD_{50} values of 150 μg/mL against leukemic and hepatocellular carcinoma cells and non-tumor cells (macrophages and myoblasts) (Cicció *et al*., 2009).

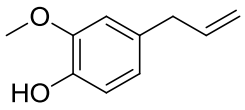
The *in vitro* antibacterial activity of the essential oil (*N. antillana*) was studied against five bacteria strains (*Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus* and *Listeria monocytogenes*) using the disc diffusion method. The essential oil (For all tests, 5 μL of essential oil were applied.) was slightly effective against nearly all bacteria tested, except for *B. subtilis* (Pino *et al*., 2014).

There is no explanation yet for the antileukemic effect of essential oil components. However some authors have suggested that the promising or significant activity *in vivo* results some diterpenoid triepoxides. Additionally, the presence of α,β-unsaturated lactone function has been shown to be important for the tumor-inhibitory activity of several classes of terpenoids) (Kupchan *et al*., 1972).

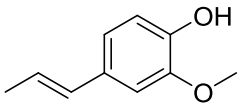
Phenylpropanoids

Phenylpropanoids have been identified in *N. amazonum* and *N. glabrescens*, including eugenol (**88**), isoeugenol (**89**), safrole (**90**), isosafrole (**91**), and nerolidol (**73**) (Barbosa-Filho *et al*., 1989), and in *N. cinnamomoides* (flowers), including *trans*-

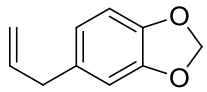
cinnamaldehyde (**92**) and methyl cinnamate (**93**), which have been identified as major components (Ballabeni *et al*., 2007a). Similarly, eugenol (**88**) was also found in *N. polita* (wood) (Suarez *et al*., 1983). From the trunk bark of *N. megapotamica* four phenylpropanoids, elemicin (**94**), isoelemicin (**95**), (±)-*erythro*-1-(3,4,5-trimethoxyphenyl)-1,2-propanediol (**96**) and (±)-*thr**eo***-1-(3,4,5-trimetoxyphenyl)-1,2-propanediol (**97**) have been isolated (Romoff *et al*., 2010).



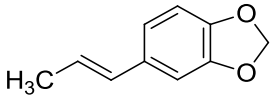
(**88**)



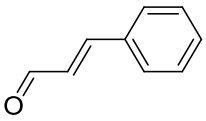
(**89**)



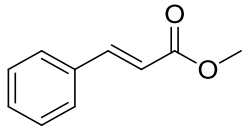
(**90**)



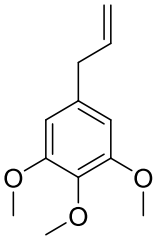
(**91**)



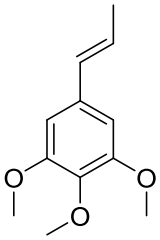
(**92**)



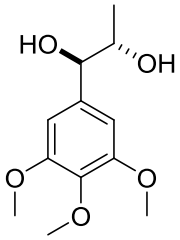
(**93**)



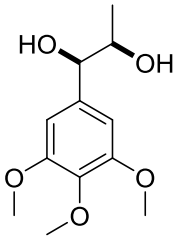
(**94**)



(**95**)



(**96**)



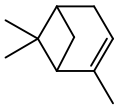
(**97**)

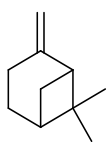
The antithrombotic bioassay of the essential oil of *N. cinnamomoides* (flowers) showed IC_{50} values of 47 µg/ml for the inhibition of arachidonic acid-induced platelet aggregation (50 µM); 163 µg/ml by collagen (5 µg/mL); 67 µg/ml by U46619 (1 µM); 70 µg/ml by ADP (3 µM), and 406 µg/ml by PMA (0.5 µM) (Ballabeni *et al*., 2007a).

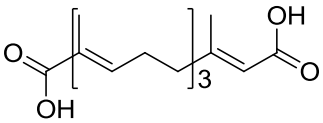
Bioassays antifungal activity (compounds elemicin (**94**), isoelemicin (**95**), (±)-*erythro*-1-(3,4,5-trimethoxyphenyl)-1,2-propanediol (**96**) and (±)-*thr**eo***-1-(3,4,5-trimetoxyphenyl)-1,2-propanediol (**97**) against strains *Candida albicans*, *C. krusei*, *C. tropicalis* and *Cryptococcus neoformans* inhibited the growth of fungi with MICs = 100 mg/mL (Garcez *et al*., 2009).

Monoterpenoids and acids

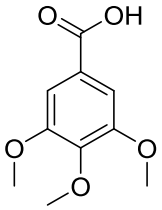
The analysis of leaves from *N. salicina* revealed the presence of α-pinene (**98**) and β-pinene (**99**) (Cicció *et al*., 2009), whereas the analysis of the wood of *N. puberula* revealed the presence of 1,6-geranylgeranodioic acid (**100**) (Moro *et al*., 1987). From the trunk bark of *N. megapotamica* has been isolated 3,4,5-trimethoxybenzoic acid (**101**) (Garcez *et al*., 2009).


(**98**)


(**99**)



(**100**)

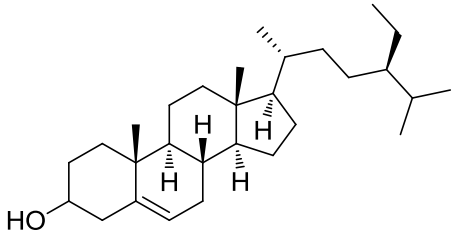


(**101**)

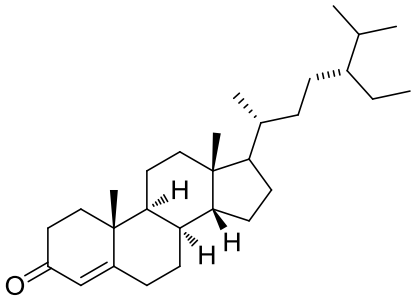
Phytosterols

In plants, more than 200 different types of phytosterols have been reported being the most abundant being β-sitosterol (24-α-ethylcholesterol), campesterol (24-α-methylcholesterol) and stigmasterol (Δ^{22},24-α-ethylcholesterol). Ergosterol $\Delta^{7,22}$,24-α -methylcholesterol is the principal sterol of yeast and is found in corn, cotton seed, peanut and linseed oils (Lampi *et al*., 2004).

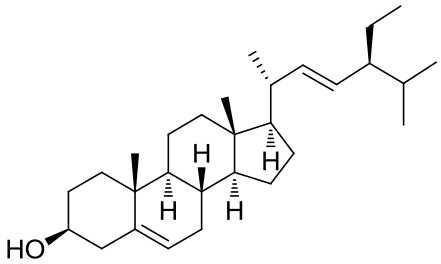
3-hydroxy and 3-ketone pentacyclic compounds are among the most representative phytosterols among the different species; for example, *N. puberula* (wood) and *N. turbacensis* (bark) have β-sitosterol (**102**) and sitostenone (**103**) (De Carvalho *et al*., 1986; Moro *et al*., 1987); *N. polita* (wood) also has β-sitosterol (**102**) (Suarez *et al*., 1983); and from *N. amazonum* and *N. glabrescens* (fruit calyces) have been reported stigmasterol (**104**) reported (Barbosa-Filho *et al*., 1989).



(**102**)



(**103**)



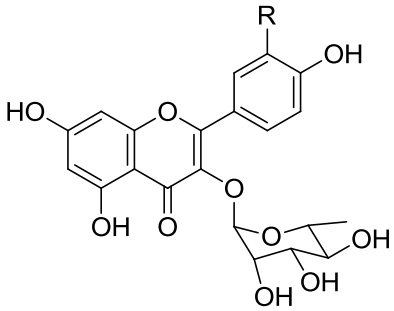
(**104**)

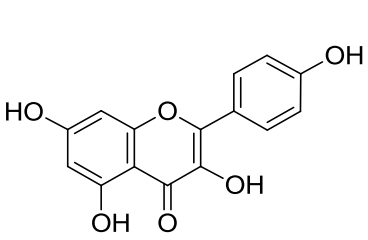
Flavonoids

Along with the phenylpropanoids or hydroxycinnamic acid derivatives (C_6C_3), flavonols and to a lesser extent flavones are found in almost every plant, while flavanones and flavones are often found together (e.g., in citrus fruits) and are connected by specific enzymes. This type of secondary metabolites, phenylpropanoids or hydroxycinnamic acid derivatives, flavonols and flavones (lesser extent) has been found in almost all plants. However, the presence of flavanones is often associated with the report of flavones in plants (for example in citrus fruits). There is a certain mutual exclusion between flavones and flavonols in many plant families and anthocyanins are almost absent in flavanone-rich plants (Rice-Evans *et al*., 1996). They occur naturally in fruit, vegetables, nuts, seeds, flowers, and bark and are an integral part of the human diet. They have been reported to exhibit a wide range of biological effects (Cook & Samman, 1996). The structural diversity of metabolites belonging to the different flavonoid classes, which are catalyzed by substrate-specific and position-oriented enzymes, contribute to the enormous diversity of flavonoid compounds that amount to >5000 chemical structures in nature and hence, to the wide spectrum of functional roles they play in the survival of plants (Wittstock *et al*., 2003).

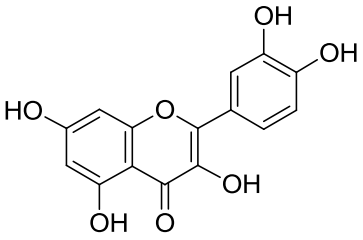
Flavonoids are reported in *N. salicina*, and a phytochemical analysis of the leaves and branches isolated 3-*O*-β-rhamnosylkaempferol (**105**) and 3-*O*-β- rhamnosylquercetin (**106**) (Bezerra-Ribeiro *et al*., 2002); whereas the analyses of *N. amazonum* and *N. glabrescens* isolated kaempferol (**107**) and quercetin (**108**) (Barbosa-Filho *et al*., 1989) and the analysis of *N. grandiflora* isolated afzelin (**109**) and quercetrin

(**110**) (Ribeiro *et al*., 2005) and (-)-epicatechin (**111**) (flavanol) in *N. megapotamica* and *N. cissiflora* (Garcez *et al*., 2010; Romoff *et al*., 2010). From *N. purpurascens* has been kumatakenin (**112**) reported (Rios-Motta & Avella, 2010). The results of analysis antioxidant demonstrate the importance of the unsaturation in the C ring allowing the electron delocalization across the molecule for stabilization of the aryloxyl radical. However, when the structure of the B ring has no neighboring hydroxyl groups, the 2,3 double bond apparently contributes little to the hydrogen-donating ability. (Rice-Evans *et al*., 1996).



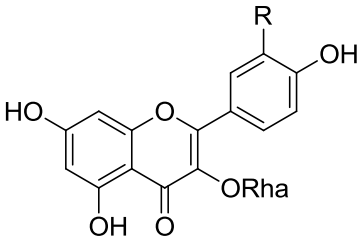


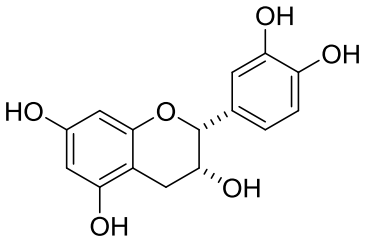
(**107**)



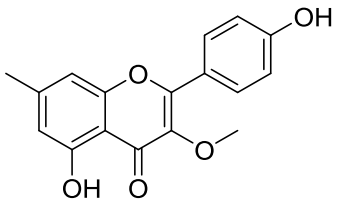
(**108**)

	R
105	H
106	OH





(**111**)



(**112**)

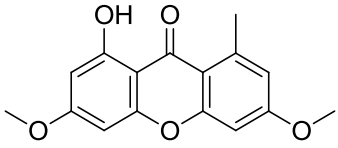
109	R=H
110	R=OH
Rha	rhamnosyl

Plant polyphenols are multifunctional and can act as reducing agents, hydrogen donating antioxidants, and singlet oxygen quenchers (Rice-Evans *et al*., 1996). Antioxidant activity assays were performed with the *N. grandiflora*, specially the compounds (**109**) and (**110**), which were shown to inhibit the oxidation of β-carotene; in compound (**109**), 2,2-diphenyl-1-picrylhydrazyl (DPPH) was inhibited at a rate of approximately 78% at a concentration of 80 µM (Ribeiro *et al*., 2005). The absence of phenolic hydroxyls in the latter renders them less effective in promoting DPPH reduction, therefore appearing as poor radical scavengers. The free radical scavenging activity of flavonoids and other phenols is mostly due to their aromatic hydroxy groups, which confer great stability to the phenolic radical as soon it is formed, after one hydrogen radical donation to DPPH. The stronger activity of compound is probably due (also) to its extended conjugation through the α,β-unsaturated carbonyl system on the C ring, which are some of the major structural features associated with antioxidant activity of flavonoids (Ribeiro *et al*., 2005). In some cases metal chelation properties have also been proposed.

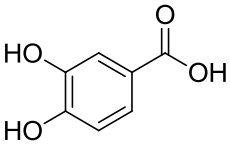
Other secondary metabolites isolated from the genus Nectandra: xanthones, phenolic acids, polyalcohols, alkene-alkynes, lactones, coumarins, benzophenones, and chromane

The only species within the genus *Nectandra* from which xanthones [corresponding to lichexanthone compound (**113**)] have been isolated is *N. rubra* (bark) (De Carvalho *et al*., 1986). Otherwhile, phenolic acids and polyalcohols, such as protocatechuic acid (**114**), piperonylic acid (**115**), and dulcitol (**116**), have been reported in *N. grandiflora* (leaves) and *N. amazonum* (fruits and calyces) (Barbosa-Filho *et al*., 1989; Ribeiro *et al*., 2005).

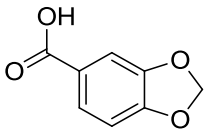
Whereas the alkene and alkinic compounds in *N. rubra* (bark) consist of the rubrenolide [(2*S*,4*R*)-2-[(2'*S*)-2',3'-dihydroxypropyl]-4-(dec-9"-enyl)-γ-lactone] (**117**) and rubrynolide [(2*S*,4*R*)-2-[(2'*S*)-2',3'-dihydroxypropyl]-4-(dec-9"- ynyl)-γ-lactone] (**118**) (Franca *et al*., 1977, Gottlieb, & Coxon, 1977; Garcez *et al*., 2009), have been reported, which may be derived as biosynthetic variants upon the acetate-malonate route to saturated fatty acids (Franca *et al*., 1972). Xanthones with moderate *in vitro* activity against several strains of *P. falciparum* have been reported (Bero *et al*., 2009). Lactones and coumarins have been identified in *N. gardneri*, including isolancifolide (**119**), fraxidin (**120**), fraxidin-8-*O*-β-D-glucopyraniside (**121**) and scopoletin (**122**) (Garcez *et al*., 1999) and benzophenones in *N. coto*, such as: cotoin (123), hydrocotoin (124), methyl hydrocotoin (125), protocotoin (126) and methyl protocotoin (127) (Seil, 1922). It has not been reported biological activity for these secondary metabolite found in the genus *Nectandra*.



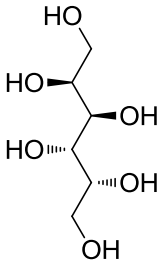
(**113**)



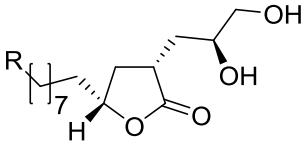
(**114**)



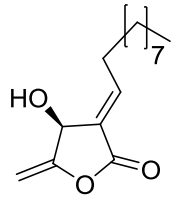
(**115**)



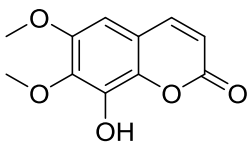
(**116**)



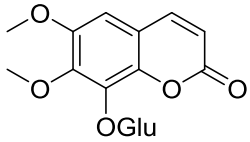
	R
117	$H_2C{=}{=}CH$
118	$HC{\equiv}CH$



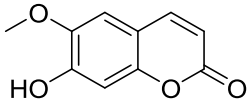
(**119**)



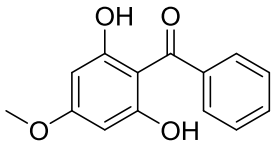
(**120**)



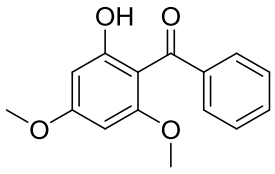
(**121**)



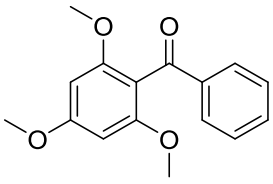
(**122**)



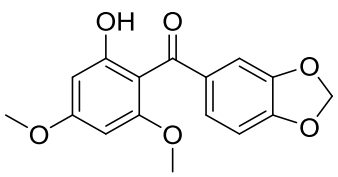
(**123**)



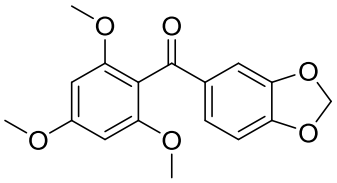
(**124**)



(**125**)



(**126**)



(**127**)

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