



Biological Activity, Botanical Characteristics, and Phytochemical Constituents of *Artemisia ciniformis*

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Abstract

Context: Humans have used plants for their medicinal needs since ancient times. *Artemisia* is an important medicinal plant genus that includes about 500 different species, many of which are known for their therapeutic effects. One of the valuable species of this genus, *Artemisia ciniformis*, exhibits interesting biological effects, yet there is no comprehensive report on its properties.

Evidence Acquisition: Data were collected through extensive literature searches in web databases, including PubMed, Scopus, Web of Science, Wiley Online Library, SpringerLink, Google Scholar, Science Direct, ResearchGate, and Plants of the World Online, up until December 2024. The chemical structures were retrieved from the PubChem database and drawn using ChemDraw Professional 16.0 software.

Results: This paper provides comprehensive information on the distribution, botanical characteristics, phytochemistry, and biological effects of this species, which may be useful for conducting further research in related fields such as pharmacognosy, pharmacology, phytochemistry, and natural product chemistry.

Conclusions: *Artemisia ciniformis*, as a valuable plant species with prominent cytotoxic, antifungal, cytoprotective, and antileishmanial effects, along with other bioactivities, can be a new source for discovering promising bioactive molecules.

Keywords: *Artemisia*, *A. ciniformis*, Biological Effects, Phytochemistry

1. Context

Humankind has long used plants to meet their healing needs. Medicinal plants remain valuable sources of therapeutic agents for combating diseases (1-4). In recent years, the demand for medicinal plants has been increasing (1, 5). The number of publications in this field has more than tripled over a 10-year period (2008 - 2018), indicating growing attention and interest in research in this area (2). *Artemisia* is a plant genus that has attracted significant interest due to its diverse biological properties and secondary metabolites. Several species in this genus have been used to prepare herbal remedies for treating major and minor ailments in the forms of herbal teas, beverages, tonics, and

cosmetics (6). The genus *Artemisia* has a long history in traditional medicine and ethnobotanical use worldwide, offering treatments for a broad range of disorders, such as malaria, inflammatory diseases, jaundice, toothache, gastrointestinal problems, menstrual pains, wounds, diarrhea, skin disorders, headache, and intestinal parasites. One of the most important uses of the genus in modern medicine is in the treatment of malaria. *Artemisia* is a promising plant genus for cancer treatment (7, 8). *Artemisia* is one of the largest and most widespread genera in the family Asteraceae (9). According to Plants of the World Online (2024), *Artemisia* includes 499 accepted species. The *Artemisia* species are widely distributed in temperate regions of the world (10). Asia is home to the highest

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species diversity, with over 170 species in the ex-USSR, 150 species in China, almost 50 species from Japan, and 35 species of this genus reported in Iran (11). About 15 species of the genus grow in the Southern Hemisphere, of which four species are native to southern Africa and five species to South America. Humans have gradually introduced six species for cultivation in the Southern Hemisphere (12). *Artemisia* species are adaptable to different habitats (13). They have a wide geographic distribution in Iran (14, 15). One of these species that grows in Iran is *Artemisia ciniformis* Krasch. & Popov ex Poljakov. In Persian, it is called “Dermaneye talaai” and “Dermaneye sakhrerooy” (15, 16). Unfortunately, unlike many other species of the genus *Artemisia*, there are only fragmentary reports about the species *A. ciniformis*. Different types of extracts, fractions, and the volatile oil of this plant species have interesting biological effects. A number of phytochemical studies have reported the presence of different classes of secondary metabolites in *A. ciniformis*. There is no complete report on the characteristics of this species. This review attempts to fill this gap and provide comprehensive information on the distribution, botanical characteristics, chemical composition, and biological effects of this beneficial plant species.

2. Evidence Acquisition

A literature search using the keywords "*Artemisia ciniformis*", "*A. ciniformis*", "*Seriphidium ciniforme*", and "*ciniformis*" was conducted in the databases of Google Scholar, Scopus, Science Direct, ResearchGate, PubMed, Web of Science, Wiley Online Library, SpringerLink, and Plants of the World Online, until December 2024. Available books were used to review some details. We carefully reviewed the available materials. All relevant materials were selected for the preparation of this report. Any data related to biological activity, botanical characteristics, folk medicine, and phytochemical constituents of *A. ciniformis* were extracted. The chemical structures and CAS registry numbers were retrieved from the PubChem database and drawn using ChemDraw Professional 16.0 software.

3. Results

3.1. Distribution

The *Artemisia* genus is distributed worldwide but is more widespread in the Northern Hemisphere, with a few species growing in the Southern Hemisphere (17). *Artemisia* species can be found in many ecosystems, from humid environments to desert communities, and from altitudes close to sea level to high mountain peaks

with an altitude of about 4000 meters (18). *Artemisia ciniformis* grows at an altitude of 1200 - 2800 meters above sea level on sandy and clay slopes (19). This species is distributed in the Irano-Turanian region, including Iran, Turkmenistan, and Afghanistan (Figure 1) (20, 21).

3.2. Botanical Characteristics

3.2.1. Taxonomic Classification and Phylogeny

The taxonomic data related to this plant species (12, 22, 23) are presented in Table 1. *Artemisia* is the largest genus within the tribe *Anthemideae* of the *Asteraceae* family (24). The adaptation of the *Artemisia* genus to its wide geographical distribution and diverse habitats has been accompanied by changes in morphology, anatomy, cellular structure, and function (25). Therefore, *Artemisia* has various ploidy levels: Dodecaploid, decaploid, octaploid, hexaploid, tetraploid, and diploid. The basic chromosome number in this genus is usually nine, but sometimes there are fewer chromosomes ($x = 8$) (26). The genus *Artemisia* is divided into several subgenera based on morphological characteristics, including pollen type and functional sexual spatial arrangement of the floret within the capitula: *Artemisia*, *Absinthium*, *Dracunculus*, *Seriphidium*, *Tridentatae* (26, 27), *Pacifica* (28). *Artemisia ciniformis* is included in the subgenus *Seriphidium*. The characteristic of this subgenus is that the capitulum lacks outer florets, contains fertile and bisexual florets, and the receptacle is glabrous (28). Also, the number of chromosomes in this subgenus is based on $x = 9$ and different ploidy levels (29). So far, the chromosomes of *A. ciniformis* have been counted three times: The first time in 1964 in the Turkmen population, where the number of chromosomes was reported as $2n = 36$ (30). The second time in 2001, in the Iranian population, where the number of chromosomes was reported as $2n = 18$, and the diploid level of this taxon was determined (31), and the third time in 2013 in the Iranian population, where the number of chromosomes was reported as $2n = 2x = 18 + 0 - 1B$ and a lower ploidy level was mentioned for it (29).

3.2.2. Life Form and Morphology

Most species of the *Artemisia* genus are perennial, with only about 10 species being biennials or annuals (27). General morphological features of the genus *Artemisia* are described as leaves alternate, capitula small, usually racemose, paniculate or capitate, inflorescence, rarely solitary; involucre bracts in few rows, receptacle flat to hemispherical, without scales and sometimes hirsute; florets all tubular, achenes obovoid, pappus absent or sometimes a tiny scarious



Figure 1. Distribution of *Artemisia ciniformis* (22)

Table 1. Taxonomic Classification of *Artemisia ciniformis*

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Asterales
Family	Asteraceae, Compositae
Tribe	Anthemideae
Genus	<i>Artemisia</i> L.
Species	<i>Artemisia ciniformis</i> Krasch. & Popov ex Poljakov synonyms: <i>Seriphidium ciniforme</i> (Krasch. & Popov ex Poljakov) Poljakov

ring (32). *Artemisia ciniformis* is a perennial plant with numerous erect stems. Its stem base is woody. The height of this plant is 20 to 35 centimeters. It has a narrow panicle or spike inflorescence. Its flowers are red and sometimes yellow. The flowering and fruiting time of this species is early to late autumn (33).

3.3. Folk Medicine

In the past, people believed that *Artemisia* plants could protect health and restore strength. *Artemisia* originated from the Greek word Artemis, which implies 'healthy' (34). Plants of this genus are traditionally used as decoctions, infusions, and tinctures for various diseases, including malaria, gastrointestinal diseases, upper respiratory tract diseases, and rheumatism. In the folk medicine of Central Asia, infusions of *Artemisia* species flowers are used for hemorrhoids, ulcerative colitis, epilepsy, bad breath, and several other diseases (35). The aerial parts and inflorescences of *A. ciniformis*

have medicinal uses. In Turkmen folk medicine, its inflorescences are used to prepare "polynnogo chaya" ("*Artemisia* tea"), which has anthelmintic properties. It is also used for malaria, typhoid fever, and convulsions. The oil prepared from *Artemisia* is also used for fever, dropsy, and scorpion stings (19). In Iran, this plant is used as an appetite stimulant and antiparasitic in folk medicine (36).

3.4. Chemical Composition

Many species of *Artemisia* are aromatic; therefore, they are rich in volatile and aromatic compounds. However, they also contain non-volatile and non-aromatic compounds. Phytochemical studies on *Artemisia* have shown that this genus mainly contains terpenoids, coumarins, and flavonoids, although other compounds are also present (37). The presence of numerous sesquiterpenoids in this genus is notable (38). Several studies have investigated and identified the


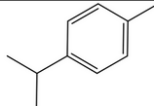
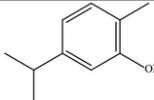

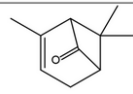
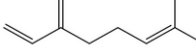
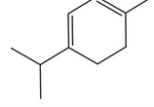
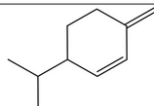
Number	Compound	CAS Registry Number	Molecular formula	Structure	References
1	trans-2-Hexenal	6728-26-3	C ₆ H ₁₀ O		(49)
2	p-Cymene	99-87-6	C ₁₀ H ₁₄		(39, 40, 50-52)
3	Carvacrol	499-75-2	C ₁₀ H ₁₄ O		(41, 42, 49, 50)
4	Pinocarvone	34-41-3	C ₁₀ H ₁₄ O		(41, 42, 49)
5	Chrysanthenone	473-06-3	C ₁₀ H ₁₄ O		(40)
6	Myrcene	123-35-3	C ₁₀ H ₁₆		(39, 40, 51, 52)
7	α-Terpinene	99-86-5	C ₁₀ H ₁₆		(39, 40, 51)
8	β-Phellandrene	555-10-2	C ₁₀ H ₁₆		(39, 51)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39-42, 49-52)

essential oil compounds of *A. ciniformis*, which indicates the presence of various monoterpenes and sesquiterpenes (39-42). The total phenolic content of the oil was 206.20 ± 4.58 mg GAE/g (43). Figure 2 lists the reported compounds of *A. ciniformis* essential oil. 1,8-cineol, camphor, borneol, and α-terpineol have been reported more frequently than other compounds. In studies conducted on *A. ciniformis*, the amount of flavonoids in the surface raw materials was measured and found to be 1.50% (44), and the flavonoid content of its methanolic extract was estimated to be 131.81 ± 6.83 mg/g CE (43). It has also been found that in this species, the amount of unsaturated sesquiterpene lactones is higher than saturated ones (45). The presence of artemisinin in the leaves of *A. ciniformis* has been reported during the vegetative stage of the plant (46).

The phytochemical investigation of *A. ciniformis* extract revealed the presence of isochlorogenic acid isomers, tetrahydrofuran-type sesquiterpenoids, acetophenone derivatives, polymethoxylated flavone, and flavonoids (47, 48). Figure 3 shows the compounds isolated from non-volatile extracts of the species.

3.5. Biological Effects

Artemisia species have a very long history of being used to treat human diseases in various parts of the world. This important medicinal genus has promising therapeutic potential for multiple problems because there are numerous reports on a broad range of bioactivities, such as antimalarial (53), hepatoprotective (54), analgesic (55), antimicrobial (56), antileishmanial

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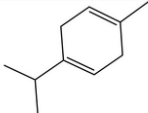
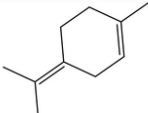
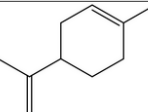
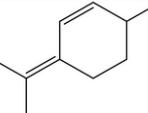
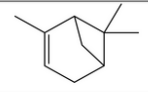
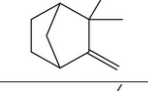


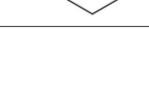
9	γ -Terpinene	99-85-4	C ₁₀ H ₁₆		(39, 40, 51)
10	Terpinolene	586-62-9	C ₁₀ H ₁₆		(39, 40, 51)
11	Limonene	138-86-3	C ₁₀ H ₁₆		(40)
12	p- Menth-2,4 (8)-diene	586-63-0	C ₁₀ H ₁₆		(40)
13	α -Pinene	80-56-8	C ₁₀ H ₁₆		(39, 40, 51)
14	Camphene	79-92-5	C ₁₀ H ₁₆		(39, 40, 51)
15	β -Pinene	127-91-3	C ₁₀ H ₁₆		(39, 40, 51)
16	2-Carene	554-61-0	C ₁₀ H ₁₆		(50)
17	3-Carene	13466-78-9	C ₁₀ H ₁₆		(50)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39, 40, 50, 51)

(57), antiparasitic (58), antitumor (59), antiulcer (60), and antidiabetic (61).

3.5.1. Antimicrobial Effects

Investigation of the in vitro antimicrobial effects of *A. ciniformis* essential oil showed moderate inhibitory activity against *Escherichia coli* (MIC = 1000 μ g/mL), *Staphylococcus aureus* (MIC = 2500 μ g/mL), *Candida albicans* (MIC = 1000 μ g/mL), *Acinetobacter baumannii* (MIC = 20 μ g/mL), *Pseudomonas aeruginosa* (MIC = 1000 μ g/mL), and clinical isolates of *Vibrio cholerae* (the diameter of inhibition zone = 24 mm) and *S. aureus* (the

diameter of inhibition zone = 58 mm) (39, 41). Hydroethanolic extract of *A. ciniformis* has inhibitory activity against bacterial strains of *P. aeruginosa* (MIC = 2000 μ g/mL), *Streptococcus pyogenes* (MIC = 2000 μ g/mL), *S. epidermidis* (MIC = 1000 μ g/mL), *Micrococcus luteus* (MIC = 500 μ g/mL), *Acinetobacter* sp. (MIC = 2000 μ g/mL) and *S. aureus* (MIC = 2000 μ g/mL), and aqueous extracts (infusion and decoction) have shown in vitro antimicrobial activity against *S. epidermidis* (MIC = 750 μ g/mL), and *Acinetobacter* sp. (MIC = 750 μ g/mL) (62, 63). The findings of Ghomi et al. showed that *A. ciniformis* extract can significantly reduce the gene expression of

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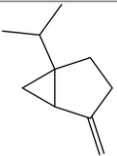
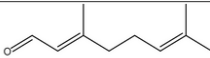
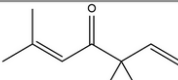
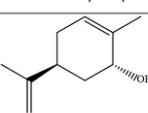
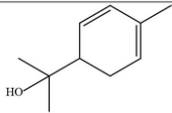
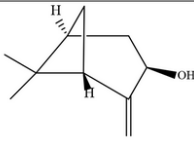
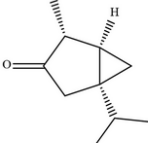
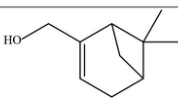
18	Sabinene	3387-41-5	C ₁₀ H ₁₆		(40)
19	Citral	5392-40-5	C ₁₀ H ₁₆ O		(39, 40, 51)
20	Artemisia ketone	546-49-6	C ₁₀ H ₁₆ O		(49)
21	trans-Carveol	1197-07-5	C ₁₀ H ₁₆ O		(41, 42, 49)
22	α- Phellandren-8-ol	1686-20-0	C ₁₀ H ₁₆ O		(40)
23	trans-Pinocarveol	547-61-5	C ₁₀ H ₁₆ O		(40-42, 49, 52)
24	α- Thujone	546-80-5	C ₁₀ H ₁₆ O		(40)
25	Myrtenol	515-00-4	C ₁₀ H ₁₆ O		(40, 41, 49)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39-42, 49, 51, 52)

the norA efflux pump in ciprofloxacin-resistant *S. aureus* and prevent the release of antibiotics and other drugs (64).

3.5.2. Antioxidant and Cytoprotective Effects

Various studies have investigated and proven the cytoprotective and antioxidant effects of *A. ciniformis*. Taherkhani evaluated the antioxidant and anti-tyrosinase capacity, iron chelation, superoxide anion, and NO radical scavenging activity of *A. ciniformis* leaf volatile oil. The essential oil exhibited a dose-dependent scavenging of DPPH, NO, and superoxide radicals with

IC₅₀ values of 10.75 mg/mL, 10.63 µg/mL, and 16.81 µg/mL, respectively. In the β-carotene-linoleic acid test system, oxidation of linoleic acid was effectively inhibited (86.39 ± 2.53%, 0.625 mg/mL). Anti-tyrosinase activity of the essential oil was also reported (IC₅₀ = 6.53 mg/mL) (42).

In a study that examined the antioxidant properties of *A. ciniformis* essential oil in the pre-and flowering stages, it was found that the antioxidant properties and phenolic content were higher in the flowering stage (52). Results of a study showed that ethyl acetate, ethanolic, and hydroethanolic extracts of *A. ciniformis* protected H9c2 cardiac muscle cells against H₂O₂-induced cell death

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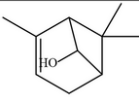
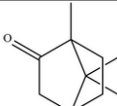
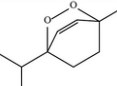
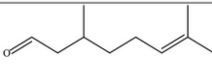
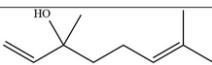
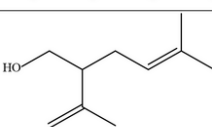
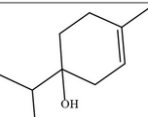
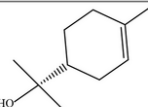

26	cis- Chrysanthanol	55722-60-6	C ₁₀ H ₁₆ O		(40)
27	Camphor	76-22-2	C ₁₀ H ₁₆ O		(39-42, 49, 51, 52)
28	Ascaridole	512-85-6	C ₁₀ H ₁₆ O ₂		(50)
29	Citronellal	106-23-0	C ₁₀ H ₁₈ O		(39-42, 49, 51, 52)
30	Linalool	78-70-6	C ₁₀ H ₁₈ O		(39, 40, 51)
31	Lavandulol	58461-27-1	C ₁₀ H ₁₈ O		(40)
32	Terpinen-4-ol	562-74-3	C ₁₀ H ₁₈ O		(39-42, 49, 51, 52)
33	α -Terpineol	98-55-5	C ₁₀ H ₁₈ O		(39-42, 49, 52)
34	cis-Sabinene hydrate	546-79-2	C ₁₀ H ₁₈ O		42, 41) (52, 49,

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39-42, 49-52)

(increase in the cell viability to 76 ± 4.53 , 72 ± 1.25 , and $82 \pm 3.21\%$ of control, respectively), possibly via the mechanism of reactive oxygen species (ROS) inhibition and/or free radical scavenging (65). An in vitro study showed that the hydroethanolic extract of *A. ciniformis* has significant antioxidant activity and high content of total phenolics (134.67 ± 0.49 mg GAE /g). The pretreatment of PC12 cells with some fractions of this extract reduced DOX-induced cytotoxicity and ROS production. An increase in superoxide dismutase (SOD) activity was also observed. One of the fractions significantly reduced the activity of caspase-3 and increased the mitochondrial membrane potential

(MMP) in the PC12 cell line (66). It has also been found that dichloromethane, ethyl acetate, and petroleum ether extracts of *A. ciniformis* can inhibit the cytotoxicity of H₂O₂ in the PC1₂ cells. Also, an increase in cell survival in the group of cells pretreated with the extracts was observed. The rate of H₂O₂-induced apoptosis was also affected. ROS scavenging, preservation of MMP, suppression of caspase-3 activity, and inhibition of SOD activity reduction were all exerted by these three extracts. The ethyl acetate extract exerted the highest antioxidant activity against H₂O₂-induced oxidative damage. This extract reduced ROS accumulation to 70%, H₂O₂-induced cell death to 35%, and caspase 3 activity to

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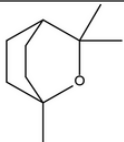
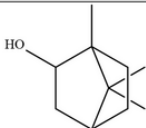
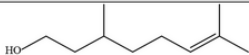
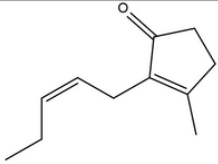
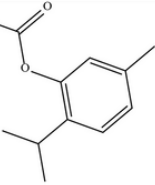
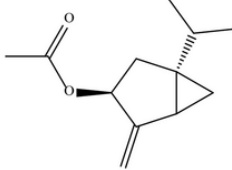
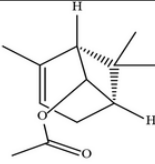
35	1,8-Cineol	470-82-6	C ₁₀ H ₁₈ O		(39-42, 49-51)
36	Borneol	6627-72-1	C ₁₀ H ₁₈ O		(39-42, 49, 51)
37	Citronellol	106-22-9	C ₁₀ H ₂₀ O		(40)
38	cis-Jasmone	488-10-8	C ₁₁ H ₁₆ O		(39-42, 49, 51)
39	Thymyl acetate	528-79-0	C ₁₂ H ₁₆ O ₂		(40)
40	trans- Sabinyol acetate	71327-37-2	C ₁₂ H ₁₈ O ₂		(40)
41	cis- Chrysanthenyl acetate	67999-48-8	C ₁₂ H ₁₈ O ₂		(40)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39-42, 49-52)

about 175%. It also increased SOD activity to 47% and mitochondrial membrane potential levels by 27% (67). In a study that examined sesquiterpene fractions from several *Artemisia* species, including *A. ciniformis*, it was found that the level of nitric oxide produced by lipopolysaccharide-primed macrophages was significantly reduced by all prepared fractions in a dose-dependent manner. However, in this study, the

unsaturated sesquiterpene lactones of *A. ciniformis* had a less modulating effect on COX-2 expression and Prostaglandin E2 (PGE2) production (68).

3.5.3. Cytotoxic and Apoptotic Effects

Studies have shown the cytotoxic effects of various extracts of *A. ciniformis*. In a study that investigated the

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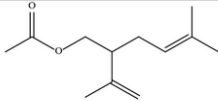
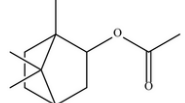
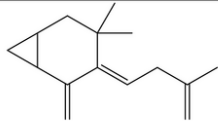
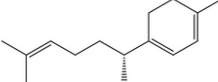
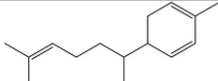
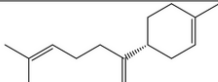
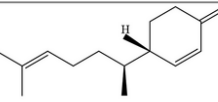
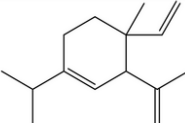
42	Lavandulyl acetate	20777-39-3	C ₁₂ H ₂₀ O ₂		(40)
43	Bornyl acetate	76-49-3	C ₁₂ H ₂₀ O ₂		(40, 52)
44	4,4-Dimethyl-3-(3-methylbut-3-enylidene)-2-methylenebicyclo[4.1.0]heptane	79718-83-5	C ₁₅ H ₂₂		(50)
45	γ-Curcumene	28976-68-3	C ₁₅ H ₂₄		(39, 40, 51)
46	α-Zingiberene	495-60-3	C ₁₅ H ₂₄		(39, 40, 51)
47	β-Bisabolene	495-61-4	C ₁₅ H ₂₄		(39, 40, 51)
48	β-Sesquiphellandrene	20307-83-9	C ₁₅ H ₂₄		(39, 40, 51)
49	δ- Elemene	20307-84-0	C ₁₅ H ₂₄		(40)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39, 40, 50-52)

cytotoxic effects of native Iranian *Artemisia* species, dichloromethane (IC₅₀ value: 35 µg/mL) and methanolic (IC₅₀ value: 60 µg/mL) extracts of *A. ciniformis* had the highest growth inhibitory effects on the human gastric adenocarcinoma cell line (AGS), and dichloromethane extract (IC₅₀ value: 29 µg/mL) had the highest inhibitory effects on human breast carcinoma (MCF-7) cells compared to other extracts studied. The human cervix carcinoma cell line (HeLa) showed high sensitivity to ethyl acetate extract of *A. ciniformis* (IC₅₀ value: 73 µg/mL). Also, the ethyl acetate extract of this species (IC₅₀ value: 94 µg/mL) was one of the most potent extracts studied in inhibiting the human colon

adenocarcinoma cell line (HT-29) (69). In another study, the dichloromethane fraction of *A. ciniformis* exerted the highest toxicity against AGS cells (IC₅₀ value: 35 µg/mL) compared to six other *Artemisia* species. Its hexane fraction also had the lowest toxicity on normal fibroblast (L929) cells (70). The petroleum ether extract of this plant showed apoptotic and anti-proliferative effects on HL-60 (IC₅₀ value: 105.20 µg/mL) and K562 human leukemic cancer cell lines (IC₅₀ value: 25.53 µg/mL). The dichloromethane extract possessed the highest anti-proliferative effects on HL-60 cells with an IC₅₀ value of 31.33 µg/mL (71). Some fractions of these two extracts exhibited potent cytotoxic and apoptotic

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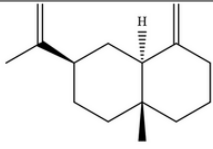
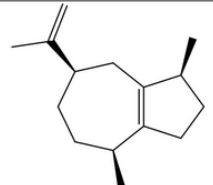
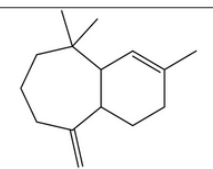
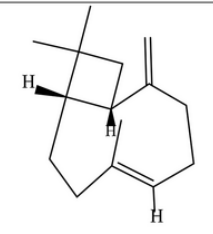
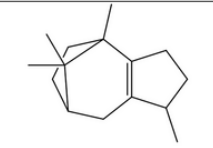
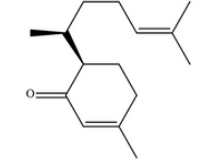
50	β - Selinene	17066-67-0	C ₁₅ H ₂₄		(40)
51	α -Guaiene	3691-12-1	C ₁₅ H ₂₄		(40-42, 49)
52	α - Himachalene	3853-83-6	C ₁₅ H ₂₄		(40)
53	(Z)-Caryophyllene	NA (PubChem CID: 6429301)	C ₁₅ H ₂₄		(41, 42, 49, 50)
54	Patchoulene	1405-16-9	C ₁₅ H ₂₄		(50)
55	(6R, 7R) Bisabolone	72441-71-5	C ₁₅ H ₂₄ O		(40)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (40-42, 49, 50)

effects on the mouse skin cancer (B16/F10) (IC₅₀ value: 53.69 ± 2.9 µg/mL), the human prostate carcinoma (PC3) (IC₅₀ value: 1.54 ± 0.7 µg/mL), and MCF-7 cell lines (IC₅₀ value: 4.15 ± 1.09 µg/mL) (72). The cytotoxic effects and apoptosis induction of free extract and alginate nanogel encapsulating *A. ciniformis* extract were compared in the AGS cell line. The nanogel was more potent in the induction of apoptosis. Flow cytometric results showed that it could inhibit cell proliferation and arrest the cell

cycle at the G0/G1 phase. The up-regulation of expression levels of pro-apoptotic genes and the down-regulation of anti-apoptotic and metastatic genes were detected (73).

3.5.4. Antileishmanial Activity

The leishmanicidal activity of *A. ciniformis* was investigated in a study by Emami et al. This study investigated the leishmanicidal activity of different

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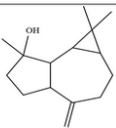
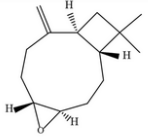
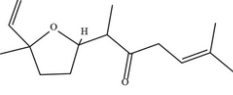
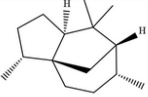
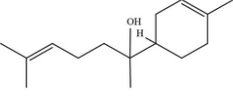
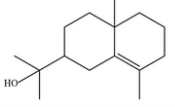
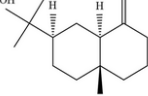
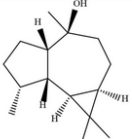
56	Spathulenol	6750-60-3	C ₁₅ H ₂₄ O		(40)
57	Caryophyllene oxide	1139-30-6	C ₁₅ H ₂₄ O		(40, 52)
58	Davanone	30810-99-2	C ₁₅ H ₂₂ O ₂		(39, 40, 50, 51)
59	Cedrane	13567-54-9	C ₁₅ H ₂₆		(41, 42, 49)
60	α -Bisabolol	515-69-5	C ₁₅ H ₂₆ O		(40)
61	8-epi-gamma-Eudesmol	NA	C ₁₅ H ₂₆ O		(50)
62	β -Eudesmol	473-15-4	C ₁₅ H ₂₆ O		(40)
63	Viridiflorol	552-02-3	C ₁₅ H ₂₆ O		(40)

Figure 2. Chemical compounds in *Artemisia ciniformis* essential oil (39-42, 49-52)

extracts of 11 *Artemisia* species in vitro. According to the results obtained, various extracts of *A. ciniformis* had a leishmanicidal effect. The ethanol extract of this species was one of the most effective extracts among the studied species and showed a strong leishmanicidal effect (IC₅₀ value: 25 ± 0.4 µg/mL) (74).

3.5.5. Antimalarial Activity

Based on the results of a study on the antimalarial activity of different extracts of three *Artemisia* species, including *A. ciniformis*, using the in vitro β -hematin formation method, the extracts with medium polarity

had antimalarial activity. Among all the extracts, the dichloromethane extract of *A. ciniformis* (IC₅₀ value: 0.92 ± 0.01 mg/mL) had the highest antimalarial activity (75).

3.5.6. Antifungal Effects

In a study, the antifungal effects of different extracts of three *Artemisia* species against *Microsporum canis*, *Trichophyton verrucosum*, *Trichophyton rubrum*, and *Epidermophyton floccosum* were investigated. According to the results of this experiment, petroleum ether extracts of all three species were the most active extracts, which showed inhibitory effects against all

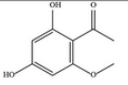
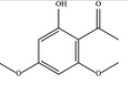
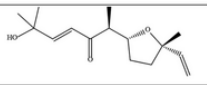
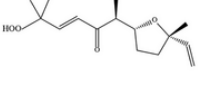
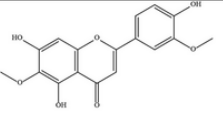
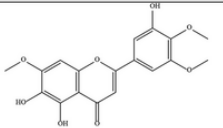
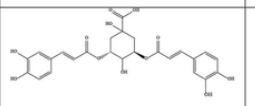
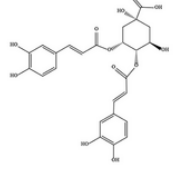
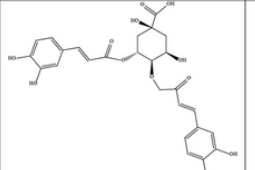
1	2',4'-Dihydroxy-6'-methoxyacetophenone	3602-54-8	C ₉ H ₁₀ O ₄		(47)
2	Xanthoxylin	90-24-4	C ₁₀ H ₁₂ O ₄		(47)
3	Hydroxydavanone	73395-08-1	C ₁₅ H ₂₄ O ₃		(47)
4	Arteincultone	88125-07-9	C ₁₅ H ₂₄ O ₄		(47)
5	Jaceosidin	18085-97-7	C ₁₇ H ₁₄ O ₇		(47)
6	Ciniformon	NA	C ₁₈ H ₁₆ O ₈		(47)
7	3,5-Dicafeoylquinic acid	89919-62-0	C ₂₅ H ₃₂ O ₁₂		(48)
8	3, 4- Dicafeoylquinic acid	89886-30-6	C ₂₅ H ₃₂ O ₁₂		(48)
9	4, 5- Dicafeoylquinic acid	89886-31-7	C ₂₅ H ₃₂ O ₁₂		(48)

Figure 3. Chemical compounds isolated from non-volatile extracts of *Artemisia ciniformis* (47, 48)

four fungi. Among the extracts examined, the lowest minimum inhibitory concentration (MIC) was recorded for the petroleum ether extract of *A. ciniformis* (78.12 µg/mL) against *T. rubrum* (76).

3.5.7. Miscellaneous Effects

In a study, Baniasadi et al. showed that an electrospun wound dressing containing polyvinyl

alcohol, nanochitosan, and an extract of *A. ciniformis* had the essential characteristics of a good wound dressing due to its significant antibacterial properties against *E. coli* and *S. aureus*, support for human fibroblast cell attachment, and rapid water absorption within the first 2 hours. Hence, the *A. ciniformis* extract can be used for biomedical applications, especially as a dressing in wound healing (77). In a study, the green synthesis of silver nanoparticles (AgNPs) was investigated using *A.*

ciniformis leaf extract and their anti-proliferative and apoptotic effects on the AGS cell line were evaluated. Green synthesized AgNPs inhibited the proliferation of human gastric carcinoma cells through apoptosis (78). In a study conducted in Turkmenistan, the use of a decoction containing *Juniperus turcomanica* and *A. ciniformis* was found to be beneficial in treating complications of oral cancer (79).

4. Conclusions

Artemisia ciniformis is a valuable plant species with a broad range of reported bioactivities such as antimicrobial, cytotoxic, cytoprotective, antioxidant, antileishmanial, antimalarial, and antifungal effects. The mono- and sesquiterpenoids comprise the majority of volatile constituents of *A. ciniformis*. So far, flavonoids, isochlorogenic acid isomers, tetrahydrofuran-type sesquiterpenoids, and acetophenone derivatives have been isolated from the non-volatile extracts of the plant species. Perhaps, the cytotoxic and antifungal effects of tetrahydrofuran-type sesquiterpenoids, and the fungicide and fungistatic activities of acetophenone derivatives (80-82) justify the biological effects of *A. ciniformis*, to some extent. The prominent cytoprotective and antioxidant effects of *A. ciniformis* are at least partly due to the presence of isochlorogenic acid isomers (6, 83, 84). Considering the diversity of phytochemicals and biological effects, this plant species is a good candidate for more extensive studies.

Footnotes

Authors' Contribution: Study concept and design: M. M.; Acquisition of data: P. J.; Analysis and interpretation of data: S. N.; Drafting of the manuscript: P. J.; Critical revision of the manuscript for important intellectual content: S. N. and M. M.; Study supervision: M. M.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

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