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Chemical composition of *Prangos ferulacea* (L.) Lindl., and *Prangos uloptera* DC. essential oils and their antifungal activities

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ABSTRACT

Introduction: *Candida albicans* is an important opportunistic pathogen that is responsible for most fungal infections in humans. Secondary metabolites are known to be antimicrobial and antifungal agents. This study aimed to investigate the chemical composition of *Prangos ferulacea* and *P. uloptera* essential oils and evaluate the sensitivity of four genera of Candida.

Methods: After collecting plant samples, their essential oils were extracted by the distillation method, and their components were analyzed using Gas chromatography–mass spectrometry to identify constituents. In total, 48 species of Candida isolated from clinical specimens were examined in this study. The antifungal activities of essential oils of *P. ferulacea* and *P. uloptera* were evaluated according to CLSI M27-A3 compared to fluconazole.

Results: Out of the two tested plants, *P. ferulacea* had the lowest minimum inhibitory concentration (MIC) against *Candida* species. However, MIC of this plant against *C. albicans* isolates was higher than 0.121 µL/mL non-albicans species. Both plants were able to inhibit non-albicans species with MIC_{90} values of 0.0097 and 0.039 µL/mL. However, their MIC_{90} values were less than fluconazole against *Candida* isolates.

Conclusion: The results of this study suggest that *P. ferulacea* and *P. uloptera* essential oils might be used as new antifungal agents.

Implication for health policy/practice/research/medical education:
This study demonstrated that *Prangos ferulacea* and *P. uloptera* essential oils have the potential to be used for the treatment of different forms of candidiasis.

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Introduction

Candidiasis is an opportunistic fungal infection caused by *Candida* species. The prevalence of candidiasis is increasing following the increase of host predisposing factors such as immunodeficiency and long-term antibiotic therapy (1). *Candida albicans* is the fourth most common causative agent of blood infections in hospitalized patients and accounts for approximately 40% of mortality (2). Various antifungal drugs such as azoles, echinocandin, and polyene have been introduced to treat *Candida* infection (3). Among these drugs, fluconazole is the main choice for treating different forms of candidiasis (4). However, it has side effects such as hepatotoxicity, nausea, vomiting, abdominal pain, diarrhea, constipation, bloating, headache, nervousness, and hepatotoxicity. Therefore, it seems that available, cheap natural herbal products with antifungal effects are a priority (5, 6). The large plant family Apiaceae (syn. Umbelliferae) includes medicinal and aromatic plants having 434 genera and 3780 species (7). Most plants of this family have secondary and considerable metabolites in their internal secretory structures in all their organs (roots, stems, leaves, flowers, seeds) (7,8). This family is growing and found in the Middle East, Irano-Turanian, and Zagros regions. Apiaceae has been known since ancient times in traditional medicine, due to the biologically active compounds, such as coumarins, flavonoids, polystyrenes, and essential oils (9,10). The genus *Prangos* is one of the

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genera of this valuable family used in traditional medicine in treating many diseases. It has many properties like antimicrobial (11), phytotoxic (12), neuroprotective (13), antihypertensive (14), anti-inflammatory (15), and antidiabetic activities (13). Among this genus, the two species *P. ferulacea* and *P. uloptera* are the research targets in various industries, including pharmaceutical, food, and cosmetics companies. This study aimed to identify the active components of aerial parts (stems, leaves, and flowers) of *Prangos ferulacea* and *P. uloptera* plants and evaluate the effects of essential oils of both plants.

Figure 1. *Prangos ferulacea (L.)* Lindl.

Figure 2. *Prangos uloptera* DC.

Materials and Methods

Plant materials

The fresh aerial parts (stems, leaves, and flowers) of *P. ferulacea* (Figure 1) and *P. uloptera* (Figure 2) with herbarium numbers of Fars Agricultural & Natural Resources Research & Education Center: FANNREC 56573 and Iranian Biological Resource Center: IBRC P1007009, respectively were collected (harvest time: May 2020) from the Kakan area of Yasuj in Kohgiluyeh and Boyer-Ahmad province, with geographical coordinates (Latitude:33 03’ 45” and Longitude: 59 26’ 20”) (Table 1). Plant materials were transferred to the laboratory of Medicinal Plants Research Center of Yasuj University of Medical Sciences to identify the plant and for essential oil extraction.

Extraction of essential oils

Essential oils were extracted by the hydrodistillation method. For this purpose, the aerial parts of the plants (stems, leaves, flowers) were divided into small pieces and prepared for the next steps. Then, 200 g from each fresh plant was distilled in water for 3 hours using a Clevenger-type instrument. The essential oils were then collected, dried with magnesium sulfate, and stored in sealed vials in the dark, at 4°C, until used. The essential oil yield percentage (%) was calculated based on fresh weight (w/w) (16).

Essential oil analysis by GC/MS method

The main active compounds of the EOs were determined using a GC-MS apparatus. A chromatography (Model 6890) coupled with an Agilent mass spectrometer (Model N-5973), an HP 5MS capillary column with 5% methylphenylsiloxane static phase (length 30 m, internal diameter 0.25 mm, layer static thickness 0.25 µm), and ionization energy of 70 eV was used for the qualitative identification of the compounds. The temperature was regulated as follows: 60°C at the beginning and then improved, at a rate of 3°C, up to 246°C. The injector and detector temperatures were maintained at 250°C, the injection volume was 1 µL with a 1.50 split, and the helium carrier gas was at a flow rate of 1.5 mL/min (17).

Identification of chemical components

Essential oil components were identified by comparing their relative retention time (RT) with valid samples or comparing their relative retention index (RRI) with a series of n-alkanes. Computer matching against commercial (Wiley GC/MS Library, MassFinder 4 Library) and in-house “Başer Library of Essential Oil Constituents” libraries built up by genuine compounds and components of known oils as well as MS literature data were used (18, 19).

Table 1. Characteristics of the studied areas and plants

Scientific name	Family	Local name	Distilled part	Plant collection time	Name of the collection area	Geographical coordinates of the region	Above mean sea level
Prangos Ferulacea (L.) Linl.	Apiaceae	Jasher dami	Aerial parts	May 2020	Kakan	Latitude:03 33 ' 45'' Longitude: 59 26' 20''	1940
Prangos uloptera DC.	Apiaceae	Jasher sakhrei	Aerial parts	May 2020	Kakan	Latitude:03 33 ' 45'' Longitude: 59 26' 20''	1900

Antifungal activity

Collection of clinical isolates of Candida genus

Candida species were isolated from clinical specimens, identified by conventional methods (CHROMagar, germ tube, chlamydoconidia formation, and growth at 42°C), and confirmed through PCR-RFLP (by ITS1 and ITS4 primers and MspI enzyme) (20, 21). These species included *C. albicans* n=13, *C. glabrata* n=13, *C. parapsilosis* n=13, and *C. krusei* n=13).

Isolates were subcultured on Sabouraud dextrose agar ((SDA) (Merck, Germany)) to confirm the purity and then preserved in sterile distilled water until use. Also, *C. albicans* ATCC10253, *C. glabrata* CBS90028, and *C. parapsilosis* ATCC22019 were used for quality control.

Determination of minimum inhibitory concentration (MIC) against Candida species

Serial dilutions of essential oils (50 µL/mL) of *P. ferulacea* and *P. uloptera essential* were prepared by RPMI-1640 media (Gibco, US) and added to 96-well microtiter plates (22). Then, the standard yeast suspensions, positive control (yeast suspension with RPMI), and negative control (essential oil with RPMI) were added to each microtiter plate and incubated at 35°C for 48 hours. The fungal growth in each well was compared with the positive controls.

To evaluate fluconazole susceptibility, serial dilutions were prepared, starting from 32 µg/mL. Then, 100 µL of the fungal suspensions were added to each well. The plates were incubated at 35°C for 24 hours, and the MICs were determined visually. The MIC was defined as the lowest concentration that caused 50% inhibition of fungal growth compared to the positive control.

Statistical analysis

The results of antifungal susceptibility tests were analyzed by SPSS software (version 24, USA) using Fisher's least significant difference (LSD). *P* value < 0.01 was considered a value significant.

Results

Essential oil yields

The essential oil yield results of *Prangos* species showed a relatively significant difference between the two species. The essential oil extracted from *P. ferulacea* was colorless and yellowish, while in *P. uloptera*, it was yellow and had a higher concentration. The highest essential oil yield belonged to *P. ferulacea* (1.8%), and the lowest belonged to *P. uloptera* (0.85%).

Chemical components of *P. ferulacea* and *P. uloptera* essential oils

The essential oils of the two plants were analyzed using GC-MS analysis to confirm the quality of the pharmacopeia. Twenty-one compounds with a ratio of 99.87% were identified in *P. ferulacea* essential oil (Table 2), and 12 with 94.94% in *P. uloptera* essential oil (Table 3). In the present study, GC analysis revealed that the major components of *P. ferulacea* essential oil were α-pinene (18.34%), β-pinene (27.01%), (δ)-3-carene (24.78%), and β-caryophyllene

Table 2. Chemical compositions of *P. ferulacea* essential oil

Compounds	Retention index	Retention index calculated	Retention index standard	Composition %
α-Thujene	6.95	934.81	966	0.27
α-Pinene	7.21	943.69	932	18.34
Camphene	7.52	954.27	946	0.35
β-Pinene	8.46	986.35	980	27.01
β--Myrcene	8.64	992.49	991	2.77
(δ)-3-Carene	9.38	1013.90	1008	24.78
β-Caryophyllene	9.97	1029.68	1031	17.69
Gamma-terpinene	10.73	1050	1062	0.87
Terpinolene	11.60	1073.26	1088	2.94
3-Carene	14.91	1155.53	1011	0.49
Terpinene-4-ol	15.62	1172.60	1177	0.49
Bornyl acetate	17.94	1227.76	1285	0.38
Caryophyllene	22.10	1326.14	1428	0.13
cis-β-Farnesene	23.07	1349.4	1458	0.12
Dehydrosesquicineol	23.54	1360.67	1504	0.50
β-Bisabolene	23.82	1367.39	1505	0.14
Dihydroagarofurane	24.02	1372.18	1509	0.16
Kessane	24.19	1376.26	1529	0.21
Elemol	25.42	1405.95	1549	1.85
Caryophyllene oxide	25.65	1411.66	1582	0.15
α-Bisabolene	30.23	1526.42	1683	0.23
Total identified (%)				99.87

Table 3. Chemical compositions of *P. uloptera* DC essential oil

Compounds	Retention index	Retention index calculated	Retention index standard	Composition %
α-Pinene	7.05	938.22	923	25.20
β-Pinene	8.24	978.84	980	3.29
Limonene	9.89	1027.54	1031	7.15
β-Ocimene	10.20	1035.83	1040	6.06
Decanal	15.58	1171.63	1193	18.03
4-Hydroxy-3-methylacetophenone	19.81	1271.76	1323	3.02
β-Caryophyllene	22.09	1325.90	1428	16.98
α-Caryophyllene	23.19	1352.28	1454	1.19
(E)-2-dodecenal	23.87	1368.58	1464	4.43
γ-Muurolene	24.14	1375.06	1477	2.20
Caryophyllene oxide	27.17	1449.38	1581	6.25
α-Bisabolol	29.55	1508.81	1683	1.14
Total identified (%)				94.94

(17.69%). Besides, for the *P. uloptera* essential oil, the major constituents included α-pinene (25.20%), limonene (7.15%), decanal (18.03%), β-caryophyllene (16.98%), and caryophyllene oxide (6.25%) in aerial parts of the plant.

Antifungal properties of *P. ferulacea* and *P. uloptera* essential oils

In the present study (Table 4), the MIC value of fluconazole against *Candida* species was 0.125-0.25 µg/mL. However, the plants' essential oils had lower MIC values on these species (0.039-0.0097 µg/mL). Also, the comparison of the activity of the two essential oils showed that the essential oil of *P. ferulacea* had a lower MIC value (0.0097-0.0195 µg/mL) than that of *P. uloptera* (0.0195-0.039 µg/mL).

As shown in Table 5, a comparison of two types of *Prangos* on different isolates of *Candida* showed that the highest p-value was obtained in *C. albicans*. On the other hand, *C. krusei* was the most susceptible species to two types of essential oil.

Discussion

The genus *Prangos* is one of the genera of this valuable family used in traditional medicine in treating many diseases. In our study, the highest essential oil yield belonged to *P. ferulacea* (1.8%) and the lowest belonged to *P. uloptera* (0.85%). In a recently published study, the percentage of essential oil yield for *P. ferulacea* in three different regions was reported to be 1.3, 1.35, and 1.02%, respectively (23), which corresponds to the values and results obtained from this study to some extent. In a study conducted on *P. uloptera*, the percentage of essential oil yield for aerial parts of *P. uloptera* in the vegetative stage (before flower emergence), flowering stage, and fruiting were reported to be 0.45, 0.42, and 3.3% (v/w), respectively, showing differences with the results of the present study (24). Probably the reason for this difference in the percentage of essential oil yield can be related to environmental and ecological factors that change the production pathways of the plant's secondary metabolites by changing the photosynthetic conditions of the plant (25-30).

Our results indicated that twenty-one compounds with a ratio of 99.87% were identified in *P. ferulacea* essential oil and 12 with 94.94% in *P. uloptera* essential oil. According to previous studies, researchers have increased the number of *P. ferulacea* compounds to 31 (89.1%) (23). In another

Table 4. The susceptibility profile of Candida isolates with the MIC range (Minimum inhibitory concentration range), MIC_{50} (MIC required to inhibit the growth of 50% of organisms), MIC_{90} MIC required to inhibit the growth of 90% of organisms) and MIC_{GM} (geometric mean)

Organisms	*P. ferulacea* (L.) Leaf+ flower EO (µL/mL) +Stem				*P. uloptera* DC. Leaf + flower EO (µL/mL) +Stem				Fluconazole (µg/mL)			
	MIC range	MIC50	MIC90	MIC_{GM}	MIC range	MIC50	MIC90	MIC_{GM}	MIC range	MIC50	MIC90	MIC_{GM}
C. albicans (n=13)	0.0097-0.0195	0.0097	0.0194	0.1213	0.039-0.0781	0.039	0.0781	0.4915	0.125-0.25	0.25	0.25	0.1984
C. parapsilosis (n=13)	0.0097	0.0097	0.0097	0.0097	0.0195-0.039	0.039	0.039	0.3258	0.125-0.25	0.125	0.2375	0.1403
C. glabrata (n=13)	0.0097	0.0097	0.0097	0.0097	0.0195-0.039	0.039	0.039	0.0306	0.125-0.25	0.125	0.25	0.1574
C. krusei (n=10)	0.0097	0.0097	0.0097	0.0097	0.0195-0.039	0.029	0.039	0.0272	0.125-0.25	0.125	0.125	0.125

Table 5. Antifungal effects of *P. ferulacea* (L.) and *P. uloptera* DC

	Candida species	Essential oil/Mean±SD	Fluconazole/Mean±SD	*P* value
P. ferulacea	*C. albicans*	0.0130±0.0048	0.2083±0.0615	<0.01
	C. parapsilosis	0.0097±0.000	0.1458±0.0487	
	C. glabrata	0.0097±0.000	0.1667±0.0615	
	C. krusei	0.0097±0.000	0.1250±0.000	
	P value	0.0027	0.0014	
P. uloptera	*C. albicans*	0.0520±0.0193	0.2083±0.0615	
	C. parapsilosis	0.0341±0.0088	0.1458±0.0487	
	C. glabrata	0.0325±0.0096	0.1667±0.0615	
	C. krusei	0.0293±0.0102	0.1250±0.000	
	P value	0.0003	0.0014	

study, the total number and percentage of compounds in fruits and flowers were 14 compounds (93.7%) and 12 compounds (94.7%), respectively (24). Also, Yousefi et al identified and reported the number of compounds and the percentage of total compounds in the province of West Azerbaijan (Iran) as 14 compounds (95.1%) (25). For *P. uloptera*, a study reported that in vegetative, flowering, and fruit stages, the number of compounds was 11, 12, 5, and the percentage of total compounds was 90.96%, 87.7%, 96.2%, respectively (26). However, Nosrati et al showed that the number of compounds was 16, and the percentage of total compounds was 90.02% (4).

Among all the components, α-pinene, β-pinene, and β-caryophyllene were common in both plants, and α-pinene was one of the main common constituents between the two plants. In a study conducted by Bazdar et al, it has been shown that the major compounds of *P. ferulacea* essential oil included α-pinene (36.82%), camphene (15.83%), β-pinene (8.73%), and limonene (10.52%), respectively (12). Also, in another study in Iran, α-pinene (4.7%), δ-3-carene (25.8%), β-phellandrene (32.1%), and m-tolualdehyde (26.2%) were identified as the main constituents of *P. ferulacea* (25). The two compounds δ -3-carene and α-pinene are consistent with the findings of the present study.

Some researches have also been done on the essential oil compounds of *P. uloptera*. Among these studies, Gholivand et al concluded that δ-3-carene, α-pinene, and camphene were the main compounds of the plant (27). Alikhah-Asl et al reported that the chemical compounds of *P. uloptera* essential oil in two different states (dry and wet) in Taleghan city of Tehran province (Iran) were α-pinene (20.29%), trans-β-ocimene (19.64%), β-caryophyllene (9.95%), δ-3-carene (8.03%), germacrene D (6.02%), and caryophyllene-oxide (11.62%) (28). It seems that habitat diversity, soil physicochemical conditions, physiography, and species type can cause differences between chemical constituents of the *Prangos* genus. Besides, the chemical and biological diversities of aromatic and medicinal plants are dependent on climatic conditions (amount and distribution of rainfall, temperature, humidity, evaporation, and transpiration), different growth stages (vegetative, flowering, seeding), and genetic changes (29). Finally, it can be said that these factors affect the biosynthetic pathways of the plant and, consequently, the quantity and quality of the main active compounds.

Antifungal susceptibility results revealed that the essential oil of *P. ferulacea* had a lower MIC value than that of *P. uloptera*. This MIC value was different from other studies performed on the essential oil of another plant of the Apiaceae family. For example, the MIC ranges against *Candida* species varied from 2.188 to 4.375 mg/mL in essential oils of *Cuminum cyminum* and *Foeniculum vulgare* (30). Also, in another study conducted by Bozovic et al, it was reported that the MIC ranged between 6.24 to 12.48 mg/mL for *Savi* subsp. *Glandulosa* and 3.12 to 12.48 mg/mL for *Calamintha nepeta* against *Candida* species (31). The MIC value varied in plants of different countries. For instance, Maxia et al showed that the MIC value of essential oil of Italian and Portuguese *Apium nodiflorum* varied from 1.25 µL/mL to 0.64 µL/mL against *Candida* species (32). Generally, these differences in the results of studies may be due to the origin of *Candida* isolates, the concentrations of essential oils, the percentage of active components in the essential oil, and their mechanism of action.

The essential oil contains some compounds that act on the fatty acid chains of membrane phospholipids and alter cell permeability and increase permeability (33,34). Another mechanism of action of essential oils on fungi may be inhibition of ergosterol synthesis, which delays membrane formation (35,36). Overall, in the present study, α-pinene was a common constituent and the main compound of the two plants, which led to increased membrane permeability, the inhibition of the respiration process, and ion transport processes in the *Candida* genus (37-39).

Conclusion

One of the main approaches of the scientific community

is the use of available herbal products for the treatment of disease, which in turn is a step towards the use of drugs with low side effects. This study aimed to investigate the essential oil compositions of two plants and compare the antifungal effects of these essential oils with the common antifungal drug fluconazole. Our results clearly showed that the essential oils of these two plants might be used as new antifungal agents.

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Authors' contributions

FH performed data analysis, MG performed the experiments, MG and SN wrote the manuscript, and DR edited the manuscript and supervised the whole project. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interests

The authors declare no conflicts of interest regarding this article.

Ethics considerations

This study was approved by the ethics committee of Yasuj University of Medical Sciences (ethical no.IR.YUMS.REC.1399.186).

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References

1. Edalatpanah Y, Rostampur S, Pouladi I, Rajaeenejad S. Evaluation of antifungal effects of *Prangos ferulace* and *Plantago major* L plants against fluconazole-resistant *Candida albicans* species in extracorporeal conditions. Navid No. 2020;23(74):44-52. doi: 10.22038/nnj.2020.46408.1201. [Persian].
2. Vandenbosch D, Braeckmans K, Nelis HJ, Coenye T. Fungicidal activity of miconazole against *Candida* spp. biofilms. J Antimicrob Chemother. 2010;65(4):694-700. doi: 10.1093/jac/dkq019.
3. Jafarzadeh L, Separdar A, Lori Gavini Z, Rafiean M, Deris F, Shahinfard N. Effect of clotrimazole-*Satureja bachtiarica* vaginal cream and clotrimazole vaginal cream in patients with vaginal candidiasis. Iran J Obstet Gynecol Infertil. 2019;21(11):14-22. doi: 10.22038/ijogi.2019.12322. [Persian].
4. Nosrati M, Behbahani M. In vitro and in silico antibacterial activity of *Prangos ferulacea* (L.) Lindl and *Prangos uloptera* DC, and their mutagenicity in the Ames test. J Microbiol Biotechnol Food Sci. 2016/17;6(3):930-6. doi: 10.15414/jmbfs.2016/17.6.3.930-936.
5. Gündüz GT, Gönül SA, Karapinar M. Efficacy of myrtle oil against *Salmonella typhimurium* on fresh produce. Int J Food Microbiol. 2009;130(2):147-50. doi: 10.1016/j.ijfoodmicro.2009.01.010.
6. Fadda A, Mulas M. Chemical changes during myrtle (*Myrtus communis* L.) fruit development and ripening. Sci Hortic. 2010;125(3):477-85. doi: 10.1016/j.scienta.2010.03.024.
7. Ercan F, Baş H, Koç M, Pandir D, Öztemiz S. Insecticidal activity of essential oil of *Prangos ferulacea* (Umbelliferae) against *Ephestia kuehniella* (Lepidoptera: Pyralidae) and *Trichogramma embryophagum* (Hymenoptera: Trichogrammatidae). Turk J Agric For. 2013;37(6):719-25. doi: 10.3906/tar-1211-15.
8. Maggi F, Papa F, Giuliani C, Maleci Bini L, Venditti A, Bianco A, et al. Essential oil chemotypification and secretory structures of the neglected vegetable *Smyrnium olusatrum* L. (Apiaceae) growing in central Italy. Flavour Fragr J. 2015;30(2):139-59. doi: 10.1002/ffj.3221.
9. Ekiert H. Medicinal plant biotechnology: the Apiaceae family as the example of rapid development. Pharmazie. 2000;55(8):561-7.
10. Mottaghipisheh J, Kiss T, Tóth B, Csupor D. The *Prangos* genus: a comprehensive review on traditional use, phytochemistry, and pharmacological activities. Phytochem Rev. 2020;19(6):1449-70. doi: 10.1007/s11101-020-09688-3.
11. Nazemisalman B, Vahabi S, Yazdinejad A, Haghghi F, Jam MS, Heydari F. Comparison of antimicrobial effect of *Ziziphora tenuior*, *Dracocephalum moldavica*, *Ferula gummosa*, and *Prangos ferulacea* essential oil with chlorhexidine on *Enterococcus faecalis*: an in vitro study. Dent Res J (Isfahan). 2018;15(2):111-6.
12. Bazdar M, Sadeghi H, Hosseini S. Evaluation of oil profiles, total phenols and phenolic compounds in *Prangos ferulacea* leaves and flowers and their effects on antioxidant activities. Biocatal Agric Biotechnol. 2018;14:418-23. doi: 10.1016/j.bcab.2018.04.009.
13. Bahadori MB, Zengin G, Bahadori S, Maggi F, Dinparast L. Chemical composition of essential oil, antioxidant, antidiabetic, anti-obesity, and neuroprotective properties of *Prangos gaubae*. Nat Prod Commun. 2017;12(12):1934578X1701201233. doi: 10.1177/1934578x1701201233.
14. Namjoyan F, Azemi ME, Abdollahi E, Goudarzi N, Nikan K. Angiotensin I converting enzyme inhibitory activities of hydroalcoholic extract of *Nardostachys jatamansi*, *Prangos ferulacea* and *Marrubium vulgare*. Jundishapur J Nat Pharm Prod. 2015;10(2):e17255. doi: 10.17795/jjnpp-17255.
15. Ghasemian M, Owlia S, Owlia MB. Review of anti-inflammatory herbal medicines. Adv Pharmacol Sci. 2016;2016:9130979. doi: 10.1155/2016/9130979.
16. Arjmand Z, Dastan D. Chemical characterization and biological activity of essential oils from the aerial part and root of *Ferula haussknechtii*. Flavour Fragr J. 2020;35(1):114-23. doi: 10.1002/ffj.3544.
17. Adams RP. Identification of Essential Oil Components by Gas Chromatography/Mass Spectrometry. Vol 456. Carol Stream, IL: Allured Publishing Corporation; 2007.
18. Göger G, Demirci B, Ilgın S, Demirci F. Antimicrobial and toxicity profiles evaluation of the Chamomile (*Matricaria recutita* L.) essential oil combination with standard

antimicrobial agents. Ind Crops Prod. 2018;120:279-85. doi: 10.1016/j.indcrop.2018.04.024.
19. Karaca N, Demirci B, Demirci F. Evaluation of *Lavandula stoechas* L. subsp. *stoechas* L., *Mentha spicata* L. subsp. *spicata* L. essential oils and their main components against sinusitis pathogens. Z Naturforsch C J Biosci. 2018;73(9-10):353-60. doi: 10.1515/znc-2017-0150.
20. Gharaghani M, Ahmadi B, Taheripour Sisakht M, Ilami O, Aramesh S, et al. Identification of *Candida* species isolated from vulvovaginal candidiasis patients by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) in Yasuj southwestern Iran. Jundishapur J Microbiol. 2018;11(8):e65359. doi: 10.5812/jjm.65359.
21. Sabz G, Gharaghani M, Mirhendi H, Ahmadi B, Gatee MA, Taheripour Sisakht M M, et al. Clinical and microbial epidemiology of otomycosis in the city of Yasuj, southwest Iran, revealing *Aspergillus tubingensis* as the dominant causative agent. J Med Microbiol. 2019;68(4):585-90. doi: 10.1099/jmm.0.000948.
22. Shafaghat A, Ghorban-Dadras O, Mohammadhosseini M, Akhavan M, Shafaghatlonbar M, Panahi A. A comparative study on chemical composition and antimicrobial activity of essential oils from *Tanacetum parthenium* (L.) Schultz. Bip. and *Tanacetum punctatum* (Desr.) Grierson. leaves from Iran. J Essent Oil Bear Plants. 2017;20(4):1143-50. doi: 10.1080/0972060x.2017.1383859.
23. Bruno M, Ilardi V, Lupidi G, Quassinti L, Bramucci M, Fiorini D, et al. Composition and biological activities of the essential oil from a Sicilian accession of *Prangos ferulacea* (L.) Lindl. Nat Prod Res. 2021;35(5):733-43. doi: 10.1080/14786419.2019.1598996.
24. Razavi SM, Nazemiyeh H, Zarrini G, Asna-Asharii S, Dehghan G. Chemical composition and antimicrobial activity of essential oil of *Prangos ferulaceae* (L.) Lindl from Iran. Nat Prod Res. 2010;24(6):530-3. doi: 10.1080/14786410802379539.
25. Yousefi K, Hamedeyazdan S, Hodaei D, Lotfipour F, Baradaran B, Orangi M, et al. An in vitro ethnopharmacological study on *Prangos ferulacea*: a wound healing agent. Bioimpacts. 2017;7(2):75-82. doi: 10.15171/bi.2017.10.
26. Razavi SM, Nazemiyeh H, Delazar A, Asnaashari S, Hajiboland R, Sarker SD, et al. Chemical variation of the essential oil of *Prangos uloptera* DC. at different stages of growth. Nat Prod Res. 2011;25(7):663-8. doi: 10.1080/14786410802270811.
27. Gholivand MB, Piryaei M, Abolghasemi MM, Papzan A. Comparison of microwave-assisted headspace single-drop microextraction (MA-HS-SDME) with hydrodistillation for the determination of volatile compounds from *Prangos uloptera*. J Essent Oil Res. 2013;25(1):49-54. doi: 10.1080/10412905.2012.747267.
28. Alikhah-Asl M, Azarnivand H, Jafari M, Arzani H, Amin G, Zare-Chahouki MA. Variations of essential oils in fresh and dried aerial parts of *Prangos uloptera*. J Nat Prod. 2012;5:5-9.
29. Salleh WM, Ahmad F. Antioxidant and anticholinesterase activities of essential oil of *Alseodaphne peduncularis* Meisn. Turk J Pharm Sci. 2016;13(3):347-50.
30. Vieira JN, Gonçalves CL, Villarreal JPV, Gonçalves VM, Lund RG, Freitag RA, et al. Chemical composition of essential oils from the Apiaceae family, cytotoxicity, and their antifungal activity in vitro against candida species from oral cavity. Braz J Biol. 2019;79(3):432-7. doi: 10.1590/1519-6984.182206.
31. Božović M, Garzoli S, Sabatino M, Pepi F, Baldisserotto A, Andreotti E, et al. Essential oil extraction, chemical analysis and anti-*Candida* activity of *Calamintha nepeta* (L.) Savi subsp. *glandulosa* (Req.) Ball-new approaches. Molecules. 2017;22(2):203. doi: 10.3390/molecules22020203.
32. Maxia A, Falconieri D, Piras A, Porcedda S, Marongiu B, Frau MA, et al. Chemical composition and antifungal activity of essential oils and supercritical CO2 extracts of *Apium nodiflorum* (L.) Lag. Mycopathologia. 2012;174(1):61-7. doi: 10.1007/s11046-011-9519-2.
33. Hammer KA, Carson CF, Riley TV. Antimicrobial activity of essential oils and other plant extracts. J Appl Microbiol. 1999;86(6):985-90. doi: 10.1046/j.1365-2672.1999.00780.x.
34. Carson CF, Hammer KA, Riley TV. *Melaleuca alternifolia* (Tea Tree) oil: a review of antimicrobial and other medicinal properties. Clin Microbiol Rev. 2006;19(1):50-62. doi: 10.1128/cmr.19.1.50-62.2006.
35. Inouye S, Takizawa T, Yamaguchi H. Antibacterial activity of essential oils and their major constituents against respiratory tract pathogens by gaseous contact. J Antimicrob Chemother. 2001;47(5):565-73. doi: 10.1093/jac/47.5.565.
36. Inouye S, Tsuruoka T, Watanabe M, Takeo K, Akao M, Nishiyama Y, et al. Inhibitory effect of essential oils on apical growth of *Aspergillus fumigatus* by vapour contact. Mycoses. 2000;43(1-2):17-23. doi: 10.1046/j.1439-0507.2000.00538.x.
37. Lima IO, Oliveira RD, Lima ED, de Souza EL, Farias NP, de Fátima Navarro D. Inhibitory effect of some phytochemicals in the growth of yeasts potentially causing opportunistic infections. Rev Bras Cienc Farm. 2005;41(2):199-203. doi: 10.1590/s1516-93322005000200007.
38. Cox SD, Mann CM, Markham JL, Bell HC, Gustafson JE, Warmington JR, et al. The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil). J Appl Microbiol. 2000;88(1):170-5. doi: 10.1046/j.1365-2672.2000.00943.x.
39. Tangarife-Castaño V, Correa-Royero J, Zapata-Londoño B, Durán C, Stanshenko E, Mesa-Arango AC. Anti-*Candida albicans* activity, cytotoxicity and interaction with antifungal drugs of essential oils and extracts from aromatic and medicinal plants. Infectio. 2011;15(3):160-7.