Nor-Lignans: Occurrence in Plants and Biological Activities - A Review

Claudio Frezza[a,*], Alessandro Venditti[b,*], Chiara Toniolo[a], Daniela De Vita[a], Marco Franceschin[b], Antonio Ventrone[a], Lamberto Tomassini[a], Sebastiano Foddai[a], Marcella Guiso[b], Marcello Nicoletti[a], Mauro Serafini[a], Armandodoriano Bianco[b,*]

a) Dipartimento di Biologia Ambientale: Università di Roma "La Sapienza", Piazzale Aldo Moro 5 - 00185 Rome (Italy)
b) Dipartimento di Chimica: Università di Roma "La Sapienza", Piazzale Aldo Moro 5 - 00185 Rome (Italy)

[*] Correspondence: claudio.frezza@uniroma1.it; alessandro.venditti@gmail.com; armandodoriano.bianco@uniroma1.it

Abstract

In this review article, the occurrence of *nor*-lignans and their biological activities are explored and described. *Nor*-lignans have proven to be present in several different families also belonging to chemosystematically distant orders as well as to have many different beneficial pharmacological activities. This review article represents the first one on this argument and is thought to give a first overview on these compounds with the hope that their study may continue if not raise after this.

Keywords: *Nor*-lignans, occurrence in plants, biological activities

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1. Introduction

A large part of secondary plant phenolic natural products derives from the aromatic amino acids couple tyrosine/phenylalanine. The de-amination of these compounds gives raise trough the shikimic acid pathway, to the intermediate metabolites C(6)-C(3), propenyl-phenols and allyl-phenols, generally named as phenylpropanoids. These are the starting points for the biosynthesis of several classes of active constituents related to the stability of the cell wall and to the defence of plants against herbivorous animals and pathogens. The first line of defence in terrestrial plants is a mechanical one, related to a polymerization process which leads to the formation of lignin, the main component of wood. Lignin is a very strong and stable macromolecule. Its introduction inside the plant cell wall instead of the carbohydrate polymer cellulose, confers force and resistance, allowing the formation of giant tree's structure and making the digestions oftheadult parts of the plant from herbivorous animals very difficult. Yet, lignin defence line has resulted to be quite insufficient in many casesandthe incoming predominance of herbal species determined the shift towards another form of defence, i.e. the chemical one. Indeed, phenylpropanoids pathway has never been dismissed, but rather it has turned to the synthesis of new smaller products having more precise targets. Among these new molecules, the dimerization process gives rise to three important classes of natural secondary metabolites: lignans, *neo*-lignans and *nor*-lignans. These present similar features due to their common biosynthetic origin. Their general structure is characterized by the presence of two terminal phenyl groups, which are more or lessfunctionalizedwith hydroxyl groups and connected by a central chain of six carbon atoms, differently arranged and oxidized. The main difference among lignans, *neo*-lignans and *nor*-lignans is due to the different type of junction between the two C(6)C(3) (= PhC3) units. In particular, in lignans this junction is through a β-β (8-8′) bond and in *neo*-lignans the junction is not a β-β type. Therefore, lignans and *neo*-lignans, and their several different derived subclasses, can be identified depending upon the carbon skeletons which they possess. For what concerns *nor*-lignans, the structure is more complicated. In fact, *nor*-lignans own a peculiar characteristic, with respect to lignans and *neo*-lignans, which is the cut of one carbon from the central chain. This loss forces this chain to be differently arranged from lignans and *neo*-lignans, such as in linear sequence or C(3)C(2) arranged meaning 8,9'-coupling and 7',8-coupling or alternatively in the bis-*nor*-lignan and cyclo-*nor*-lignan skeletons (8,8') where chirality plays a central role. From this description, it is quite easy to understand the other definition of the structure of *nor*-

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lignans i.e. natural compounds based on diphenyl-pentanes, derived by the union of two phenylpropanoid units in the positions α, β' or β, γ' and characterized with the loss of the terminal carbon of thechain [1-3].

Figure 1 shows the possible different arrangements for *nor*-lignans.

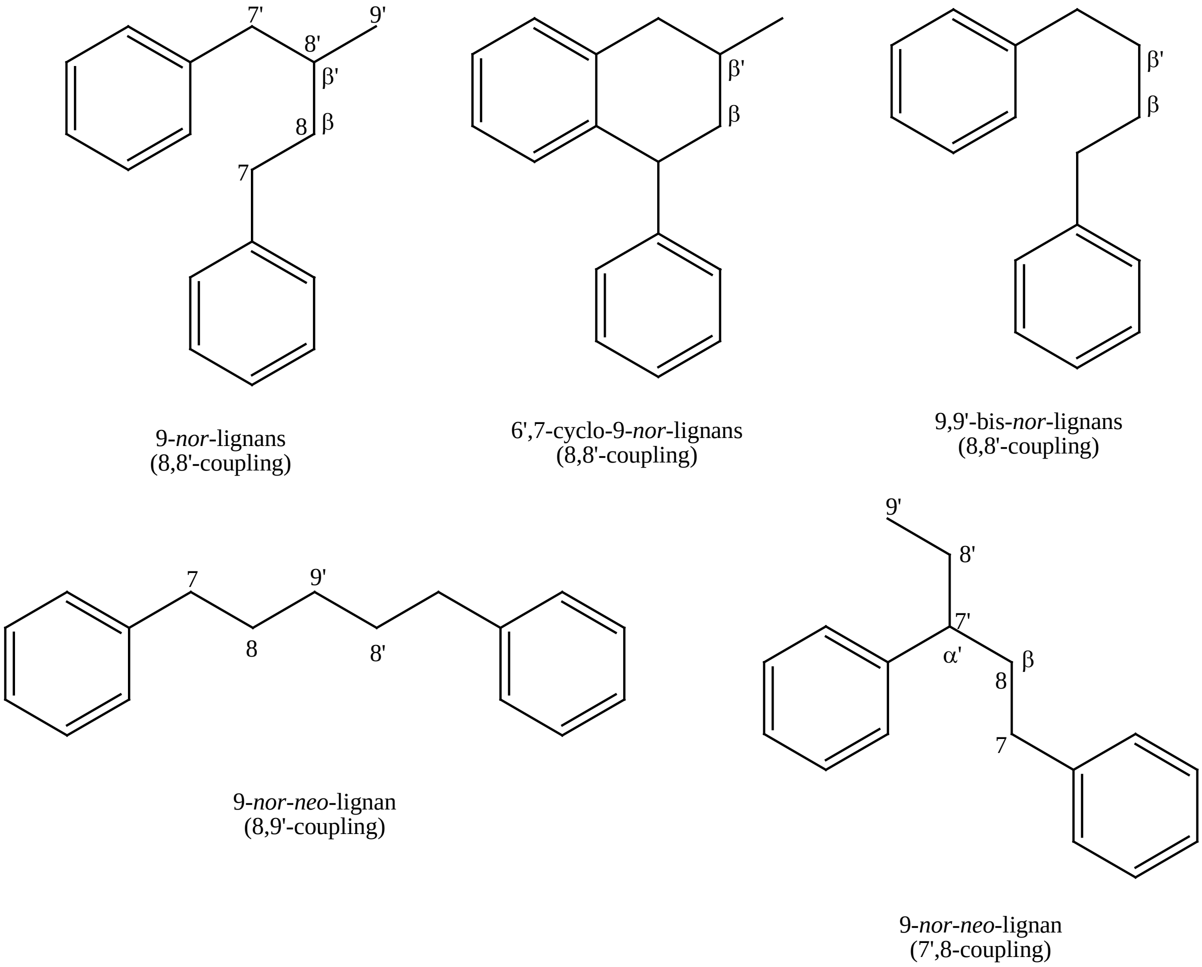

Figure 1: Overview on the general *nor*-lignanbasic structures

2. Occurrence of *nor*-lignans in the plant kingdom

From the environmental and taxonomical points of view, lignans are mainly biosynthesized in woody plants, since main occurrences are related to Gymnospermae and Angiospermae. In particular, they can be found in the trees' members of ancient forests like the Amazonian one, but, probably because of their simple biosynthetic pathway, they can be present also in herbal plants like those of monocotyledons.

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In this review article, the attention is focused on *nor*-lignans, their occurrence in the plant kingdom and their importance as bioactive molecules.

Table 1 reports on the *nor*-lignans identified in the plant kingdom differentiating them according to the species, genus and family. In addition, the organs from which these compounds have been isolated, and the techniques used for their isolation and identification were completely added.

Family	Species	Studied organs	Compounds	Methods	References
Acanthaceae	*Justicia patentflora* Hemsl.	Leaves and stems	justiflorinol	SE, CC, HPLC, $[\alpha]_D$, UV, IR, NMR, MS	[4]
Acoraceae	*Acorus tatarinowii* Schott	Rhizomes	(+)-acortatarinowin A, (+)-acortatarinowin B, (+)-acortatarinowin C, (-)-acortatarinowin A, (-)-acortatarinowin B, (-)-acortatarinowin C	SE, CC, HPLC, ECD, $[\alpha]_D$, UV, IR, NMR, MS	[5]
			acorusin B	SE, CC, $[\alpha]_D$, UV, IR, NMR, MS	[6]
Annonaceae	*Duguetia confinis* (Engl. & Diels) Chatrou	Bark	pachypostaudin A, pachypostaudin B	SE, CC, TLC, NMR,MS	[7]
	*Pachypodanthium staudlii (*Engl. & Diels) Engl. &Diels	Bark	pachypostaudin A, pachypostaudin B, pachypophyllin	SE, MP, NMR, MS	[8]
Araucariaceae	*Araucaria angustifolia* (Bertol.) Kuntze	Knotresin	2,3-*bis*-(*p*-hydroxyphenyl)-2-cyclopentene-1-one, nyasol, cryptoresinol	SE, CC, HPLC, TLC, UV, IR, NMR, MS	[9]
Asparagaceae	*Anemarrhena asphodeloides* Bunge	Rhizomes	nyasol, 4'-*O*-methyl-nyasol, 1,3-di-*p*-hydroxyphenyl-4-penten-1-one	SE, CC, LC, $[\alpha]_D$, NMR, MS	[10, 11]
			nyasol, 4′-O-methyl-nyasol, 3″-methoxy-nyasol, 3″-hydroxy-4″-methoxy-4″-dehydroxy-nyasol	SE, CC, NMR, MS	[12]
			nyasol	SE, CC, HPLC, UV, NMR, MS	[13]
	Asparagus africanus Lam.	Roots	nyasol	CC, LC, HPLC, NMR, MS	[14]
	Asparagus cochinchinensis (Lour.) Merr.	Roots	*iso*-agatharesinoside, *iso*-agatharesinol	SE, CC, $[\alpha]_D$, UV, IR, NMR, MS	[15]
		Tubers	nyasol	SE, CC, $[\alpha]_D$, IR, NMR, MS	[16]
		Roots	3'-hydroxy-4'-methoxy-4'-dehydroxy-nyasol, nyasol, 3'-methoxy-nyasol, 1,3-*bis*-di-*p*-hydroxyphenyl-4-penten-1-one, asparenydiol, 3″-methoxy-asparenydiol	SE, CC, $[\alpha]_D$, UV,IR, NMR, MS	[17]
	Asparagus gobicus N.A.Ivanova ex Grubov	Roots	3′-methoxy-nyasin, *iso*-agatharesinol, gobicusin A, gobicusin B, nyasol, 4-[5-(4-methoxyphenoxy)-3-penten-1-ynyl]phenol, sequirinC	SE, CC, $[\alpha]_D$, UV, IR, NMR, MS	[18]
	*Asparagus racemosus*Willd.	Whole plant	*iso*-agatharesinol, gobicusin A	SE, CC, NMR, MS	[19]
	Drimiopsis burkei Baker	Bulbs	(-)-nyasol	SE, CC, $[\alpha]_D$, NMR	[20, 21]
	Drimiopsis maculata Lindl.	Bulbs	(-)-(*E*)-1,3-bis(4-	SE, CC, $[\alpha]_D$,	[20]

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	&Paxton		hydroxyphenyl)-1,4-pentadiene	NMR	
	Ledebouria ovatifolia (Baker) Jessop	Whole plant	5-((*S*,*Z*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-yl)-2,3-dimethoxyphenol	n.r.	[21]
	Rhodocodon campanulatus H. Perrier	Bulbs	(7*S*,8'*R*)-3,3'-dimethoxy-4,4'-diacetoxy-7'-ketolignano-9,9'-lactone	SE, CC, $[\alpha]_D$, ECD, IR, NMR, MS	[22]
Berberidaceae	*Dysosma versipellis* (Hance) M.Cheng	Roots	dysosmanorlignan A, dysosmanorlignan B	SE, CC, HPLC, TLC,$[\alpha]_D$, IR, UV, NMR, MS	[23]
Brassicaceae	*Descurainia sophia* (L.) Webb ex Prantl	Roots	descuraic acid	SE, LC, CC, $[\alpha]_D$, NMR, MS	[24]
Compositae	*Saussurea macrota* Franch	Whole plant	egonol	SE, CC, TLC, $[\alpha]_D$, IR, NMR, MS	[25]
Cucurbitaceae	*Herpetospermum pedunculosum* (Ser.) C.B. Clarke	Whole plant	herpetone	SE, CC, HPLC, IR, UV, NMR, MS	[26]
Cupressaceae	*Chamaecyparis formosensis* Matsum.	Wood	yateresinol, nyasol	SE, CC, UV, IR, NMR	[27]
	Chamaecyparis obtusa var. *formosana* (Hayata) Hayata	Heartwood	chamaecypanone C, obtunorlignan A	SE, CC, $[\alpha]_D$, UV, IR, NMR, MS	[28]
		Wood	*trans*-nyasol	SE, $[\alpha]_D$, MP, IR, MS	[29]
	Cryptomeria japonica (Thunb. ex L.f.) D.Don	Whole plant	agatharesinol	IM	[30]
		n.a.	yateresinol	n.a.	[31]
	Libocedrus yateensis Guillaumin	Heartwood	yateresinol, nyasol	SE, CC, $[\alpha]_D$, IR, NMR, MS	[32]
	Metasequoia glyptostroboides Hu&W.C.Cheng	Stems and leaves	metasequirin D, metasequirin E, metasequirin F, sequosempervirin B, sequosempervirin D, sequosempervirin F, agatharesinol, agatharesinol acetonide, sequirin C, nyasol	SE, CC, LC, HPLC, $[\alpha]_D$,IR, NMR, MS	[33]
		Branches and stems	metasequirin G, metasequirin H, metasequirin I	SE, CC, LC, HPLC, $[\alpha]_D$, UV, IR, NMR, MS	[34]
	Sequoia sempervirens (D.Don) Endl.	Branches and leaves	sequosempervirin B, sequosempervirin C, sequosempervirin D, sequosempervirin E, sequosempervirin F, sequosempervirin G, agatharesinol, agatharesinolacetonide, sugiresinol	SE, CC, $[\alpha]_D$, UV, NMR, MS	[35]
		Heartwood	sugiresinol, sequirin B, sequirin C, sequirin D, dimethyl-agatharesinol	SE, CC, LC, NMR, MS	[36]
	Sequoiadendron giganteum (Lindl.) J.Buchholz	Heartwood	sequirin E, sequirin F, sequirin G, agatharesinol, dimethyl-agatharesinol, dimethyl-agatharesinol acetonide	SE, CC, TLC, NMR, MS	[36]
	Taxodium ascendens Brongn.	Leaves and branches	(2*R*,3*R*,4*S*,5*S*)-2,4-bis(4-hydroxyphenyl)-3,5-dihydroxy-tetrahydropyran, sequosemperverin B, agatharesinol, cryptoresinol	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[37]
	Taxodium distichum var. *imbricatum* (Nutt.) Croom	Leaves and branches	taxodascendin, cryptoresinol, sequosempervirin B, agatharesinol	SE, CC, NMR, IR, UV, MS	[38]

Hypericaceae	*Hypericum chinense* L.	Leaves	hyperione A, hyperione B	SE, CC, $[\alpha]_D$,IR, NMR, MS	[39]
Hypoxidaceae	*Curculigo breviscapa* S.C.Chen	Rhizomes	breviscapin C, breviscaside B, curcapital, capituloside, pilosidine, cucapitoside, crassifoside H, crassifoside F	SE, CC, LC, $[\alpha]_D$,IR, UV, NMR, MS	[40]
	Curculigo capitolata (Lour.) Kuntze	Rhizomes	(2*S*)-1-*O*-butyl-*iso*-nyasicoside, (2*S*)-1-*O*-butyl-nyasicoside, nyasicoside, 3″-dehydroxy-nyasicoside, 1-*O*-methyl-nyasicoside, curlignan	SE, CC, IR, UV, CD, NMR, MS	[41]
			capituloside, curculigenin, *iso*-curculigenin, curculigine,*iso*-curculigine, 1-*O*-methyl-curculigine, 1-*O*-methyl-*iso*-curculigine	SE, TLC, CC, IR, UV, NMR, MS	[42]
			crassifoside I, sinensigenin C, 1,1-*bis*-(3,4-dihydroxyphenyl)-1-(2-furan)-methane, crassifogenin B, crassifoside A, breviscaside A, crassifoside D, curcapital	SE, CC, $[\alpha]_D$,IR, UV, NMR, MS	[43]
	Curculigo crassifolia (Baker) Hook.f.	Rhizomes	crassifogenin C, curcapital, crassifoside E, crassifoside F	SE, CC, IR, UV, NMR, MS	[44]
			1-*O*-methyl-nyasicoside, 1-*O*-methyl-*iso*-nyasicoside, (1*R*)-crassifogenin D, (1*S*)-crassifogenin D	SE, CC, LC, $[\alpha]_D$,IR, UV, NMR, MS	[45]
			crassifogenin A, crassifogenin B, crassifoside A, crassifoside B	SE, CC, $[\alpha]_D$,IR, UV, NMR, MS	[46]
	Curculigo pilosa (Schumach. &Thonn.) Engl.	Rhizomes	nyasicoside, curculigine, pilosidine	SE, CC, $[\alpha]_D$,IR, UV, NMR, MS	[47, 48]
	Curculigo recurvata W.T.Aiton	Rhizomes	curculigine, *iso*-curculigine, 1-*O*-methyl-curculigine, 1-*O*-methyl-*iso*-curculigine, nyasicoside	SE, CC, CE, CD, NMR, MS,	[49, 50]
	Curculigo sinensis S.C.Chen	Rhizomes	sinensigenin A, sinensigenin B, crassifogenin B, cucapitoside, crassifoside B, crassifoside H, curculigine, *iso*-curculigine	SE, CC, LC, $[\alpha]_D$, IR, UV, NMR, MS	[51]
			sinenside A, sinenside B, crassifoside D, capituloside, 1-*O*-methyl-nyasicoside, 1-*O*-methyl-*iso*-nyasicoside, 1-*O*-methyl-curculigine, 1-*O*-methyl-*iso*-curculigine	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[52]
	Hypoxis angustifolia Lam.	Rhizomes	nyasol, hypoxoside, nyasosidenyaside, mononyasine A, mononyasine B	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[53]
	Hypoxis hemerocallidea Fisch., C.A.Mey. &Avé-Lall.	Rhizomes	hypoxoside, dehydroxy-hypoxoside, *bis*-dehydroxy-hypoxoside, rooperol, dehydroxy-rooperol, *bis*-dehydroxy-rooperol	SE, HPLC, LC, UV, NMR, MS	[54]
	Hypoxis interjecta Nel	Rhizomes	interjectin	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[55]
	Hypoxis multiceps Buchinger ex Baker	Rhizomes	interjectin	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[55]
	Hypoxis nyasica Baker	Rhizomes	nyasicoside, mononyasine A, mononyasine B, nyaside, hypoxoside, nyasoside	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[56-58]

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	Hypoxis obtuse Burch. ex Ker Gawl.	Rhizomes	hypoxoside	SE, CC, NMR, MS	[59]
			rooperol. obtuside A, obtuside B	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[60]
Jungermanniaceae	*Jungermannia exsertifolia* Stephani	Whole plant	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene, 3-carboxy-6,7-dihy-droxy-1-(3',4'-dihydroxyphenyl)-naphthalene-9,5''-*O*-shikimic acid ester	SE, CC, LC, HPLC, $[\alpha]_D$, NMR, MS	[61]
Krameriaceae	*Krameria cytisoides* Cav.	Roots	(2*R*,3*R*)-2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran, (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-3-methyl-5-(E)-propenylbenzofuran , (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxyphenyl)-7-methoxy-3-methyl-5-(*E*)-propenylbenzofuran, conocarpan, rataniaphenol II, eupomatenoid 13, 3-formyl-2-(4-hydroxyphenyl(-7-methoxy-5-(*E*)-propenylbenzofuran, 2-(2,4-dimethoxyphenyl)-5-(*E*)-propenylbenzofuran, rataniaphenol I, toltecol, 2-(4-hydroxyphenyl)-7-methoxy-5-(*E*)-propenylbenzofuran, 2-(2,4-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran, 2-(2,4-dihydroxyphenyl)-7-methoxy-5-(*E*)-propenylbenzofuran, olmecol,3,3'-didemethoxy-nectandrin B, 3'-demethoxy-nectandrin B	SE, CC, TLC, UV, IR, NMR, MS	[62]
	Krameria grayi Rose & Painter	Roots	rataniaphenol I, eupomatenoid 6, 2-(2,4-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran, (*E*)-2-(4-methoxyphenyl)-3-methyl-5-(prop-1-enyl)benzo[b]furan, rataniaphenol III, 2-(2,4-dimethoxyphenyl)-5-(*E*)-propenylbenzofuran, 2-(4-hydroxyphenyl)-5-(*E*)-propenylbenzofuran, 2-(4-hydroxy-2-methoxyphenyl)-5-3-hydroxy-(*E*)-1-propen-1-yl-benzofuran, 2-(2-hydroxy-4-methoxyphenyl)-5-3-hydroxy-(*E*)-1-propen-1-yl-benzofuran, (2*R*,3*R*)-2,3-dihydro-2-(4-methoxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran, (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxyphenyl)-7-methoxy-3-methyl-5-(*E*)-propenylbenzofuran, (+)-licarin A, (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran, 4-(5-((*R*)-2-hydroxypropyl)-3-methylbenzofuran-2-	SE, CC, TLC, IR, UV, NMR, MS	[63]

			yl)phenol		
	Krameria ixine L.	Roots	conocarpan, ratanhiaphenol I, ratanhiaphenol II, 2-(4,6-dimethoxyphenyl-2-hydroxyphenyl)-5-(*E*)-propenylbenzofuran, 2-(4-hydroxyphenyl)-5-((*E*)-prop-2-en-1-yl)benzofuran, 2-(2,4-dihydroxyphenyl)-5-((*E*)-prop-2-en-1-yl)benzofuran, 5-(*E*)-propenyl-2-(2,4,5-trimethoxyphenyl)benzofuran, eupomatenoid15, 5-allyl-2-(4-hydroxyphenyl)-3-methylbenzofuran, hermosillol, 4-2-(5-allyl-2-methoxyphenyl)allyl-phenol, *trans*-(2'*S*)-2-1'-(4-methoxyphenyl)prop-2'-yl-anethol, 3,3'-didemethoxy-nectandrin B	SE, CC, TLC, $[\alpha]_D$,CD, UV, IR, NMR, MS	[64]
	Krameria tomentosa A. St.-Hil.	Roots	krametosan, ratanhiaphenol II, 2-(2′-hydroxy-4′,6′-dimethoxyphenyl)-5-[(*E*)-propenyl]benzofuran, conocarpan, decurrenal(*S*)	SE, CC, $[\alpha]_D$, IR, NMR, MS	[65]
Lamiaceae	*Glechoma longituba* (Nakai) Kuprian.	Whole plant	glechomol A, glechomol B, glechomol C	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[66]
	Tectona grandis L.f.	Leaves	balaphonin, tectonoelin A, tectonoelin B	SE, CC, HPLC, IR, NMR, MS	[67]
	Vitex negundo var. *cannabifolia* (Siebold&Zucc.) Hand.-Mazz.	Fruits	vitrofolal E, vitrofolal F	SE, CC, HPLC, NMR, MS	[68]
		Seeds	6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, vitexdoin A, vitexdoin E, vitexdoin C, vitexdoin D, vitexdoin B, vitexdoin F, vitrofolal A, vitrofolal B, vitrofolal E, vitrofolal F, negundin B, detetrahydro-conidendrin, vitedoin A, negundin B, 4-(3,4-dimethoxyphenyl)-6-hydroxy-5-methoxynaphtho[2,3-c]furan-1(3*H*)-one, 4-(3,4-dimethoxyphenyl)-6-hydroxy-7-methoxynaphtho[2,3-c]furan-1(3*H*)-one, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-7-methoxy-naphtho[2,3-c]furan-1,3-dione, 1,2-dihydro-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-6-methoxy-(1*S*,2*R*)-2-naphthalenecarboxaldehyde, 3,4-dihydro-4-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-6,7-dimethoxy-(3*R*,4*S*)-2-naphthalenecarboxaldehyde	SE, CC, LC, HPLC, $[\alpha]_D$,CD, NMR, MS	[69]
	Vitex negundo L.	Roots	negundin A, negundin B, 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-	SE, CC, TLC, IR, UV, NMR, MS	[70, 71]

			7-methoxy-3,4-dihydro-2-naphthaledehyde, (+)-lyoniresinol, (+)-lyoniresinol 3a-*O*-β-glucopyranoside, vitrofolal E, vitrofolal F		
			negundin A, negundin B, 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaledehyde, (+)-lyoniresinol, (+)-lyoniresinol 3a-*O*-β-glucopyranoside, vitrofolal E	SE, CC, $[\alpha]_D$, IR, UV, NMR, MS	[72]
		Seeds	vitedoin A, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, detetrahydro-conidendrin, vitrofolal E, vitrofolal F, 2α,3β-7-*O*-methyl-cedrusin	SE, CC, $[\alpha]_D$, NMR, MS	[73]
			vitexnegheteroin E, vitexnegheteroin F, vitexnegheteroin G, vitecannaside B, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, vitedoin A, vitexdoin A	SE, CC, $[\alpha]_D$, CD, UV, IR, NMR, MS	[74]
			vitexdoin A, vitexdoin B, vitexdoin C, vitexdoin D, vitexdoin E, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, vitrofolal E, vitrofolal F	SE, CC, LC, $[\alpha]_D$, CD, UV, IR, NMR, MS	[75]
		Aerial parts	vitedoin A, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, 2α,3β-7-*O*-methyl-cedrusin, vitexdoin F, vitexdoin A, (-)-lyoniresinol-3a-*O*-β-D-glucopyranoside, (+)-lyoniresinol-3*a*-*O*-*β*-D-glucopyranoside,vitecannaside B, ovafolinin E, (7*S*,8*R*)-dihydrodehydrodiconiferyl alcohol, vitecannaside C, vitexdoin G	SE, CC, LC, $[\alpha]_D$, UV, IR, NMR, MS	[76]
	Vitex rotundifolia L.f.	Roots	vitrofolal A, vitrofolal B, vitrofolal C, vitrofolal D, vitrofolal E, vitrofolal F, detetrahydro-conidendrin, 4-(3,4-dimethoxyphenyl)-6-hydroxy-5-methoxynaphtho[2,3-c]furan-1(3*H*)-one, 4-(3,4-dimethoxyphenyl)-6-hydroxy-7-methoxynaphtho[2,3-c]furan-1(3*H*)-one	SE, CC, MP, UV, IR, NMR, MS	[77]
Lauraceae	*Nectandra lineata* (Kunth) Rohwer	Young leaves	3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-nor-8,5'-neolignan-9'-acetoxy, 3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-nor-8,5'-neolignan-7,8'-	SE, CC, IR, NMR, MS	[78]

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			diene		
Lepidoziaceae	*Bazzania trilobata* (L.) Gray	Whole plant	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene	SE, CC, HPLC, NMR ,MS	[79]
	Lepidozia incurvata Lindenb.	Whole plant	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene, 3-carboxy-6-methoxy-1-(3',4'-dihydroxyphenyl)-naphthalene-7-*O*-α-L-rhamnopyranoside	SE, CC, LC, HPLC, $[\alpha]_D$, NMR, MS	[61]
	Lepidozia reptans (L.) Dumort.	n.a.	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene	n.a.	[80]
Lophocoleaceae	*Chiloscyphus polyanthos* (L.) Corda	Whole plant	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene, 3-carboxy-6,7-dihydroxy-1-(3',4'-dihydroxy-phenyl)-naphthalene-9,2''-*O*-malic acid ester	SE, CC, LC, HPLC, $[\alpha]_D$, NMR, MS	[80]
Lythraceae	*Sonneratia caseolaris* (L.) Engl.	Fruits	nyasol, 4'-*O*-methyl-nyasol	SE, CC, TLC, NMR, MS	[81]
	Sonneratia ovata Backer	Fruits	nyasol, 4'-*O*-methyl-nyasol	SE, CC, TLC, NMR, MS	[81]
	Trapa natans L.	Whole plant	nyasol	SE, CC, $[\alpha]_D$,IR, NMR, MS	[82]
Magnoliaceae	*Magnolia odora* (Chun) Figlar&Noot.	Twigs	glaberide I, salicifoliol, 6-hydroxy-2-(4-hydroxy-3,5-dimethoxyphenyl)-3,7-dioxabicyclo-[3.3.0]-octane,ficusal, *erythro*-guaiacylglycerol 8'-vanillin ether, *threo*-guaiacylglycerol 8'-vanillin ether	SE, CC, LC, HPLC, NMR, MS	[83]
Meliaceae	*Aglaia cordata* Hiern	Stem barks	aglacin H	SE, CC, HPLC, NMR, MS	[84]
	Cedrela sinensis Juss.	Leaves	cedralin A, cedralin B	SE, IR, UV, NMR, MS	[85]
	Toonasinensis(Juss.) M.Roem.	Roots	toonin C	SE, CC, HPLC, $[\alpha]_D$, IR, NMR, MS	[86]
Oleaceae	*Syringa pinnatifolia* Hemsl.	Stem barks	noralashinol A, vitrofolal E	SE, CC, UV, IR, NMR, MS	[87, 88]
			noralashinol B, noralashinol C	SE, CC, LC, $[\alpha]_D$, UV, IR, ECD, NMR, MS	[89]
Pelliaceae	*Pellia epiphylla* (L.) Corda	Gametophytes	3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene	SE, CC, IR, NMR, MS	[90]
Phyllanthaceae	*Phyllanthus virgatus* G.Forst.	Whole plant	virgatyne	SE, CC, LC, $[\alpha]_D$, UV, NMR, MS	[91]
Piperaceae	*Peperomia tetraphylla* (G.Forst.) Hook. &Arn.	Whole plant	methyl *rel*-(1*R*,2*S*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate, methyl*rel*-(1*R*,2*R*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate	SE, CC, LC, $[\alpha]_D$, UV, IR, CD, NMR, MS	[92]
			peperotetraphin	SE, CC, LC, $[\alpha]_D$, UV, IR, NMR, MS	[93]
	Piper obliquum Ruiz &Pav.	Leaves	justiflorinol	SE, CC, $[\alpha]_D$, UV,IR, NMR, MS	[94]
Poaceae	*Imperata cilindrica* (L.) Raeusch.	Rhizomes	(*S*)-(+)-imperanene	SE, CC, $[\alpha]_D$,	[95]

				NMR, MS	
Saururaceae	*Gymnotheca chinensis* Decne.	Whole plant	gymnothedelignan A, gymnothedelignan B	SE, CC, X-ray, NMR, MS	[96]
Selaginellaceae	*Selaginella moellendorffii* Hieron.	Whole plant	moellenoside B	SE, CC, LC, TLC, $[\alpha]_D$, CD, UV, IR, NMR, MS	[97]
Schisandraceae	*Schisandra bicolor* W.C.Cheng.	Fruits	marphenol C, marphenol D, marphenol E, marphenol F	SE, CC, LC, HPLC, $[\alpha]_D$, UV, IR, NMR, MS	[98]
Solanaceae	*Cestrum diurnum* L.	Leaves	cestrumoside, berchemol-4'-*O*-β-glucopyranoside, dehydrodiconiferyl alcohol-4-*O*-β-glucopyranoside, (+)-lyoniresinol 3a-*O*-β-glucopyranoside, (–)-lyoniresinol 3a-*O*-β-glucopyranoside	SE, CC, $[\alpha]_D$, UV, CD, IR, NMR, MS	[99]
	Cestrum parqui (Lam.) L'Hér.	Leaves	9'-*nor*-3',4,4'-trihydroxy-3,5-dimethoxylign-7-eno-9,7'-lactone	SE, CC, $[\alpha]_D$, NMR,MS	[100]
	Nicotiana tabacum L.	Roots and stems	nicotnorlignan C, recurphenol C, recurphenol D, sequirin C, benzodioxane	n.r.	[101, 102]
		Leaves	nicotnorlignan A, sequirin C, benzodioxane	n.r.	[101]
	Solanum melongena L.	Roots	guaiacylglycerol 8′-vanillin ether, ficusal, polystachyol	SE, CC, HPLC, $[\alpha]_D$, NMR,MS	[103]
Styracaceae	*Styrax campo rum* Pohl	Whole plant	egonol, homoegonol	SE, pTLC, CC, HPLC-UV, NMR	[104]
	Styrax ferrugineus Nees& Mart.	Leaves	egonol, homoegonol, egonol glucoside, homoegonol glucoside	SE, FCC, IR, NMR, MS	[105]
	Styrax japonica Sieb. et Zucc.	Stem bark	styraxlignolide A, egonol, masutakeside I	SE, CC, LC,$[\alpha]_D$, UV, NMR, MS	[106]
	Styrax obassis Sieboldi&Zucc.	Aerial parts	1''-hydroxylegonol gentiobioside, egonol glucoside	SE, CC, LC, NMR, MS	[107]
	Styrax officinalis L.	Fruits	egonol, dimethyl-egonol, homoegonol	SE, CC, NMR, MS	[108]
	Styrax pohlii A. DC.	Aerial parts	egonol, homoegonol, homoegonol gentiobioside, homoegonol glucoside, egonol gentiobioside	SE., CC, HPLC, NMR	[109]
	Styrax ramirezii Greenm.	Fruits	egonol, homoegonol, egonol glucoside, homoegonol glucoside, 7-demethoxy-egonol, 4-*O*-demethyl-homoegonol	SE, HPLC-DAD-MS	[110]
Thelypteridaceae	*Abacopteris penangiana* (Hook.) Ching	Rhizomes	penangianol A, penangianol B	SE, CC, $[\alpha]_D$, UV, IR, NMR, MS	[111]
Urticaceae	*Pouzolzia occidentalis* (Liebm.) Wedd.	Aerial parts	pouzolignan A, pouzolignan B	SE, CC, LC,$[\alpha]_D$, UV,IR, NMR, MS	[112]
	Pouzolzia zeylanica var. *microphylla* (Wedd.) Masam.	Aerial parts	pouzolignan D, pouzolignan K	n.a.	[113]

Table 1: Occurrence of *nor*-lignans in the plant kingdom

Figures (2-24) show the structures of all the identified *nor*-lignans.

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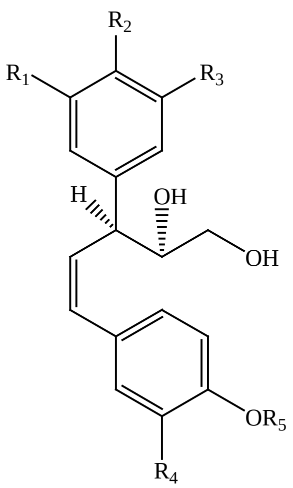
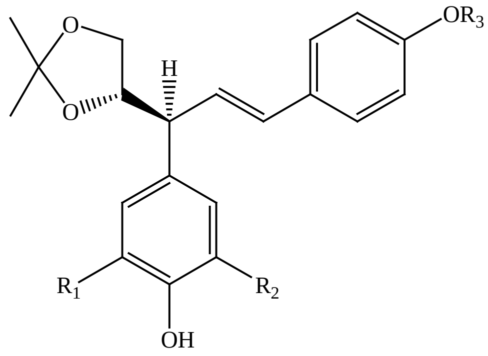
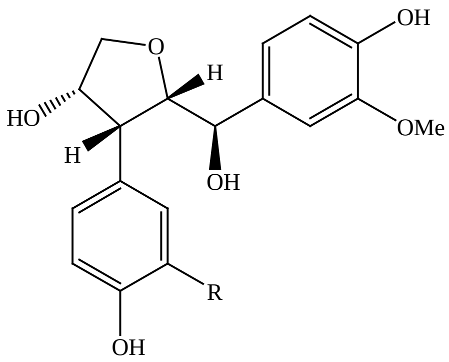


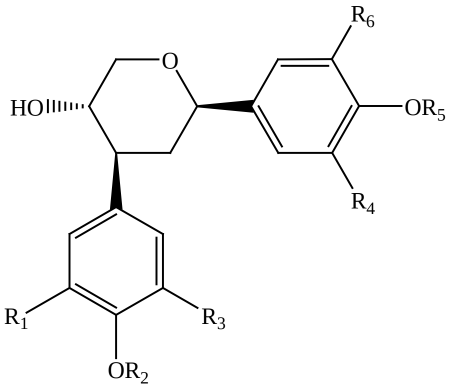
$R_1 = R_4 = R_5 = H$, $R_2 = OH$, $R_3 = OMe$: sequosempervirin B
$R_1 = R_3 = OMe$, $R_2 = OH$, $R_4 = R_5 = H$: sequosempervirin C
$R_1 = R_3 = R_4 = R_5 = H$, $R_2 = OH$: agatharesinol
$R_1 = OMe$, $R_2 = OH$, $R_3 = R_4 = H$, $R_5 = Me$: dimethyl-agatharesinol
$R_1 = R_4 = OMe$, $R_2 = OH$, $R_3 = R_5 = H$: metasesquirin D



$R_1 = R_3 = H$, $R_2 = OMe$: sequosempervirin D
$R_1 = R_2 = OMe$, $R_3 = H$: sequosempervirin E
$R_1 = R_2 = R_3 = H$: agatharesinol acetonide
$R_1 = OMe$, $R_2 = H$, $R_3 = Me$: dimethyl-agatharesinol acetonide



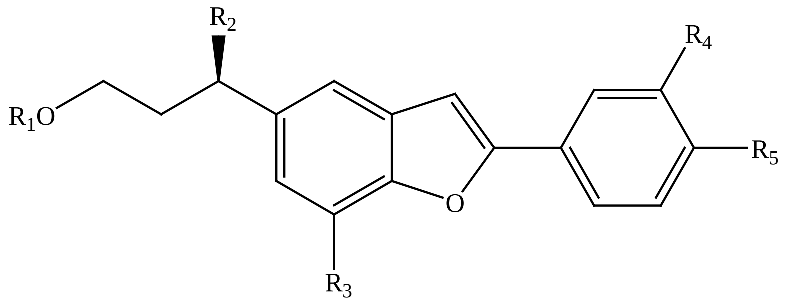
R = OMe: metasesquirin E
R = H: metasesquirin F



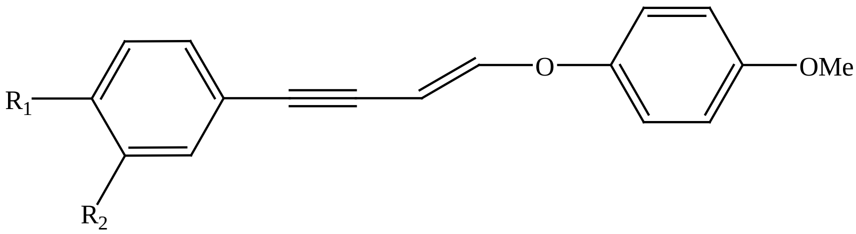
$R_1 = R_2 = R_5 = R_4 = R_6 = H$, $R_3 = OMe$: sequosempervirin F
$R_1 = R_3 = OMe$, $R_2 = R_4 = R_5 = R_6 = H$: sequosempervirin G
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = H$: sugiresinol
$R_1 = R_2 = R_4 = R_5 = R_6 = H$, $R_3 = OH$: sequirin B
$R_1 = R_3 = R_4 = H$, $R_2 = R_5 = Me$, $R_6 = OMe$: sequirin D
$R_1 = R_4 = H$, $R_2 = R_5 = Me$, $R_3 = R_6 = OMe$: sequirin E
$R_1 = R_3 = R_6 = OMe$, $R_2 = R_5 = Me$, $R_4 = H$: sequirin F

Figure 2: Structures of the isolated *nor*-lignans in the plant kingdom - part 1

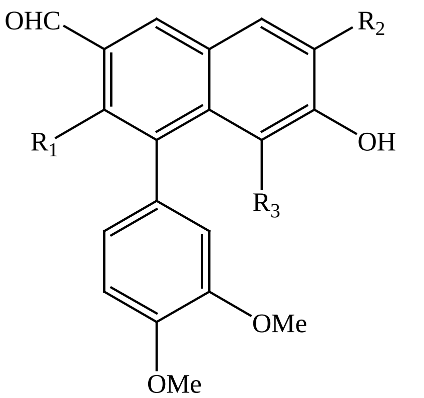
 doi:10.20944/preprints201911.0367.v1



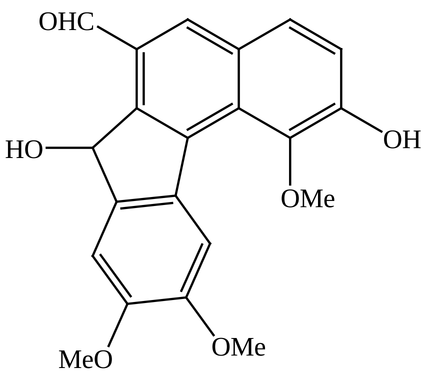
$R_1 = R_2$ = H, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-:egonol
$R_1 = R_2$ = H, R_3 = OMe, $R_4 = R_5$ = OMe: homoegonol
$R_1 = R_2$ = H, R_3 = OH, $R_4 = R_5$ = -O-CH_2-O-: demethyl-egonol
$R_1 = R_2$ = H, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-: 7-demethoxy-egonol
$R_1 = R_2$ = H, $R_3 = R_4$ = OMe, R_5 = OH: 4-*O*-demethyl-homoegonol
R_1 = β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-: egonol glucoside
R_1 = β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = OMe: homoegonol glucoside
R_1 = 6-O-β-D-Glc-β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-: egonol gentiobioside
R_1 = 6-O-β-D-Glc-β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = OMe: homoegonol gentiobioside
R_1 = 6-O-β-D-Xyl-β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = OMe: styraxlignolide A
R_1 = 6-O-β-D-Xyl-β-D-Glc, R_2 = H, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-: masutakeside I
R_1 = 6-O-β-D-Glc-β-D-Glc, R_2 = OH, R_3 = OMe, $R_4 = R_5$ = -O-CH_2-O-: 1''-hydroxylegonol gentiobioside



R_1 = OMe, R_2 = OH: gobicusin B
R_1 = OH, R_2 = H: 4-[5-(4-methoxyphenoxy)-3-penten-1-ynyl]phenol



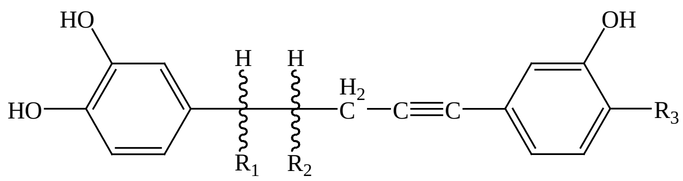
$R_1 = R_2$ = H, R_3 = OMe: vitrofolal A
R_1 = OH, R_2 = H, R_3 = OMe: vitrofolal B



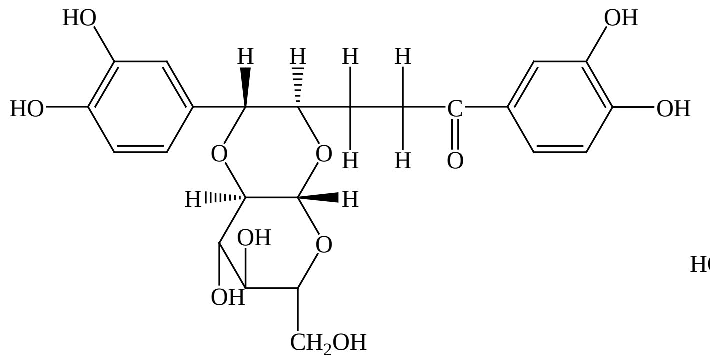
vitrofolal C

Figure 3: Structures of the isolated *nor*-lignans in the plant kingdom - part 2

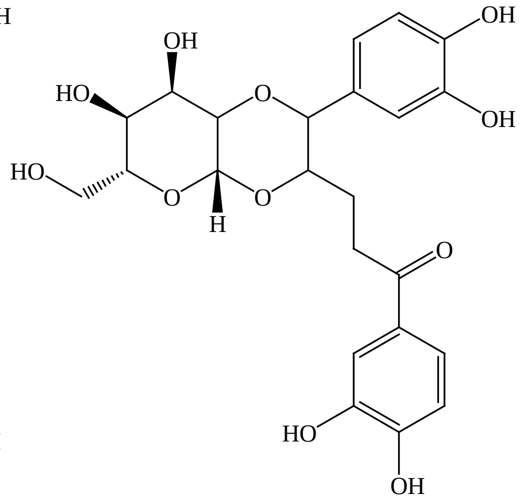
 doi:10.20944/preprints201911.0367.v1



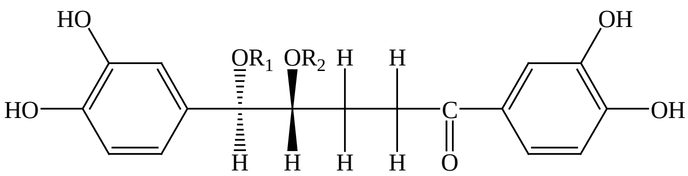
R_1 = (*R*)-OH, R_2 = (*R*)-O-β-D-Glc, R_3 = OH: nyasicoside
R_1 = (*R*)-Obutyl, R_2 = (*S*)-O-β-D-Glc, R_3 = OH: (2*S*)-1-*O*-butyl-*iso*-nyasicoside
R_1 = (*S*)-Obutyl, R_2 = (*S*)-O-β-D-Glc, R_3 = OH: (2*S*)-1-*O*-butyl-nyasicoside
R_1 = (*R*)-OH, R_2 = (*R*)-O-β-D-Glc, R_3 = H: 3"-dehydroxy-nyasicoside
R_1 = (*S*)-OMe, R_2 = (*R*)-O-β-D-Glc, R_3 = OH: 1-*O*-methyl-nyasicoside
R_1 = (*R*)-OMe, R_2 = H, R_3 = OH: (1*R*)-crassifogenin D
R_1 = (*S*)-OMe, R_2 = H, R_3 = OH: (1*S*)-crassifogenin D
R_1 = (*R*)-OMe, R_2 = (*R*)-O-β-D-Glc, R_3 = OH: 1-*O*-methyl-*iso*-nyasicoside
R_1 = (*R*)-OH, R_2 = *p*-hydroxy-cinnamoyl-2-O-β-D-Glc, R_3 = (*R*)-O-β-D-Glc: interjectin



pilosidine



capituloside



R_1 = Me, R_2 = H : curculigenin
R_1 = H, R_2 = β-D-Glc: curculigine
R_1 = Me, R_2 = β-D-Glc: 1-*O*-methyl-curculigine

Figure 4: Structures of the isolated *nor*-lignans in the plant kingdom - part 3

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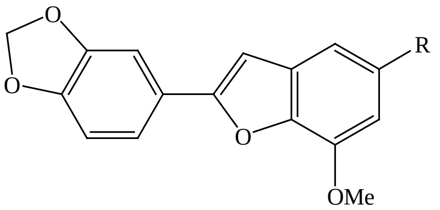
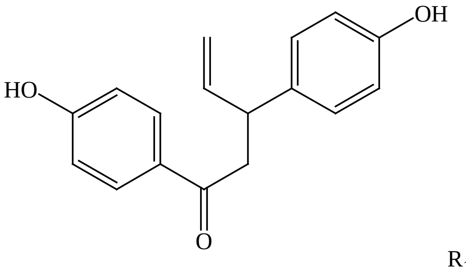
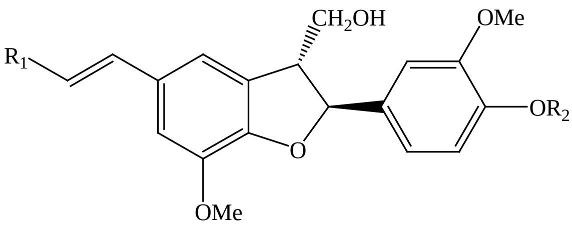


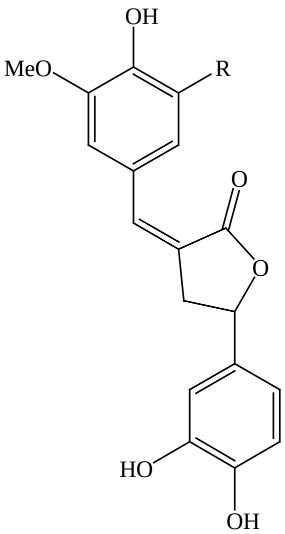
R = $-CH_2CH_2CH_2OCOCH_3$: 3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-*nor*-8,5'-neolignan-9'-acetoxy
R = $-CH_2CHCH_2$: 3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-*nor*-8,5'-neolignan-7,8'-diene



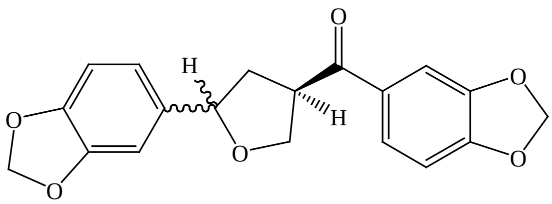
1,3-di-*p*-hydroxyphenyl-4-penten-1-one



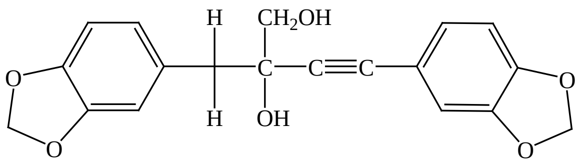
R_1 = CHO, R_2 = H: balaphonin
R_1 = CH_2OH, R_2 = β-D-Glc: dehydrodiconiferyl alcohol-4-*O*-β-glucopyranoside



R = H: tectonoelin A
R = OMe: tectonoelin B



H in *trans* to ketone: hyperione A
H in *cis* to ketone: hyperione B



virgatyne

Figure 5: Structures of the isolated *nor*-lignans in the plant kingdom - part 4

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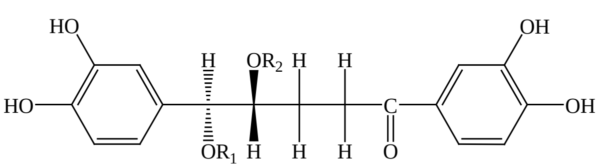
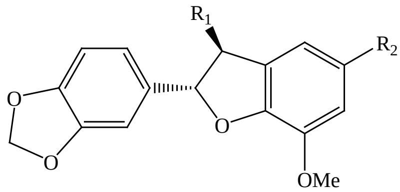
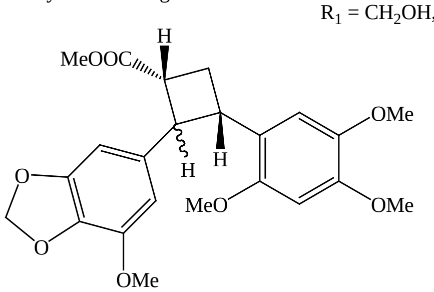


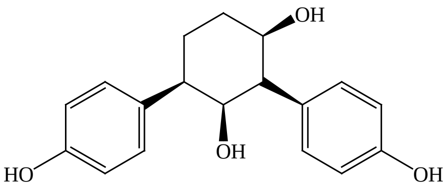
R_1 = Me, R_2 = H : *iso*-curculigenin
R_1 = H, R_2 = β-D-Glc: *iso*-curculigine
R_1 = Me, R_2 = β-D-Glc: 1-*O*-methyl-*iso*-curculigine



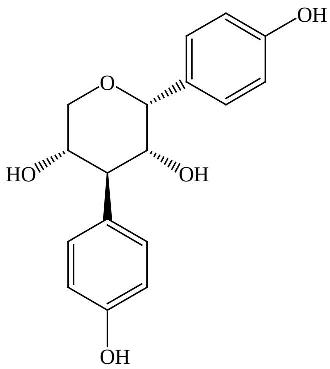
R_1 = COOH, R_2 = CH_2OH: cedralin A
R_1 = COOMe, R_2 = CH_2O-β-D-Glc: cedralin B
R_1 = CH_2OH, R_2 = COOMe: toonin C



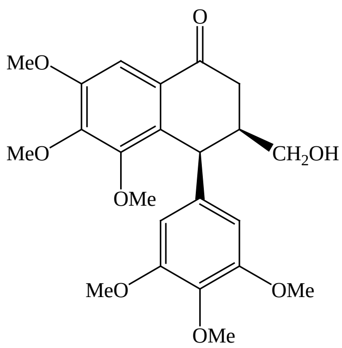
H in *trans* to carboxyl: methyl *rel*-(1*R*,2*S*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate
H in *cis* to carboxyl: methyl *rel*-(1*R*,2*R*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate



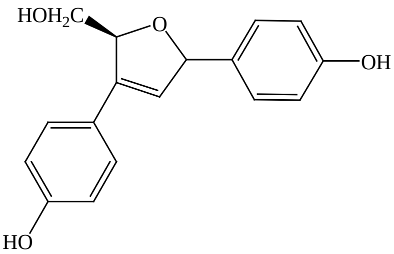
taxodascendin



(2*R*,3*R*,4*S*,5*S*)-2,4-bis(4-hydroxyphenyl)-3,5-dihydroxy-tetrahydropyran

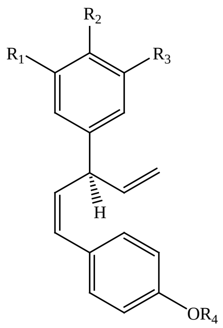


aglacin H

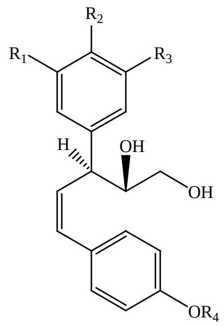


cryptoresinol

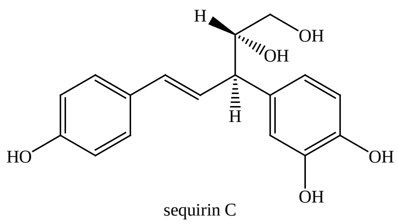
Figure 6: Structures of the isolated *nor*-lignans in the plant kingdom - part 5



$R_1 = R_4 = H$, $R_2 = OH$, $R_3 = OMe$: 3'-methoxy-nyasin
$R_1 = R_3 = R_4 = H$, $R_2 = OH$: nyasol
$R_1 = R_3 = H$, $R_2 = OH$, $R_4 = Me$: 4'-*O*-methyl-nyasol
$R_1 = OH$, $R_2 = OMe$, $R_3 = R_4 = H$: 3'-hydroxy-4'-methoxy-4'-dehydroxy-nyasol
$R_1 = OMe$, $R_2 = OH$, $R_3 = R_4 = H$: 3'-methoxy-nyasol
$R_1 = R_3 = H$, $R_2 = O$-β-D-Glc, R_4 = β-D-Glc: nyasoside
$R_1 = R_3 = R_4 = H$, $R_2 = O$-β-D-Glc: mononyasine A
$R_1 = R_3 = H$, $R_2 = OH$, R_4 = β-D-Glc: mononyasine B
$R_1 = R_3 = H$, $R_2 = O$-α-L-Api-(1-6)-β-D-Glc, R_4 = β-D-Glc: nyaside
$R_1 = R_2 = OMe$, $R_3 = OH$, $R_4 = H$: 5-((*S*,*Z*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-yl)-2,3-dimethoxyphenol

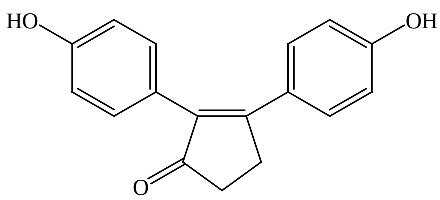


$R_1 = R_3 = R_4 = H$, $R_2 = OH$: *iso*-agatharesinol
$R_1 = OH$, $R_2 = R_4 = H$, $R_3 = OMe$: gobicusin A
$R_1 = R_3 = H$, $R_2 = OH$, R_4 = β-D-Glc: *iso*-agatharesinoside

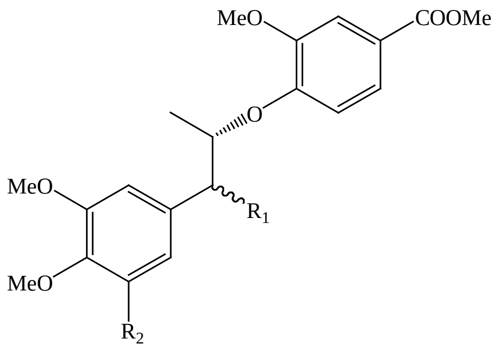


sequirin C

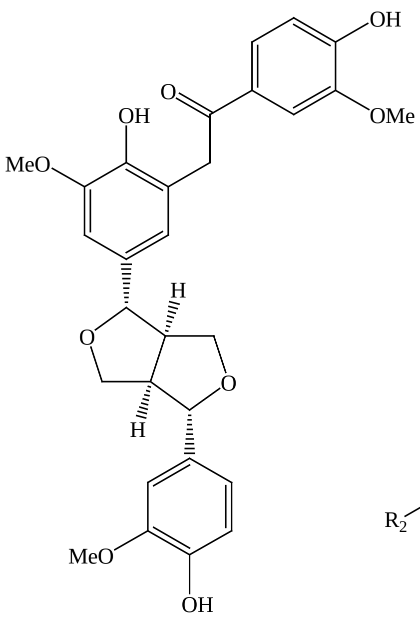
Figure 7: Structures of the isolated *nor*-lignans in the plant kingdom - part 6



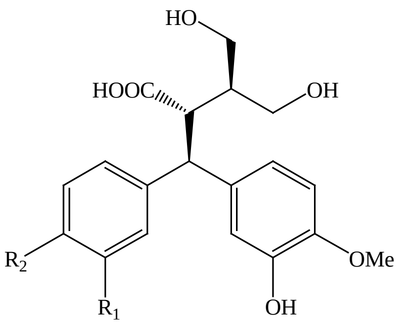
2,3-bis-(*p*-hydroxyphenyl)-2-cyclopentene-1-one



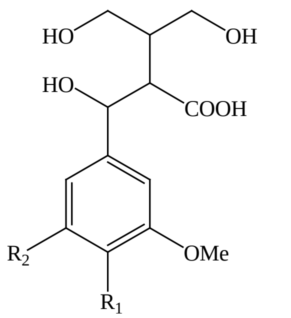
R_1 = (*S*)-OH, $R_2 = H$: (+)-acortatarinowin A
R_1 = (*R*)-OH, $R_2 = H$: (+)-acortatarinowin B
R_1 = (*S*)-OH, $R_2 = OMe$: (+)-acortatarinowin C
R_1 = (*R*)-OH, $R_2 = H$: (-)-acortatarinowin A
R_1 = (*S*)-OH, $R_2 = H$: (-)-acortatarinowin B
R_1 = (*R*)-OH, $R_2 = OMe$: (-)-acortatarinowin C



herpetone



$R_1 = OH$, $R_2 = OMe$: marphenol E
$R_1 = R_2 = -OCH_2O$: marphenol F



$R_1 = OH$, $R_2 = H$: marphenol C
$R_1 = OMe$, $R_2 = OH$: marphenol D

Figure 8: Structures of the isolated *nor*-lignans in the plant kingdom - part 7

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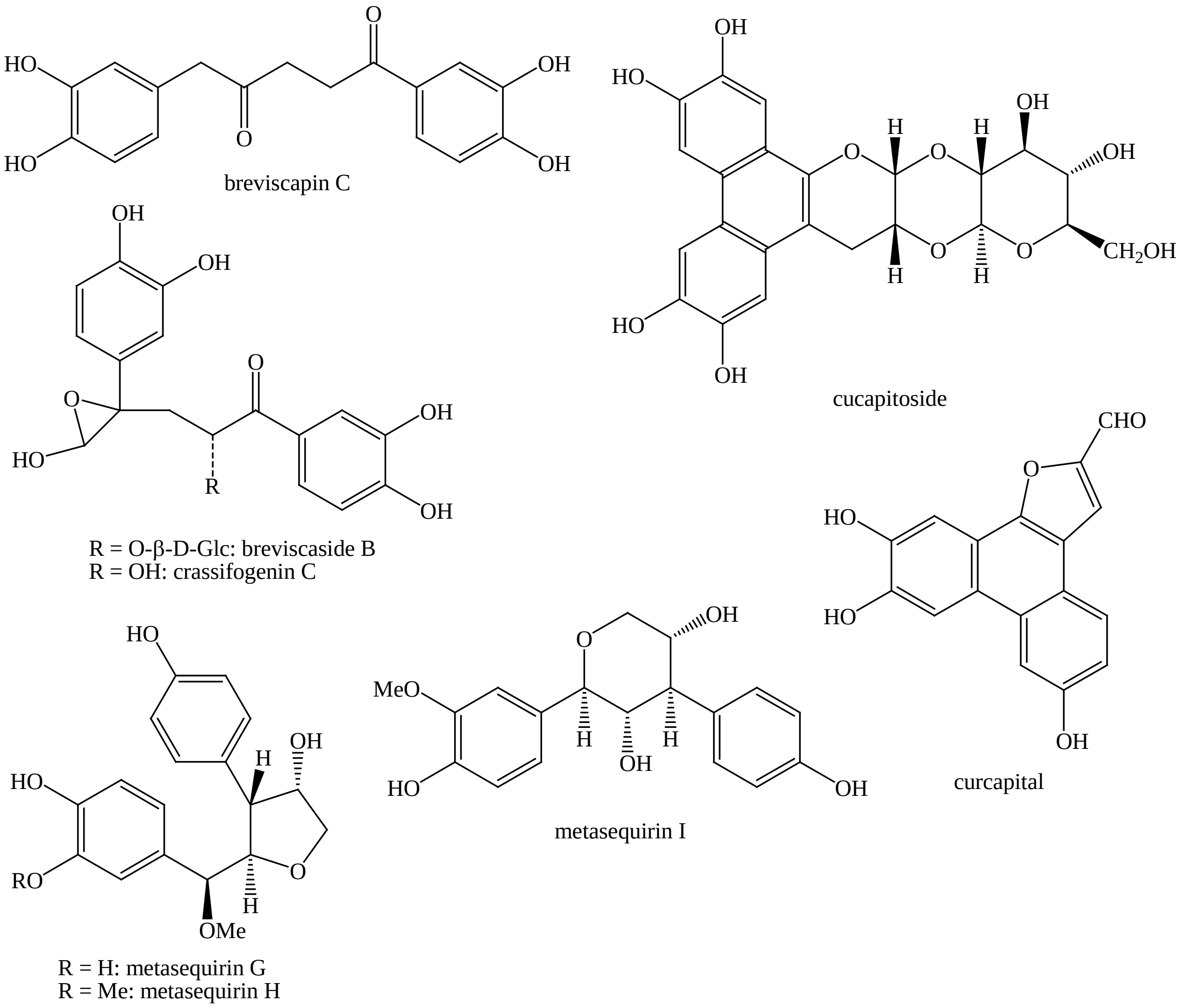
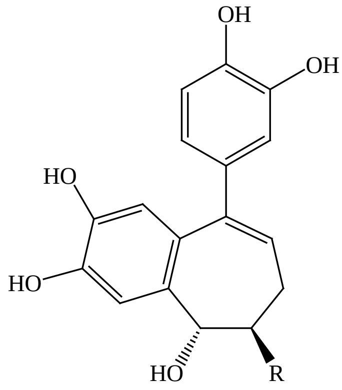
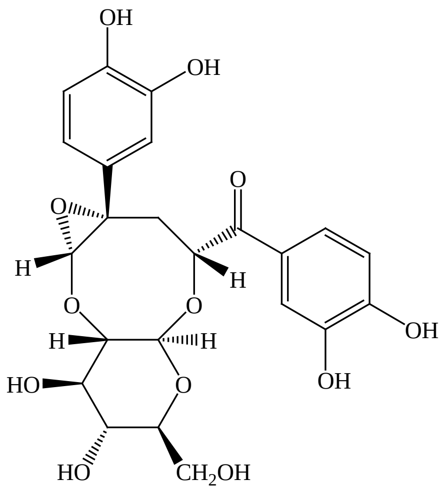


Figure 9: Structures of the isolated *nor*-lignans in the plant kingdom - part 8

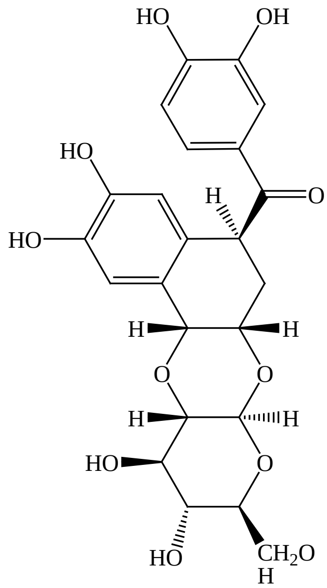
 doi:10.20944/preprints201911.0367.v1



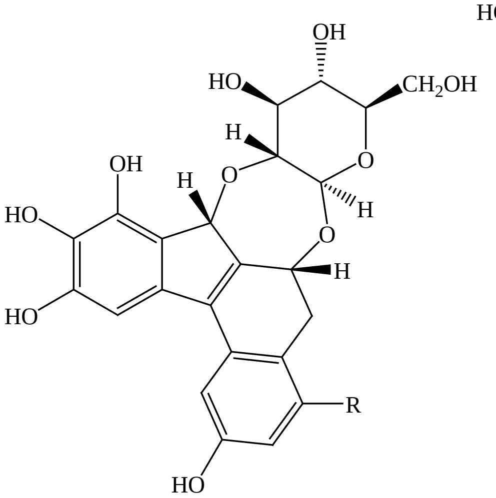
R = O-β-D-Glc: crassifoside D

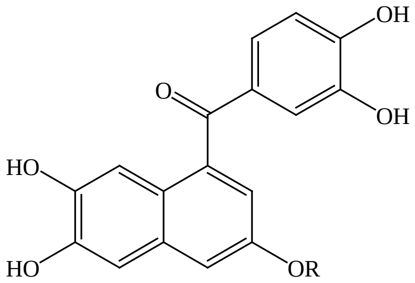


crassifoside F



crassifoside I





R = H: crassifogenin B
R = α-D-Glc crassifoside A

R= Cl: crassifoside H
R = OEt: crassifoside E

Figure 10: Structures of the isolated *nor*-lignans in the plant kingdom - part 9

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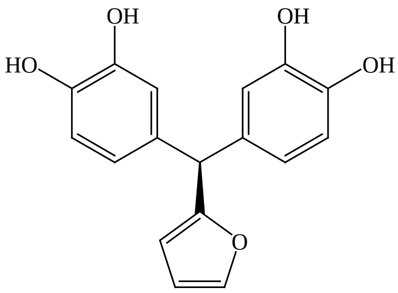
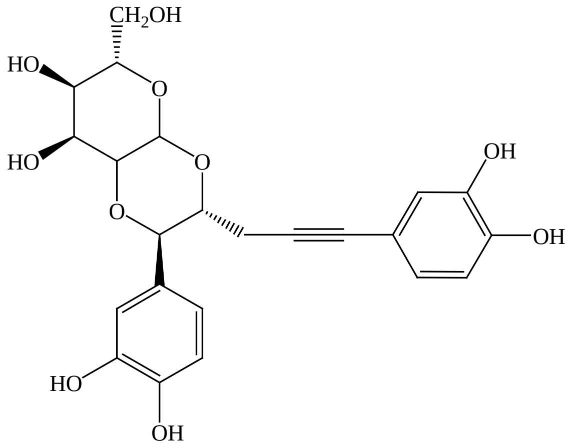
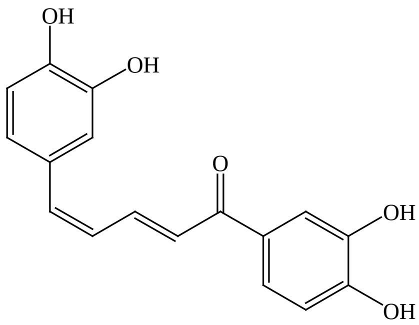


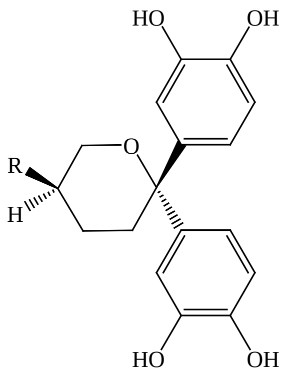
1,1-*bis*-(3,4-dihydroxyphenyl)-1-(2-furan)-methane



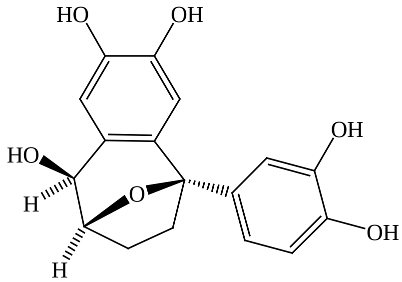
crassifoside B



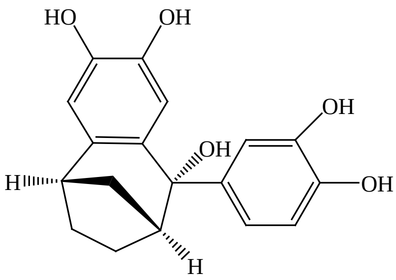
sinensigenin B



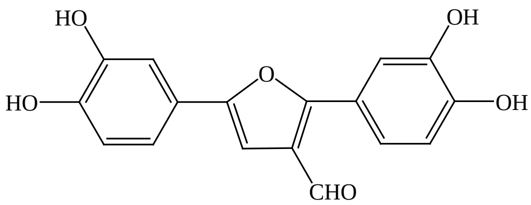
R = O-β-D-Glc: breviscaside A



sinensigenin C



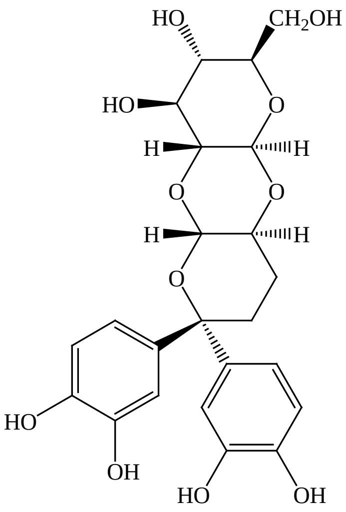
sinensigenin A



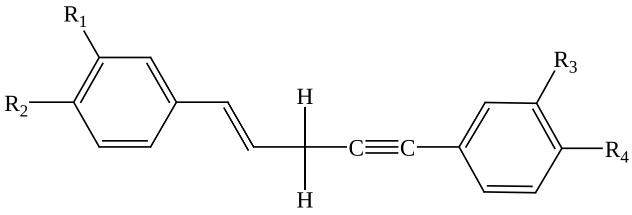
crassifogenin A

Figure 11: Structures of the isolated *nor*-lignans in the plant kingdom - part 10

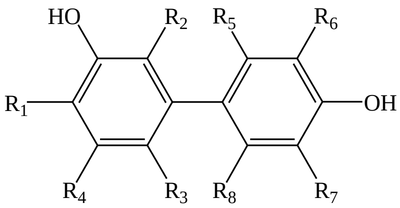
 doi:10.20944/preprints201911.0367.v1



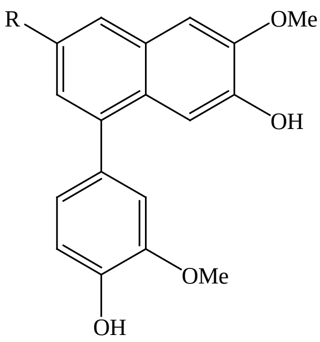
sinenside A



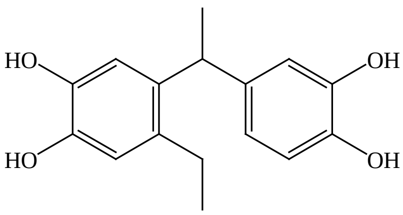
$R_1 = R_3$ = OH, $R_2 = R_4$ = O-β-D-Glc: hypoxoside
R_1 = H, $R_2 = R_4$ = O-β-D-Glc, R_3 = OH: dehydro-hypoxoside
$R_1 = R_3$ = H, $R_2 = R_4$ = O-β-D-Glc: *bis*-dehydro-hypoxoside
$R_1 = R_2 = R_3 = R_4$ = OH: rooperol
R_1 = H, $R_2 = R_3 = R_4$ = OH: dehydro-rooperol
$R_1 = R_3$ = H, $R_2 = R_4$ = OH: *bis*-dehydro-rooperol
$R_1 = R_3 = R_4$ = OH, R_2 = O-β-D-Glc: obtuside A
$R_1 = R_2 = R_3$ = OH, R_4 = O-β-D-Glc: obtuside B



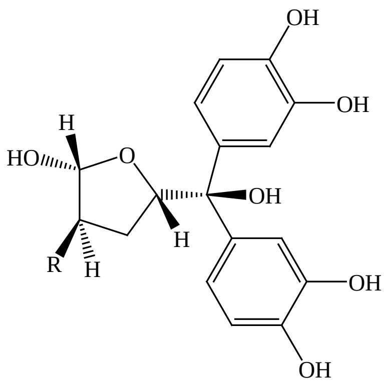
$R_1 = R_3 = R_5 = R_7$ = H, $R_2 = R_6$ = OH, $R_4 = R_8$ = Et: glechomol A
$R_1 = R_7$ = OH, $R_2 = R_4 = R_6 = R_8$ = H, $R_3 = R_5$ = Et: glechomol B



R = $CH(OMe)_2$: noralashinol A
R = CH_2OH: noralashinol C



glechomol C



R = O-β-D-Glc: sinenside B

Figure 12: Structures of the isolated *nor*-lignans in the plant kingdom - part 11

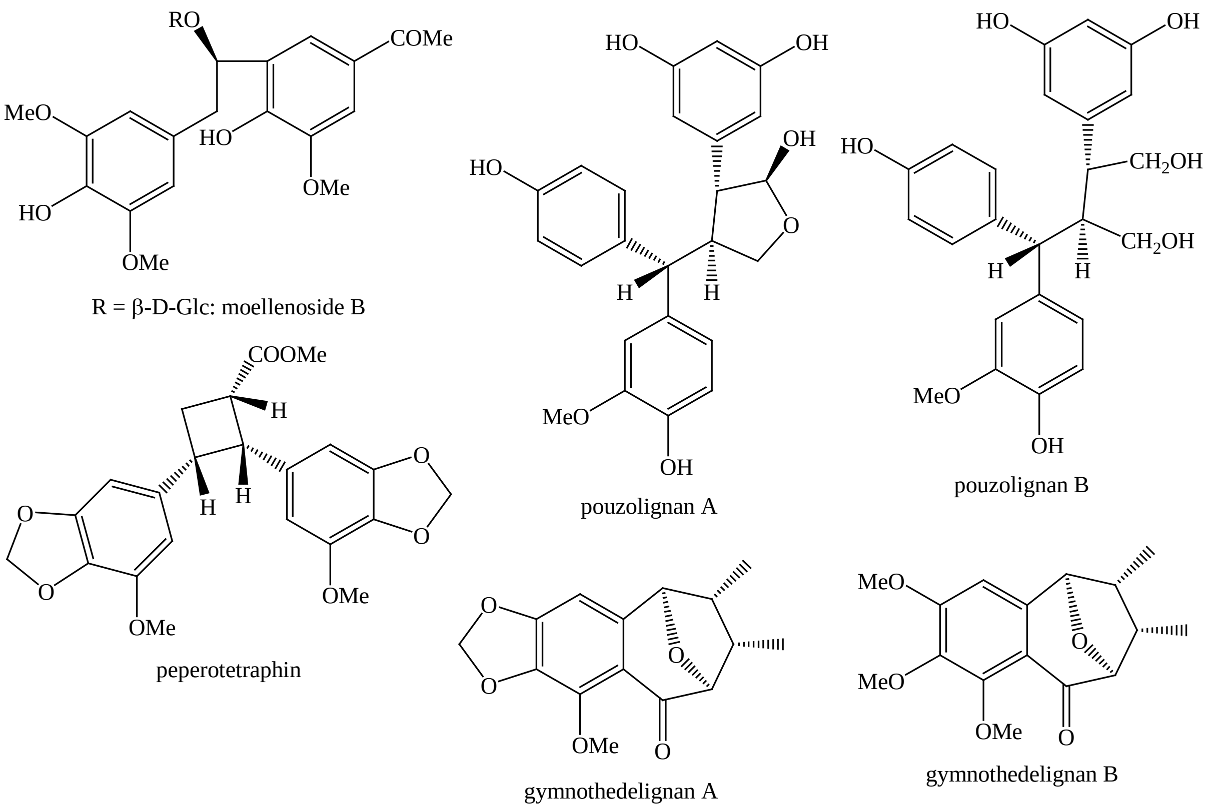
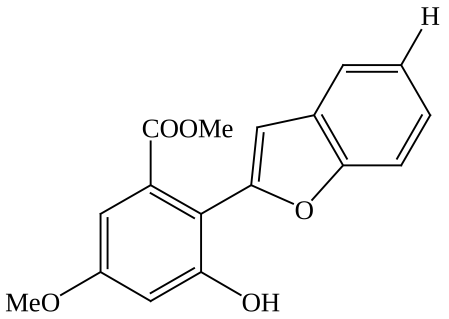
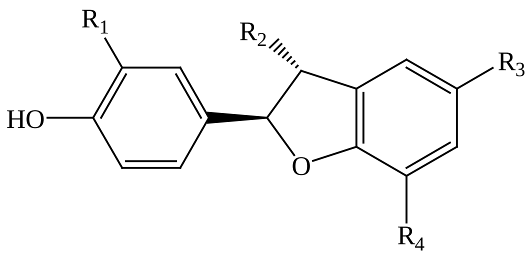


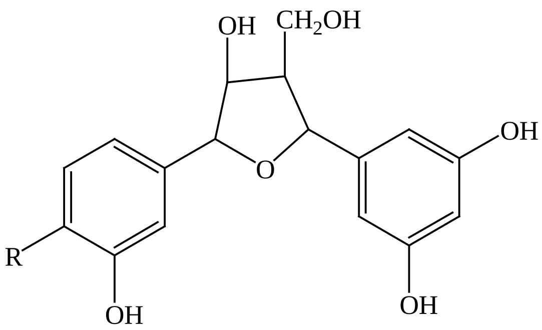
Figure 13: Structures of the isolated *nor*-lignans in the plant kingdom - part 12



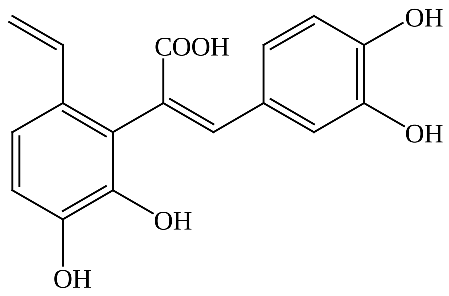
krametosan



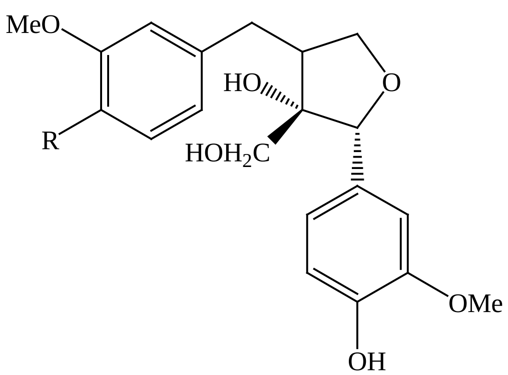
R_1 = R_4 = H, R_2 = Me, R_3 = CHO: decurrenal (*S*)
R_1 = R_4 = OMe, R_2 = CH_2OH, R_3 = COOMe: curlignan



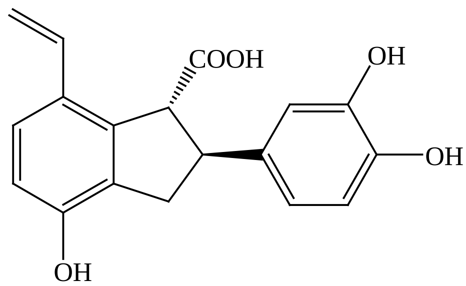
R = O-β-D-Glc: cestrumoside



penangianol B



R = O-β-D-Glc: berchemol-4'-O-β-glucopyranoside



penangianol A

Figure 14: Structures of the isolated *nor*-lignans in the plant kingdom - part 13

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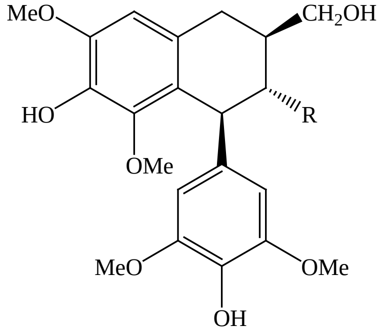
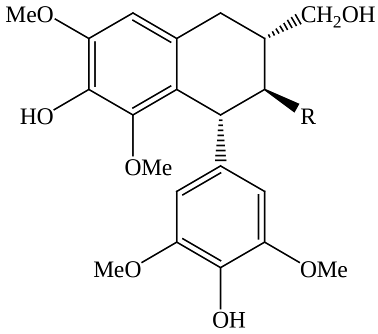
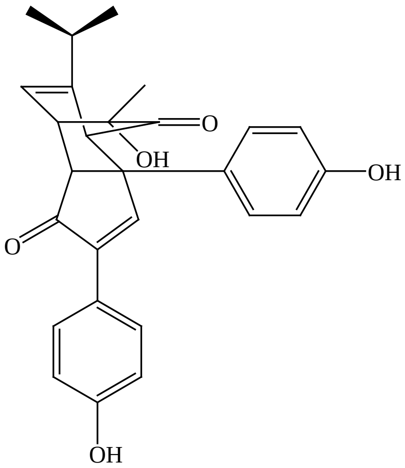


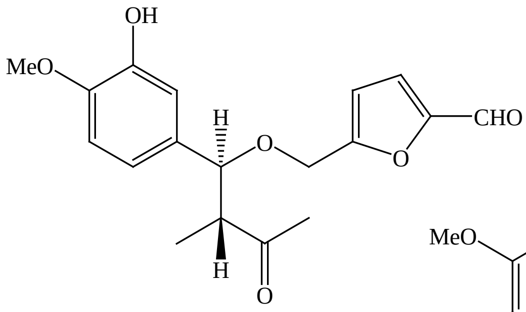
R = CH$_2$OH: (+)-lyoniresinol
R = CH$_2$O-β-D-Glc: (+)-lyoniresinol 3a-*O*-β-glucopyranoside



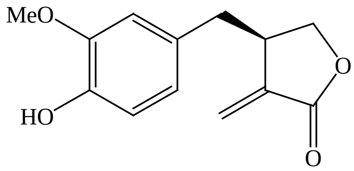
R = CH$_2$O-β-D-Glc: (-)-lyoniresinol 3a-*O*-β-glucopyranoside



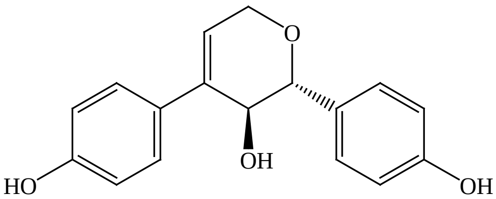
chamaecypanone C



acorusin B

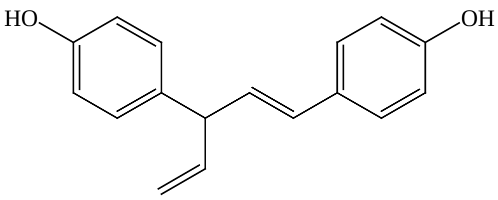


noralashinol B

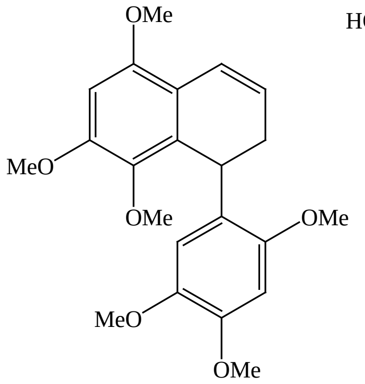


obtunorlignan A

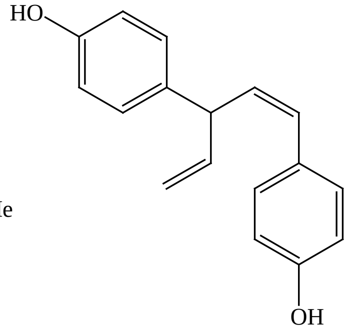
Figure 15: Structures of the isolated *nor*-lignans in the plant kingdom - part 14



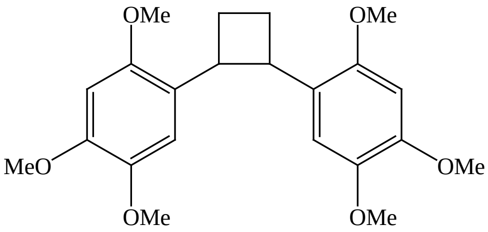
(-)-(*E*)-1,3-bis(4-hydroxyphenyl)-1,4-pentadiene



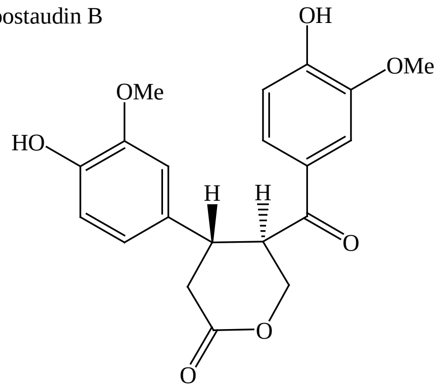
pachypostaudin B



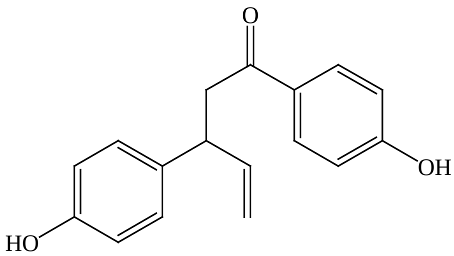
(-)-nyasol



pachypophyllin



(7*S*,8'*R*)-3,3'-dimethoxy-4,4'-diacetoxy-7'-ketolignano-9,9'-lactone



1,3-*bis*-di-*p*-hydroxyphenyl-4-penten-1-one

Figure 16: Structures of the isolated *nor*-lignans in the plant kingdom - part 15

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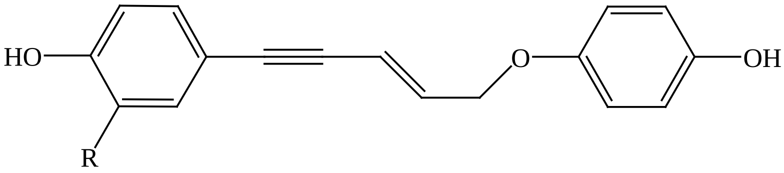
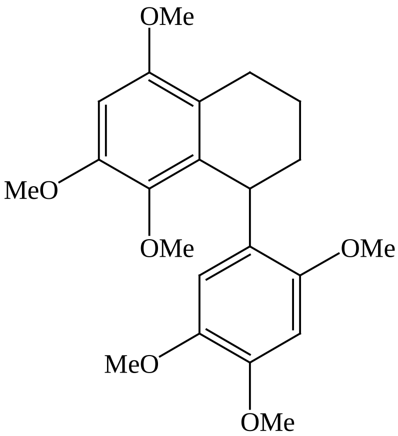
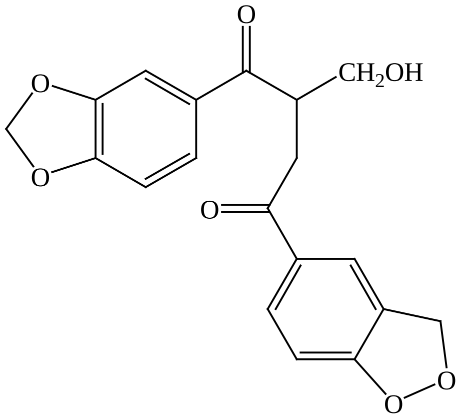


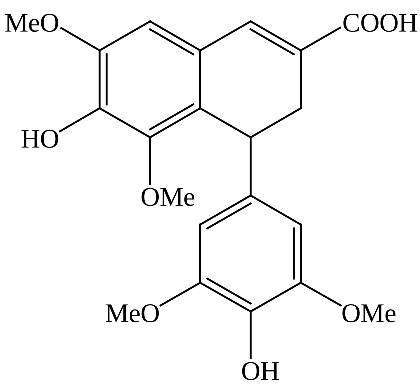
R = H: asparenydiol
R = OMe: 3''-methoxy-asparenydiol



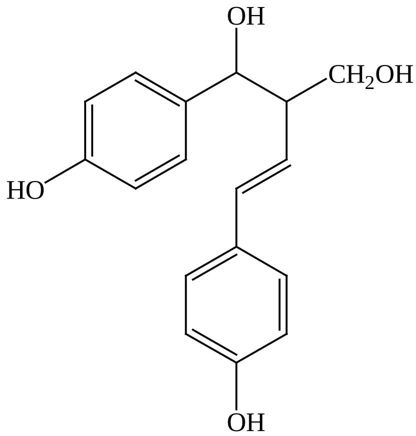
pachypostaudin A



justiflorinol

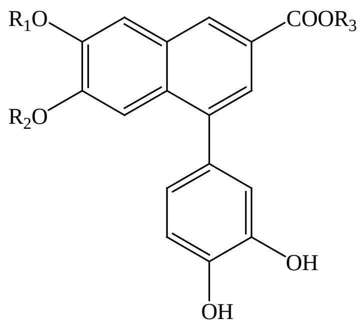


descuraic acid

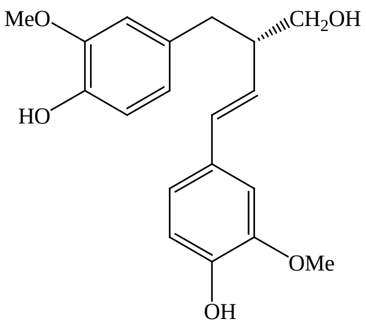


yateresinol

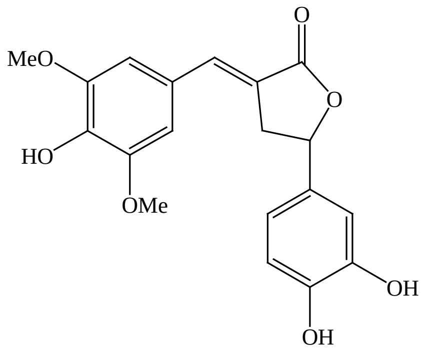
Figure 17: Structures of the isolated *nor*-lignans in the plant kingdom - part 16



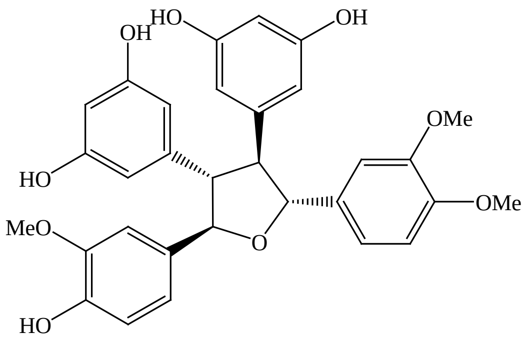
R_1 = R_2 = R_3 = H: 3-carboxy-6,7-dihydroxy-l-(3',4'dihydroxyphenyl)-naphthalene
R_1 = Me, R_2 = O-α-L-Rha, R_3 = H: 3-carboxy-6-methoxy-1-(3',4'-dihydroxyphenyl)-naphthalene-7-*O*-α-L-rhamnopyranoside
R_1 = R_2 = H, R_3 = CH(COOH)CH_2COOH: 3-carboxy-6,7-dihydroxy-1-(3',4'-dihydroxy-phenyl)-naphthalene-9,2''-*O*-malic acid ester
R_1 = R_2 = H, R_3 = shikimic acid: -carboxy-6,7-dihy-droxy-1-(3',4'-dihydroxyphenyl)-naphthalene-9,5''-*O*-shikimic acid ester



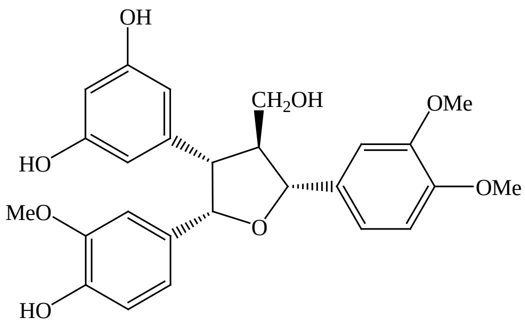
(*S*)-(+)-imperanene



9'-*nor*-3',4,4'-trihydroxy-3,5-dimethoxylign-7-eno-9,7'-lactone



pouzolignan K



pouzolignan D

Figure 18: Structures of the isolated *nor*-lignans in the plant kingdom - part 17

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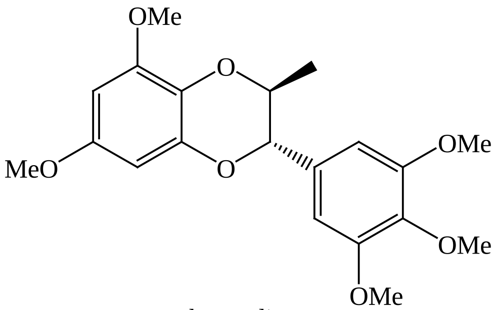
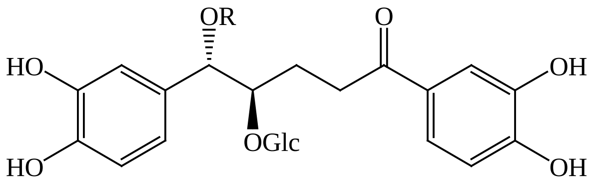
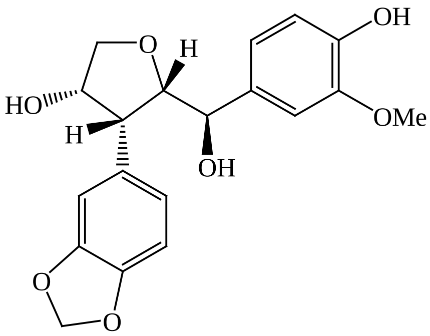


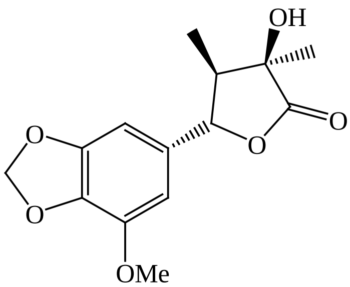
benzodioxane



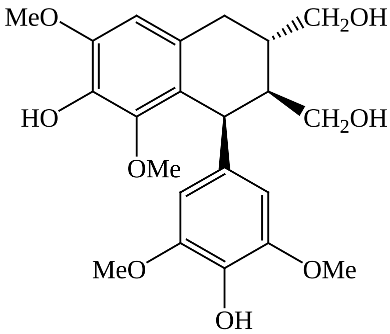
R = H: recurphenol C
R = Me: recurphenol D



nicotnorlignan A

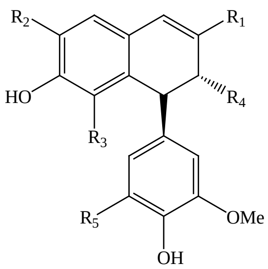


nicotnorlignan C

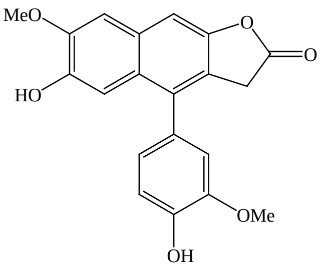


polystachyol

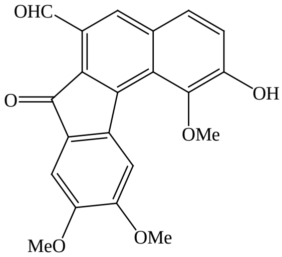
Figure 19: Structures of the isolated *nor*-lignans in the plant kingdom - part 18



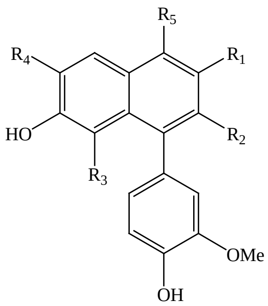
R_1 = CH_2OH, R_2 = OMe, R_3 =R_5 = H, R_4 = CH_2OH: negundin B
R_1 = CHO, R_2 = OMe, R_3 = R_5 = H, R_4 = CH_2OH: 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaledehyde
R_1 = CHO, R_2 = R_5 = H, R_3 = OMe, R_4 = CH_2OH: vitedoin A
R_1 = CHO, R_2 = R_3 = OMe, R_4 = CH_2OH, R_5 = H: vitexdoin F
R_1 = CHO, R_2 = OH, R_3 = R_5 = H, R_4 = CH_2OH: vitexdoin A
R_1 = CHO, R_2 = H, R_3 = OMe, R_5 = H, R_4 = CH_2O-β-D-Glc: vitexnegheteroin E
R_1 = CHO, R_2 = R_3 = OMe, R_4 = CH_2O-β-D-Glc, R_5 = H: vitexnegheteroin F
R_1 = CHO, R_2 = OMe, R_3 = H, R_4 = CH_2O-β-D-Glc, R_5 = H: vitecannaside B
R_1 = CHO, R_2 = R_3 = OMe, R_4 = CH_2O-β-D-Glc, R_5 = H: vitecannaside C
R_1 = CHO, R_2 = R_3 = R_5 = OMe, R_4 = CH_2OH: ovafolinin E



negundin A



vitrofolal D



R_1 = CHO, R_2 = R_3 = R_5 = H, R_4 = OMe: vitrofolal E
R_1 = CHO, R_2 = OH, R_3 = R_5 = H, R_4 = OMe: vitrofolal F
R_1 = COOH, R_2 = OH, R_3 = R_5 = H, R_4 = OMe: vitexnegheteroin G
R_1 = CHO, R_2 = R_5 = H, R_3 = OMe, R_4 = H: vitexdoin B
R_1 = R_3 = R_5 = H, R_2 = CHO, R_4 = OMe: vitexdoin C
R_1 = OH, R_2 = CHO, R_3 = R_5 = H, R_4 = OMe: vitexdoin D
R_1 = CHO, R_2 = R_3 = H, R_4 = OMe, R_5 = OH: vitexdoin E

Figure 20: Structures of the isolated *nor*-lignans in the plant kingdom - part 19

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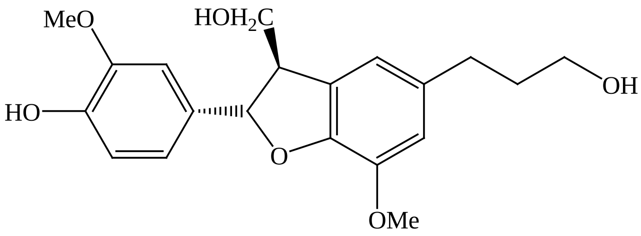
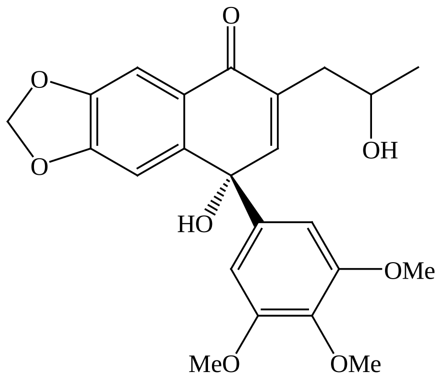
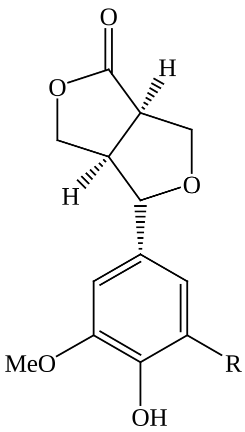


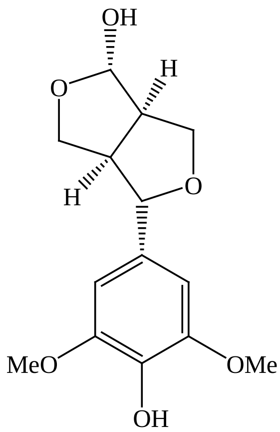
2α,3β-7-*O*-methyl-cedrusin



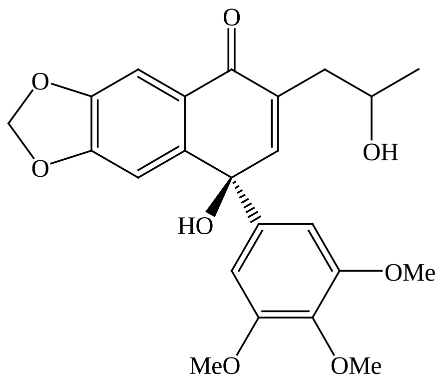
dysosmanorlignan B



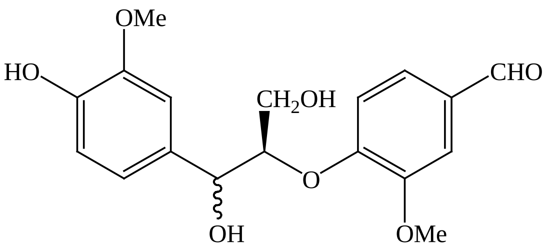
R = H: salicifoliol
R = OMe: glaberide I



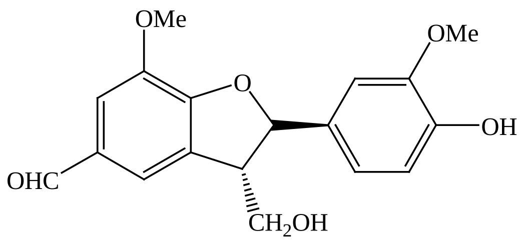
6-hydroxy-2-(4-hydroxy- 3,5-dimethoxyphenyl)-3,7-dioxabicyclo-[3.3.0]-octane



dysosmanorlignan A



erythro: *erythro*-guaiacylglycerol 8'-vanillin ether
threo: *threo*-guaiacylglycerol 8'-vanillin ether



ficusal

Figure 21: Structures of the isolated *nor*-lignans in the plant kingdom - part 20

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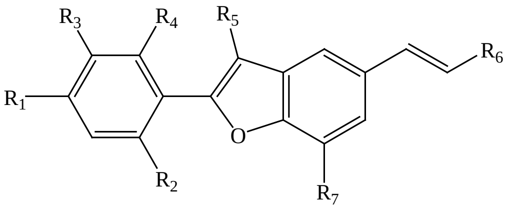
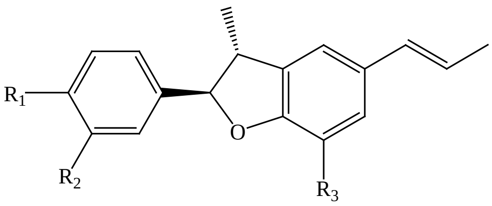


R_1 = OMe, R_2 = OH, R_3 = R_4 = R_5 = R_7 = H, R_6 = Me: rataniaphenol I
R_1 = OH, R_2 = R_3 = R_4 = R_7 = H, R_5 = R_6 = Me: rataniaphenol II
R_1 = OMe, R_2 = OH, R_3 = R_4 = R_5 = R_7 = H, R_6 = Me: rataniaphenol III
R_1 = OH, R_2 = R_3 = R_4 = R_7 = H, R_5 = R_6= Me: eupomatenoid 6
R_1 = OH, R_2 = R_3 = R_4 = H, R_5 = R_6 = Me, R_7 = OMe: eupomatenoid 13
R_1 = OMe, R_2 = R_3 = R_4 = R_7 = H, R_5 = R_6 = Me: eupomatenoid 15
R_1 = R_7 = OMe, R_2 = OH, R_3 = R_4 = R_5 = H, R_6 = Me: toltecol
R_1 = R_2 = R_3 = OMe, R_4 = R_5 = R_7 = H, R_6 = Me: 5-(*E*)-propenyl-2-(2,4,5-trimethoxyphenyl)benzofuran
R_1 = R_4 = OMe, R_2 = OH, R_3 = R_5 = R_7 = H, R_6 = Me: 2-(4,6-dimethoxyphenyl-2-hydroxyphenyl)-5-(*E*)-propenylbenzofuran
R_1 = OMe, R_2 = R_3 = R_4 = R_7 = H, R_5 = R_6 = Me: (*E*)-2-(4-methoxyphenyl)-3-methyl-5-(prop-1-enyl)benzo[b]furan
R_1 = R_2 = OH, R_3 = R_4 = R_5 = R_7 = H, R_6 = Me: 2-(2,4-dihydroxyphenyl)-5-(*E*)-propenylbenzofuran
R_1 = R_2 = OH, R_3 = R_4 = R_5 = H, R_6 = Me, R_7 = OMe: 2-(2,4-dihydroxyphenyl)-7-methoxy-5-(*E*)-propenylbenzofuran
R_1 = R_2 = OMe, R_3 = R_4 = R_5 = R_7 = H, R_6 = Me: 2-(2,4-dimethoxyphenyl)-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = R_3 = R_4 = R_5 = R_7 = H, R_6 = Me: 2-(4-hydroxyphenyl)-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = R_3 = R_4 = R_5 = H, R_6 = Me, R_7 = OMe: 2-(4-hydroxyphenyl)-7-methoxy-5-(*E*)-propenylbenzofuran
R_1 = OMe, R_2 = OH, R_3 = R_4 = R_5 = R_7 = H, R_6 = CH_2OH: 2-(2-hydroxy-4-methoxyphenyl)-5-3-hydroxy-(E)-1-propen-1-yl-benzofuran
R_1 = OH, R_2 = OMe, R_3 = R_4 = R_5 = R_7 = H, R_6 = CH_2OH: 2-(4-hydroxy-2-methoxyphenyl)-5-3-hydroxy-(E)-1-propen-1-yl-benzofuran
R_1 = OH, R_2 = R_3 = R_4 = H, R_5 = CHO, R_6 = Me, R_7 = OMe: 3-formyl-2-(4-hydroxyphenyl(-7-methoxy-5-(*E*)-propenylbenzofuran



R_1 = OMe, R_2 = R_3 = H: (2*R*,3*R*)-2,3-dihydro-2-(4-methoxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = H, R_3 = OMe: (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxyphenyl)-7-methoxy-3-methyl-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = R_3 = OMe: (2R,3*R*)-2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-3-methyl-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = OMe, R_3 = H: (2*R*,3*R*)-2,3-dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-methyl-5-(*E*)-propenylbenzofuran
R_1 = OH, R_2 = R_3 = OMe: (+)-licarin A
R_1 = OH, R_2 = R_3 = H: conocarpan

Figure 22: Structures of the isolated *nor*-lignans in the plant kingdom - part 21

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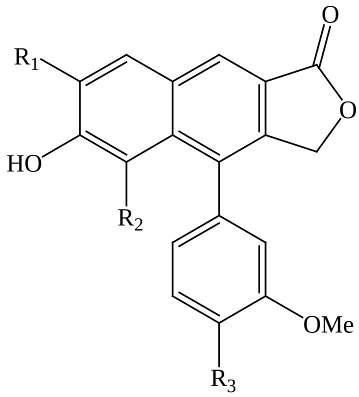
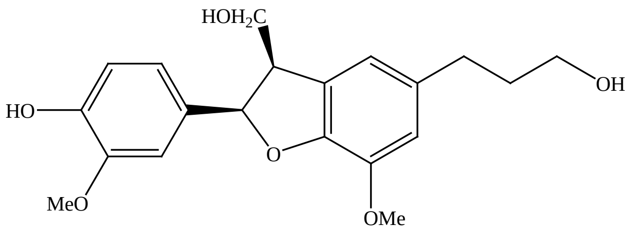
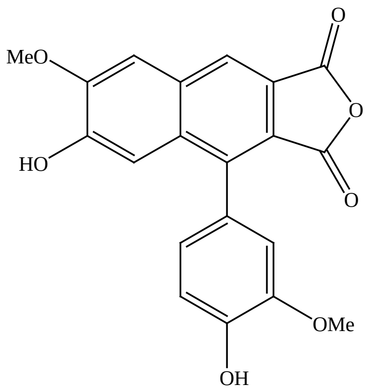


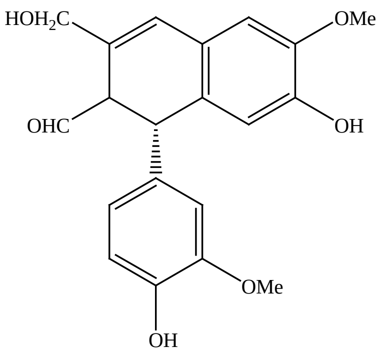
R_1 = OMe, R_2 = H, R_3 = OH: detetrahydro-conidendrin
R_1 = H, R_2 = R_3 = OMe: 4-(3,4-dimethoxyphenyl)-6-hydroxy-5-methoxynaphtho[2,3-c]furan-1(3*H*)-one
R_1 = R_3 = OMe, R_2 = H: 4-(3,4-dimethoxyphenyl)-6-hydroxy-7-methoxynaphtho[2,3-c]furan-1(3*H*)-one
R_1 = R_3 = OH, R_2 = H: vitexdoin G



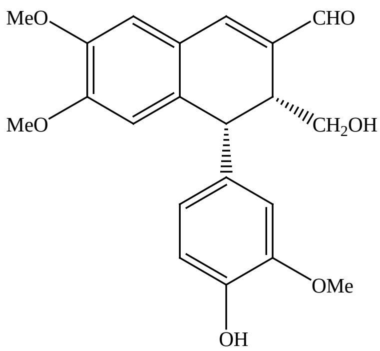
(7*S*,8*R*)-dihydrodehydrodiconiferyl alcohol



6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-7-methoxynaphtho[2,3-c]furan-1,3-dione



1,2-dihydro-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-6-methoxy-(1*S*,2*R*)-2-naphthalenecarboxaldehyde



3,4-dihydro-4-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-6,7-dimethoxy-(3*R*,4*S*)-2-naphthalenecarboxaldehyde

Figure 23: Structures of the isolated *nor*-lignans in the plant kingdom - part 22

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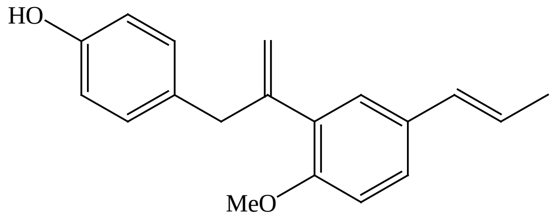
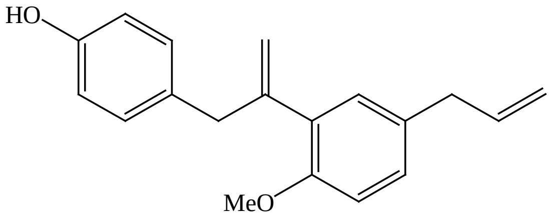
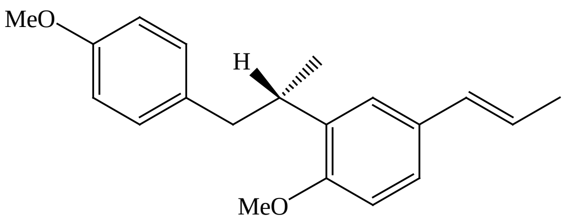


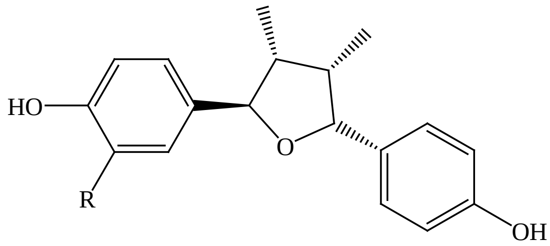
hermosillol



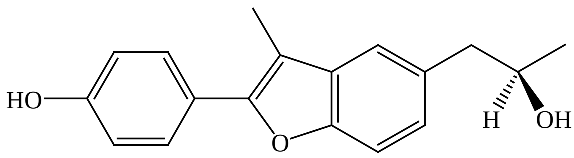
4-2-(5-allyl-2-methoxyphenyl)allyl-phenol



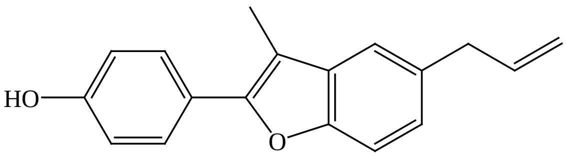
trans-(2'*S*)-2-1'-(4-methoxyphenyl)prop-2'-yl-anethol



R = H: 3,3'-didemethoxy-nectandrin B
R = OMe: 3'-demethoxy-nectandrin B



4-(5-((*R*)-2-hydroxypropyl)-3-methylbenzofuran-2-yl)phenol



5-allyl-2-(4-hydroxyphenyl)-3-methylbenzofuran

Figure 24: Structures of the isolated *nor*-lignans in the plant kingdom - part 23

3. Chemotaxonomy

As Table 1 clearly shows, *nor*-lignans have been recognized as phytochemical constituents of several families, even chemosystematically far away from each other.

Nevertheless, some specific compounds can be evidenced as chemotaxonomic makers at every classification level.

In particular, (+)-acortatarinowins A-C, (-)-acortatarinowins A-C and acorusin B may be useful chemotaxonomic markers for the species *Acorus tatarinowii* Schott. since they have been isolated only from that species [5, 6].

Pachypostaudins A-B and pachypophyllin may be chemotaxonomic markers for the entire Annonaceae family given their specific occurrence here [7, 8].

Asparenydiol and its derivatives are considered as some of the chemotaxonomic markers for the genus *Asparagus* L. [17].

Capituloside and the crassifosides may be used as chemotaxonomic markers for the genus *Curculigo* Gaertn. given their occurrence limited to only it [40, 43, 44, 46, 51, 52].

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For the same reason hypoxoside is a possible chemotaxonomic marker for the genus *Hypoxis* L. [54, 56, 59] and rataniaphenols I-II may serve as chemotaxonomic markers for the genus *Krameria* L. [62-64].
Within the Lamiaceae family, surely negundins A-B are chemotaxonomic markers for the species *Vitex negundo* L given their occurrence in several exemplars of this species [69-71].
Indeed, egonol, homoegonol and their derivatives can serve as chemotaxonomic markers for the *Styrax* L. genus since their occurrence is quite limited to it [104-110].

4. Biological activities

Nor-lignans show several interesting biological activities i.e. antioxidant, antifungal, antibacterial, antiallergic, antiasthma, analgesic, anticomplement, antiatherogenic, antiparasitic, vascular, anti-inflammatory, cytotoxic, phytotoxic, inhibitory of enzymes, proteins and platelet aggregation. In the following pages, these are characterized one by one.

4.1. Antioxidant

Egonol highly inhibits the production of NO and highly reduces the release of ROS in a dose dependent manner. The same is valid for homoegonol but in a minor way [110].
Indeed, curcapital, crassifogenin C, crassifoside E and crassifoside F show strong radical scavenging activity by the 1,1-diphenyl-2-picrylhydrazyl (DPPH$^•$) assay with IC_{50} values equal to 7.76 13.48, 15.54 and 17.07 μM, respectively, which are much higher than the control, L-ascorbic acid (IC_{50} = 27.59 μM) [44].
Moreover, hypoxoside and rooperol show high effects towards the inhibition of lipid peroxidation withIC_{50} values equal to 12.6 and 2.6 μM, respectively [54].
Nyasol exerts medium effects against ABTS$^{•+}$ cation and superoxide anion radicals with IC_{50} values equal to 45.6 and 40.5 μM, respectively [82].
Vitexdoin F, vitedoin A, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, vitexdoin A, negundin B, vitexdoin E, vitrofolal F, 1,2-dihydro-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-6-methoxy-(1*S*,2*R*)-2-naphthalenecarboxaldehyde, vitexdoin C, vitexdoin D, vitrofolal E, vitexdoin B, vitrofolal A, detetrahydro-conidendrin showed stronger effects than ascorbic acid [69,73].

4.2. Antiradical

Vitrofolal E, vitrofolal F, viteodin A, 6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde, detetrahydro-conidendrin and 2α,3β-7-*O*-methyl-cedrusin exert high effects against the stable free radical, 1,1-diphenyl-2-picrylhydrazyl (DPPH$^{\bullet}$), more than*L*-cysteine and in most cases similar to α-tocopherol [73].
Also,vitexnegheteroin E, vitexnegheteroin F, vitexnegheteroin G, vitecannaside B and vitexdoin A exhibit strong effects in the ABTS assay with IC_{50} values lower than 3.20 µM[74].
Vitexdoin A, vitexdoin B, vitexdoin C, vitexdoin D, vitexdoin E, vitrofolal E and vitrofolal F are potent NO production inhibitors with IC_{50} values equal to 0.38 µM, 0.20 µM, 0.57 µM, 0.13 µM, 0.15 µM, 0.50 µM and 0.11 µM, respectively. Instead, 6-Hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde has a weaker effect with an IC_{50} value equal to 3.54 µM. Anyway, they were all more powerful than the positive control L-nitroarginine (IC_{50}= 43.6 µM) [75].

4.3. Antifungal and antibacterial

Homoegonol and egonol exhibit strong effects against *Candida albicans*, *Cladosporium sphaerospermum* and *Staphylococcus aureus* with MIC values equal to 10, 5, 10 µg/mL respectively for the former compound and 12, 10, 10 µg/mL respectively for the latter compound. Indeed, egonol and 5-[3"-(β-D-glucopyranosyloxy)propyl]-7-methoxy-2-(3',4'-methylenedioxyphenyl)-benzofuran exhibit lower effects only against *Candida albicans* and*Staphylococcus aureus* with MIC values equal to 15, 15 µg/mL respectively for the former compound and 20, 20, µg/mL respectively for the latter compound [105].
Conversely, homoegonol is totally inactive against *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenza*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia* showing MIC values higher than 400 µg/mL. Instead, egonol is weakly active only against *Streptococcus pneumonia* showing a MIC value equal to 400 µg/mL [114]. Also, *iso*-agatharesinol and gobicusin A are able to exert these effects. In particular, gobicusin A is a better antibacterial compound against *Escherichia coli*, *Staphylococcus aureus* than *iso*-agatharesinol given its MIC values (0.12 and 0.05 mg/mL vs. 0.25 and 0.12 mg/mL,

respectively) and its efficacy is extremely comparable to streptomycin especially against *Staphylococcus aureus* (MIC = 0.01 mg/mL) [19].

Nyasol is able to inhibit the mycelial growth of *Colletotrichum orbiculare*, *Phytophthora capsici*, *Pythium ultimum*, *Rhizoctonia solani* and *Cladosporium cucumerinum* in a MIC range comprised between 1 and 50mg/mL [13]. Moreover, it potently inhibits the growth of *Leishmania major* with an IC_{50} value equal to 12 µM and moderately inhibits *Plasmodium falciparum* with an IC_{50} value equal to 49 µM[14].

Vitrofolal C, vitrofolal D, vitrofolal E and detetrahydro-conidendrin have good activity against methicillin-resistant *Staphylococcus aureus* with a MIC value below 64 µg/mL [77].

4.4. Antiviral

Nicotnorlignan A, sequirin C and benzodioxane showed high effects against HIV-1 with IC_{50} values equal to 3.15,9.56 and 7.62 µM, respectively [102].

Moreover, nicotnorlignan C, recurphenol C, recurphenol D, sequirin C and benzodioxane possess moderate activity against the anti-Tobacco mosaic virus with inhibition rates equal to 14.7 %, 22.5 %, 23.4 %, 17.6 % and 21.4 %, respectively [102]. Also, nicotnorlignan A show similar effects [102].

4.5. Anti-allergic

Nyasol and 4'-*O*-methyl-nyasol exert good effects with IC_{50} values equal to 2.06 and 1.89 µM, respectively. These values are extremely compatible with that of DSCG (IC_{50} = 1.78 µM), a very common antiallergic compound used in pharmacy [10].

4.6. Antiasthma

Homoegonol is the only compound able to exert antiasthma effects by a complex mechanism of action composed by several paths [115].

4.7. Analgesic

Hypoxoside does not display any effect on the locomotor activity in mice but exerts a high analgesic effect even at low doses (5 mg/Kg) probably via an anti-inflammatorymechanism [59].

4.8. Anticomplement

Styraxlignolide A, egonol and masutakeside I show a strong effect with IC_{50} values equal to 123, 33 and 166 μM, respectively. This activity in the case of egonol is much higher than the control i.e. rosmarinic acid which shows an IC_{50} value equal to 182 μM [106].

4.9. Antiatherogenic

Nyasol is able to act as inhibitor against LDL-oxidation with an IC_{50} value equal to 5.6 μM, which is very similar to that probucol (IC_{50} = 2.0 μM), the typical compound uses for these purposes. Indeed, it exerts extremely weak inhibitory effects against hACAT1, hACAT2 (cholesterol acyltransferases)and Lp-PLA2 (lipoprotein-associated phospholipase A2) with IC_{50} values equal to 280.6, 398.9 and 284.7 μM, respectively[82].

4.10. Antiparasitic

3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-nor-8,5'-neolignan-9'-acetoxy has a medium effect against *Trypanosoma cruzi* with an IC_{50} value equal to 111 μM whereas 3'-methoxy-3,4-methylenedioxy-4',7-epoxy-9-nor-8,5'-neolignan-7,8'-diene is a good compound in this context with an IC_{50} value equal to 60 μM [78].

4.11.Vascular

Pilosidine, nyasicoside and curculigine in low doses ranging from 1 to 30 mM are able to induce a reversible facilitating effect on adrenaline evoked contractions [47]. Moreover, they all have a dose dependent vasoconstricting effect on rabbit aorta strips [48].

(2*S*)-1-*O*-butyl-nyasicoside and nyasicoside possess high effects against the ouabain-induced arrhythmia in the heartpreparations of guineapigat the doses of 3 µM, especially at the left atrium level. (-)-(1*S*,2*S*)-1-*O*-butyl-nyasicosidehas the sameeffectbut in minor extent [41].

Lastly, 2-(2′-hydroxy-4′,6′-dimethoxyphenyl)-5-[(*E*)-propenyl]benzofuran inhibits the vasodilator effect produced by acetylcholine with an IC_{50} value equal to 31.2 µM. This effect is concentration-dependent. Moreover, the compound inhibits basal nitric oxide production [116].

4.12.Anti-inflammatory

Egonol, homoegonol, homoegonol gentiobioside, homoegonol glucoside and egonol gentiobioside were found to exert weak or medium effects against COX1 and COX2 with percentages of inhibition ranging from 1.3 for homoegonol gentiobioside against COX1 to 35.7 of homoegonol glucoside against COX1 at the concentration of 30 mM [109]. Yet, egonol is able to reduce the mRNA expression levels of inducible nitricoxide synthase (iNOS), COX-2, interleukin-1β (IL-1β) and interleukin-6 (IL-6). The same effect was observed also for homoegonol but in a minor extent[110].

Lastly, nyasol and 5-((*S*,*Z*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-yl)-2,3-dimethoxyphenolshow high effects. In particular, nyasol is able to inhibit microsomal cells by 100 % as well as COX-1 while it inhibits COX-2 by 19%. Conversely, 5-((*S*,*Z*)-1-(4-hydroxyphenyl)penta-1,4-dien-3-yl)-2,3-dimethoxyphenol inhibits microsomal cells by 72% and COX-2 by 23% [21].

4.13. Cytotoxic

3′-methoxy-nyasin and nyasol possess moderate effects against HO-8910 (human ovarian carcinoma) and Bel-7402 (human hepatoma) cell lines. In particular, the former compound shows IC_{50} values equal to 84.0 and 26.2 µM, respectively whereas the latter compound shows IC_{50} values equal to 30.6 and 29.4 µM, respectively [18]. Nyasol and 4'-*O*-methyl-nyasol exert moderate effects against the rat glioma C-6 cell line with IC_{50} values equal to 19.02 and 20.21 mg/mL, respectively [81]. Nyasol is also able to inhibit the basic fibroblast growth factor (bFGF) and the vascular endothelial growth factor (VEGF)-induced endothelial cell proliferation[11]. In addition, it has medium effects against the human HL60 cancer cell line with IC_{50} value equal to 15.5 µM [27]. Moreover, nyasol, 4'-*O*-methyl-nyasol and 3"-methoxy-nyasolhave a modest effect on the inhibitionof β-hexosaminidase release in RBL-2H3 cells stimulated by DNP-BSA with IC_{50} values ranging from 18.08 µM for the latter to 52.67 for the second compound. These values are higher than the control compound ketotifen which owns an IC_{50} value equal to 10.12. Conversely, 3"-hydroxy-4"-methoxy-4"-dehydroxy-nyasol is more efficient than the control displaying an IC_{50} value equal to 2.85 [12].

Egonol and homoegonol exhibit medium effects against B16F10 (murine melanoma), MCF-7 (human breast adenocarcinoma), HepG2 (human hepatocellular liver carcinoma), HeLa (human cervical adenocarcinoma) and MO59J (human glioblastoma) cell lines. These effects were observed to be higher with the passing of time reaching their peaks after 72 h. Anyway, they were not better than the controls doxorubicin, camptotechin and etoposide [104]. For what concerns egonol, the results for MCF-7 and HeLa were confirmed in another study and it was also observed that it is active against theHL-60 (human leukemia) cell line with an IC_{50} value equal to 47.8 µM [107].

Agatharesinol acetonide exhibits strong effects on the A549 cell line (non-small-cell lung cancer) with an IC_{50} value equal to 27.1 µM, much higher than taxol 33.72 µM [35].

Sequirin C exert good effects against the HL-60 cell line with an IC_{50} value of 5.5 µM which is comparable to that of cisplatin (2.0 µM) [33].

Cedralin A has weak activities against the HL-60 and K562 (myelogenous leukemia) cell lines with IC_{50} values equal to 26.2 and 22.4 mg/ml, respectively [85].

Methyl *rel*-(1*R*,2*S*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate and methyl *rel*-(1*R*,2*R*,3*S*)-2-(7-methoxy-1,3-benzodioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)-cyclobutane-carboxylate exert modest effects against the HepG2, A549, and HeLa cell lines with IC_{50} values equal to 38.0, 56.4, 64.9 µM for the former in corresponding order, and 42.4, 66.3, 77.7 µM for the latter in corresponding order [52].

Noralashinol B exhibits a weak activity against the HepG2 cancer cell line with an IC_{50} value equal to 31.7 µM which is higher than the positive control, methotrexate showing an an IC_{50} value equal to 15.8µM[89].

Metasequirin G, metasequirin H and metasequirin I possess low cytotoxic effects against the A549 cell line with IC_{50} values close to 100 µM [34].

Chamaecypanone C exertspotent effects against KB (human oralepidermoid carcinoma), HONE-1 (human nasopharyngeal carcinoma) and TSGH (human gastric carcinoma) cell lines with IC_{50} values equal to 0.19,0.24 and 0.52 µM, respectively [28].

Acorusin B exert moderate effects against the CI-H1650 (non-small cell lung carcinoma), HepG2, BGC 823 (human stomach carcinoma), HCT-116 (human colon carcinoma), and MCF-7 cancer cell lines with IC_{50} values equal to 6.51,4.80, 7.23, 8.81 and 3.58 and 0.52 µM, respectively [6].

Yateresinol is a decent cytotoxic compound against the human HL60 and Hepa G2 cancer cell lines with IC_{50} values higher than 20 µM[27].

Vitedoin A exerts moderate effects against HCT116 cell lines with an IC_{50} value equal to 10.18 µM [74].

6-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaldehyde shows high effects against HepG2 cell lines with an IC_{50} value equal to 8.24 µM which is comparable to doxorubicin (IC_{50} = 6.49 µM) [74].

4.14.Phytotoxic

9'-*nor*-3',4,4'-trihydroxy-3,5-dimethoxylign-7-eno-9,7'-lactone is a phytotoxic compound against *Lactuca sativa* L. (lettuce) and *Lycopersi conesculentum* Mill. (tomato) preventing their growth [100].

4.15. Inhibition on enzymes, proteins and platelet aggregation

Negundin A, negundin B, 6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaledehyde, vitrofolal E and (+)-lyoniresinol have shown medium effects against tyrosinase with IC_{50} values equal to 10.06, 6.72, 7.81, 9.76 and 3.21 µM which are, anyway, higher than kojic acid (IC_{50} = 16.67µM) [71].

Indeed, negundin B has potent effect against lipoxygenase with an IC_{50} value equal to 6.25 µM [70].

Vitrofolal E shows also moderate effects against butyryl-cholinesterase with an IC_{50} value equal to 35.0 µM [70].

6-hydroxy-4-(4-hydroxy-3-methoxy)-3-hydroxymethyl-7-methoxy-3,4-dihydro-2-naphthaledehyde and vitrofolal E have modest α-chymotrypsin (serine protease) competitive inhibitory effectswith $K_i$values equal to 31.75 and 47.11 µM, respectively [72].

Cestrumoside is a strong protein kinase C inhibitor in an animal feed additive [117].

Lastly, (*S*)-(+)-imperanene strongly inhibits tyronase isolated from HMV-II cells with an IC_{50} value equal to 1.85 mM [118] and shows a high effect in rabbits giving a complete inhibition at the concentration of $6*10^{-4}$ M when the platelet aggregation is induced by thrombin [95].

5. Conclusions

Nor-lignans have proven to be quite present in the plant kingdom. Nevertheless, some of them can be even considered to be chemotaxonomic markers. In addition, they are endowed with a vast number of biological activities with a myriad of possible application in several medicinal and pharmacological fields. Actually, some of these biological activities are peculiar for specific compounds, some are in common among more compounds and some compounds are able to exert more of them. Yet, not all the *nor*-lignans have been studied and discovered at the present. This review article means to be a first step towards the understanding of how important *nor*-lignans are and an incentive, it is hoped, to continue their research and study.

Abbreviations: $[\alpha]_D$: Optical Rotation Spectroscopy; ECD: Electronic Circular Dichroism Spectroscopy; CC: Column Chromatography; CD: Circular Dichroism Spectroscopy; FCC: Flash Column Chromatography; HPLC: High Performance Liquid Chromatography; IM: Immunohistochemistry Methods; IR: Infrared Spectroscopy; LC: Liquid Chromatography; MP: Melting Point; MS: Mass Spectrometry; NMR: Nuclear Magnetic Resonance Spectroscopy; n.a.: not accessible; n.r.: not reported; pTLC: Performance Thin Layer Chromatography; SE: solvent extraction; TLC: Thin Layer Chromatography; UV: Ultra-Violet Spectroscopy.

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