

Review article

Biological activities of essential oils from the genus *Ferula* (Apiaceae)

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The genus *Ferula* (Apiaceae) comprises about 170 species occurring from central Asia westward to northern Africa. This genus is well-known in folk medicine for the treatment of various organ disorders. Most of *Ferula* species possess strong aromatic smell that is due to the presence of essential oil or oleoresin in their different organs. This article reviews anti-bacterial, anti-fungal and other biological activities of *Ferula* oils reported to date. For medicinal applications, the chemical composition of volatile oils obtained from different *Ferula* species is summarized in Appendix.

Keywords: Apiaceae, essential oil, *Ferula*

The Apiaceae or Umbelliferae is a family of usually aromatic plants with hollow stems commonly known as umbellifers. This family is well represented in the Iranian flora, at least with 112 genera, 316 species, and 75 endemic species [1]. Notable members of this family include *Anethum graveolens* (Dill), *Anthriscus cerefolium* (chervil), *Angelica* spp. (*Angelica*), *Apium graveolens* (celery), *Carum carvi* (caraway), *Coriandrum sativum* (coriander), *Cuminum cyminum* (cumin), *Foeniculum vulgare* (fennel), *Ferula gummosa* (galbanum), and *Pimpinella anisum* (anise). The aromatic smell of most species is due to the presence of essential oil or oleoresin in their different organs [2]. Pictures of *Ferula* species are shown in **Fig. 1**.

The genus *Ferula*, belonging to the family Apiaceae, comprises about 170 species. These are produced from central Asia westward to northern Africa [3]. The Iranian flora comprises of 30 species of *Ferula*, of which some are endemic [4, 5]. The popular Persian name of the most species is "Koma" [5].

The chemistry of this genus has been studied by many investigators. To date, more than 70 species of

Ferula have been investigated chemically [6-8]. The plants of this genus are well documented as a good source of biologically active compounds such as derivatives [9-17], and sulfur containing compounds [18-24].

Several species of this genus have been used in traditional medicine for the treatment of various organ disorders. Among different *Ferula* species that have been used as natural remedies, *F. assa-foetida* (used as anticonvulsant, carminative, antispasmodic, diuretic, aphrodisiac, antihelmintic, tonic, and laxative, alterative, etc.), *F. badrakema* and *F. gummosa* (both used as anti-convulsant, tonic, anti-hysterical, decongestant, treatment of neurological disorders, and stomachache), and *F. persica* (used as laxative, carminative, anti-hysterical, treatment of lumbago, diabetes, rheumatism, and backache) are most famous [25-28].

Recent investigations have led to the discovery of some new biological activities of the plants of this genus. These include anti-microbial, anti-fungal, antinociceptive, anti-inflammatory, anti-convulsant, antioxidant, anti-mycobacterial, anti-spasmodic, and hypotensive activities [29-39]. At least, part of the biological activities of the plants of this genus can be attributed to their essential oils [29-31].

Essential oils are the subtle, highly concentrated, aromatic, and volatile liquids. These are extracted from the flowers, seeds, leaves, stems, bark, and roots of

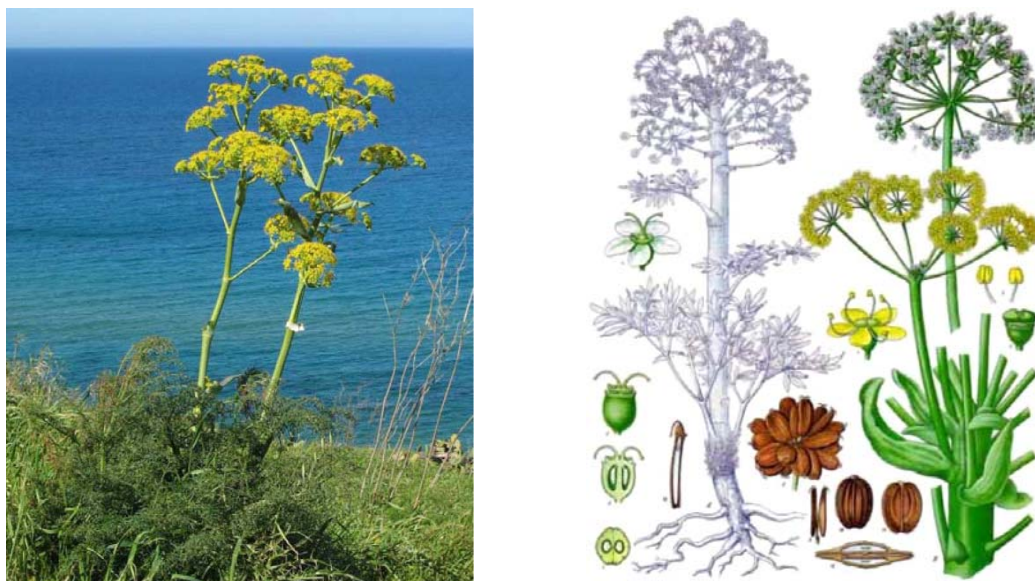


Fig. 1 Natural and schematic pictures of *Ferula* species.

plants, usually through steam or hydro-distillation. These natural oils are mixtures of complex and volatile compounds that are synthesized by aromatic plants as secondary metabolites. The importance of essential oils is not only confined to their natural protecting role for the host plants, but also to the fact that these oils contain properties many times more powerful than dried herbs. Among these properties are the anti-bacterial, anti-microbial, anti-viral, and anti-fungal activities, together with some particular medicinal effects that make essential oils a very important consideration [29-31, 40-43]. Regarding the strong odor of many *Ferula* species and reported effects of some isolated volatile components, it seems that essential oils of this genus have an important role in the observed biological effects of these plants.

In this article, we review biological activities of *Ferula* oils where stress is put on anti-microbial and anti-fungal activities of *Ferula* oils. Considering a recent trend to natural products including essential oils for medicinal applications, we summarize the chemical composition of volatile oils obtained from different *Ferula* species in Appendix.

Antimicrobial activities

In a previous survey, the essential oil from the fruits of *F. badrakema* was found to be moderately active against *Staphylococcus aureus* and *Bacillus cereus* as Gram-positive bacteria, and *Candida albicans* as fungal strain. However, Gram-negative

bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) appeared not to be susceptible to inhibitory effects of this essential oil [29]. In another study, the essential oils from *F. glauca* were evaluated for antibacterial and antifungal activity. The results showed that the Gram-positive *B. subtilis* was the most sensitive strain. The essential oils also showed moderate inhibitory activity against *Streptococcus mutans*, *Enterococcus faecalis* and *E. coli* whereas no remarkable activity was observed against *S. aureus* and the yeast *C. albicans* (which was the most resistant strain). Findings also demonstrated that leaves and fruits essential oils were the most active oils of the plant on the tested microorganisms [30]. Concerning the *F. latisecta*, the polysulfide-rich fruit oil of this plant was shown to possess antibacterial activity against Gram-positive (*B. cereus* and in particular *S. aureus*) but not Gram-negative bacteria (*P. aeruginosa* and *E. coli*) and a relatively potent inhibitory activity against *C. albicans* [44]. Moreover, this oil was tested for its antifungal activity against a range of human pathogenic dermatophytes (*Trichophyton mentagrophytes*, *T. rubrum*, *T. verrucosom*, *Microsporum canis* and *M. gypseum*). The results showed that the oil was active against all tested dermatophytes with the most significant activity against *T. rubrum* and *T. verrucosom* [31]. In another study, the essential oil from the aerial parts of *F. latisecta* was reported to exert high inhibitory activity against the Gram-positives *B. subtilis* and *E. faecalis*,

moderate activity against *S. aureus*, *E. coli* and *Klebsiella pneumoniae* and was inactive against *P. aeruginosa* [45]. Concerning the *F. gummosa*, it was found that the essential oil from the fruits of the plant possesses strong antibacterial and antifungal activities against Gram-positive (*S. aureus*, *S. epidermis* and *B. subtilis*) and negative (*E. coli*, *Salmonella typhi* and *Pseudomonas aeruginosa*) bacteria and fungi (*C. albicans* and *C. kefyr*) [46]. In another study, *F. gummosa* seed oil was also reported to be active against Gram-positive bacteria (*S. aureus*, *B. subtilis* and *E. faecalis*) and *E. coli*. However, unlike the former study, little antibacterial activity was found from this oil against *P. aeruginosa* [47]. For *F. szowitsiana*, the leaf oil of the plant possessed antimicrobial activity against two strains of Gram-positive bacteria (methicillin-resistant *S. aureus* and *S. epidermidis*), four strains of Gram-negative bacteria (*E. coli*, *P. aeruginosa*, *Proteus vulgaris* and *Salmonella typhimurium*) and a yeast (*Candida albicans*). The minimal inhibitory concentration (MIC) values of the leaf oil towards the selected human pathogenic bacteria and the fungus were determined as 0.156-1.25 µg/mL. Noteworthy, the strong antibacterial activity of this oil against methicillin-resistant *S. aureus* (MRSA, MIC = 0.156 µg/mL) was an interesting finding [48]. In another investigation on the essential oil obtained from the aerial parts of this plant, *B. subtilis* was found to be the most sensitive strain compared with the *S. aureus*, Gram-negative bacteria (*E. coli*, *P. aeruginosa*) and fungal strains (*Aspergillus niger* and *C. albicans*) for which weaker activities of the oil were observed [49]. Finally, there is a previous report indicating the antifungal activity of *F. assa-foetida* seed oil against five species of the food borne mold *Aspergillus* (*A. awamori*, *A. niger*, *A. flavus*, *A. foetidus* and *A. oryzae*). The oil was shown to inhibit all the three stages of asexual reproduction of *Aspergillus* species i.e., spore germination, mycelial growth, and spore formation [50]. Findings on the antimicrobial activities of *Ferula* oils have been summarized in **Table 1**.

Miscellaneous activities

Together with the anti-microbial activities, a few miscellaneous activities have also been reported from essential oils of *Ferula* species. Concerning the *F. gummosa*, the fruit oil of the plant was evaluated

for anticonvulsant activity against experimental seizures. The essential oil had no effect against seizures induced by maximal electroshock but protected mice against pentylenetetrazole-induced tonic seizures. However, the protective dose produced neurotoxicity and was too close to the LD₅₀ of the essential oil [51]. In another investigation, the oleo-gum-resin oil of *F. gummosa* was reported to possess relaxant effect on rat-isolated ileum against contractions induced by KCl and acetylcholine. The authors stated that at least part of this inhibitory effect might be due to the α-pinene and β-pinene components of the oil [52]. In connection with *F. harmonis*, it was revealed that seed oil of the plant could enhance erectile function in rats. However, it was reported that this oil could also cause certain toxicities if it is used for a long period and even may become a male contraceptive agent [53]. Finally, the essential oil from *F. orientalis* aerial parts was found to possess antioxidative potential in 2'-diphenyl-1-picrylhydrazyl radical (DPPH) as well as β-carotene/linoleic acid assay, though it was not as strong as that of positive control (BHT) [32].

Concluding remarks

There are only few reports on the biological activity of essential oils from *Ferula* species, of which the majority have investigated the anti-microbial activity of these oils. Previous findings indicate the anti-microbial activity of *Ferula* essential oils and their potential application as natural aromatic anti-bacterial and anti-fungal agents. The bacteriostatic and fungistatic properties of these essential oils may be associated to the high content of α-pinene and β-pinene or polysulfides that are present in these oils and for which strong anti-microbial activities have been reported previously [54-56].

Asian countries have used herbs and minerals as nutrients, and medicine for a long time. However, their analytical studies have not been completed yet [59, 60]. Some reports indicate side effects of traditional medicine to acknowledgement of the value of the long heritage in traditional medicine. Further analysis and understanding of herbal and mineral medicine will increase to current medical practice.

The authors have no conflict of interest to report.

Appendix

The chemical composition of volatile oils obtained from different *Ferula*

Different *Ferula* species share some similarities in their volatile components, but there are many compositional differences. We can classify their essential oils based on their compositional differences.

The most prominent measure that can be applied to categorize *Ferula* oils is the presence of sulfur-containing compounds. The essential oils obtained from *F. assa-foetida*, *F. fukanensis*, *F. latisecta*, *F. persica* and *F. sinkiangensis* contained sulfur compounds. On the other hand, other oils were devoid of these compounds among their identified components. *sec*-Butyl-(*Z*)-propenyl disulfide and *sec*-butyl-(*E*)-propenyl disulfide were found to be the most prevalent sulfur-containing compounds in the essential oils of some *Ferula* species. The terpenoid compounds were almost the most abundant

components of *Ferula* oils. The most frequent terpenoid compounds that occurred as main components in the essential oils were α -pinene, β -pinene, myrcene and limonene (among monoterpene hydrocarbons); linalool, α -terpineol and neryl acetate (among oxygenated monoterpenes); β -caryophyllene, germacrene B, germacrene D and δ -cadinene (among sesquiterpene hydrocarbons) and caryophyllene oxide, α -cadinol, guaialol and spathulenol (among oxygenated sesquiterpenes). Despite the existing reports and considering the total number of identified *Ferula* species (more than 170), there are still many species uninvestigated. Therefore, conducting future studies on the chemical composition and particularly biological activities of uninvestigated *Ferula* oils is greatly recommended. The tabulated overviews of chemical components of *Ferula* species essential oils, together with the structures of the main components, are shown in **Fig. 2-7**.

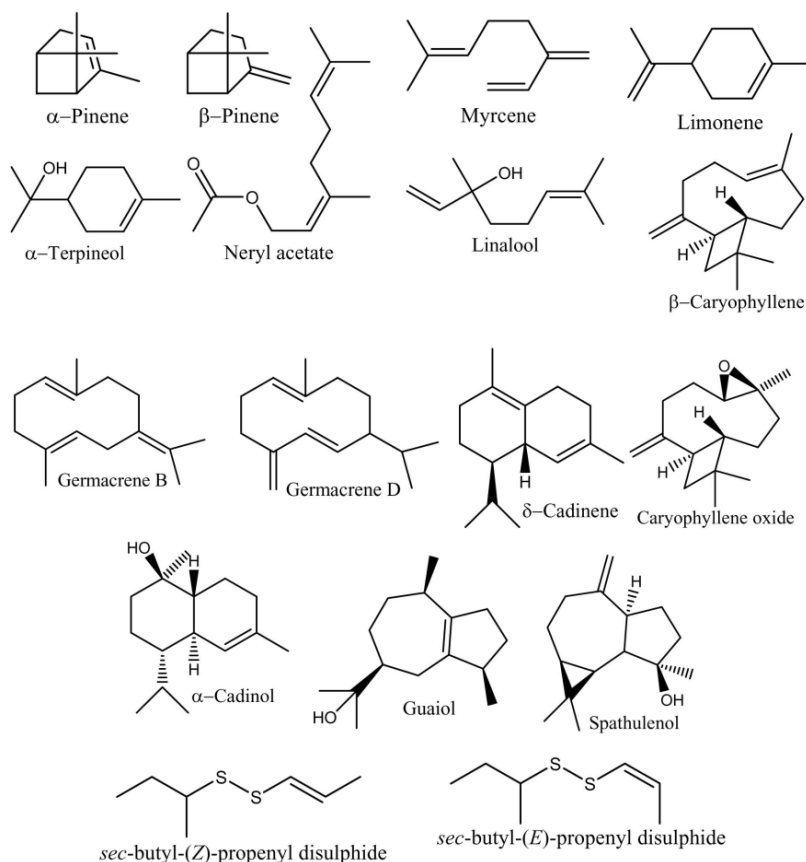


Fig. 2 Chemical structure of the most frequent main components present in the essential oils of *Ferula* species.

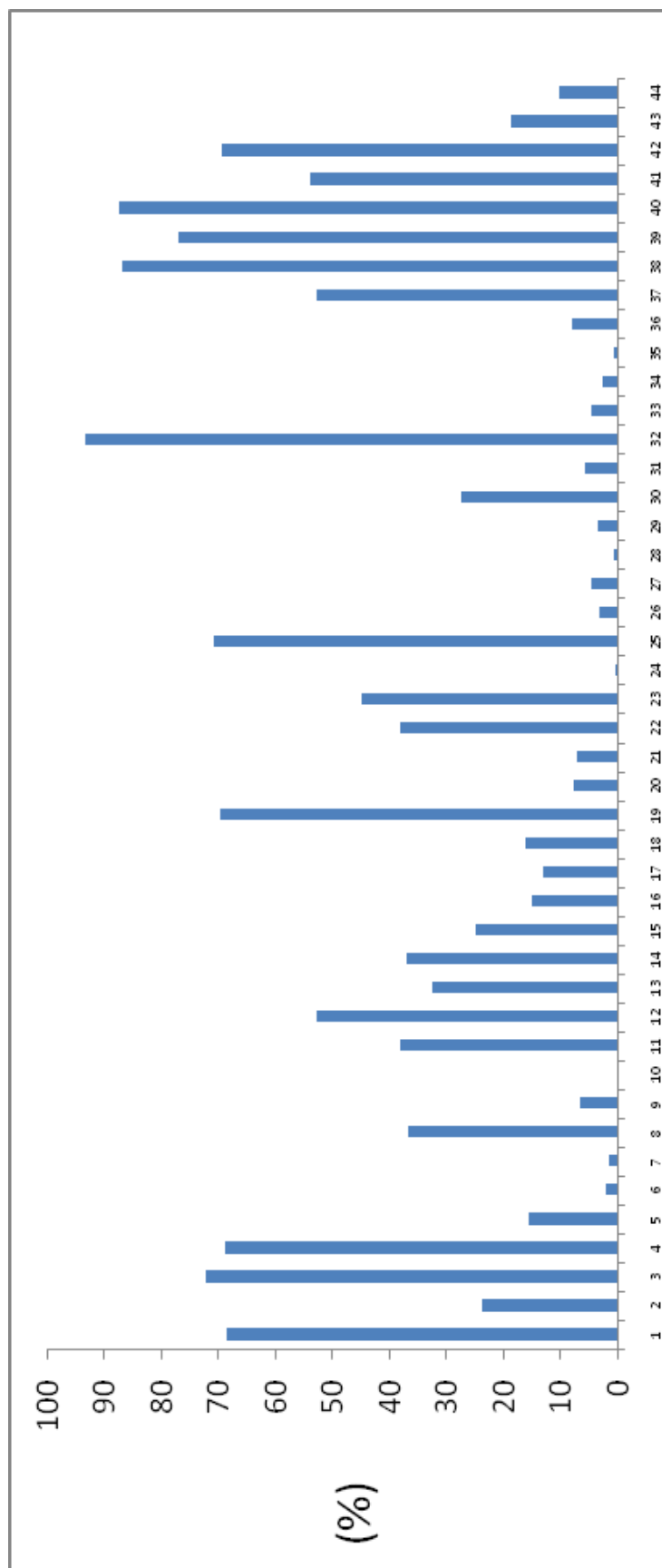


Fig. 3 Relative abundance of monoterpene hydrocarbons in the essential oils of *Ferula* species. **1:** *F. ovina* (fruits); **2:** *F. ovina* (aerial parts from Isfahan province of Iran); **3:** *F. ovina* (aerial parts from Azerbaijan province of Iran); **4:** *F. badrakema* (fruits); **5:** *F. elaeochoyris* (fruits); **6:** *F. sinkiangensis* (oleogum resin); **7:** *F. fukanensis* (oleogum resin); **8:** *F. arrigonii* (leaves); **9:** *F. persica* (aerial parts); **10:** *F. persica* (roots); **11:** *F. hirtella* (aerial parts); **12:** *F. microcolea* (aerial parts); **13:** *F. macrocolea* (aerial parts); **14:** *F. szowitziana* (stems/leaves); **15:** *F. szowitziana* (stems/leaves); **16:** *F. szowitziana* (flowers/fruits); **17:** *F. szowitziana* (stems); **18:** *F. szowitziana* (leaves); **19:** *F. orientalis* (aerial parts); **20:** *F. feruloides* (roots); **21:** *F. glauca* (leaves); **22:** *F. glauca* (flowers); **23:** *F. glauca* (fruits); **24:** *F. glauca* (roots); **25:** *F. communis* (leaves); **26:** *F. communis* (flowerheads obtained by SFE); **27:** *F. communis* (flowerheads obtained by hydro-distillation); **28:** *F. communis* (mixed different parts from poisonous chemotype); **29:** *F. communis* (mixed different parts from non-poisonous chemotype); **30:** *F. flabelliloba* (aerial parts); **31:** *F. flabelliloba* (fruits); **32:** *F. stenocarpa* (aerial parts); **33:** *F. latisecta* (fruits); **34:** *F. latisecta* (leaves); **35:** *F. latisecta* (roots); **36:** *F. latisecta* (aerial parts); **37:** *F. jaeschkeana* (rhizomes); **38:** *F. gummosa* (fruits from the Tehran province of Iran); **39:** *F. gummosa* (fruits from the Isfahan province of Iran); **40:** *F. gummosa* (oleogum resin/latex); **41:** *F. gummosa* (stems); **42:** *F. gummosa* (roots); **43:** *F. assa-foetida* (seeds); **44:** *F. assa-foetida* (oleogum resin).

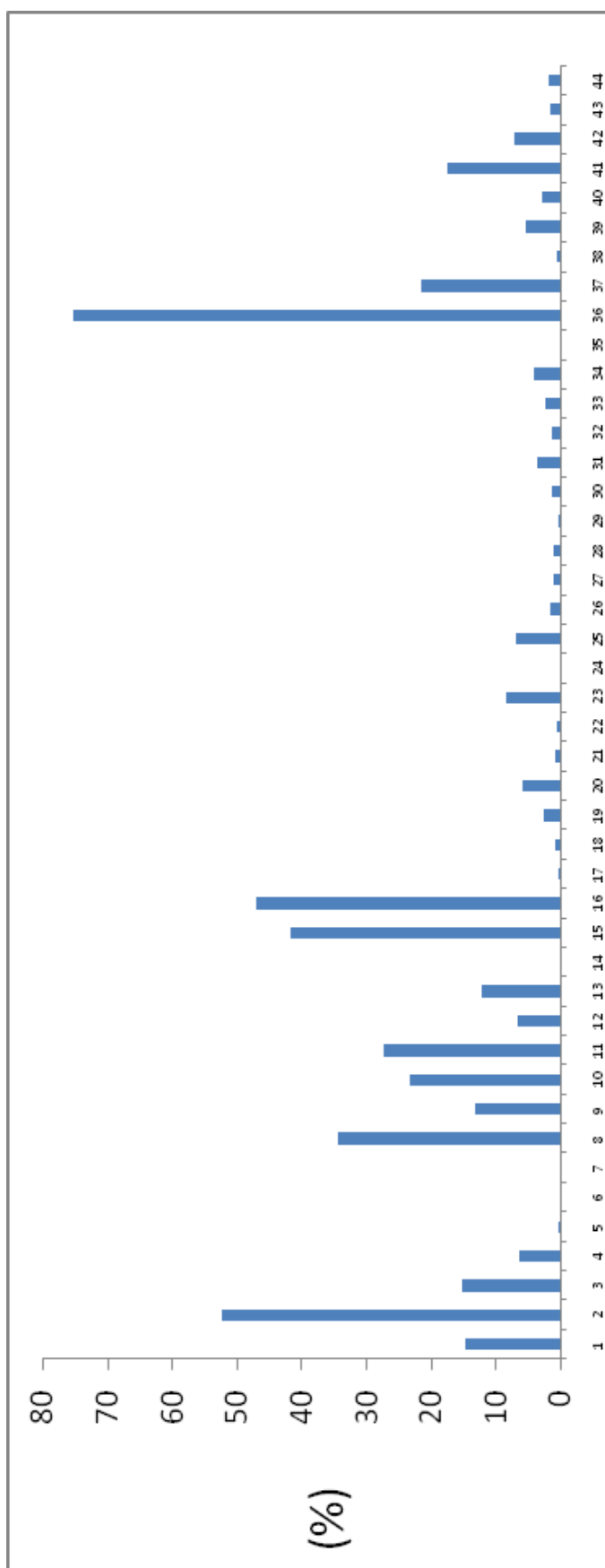


Fig. 4 Relative abundance of oxygenated monoterpenes in the essential oils of *Ferula* species. **1:** *F. ovina* (fruits); **2:** *F. ovina* (aerial parts from Isfahan province of Iran); **3:** *F. ovina* (aerial parts from Azerbaijani province of Iran); **4:** *F. badrakema* (fruits); **5:** *F. elaeochytris* (fruits); **6:** *F. sinkiangensis* (oleogum resin); **7:** *F. fukanensis* (oleogum resin); **8:** *F. arrigonii* (leaves); **9:** *F. persica* (aerial parts); **10:** *F. persica* (roots); **11:** *F. hirtella* (aerial parts); **12:** *F. microcolea* (aerial parts); **13:** *F. macrocolea* (aerial parts); **14:** *F. szowitsiana* (aerial parts); **15:** *F. szowitsiana* (stems/leaves); **16:** *F. szowitsiana* (flowers/fruits); **17:** *F. szowitsiana* (stems); **18:** *F. szowitsiana* (leaves); **19:** *F. orientalis* (aerial parts); **20:** *F. feruloides* (roots); **21:** *F. glauca* (leaves); **22:** *F. glauca* (flowers); **23:** *F. glauca* (fruits); **24:** *F. glauca* (roots); **25:** *F. communis* (leaves); **26:** *F. communis* (flowerheads obtained by SFE); **27:** *F. communis* (flowerheads obtained by hydro-distillation); **28:** *F. communis* (mixed different parts from poisonous chemotype); **29:** *F. communis* (flowerheads from non-poisonous chemotype); **30:** *F. flabelliloba* (aerial parts); **31:** *F. flabelliloba* (fruits); **32:** *F. stenocarpa* (aerial parts); **33:** *F. latisecta* (leaves); **34:** *F. latisecta* (fruits); **35:** *F. latisecta* (roots); **36:** *F. latisecta* (aerial parts); **37:** *F. joeschkeana* (rhizomes); **38:** *F. gummosa* (fruits from the Tehran province of Iran); **39:** *F. gummosa* (fruits from the Isfahan province of Iran); **40:** *F. gummosa* (oleogum resin/latex); **41:** *F. gummosa* (stems); **42:** *F. assa-foetida* (seeds); **43:** *F. assa-foetida* (oleogum resin); **44:** *F. assa-foetida* (oleogum resin).

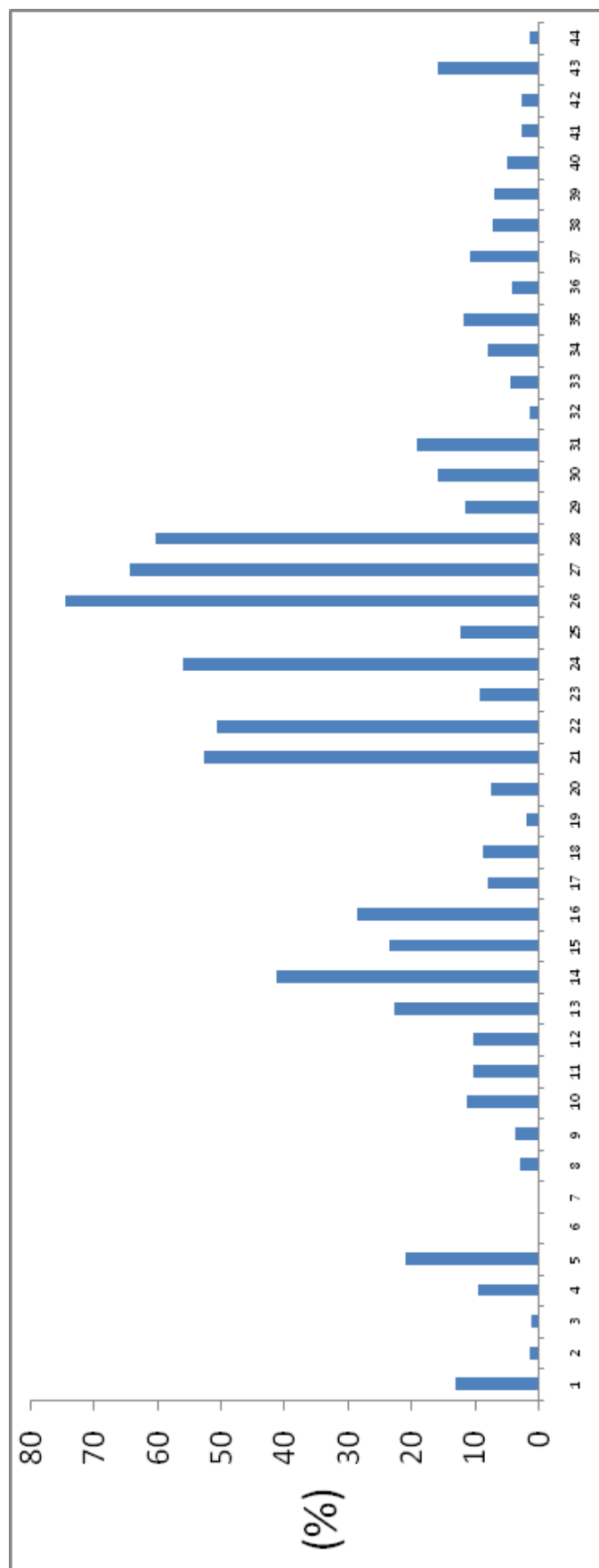


Fig. 5 Relative abundance of sesquiterpene hydrocarbons in the essential oils of *Ferula* species. **1:** *F. ovina* (fruits); **2:** *F. ovina* (aerial parts from Isfahan province of Iran); **3:** *F. ovina* (aerial parts from Azerbaijan province of Iran); **4:** *F. badrakema* (fruits); **5:** *F. elaeochytris* (fruits); **6:** *F. sinkiangensis* (oleogum resin); **7:** *F. fukanensis* (oleogum resin); **8:** *F. arrigonii* (leaves); **9:** *F. persica* (aerial parts); **10:** *F. hirtella* (aerial parts); **11:** *F. hirtella* (aerial parts); **12:** *F. microcolea* (aerial parts); **13:** *F. macrocolea* (aerial parts); **14:** *F. szowitsiana* (aerial parts); **15:** *F. szowitsiana* (stems/leaves); **16:** *F. szowitsiana* (flowers/fruits); **17:** *F. szowitsiana* (stems); **18:** *F. szowitsiana* (leaves); **19:** *F. feruloides* (roots); **20:** *F. feruloides* (roots); **21:** *F. glauca* (leaves); **22:** *F. glauca* (flowers); **23:** *F. glauca* (fruits); **24:** *F. glauca* (roots); **25:** *F. communis* (flowerheads obtained by SFE); **26:** *F. communis* (flowerheads obtained by hydro-distillation); **27:** *F. communis* (mixed different parts from poisonous chemotype); **28:** *F. communis* (mixed different parts from non-poisonous chemotype); **29:** *F. flabelliloba* (aerial parts); **30:** *F. flabelliloba* (fruits); **31:** *F. flabelliloba* (fruits); **32:** *F. stenocarpa* (rhizomes); **33:** *F. latisecta* (leaves); **34:** *F. latisecta* (leaves); **35:** *F. latisecta* (roots); **36:** *F. latisecta* (aerial parts); **37:** *F. jaeschkeana* (rhizomes); **38:** *F. gummosa* (fruits from the Tehran province of Iran); **39:** *F. gummosa* (fruits from the Isfahan province of Iran); **40:** *F. gummosa* (oleogum resin/latex); **41:** *F. gummosa* (stems); **42:** *F. gummosa* (roots); **43:** *F. assa-foetida* (seeds); **44:** *F. assa-foetida* (oleogum resin).

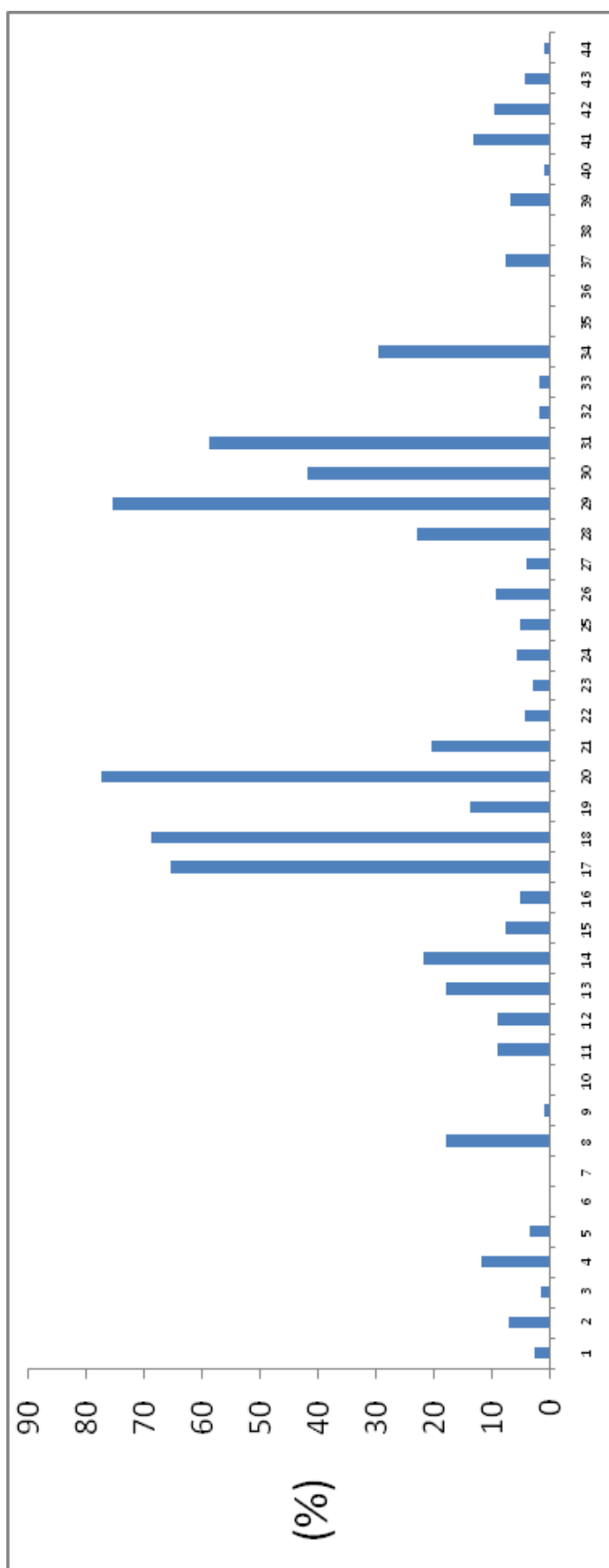


Fig. 6 Relative abundance of oxygenated sesquiterpenes in the essential oils of *Ferula* species. **1:** *F. ovina* (fruits); **2:** *F. ovina* (aerial parts from Isfahan province of Iran); **3:** *F. ovina* (aerial parts from Azerbaijan province of Iran); **4:** *F. badrakema* (fruits); **5:** *F. elaeochytris* (fruits); **6:** *F. sinkiangensis* (oleogum resin); **7:** *F. fukanensis* (oleogum resin); **8:** *F. arrigonii* (leaves); **9:** *F. persica* (aerial parts); **10:** *F. persica* (roots); **11:** *F. hirtella* (aerial parts); **12:** *F. microcolea* (aerial parts); **13:** *F. macrocolea* (aerial parts); **14:** *F. szowitziana* (aerial parts); **15:** *F. szowitziana* (stems/leaves); **16:** *F. szowitziana* (flowers/fruits); **17:** *F. szowitziana* (stems); **18:** *F. szowitziana* (leaves); **19:** *F. orientalis* (aerial parts); **20:** *F. feruloides* (roots); **21:** *F. glauca* (leaves); **22:** *F. glauca* (flowers); **23:** *F. glauca* (fruits); **24:** *F. glauca* (roots); **25:** *F. communis* (leaves); **26:** *F. communis* (flowerheads obtained by SFE); **27:** *F. communis* (flowerheads obtained by hydro-distillation); **28:** *F. communis* (mixed different parts from poisonous chemotype); **29:** *F. communis* (mixed different parts from non-poisonous chemotype); **30:** *F. flabelliloba* (aerial parts); **31:** *F. flabelliloba* (fruits); **32:** *F. flabelliloba* (aerial parts); **33:** *F. latisecta* (fruits); **34:** *F. latisecta* (leaves); **35:** *F. latisecta* (roots); **36:** *F. latisecta* (aerial parts); **37:** *F. jaeschkeana* (rhizomes); **38:** *F. gummosa* (fruits from the Tehran province of Iran); **39:** *F. gummosa* (fruits from the Isfahan province of Iran); **40:** *F. gummosa* (oleogum stems); **41:** *F. gummosa* (oleogum resin/latex); **42:** *F. gummosa* (roots); **43:** *F. assa-foetida* (seeds); **44:** *F. assa-foetida* (oleogum resin).

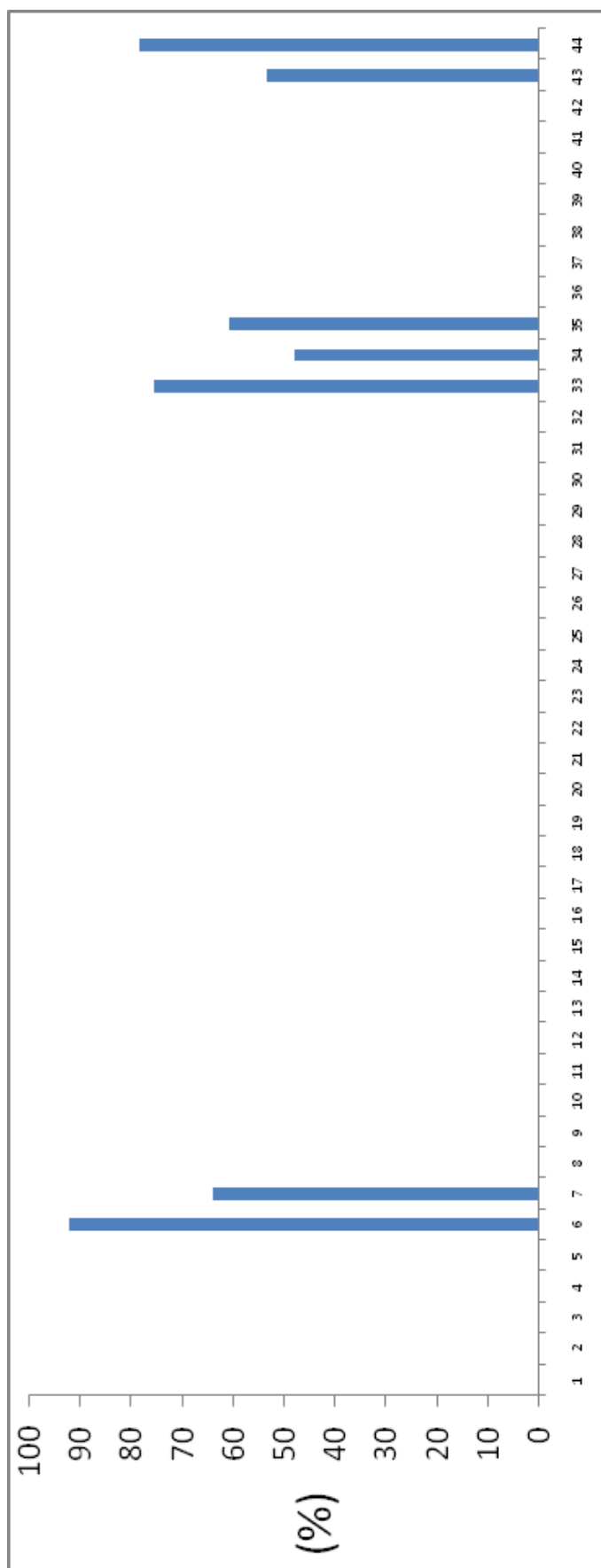


Fig. 7 Relative abundance of sulfur-containing compounds in the essential oils of *Ferula* species. **1:** *F. ovina* (fruits); **2:** *F. ovina* (aerial parts from Isfahan province of Iran); **3:** *F. ovina* (aerial parts from Azerbaijan province of Iran); **4:** *F. badrakema* (fruits); **5:** *F. elaeochoytris* (fruits); **6:** *F. sinkiangensis* (oleogum resin); **7:** *F. fukanensis* (oleogum resin); **8:** *F. arrigonii* (leaves); **9:** *F. persica* (aerial parts); **10:** *F. persica* (roots); **11:** *F. hirtella* (aerial parts); **12:** *F. microcolea* (aerial parts); **13:** *F. macrocolea* (aerial parts); **14:** *F. szowitziana* (aerial parts); **15:** *F. szowitziana* (stems/leaves); **16:** *F. szowitziana* (flowers/fruits); **17:** *F. szowitziana* (stems); **18:** *F. szowitziana* (leaves); **19:** *F. orientalis* (aerial parts); **20:** *F. feruloides* (roots); **21:** *F. glauca* (leaves); **22:** *F. glauca* (flowers); **23:** *F. glauca* (fruits); **24:** *F. glauca* (roots); **25:** *F. communis* (leaves); **26:** *F. communis* (flowerheads obtained by SFE); **27:** *F. communis* (flowerheads obtained by hydro-distillation); **28:** *F. communis* (mixed different parts from poisonous chemotype); **29:** *F. communis* (mixed different parts from non-poisonous chemotype); **30:** *F. flabelliloba* (aerial parts); **31:** *F. flabelliloba* (fruits); **32:** *F. stenocarpa* (aerial parts); **33:** *F. latisecta* (fruits); **34:** *F. latisecta* (leaves); **35:** *F. latisecta* (roots); **36:** *F. latisecta* (aerial parts); **37:** *F. jeschkeana* (rhizomes); **38:** *F. gummosa* (fruits from the Tehran province of Iran); **39:** *F. gummosa* (fruits from the Isfahan province of Iran); **40:** *F. gummosa* (stems); **41:** *F. gummosa* (oleogum resin/latex); **42:** *F. gummosa* (roots); **43:** *F. assa-foetida* (seeds); **44:** *F. assa-foetida* (oleogum resin).

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