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PIPER MARGINATUM JACQ. (PIPERACEAE): PHYTOCHEMICAL, THERAPEUTIC, BOTANICAL INSECTICIDAL AND PHYTOSANITARY USES

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Abstract

Piper marginatum is a neotropical native plant found from Guatemala to Brazil including the Caribbean. This species is known for its healing properties in traditional medicine. It is employed for treating inflammation, malaria, wound healing, snakebites, pathologies related to bile or liver, dental caries, as a diurectic, sudoriferous agent, haemostatic, and for its analgesic effects. In foods it is used as a flavouring agent and a sweetener. It has been reported to have phytosanitary activity, thus it has been adopted as a botanical insecticide. This study gathers information regarding its taxonomic, etnobotanical, phytochemical, and toxicity properties. In addition, we apprise its phytosanitory activity and botanical insecticide use. *Piper marginatum* is an important plant species for the development of future alternative medicinal products.

Keywords: *Piper marginatum*, curadientes, heal teeth, ethnobotany, phytochemistry, medicinal plant, Colombia

Introduction

Piper marginatum is a shrub found from Guatemala to Ecuador, Brazil, and the Caribbean. This plant is commonly known in Colombia as "curadientes and cordoncillo", "wild-piper" in the Amazon region, "caapaeba cheirosa, pimenta do mato, malvarisco, soldier's herb" in Brazil, "Ti bombe" in French Guiana, "lanie bois" in Trinidad and Tobago [1-3]. Custums and traditions from various countries demonstrate its medicinal properties to treat and relieve different illnesses. Likewise, it is used as a flavoring agent and a sweetener.

Taxonomic Aspects

Shrubs can grows as tall as 3 m high, with glabrous branches. Leaves are 8.5 - 17 x 6 - 14 cm, cordate leaves of symmetrical base with an acuminate leaf apex, membranaceous when dry, brown glands are frequent, glabrescent to hispida, ciliated margin, palmate venation 9 – 11, 1.5 – 4 cm peduncle, glabrous or slightly pilose, with leaflets almost to all its extension. Segment 10 – 16 cm long, arched, 0.6 – 1.5 cm peduncle, glabrous, glabrous rachis. Orbicular to almost triangular floral bracts, sessile stigma inserted at the apical depression of the fruit. Drupe fruit up to 1 x 1 mm, oblong, and glabrous [4]. The plant taxonimic position is as follows: *Plantae* Kingdom, Phylum: *Magnoliophyta*, Class: *Magnoliopsida*, Order: *Piperales*, Family: *Piperaceae*, Genus: *Piper*, Species: *P. marginatum*. The plant was collected in Mogambo environmental trail, Municipality of Viotá in the Department of Cundinamarca- Colombia. The Colombian National Herbarium has taxonomically determined this species under the voucher COL575454 (identified by A. Jara, June 12 of 2014).

Tradicional use

Piper marginatum is a native neotropical species with presence in Colombia. It is known with the popular name of curadientes, since it presents a medicinal activity against tooth cavities according to García in 1992, "...the stem is macerated and topically applied, as a tookpaste against tooth cavities..." [1]. The plant is commonly used in folk medicine as a tonic with with antispasmodic action, for treating inflammation, snakebites, wound healing, pathologies related to bile or liver, to prevent tooth cavities. In addition, it is recognized as having cercaricidal activity. Its fruits are used in food as a flavouring agent, usually used to replace black pepper [2, 5-8]. Amazon tribes use cooked leaves to treat illnesses of the bile and liver, and as a tonic with carminative action and antispasmodic [9]. Women from the Sonia indigenous reserve in Colombia use P*iper marginatum* as an as infusion and as compression to calm pain [10]. *Piper marginatum* in combinaion with *Quassia amara* are used to treat malaria [11]. The root is used as a diuretic and as an agent to promote sweating [6]. Leaf infusion is used as a cholagogue. It is also employed for molar tooth ache, to treat rheumatism, tumors, bleeding wounds, rashes, diarrhea, and chronic dysentery [6, 12-14]. Leaf dye is used as an astringent and for digestive disorders [15]. It presents analegesic and anti-inflammatory properties, reducing fever and lung secretions [12, 13]. Due to its potent hemostatic effect it is known as the soldier's herb. Cooking its leaves is used to dimish menstruation bleeding, control uterine bleeding, and against infections of the uterus [3, 12, 14]. Likewise, cooked leaves are added to a bath or used as a fricton treat rashes and calm insect bite itching [6]. Dried leaves are used as a sweetner with a greater sweetening power than sugar [16, 17].

Phytochemistry

Piper marginatum first registries indicate a total ash content of 10.7%, insoluble acid ashes of 2.9%, humidity between 8.6 and 14.7% when using the Toluene determination of moisture and oven method respectively. Additionally, it contains volatile oil (6.9 to 7.6%), reducing sugars, phytoesterols, fat, alcaloids and tannins expressed as gallotannic acid 0.7% (method of the Assoc. Official Agr. Chem.), yet when employing the hide powder method the percentage was 0.3%. Sensorial volatile acid evaluation presented the following characteristics: colorless turining yellowish, aroma similar to sassafras with a minty flavour. It has a relative density of 1.0560 and a refraction index of 1.5475 [14]. Foungbe and collaborators revelaed alcaloid traces, flavonoids, and escential oil. The main components of essential oil were anethole, methyleugenol, methylisoeugenol, a-pinene and b-pinene. C-flavonoids corresponded to Apigenin 8-C-β-D-glucopyranoside [6]. Phytochemical preliminary analysis from alchol extract of collected leaves from the Municipality of San Luis and Puerto Triunfo in the Departament of Antioquia (Colombia) evidenced a moderate content of flavonoids, phenolic compounds, terpenes/steroids and alcaloids [18].

Piper marginatum derived from leaves and stems from Itacoatiara (Brazil) contained principally: 3, 4-methylenedioxypropiophenone (8.0 - 8.9%), b-caryophyllene (4.0 - 5.6%), g-elemene (3.8%), a-copaene (2.5 - 1.7%), *trans*-ocimene (2.3-0.7%), g-terpinene (1.9 -1.3%), d-elemene (1.8 - 1.4%), a-

humulene (1.3 - 0.6%), *cis*-ocimene (1.3 - 0.3%), elemicin (1.3 - 1.5%), D^3-carene (1.2-3.3%), a-Terpinolene (1.1 - 0.9%), 2-hydroxy-4,5-methylenedioxypropiophenone (1.1 - 1.4%), methyleugenol (1.0 - 1.5%), and myristicin (0.2 - 9.2%) [2]. Researchers from Cuba performed *Piper marginatum* essential oil Column chromatography chemical fractionation. Chemical composition of the fractions obtained were analyzed by gas chromatography/mass spectrometry (GS/MS) with the following main components obtained: isosafrole (37.3%), notosmirnole (22.7%), methyl-eugenol (7.3%), safrole (7.0%) trans-a-asarone (5.9%), myristicin (4.3%), eusarone (1.3%) and asarone (1.0%), among others [19].

In Brazil essential oil presented a main composition of: (Z)-asarone (30.4%), patchouil alcohol (16%), elemol (9.7%), bicyclogermacrene (9.4%), (e)-caryophyllene (7.5%), (e)-asarone (6.4%), a-acoradiene (5.1%), a-cadinene (1.4%), a-elemene (3.4%), b-acoradiene (1.3%), g-himachalene (1.3%), and b-elemene (1.1%), among others [20]. In Costa Rica *Piper marginatum* essential oil originated from the Monteverde region. Its predominant component was trans-anethole (80.5%). This compound is used as a flavoring agent in drinks, sweets, pastry, chewing gum, and candy in concentrations up to 1500 ppm of the finished product (16, 21). *Piper marginatum* volatile fraction originating from los Llanos Orientales in Colombia evidenced a monoterpenic hydrocarbon value of 50.8%. The main compounds in the volatile fraction were: g-terpinene (9.5%), a-terpinene (7.1%), a-pinene (6.9%), b-pinene (6.9%), a-terpinolene (6.7%), (Z)-1,3,5-trimethoxy-2-propenyl benzene (5.6%), -(E) - b-ocimene (3.7%), (Z) - b-ocimene (3.2%), and in a lesser proportion limonene (2.1%), trans-caryophyllene (1.8%), and bicyclogermacrene (2.4%) [22]. From the acqueous extract obtained by cooking the leaves of *Piper marginatum* followed by ethyl ether extraction, ehtyl acetate, and butanol the following flavonoid-type compounds were isolated: vitexin and marginatoside (6"-O-b-gentiobiosyl vitexin). This last one is a gycosilated vitexin [6, 23]. A Me_2CO extract isolated from the aereal parts of *Piper marginatum* origintaing from Trinidad and Tobago contained 3-farnesyl-4-hydroxybenzoic acid and methylated derivatives [24]. Croweacin was isolated from *Piper marginatum* root derived ethanol extract fractioned on silica gel using $CHCl_3$ [25]. Other compounds were obtained when using other solvents such as hexane-$CHCl_3$, $CHCl_3$, $CHCl_3$-MeOH, and MeOH. The compounds obtained were the following: 3,4-methylenedioxy-1-(2 E-octenyl)-benzene (marginatine), 1-(1E-propenyl-)-2,4,6-trimethoxybenzene (pipermargine), 2,6-dimethoxy-3,4-methylenedioxy-1-(2-propenyl)-benzene, apiole, isoasarone [26], 2,4,5-trimethoxypropiophenone [27], (E,E)-N-Isobutyl-2,4-octadienamide [28], and 2-methoxy-4,5-methylenedioxypropiophenone [29].

Hexane extracts from *Piper marginatum* fruits collected in Joao Pessoa (Brazil), contained 1-(1-Z-propenyl)-2,4,6-trimethoxybenzene, 3-farnesyl-4-hydroxybenzoic acid. From the extract in chloroform caryophyllene oxide was isolated [30]. 1-cinnamoyl pyrrolidine was obtained from ethanol extracted stems collected in Santa Rita (Brazil) fractioned on silica gel using petroleum and ethanol acetate [31]. From whole plant ethanol extract followed by silica gel fractioning using hexane, EtOAc, and MeOH, aristolactams cepharanone B and piperolactam A were isolated [32]. An EtOAC fraction was obtained from leaf methanol crude extract, fractioned on silica gel using an increasing polarity gradient from hexane to EtOAc. The following compunds were isolated: 3,4-methylenedioxypropiophenone, 2-methoxy-4,5-methylenedioxypropiophenone, 1-(3,4-methylenedioxyphenyl)propan-1-ol (marginatumol), 5,4'-dihydroxy-7-methoxyflavanone, and 5,7-dihydroxy-4'-methoxyflavanone [33].

Depending on the latitude where the plant is found, its chemical composition changes. Thus, they can be classified in families with characteristic compunds. For the French Guiana anethole, methyleugenol, and the heteroside marginatoside was reported. In the Brazilian Amazon wild species contain propiophenones, in Trinidad and Tobago compounds corresponded to 3-farnesyl-4-hydroxybenzoic acid and derivatives. Last, in Piraíba (Brazil) this plant contained phenylpropanoids, phenylalkanoids, octadienamide, 1-cinnamoyl pyrrolidide, and aristolactams [9, 32, 34]. Main compound essential oil analysis allowed to establish seven different types of chemotypes, providing a chemical, biological, and botanical means of classification. The chemotype allows to determine therapautic properties in a clear and safe way, with/or variations in its toxicity. Main compunds in chemotype I correspond to safrole (63.9%) and 3,4-(methylenedioxy) propiophenone (33.2%); for chemotype II: 3,4-(methylenedioxy)propiophenone (40.7%) and p-mentha-1(7),8-diene (22.9%); for the chemotype III: 3,4-(methylenedioxy)propiophenone (40.2%), myristicin (16.0%), (E)-b-ocimene (15.2%), and g-terpinene (14.4%); in chemotype IV: b-caryophyllene (13.3%), a-copaene (11.4%), and 3,4-(methylenedioxy)propiophenone (10.4%); in

chemotype V: (E)-isoosmorhizole (46.8%), (E)-anethole (26.4%), and isoosmorhizole (24.5%); for the chemotype VI: 2-methoxy-4,5-(methylenedioxy)propiophenone (26.5%), methoxy-4,5-(methylenedioxy)propiophenone isomer (21.9%) , and (E)-isoosmorhizole (15.8%); last for the chemotype VII: b-caryophyllene (13.6%), bicyclogermacrene (11.7%), and (E)-asarone (10.8%) [9, 35]. *Piper marginatum* cyrcadian cycle influences essential oil chemical composition, where the predominant compounds correspond to phenylpropanoids such as (Z)-asarone (33.8%) and (E)-asarone (20.6%), and sesquiterpenes such as α-acoradiene (11.6%). Abiotic and biotic stress, as well as an antibacterial activity induce phenylpropanoid production as the plant's chemical response [36]. Figure 1 depicts some chemical structures of compounds which are present in *Piper marginatum* [37].

Medicinal properties

Early phramacological studies indicated its relaxation action on smooth muscle, an aparent reduction in cuagulation time and bleeding [14].

In rat models *Piper marginatum* extract in concentrations of 0.5 and 1.0 g/kg has been reported to reduce carrageenan-induced paw edema. Furthermore, it presents a slight analgesic effect to a writhing reponse in mice under acetic acid induction. Edema reduction is associated with vasoconstrictor compounds, such as noradrenalin present in the crude extract and responsible for its action after oral administration [12, 38]. Acqueous extract demonstrated hemostatic, analgesic, and antiinflammatory properties associated with noradrenalin vasoconstrictor effects present in the plant [9]. Furthermore, in addition to its anti-inflammtory attributes *Piper marginatum* acqueous extract displays anti-tumoral activity. *In vitro* cytostatic effect was evaluated in three cell lines at high concentrations (>300 mg/ml), resulting in reduced cell proliferation. Its anti-inflammatory properties were evaluated determining TNF reduction, which resulted in 50% decreased cytokine production. In addition, tumor growth and metastasis was evaluated in C57BL/6 inoculated with B16/BL6 melanoma with an 80% reducion in primary tumor. It has also been reported to inhibit lung metastasis between 40 a 60% [39, 40]. The plant's hydroalcoholic extract exhibited antimicrobial activity against *Staphylococcus aureus* and *Bacillus subtillis* with a minimum inhibitory concentration (MIC) of 0.2 mg/ml for each organism [41]. Anticandidal activity was performed on a MIC greater than 2.0 mg/ml for each [42]. *Piper marginatum* leaf essential oil has an activity against *Escherichia coli* for serotypes EPEC 0031-2 and STEC 0157 at concentrations between 0.7 and 0.9 mg/ml, respectively [43]. *Piper marginatum* leaf essential oil and fruit demonstrated a robust antithelmic activity, with 96% *Schistosoma mansoni* death after 15 minute treatment at a 10 mg of essential oil emulsified in water. Thus, it can be considered as an alternative treatment against schistosomiasis [44].

Piper marginatum leaf ethanol extract did not present an antiplasmodial activity (IC_{50} > 50 µg/mL) with modearte cytotoxicity CC_{50} = 41.3 µg/mL. In contrast stem extract antiplasmodial activity was low with an IC_{50} = 31.8 µg/mL, and it has a cytotoxic effect of CC_{50} = 25.9 µg/mL [18]. Antidermatophytic activity against *Trichophyton rubrum* and *Trichophyton mentagrophytes* was determined using *P. marginatum* essential oil, finding minimal inhibitory values of 500 and 250 mg/mL, respectively. Dermatophytic activity could be associated with elemicin, trans-β-caryophyllene, and α-phellandrene isoelemicin, present in essential oil [45].

Phytosanitary activity

Piper marginatum methanol leaf and seed extract evidenced antifungal activity against *Colletotrichum scoville,* responsible for bell pepper anthrancnose. *In vitro Piper marginatum* methanol extract evaluation at 250 ppm inhibited *Colletotrichum scoville* mycelium. Ethyl acetate fraction of this extract reduced *in vitro* growth significantly. Moreover, the purified fraction presented an *in vitro* effect and post-crop with a better efficiency than the fungicide mancozeb [46]. Essential oil antimicrobial activity obtained by hydrodestilation was evaluated againt *Xhantomonas albilineans* determined by MIC and minumum bactericiadial concentration (MBC) in 0.12 mg/mL. Such activities were attributed to the presence of oxygenated compounds (phenolic terpenes) like isosafrole and notosimirnole [19, 47]. Likewise,essential oil presented bactericidal effect against *Xanthomas campestris* and fungistatic effect against *Alternaria solani* Sor [19, 48]. Leaf essential oil (10 uL) presented an inhibitory effect on *Fusarium oxyporum* growth, with a diffusion diameter of 22.5 mm compared with 69.9 mm in controls. Results suggest a potential use in agriculture, mainly for plantane, bean and soy [49]. *Piper marginatum* leaf methanol extract isolated and purified flavonones displayed a fungicidal activity (bioautographic assay), inhibiting *Cladosporium cladosporoides* and *Cladosporium sphaerospermum* fungal growth by

using 1 µg of pure compound on a chromatographic plate [33]. *Tyrophagus putrescentiae* (Schrank) and *Suidasia pontifica* Oudemans (Acari: Astigmata) mite control by spraying was evaluated using *Piper marginatum* essential oil with a percentage mortality lower than 50% [50]. Phythopathogens such as *Crinipellis perniciosa*, *Phytophthora palmivora* and *Phytophthora capsici* are responsible for low cacao yield, due to fungal attack. *Piper marginatum* essential oil to was used to inhibit total mycelium growth with a MIC value of 1.0 mL/mL for *Crinipellis perniciosa* and a higher concentration for *Phytopthora palmivora* and *Phytopthora capsici* [51]. *Piper marginatum* essential oil MIC against *Fusarium oxysporum* was greater than 500 mg/mL. Antifungal activity could be associated with trans-β-caryophyllene, β-pinene, and α-pinene [45].

Botanical insecticides

In search of less toxic products, biodegradable, and safe for the environment, analysis by combining HPLC fingerprints and chemometric methods of methanolic extract of leaves and inflorescences of *Piper marginatum* and other *Piper* species could offer components that can contribute biological activity as botanical insecticides [52].

Inflorescence essential oil presented a strong activity against *Aedes aegypti* mosquito larvae with LC_{10} and LC_{50} of 13.8 and 20.0 ppm, respectively. Essential oil extracted from the fruit had an LC_{50} of 8.29 ppm, representing a potential source of larvicidal compounds [5, 20, 53, 54]. Another study found (E)-methyl isoeugenol (27.1%), (E)-anethole (23.9%), and (Z)-methyl isoeugenol (12.1%) as possible compounds responsible for high larvicidal activity against *Aedes aegypti* with a mortality percentage of 78% for a 50 ppm concentration after 96 h treatment. In addition, LC_{50} of 34 ppm and LC_{90} of 85 ppm for third and fourth larval stages [55].

Piper ethanol extract application of 10 species including *Piper marginatum*, obtained from the Sumapaz region in Cundinamarca, Colombia was used against *Spodoptera frugiperda* third instar larvae. Treatment resulted in larvae antifeedant activity, producing high mortality percentages similar to those presented by the commercial biological control in *Bacillus thurigiensis* larvae [56, 57]. *Piper marginatum* leaf and fruit essential oil protects in an efficient manner maize seeds against *Sitophilus zeamais* weevil during 120 days of storage. By using an essential oil concentration of 1 uL/g a 92.2 and 53.1% mortality percentage was obatined against the insect for day 30 and day 120 of storage, respectively. This effectiveness could be related to the high content of (Z)-asarone (30.5%) present in the plant as a principal compound (58). Toxicity measured as lethal concentration LC_{50} by contact and intake of essential oil in adult *Sitophilus zeamais* was 21.1 uL per 40 g of maize and the spraying effect (LC_{50}) ranged between 38.8 and 52.9 uL per litre of air [59]. Arm-in-cage testing of *Piper marginatum* essential oil demonstrated 50 mL applied on the back of the hand did not have a repellent effect on *Lutzomyia migonei* sandfly female mosquito with a protection time of 10.3 minutes [60]. Water bodies held by terrestrial plants known as phytotelmata, serve as a habitat for insect development such as some *Anopheles* and *Aedes* genera, vectors of malaria and yellow fever, among others. The main practice to control insects is insecticide solution immersion. Research has revealed *Piper marginatum* essential oil used at a 1% concentration can result in 44.4% insect removal for the *Diptera* genus, and mortality percentages of 33.3%, 33.4%, and 6.7% for *Coleoptera*, *Hymenoptera* and *Diptera* genus, respectively [61].

Capuchin monkeys (*Cebus capucinus*) from Costa Rica use *Piper marginatum* stems, leaves, and seeds mixed with saliva to repel insects by rubbing it vigorously to their bodies [62, 63]. Insecticidal activity against fire ant workers *Solenopsis saevissima* (Smith) was evaluated using *Piper marginatum* essential oil at a LC_{50} of 122.4 and 167 mg/L for chemotype A and B, respectively. Main constituenrs responsible for insecticidal activity were p-mentha-1(7),8-diene (39%), 3,4-methylenedioxypropiophenone (19%), and (E)-β-ocimene (9.8%) for *Piper marginatum* chemotype A. On the other hand, for *Piper marginatum* chemotype B the following compounds were detected: (E)-isoosmorhizole (32.2%), (E)-anethole (26.4%), isoosmorhizole (11.2%), and (Z)-anethole (6%) [64].

Toxicity

Prolongued exposure to trans-anethol present in *Piper marginatum* can be a health risk, since it has been reported to produce hepatocarcinoma in female rats [17]. Additionally, estragole present in this species is also a hepatic carcinogenic agent. These constituents are closely realted to phenylpropanoid safrol, a hepatocarcinogen [16, 17]. Mice and rat *Piper marginatum* extract intraperitoneal administration between 0.1 and 1.0 mg/kg causes piloerection, sialorrhea, lacrimation, muscle relaxation, and dispnea. At higher doses (> 1 mg/kg) it produces respiratory failure and death. Anesthesized rats given intravenous injection of extract between 0.1 and 0.5 mg/kg result in

hypertension. Oral and intragastric administration of extract also causes increased blood pressure [12]. Brine shrip *Artemia franciscana* lethality test is used to evaluate essential oil toxicity. *Piper marginatum* essential oil presents a low toxicity LC_{50}value of 22.4 and 12.6 mg/mL at 24 and 48 h, respectively. Oil chemical composition evidenced a content of elemecin (18.0%), trans-β-caryophyllene (11.0%), α-phellandrene (11.1%), isoelemecine (9.2%), limonene (7.5%), bicyclogermacrene (4.1%), β-elemene (4.0%), trans-anethol (3.4%), exalatacin (3.2%), α-pinene (2.5%), cis-methyl isoeugenol (2.4%), β-phellandrene (2.2%), cis-nerolidol (1.8%), α-humulene (1.7%), trans-methyl isoeugenol (1.7%), β-pinene (1.4%), cis-asarone (1.3%) and β-myrcene (1.1%) [65]. Moreover, *Piper marginatum* was evaluated on Vero cells (African Green Monkey -*Cercopithecus aethiops* epithelial kidney cells to determine its half maximal inhibitory concetration IC_{50}. A value of 30.3 mg/mL was determined. According to the American National Cancer Institute (USA) criteria, plant derivate extracts are cytotoxic with IC_{50} value less than 30 µg/mL [45, 66]. Primary constituents in oil were: elemicin (18%), trans-β-caryophyllene (11%), α-phellandrene (11.1%), and isoelemicin (9.2%) [45].

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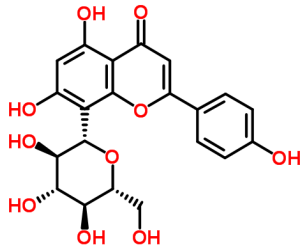
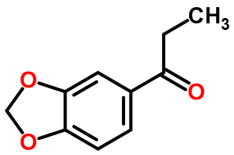
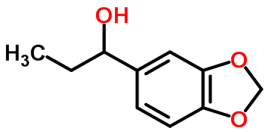
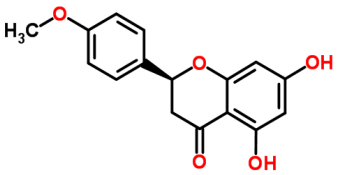
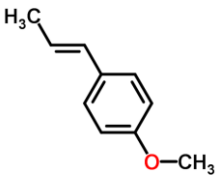
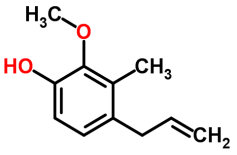
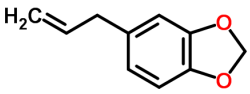
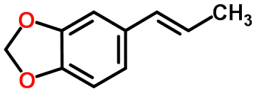
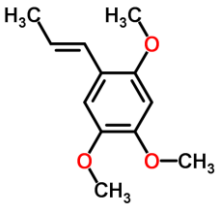
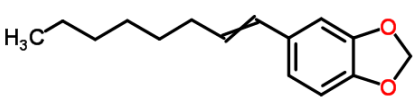
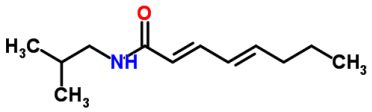
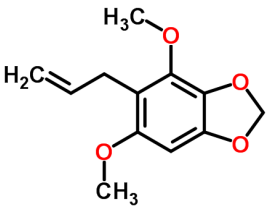
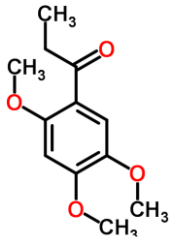
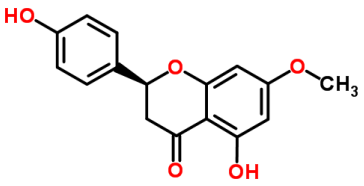
 Vitexin: Apigenin 8-C-β-D-glucopyranoside. ACD/IUPAC Name: (1S)-1,5-Anhydro-1-[5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-8-yl]-D-glucitol	 3,4 methylenedioxypropiophenone ACD/IUPAC Name: 1-(1,3-Benzodioxol-5-yl)-1-propanone	 1-(3,4-methylenedioxyphenyl)propan-1-ol ACD/IUPAC Name: 1-(1,3-Benzodioxol-5-yl)-1-propanol
 5,7-dihydroxy-4'-methoxyflavanone ACD/IUPAC Name: (2S)-5,7-Dihydroxy-2-(4-methoxyphenyl)-2,3-dihydro-4H-chromen-4-one	 trans-Anethole ACD/IUPAC Name: 1-Methoxy-4-[(1Z)-1-propen-1-yl]benzene	 Methyleugenol ACD/IUPAC Name: 4-Allyl-2-methoxy-3-methylphenol
 Safrole ACD/IUPAC Name: 5-Allyl-1,3-benzodioxole	 trans-Isosafrole ACD/IUPAC Name: 5-[(1E)-1-Propen-1-yl]-1,3-benzodioxole	 (E)-Asarone ACD/IUPAC Name: 1,2,4-Trimethoxy-5-[(1E)-1-propen-1-yl]benzene
 Marginatine 3,4-methylenedioxy-1-(2E-octenyl)-benzene ACD/IUPAC Name: 5-(1-Octen-1-yl)-1,3-benzodioxole	 (E,E)-N-Isobutyl-2,4-octadienamide ACD/IUPAC Name: (2E,4E)-N-Isobutyl-2,4-octadienamide	 2,6-dimethoxy-3,4-methylenedioxy-1-(2-propenyl)-benzene ACD/IUPAC Name: 5-Allyl-4,6-dimethoxy-1,3-benzodioxole

Figure 1. Compounds from *Piper marginatum*.



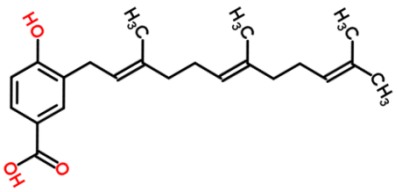
2,4,5-trimethoxypropiophenone

ACD/IUPAC Name: 1-(2,4,5-Trimethoxyphenyl)-1-propanone



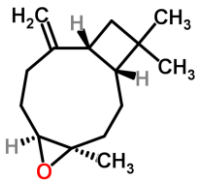
5,4'-dihydroxy-7-methoxyflavanone

ACD/IUPAC Name: : (2S)-5-Hydroxy-2-(4-hydroxyphenyl)-7-methoxy-2,3-dihydro-4H-chromen-4-one



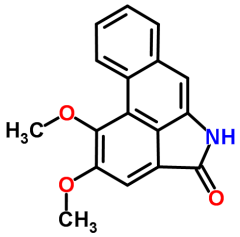
3-farnesyl-4-hydroxybenzoic acid

ACD/IUPAC Name: 4-Hydroxy-3-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl]benzoic acid



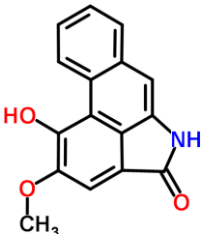
Caryophyllene oxide

ACD/IUPAC Name: (1R,4R,6S,10R)-4,12,12-Trimethyl-9-methylene-5-oxatricyclo[8.2.0.04,6]dodecane



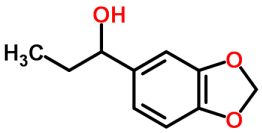
Cepharanone B

ACD/IUPAC Name: 1,2-Dimethoxydibenzo[cd,f]indol-4(5H)-one



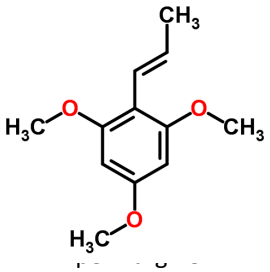
Piperolactam A

ACD/IUPAC Name: 1-Hydroxy-2-methoxydibenzo[cd,f]indol-4(5H)-one



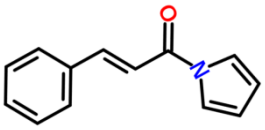
Marginatumol
1-(3,4-methylenedioxyphenyl)propan-1-ol

ACD/IUPAC Name: 1-(1,3-Benzodioxol-5-yl)-1-propanol



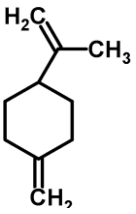
1-(1E-propenyl-)-2,4,6-trimethoxybenzene

ACD/IUPAC Name: 1,3,5-Trimethoxy-2-[(1E)-1-propen-1-yl]benzene



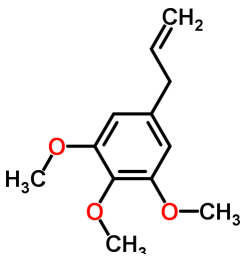
1-cinnamoyl pyrrolidide

ACD/IUPAC Name: (2E)-3-Phenyl-1-(1H-pyrrol-1-yl)-2-propen-1-one



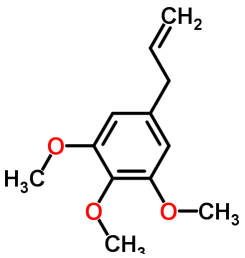
p-mentha-1(7),8-diene

ACD/IUPAC Name: 1-Isopropenyl-4-methylenecyclohexane



Elemecin

ACD/IUPAC Name: 5-Allyl-1,2,3-trimethoxybenzene



Nothosmyrnol

ACD/IUPAC Name: 2,4-Dimethoxy-1-[(1E)-1-propen-1-yl]benzene

Figure 1. Compounds from *Piper marginatum*.