The Apiaceae family comprises a set of medicinal and aromatic plants that store important secondary metabolites in internal secretory structures known as ducts and vittae, which occur in all plant organs [1]. They have been used since ancient times in traditional medicine as well as in cooking for their bioactive compounds content, including coumarins, flavonoids, polyacetylenes, and essential oils [2]. The relatively safety of these compounds, along with the availability of the raw material from which they are obtained, make them exploitable in different fields [3]. The main examples of useful Apiaceae are anise, cumin, fennel, dill, caraway, and coriander [4]. Other Apiaceae, in particular the Cachrys group, deserve further exploration for possible use on the industrial level.

The Cachrys group (fam. Apiaceae, subfam. Apioideae) is divided into several genera: Prangos, Allocarpum, Cachrys, Bilacunaria, Ferulago, Diplotaenia, Eriocycla, and Azilia [5].

According to the Plant List [6], there are 19 accepted Prangos species. They are mainly distributed in the eastern Mediterranean area, the Balkans, the Middle East, and western Asia and many of them are endemic in Turkey. Species of the genus Prangos found in Italy are Prangos ferulacea Lindl. and Prangos trifida (Miller) Herrn. & Heyn, whereas in western Europe, only P. trifida occurs [7].

Abstract

Prangos ferulacea (L.) Lindl. (Fam. Apiaceae), an orophilous species of eastern Mediterranean and western Asia, possesses a number of biological properties that are worthy of exploitation in different fields. Phytochemical investigations revealed the presence of coumarins, prenyl-coumarins, and furanocoumarins as the main constituents of this species, as well as several flavonoids. Among prenyl-coumarins, osthol is a promising apoptotic agent quite selective toward cancer cells. In addition, the essential oils have been extensively investigated, and several chemotypes have been identified. This work reviews the literature on this species published between 1965 and 2018, describes its volatile and nonvolatile metabolites, and outlines its pharmacological effects.
The Prangos Lindl. genus [8] consists of perennial herbaceous plants. Its stems are well branched, without coasts, at the base, with a well-developed and persistent collar of fibrous parts. Its leaves are 4–7-(3)-pinnate, glabrous, with numerous thread-like, acute leaflets. The umbels are composed of numerous flowers. The bracts and bracteoles are sometimes deciduous, and the flowers are hermaphrodite and male. The goblet has more or less evident teeth. Its petals are yellow, broadly ovate, with curved peak, and homogeneous. The fruits are oblong, more or less compressed laterally, and hairless. The mericarps are smooth, free of externally marked coasts, with semielliptical or semicircular sections, with spongy mesocarp; vittae are numerous and form a continuous ring. The seeds have the endosperm convoluted on the commissural face [9].

Prangos ferulacea (synonyms: Cachrys alata Hoffm., C. alata M. Bieb., Cachrys ferulacea [L.] Calest., Cachrys goniocarpa Boiss., Cachrys prangoides Boiss., Laserpitium ferulaceum L., Prangos alata Grossh., Prangos biebersteinii Karjagin, Prangos caninata Griseb. ex Grecescu) [6] is an orophilous species of the eastern Mediterranean and western Asia, where it grows in arid, stony, mountain pastures, preferentially on basic soils. In Sicily, it is fairly widespread on the carbonate mountains, above 1000 m of altitude; it flowers in May to June and fruits in July to August. In the Madonie Mountains (Sicily), the species is usually consumed by grazing cattle and sheep and imparts characteristic smells and flavors to their milk, which are transmitted to the derived dairy products such as cheese and salted ricotta, very appreciated and sought after by local communities [10]. In Turkey, P. ferulacea is known as “heliz” and is used as an ingredient of the very famous cheese, “öztü”, produced traditionally in eastern cities, particularly around Van province, as it provides characteristic appearance and special aroma as well as antimicrobial preservation [11]. In the central, southern, and eastern mountains of Turkey, where it is called “çaşıri”, the young shoots of this plant are used as a vegetable, consumed boiled, fried, and pickled [12]. In Persian folk medicine, P. ferulacea has been used as a carminative, emollient tonic for gastrointestinal and liver disorders, and as anti-flatulent, sedative, anti-inflammatory, anti-virul, anti-helminthic, antifungal and anti-bacterial agent [13]. It is locally known as “jasbir” and also serves as food and yogurt seasoning [14].

This work reviews reports published between 1965 and 2018 on the volatile and nonvolatile secondary metabolites and the biological activities of P. ferulacea with the aim of stimulating further research that may open the way to new applications of this species.

Nonvolatile Metabolites

Occurrence

The roots from different P. ferulacea populations growing in Armenia, Bulgaria, Iran, Russia, Sardinia, and Turkey have been the subject of extensive phytochemical investigations (Table 1). They were shown to be extremely rich in coumarins, the main class of secondary metabolites detected so far. In addition, the aerial parts contain not only coumarin derivatives, but also several flavonoid glycosides and the trisaccharide umbelliferose (46) (in a Sar-}

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findings suggest that osthol (S) might prove to be useful as a therapeutic agent in carcinoma treatment mainly in phenotypic-resistant cell lines due to defect in p53 function. Randomized clinical trials are important to evaluate the safety and efficacy of osthol in patients with different types of cancers.

<table>
<thead>
<tr>
<th>Parts</th>
<th>Origin</th>
<th>Other metabolites</th>
<th>Coumarins</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>roots</td>
<td>Armenia</td>
<td>quercetin 3-O-β-glucoside (41),isorhamnetin 3-O-β-glucoside (42), isorhamnetin 3-O-glucorhamnoside (43)</td>
<td>celeroside (23)</td>
<td>[19]</td>
</tr>
<tr>
<td>roots</td>
<td>Bulgaria</td>
<td>quercetin 3-O-β-glucoside (41),isorhamnetin 3-O-β-glucoside (42), isorhamnetin 3-O-glucorhamnoside (43)</td>
<td>celeroside (23)</td>
<td>[19]</td>
</tr>
<tr>
<td>roots</td>
<td>Iran, Tochal</td>
<td>quercetin 3-O-glucuronide (44)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Iran, West-Azerbaijan</td>
<td>quercetin 3-O-β-glucoside (41),isorhamnetin 3-O-β-glucoside (42), isorhamnetin 3-O-glucorhamnoside (43)</td>
<td>imperatorin (24), ferudeno1 (13)</td>
<td>[23]</td>
</tr>
<tr>
<td>roots</td>
<td>Iran</td>
<td>quercetin 3-O-glucuronide (44)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Italy, Sardinia</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>seeds</td>
<td>Italy, Sardinia</td>
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<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>fruits</td>
<td>Italy, Sicily</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Russia, Bichenak Mt</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Russia, Bichenak Mt</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Russia, Bichenak Mt</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Russia, Nakhichevan</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
<tr>
<td>roots</td>
<td>Turkey</td>
<td>quercetin 3-O-glucuronide (44),isorhamnetin 3-O-β-glucuronide (45)</td>
<td>imperatorin (24), heraclein (26), oxypeucedanin (34), sprengelianin (38), xanthotoxin (methoxsalen) (17), imperatorin (24)</td>
<td>[22]</td>
</tr>
</tbody>
</table>

**Table 1** Occurrence of nonvolatile metabolites in different populations of *P. ferulacea*.

**Antioxidant and antimicrobial activities**

The methanolic extract from aerial parts of *P. ferulacea* collected in eastern Turkey was found to be a good antioxidant with 50% inhibitory concentration values at 0.242 and 0.152 mg/mL in DPPH (2,2-Diphenyl-1-pirclyhydrazyl) radical scavenging and lipid per-
oxidation inhibition assays, respectively. It was also evaluated for its effect on glutathione-S-transferase activities showing an IC\textsubscript{50} value of 79.25 µg/mL [44,45].

Various solvent extracts (water, methanol, ethanol, and ethyl acetate) of different herbs, traditionally used in eastern Turkey to enhance the aromatic properties of cheese, were tested for their antioxidant properties. The methanolic extract of \textit{P. ferulacea} showed the highest DPPH and ABTS (2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt) radical-scavenging activities. Furthermore, a moderate antimicrobial activity against \textit{Enterococcus faecalis} (MIC [minimal inhibitory concentration] value of 250 µg/mL) was observed [11]. Quercetin glucoside (41) and isorhamnetin glucoside (42), isolated from the methanolic extract of \textit{P. ferulacea} aerial parts collected in Eastern Azerbaijan province, Iran, exhibited strong antioxidant activity in the DPPH assay with RC\textsubscript{50} values of 36.2 and 64.4 µg/mL, respectively [19]. Cytotoxic, phytotoxic, antimicrobial, and antioxidant effects of quercetin glucoside (41) isolated from aerial parts of \textit{P. ferulacea} and characterized by HPLC were studied by MTT assay, lettuce germination assay, disk diffusion, and DPPH methods. Quercetin glucoside (41) exhibited the highest antioxidant activity in the DPPH assay with an RC\textsubscript{50} value of 22 µg/mL, whereas no activity against \textit{Bacillus cereus}, \textit{Escherichia coli}, \textit{Staphylococcus epidermidis}, \textit{Pseudomonas aeruginosa}, and \textit{Candida kefyr} was detected [46].

The antibacterial effects of 4 extracts (ethanolic, methanolic, aqueous, and hexanic) of \textit{P. ferulacea} against several gram-positive bacteria such as \textit{B. cereus}, \textit{Bacillus subtilis}, \textit{Micrococcus luteus}, and \textit{Staphylococcus aureus} were evaluated. The highest inhibitory effects were observed against \textit{M. luteus} and \textit{S. aureus} for ethanolic (16 and 16 mm inhibition zone diameters, respectively) and methanolic extracts (12 and 16 mm inhibition zone diameters, respectively) [47].

Recently, a clinical trial showed that \textit{P. ferulacea} vaginal cream, containing its extract plus oral metronidazole, prepared in the laboratory of the School of Pharmacy of Shahid Beheshti Univer-
sity of Medical Sciences, accelerated the recovery of patients with bacterial vaginosis. Thus, it can be used effectively as a complementary treatment with oral metronidazole in cases of medication resistance [48].

Hypoglycemic activity

The hypoglycemic and hypolipidemic effects of the *P. ferulacea* root hydroalcoholic extract in alloxan-induced diabetic rats were studied. A 4-wk treatment of diabetic rats with a hydroalcoholic extract of roots (100 mg/kg) caused significant decrease in blood glucose (from 383 to 309 mg/dL), similar to the results obtained with 1 IU/kg of insulin (298 mg/dL). On the basis of these results, it was concluded that the *P. ferulacea* extract can be used in the treatment of diabetes to reduce the blood glucose and lipid profile. Furthermore, the extract was found to influence changes of aminotransferases and to prevent the histopathological changes of liver in diabetic rats [49,50]. Other researchers confirmed these results; in fact, a 3-wk diet with antihyperglycemic treatment of diabetes to reduce the blood glucose and lipid properties through peripheral and central analgesia [53]. The results showed that both extracts exerted analgesic properties through peripheral and central analgesia [53].

Analgesic effects

The analgesic effects of aqueous and methanolic extracts of *P. ferulacea* on formalin-induced pain in female rats were examined. The results showed that both extracts exerted analgesic properties through peripheral and central analgesia [53].

Noteworthy antispasmodic effects of the *P. ferulacea* acetone extract and its main constituents, namely osthol (5) and prenylated coumarins, on rat ileum contraction and uterus smooth muscle motility have also been reported. The relaxation effects of osthol (5) might be mediated through Ca²⁺ channel blocking activity, as it inhibited the response to KCl [14,54].

Other properties

*P. ferulacea* is used in Iranian traditional medicine for the treatment of gastrointestinal disorders. However, it seems to exert an abortifacient effect on pregnant women. A study by Kazeroomi and Mousavizadeh [55] showed that the leaf aqueous and hydroalcoholic extracts of *P. ferulacea* did not significantly increase the rate of abortion in pregnant rats. However, further investigations should be conducted to test the safety of these extracts in other animals [56].

The n-hexane extract was evaluated for inhibitory activity on acetylcholinesterase enzyme (AChE), a key target for the discovery of new treatments of Alzheimer’s disease. This extract showed a significant AChE inhibitory activity, with 75.6% inhibition at a concentration of 50 µg/mL. A further bio-assay-guided fractionation showed that the fraction containing imperatorin (24), oxy-

peucedanin (34), oxypeucedanin hydrate (35), oroseroI (37), rivulobirin A (39), quercetin (40), and quercetin 3-O-glucuronide (44) was the most active against AChE, showing an IC₅₀ value of 25.2 µg/mL as well as good docking scores of its constituents [22].

Volatile Metabolites

Essential oils

With regard to the composition of the essential oils obtained from different parts of *P. ferulacea* from different geographic origin, several papers have been published. Most of them refer to natural populations growing in Iran, while a few studies have been performed on those from Turkey, Greece, Montenegro, and Italy (Table 2). The essential oil derived from whole aerial parts contains different chemotypes. Terpinolene (38.1–56.3%) [57], δ-3-carene (45.9%), limonene (55.1%) [58] and β-pinene (43.0%) [59] were found as the major constituents in the oils obtained from samples during the vegetative stage. α-Pinene (41.3%) and δ-3-carene (34.6%) [58], (E)-caryophyllene (48.2%) [60], α-pinene (37.1%), and β-pinene (33.8%) [59] were found as the most abundant volatile components in flowering aerial parts. α-Pinene (31.7%) and β-pinene (38.5%) were the major components in the oil obtained from aerial parts during the fruiting stage [59]. The leaf oil was mostly characterized by linalool (36.7%) [61], (E)-β-ocimene (13.6–28.2%) [62,63], and β-pinene (29.6%) [64], with minor contributions of limonene (12.2–15.2%) and 2,3,6-trimethylbenzaldehyde (12.7%), and α-pinene (19.8%) and δ-3-carene (11.4%). Interestingly, a significant variation was found when the leaf oil sample obtained from the vegetative stage was compared with that from the flowering stage [65]. Indeed, the former was characterized by α-pinene (57.0%), whereas the latter was dominated by (E)-anethole (95.5%). The oil obtained from umbels was characterized by α-pinene (42.2%) [66], linalool (19.0%) and lavandulyl acetate (16.0%) [61], and β-pinene (20.6%) and δ-3-carene (10.4%) [64,67]. Fruit oil exhibited a different chemical profile, with α-pinene (18.0–26.3%) [66,68], chrysanthenyl acetate (26.5%) [69], and γ-terpine (27.8–30.2%) [70,71] as the major constituents. The stem oil was characterized by 1,8-cineole (19.0%) and α-pinene (10.3%) [61]. The root oil was found to be rich in β-phellandrene (11.8–32.1%) and δ-3-carene (22.5–25.8%) [72,73] and 3,5-nonadiene (85%) [74]. The significant variability observed in the various studies can be mainly ascribed to differences in geographic origin (related, for example, to pedoclimatic factors), phenological stage, and genetics of the samples.

Biological properties of essential oils

Antioxidant and antimicrobial activities

The essential oil obtained from the aerial parts of *P. ferulacea* growing in Semnan province, Iran (main components: β-phellandrene [20.4%], α-terpinolene [15.3%], α-pinene [11.6%], δ-3-carene [11.1%], (E)-β-ocimene [9.7%], and α-phellandrene [9.1%]), showed antibacterial activity against *E. coli* and *Staphylococcus saprophyticus*, with MIC values of 3.27 and 8.19 µg/mL, respectively [78], whereas the essential oils of fruits and flowers of plants growing in East Azerbaijan, Iran, both rich in α-pinene and...
<table>
<thead>
<tr>
<th>Plant part</th>
<th>Origin</th>
<th>Compounds (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>aerial parts</td>
<td>Greece, Crete</td>
<td>γ-pinene (27.5), α-pinene (10.4), α-terpinolene (9.0), (E)-β-ocimene (8.8), p-cymene (6.8), apiole (5.5), myrcene (4.4)</td>
<td>[75]</td>
</tr>
<tr>
<td>leaves (veget. stage)</td>
<td>Iran, E. Azerbaijan</td>
<td>α-pinene (57.0), 3-ethyliden-2-methyl-1-hexen-4-yne (5.3), β-pinene (4.5), (E)-anethole (3.9), caryophyllene oxide (3.5)</td>
<td>[65]</td>
</tr>
<tr>
<td>leaves (flow. stage)</td>
<td>Iran, E. Azerbaijan</td>
<td>(E)-anethole (95.5)</td>
<td>[65]</td>
</tr>
<tr>
<td>fruits</td>
<td>Iran, E. Azerbaijan</td>
<td>α-pinene (63.1), cis-ocimene (9.7), β-pinene (8.3), myrcene (4.8)</td>
<td>[66]</td>
</tr>
<tr>
<td>umbels</td>
<td>Iran, E. Azerbaijan</td>
<td>α-pinene (42.2), cis-ocimene (36.3), myrcene (5.0), β-phellandrene (3.3)</td>
<td>[66]</td>
</tr>
<tr>
<td>roots</td>
<td>Iran, W. Azerbaijan</td>
<td>β-phellandrene (32.1), m-tolualdehyde (26.2), δ-3-carene (25.8), α-pinene (4.7)</td>
<td>[72]</td>
</tr>
<tr>
<td>aerial parts</td>
<td>Iran, Azerbaijan</td>
<td>β-pinene (43.1), α-pinene (22.1), δ-3-carene (16.9), α-terpinolene (3.9)</td>
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<tr>
<td>leaves</td>
<td>Iran, Esfahan</td>
<td>linalool (36.7), caryophyllene oxide (16.3), α-pinene (12.1), 1,8-cineole (8.9)</td>
<td>[61]</td>
</tr>
<tr>
<td>stems</td>
<td>Iran, Esfahan</td>
<td>1,8-cineole (19.0), α-pinene (10.3), caryophyllene oxide (4.2), linalool (3.7)</td>
<td>[61]</td>
</tr>
<tr>
<td>flowers</td>
<td>Iran, Esfahan</td>
<td>linalool (19.0), lavandulyl acetate (16.0), 1,8-cineole (14.5), α-pinene (12.4), geranyl isobutryate (12.2), α-campholenal (7.0), α-cadinol (6.4)</td>
<td>[61]</td>
</tr>
<tr>
<td>leaves</td>
<td>Iran, Fars</td>
<td>(E)-β-ocimene (13.6), 2,3,6-trimethylbenzaldehyde (12.7), p-cymene (9.7), terpinolene (8.3), (E)-caryophyllene (5.4), β-elemene (5.3), germacre D (5.0), α-bisabolol (4.9), linalool (4.5), kessane (3.4), γ-pinene (3.4), α-pinene (3.0)</td>
<td>[62]</td>
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<td>leaves</td>
<td>Iran, Fars</td>
<td>(E)-β-ocimene (23.6), linalool (13.3), p-cymene (12.2), 2,3,6-trimethylbenzaldehyde (7.4), terpinolene (6.7), α-pinene (3.9), (E)-caryophyllene (3.1)</td>
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<td>leaves</td>
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<td>(E)-β-ocimene (28.2), linalool (12.2), terpinolene (8.7), p-cymene (7.1), 2,3,6-trimethylbenzaldehyde (7.0), germacre D (5.0), (E)-caryophyllene (3.9), α-pinene (3.7), β-elemene (3.5), γ-pinene (3.3)</td>
<td>[63]</td>
</tr>
<tr>
<td>aerial parts (grow. stage), fresh</td>
<td>Iran, North Fars</td>
<td>terpinolene (56.3), (E)-caryophyllene (4.7), bornyl acetate (3.0)</td>
<td>[57]</td>
</tr>
<tr>
<td>aerial parts (grow. stage), dry</td>
<td>Iran, North Fars</td>
<td>terpinolene (38.1), (E)-caryophyllene (3.6), bornyl acetate (1.8)</td>
<td>[57]</td>
</tr>
<tr>
<td>aerial parts (veget. stage), fresh</td>
<td>Iran, North Fars</td>
<td>δ-3-carene (45.9), indole (11.6), terpinolene (9.6), p-cymen-8-ol (6.2), n-pentadecanol (5.5)</td>
<td>[58]</td>
</tr>
<tr>
<td>aerial parts (veget. stage), dry</td>
<td>Iran, North Fars</td>
<td>limonene (55.1), γ-pinene (10.7), bornyl acetate (8.5)</td>
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</tr>
<tr>
<td>aerial parts (flow. stage), fresh</td>
<td>Iran, North Fars</td>
<td>α-pinene (41.3), δ-3-carene (34.6), limonene (14.6), β-pinene (9.5), terpinolene (8.1), myrcene (7.4), sabine (4.7), α-phellandrene (4.1)</td>
<td>[58]</td>
</tr>
<tr>
<td>aerial parts (flow. stage), dry</td>
<td>Iran, North Fars</td>
<td>α-pinene (24.2), δ-3-carene (7.7), β-pinene (8.6), terpinolene (3.8), β-phellandrene (4.4)</td>
<td>[58]</td>
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<tr>
<td>aerial parts (flow. stage)</td>
<td>Iran, Kermanshah</td>
<td>(E)-caryophyllene (48.2), α-humulene (10.2), spathulenol (9.3), linalool (3.5), δ-3-carene (3.4)</td>
<td>[58]</td>
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<tr>
<td>leaves</td>
<td>Iran, Kurdistan</td>
<td>β-pinene (29.6), α-pinene (19.8), δ-3-carene (11.4), β-phellandrene (11.1), β-caryophyllene (3.7)</td>
<td>[67]</td>
</tr>
<tr>
<td>flowers</td>
<td>Iran, Kordestan</td>
<td>β-pinene (20.6), δ-3-carene (10.4), α-pinene (8.8), β-phellandrene (8.1), germacre D (5.8), α-humulene (5.3), p-cymene (3.8), δ-cadinene (3.3)</td>
<td>[67]</td>
</tr>
<tr>
<td>leaves</td>
<td>Iran, Khorasan</td>
<td>β-pinene (29.6), α-pinene (19.8), δ-3-carene (11.4), β-phellandrene (11.1), (E)-caryophyllene (3.7)</td>
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<tr>
<td>flowers</td>
<td>Iran, Khorasan</td>
<td>β-pinene (20.6), δ-3-carene (10.4), α-pinene (8.8), β-phellandrene (8.1), germacre D (5.8), p-cymene (3.8), δ-cadinene (3.3)</td>
<td>[64]</td>
</tr>
<tr>
<td>roots</td>
<td>Iran, Kohgiluyeh-Boirahmad</td>
<td>δ-3-carene (22.5), β-phellandrene (11.8), α-pinene (8.6), terpinolene (7.2), p-cymene (6.3), α-phellandrene (6.2), myrcene (4.5), sabine (3.6), bornyl acetate (3.2), γ-pinene (3.0)</td>
<td>[73]</td>
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<tr>
<td>aerial parts</td>
<td>Iran, Lorestan</td>
<td>α-pinene (36.6), β-pinene (31.9), β-phellandrene (11.7), terpinolene (6.9), α-phellandrene (3.9), (E)-caryophyllene (3.1)</td>
<td>[76]</td>
</tr>
<tr>
<td>aerial parts (pre-flow. stage)</td>
<td>Iran, Lorestan</td>
<td>β-pinene (43.0), α-pinene (40.0), β-phellandrene (6.5), α-terpinene (5.1)</td>
<td>[59]</td>
</tr>
</tbody>
</table>

*cont.*
cis-ocimene, displayed antibacterial effects against *B. cereus* (15 mm of inhibition zone diameter) [65, 80].

It was found that the essential oil from leaves of *P. ferulacea* growing in Esfahan, Iran, rich in linalool (36.7%), caryophyllene oxide (16.3%), α-pinene (12.1%), and 1,8-cineole (9.8%), exhibited particularly strong antibacterial activity, especially against Gram-positive organisms with MIC values of 0.0625, 0.25, 0.50, respectively [61]. Also, the oil from the fruits collected near Teheran, Iran, whose main components were chrysanthenyl acetate (26.5%), limonene (19.6%), α-pinene (19.5%), δ-3-carene (6.6), menthadiol (6.1), germacrene B (3.5) [69].

The essential oil of the aerial parts of *P. ferulacea* collected in the Broujerd mountains of Lorestan province, Iran, showed good antibacterial activity against several Gram-positive and Gram-negative bacteria, especially *S. aureus* [69]. The inhibition of bacterial growth was attributed to the large content of monoterpenes such as α-pinene (36.6%) and β-pinene (31.1%) [76].

The essential oil from the flowering aerial parts of *P. ferulacea* collected in East Azerbaijan, Iran, characterized by a large content of (E)-anethole, exhibited significant phytotoxic activity (IC₅₀ = 244.19 µg/mL) on lettuce and fungitoxic effects (0.01 mg/mL) against *Sclerotinia sclerotiorum* [65].

It was seen that ultrasonic pre-treatment of sample had no adverse effects on the biological properties of *P. ferulacea* essential oils and particularly improved the antioxidant activity [63].

The roots of *P. ferulacea* are traditionally used as an effective wound healing agent especially for pus-filled wounds both in human and livestock in the northwest of Iran. The antimicrobial properties of the root essential oil (major constituents: β-phellandrene [32.1%], m-tolualdehyde [26.2%], and δ-3-carene [25.8%]) were evaluated against *Staphylococcus aureus*, *S. epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi* and *Candida albicans* using the agar dilution method. Very good growth inhibition of *S. aureus* and *P. aeruginosa* with a MIC value of 20 µg/mL, for both pathogens, was shown. In addition, the oil, at concentrations of 4 and 16 µg/mL, significantly enhanced the migration rate of L929 cells (63% and 87%, respectively, after 2 d), with a significant increase of collagen production [72].

**Other properties**

3,5-Nonadiyne, isolated from the root essential oil of *P. ferulacea* collected in Montenegro, selectively inhibited the endogenous nitric oxide release in rat peritoneal macrophages (IC₅₀ = 6.7 µM) without inhibiting T cell proliferation [74].

Essential oil obtained from *P. ferulacea*, containing mainly 2,3,6-trimethylbenzaldehyde (66.6%) and chrysanthenyl acetate (15.1%), was tested on different stages of *Ephesia kuehniella* Zeller (Lepidoptera: Pyralidae) and against the egg parasite *Trichogramma embryoagrum* Hartig (Hymenoptera: Trichogrammatidae). The essential oil was toxic to the adult stages of both pests with 100% mortality obtained after 24 h at 1.0 and 0.25 µL/L air, respectively. The LC₅₀ and LC₉₉ values of the essential oil against the egg stages of *E. kuehniella* and *T. embryoagrum* were 320.372–486.839 and 2.121–5.662 µL/L air, respectively. The results of this study indicated that essential oil of *P. ferulacea* should be used as a control agent against these pests for integrated pest management programs [79].
Conclusions and Perspectives

This review summarized the main phytochemicals and biological properties of *P. ferulacea*, a species traditionally used in different countries for its antispasmodic, sedative, analgesic, anti-inflammatory, antiseptic, anti-viral, and antimicrobial properties. In several cases, scientific evidence has supported and validated its traditional uses. The most investigated characteristic of this species has been its antimicrobial activity, and both extracts and essential oils have been shown to possess promising effects, thus confirming the ethno-traditional uses. Coumarins are the main class of constituents isolated to date, although a few flavonoids have also been detected. These secondary metabolites, including mainly prenyl-coumarins and furano-coumarins, showed notable cytotoxic activity that is worthy of further investigation. Despite the large number of investigations reported, other studies should be carried out in order to increase our knowledge about this species. Most of the phytochemical studies examined the less polar fractions; consequently, a complete metabolic profile that also includes polar compounds is lacking. Furthermore, the biological activities of the extracts, essential oils, and pure compounds were mainly investigated using in vitro tests. Given that the potential health risks of *P. ferulacea*-derived products have not been investigated in depth, more detailed studies will be needed before they can be used for future pharmacological and commercial purposes.

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Conflict of Interest

The authors declare no conflicts of interest.

References

Kuznetsova GA, Abyshev AZ. Natural...

Bruno M et al. The Nonvolatile and...

Nikonov GK, Saidkhodzhaev AI. Structure of pranferin, a new coumarin...

Abyshev AZ, Denisenko PP, Kostyuchenko NP, Anisimova OS, Ermakov AI,

Cachrys...

Coruh N, Sagdicoglu CAG, Oezgoekce F. Antioxidant properties of...

Melough MM, Cho E, Chun OK. Furocoumarins: a review of biochemical...

Mavi A, Terzi Z, Ozgen U, Yildirim A, Coskun M. Antioxidant properties of...

Razavi SM, Zahri S, Zarrini G, Nazemiyeh H, Mohammadi S. Biological ac-


Seidi Damyeh M, Niakousari M, Saharkhiz MA. Ultrasound pretreatment impact on Prangos ferulacea Lindl. and Satureja macrocephala Boiss. essential oil extraction and comparing their phycosicochemical and biological properties. Ind Crops Prod 2016; 87: 105–115

Taherkhani M, Rustaiyan A, Masoudi S. Volatile constituents of the aerial parts of Ferula subvelutina Rech. f., Ferula stellata Boiss., leaves and flowers of Prangos ferulacea (L.) Lindl. and leaves of Ferula ovina (Boiss.) Boiss.: four Umbelliferae herbs from Iran. Asian J Chem 2012; 24: 1601–1606


Bruno M et al. The Nonvolatile and...


