Achillea eriophora DC.: An ethnobotanical, pharmacological and phytochemical review

Toktam Mohammadi, Atefeh Pirani, Hamid Moazzeni and Jamil Vaezi

Review

Abstract

Background: *Achillea eriophora* DC. (Asteraceae) is a less-known medicinal plant endemic to South and East Iran. It is traditionally used for treating a variety of health problems by local people. This review aims to provide up-to-date information on *A. eriophora*, including its traditional uses, phytochemistry, and pharmacological properties, in exploring future therapeutic and scientific potentials.

Methods: The information on ethnobotany, phytochemistry, and pharmacological aspects of *A. eriophora* was collected from the scientific literature databases, Iranian Pharmacopoeia, published books, Ph.D. and MS dissertations.

Results: *Achillea eriophora* is traditionally considered to have antipyretic, diuretic, and carminative effects. It is also used to treat digestive problems, diarrhea, fever, diabetes, bone pain, wounds, and insect bite. It has considerable pharmacological properties, including antimicrobial, hypotensive, wound healing, and antioxidant. A total of 128 compounds such as terpenes, sesquiterpenes, alcohols, esters, and phenols have been isolated from this species. Its major chemical components are 1,8-cineole and camphor.

Conclusions: The high number of isolated constituents signify considerable pharmacological properties of *Achillea eriophora*. The present pharmacological investigations of this plant are limited and often lack exact information on active compounds and their mechanisms of action. Most of the medicinal properties attributed to *A. eriophora*, such as healing digestive disorders, fever, and diabetes have not yet been investigated and proven under a scientific study. This highlights the importance of *A. eriophora* as a valuable candidate for future studies on medicinal plants. Due to its wide range of traditional uses, the whole plant parts of *A. eriophora*, including roots, are harvested by local communities. Therefore, a conservation planning for this threatened species is needed.

Keywords: *Achillea*, Asteraceae, digestive disorders, ethnobotany, Iran, phytochemistry, pharmacology

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Background

The family Asteraceae includes a considerable number of genera traditionally used as herbal medicines (Saeidnia *et al.* 2011, Suntar 2014). *Achillea* L. is among the large genera of Asteraceae, best known for its nice fragrant smell (Misra & Misra 2017) and medicinal properties. It is distributed throughout the Mediterranean region and Eurasia. *Achillea* species inhabit various natural ecosystems, including deserts (*A. tomentosa* L., *A. micrantha* Willd.), wetland habitats (*A. ageratum* L., *A. impatiens* L., *A. pyrenaica* Sibth. ex Godr.), seashore (*A. millefolium* L.) and the sub-nival zone of high mountains (*A. clusiana* Tausch) (Ehrendorfer & Guo 2006, Misra & Misra 2017, Tutin *et al.* 1976). A high number of *Achillea* species are endemics restricted to certain geographical ranges (*A. aucherii* Boiss., *A. eriophora* DC., and *A. pachycephala* Rech.f. which

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are endemic to Iran), while the others extend over a vast geographical region (*A. millefolium* and *A. alpina* L.) (Mozaffarian 2008, Rechinger 1986, Tutin *et al*. 1976).

Achillea represents a high therapeutic potential that its identification dates back to 6500 B.C. as it was found in a Middle Paleolithic grave at Shanidar (Leori-Gourhan 1975, Lietava 1992, Solecki 1975). Homer and Plinius considered *Achillea* as useful for wounds (Lietava 1992) and Dioscorides used *Achillea* for dysentery (Ross 2003). Anglo-Saxons used *Achillea* (*A*. *millefolium*) as a panacea (Lietava 1992). *Achillea* species are currently known to exhibit a wide range of pharmacological properties including antioxidant, antimicrobial, antibacterial, anti-inflammatory, antispasmodic, diaphoretic, diuretic and herbicidal (Barbour *et al.* 2004, Cakilcioglu *et al.* 2011, Giorgi *et al.* 2009, Hegazy *et al.* 2008, Konyalioglu & Karamenderes 2005, Karamenderes & Apaydin 2003, Maggi *et al.* 2009, Mohammadhosseini *et al.* 2017, Ozlem *et al.* 2006, Yaeesh *et al.* 2006). The most used and cited medicinal species of *Achillea* is *A. millefolium* (Applequist & Moerman 2011, Banh-nhu *et al.* 1979, Benedek *et al.* 2008, Falk *et al.* 1975, Kindlovits & Nemeth 2012). It is one of the most significant economic plants of Anatolia. Herbal teas prepared from *A. millefolium* are traditionally used for abdominal pain and flatulence in Turkey (Honda *et al.* 1996).

Iran, with a rich flora of over 8000 plant species, hosts many endemics and unique species of medicinal plants from the family Asteraceae (Ghahremaninejad & Nejad-Falatoury 2016, Mohammadhosseini *et al*. 2017). *Achillea* is represented in Iran by 18 species, among which 10 are endemics (Mozaffarian 2008). Fourteen species of the genus are considered as medicinal plants in Iran, of which *A. millefolium*, *A. tenuifolia* Lam., and *Achillea santolinoides Lag.* subsp. *wilhelmsii* (K.Koch) Greuter (Formerly known as *A*. *wilhelmsii* K.Koch) are more popular (Ghorbani 2005, Hamzeloo-Moghadam *et al.* 2015, Khosravitabar *et al.* 2017, Mosaddegh *et al.* 2012, Nadaf *et al.* 2019). *Achillea eriophora* is another popular species extensively used by local people and traditional healers as a medicinal plant. This species is distributed in South and East Iran. It is mostly misidentified as *A*. *santolinoides* subsp. *wilhelmsii* due to morphological similarities (see below).

The aims of this study are: (1) to highlight *A. eriophora* as a valuable medicinal plant by reviewing its pharmacological and phytochemical aspects, (2) to give an overview of traditional knowledge about *A. eriophora* and its uses.

Materials and Methods

We performed a review on *A. eriophora* using articles and books that were published until August 2019. We considered different online and offline resources, including journals and books published in English and Persian. Information was collected from medicinal plants textbooks, ethnobotanical, pharmacological and phytochemical studies, and scientific databases, including PubMed, Scopus, EBSCO, Science Direct, ResearchGate, Tropicos, Academia, Google Scholar, Ph.D. and MSc dissertations. Since *A. eriophora* is an endemic species, ethnobotanical surveys on this species are limited. Therefore, we considered all publications on traditional and folklore medical uses of *A. eriophora*. Regarding pharmacological and phytochemical data, we tried to use more recent publications as well as a few older ones to highlight some important points. The distribution maps are prepared using the species incidence data in ArcMap 10.3 (Esri, 2011).

Botany, etymology and vernacular names of *Achillea eriophora*

Achillea eriophora is endemic to the south and east of Iran. This species belongs to the Irano-Turanian and Sahara-Sindian floristic regions. It inhabits altitudinal ranges of 700 to 2000 m in Fars, Hormozgan, Khorassan, Khuzestan, Sistan and Baluchestan, and Yazd provinces (Fig. 1). *Achillea eriophora* is a perennial herb with woody branches at the base covered with dense woolly hairs. The stem is 25-55 cm high. Leaves are linear, pinnatipartite. The inflorescence is a dense corymb. Capitules are 10-20, sessile or with a short peduncle (2 mm). Ligulate and disc flowers are present; ligulate flowers are yellow, trilobate; disc flowers 4-9, 3-3.5 mm long (Fig. 2) (Mozaffarian 2008, Rechinger 1986). The flowering period of *A. eriophora* is from May to June (Ghahraman 1989). It prefers warm and sunny habitats (Ghani *et al.* 2008). Ploidy level of *A. eriophora* has been recorded as diploid (2n = 2x = 18) (Sheidai *et al.* 2009).

The genus *Achillea* is named after Achilles, the Greek hero of the Trojan War, as he used the leaves of *Achillea* to check the bloodstream and treat the wounds of his soldiers (Applequist & Moerman 2011, Chandler *et al.* 1982, Harvey 1982, Iranshahr 2007). The specific epithet “eriophora” comes from Greek origin. The prefix erio- in Greek means wool and the suffix -phorum or -phorus means carrying. So, “eriophorus” means wool-bearing (Stearn 2004), which refers to the tomentose-lanate appearance of *A. eriophora*.

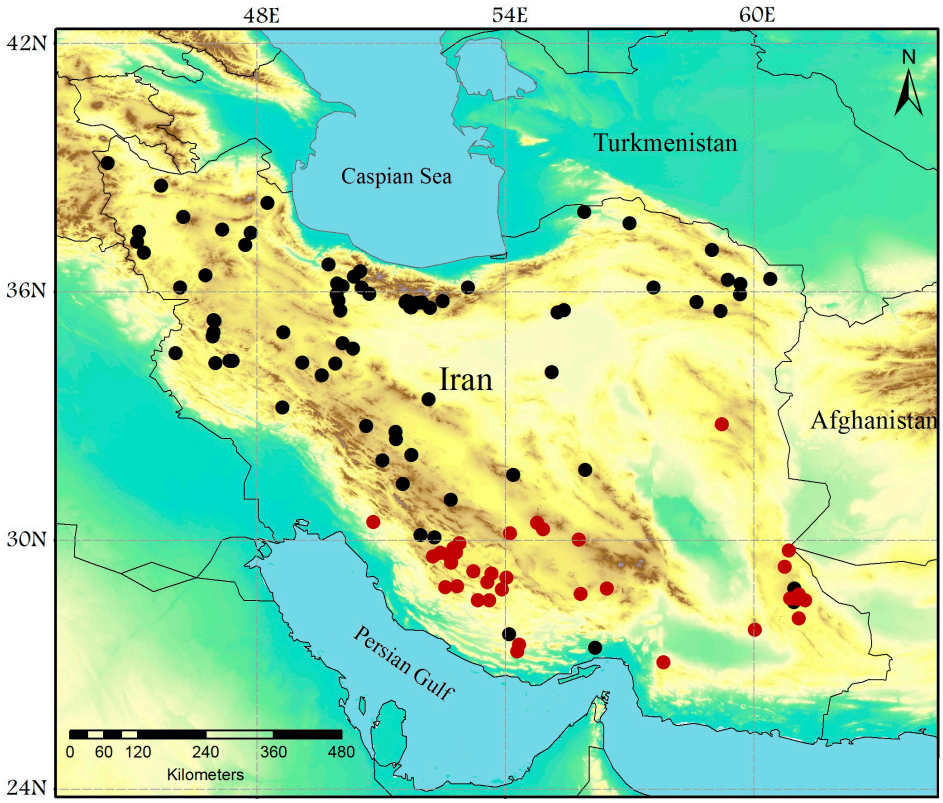

Figure 1. Distribution map of *A. eriophora* (in red) and *A. santolinoides* subsp. *wilhelmsii* (in black) in Iran.

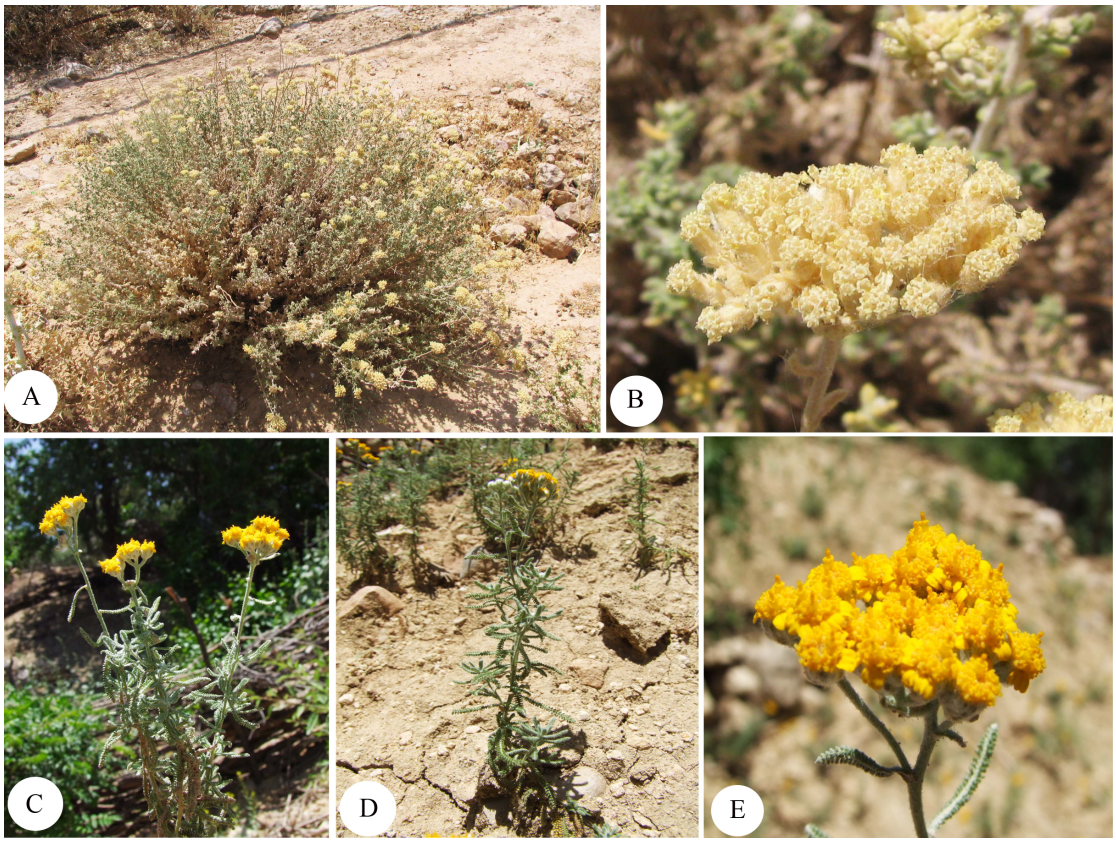

Figure 2. A-B: *Achillea eriophora*, A. habit, B. inflorecence. C-E. *A. santolinoides* subsp. *wilhelmsii*, C-D. habit. E. inflorescence.

Different species of *Achillea* are commonly called Bumadaran (buːmɑːdærʌn) in Persian (Moein *et al.* 2015, Sadat-Hosseini *et al.* 2017, Zargari 1996). *Achillea eriophora* is known as Boumadaran-e Jonoubi, Boumadaran-e Shiraz or Sarzardou (Mozaffarian 1996), Berenjasf (Safa *et al.* 2013), Bozhana (Azizi & Keshavarzi 2015), Zanboul and/or Zamboul (Maleki & Akhani 2018) in different parts of South Iran. Moreover, People in Birjand and its adjacent villages (South Khorassan province), call *Achillea eriophora* as 'Kalpoureh'. Interestingly, 'Kalpoureh' is used as the common name for *Teucrium polium* L. (Lamiaceae) in most parts of Iran. Although *T. polium* is a well-known medicinal plant, it is absent in South Khorassan province. The identical common name for these two species might have arisen from the similarity of their local uses (Mohammadi *et al*., in prep.). Table 1 lists all local names documented for *A. eriophora*.

Table 1. Vernacular names of *Achillea eriophora* in Iran.

Province/ Area	Vernacular name(s)	Reference(s)
Kerman, Sirjan	Boumadaran	(Sharififar *et al.* 2011)
Bushehr, Helleh River	Sar-berenjas (berenjasf)	(Rastegar *et al.* 2012)
Hormozgan	Benjerashk, Berenjasf, Sarzardu	(Safa *et al.* 2013)
North-east watershed of Persian Gulf	Bimadaroun	(Dolatkhahi & Nabipour 2014)
Kerman, Baft	Boumadaran-e-jonoubi, Berenjasf	(Mehrabani *et al.* 2014)
Kerman, Joupar	Boumadaran	(Sharififar *et al.* 2014)
Western Azerbaijan, Sardasht	Bozhana	(Azizi & Keshavarzi 2015)
Fars, Darab	Boomadaran	(Moein *et al.* 2015)
Kerman, Khabr and Rouchon region	Boumadaran	(Mohamadi *et al.* 2015)
Bushehr, Southwest Mand mountain	Sar-berenjasf	(Lavari *et al.* 2017)
South of Kerman	Boumadaran	(Sadat-Hosseini *et al.* 2017)
Fars, Jahrom	Boomadaran-e Gol Sefidoo	(Khajoei Nasab & Esmailpour 2018)
Sistan and Baluchestan, Mountain Taftan	Zanboul and/or Zamboul	(Maleki & Akhani 2018)
South Khorassan, Birjand	Kalpoureh	(Unpublished data, Mohammadi *et al*.)

Achillea eriophora is mostly misidentified with *A. santolinoides* subsp. *wilhelmsii* by local people. *Achillea eriophora* occurs only in Iran, while the latter has a broader distribution area ranging from North Africa and East Mediterranean to central Asia (POWO, 2019). Distribution ranges of *A. eriophora* and *A. santolinoides* subsp. *wilhelmsii* overlap in south of Iran (Fig. 1). They also have morphological similarities. Therefore, the local inhabitants of South Iran mostly attribute the same common name (Bumadaran, Berenjasf; see Table 1) to both species. Due to the nominal and morphological similarities between *A. santolinoides* subsp. *wilhelmsii* and *A. eriophora* (Fig. 2), and co-occurrence of both species in several parts of South Iran, local people usually do not distinguish between them and use both species for common purposes. Only practiced traditional healers recognize them as separate. This uncertainty has partly led *A. eriophora* to be underestimated by recent literature.

Traditional medicine and ethnobotany

The aerial plant part of *Achillea eriophora* (stem, leaf and flower) is considered as diuretic and antipyretic, and best known for healing digestive disorders in Iranian traditional medicine (Amin 1991). In the recent decade, a few numbers of ethnobotanical studies have been conducted in South Iran documenting new aspects of medicinal usage of *A. eriophora*. The results of these studies are summarized in Table 2. Based on these data, the mostly used plant part of *A. eriophora* is the aerial part (Khajoei Nasab & Esmailpour 2018, Maleki & Akhani 2018, Sadat-Hosseini *et al.* 2017, Azizi & Keshavarzi 2015, Moein *et al.* 2015, Mohamadi *et al.* 2015, Dolatkhahi & Nabipour 2014, Mehrabani *et al.* 2014, Safa *et al.* 2013, Sharififar *et al.* 2011; 2014). Application of roots is reported only in Taftan mts (Sistan and Baluchestan province) by Maleki and Akhani (2018). Moreover, these data indicate that digestive complains and fever are the most common problems trated using *A. eriophora* by folk medicine. The other disorders include diabetes, menstrual cramps, bone pain, insect and snake bite, common cold, wound healing. Anti-epileptic and diuretic effects have been mentioned by single studies (Sadat-Hosseini *et al.* 2017, Mehrabani *et al.* 2014, respectively). The common modes of preparation of this species are decoction and powder, followed by maceration and bath and poultice. Administration of flowers' smoke is reported only by Khajoei Nasab and Esmailpour (2018). Although the preparation method(s) by Iranian traditional medicine is not mentioned in detail (Amin 1991), it seems that the administration mode of the plant is oral. Routes of administration have been recorded by few ethnobotanical studies documenting both oral and topical uses of the plant.

Table 2. Ethnobotanical uses regarding *Achillea eriophora* in Iran.

Plant part used	Preparation mode(s)	Medicinal uses	Routes of administration	Reference (s)
Stem	Maceration, decoction, baths, powder	Bellyache, stomach cramps, diarrhea, vomit, nausea, food poisoning, stomachache, fever, digestion, diabetes, bone pain	-	(Maleki & Akhani 2018)
Leaves	-	Anti-colic, anti-diarrhea, carminative, treatment of stomach problems, and treatment of menstrual cramping	-	(Sharififar *et al.* 2011)
	Poultice, powder	Anti-pyretic, treatment of insect bite, bee bite, snake bite, scorpions bite, and wound healing	-	(Safa *et al.* 2013)
	Poultice, powder	Anti-pyretic, treatment of insect bite, and bee bite	Powder (oral), poultice (topical)	(Dolatkhahi & Nabipour 2014)
	-	Anti-diarrhea		(Azizi & Keshavarzi 2015)
	Maceration	Antipyretic, common cold	-	(Moein *et al.* 2015)
	Decoction	Anti-colic, anti-diarrhea and cramping, carminative, stomach problems, and menstrual cramping	-	(Mohamadi *et al.* 2015)
	Maceration, decoction, baths, powder	Bellyache, stomach cramps, diarrhea, vomit, nausea, food poisoning, stomachache, fever, digestion, diabetes, bone pain	-	(Maleki & Akhani 2018)
Flower	Poultice, powder	Anti-pyretic, treatment of insect bite, bee bite, snake bite, scorpions bite, and wound healing	-	(Safa *et al.* 2013)
	Poultice, powder	Anti-pyretic, treatment of insect bite, and bee bite	-	(Dolatkhahi & Nabipour 2014)
	Powder, decoction	Anti-epileptic	Powder (oral)	(Sadat-Hosseini *et al.* 2017)
	Smoke, decoction	Treatment of common cold, and accelerating wound healing of circumcision	Poultice (topical)	(Khajoei Nasab & Esmailpour 2018)
	Powder, decoction	Treatment of stomachache, foot pains, and digestive disorders	Oral	(Unpublished data, Mohammadi *et al*.)
Flowering branches	-	Anti-colic, anti-diarrhea, carminative, treatment of stomach problems, and treatment of menstrual cramping	-	(Sharififar *et al.* 2011)
	-	Treatment of digestive disorders, diuretic, and febrifuge	Oral	(Mehrabani *et al.* 2014)
	Decoction	Anti-colic, anti-diarrhea and cramping, carminative, stomach problems, and menstrual cramping	-	(Mohamadi *et al.* 2015)
The aerial parts	-	Digestive pain treatment, and anti-diarrhea	-	(Sharififar *et al.* 2014)

Twig	Maceration	Anti-pyretic, common cold	-	(Moein *et al.* 2015)
Latex	Maceration, decoction, baths, Powder	Bellyache, stomach cramps, diarrhea, vomit, nausea, food poisoning, stomachache, fever, digestion, diabetes, bone pain	-	(Maleki & Akhani 2018)
Root	Maceration, decoction, baths, powder	Bellyache, stomach cramps, diarrhea, vomit, nausea, food poisoning, stomachache, fever, digestion, diabetes, bone pain	-	(Maleki & Akhani 2018)
-	-	Treatment of stomachache and anti-diabetes	-	(Rastegar *et al.* 2012)
-	-	Treatment of stomachache and diarrhea	-	(Lavari *et al.* 2017)

Some of the mentioned medicinal properties of *A. eriophora*, e.g., wound healing effects, have been evaluated in recent pharmacological surveys (Khosravitabar *et al.* 2017), while others, e.g., healing digestive disorders, fever, diabetes and body pain have not been subjected to pharmacological studies yet.

Traditional and folklore medicine agree in application of *A. eriophora* for treatment of digestive disorders and fever. But using this species as diuretic by traditional medicine is reported only by a single ethnobotanical study conducted in Kerman province (Mehrabani *et al.* 2014). Folk medical administration of *A. eriophora* for diabetes, menstrual cramps, bone pain, insect and snake bite, common cold, wound healing, and epilepsy has not been considered by Iranian traditional medicine.

Phytochemistry

Phytochemical surveys have revealed that *Achillea* species possess highly bioactive compounds such as flavonoids, terpenoids, lignans, amino acid derivatives, fatty acids, and alkamides (Saeidnia *et al.* 2011). The first natural proazulene, achillicin III, anti-spasmodic flavonoids, cynaroside I and cosmosiin II, were isolated from *A. millefolium* (Banh-nhu *et al.* 1979, Falk *et al.* 1975).

Several phytochemical studies have been performed on chemical composition and essential oil of *A. eriophora*. Phytochemical analyses revealed about 128 compounds (Appendix 1).

The most abundant and important chemical components of the essential oil, analyzed by Head Space-Solid Phase Microextraction (HS-SPME), Gas Chromatography (GC), Gas Chromatography-Mass Spectrometry (GC-MS), Nuclear magnetic resonance (NMR) spectroscopy, can be listed as 1,8-cineole, α-pinene, β-pinene, camphor, camphene, linalool, α-terpineol, geranyl acetate, germacrene-D, bicyclogermacrene, borneol, spathulenol, bornyl acetate, β-phellandrene, δ-3-carene, artemisia ketone, α-thujone, and yomogi alcohol (see Table 3; Azizi *et al.* 2010, Dokhani *et al.* 2005, Doozandeh *et al.* 2015, Ghani *et al.* 2008; 2011, Gharibi *et al.* 2015, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian *et al.* 2010, Weyerstahl *et al.* 1997). Among the mentioned compounds, monoterpenes (1, 8-cineole and camphor; Fig. 3) are reported to be the main ingredients of essential oil in *A. eriophora* (Azizi *et al.* 2010, Karami-Osboo *et al.* 2015, Saeidnia *et al.* 2011). The results of these studies are summarized in Appendix 1.

Table 3. Main components of essential oils and extracts from *Achillea eriophora*.

Main components	**Plant part(s)**	**References**
1,8-Cineole and the pinenes	Leaves and flower	(Weyerstahl *et al.* 1997)
1,8-Cineole, α-pinene, and β-pinene	Leaves and flower	(Dokhani *et al.* 2005)
1,8-Cineole, camphor, and camphene	Aerial parts	(Ghani *et al.* 2008)
1,8-Cineole, linalool, α-terpineole, and geranyl formate	-	(Ghasemi *et al.* 2008)
1,8-Cineole, camphor, germacrene-D, bicyclogermacrene, borneol, spathulenol, and bornyl acetate	-	(Azizi *et al.* 2010)
1,8-Cineole	Leaves	(Azizi *et al.* 2010)
1,8-Cineole, camphor, camphene, α-pinene, β-pinene, and borneol	Aerial parts and flowers	(Oroojalian *et al.* 2010)
1,8-Cineole, camphor, and camphene	Flowering parts	(Ghani *et al.* 2011)
1,8-Cineole, camphor, borneol, β-phellandrene, α-pinene, 3-carene and β-pinene	Aerial parts	(Doozandeh *et al.* 2015)
Germacrene-D, camphor, and spathulenol	-	(Gharibi *et al.* 2015)
1,8-Cineole, camphor, camphene and germacrene-D	-	(Karami-Osboo *et al.* 2015)
Camphor, artemesia ketone, α-thujone, and yomogi alcohol	Aerial parts	(Mottaghipisheh *et al.* 2015)

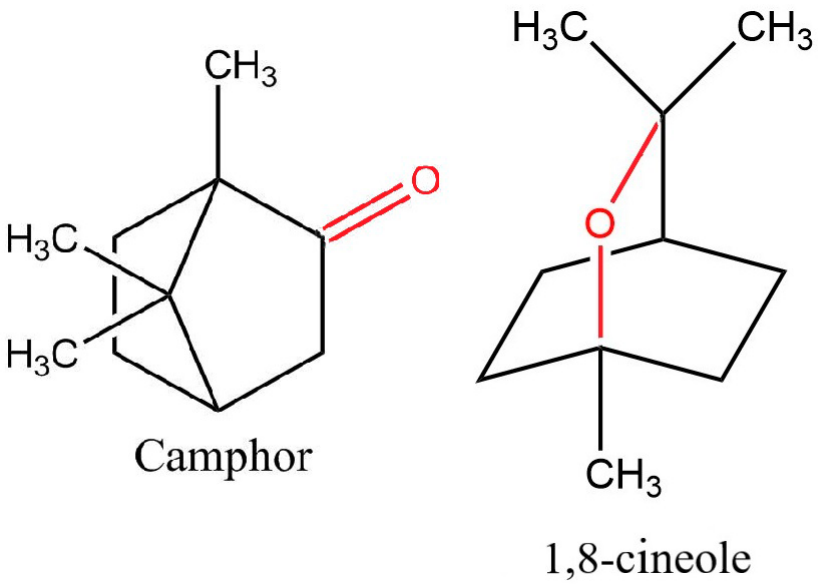

Figure. 3. Most abundant phytochemical compounds of *Achillea eriophora.*

Monoterpenes

Monoterpenes are the most generally reported ingredients in *A. eriophora* (about 90%); the amounts of oxygen-containing monoterpenes are higher than monoterpene hydrocarbons (Doozandeh *et al.* 2015, Ghani *et al.* 2008; 2011). Monoterpenes are economically important and mostly used in perfumes, fragrances, food, and medicine. Various pharmacological properties of monoterpenes can be listed as antimicrobial, antioxidant, antiarrhythmic, antidiabetics, local anesthetic, anti-inflammatory, antihistaminic, anti-spasmodic activities and insect repellants (Eggersdorfer 2012, Koziol *et al.* 2014).

Oxygenated monoterpenes

Camphor (Fig. 3) is an oxygenated monoterpene (Cooper & Nicola 2015, Karami-Osboo *et al.* 2015). It is a volatile oil and mostly used for its smell (Cooper & Nicola 2015). Camphor has many uses in the perfume industry, traditional and modern medicine (Donkin 1999). A wide range of pharmacological properties such as antimicrobial, analgesic, antioxidative have been reported for camphor (Doozandeh *et al*. 2015). The general effects of camphor are tachycardia (increased heart rate), slower breathing, reduced appetite, and increased secretions and excretions, such as perspiration and urination (Hempel *et al.* 2005, Smith & Margolis 1954). It should be considered that using high dosage of camphor can be toxic, especially for children (Zuccarini & Soldani 2009). Since camphor is one the major ingredients of *A. eriophora*, the use dosage should follow the prescriptions to avoid toxicity risk.

Hydrocarbonic monoterpenes

1,8-cineole (Fig. 3), also called eucalyptol, is a cyclic ether and monoterpenoid, which reduces germination and strongly inhibits mitosis in plants (Osbourn & Lanzotti 2009). 1,8-cineole represents one of the main aroma components of *Achillea eriophora* (Dokhani *et al*. 2005). Brown *et* al. (2017) reported 1,8-cineole has a range of pharmacological activities including anti-inflammatory, anti-microbial and anti-oxidant. Moreover, 1,8-cineole has been reported to be an important ulcer healing compound with gastroprotective effect by Cladas *et* al. (2015). The healing effect on digestive disorders, attributed to *A. eriophora* by Iranian traditional and folk medicine, might be related to its 1,8-cineole content.

α-Pinene and β-pinene are monoterpenes that represent two isomers of pinene (Budavari 1989, Cooper & Nicola 2015). Both these pinenes are among the major aroma components of *A. eriophora* (Dokhani *et al*, 2005). α-Pinene has anti-inflammatory effects and seems to be an antimicrobial agent (Nissen *et al.* 2010, Russo 2011). β-Pinene has a pine-like smell and demonstrates moderate in vitro antitumoral activity (Tisserand & Young 2013).

Camphene, as one of the minor aroma components of *A. eriophora*, is a bicyclic monoterpene with a spicy odor (Budavari 1989, Dokhani *et al*. 2005). A hypolipidemic effect of camphene and its mechanism of action has been reported by Vallianou and Hadzopoulou-Cladaras (2016).

Linalool is a fragrant monoterpene present in many plants. It has a range of different activities such as antimicrobial, antioxidant, anti-inflammatory, as well as spasmolytic effects (Peana *et al.* 2002).

α-terpineol is a monoterpene alcohol (Budavari 1989, Khaleel *et al*. 2018). It has a pleasant odor and

is a popular component in perfumes, cosmetics, and flavors (Khaleel *et al*. 2018, Yao *et al.* 2005). α-terpineol has various biological and medicinal properties such as cardiovascular and antihypertensive effects, as well as antioxidant, anticancer, anti-nociceptive, antiulcer, anti-bronchitis, skin penetration enhancing, insecticidal, and anticonvulsant and sedative activities (Khaleel *et al*. 2018).

Borneol is a bicyclic monoterpene alcohol with anti-nociceptive and anti-inflammatory activity (Almeida *et al*. 2013) and improves drug delivery to the brain (Zhang *et al.* 2017).

Bornyl acetate is a monoterpene compound reported to have analgesic, anti-inflammatory, and sedative effect as well as antitumor activity (Wu *et al.* 2004, Yang *et al.* 2014). Analgesic effect of borneol and bornyl acetate might provide a pharmacological evidence for folklore use of *A. eriophora* for treating body pains.

Geranyl acetate is a fragrant monoterpene with antifungal activity and hepatoprotective, insecticide, and antinociceptive anti-inflammatory effects (Ali *et al.* 2013, Budavari 1989, Quintans- Júnior *et al*. 2013, Rath *et al.* 2005).

As a cyclic monoterpene, β-phellandrene is one of the minor aroma components of *A. eriophora* (Dokhani *et al*., 2005). Different biological properties such hyperthermic, irritant, spasmogenic and tumor-promoter have been reported for β-phellandrene (Doozandeh *et al*. 2015).

δ-3-Carene is a bicyclic monoterpene. Pharmacological properties or potential toxicology of this compound were not found by our literature survey.

α-Thujone is a ketone and a monoterpene with psychoactive and neurotoxic effects (Mojarrab *et al.* 2012, Pelkonen *et* al. 2013, Szopa *et al*. 2020).

Yomogi alcohol is a monoterpenoid compound with antibacterial potential (Muselli *et al.* 2007).

Sesquiterpenes

Germacrene-D is a sesquiterpene (Osbourn & Lanzotti 2009) with cytotoxic, antimicrobial and insecticidal properties (Adio 2009, Da Silva *et al*. 2013, Xiong *et al*. 2013).

Bicyclogermacrene is a sesquiterpene derived from germacrene (Yang *et al*. 2005). This compound has cytotoxic and fungitoxic activities (Da Silva *et al*. 2007, Da Silva *et al*. 2013).

Spathulenol is a tricyclic sesquiterpene alcohol, which is a colorless and viscous compound with an earth-aromatic smell and bitter-spicy flavor (Juell *et al.* 1976, Lou *et al.* 2019). It possesses antibacterial and antifungal properties as well as anti-inflammatory and anticancer activity (Ghavam *et al*. 2020).

Phenolic compounds

Phenolic compounds possess a hydroxyl group (-OH) bonded directly to an aromatic hydrocarbon group. One of the most prevalent subgroups of phenolic compounds are Flavonoids that ubiquitously present in plants (Kumar & Pandey 2013). Phenolic compounds are natural antioxidants with variety of biological activities such as analgesic, cytotoxic, cardioprotective, neuroprotective, antidiabetic, antiviral, anti-inflammatory, anti-cancer, anti-proliferative and antimicrobial (Mahdi *et al*. 2013, Tanase *et al*. 2019, Tungmunnithum *et al*. 2018).

Pharmacological activities

Antimicrobial activity

Ethanol extract of *A. eriophora* has inhibitory effect against the growth of pathogenic microorganisms, and its essential oil presents antimicrobial effect (Ghasemi *et al.* 2008). Antimicrobial activity of *A. eriophora* could partly be due to its monoterpene compounds such as 1,8-cineole, camphor, α-pinene, α-terpineol. The folklore application of *A. eriophora* for treating common cold might be attributed to its antimicrobial activity.

Antioxidant activity

Achillea eriophora has notable antioxidant properties, especially on Human Foreskin Fibroblast (HFF3) cells (Varasteh-Kojourian *et al.* 2017). Alizadeh *et al.* (2012) reported a good correlation between the total phenolic content and antioxidant activity in *A. eriophora* and some other taxa of the family Asteraceae. The antioxidant activity of *A. eriophora* could be attributed to its phenolic and flavonoid content (Procházková *et al.* 2011, Varasteh-Kojourian *et al.* 2017).

Hypotensive effect

The hydroethanolic extract of the leaves and flowers of *A. eriophora* has hypotensive effects on rats (Anvari *et al.* 2016, Anvari *et al.* 2017). The hypotensive effect of the plant might be attributed to its 1,8- cineole (Lahlou *et al.* 2002) and flavonoid content (De Souza *et al.* 2011, Jiang *et al.* 2005, Morello *et al.* 2006).

Wound healing potentials

Khosravitabar *et al.* (2017) showed that methanolic extract of the leaves of *A. eriophora* improves the wound healing activity in Human Foreskin Fibroblast (HFF3) cells. They suggested the flavonoid content of the extract as a potential component responsible for this improved wound healing effect.

Cytotoxic effect

Methanolic extract of the leaves of *A. eriophora* has cytotoxic effects on Human Foreskin Fibroblast (HFF3) cells (Varasteh-kojourian *et al.* 2017). Cytotoxic effect of *A. eriophora* could possibly be ascribed to its sesquiterpene derivatives such as germacrene-D and bicyclogermacrene (Da Silva *et al*. 2013).

Conclusions

Achillea eriophora is a valuable medicinal plant that is used for different purposes by Iranian traditional and folk medicine. Regarding the considerable number of isolated constituents and highly variable ethnobotanical uses of the plant, pharmacological studies on this species seem poor. Moreover, the present pharmacological data lack detailed information on active compounds and their mechanisms of action. We suggest digestive disorders, fever and diabetes as future fields of study on *A. eriophora* to evaluate the pharmacological evidence for traditional and folklore claim of this species to be used as gastroprotective, antipyretic and antidiabetic.

The whole aerial parts of *Achillea eriophora* are widely harvested for medicinal purposes by local people. In Sistan and Baluchestan province roots are also used. Therefore, a conservation planning for this threatened endemic species is needed.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: The data was not deposited in public repositories.

Competing interests: The authors declare no conflict of interest.

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Appendix 1. Chemical composition of *Achillea eriophora*.

No.	Compound	References
1	1,8-Cineole	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Gharibi *et al.* 2015, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
2	13-Tetradecanolide	(Weyerstahl *et al.* 1997)
3	13-Tetradecanolide	(Weyerstahl *et al.* 1997)
4	15-Hexadecanolide	(Weyerstahl *et al.* 1997)
5	2-Methylbutyl-3-phenyl-propionate	(Weyerstahl *et al.* 1997)
6	2,2,6-Trimethyl-6-vinyl dihydropyran-3-one	(Weyerstahl *et al.* 1997)
7	α-Bisabolol	(Doozandeh *et al.* 2015)
8	α-Campholenal	(Azizi *et al.* 2010, Doozandeh *et al.* 2015)
9	α-Campholene aldehyde	(Weyerstahl *et al.* 1997)
10	α-Eudesmol	(Ghani *et al.* 2008, 2011)
11	α-Fenchene	(Doozandeh *et al.* 2015)
12	α-Gurjunene	(Doozandeh *et al.* 2015)
13	α-Humulene	(Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
14	α-Phellandrene	(Doozandeh et al., 2015)
15	α-Pinene	(Azizi *et al.* 2010, Dokhani *et al.* 2005, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
16	α-Santalene	(Ghani *et al.* 2008, 2011)
17	α-Terpinene	(Azizi *et al.* 2010, Dokhani *et al.* 2005, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Rahimmalek *et al.* 2009, Weyerstahl *et al.* 1997)
18	α-Terpineol	(Azizi *et al.* 2010, Ghasemi *et al.* 2008, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
19	α-Thujene	(Azizi *et al.* 2010, Dokhani *et al.* 2005, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
20	β-Caryophyllene	(Azizi *et al.* 2010, Ghani *et al.* 2011, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
21	β-Chamigrene	(Rahimmalek *et al.* 2009)
22	β-Eudesmol	(Ghani *et al.* 2008, Ghasemi *et al.* 2008, 2011, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
23	β-Pinene	(Azizi et al. 2010, Dokhani et al. 2005, Doozandeh et al. 2015, Ghani et al. 2008, 2011, Ghasemi et al. 2008, Karami-Osboo et al. 2015, Mottaghipisheh et al. 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl et al. 1997)
24	β-Sabinene	(Weyerstahl *et al.* 1997)
25	β-Selinene	(Ghasemi *et al.* 2008, Weyerstahl *et al.* 1997)
26	β-Thujone	(Doozandeh *et al.* 2015 Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
27	γ -Cadinene	(Doozandeh *et al.* 2015)
28	γ-Terpinene	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, Ghasemi *et al.* 2008, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
29	γ-Terpineol	(Ghani *et al.* 2011, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
30	γ-Eudesmol	(Azizi *et al.* 2010)
31	δ-3-Carene	(Doozandeh *et al.* 2015, Ghani *et al.* 2011)
32	*cis*-β-Menth-2-en-1-ol	(Doozandeh *et al.* 2015)
33	*cis*-Chrysanthenyl acetate	(Weyerstahl *et al.* 1997)
34	*cis*-*p*-Mentha-1(7),8-dien-2-ol	(Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
35	*cis*-*p*-Menth-2en-1-ol	(Azizi *et al.* 2010)
36	*cis*-Muurola-3,5-dien	(Doozandeh *et al.* 2015)

37	*cis*-Pinocamphone	(Karami-Osboo *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010)
37	*cis*-Piperitenol	(Weyerstahl *et al.* 1997)
39	*cis*-Sabinene hydrate	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
40	*p*-Cymene	(Azizi *et al.* 2010, Dokhani *et al.* 2005, Doozandeh *et al.* 2015, Weyerstahl *et al.* 1997)
41	*p*-Cymen-9-ol	(Weyerstahl *et al.* 1997)
42	*p*-Mentha-2,4(8)-diene	(Doozandeh *et al.* 2015, Ghani *et al.* 2011)
43	*trans*-β-Farnesene	(Rahimmalek *et al.* 2009)
44	*trans*-Carveol	(Doozandeh *et al.* 2015, Ghani *et al.* 2011, Rahimmalek *et al.* 2009, Weyerstahl *et al.* 1997)
45	*trans*-Jasmone	(Ghani *et al.* 2008, 2011, Oroojalian & Kasra-Kermanshahi, 2010)
46	*3trans-p*-Mentha-1(7),8-dien-2-ol	(Weyerstahl *et al.* 1997)
47	*trans*-Pinocarveol	(Weyerstahl *et al.* 1997)
48	*trans*-Sabinene hydrate	(Azizi *et al.* 2010, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
49	*trans*-Verbenol	(Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
50	*Allo*-Aromadendrene	(Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)
51	Artemesia alcohol	(Mottaghipisheh *et al.* 2015)
52	Artemisia ketone	(Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
53	Artemisia triene	(Mottaghipisheh *et al.* 2015)
54	Benzene propanoic acid,2-pentyl ester	(Mottaghipisheh *et al.* 2015)
55	Bicyclogermacrene	(Ghani *et al.* 2008, Gharibi *et al.* 2015, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Rahimmalek *et al.* 2009, Weyerstahl *et al.* 1997)
56	Bisabolene oxide A	(Weyerstahl *et al.* 1997)
57	Borneol	(Azizi *et al*. 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Gharibi *et al.* 2015, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
58	Cabreuva oxide (A^d, B^d, C^d, D^d)	(Weyerstahl *et al.* 1997)
59	Camphene	(Azizi *et al*. 2010, Dokhani et al. 2005, Doozandeh *et al.* 2015, Ghani *et al.* 2011, Karami-Osboo *et al.* 2015, Karami-Osboo *et al.* 2015; Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
60	Camphor	(Ghani *et al.* 2008, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Rahimmalek *et al.* 2009, Weyerstahl *et al.* 1997)
61	Caryophylla-3,8(15)-dien-5-one	(Weyerstahl *et al.* 1997)
62	Caryophylla-3,8(15)-dien-5α-ol	(Weyerstahl *et al.* 1997)
63	Caryophylla-3,8(15)-dien-5β-ol	(Weyerstahl *et al.* 1997)
64	Caryophylla-4(14),8(15)-dien-5α-ol	(Weyerstahl *et al.* 1997)
65	Caryophylla-4(14),8(15)-dien-5β-ol	(Weyerstahl *et al.* 1997)
66	Caryophylla-4(14),8(15)-dien-5-one	(Weyerstahl *et al.* 1997)
67	Caryophyllene epoxide	(Weyerstahl *et al.* 1997)
68	Caryophyllene oxide	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al*. 2008, 2011, Ghasemi *et al*. 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015)
69	Carvone	(Azizi *et al*. 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2011, Weyerstahl *et al.* 1997)
70	Chamazulene	(Ghasemi *et al.* 2008, Weyerstahl *et al.* 1997))
71	Cumin aldehyde	(Doozandeh *et al.* 2015, Weyerstahl *et al.* 1997)
72	Cryptone	(Doozandeh *et al.* 2015)
73	Dehydro-1,8-cineole	(Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997))
74	Dehydrocineol	(Azizi *et al.* 2010)
75	Dehydrosabinene	(Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997))
76	Dillapiole	(Ghani *et al.* 2011)
77	E-β-Ocimene	(Doozandeh *et al.* 2015)
78	E, E-3,7,11-Trimethyl-7,10-epoxydodeca-2,5,11-trien-1-ol	(Weyerstahl *et al.* 1997)
79	E, E-3,7,11-Trimethyl-7,10-epoxydodeca-2,5,11-trien-1-yl acetate	(Weyerstahl *et al.* 1997)

80	E, E-5-Hydroxy-3,7,11-trimethyldodeca-2,6,10-trien-1-yl acetate	(Weyerstahl *et al.* 1997)
81	E, E-Farnesol	(Ghani *et al.* 2011, Oroojalian & Kasra-Kermanshahi 2010)
82	epi-α-Cadinol	(Doozandeh *et al.* 2015)
83	Estragol	(Weyerstahl *et al.* 1997)
84	Eugenol	(Azizi *et al.* 2010, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
85	Eugenol methyl ether	(Weyerstahl *et al.* 1997)
86	Geraniol	(Doozandeh *et al.* 2015, Weyerstahl *et al.* 1997)
87	Geranyl acetate	(Doozandeh *et al.* 2015)
88	Germacrene-B	(Ghani *et al.* 2008, 2011, Oroojalian & Kasra-Kermanshahi 2010)
89	Germacrene-D	(Dokhani *et al.* 2005, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Rahimmalek *et al.* 2009)
90	Hexyl tiglate	(Doozandeh *et al.* 2015)
91	Hotrienol	(Weyerstahl *et al.* 1997)
92	Isobornyl acetate	(Ghani *et al.* 2008, 2011, Oroojalian & Kasra-Kermanshahi 2010;)
93	Isobornyl formate	(Doozandeh *et al.* 2015)
94	Isopinocamphone	(Weyerstahl *et al.* 1997)
95	Isopiperitenol	(Weyerstahl *et al.* 1997)
96	Isovaleryl-3-phenyl-proprionate	(Weyerstahl *et al.* 1997)
97	Jasmone	(Azizi *et al.* 2010)
98	Lavandulol	(Weyerstahl *et al.* 1997)
99	Lavandulyl acetate	(Weyerstahl *et al.* 1997)
100	Limonene	(Weyerstahl *et al.* 1997)
101	Linalol	(Weyerstahl *et al.* 1997)
102	Linalol oxide furanoid A, B	(Weyerstahl *et al.* 1997)
103	Linalol oxide pyranoid A	(Weyerstahl *et al.* 1997)
104	Longipinocarvone	(Azizi *et al.* 2010, Mottaghipisheh *et al.* 2015)
105	Methyl eugenol	(Azizi *et al.* 2010, Ghani *et al.* 2008, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Rahimmalek *et al*. 2009)
106	Methyl jasmonate	(Weyerstahl *et al.* 1997)
107	Myrtenal	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
108	Myrtenol	(Azizi *et al.* 2010, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015; Mottaghipisheh *et al.* 2015, Rahimmalek *et al.* 2009, Weyerstahl *et al.* 1997)
109	Oxacyclo tetradecan-2-one,14-methyl	(Mottaghipisheh *et al.* 2015)
110	Perilla aldehyde	(Weyerstahl *et al.* 1997)
111	Pinocamphone	(Azizi *et al.* 2010)
112	Pinocarvone	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
113	Pinol	(Weyerstahl *et al.* 1997)
114	Piperitone	(Rahimmalek *et al.* 2009)
115	Sabinene	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011, Karami-Osboo *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010)
116	Santolina alcohol	(Weyerstahl *et al.* 1997)
117	Santolina triene	(Weyerstahl *et al.* 1997)
118	Spathulenol	(Ghani *et al.* 2011, Gharibi *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Rahimmalek *et al.* 2009)
119	T-Cadinol	(Ghani *et al*. 2008, 2011)
128	Terpinen-4-ol	(Azizi *et al.* 2010, Doozandeh *et al.* 2015, Ghasemi *et al.* 2008, Karami-Osboo *et al.* 2015, Mottaghipisheh *et al.* 2015, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl *et al.* 1997)
121	Terpinolene	(Azizi *et al.* 2010, Doozandeh *et al*. 2015, Ghani *et al.* 2011, Ghasemi *et al.* 2008; Karami-Osboo *et al*. 2015, Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
122	Thuj-3-en-10-al	(Karami-Osboo *et al.* 2015, Weyerstahl *et al.* 1997)

123	Thymol acetate	(Ghani *et al.* 2011, Oroojalian & Kasra-Kermanshahi 2010)
124	Tricyclene	(Azizi *et al*. 2010, Doozandeh *et al.* 2015, Ghani *et al.* 2008, 2011)
125	Verbenone	(Weyerstahl *et al.* 1997)
126	Yomogi alcohol	(Mottaghipisheh *et al.* 2015, Weyerstahl *et al.* 1997)
127	Z-β-Ocimene	(Doozandeh *et al*. 2015)
128	Z-Jasmone	(Ghasemi *et al.* 2008, Weyerstahl *et al.* 1997)