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The volatile components of parsley, *Petroselinum crispum* (Mill.) Fuss

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Abstract
The leaf essential oils of two different samples of curly leaf parsley (*Petroselinum crispum* var. *crispum*) and two samples of flat leaf parsley (*P. crispum* var. *neapolitanum*) were obtained by hydrodistillation and analyzed by gas chromatography (GC-FID and GC-MS). Curley leaf parsley was rich in myristicin (39.4% and 43.2%), β-phellandrene (32.7% and 35.0%), and 1,3,8-*p*-menthatriene (14.9% and 7.9%). Flat leaf parsley, on the other hand, was dominated by apiole (52.9% and 33.0%) and β-phellandrene (10.0% and 17.0%). One sample of flat leaf parsley was rich in *p*-cymene (17.3%), while the other was rich in 1,3,8-*p*-menthatriene (23.4%). A cluster analysis of parsley leaf oils reported in the literature revealed three different categories based on composition: myristicin/β-phellandrene, 1,3,8-*p*-menthatriene/β-phellandrene, and apiole/β-phellandrene.

Keywords: Chemical composition, essential oil, cluster analysis, myristicin, apiole, 1,3,8-*p*-menthatriene, β-phellandrene.

1. Introduction
Parsley, *Petroselinum crispum* (Mill.) Fuss (Apiaceae), is a widely cultivated and used herb. The plant is native to the Mediterranean region (Spain, Italy, Greece, Malta, Algeria, Tunisia, and Morocco), but it has been introduced into cultivation worldwide [1]. There are three common varieties (or cultivars) of parsley, the curly leaf variety (*P. crispum* var. *crispum*) that is often used as a garnish, the flat leaf or Italian variety (*P. crispum* var. *neapolitanum*) used in tabbouleh and other Mediterranean dishes, and root parsley (*P. crispum* var. *tuberosum*), which is grown as a root vegetable. In addition to its culinary uses, parsley has also been used as a medicinal herb; some of the ethnopharmacological uses of parsley are summarized in Table 1.

2. Materials and Methods
2.1 Plant Material
Two different samples of *P. crispum* var. *crispum* were purchased from a local grocery store in Huntsville, Alabama on February 26, 2017 (sample #1 from Braga Fresh Family Farms, Soledad, California; sample #2 from Cal-Organic Farms, Bakersfield, California). Likewise, two samples of *P. crispum* var. *neapolitanum* were purchased on March 11, 2017 (sample #3 from Walter P. Rawl & Sons, Inc., Pelion, South Carolina; sample #4 from Cal-Organic Farms, Bakersfield, California). In each case, the fresh leaves were hydrodistilled using a Likens-Nickerson apparatus with continuous extraction with dichloromethane to give pale yellow essential oils (Table 2).

2.2 Gas Chromatography – Mass Spectrometry
The leaf essential oils of *Petroselinum crispum* were analyzed by GC-MS using an Agilent 6890 gas chromatograph coupled to an Agilent 5973 mass selective detector (MSD), operated in the electron impact mode with electron energy = 70 eV, a scan range of 40-400 amu, a scan rate of 3.99 scans/sec, and operated through an Agilent ChemStation data system. The GC column was an HP-5ms fused silica capillary column with a (5% phenyl)-polydimethylsiloxane stationary phase, a film thickness of 0.25 μm, a length of 30 m, and an internal diameter of 0.25 mm. The carrier gas was helium with a column head pressure of 92.4 kPa and a flow rate of 1.5 mL/min. The inlet temperature was 250 °C and the interface temperature was 280 °C. The GC oven temperature was programmed, 60 °C initial temperature, which was held for 5 min, temperature increased at a rate of 3 °C/min up to 280 °C

Solutions of essential oils (1% in CH_2Cl_2) were prepared and 1-μL injections were carried out using a splitless mode. Identification of the oil components was based on their retention indices determined by reference to a homologous series of *n*-alkanes, and by comparison of their mass spectral fragmentation patterns with those reported in the literature [19], and stored in our in-house MS library.

2.3 Quantitative Gas Chromatography

Quantitative GC was carried out using an Agilent 6890 GC with Agilent flame ionization detector (FID), HP-5ms column, helium carrier gas (head pressure = 144.1 kPa, flow rate = 2.0 mL/min), same oven temperature program as GC-MS (above). The percentages of each component in the essential oils are reported as raw percentages without standardization.

2.4 Hierarchical Cluster Analysis

A total of 29 *P. crispum* leaf essential oil compositions from the published literature [20–35], as well as the four compositions from this study were treated as operational taxonomic units (OTUs). The percentage composition of nine major essential oil components (α-pinene, β-pinene, myrcene, β-phellandrene, terpinolene, *p*-cymenene, 1,3,8-*p*-menthatriene, myristicin, and apiole) was used to determine the chemical relationship between the various *P. crispum* essential oil samples by agglomerative hierarchical cluster (AHC) analysis using the XLSTAT software, version 2015.4.01. Pearson correlation was selected as a measure of similarity, and the unweighted pair-group method with arithmetic average (UPGMA) was used for cluster definition.

Table 1: Mediterranean ethnopharmacological uses of parsley (*Petroselinum crispum*).

Geographical Location	Ethnopharmacological Uses	Ref.
Thessaloniki (northern Greece)	Leaf decoction taken to relieve hypertension, treat cystitis, kidney stones, and prostatism.	[2]
Cyprus (Greece)	Infusion of the leaves taken as a tonic to treat anemia, as a stimulant, and a diuretic.	[3]
Riviera Spezzina, Liguria (northwestern Italy)	Leaves used externally to disinfect wounds.	[4]
Nebrodi Regional Park (northeastern Sicily, Italy)	Decoction of the aerial parts taken orally as a diuretic. Poultice of leaves used to treat insect bites.	[5]
Chieti, Abruzzo (central Italy)	Leaves used externally on wasp or bee stings. Leaf juice used on skin wounds as a disinfectant.	[6]
Acquapendente, Latium (central Italy)	Chopped leaves used externally on insect bites, pimples, and whitlows.	[7]
Dolomiti Lucane (southern Italy)	Decoction of the aerial parts used as abortifacient. Ground leaves topically applied to insect bites.	[8]
Maratea, Basilicata (southern Italy)	Leaf decoction taken as abortifacient.	[9]
Basilicata region (southern Italy)	Decoction of the aerial parts used as abortifacient. Ground leaves topically applied to insect bites.	[10]
Vesuvio National Park, Campania (southern Italy)	Decoction of the aerial parts taken orally as an abortifacient.	[11]
El Caurel, Galicia (northwestern Spain)	Decoction of the leaves taken as a diuretic.	[12]
Arribes del Duero (western Spain)	Decoction of the leaves taken orally as an abortifacient.	[13]
Granada province (southern Spain)	Decoction of the leaves taken orally as an abortifacient, to treat kidney stones, dysmenorrhea, prostatism, diabetes, and hypertension.	[14]
Granada, Andalusia (southern Spain)	Infusion of the aerial parts used externally to treat wounds on animals.	[15]
Serra de Mariola (southeastern Spain)	Leaves used externally on wounds and sores or gynecological issues. Leaf decoction taken orally for urinary problems, to stimulate appetite, or treat constipation.	[16]
Edremit Bay, Balıkesir (south central Turkey)	Infusion of the aerial parts taken orally as a diuretic, to treat kidney stones and abdominal aches.	[17]
Elazığ (eastern Turkey)	Decoction of the leaves taken orally to treat kidney stones and mouth sores.	[18]

Table 2: Essential oil yields from hydrodistillation of parsley (*Petroselinum crispum*) leaves.

Sample	*P. crispum* var. *crispum*		*P. crispum* var. *neapolitanum*	
	#1	#2	#3	#4
Mass of plant material	53.86 g	75.66 g	49.36 g	51.58 g
Essential oil yield	104.0 mg	165.3 mg	299.2 mg	165.7 mg

3. Results and Discussion

The essential oils from two different samples of *P. crispum* var. *crispum* (curly leaf parsley) and two different samples of *P. crispum* var. *neapolitanum* (flat leaf parsley) were obtained by hydrodistillation in yields of 0.193-0.606%. The essential oils were analyzed by GC-MS and GC-FID (see Table 2). A total of 38 compounds were identified in the oils. The major components in *P. crispum* var *crispum* were myristicin (39.4 and 43.2%), β-phellandrene (31.7 and 35.0%), and 1,3,8-*p*-menthatriene (14.9 and 7.9%).

Table 3: Chemical compositions of *Petroselinum crispum* leaf essential oils.

RI[a]	Compound	Percent Composition			
		***P.c.c.*#1**[b]	***P.c.c.*#2**[c]	***P.c.n.*#3**[d]	***P.c.n.*#4**[e]
882	(2*E*)-Hexenal	---	---	0.3	1.8
883	(4*Z*)-Hexenol	---	---	0.1	0.5
935	α-Pinene	1.1	0.9	2.2	3.0
971	Sabinene	0.2	0.1	---	0.1
973	β-Pinene	0.6	0.5	0.8	1.7

988	Myrcene	3.2	3.1	1.3	2.5
1000	α-Phellandrene	1.6	1.9	2.1	1.1
1012	α-Terpinene	---	---	0.4	---
1020	*p*-Cymene	0.2	0.1	17.3	0.3
1025	β-Phellandrene	31.7	35.0	10.0	17.0
1056	γ-Terpinene	---	0.1	0.2	0.6
1087	Terpinolene	2.3	0.9	0.1	1.0
1088	*p*-Cymenene	---	---	2.5	0.9
1111	1,3,8-*p*-Menthatriene	14.9	7.9	1.5	23.4
1184	*p*-Methylacetophenone	---	---	0.4	0.1
1186	*p*-Cymen-8-ol	---	---	0.6	0.1
1323	Myrtenyl acetate	---	---	---	0.1
1356	α-Cubebene	---	0.1	---	---
1373	α-Copaene	---	---	0.3	0.3
1388	β-Cubebene	---	---	---	0.1
1391	β-Elemene	0.5	0.5	---	---
1418	(*E*)-Caryophyllene	---	0.2	2.0	4.7
1430	γ-Elemene	---	---	0.2	---
1450	α-Humulene	---	---	0.1	0.2
1459	(*E*)-β-Farnesene	---	---	tr	0.1
1475	γ-Muurolene	---	---	1.0	---
1478	Germacrene D	0.4	0.9	0.2	5.2
1486	4-*epi*-*cis*-Dihydroagarofuran	0.2	0.3	0.2	0.2
1493	γ-Amorphene	---	---	0.2	---
1502	Isodaucene	1.3	1.2	---	---
1512	γ-Cadinene	---	---	0.3	---
1522	Myristicin	39.4	43.2	---	---
1523	δ-Cadinene	---	---	1.8	0.4
1524	β-Sesquiphellandrene	1.1	0.7	---	0.4
1536	α-Cadinene	---	---	0.1	---
1554	Germacrene B	0.5	1.4	---	---
1683	Apiole	0.7	0.9	52.9	33.0
1841	1-Phytadiene	---	---	0.2	0.2
	Total Identified	100.0	100.0	99.1	99.0

[a] RI = Retention Index determined in reference to a homologous series of *n*-alkanes on an HP-5ms GC column.
[b] *P. selinum* var. *crispum* (sample #1).
[c] *P. selinum* var. *crispum* (sample #2).
[d] *P. selinum* var. *neapolitanum* (sample #3).
[e] *P. selinum* var. *neapolitanum* (sample #4).

There have been several leaf essential oils of parsley identified as *P. crispum* var. *crispum* reported in the literature. Petropoulos and co-workers examined curly leaf parsley at two different growth stages and sowing dates in Athens, Greece [31]. These workers also found myristicin, β-phellandrene, and 1,3,8-*p*-menthatriene to dominate the leaf oils. There was observed, however, a dramatic decrease in monoterpene concentrations with concomitant increase in myristicin in the leaf oil one month after the first collection. Likewise, plants sown in December and harvested in April showed a higher concentration of apiole compared to plants sown in September and harvested in either December or January. Thus, seasonal variation had a profound effect on the chemistry of parsley leaf oils. In contrast, curly leaf parsley grown in Dokki, Giza, Egypt, also showed an abundance of myristicin (28.7-33.6%) and β-phellandrene (12.5-16.4%), but also showed relatively high concentrations of myrcene (9.8-10.4%), terpinolene (6.0-7.1%), and *p*-cymene (7.5-8.2%) [20]. Additionally, there was very little seasonal variation observed in the leaf oils from Egypt. Lechtenberg and co-workers examined two samples of curly leaf parsley from different sources [24]. One sample was rich in myristicin (59.4%), apiole (27.8%) and myrcene (9.6%), while the other sample was dominated by myristicin (82.3%). A leaf oil sample from Rockdale, New South Wales, Australia, was rich in 1,3,8-*p*-menthatriene, apiole, and β-phellandrene, but was devoid of myristicin [28]. Apparently, geographical location also plays a key factor in parsley leaf oil composition.

In contrast to the leaf oils of curly leaf parsley, flat leaf parsley oil in this work showed high concentrations of apiole (52.9 and 33.0%), but no detectible myristicin. Concentrations of β-phellandrene were high in both samples (10.0 and 17.0%), but *p*-cymene was high in the sample from South Carolina, #3 (17.3%), while 1,3,8-*p*-menthatriene was high in the sample from California, #4 (23.4%). Flat leaf parsley from Greece [31] and Mexico [26] showed relatively low concentrations apiole (0-17.8% and 3.8-13.8%, respectively). López and co-workers observed a dramatic decrease in the concentrations of β-phellandrene (58.3% → 0%) and myristicin (12.0% → 0%) through the growth cycle, while 1,3,8-*p*-menthatriene concentrations increased dramatically (0.4% → 79.9%) [26].

There are many reports in the literature on the chemical compositions of parsley leaf oils where the particular cultivar (or wild type) was not indicated. In order to place the parsley leaf oil compositions into context, but realizing that there can be significant seasonal and geographical variation possible, a hierarchical cluster analysis was carried out (Figure 1). The cluster analysis reveals three clusters: (1) a myristicin-rich cluster, (2) an apiole-rich cluster, and (3) a 1,3,8-*p*-menthatriene-rich cluster. All three clusters were also rich in β-phellandrene. Interestingly, most of the curly leaf parsley (*P. crispum* var. *crispum*) samples, including the two *crispum* samples from this study, fell into the myristicin cluster, while most of the flat leaf parsley (*P. crispum* var. *neapolitanum*) samples fell into the 1,3,8-*p*-menthatriene cluster; the apiole cluster had representatives from each, including the two *neapolitanum* samples from this current study.

The phenylpropanoid myristicin (4-methoxy-6-(2-propenyl)-1,3-benzodioxole) is not only a major component of parsley leaf oils, but also a major component of nutmeg (*Myristica fragrans*) [36]. The compound is known to form liver DNA adducts in mice [37] and has shown neurotoxicity in human neuroblastoma cells [38]. Myristicin has also shown anxiolytic effects in rats [39], locomotor inhibitory activity in mice [40], insecticidal activity [41–43], and anti-inflammatory activity [44]. Myristicin has also demonstrated cancer chemopreventive activity in a mouse model [45] and hepatoprotective effects in rats [46]. It is also a monoamine oxidase inhibitor [47], serotonin receptor agonist, and a hallucinogen [48], which has been attributed to one of its metabolites, 3-methoxy-4,5-methylenedioxyamphetamine (MMDA) [49]. There have been reports of myristicin poisoning due to nutmeg abuse [50].

Apiole (4,7-dimethoxy-5-(2-propenyl)-1,3-benzodioxole) has shown antipyretic, diuretic, insecticidal, and antitumor activities [51]. This compound has also been reported to cause human poisoning [52]. The monoterpene 1,3,8-*p*-menthatriene has been determined to be the key odorant and character impact flavor component of parsley leaves [53].

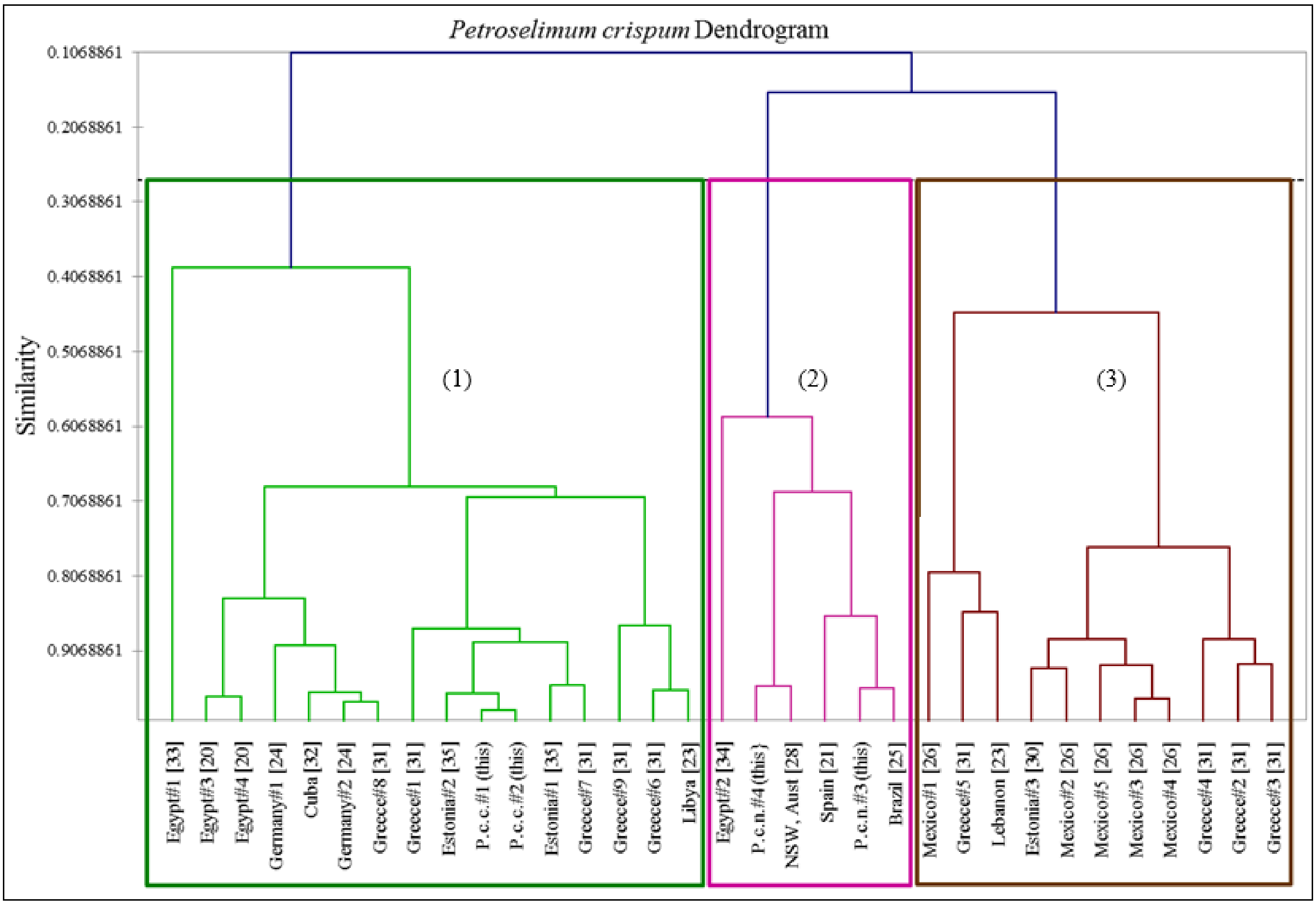

Fig 1: Dendrogram obtained from the agglomerative hierarchical cluster analysis of 33 *Petroselinum crispum* essential oil compositions. (1) myristicin/β-phellandrene cluster, (2) apiole/β-phellandrene cluster, (3) 1,3,8-*p*-menthatriene/β-phellandrene cluster.

4. Conclusions

The leaf essential oils of two varieties of parsley, curly leaf parsley and flat leaf parsley were examined by GC and GC-MS. The leaf essential oils of two samples of *P. crispum* var. *crispum* (curly leaf parsley) were found to be rich in myristicin, β-phellandrene, and 1,3,8-*p*-menthatriene, but very low in apiole. Two samples of flat leaf parsley (*P. crispum* var. *neapolitanum*) were rich in apiole, but devoid of myristicin. There is wide variation in the chemical compositions of parsley leaf oils, but they can be classified into three different categories based on composition: myristicin/β-phellandrene, including the two curly leaf samples from this work and most of the other curly leaf samples reported in the literature; 1,3,8-*p*-menthatriene/β-phellandrene, which includes most of the flat leaf samples reported in the literature; and apiole/β-phellandrene, including the two samples of flat leaf parsley in this work.

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