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Chemical Composition and Terpenoid Enantiomeric Distribution of the Essential oil of *Artemisia tridentata* Subsp. *tridentata* From Southwestern Idaho

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Abstract

Big sagebrush (*Artemisia tridentata*) is a common shrub growing in the cold intermountain regions of western North America. The plant is an important food source for herbivores and was used in Native American traditional medicine. In this work, the essential oils were obtained from 3 individuals of *A tridentata* subsp. *tridentata* growing in southwestern Idaho. The essential oils were analyzed by gas chromatographic methods including chiral gas chromatography. The major components in the essential oils were yomogi alcohol (5.8%-30.8%), santolina epoxide (1.7%-10.5%), camphor (5.2%-20.1%), and (*Z*)-tagetone (0.9%-8.9%). (+)-α-Pinene, (+)-β-pinene, (+)-verbenone, (−)-(*E*)-β-caryophyllene, and (−)-δ-cadinene were the only enantiomers observed for these compounds. Camphene and camphor, on the other hand, showed wide variability in enantiomeric distribution. The enantiomeric distributions in *A tridentata* subsp. *tridentata* differ widely compared to other *Artemisia* species. There are large variations in the chemical compositions in *A tridentata*, both between subspecies and within subspecies.

Keywords

big sagebrush, basin sagebrush, essential oil, chiral, gas chromatography

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Introduction

Artemisia is a large genus of the Asteraceae with around 1550 species worldwide[1] and 60 species native to North America, north of Mexico.[2] *Artemisia tridentata* Nutt. (Asteraceae), commonly known as big sagebrush or basin sagebrush, is found in western North America from Montana, Wyoming, Colorado, and New Mexico, west in Washington, Oregon, and California, including Idaho,[2] and is most prevalent in the cold intermountain regions.[3] Although the species has undergone extensive taxonomic revision[4] and hybridization is common,[5] there are 3 generally recognized subspecies: *A tridentata* subsp. *tridentata*, *A tridentata* subsp. *vaseyana* (Rydb.) Beetle, and *A tridentata* subsp. *wyomingensis* Beetle and A.L. Young.[3]

A tridentata is an important cover and food source for the pygmy rabbit (*Brachylagus idahoensis*), the greater sage-grouse (*Centrocercus urophasianus*), Gunnison sage-grouse (*Centrocercus minimus*), pronghorn (*Antilocapra americana*), mule deer (*Odocoileus hemionus*), elk (*Cervus canadensis*), and bighorn sheep (*Ovis canadensis*).[6–8] Indigenous peoples of western North America used *A tridentata* in traditional herbal medicine. An infusion of leaves of *A tridentata* was taken for colds, coughs, and bronchitis (Diegueño, Flathead, Gosiute, and Havasupai); the burning plant was inhaled for headache (Paiute); a poultice or decoction of leaves was used as a liniment (Gosiute, Montana; Okanagan-Colville, and Shoshoni), and to treat cuts, sores, and wounds (Okanagan-Colville, and Shoshoni).[9]

The phytochemistry of *A tridentata* has been dominated by monoterpenoids, sesquiterpenoids, and phenolics.[10] Previous reports on the essential oils of *A tridentata* indicate the plant to be composed largely of camphor (20%-45%), camphene (3%-21%), 1,8-cineole (12%-30%), thujone (6%), and borneol (5%).[11–16] In addition, several irregular monoterpenoids have been isolated and characterized,[17–21] including artemiseole, lyratrol, lyratral, neolyratrol, rothrockene, *trans*-chrysanthemol, santolinolides A, B, and C, 1-(3-hydroxymethyl-2,2-dimethylcyclopropyl)-2-methyl-

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2-propen-1-one, and 1-(3-hydroxymethyl-2,2-dimethylcyclopropyl)-2-methyl-1-propanone. Sesquiterpene lactones are major components of the nonvolatile phytochemicals found in *A tridentata*.[22] These include the eudesmanolides dentatin A, dihydroreynosin, and 11β,13-dihydrosantamarine; the germacranolides artevasin, tatridin A, and tatridin B; and the guaianolides dehydroleucodine, parishins A, B, and C. The volatile components of *A tridentata* are likely responsible for the traditional uses of the plant by Native Americans. 1,8-cineole and camphor have demonstrated antitussive activity,[23,24] camphor has shown activity against H1N1 influenza virus[25] and 1,8-cineole-rich essential oils (eg, *Eucalyptus* oil) have shown anti-influenza virus activity.[26] In a double-blind, placebo-controlled clinical trial, 1,8-cineole showed significant relief in patients suffering from acute bronchitis.[27]

Different sagebrush taxa have different palatability characteristics toward herbivores. For example, *A tridentata* subsp. *vaseyana* and *A tridentata* subsp. *wyomingensis* are generally palatable to most herbivores, while *A tridentata* subsp. *tridentata* is the least palatable of the *A tridentata* subspecies.[28] The phytochemical makeup of *A tridentata* is likely a fundamental factor in palatability and food selection by herbivores.[6,28,29] It has been found that high levels of monoterpenoids reduce rumen microbial activity and affect palatability of *A tridentata* to browsing animals.[30] However, monoterpene and sesquiterpene hydrocarbons have been shown to enhance fermentation by rumen microorganisms, whereas oxygenated monoterpenoids inhibit microbial fermentation.[13]

The purpose of this study was to expand our understanding of the volatile phytochemistry of sagebrush. To our knowledge, this is the first report on the essential oil composition of *A tridentata* subsp. *tridentata* from southwestern Idaho (Figure 1) and the first evaluation of the enantiomeric distributions of the terpenoid components. Additionally, a comparison of enantiomeric distributions with other *Artemisia* species is presented.

Results and Discussion

Essential oil Composition

The pale yellow essential oils from the aerial parts of *A tridentata* subsp. *tridentata* were obtained from 3 individual plants growing along the Snake River in southwestern Idaho with yields of 1.29%, 1.43%, and 1.72%. The essential oils were analyzed by gas chromatography–flame inonization detection (GC-FID) and gas chromatography–mass spectrometry (GC-MS) (Table 1). A total of 46, 47, and 51 compounds were identified in the 3 essential oils, accounting for 82.6%, 83.7%, and 92.1%, for samples #1, #2, and #3, respectively.

Oxygenated monoterpenoids dominated the essential oils of *A tridentata* subsp. *tridentata* from southwestern Idaho with yomogi alcohol (5.8%-30.8%), santolina epoxide (1.7%-10.5%), camphor (5.2%-20.1%), and (*Z*)-tagetone (0.9%-8.9%) as major components. Zheljazkov and co-workers have carried out an extensive investigation of sagebrush species from the Bighorn Mountains of Wyoming, including *A tridentata* subsp. *tridentata*.[29] There are some notable differences between the Wyoming essential oil compositions and the Idaho compositions. While yomogi alcohol, santolina epoxide, (*Z*)-tagetone, and α-santolina alcohol were relatively abundant in the Idaho essential oils, they were not detected in the Wyoming essential oils. Conversely, camphene (10.5% and 21.5%) and 1,8-cineole (13.6% and 21.2%) were relatively abundant in the Wyoming oils, but they were relatively minor components in the Idaho oils (0.8%-1.6% and 0.3%-2.5%, respectively). Likewise, camphor was much more abundant in the Wyoming oils (41.3% and 43.2%) than in the Idaho oils (5.2%-20.1%). Chrysanthenone (1.1% and 11.3%) in the Wyoming oil was not detected in the Idaho oils. There is much variability in essential oil compositions between subspecies and within subspecies of *A tridentata*.[29] The differences in composition between the Wyoming and Idaho collections may be attributed to genetic/chemotypic variation, latitudinal (44°34′ in Wyoming and 43° 15′ in Idaho) and altitudinal differences (2100 and 2300 m in Wyoming and 700 m in Idaho), or seasonality (30 September for the Wyoming collection and 28 July for the Idaho collection).

Although the concentrations of coumarins[5] and sesquiterpene lactones[28] may affect palatability, essential oil constituents likely also affect palatability and herbivory.[8] As previously noted, monoterpene and sesquiterpene hydrocarbons have been shown to enhance fermentation by rumen microorganisms, whereas oxygenated monoterpenoids inhibit microbial fermentation.[13] Notably, the essential oils of *A. tridentata* subsp. *tridentata* in this study were dominated by oxygenated monoterpenoids (72.8%-85.9%).

Terpenoid Enantiomeric Distributions

The enantiomeric distributions of chiral terpenoid components of *A tridentata* subsp. *tridentata* were evaluated using chiral GC-MS (Table 2). As far as we are aware, this is the first presentation of the chiral terpenoid components of *A tridentata*, and one of only a few descriptions of chiral terpenoid components of *Artemisia*. As a comparison, the essential oils of 2 commercial *Artemisia vulgaris* essential oils from Nepal were also analyzed by chiral GC-MS (Table 3).

(+)-α-Pinene and (+)-β-pinene, were the only enantiomers identified in *A tridentata* subsp. *tridentata* essential oils. In contrast, the essential oil of *Artemisia vulgaris* showed variability in the distributions of α- and β-pinene, while the essential oil of *Artemisia annua* showed variable distributions of α-pinene but only (−)-β-pinene was observed.[37] (−)-β-Pinene also dominated the enantiomeric distribution in *Artemisia arborescens*.[38] Camphene showed variability in enantiomeric distribution ranging from 17.4% to 96.1% (+)-camphene in *A tridentata* subsp. *tridentata*. Camphene enantiomers in *A. vulgaris* (Table 3) were variable with 98.3% (+)-camphene in one sample and 90.0% (−)-camphene in the other. Camphene in *A. arborescens* were also variable with 44.0% to 65.8% (+)-camphene.[38]

Table 1. Essential oil Compositions (%) of *Artemisia tridentata* Subsp. *tridentata* From Southwestern Idaho.

RI_{calc}	RI_{db}	Compound	#1	#2	#3
888	888	Ethyl pent-4-enoate	0.8	1.3	0.2
904	902	Santolina triene	4.3	4.0	---
904	909	2-Acetylfuran	---	---	0.8
914	913	Isobutyl isobutyrate	0.3	0.2	0.1
922	922	Artemisia triene	0.1	0.3	0.6
933	933	α-Pinene	0.2	0.1	0.1
950	950	Camphene	1.6	0.4	0.8
972	971	Artemiseole	3.5	2.1	0.7
978	978	β-Pinene	0.1	tr	tr
982	---	*epi*-Artemiseole	0.3	0.2	0.1
998	996	Yomogi alcohol	5.8	20.6	30.8
1004	1003	Isobutyl 2-methylbutanoate	0.1	0.1	0.1
1008	1007	α-Phellandrene	0.1	tr	---
1010	1008	Allyl tiglate	0.7	1.5	0.3
1025	1025	*p*-Cymene	0.7	0.6	0.5
1032	1031	Santolina alcohol	0.6	0.4	0.1
1033	1032	1,8-Cineole	2.5	1.6	0.3
1047	---	Oxido santolina triene (=Santolina epoxide)[17]	10.5	5.8	1.7
1055	1053	*epi*-Isolyratol[31]	0.4	0.2	---
1058	1056	Artemisia ketone	---	---	0.1
1060	1054	Methyl 2,6-dimethylheptanoate	---	0.2	0.1
1064	1066	1-Methyl-2-oxopropyl butyrate	---	---	0.2
1070	---	Isolyratol[32]	1.4	0.6	1.2
1072	---	α-Santolina alcohol[21]	4.8	4.1	0.8
1075	---	*epi*-α-Santolina alcohol[21]	3.0	2.0	---
1081	1079	Artemisia alcohol	1.7	4.0	4.5
1105	1104	Hotrienol	---	---	0.1
1110	---	Unidentified[a]	1.7	0.3	0.3
1113	---	Unidentified[b]	1.7	0.6	0.3
1114	---	Unidentified[c]	1.3	1.2	0.8
1131	1129	Methyl santolinate	1.1	0.9	0.4
1150	1149	Camphor	9.6	5.2	20.1
1152	1152	(*Z*)-Tagetone	8.9	7.7	0.9
1156	---	Lyratol[31]	1.5	---	---
1163	1164	Pinocarvone	---	---	0.3
1165	1164	β-Artemisyl acetate	0.7	6.9	15.9
1181	1180	Terpinen-4-ol	0.4	0.3	0.2
1207	1208	Verbenone	0.2	0.2	1.3
1249	1253	*trans*-Chrysanthenyl acetate	4.2	2.3	0.5
1255	1255	Geraniol	1.3	0.9	0.6
1258	---	Santolinolide B′[18]	1.0	1.0	1.4
1259	---	Santolinolide B[18]	1.8	1.5	1.5
1267	1266	*cis*-Chrysanthenyl acetate	2.2	2.1	0.5
1285	1284	Lavandulyl acetate	2.8	1.0	0.3
1292	---	Santolinolide C[18]	1.2	1.0	1.3
1369	---	Unidentified[d]	2.1	1.7	0.6
1373	1372	Linalyl isobutanoate	0.3	0.1	---
1397	1396	(2*E*)-13,7-Trimethyl-2,6-octadienyl acetate	---	---	0.1
1415	1415	Lavandulyl isobutanoate	0.2	0.2	0.1
1418	1417	(*E*)-β-Caryophyllene	---	---	0.1
1432	1432	6-Oxobornyl acetate	0.5	0.3	---
1479	1480	Germacrene D	0.1	0.2	---
1480	1480	*ar*-Curcumene	---	---	0.3
1490	1490	Benzyl phenylacetate	---	---	0.2
1495	1497	Anisylacetone	---	0.2	---
1501	1501	Lavandulyl isovalerate	0.2	0.2	0.1
1516	1518	δ-Cadinene	0.1	0.1	0.1
1554	---	Unidentified[e]	4.6	4.7	0.6

(Continued)

Table 1. Continued.

RI_{calc}	RI_{db}	Compound	#1	#2	#3
1560	1561	(*E*)-Nerolidol	---	0.3	0.5
1563	1560	Dodecanoic acid	---	0.3	---
1576	1576	Spathulenol	0.1	0.1	0.2
1596	1596	Fokienol	---	---	0.1
1601	1600	β-Oplopenone	---	---	0.1
1603	1605	Ledol	---	---	0.1
1640	1642	Methyl (*Z*)-jasmonate	---	0.3	0.2
1640	1643	τ-Cadinol	0.2	---	---
1642	1644	τ-Muurolol	0.1	0.1	0.2
1653	1655	α-Cadinol	0.3	0.2	0.4
		Monoterpene hydrocarbons	7.0	5.5	2.0
		Oxygenated monoterpenoids	72.8	73.3	85.9
		Sesquiterpene hydrocarbons	0.3	0.3	0.6
		Oxygenated sesquiterpenoids	0.7	0.8	1.4
		Esters	1.9	3.4	1.2
		Benzenoid aromatics	0.0	0.2	0.2
		Others	0.0	0.3	0.9
		Total identified	82.6	83.7	92.1

[a]MS(EI): 152(2%), 137(6%), 121(45%), 107(14%), 105(14%), 94(23%), 93(58%), 91(43%), 79(100%), 77(42%), 67(14%), 55(18%), 43(21%), 41(30%).
[b]MS(EI): 149(2%), 137(35%), 135(33%), 121(33%), 109(27%), 107(31%), 105(24%), 96(61%), 95(34%), 93(49%), 91(86%), 79(100%), 77(67%), 67(18%), 65(20%), 55(24%), 53(37%), 43(55%), 41(65%).
[c]MS(EI): 154(1%), 138(45%), 123(47%), 95(58%), 82(54%), 68(54%), 67(100%), 59(40%), 43(87%), 41(55%).
[d]MS(EI): 139(3%), 117(41%), 96(34%), 81(33%), 75(33%), 67(10%), 55(9%), 43(100%), 41(7%). e MS(EI): 150(17%), 149(25%), 134(10%), 107(12%), 91(12%), 79(11%), 43(100%).
Abbreviations: RI_{calc}, Calculated retention index with respect to a homologous series of *n*-alkanes on a ZB-5ms column; RI_{db}, Reference retention index from the databases;[33–36] tr, trace (< 0.05%).

Table 2. Enantiomeric Distribution of Terpenoid Constituents of *Artemisia tridentata* Subsp. *tridentata* Essential Oils From Southwestern Idaho.

	(+)% : (−)%		
Compounds	#1	#2	#3
α-Pinene	(+)100.0 : (−)0.0	(+)100.0 : (−)0.0	(+)100.0 : (−)0.0
Camphene	(+)17.4 : (−)82.6	(+)67.8 : (−)32.2	(+)96.1 : (−)3.9
β-Pinene	(+)100.0 : (−)0.0	(+)100.0 : (−)0.0	---
Camphor	(+)41.0 : (−)59.0	(+)91.6 : (−)8.42	(+)100.0 : (−)0.0
Terpinen-4-ol	(+)27.7 : (−)72.3	(+)29.8 : (−)70.2	(+)25.7 : (−)74.3
Verbenone	(+)100.0 : (−)0.0	(+)100.0 : (−)0.0	(+)100.0 : (−)0.0
(*E*)-β-Caryophyllene	---	---	(+)0.0 : (−)100.0
δ-Cadinene	(+)0.0 : (−)100.0	(+)0.0 : (−)100.0	(+)0.0 : (−)100.0
(*E*)-Nerolidol	---	(+)8.1 : (−)91.9	(+)7.9: (−)92.1

Camphene enantiomers in *A. annua* were also variable, but (−)-camphene predominated.[37] Camphor also showed variability in enantiomeric distribution in *A tridentata* subsp. *tridentata* with (+)-camphor ranging from 41.0% to 100.0%. Interestingly, (−)-camphor dominated the essential oil compositions of *A. vulgaris* (Table 3), *A. arborescens*,[38,39] and *Artemisia herba-alba*.[40] The (−)-enantiomer predominated for terpinene-4-ol in *A tridentata* subsp. *tridentata* (70.2%-74.3%) in contrast to that observed in *A. arborescens* (67.5%-72.2% (+)-terpenen-4-ol).[38,39] (+)-Verbenone, (−)-(*E*)-β-caryophyllene, and (−)-δ-cadinene were the only enantiomers observed in *A tridentata* subsp. *tridentata*, while (−)-(*E*)-nerolidol was the predominant enantiomer, consistent with the distributions found in *A vulgaris*.

Table 3. Enantiomeric Distribution of Terpenoid Constituents of Commercial *Artemisia vulgaris* Essential Oils From Kirtipur, Kathmandu, Nepal.

	(+)% : (−)%	
Compounds	Sample 210913M	Sample 220125J
α-Pinene	(+)87.3 : (−)12.7	(+)18.0 : (−)82.0
Camphene	(+)93.8 : (−)6.2	(+)10.0 : (−)90.0
β-Pinene	(+)8.6 : (−)91.4	(+)42.5 : (−)57.5
Camphor	(+)0.0 : (−)100.0	(+)28.0 : (−)72.0
Terpinen-4-ol	(+)48.1 : (−)51.9	(+)66.9 : (−)33.1
Verbenone	---	(+)0.0 : (−)100.0
(*E*)-β-Caryophyllene	(+)0.0 : (−)100.0	(+)0.0 : (−)100.0
δ-Cadinene	(+)0.0 : (−)100.0	(+)0.0 : (−)100.0
(*E*)-Nerolidol	(+)5.5 : (−)94.5	---

Figure 1. *Artemisia tridentata*, subsp. *tridentata* from Swan Falls, Snake River, Idaho.

Conclusions

The essential oil compositions of *A tridentata* subsp. *tridentata* collected from southwestern Idaho showed remarkable differences compared to *A tridentata* essential oils from different geographical locations or from different subspecies. Sagebrush essential oil compositions are apparently very variable. Nevertheless, the high concentrations of oxygenated monoterpenoids may account for the known unpalatability of *A tridentata* subsp. *tridentata* toward herbivores. The enantiomeric distributions of terpenoid components of *A tridentata* subsp. *tridentata* were vastly different from enantiomers of other species of *Artemisia*. Additional research is required to more fully understand the terpenoid enantiomeric distributions in sagebrush species.

Materials and Methods

Plant Material

Aerial parts from 3 different individuals of *A tridentata* subsp. *tridentata* were collected from the Swan Falls area of the Snake River, Idaho (#1, 43°14′45″N, 116°22′40″W, 707 m elevation; #2, 43°14′46″N, 116°22′46″W, 702 m elevation; #3, 43° 14′45″N, 116°22′40″W, 707 m elevation) on July 28, 2021, 9:30 to 10:00 am. The plant was identified by W.N. Setzer; a voucher specimen was deposited in the University of Alabama in Huntsville Herbarium (voucher number WNS21123002). The fresh aerial parts of each plant (118.38 g, 80.64 g, and 59.00 g, respectively) were chopped and hydrodistilled using a Likens-Nickerson apparatus for 4 h to give pale yellow essential oils (1.5275 g, 1.1551 g, and 1.0164 g, respectively).

The commercial essential oil samples of *A. vulgaris* from Kirtipur, Kathmandu, Nepal, were analyzed as received in the laboratory of the Aromatic Plant Research Center (APRC, Lehi, Utah, USA).

Gas Chromatography

GC-MS was carried out using a Shimadzu GC-MS-QP2010 Ultra (Shimadzu Scientific Instruments) equipped with a ZB-5ms GC column (5% phenyl polydimethylsiloxane, 60 m × 0.25 mm × 0.25 μm film thickness) (Phenomenex). The injector and detector temperatures were 260 °C, the carrier gas was helium with a column head pressure of 208.3 kPa, and a flow rate of 2.00 mL/min. The GC oven temperature was programmed to start at 50 °C and ramp up to 260 °C at a rate of 2 °C/min. For each essential oil sample, 1.0 μL of a 5% (w/v) solution in dichloromethane was injected with a splitting mode of 24.5:1. Retention index (RI) values were calculated using a homologous series of *n*-alkanes.[41] The essential oil components were identified by comparing their RI values and their MS fragmentation patterns with those reported in the databases[33-36] using the LabSolutions GCMS solution software version 4.45 (Shimadzu Scientific Instruments).

GC-FID was carried out using a Shimadzu GC 2010 with an FID detector (Shimadzu Scientific Instruments) and a ZB-5 GC column (60 m × 0.25 mm × 0.25 μm film thickness) (Phenomenex), using the same operating conditions as above for GC-MS. The percent compositions were determined from raw peak areas without standardization.

The *A tridentata* essential oils were analyzed by chiral GC-MS using a Shimadzu GC-MS-QP2010S (Shimadzu Scientific Instruments) instrument fitted with a Restek B-Dex 325 column (30 m × 0.25 mm diameter × 0.25 μm film thickness)

(Restek Corp.). The injector and detector temperatures were 240 °C. Helium was the carrier gas with a column head pressure of 53.6 kPa and a flow rate of 1.00 mL/min. The GC oven was programmed with an initial temperature of 50 °C, held for 5 min, then 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 essential oil sample, 0.3 μL of a 5% (w/v) solution in dichloromethane was injected using a splitting mode of 24.0:1. The enantiomeric distributions were determined by comparison of retention times with authentic samples obtained from Sigma-Aldrich (Milwaukee, WI, USA). The enantiomer percentages were determined from raw peak areas.

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