TERPENOIDS FROM *ARTEMISIA* SPECIES AND THEIR ACTIVITIES

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Annotation: At present, the demand for natural compounds and medicinal products derived from them is steadily increasing. Species belonging to the genus *Artemisia* are recognized as rich sources of secondary metabolites, particularly terpenoid compounds, which exhibit a wide range of pronounced biological activities. In this context, the present article provides a comprehensive analysis of terpenoid compounds identified in *Artemisia* species, with emphasis on their chemical composition and associated biological activities.

Key words: *Artemisia* genus, sesquiterpene, monoterpene, antimicrobial, antifungal, antibacterial.

ARTEMISIA OILASIGA MANSUB O‘SIMLIKLARNING TERPENOID BIRIKMALARI VA ULARNING AKTIVLIKLARI

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Annotatsiya: Hozirgi kunda tabiiy birikmalar va ular asosida olingan dori vositalariga bo‘lgan talab ortib bormoqda. *Artemisa* oilasiga mansub o‘simliklar o‘zida ko‘plab ikkilamchi metabolitlarini saqlaydigan o‘simliklar hisoblanib, ayniqsa ulardan ajratib olingan terpenoidlar o‘zlarining yuqori biologik faolliklari bilan ajralib turadi. Shuni hisobga olgan holda ushbu maqolada *Artemisia*

turkumiga mansub o‘simliklarning terpenoid birikmalari, ularning kimyoviy tarkibi hamda biologik faolliklari tahlil qilindi.

Kalit so’zlar: *Artemisia, seskviterpen, monoterpene, mikroblarga qarshi, zamburug‘larga qarshi, antibakterial.*

ТЕРПЕНОИДЫ ВИДОВ РОДА *ARTEMISIA* И ИХ АКТИВНОСТЬ

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Аннотация. В настоящее время спрос на природные соединения и лекарственные препараты, полученные на их основе, неуклонно возрастает. Виды, относящиеся к роду *Artemisia*, признаны богатыми источниками вторичных метаболитов, в частности терпеновых соединений, которые проявляют широкий спектр выраженной биологической активности. В данном контексте в настоящей статье представлен комплексный анализ терпеновых соединений, идентифицированных у видов рода *Artemisia*, с акцентом на их химический состав и соответствующие биологические активности.

Ключевые слова: род *Artemisia*, сесквитерпены, монотерпены, антимикробная активность, противогрибковая активность, антибактериальная активность.

Sesquiterpenes are recognized as key and often defining constituents within the *Artemisia* genus. These compounds represent a large class of natural products, with over 5000 individual molecules having been characterized to date [1]. Sesquiterpene lactones are fifteen carbon compounds formed from condensation of three isoprene units, followed by cyclization and oxidative transformation to make

a *cis* or *trans*-fused lactone. The *γ*-lactone ring, usually with an a-methylene group, is a significant characteristic of sesquiterpene lactones. Their molecule may present hydroxyls, esterified hydroxyls, or epoxide groups, some sesquiterpene lactones occur in glycosylated form, and few contain halogen or sulfur atoms [2]. Sesquiterpene lactones are characterized as bitter, colorless compounds exhibiting lipophilic properties and a diverse array of structural arrangements. Classification is based on their carboxylic skeleton, leading to the identification of the following primary groups: germacranolides (10-membered rings), the largest group and biogenetic precursors of the majority of sesquiterpene lactones; eudesmanolides and eremophilanolides (6/6-bicyclic compounds); and guaianolides, pseudoguaianolides, and hypocretenolides (all 5/7-bicyclic compounds) [3].

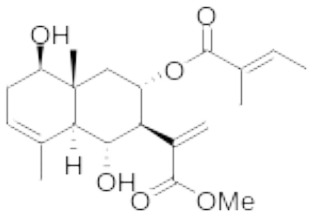
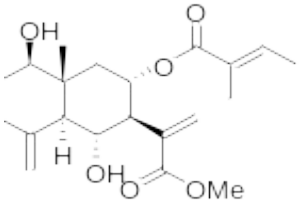
Sesquiterpenes are causing considerable attention thanks to their diverse range of biological activities, including, antitumor, antimicrobial, anti-inflammatory, antioxidant, antidiabetic, anti-vitiligo, cytotoxic and neuroprotective [18,23]. While terpenoids show beneficial properties, they can also elicit adverse effects, including respiratory distress, central nervous system disturbances, emesis, and nausea. Terpenoid ingestion disproportionately affects children, often resulting in gastrointestinal distress [4].

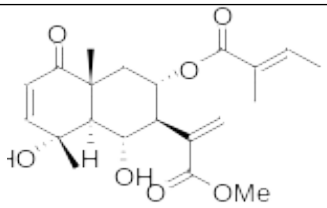
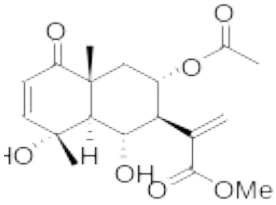
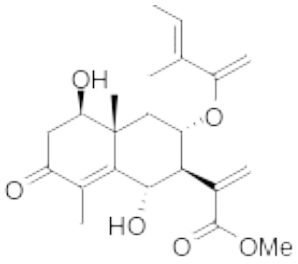
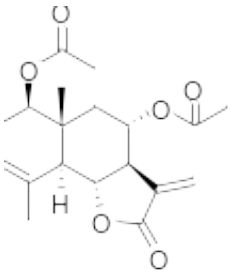
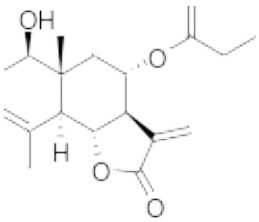
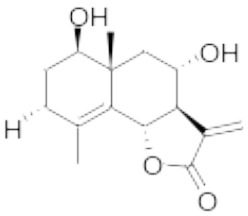
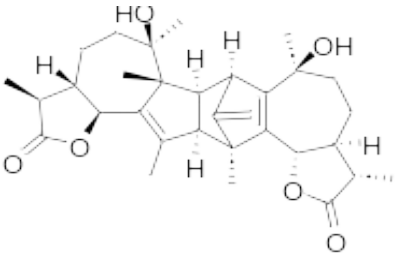
The biological activity of sesquiterpene lactones is mainly attributed to the a-methylene-*γ*-lactone group (aMyL) in their structure. The aMyL acts as a Michael acceptor and reacts with nucleophiles (sulfhydryl or amino groups) in enzymes, transcription factors, and other proteins, alkylating them irreversibly. The alkylation will disrupt the proper function of the biological macromolecule due to steric and chemical changes. This is considered to be the primary mechanism of action of sesquiterpene lactones that underlies their cytotoxicity. It also explains cell wall damage in microbes and prevalence of contact dermatitis in humans. Yet, other factors can influence the potency of sesquiterpene lactones: number of alkylating groups, lipophilicity, molecular geometry and size, chemical environment, other functional groups neighboring the aMyL, and the target sulfhydryl [3-5].

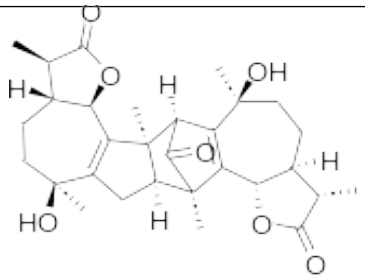
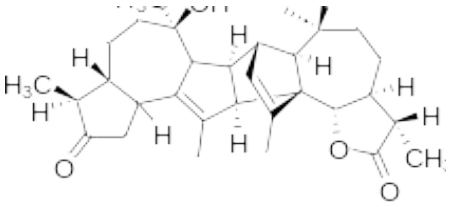
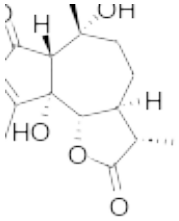
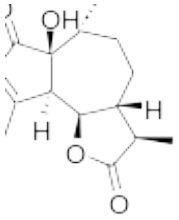
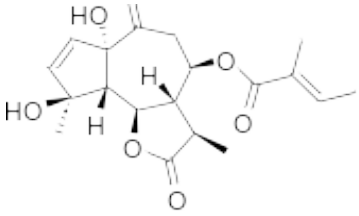
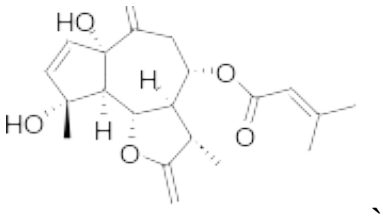
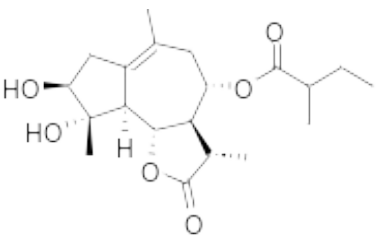
An analysis of the article presented by Amin Rezaei Do, Seyed Ahmad Emami, and Maryam Akaberi reveals that it provides data on 914 sesquiterpenes, primarily of the eudesmane, guaiane, germacrene, and cadinane subtypes, isolated from 53 *Artemisia* species between 2015 and December 2023 [6]. Based on this information, 94 previously undescribed terpenoids, isolated from 8 *Artemisia* species in 2024-April 2025, are presented below (Table 1-1).

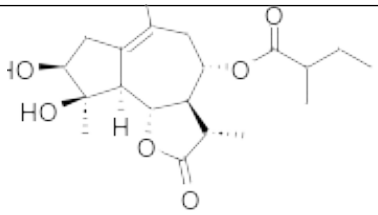
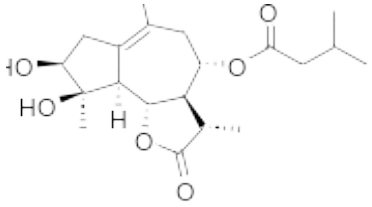
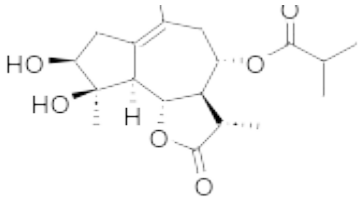
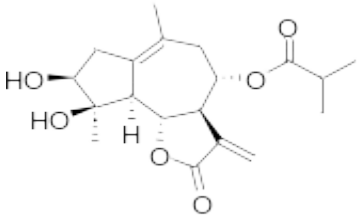
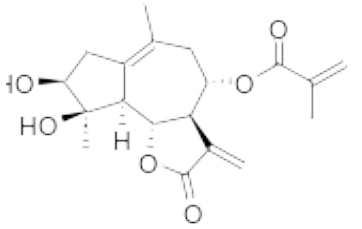
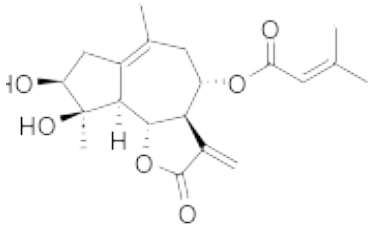
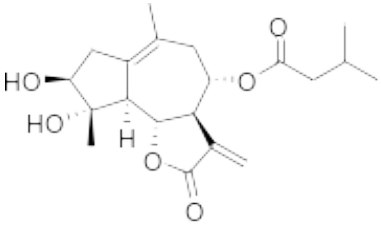
Monoterpene. Monoterpenes and monoterpenoids constitute a diverse class of organic compounds characterized by the presence of two isoprene units. Monoterpenes consist exclusively of carbon and hydrogen atoms with a molecular formula $C_{10}H_{16}$. In contrast, monoterpenoids are modified monoterpenes incorporating diverse functional groups, including alcohols, carboxylic acids, ketones, aldehydes, and phenols; thus, monoterpenoids represent a subclass of monoterpenes. Monoterpenes are prevalent natural products within the plant kingdom, significantly contributing to the distinctive organoleptic properties characteristic of various herbs, spices, citrus fruits, conifers, flowers, and fruits. These compounds perform diverse ecological roles, including broad-spectrum antimicrobial activity, allelopathic effects, herbivore deterrence (both direct and indirect), and pollinator attraction [7-9].

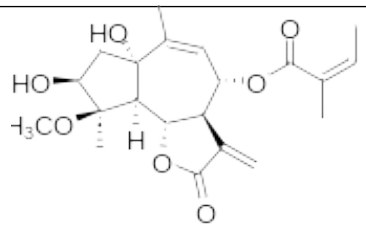
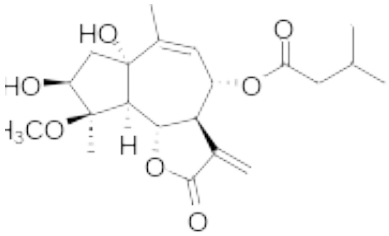
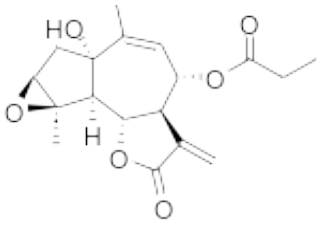
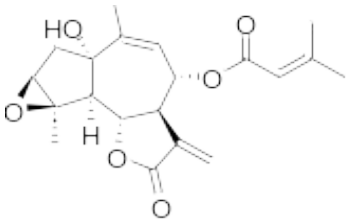
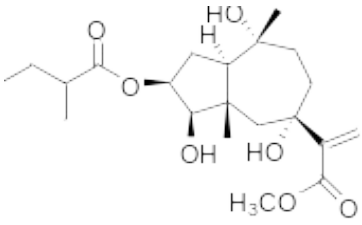
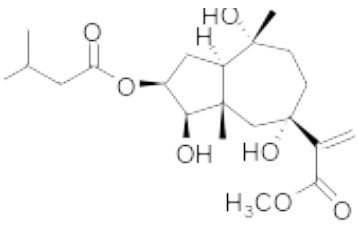
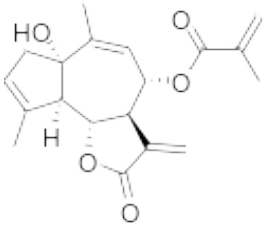
Table 1-1 Main terpenoid compounds from *Artemisa* species

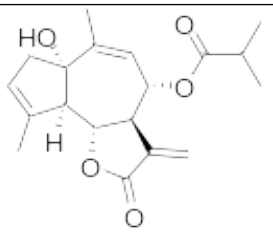
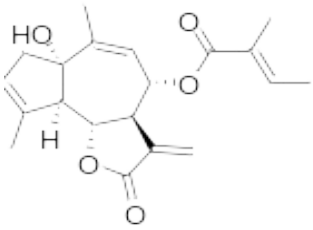
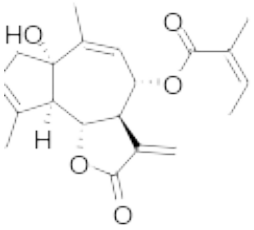
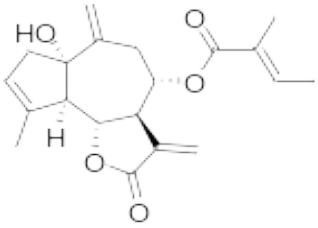
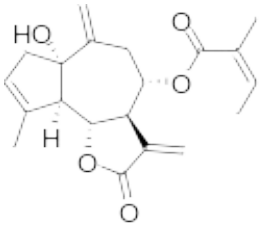
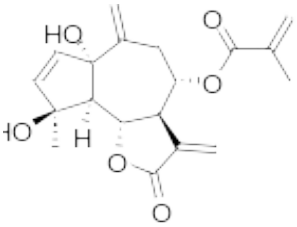
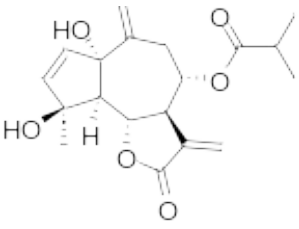
№	Compounds name	Structure	Source	Ref.
1.	Artemiprinin A		*A. princeps*	[10]
2.	Artemiprinin B		*A. princeps*	[10]

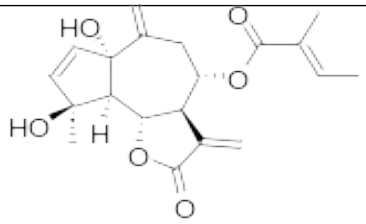
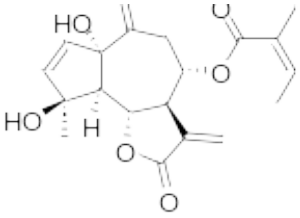
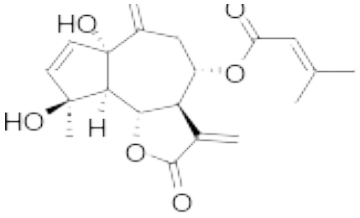
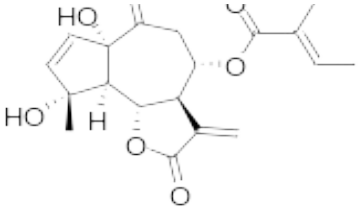
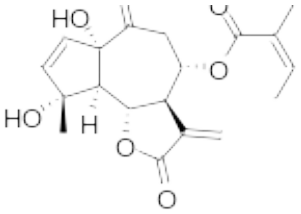
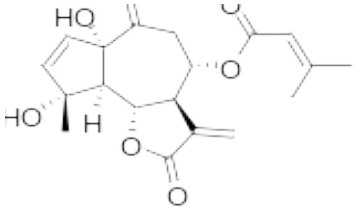
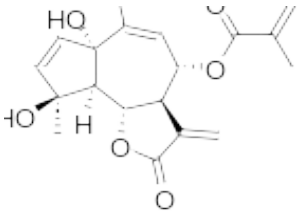
№	Compounds name	Structure	Source	Ref.
3.	Artemiprinin C (3)		*A. princeps*	[10]
4.	Artemiprinin D (4)		*A. princeps*	[10]
5.	Artemiprinin E (5)		*A. princeps*	[10]
6.	Artemiprinin F (6)		*A. princeps*	[10]
7.	Artemiprinin G (7)		*A. princeps*	[10]
8.	Artemiprinin H (8)		*A. princeps*	[10]
9.	Artemongolide G		*A. mongolica*	[11]

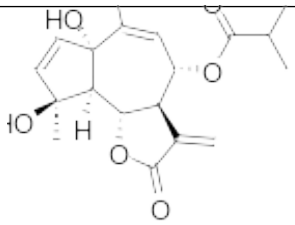
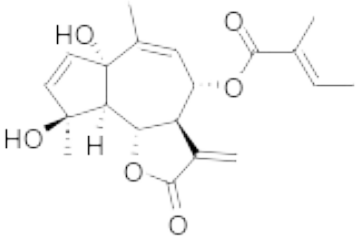
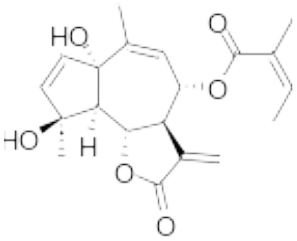
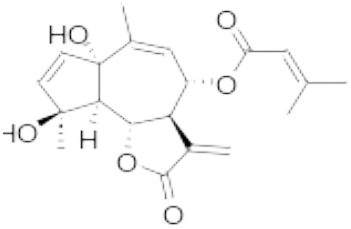
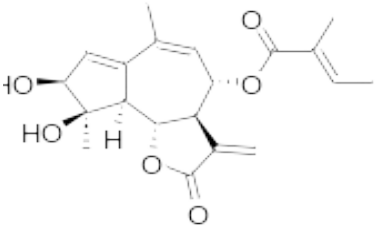
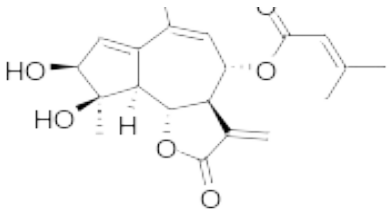
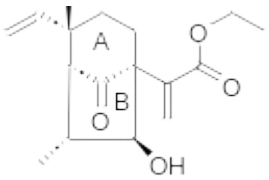
№	Compounds name	Structure	Source	Ref.
10.	Artemongolide H		*A. mongolica*	[11]
11.	Artemongolide I		*A. mongolica*	[11]
12.	Artemanomalide D		*A. mongolica*	[11]
13.	Artemanomalide E		*A. mongolica*	[11]
14.	Artemanomalide F		*A. mongolica*	[11]
15.	Artemanomalide G		*A. mongolica*	[11]
16.	Artemisol A		*A. argyi*	[11]

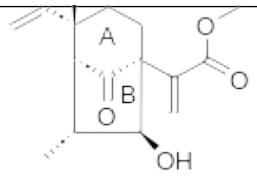
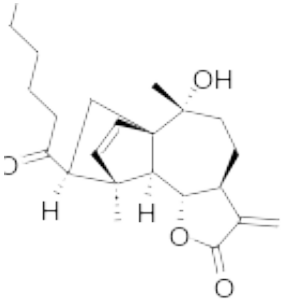
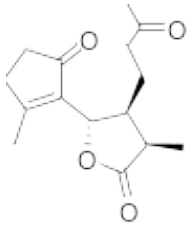
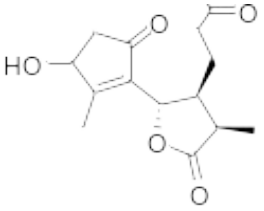
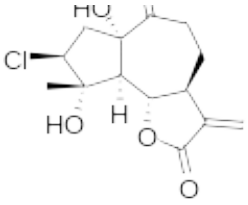
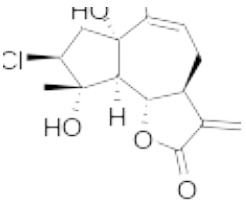
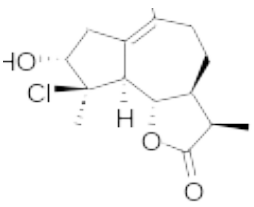
№	Compounds name	Structure	Source	Ref.
17.	Artemisol B		*A. argyi*	[11]
18.	Artemisol C		*A. argyi*	[11]
19.	Artemisol D		*A. argyi*	[11]
20.	Artemisol E		*A. argyi*	[11]
21.	Artemisol F		*A. argyi*	[11]
22.	Artemisol G		*A. argyi*	[11]
23.	Artemisol H		*A. argyi*	[11]

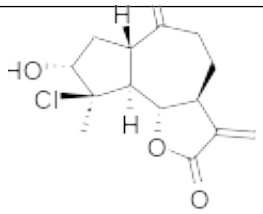
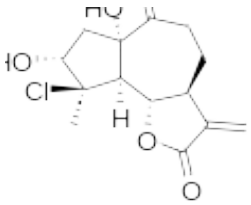
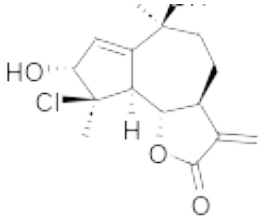
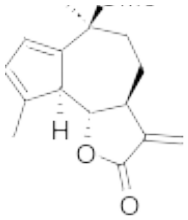
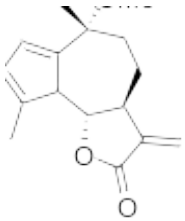
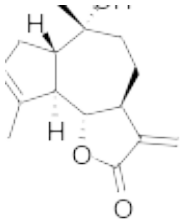
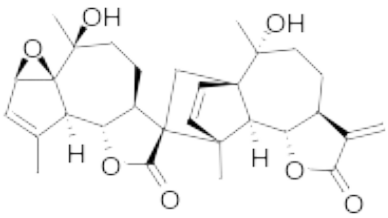
№	Compounds name	Structure	Source	Ref.
24.	Artemisol I		*A. argyi*	[11]
25.	Artemisol J		*A. argyi*	[11]
26.	Artemisol K		*A. argyi*	[11]
27.	Artemisol L		*A. argyi*	[11]
28.	Artemisol M		*A. argyi*	[11]
29.	Artemisol N		*A. argyi*	[11]
30.	Artemisacrolide A		*A. sacrorum*	[12]

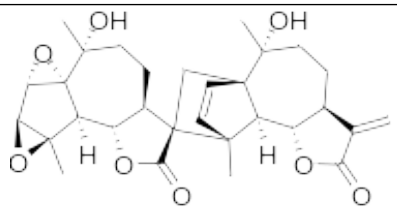
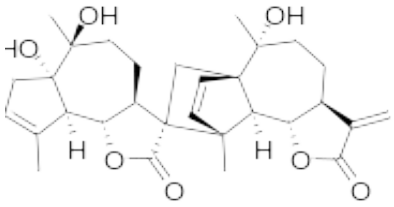
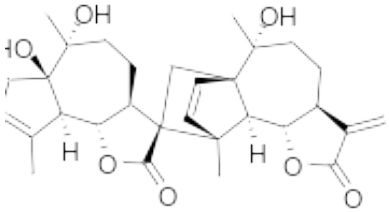
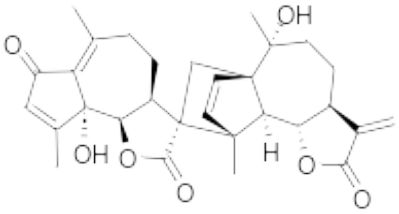
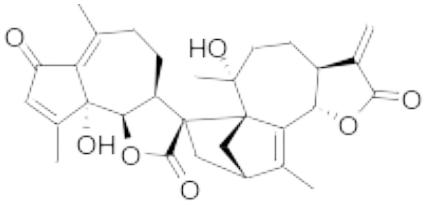
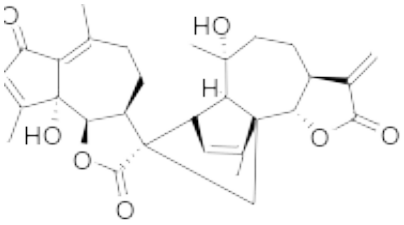
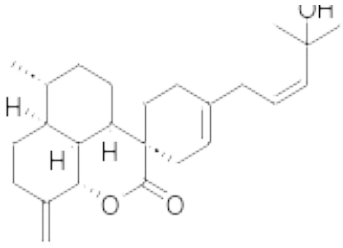
№	Compounds name	Structure	Source	Ref.
31.	Artemisacrolide B		*A. sacrorum*	[12]
32.	Artemisacrolide C		*A. sacrorum*	[12]
33.	Artemisacrolide D		*A. sacrorum*	[12]
34.	Artemisacrolide E		*A. sacrorum*	[12]
35.	Artemisacrolide F		*A. sacrorum*	[12]
36.	Artemisacrolide G		*A. sacrorum*	[12]
37.	Artemisacrolide H		*A. sacrorum*	[12]

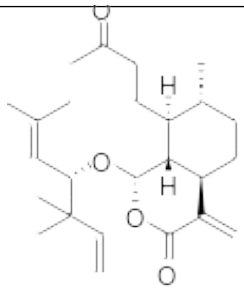
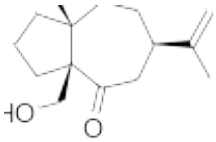
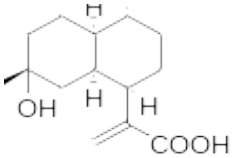
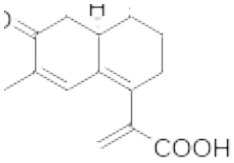
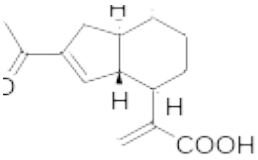
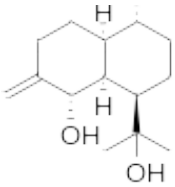
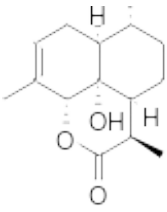
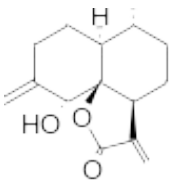
№	Compounds name	Structure	Source	Ref.
38.	Artemisacrolide I		*A. sacrorum*	[12]
39.	Artemisacrolide J		*A. sacrorum*	[12]
40.	Artemisacrolide K		*A. sacrorum*	[12]
41.	Artemisacrolide L		*A. sacrorum*	[12]
42.	Artemisacrolide M		*A. sacrorum*	[12]
43.	Artemisacrolide N		*A. sacrorum*	[12]
44.	Artemisacrolide O		*A. sacrorum*	[12]

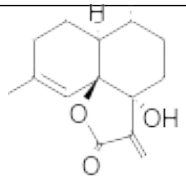
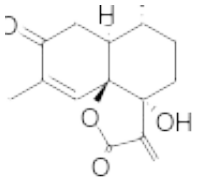
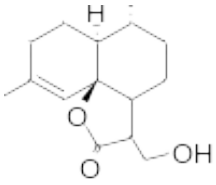
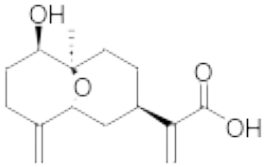
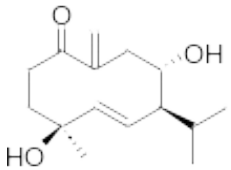
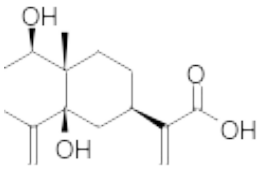
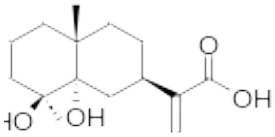
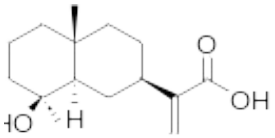
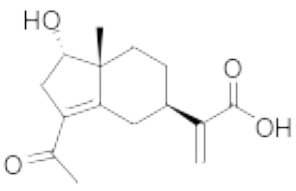
№	Compounds name	Structure	Source	Ref.
45.	Artemisacrolide P		*A. sacrorum*	[12]
46.	Artemisacrolide Q		*A. sacrorum*	[12]
47.	Artemisacrolide R		*A. sacrorum*	[12]
48.	Artemisacrolide S		*A. sacrorum*	[12]
49.	Artemisacrolide T		*A. sacrorum*	[12]
50.	Artemisacrolide U		*A. sacrorum*	[12]
51.	Artemdubinoid A		*A. dubia*	[13]

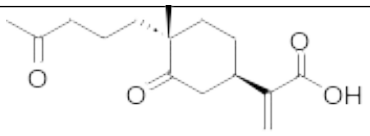
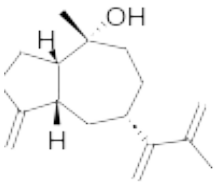
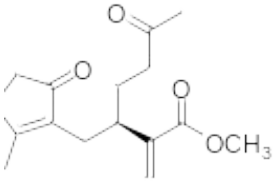
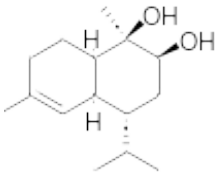
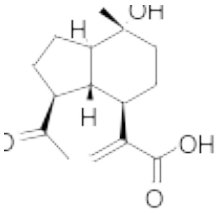
№	Compounds name	Structure	Source	Ref.
52.	Artemdubinoid B		*A. dubia*	[13]
53.	Artemdubinoid C		*A. dubia*	[13]
54.	Artemdubinoid D		*A. dubia*	[13]
55.	Artemdubinoid E		*A. dubia*	[13]
56.	Artemdubinoid F		*A. dubia*	[13]
57.	Artemdubinoid G		*A. dubia*	[13]
58.	Artemdubinoid H		*A. dubia*	[13]

№	Compounds name	Structure	Source	Ref.
59.	Artemdubinoid I		*A. dubia*	[13]
60.	Artemdubinoid J		*A. dubia*	[13]
61.	Artemdubinoid K		*A. dubia*	[13]
62.	Artemdubinoid L		*A. dubia*	[13]
63.	Artemdubinoid M		*A. dubia*	[13]
64.	Artemdubinoid N		*A. dubia*	[13]
65.	Artemyriantholidimer A		*A. myriantha*	[13]

№	Compounds name	Structure	Source	Ref.
66.	Artemyriantholidimer B		*A. myriantha*	[13]
67.	Artemyriantholidimer C		*A. myriantha*	[13]
68.	Artemyriantholidimer D		*A. myriantha*	[13]
69.	Artemyriantholidimer E		*A. myriantha*	[13]
70.	Artemyriantholidimer F		*A. myriantha*	[13]
71.	Artemyriantholidimer G		*A. myriantha*	[13]
72.	Artemordosin A		*A. ordosica*	[14]

№	Compounds name	Structure	Source	Ref.
73.	Artemordosin B		*A. ordosica*	[14]
74.	Artemordosin C		*A. ordosica*	[14]
75.	Artemordosin D		*A. ordosica*	[14]
76.	Artemordosin E		*A. ordosica*	[14]
77.	Artemordosin F		*A. ordosica*	[14]
78.	Artemordosin G		*A. ordosica*	[14]
79.	Artemordosin H		*A. ordosica*	[14]
80.	Artemordosin I		*A. ordosica*	[14]

№	Compounds name	Structure	Source	Ref.
81.	Artemordosin J		*A. ordosica*	[14]
82.	Artemordosin K		*A. ordosica*	[14]
83.	Artemordosin L		*A. ordosica*	[14]
84.	Vachanin A		*A. vachanica*	[15]
85.	Vachanin B		*A. vachanica*	[15]
86.	Vachanin C		*A. vachanica*	[15]
87.	Vachanin D		*A. vachanica*	[15]
88.	Vachanin E		*A. vachanica*	[15]
89.	Vachanin F		*A. vachanica*	[15]

№	Compounds name	Structure	Source	Ref.
90.	Vachanin J		*A. vachanica*	[15]
91.	Vachanin H		*A. vachanica*	[15]
92.	Vachanin I		*A. vachanica*	[15]
93.	Vachanin J		*A. vachanica*	[15]
94.	Vachanin K		*A. vachanica*	[15]

1.1.1 Pharmocological studies on *Artemisia* species

Plants belonging to the *Artemisia* family are widely used in traditional and modern medicine. Their antioxidant, antimicrobial, antifungal, antibacterial, antidiabetic, antiviral, anticarcinogenic, antiulcer activity, anti-asthmatic, anti-inflammatory, antifeedant, antiparasitic, antiosteoclastogenic, antimalarial, antiparkinson's, antiprotozoal, cytotoxic, immunosuppressant, nematocidal, and neurotrophic activities, along with a number of other activities, have been studied. Some of these activities are presented as followings [15-18].

1.1.3.1 Antimicrobial, antifungal and antibacterial activities

11-*epi*-artapshin, an eudesmane compound extracted from *A. herba-alba*, was evaluated for its antimicrobial properties against various bacterial and fungal species by Mohamed. At a concentration of 100 μg/5 μL DMSO/disk, compound 11-*epi*-artapshin exhibited activity against *Bacillus subtilis* (ATCC 6633), *S. aureus* (ATCC 29213), *E. coli* (ATCC 25922), and *P. aeruginosa* (ATCC 27953), as well as against the fungi *Candida tropicalis* (ATCC 750) and *Fusarium solani* (NRC 15) at 100 lg/5 μL DMSO/disk with inhibition zone diameters between 6 and 8 mm in comparison to thiophenicol and treflucan as positive controls (11-25 mm). Blagojević studied the antibacterial properties of *A. vulgaris* essential oil against a panel of bacteria. The essential oil was gained through steam distillation of both aboveground and underground plant parts. The zones of pathogen growth suppression on the paper filters were investigated 10 and 30 times. Oil extracted from the aerial parts of *A. vulgaris* demonstrated inhibitory activity against *Salmonella enteritidis*, *P. aeruginosa*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *E. coli*. In an effort to generate antimicrobial and toxicity profiles, Hubsch examined the interaction of herbal extracts, including *A. afra*, with a range of antibiotics. Their analysis of 420 antibiotic-plant extract combinations revealed that 14.29% exhibited synergistic activity, 7.56% antagonistic activity, 35.71% additive effects, and 42.44% indifferent interactions. Notably, *A. afra* exhibited antagonistic effect in combination with ciprofloxacin against *E. coli* [19-21].

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