Achillea eriophora DC.: An ethnobotanical, pharmacological and phytochemical review
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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. aucheri Boiss., A. eriophora DC., and A. pachycephala Rech.f. which
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. Capitulescences 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. inflorescence. C-E. *A. santolinoides* subsp. *wilhelmsii*, C-D. habit. E. inflorescence.
Different species of Achillea are commonly called Bumadaran (bu mo daeæn) in Persian (Moein et al. 2015, Sadat-Hosseini et al. 2017, Zargari 1996). Achillea eriophora is known as Bumadaran-e Jonoubi, Bumadaran-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 ‘Kalpoure’. Interestingly, ‘Kalpoure’ 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 | Bumadaran         | (Sharififar et al. 2011) |
| Bushehr, Helhe River | Sar-berenasf (berenjasf) | (Rastegar et al. 2012) |
| Hormozgan | Benjeraskas, Berenjasf, Sarzardu | (Safa et al. 2013) |
| North-east watershed of Persian Gulf | Bimadaroun | (Dolatkhahi & Nabipour 2014) |
| Kerman, Baft | Bumadaran-e-jonoubi, Berenjasf | (Mehrabani et al. 2014) |
| Kerman, Joupar | Bumadaran | (Sharififar et al. 2014) |
| Western Azerbaijan, Sarsasht | Bozhana | (Azizi & Keshavarzi 2015) |
| Fars, Darab | Bumadaran | (Moein et al. 2015) |
| Kerman, Khab and Rouchon region | Bumadaran | (Mohamadi et al. 2015) |
| Bushehr, Southwest Mand mountain | Sar-berenasf | (Lavari et al. 2017) |
| South of Kerman | Bumadaran | (Sadat-Hosseini et al. 2017) |
| Fars, Jahrom | Bumadaran-e Gol Sefidoo | (Khajoei Nasab & Esmaillpour 2018) |
| Sistan and Baluchestan, Mountain | Zanboul and/or Zamboul | (Maleki & Akhani 2018) |
| Taftan | Kalpoure | (Unpublished data, Mohammadi et al.) |

Achillea eriophora is mostly misidentified with A. santolínoides 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. santolínoides 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. santolínoides 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 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 & Esmaillpour 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 complaints and fever are the most common problems treated 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 Esmaillpour (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) |
| Poultrice, powder | - | Anti-pyretic, treatment of insect bite, bee bite, snake bite, scorpions bite, and wound healing | - | (Safa et al. 2013) |
| Poultrice, powder | - | Anti-pyretic, treatment of insect bite, and bee bite | Powder (oral), poultice (topical) | (Dolatkhahi & Nabipour 2014) |
| **Flower**      | Maceration, decoction, baths, powder | Bellyache, stomach cramps, diarrhea, vomit, nausea, food poisoning, stomachache, fever, digestion, diabetes, bone pain | - | (Maleki & Akhani 2018) |
| **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, among the mentioned compounds, monoterpenes (1,8-cineole and camphor; Fig. 3) are reported to be the main ingredients of essential oil in A. millefolium (Banhnhu 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 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-terpineol, 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, artemisia ketone, α-thujone, and yomogi alcohol | Aerial parts | (Mottaghipisheh et al. 2015) |
Monoterpenes
Monoterpenes are the most generally reported ingredients in *A. eriophora* (about 90%); the amounts of oxygen-containing monoterpenes are higher than monoterpane 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 (Osborn & 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 monoterpenoid 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 monoterpenoid present in many plants. It has a range of different activities such as antimicrobial, antioxidant, anti-inflammatory, as well as spasmyloytic effects (Peana et al. 2002).

α-terpineol is a monoterpenoid alcohol (Budavari 1989, Khaleel et al. 2018). It has a pleasant odor and
Borneol is a bicyclic monoterpane 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 monoterpane 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 monoterpane with antifungal activity and hepatoprotective, insecticidal, and antinociceptive anti-inflammatory effects (Ali et al. 2013, Budavari 1989, Quintans- Júnior et al. 2013, Rath et al. 2005).

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

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

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

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

Sesquiterpenes
Germacrene-D is a sesquiterpene (Osborn & 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, anti-diabetic, 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 monoterpane 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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**Authors’ contributions:** Toktam Mohammadi prepared the first draft of the manuscript; Atefeh Pirani supervised the study and contributed to the manuscript preparation; Hamid Moazzeni supervised the study and contributed to the manuscript preparation; Jamil Vaezi advised the study and revised the manuscript.

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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, Ghasemi et al. 2008, Oroojalian & Kasra-Kermanshahi 2010, Weyerstahl et al. 1997) |
| 18  | α-Terpineol                                    | (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) |
| 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-p-Menth-2-en-1-ol                          | (Doozandeh et al. 2015)                                                    |
| 33  | cis-Chrysantheryl acetate                      | (Weyerstahl et al. 1997)                                                   |
| 34  | cis-p-Menth-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-β-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 | Artemisia 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<sup>d</sup>, B<sup>d</sup>, C<sup>d</sup>, D<sup>d</sup>) | (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-5u-ol | (Weyerstahl et al. 1997) |
| 63 | Caryophylla-3,8(15)-dien-5β-ol | (Weyerstahl et al. 1997) |
| 64 | Caryophylla-4(14),8(15)-dien-5u-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 | Dehydrocinone | (Azizi et al. 2010) |
| 75 | Dehydroasabinene | (Mottaghipisheh et al. 2015, Weyerstahl et al. 1997)) |
| 76 | Dillapiole | (Ghani et al. 2011) |
| 77 | Eβ-3α,7β,11α-Epoxidodeca-2,5,11-trien-1-ol | (Weyerstahl et al. 1997) |
| 78 | E, E-3,7,11-Trimethyl-7,10-epoxypododeca-2,5,11-trien-1-ol | (Weyerstahl et al. 1997) |
| 79 | E, E-3,7,11-Trimethyl-7,10-epoxypododeca-2,5,11-trien-1-yl acetate | (Weyerstahl et al. 1997) |
|   | Chemical Name                                      | References                                                                 |
|---|---------------------------------------------------|-----------------------------------------------------------------------------|
| 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| Jasnone                                            | (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, Oroojalian & Kasra-Kermanshahi 2010, 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, Mottaghipisheh 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, Ghariabi et al. 2015, Oroojalian & Kasra-Kermanshahi 2010, Rahimmalek et al. 2009) |
| 119| T-Cadinol                                          | (Ghani et al. 2008, 2011)                                                   |
| 120| Terpinen-4-ol                                      | (Azizi et al. 2010, Doozandeh et al. 2015, Ghani 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)                          |
|   | Substance          | References                                                                 |
|---|--------------------|---------------------------------------------------------------------------|
| 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)                            |