Essential oil composition of *Monardella odoratissima* Benth. (Lamiaceae) from the Owyhee Mountains, Idaho

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ABSTRACT

Two plant samples of *Monardella odoratissima* were collected from southwestern Idaho. The fresh aerial parts were hydrodistilled to give pale-yellow essential oils (3.67% and 3.38% yield), which were analyzed by gas chromatography (GC/MS, GC-FID, and enantioselective GC-MS). The essential oils were dominated by (+)-pulegone (76.3% and 72.7%) along with *p*-menth-3-en-8-ol (5.3% and 12.8%) and linalool (5.9% and 3.4%, > 96% (+)-linalool) as major components. The essential oil composition of *M. odoratissima* from Idaho is very different from that from Utah. This essential oil has been scarcely researched and likely represents a new chemical variant described for the species. With such a paucity of information, additional research is needed from other geographical locations within the range of *M. odoratissima*.

INTRODUCTION

Monardella Benth. (Lamiaceae) is a genus of 37 species (World Flora Online, 2024) distributed in western North America (Kartesz, 2015), several of which have been used as herbal medicines by western North American native peoples (Moerman, 1998). However, there has been very little work on the phytochemical constituents of this genus. *Monardella odoratissima* Benth. (mountain mint, desert mint, Lamiaceae) is a perennial plant that is found in sagebrush scrub to subalpine forests in the mountains of the Great Basin (Estiandan, 2017), including California, Oregon, Washington, Idaho, Nevada, Arizona, and as far east as western Colorado and western New Mexico (Figure 1). The plant is around 30-100 cm tall; the inflorescence of *M. odoratissima* is a head (16-22 mm wide) and is colored rose to purple; the leaves are opposite, lanceolate to ovate, and measure 18-27 mm (up to 45 mm) long, and 6-10 mm (up to 20 mm) wide (Estiandan, 2017) (Figure 2). The plant was used by Native American tribes, including the Paiute and Shoshoni people, as traditional medicines. A decoction of the plant was taken as a remedy for colds and as a gastrointestinal aid for indigestion, flatulence, or minor indigestion (Moerman, 1998). The purpose of this work is to obtain and characterize the essential oil of *M. odoratissima* growing in the Owyhee Mountains of Idaho. Previously, three essential oil samples of *Monardella undulata* Benth., *Monardella undulata* var. *undulata* (syn. *Monardella undulata* Benth.), *Monardella undulata* var. *frutescens* Hoover (syn. *Monardella undulata* subsp. *undulata*), and *Monardella crispa* Elmer (syn. *Monardella undulata* subsp. *crispa* (Elmer) Elvin & A.C. Sanders), have been reported and were rich in pulegone (Tanowitz et al., 1987). *Monardella hypoleuca* A. Gray essential oil, on the other hand, was dominated by (*E*)-β-farnesene (Tanowitz et al.,

1984). While this project was underway, a report on the essential oil of *M. odoratissima* from Utah appeared (Wilson et al., 2023). This work, then, compares the essential oil compositions of *M. odoratissima* from the Owyhee Mountains of Idaho and that from the Oquirrh Mountains of Utah.

Figure 1. Range of *Monardella odoratissima*, based on (Estiandan, 2017).

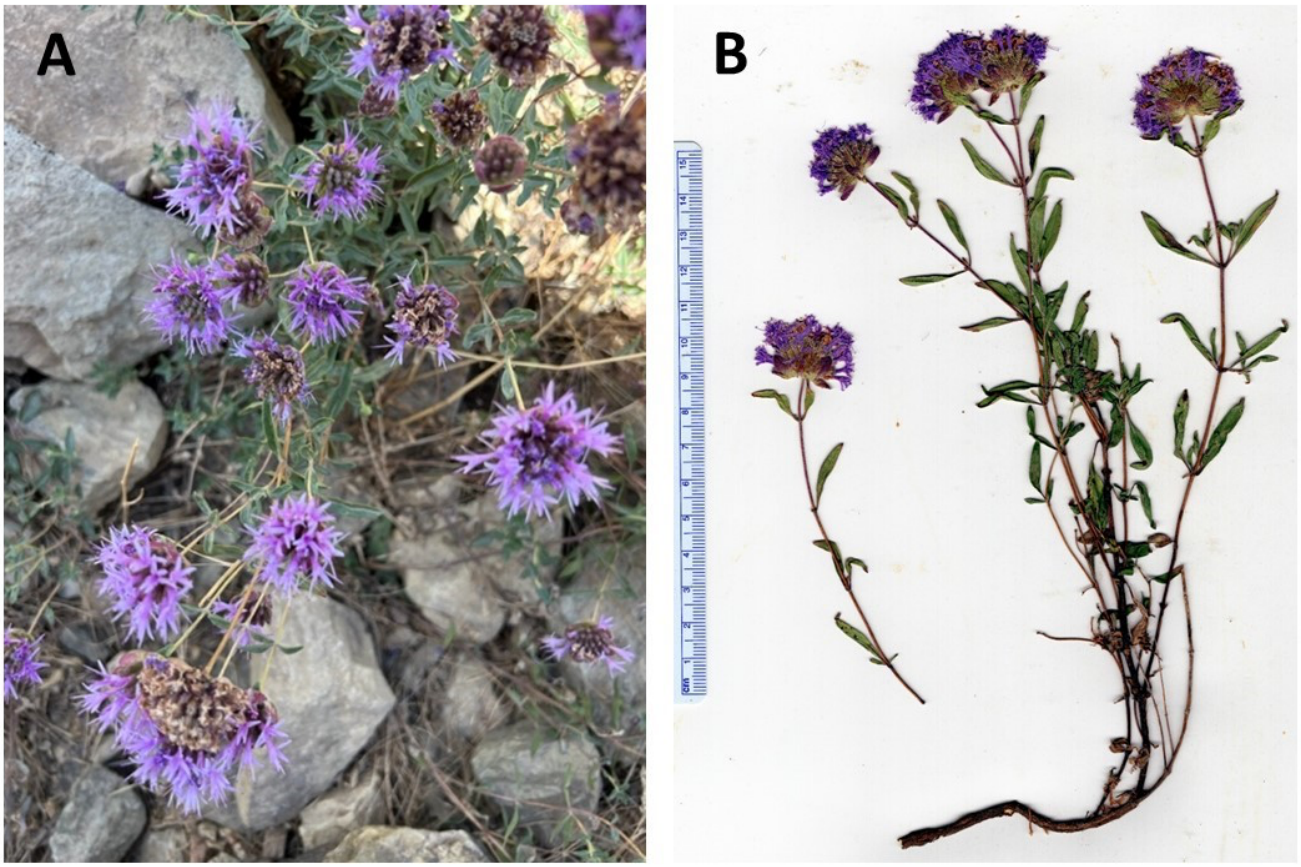

Figure 2. *Monardella odoratissima* Benth. collected near Silver City, Idaho (43°2′43″ N, 116°46′36″ W, 1808 m asl). **A**: Photograph (by K. Swor). **B**: Scan of pressed plant (by W.N. Setzer).

MATERIALS AND METHODS

Plant Material. Two different individual *Monardella odoratissima* plants were collected on 11 August 2023, Owyhee Mountains, near Silver City, Idaho (43°2′43″ N, 116°46′36″ W, 1808 m asl). The plant was identified in the field by W.N. Setzer using a field guide (Turner and Gustafson, 2006) and verified by comparison with herbarium samples from the New York Botanical Garden (New York Botanical Garden). A voucher specimen (WNS-Mog-7788) has been deposited with the University of Alabama in Huntsville herbarium. The fresh plant materials were frozen (−20 °C) until distilled.

Essential Oil Extraction. The fresh/frozen aerial parts of *M. odoratissima* were each hydrodistilled using a Likens-Nickerson apparatus (Likens and Nickerson, 1964; Au-Yeung and MacLeod, 1981; Bouseta and Collin, 1995). The chopped plant samples (56.70 g and 34.36 g) were added to a 500-mL flask, enough distilled water was added to cover the plant material, and distillation was carried with continuous extraction of the distillate with dichloromethane (20 mL) for 3 h, to give pale-yellow essential oils (2.08 g and 1.16 g, respectively).

Gas Chromatographic Analysis. The *M. odoratissima* essential oils were analyzed by gas chromatography / mass spectrometry (GC/MS), gas chromatography with flame ionization detection (GC-FID), and enantioselective GC/MS as previously described (Satyal et al., 2023; Swor et al., 2022). GC/MS: Shimadzu GCMS-QP2010 Ultra instrument (Shimadzu Scientific Instruments, Columbia, MD, USA), electron impact (EI) mode

(electron energy = 70 eV), scan range = 40–400 atomic mass units, scan rate = 3.0 scans/s, ZB-5ms capillary column (Phenomenex, Torrance, CA, USA, 60 m length, 0.25 mm inner diameter, 0.25 μm film thickness), helium carrier gas (column head pressure = 208.2 kPa, flow rate = 2.0 mL/min, injector temperature = 260 °C, ion source temperature = 260 °C; GC oven temperature program (50 °C initial temperature, increased at 2 °C/min to 260 °C, then held at 260 °C for 5 min). For each essential oil sample, 0.1 μL (5% w/v solution in dichloromethane) was injected, splitting mode = 24.5:1. Retention indices (RI) were calculated based on a homologous series of *n*-alkanes (C_8-C_{28}) (van den Dool and Kratz, 1963). The components in the essential oils were identified by comparison of RI values (within 5 RI units) and MS fragmentation (> 80% similarity) with reference compounds available in the Adams (Adams, 2007), FFNSC 3 (Mondello, 2016), NIST20 (NIST20, 2020), and Satyal (Satyal, 2015) databases. GC-FID: Shimadzu GC 2010 instrument with FID detector (Shimadzu Scientific Instruments, Columbia, MD, USA), ZB-5 GC column (Phenomenex, Torrance, CA, USA, 60 m × 0.25 mm × 0.25 μm film thickness), same operating conditions as above for GC/MS. The component percentages were calculated from raw peak integration without standardization (% compound = 100% × compound peak area / total integration). Chiral GC/MS: Shimadzu GCMS-QP2010S instrument (Shimadzu Scientific Instruments, Columbia, MD, USA), Restek B-Dex 325 column (Restek Corp., Bellefonte, PA, USA, 30 m × 0.25 mm diameter × 0.25 μm film thickness), injector and detector temperatures = 240 °C. He carrier gas (column head pressure = 53.6 kPa, flow rate = 1.00 mL/min); GC oven temperature program (50 °C initial temperature held for 5 min, increased to 100 °C at a rate of 1.0 °C/min, then increased to 220 °C at a rate of 2 °C/min). For each sample, 0.3 μL (5% w/v solution in dichloromethane) was injected, splitting mode = 24.0:1. The enantiomers were determined by comparison of RI values with authentic samples (Sigma-Aldrich, Milwaukee, WI, USA), which are compiled in our in-house database; enantiomer ratios were calculated from raw peak areas.

Multivariate Analyses. A hierarchical cluster analysis (HCA) was carried out to visualize the similarity and differences of the essential oil samples using the distribution of essential oil components from this study and the study by Wilson and co-workers (Wilson et al., 2023). The three *M. odoratissima* samples were treated as operational taxonomic units (OTUs), Pearson correlation was used to measure of similarity, and the unweighted pair group method with arithmetic average (UPGMA) was used to define the clusters. Principle component analysis (PCA) was undertaken to verify the HCA analysis. The HCA and PCA analyses were performed using XLSTAT v. 018.1.1.62926 (Addinsoft, Paris, France).

In-Silico Bioactivity Predictions. The structure of the major essential oil component, pulegone, was entered into the PASS Online server (Filimonov et al., 2014; Way2Drug, 2024), which automatically generated potential biological activities. The physicochemical properties of pulegone were obtained by entering the structure into the Swiss-ADME online server (Daina et al., 2017; Swiss Institute of Bioinformatics, 2024).

RESULTS AND DISCUSSION

Hydrodistillation of the aerial parts of *M. odoratissima* gave pale-yellow essential oils in yields of 3.67% and 3.38% for samples #1 and #2, respectively. Gas chromatographic analysis (GC/MS and GC-FID) led to identification of 89 components in the essential oils (Table 1), which accounted for 100% and 99.9% of the compositions of the two samples. The major components in the essential oils were the oxygenated monoterpenoids pulegone (76.3% and 72.7% for samples #1 and #2, respectively), *p*-menth-3-en-8-ol (5.3% and 12.8%), and linalool (5.9% and 3.4%).

The essential oil composition of *M. odoratissima* from southwestern Idaho is in complete contrast to that reported previously from the Oquirrh Mountains of Utah (Wilson et al., 2023). In the previous report, the major components were limonene (27.7%), 1,8-cineole (12.1%), (*E*)-β-ocimene (6.9%), and pulegone (4.3%). Furthermore, linalool was only

0.04% and *p*-menth-3-en-8-ol was not observed. To visualize the similarities between the Idaho samples and the difference compared to the Utah sample, both hierarchical cluster analysis (HCA) and principal component analysis (PCA) were carried out (Figures 3 and 4, respectively). The HCA clearly shows striking similarity between the two Idaho samples (> 99% similarity) and differences compared to the Utah sample (only 12% similarity). The PCA confirms the similarities between the two Idaho samples, with correlations to pulegone, *p*-menth-3-en-8-ol, and linalool, and differences compared to the Utah sample (correlating with limonene, 1,8-cineole, and (*E*)-β-ocimene).

Table 1. Chemical composition (%) of *Monardella odoratissima* essential oil from the Owyhee Mountains, Idaho.

RI_{calc}[1]	RI_{db}[2]	Compound	#1	#2
850	850	(2*E*)-Hexenal	0.1	0.1
875	873	2-Methylbutyl acetate	tr[3]	tr
913	913	Isobutyl isobutyrate	tr	tr
923	923	Tricyclene	tr	-
926	927	α-Thujene	tr	tr
933	933	α-Pinene	0.7	0.3
949	950	Camphene	0.4	tr
953	951	3-Methylcyclohexanone	tr	tr
962	964	Benzaldehyde	-	tr
969	967	Isoamyl propionate	0.1	tr
972	972	Sabinene	0.4	0.3
976	973	1-Octen-3-one	0.1	0.2
977	978	β-Pinene	0.6	0.4
979	978	1-Octen-3-ol	0.1	tr
984	984	3-Octanone	0.1	tr
988	989	Myrcene	0.3	0.2
1005	1004	*p*-Mentha-1(7),8-diene	tr	tr
1015	1015	2-Methylbutyl isobutyrate	tr	tr
1017	1017	α-Terpinene	tr	-
1024	1025	*p*-Cymene	tr	tr
1027	1026	2-Acetyl-3-methylfuran	-	tr
1029	1030	Limonene	1.4	0.9
1031	1031	β-Phellandrene	tr	tr
1032	1032	1,8-Cineole	1.0	0.9
1035	1035	(*Z*)-β-Ocimene	tr	tr
1044	1045	Phenylacetaldehyde	0.1	tr
1045	1046	(*E*)-β-Ocimene	0.1	tr
1057	1056	Artemisia ketone	0.2	tr
1058	1058	γ-Terpinene	tr	tr
1070	1073	*p*-Mentha-3,8-diene	0.1	0.2
1070	1069	*cis*-Linalool oxide (furanoid)	0.1	tr
1085	1086	Terpinolene	0.1	tr
1086	1086	*trans*-Linalool oxide (furanoid)	tr	0.1

RI_{calc}[1]	RI_{db}[2]	Compound	#1	#2
1101	1101	Linalool	5.9	3.4
1103	1103	2-Methylbutyl 2-methylbutyrate	0.1	0.1
1105	1107	2,2,6-Trimethyl-3-keto-6-vinyltetrahydropyran	0.1	0.1
1122	1122	*trans*-*p*-Mentha-2,8-dien-1-ol	0.1	0.1
1137	1137	*cis*-*p*-Mentha-2,8-dien-1-ol	0.1	0.1
1146	1146	*trans*-Verbenol	0.1	0.1
1151	1149	*p*-Menth-3-en-8-ol	5.3	12.8
1163	1164	Menthofuran	tr	0.1
1165	1166	*iso*-Menthone	0.3	0.4
1172	1170	δ-Terpineol	-	tr
1173	1170	Borneol	0.7	-
1175	1176	*trans*-*iso*-Pulegone	1.1	1.6
1181	1180	Terpinen-4-ol	0.1	0.1
1196	1195	α-Terpineol	0.4	0.5
1201	1201	*cis*-Piperitol	0.1	0.1
1209	1208	Verbenone	0.1	0.1
1217	1216	Octadec-1-ene	0.1	0.2
1220	1221	*m*-Isopropylbenzaldehyde	0.2	0.2
1241	1241	Pulegone	76.3	72.7
1244	1246	2,4-Diisopropyl-1,1-dimethyl cyclohexane	0.1	0.1
1262	1262	Pulegone oxide A	tr	tr
1269	1270	*iso*-Piperitenone	-	tr
1276	1276	Neryl formate	tr	tr
1280	1278	*neo*-*iso*-Pulegyl acetate	-	tr
1284	1285	Bornyl acetate	tr	tr
1288	1287	Pulegone oxide B	0.2	0.5
1291	1290	Menthyl acetate	tr	0.1
1291	1290	Indole	0.2	0.3
1307	1308	*neo*-*iso*-*iso*-Pulegyl acetate	-	tr
1310	1306	Dihydrocarvyl acetate	0.1	0.2
1338	1339	Piperitenone	0.3	0.2
1375	1375	α-Copaene	tr	tr
1383	1382	β-Bourbonene	0.2	0.2
1384	1385	(*E*)-Jasmone	0.1	-
1389	1390	*trans*-β-Elemene	tr	tr
1392	1394	(*Z*)-Jasmone	0.4	0.2
1417	1417	(*E*)-β-Caryophyllene	tr	tr
1426	1427	γ-Elemene	tr	tr
1429	1430	β-Copaene	tr	tr
1432	1432	*trans*-α-Bergamotene	-	tr
1446	1447	Geranyl acetone	-	tr
1451	1452	(*E*)-β-Farnesene	0.1	0.3

RI_{calc}[1]	RI_{db}[2]	Compound	#1	#2
1480	1482	Germacrene D	0.7	0.4
1489	1489	(*Z*,*E*)-α-Farnesene	0.2	0.2
1494	1497	Bicyclogermacrene	tr	0.1
1503	1504	(*E*,*E*)-α-Farnesene	0.5	0.6
1517	1518	δ-Cadinene	tr	tr
1576	1576	Spathulenol	-	0.1
1606	1607	Lauryl acetate	tr	tr
1639	1639	Phenethyl hexanoate	tr	tr
1640	1642	Methyl (*Z*)-jasmonate	-	tr
1839	1841	Phytone	tr	tr
2144	2143	Serratol	-	0.1
2300	2300	Tricosane	tr	tr
2500	2500	Pentacosane	0.1	0.1
2700	2700	Heptacosane	0.1	0.1
		Monoterpene hydrocarbons	4.0	2.3
		Oxygenated monoterpenoids	92.4	94.1
		Sesquiterpene hydrocarbons	1.7	1.7
		Oxygenated sesquiterpenoids	0.0	0.1
		Benzenoid aromatics	0.5	0.5
		Others	1.3	1.2
		Total identified	100.0	99.9

[1] RI_{calc} = Retention index determined with respect to a homologous series of *n*-alkanes on a ZB-5ms column.
[2] RI_{db} = Reference retention index obtained from the databases (Adams, 2007; Satyal, 2015; Mondello, 2016; NIST20, 2020).
[3] tr = trace (< 0.05%).

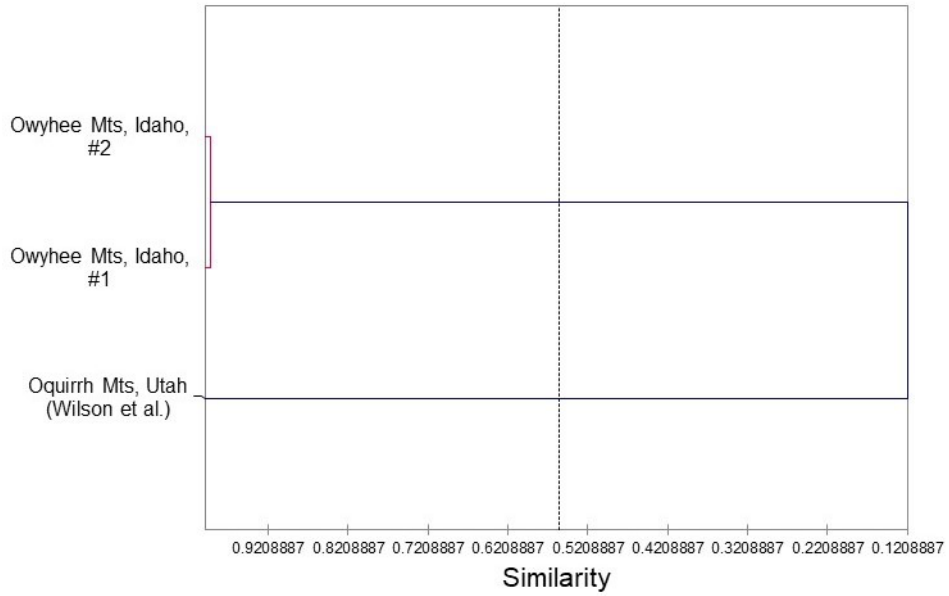

Figure 3. Dendrogram obtained by cluster analysis of the compositions of *Monardella odoratissima* essential oils from Idaho (this work) and from Utah (Wilson et al., 2023).

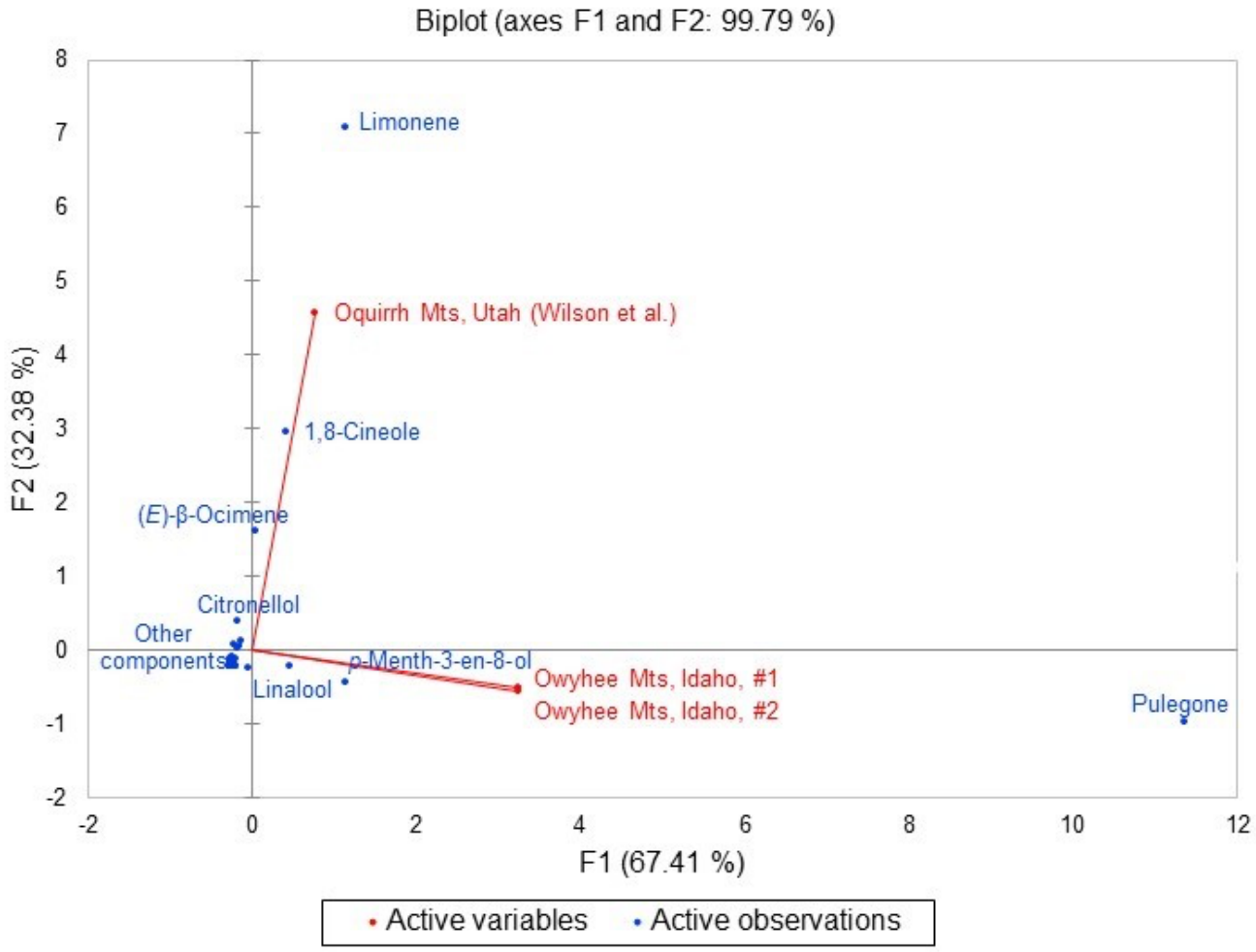

Figure 4. Principal component analysis of the essential oils of *Monardella odoratissima* from Idaho (this work) and from Utah (Wilson et al., 2023).

The reasons for the vast differences are not clear. Climatic (Jaouadi et al., 2023), edaphic (Karimi et al., 2020; Vaičiulytė et al., 2022), phenological (Porres-Martínez et al., 2014; Mounira et al., 2022), seasonal (Lakušić et al., 2013; Méndez-Tovar et al., 2016), or genetic (Martínez-Natarén et al., 2014; Leontaritou et al., 2020) differences can be responsible the variations in essential oil compositions. In this work, the plants were collected in the second week of August (the plants were in full flower) while the Utah sample was collected in the third week of July (also full flower), so seasonal variation does not seem likely. The differences in composition may not be surprising, however; the two populations are disjunct (see Figure 1), so phytochemical divergence may be expected. In addition, the elevations of the collection sites were different (1808 m in the Idaho collection and 3015 m in the Utah collection), which may account for the difference in compositions (Alimohammadi et al., 2017; Talebi et al., 2019). It is likely that the Idaho samples and the Utah sample represent different chemotypes of *M. odoratissima*. *Monarda fistulosa* L. essential oil compositions indicate at least five different chemotypes (thymol, carvacrol, p-cymene/carvacrol, geraniol, and α-terpineol), which can be attributed to different geographical areas of cultivation (Lawson et al., 2021a).

Pulegone concentrations in members of the Lamiaceae are known to show seasonal effects.

Pulegone is the precursor in the biosynthesis of isomenthone and menthone (Croteau and Venkatachalam, 1986; Fuchs et al., 1999), and a seasonal study of *Pycnanthemum virginianum* showed a seasonal reduction in pulegone concentration with concomitant increase in isomenthone and menthone concentrations over the growing season (Setzer et al., 2021). Thus, it would be interesting to compare *M. odoratissima* essential oil compositions from samples collected earlier and later in the season.

The high concentration of pulegone in this study may account for the traditional use of the plant to treat colds and indigestion. Pulegone was used for Prediction of Activity Spectra for Substances (PASS) (Table 2) and Absorption, Distribution, Metabolism, and Excretion (ADME) *in-silico* predictions (Table 3). In the PASS prediction, the *Pa* is the probability for the compound to be active for the activity while the *Pi* is the probability to be inactive. The *Pa* reflects the similarity of the structure of a given compound to the structures of the typically active compounds in the training set. If the *Pa* is greater than 0.70 the chances of finding experimental activity are high (Filimonov et al., 2014).

Table 2. Prediction of biological activities by the Prediction of Activity Spectra for Substances (PASS) online webserver for pulegone, the major component in the essential oil of *Monardella odoratissima*.

Biological Activity	*Pa* [1]	*Pi* [2]
Carminative	0.937	0.001
Antieczematic	0.886	0.006
Antiseborrheic	0.783	0.022
Immunosupressant	0.708	0.016
Dermatologic	0.607	0.015
Phobic disorders treatment	0.669	0.090
Anti-inflammatory	0.060	0.033
Antipruritic	0.573	0.020
Anti-picornavirus	0.558	0.030

[1] *Pa* = Probability to be active. [2] *Pi* = Probability to be inactive.

The predicted carminative activity of pulegone is consistent with the use of *M. odoratissima* to treat gastrointestinal disturbances, including flatulence, while the predicted anti-picornavirus activity of pulegone is consistent with the use of the plant to treat colds. Rhinovirus (a picornavirus) is the most common viral infectious agent in humans and is the predominant cause of the common cold (Andrews, 1966). Interestingly, pulegone is predicted to show antieczematic, antiseborrheic, dermatological, anti-inflammatory, and antipruritic activities, but there are apparently no reports on traditional uses of *M. odoratissima* to treat dermatological conditions.

The drug-likeness and ADME properties (Table 3) are consistent with oral bioavailability of pulegone. Note, however, that pulegone and its metabolites have exhibited long-term toxicity in rodent models (Cohen et al., 2020), including carcinogenic activities in mice (liver tumors) and female rats (urinary bladder tumors) (National Toxicology Program, 2011; Da Rocha et al., 2012).

Table 3. Drug-likeness and ADME properties predicted by *in-silico* studies using the SwissADME online webserver for pulegone.

Physico-Chemical Properties	
Molecular weight	152.23 g/mol
Hydrogen bond acceptors	1
Hydrogen bond donors	0
Number of rotatable bonds	0
Topological polar surface area (tPSA)	17.07 $Å^2$
Absorption Parameters	
Water solubility (Consensus Log *S*)	-2.74
Lipophilicity (Consensus Log $P_{o/w}$)	2.62
Water solubility prediction	Soluble [a]
Drug Likeness Prediction	
Lipinski "Rule of Five" [b]	Yes, 0 violations
Bioavailability	
Bioactivity score	0.55 [c]
Distribution Parameters Prediction	
Skin permeability (Log K_p (cm/s) [d]	-5.04
Gastrointestinal Absorption [e]	High
Blood-Brain Barrier (BBB) Permeability [e]	Yes

[a] Pulegone is water soluble, albeit to a small degree, as the Log S suggests; the water solubility of pulegone has been experimentally determined (1.38 g/L at 20 °C) (Smyrl & LeMaguer 1980). [b] Lipinski's Rule of Five: An orally active drug should have no more than 5 hydrogen bond donors, no more than 10 hydrogen bond acceptors, a molecular weight less than 500 g/mol, and a calculated octanol-water partition coefficient (Log P) less than 5 (Lipinski et al,. 1997). [c] A bioavailability score of 0.55 suggests > 10% bioavailability in rat or measurable Caco-2 permeability (Martin, 2005). [d] (Potts and Guy, 1992). [e] Gastrointestinal absorption and BBB permeability are predicted using the Brain Or IntestinaL EstimateD permeation (BOILED-Egg) method (Daina and Zoete, 2016).

The enantiomeric distributions of chiral essential oil components of *M. odoratissima* were determined using enantioselective GC/MS (Table 4). The (–)-enantiomers were dominant for α-pinene (> 76%), camphene (97%), sabinene (> 72%), limonene (97%), 1-octen-3-ol (100%), borneol (100%), α-terpineol (100%), and germacrene D (100%). On the other hand, the (+)-enantiomers predominated in linalool (> 96%), *iso*-menthone (100%), and pulegone (100%). β-Pinene was nearly racemic in *M. odoratissima*. In comparison, the enantiomeric distribution observed in *M. odoratissima* from Utah was 70.6% (−)-α-pinene, 59.0% (+)-sabinene, 66.1% (−)-β-pinene, 80.8% (−)-limonene, 100% (+)-pulegone, and 75.0% (+)-α-terpineol (Wilson et al., 2023). Thus, the enantiomeric distributions are consistent between the Idaho and Utah samples for α-pinene, β-pinene, limonene, and pulegone, but the major enantiomers are reversed for sabinene and α-terpineol.

Table 4. Enantiomeric distribution (% enantiomer) of chiral components in the essential oil of *Monardella odoratissima*.

Compound	RI_{db}	RI_{calc}	#1	#2
(–)-α-Pinene	976	978	79.6	76.9
(+)-α-Pinene	982	984	20.4	23.1
(–)-Camphene	998	999	97.3	-
(+)-Camphene	1005	1006	2.7	-
(+)-Sabinene	1021	1021	27.6	26.1
(–)-Sabinene	1030	1030	72.4	73.9
(+)-β-Pinene	1027	1027	43.6	46.5
(–)-β-Pinene	1031	1030	56.4	53.5
(–)-Limonene	1073	1071	97.1	96.8
(+)-Limonene	1081	1079	2.9	3.2
(–)-1-Octen-3-ol [1]	1218	1220	100.0	-
(–)-Linalool	1228	1229	1.6	3.2
(+)-Linalool	1231	1232	98.4	96.8
(+)-*iso*-Menthone [2]	1302	1301	100.0	100.0
(–)-Borneol	1335	1332	100.0	100.0
(+)-Borneol	1340	-	0.0	0.0
(–)-α-Terpineol	1347	1350	100.0	100.0
(+)-α-Terpineol	1356	-	0.0	0.0
(+)-Pulegone [3]	1408	1409	100.0	100.0
(+)-Germacrene D	1519	-	0.0	0.0
(–)-Germacrene D	1522	1522	100.0	100.0

[1] Only (–)-Octen-3-ol was available as a standard. [2] Only (+)-*iso*-Menthone was available as a standard. [3] Only (+)-Pulegone was available as a standard.

Although there are no additional comparisons to be made within the *Monardella* genus in terms of enantiomeric distributions, comparisons are possible with *Monarda* (Lawson et al., 2021a; 2021b). While (–)-α-pinene was the major enantiomer in *M. odoratissima*, the (+)-enantiomer predominated in *Monarda* essential oils. (–)-Limonene was the major enantiomer in *M. odoratissima* as well as *Monarda fistulosa* essential oils. (+)-Linalool dominated in *M. odoratissima*, but (–)-linalool was the major enantiomer in *M. fistulosa* and *M. bradburiana*. (–)-Borneol was the exclusive enantiomer in *M. odoratissima* as well as *Monarda*. (+)-α-Terpineol dominated in *Monarda* essential oils.

CONCLUSIONS

The essential oil composition of *Monardella odoratissima* from the Owyhee Mountains, Idaho, has been determined and complements an investigation from the Oquirrh Mountains of Utah. A comparison with *M. odoratissima* from the Oquirrh Mountains shows remarkable differences in both essential oil composition as well as differences in the distribution of enantiomeric monoterpenoids. The differences may be due to the disjunct populations of the two collections, differences in elevation as well as other environmental differences between the two collection sites. The Utah and Idaho samples likely represent different chemotypes and additional research is needed to explore this. Pulegone dominated the essential oil composition from Idaho, but pulegone concentrations are known exhibit seasonal variation in members of the Lamiaceae. It would be interesting to compare the essential oil compositions from other separate populations such as locations in New Mexico, central Washington,

central Oregon, and southern Nevada. It would also be informative to study the seasonal variation of essential oil compositions of this plant in as well as sampling *M. odoratissima* from other geographical locations and elevations.

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REFERENCES

Adams, R.P. 2007. *Identification of Essential Oil Components by Gas Chromatography/Mass Spectrometry*. 4th ed. Allured Publishing, Carol Stream, IL, USA.

Alimohammadi, M., Yadegari, M., and Shirmardi, H.A. 2017. Effect of elevation and phenological stages on essential oil composition of *Stachys*. Turkish J. Biochem. 42(6):647–656.

Andrews, C.H. 1966. Rhinoviruses and common colds. Annu. Rev. Med. 17(1):361–370.

Au-Yeung, C.Y. and MacLeod, A.J. 1981. A comparison of the efficiency of the Likens and Nickerson extractor for aqueous, lipid/aqueous, and lipid samples. J. Agric. Food Chem. 29(3):502–505.

Bouseta, A. and Collin, S. 1995. Optimized Likens-Nickerson methodology for quantifying honey flavors. J. Agric. Food Chem. 43(7):1890–1897.

Cohen, S.M., Eisenbrand, G., Fukushima, S., Gooderham, N.J., Guengerich, F.P., Hecht, S.S., Rietjens, I.M.C.M., Bastaki, M., Davidsen, J.M., Harman, C.L., McGowen, M.M., and Taylor, S.V. 2020. FEMA GRAS assessment of natural flavor complexes: Mint, buchu, dill and caraway derived flavoring ingredients. Food Chem. Toxicol. 135:110870.

Croteau, R. and Venkatachalam, K.V. 1986. Metabolism of monoterpenes: Demonstration that (+)-*cis*-isopulegone, not piperitenone, is the key intermediate in the conversion of (–)-isopiperitenone to (+)-pulegone in peppermint (*Mentha piperita*). Arch. Biochem. Biophys. 249(2):306–315.

Daina, A., Michielin, O., and Zoete, V. 2017. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci. Rep. 7:42717.

Daina, A. and Zoete, V. 2016. A BOILED-egg to predict gastrointestinal absorption and brain penetration of small molecules. ChemMedChem. 11(11):1117–1121.

Da Rocha, M.S., Dodmane, P.R., Arnold, L.L., Pennington, K.L., Anwar, M.M., Adams, B.R., Taylor, S.V., Wermes, C., Adams, T.B., and Cohen, S.M. 2012. Mode of action of pulegone on the urinary bladder of F344 rats. Toxicol. Sci. 128(1):1–8.

Estiandan, M. 2017. Morphological Variation in the *Monardella odoratissima – Monardella villosa* Complex. M.S. thesis, University of the Pacific, Stockton, California, USA.

Filimonov, D.A., Lagunin, A.A., Gloriozova, T.A., Rudik, A.V., Druzhilovskii, D.S., Pogodin, P.V., and Poroikov, V.V. 2014. Prediction of the biological activity spectra of organic compounds using the PASS online web resource. Chem. Heterocycl. Compd. 50(3):444–457.

Fuchs, S., Beck, T., Sandvoss, M., and Mosandl, A. 1999. Biogenetic studies in *Mentha* × *piperita*. 2. Stereoselectivity in the bioconversion of pulegone into menthone and isomenthone. J. Agric. Food Chem. 47(8):3058–3062.

Jaouadi, R., Boussaid, M., and Zaouali, Y. 2023. Variation in essential oil composition within and among Tunisian *Thymus algeriensis* Boiss et Reut. (Lamiaceae) populations: Effect of ecological factors and incidence on antiacetylcholinesterase and antioxidant activities. Biochem. Syst. Ecol. 106:104543.

Karimi, A., Krähmer, A., Herwig, N., Schulz, H., Hadian, J., and Meiners, T. 2020. Variation of secondary metabolite profile of *Zataria multiflora* Boiss. populations linked to geographic, climatic, and edaphic factors. Front. Plant Sci. 11:969.

Kartesz, J.T. 2015. The biota of North America program (BONAP). North American Plant Atlas. Accessed February 24, 2024 at http://www.bonap.org/

Lakušić, D., Ristić, M., Slavkovska, V., and Lakušić, B. 2013. Seasonal variations in the composition of the essential oils of rosemary (*Rosmarinus officinalis*, Lamiaceae). Nat. Prod. Commun. 8(1):131–134.

Lawson, S.K., Satyal, P., and Setzer, W.N. 2021a. The volatile phytochemistry of *Monarda* species growing in south Alabama. Plants. 10(3):482.

Lawson, S.K., Satyal, P., and Setzer, W.N. 2021b. Leaf essential oil composition and terpenoid enantiomeric distribution of *Monarda bradburiana* Beck cultivated in South Alabama. Am. J. Essent. Oils. Nat. Prod. 9(4):10–13.

Leontaritou, P., Lamari, F.N., Papasotiropoulos, V., and Iatrou, G. 2020. Morphological, genetic and essential oil variation of Greek sage (*Salvia fruticosa* Mill.) populations from Greece. Ind. Crops Prod. 150:112346.

Likens, S.T. and Nickerson, G.B. 1964. Detection of certain hop oil constituents in brewing products. Proceedings Annu. Meet. - Am. Soc. Brew. Chem. 22(1):5–13.

Lipinski, C.A., Lombardo, F., Dominy, B.W., and Feeney, P.J. 1997. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Deliv. Rev. 23(1–3):3–25.

Martin, Y.C. 2005. A bioavailability score. J. Med. Chem. 48(9):3164–3170.

Martínez-Natarén, D.A., Parra-Tabla, V., Ferrer-Ortega, M.M., and Calvo-Irabién, L.M. 2014. Genetic diversity and genetic structure in wild populations of Mexican oregano (*Lippia graveolens* H.B.K.) and its relationship with the chemical composition of the essential oil. Plant Syst. Evol. 300(3):535–547.

Méndez-Tovar, I., Novak, J., Sponza, S., Herrero, B., and Asensio-S-Manzanera, M.C. 2016. Variability in essential oil composition of wild populations of Labiatae species collected in Spain. Ind. Crops Prod. 79:18–28.

Moerman, D.E. 1998. *Native American Ethnobotany*. Timber Press, Inc., Portland, OR, USA.

Mondello, L. 2016. *FFNSC 3*. Shimadzu Scientific Instruments, Columbia, MD, USA.

Mounira, G.M., Ahlem, Z., Mariem, B.A., Romdhane, M., Okla, M.K., Al-Hashimi, A., Alwase, Y.A., Madnay, M.M., Abdelgayed, G., Asard, H., Beemster, G.T.S., and AbdElgawad, H. 2022. Essential oil composition and antioxidant and antifungal activities of two varieties of *Ocimum basilicum* L. (Lamiaceae) at two phenological stages. Agronomy. 12(4):825.

National Toxicology Program (NTP). 2011. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Naphthalene in F344 /N Rats (Inhalation Studies) National Toxicology Program. Research Triangle Park, NC. https://ntp.niehs.nih.gov/sites/default/files/ntp/htdocs/lt_rpts/tr563.pdf

New York Botanical Garden (NYBG). C. V. Starr Virtual Herbarium. Accessed on August 15, 2023 at https://sweetgum.nybg.org/science/vh/

NIST20. 2020. National Institute of Standards and Technology, Gaithersburg, MD, USA.

Porres-Martínez, M., González-Burgos, E., Carretero, M.E., and Gómez-Serranillos, M.P. 2014. Influence of phenological stage on chemical composition and antioxidant activity of *Salvia lavandulifolia* Vahl. essential oils. Ind. Crops Prod. 53:71–77.

Potts, R.O. and Guy, R.H. 1992. Predicting skin permeability. Pharm. Res. 9:663–669.

Satyal, P. 2015. Development of GC-MS Database of Essential Oil Components by the Analysis of Natural Essential Oils and Synthetic Compounds and Discovery of Biologically Active Novel Chemotypes in Essential Oils, Ph.D. dissertation, University of Alabama in Huntsville, Huntsville, AL, USA.

Satyal, P., Dosoky, N.S., Poudel, A., Swor, K., and Setzer, W.N. 2023. Chemical composition of the aerial parts essential oil of *Chrysothamnus viscidiflorus* from southwestern Idaho. J, Essent. Oil Plant Compos. 1(2):115–121.

Setzer, W.N., Duong, L., Pham, T., Poudel, A., Nguyen, C., and Mentreddy, S.R. 2021. Essential oils of four Virginia mountain mint (*Pycnanthemum virginianum*) varieties grown in North Alabama. Plants. 10(7):1397.

Smyrl, T.G. and LeMaguer, M. 1980. Solubilities of terpenic essential oil components in aqueous solutions. J. Chem. Eng. Data. 25(2):150-152.

Swiss Institute of Bioinformatics (SIB). 2024. Swiss-ADME. Accessed on January 14, 2024 at http://www.swissadme.ch/index.php

Swor, K., Satyal, P., Timsina, S., and Setzer, W.N. 2022. Chemical composition and terpenoid enantiomeric distribution of the essential oil of *Artemisia tridentata* subsp. *tridentata* from southwestern Idaho. Nat. Prod. Commun. 17(7):1934578X2211174.

Talebi, S.M., Nohooji, M.G., Yarmohammadi, M., Khani, M., and Matsyura, A. 2019. Effect of altitude on essential oil composition and on glandular trichome density in three *Nepeta* species (*N. sessilifolia*, *N. heliotropifolia* and *N. fissa*). Mediterr. Bot. 40(1):81–93.

Tanowitz, B.D., Smith, D.M., and Junak, S.A. 1984. Terpenoids of *Monardella hypoleuca*. J. Nat. Prod. 47(4):738–739.

Tanowitz, B.D., Smith, D.M., and Junak, S.A. 1987. Terpenoid constituents of three taxa of *Monardella*. Phytochemistry. 26(10):2751–2752.

Turner, M. and Gustafson, P. 2006. *Wildflowers of the Pacific Northwest*. Timber Press, Inc., Portland, OR, USA.

Vaičiulytė, V., Ložienė, K., and Taraškevičius, R. 2022. Impact of edaphic and climatic factors on *Thymus pulegioides* essential oil composition and potential prevalence of chemotypes. Plants. 11(19):2536.

van den Dool, H. and Kratz, P.D. 1963. A generalization of the retention index system including linear temperature programmed gas-liquid partition chromatography. J. Chromatogr. A. 11:463–471.

Way2Drug. 2024. PASS online, version 2.0. Accessed on January 14, 2024 at http://www.way2drug.com/passonline/

Wilson, T.M., Davis, A., Sonstrom, R.E., Neill, J.L., Ziebarth, E.A., Poulson, A., and Carlson, R.E. 2023. Essential oil composition and enantioselective profile of *Agastache urticifolia* (Lamiaceae) and *Monardella odoratissima* (Lamiaceae) from Utah. Molecules. 28(5):2249.

World Flora Online, WFO. 2024. *Monardella* Benth. The World Flora Online. Accessed on February 24, 2024 at https://www.worldfloraonline.org/taxon/wfo-4000024633

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