

A REVIEW ON CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF
FURTHER IRANIAN ARTEMISIA SPECIES

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P.O. Box 14515-775, Tehran, Iran.*Corresponding Author Email: arustaiyan@yahoo.it**ABSTRACT:**

Artemisia is fascinating plant genus, one of the widest-spread member of the Asteraceae family, it features prominently in the pharmacopeia of many countries throughout the world. *Artemisia* is a large diverse genus of plants with between 400 to 500 species belong to the daisy family Compositae, one of the most bulky vegetal groupings, which comprises about 1000 genera and over 20000 species. The genus *Artemisia* are considered of one of state-of-art chemical laboratories capable of biosynthesizing number of biomolecules of different chemical classes. The present review describes the Chemical and Biological activities of further Iranian *Artemisia* species: *A.biennis*, *A.dracunculus* L., *A.fragrans* Wild, *A.hassknechtii* Boiss, and *A.persica* Boiss.

KEYWORDS:

Further Iranian *Artemisia* Species, Compositae, Secondary metabolite, Biological activities.

INTRODUCTION^{1,2,3,4,5,6}

Artemisia comprises hardy herbs and shrubs known for their volatile oils. Most species have strong aromas and bitter tastes from terpenoids specially sesquiterpene lactones. Within this family, *Artemisia* is included into the tribe Anthemideae and comprises itself over 500 species. The 500 species of *Artemisia* are mainly found in Asia, Europe and North America. Asia seems to show the greatest concentration of species with 150 accessions for China, 174 in the ex U.S.S.R., about 50 reported to occur in Japan and 35 species of the genus are found in Iran. *Artemisia* is highly evolved genus with a wide range of life forms, from tall shrubs to dwarf herbaceous alpine plants, occurring in a variety of habitats between Arctic alpine or mountain environments to the dry deserts. The genus *Artemisia* has always been of great botanical and pharmaceutical interest and is useful in traditional medicines for the treatment of a variety of diseases and complaints. *Artemisia annua* is a traditional medicinal herb of China. It is presently being cultivated on a commercial scale in China and Vietnam for its

antimalarial sesquiterpene lactone artemisinin and its essential oil.

The 500 species of *Artemisia* share the common morphological characters: Herbs or small shrubs, frequently aromatic, leaves alternate, capitate small, usually pendent, racemose, paniculate or capitate inflorescences, rarely solitary. The Iranian species has been investigated chemically and presence of monoterpenes, sesquiterpenes, especially sesquiterpene lactones and essential oils reported. The extract of the aerial parts of *A. diffusa* Krasch ex P. Poljakov collected in the Province of Khorassan (Iran) afforded, in addition to several eudesmanolides and a new type of sesquiterpene lactone Artediffusin (Tehranolide), with an endoperoxide group that probably has the same effect as the antimalarial agent artemisinin. In fact, the Iranian *Artemisia* spp. has yielded a considerable amount of new, interesting terpenoids.

Artemisia biennis Wild.⁷

Artemisia biennis is a species of sagebrush known by the common name biennial wormwood. It is native to Europe. This is an annual or biennial herb producing a single erect green to reddish stem up to 2 meters in maximum height. It is generally hairless and unscented. The frilly leaves are up to 13 centimeters long and divided into thin, lance-shaped segments with long teeth. The inflorescence is a dense rod of clusters of flower heads interspersed with leaves. The flowers are hermaphrodite (have both male and female organs) and are pollinated by wind. The fruit is a tiny achene less than a millimeter wide.

It is an invasive species and noxious weed in parts of North America. It is a weed of several agricultural crops, particularly soybeans, other types of dry edible beans, and sunflowers.

The plant prefers light (sandy) and medium (loamy) soils and requires well-drained soil. The plant prefers neutral and basic (alkaline) soils. It can grow in semi-shade (light woodland) or no shade. It requires dry or moist soil and can tolerate drought.

Propagation: Seed - surface sow spring in a greenhouse. Do not allow the compost to dry out. When large enough to handle, prick the seedlings out into individual pots and plant them out in early summer. The seed can also be sown in situ during late spring.

Artemisia biennis is naturalized and weedy in the eastern portion of its range. It is morphologically similar to *A. annua*, differing primarily in the coarser leaf lobes and larger heads that are sessile in axils of leaflike bracts. *Artemisia biennis* is considered native to the northwest United States; it may be introduced in other parts of its range. The type specimen is a horticultural specimen from New Zealand.

Germination Ecology of Biennial Wormwood (*Artemisia biennis*) Seeds⁸

Biennial wormwood has become serious weed of several crops within the northern Great Plains of the United States and Canada. The species is prolific seed producers but little is known about its potential for developing persistent seed banks. Field studies were conducted to determine the influence of duration (7, 8, 11, 19, 20, and 23 mo) and depth of burial (0, 2.5, and 10 cm) on biennial wormwood seed viability and decay. Biennial wormwood seed was buried in September 2003 (burial 1) and September 2004 (burial 2). In burial 1, biennial wormwood seed viability was 65, after 23 mo of burial. In burial 2, biennial wormwood seed viability was 8 %, after 23 mo of burial. The difference was likely because of higher soil moisture during burial 2, which promoted seed decay. Controlled-environment studies sought to determine the influence of stratification environments (freezing, chilling, and freeze-thaw) followed by exposure to diurnally fluctuating temperatures on germination of biennial wormwood seeds.

CHEMICAL CONSTITUENTS⁹

Essential Oil:

Aerial parts of *A. biennis* were collected in March 2001 from Ramsar, Province of Mazandaran, northern Iran, at flowering stage. The oil obtained by hydrodistillation from aerial parts of *Artemisia biennis* was analyzed by means of GC and GC/MS. The major components of the oil of *Artemisia biennis* were camphor (24.6%), artemisia ketone (11.4%) and α -pinene (10.2%).

Identification of the constituents was based on comparison of their mass spectra and retention indices with those obtained from authentic samples and Wiley library spectra.

Artemisia dracunculus L.^{10, 11, 12, 13, 14}

Corresponding to its species names, a common term for the plant is “dragon herb”. It is native to a wide area of the Northern Hemisphere from easternmost Europe across central and eastern Asia to India, western North

America, and south to northern Mexico. The North America populations may, however, be naturalized from early human introduction.

Tarragon grows to 120-150 cm tall, with slender branched stems. The leaves are lanceolate, 2-8 cm long and 2-10 mm broad, glossy green, with an entire margin. The flowers are produced in small capitulate 2-4 mm diameter, each capitulum containing up to 40 yellow or greenish-yellow florets (French tarragon, however, seldom produces flowers).

French tarragon is the variety generally considered best for the kitchen, but is difficult to grow from seed. It is best cultivated by root division. It is normally purchased as a plant, and some care must be taken to ensure that true French tarragon is purchased. *Artemisia dracunculus* is a perennial herb it normally goes dormant in winter. It likes a hot, sunny spot, without excessive watering.

French tarragon grows best in sunny sheltered sites, growing easily on rich, light and well drained soil. Attempts have been made to grow French tarragon on waste ground with only 10-15 cm layers of soil. Propagation is by cuttings or division of roots in spring. French tarragon does not set seed, so all propagation is by these techniques. The grey-green leaves are long, smooth and shiny and mostly entire although the lower leaves are 3-toothed at their tips while the unobtrusive yellow globose flowers are clustered in a spike, drooping on down curved stalks, blooming from June to August.

Russian tarragon (*A. dracunculus* L.) can be grown from seed but is much weaker in flavor when compared to the French variety. However, Russian tarragon is a far more hardy and vigorous plant, spreading at the roots and growing over a meter tall. This tarragon actually prefers poor soils and happily tolerates drought and neglect. It is not as strongly aromatic and flavorsome as its French cousin, but it produces many more leaves from early spring onwards that are mild and good in salads and

cooked food. The young stems in early spring can be cooked as an asparagus substitute. Horticulturists recommend that Russian tarragon be grown indoors from seed and planted out in the summer. The spreading plants can be divided easily.

Tarragon has an aromatic property reminiscent of anise, due to the presence of estragole, a known carcinogen and teratogen in mice. The European Union investigation revealed that the danger of estragole is minimal even at 100-1000 times the typical consumption seen in humans.

Chemical constituents and biological activities: ^{15, 16, 17, 18, 19, 20, 21, 22,23}

Artemisia dracunculus L., tarragon, is an herbaceous plant. Two chemical races of tarragon are distinguished. Plants originating mainly from France have yielded 0.15-3% essential oil, with methyl chavicol (estragol) (Fig. 1) as the principle constituent (68-80%). Further important constituents of this oil are cis- and trans-ocimene (6-12%) and limonene (2-6%). This oil has an aniseed-like taste. Plants from German or Russian provenance contain 0.25-2% essential oil with sabinene, elemicine and trans-isoelemicin as the principal components. This oil has a bitter chervil-like taste.

The herb is principally used as a seasoning for food and as a source of essential oil. Medicinally, aerial parts of tarragon are used to treat symptoms of various digestive ailments and as an adjunctive therapy for the painful component of spasmodic colitis. Further medicinal properties that are claimed for the plant include antiseptic, antipyretic, emmenagogue, anthelmintic, diuretic and calming effects.

In greenhouse and phytotron studies, French tarragon was grown under various temperature and daylength regimes, with the highest yield of herbage and volatile oil being realized under long daylength and constant temperature. It was found that under these conditions, there was an elevated level of elemicin content in the volatile oil, with a corresponding reduction in levels of

methyl chavicol, ocimene, β -pinene and sabinene . In a second study, comparing French, Russian and polish forms of tarragon, Olszewska-Kaczynska and Suchorska reported that the elevated levels of methyl chavicol found in *A. dracunculus* resulted in a strong anise aroma which they considered unacceptable. In other reports on Russian tarragon, elemicin was the major component in the volatile oil. Werker and co-workers (1994) reported that the leaves of French tarragon had both glandular and

non-glandular hairs, the glandular hairs secreting volatile oil when the leaves were young, where the major component in the oil was methyl chavicol. Chalvia in 1992 reported the main oil constituent in leaves of *Persea gratissima* to be methyl chavicol at leaves up to 78% making this a better commercial source of this compound for the flavor and fragrance industry compared with *A. dracunculus*. (Fig. 1).

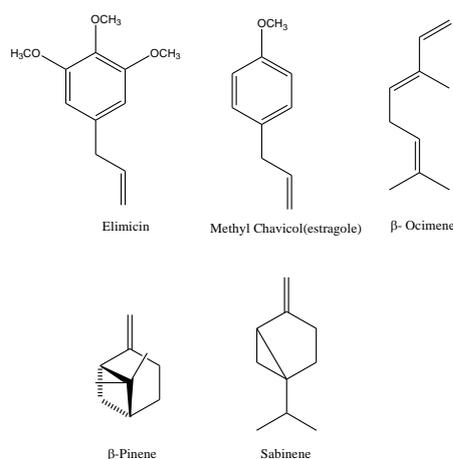


Figure 1: Monoterpenes from *Artemisia dracunculus*.

A number of studies have been undertaken into the bioactive properties of the volatile oil from *A. dracunculus* . In two studies into insect responses to the volatile oil and its constituents, *Papilio* spp. Evoked different reactions to the oil.

Culinary use ^{24, 25, 26}

Tarragon is one of the four fines herbs of French cooking, and is particularly suitable for chicken, fish, and egg dishes. Tarragon is the main flavoring component of Bearnaise sause. Fresh, lightly bruised sprigs of tarragon are steeped in vinegar to produce tarragon vinegar.

Tarragon is used to flavor a popular carbonated soft drink in the countries of Azerbaijan, Armenia, Georgia and, by extension, Russia, Ukraine and Kazakhstan. The drink, named Tarhun, is made out of sugary tarragon concentrate and colored bright green.

In Slovenia, tarragon is used as a spice for a traditional sweet cake called potica. In Hungary a popular kind of chicken soup is flavored with tarragon. In Iran is used for a traditional Kufte Tabrizi which is delicious.

The names of tarragon on modern languages of Europe and Western Asia are: English *tarragon*, Finnish *rakuna*, Spanish *tarragona* and Iranian *tarkhun*.

An ethanolic extract of Russian tarragon, *Artemisia dracunculus* L., with antihyperglycemic activity in animal models was reported to decrease phosphoenolpyruvate carboxykinase (PEPCK) mRNA expression in STZ-induced diabetic rats. A quantitative polymerase chain reaction (qPCR) assay was developed for the bioactivity-guided purification of the compounds within the extract that decrease PEPCK expression. The assay was based on the inhibition of dexamethasone-

stimulated PEPCK upregulation in an H4IIE hepatoma cell line. Two polyphenolic compounds that inhibited PEPCK mRNA levels were isolated and identified as 6-demethoxycapillarisin and 2', 4'-dihydroxy-4-methoxydihydrochalcone with IC₅₀ values of 43 and 61 μM, respectively. The phosphoinositide-3 kinase (PI3K) inhibitor LY-294002 showed that 6-demethoxycapillarisin exerts its effect through the activation of the PI3K pathway, similarly to insulin. The effect of 2', 4'-dihydroxy-4-methoxydihydrochalcone is not regulated by PI3K and dependent on activation of AMPK pathway. These results indicate that the isolated compounds may be responsible for much of the glucose-lowering activity of the *Artemisia dracunculus* extract.

Essential Oil: French and Russian tarragon, *Artemisia dracunculus* L., leaves have glandular hairs distributed over the whole surface and secretory cavities arranged in files along the major veins in the mesophyll. Chemical composition analysis of leaves, leaf epidermis, and leaf mesophyll by hydrodistillation

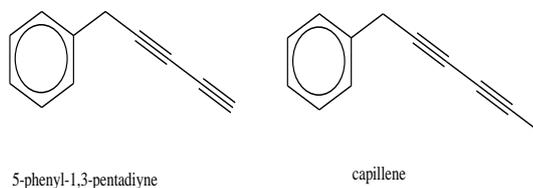


Figure 2: Molecular structure of 5-phenyl-1, 3-pentadiyne and capillene

***Artemisia fragrans* Willd.²⁷**

Essential Oil

Hydrodistillation of leaves and roots of *Artemisia fragrans* Willd. Yielded 0.9% and 0.1% (v/w) essential oils, respectively. GC/MS analysis allowed identification of 19 components, which made up 91.1% of the total oil from the leaves, while only 9 compounds (93.8%) were identified in the roots. The main components of the leaf oil were chrysanthenon (23.8%), 1, 8-cineole (23.7%), β-caryophyllene (9.6 %), *p*-cymene (7.7 %), filifolide-A (5.7%) and filifolone (5.7%). In the root oil, the main constituents were camphor (67.0%) and camphene (16.9%). Antibacterial activity was tested against Gram-positive and Gram-negative bacteria using the agar

and solvent extraction indicate quantitative differences in composition between the epidermis and the mesophyll. The main components in the essential oils, methyl chavicol in French tarragon and elemicin and methyl eugenol in the Russian tarragon, were observed to accumulate primarily in the mesophyll.

The volatile oil of *Artemisia dracunculus* L. var. *dracunculus* grown in Oregon was obtained by steam distillation and analyzed by GC/MS. The chemical composition of the oil was very different than the typical oil of tarragon (*Artemisia dracunculus* L. var. *sativa*), with very little (0.1%) methyl chavicol detected. The main components found were terpinolene (25.4%) and (Z)-β-ocimene (22.2%). Perhaps the most interesting characteristic of the oil was the presence of two unusual and rarely occurring alkynes, 5-phenyl-1,3-pentadiyne (11.7%) and 6-phenyl-2,4-hexadiyne (also capillene)(4.8%).(Fig. 2).

diffusion method. Activity was observed against both Gram-positive and one Gram-negative bacteria.

The twiglets of *Artemisia fragrans* Willd were collected from Tabriz in northwestern Iran and hydrodistilled to produce a light-yellow oil in a yield of 1.3%. The oil was analyzed by GC/MC. Twenty-eight compound were identified, among which 1, 8-cineole (52.1%) and α-thujone (34.8%) were the major constituents.

***Artemisia haussknechtii* Boiss^{28, 29, 30}**

Essential Oil

The water distilled essential oils from aerial parts of *A.haussknechtii* Boiss has been analyzed by a combination of GC/MS. In the oil of *A.haussknechtii*

1,8-cineole (16.5%), camphor (14.5%) and Artemisia ketone (10.5%) were found to be the major constituents. Another study Investigate chemical composition of the essential oil of *A.haussknechtii*. Also potential antioxidant and anti microbial activities of the essential oil and ethanolic extract were studied Antioxidant activity was evaluated by methods; namely DPPH, free radical scavenging, FTC system and total phenolic compounds analyzing. The antimicrobial activities of the extract were individually tested against a panel of microorganisms using disc diffusion method and MIC (minimum inhibitory concentration) measurement. Results: Forty-eight components were identified constituting 98.4% of total oil. Camphor (12.4%), α -Terpineol (9.9%), Davana bis ether (6.2%), and Bornyl acetate (3.8%) were the major components. (Fig.3) Good antioxidant activity of extract; increasing with the increment of concentration of plant extract was revealed. Ethanolic extract of *A.haussknechtii* inhibited both Gram-positive and Gram-negative bacteria. MIC of the extract against yeast was the lowest (2.5 μ g/ml). A novel

method for extraction and analysis of volatile compounds of *Artemisia haussknechtii* Boiss., using simultaneous hydro-distillation and static headspace liquid micro extraction followed by gas chromatography-mass spectrometry (SHD-SHLPME-GCMS) is developed. SHLPME parameters including nature of extracting solvent, headspace volume and design, extraction time, sample weight and micro drop volume were optimized. Comparison of hydro-distillation gas chromatography-mass spectrometry and HD-SHLPME-GCMS showed that the latter method is fast, simple, inexpensive and effective for the analysis of volatile compounds of aromatic plants. By using this method, 56 compounds were extracted and identified for *Artemisia haussknechtii* Boiss. The main constituents of its essential oil that were extracted by HD-SHLPME-GCMS method, include camphor (41.01%), 1,8-cineol (32.35%), cis-davanone (3.68%), 4-terpineol (2.99%), linalool (2.84%), beta-fenchyl alcohol (2.72%), and borneol (2.58%).

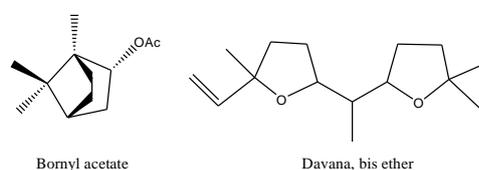


Figure 3: Structure of Bornyl acetate and Davana, bis ether

***Artemisia persica* Boiss**^{31, 32, 33, 34 35}

Essential oil:

Sixty constituents were identified in essential oil from aerial parts, leaves, flowers and roots of *Artemisia persica* Boiss. from Iran. The oils were obtained by hydrodistillation and the composition of the oils were analysed by a combination of GC and GC/MS. The oils obtained from aerial parts were rich in (Z)-ocimene (38.8%), ascaridole (16.0%) and α -terpinene (10%). The major components of the leaves oil were cis-sabinene hydrate (38.8%) and terpinolene (13.3%). The flowers oil was characterized by higher amounts of cis-sabinene hydrate (41.2%) and ethyl-2-nonyloate (24.4%). β -cedren-9-one (76.7%) was the predominate

compound in the roots oil. The steam – distilled essential oil from *Artemisia persica* growing wild in Iran was analyzed by GC/MS. In all 50 compounds were identified; Davanone (60.6%), Cis Chrysanthenyl acetate (8.6%), Limonene (5.7%), α - Pinene (3.7%), Davanone ether isome- (3.6%) and a Thujene (3.6%) were the main components of the oil respectively.

The essential oil from *Artemisia persica* (compositae) from Ladakh, India was found to contain mainly functionalized monoterpenes with artemisyl (*Artemisia* ketone, yomogi alcohol) and thujyl skeleton (sabinene, trans- sabinol, cis and trans- sabinene hydrate, α - and β - thujone, thujenal , trans- sabinyl acetate).

The roots of *Artemisia persica* afforded in addition to isofraxidin-derived sesquiterpene ethers, the scopoletin farnesyl ether scopofarnol and a new scopoletin dimethyl ether scopodrimol A. The structures and stereochemistries were elucidated by spectroscopic methods. According to the leaf morphology the accumulation of coumarin sesquiterpene ethers also suggests that the species should be transferred from the section Absinthium to the section Abrotanum.(Fig. 4)

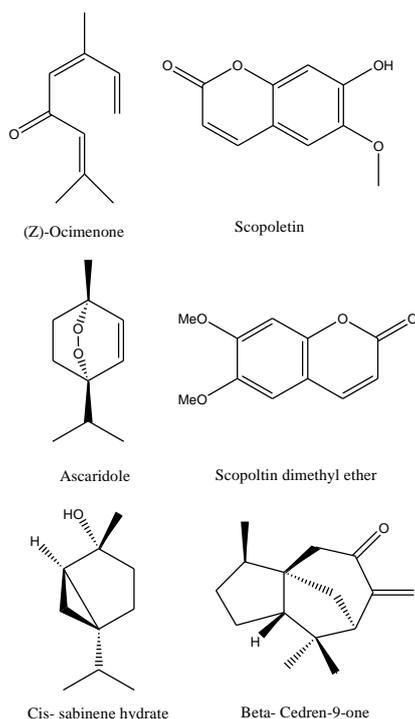


Figure 4: Structures from components of *Artemisia persica*. Boiss.

An experimental protocol was designed to investigate the total flavonoids, phenolics and antioxidant potential of methanol extract of *Artemisia persica*. For initial screening of antioxidant activity DPPH on TLC was employed. After the qualitative confirmation of antioxidant potential, spectroscopic measurements were made through DPPH assay. Free fatty acids (FFA), peroxide values (PV) and Iodine values were monitored in refined, bleached and deodorized (RBD) sunflower oil. Plant extract was found to possess strong antioxidant potential in all mentioned assays. Total phenolic and flavonoids contents were 407 mg/g respectively.

CONCLUSION^{36, 37, 38, 39, 40}

As mentioned in this review Constituents and Biological Activities of some Iranian species including: *A.biennis*, *A.dracunculus* L., *A.fragrans* Wild, *A.hassknechtii* Boiss, and *A.persica* Boiss. have been described. *Artemisia* species produce at least three classes of compounds: Terpenoids especially Sesquiterpene lactones, Flavonoids and Polyacetylenes.

Most attention has been focused on sesquiterpene lactones. Recently we have prepared and submitted a review article, on some *Artemisia* species: *A. aucheri* Boiss., *A. austriaca* Jacq., *A. chamaemelifolia* Vill, *A. ciniformis* Krasch, *A. deserti* Krasch and *A. diffusa*. Krasch. A new type of Sesquiterpene lactone (Tehranolide) with the endoperoxide group that probably has the same effect of artemisinin or qinghaosu which has been found to be responsible for the anti malarial activity of *A. annua*. In morphology, the *Artemisia* genus is endowed with head-like inflorescences and is considered to be one of the most evolutionary taxa in the Dicotyledonae. This advancement in taxonomy may increase the chemical diversity as the advance species may synthesize more complex (cyclized, rearranged and/or oxygenated) secondary metabolites.

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