Canarium L. : A Phytochemical and Pharmacological Review

Article · January 2011

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R.Mogana et al. / Journal of Pharmacy Research 2011,4(8),2482-2489

Review Article
ISSN: 0974-6943

Available online through
www.jpronline.info

Canarium L. : A Phytochemical and Pharmacological Review

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Received on: 17-05-2011; Revised on: 12-06-2011; Accepted on:16-07-2011

ABSTRACT

The genus *Canarium* L. consists of 75 species of aromatic trees which are found in the rainforests of tropical Asia, Africa and the Pacific. The medicinal uses, botany, chemical constituents and pharmacological activities are now reviewed. Various compounds are tabulated according to their classes their structures are given. Traditionally *Canarium* L. species have been used to treat a broad array of illnesses. Pharmacological actions for *Canarium* L. as discussed in this review include antimicrobial, antioxidant, anti-inflammatory, hepatoprotective and antitumor activity.

Keywords: *Canarium* L., Burseraceae, antibacterial, antioxidant, pharmacology, secondary metabolites

INTRODUCTION

Canarium L. belongs to the family of Burseraceae Kunth. in the order Sapindales Juss. ex Bercht. & J. Pearl. This family consists of 18 genera and about 700 species of tropical trees[1]. The word *Canarium L.* derives from the Malay name 'kanari'[2]. *Canarium* L. species often produce edible kernels, called canarium nut of commercial interest: *Canarium indicum* L., *Canarium solomonense* B.L.Burtt, *Canarium harveyi* Seem, *Canarium odontophyllum* Miq. and *Canarium album* L. Another economical interest of *Canarium* L. species, is the production of resins used in foods (*Canarium luzonicum* Miq.), in the making of incense and varnishing.

In spite of these commercial potentials of *Canarium* L., little attention has been given to the collection and conservation of *Canarium* L. species [3]. The genetic diversity thus derogates at an alarming rate.

BOTANICAL DESCRIPTION

The genus *Canarium* L. probably originated from the North American continent, not Gondwanaland [1]. This clade embraces 75 species of trees which are mainly found in tropical Asia and the Pacific, and a few species in tropical Africa [2]. About 9 species were found in the Philippines [2]. The geographical centre of their genetic diversity is the Molucca Islands of eastern Indonesia, but their centre of cultivated diversity is undoubtedly western Melanesia. Twenty to 25 species are found in the South Pacific, of which 21 are in Papua New Guinea [4], eight in the Solomon Islands [5] and 3 or 4 in Vanuatu [6]. The members of the genus *Canarium* L. consist of medium to large buttressed trees up to 40-50m tall, or rarely a shrub. The barks are greenish grey, fawn or light yellow brown that are usually smooth, scaly or dippled with many small lenticels. Outer bark are thin while the inner barks are pinkish brown or reddish brown, laminated, soft and aromatic with a clear sticky or rarely oily exudate. The stems are usually terete.

The leaves are pinnate, spiral and stipulated. The rachis is terete flattened to channeled swollen at base, and bears 5-21 folioles. The folioles are oblique at base, entire, dentate or serrate at margin, often thick and acuminiate at apex. The secondary nerves are arching and joined near margin. The tertiary nerves are reticulate. The infloresence is an axillary or terminal panicle.

The calyx is cupular. The corolla includes 3 creamy petals. The androecium comprises a whorl of 6 stamens. The disc within the stamens is 6 lobed. The gynaecium consist of 3 carpels united into a 3 lobular ovary. The drupes are seated on a persistent enlarged calyx and enclose a woody stone [7].

TRADITIONAL MEDICINAL USE

Elemi (British Pharmaceutical Codex, 1934) is an oleoresin exuded through the bark of *Canarium luzonicum* Miq. or *Canarium commune* L. which has been used in the form of an ointment as a stomach stimulant and as an expectorant [8]. The barks of *Canarium indicum* L. has been used for chest pains where else the oil has been patented for treatment of arthritis pain and the oleoresin of the tree is applied as a poultice for ulcerated wounds. The resin of *Canarium tonkinense* Engl. has been used as a stimulant, rubefacient and antirheumatic when applied externally. The oleoresin has been applied as ointment for ulcers [9].

The dried fruit of chinese olive or *Canarium album* (Lour.) Raeusch. is used in China and used to treat bacterial and viral infections, inflammation, poisoning and for detoxification [10]. In Chinese folk medicine, the dried fruits of *Canarium album* (Lour.) Raeusch have been used for treatment of angina, dysentery, snake bites, cough-hematemesis, enteritis, diarrhoea, toxicosis from swellfish and alcohol [11].

Canarium schweinfurthii Engl. is used by traditional healers as a remedy for diabetes mellitus in southern Senegal [12] while in Congo and Central African Republic the plant is used in fever, as stimulant, emollient, in post-partum pain, constipation, malaria, diarrhoea, sexual infections and rheumatism [13]. In Indonesia, the bark of *Canarium littorale* Bl. is used to make a decoction taken to heal haemorrhoids [3].

CHEMICAL CONSTITUENTS

Isolation and structure elucidations of secondary metabolites in *Canarium* L. has been carried out since the 50s [14] Majority of investigations include the resin and the fruit of the species.

To date about 99 compounds have been isolated from 9 species, which are *Canarium schweinfurthii* Engl., *Canarium boivinii* Engl., *Canarium odontophllum* Miq., *Canarium manii* King., *Canarium album* (Lour) Raeusch, *Canarium zeylanicum* (Retz.) Blume, *Canarium commune* L., *Canarium muelleri* F.M. Bailey and *Canarium bengalense* Roxb. The extensively researched species are *Canarium schweinfurthii* Engl. *and Canarium album* (Lour.) Raeusch [10,11,15-17]

Among the secondary metabolites isolated from members of the genus *Canarium* L. are terpenes (monoterpenes, triterpenes, tetraterpenes like carotenoids, sesquiterpenes, cyclohexane and sterols), carboxylic acids, coumarins, furans, lipids and phenols (flavonoids, tannins, phenolic acids). The main secondary metabolites isolated so far from the genus *Canarium* L. consists of terpenes with 58 compounds and flavonoids with 11 compounds. The profile of all known secondary metabolites of *Canarium* L. as found in literature and their structures are included in Table 1.

METHODS OF ISOLATION AND STRUCTURAL DETERMINATIONS

The isolation and separation technique is very much dependent on the type of fractions. Essential oils are analysed with gas chromatography (GC) and mass spectroscopy (MS) [13,18,19]. Other substances are separated with liquid chromatography using different solvent mixtures with silica gel [20,21], charcoal [22], sephadex [11] and multiple column packing such as AB-8 adsorption resin, polyamide, and TSK Toyopearl HW-40(S). Other types of analytical techniques include thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) [10,17,23-25].

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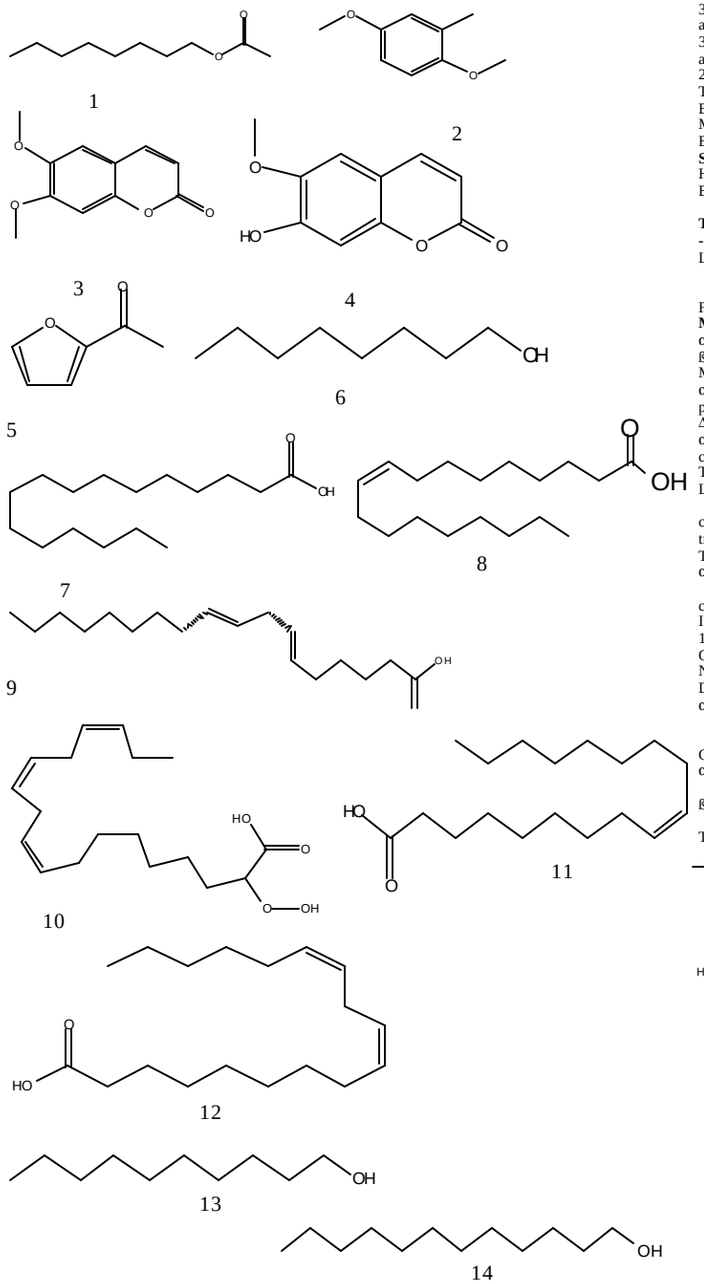
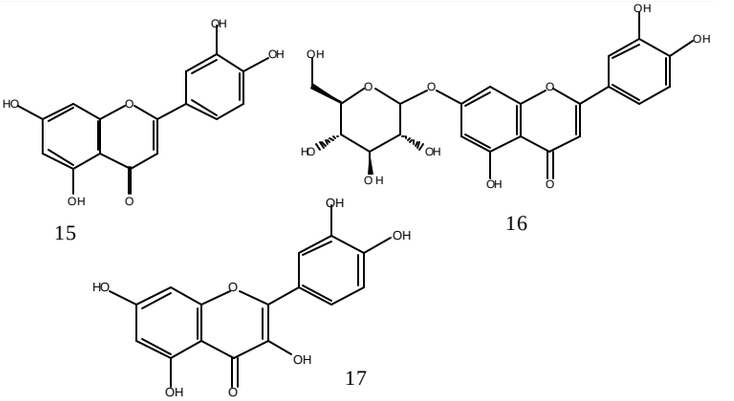
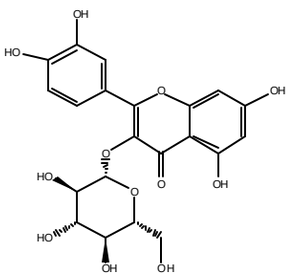
Table 1. Secondary metabolites of *Canarium* L.

Compound name	Species	Chemical Formula	Structure Number	Plant part	Reference
CARBOXYLIC ACIDS					
Octylacetate	*Canarium schweinfurthii* Engl.	$C_{10}H_{20}O_2$	1	resin,oil	[13]
2,5-Dimethoxytoluene	*Canarium schweinfurthii* Engl.	$C_9H_{12}O_2$	2	resin,oil	[13]
COUMARINS					
Scoparone	*Canarium album* (Lour.) Raeusch	$C_{11}H_{10}O_4$	3	fruit	[38]
Scopoletin	*Canarium album* (Lour.) Raeusch	$C_{10}H_8O_4$	4	fruit	[38]
HETEROCYCLIC COMPOUNDS- FURANS					
2-acetylfuran	*Canarium schweinfurthii* Engl.	$C_6H_6O_2$	5	resin,oil	[13]
n-octanol	*Canarium schweinfurthii* Engl.	$C_8H_{18}O$	6	resin,oil	[13]
LIPIDS					
Hexadecanoic acid	*Canarium schweinfurthii* Engl.	$C_{16}H_{32}O_2$	7	fruit,oil	[39]
9-octadecenoic acid	*Canarium schweinfurthii* Engl.	$C_{18}H_{34}O_2$	8	fruit,oil	[39]
6,9-octadecadienoic acid	*Canarium schweinfurthii* Engl.	$C_{18}H_{32}O_2$	9	fruit,oil	[39]
9,12,15-octadecatrienoic acid	*Canarium schweinfurthii* Engl.	$C_{18}H_{30}O_4$	10	fruit,oil	[39]
Oleic acid(cis-C18:1n9)	*Canarium schweinfurthii* Engl.	$C_{18}H_{34}O_2$	11	fruit,oil	[40]
Linoleic acid(cis-C18:2n6)	*Canarium schweinfurthii* Engl.	$C_{18}H_{32}O_2$	12	fruit,oil	[40]
n-decanol	*Canarium schweinfurthii* Engl.	$C_{10}H_{22}O$	13	resin, oil	[13]
n-dodecanol	*Canarium schweinfurthii* Engl.	$C_{12}H_{26}O$	14	resin,oil	[13]
PHENOLS					
FLAVONOIDS					
Luteolin	*Canarium album* (Lour.) Raeusch	$C_{15}H_{10}O_6$	15	fruit	[11]
Luteolin-7-*O*-ß-D-glucoside	*Canarium album* (Lour.) Raeusch	$C_{21}H_{20}O_{11}$	16	fruit	[11]
Quercetin	*Canarium album* (Lour.) Raeusch	$C_{15}H_{10}O_7$	17	fruit	[11]
Quercetin-3-*O*-ß-D-glucoside	*Canarium album* (Lour.) Raeusch	$C_{21}H_{19}O_{12}$	18	fruit	[11]
Kaempferol	*Canarium album* (Lour.) Raeusch	$C_{15}H_{10}O_6$	19	fruit	[11]
7,8,3',4'-tetrahydroxyflavanone	*Canarium album* (Lour.) Raeusch		20	fruit	[11]
3,5,7,3'-tetrahydroxy-4'-methoxyflavanonol	*Canarium album* (Lour.) Raeusch		21	fruit	[11]
Hyperin/Quercetin-3-galactoside	*Canarium album* (Lour.) Raeusch	$C_{21}H_{20}O_{12}$	22	dried stem, leaf,fruit	[27],10]
Kaempferol-3-glucoside	*Canarium album* (Lour.) Raeusch	$C_{21}H_{20}O_{11}$	23	fruit	[10]
Amentoflavone	*Canarium album* (Lour.) Raeusch	$C_{30}H_{18}O_{10}$	24	fruit	[10]
Agathisflavone	*Canarium manii* King.	$C_{30}H_{18}O_{10}$	25	stem,bark	[21]
PHENOLIC ACIDS					
Sinapic acid	*Canarium album* (Lour.) Raeusch	$C_{11}H_{12}O_5$	26	fruit	[17]
Corilagin	*Canarium album* (Lour.) Raeusch	$C_{27}H_{22}O_{18}$	27	fruit	[10]
Gallic acid	*Canarium album* (Lour.) Raeusch	$C_7H_6O_5$	28	fruit	[38],[10]
Ellagic acid	*Canarium album* (Lour.) Raeusch	$C_{14}H_6O_8$	29	dried stem,leaf	[27]
Brevifolin carboxylic acid	*Canarium album* (Lour.) Raeusch	$C_{13}H_8O_8$	30	fruit	[17]
3-O-galloyl quinic acid butyl ester	*Canarium album* (Lour.) Raeusch	$C_{18}H_{24}O_{10}$	31	fruit	[16]
3,4-dihydroxybenzoic acid ethyl ether	*Canarium album* (Lour.) Raeusch	$C_9H_{10}O_4$	32	fruit	[11]
2-hydroxybenzoic acid	*Canarium album* (Lour.) Raeusch	$C_7H_6O_3$	33	fruit	[11]
TANNINS					
Ethyl gallate	*Canarium album* (Lour.) Raeusch	$C_9H_{10}O_5$	34	fruit	[11],[10]
Methyl gallate	*Canarium album* (Lour.) Raeusch	$C_8H_8O_5$	35	fruit	[10]
Elemicin	*Canarium commune* L.	$C_{12}H_{16}O_3$	36	fruit	[34]
SAPONINS					
HYDROXY ACIDS					
Elemadienonic acid	*Canarium boivinii* Engl.	$C_{30}H_{46}O_3$	37	resin	[41]
	Canarium schweinfurthii Engl.			resin	[14]
TERPENES					
- CYCLOHEXANE	*Canarium schweinfurthii* Engl.	$C_{10}H_{16}$	38	resin,oil	[13]
Limonene	*Canarium boivinii* Engl. *Canarium zeylanicum* (Retz.) Blume		39	resin oleoresin	[20,41]
Furfuryl butanoate	*Canarium schweinfurthii* Engl.	$C_9H_{12}O_3$	40	resin,oil	[13]
MONOTERPENES					
α-pinene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	41	resin	[18]
ß-Pinene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	42	resin	[18]
Myrcene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	43	resin	[18]
α-Fenchene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	44	resin	[18]
p-1-Menthene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{18}$	45	resin	[18]
Δ-3-Carene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	46	resin	[18]
α-Terpinene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	47	resin	[18]
cis-Sabinene hydrate	*Canarium album* (Lour.) Raeusch	$C_{10}H_{18}O$	48	resin	[18]
Terpinolene	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}$	49	resin	[18]
Linalool	*Canarium album* (Lour.) Raeusch *Canarium schweinfurthii* Engl.	$C_{10}H_{18}O$	50	resinresin,oil	[18] [13]
cis-p-Menth-2-en-1-ol	*Canarium album* (Lour.) Raeusch	$C_{10}H_{18}O$	51	resin	[18]
trans-p-Menth-2-en-1-ol	*Canarium album* (Lour.) Raeusch	$C_{10}H_{18}O$	52	resin	[18]
Terpinen-4-ol	*Canarium album* (Lour.) Raeusch	$C_{10}H_{18}O$	53	resin	[18]
α-Terpineol	*Canarium album* (Lour.) Raeusch *Canarium schweinfurthii* Engl.	$C_{10}H_{18}O$	54	resin resin,oil	[18] [13]
cis-Piperitone	*Canarium album* (Lour.) Raeusch	$C_{10}H_{16}O_2$	55	resin	[18]
Isobornyl acetate	*Canarium album* (Lour.) Raeusch	$C_{12}H_{20}O_2$	56	resin	[18]
1,8-cineole	*Canarium schweinfurthii* Engl.	$C_{10}H_{18}O$	57	reisn,oil	[13]
Citronellyl acetate	*Canarium schweinfurthii* Engl.	$C_{12}H_{22}O_2$	58	resin,oil	[13]
Neryl acetate	*Canarium schweinfurthii* Engl.	$C_{12}H_{20}O_2$	59	resin,oil	[13]
Decyl Acetate	*Canarium schweinfurthii* Engl.	$C_{12}H_{24}O_2$	60	resin,oil	[13]
α-pinene/α-pinene	*Canarium boivinii* Engl. *Canarium zeylanicum* (Retz.) Blume	$C_{10}H_{16}$	61	Resin Oleoresin, timber	[20,41]
Carvone	*Canarium zeylanicum* (Retz.) Blume	$C_{10}H_{14}O$	62	oleoresin	[20]
α-phellandrene	*Canarium zeylanicum* (Retz.) Blume	$C_{10}H_{16}$	63	oleoresin, bark,timber	[20]
ß-phellandrene	*Canarium zeylanicum* (Retz.) Blume	$C_{10}H_{16}$	64	oleoresin, bark,timber	[20]
Terpineol	*Canarium zeylanicum* (Retz.) Blume	$C_{10}H_{18}O$	65	oleoresin, bark	[20]







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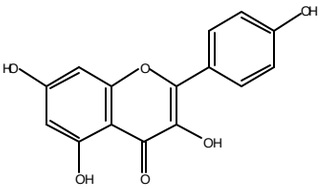

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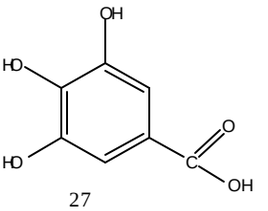

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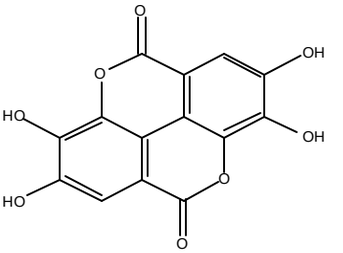

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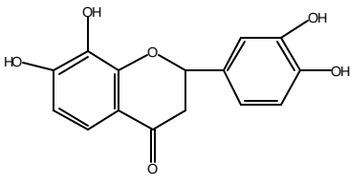

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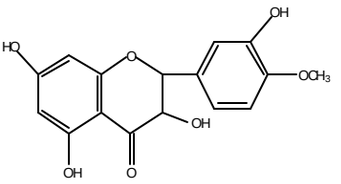

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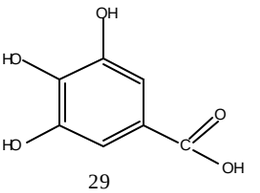

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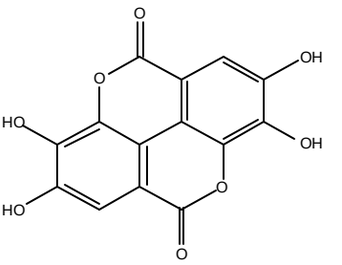

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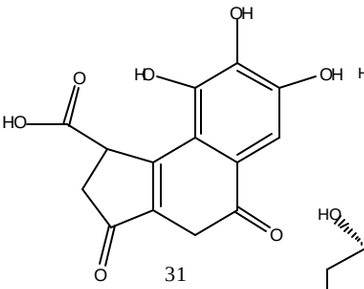

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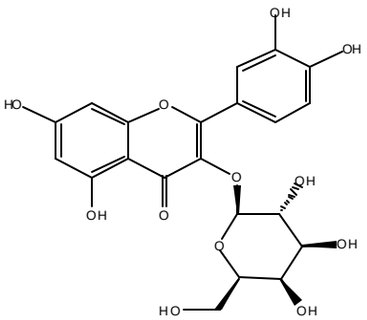

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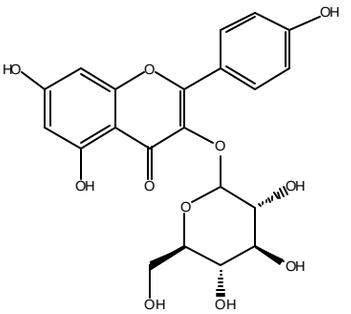

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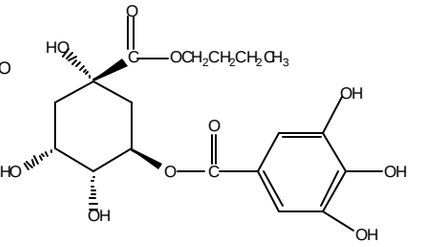

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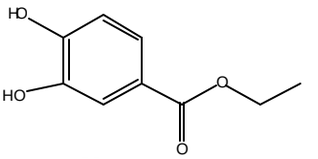

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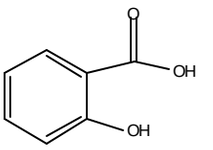

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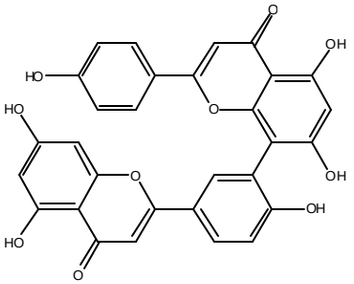

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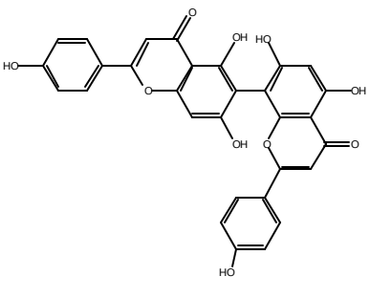

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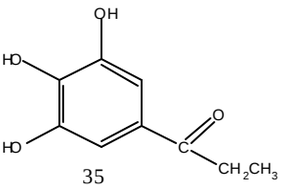

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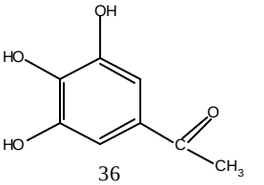

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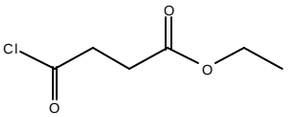

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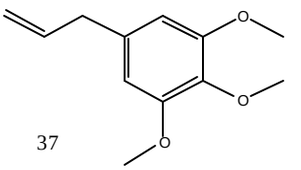

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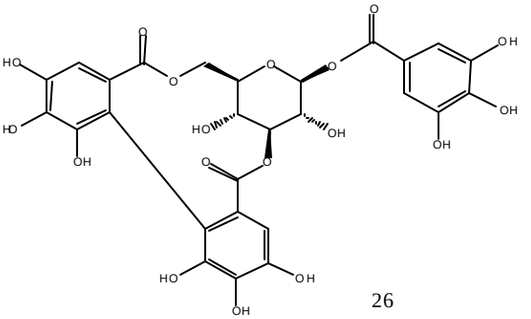

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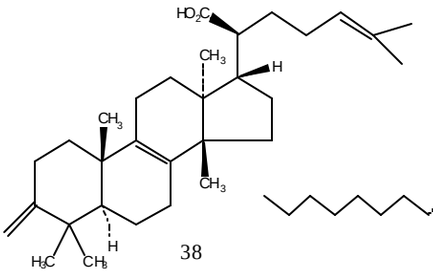

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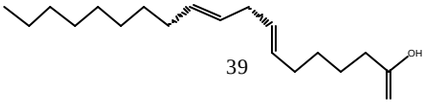

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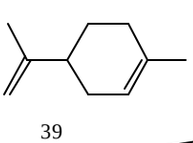
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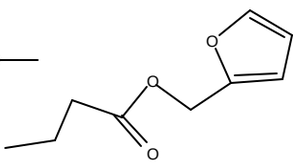
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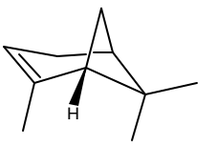
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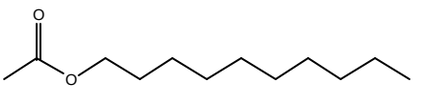
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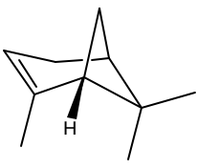
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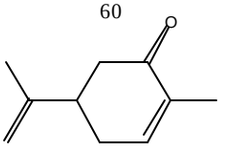
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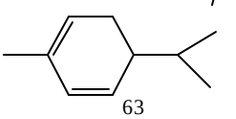
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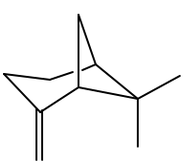
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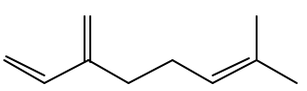
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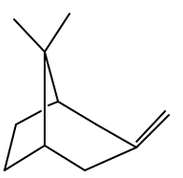
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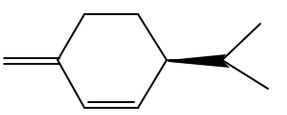
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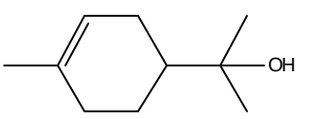
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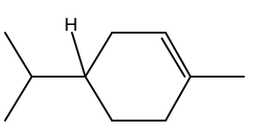
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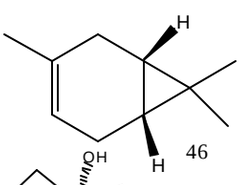
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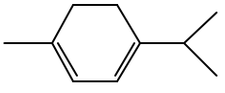
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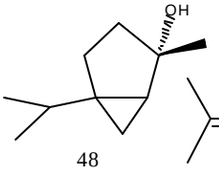
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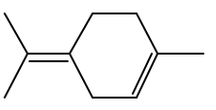
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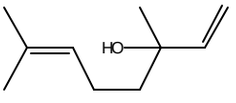
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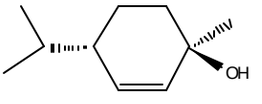
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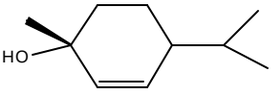
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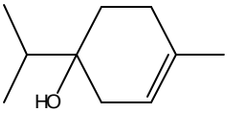
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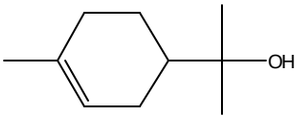
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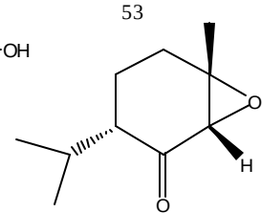
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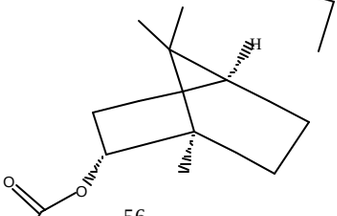
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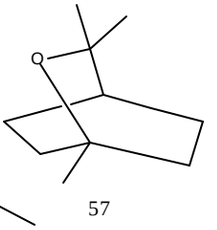
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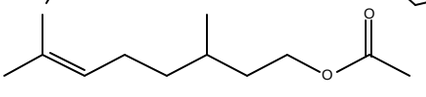
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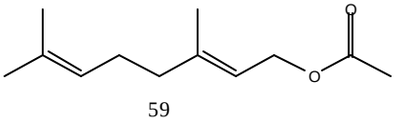
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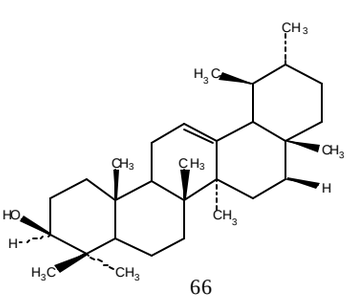
Compound name	Species	Chemical Formula	Structure Number	Plant part	Reference
TRITERPENES					
α-amyrin/α-amyrin/ (urs-12-en-3ß-ol)	*Canarium album* (Lour.) Raeusch *Canarium boivinii* Engl. *Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{50}O$	66	Dried stem, leaf Resin oleoresin, bark,timber	[20,32,41]
ß-amyrin(olean-12-en-3ß-ol)	*Canarium album* (Lour.) Raeusch *Canarium boivinii* Engl. *Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{50}O$	67	dried stem, leaf Resin oleoresin, bark,timber	[20,32,41]
3-epi-α-amyrin	*Canarium album* (Lour.) Raeusch	$C_{30}H_{50}O$	68	dried stem, leaf	[32]
3-epi-ß-amyrin	*Canarium album* (Lour.) Raeusch	$C_{30}H_{50}O$	69	dried stem, leaf	[32]
α-Amyrenone (urs-12-en-3-one)	*Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{48}O$	70	oleoresin	[20]
ß-Amyrenone (olean-12-en-3-one)	*Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{48}O$	71	oleoresin	[20]
Taraxerol	*Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{50}O$	72	bark	[20]
urs-12-ene-3α, 16ß-diol	*Canarium album* (Lour.) Raeusch	$C_{30}H_{50}O_2$	73	dried stem,leaf	[32]
olean-12-ene-3α, 16ß diol	*Canarium album* (Lour.) Raeusch	$C_{30}H_{50}O_2$	74	dried stem, leaf	[32]
TETRATERPENES					
CAROTENOIDS					
All-trans-lutein	*Canarium odontophyllum* Miq.	$C_{40}H_{56}O_2$	75	peel,pulp, seed	[29]
9-cis-lutein	*Canarium odontophyllum* Miq.	$C_{40}H_{56}O_2$	76	peel,pulp, seed	[29]
13-cis-lutein	*Canarium odontophyllum* Miq.	$C_{40}H_{56}O_2$	77	peel,pulp, seed	[29]
15-cis-ß-carotene	*Canarium odontophyllum* Miq.	$C_{40}H_{56}$	78	peel,pulp, seed	[29]
9-cis-ß-carotene	*Canarium odontophyllum* Miq.	$C_{40}H_{56}$	79	peel,pulp, seed	[29]
All-trans-ß-carotene	*Canarium odontophyllum* Miq.	$C_{40}H_{56}$	80	peel,pulp, seed	[29]
SESQUITERPENES					
α-Cubenene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	81	resin	[18]
α-Copaene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	82	resin	[18]
ß-Cubebene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	83	resin	[18]
Canaric acid	*Canarium muelleri* F.M. Bailey *Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{48}O_2$	84	oleoresin	[20,22]
(E)-ß-Caryophyllene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	85	resin	[18]
α-Humelene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	86	resin	[18]
Germacrene D	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	87	resin	[18]
Spathulenol	*Canarium album* (Lour.) Raeusch *Canarium schweinfurthii* Engl.	$C_{15}H_{24}O$	88	Resin resin,oil	[13,18]
Viridiflorol	*Canarium schweinfurthii* Engl.	$C_{15}H_{26}O$	89	resin, oil	[13]
Caryophyllene epoxide	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}O$	90	resin	[18]
(E)- Nerolidol	*Canarium schweinfurthii* Engl.	$C_{15}H_{26}O$	91	resin,oil	[13]
Elemene	*Canarium zeylanicum* (Retz.) Blume	$C_{15}H_{24}$	92	oleoresin, bark	[20]
Elemol	*Canarium zeylanicum* (Retz.) Blume	$C_{15}H_{24}O$	93	oleoresin, bark	[20]
Brevifolin	*Canarium album* (Lour.) Raeusch	$C_{10}H_{12}O_4$	94	dried stem, leaf	[27]
δ-Elemene	*Canarium album* (Lour.) Raeusch	$C_{15}H_{24}$	95	resin	[18]
STEROLS					
Sitosterol	*Canarium zeylanicum* (Retz.) Blume	$C_{29}H_{50}O$	96	oleoresin, bark,timber	[20]
ß-sitosterol	*Canarium benglense* Roxb.	$C_{29}H_{50}O$	97	bark	[42]
Neoilexonol (3ß-Hydroxyurs -12-en-11-one)	*Canarium zeylanicum* (Retz.) Blume	$C_{30}H_{48}O_2$	98	oleoresin, bark	[20]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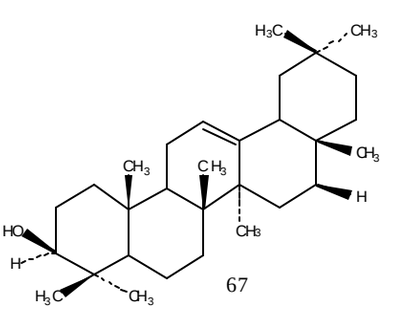
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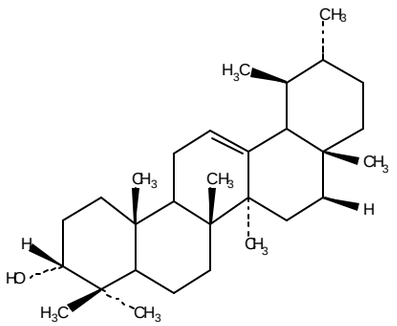

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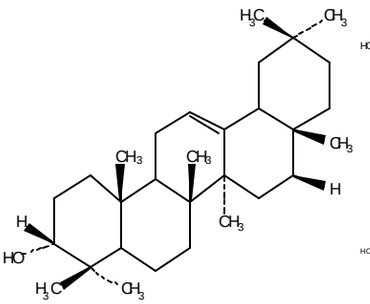

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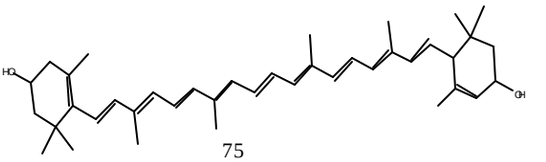

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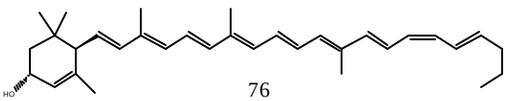

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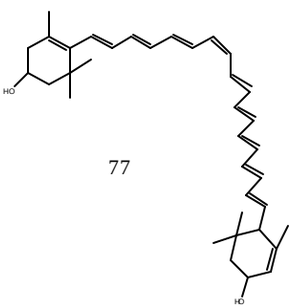

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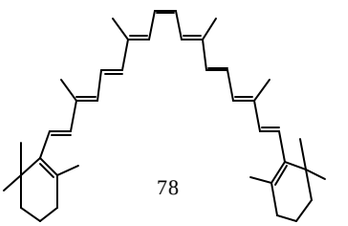

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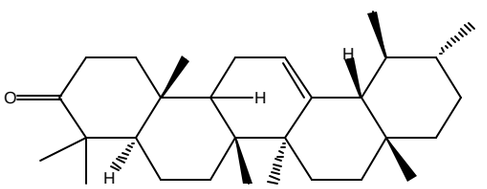

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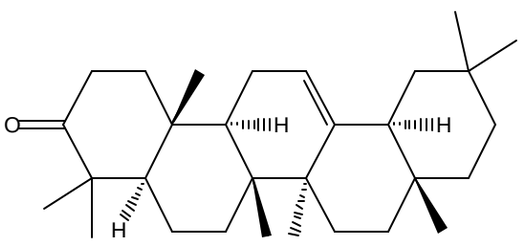

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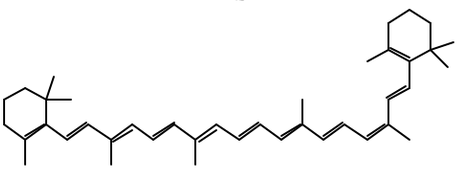

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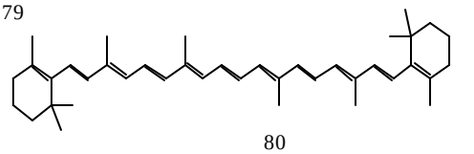

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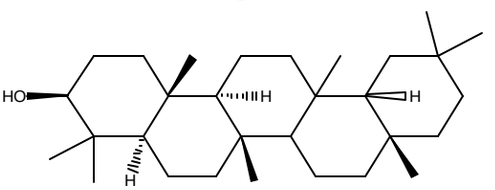

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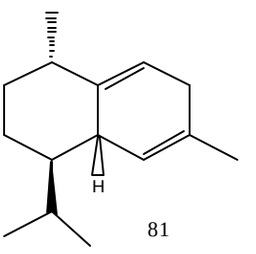

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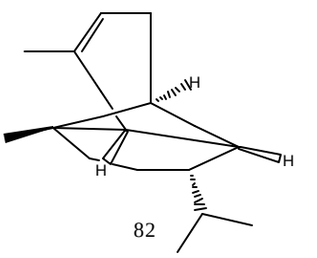

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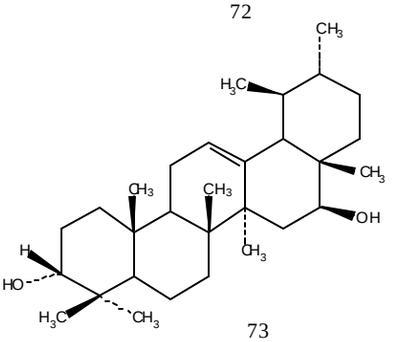

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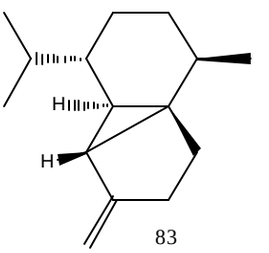

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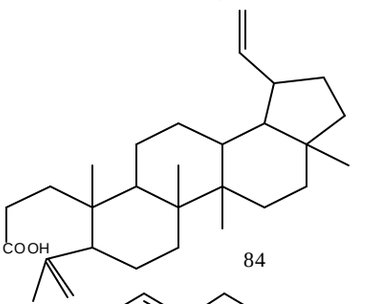

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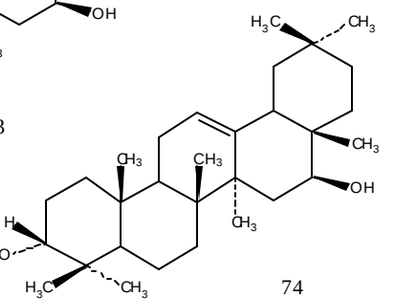

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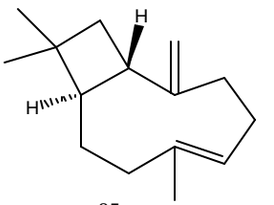

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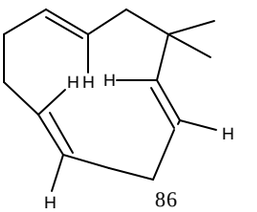

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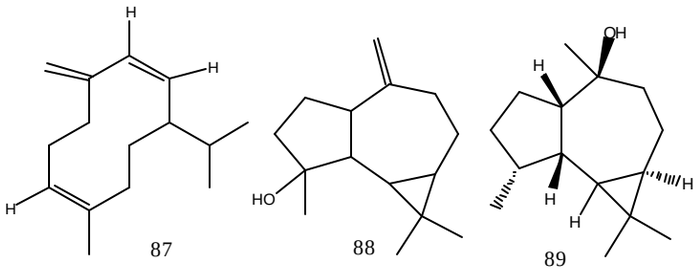

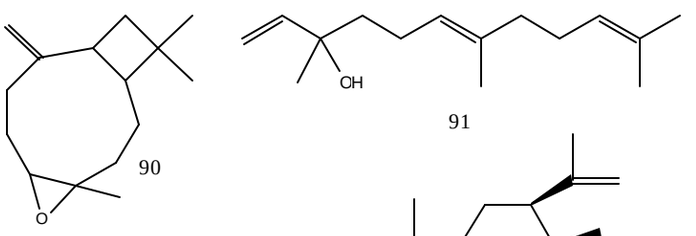

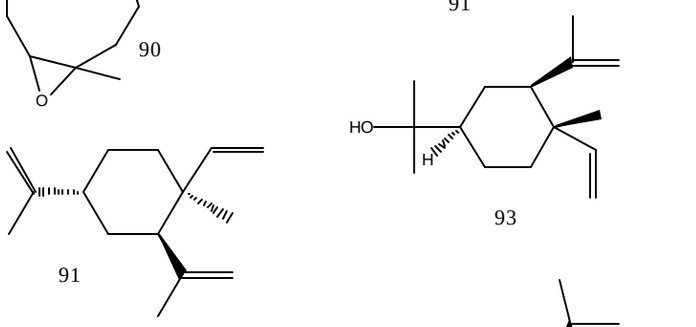

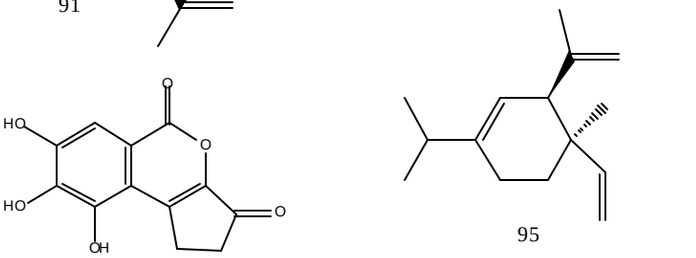

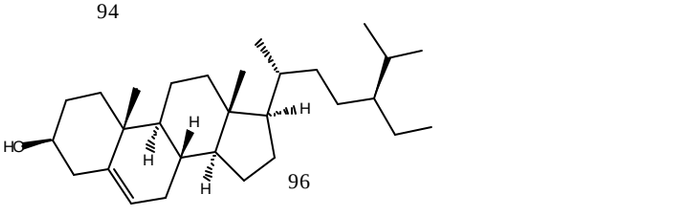

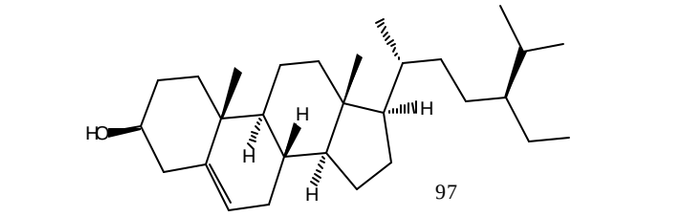

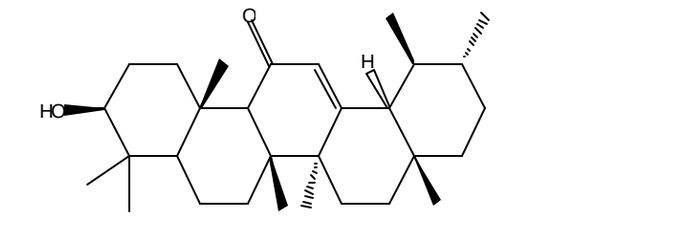

The structures are mainly established by mass spectroscopy (MS), ultra-violet spectroscopy (UV), infrared spectroscopy (IR) and ^{1}H and/or ^{13}C nuclear magnetic resonance (NMR). ^{1}H and/or ^{13}C spectroscopy is probably the most useful method in structure elucidation [21].

PHARMACOLOGICAL ACTIVITIES

Only 12% of 75 species have been studied for their pharmacological activities. Extracts and pure compounds derived from *Canarium* L. were reported to have a variety of pharmacological activities of which antioxidant, antibacterial, antifungal, antitumor, anti-inflammatory, hepatoprotective, analgesic and anti-diabetic (Table 2).

Antioxidant

Antioxidant activities were reported in *Canarium album* (Lour.) Raeusch, *Canarium odontophyllum* Miq., *Canarium schweinfurthii* Engl. and *Canarium patentinervium* Miq. A tonic soup made of *Canarium album* (Lour.) Raeusch used mainly in China displayed significant antioxidant activity by 1,1,-diphenyl-2-2-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assay [26]. Tannins extracted from the leaves, twigs and stem barks of *Canarium album* (Lour.) Raeusch showed potent antioxidant activity in the DPPH radical scavenging activity with IC_{50} values of 56.86 µg/ml, 62.31 µg/ml and 54.80 µg/ml respectively and ferric reducing power of 4.28, 3.74 and 4.49 mmol AAE/g equivalent of dried tannin [15]. Pure compounds from this species includes brevifolin, hyperin and ellagic acid which showed free radical scavenging activity in DPPH assay [27].

The essential oil of *Canarium schweinfurthii* Engl. was tested for the antioxidant activity with the DPPH assay and by ß-carotene bleaching test. It exhibited highest antioxidant activity at 150 µg/ml activity in both assay [28]. The ethyl acetate fraction of peel of *Canarium odontophyllum* Miq. exhibited 95±1.00% scavenging activity at the concentration of 40µg/ml [25,29]. The bark and leaf ethanol extracts of *Canarium patentinervium* Miq. exhibited excellent antioxidant activities in the DPPH assay with EC_{50} value of 2.33 µg/ml and 2.93µg/ml . It exhibited 77.80±0.01 and 65.80±0.01 % DPPH radical scavenging activity at the concentration of 10µg/ml [30].

Antibacterial and antifungal activities

Antibacterial activities were reported in *Canarium schweinfurthii* Engl. and *Canarium patentinervium* Miq. Dichloromethane extract of *Canarium schweinfurthii* Engl. had bactericidal activity against Gram-negative *Vibrio cholerae* with minimum inhibitory concentration (MIC) of 0.62mg/ml while the ethylacetate extract was active against Gram- positive and Gram-negative bacteria namely *Staphylococcus aureus* and *Proteus vulgaris* with MIC values of 10mg/ml and 5mg/ml respectively. Ethanol extract was active against Gram-negative *Vibrio cholerae* and *Proteus vulgaris* with MIC values of 0.62mg/ml and 10mg/ml respectively [31].

In a separate disc diffusion assay, the essential oil of *Canarium schweinfurthii* Engl. abrogated the survival of Gram-negative *Salmonella enterica*, Gram-positive *Streptococcus pyogens* and *Staphylococcus aureus* with an inhibition zone of 27mm, 25mm and 18mm respectively. However the author did not inform on the concentration of the extract per disc. The oil was also fungicidal against *Candida albicans* with an inhibition zone of 23mm [28].

The ethanol extract of leaves and barks and hexane extract of barks of *Canarium patentinervium* Miq, exhibited significant antimicrobial activity against Gram-positive bacteria *Staphylococcus aureus, Bacillus cereus,* methicillin-resistant *Staphylococcus aureus* and Gram-negative *Pseudomonas aeruginosa*. The highest sensitivity obtained was with the ethanol extract of leaves which inhibited the growth of Gram-positive *Staphylococcus aureus, Bacillus cereus,* methicillin-resistant *Staphylococcus aureus* and Gram-negative *Pseudomonas aeruginosa* with an inhibition zone of 14mm, 13mm, 13mm and 15mm respectively. Disc diffusion assay was done at a concentration of 2mg/disc and the extracts were more active than ampicillin and streptomycin [30]

Hepatoprotective activities

Hepatoprotective activity was exhibited in *Canarium manii* King. and *Canarium album* (Lour.) Raeusch. The biflavanoid agathisflavone from *Canarium manii* King. preserved the integrity of the liver cells membrane of rodents as evidenced by the decrease in the CCl_4-induced rise of glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) levels. GPT which is predominantly found in the liver showed a dose-dependent and significant reduction [21].

The triterpenes urs-12-ene-3a,16ß-diol, olean-12-ene-3a,16ß-diol and urs-

Table 2. Biological and pharmacological acitivities (*in vitro* and *in vivo*) of *Canarium* L. extracts and pure constituents

Extract/Compound	Species	Pharmacological activity	References
***In Vitro* Models**			
Polymeric procyanidins(tannins) from leaves, twigs and stem bark	*Canarium album* (Lour.) Raeusch	Significant DPPH radical scavenging activity, Ferric reducing antioxidant activity	[15]
Ethyl acetate fraction of the fruit peel	*Canarium odontophyllum* Miq.	Antioxidant activity with DPPH assay, FRAP assay and hemoglobin oxidation assay	[29]
Carotenoids from peel,pulp and seed extracts	*Canarium odontophyllum* Miq.	Significant antioxidant activity with beta-carotene bleaching assay, ABTS assay, DPPH assay and hemoglobin oxidation assay	[25]
Essential oil of resins	*Canarium schweinfurthii* Engl.	Bactericidal for *E.faecalis*, *L.innocua*, *S.enterica*, *S.aureus*, *S. camorum*.Fungicidal for *C.albicans* Antioxidant for DPPH and β-carotene bleaching test	[28]
Essential oil of resins(monoterpenes hydrocarbon)	*Canarium schweinfurthii* Engl.	Significant anti-inflammatory activity via lipooxygenase method with IC_{50} of 62.6ppm	[19]
brevifolin, ellagic acid and hyperin	*Canarium album* (Lour.) Raeusch	Significant antioxidant activity and inhibitory effect on lipid peroxidation assay	[27]
Ethanol extracts of leaves and barks	*Canarium patentinervium* Miq.	Significant antimicrobial activity via disc diffusion assay against *S.aureus*, *B.cereus*, methicillin-resistant *S.aureus* and *P.aeruginosa* Significant antioxidant activity in DPPH assay with EC_{50} of 2.93µg/ml and 2.33µg/ml respectively	[30]
Chloroform and ethanol extract of barks	*Canarium patentinervium* Miq..	Singnificant antitumor activity against breast cancer cell line MDA468	[33]
Dichloromethane extract of barks	*Canarium schweinfurthii* Engl.	Antimicrobial activity against *V.cholerae*	[31]
Extract of whole plant	*Canarium album* (Lour.) Raeusch	Antioxidant activities in DPPH and FRAP assay	[26]
In Vivo Models			
agathisflavone (biflavanoid)	*Canarium manii* King.	Hepatoprotective activity against experimentally-induced carbon tetrachloride-hepatotoxicity in rats and mice	[21]
urs-12-ene-3a, 16ß-diol, olean-12-ene-3a, 16ß diol (triterpene)	*Canarium album* (Lour.) Raeusch	Hepatoprotective activity in primary cultured rat hepatocytes intoxicated with D-galactosamine	[32]
brevifolin, ellagic acid	*Canarium album* (Lour.) Raeusch	Reduction of carbon tetrachloride induced liver damage in mice. Reduction in elevated GPT and GOT levels after intraperitoneal administration	[27]
Essential oil of resins(composed mainly of nerolidol and octylacetate)	*Canarium schweinfurthii* Engl.	Significant analgesic effect using acetic acid-induced writhing and hot plate methods with swiss mice	[13]
Methanol/methylene chloride extract of stem barks	*Canarium schweinfurthii* Engl.	Anti-diabetic activity that reverses hyperglycemia, polyphagia and polydipsia in streptozotocin-induced diabetic rats. Significant reduction of 69.9% reduction in blood glucose level after 14 days at 300mg/kg	[12]

12-ene-3ß,16ß-diol from from *Canarium album* (Lour.) Raeusch markedly reduced the amount of alanine aminotransferase leakage from the primary cultured hepatocytes intoxicated with 0.2mM of D-galactosamine (GaIN) [32]. The phenols brevifolin and ellagic acid protected rat hepatocytes against GaIN-induced insults [27].

Other Biological Activities

The essential oil of *Canarium schweinfurthii* Engl. collected from the region of Cameroon inhibited the enzymatic activity of lipoxygenase with an IC_{50} value of 62.6ppm [19]. However in a separate study of the same species collected from central African region did not show any activity in the cotton pellet induced granuloma formation experiment [13]. This may suggest possible evidence of variety between secondary metabolites constituents according to regions.

The essential oil of *Canarium schweinfurthii* Engl. at a dose of 1, 2 and 3 mg/kg i.p. displayed potent analgesic effect in the acetic acid-induced writhing and hot plate experiments [13].

Anti-diabetic activity was reported in the methanol/methylene chloride extract of stem bark of *Canarium schweinfurthii* Engl. At a dose of 300mg/kg there was 67.1% reduction in blood glucose levels after a once daily subcutaneous injection on streptozotocin-induced diabetic male rats over 14 days, versus insulin that had 76.8% reduction. Weight gain was only 6.6% as opposed to untreated rats that had lost 14.1% of body weight. There was also significant reduction in food and fluid consumption by 68.5% and 79.7%. These results showed the extract could reverse hyperglycemia, polyphagia and polydipsia provoked by streptozotocin, thus having anti-diabetic activity [12].

Antitumor potential was demonstrated by the chloroform and ethanol extract of bark of *Canarium patentinervium* Miq. significant with GI_{50} value of 23.44 µg/ml and 34.40 µg/ml respectively via the MTT biological assay. Extracts were most sensitive to the breast cancer cell line MDA 468 [33].

Commercial uses of *Canarium* L. Produces

Elemi derived from the Arabic 'Al-lami' is a collective term applied to several oleoresins obtained from different plants of the family Burseraceae Kunth. The most important and widely known of these oleoresins is Manila Gum Elemi which exudates from the trunk of *Canarium luzonicum* Miq. or *Canarium commune* L. The natural constituent of elemi oil is elemicin. Variety of foodstuffs are flavoured with elemi oil and in Europe its used in spices and seasonings. In US elemi oil is also used in fragrances to approximately 1000lb/year [34].

At present, at least 4 species of *Canarium* L. nuts are of economic importance. *Canarium ovatum* Engl. (known locally as 'pili' and 'pilaui') is the most important nut-producing species in the Philippines. *Canarium luzonicum* Miq. most commonly known in the Philippines as 'pisa' and 'basiad', is important, not as an edible nut but for its oily resin (known locally as 'sahing'), which is tapped from the trunk. When processed, it is called 'brea blanca'(white pitch) and is exported as Manila elemi *Canarium indicum* L. is an important nut-producing species in the Solomon Islands (locally called 'ngali'), Papua New Guinea (locally called 'galip') and Vanuatu (where it is known as 'nangai') [5]. *Canarium album* (Lour) Raeusch., known in English as Chinese olive, 'samo cheen' in Thailand and 'tram trang' in Vietnam, is important in these countries for its edible pulp and kernel [35].

In Melanesia, marketing operations for *Canarium indicum* L. and *Canarium harveyi* Seem. range from private and community based production, processing, and marketing of kernel oil for cosmetic and medicinal use, to government-backed nationwide purchasing of kernels for sale as confections and oil. *Canarium solomonense* B.L. Burtt in the Solomons islands are used as general-purpose timber [36].

Because of the potential of *Canarium* L. as a high-value export crop for nuts (for confections) and/or oil extraction, some research is being done on its taxonomy, production and marketing. Additional research needs include selection, evaluation, and improvement of promising varieties for timber production, investigation of cultural aspects, phenological studies, and vegetative propagation [37]

CONCLUSION

This review highlights the fact that only about 12% of the total *Canarium* L. species have been studied for chemistry and pharmacological activities. The diversity of secondary metabolites and pharmacological actions reviewed in this work demonstrate that there is much to be discovered in this family. Indeed, as compared to many other genus in this family, *Canarium* L. is still very much under studied. This could be explained by the fact that *Canarium* L. species are mainly found in primary rainforest where they face extinction due to intensive logging and little conservation. There is therefore a compelling need to study *Canarium* L. species which may shelter some drugs for the future.

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Source of support: Nil, Conflict of interest: None Declared