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Phytochemistry and Biological Activities of the Genus *Ocotea* (Lauraceae): A Review on Recent Research Results (2000-2016)

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ABSTRACT

Ocotea (family: Lauracea), which comprises nearly 350 species, are distributed throughout tropical America, Africa, and Asia. Up to now, the reported constituents from the genus *Ocotea* involve neolignans, alkaloids, sesquiterpenes, flavonoids, lignans, butanolides, benzopyrans, steroids, essential oils and several other types of compounds (alkylphenols, arylpropene, coumarin, ester, saponin). Studies have shown that *Ocotea* and its active principles possess a wide range of pharmacological activities, such as anti-inflammatory, cytotoxicity, antimicrobial, larvicidal, and antiproliferative activities. The outcome of these studies will further support the therapeutic potential of the genus *Ocotea*, and provide convincing evidences to its future clinical applications in modern medicine. Thus, increasing amount of data supports application and exploitation for new drug development.

INTRODUCTION

The plant genus *Ocotea*, one of the largest members of the Lauraceae family, comprises approximately 350 species that are distributed throughout tropical and subtropical climates. Most species are found in America from Mexico to Argentina, seven species are found in Africa, one species is found in the Canary Islands, and about 34 recognized species are found in Madagascar (Rohwer, 2000; van der Werff, 2013). It can be recognized by the simple, alternate, stiff and aromatic elliptic to obovate leaves and fruits often borne in a cup. This family has a considerable economic importance worldwide because it is used as a source of timber for construction and furniture (*Nectandra*, *Ocotea*, *Persea* spp.), as a crop (*Persea americana*), and to obtain flavours for food industry, perfumery, and medicines (*Cinnamomum zeylanicum*, *C. cassia*) (Chaverri *et al*., 2011). Several plants of this genus have been used for the treatment of various diseases. Among them, the stem wood of *O. bullata* has been used to treat headache and male urinary tract infections (Rakotondraibe *et al*., 2015). *O. puchury-major* is popular in local medicine, as possible sedative, gastroenteric, and antirheumatic properties. It is reported mainly for its leaves and bark, as well as cosmetic applications involving the essential oil of the leaves (Christophel *et al*., 1996). *O. quixos* is used as disinfectant, local anaesthetic and anti-diarrheic infusion (Ballabeni *et al*., 2007). Meanwhile,*O. lancifolia* is used as antiparasitic, and *O. caparrapi* is used to treat insect bites, snake bites, bronchitis, and cancerous tumours (Fournet *et al*., 2007). The woody calyces of *O. bofo* collected from mature fruits are traditionally used to aromatize infusions by ethnic groups. It possesses a strong anise like aroma and thus may represents a potential aniseed, fennel, or tarragon substitute or adulterant (Guerrini *et al*., 2006). A number of plants in the genus *Ocotea* are the sources of secondary metabolites, including neolignans, alkaloids, flavonoids, sesquiterpenes, lignans, butanolides, benzopyrans, steroids, alkylphenols, arylpropenes, coumarins, esters, and saponins; many of which exhibited interesting antiproliferative, antifungal, antiherpetic, anti-inflammatory, and antimicrobial activities (Camargo *et al*., 2013; Castro *et al*., 2011; Cuca *et al*., 2009; Destryana *et al*., 2014; Garcez *et al*., 2011; Garett *et al*., 2012; Yamaguchi *et al*., 2013).

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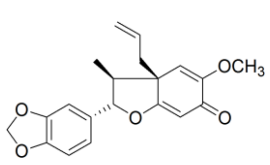
The extensive reading and investigation were actualized by systematically searching the scientific databases (PubMed, Scopus, SciFinder, and the Web of Science) for topics related to factors like the essential oils composition, chemical constituents, and pharmacological effects of the genus *Ocotea*. A bibliographic search, carried out from the year 2000 to 2016 of the genus *Ocotea* revealed that about 43 species were investigated at chemical or biological level.

Due to the ethnobotanic importance of this genus, further studies on *Ocotea* species are urgently needed. Thus, the aim of this review is to provide an overview on chemical and pharmacological studies on the essential oil, extracts, and isolated compounds from the genus *Ocotea* from year 2000 to 2016. Also included are the biological activities of compounds isolated in recent years. This should be helpful for professionals in ethnopharmacology and natural product chemistry and promote the application of plants of this genus.

PHYTOCHEMISTRY STUDIES

The chemical constituents of *Ocotea* compounds (**Figure 1**) includeneolignans, alkaloids, sesquiterpenes, flavonoids lignans, butanolides, benzopyrans, steroids, alkylphenols, arylpropene, coumarins, ester, and saponin. Their structures are shown below, and their names and the corresponding plant sources are listed in the **Table 1.** In addition, the chemical compositions of the *Ocotea* essential oils are also discussed and summarized in **Table 2**.



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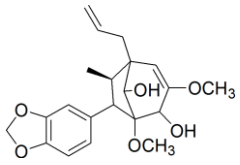

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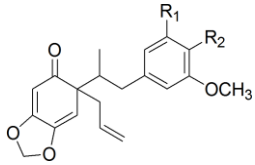
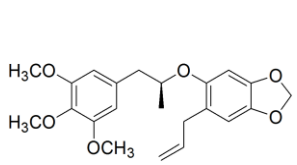


3 $R_1 = R_2 = OCH_3$
4 $R_1 = H$; $R_2 = OCH_3$
5 $R_1 = OCH_3$; $R_2 = OH$



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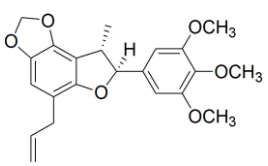

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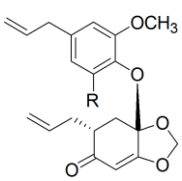
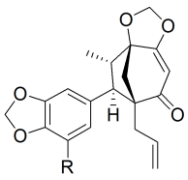
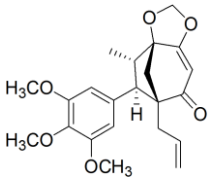


8 R = H
9 R = OCH_3



10 R = H
11 R = OCH_3
12 R = OH



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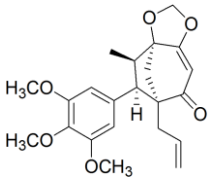

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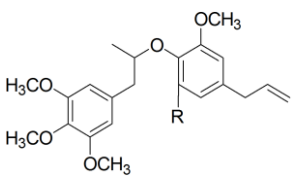

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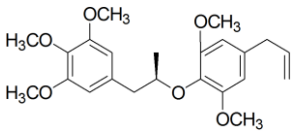
16 R = H



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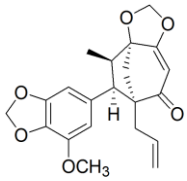

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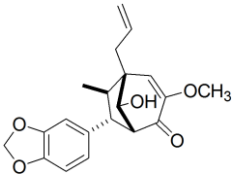

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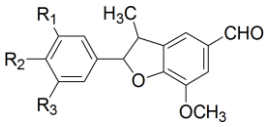
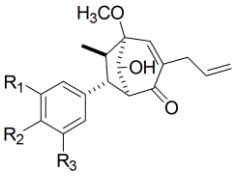
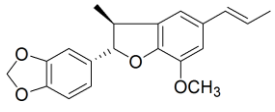


20 $R_1 = R_2 = OCH_2O$; $R_3 = H$
21 $R_1 = R_2 = R_3 = OCH_3$



22 $R_1 = R_2 = OCH_2O$; $R_3 = H$
23 $R_1 = R_2 = OCH_3$; $R_3 = H$
24 $R_1 = R_2 = R_3 = OCH_3$



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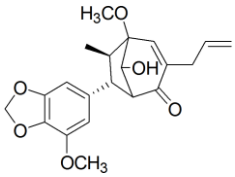

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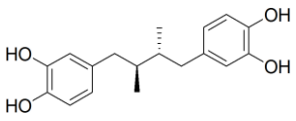

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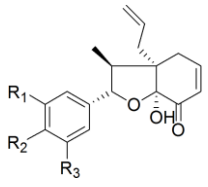
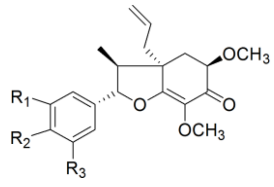
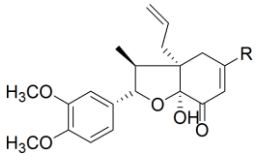


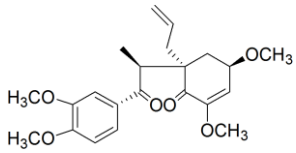
28 $R_1 = R_2 = OCH_2O$; $R_3 = H$
29 $R_1 = R_2 = OCH_3$; $R_3 = H$
30 $R_1 = R_2 = R_3 = OCH_3$



31 $R_1 = R_2 = OCH_2O$; $R_3 = H$
32 $R_1 = R_2 = OCH_3$; $R_3 = H$
33 $R_1 = R_2 = R_3 = OCH_3$



34 R = H
35 R = OCH_3



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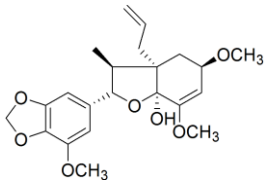

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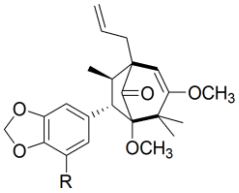
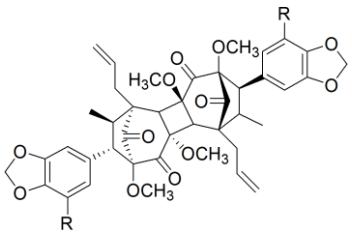
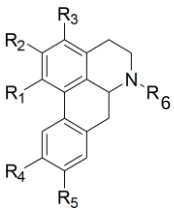


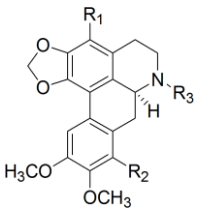
38 R = H
39 R = OCH_3



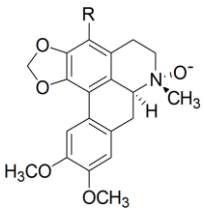
40 R = H
41 R = OCH_3



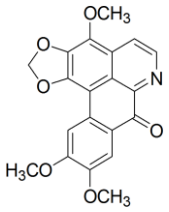
42 $R_1 = R_2 = OCH_2O$; $R_3 = H$; $R_4 = R_5 = OCH_3$; $R_6 = CH_3$; (6aS)
48 $R_1 = R_2 = OCH_2O$; $R_3 = H$; $R_4 = R_5 = OCH_2O$; $R_6 = CH_3$; (6aS)
53 $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = R_5 = OCH_2O$; $R_6 = CH_3$; (6a-7)
54 $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = R_5 = OCH_2O$; $R_6 = CH_3$; (6aS)
55 $R_1 = R_2 = OCH_3$; $R_3 = H$; R4 = $R_5 = OCH_2O$; $R_6 = COCH_3$; (6aS)
56 $R_1 = R_2 = OCH_2O$; $R_3 = OCH_3$; $R_4 = R_5 = OCH_2O$; $R_6 = H$; (6aS)
57 $R_1 = R_2 = OCH_2O$; $R_3 = OCH_3$; $R_4 = R_5 = OCH_3$; $R_6 = CH_3$; (6a-7)



43 $R_1 = OCH_3$; $R_2 = H$; $R_3 = CH_3$
45 $R_1 = H$; $R_2 = OH$; $R_3 = CH_3$
46 $R_1 = OCH_3$; $R_2 = OH$; $R_3 = H$



44 R = OCH_3
72 R = H



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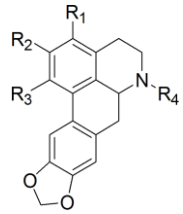
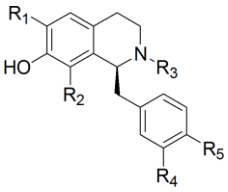
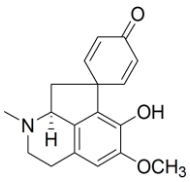


49 $R_1 = R_2 = OCH_3$; $R_3 = OH$; R_4= H
50 $R_1 = R_2 = OCH_3$; $R_3 = OH$; R_4= $COOCH_2CH_3$
51 $R_1 = R_2 = OCH_3$; $R_3 = OH$; R_4= COH
52 $R_1 = R_2 = OCH_3$; $R_3 = OH$; R_4= $COOCH_3$



58 $R_1 = OCH_3$; $R_2 = R_3 = R_4 = H$; $R_5 = OH$
59 $R_1 = OCH_3$; $R_2 = R_4 = H$; $R_3 = CH_3$; $R_5 = OH$
69 $R_1 = R_3 = R_4 = H$; $R_2 = OCH_3$; $R_3 = H$; $R_5 = OH$
70 $R_1 = R_5 = OCH_3$; $R_2 = H$; $R_3 = CH_3$; $R_4 = OH$



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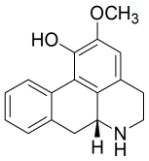

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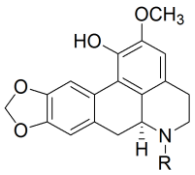
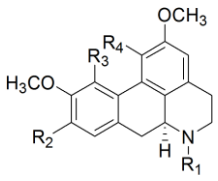
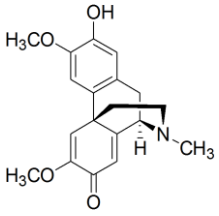


63 R = H
66 R = CH_3



62 $R_1 = R_3 = H$; $R_2 = OH$; $R_4 = OCH_3$
64 $R_1 = R_3 = H$; $R_2 = R_4 = OH$
65 $R_1 = CH_3$; $R_2 = H$; $R_3 = R_4 = OH$
67 $R_1 = CH_3$; $R_2 = R_4 = OH$; $R_3 = H$



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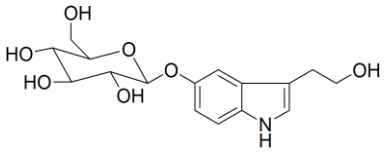

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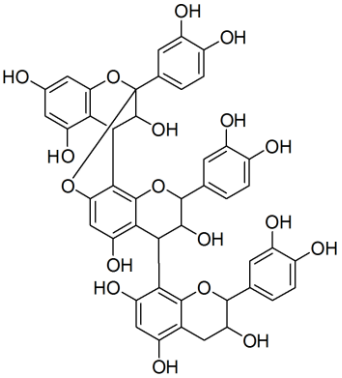

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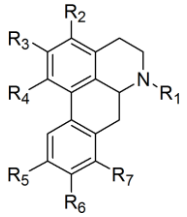
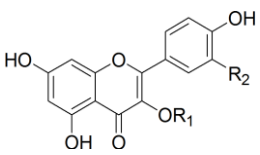
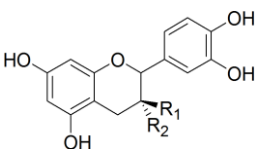


73 $R_1 = CH_3$; $R_2 = R_5 = R_6 = OCH_3$; $R_3 = R_4 = OCH_2O$; $R_7 = OH$
74 $R_1 = R_7 = H$; $R_2 = R_5 = R_6 = OCH_3$; $R_3 = R_4 = OCH_2O$
75 $R_1 = R_2 = R_7 = H$; $R_3 = R_4 = OCH2O$; $R_5 = R_6 = OCH_3$
76 $R_1 = CH_3$; $R_2 = R_3 = R_4 = R_5 = R_6 = OCH_3$; $R_7 = H$
77 $R_1 = R_2 = R_7 = H$; $R_3 = OH$; $R_4 = OCH_3$; $R_5 = R_6 = OCH_2O$
78 $R_1 = CH_3$; $R_2 = R_7 = H$; $R_3 = OH$; $R_4 = R_5 = R_6 = OCH_3$
79 $R_1 = CH_3$; $R_2 = R_7 = H$; $R_3 = R_4 = R_5 = OCH_3$; $R_6 = OH$



81 R_1 = Glucose ; R_2 = OH
82 R_1 = Xylose ; R_2 = OH
83 R_1 = Glucuronic acid ; R_2 = OH
84 R_1 = Rhamnose ; R_2 = OH
85 R_1 = Rhamnose ; R_2 = H
88 R_1 = H ; R_2 = OH
89 $R_1 = R_2$ = H



86 R_1 = OH ; R_2 = H
87 R_1 = H ; R_2 = OH

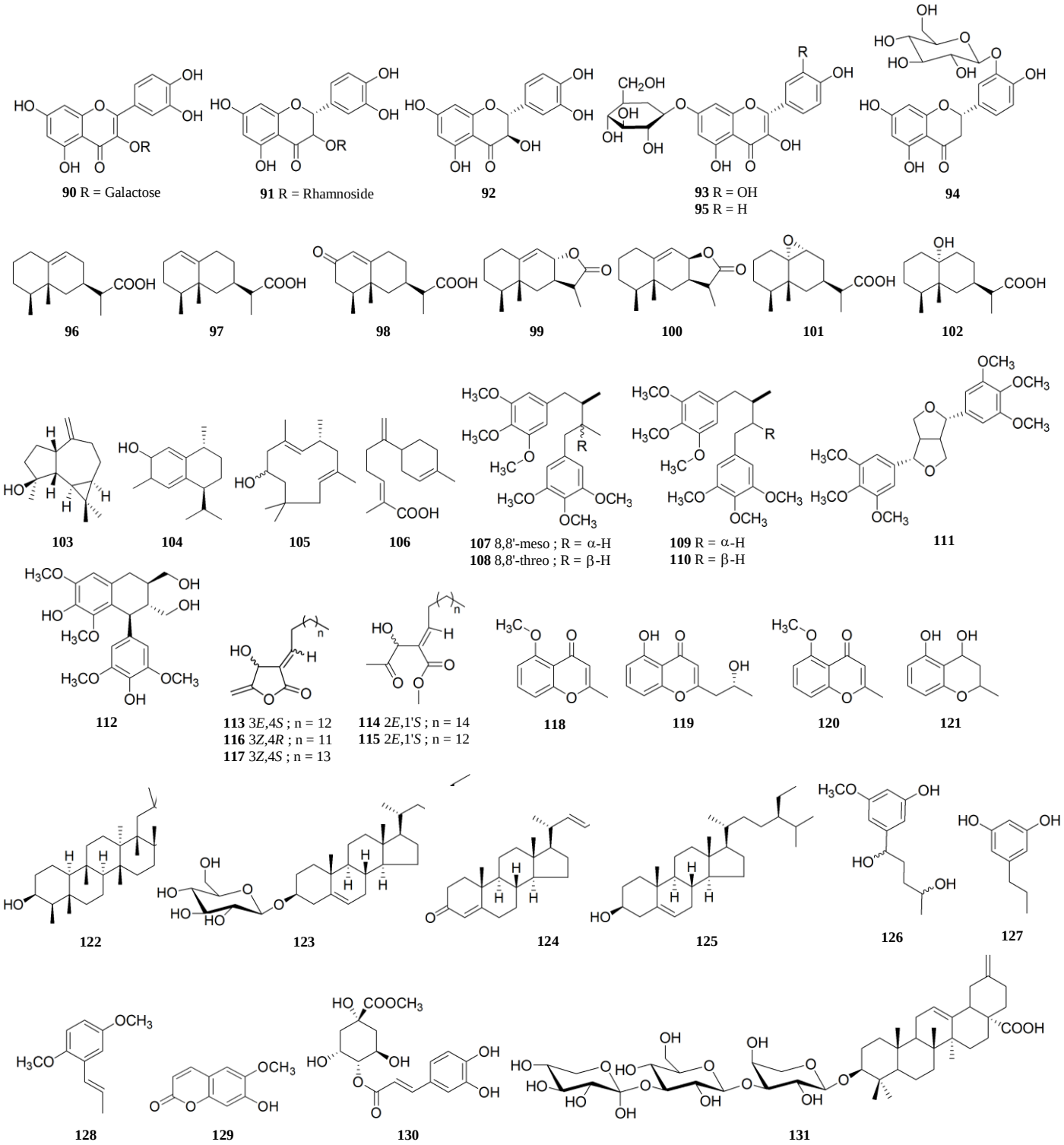


Fig. 1: Chemical structures of the compounds isolated from the genus *Ocotea*.

Table 1: Chemical constituents isolated from the genus *Ocotea* (2000-2016).

No.	Compound class and name	Source	References
	Neolignans		
1	Burchellin	*O. cymbarum*	Narciso *et al*., 2014
		O. elegans	Oliveira *et al*., 2006
2	Canelin	*O. elegans*	Oliveira *et al*., 2006
3	Cymosalignan A	*O. cymosa*	Rakotondraibe *et al*., 2015
4	Cymosalignan B	*O. cymosa*	Rakotondraibe *et al*., 2015
5	Cymosalignan C	*O. cymosa*	Rakotondraibe *et al*., 2015
6	3′,4′-Methylenedioxy-3,4,5-trimethoxy-$\Delta^{8'}$-8.O.6′-neolignan	*O. cymosa*	Rakotondraibe *et al*., 2015
7	Ococymosin	*O. cymosa*	Rakotondraibe *et al*., 2015
8	Didymochlaenone B	*O. cymosa*	Rakotondraibe *et al*., 2015
9	Didymochlaenone C	*O. cymosa*	Rakotondraibe *et al*., 2015
10	Sibyllenone	*O. bullata*	Zschocke *et al*., 2000
11	Demethoxysibyllenone	*O. cymosa*	Rakotondraibe *et al*., 2015
12	5-*O*-Demethylsibyllenone	*O. cymosa*	Rakotondraibe *et al*., 2015
13	(7*R*,8*S*,1′*S*,3′*S*)-$\Delta^{8'}$-3,4,5-Trimethoxy-3′,4′-methylenedioxy-1′,2′,3′,6′-tetrahydro-6′-oxo-7.1′-8.3′-neolignan	*O. cymosa*	Rakotondraibe *et al*., 2015
14	(7*R*,8*R*,1′*R*,3′*R*)-$\Delta^{8'}$-3,4,5-Trimethoxy-3′,4′-methylenedioxy-1′,2′,3′,6′-tetrahydro-6′-oxo-7.1′-8.3′-neolignan	*O. cymosa*	Rakotondraibe *et al*., 2015
15	3,4,5,3′,5′-Pentamethoxy-1′-allyl-8.O.4′-neolignan	*O. cymosa*	Rakotondraibe *et al*., 2015
16	3,4,5,3′-Tetramethoxy-1′-allyl-8.O.4′-neolignan	*O. cymosa*	Rakotondraibe *et al*., 2015
17	Virolongin B	*O. cymosa*	Rakotondraibe *et al*., 2015
18	Ocobullenone	*O. cymosa*	Rakotondraibe *et al*., 2015
		O. bullata	Zschocke *et al*., 2000
19	2′-Epiguianin	*O. macrophylla*	Suárez *et al*., 2011
		O. macrophylla	Coy-Barerra *et al*., 2009
20	Ocophyllal A	*O. macrophylla*	Coy-Barerra *et al*., 2009
		O. macrophylla	Suárez *et al*., 2011
21	Ocophyllal B	*O. macrophylla*	Coy-Barerra *et al*., 2009
		O. macrophylla	Suárez *et al*., 2011
22	Ocophyllol A	*O. macrophylla*	Coy-Barerra *et al*., 2009
		O. macrophylla	Suárez *et al*., 2011
23	Ocophyllol B	*O. macrophylla*	Coy-Barerra *et al*., 2009
		O. macrophylla	Suárez *et al*., 2011
24	Ocophyllol C	*O. macrophylla*	Coy-Barerra *et al*., 2009
25	(+)-Licarin B	*O. macrophylla*	Coy-Barerra *et al*., 2009
26	*rel*- (7*S*,8*R*,1'*S*,2'*R*,3'*S*)-$\Delta^{8'}$-2'-hydroxy-5,1',3'-trimethoxy-3,4-methylenedioxy-7,3',8,1'-neolignan	*O. heterochroma*	Cuca *et al*., 2009
27	*meso*-Dehydroguaiaretic acid	*O. heterochroma*	Cuca *et al*., 2009
28	Ferrearin C	*O. catharinensis*	Funasaki *et al*., 2009
29	Ferrearin E	*O. catharinensis*	Funasaki *et al*., 2009
30	Ferrearin G	*O. catharinensis*	Funasaki *et al*., 2009
31	Armenin B	*O. catharinensis*	Funasaki *et al*., 2009
32	5′-Methoxyporosin	*O. catharinensis*	Funasaki *et al*., 2009
33	(7*S*,8*S*,1′*R*,3′*R*)-3,4,5,3′,5′-Pentamethoxy-4′-oxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.O.6′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
34	*rel*- (7*S*,8*S*,l′*R*,2′*S*)-2′-Hydroxy-3,4-dimethoxy-3′-oxo-$\Delta^{1,3,5,4',8'}$-8.1′,7.O.2′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
35	*rel*- (7*R*,8*S*,1′*R*,2′*S*)-2′-Hydroxy-3,4,5′-trimethoxy-3′-oxo-$\Delta^{1,3,5,4',8'}$-8.1′,7.O.2′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
36	*rel*- (8*S*,1′*R*,5′*R*)-3,4,3′,5′-Tetramethoxy-7,2′-dioxo-$\Delta^{1,3,5,3',8'}$-8.1′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
37	*rel*- (7*R*,8*S*,1′*R*,2′*S*)-2′-Hydroxy-3,4-methylenedioxy-5,3′,5′-trimethoxy-$\Delta^{1,3,5,3',8'}$-8.1′,7.O.2′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
38	*rel*- (7*S*,8*R*,1′*R*,3′*R*)-4′-Hydroxy-3,4-methylenedioxy-3′,5′-dimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
39	(7*S*,8*R*,1′*R*,3′*R*)-4′-Hydroxy-3,4-methylenedioxy-3′,5′,5-trimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan	*O. catharinensis*	Funasaki *et al*., 2009
40	*rel*- (7*S*,8*R*,1′*R*,3′*R*)-4′-Hydroxy-3,4-methylenedioxy-3′,5′-dimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan dimer	*O. catharinensis*	Funasaki *et al*., 2009
41	(7*S*,8*R*,1′*R*,3′*R*)-4′-Hydroxy-3,4-methylenedioxy-3′,5′,5-trimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan dimer	*O. catharinensis*	Funasaki *et al*., 2009
	Alkaloids		
42	(+)-Dicentrine	*O. puberula*	Montrucchio *et al*., 2012
		O. macrophylla	Coy-Barrera and Cuca-Suárez, 2009
		O. acutifolia	Garcez *et al*., 2011; Guterres *et al*., 2013
43	(+)-Ocoteine	*O. acutifolia*	Garcez *et al*., 2011; Guterres *et al*., 2013
44	(+)-6*S*-Ocoteine *N*-oxide	*O. acutifolia*	Garcez *et al*., 2011; Guterres *et al*., 2013
45	(+)-Leucoxine	*O. acutifolia*	Garcez *et al*., 2011; Guterres *et al*., 2013

46	(+)-Norocoxylonine	*O. acutifolia*	Garcez *et al*., 2011
47	(+)-Thalicminine	*O. acutifolia*	Garcez *et al*., 2011; Guterres *et al*., 2013
48	(+)-Neolitsine	*O. acutifolia*	Garcez *et al*., 2011; Guterres *et al*., 2013
		O. macrophylla	Coy-Barrera and Cuca-Suárez 2009
49	*S*-3-methoxy-nordomesticine	*O. macrophylla*	Pabon and Cuca 2010
50	*S*-*N*-ethoxycarbonyl-3-methoxy-nordomesticine	*O. macrophylla*	Pabon and Cuca 2010
51	*S*-*N*-formyl-3-methoxy-nordomesticine	*O. macrophylla*	Pabon and Cuca 2010
52	*S*-*N*-methoxycarbonyl-3-methoxy-nordomesticine	*O. macrophylla*	Pabon and Cuca 2010
53	Dehydronantenine	*O. macrophylla*	Coy-Barrera and Cuca-Suárez 2009
54	(+)-Nantenine	*O. macrophylla*	Coy-Barrera and Cuca-Suárez 2009
55	(+)-*N*-acetyl-nornantenine	*O. macrophylla*	Coy-Barrera and Cuca-Suárez 2009
56	(+)-Cassythidine	*O. macrophylla*	Coy-Barrera and Cuca-Suárez 2009
57	Didehydroocoteine	*O. macrophylla*	Coy-Barrera and Cuca-Suárez 2009
58	Coclaurine	*O. lancifolia*	Fournet *et al*., 2007
		O. duckei	Silva *et al*., 2002
59	(-)-*N*-Methycoclaurine	*O. lancifolia*	Fournet *et al*., 2007
NMS	Crostparine	*O. lancifolia*	Fournet *et al*., 2007
60	Glaziovine	*O. lancifolia*	Fournet *et al*., 2007
61	(-)-Caaverine	*O. lancifolia*	Fournet *et al*., 2007
62	(+)-Laurotetanine	*O. lancifolia*	Fournet *et al*., 2007
63	(+)-Nordomesticine	*O. lancifolia*	Fournet *et al*., 2007
64	(+)-Norisoboldine	*O. lancifolia*	Fournet *et al*., 2007
NMS	(+)-Norantenine	*O. lancifolia*	Fournet *et al*., 2007
65	(+)-Corytuberine	*O. lancifolia*	Fournet *et al*., 2007
66	(+)-Domesticine	*O. lancifolia*	Fournet *et al*., 2007
67	(+)-Isoboldine	*O. lancifolia*	Fournet *et al*., 2007
68	(*S*)-Pallidine	*O. lancifolia*	Fournet *et al*., 2007
69	(+)-Norjuziphine	*O. lancifolia*	Fournet *et al*., 2000
70	(+)-Reticuline	*O. lancifolia*	Fournet *et al*., 2007
71	Tryptophol-5-*O*-β-D-glucopyranoside	*O. minarum*	Garcez *et al*., 2005
NMS	Lequesnamine	*O. leucoxylon*	Imler *et al*., 2003
72	(+)-6*S*-Dicentrine *N*-oxide	*O. acutifolia*	Garcez *et al*., 2011
73	(+)-Oxocylonine	*O. acutifolia*	Garcez *et al*., 2011
74	(+)-*O*-Methylcassyfiline	*O. acutifolia*	Garcez *et al*., 2011
75	(+)-Nordicentrine	*O. acutifolia*	Garcez *et al*., 2011
76	(+)-Thalicsimidine	*O. acutifolia*	Garcez *et al*., 2011
77	(+)-Isodomesticine	*O. acutifolia*	Garcez *et al*., 2011
78	(+)-Predicentrine	*O. acutifolia*	Garcez *et al*., 2011
79	(+)-*N*-Methyllaurotethanine	*O. acutifolia*	Garcez *et al*., 2011
	Flavonoids		
80	A-type proanthocyanidin trimer	*O. notata*	Garett *et al*., 2012
81	Isoquercitrin	*O. notata*	Garett *et al*., 2012
		O. corymbosa	Batista *et al*., 2010
82	Reynoutrin	*O. notata*	Garett *et al*., 2012
		O. corymbosa	Batista *et al*., 2010
83	Miquelianin	*O. notata*	Garett *et al*., 2012
84	Quercitrin	*O. notata*	Garett *et al*., 2012
85	Afzelin	*O. notata*	Garett *et al*., 2012
86	Catechin	*O. notata*	Garett *et al*., 2012
87	Epicatechin	*O. notata*	Garett *et al*., 2012
88	Quercetin	*O. notata*	Garett *et al*., 2012
89	Kaempferol	*O. acutifolia*	Garcez *et al*., 2011
90	Quercetin-3-*O*- β-D-galactoside	*O. corymbosa*	Batista *et al*., 2010
91	*rel*- (2*R*,3*R*)-dihydroquercetin-3-*O*-α-L-rhamnoside (astilbin)	*O. elegans*	Batista *et al*., 2010
92	Taxifolin	*O. minarum*	Garcez *et al*., 2005
93	Quercetin-7-*O*-β-D-glucopyranoside	*O. minarum*	Garcez*et al*., 2005
94	Eriodictyol-3'-*O*-β-D-glucopyranoside	*O. minarum*	Garcez *et al*., 2005
95	Naringenin-7-*O*-β-D-glucopyranoside	*O. minarum*	Garcez *et al*., 2005
	Sesquiterpenes		
96	*rel*-4β,5β,7β-eremophil-9-en-12-oic acid	*O. lancifolia*	Camargo *et al*., 2013
97	*rel*-4β,5β,7β-eremophil-1 (10)-en-12-oic acid	*O. lancifolia*	Camargo *et al*., 2013
98	*rel*-4β,5β,7β-eremophil-1 (10)-en-2-oxo-12-oic acid	*O. lancifolia*	Camargo *et al*., 2013
99	*rel*-4β,5β,7β-eremophil-9-en-12,8α-olide	*O. lancifolia*	Camargo *et al*., 2013
100	*rel*-4β,5β,7β-eremophil-9-en-12,8β-olide	*O. lancifolia*	Camargo *et al*., 2013

101	*rel*-4β,5β,7β-eremophil-9α,10α-epoxy-12-oic acid	*O. lancifolia*	Camargo *et al*., 2013
102	4β,5β,7β-eremophil-11-en- 10α-ol	*O. lancifolia*	Camargo *et al*., 2013
103	Spathulenol	*O. lancifolia*	Camargo *et al*., 2013
104	*rel*- (1*R*, 4*S*)-7-hydroxycalamenene	*O. elegans*	Batista *et al*., 2010
105	*rel*- (8*R*)-Humulan-1,4-dien-8-ol	*O. catharinensis*	Funasaki *et al*., 2009
106	Lanceolic acid	*O. minarum*	Garcez *et al*., 2005
	Lignans		
107	*meso*-3,4,5,3′,4′,5′-Hexamethoxy-8.8′-lignan	*O. macrophylla*	Coy-Barerra *et al*., 2011
108	*threo*-3,4,5,3′,4′,5′-Hexamethoxy-8.8′-lignan	*O. macrophylla*	Coy-Barerra *et al*., 2011
109	*erythro*-Diarylbutane	*O. macrophylla*	Suárez *et al*., 2011
110	*threo*-Diarylbutane	*O. macrophylla*	Suárez *et al*., 2011
111	Yangambin	*O. heterochroma*	Cuca *et al*., 2009
		O. duckei	Neto *et a*l., 2007; 2008
112	Lyonyresinol	*O. minarum*	Garcez *et al*., 2005
	Butanolides		
113	Macrocarpolide A	*O. macrocarpa*	Liu *et al*., 2015
114	Macrocarpolides B	*O. macrocarpa*	Liu *et al*., 2015
115	Macrocarpolides C	*O. macrocarpa*	Liu *et al*., 2015
116	Linderanolide B	*O. macrocarpa*	Liu *et al*., 2015
117	Isolinderanolide	*O. macrocarpa*	Liu *et al*., 2015
	Benzopyrans		
118	2-Methyl-5-methoxy-benzopyran-4-one	*O. corymbosa*	Teles *et al*., 2005
119	(2′*S*)-2- (propan-2′-ol)-5-hydroxy-benzopyran-4-one	*O. corymbosa*	Teles *et al*., 2005
120	(2*R*)-2,3-dihydro-2-methyl-5-methoxy-benzopyran-4-one	*O. corymbosa*	Teles *et al*., 2005
121	2,3-Dihydro-2-methyl-benzopyran-4,5-diol	*O. corymbosa*	Teles *et al*., 2005
	Steroids		
122	β-Friedelanol	*O. heterochroma*	Cuca *et al*., 2009
123	3-*O*-β-D-glucopyranosyl stigmasterol	*O. minarum*	Garcez *et al*., 2005
124	Stigmasta-4,22-dien-3-one	*O. minarum*	Garcez *et al*., 2005
125	β-Sitosterol	*O. minarum*	Garcez *et al*., 2005
	Alkylphenols		
126	3- (1,4-Dihydroxypentyl)-5-methoxyphenol	*O. minarum*	Garcez *et al*., 2005
127	5-Propylresorcinol	*O. minarum*	Garcez *et al*., 2005
	Arylpropene		
128	*trans*-Asarone	*O. minarum*	Garcez *et al*., 2000
	Coumarin		
129	Scopoletin	*O. minarum*	Garcez *et al*., 2005
	Ester		
130	4-*O*-*E*-caffeoylquinic acid methyl ester	*O. corymbosa*	Batista *et al*., 2010
	Saponin		
131	Guaianin	*O. elegans*	Oliveira *et al*., 2006

NMS – no molecular structure provided.

Table 2: Chemical components identified in the essential oils of the genus *Ocotea (*2000-2016).

Species	Locality	Parts/Major components	References
O. odorifera	Brazil	**Leaves:** Safrole (92.0%)	Oltramari *et al*., 2004
	Brazil	**Leaves:** Camphor (43.0%), safrole (42.0%)	Mossi *et al*., 2014
O. quixos	Italy	**Leaves:** 1,8-Cineole (8.2%), sabinene (4.6%), α-pinene (4.3%)	Enrico *et al*., 2014
	USA	**Leaves:** *trans*-Caryophyllene (28.2%), methyl cinnamate (19.5%), β-selinene (10.4%), α-humulene (10.1%)	Destryana *et al*., 2014
	Ecuador	**Leaves:** *trans*-Cinnamaldehyde (27.8%), methyl cinnamate (21.6%)	Tognolini *et al*., 2006
	Ecuador	**Leaves:** β-Caryophyllene (15.1%), cinnamyl acetate (11.4%), sabinene (7.6%), geranial (5.6%)	Sacchetti *et al*., 2006
	Ecuador	**Flower calices:** *trans*-Cinnamaldehyde (27.9%), methylcinnamate (21.6%), 1,8-cineole (8.0%)	Bruni *et al*., 2003
O. nigrescens	Brazil	**Leaves:** β-Caryophyllene (37.9%), α-pinene (6.7%), β-pinene (6.9%), α-copaene (6.2 %)	Yamaguchi *et al*., 2013
O. splendens	Brazil	**Leaves:** β-Caryophyllene (51.0%), caryophyllene oxide (9.9%), α-humulene (6.2%)	Yamaguchi *et al*., 2013
O. puchury-major	Brazil	**Leaves:** Safrol (39.4%), eucaliptol (28%), sabinene (8.5%), α-terpineol (7.9%)	Leporatti *et al*., 2014
O. macrophylla	Brazil	**Leaves:** Germacrene A (22.7 %), β-caryophyllene (22.9 %), α-pinene (8.7%), β-pinene (6.9%)	Garrett *et al*., 2010
	Colombia	**Leaves:** Spathulenol (15.9%), γ-muurolene (15.4%), bicyclogermacrene (14.5%)	Prieton *et al*., 2010
O. gomezii	Costa Rica	**Leaves:** Pentan-2-ol (12.5%), epi-α-cadinol (9.8%), δ-cadinene (7.7%), 1,8-cineole (6.0%)	Chaverri *et al*., 2011
		Bark: δ-Cadinene (14.5%), 1,10-diepi-cubenol (7.7%), α-muurolene (6.9%)	Chaverri *et al*., 2011
		Wood: epi-α-Muurolol (15.0%), epi-α-cadinol (10.0%), δ-cadinene (7.7%)	Chaverri *et al*., 2011
O. morae	Costa Rica	**Leaves:** β-Pinene (17.5%), α-pinene (10.4%), bicyclogermacrene (8.8%), germacrene D (7.5%), 1,8-cineole (7.3%), β-caryophyllene (7.1%)	Chaverri *et al*., 2011
		Bark: 1,8-Cineole (12.8%), β-caryophyllene (6.1%)	Chaverri *et al*., 2011
		Wood: (*E*)-Nerolidol (11.4%), 1,8-cineole (7.1%), epi-α-muurolol (6.3%), δ-cadinene (6.2%), α-cadinol (6.0%)	Chaverri *et al*., 2011
O. puberula	Brazil	**Bark:** Spathulenol, β-pinene, bicyclogermacrene, germacrene D and α-pinene	Farago *et al*., 2010
O. longifolia	Colombia	**Leaves:** α-Terpinolene (80.9%), α-phellandrene (4.7%)	Prieto *et al*., 2010
O. sp.	Colombia	**Stem/leaves/flowers:** α-Pinene (42.0%), *p*-cymene (14.6%), β-pinene (12.7%)	Olivero *et al*., 2010
O. duckei	Brazil	**Roots:** Elemol (24.3%), β-elemene (16.6%), β-eudesmol (13.4%), (%)	Barbosa-Filho *et al*., 2008
		Stems: β-Eudesmol (27.5%), α-pinene (9.0%), dl-limonene (6.6%), 1-borneol (6.1%)	Barbosa-Filho *et al*., 2008
		Leaves: *trans*-Caryophyllene (60.5%), α-humulene (4.6%), δ-selinene (4.4%)	Barbosa-Filho *et al*., 2008
		Fruits: dl-Limonene (30.1%), β-pinene (12.2%), α-pinene (9.8%), epiglobulol (8.1%)	Barbosa-Filho *et al*., 2008
O. endresiana	Costa Rica	**Leaves:** α-Pinene (47.9%), β-pinene (21.0%), α-humulene (14.3%)	Agius *et al*., 2007
O. praetermissa	Costa Rica	**Leaves:** α-Pinene (30.1%), β-pinene (19.0%), (*E*)-caryophyllene (9.1%), limonene (9.0%)	Agius *et al*., 2007
O. veraguensis	Costa Rica	**Leaves:** Bulnesol (29.5%), *p*-cymene (19.8%), spathulenol (8.5%)	Moriarity *et al*., 2007; Takaku *et al*., 2007
O. whitei	Costa Rica	**Leaves:** Spathulenol (15.3%), β-caryophyllene (15.2%), (*E*,*E*)-farnesyl acetate (10.1%)	Moriarity *et al*., 2007; Takaku *et al*., 2007
O. meziana	Costa Rica	**Leaves:** Germacrene D (50.6%), β-caryophyllene (13.2%), δ-cadinene (8.0%)	Moriarity *et al*., 2007; Takaku *et al*., 2007
O. sp. nov. "los llanos"	Costa Rica	**Leaves:** α-Pinene (27.5%), β -pinene (17.2%)	Wright *et al*., 2007
O. sp. nov. "small leaf"	Costa Rica	**Leaves:** Germacrene D (60.4%), α-pinene (4.3%)	Wright *et al*., 2007
O. floribunda	Costa Rica	**Leaves:** α-Pinene (22.5%), β -pinene (21.3%)	Takaku *et al*., 2007; Werka *et al*., 2007
O. bracteosa	Brazil	**Stem bark:** δ-Cadinene (12.4%), ledene (11.1%), globulol (10.1%)	Coutinho *et al*., 2007
O. austinii	Costa Rica	**Leaves:** α-Pinene (33.2%), β-pinene (13.0%) and δ-cadinene (5.7%)	Chaverri *et al*., 2007
		Twig wood: α-Pinene (14.9%), β-pinene (8.2%), β-eudesmol (9.1%), α-eudesmol (8.8%)	Chaverri *et al*., 2007
O. tonduzii	Costa Rica	**Leaves:** α-Pinene (41.4%), β-pinene (25.1%), α-humulene (6.9%), β-caryophyllene (5.8%)	Takaku *et al*., 2007; Bansal *et al*., 2007
O. holdridgeana	Costa Rica	**Leaves:** α-Pinene (29.9%), germacrene D (19.9%), *trans*-2-hexenal (8.4%)	Takaku *et al*., 2007
O. sinuate	Costa Rica	**Leaves:** *trans*-2-hexenal (17.0%), camphene (16.2%), germacrene D (15.4%), α-pinene (15.0%)	Takaku *et al*., 2007
O. valeriana	Costa Rica	**Leaves:** Germacrene D (69.7%), α-cadinol (4.5%)	Takaku *et al*., 2007
	USA	**Leaves:** 1,4-Cineole (19.6%), (*Z*)-anethole (13.4%), β-pinene (6.8%), α-gurjunene (6.5%)	Scora and Scora, 2001
O. bofo	Ecuador	**Floral calyces:** Stragole (48.7%), *R*-phellandrene (19.6%), sabinene (10.4%)	Guerrini *et al*., 2006
O. foetens	Portugal	**Aerial parts:** *p*-Coumarate (69.6%), γ-muurolene (5.2%), β-caryophyllene (4.9%)	Pino *et al*., 2004
O. comoriensis	Africa	**Bark:** Camphene (18.1%), α-pinene (13.7%), bornyl acetate (13.8%)	Menut *et al*., 2002
O. opifera	Bolivia	**Stem bark:** Asaricin (84.6%)	Lorenzo *et al*., 2001
O. botrantha	USA	**Leaves:** Germacrene D (35.2%), β-caryophyllene (13.4%), δ-elemene (11.2%)	Scora and Scora, 2001

Neolignans

Forty one neolignans were isolated from eight *Ocotea* species. Rakotondraibe *et al.* (2015)successively isolated ten new neolignans including the 6′-oxo-8.1′-lignans, cymosalignan A-C (**3**-**5**), 8.O.6′-neolignan (**6**), ococymosin (**7**), didymochlaenone C (**9**), and the bicyclo[3.2.1]octanoids (**11**-**14**) were isolated along with the known compounds, didymochlaenone B (**8**), 3,4,5,3′,5′-pentamethoxy-1′-allyl-8.O.4′-neolignan (**15**), 3,4,5,3′-tetramethoxy-1′-allyl-8.O.4′-neolignan (**16**), virolongin B (**17**), ocobullenone (**18**), and sibyllenone (**10**) from the stems or bark of the Madagascan plant *O. cymosa*. Compound (**10**) and (**18**) were also identified from the stem bark of *O. bullata (*Zschocke *et al*., 2000). Phytochemical exploration of the leaves of *O. macrophylla* afforded two new di-*nor*-benzofuran neolignan aldehydes, ocophyllals (**20**-**21**), and three new macrophyllin-type bicyclo[3.2.1]octanoid neolignans, ocophyllols A–C (**22**-**24**). The known compounds of 2′-*epi*-guianin (**19**) and licarin B (**25**) were also isolated (Coy-Barrera *et al*., 2009; Suarez *et al*., 2011). Funasaki *et al*., (2009) reported the isolation of fourteen neolignans (**28**-**41**) from the leaves of *O. catharinensis.* They managed to isolate seven new compounds; (7*S*,8*S*,1′*R*,3′*R*)-3,4,5,3′,5′-pentamethoxy-4′-oxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.O.6′-neolignan (**33**), *rel*- (7*R*,8*S*,1′*R*,2′*S*)-2′-hydroxy-3,4,5′-trimethoxy-3′-oxo-$\Delta^{1,3,5,4',8'}$-8.1′,7.O.2′-neolignan (**35**), *rel*- (8*S*,1′*R*,5′*R*)-3,4,3′,5′-tetramethoxy-7,2′-dioxo-$\Delta^{1,3,5,3',8'}$-8.1′-neolignan (**36**), *rel*-(7*R*,8*S*,1′*R*,2′*S*)-2′-hydroxy-3,4-methylenedioxy-5,3′,5′-trimethoxy-$\Delta^{1,3,5,3',8'}$-8.1′,7.O.2′-neolignan (**37**), *rel*-(7*S*,8*R*,1′*R*,3′*R*)-4′-hydroxy-3,4-methylenedioxy-3′,5′-dimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan (**38**), *rel*- (7*S*,8*R*,1′*R*,3′*R*)-4′-hydroxy-3,4-methylenedioxy-3′,5′-dimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan dimer (**40**), and (7*S*,8*R*,1′*R*,3′*R*)-4′-hydroxy-3,4-methylenedioxy-3′,5′,5-trimethoxy-2′,4′-dioxo-$\Delta^{1,3,5,5',8'}$-8.1′,7.3′-neolignan dimer (**41**). In addition, burchellin (**1**) was isolated from the leaves of *O. cymbarum* (Narciso *et al*., 2014), while canelin (**2**) from the stem of *O. elegans* (Oliveira *et al*., 2006). Besides, a new bicyclo[3.2.1]octanoid neolignan (**26**) was isolated from the fruit of *O. heterochroma*, together with a known compound, meso-dehydroguaiaretic acid (**27**) (Cuca *et al*., 2009).

Alkaloids

Most of alkaloids isolated from several *Ocotea* species were aporphine and benzylisoquinoline alkaloids. Forty one alkaloids were successfully identified from six *Ocotea* species. Garcez *et al*. (2005) isolated a new indole alkaloid; tryptophol-5-*O*-β-D-glucopyranoside (**71**) from the fruit of *O. minarum*. Six years later, they managed to isolate two new aporphinoid alkaloids; (+)-6*S*-ocoteine *N*-oxide (**44**) and norocoxylonine (**46**) from the leaves and trunk bark of *O. acutifolia*, along with thirteen aporphine analogues (+)-dicentrine (**42**), (+)-ocoteine (**43**), (+)-leucoxine (**45**), (+)-thalicminine (**47**), (+)-neolitsine (**48**), (*S*)-pallidine (**68**), (+)-reticuline (**70**), tryptophol-5-*O*-β-D-glucopyranoside (**71**), lequesnamine (**NMS**), (+)-6*S*-dicentrine *N*-oxide (**72**), (+)-oxocylonine (**73**), (+)-*O*-methylcassyfiline (**74**), (+)-nordicentrine (**75**), and (+)-thalicsimidine (**76**) and one morphinan alkaloid, *N*-methyllaurotethanine (**79**) (Garrett *et al*., 2010). Compound (**42**) was also isolated from the fruit of *O. puberula (*Montrucchio *et al*., 2012). Coy-Barrera *et al*., (2009) reported the isolation of seven aporphine alkaloids from the leaves of *O. macrophylla*. They were identified as dicentrine (**42**), neolitsine (**48**), dehydronantenine (**53**), nantenine (**54**), *N*-acetyl-nornantenine (**55**), cassythidine (**56**), and didehydroocoteine (**57**). A year later, Pabon and Cuca (2010) managed to isolate four aporphine alkaloids from the wood of *O. macrophylla*, which were (*S*)-3-methoxy-nordomesticine (**49**), (*S*)-*N*-ethoxycarbonyl-3-methoxy-nordomesticine (**50**), (*S*)-*N*-formyl-3-methoxy-nordomesticine (**51**), and (*S*)-*N*-methoxycarbonyl-3-methoxy-nordomesticine (**52**). Fournet and co-workers (2007)had successfully isolated thirteen known isoquinoline alkaloids from the stem bark of *O. lancifolia.* It comprises three benzyl-tetrahydroisoquinolines, coclaurine (**58**), *N*-methycoclaurine (**59**), norjuziphine (**69**), reticuline (**70**); two pro-aporphines: crostparine (**NMS**), glaziovine (**60**); eight aporphines, laurotetanine (**62**), nordomesticine (**63**), norisoboldine (**64**), domesticine (**66**), isoboldine (**67**), norantenine (**NMS**), caaverine (**61**), corytuberine (**65**), and the morphidanedienone alkaloid (*S*)-pallidine (**68**). Compound (**58**) was also isolated from the stem bark of *O. duckei* (Silva *et al*., 2002). Besides, Imler *et al*., (2003)had successfully isolated a new oxoaporphine alkaloid, lequesnamine from the wood of *O. leucoxylon.*

Flavonoids

Sixteen flavonoids were isolated from five *Ocotea* species. Garett *et al*., (2012) have successfully isolated an A-type proanthocyanidin trimer (**80**), isoquercitrin (**81**), reynoutrin (**82**), miquelianin (**83**), quercitrin (**84**), afzelin (**85**), and four minor compounds; catechin (**86**), epicatechin (**87**), quercetin (**88**), and kaempferol (**89**) from the leaves of *O. notata*. They also managed to isolate compound (**89**) from the leaves of *O. acutifolia* (Garcez *et al*., 2011). Compounds (**81**-**82**) were also isolated from the leaves of *O. corymbosa*, together with quercetin-3-*O*-β-D-galactoside (**90**) (Batista *et al*., 2010). In addition, Batista *et al*., (2010) also isolated a flavonoid, *rel*- (2*R*,3*R*)-dihydroquercetin-3-*O*-α-L-rhamnoside (**91**) from the leaves of *O. elegans*. Garcez *et al*., (2005) obtained four flavonoids which were taxifolin (**92**), quercetin-7-*O*-β-D-glucopyranoside (**93**), eriodictyol-3'-*O*-β-D-glucopyranoside (**94)**, and naringenin-7-*O*-β-D-glucopyranoside (**95**) from the fruit of *O. minarum.*

Sesquiterpenes

Eleven sesquiterpenes were isolated from four species of *Ocotea*. Camargo *et al*., (2013) isolated six new eremophilane sesquiterpenes, *rel*-4β,5β,7β-eremophil-9-en-12-oic acid (**96**), *rel*-4β,5β,7β-eremophil-1 (10)-en-12-oic acid (**97**), *rel*-4β,5β,7β-eremophil-1 (10)-en-2-oxo-12-oic acid (**98**), *rel*-4β,5β,7β-eremophil-9-en-12,8α-olide (**99**), *rel*-4β,5β,7β-eremophil-9-en-12, 8β-olide (**100**), and *rel*-4β,5β,7β-eremophil-9α,10α-epoxy-12-oic acid (**101**), from the leaves of *O. lancifolia*, together with two

known sesquiterpenes, 4β,5β,7β-eremophil-11-en-10α-ol (**102**) reported fors the first time in the genus *Ocotea*, and the aromadendrene sesquiterpene, spathulenol (**103**). Besides, the sesquiterpene *rel*- (1*R*,4*S*)-7-hydroxycalamenene (**104**) isolated from the leaves of *O. elegans*, has already been isolated from *O. corymbosa*. However, there was no report regarding this compound on other Lauraceae genera (Batista *et al*., 2010). Additionally, a new sesquiterpene of humulane type, *rel*- (8*R*)-humulan-1,4-dien-8-ol (**105**), besides known spathulenol (**103**) was isolated form the leaves of *O. catharinensis* (Suarez *et al*., 2011), while lanceolic acid (**106**) was identified from the trunk bark of *O. minarum* (Garcez *et al.*, 2005).

Lignans

Six lignans were isolated from four species of *Ocotea*. Two known lignans were isolated from the leaves of *O. macrophylla* which were *meso*-3,4,5,3′,4′,5′-hexamethoxy-8.8′-lignan (**107**) and *threo*-3,4,5,3′,4′,5′-hexamethoxy-8.8′-lignan (**108**) (Coy-Barrera *et al*., 2011). Meanwhile, Suarez *et al*., (2011)also managed to isolate*erythro*-diarylbutane (**109**) and *threo*-diarylbutane (**110**) from the same species. Yangambin (**111**), a furofuran lignan was obtained from the leaves of *O. duckei* (Neto *et al*., 2007, 2008) and fruits of *O. heterochroma* (Cuca *et al*., 2009). Besides, lyonyresinol (**112**) was isolated from the heartwood of *O. minarum* (Garcez *et al*., 2005).

Butanolides

Five butanolides were isolated from the root of *O. macrocarpa*. Macrocarpolide A (**113**), B (**114**) and C (**115**) were isolated for the first time from genus *Ocotea*. Compounds (**114-115**) belong to the class of secobutanolides (Liu *et al*., 2015).

Benzopyrans

Four benzopyrans derivatives were isolated from the leaves of *O. corymbosa*. (2′*S*)-2- (propan-2′-ol)-5-hydroxy-benzopyran-4-one (**119**) and 2,3-dihydro-2-methyl-benzopyran-4,5-diol (**121**) were firstly isolated from the genus *Ocotea* (Teles *et al*., 2005).

Steroids

Three steroids, 3-*O*-β-D-glucopyranosyl stigmasterol (**123**), stigmasta-4,22-dien-3-one (**124**), and β-sitosterol (**125**) were isolated from the heartwood and trunkbark of *O. minarum* (Garcez *et al*., 2005). β-Friedelanol (**122**) was obtained from the fruit of *O. heretochroma* (Cuca *et al*., 2009).

Alkylphenols

Two alkylphenols, 3- (1,4-dihydroxypentyl)-5-methoxyphenol (**126**) and 5-propylresorcinol (**127**) were isolated from the heartwood of *O. minarum* (Garcez *et al*., 2005)

Miscellaneous compounds

The arylpropene, *trans*-asarone (**128**), and a coumarin, scopoletin (**129**) were successfully isolated from the heartwood and fruits of *O. minarum* (Garcez *et al*., 2005). An ester, 4-*O*-*E*-caffeoylquinic acid methyl ester (**130**) was obtained from the leaves of *O. corymbosa* (Batista *et al.*, 2010), while a saponin, guaianin (**131**) was found from the leaves of *O. elegans* (Oliveira *et al*., 2006).

Essential oils

Since 2000 to 2016, thirty one *Ocotea* species have been reported on their essential oils composition as shown in **Table 2**. Sesquiterpenoids were found as the major group components in most of the *Ocotea* essential oils, which are *O. quixos*, *O. nirescens*, *O. splendens*, *O. macrophylla*, *O. gomezii*, *O. puberula*, *O. duckei*, *O. veraguensis*, *O. whitei*, *O. meziana*, and *O. bracteosa* (Barbosa-Filho *et al*., 2008; Chaverri *et al*., 2007;Coutinho *et al*., 2007; Destryana *et al*., 2014; Farago *et al*., 2010; Garrett *et al.*, 2010; Moriarity *et al*., 2007; Prieto *et al*., 2010; Sacchetti *et al*., 2006; Takaku *et al*., 2007; Wright *et al*., 2007; Yamaguchi *et al*., 2013). In addition, monoterpenoids were also detected from the essential oils of *O. marae*, *O. longifolia*, *O. endresiana*, *O. praetermissa*, *O. floribunda*, *O. austinii*, *O. tonduzii*, and *O. holdridgeana* (Agius *et al*., 2007; Bansal *et al*., 2007; Chaverri *et al*., 2011; Chaverri and Ciccio, 2007; Moriarity *et al*., 2007; Prieto *et al*., 2010; Takaku *et al*., 2007; Werka *et al*., 2007). Meanwhile, phenylpropanoids were also reported as the major group components isolated in *O. odorifera*, *O. puchury-major*, and *O. opifera* (Leporatti *et al*., 2014; Lorenzo *et al*., 2001; Mossi *et al*., 2014; Oltramari *et al*., 2004).

BIOLOGICAL ACTIVITIES

The traditional medicinal applications of the *Ocotea* species have inspired many pharmacological investigations. The pharmacological activities were compiled in this section. Nineteen different biological activities have been reported from the extracts, essential oils, and their isolated compounds.

Cytotoxicity activity

The cytotoxicity of *O. gomezii* and *O. morae* essential oils were tested on cell lines (CCF-STTG1, Hep3B, HepG2, H-460, AGS, N-87, SW-620, MCF-7, and VERO), and found that astrocytoma cells were the most resistant. The leaves and bark oils of *O. gomezii* gave the best activity against SW620 (colon) with LD_{50} of 122 and 94 µg/mL, respectively. While, the wood oil showed cytotoxicity activity against HepG2 (liver) with LD_{50} of 94 µg/mL. In addition, the leaf, bark, and wood oils of *O. morae* showed activity against AGS (stomach) (LD_{50} of 183 µg/mL), SW620 (colon) (LD_{50} of 166 µg/mL), and HepG2 (liver) (LD_{50} of 183 µg/mL), respectively (Chaverri *et al*., 2011). *O. praetermissa* and *O. endresiana* leaf oils were notably cytotoxic on MCF-7 cells (with >97% killing at 100 µg/mL) (Agius *et al*., 2007). *O. whitei* oil showed activity against M-14 melanoma cells (with 65% killing at 100 µg/mL). In addition, *O. veraguensis* oil was active against the estrogen receptor (ER) negative cell line, MDA-MB 231 (with 93% killing at 100 µg/mL) (Moriarity *et al*., 2007). *O.*

meziana, *Ocotea* sp. nov. 'los llanos', and *Ocotea* sp. nov. 'small leaf' have been reported to exhibit *in vitro* cytotoxic activity on MCF-7 human mammary adenocarcinoma cells (with 100% killing at 100 µg/mL) (Wright *et al*., 2007). *O. floribunda* oil has showed notable cytotoxic activity (≥ 50% killing on at least one cell line) with the best activity against HepG2 cell (78.8% killing at 100 µg/mL) (Werka *et al*., 2007). The (+)-ocoteine (**43**) showed the most potent effect against Hep-2 cells and (+)-neolitsine (**48**) being the most cytotoxic alkaloid to MCF-7 and B16-F10 cells. Thalicminine (**47**) on the other hand, was the most active compound against 786-0 cells, although it proved only marginally inhibitory to Hep-2 cells and nontoxic to MCF-7 and B16-F10 cells. While, (+)-6*S*-ocoteine *N*-oxide (**44**) was found to be only weakly active against Hep-2 and B16-F10 cells (IC_{50} of 32.7 and 30.7 µg/mL, respectively) and to be devoid of cytotoxicity against MCF-7 and 786-0 cells, as demonstrated by an IC_{50} value higher than 50 µg/mL in both cases. These results indicated that, compared with (+)-ocoteine (**43**), *N*-oxide functionality in (**44**) reduces its cytotoxic activity (Garcez *et al*., 2011). Yangambin (**111**) isolated from *O. duckei* presented cytotoxicity to murine macrophages, measured by the Trypan blue dye exclusion test and MTT reduction assay, resulting in high IC_{50} values of 187.0 µg/mL and 246.7 µg/mL, respectively (Neto *et al*., 2008).

Antibacterial and antifungal activities

O. praetermissa and *O. endresiana* leaf oils were slightly antibacterial against *Bacillus cereus* with MIC values of 78 and 156 µg/mL, respectively (Agius *et al*., 2007). *O. bofo* oil showed fair inhibiting properties against *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis* with MIC values of 0.16 mg/mL, while a good inhibition against yeast, *Yarrowia lypolytica* with MIC values of 0.10 mg/mL (Guerrini *et al*., 2006). The *O. quixos*oil also showed a dose-dependent antifungal activity against C*andida albicans* and *Saccharomyces cerevisiae* (MIC of 0.024 mg/ml), while the antifungal activity against the dermatophyte and phytopathogen strains by the essential oil was relatively good. The growth inhibition percentage against the dermatophyte *Trichophyton mentagrophytes* was 60% at the highest concentration tested. However, *O. quixos*oil performed better against the phytopathogen *Pythium ultimum*, with an inhibitory action of 85% at 500 mg/mL (Bruni *et al*., 2003). The *in vitro* antifungal activity of essential oil from *O. odorifera* had weak activity against *C. albicans* and *C. tropicalis* strains involved in oral cavity infections.

A slight antifungal activity was observed with 2.5 mg/mL and MIC in 68% strains (Castro *et al*., 2011). The essential oil of *O. longifolia* showed significant fumigant activity against *Sitophilus zeamais (*CL_{50} of 280.5 µL/L) (Prieto *et al*., 2010). The alkaloid fraction of *O. macrophylla* was active against *Fusarium oxysporum* at 250 µg/µL. The inhibitory activity against the growth of the fungi was moderate at 5 µg/µL for (*S*)-3-methoxy-nordomesticine (**49**) while the other alkaloids were ineffective, suggesting that the presence of electron withdrawing substituents on nitrogen atom decreased the antifungal activity. In addition, alkaloid (**49**) also showed antimicrobial activity against *Staphylococcus aureus* and *Enterococcus faecalis* with values of 30 AU (Pabon and Cuca, 2010).

Anti-inflammatory activity

The essential oils of *O. nigrescens* and *O. splendens* have showed a low anti-aggregant factor with 10.8% and 11.74%, respectively, as compared with the positive standard acetylsalicylic acid which strongly inhibits platelet aggregation (100%). The low antiplatelet activity against ADP shown by both essential oils might be due to the absence of phenylpropanoids in their composition (Yamaguchi *et al*., 2013). *O. quixos* essential oil significantly reduced LPS-induced NO release from J774 macrophages at non-toxic concentrations, inhibited LPS-induced COX-2 expression and increased forskolin-induced cAMP production. The essential oil in carrageenan-induced rat paw edema showed anti-inflammatory effect without damaging gastric mucosa (Ballabeni *et al*., 2010). The diastereomeric lignans, the *meso*-isomer (**107**) and*threo*-isomer (**108**) were found to be the potent COX-2/5-LOX dual inhibitor and PAF-antagonist. Compound (**107**) displayed a lower IC_{50} value than (**108**), in contrast to their COX-inhibition. The IC_{50} value of (**107**) for 5-LOX and PAFwere 46.4 and 38.9 µM, respectively, while COX-2 for (**108**) was 15.6 µM (Coy-Barrera *et al*., 2011). 2′-*epi*-Guianin (**19**) showed the most potent inhibition of platelet activating factor (PAF)-induced aggregation of rabbit platelets among other neolignans isolated from *O. macrophyla*, with IC_{50} value 1.6 µM (Coy-Barrera *et al*., 2009). Sibyllenone (**10**) was the only compound from *O. bullata* which showed good inhibitory activity towards 5-lipoxygenase with IC_{50} value of 18.6 µM (Zschocke *et al*., 2000).

Antileishmanial activity

The ethanolic leaves extract of *O. macrophylla* showed the efficacy assay against both Leishmania parasites, *L. panamensis* and *L. braziliensis* with EC_{50} values of 98.0 and 85.7 µg/mL,respectively. In addition, *erythro*-diarylbutane (**109**) and ocophyllal B (**21**) the isolated compounds from *O. macrophylla* have shown the best activity against *L. panamensis (*IC_{50} value 26.6 µg/mL) and *L. braziliensis (*IC_{50} value 36.3 µg/mL), respectively (Suarez *et al*., 2011). The crude ethanolic extract, lignoid fraction, and the purified compound, yangambin (**111**) obtained from *O. duckei* presented antileishmanial activity with IC_{50} values of 135.7, 26.5, and 49.0 µg/mL, respectively on *Leishmania chagasi*. Meanwhile, for *Leishmania amazonensis*, the IC_{50} values were 143.7, 48.2, and 64.9 µg/mL for the crude ethanolic extract, the lignoid fraction, and the purified compound yangambin (**111**), respectively (Neto *et al*., 2007).

Cruzain inhibitory activity

O. praetermissa and *O. endresiana* leaf oils inhibited cruzain with IC_{50} values of 87.5 and 18.8 µg/mL, respectively (Agius *et al*., 2007). The leaf essential oils of ten species of *Ocotea* from Costa Rica were examined on the enzyme inhibitory

activities against cruzain using a fluorometric assay. The *O. meziana* leaf oil was the most active (IC_{50} value 14.9 µg/mL) followed by *O. whitei (*15.8 µg/mL), *Ocotea* sp. nov. 'los llanos' (17.1 µg/mL), *Ocotea* sp. nov. 'small leaf' (19.2 µg/mL), and *O. holdridgeana (*76.9 µg/mL). The leaf oils of *O. floribunda*, *O. tonduzii*, and *O. valeriana* were somewhat active (IC_{50} value 100-200 µg/mL), but *O. sinuata* and *O. veraguensis* essential oils were inactive (IC_{50} >500 µg/mL). The cruzain inhibitory activities of the essential oils can be attributed to active sesquiterpenoid components as well as synergistic effects between two or more components (Setzer *et al*., 2006).

Mutagenic and recombinogenic activities

The somatic mutation and recombination test (SMART) in wing cells of *Drosophila melanogaster* was used to test the mutagenic and recombinogenic activities of alkaloids isolated from *O. acutifolia*. Third-stage larvae derived from the standard cross with wing cell markers *mwh* and/or flr^3 were treated chronically. The frequencies of mutant spots observed in marked heterozygous descendants revealed significant dose-dependent genotoxicity for alkaloids; thalicminine (**47**), (+)-dicentrine (**42**), (+)-ocoteine (**43**), and (+)-6*S*-ocoteine *N*-oxide (**44**). These alkaloids also induced mitotic recombination. The presence of a methoxyl group at C-3 (as in compound **43**) lowers its genotoxic effect relative to that of unsubstituted analogue (**42**), and the introduction of *N*-oxide functionality (**43** vs. **44**) further reduces its genotoxicity. The very planar conformation of oxoaporphine alkaloid (**47**) may account for its higher genotoxicity vs. its less-planar analogues (**43**) and (**44**) (Guterres *et al*., 2013).

Antiherpetic activity

The flavonoid fraction from *O. notata* leaves extract showed antiherpes activity against both herpes simplex viruses;type 1 (HSV-1) and 2 (HSV-2) with EC_{50} values of 35.8 and 23.5 µg/mL, respectively. Moreover, this fraction was more active against HSV-2 than HSV-1. The mechanisms of antiviral action of the flavonoid fraction against the herpesvirus types 1 and 2 were evaluated and the inhibition of different steps of the virus replication cycle was observed. The percentage inhibition obtained for HSV-2 was higher than 90% in all performed experiments. Differently, for HSV-1, the flavonoid fraction had no effect in pre-treatment of cells and showed 60% of inhibition in virucidal assay (Garett *et al*., 2012).

Antioxidant activity

The antioxidant activity (TBARS method) of the essential oil from *Ocotea* sp., showed the lowest mean effective concentration with EC_{50} value of 31.1 µg/mL (Olivero *et al*., 2010). *O. bofo* oil revealed a remarkable inhibitory scavenging effect on DPPH with inhibition of 64.4%, while in β-carotene bleaching test gave 75.8% inhibition. In the photochemiluminescence (PCL) assay, the oil gave 3.14 mmol of Trolox/L (Guerrini *et al*., 2006). The *O. quixos* oil exerted a relatively good capacity to act as a non-specific donor of hydrogen atoms or electrons whenchecked by the DPPH assay, quenching 52% of the radical. On the other hand, it showed weak effects in inhibiting theoxidation of linoleic acid when assayed by the β-carotene bleaching test (Bruni *et al*., 2003).

Cardiovascular activity

The pharmacological activity of *O. duckei* essential oil showing significant cardiovascular effects. The leaves oil induced significant hypotension, followed by intense bradycardia. The fruits also induced a marked hypotension, which was followed by bradycardia. The stem bark and roots were both able to induce hypotension and bradycardia. Among all of the essential oils tested, the hypotensive effect was more potent on diastolic arterial blood pressure compared with the effect induced on systolic pressure (Barbosa-Filho *et al*., 2008).

Antithrombotic activity

O. quixos essentially possesses potent and safe antithrombotic activity attributable to its antiplatelet and vasorelaxant effects. The best inhibitory potency against platelet aggregation in guinea pig PRP induced by arachidonic acid (IC_{50} of 47 µg/mL), while platelet aggregation in human PRP induced by thromboxane A_2 receptor agonist U46619 (IC_{50} of 115 µg/mL). The antithrombotic activity could be related to its ability to block both platelet aggregation and clot retraction and to inhibit vasoconstriction (Ballabeni *et al*., 2007).

Antiproliferative activity

Macrocarpolides A-C (**113-115**), linderanolide B (**116**), and isolinderanolide (**117**) showed good antiproliferative activities against the A2780 ovarian cell line, with IC_{50} values of 2.57, 1.98, 1.67, 2.43, and 1.65 µM, respectively. The similar IC_{50} values for the five compounds suggested that they have a similar mechanism of action, possibly as Michael acceptors (Liu *et al*., 2015). A benzopyran (**119**) was found to induce cell proliferation: 70% on HeLa (human cervix tumour) cells and 25% on CHO (Chinese hamster ovary) cells (Teles *et al*., 2005).

Antinociceptive activity

Dicentrine (**42**) produced dose-related inhibition of acetic acid-induced pain without causing changes in the motor performance of mice. Furthermore, the chloroform fraction from *O. puberula* fruit produced marked antinociception in different models of chemical pain, and this effect appears to be, at least in part, due to the presence of dicentrine (**42**). The mechanisms by the extract and the alkaloid produced antinociception still remains unclear, but the adenosinergic or opioid system seems unlikely to be involved in this action (Montrucchio *et al*., 2012).

Larvicidal activity

Burchellin (**1**) isolated from *O. cymbarum* interfered with the development cycle of *Aedes aegypti*, where its strongest toxic effect was 100% mortality in larvae (L3) at concentrations ≥30 ppm (Narciso *et al*., 2014). The new 8.O.6′-neolignan (**6**),

dihydrobenzofuranoid (**7**), and bicyclo[3.2.1]octanoid (**11**) have *in vitro* activities against *Aedes aegypti*, with ≥80% mortality at 4 mg/mL (Rakotondraibe *et al*., 2015).

Lethality activity

O. praetermissa and *O. endresiana* leaf oils were active in the brine shrimp lethality test against *Artemia salina* with LC_{50} values of 31.6 and 6.9 µg/mL, respectively (Agius *et al*., 2007). The *O. floribunda* oil showed notable brine shrimp toxicity against *Artemia salina* with LC_{50} value of 3.7 µg/mL. On the other, the oil also showed antibacterial activity on *Staphylococcus aureus* with MIC value of 78 µg/mL (Werka *et al*., 2007).

Antiprotozoal activity

(-)-Caaverine (**61**) has shown the most interesting antiprotozoal activity against *Leishmaniabraziliensis*, *Leishmania amazonensis*, and *Leishmania donovani* with IC_{100} of 10 µg/mL, respectively. Meanwhile, (-)-caaverine (**61**) and (+)-domesticine (**66**) showed the best activity against *Trypanosoma cruzi* parasite with IC_{50} of 155 and 105 µg/mL, respectively (Fournet *et al*., 2007).

Toxicity activity

The essential oil of *O. notata* was evaluated by means of the brine shrimp lethality test and showed a high toxicity with an LC_{50} value of 2.37 µg/mL (Garrett *et al*., 2010). The *Ocotea* sp. essential oil has showed high cytotoxicity (LC_{50} value 7.84 µg/mL) against *Artemia franciscana* on the brine shrimp assay (Olivero *et al*., 2010).

Molluscicidal activity

The stem bark oil of *O. bracteosa* showed significant molluscicidal activity against *Biomphalaria glabrata*, with an LC_{90} value of 8.3 µg/mL, which falls below the threshold of 100 µg/mL, set for potential molluscicidal activity by the World Health Organization (Coutinho *et al*., 2007).

Antiplasmodial activity

Ococymosin (**7**) was the most active antiparasitic component than other neolignans, with an IC_{50} value of 0.45 µM against the Dd2 strain of *Plasmodium falciparum* (Rakotondraibe *et al*., 2015).

Antilmalarial activity

The antimalarial activity of the *O. comoriensis* oil is interesting, with an IC_{50} value of 10 µg/mL (Menut *et al*., 2002).

CONCLUSION

The genus *Ocotea* is widespread all over the world, and many species of this genus have been used as traditional herbal medicines. The chemical investigation of *Ocotea* species has revealed that many components from this genus exhibit significant bioactivities. Nevertheless, there are still several *Ocotea* species that have received no or only little attention, and phytochemical and biological studies now should focus on these plants.

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