



ANGELICA SYLVESTRIS VAR. SYLVESTRIS L.: ESSENTIAL OILS AND ANTIOXIDANT ACTIVITY EVALUATION

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ABSTRACT

In this study, the essential oils and antioxidant activities of *A. sylvestris* var. *sylvestris* belongs to the Apiaceae family were evaluated. The essential oils from dried roots, leaves, flowers and fruits obtained by hydrodistillation were analyzed by Gas Chromatography and Gas Chromatography-Mass Spectroscopy, simultaneously. The volatile compounds were characterized by using *in-house* and commercially libraries. The major compounds were spathulenol (12.4%), germacrene D (10.6%), α -humulene (7.6%) in the leave essential oil; elemol (5.4%), 10-epi- γ -eudesmol (5.4%), spathulenol (4.8%) in the root oil; α -pinen (42.0, 23.2%) and β -phellandrene (25.5, 9.1%) in the flower and the fruit essential oils, respectively. The possible antioxidant activities of each essential oil were determined at *in vitro* conditions. Any essential oil at 10 mg/ml concentration showed DPPH• scavenging activity while the fruit essential oil was found to be most active against ABTS• radical. But this effect was lower than gallic acid.

Keywords: *Angelica sylvestris* var. *sylvestris*, Apiaceae, Essential oil, Antioxidant activity

1. INTRODUCTION

Apiaceae family (formerly called Umbelliferae), which has approximately 455 genera and 3751 species and usually spreads in temperate regions, is represented by 102 genus and 451 species in Turkey, according to Flora of Turkey. Later on, 4 genera and 53 species were added to Flora of Turkey [1-7]. Turkey is one of the largest centers of biodiversity for the family among Asian countries [8].

Species belonging to Apiaceae family are generally rich essential oil sources and also contain resin. Essential oil is found in the secretion channels located in all parts of fruit, leaf, root or plant. Some types of Apiaceae are used as both spices and food, and therefore their cultures are also made. Most of the species have economic value and are commercially important [9, 10]. Members of the Apiaceae family are among economically assessed species in the world and are widely used in food, animal feed, ornamental plants, health and cosmetics industries [11].

This family is very rich in terms of secondary metabolites. Coumarin [12, 13], flavonoid [13-15], acetylenic compounds [13], sesquiterpene lactones [16-18] and essential oils [19- 23] are obtained from many genera of the family.

More than 90 species of *Angelica* L. genus, one of the family members, are known. More than half of these species are used in traditional medicine [24].

Angelica sylvestris L. is known by names of ‘wild angelica, European wild angelica’, it is similar to *A. archangelica* L. in terms of their general characteristics. They grow on waterfronts and wetlands. *A. sylvestris* is among medicinal plants used for its roots. It tastes bitter, its scent is light and special. Its

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appetizing, bitter, diaphoretic, carminative and stimulant effects are known. It is also recorded that tea or tincture prepared from its roots are used against respiratory system and nervous system disorders, in cases of fever and colds. The tea is prepared by boiling 2 teaspoons of dry root, which is collected in spring and dried, into 1 cup of water for 5-10 min. and it is drunk as a cup a day. The use of powdered roots in a quarter or half a teaspoon and three times a day is also encountered in the sources. In ethnobotanical studies, uses of *A. sylvestris* have been indicated in cases of indigestion (Italy), disorders of digestive, respiratory and nervous systems, fever, infection and influenza (Austria), antipyretic (Thailand), analgesic, anticarcinogenic effect, arthritis and headache (China) [25-27]. In our country, jam is prepared from stems of this plant grown in the foothills of Bursa, Uludağ, and the plant is known to be fragrant [25].

In studies conducted with *Angelica sylvestris*, secondary metabolites such as simple coumarins and furanocoumarins (umbelliprenin, bergapten, isoimperatorin, aviprin, byakangelicin, imperatorin, xanthotoxol, bisabolangelone, 5- β -cyclohexenylpsoralen, 4-[(2,4,4-trimethyl-1-cyclohexen-1-yl)methoxy]-7H-furo[3,2-g][1]-benzopyran-7-one, 1'-*O*- β -D-glucopyranosyl-(2*S*,3*R*)-3-hydroxymarmesin) [28-31], sterols (sitosterol, stigmasterol, campesterol, cholesterol, stigmast-7-en-3-ol, ergosta-5,24-dien-3 α -ol, α -saccharostenon [32], essential oils (major compounds as (+)-globulol, limonene, α -pinene, farnesol, nonane, β -phellandrene) [26, 33-36] were defined. Studies conducted with essential oils of species and varieties are limited in numbers. In a study conducted in France, it was reported that the yield of essential oil was 0.17% in fresh roots of *A. sylvestris* var. *elatior* Wahlenb., there were nonane (18.7%), α -pinene (16.2%) and β -phellandrene (12.0%) as main compounds. The yields of the dried for one month and fresh root essential oils of *A. heterocarpa* Lloyd were calculated as 0.03% and 0.07%, respectively. The main compounds were characterized as nonane (5.2%), isoheptyl-2-methylbutyrate (3.1%) and 1-(5-methyl-furanyl)-but-1-en-3-one (2.4%) [33]. It was determined that fruit essential oil yield of *A. sylvestris* var. *vulgaris* Ave-Lallemant was 1.78%, and its main compounds were limonene (56.1%), α -pinene (16.2%) and α -bisabolol (% 5.8) [34]. From 22 compounds defined in essential oils of *A. sylvestris* L. seeds growing naturally in Serbia, limonene (66.6%) and α -pinene (19.0%) were detected as main compounds [35].

Two varieties of *Angelica sylvestris* grow in Turkey: *Angelica sylvestris* var. *sylvestris* L. and *A. sylvestris* var. *stenoptera* Lallemand. *A. sylvestris* var. *stenoptera* are endemic to Turkey and they grow in Rize. *A. sylvestris* var. *sylvestris*, on the other hand, spread in Northern Anatolia, and they grow in provinces of Bolu, İstanbul, Sinop, Trabzon, Bursa, Hatay, Maraş and Karabük in Turkey. Composition of essential oil obtained from hydrodistillation of the fruit of *Angelica sylvestris* L. var. *sylvestris* was examined by Özek et al. [26], α -pinene (25.6%), β -phellandrene (9.1%) and limonene (5.6%) were determined as main compounds [26].

Nowadays, the essential oils have been gained popularity in industries such as pharmaceuticals, food and cosmetics. Essential oils are complex mixtures that contain different compounds thus, they vary in their biological effects. The researches revealed the effects of various essential oils such as antibacterial, antifungal, antiviral, carminative, choloretic, sedative, diuretic, antispasmodic, analgesic and anticancer effects. In particular, practices of phytotherapy and aromatherapy also increase. This has increased the interest of researchers on essential oils [18, 37- 44].

There is literature information available on antibacterial [45- 48], antiinflammatory [46], antioxidant activities [45, 48] and general toxic effects [45] of several extracts of *Angelica sylvestris*. However, studies on its essential oils seem to be a limited in number [35].

Within the scope of this research, essential oil compounds in roots, leaves, flowers and fruits of *Angelica sylvestris* var. *sylvestris* were evaluated separately, and the possible antioxidant effects of each essential oil were examined *in vitro*.

2. MATERIAL AND METHODS

2.1. Chemicals, standards and analytical systems

Clevenger type apparatus for hydrodistillation (Ildam); UV-spectrophotometer (Shimadzu), microplate reader (BioTek Power Wave XS) and vortex (Heidolph reaxtop) for antioxidant assays; Gas Chromatography system (Agilent 6890 N GC) and Gas Chromatography-Mass Spectrometry (Agilent 5975 GC-MSD) were used for essential oil analyzes. Chemicals and standards: 1,1-diphenyl-2-picrylhydrazyl (DPPH[•]) (Aldrich), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) diammonium salt (ABTS) ≥ 98% (HPLC) (Sigma), Ethanol absolute (Riedel), Gallic acid (Sigma), Methanol Chromasolv (HPLC grade) (Sigma Aldrich), Sodium persulphate (Sigma), Trolox % 97 (Aldrich).

2.2. Plant Material

The plant was gathered from Bursa: Harmancık Village: from Küplü Hill to Ballisaray, near Ayıcık River and dampy road, Turkey (692118D, 4388556N, 985 m) in 2015. The plant was collected and identified by Prof. Dr. Hulusi Malyer. The herbarium samples were kept at Anadolu University, Pharmacy Faculty Herbarium with ESSE number 14712. The plant materials separated as roots, leaves, flowers and fruits were dried in the shade.

2.3. Hydrodistillation

The dry samples were subjected to hydrodistillation for 3 h by Clevenger type apparatus [49]. The yields of the essential oils were calculated on dry materials. The essential oils were kept at 4°C in amber vials.

2.4. Gas Chromatography (GC) and Gas Chromatography-Mass Spectrometry (GC-MS) Analyzes

GC-FID and GC-MS analyzes processes were performed with reference to Demirci et al. [49].

2.5. Antioxidant Activity Evaluation

2.5.1. 1,1-Diphenyl-2-picrylhydrazyl (DPPH[•]) radical scavenging activity

The DPPH radical scavenging assay was performed according to Duymuş et al. [50]. Gallic acid was used as positive control. The percentage inhibition was calculated.

2.5.2. Trolox equivalent antioxidant capacity (TEAC assay)

This assay assesses the capacity of a compound to scavenge the stable ABTS radical in comparison to the antioxidant activity of Trolox, a water-soluble form of vitamin E that is used as a standard. The TEAC assay was performed according to Duymuş et al. [50].

3. RESULTS

3.1. The Yields of the Essential Oils

The yields of the essential oils were calculated as 0.08% for leaves; 0.52% for flowers; 1.1% for fruits and 0.16% for roots.

3.2. The Essential Oil Analyzes

The each essential oil was analyzed by GC and GC-MS systems, simultaneously. The volatile compounds were characterized by using in house “Baser Library of Essential Oil Constituents” and commercially libraries “Adams Library, MassFinder Library, Wiley GC/MS Library [51- 53]. The identifications were accomplished by comparison of retention times with authentic samples or by comparison of their relative retention index (RRI) to series of *n*-alkanes (C₈-C₂₁). The identified volatile compounds, RRI values and relative percentages were given in Table 1.

Table 1. *Angelica sylvestris* var. *sylvestris* essential oil compositions

RRI	Compound	A (%)	B (%)	C (%)	D (%)
1032	α-Pinene	-	23.2	42.0	1.7
1035	<i>α</i> -Tujene	-	0.3	-	-
1076	Camphene	-	2.7	4.8	0.5
1118	<i>β</i> -Pinene	-	1.4	1.7	0.1
1132	Sabinene	-	6.9	1.4	0.1
1174	Myrcene	-	2.8	4.4	3.7
1176	<i>α</i> -Phellandrene	-	1.0	1.0	-
1183	Pseudolimonene	-	0.3	0.2	-
1188	<i>α</i> -Terpinene	-	0.2	-	-
1203	Limonene	0.4	3.4	4.2	1.3
1218	β-Phellandrene	0.5	34.5	25.5	0.5
1244	2-Pentylfuran	-	-	-	tr
1246	(<i>Z</i>)- <i>β</i> -Ocimene	tr	-	-	-
1255	<i>γ</i> -Terpinene	-	0.4	0.2	-
1266	(<i>E</i>)- <i>β</i> -Ocimene	tr	-	-	-
1280	<i>p</i> -Cymene	0.7	1.9	1.0	0.1
1286	2-Methylbutyl-2-methylbutyrate	-	tr	0.1	0.2
1296	Octanal	-	-	-	0.6
1290	Terpinolene	-	tr	0.2	-
1299	2-Methylbutyl-3-methylbutyrate	-	-	0.1	3.0
1457	Hexyl isovalerate	-	-	-	0.3
1495	Bicycloelemene	1.4	-	-	-
1535	<i>β</i> -Bourbonene	0.6	-	-	-
1549	<i>β</i> -Cubebene	0.5	-	-	-
1590	Bornyl acetate	0.9	2.7	4.1	2.9
1600	<i>β</i> -Elemene	1.6	tr	0.2	2.1
1610	<i>β</i> -Copaene	1.2	-	-	-
1611	Terpinen-4-ol	-	0.9	0.3	-
1612	<i>β</i> -Caryophyllene	0.6	-	-	-
1638	<i>β</i> -Cyclocitral	0.3	-	-	-
1650	<i>γ</i> -Elemene	0.9	-	-	0.5
1659	<i>γ</i> -Gurjunene	0.4	-	-	-
1669	Sesquisabinene	0.3	-	-	-
1687	α-Humulene	7.6	-	0.2	1.3
1688	Selina-4,11-diene	-	-	-	tr
1690	Cryptone	-	1.7	1.1	-
1704	<i>γ</i> -Muuroolene	0.8	-	-	0.3
1719	Borneol	0.4	-	0.1	-
1726	Germacrene D	10.6	-	0.3	1.2
1740	<i>α</i> -Muuroolene	0.6	-	-	1.4
1744	<i>α</i> -Selinene	0.4	-	-	1.8
1744	Phellandral	-	-	0.2	-
1755	Bicyclogermacrene	3.5	-	-	1.1
1762	<i>α</i> -Chamigrene	1.0	-	-	-
1765	Geranyl acetate	0.2	8.4	-	-
1773	<i>δ</i> -Cadinene	1.0	-	-	2.0
1776	<i>γ</i> -Cadinene	-	-	-	0.8
1796	Selina-3,7(11)-diene	-	-	-	0.1
1797	Aromadendra-1(10),4-(15) diene	0.2	-	-	-
1802	Cumin aldehyde	-	0.2	-	-

1802	(E, E)-2,4-Decadienal	0.3	-	-	-
1811	<i>p</i> -Mentha-1,3-dien-7-al	-	0.2	-	-
1838	(E)- β -Damascenone	0.2	-	-	-
1853	Calamenene	0.6	-	-	-
1854	Germacrene B	-	-	0.3	2.6
1857	Geraniol	-	1.1	-	-
1868	(E)-Geranyl acetone	0.9	-	-	-
1900	<i>epi</i> -Cubebol	0.2	-	-	-
1933	Neophytadiene isomer	1.3	-	-	-
1942	4-Hydroxy-2-methyl acetophenone	3.6	2.6	3.6	1.7
1957	Cubebol	0.4	-	-	-
1958	(E)- β -Ionone	0.9	-	-	-
2037	Salvial-4(14)-en-1-one	0.9	-	-	-
2053	Germacrene D-1,10-epoxide	0.2	-	-	-
2071	Humulene epoxyde II	2.3	-	-	0.6
2080	Cubebol	-	-	-	0.1
2080	1,10- <i>diepi</i> -Cubebol	-	-	-	0.1
2081	Humulene epoxide III	0.5	-	-	-
2084	Octanoic acid	-	-	-	0.3
2094	<i>p</i> -Cresol	-	0.7	0.5	-
2096	Elemol	-	-	-	5.4
2103	Guaiol	-	-	-	4.1
2127	10-<i>epi</i>-γ-Eudesmol	-	-	-	5.4
2130	Salviadienol	0.7	-	-	-
2131	Hexahydrofarnesyl acetone	0.6	-	-	-
2144	Spathulenol	12.4	-	0.2	4.8
2179	3,4-Dimethyl-5-pentyliden-2-(5H)-furanone	0.6	-	-	-
2209	T-Muurolol	0.4	-	-	0.3
2232	α -Bisabolol	-	0.1	0.6	-
2237	Valerianol	-	-	-	3.5
2247	<i>trans</i> - α -Bergamotol	1.0	-	-	-
2248	Bulnesol	-	-	-	4.1
2250	α -Eudesmol	-	-	-	3.0
2255	α -Cadinol	0.6	-	-	3.6
2257	β -Eudesmol	-	-	-	3.0
2273	Selina-11-en-4 α -ol	-	-	-	1.2
2278	Torrilenol	1.0	-	-	-
2368	Eudesma-4(15)-7-dien-1- β -ol	1.7	-	-	-
2392	Caryophyllenol II	1.2	-	-	-
2500	Pentacosane	0.4	-	-	-
2503	Dodecanoic acid	0.3	-	-	-
2568	14-Hydroxy- α -muurolene	0.1	-	-	-
2607	1-Octadecanol	0.7	-	-	-
2607	14-Hydroxy- δ -cadinene	0.3	-	-	-
2622	Phytol	3.6	-	-	-
2670	Tetradecanoic acid	0.4	-	-	-
2822	Pentadecanoic acid	0.2	-	-	-
2931	Hexadecanoic acid	4.3	-	0.2	-
Total		79.4	97.6	98.7	66.4

(A), leaves; (B), fruits; (C), flowers; (D), roots; RRI, Relative retention time indices were calculated according to *n*-alkane series; %, relative percentages were calculated according to FID data; tr: trace amount (< % 0.1).

Fifty nine volatile compounds were characterised representing 79.4% of the leave oil. Spathulenol (12.4%), germacrene D (10.6%) and α -humulene (7.6%) were found as major compounds. Sesquiterpenes were the major group in the leave essential oil. Bicycloelemene, β -elemene, β -copaene, bicyclogermacrene, α -chamigrene, δ -cadinene, neophytadiene isomer, 4-hydroxy-2-methyl acetophenone, humulene epoxide II, *trans*- α -bergamotol, torrilenol, eudesma-4(15)-7-dien-1- β -ol, caryophyllenol II, phytol and hexadecanoic acid were other major compounds.

Twenty six compounds were characterized in the fruit essential oil representing by 97.6% of the oil. Monoterpenes such as α -pinene (23.2%) and β -phellandrene (34.5%) were the main group in the oil. In

the same time, the relative percentages of camphene, β -pinene, sabinene, myrcene, α -phellandrene, limonene, *p*-cymene, bornyl acetate, cryptone, geranyl acetate, geraniol ve 4-hydroxy-2-methyl acetophenone were calculated more than 1% of the oil.

Twenty eight compounds were detected in the flower oil representing by 98.7% of the oil. α -Pinene (42%) ve β -phellandrene (25.5%) were the major. Also, camphene, β -pinene, sabinene, myrcene, α -phellandrene, limonene, *p*-cymene, bornyl acetate, cryptone and 4-hydroxy-2-methyl acetophenone were found as >1% of the oil.

Forty three compounds were identified in the root essential oil (66.4%). Oxygenated sesquiterpenes such as elemol (5.4%), 10-epi- γ -eudesmol (5.4%) and spathulenol (4.8%) were the major compounds. The relative percentages more than 1% compounds were α -pinene, myrcene, limonene, 2-methylbutyl-3-methylbutyrate, bornyl acetate, β -elemene, α -humulene, germacrene D, α -muurolene, α -selinene, bicyclogermacrene, germacrene B, 4-hydroxy-2-methyl acetophenone, guaiol, valerianol, bulnesol, α -eudesmol, α -cadinol, β -eudesmol and selina-11-en-4 α -ol.

3.3. Antioxidant activity results

3.3.1. DPPH radical scavenging activity

The IC₅₀ values of tested essential oils except the leaves oil were calculated as more than 10 mg/ml. The leave essential oil had no radical scavenging activity at 2 mg/ml, therefore, the IC₅₀ value was not calculated. The radical scavenging activity was calculated for gallic acid as IC₅₀ value at 0.007 \pm 0.0004 mg/ml. According to results, any essential oil showed DPPH radical scavenging activity.

3.3.2. TEAC assay

The each essential oil was tested at two different concentrations (1 and 10 mg/ml). Any essential oil at 1 mg/ml was not effective against ABTS radical. At 10 mg/ml concentration, the most active essential oil was the fruit oil. The TEAC value was calculated as 1.74 \pm 0.3 mM for the fruit essential oil while the TEAC value of the gallic acid was 2.77 \pm 0.05 mM even at 1 mg/ml.

4. CONCLUSION and DISCUSSION

As a result of review on *Angelica sylvestris* var. *sylvestris* which grows commonly in Turkey, it was determined that there are not many studies available on this subject.

In a study conducted on its fruits, compounds of fruit essential oils obtained by different methods were compared. According to this source, the main compounds of essential oil obtained by hydrodistillation are α -pinene (25.6%) and β -phellandrene (9.1%) [26]. In this study, it was determined that essential oil obtained by hydrodistillation of fruits similarly carried α -pinene (23.2%) and β -phellandrene (34.5%) as main compounds. This composition also shows similarity to the fruit essential oils of *A. archangelica* species, which are widely used medically [54]. *A. sylvestris* var. *vulgaris* fruit essential oil also includes limonene (56.1%) and α -pinene (11.3%), and it is similar to other subspecies as an essential oil rich in monoterpenes [34].

The amount of essential oil obtained from the roots is 0.16%. Although this amount is close to the amount of essential oil of *A. sylvestris* var. *elatior* (the essential oil yield, 0.17%) in literature [55], it is different from this subspecies containing an oil rich in monoterpene in terms of compound. Root essential oil obtained within the scope of this research was found to be rich in sesquiterpenes.

Uses of leaves and flower states of *A. sylvestris* var. *sylvestris* as a plant material were not found in any studies. Spathulenol, germacrene D and α -humulene were identified as main compounds in leaf essential oil. Sesquiterpenes are the major group in leaf essential oil, which is similar to root essential oil. In the flower essential oil, α -pinene (42%) and β -phellandrene (25.5%) were identified as major compounds, and the composition of the flower essential oil was found different from leaves and similar to fruit essential oils.

Only one study on antioxidant activity of *Angelica sylvestris* was found in literature [56]. In that study, the antioxidant activity of methanol extract of *A. sylvestris* sections above soil was examined, and a significant effect was not determined compared with positive controls in experiment systems. As part of our project, it was determined that *A. sylvestris* var. *sylvestris* essential oils had also low in antioxidant activity, similar to the activity results mentioned in the literature. Although the experimental systems and extraction procedures differ from each other, when the findings were examined, it is the common finding of two studies that *A. sylvestris* was not a potential antioxidant source.

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