Research Journal of Pharmacognosy (RJP) 9(4), 2022: 29–38
Received: 7 June 2022
Final revision: 28 Aug 2022
Accepted: 5 Sep 2022
Published online: 10 Sep 2022
DOI: 10.22127/RJP.2022.345563.1917

Original article

Remarkable Variation in Phytochemicals of *Ferula gummosa* Bioss. Essential Oils Collected From Different Parts of Iran

Saied Goodarzi[1*], Mansour Mofasseri[1], Zahra Tofighi[2], Mostafa Pirali Hamedani[2], Abbas Hadjiakhoondi[3], Saeed Tavakoli[4], Zahra Moein[3], Zahra Baharipour[5]

[1]Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
[2]Department of Pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
[3]Department of Pharmacognosy and Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
[4]Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran.
[5]Department of Pharmacognosy, School of Pharmacy, International Campus, Tehran University of Medical Sciences, Tehran, Iran.

Abstract
Background and objectives: The oleo-gum resin from *Ferula gummosa* Bioss. is commercially important. Variability of geographic location has shown a deep effect on essential oil of different genus of plants. Thus, evaluation of oleo-gum resin of *Ferula gummosa* from different locations is important for further studies. In the present study, phytochemicals profile of essential oil of oleo-gum resins from *F. gummosa* in different geographic location and various bioclimates of Iran, were studied. **Methods:** The oleo-gum resin of *F. gummosa* was collected from different regions of Iran. The essential oils of the samples were extracted by Clevenger apparatus and were analyzed by GC-MS. **Results:** The highest amount of essential oil compared was observed in the samples from Damghan area (24.0%), Firuzkuh area (22%) and Kalat-e-Naderi area (22%). The variability in the oil composition of different samples exhibited a notable difference in monoterpenes content from 39.15 % to 87.48%. Based on GC-MS analysis, the major components were β-pinene (5.11-63.80 %), sabinene (3.37-30.69%), α-pinene (4.43-12.72%) and δ-carene (2.38-10.23 %). The highest concentrations of β-pinene (63.80%) and sabinene (30.69%) were observed in the Shiraz and Torbat-e-Jam essential oils, respectively. The highest amounts of α-pinene (12.72%) and δ-carene (10.23%) were recorded in Firuzkuh and Shiraz areas, respectively. **Conclusion:** Significant variation in the component of the essential oils from different oleo-gum resins can be used to improve the knowledge about the endemic medicinal plants.

Keywords: *Ferula gummosa*; oleo-gum resin; β-pinene; sabinene; volatile oil

Citation: Goodarzi S, Mofasseri M, Tofighi Z, Pirali Hamedani M, Hadjiakhoondi A, Tavakoli S, Moein Z, Baharipour Z. Remarkable variation in phytochemicals of *Ferula gummosa* Bioss. essential oils collected from different parts of Iran. Res J Pharmacogn. 2022; 9(4): 29–38.

Introduction
Medicinal plants have been used as alternative treatments for several diseases in developing countries. They play a crucial role in developing new drugs. From ancient to recent time, polyphenolic compounds have shown vital roles in human health [1]. In this regard, essential oils

*Corresponding author: goodarzi_s@tums.ac.ir

from natural products and their phytochemicals have unique chemical properties that make them proper candidates for drug design. Also many studies have documented the efficacy of essential oils and their constituents as sources of bioactive natural products [2]. Essential oils of different plants have shown various properties including antibacterial [3], antiviral [4], antioxidant [5], antinociceptive and anti-inflammatory [6] effcets. They are also known for relieving stress and are significantly used in treatments of sleep disorders. They are also reported beneficial in Alzheimer disease [7], cardiovascular issues [8], cancer [9], and as antifungal and antimycotoxigenic [10], immunomodulatory [11], antispasmodic [12], cytotoxic [13] and anxiolytic [14] agents.

Ferula is the third largest genus of Apiaceae family and is categorized in the Peucedaneae tribe and Ferulinae subtribe of the family. At present, about 180 *Ferula* species have been reported [15]. This genus has a wide distribution all over central and south–west Asia (especially Iran and Afghanistan), the far-east, North India, and the Mediterranean region [16,17], and some desert areas. Most of the *Ferula* species grow in mountainous regions and arid climates [18]. *Ferula gummosa* Boiss. is a native plant in Iran that grows in the western and northern mountainous regions [19]. In Iranian traditional medicine, *F. gummosa* is used for treating different diseases. *Ferula gummosa* acts as an anti-oxidant and anti-inflammatory agent as well [20,21]. Other pharmacological effects of this plant include anticonvulsant, anti-neurological, anti-diabetes, anti-rheumatic and anti-inflammatory activities. In addition, pharmacological studies have shown that *F. gummosa* resins show antibacterial, anti-catarrh, anti-microbial, antiepileptic, analgesic, digestive, carminative, aphrodisiac, laxative and expectorant properties. Moreover, the anti-hemolytic and anti-oxidant attributes of the leaves, fruits, and stems extracts of *F. gummosa* have been already reported [20]. *Ferula gummosa* has also exhibited significant anti-proliferation and apoptosis-inducing effects in gastric cancer [22].

Chemical composition of various essential oils of plants may be affected by genetic and environmental factors such as geographical conditions, climate and seasonal variations and the stage of the plant growth [23-25]. Accordingly, Malekzadeh et al., studied chemical composition of *F. gummosa* gathered from different bioclimates of Iran. They demonstrated that there was a considerable variation in the oils of collected samples depending on their geographic location. The high variability in the oil contents and composition in different populations showed a remarkable difference in monoterpenes content from 79.47 to 86.48% [26]. Ghasemi *et al.*, identified 73 components from *F. gummosa* fruits gathered from one region (Isfahan, Iran) in which the major components were β-pinene (43.78%), α-pinene (27.27%), and myrcene (3.37%) [27]. Composition and the antifungal activities of the essential oils of *F. gummosa* from three localities (Kashan, Ilam and Semnan) in Iran were evaluated. Analysis of the oil samples gave 34 components. The major components were β-pinene (28.44 - 40.99 %), α-pinene (1.42 - 33.91 %), δ -3-carene (1.36 – 10.23 %) and limonene (5.09 - 9.15 %) [28].

It seems that geographic location plays a vital role in the variation of chemical content of essential oils. Thus, the purpose of the present study was evaluation of variation in *F. gummosa* essential oils from eight different locations of Iran.

Materials and Methods

Ethical considerations

The study was approved by the ethics committee of Tehran University of Medical Sciences (IR.TUMS.NIHR.REC.1397.026).

Plant material

The oleo-gum resin of roots and aerial parts of *F. gummosa* were obtained from eight different parts of Iran including Firuzkuh (M1), Torbat-e-Jam (M2), Sabzevar (M3), Kalat-e-Naderi (M4), Shiraz (M5), Shahmirzad (M6), Damghan (M7) and Jajarm (M8) during September 2018. All specimens were authenticated at the Herbarium of Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran , Iran (Table 1).

Essential oil extraction

The oleo-gum resin of each sample was powdered separately and subjected to hydrodistilation for 4 h using a Clevenger-type apparatus [29]. The oils were dried over anhydrous sodium sulphate and kept at 4°C until they were analyzed.

Table 1. Geographical properties of natural habitats and herbal market code of *Ferula gummosa* from different sites of Iran

Sample*	Average annual rainfall (mm)	Mean annual temperature (°C)	Latitude (E)	Longitude (N)	Altitude (m)	Herbal market code
M1	269.2	25.2	35° 45' 17.9496"	52° 46' 20.4744"	1943	PMP-846
M2	168.0	19.3	35° 13' 54.0696"	60° 38' 24.4392"	898	PMP-847
M3	190.0	22.1	36° 11' 60.00"	57° 42' 59.99"	978	PMP-848
M4	127.0	22.5	36° 14' 60.00"	49° 30' 59.99"	2100	PMP-850
M5	255.0	26.6	29° 35' 30.3648"	52° 35' 1.3128"	1545	PMP-849
M6	266.5	18.3	35° 46' 1.79"	53° 19' 18.00"	1960	PMP-1803
M7	189.5	15.5	36° 10' 4.44"	54° 20' 34.51"	1154	PMP-1804
M8	346.5	17.9	37° 19' 31.01"	56° 44' 29.00"	1000	PMP-1838

*Oleo-gum resin of *Ferula gummosa* from different regions of Iran; M1: Firuzkuh, M2: Torbat-e-Jam, M3: Sabzevar, M4: Kalat-e-Naderi, M5: Shiraz, M6: Shahmirzad, M7: Damghan, M8: Jajarm

GC-MS analysis of the essential oils

Essential oils of *F. gummosa* oleo-gum resins were analyzed on a HP-6890 gas chromatograph with a HP-5MS column (30 m×0.25 mm id, 0.25 µm film thickness), equipped with HP-5973 mass detector (ionization energy: 70 eV) under the following conditions; temperature program: 60 °C (0–3 min), 60–280 °C at the rate of 3 °C/min (3–65 min), injector temperature: 240 °C, detector temperature: 250 °C, injection volume: 1.0 µL, split ratio: 1:50, carrier gas: helium (flow rate: 1 mL/min). Identification of the compounds were carried out based on computer matching with the Wiley275.L and Wiley7n.L libraries, as well as by comparison of Kovats indices (KIs) and patterns mass fragmentation with those published for standard compounds [30]. The reported KIs of each identified compound for HP-5 column were found in identification of essential oil components by gas chromatography/mass spectrometry book and National Institute of Standards and Technology (NIST) website. Also, the calculated KIs (based on retention indices, KIc) were calculated based on below formula:

$$KIc = 100 \times [n + (\frac{\text{Retention time compound - Retention time smaller alkane}}{\text{Retention time large alkane - Retention time smaller alkane}})]$$

Results and Discussion

The results of essential oils contents for *F. gummosa* are provided in Table 2. It is worth noting that the highest essential oil yield in dry weight of oleo-gum resin (24%) was recorded in the samples from Damghan (M7), Firuzkuh (M1) area (22%) and Kalat-e-Naderi (M4) area (22%), respectively. However, samples from Sabzevar (M3) and Shahmirzad (M6) showed the lowest essential oils yield in this regard. There was no considerable difference between others areas in terms of essential oil yield in oleo-gum resins (Table 2). Percentages of phytochemical compositions of the essential oils of 8 locations of *Ferula gummosa* from Iran are summarized in the Table 3.

Table 2. Essential oil properties from oleo-gum of *Ferula gummosa* from different regions

Sample*	M1	M2	M3	M4	M5	M6	M7	M8
Essential oil Color	Colorless	Pale yellow	Pale yellow	Colorless	Colorless	Colorless	Pale yellow	Colorless
Essential oil Contents (%v/w)	22.0	12.50	6.0	22.0	19.35	9.25	24.0	18.60

*Oleo-gum resin of *Ferula gummosa* from different regions of Iran; M1: Firuzkuh, M2: Torbat-e-Jam, M3: Sabzevar, M4: Kalat-e-Naderi, M5: Shiraz, M6: Shahmirzad, M7: Damghan, M8: Jajarm

Table 3. The essential oil compositions of *Ferula gummosa* from eight locations in Iran

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
***β*-Thujene**	920	-	-	-	-	-	-	0.63 (924)	-
***α*-Thujene**	931	2.14 (935)	2.77 (934)	4.76 (943)	0.82 (941)	0.66 (925)	2.75 (930)	-	0.65 (930)
***α*-Pinene**	939	12.72 (944)	11.0 (941)	4.43 (949)	4.85 (946)	7.33 (931)	8.70 (939)	4.61 (931)	6.42 (936)

Table 3. Continued

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
Camphene	953	0.32 (946)	0.18 (948)	0.47 (954)	-	-	-	-	0.53 (947)
2,4 (10)-Thujadien	955	-	-	0.06 (956)	-	-	-	-	-
Sabinene	976	-	30.69 (980)	14.90 (980)	-	3.37 (979)	29.54 (996)	-	-
***β*-Pinene**	980	25.88 (990)	5.11 (984)	11.79 (986)	40.46 (990)	63.80 (997)	-	48.27 (978)	54.34 (986)
Nopinene	981	-	-	-	-	-	6.47 (999)	-	-
***β*-Myrcene**	992	2.55 (996)	0.64 (996)	0.13 (997)	3.02 (996)	-	-	-	-
Phellandrene	1005	0.58 (1008)	0.75 (1000)	0.15 (1001)	0.64 (1005)	-	0.52 (1005)	0.56 (993)	0.62 (1000)
***δ*-3-Carene**	1009	8.72 (1012)	2.38 (1005)	0.15 (1007)	8.19 (1010)	10.23 (1010)	0.75 (1015)	0.58 (1009)	0.69 (1005)
4-Carene	1014	-	-	-	-	-	-	0.13 (1014)	0.33 (1014)
***α*-Terpinene**	1018	0.67 (1020)	0.62 (1014)	1.48 (1017)	1.33 (1020)	-	-	-	-
***o*-Cymene**	1027	0.46 (1026)	3.63 (1020)	6.52 (1036)	0.18 (1027)	-	6.13 (1036)	-	-
Limonene	1031	5.48 (1030)	-	1.31 (1040)	3.51 (1033)	-	-	-	2.48 (1026)
***trans*-*β*-Ocimene**	1047	-	-	-	2.1 (1051)	1.33 (1030)	-	1.45 (1052)	1.26 (1048)
***β*-Ocimene**	1050	3.29 (1063)	0.17 (1053)	-	-	-	-	0.42 (1052)	-
10-*cis*-*β*-Ocimene	1052	0.69 (1064)	0.17 (1060)	-	-	0.25 (1052)	-	-	0.42 (1057)
ɤ-Terpinene	1061	0.13 (1075)	1.39 (1074)	2.21 (1072)	0.19 (1078)	0.14 (1075)	1.36 (1058)	0.10 (1062)	0.29 (1061)
***trans*-Sabinene hydrate**	1071	-	0.47 (1077)	-	-	-	0.56 (1075)	-	0.11 (1068)
***α*-Terpinolene**	1088	0.84 (1095)	0.90 (1085)	0.90 (1077)	0.70 (1088)	0.37 (1089)	0.70 (1093)	1.54 (1097)	0.16 (1077)
***cis*-Sabinene hydroxide**	1097	-	-	-	-	-	0.48 (1104)	-	-
Isovaleric acid	1104	-	-	-	-	-		0.09 (1102)	0.13 (1109)
***β*-Thujone**	1114	-	0.11 (1099)	0.42 (1100)	-	-	-	-	-
***trans*-*ρ*-Menth-2-enol**	1119	-	0.14 (1108)		-	-	-	-	-
Neo-Allo-ocimene	1131	0.08 (1134)	-	-	0.1 (1117)	-	-	-	-
Nopinone	1138	-	-	-	-	-	0.19 (1134)	-	0.17 (1137)
Pinocarveol	1141	-	1.56 (1136)	2.9 (1139)	0.36 (1138)	0.38 (1131)	1.13 (1142)	1.08 (1145)	-
***trans*-Verbenol**	1147	-	-	-	-	-	0.36 (1153)	-	-
***cis*-Verbenol**	1143	0.44 (1145)	-	-	-	-	-	-	-
4-Terpineol	1159	-	-	4.96 (1158)	-	-	-	-	-
Pinocarvone	1162	0.14 (1163)	0.90 (1159)	1.02 (1160)	0.17 (1169)	-	0.94 (1160)	0.13 (1158)	0.49 (1163)
Terpinen-4-ol	1171	-	1.44 (1177)	-	-	-	-	-	-
1,3,5-Undecatriene	1173	4.37 (1172)	-	-	4.37 (1176)	1.90 (1183)	-	3.19 (1169)	2.69 (1175)
4-Terpineneol	1175	-	-	-	-	-	1.99 (1177)		

Table 3. Continued

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
Myrtenal	1178	-	-	-	-	-	1.13 (1180)	0.19 (1176)	0.59 (1181)
***ρ*-Cymen-8-ol**	1179	-	0.32 (1188)	0.81 (1172)	-	-	-	-	-
1,3,5-Undecatriene	1181	0.23 (1189)	-	-	0.72 (1186)	-	-	-	-
***β*-Terpineol**	1183	-	-	0.36 (1187)	-	-	-	-	-
2-Pinen-10-ol	1188	-	-	2.80 (1189)	-	-	1.17 (1194)	-	-
Myrtenol	1191	0.38 (1192)	2.24 (1192)	-	0.28 (1194)	-	-	-	0.61 (1189)
n-Hexyl butanoate	1192	-	-	-	-	0.56 (1188)	-	-	-
Octyl acetate	1194	-	-	-	-	0.38 (1192)	-	-	-
***cis*-Piperitol**	1195	-	-	0.13 (1198)	-	-	-	-	-
Levoverbenone	1200	-	0.16 (1109)	0.15 (1191)	-	-	-	-	-
Fenchyl acetate	1217	2.21 (1207)	0.27 (1214)	0.48 (1214)	0.15 (1218)	-	0.44 (1218)	-	-
2,4,6-Undecatriene	1232	0.05 (1235)	-	-	-	-	-	0.26 (1226)	-
Citral	1240	-	0.43 (1257)	-	0.38 (1238)	-	-	-	-
Prenyl senecioate	1242	-	-	-	-	-	-	-	0.25 (1232)
Carvone	1244	-	-	0.14 (1245)	-	-	-	-	-
Bornyl acetate	1284	-	-	0.12 (1289)	0.15 (1276)	-	0.17 (1288)	0.24 (1270)	0.56 (1287)
***trans*-Pinocarvyl acetate**	1298	-	-	-	0.12 (1283)	-	0.54 (1295)	0.11 (1282)	0.20 (1294)
Cumic alcohol	1301	-	-	0.32 (1296)	-	-	-	-	-
2,4-Decadienal	1308	0.14 (1303)	-	-	-	-	-	-	-
***ρ*-Cymen-2-ol**	1311	-	-	0.33 (1310)	-	-	-	-	-
***α*-Terpinyl acetate**	1326	-	-	-	-	0.55 (1327)		1.07 (1303)	1.18 (1328)
***α*-Cubebene**	1339	-	0.13 (1338)	0.10 (1339)	-	-	-	0.05 (1340)	-
***α*-Longipinene**	1347	0.1 (1355)	-	-	-	-	-	-	-
Cyclosativene	1365	-	-	1.26 (1360)		0.13 (1358)	0.77 (1355)	0.37 (1354)	-
Cycloisosativene	1368	-	0.58 (1367)	0.28 (1367)	0.29 (1365)	-	-	-	-
Copaene	1370	1.11 (1361)	1.08 (1372)	0.92 (1372)	0.26 (1369)	0.18 (1377)	0.88 (1369)	0.51 (1367)	0.61 (1372)
Ylangene	1371	-	-	-	0.40 (1377)	0.25 (1381)	-	-	-
Longifolene	1377	-	-	-	-	-	-	-	0.5 (1376)
***β*-Elemene**	1381	0.52 (1379)	0.45 (1380)	2.84 (1381)	0.39 (1401)	0.14 (1387)	-	-	-
***β*-Bourbonene**	1382	-	0.57 (1383)	0.92 (1386)	-	-	0.95 (1388)	-	0.33 (1389)
5-Tetradecene	1387	-	0.50 (1385)	0.56 (1390)	-	-	-	-	-
***β*-Cubebene**	1390	0.47 (1385)	0.38 (1389)	2.46 (1393)	-	-	-	-	-

Table 3. Continued

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
***β*-Funebrene**	1392	-	-	-	-	-	0.53 (1393)	-	-
Himachala-3(12),4-diene	1398	1.23 (1390)	-	-	-	-	-	-	-
***β*-Cedrene**	1406	-	-	-	-	-	0.13 (1404)	-	-
Valerena-4,7(11)-diene	1409	-	-	-	-	-	1.27 (1412)	-	-
Elixene	1414	-	-	-	-	-	0.65 (1418)	0.21 (1411)	0.29 (1417)
Cedr-8(15)-ene	1415	-	-	0.38 (1413)	0.11 (1413)	-	-	-	-
***α*-Cedrene**	1417	0.97 (1406)	0.32 (1405)	-	-	-	2.53 (1421)	0.69 (1417)	0.16 (1420)
***trans*-Caryophyllene**	1418	-	0.53 (1415)	-	0.47 (1417)	-	-	-	0.25 (1423)
***α*-Caryophyllene**	1426	0.76 (1418)	-	-	-	0.28 (1427)	-	-	-
***β*-Gurjurene**	1429	-	-	-	-	-	-	-	0.26 (1437)
***α*-Bergamotene**	1432	0.09 (1432)	-	1.09 (1439)		-	-	-	-
ɤ-Elemene	1433	-	-	-	1.25 (1428)	0.66 (1437)	-	-	-
Guaia-6,9-diene	1440	-	-	-	-	0.28 (1448)	-	0.27 (1437)	1.33 (1453)
***α*-Guaiene**	1442	0.14 (1444)	-	-	0.23 (1440)	-	-	-	-
Isoledene	1445	-	-	-	0.55 (1444)	-	-	-	-
Longifolen-V1	1446	-	-	-	0.23 (1448)	-	-	-	-
***α*-Humulene**	1449	-	0.37 (1442)	-	0.86 (1449)	0.34 (1449)	-	-	-
***α*-Amorphene**	1450	-	0.40 (1448)	0.39 (1459)	0.63 (1452)	0.55 (1452)	2.57 (1456)	-	-
***α*-Muurolene**	1455	0.72 (1454)	-	-	-	-	1.55 (1460)	-	-
***trans*-*α*-Farnesene**	1458	-	-	-	-	-	-	-	0.30 (146)
***cis*-Muurola-4(15),5-diene**	1462	-	-	-	-	-	2.54 (1462)	0.16 (1468)	0.51 (1473)
Viridiflorene	1466	-	-	-	-	-	0.16 (1467)	-	-
***γ* -Himachalene**	1471	-	-	-	-	-	-	2.15 (1470)	-
ɤ-Muurolene	1475	1.12 (1473)	-	0.23 (1471)		0.26 (1472)	0.37 (1477)	0.33 (1477)	-
Virdiflorene	1477	-	-	-	-	-	-	0.69 (1488)	-
Germacrene-D	1479	2.6 (1478)	0.32 (1478)	0.34 (1478)	2.93 (1481)	-	-	-	-
Dihydroagarofurane	1480	0.83 (1480)	-	-	-	0.31 (1482)	-	-	1.34 (1477)
***β*-Selinene**	1482	0.21 (1483)	-	0.16 (1485)	0.40 (1483)	-	-	-	2.01 (1491)
Bicyclogermacrene	1483	1.0 (1485)	-	-	-	-	-	-	-
***α*-Gurjunene**	1484	0.25 (1487)	1.01 (1488)	-	-	-	-	0.41 (1493)	0.52 (1498)
***α*-Selinene**	1486	0.35 (1488)	-	1.55 (1493)	0.48 (1490)	-	-	-	-
Albicanol	1489	-	-	-	0.88 (1492)	-	-	-	-

Table 3. Continued

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
***α*-Eudesmol**	1495	-	-	-	0.38 (1495)	-	-	-	-
***α*-Himachalene**	1498	0.2 (1497)	-	-	-	-	-	-	-
Epizonarene	1500	0.41 (1502)	-	-	-	-	-	-	-
***β*-Bisabolene**	1501	0.7 (1505)	0.76 (1506)	0.51 (1502)	-	-	0.71 (1500)	-	-
***β*-Patchoulene**	1509	-	-	-	-	-	-	0.34 (1503)	-
ɤ-Cadinene	1511	0.19 (1509)	2.73 (1507)	2.83 (1514)	0.93 (1513)	0.23 (1525)	2.44 (1525)	0.55 (1516)	0.60 (1504)
***δ*-Cadinene**	1513	1.35 (1511)	0.42 (1513)	2.65 (1517)	1.10 (1515)	-	-	-	-
***δ*-Amorphene**	1514	-	1.92 (1515)	-	-	-	-	-	-
***β*-Guaiene**	1517	-	-	-	0.78 (1521)	-	-	-	-
Epicubebol	1519	-	-	-	-	-	1.13 (1530)	-	-
***α*-Farnesene**	1522		0.64 (1519)	-	-	-	-	-	-
ɤ-Selinene	1524	-	-	-	0.31 (1526)	-	-	-	-
***δ*-Selinene**	1529	-	-	-	0.26 (1529)	-	-	-	-
***cis*-*α*-Bisabolene**	1535	-	0.43 (1530)	-	-	-	-	-	-
3,7(11)-Selinadiene	1541	-	-	-	0.34 (1537)	-	-	-	-
Elemol	1548	0.3 (1540)	-	0.42 (1552)	0.27 (1542)	-	0.17 (1540)	-	-
***γ*-Eudesmol**	1555	-	-	-	-	0.20 (1540)	-	0.66 (1547)	
Germacrene -B	1559	0.47 (1555)	-	-	4.49 (1555)	1.34 (1552)	-	-	-
Calarene	1570				0.11 (1563)	-	-	-	-
ɤ-Gurjunene	1571	0.61 (1568)	-	0.23 (1568)	-	-	-	-	-
Spathulenol	1573	0.26 (1570)	-	-	-	-	-	-	-
Cadina-1(6),4-diene	1575	-	-	-	-	-	-	-	0.72 (1576)
Veridiflorol	1590	0.42 (1588)	-	-	-	-	-	-	-
Guaiol	1595		0.87 (1588)	0.93 (1584)	1.44 (1586)	0.75 (1590)	1.58 (1588)	7.41 (1592)	3.24 (1593)
***β*-Gurjunene**	1609	1.08 (1601)	-	0.51 (1598)	-	-	0.19 (1604)	0.31 (1606)	-
Fenobucarb	1616	-	-	-	-	-	-	-	0.16 (1611)
Epi-bicyclosesquiphellandrene	1620	-	2.81 (1612)	1.55 (1613)	-	-	-	-	-
Epicubenol	1628	-	-	-	-	-	0.49 (1624)	-	-
***τ*-Cadinol**	1636	-	-	-	-	-	2.41 (1630)	-	-
epi-*α*-Muurolene	1642	0.27 (1647)	-	-	-	-	-	-	-
***trans*-Muurolol**	1645	-	0.19 (1640)	-	-	-	-	-	-
***β*-Eudesmol**	1646	0.29 (1649)	0.17 (1647)	0.17 (1647)	0.42 (1644)	-	-	-	-

Table 3. Continued

		Percentage of compounds in samples* (KIc**)							
Compounds	**KI*** **	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**
epi-γ-Eudesmol	1657	-	-	-	-	0.40 (1644)	-	0.40 (1648)	0.69 (1642)
β-Atlantone	1659	-	-	-	-	-	-	0.43 (1652)	-
Aromandendrene	1661	-	0.14 (1659)	0.23 (1658)	-	0.29 (1664)	-	1.26 (1666)	0.16 (1658)
Agarospirol	1663	0.26 (1660)	-	-	-	-	-	-	-
α-epi-7-epi-5-Eudesmol	1664	-	-	-	-	-	-	-	0.37 (1666)
Bulnesol	1666	0.95 (1662)	0.74 (1662)	0.80 (1660)		0.47 (1668)	-	0.30 (1670)	2.68 (1672)
Guai-1(10)-en-11-ol	1668	-	-	-	-	-	1.44 (1674)	6.79 (1673)	-
Guaiac acetate	1710	1.24 (1703)	-	-	-	-	-	-	-
Acorenone B	1716	-	0.19 (1711)	0.73 (1715)	-	-	0.38 (1717)	-	-
Guaiol acetate	1720	-	-	-	-	-	-	1.26 (1705)	
Monoterpene hydrocarbons		63.63	61.27	49.59	65.99	87.11	57.48	58.29	68.47
Oxygenated monoterpenes		3.39	7.37	14.23	1.82	1.31	8.54	2.82	4.05
Sesquiterpene hydrocarbons		18.42	16.68	22.72	17.8	4.93	20.06	15.09	8.92
Oxygenated sesquiterpenes		3.34	1.23	1.52	3.41	1.66	7.22	16.95	5.27
Diterpene hydrocarbons		-	-	-	-	-	-	-	-
Oxygenated diterpenes		-	-	-	-	-	-	-	-
Other		5.60	0.74	0.80	5.09	2.93	0.00	3.75	5.50
Total identified		**94.38**	**87.29**	**88.86**	**94.11**	**97.94**	**93.30**	**96.90**	**92.21**
Unknown		5.62	12.71	11.14	5.89	2.06	6.70	3.10	7.79

*Oleo-gum resin of *Ferula gummosa* from different regions of Iran; M1: Firuzkuh, M2: Torbat-e-Jam, M3: Sabzevar, M4: Kalat-e-Naderi, M5: Shiraz, M6: Shahmirzad, M7: Damghan, M8: Jajarm; ** KIc: index calculated based on Kovats index formula; *** KI: Kovats index based on NIST website & identification of essential oil components by gas chromatography/ mass spectrometry [31]

In the pharmacological effects observed from plants, all components of the essential oils are important and it is usually not possible to relate a specific effect to a specific component of the essential oil. However, in essential oils of *Ferula gummosa*, components such as α-pinene, β-pinene, δ-3-carene and sabinene are commercially important.

According to the GC-MS analysis, the main components of essential oils of all samples were monoterpene hydrocarbons among which the major compounds were β-pinene (5.11-63.80 %), sabinene (3.37-30.69%), α-pinene (4.43-12.72%) and δ-3-carene (2.38-10.23 %). The variability in the oil content and composition of different samples exhibited a notable difference in hydrocarbon monoterpenes content variation from 49.59 % (M3) to 87.11% (M5), but when we consider the sum of monoterpenoids, this difference becomes smaller from 61.11 % (M7) to 88.42% (M5).

It is also important to note that the highest concentration of β-pinene (63.80%) and sabinene (30.69%) were found in the M5 (Shiraz) and M2 (Torbat-e-Jam) samples, respectively.

Also, the highest concentration of α -pinene (12.72%) and δ-3-carene (10.23%) were found in the M1 (Firuzkuh) and M5 (Shiraz) samples, respectively.

The results of this study is in agreement with the previous study of Malekzadeh et al. that demonstrated the effect of geographic location on variability of chemical composition of essential oils from roots and aerial parts of *F. gummosa.* According to their study, monoterpenes hydrocarbons including (α-pinene (17-56.55 %), β-pinene (10.44-37.04 %), δ-3-carene (9.16-10.75 %) and limonene (0-13.23) were the predominant components of *F. gummosa* [26]. Essential oils colors were different depending on the location of growth. In accordance with phytochemical screening, the environmental factors including average annual rainfall, mean annual temperature, latitude, longitude, and altitude remarkably change the phytochemical content of the same plant in different locations.

Accordingly, variation in secondary metabolites of the same genus is economically and therapeutically important and plays a highly effective role in the area of investigation for more influential secondary metabolites. In fact, by changing the location and environmental factors, desirable plants with target contents can be acquired which is a big step toward better therapeutic and economic purposes in the field of natural products and compounds.

Conclusion

Chemical composition of essential oils from oleo-gum resins are highly affected by the environmental elements such as annual temperature and rainfall, altitude, longitude and latitude. As a result, the therapeutic effect of medicinal plants depends on variation of geographic location. Therefore, analysis of one species from different geographic locations and climate leads to identification of varied percentages of compounds which provide the basis for more medicinal investigations and wide variety of healing properties. Thus, remarkable variation in the chemical composition of essential oils can be used as basic rule for growing medicinal plants in order to meet more specific pharmaceutical goals.

Acknowledgments

This research was supported by Medicinal Plants Research Center, Faculty of Pharmacy, and Research and Technology Office, Tehran University of Medical Sciences, Tehran, Iran (No.38878).

Author contributions

Mansour Mofasseri, Zahra Moein, and Zahra Baharipour accomplished the experiments; Zahra Tofighi, Mostafa Pirali Hamedani, and Saeed Tavakoli analyzed the data; Abbas Hadjiakhoondi administrated the study; Saied Goodarzi designed the study and supervised study.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

References

[1] Selamoglu Z. Polyphenolic compounds in human health with pharmacological properties. *J Tradit Med Clin Naturopat*. 2017; 6(4): 1.

[2] Mehdizadeh L, Moghaddam M. Essential oils: biological activity and therapeutic potential. In: Grumezescu AM, Holban AM, Eds. Therapeutic, probiotic, and unconventional foods. Academic Press, 2018.

[3] Bonda AF, Regis L, Giovannelli L, Segale L. Alginate/maltodextrin and alginate/shellac gum core-shell capsules for the encapsulation of peppermint essential oil. *Int J Biol Macromol.* 2020; 162: 1293–1302.

[4] Alikhani-Koupaei M. Liposome-entrapped essential oils on in vitro and in vivo antioxidant activity in leafy vegetables. *Qual Assur Saf Crop Food.* 2015; 7(3): 369–373.

[5] Hajhashemi V, Ghannadi A, Pezeshkian SK. Antinociceptive and anti-inflammatory effects of *Satureja hortensis* L. extracts and essential oil. *J Ethnopharmacol*. 2002; 82(2-3): 83–87.

[6] Ayaz M, Sadiq A, Junaid M, Ullah F, Subhan F, Ahmed J. Neuroprotective and anti-aging potentials of essential oils from aromatic and medicinal plants. *Front Aging Neurosci*. 2017; 9: 1–16.

[7] Alves-Silva JM, Zuzarte M, Girão H, Salgueiro L. The role of essential oils and their main compounds in the management of cardiovascular disease risk factors. *Molecules*. 2021; 26(12): 1–26.

[8] Bhalla Y, Gupta VK, Jaitak V. Anticancer activity of essential oils: a review. *J Sci Food Agric*. 2013; 93(15): 3643–3653.

[9] Mutlu-Ingok A, Devecioglu D, Dikmetas DN, Karbancioglu-Guler F, Capanoglu E. Antibacterial, antifungal, antimycotoxigenic, and antioxidant activities of essential oils: an updated review. *Molecules.* 2020; 25(20): 1–49.

[10] Valdivieso-Ugarte M, Gomez-Llorente C, Plaza-Díaz J, Gil Á. Antimicrobial, antioxidant, and immunomodulatory properties of essential oils: a systematic review. *Nutrients*. 2019; 11(11): 1–29.

[11] Heghes SC, Vostinaru O, Rus LM, Mogosan C, Iuga CA, Filip L. Antispasmodic effect of essential oils and their constituents: a review. *Molecules.* 2019; 24(9): 1–29.

[12] García-Salinas S, Elizondo-Castillo H, Arruebo M, Mendoza G, Irusta S. Evaluation of the antimicrobial activity and cytotoxicity of different components of natural origin

present in essential oils. *Mol J Synth Chem Nat Prod Chem*. 2018; 23(6): 1–18.
[13] Zhang N, Yao L. Anxiolytic effect of essential oils and their constituents: a review. *J Agric Food Chem*. 2019; 67(50): 13790–13808.
[14] Mortazaienezhad F, Sadeghian M. Investigation of compounds from galbanum (*Ferula gummosa*) Boiss. *Asian J Plant Sci*. 2006; 5(5): 905–906.
[15] Bahrami G, Soltani R, Sajjadi SE, Kanani MR, Naderi R, Ghiasvand N, Shokoohinia Y. Essential oil composition of *Ferula assa-foetida* L. fruits from Western Iran. *J Rep Pharm Sci*. 2013; 2(2): 90–97.
[16] Hosseinzadeh N, Shomali T, Hosseinzadeh S, Raouf Fard F, Pourmontaseri M, Fazeli M. *J Pharm Pharmacol*. 2020; 72(8): 1013–1025.
[17] Yaqoob U, Nawchoo IA. Distribution and taxonomy of *Ferula* L.: a review. *Res Rev J Biotechnol*. 2016; 5(3): 15–23.
[18] Pirbalouti AG, Ghahfarokhi BB, Ghahfarokhi SAM, Malekpoor F. Chemical composition of essential oils from the aerial parts and underground parts of Iranian valerian collected from different natural habitats. *Ind Crops Prod*. 2015; 63: 147–151.
[19] Nabavi SF, Habtemariam S, Sureda A, Nabavi SM. *Ferula gummosa* Boiss. as a rich source of natural antioxidants with numerous therapeutic uses-a short review. In: Capasso A, Ed. Medicinal plants as antioxidant agents: understanding their mechanism of action and therapeutic efficacy. Kerala: Research Signpost, 2012.
[20] Mousavi SH, Tayarani NZ, Hersey P. Apoptosis: from signalling pathways to therapeutic tools. *Iran J Basic Med Sci.* 2008; 11(3): 121–142.
[21] Gharaei R, Akrami H, Heidari S, Asadi MH, Jalili A. The suppression effect of *Ferula gummosa* Boiss. extracts on cell proliferation through apoptosis induction in gastric cancer cell line. *Eur J Integr Med*. 2013; 5(3): 241–247.
[22] Iranshahy M, Iranshahi M. Traditional uses, phytochemistry and pharmacology of asafoetida (*Ferula assa-foetida* oleo-gum-resin), a review. *J Ethnopharmacol*. 2011; 134(1): 1–10
[23] Moosavy MH, Shavisi N. Determination of antimicrobial effects of nisin and *Mentha spicata* essential oil against *Escherichia coli* O157: H7 under various conditions (pH, temperature and NaCl concentration). *Pharm Sci*. 2013; 19(2): 61–67.
[24] Rajabi Z, Ebrahimi M, Farajpour M, Mirza M, Ramshini H. Compositions and yield variation of essential oils among and within nine *Salvia* species from various areas of Iran. *Ind Crops Prod*. 2014; 61: 233–239.
[25] Bajalan I, Pirbalouti AG. Variation in chemical composition of essential oil of populations of *Lavandula* × *intermedia* collected from Western Iran. *Ind Crops Prod*. 2015; 69: 344–347.
[26] Malekzadeh M, Rabbi Angourani H, Yazdinezhad A, Hassan M, Abiodun F, Hazrati S. Evaluation of volatile oil in indigenous populations of *Ferula gummosa* Boiss. *J Essent Oil Bear Plants*. 2018; 21(1): 206–213.
[27] Talebi Kouyakhi E, Naghavi MR, Alayhs M. Study of the essential oil variation of *Ferula gummosa* samples from Iran. *Chem Nat Compd*. 2008; 44: 124–126.
[28] Jahansooz F, Ebrahimzadeh H, Najafi A, Naghavi M, Talebi Kouyakhi E, Farzaneh H. Composition and antifungal activity of the oil of *Ferula gummosa* samples from Iran. *J Essent Oil Bear Plants*. 2008; 11(3): 284–291.
[29] Editorial board. British pharmacopeia. London: The Stationary Office, 1988.
[30] Adams RP. Identification of essential oil components by gas chromatography/ quadruple mass spectroscopy. Carol Stream: Allured publishing cor., 2004.
[31] Adams RP. Identification of essential oil components by gas chromatography/mass spectrometry. Carol Stream: Allured publishing cor., 2007.

Abbreviations

GC-MS: Gas Chromatography- Mass Spectrometry; KI: Kovats Index; KIc: Calculated Kovats Index; NIST: National Institute of Standards and Technology