Journal of Pharmaceutics and Drug Research
JPDR, 5(2): 566-597
www.scitcentral.com

ISSN: 2640-6152

Review Article: Open Access

Phytoconstituents and Biological Activities of Genus Artemisia (Asteraceae): A Review

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Received May 25, 2021; Revised May 29, 2021; Accepted June 02, 2021

ABSTRACT

The genus "*Artemisia*" is one of the largest and widely distributed genus of the plant family "*Asteraceae"*, comprising more than 400 accepted species. Due to the structurally diverse bioactive phytochemical constituents from the *Artemisia* species, this genus has been used as folk remedies in various treatments since ancient times. The genus contains various classes of secondary metabolites comprising alkaloids, flavonoids, coumarins, lignans, phenylpropanoids, terpenes, monoterpenes, terpenoids, sesquiterpenoids, sterols, phenolics, fatty acids, caffeoylquinic acids and acetylenes. Phytochemicals and extracts of *Artemisia* species exhibit diverse pharmacological activities including anti-malarial, anti-cancerous, anti-oxidant, anticoagulant activity, anti-parasitic, anti-inflammatory, antiulcerogenic, anti-viral activity, anti-microbial, anti-tumor and anti-diabetic activity. The present review compiles phytochemical constituents and various pharmacological activities of the *Artemisia* species.

The aim of this review is to bring together most of the information about the phytochemical constituents and pharmacological activities to attract researcher for further research in drug discovery.

Keywords: Asteraceae, *Artemisia*, Phytochemicals, Flavonoids, Alkaloids, Coumarins, Lignans NMR, Pharmacological activities

Abbreviations: NMR: Nuclear magnetic resonance; CDCl3: Deuterated chloroform; CD3OD: Deuterated methanol; DMSO-d6: Dimethyl sulfoxide-d□

INTRODUCTION

Since ancient times, medicinal plants have been used in healthcare. A number of plants have been used in traditional medicine for various treatments. According to WHO about 80% of the world population used medicinal plants and relies on traditional remedies for their preliminary health care [1].

The aster family (Asteraceae), also called *Compositae* is one of the largest angiosperm families, consisting of more than 1,620 genera and 23,600 species of herbaceous plants, shrubs, and trees. The Asteraceae family also recognized as, 'sunflower family', 'thistle family' or 'daisy family'. The family has a widespread distribution throughout the world, except Antarctica. The plants are characterized by their composite flower heads and one-seeded achene fruits. Members of this family possess medicinal properties and are used as traditional medicine due to their various phytoconstituents [2,3].

The word '*Artemisia*' comes from the ancient Greek word 'Artemis' means The Goddess (the Greek Queen *Artemisia*) and 'absinthium' means Unenjoyable or without sweetness. The genus "*Artemisia*", is one of the largest and widely distributed genus belongs to the flowering plant family *Asteraceae*, comprises hardy herbaceous plants and small shrubs, distributed mainly in the temperate zones of Europe, Asia and North America [4,5]. The genus consisting over 500 diverse species, out of which 474 are accepted species names [6]. Various species of the genus are called by the

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Citation: Eira BN, Mitra JR & Tuz-Zohora F. (2022) Phytoconstituents and Biological Activities of Genus Artemisia (Asteraceae): A Review. J Pharm Drug Res, 5(2): 566-597.

common names include mugwort, wormwood, sagebrush, southernwood, slovenwood, sweet Annie, sagewort, tarragon [7]. Most of the *Artemisia* species found in the temperate sectors of northern hemisphere, but limited numbers of species are also found in the southern hemisphere of the world. However, its center of diversification is Central Asia [8]. Plants of this genus have been used in various treatment as folk remedies due to the presence of diverse bioactive phytochemical compound. Phytochemical investigation on *Artemisia* species revealed that the genus contains various classes of secondary metabolites comprising alkaloids, flavonoids, coumarins, lignans, phenylpropanoids, terpenes, monoterpenes, terpenoids, sesquiterpenoids, sterols, phenolics, fatty acids, caffeoylquinic acids and acetylenes etc. which are reported to possess various biological activities including antimicrobial, antioxidant, cytotoxic, insecticidal, [9,10] anti-malarial [11], anti-cancerous[12], anti-tumor[13], anthelmintic activity [14] , anti-diabetic [15], antiulcerogenic [16], anti-inflammatory [17] and anti-viral activity [18].

The aim of this paper is to compile and accumulate information about the phytochemical constituents and various pharmacological studies of the different species of *Artemisia*.

BOTANICAL DESCRIPTION

Habitat

Artemisia species are widely distributed in temperate regions of North America (Mexico, the United States, and Canada), the Mediterranean region, Asia, Africa, and Australia. The majority of species have been found in Asia, including China, Japan, Iran, India, and Turkey [19]. The genus is mostly found in temperate areas of the northern hemisphere, with just few species recorded from the southern hemisphere [20]. However, Central Asia is the center of diversification, with around 150 species in China, 50 species in Japan, and 35 species in Iran, while the speciation areas are North West America, Irano-Turanian, 29 species in Pakistani flora, and the Mediterranean region. From Africa and Europe, only few species have been recorded [21].

Artemisia is thought to have originated in the northwestern Asian mountain regions, probably from meso-thermic subarctic or semihumid forest steppe conditions near the Ural Mountains [22].

Taxonomic classification [23]

Kingdom	: Plantae
Phylum	: Magnoliophyta
Class	: Magnoliopsida
Order	: Asterales
Family	: Asteraceae
Genus	: *Artemisia*

Morphology

The leaves of the genus *Artemisia* are of various sizes, shapes, and textures, according to taxonomic characteristics. These are alternate and pinnatifid to pinnatisect. The inflorescence capitulum is small, often ellipsoid to ovate, arranged in the form of Paniculate Racemose, and contains tubular florets inserted on receptacle covered by involucral bracts, present in few rows. The corollas come in a variety of colors, including white, green, yellow, purplish, and sometimes brown [24] **(Figure 1)**.

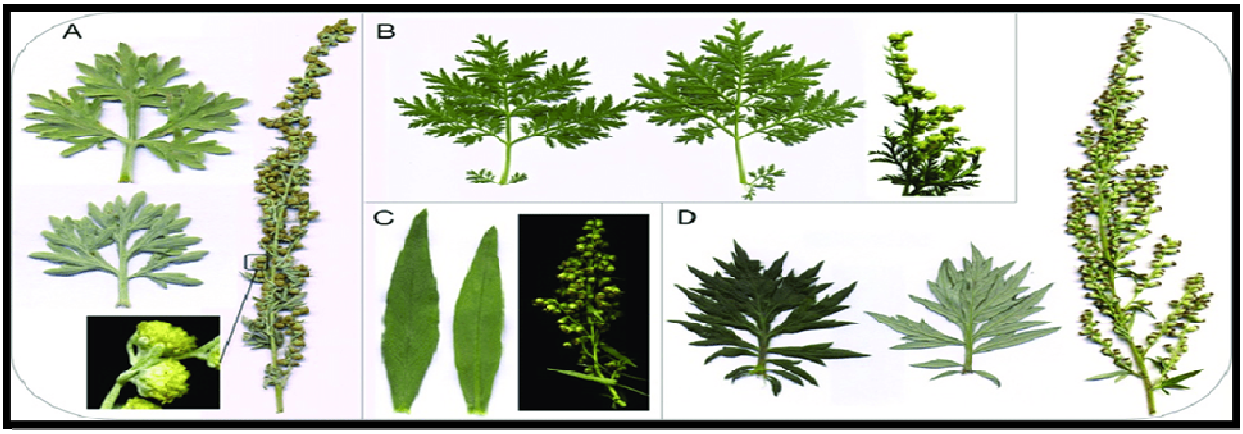


Figure 1. Morphological features of different *Artimesia* species [26] **(A)** *Artemisia absinthium.* **(B)** *Artemisia annua.* **(C)** *Artemisia dracunculus.* **(D)** *Artemisia vulgaris.*

[Photographs by P. Barnola, A. Mallol and L. Vilar (synflorescences of A. absinthium-detail-and A. dracunculus), G. Pié (synflorescence of A. annua) and J. Vallès (A. vulgaris)]

Cypsela may be oblique or terminal, with a scarred corolla, or elliptical, spheroidal, ovate, or compressed. Its color ranges from light brown to dark brown, and its surface can be glabrous or finely striated. Cypsela is 0.5-1.5×0.25-0.75mm in size [25]. Many species in this genus begin flowering at the end of the summer or during winter [26,27].

Ethnopharmacology

The genus *Artemisia* contains economically valuable plant species that have been used in pharmacology and various culinary applications for a long time. *Artemisia* extracts are used in a variety of biopharmaceutical products available on the market to treat a variety of ailments. In Chinese traditional medicine, *Artemisia annua* is used to treat malaria and chills. Decoctions of *Artemisia herba- alba* (*Artemisia brevifolia* Wall., *Artemisia meritima* L.) is used in traditional medicines to treat fever and nervous problems [28]. In addition, *Artemisia absinthium* (wormwood) has antiparasitic properties and is used to treat indigestion and anorexia. It is also used in gastric herbal preparations and in alcoholic beverages [29]. Among other species *Artemisia biennis* is used as antiseptics and spices. It's used to treat cuts, inflammation, and infections of the chest. Stomach cramps and painful menstruation are treated with the whole plant and seeds. It has been used to treat wounds and sores externally [30]. *Artemisia argyi* is a plant that grows primarily in China (where it is known as ai ye) and Japan (where it is known as gaiyou) and is used in herbal medicine to treat kidney, liver, and spleen disorder [31]. Essential oils are produced by the aerial parts of *Artemisia scoparia* (redstem wormwood) and are used as antibacterial, antipyretic, antiseptic, anti-cholesterolemic, insecticidal, purgative, diuretic, and gall bladder inflammation remedies [32].

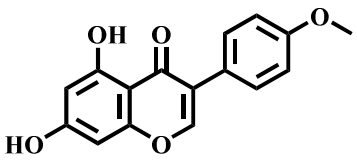
Phytochemical Constituents

The genus *Artemisia* contains a rich source of structurally diverse secondary metabolites. Phytochemical investigation on *Artemisia* species showed the presence of various classes of phytochemicals comprising alkaloids, flavonoids, coumarins, lignans, phenylpropanoids, terpenes, monoterpenes, terpenoids, sesquiterpenoids, sterols, phenolics, fatty acids, caffeoylquinic acids and acetylenes etc. Among these the present review compiles and focuses mainly on flavonoids, alkaloids, coumarins and lignans.

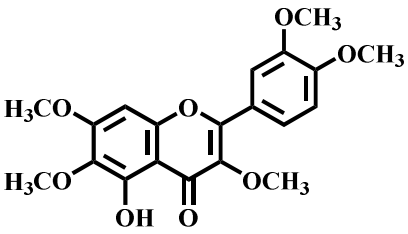
Flavonoids isolated from the *Artemisia* species are compiled in **Table 1** and the chemical structure of this isolated flavonoids compound are illustrated in **Figure 2.**

Table 1. Flavonoids found in *Artemisia* species.

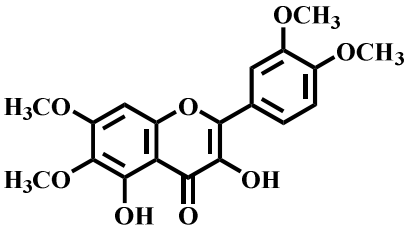
Compound	References
Artemetin, Quercetagetin 6,7,3',4'-tetramethyl ether	[33]
Quercetagetin 4'-methyl ether, 2,2-Dihydroxy-6-methoxychromene, 2,2,6- Trihydroxychromene, Quercimeritrin	[34]
Casticin	[35]
Chrysoplenetein	[36]
Eupatin	[37]
Chrysoplenetein B, Tricin, Retusin C	[38]
Naringenin, Sakuranetin, Isosakuranetin, Eriodictyol-7-methyl ether, Eriodictyol-7,4'-dimethyl ether, Eriodictyol-7,3'-dimethyl ether	[39]
2',4',5,7-tetrahydroxy-5',6-dimethoxyflavone, Eupatilin, Dimethoxycentaureidin, Cirsiliol	[40]
Quercetin, Quercetin-3-rutinoside, Robinin, Luteolin-7-glucoside	[41]
Kaempferol, Apigenin, Luteolin	[42]
Catechin, Myristin	[43]
Pinocembrin	[44]
Acacetin, 5□hydroxy□7,4′□dimethoxyflavanone, 3,5□dihydroxy□7,4′□dimethoxyflavone, 5,4′□dihydroxy□7□methoxyflavanone, 5,4′□dihydroxy□7,3′□dimethoxyflavanone	[45]
Myricetin, Spinacetin	[46]
Isorhamnetin	[47]
Angophorol	[48]
Rhamnetin	[49]
Isokaempferide	[50]
Cirsilineol, Hispidulin, Isovitexin, Pultetin 3-rutinoside, Pultetin 3-glucoside, Vicecin-2, Schaftoside, Isoschaftoside	[51]
Jaceosidin	[52]
Chrysoeriol	[53]
Diosmetin, Eriodictyol	[54]
Formononetin	[55,56]



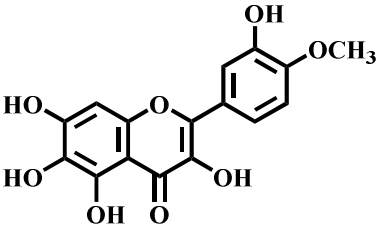
Formononetin



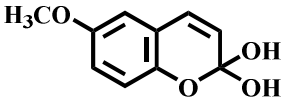
Artemetin



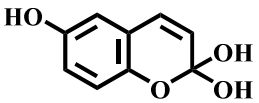
Quercetagetin 6,7,3′,4′-tetramethyl ether



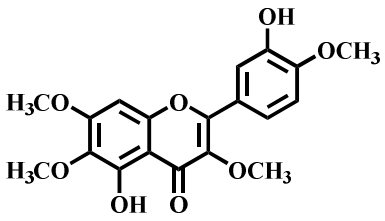
Quercetagetin 4'- methyl ether



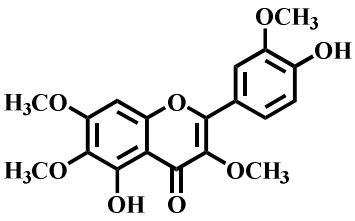
2,2-Dihydroxy-6-methoxychromene



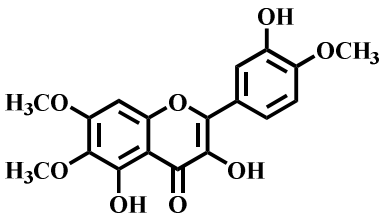
2,2,6-Trihydroxychromene



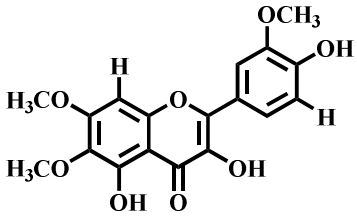
Casticin



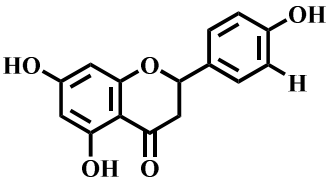
Chrysosplenetein



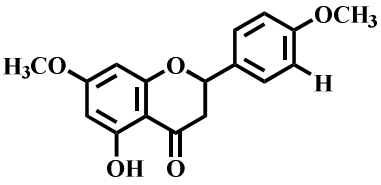
Eupatin



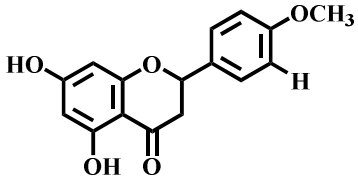
Chrysosplenetein B



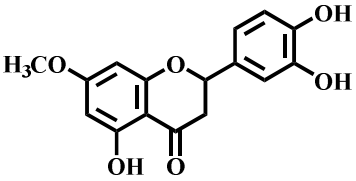
Naringenin



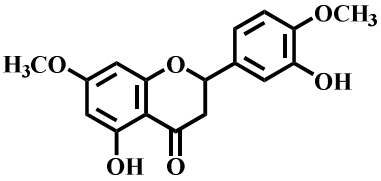
Sakuranetin



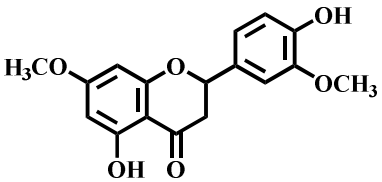
Isosakuranetin



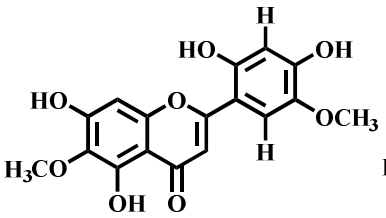
Eriodictyol-7-methyl ether



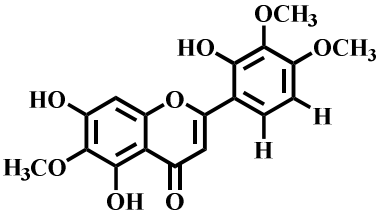
Eriodictyol-7,4'-dimethyl ether



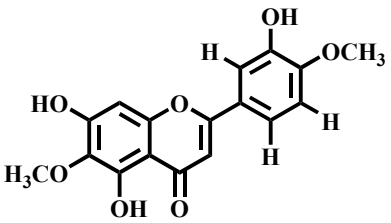
Eriodictyol-7,3'-dimethyl ether



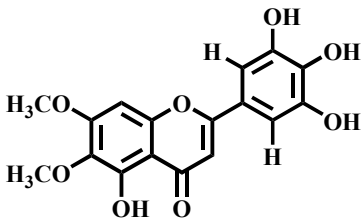
2',4',5,7-tetrahydroxy-5',6-dimethoxyflavone



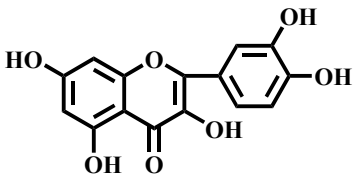
Eupatilin



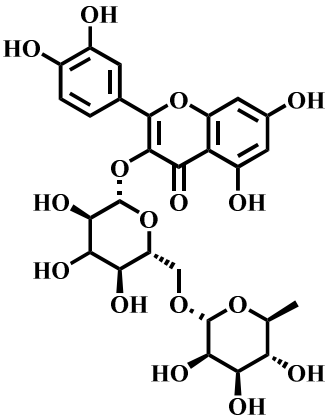
Dimethoxycentaureidin



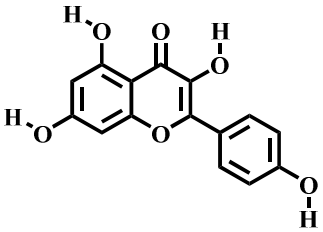
Cirsiliol



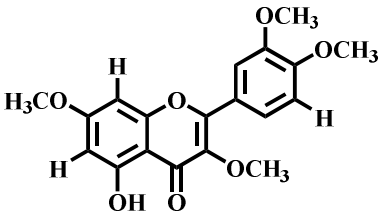
Quercetin



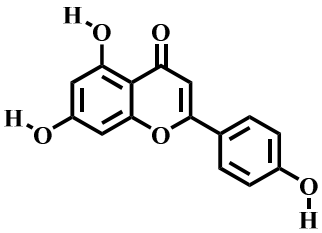
Quercetin-3-rutinoside



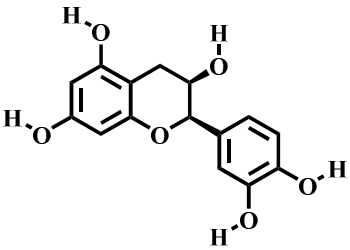
Kaempferol



Retusin C



Apigenin



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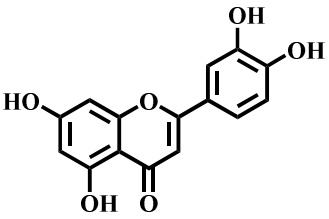

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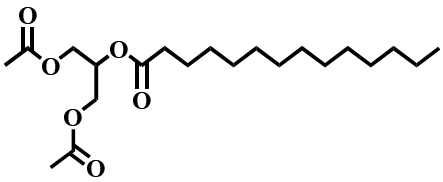
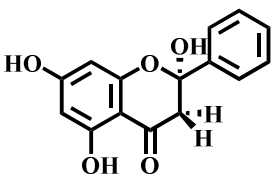


Myristin



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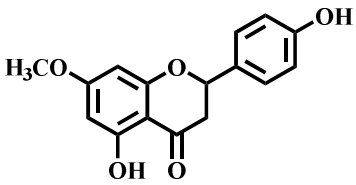

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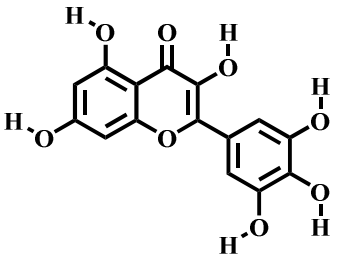

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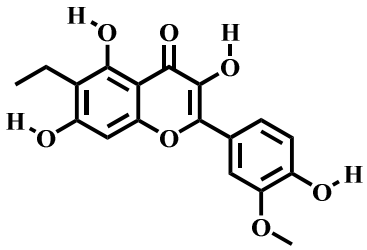

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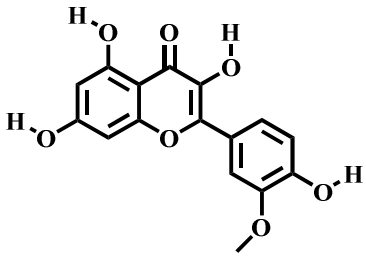

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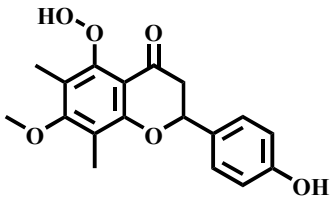

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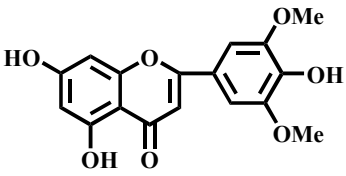
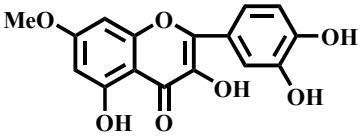
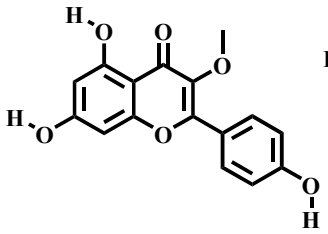


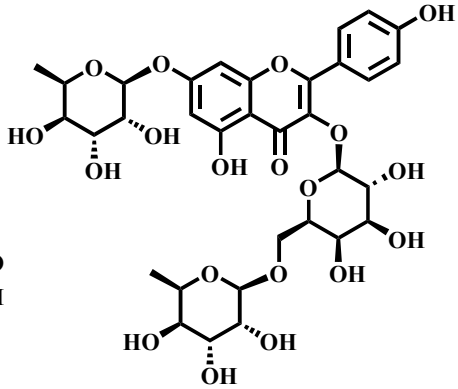
Tricin



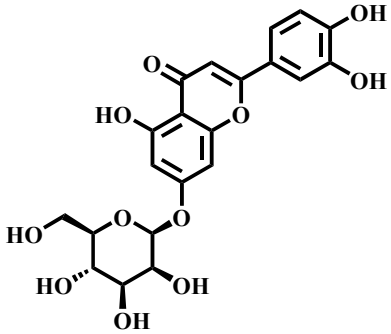
Rhamnetin



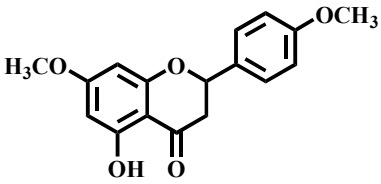
Isokaempferide



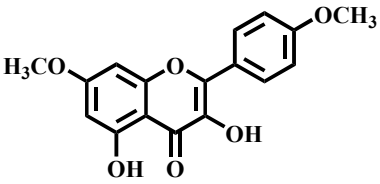
Robinin



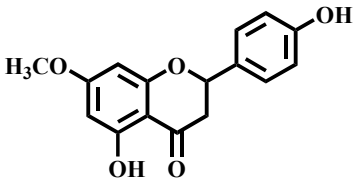
Luteolin-7-glucoside



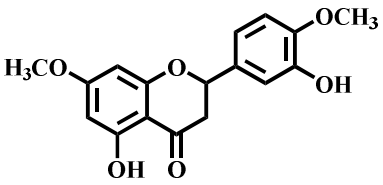
5-hydroxy-7,4'-dimethoxyflavanone



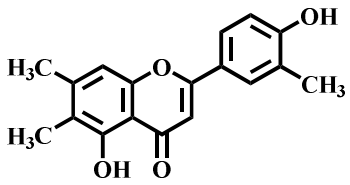
3,5-dihydroxy-7,4'-dimethoxyflavone



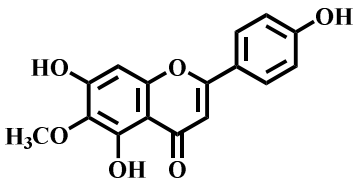
5,4'-dihydroxy-7-methoxyflavanone



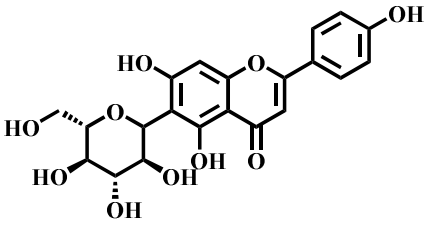
5,4'-dihydroxy-7,3'-dimethoxyflavanone



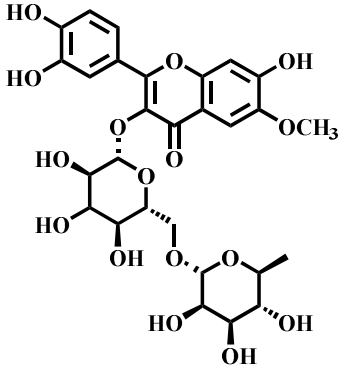
Cirsilineol



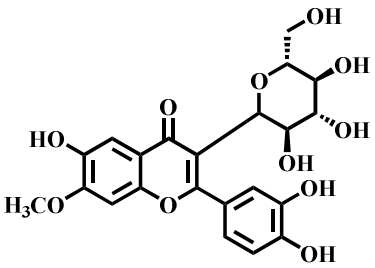
Hispidulin



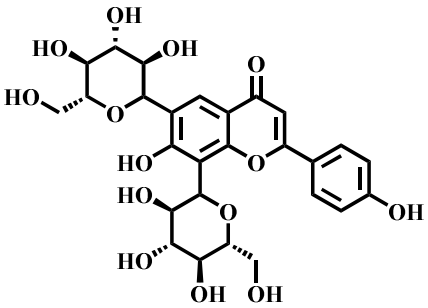
Isovitexin



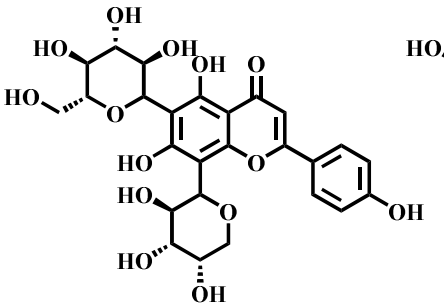
Pultetin 3- rutinoside



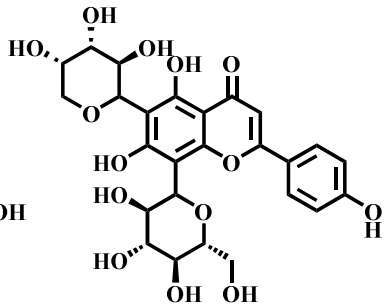
Pultetin 3- glucoside



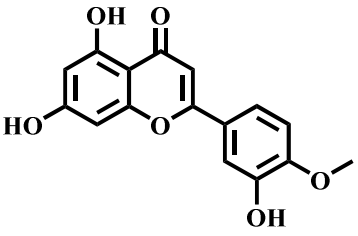
Vicecin- 2



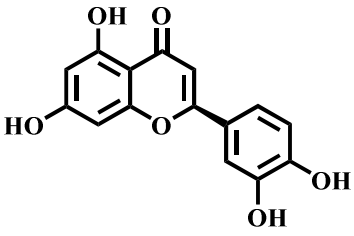
Schaftoside



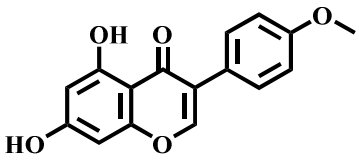
Isochaftoside



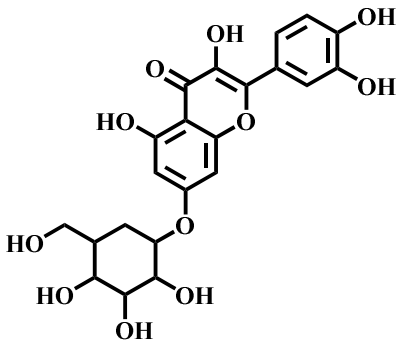
Diosmetin



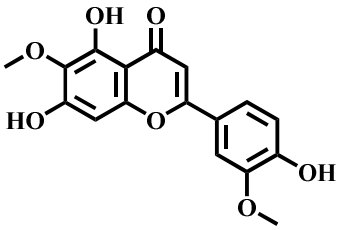
Eriodictyol



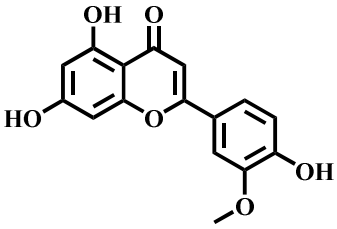
Formononetin



Quercimeritrin



Jaceosidin



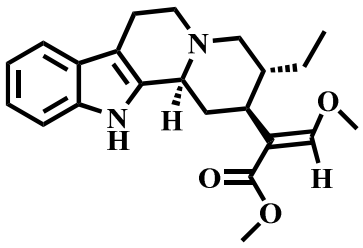
Chrysoeriol

Figure 2. Chemical Structure of Flavonoids Isolated from *Artemisia* Species.

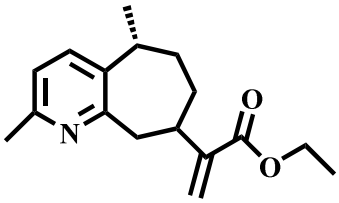
Alkaloids isolated from the *Artemisia* species are compiled in **Table 2** and the chemical structure of this isolated alkaloids compound are illustrated in **Figure 3.**

Table 2. Alkaloids found in *Artemisia* species.

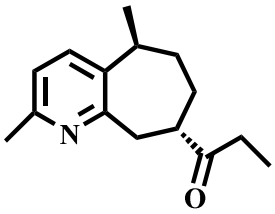
Compound	References
Hirsutine	[41]
Rupestine A, Rupestine B, Rupestine C, Rupestine D	[57]
Rupestine E	[58]
Rupestine F, Rupestine G, Rupestine H, Rupestine I, Rupestine J, Rupestine K, Rupestine L, Rupestine M	[59]
Artekorine, 6-ketoartekorine, Lappaconitine	[60]
Usaramine, Chromonar	[61]
6□amino□7,8□dihydro□2□hydroxypurin	[62]
6□amino□9□[1□(3,4□dihydroxyphenyl) ethyl] □9H□purine	[63]
Zeatin	[64]
Indole□3□acetic acid, 6□isoprenylindole□3□carboxylic acid	[65]
Tryptophan	[66]
Benzo[d]thiazole	[67]
1H□indole	[68]
6□methoxy□1H□indole□3□methyl carboxylate	[69]
Burnamicine	[70]
Serotonin	[71]
Ficine, Isoficine	[70,72]



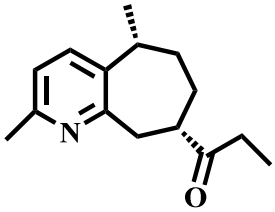
Hirsutine



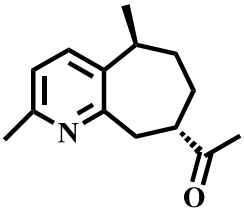
Rupestine A



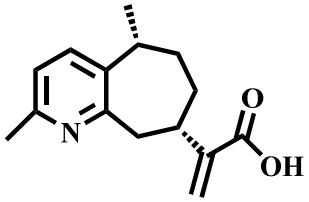
Rupestine B



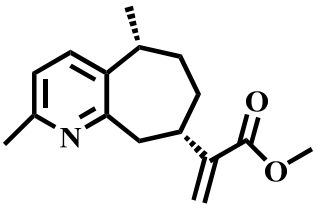
Rupestine C



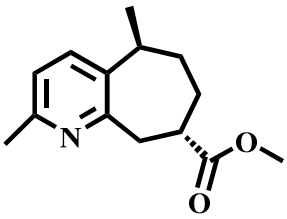
Rupestine D



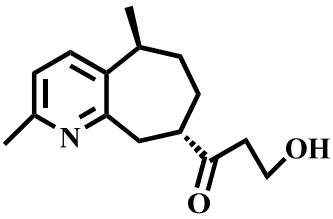
Rupestine E



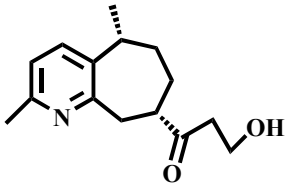
Rupestine F



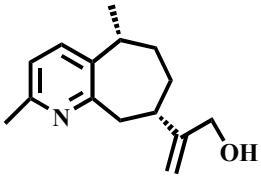
Rupestine G



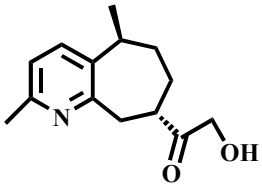
Rupestine H



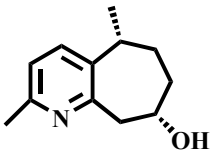
Rupestine I



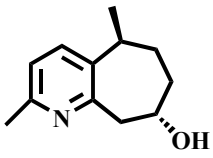
Rupestine J



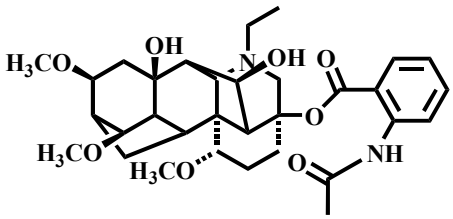
Rupestine K



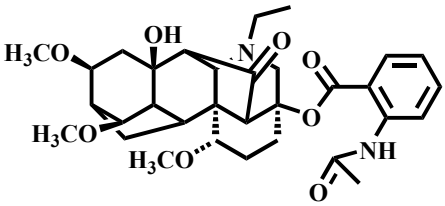
Rupestine L



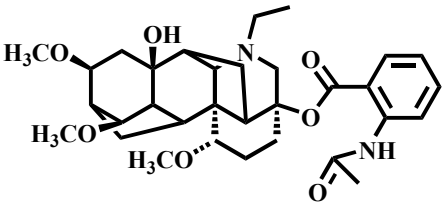
Rupestine M



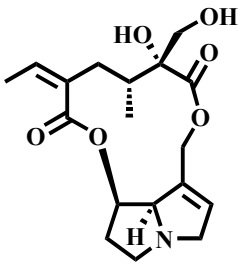
Artekorine



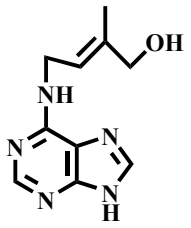
6-Ketoartekorine



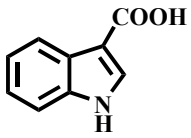
Lappaconitine



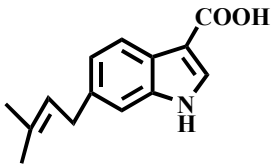
Usaramine



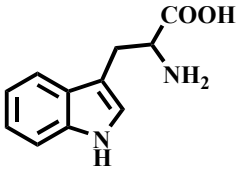
Zeatin



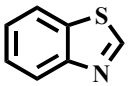
Indole-3-acetic acid



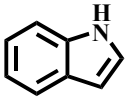
6-Isoprenylindole-3-carboxylic acid



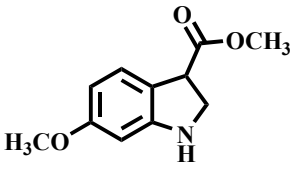
Tryptophan



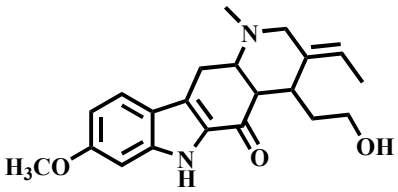
Benzo[d]thiazole



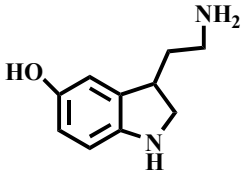
1H-indole



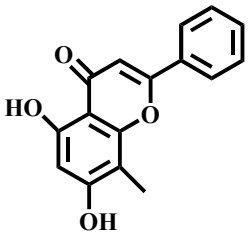
6-methoxy-1H-indole-3-methyl carboxylate



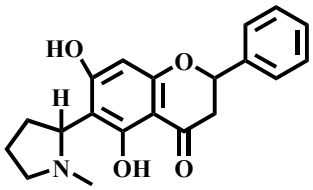
Burnamicine



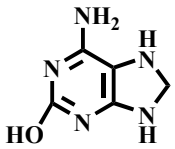
Serotonin



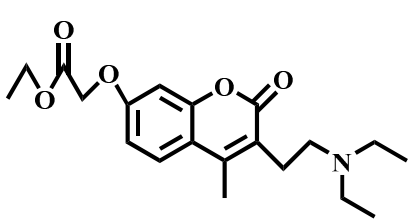
Ficine



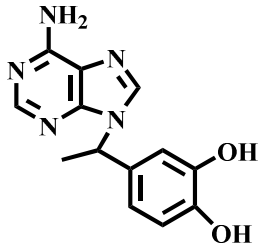
Isoficine



6-amino-7,8-dihydro-2-hydroxypurin



Chromonar



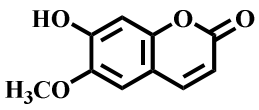
6-amino-9-[1-(3,4-dihydroxyphenyl)ethyl]-9H-purine

Figure 3. Chemical Structure of Alkaloids Isolated from *Artemisia* Species.

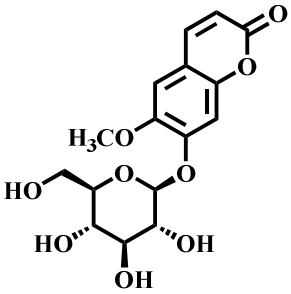
Coumarins isolated from the *Artemisia* species are compiled in **Table 3** and the chemical structure of this isolated coumarins compound are illustrated in **Figure 4.**

Table 3. Coumarins found in *Artemisia* species.

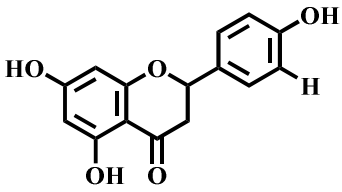
Compound	**References**
Scopoletin	[36]
Scopolin	[73,74]
Arteordocoumarin A, 6,7-dimethoxycoumarin, 6,7,8-trimethoxycoumarin, 6-hydroxy-7-methoxycoumarin, 4-hydroxylacetophenone, 4-hydroxy-5-methoxylacetophenone, 4-hydroxybenzaldehyde, 4-hydroxy-5-methoxybenzaldehyde, 4,5-dihydroxybenzaldehyde	[75]
Esculetin	[76]
Fraxidin, Artemidinal, Artemidin, (+)-Epoxyartemidin	[74]
Isofraxidin, Dracunculin	[77]
Herniarin	[50]
Unbelliferone	[47]
Scoparone	[78]



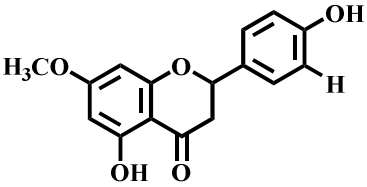
Scopoletin



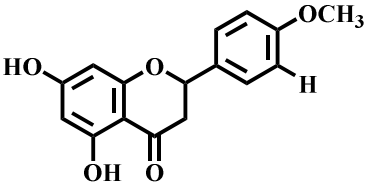
Scopolin



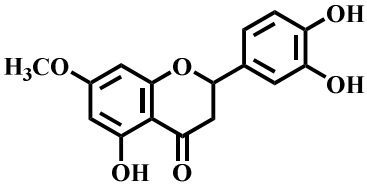
Arteordocoumarin A



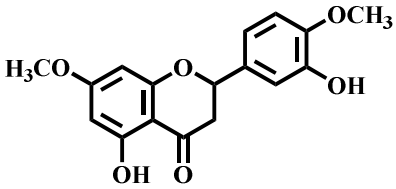
6,7-dimethoxycoumarin



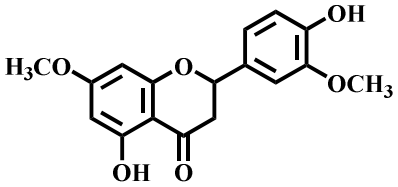
6,7,8-trimethoxycoumarin



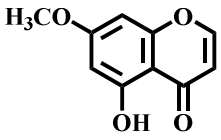
6-hydroxy-7-methoxycoumarin



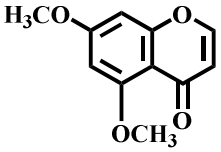
4-hydroxylacetophenone



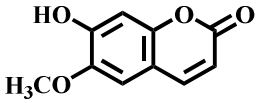
4-hydroxy-5-methoxylacetophenone



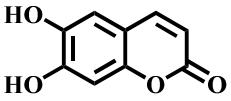
4-hydroxybenzaldehyde



4-hydroxy-5-methoxybenzaldehyde



4,5-dihydroxybenzaldehyde



Esculetin

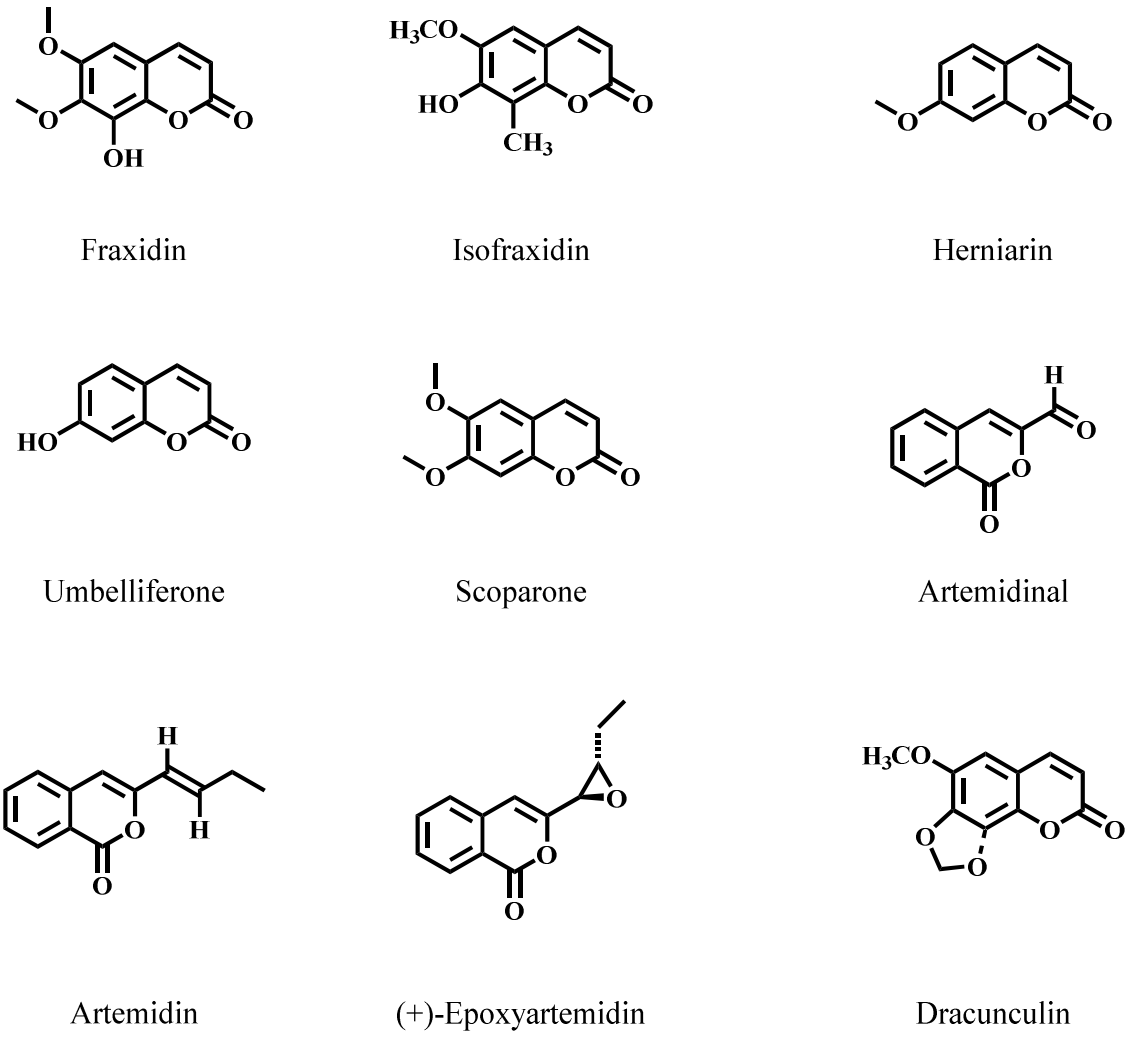
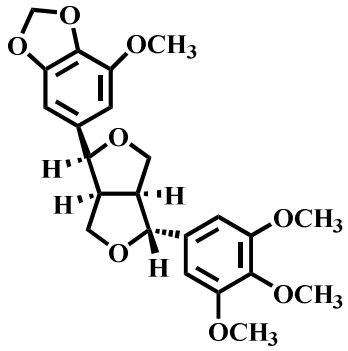


Figure 4. Chemical structure of coumarins isolated from *Artemisia* species.

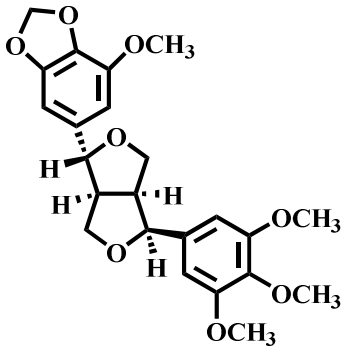
Lignans isolated from the *Artemisia* species are compiled in **Table 4** and the chemical structure of this isolated Lignans compound are illustrated in **Figure 5.**

Table 4. Lignans found in *Artemisia* species.

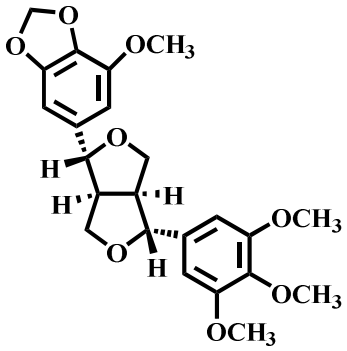
Compound	References
Episesartemin A, Episesartemin B, Diasesartemin, Fargesin, Epifargesin, Epimagnolin, Epieudesmin, Sesamin, Aschantin	[79]
Kobusin, Magnolin, Eudesmin	[80]
5-Methoxysesamin, Phillyrin, Simplocosin, Sieversol	[81,82]
Spinescen, Pinoresinol, Demethoxyexcelsin	[79,83]
Carulignan A, Carulignan B, Carulignan D	[84]
Carulignan C, 7-β- Carulignan C, Syringaresinol, (+) Arborone, Epiyangambin, Diayangambin, Sesartemin, Epiaschantin, Yangambin	[85]
Diasyringaresinol	[86]



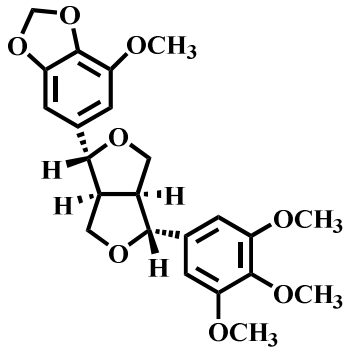
Episesartemin A



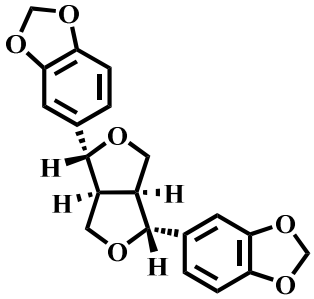
Episesartemin B



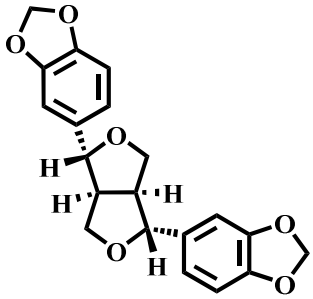
Sesartemin



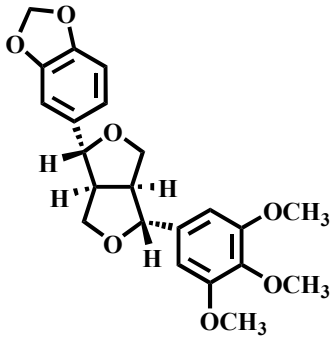
Diasesartemin



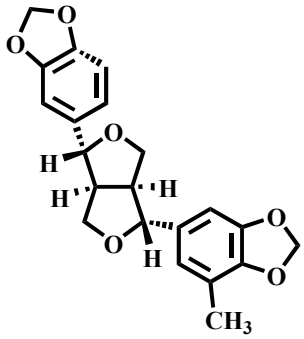
Sesamin



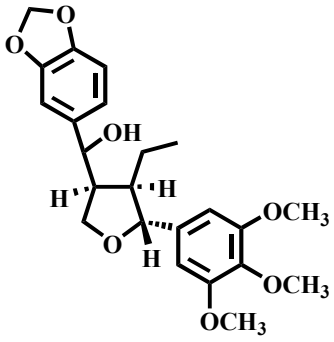
Kobusin



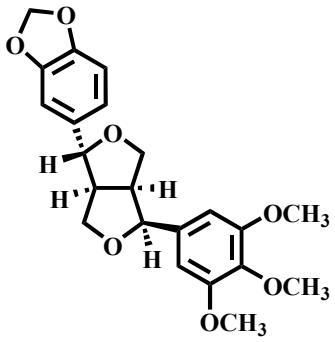
Aschantin



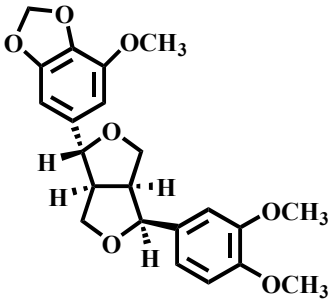
5-Methoxysesamin



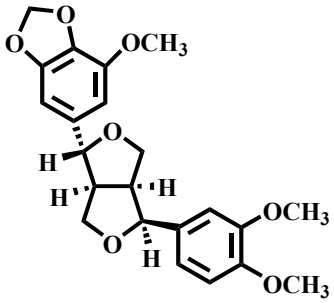
Sieversol



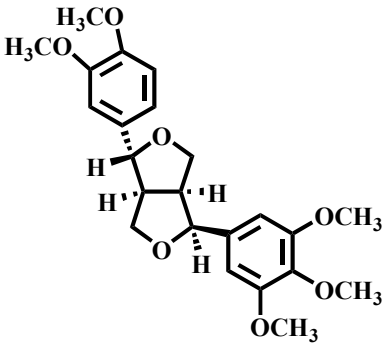
Epiaschantin



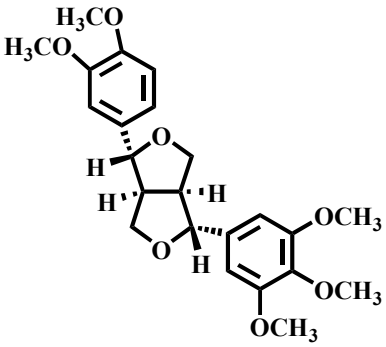
Fargesin



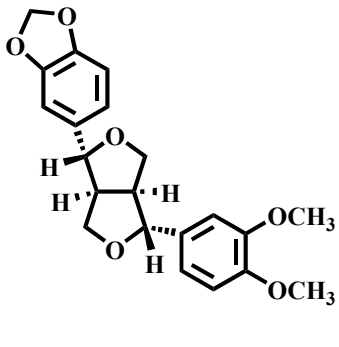
Epifargesin



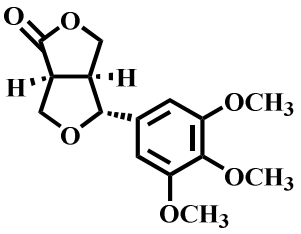
Epimagnolin



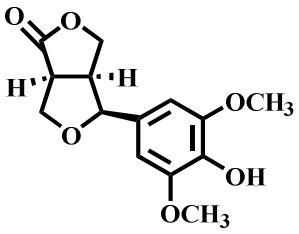
Magnolin



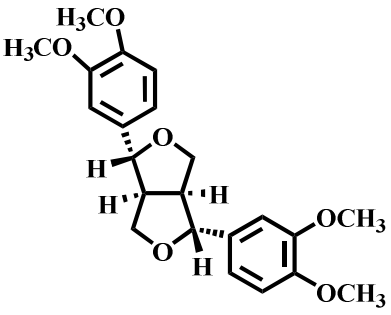
Spinescen



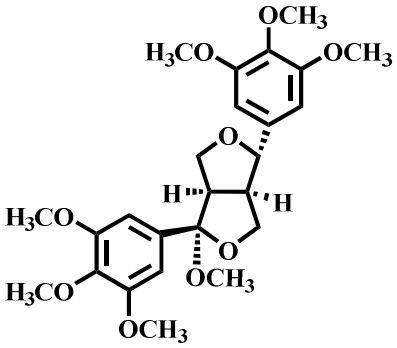
7-β-Caruilignan C



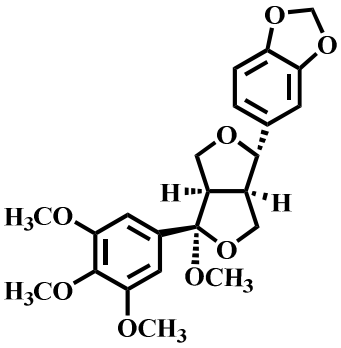
Caruilignan D



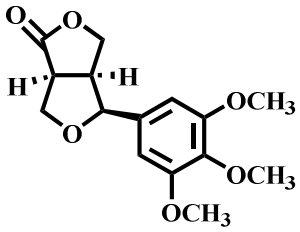
Eudesmin



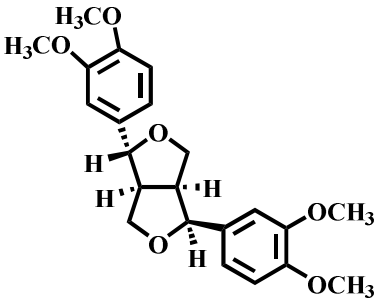
Caruilignan A



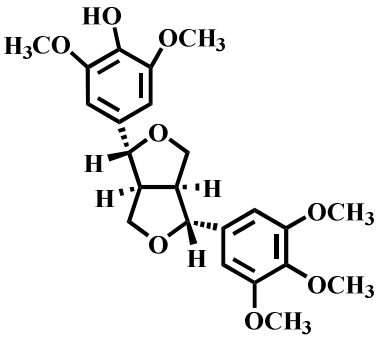
Caruilignan B



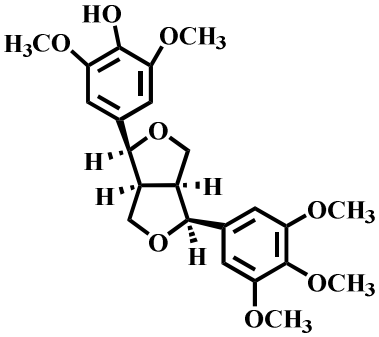
Caruilignan C



Epieudesmin



Syringaresinol



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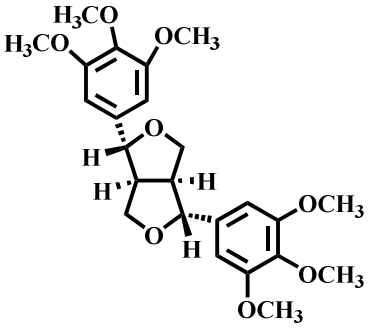
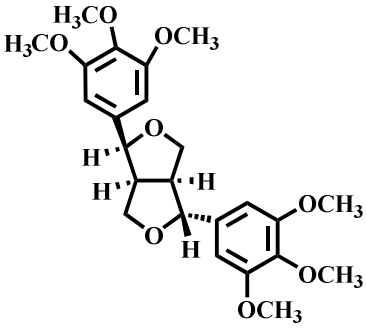


Yangambin



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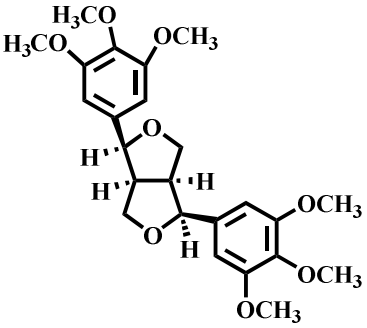
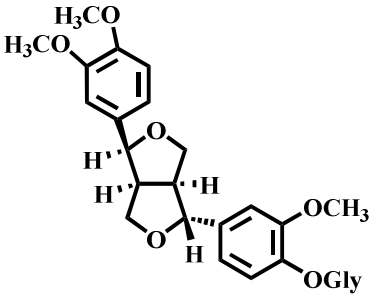
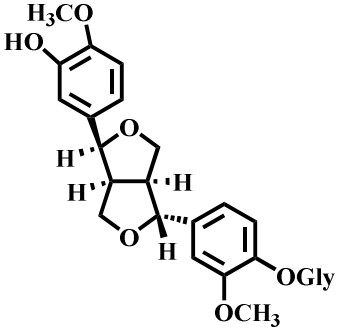


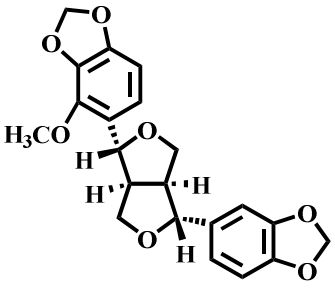
Diayangambin



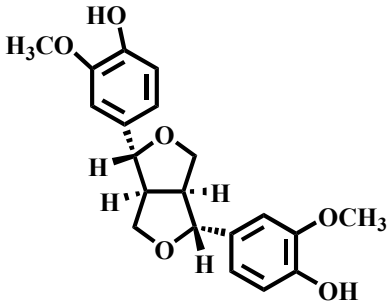
Phillyrin



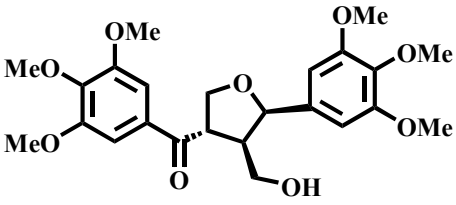
Simplocosin



Demethoxyexcelsin



Pinoresinol



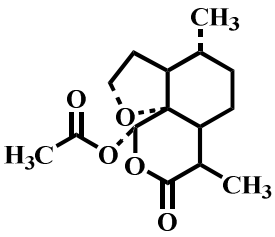
(+) Arborone

Figure 5. Chemical Structure of Ligands Isolated from *Artemisia* species.

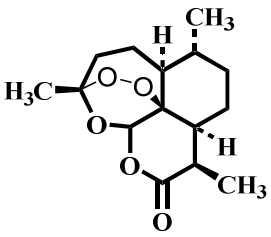
Some terpenes isolated from the *Artemisia* species are compiled in **Table 5** and the chemical structure of this isolated terpenes and their derivatives are illustrated in **Figure 6.**

Table 5. Terpenes and their derivatives found in *Artemisia* species.

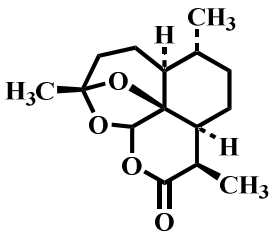
Compound	**References**
Artemisinin, Deoxyartemisinin, Arteannuin-B, Friedelin, Friedelin-3-β-ol	[33]
Artemisinin G	[87]
Artecanin	[88]
Argyinolides A, Argyinolides B	[89]
Vulgarolides A, Vulgarolides B	[90]
Eudesmanolide, Artanomadimers A, Artanomadimers B, Artanoate	[91-93]



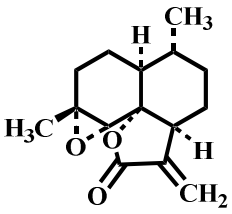
Artemisinin G



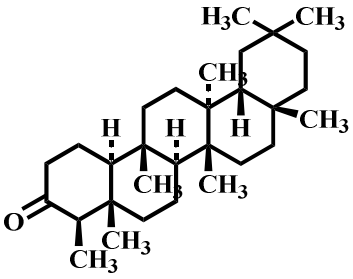
Artemisinin



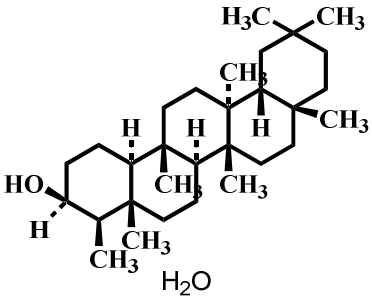
Deoxyartemisinin



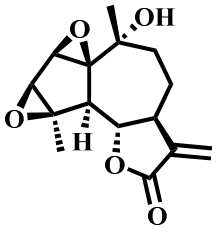
Arteannuin-B



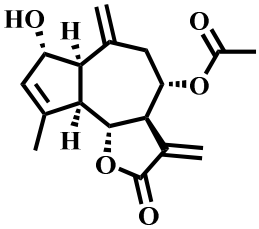
Friedelin



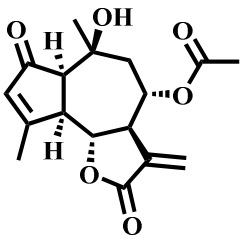
Friedelin -3β- ol



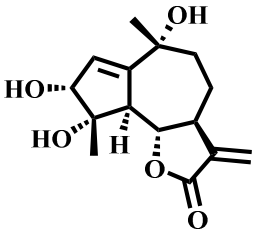
Artecanin



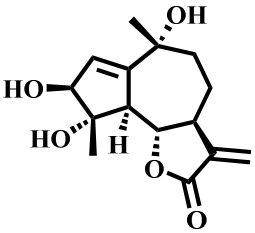
Argyinolides A



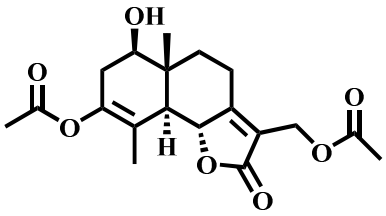
Argyinolides B



Vulgarolides A



Vulgarolides B



Eudesmanolide

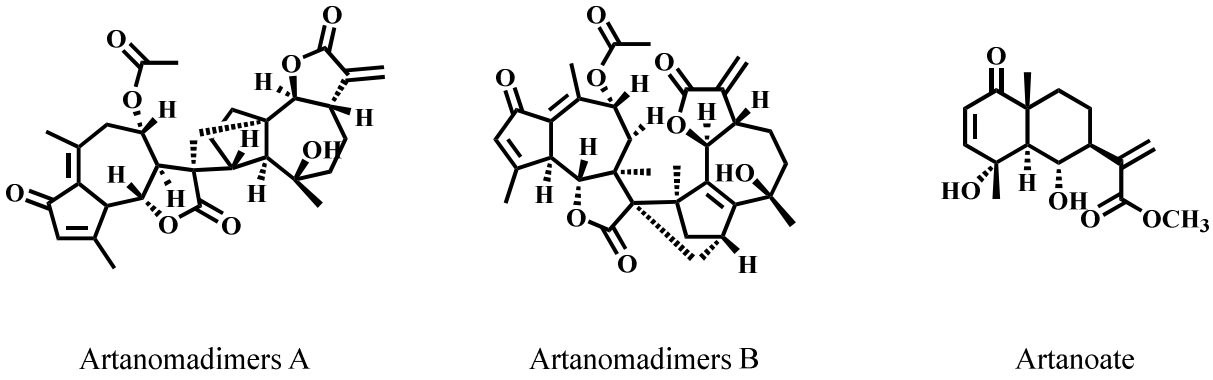


Figure 6. Chemical structure of some Terpenes and their derivatives isolated from *Artemisia* species.

NMR

Artemetin [33]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (1H, dd, *J*=8.4Hz, 2.2Hz, H-6'), 7.66 (1H, d, *J*=2.2Hz, H-2'), 6.99 (1H, d, *J*=8.4Hz, H-5'), 6.86(1H, s, H-8), 3.99 (3H, s, 7-OMe), 3.97 (3H, s, 3-OMe), 3.97 (3H, s, 3'- or 4'-OMe), 3.86 (3H, s, 6-OMe), 3.79 (3H, s, 4' - or 3'-OMe), 2.52 (3H, s, 5-OAc).

Artemisinin [37]

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31(m, H-1), 2.00/1.44 (m, H-2a/H-2b), 2.43/2.06 (ddd, H-3a/H-3b), 5.86 (s, H-5), 1.75 (m, H-7), 1.85/1.05 (m, H-8a/H-8b), 1.75/1.05 (m, H-9a/H-9b), 3.39 (dq, H–H), 1.18(d, 7.0 Hz, H-13), 0.98 (d, 6.0 Hz, H-14) and 1.42 (s, H-15).

^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1(C-1), 105.4(C-2), 93.7(C-3), 79.5 (C-4), 50.1(C-5), 44.9(C-6), 37.5(C-7), 35.9(C-8), 33.6(C-9), 32.9(C-10), 25.2(C-11), 24.8(C-12), 23.4(C-13), 19.8(C-14), 12.5(C-15).

Scopoletin [37]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.20 (d, 9.4 Hz, H-3) 7.51 (d, 9.4 Hz, H-4), 6.86 (s, H-5), 6.82(s, H-8) and 3.82 (s, OCH_3).

Chrysosplenetin [37]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.50 (s, H-1) 7.66 (d,2,1 Hz, H-2′), 7.05 (d,8.6 Hz, H-5′), 7.71 (dd,8.6 Hz, 2.1 Hz, H-6′), 12.61 (s, 5-OH), 5.74 (s, 4′-OH), 3.86 (s, 3′-OCH_3), 3.93 (s, 6-OCH_3), 3.99 (s, 7-OCH_3), 3.96 (s, 3′-OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9(C-2), 105.40(C-2), 138.7(C-3), 178.9(C-4), 152.8(C-5), 132.3(C-6), 158.7(C-7), 90.3(C-8), 152.3(C-9), 106.6(C-10), 122.4(C-1′), 110.9(C-2′), 146.3(C-3′), 148.4(C-4′), 114.6(C-5′), 122.6(C-6′), 60.1(3-OCH_3), 60.9(6-OCH_3), 56.1(7-OCH_3), 56.3(3′CH_3).

Eupatin [37]

^{1}H NMR (300 MHz, $CDCl_3$): δ 12.75 (s,5-OH), 7.74 (dd,3.0Hz,12Hz, H-6′), 7.61(d,3.0Hz, H-2′), 7.01(d,12Hz, H-5′), 6.81(s, H-8), 4.00(CH_3O-6), 3.88(CH_3O-7), 3.81(4′-OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ 148.2(C-4′), 144.9(C-3′), 121.2(C-6′), 115.5(C-2′), 115.3(C-1′), 90.8(C-8), 59.6(6-OCH_3), 59.3(7-OCH_3), 55.9(4′-OCH_3).

Casticin [35]

^{1}H NMR (500 MHz, DMSO-d_6): δ 12.61 (1H, s, 5-OH), 9.90 (1H, s, 3-OH), 7.65 (1H, d, *J* = 2.0 Hz, H-2), 7.61(1H, dd, *J* = 8.0 Hz, 2.0 Hz, H-6), 6.94(1H, d, *J* = 8.0 Hz, H-5), 6.90(1H, s, H-5), 3.90 (3H, s, 7- OCH_3), 3.85(3H, s, 4 - OCH_3), 3.78(3H, s,3- OCH_3), 3.71(3H, s, 6- OCH_3).

^{13}C NMR (500 MHz, DMSO-d_6): δ 178.3(C-4), 158.7(C-7), 155.8(C-2), 151.8(C-9), 151.7(C-5), 150.0(C-3), 147.5(C-4), 137.8(C-3), 131.7(C-6), 122.4(C-1), 120.8(C-6), 115.7(C-2), 112.1(C-5), 105.6(C-10), 91.5(C-8), 60.1(6- OCH_3), 59.8(3-OCH_3), 56.6(7- OCH_3),55.9(4- OCH_3).

Artemisinin G [87]

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97(3H. d, *J*=6.3Hz), 1.19 (3H, d, *J*=7.1Hz), 2.15(3H. s), 3.15(IH, m), 3.93 (1H, m), 4.20 (IH, m), 6.63(1H, s).

^{13}C NMR (90 MHz, $CDCl_3$): δ 12.40, 20.26, 21.10, 24.22, 27.58, 30.82, 34.56 34.92, 46.59, 54.75, 69.14, 79.31, 92.94, 168.30, 171.50.

Quercetagetin 4'-methylether [34]

^{1}H NMR (CD_3OD): δ 7.80 (1H, d, *J*=2 Hz, C-2'), 7.65 (1H, dd, *J*=9 and 2 Hz, C-6'), 6.90 (1H, d, *J*=9 Hz, C-5'), 6.72 (1H, s, C-8), 4.01 (3H, s, C-4'-OMe).

2,2-Dihydroxy-6-methoxychromene [34]

^{1}H NMR (CD_3OD): δ 7.60 (1H, d, *J*=10 Hz, C-3), 7.18 (1H, d, *J*=2 Hz, C-5), 7.04 (1H, dd, *J*=6 and 2 Hz, C-7), 6.82 (1H, d, *J*=6 Hz, C-8), 6.31 (1H, d, *J*=l0 Hz, C-4), 3.86 (3H, s, C-6-OMe).

2,2,6-Trihydroxychromene [34]

^{1}H NMR (CD_3 OD): δ 7.48 (1H, d, *J*= 10Hz, C-3), 7.05 (1H, d, *J*= 2Hz, C-5), 6.90 (1H, dd, *J*=6 and 2 Hz, C-7), 6.72 (1H, d, *J*=6 Hz, C-8), 6.20 (IH, d, *J*=10 Hz, C-4).

2',4',5,7-tetradroxy-5',6-dimethoxyflavone [40]

^{1}H NMR (300 MHz, DMSO-d_6): δ 3.74 (3H, s, 5'- OCH_3), 3.79 (3H, s, 6- OCH_3), 6.55 (1H, s, H-3'), 6.61 (1H, s, H-8), 7.02 (1H, s, H-3), 7.37 (1H, s, H-6′), 9.99 (1H, s, 4'-OH), 10.33 (1H, s, 2'-OH), 10.38 (1H, s, 7-OH), 13.00 (1H, s, 5-OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ 182.6 (C-4), 162.2 (C-2), 157.4 (C-7), 153.4 (C-2′), 153.1 (C-4′), 152.8 (C-5), 152.8 (C-9), 148.1 (C-3′), 131.5 (C-6), 112.1 (C-6′), 106.9 (C-3), 94.7 (C-8), 107.4 (C-1′), 104.8 (C-5′), 104.3 (C-10), 60.4 (3'- OCH_3), 56.9 (6-OCH_3).

Eupatilin [40]

^{1}H NMR(300 MHz, DMSO-d_6): δ 3.76 (3H, s, 6- OCH_3), 3.85 (3H, s, 3'- OCH_3), 3.87 (3H, s, 4'- OCH_3), 6.63 (1H, s, H-8), 6.95 (1H, s, H-3), 7.10 (1H, d, *J*=3.0 Hz, H-2'), 7.55 (1H, d, *J* = 9.0 Hz, H-5'), 7.66 (1H, dd, *J*=9.0,3.0 Hz, H-6'), 7.66 (1H, s, H-3), 13,00 (1H, s, 5-OH), 10.69 (1H, s, 7-OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ 182.6 (C-4), 163.8 (C-2), 157,8 (C-5), 153.2 (C-7), 152.9 (C-9), 152.6 (C-4'), 149.4(C-3'), 131.8 (C-6), 123,4 (C-1'), 120.5 (C-6'), 112.1 (C-2'), 109.8 (C-5'), 104.6 (C-10), 103.8 (C-3), 94.8 (C-8), 60.4 (6- OCH_3), 56,3 (3´- OCH_3) 56,2 (4´- OCH_3).

Dimethoxycentaureidin [40]

^{1}H NMR(300 MHz, DMSO-d_6): δ 3.79 (3H, s, 6- OCH_3), 3.92 (3H, s, 4'- OCH_3), 6.65 (1H, s, H-8), 6.93 (1H, s, H-3), 6.95 (1H, d, *J*=9.0 Hz, H-5′), 7.60 (1H, d, *J*=2.0 Hz, H-2′), 7.58 (1H, dd, *J*=9.0,2.0 Hz, H-6′), 13.12 (1H, s, 5-OH), 9.99 (1H, s, 3'-OH), 10.71 (1H, s, 7-OH).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 182.6 (C-4), 164.2 (C-2), 157.7 (C-7), 153.2 (C-5), 152.8 (C-9), 151.1 (C-3′), 148.1 (C-4′),131.8 (C-6), 122.0 (C-1′), 120.8 (C-6′), 116.2 (C-5′), 110.6 (C-2′), 104.5 (C-10), 103.2 (C-3), 94.8 (C-8), 60.5 (4'-OCH_3), 56.4 (6- OCH_3).

Cirsiliol [40]

^{1}H NMR (300 MHz, DMSO-d_6): δ 3.75 (3H, s, 6- OCH_3), 3.95 (3H, s, 7- OCH_3), 6.76 (1H, s, H-3), 6.90 (1H, d, *J*=9.0 Hz, H-5′), 6.93 (1H, s, H-8), 7.46 (1H, s, H-2'), 7.49 (1H, d, *J*=9.0 Hz, H-6′), 13.09 (1H, s, 5-OH), 8.32 (1H, s, 3'-OH), 8.27 (1H, s, 4'-OH).

^{13}C NMR (75 MHz, DMSO-d_6) δ: 182.6 (C-4), 164.7 (C-2), 159.0 (C-7), 153.0 (C-5), 152.8 (C-9), 150.4 (C-4′), 146.3 (C-3′), 132.3 (C-6), 121.8 (C-1′), 119.5 (C-6′), 116.4 (C-5′), 113.9 (C-2′), 105.5 (C-10), 103.1 (C-3), 91.9 (C-8), 60.5 (7-OCH_3), 56.4 (6- OCH_3).

Luteolin [42]

^{1}H NMR (400 MHz, CD_3OD): δ 6.22 (1H, d, *J* = 2.0 Hz, H-6), 6.45 (1H, d, *J* = 2.0 Hz, H-8), 6.55 (1H, s, H-3), 6.92 (1H, d, *J* = 8.8 Hz, H-5´), 7.39 (1H, d, *J* = 2.0 Hz, H-2´), 7.40 (1H, dd, *J* = 2.0, 8.8 Hz, H-6´).

Kaempferol [42]

^{1}H NMR (400 MHz, CD_3OD): δ 6.20 (1H, d, *J* = 2.0 Hz, H-6), 6.41 (1H, d, *J* = 2.0 Hz, H-8), 6.93 (2H, d, *J* = 8.4 Hz, H-3´,5´), 8.11 (2H, d, *J* = 8.4 Hz, H-2´, 6´).

Apigenin [42]

^{1}H NMR (400 MHz, CD_3OD): δ 6.22 (1H, d, *J* = 2.0 Hz, H-6), 6.47 (1H, d, *J* = 2.0 Hz, H-8), 6.61 (1H, s, H-3), 6.95 (2H, d, *J* = 8.8 Hz, H-3´, 5´), 7.87 (2H, d, *J* = 8.8 Hz, H-2´, 6´).

Scoparone [78]

^{1}H NMR (400 MHz, CD_3OD): δ 3. 87 (3H, s, 7- OCH_3), 3.92 (3H, s, 6- OCH_3), 6.26 (H, d, *J*=9.6 Hz, H-3), 7.88 (1H, d, *J*=9.6 Hz, H-4), 7.13 (1H, s, H-5), 6.98 (1H, s, H-8).

^{13}C NMR (100 MHz, CD_3OD): δ 56.9 (2x– OCH_3), 163.8 (C-2), 110.0 (C-3), 145.9 (C-4), 113.6 (C-5),148.2 (C-6), 154.8 (C-7), 101.0 (C-8), 151.3 (C-9), 113.1 (C-10).

Isofraxidin [78]

^{1}H NMR (400 MHz, CD_3OD): δ 3.87 (3H, s, 7- OCH_3), 3.92(3H, s, 6- OCH_3), 6.26 (1H, d, *J*=9.4 Hz, H-3), 7.13 (1H, s, H-5), 7.88 (1H, d, *J*=9.4 Hz, H-4).

^{13}C NMR (100 MHz, CD_3OD): δ 56. 9 (2×– OCH_3), 101.0 (C-8), 110.0 (C-3), 113.1 (C-10), 113.6 (C-5), 145.9 (C-4), 148.2(C-6), 151.3 (C-9), 154.8 (C-7), 163.8 (C-2).

6,7-dimethoxycoumarin [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.31 (1H, d, *J* = 9.5 Hz, H-3), 7.65 (1H, d, *J* = 9.5 Hz, H-4), 6.86 (1H, s, H-5), 6.88 (1H, s, H-8), 3.94 (3H, s, 6-OCH_3), 3.97 (3H, s, 7-OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5 (C-2), 113.6 (C-3), 143.3 (C-4), 107.9 (C-5), 146.3 (C-6), 152.8 (C-7), 100.0 (C-8), 150.0 (C-9), 111.4 (C-10), 56.4 (6-OCH_3), 56.3 (7-OCH_3).

6,7,8-trimethoxycoumarin [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.06 (1H, d, *J* = 9.0 Hz, H-3), 7.52 (1H, d, *J* = 9.0 Hz, H-4), 7.30 (1H, s, H-5), 3.88 (3H, s, 6-OCH_3), 3.86 (3H, s, 8-OCH_3), 3.82 (3H, s, 7-OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4 (C-2), 115.5 (C-3), 140.3 (C-4), 114.9(C-5), 145.0 (C-6), 125.1 (C-7), 133.5 (C-8), 134.4 (C-9), 120.7 (C-10), 56.4 (6-OCH_3), 56.1 (8-OCH_3), 55.8 (7- OCH_3).

6-hydroxy-7-methoxycoumarin [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.31 (1H, d, *J* = 9.5 Hz, H-3), 7.64 (1H, d, *J* = 9.5 Hz, H-4), 6.93 (1H, s, H-5), 6.85 (1H, s, H-8), 3.91 (3H, s, 7-OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 161.6 (C-2), 113.5 (C-3), 143.5 (C-4), 108.3 (C-5), 147.3 (C-6), 152.0(C-7), 103.0 (C-8), 153.0 (C-9), 113.4 (C-10), 56.5 (7-OCH_3).

4-hydroxylacetophenone [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (2H, d, *J* = 8.5 Hz, H-2,6), 6.91 (2H, d, *J* = 8.5 Hz, H-3,5), 2.58 (3H, s, - CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 130.4 (C-1), 131.0 (C-2), 115.3 (C-3), 160.1 (C-4), 115.3 (C-5), 131.0 (C-6), 197.9 (C=O), 26.3 (-CH_3).

4-hydroxy-5-methoxylacetophenone [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (1H, d, *J* = 2.0 Hz, H-2), 6.98 (1H, d, *J* = 8.0 Hz, H-5), 7.62 (1H, d, *J* = 8.0, 2.0 Hz, H-6), 3.90 (3H, s, -OCH_3), 2.51 (3H, s, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 129.9 (C-1), 111.1 (C-2), 147.0 (C-3)146.8(C-4), 114.4 (C-5), 126.9 (C-6), 190.3 (C=O), 56.8 (-OCH_3), 26.3 (-CH_3).

4-hydroxybenzaldehyde [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (2H, d, *J* = 8.5 Hz, H-2,6), 7.02 (2H, d, *J* = 8.5 Hz, H-3,5), 9.85 (1H, s, -CHO).

^{13}C NMR (125 MHz, $CDCl_3$): δ 139.3 (C-1), 132.5 (C-2), 116.0 (C-3), 162.0 (C-4), 116.0 (C-5), 132.5 (C-6), 191.3 (-CHO).

4-hydroxy-5-methoxybenzaldehyde [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (1H, brs, H-2), 7.05 (1H, d, *J* = 8.5 Hz, H-5), 7.45 (1H, brd, *J* = 8.5 Hz, H-6), 9.83 (1H, s, -CHO), 3.99 (3H, s, -OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ 129.9 (C-1), 108.8 (C-2), 151.7 (C-3), 147.2 (C-4), 114.4 (C-5), 127.6 (C-6), 191.0 (C=O), 56.1 (-OCH_3).

4,5-dihydroxybenzaldehyde [75]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (1H, d, *J* = 2.0 Hz, H-2), 6.96 (1H, d, *J* = 8.0 Hz, H-5), 7.46 (1H, brd, *J* = 8.0, 2.0 Hz, H-6), 9.85 (1H, s, -CHO).

^{13}C NMR (125 MHz, $CDCl_3$): δ 129.8 (C-1), 108.9 (C-2), 146.8 (C-3), 146.2 (C-4), 114.3 (C-5), 127.7 (C-6), 191.0 (C=O).

Rupestine A [57]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92 (d, *J* =8.0 Hz, H-3), 7.31 (d, *J*=8.0 Hz, H-4), 3.04 (m, H-5), 1.76 – 1.84 (m, Ha-6, Hb-6), 1.76 – 1.84 (m, Ha-7, Hb-7), 2.75 – 2.85 (m, H-8), 3.15 (d, *J*= 13.6 Hz, Ha-9), 3.29 (dd, *J*= 14.4,10 Hz, Hb-9), 5.58 (s, Ha-14), 6.18 (s, Hb-14), 2.50 (s, CH_3-15), 1.30 (d, *J*=7.2 Hz, CH_3-16), 4.21 (q, *J*=7.2 Hz, CH_2-1'), 1.31 (t, *J*= 7.2 Hz, CH_3-2').

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.63 (C-2), 121.04 (C-3), 136.79 (C-4), 37.94 (C-5), 33.03 (C-6), 31.68 (C-7), 38.10 (C-8), 43.78 (C-9), 158.61 (C-10), 137.61 (C-11), 146.45 (C-12), 167.04 (C-13), 122.86 (C-14), 23.86 (C-15), 18.33 (C-16), 60.66 (C-1'), 14.22 (C-2').

Rupestine B [57]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J*=8 Hz, H-3), 7.38 (d, *J*= 8 Hz, H-4), 2.99 – 3.04 (m, H-5), 1.22 – 1.27 (m, H_a-6), 1.82 – 1.94 (m, H_b-6), 1.82 – 1.94 (m, H_a-7), 1.98 – 2.08 (m, H_b-7), 2.47 – 2.60 (m, H-8), 3.09 (d, *J*=14 Hz, H_a-9), 3.24 (dd, *J*=14, 10.8 Hz, H_b-9), 2.52 (q, *J*= 7.2 Hz, CH_2-13), 1.04 (t, *J*=7.2 Hz, H_a-14), 2.51 (s, CH_3-15), 1.31 (d, *J*=7.6 Hz, CH_3-16).

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.39 (C-2), 121.17 (C-3), 132.48 (C-4), 34.79 (C-5), 35.08 (C-6), 33.22 (C-7), 48.60 (C-8), 39.73 (C-9), 159.36 (C-10), 137.90 (C-11), 213.71 (C-12), 34.38 (C-13), 7.83 (C-14), 23.79 (C-15), 20.38 (C-16).

Rupestine C [57]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (d, *J*=7.6 Hz, H-3), 7.33 (d, *J*=7.6 Hz, H-4), 2.95 – 3.04 (m, H-5), 1.72 – 1.88 (m, H_a-6), 1.72 – 1.88 (m, H_a-7), 2.00 – 2.10 (m, H_b-7), 2.67 – 2.75 (m, H-8), 3.16 – 3.24 (m, H_a-9), 3.31 – 3.41 (m, H_b-9), 2.60 (q, *J*=7.2 Hz, CH_2-13), 1.02 (q, *J*=7.2 Hz, H_a-14), 2.50 (s, CH_3-15), 1.31 (d, *J*=7.6 Hz, CH_3-16).

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.63 (C-2), 121.42 (C-3), 136.59 (C-4), 37.65 (C-5), 32.11 (C-6), 28.40 (C-7), 48.50 (C-8), 39.57 (C-9), 157.63 (C-10), 138.14 (C-11), 213.38 (C-12), 34.29 (C-13), 7.76 (C-14), 23.56 (C-15), 18.85 (C-16).

Rupestine D [57]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, *J*=8.0 Hz, H-3), 7.40 (d, *J*= 8.0 Hz, H-4), 2.94 - 3.04 (m, H-5), 1.23 - 1.30 (m, H_a-6), 1.82 - 1.94 (m, H_b-6), 1.82 - 1.94 (m, H_a-7), 2.04 – 2.11 (m, H_b-7), 2.54 - 2.60 (m, H-8), 3.13 - 3.28 (m, H_a-9), 2.23 (s, CH_2-13), 2.51 (s, H_a-14), 1.35 (d, *J*= 7.2 Hz, CH_3-15).

^{13}C NMR (100 MHz, $CDCl_3$): δ 154.36 (C-2), 121.24 (C-3), 132.60 (C-4), 34.76 (C-5), 34.96 (C-6), 32.92 (C-7), 49.47 (C-8), 39.43 (C-9), 159.05 (C-10), 137.90 (C-11), 211.07 (C-12), 28.49 (C-13), 23.71 (C-14), 20.32 (C-15).

Caruilignan C [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.51 (s, 2H, H-2,6), 4.95 (d, 1H, *J*=6.0 Hz, H-7), 4.53 (d, 1H, *J*= 9.5 Hz, Hβ-9), 4.10 (dd, 1H, J_1=8.0 Hz, J_2=9.5 Hz, H β-9′), 3.98 (dd, 1H, J_1= 6.5 Hz, J_2 =9.5 Hz, Hα-9), 3.88 (s, 6H, 3,5-OCH_3), 3.85 (s, 3H, 4-OCH_3), 3.83 (dd, 1H, overlapped, Hα-9′), 3.39 (m, 1H, H-8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 178.6 (C-7′), 153.5 (C-3,5), 137.4 (C-4), 132.1 (C-1), 102.7 (C-2,6), 84.2 (C-7), 70.9 (C-9), 68.4 (C-9′), 60.9 (4-OCH_3), 56.2 (3,5-OCH_3), 45.9 (C-8), 43.5 (C-8′).

7β-Caruilignan C [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.57 (s, 2H, H-2,6), 4.62 (d, 1H, *J*=7.0 Hz, H-7), 4.52 (dd, 1H, J_1=6.5 Hz, J_2=9.5 Hz, Hβ-9), 4.40 (t, 1H, *J*= 9.0 Hz, Hβ-9′), 4.37 (dd, 1H, J_1=2.0 Hz, J_2=9.8 Hz, Hα-9), 4.22 (dd, 1H, J_1=4.0 Hz, J_2=9.0 Hz, Hα-9′), 3.88 (s, 6H, 3′,5′-OCH_3), 3.85 (s, 3H, 4′-OCH_3), 3.46 (dt, 1H, J_1=4.0 Hz, J_2=9.0 Hz, $J_3$9.0 Hz, H-8′), 3.14 (m, 1H, H-8).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 178.0 (C-7′), 153.6 (C-3,5), 138.0 (C-4), 134.5 (C-1), 102,8 (C-2,6), 86.2 (C-7), 70.2 (C-9′), 69.8 (C-9), 60.8 (4-OCH_3), 56.2 (3,5-OCH_3), 48.5 (C-8), 46.0 (C-8′).

Yangambin [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.58 (s, 4H, H-2,6,2′,6′), 4.76 (d, 2H, *J* =4.0 Hz, H-7,7′), 4.32 (dd, 2H, J_1=7.0 Hz, J_2=9.0 Hz, Hα-9,9′), 3.94 (dd, 2H, J_1=3.0 Hz, J_2=9.0 Hz, Hβ-9,9′), 3.88 (s, 12H, 3,3′,5,5′-OCH_3), 3.85 (s, 6H, 4,4′-OCH_3), 3.11 (m, 2H, H-8,8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.4 (C-3,5,3′,5′), 136.7 (C-1,1′), 137.5 (C-4,4′), 102.8 (C-2,6,2′,6′), 85.9 (C-7,7′), 72.0 (C-9,9′,60.8 (4,4′-OCH_3), 56.2 (3,5,3′,5′-OCH_3), 54.3 (C-8,8′).

Diayangambin [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.61 (s, 4H, H-2,6,2′,6′), 4.92 (d, 2H, *J*=4.5 Hz, H-7,7′), 3.89 (s, 12H,3,5,3′,5′-OMe), 3.86 (s,6H, 4,4′-OMe), 3.75 (dd, 2H, J_1=1.5 Hz, J_2=9.5 Hz, Hα-9,9′), 3.60 (dd, 2H, J_1=7 Hz, J_2=10 Hz, Hβ-9,9′), 3.21 (m, 2H, H-8,8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.2 (C-3,5,3′,5′), 137.1 (C-1,1′), 134.6 (C-4,4′), 103.2 (C-2,6,2′,6′), 84.1 (C-7,7′), 68.9 (C-9,9′), 60.9 (4,4′-OMe), 56.1 (3,5,3′,5′-OMe), 49.4 (C-8,8′).

Epiyangambin [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.60 (s, 2H, H-2,6), 6.59 (s, 2H, H-2′,6′), 4.87 (d, 1H, *J* = 5.5 Hz, H-7), 4.45 (d, 1H, *J* =7.0 Hz, H-7′), 4.17 (d, 1H, *J* =9.5 Hz, Hβ-9′), 3.91 (m, 2H, Hα-9,9′), 3.89-3.85 (m, 18H, 3,4,5,3′,4′,5′-OMe), 3.37 (m, 1H, H-8), 3.36 (m, 1H, Hβ-9), 2.93 (m, 1H, H-8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.4 (C-3′,5′), 153.2 (C-3,5), 137.6 (C-4′), 137.0 (C-4), 136.8 (C-1′), 134.0 (C-1), 103.0 (C-2′,6′), 102.6 (C-2,6), 87.8 (C-7′), 82.2 (C-7), 71.1 (C-9′), 69.8 (C-9), 60.9 (4′-OMe), 60.8 (4-OMe), 56.2 (3,5,3′,5′-OMe), 54.5 (C-8′), 50.0 (C-8).

Sesartemin [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.57 (s, 2H, H-2,6), 6.55 (d, 1H, *J*=1.5 Hz, H-6′), 6.53 (d, 1H, *J*=1.5 Hz, H-2′), 5.95 (s, 2H, OCH_2O), 4.72 (d, 2H, *J*=4.5 Hz, H-7,7′), 4.29 (dd, 1H, J_1=6.7 Hz, J_2=9.2 Hz, Hα-9), 4.26 (dd, 1H, J_1=6.7 Hz, J_2=9.2 Hz, Hα-9′), 3.92 (dd, 1H, J_1=3.6 Hz, J_2=9.2 Hz, Hβ-9), 3.91 (s, 3H,5′-OMe), 3.90 (dd, 1H, J_1=3.6 Hz, J_2=9.2 Hz, Hβ-9′), 3.87 (s, 6H, 3,5-OMe), 3.83 (s, 3H, 4-OMe), 3.07 (m, 2H, H-8,8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.4 (C-3,5), 149.1 (C-3′), 143.4 (C-5′), 137.4 (C-4), 136.7 (C-1), 135.7 (C-1′), 134.6 (C-4′), 105.5 (C-6′), 102.8 (C-2,6), 101.4 (OCH_2O), 100.0 (C-2′), 85.9 (C-7′), 85.7 (C-7), 71.9 (C-9), 71.7 (C-9′), 60.8 (4-OMe), 56.6 (5′-OMe), 56.1 (3,5-OMe), 54.3 (C-8,8′).

(+) Arborone [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.43 (s, 2H, H-2,6), 6.55 (s, 2H, H-2′,6′), 5.03 (d, 1H, *J*=6.0 Hz, H-7′), 4.44 (t, 1H, *J*=8.0 Hz, Hβ-9), 4.33 (d, 1H, J_1=2.8 Hz, J_2=5.6 Hz, J_3=8.0 Hz, H-8), 4.26 (d, 1H, J_1=2.8 Hz, J_2=8.0 Hz, Hα-9), 3.94 (s, 3H, 4-OMe), 3.93 (s, 6H, 3,5-OMe), 3.87 (s, 6H, 3′,5′-OMe), 3.84 (s, 3H, 4′-OMe), 3.44 (d, 2H, *J*=6.8 Hz, H-9′), 2.91 (m, 1H, H-8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 198.5 (C-7), 153.4 (C-3,5), 153.2 (C-3′,5′), 143.0 (C-4), 137.1 (C-4′), 133.6 (C-1′), 131.3 (C-1), 106.4 (C-2,6), 102.5 (C-2′,6′), 81.6 (C-7′), 69.1 (C -9), 62.0 (C-9′), 61.0 (4-OMe), 60.9 (4′-OMe), 56.4 (3,5-OMe), 56.2 (3′,5′-OMe), 49.6 (C-8′), 48.8 (C-8).

Syringaresinol [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.59 (s, 4H, H-2,6,2′,6′), 5.52 (brs, 2H, 4,4′-OH), 4.74 (d, 2H, *J*=4.0 Hz, H-7,7′), 4.29 (dd, 2H, J_1=6.5 Hz, J_2=8.5 Hz, Hβ-9,9′), 3.92 (dd, 2H, J_1=2.9 Hz, J_2=8.5 Hz, Hα-9,9′), 3.90 (s, 12H, 3,5,3′,5′-OMe), 3.10 (m, 2H, H-8,8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 147.1 (C-3,5,3′,5′), 134.3 (C-4,4′), 132.1 (C-1,1′), 102.7 (C-2,6,2′,6′), 86.0 (C-7,7′), 71.8 (C-9,9′), 56.4 (3,5,3′,5′-OMe), 54.3 (C-8,8′).

Epiashchantin [85]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.78-6.88 (m, 3H, H-2′,5′,6′), 6.59 (s, 2H, H-2,6), 5.96 (s, 2H, OCH_2O), 4.86 (d, 1H, *J*=5.5 Hz, H-7), 4.44 (d, 1H, *J*=7.0 Hz, H-7′), 4.13 (dd, 1H, J_1=1.4 Hz, J_2=9.5 Hz, Hβ-9′), 3.89 (s, 6H, 3,5-OMe), 3.86 (s, 3H, 4-OMe), 3.85 (m, 2H, Hα-9,9′), 3.36 (m, 1H, H-8), 3.34 (m, 1H, Hβ-9), 2.89 (m, 1H, H-8′).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 153.2 (C-3,5), 148.0 (C-3′), 147.2 (C-4′), 136.9 (C-4), 135.1 (C-1′), 134.0 (C-1), 119.5 (C-6′), 108.2 (C-5′), 106.5 (C-2′), 102.6 (C-2,6), 101.0 (OCH2O), 87.6 (C-7′), 82.2 (C-7), 71.0 (C-9′), 69.7 (C-9), 60.9 (4-OMe), 56.2 (3,5-OMe), 54.5 (C-8′), 50.1 (C-8).

PHARMACOLOGICAL ACTIVITY

Antioxidant activity

The antioxidant properties of plant extracts are primarily due to their phenolic compounds/flavonoids. An antioxidant activity of A. Vulgaris has been studied in vitro by free radical scavenging activity. The radical scavenging activity of methanolic extract of *A. vulgaris* (MEAV) leaves was determined by Calorimetric assay using 2,2-diphenyl-1-picrylhydrazyl (DPPH) according to the method of Blois with a slight modification. This study found that the percentage inhibition of MEAV extract was 68.06% at 60 µg/ml concentrations comparable to that of ascorbic acid (93.53%). The results showed a concentration dependent DPPH radical scavenging property, that estimated that the inhibition percentage was also increase with increase in concentration of MEAV, it showed that methanolic extract of *A. vulgaris* (MEAV) leaves has a potential antioxidant activity. In order to confirm the antioxidant activities, the plant extract was further analyzed by reducing power assay. where it was found that the ferric reducing power of MEAV was 0.95 ± 0.05 at100 µg/ml concentration comparable to ascorbic acid (1.04 ± 0.05). It showed that the tested extract has ability to transform the ferric ion (Fe3+) to ferrous ion (Fe2+) as reducing power with the increase of concentration of the extract [94]. Another study investigated the methanolic extract of *A. absinthium* aerial part at flowering stage and reported to have DPPH radical-scavenging activity [95].

The methanolic extracts of eight *Artemesia sp.* were investigated to evaluate potential antioxidant activity. This investigation reported that the extract of *A. keiskeana, A. selengensis, A.capillaries, A.japonica, A scoparia, A stolonifera, A.montana, A.sylvatica* showed Potent antioxidant activity in DPPH/ ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical quenching activity [96].

Anticancer activity

Hye-Yeon Han and his colleagues were investigated the anticancer properties of a flavonoid compound jaceosidin from *A. princeps* using MTT assay. Their investigation has reported that jaceosidin selectively inhibits OSCC (oral squamous cell carcinoma) cell proliferation by inducing caspase-dependent apoptosis and inhibiting the Akt pathway by blocking Akt phosphorylation in OSCC cells. The study also demonstrates that jaceosidin does not show any effect on normal epithelial keratinocyte cells [52].

Methanolic extract from *A. capillaris, A. sylvatica* and *A. selengensis* also has been reported to shows anticancer activity [97-100]. Artemisinin, the active ingredient of *A. annua*, showed cell toxicity against human lymphoid leukemia (Molt-4) cells [101]. An in vitro study of ethanol extract of *A. kulbadica, A. diffusa, A. sieberi, A. santolina* and *A. turanica* against HepG-2 and Hep-2 cell lines were investigated. Results shown a concentration-dependent toxicity for all the extracts and the overall toxicity on HepG-2 cells are more than that on Hep-2 cells [102].

Anticoagulant activity

β-sitosterol and a known compound 2-(3,4-dimethoxyphenyl)-6-methoxy-4-oxo-4H-chromene-5,7-dicarboxylic acid was isolated from *A. argyi* for the first time in 1992, and both were shown to inhibit platelet aggregation [103]. In vitro anticoagulation activities of two newly purified flavonoids, eupatilin 7-O-β-D-glucopyranoside and 5,6,2′,4′-tetrahydroxy-7,5′-dimethoxyflavone, were recently investigated [104]. Both compounds retarded blood clotting by extending thrombin time (TT) and prothrombin time (PT), according to the findings. The anticoagulant property of *A. argyi* essential oil (AAEO) was confirmed in vivo by using an ice water bath to create an acute blood stasis rat model. AAEO decreased the blood viscosity of low, medium, and high shear rates at a skin administration dosage of 0.125–0.50 mL/kg. Additionally, this behavior has been linked to the ability to reduce erythrocyte aggregation [105].

Anti-inflammatory activity

A study was carried out to investigate the anti-inflammatory activity of three eudesmanolides compound from *Artemisia burrelieri*. This study has tested the anti-inflammatory effect of three eudesmanolides, barrelierin, artemalin and barrelin, isolated from aerial parts of *A. burrelieri* by studying their influence on carrageenan-induced rat paw oedema. According to the findings the percentage inhibition of barrelin was 33% at 15 mg/kg, more than 50% at 30mg/kg, and about 80% at 90 mg/kg. On the other hand, compound barrelierin and artemalin showed similar activity, but appears to be less potent, since with the lowest and highest doses the reduction of the inflammation was about 15% and 40%, respectively. This demonstrates that the compounds were reduced the inflammation in a dose-dependent manner [17]. Inhibition of nitrite synthesis in lipopolysaccharide (LPS)-stimulated macrophage cultures were investigated to assess the extracts' anti-inflammatory activity. In the presence of LPS, methanolic extracts of *A. stolonifera, A. selengensis, A. capillaris, and A. keiskeana* were found to reduce nitric oxide production at higher concentrations than control cells [97]. Methanolic leaf extract of *A. vulgaris* were also assessed to evaluate anti-inflammatory activity in wister albino rats by cotton pellet granuloma method. The result revealed that *A. vulgaris* extract possess a significant anti-inflammatory activity [106].

Antimalarial Activity

The aqueous, cold alcoholic and hot alcoholic extract of *Artemisia absinthium* was conducted to tested their antimalarial activity in vitro. The result of in vitro assay showed 35%, 55% and 21% inhibition in growth of *Plasmodium falciparum*, respectively at 2.00 mg/ml [107]. Another in vivo study was undertaken to investigate the antimalarial activity of ethanolic leaf extract from *A. vulgaris* against the *P. berghei murine* malaria model in

terms of antiparasitic activity. The assay revealed that the leaf extract possesses potent antimalarial action [108]. The various organic (n-hexane, chloroform, petroleum ether, ethanol, methanol and aqueous) leaf extracts of *A. nilagirica* were assayed for antimalarial activity against *P. falciparum* FCR-3 strain. It was observed that, all tested leaf extracts showed a significant IC50 value [109]. The dichloromethane extract of *A. armeniaca, A. aucheri and A. ciniforms* was also investigated and reported to has antimalarial activity [109-114]. Another study revealed that by potentiating artemisinin activity the hydro alcoholic and aqueous extracts of *A. annua* L. showed antimalarial activity on *plasmodium* [115].

Antifungal and Antibacterial activity

The antibacterial and antifungal activity of ethanolic extracts of *A. abrotanum* and *A. pallens* against both gram positive and gram-negative bacteria was tested using the cup plate method. These extracts showed maximum zone of inhibition against *Pseudomonas cepacia* (28.6mm) and *Bacillus stearothermophilus* (27.6mm) respectively. The antifungal activity of both plant extracts was maximum against *Trichosporon beigelii* (17mm). These findings indicate that *A. abrotanum* and *A. pallens* ethanolic extracts have antibacterial and antifungal properties [116]. The antifungal and antibacterial activities of essential oils isolated from *A. absinthium, A. dracunculus, A. santonicum, and A. spicigera* (20 L/Petri dish) were tested against phytopathogenic fungal species and bacterial strains. This extract exhibited significant antifungal activity and antibacterial activity against microbial growth [117]. Three Gram positive bacteria, *Staphylococcus aureus, Enterococcus faecalis, Bacillus cereus*, and three Gram negative bacteria, *Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Escherichia coli*, were tested to evaluate the antibacterial activity of ethanol extract of *A. nilagirica*. In terms of zone of inhibition, the results revealed that the extract has good antibacterial activity [118]. An antibacterial analysis of methanolic extract of *A. campestris* was performed, and the extract was found to have antibacterial properties [119,120]. The antibacterial properties of water extracts of *A. annua* have been studied, and the results indicate that the water extracts have stronger antibacterial properties [121].

Antitumor Activity

The methanolic extracts of the aerial parts of *A. argyi* were investigated for antitumor activity. The study showed that the compound 5,6,4'-trihydroxy-7,3'-dimethoxyflavone isolated from extract inhibit proliferation of a couple of tumor cell lines [122]. Flavonoids of *A. absinthium, A. sieversiana* and *A. xanthochroa* were assessed for antitumor activity in mice with melanoma 16, they possessed a slight inhibitory effect on Pliss lymphosarcoma in rats [123]. Ethyl acetate extract of *A. indica* also have been reported to showed antitumor activity [124].

Antiviral Activity

Hot water extract of *A. capillaris* were investigated and reported to possess antiviral activity against enterovirus 71(EV71) [98]. Artemisinin used in the treatment of malaria have been reported to have broad spectrum of potential antiviral effect. Artemisinin from *A. annua* give antiviral effect against Bovine Viral Diarrhoea Virus (BVDV) [18]. Other's artemisinin derivatives such as arteannuin B is a structural derivative of artemisinin that reported to showed an anti-SARS-CoV-2 effect in vitro [125]. An In vitro study of antiviral activity of subset extracts from *A. incana, A. chamaemelifolia, A. campesteris, A. fragrans, A. annua, A. vulgaris, and A. persica* was investigated against Herpes Simplex virus type 1 (HSV1). Results showed that the extracts of aerial parts of *A. annua* had the highest anti-herpetic activity while those of *A. chamaemelifolia* showed the lowest activity [126].

Antidiabetic Activity

Antidiabetic study was carried out on the water and alcoholic extracts of *A. judaica* in diabetic rats. The result showed that oral administration of all doses of the aqueous and ethanolic extracts produced significant decrease in blood glucose level when compared to the control diabetic group [125]. Oral administration of an aqueous extract (0.39 g/kg) of the aerial parts of *A. herba alba* to normoglycemic and to alloxandiabetic rabbits was investigated and found to have significant hypoglycemic activity, which was consistent and time-dependent [126].

Another study used an aqueous extract of the aerial parts of the *A. herba alba* plant on diabetic rats and rabbits weighing 0.39 g/kg body weight. In this research these extracts also demonstrated a substantial reduction in blood glucose levels [127]. The anti-diabetic properties of petroleum ether, ethyl acetate, methanol, and hydroethanolic extracts of *A. amygdalina* were investigated in diabetic rats. The result confirms that the extract was significantly reduced glucose levels in diabetic rats [128]. According to a study, the methanolic leaf extract of *A. absinthium* showed possible antidiabetic activity against hyperglycemia and hypoinsulinemia in experimental Streptozotocin (STZ) induced diabetic rats [129].

Antiulcerogenic activity

The compounds artemisinin, dihydro-epideoxyarteannuin B and deoxyartemisinin obtained from ethanolic extract of *A. annua* were tested on ethanol and indomethacin induced ulcer models. The result indicated that the extract showed an inhibitory effect on the ulcerative lesion index in all experimental models tested, in rats [16]. Another study was undertaken to investigate the protective effect of *A. campestris* aqueous extract on aspirin-induced gastric ulceration. The result showed that the extract possesses potent antiulcer activity [130-132].

CONCLUSION

The genus *Artemisia* (Asteraceae) is a rich source of bioactive secondary metabolites. Species of this genus possess potential sources of pharmacological activity. Phytochemical investigation on *Artemisia* species revealed that the genus contains various classes of secondary metabolites with promising pharmacological activity. Terpenoids, flavonoids, coumarins, alkaloids, lignans caffeoylquinic acids and sterols constitute are major classes of phytoconstituents of the genus. The present review emphasizes the phytochemical constituents, pharmacological activities and NMR of structurally diverse phytochemicals. This review concluded that the presence of structurally diverse bioactive phytochemical constituents may attract the researchers for further research in new drug lead secondary metabolites from the genus. The included NMR of different phytochemical compound obtained from *Artemisia* species may help the researcher to elucidate structures.

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