

Supplementary Material for:

# Labdane Diterpenoids from *Salvia tingitana* Etl. Synergize with Clindamycin against Methicillin-Resistant *Staphylococcus aureus*

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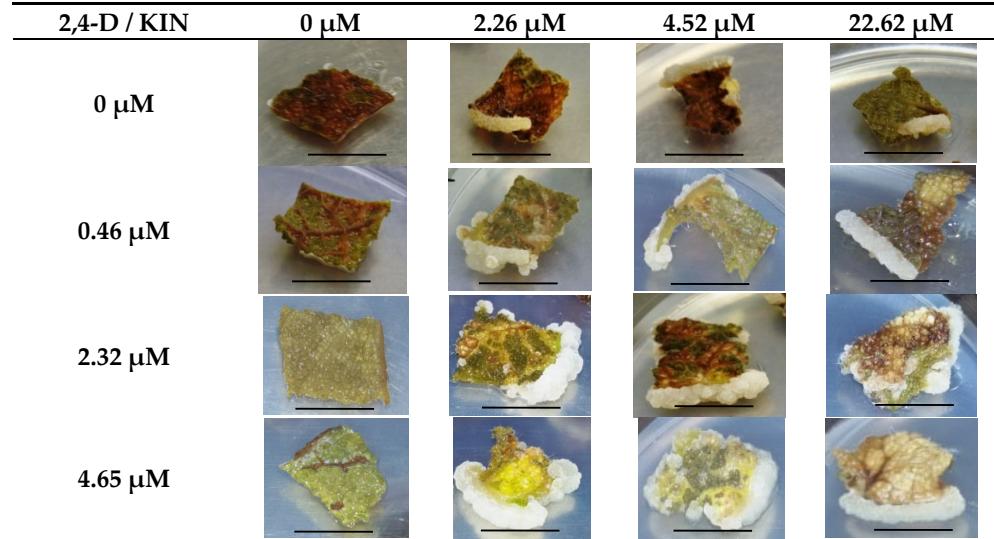
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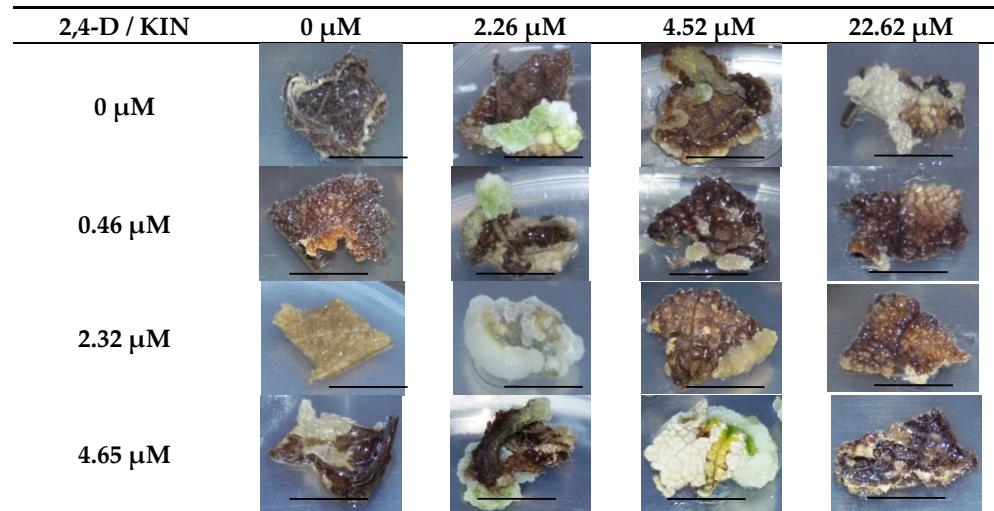
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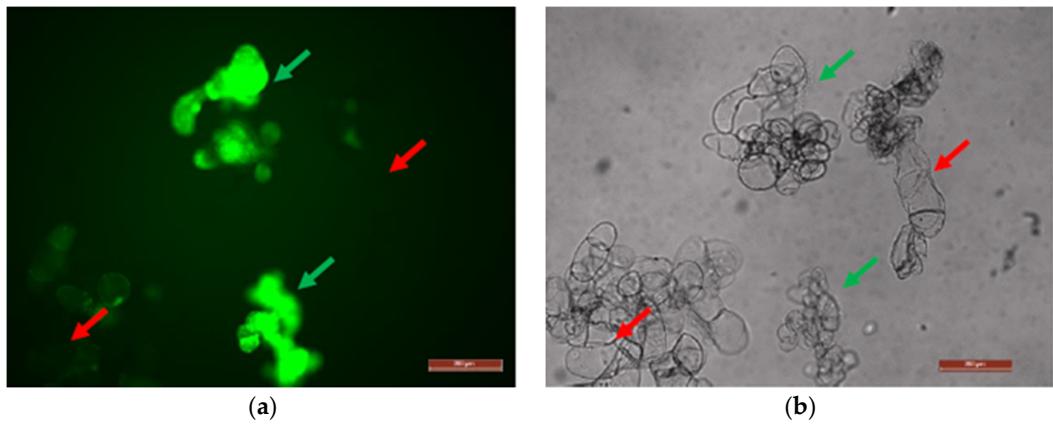
**Table S1.** Literature survey about the presence of sclareol (**1**) and manool (**2**) in *Salvia* spp.<sup>a</sup> ..... 10



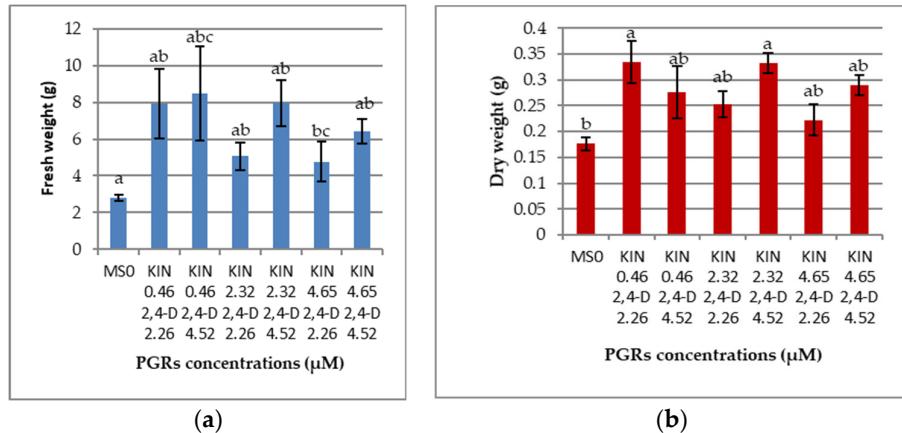
**Figure S1.** Callus of *S. tingitana* developed from leaf explants in dark condition on MS supplemented with different combination of PGRs and 10 mg/L of ascorbic acid after 4 weeks. MS: Murashige and Skoog medium; PGRs: plant growth regulators; 2,4-D: 2,4-dichlorophenoxyacetic acid; KIN: kinetin. Bars = 1 cm.



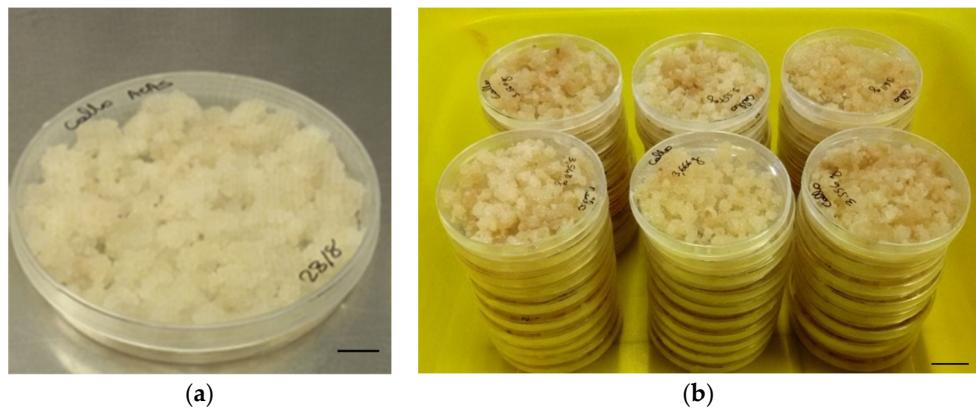
**Figure S2.** Callus of *S. tingitana* developed from leaf explants in light condition on MS supplemented with different combination of PGRs and 10 mg/L of ascorbic acid after 4 weeks. MS: Murashige and Skoog medium; PGRs: plant growth regulators; 2,4-D: 2,4-dichlorophenoxyacetic acid; KIN: kinetin. Bars = 1 cm.



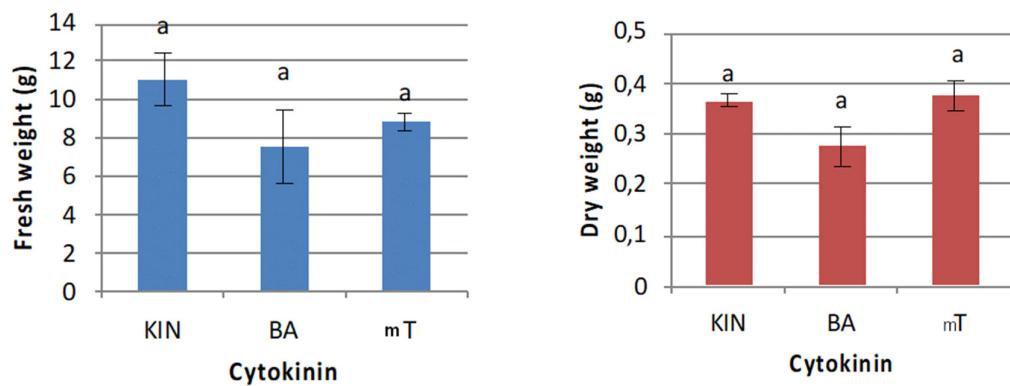
**Figure S3.** FDA staining of *S. tingitana* callus.a: fluorescent observation; b: bright field observation (40×). Green arrows mean living cell while red mean dead cells. FDA: fluoresceine diacetate. Bars = 200  $\mu$ m.



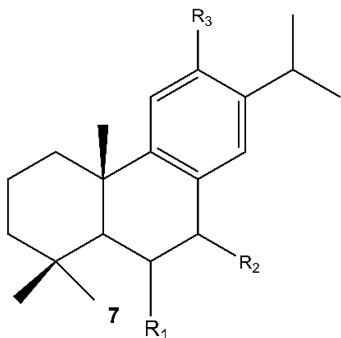
**Figure S4.** Effect of different combination of plant growth regulators to *S. tingitana* callus biomass production.a: fresh weight; b: dry weight. Data are reported as mean of six replicates  $\pm$  SE, n=6. Different letters identify values which differ at  $p \leq 0.05$ .



**Figure S5.** Callus of *S. ttingitana*. a: friable callus obtained after several subculture in MS medium supplemented with KIN 2.32  $\mu$ M and 2,4-D 4.52  $\mu$ M and ascorbic acid 10 mg/L. MS: Murashige and Skoog medium; KIN: kinetin; 2,4-D: 2,4-dichlorophenoxyacetic acid. Bar=1 cm. b: biomass production. Bar = 2 cm.



**Figure S6.** Effect of equimolar concentration of different cytokinins on callus growth. KIN: kinetin; BA: 6-benzylamino-purine; mT: meta Topolin. Values represent the mean  $\pm$  standard error (SE)  $n=4$ .

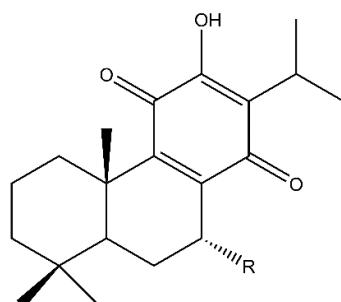


4 R<sub>1</sub>: H, R<sub>2</sub>: H, R<sub>3</sub>: H

**6** R<sub>1</sub>: H, R<sub>2</sub>: =O, R<sub>3</sub>: H

7 R<sub>1</sub>: H, R<sub>2</sub>: H, R<sub>3</sub>: OH

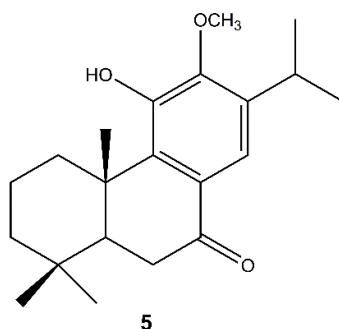
**8** R<sub>1</sub>: =O, R<sub>2</sub>: =O, R<sub>3</sub>: OH



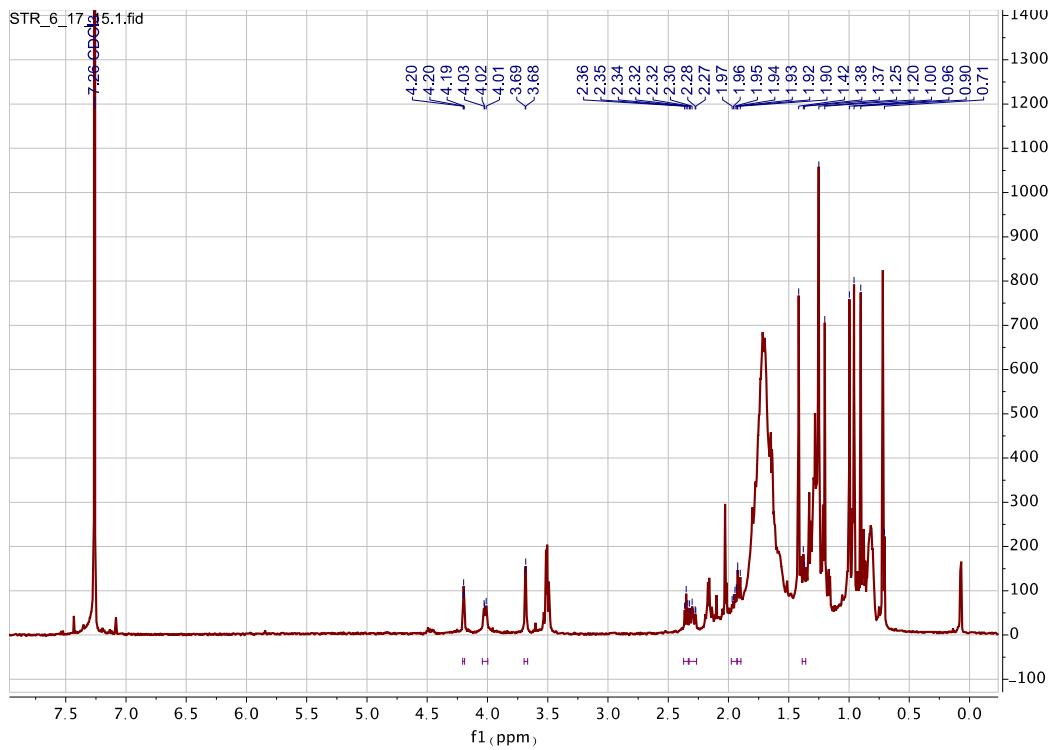
$$3 \quad R = T$$

9 R = OH

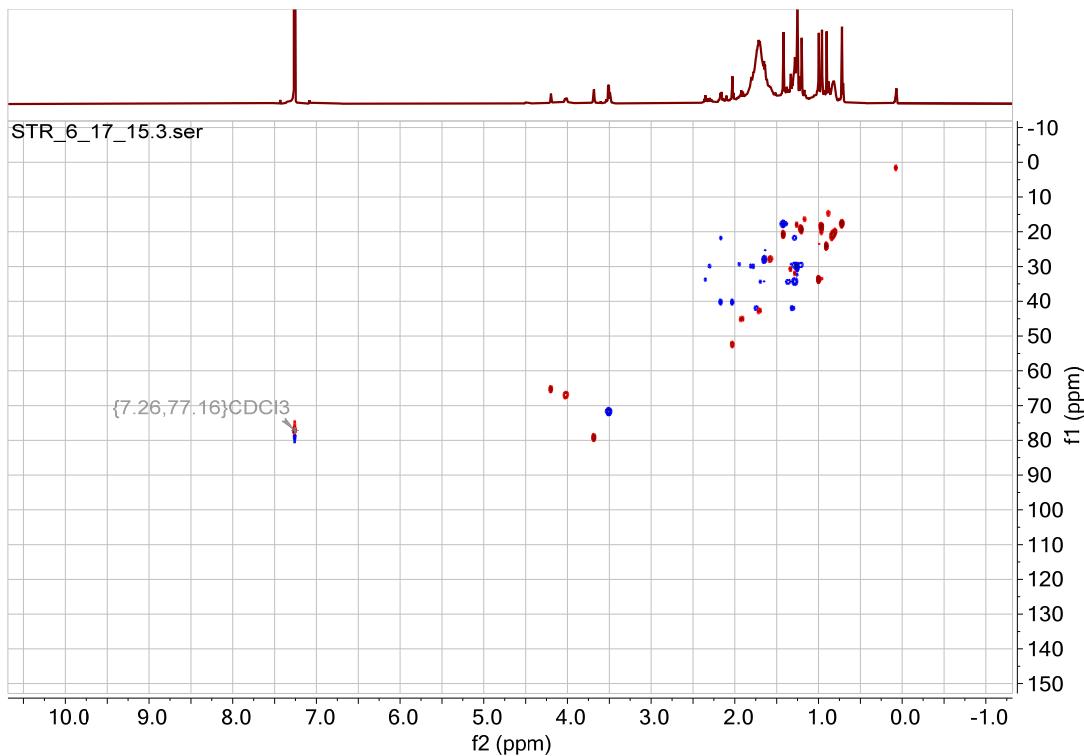
**10** R =OCH<sub>3</sub>



**Figure S7.** Abietane diterpenoids isolated from the roots of *S. tingitana*.**3:** royleanone; **4:** abiet-8,11,13-triene; **5:** cryptojaponol; **6:** abiet-8,11,13-trien-7-one; **7:** ferruginol; **8:** 12-hydroxyabiet-8,11,13-triene-6,7-dione (hypargenin C); **9:** horminone; **10:** 7-O-methylhorminone



**Figure S8.**  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of compound **13**.



**Figure S9.** HSQC (600 MHz,  $\text{CDCl}_3$ ) spectrum of compound **13**.

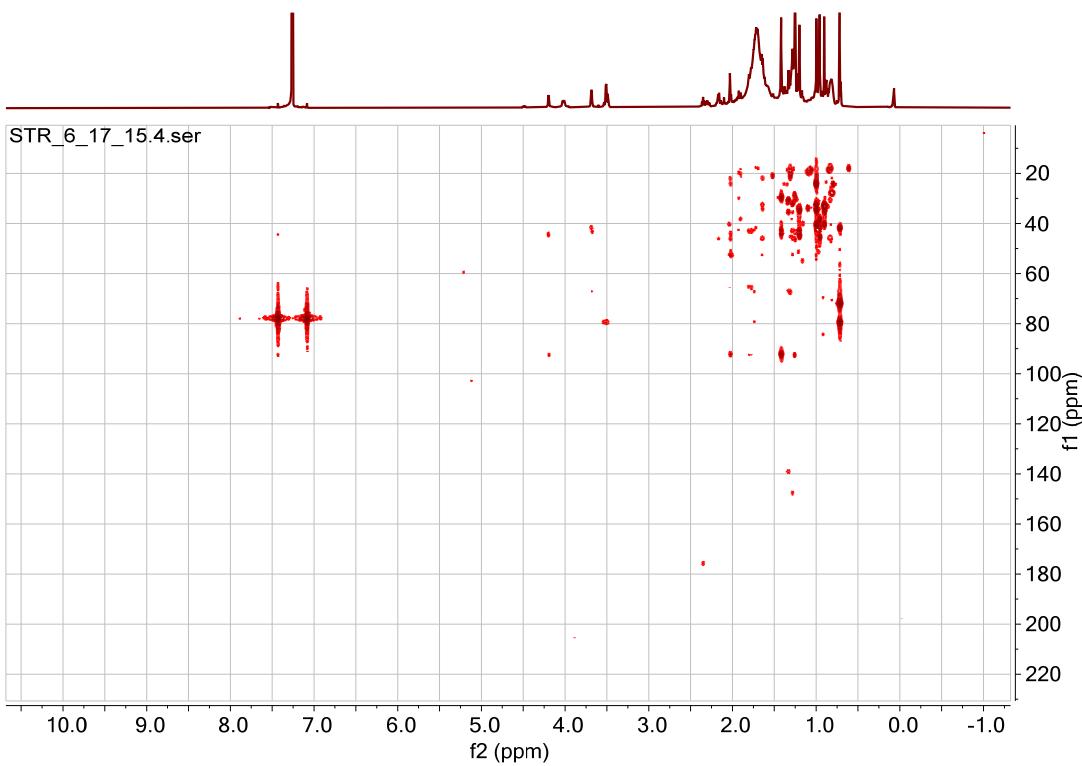


Figure S10. HMBC (600 MHz,  $\text{CDCl}_3$ ) spectrum of compound 13.

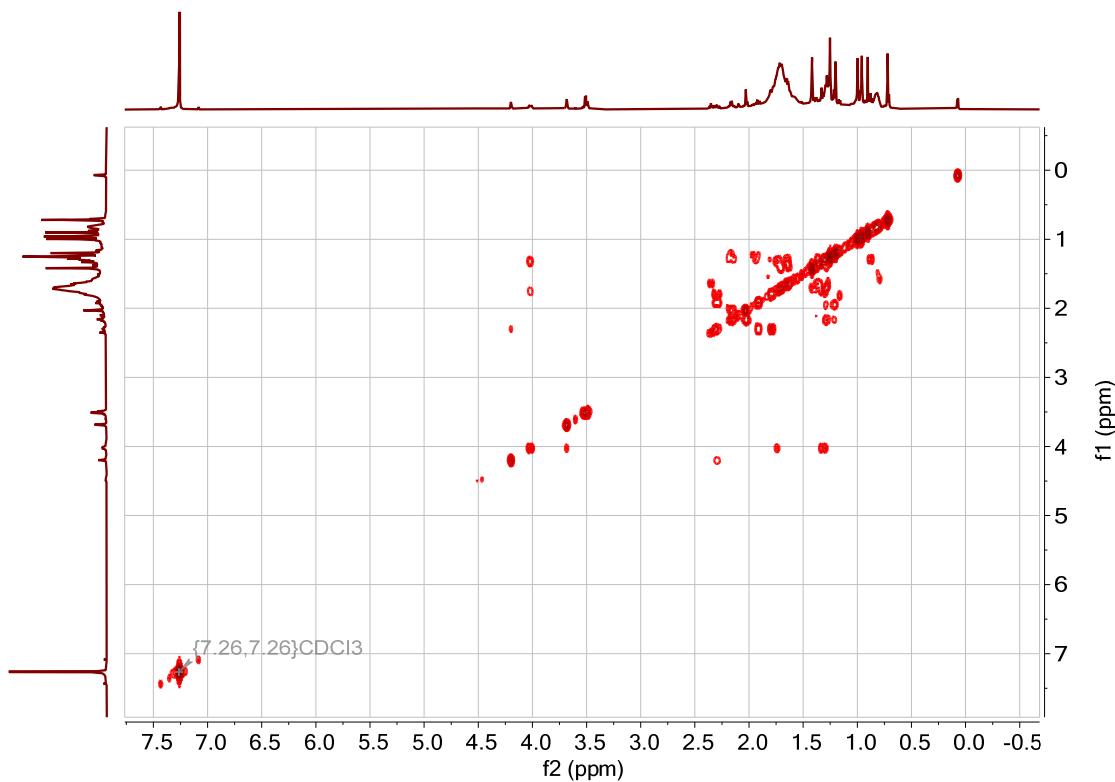
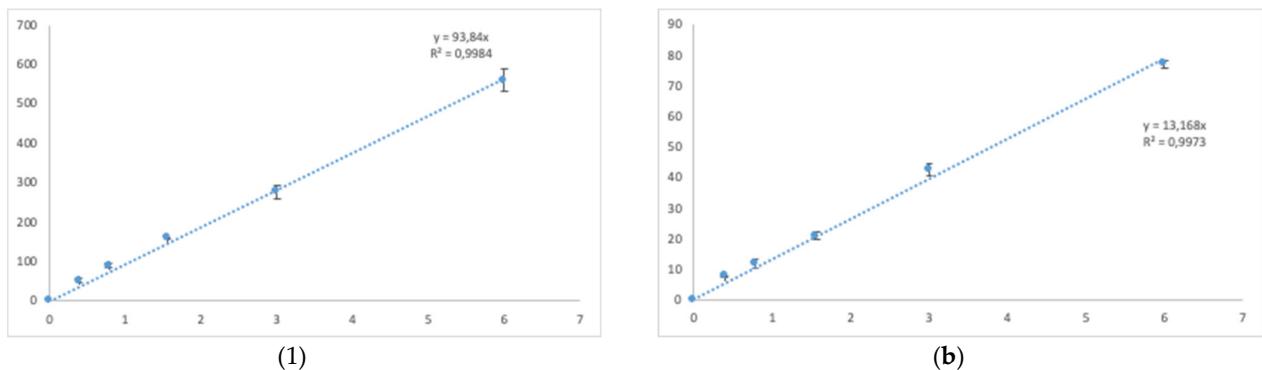
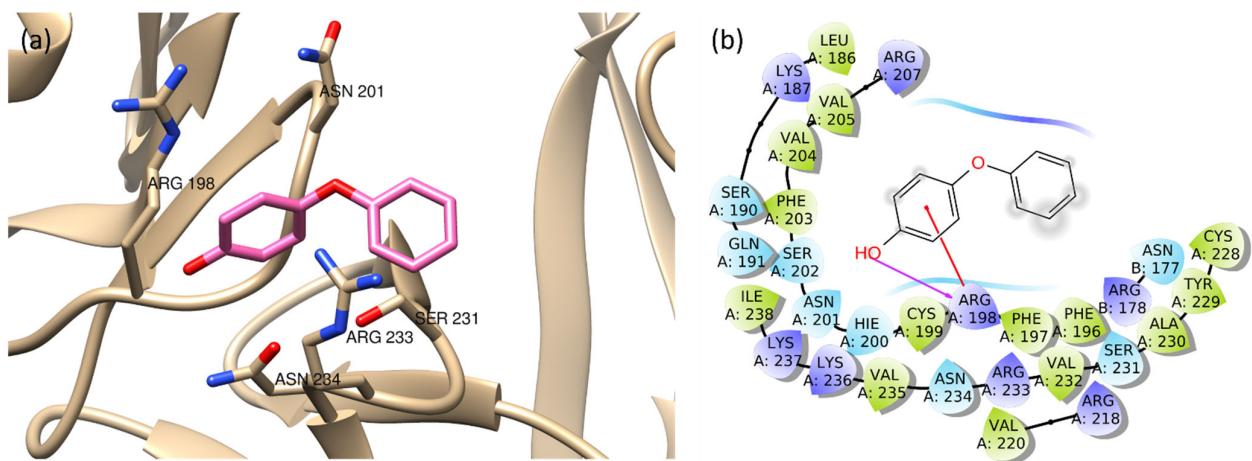


Figure S11. COSY (600 MHz,  $\text{CDCl}_3$ ) spectrum of compound 13.

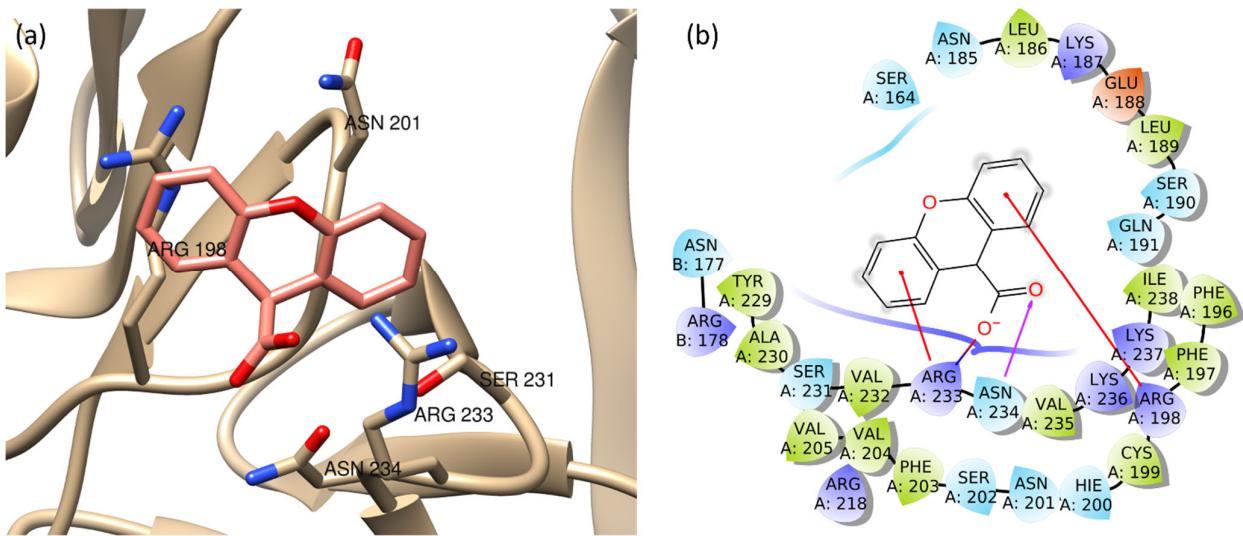


**Figure S12.** Calibration curves obtained for the LC/MS/MS analysis of sclareol (1) and manool (2) using pure compounds.

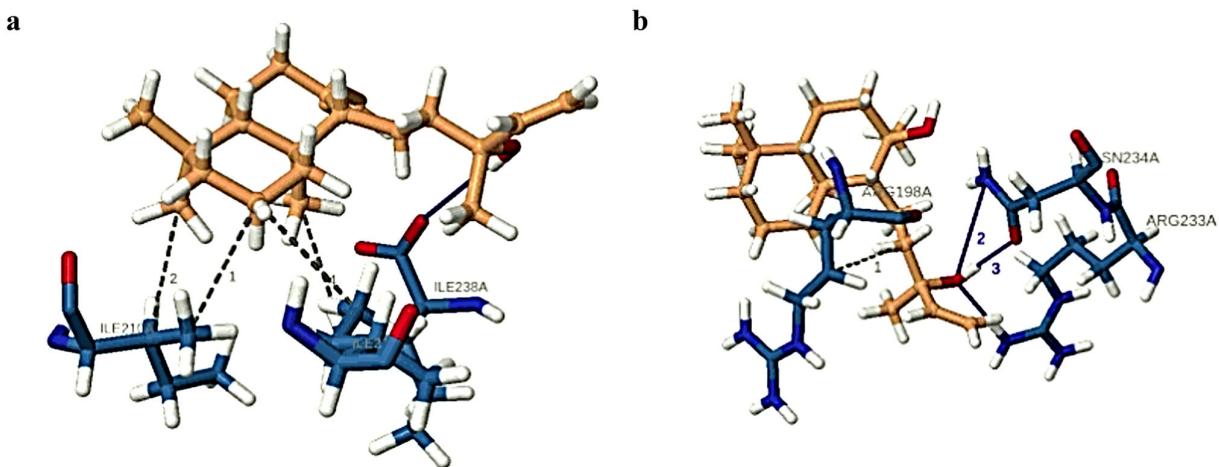


**Figure S13.** Binding pose and ligand interaction plot of 4-phenoxyphenol at the conserved AgrA active site.

(a): protein is reported as light brown ribbons, 4-phenoxyphenol is reported as capped sticks and is colored in magenta. (b): 4-phenoxyphenol is surrounded by the protein residues represented as follows: the negatively charged residues are indicated in red, polar residues are in cyan, hydrophobic residues are shown in green, H-bonds are presented as purple arrows and pi-cation as red line..



**Figure S14.** Binding pose and ligand interaction plot of 9H-xanthene-9-carboxylic acid at the conserved AgrA active site.(a): the protein is reported as light brown ribbons, 9H-xanthene-9-carboxylic acid is reported as capped sticks and is colored in salmon. (b): 9H-xanthene-9-carboxylic acid is surrounded by the residues represented as follows: the negatively charged residues are indicated in red, polar residues are in cyan, hydrophobic residues are shown in green, H-bonds are presented as purple arrows and pi-cation as red line.



**Figure S15.** Manool and sclareol interactions with the key residues into the binding cavity.a: manool interactions; b: sclareol interactions; blue lines: H-bonds; broken grey lines: Van der Waals interactions.

**Table S1.** Literature survey about the presence of sclareol (1) and manool (2) in *Salvia* spp.<sup>a</sup>

Accepted Name, Proto-logue [1]	Synonyms [1]	Part/s of the Plant	Sclareol (1)	Manool (2)	References
<i>Salvia aethiopis</i> L., Sp. Pl.: 27 (1753)	Homotypic Names: <i>Sclarea aethiopis</i> (L.) Mill., Gard. Dict. ed. 8: n.º 2 (1768); <i>Sclarea lanata</i> Moench, Methodus: 374 (1794), nom. superfl.; <i>Salvia lanata</i> Stokes, Bot. Mat. Med.: 52 (1812), nom. illeg. Heterotypic Synonyms: <i>Salvia kochiana</i> Kunze, Index Seminum (LZ, Lipsiensis) 1847: 4 (1847); <i>Salvia leuconeura</i> Boiss., Diagn. Pl. Orient., ser. 2, 4: 20 (1859); <i>Aethiopis vera</i> Fourr., Ann. Soc. Linn. Lyon, n.s., 17: 134 (1869); <i>Salvia idanensis</i> Gand., Fl. Lyon.: 171 (1875). Homotypic Names: <i>Sclarea argentea</i> (L.) Mill., Gard. Dict. ed. 8: n.º 15 (1768); <i>Salvia argentea</i> var. <i>fontanesiana</i> Maire in É.Jahandiez & al., Cat. Pl. Maroc 3: 642 (1934), not validly publ. Heterotypic Synonyms: <i>Salvia patula</i> Desf., Fl. Atlant. 1: 25 (1798); <i>Salvia atlantica</i> Pers., Syn. Pl. 1: 29 (1805); <i>Salvia tmolea</i> Boiss., Diagn. Pl. Orient. 5: 9 (1844); <i>Salvia saccata</i> Pourr. ex Willk. & Lange, Prodr. Fl. Hispan. 2: 424 (1868); <i>Salvia aurasiaca</i> Pomel, Nouv. Mat. 38 (1762) Fl. Atl.: 306 (1874); <i>Salvia suaveolens</i> Pomel, Nouv. Mat. Fl. Atl.: 306 (1874); <i>Salvia argentea</i> var. <i>gussonei</i> Boiss. ex Nyman, Conspl. Fl. Eur.: 569 (1881), nom. nud.; <i>Salvia argentea</i> var. <i>patula</i> (Desf.) Nyman, Conspl. Fl. Eur.: 569 (1881); <i>Salvia alpestris</i> Hausskn. ex Nyman, Conspl. Fl. Eur., Suppl. 2, 1: 248 (1889); <i>Salvia rhodopea</i> Velen., Sitzungsber. Königl. Böhm.	flower, leaf and stems	ND	5.7% in stems, 0.6% p/V in flower, 2.1% in leaf of ex-tract	[2]
<i>Salvia argentea</i> L., Sp. Pl. ed. 2: 38 (1762)	leaves and inflorescences	ND	0.8% of the essential oil	[3]	

	Ges. Wiss., Math.-Naturwiss. Cl. 37: 388 (1892 publ. 1893); <i>Salvia argentea</i> subsp. <i>patula</i> (Desf.) Maire, Bull. Soc. Hist. Nat. Afrique N. 15: 90 (1924); <i>Salvia argentea</i> var. <i>pomelii</i> Maire, Bull. Soc. Hist. Nat. Afrique N. 15: 90 (1924); <i>Salvia argentea</i> var. <i>aurasiaca</i> (Pomel) Maire, Mém. Soc. Sci. Nat. Maroc 21-22: 13 (1930); <i>Salvia argentea</i> var. <i>mesatlantica</i> Maire, Mém. Soc. Sci. Nat. Maroc 21-22: 13 (1930).	Heterotypic Synonyms: <i>Salvia bachtiarica</i> Bunge, Labiat. Persic.: 47 (1873); <i>Salvia hypochionea</i> Buhse ex Boiss., Fl. Orient. 4: 620 (1879); <i>Salvia montbretii</i> var. <i>virescens</i> Freyn, Bull. Herb. Boissier, sér. 2, 1: 278 (1901); <i>Salvia atropatana</i> Kudr., Trudy Sektora Rast. Res. Bunge, Komit. Nauk Uzbeksk. SSR Labiad. 3: 26 (1937); <i>Salvia linczevskii</i> Persic.: 47 Kudr., Trudy Sektora Rast. (1873) Res. Komit. Nauk Uzbeksk. SSR 3: 22 (1937); <i>Salvia kourossia</i> Parsa, Kew Bull. 3: 224 (1948); <i>Salvia lurorum</i> Rech.f., Oesterr. Bot. Z. 99: 57 (1952); <i>Salvia linguifolia</i> Hedge & Hub.-Mor., Notes Roy. Bot. Gard. Edinburgh 22: 181 (1957). Heterotypic Synonyms: <i>Salvia albida</i> Jacq., Observ. Bot. 1: 10 (1764), name not found; <i>Salvia crassifolia</i> Sm. in J.Sibthorp & J.E.Smith, Fl. Graec. Prodr. 1: 17 (1806), nom. illeg.; <i>Salvia albida</i> Spreng., Index Seminum (HAL, Halensis) 1807: 53 <i>candidissima</i> (1807), nom. illeg.; <i>Salvia odo-</i> <i>rata</i> Willd., Enum. Pl.: 43 <i>candidissima</i> (1809); <i>Salvia argentea</i> Benth., Labiad. Gen. Spec.: 223 (1833), nom. illeg.; <i>Salvia ar-</i> <i>mrena</i> K.Koch, Linnaea 21: 654	13.3% of the essential oil	1% of the es- sential oil	[5]
	aerial parts	0.3% of the es- sential oil	ND	[6]	
	roots	NQ	NQ	[7]	

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	(1849); <i>Salvia pycnophylla</i> Greuter & Burdet, Will- denowia 14: 301 (1984 publ. 1985).						
<i>Salvia</i> <i>candidissima</i> Vahl, Enum. Pl. Obs. 1: 278 (1804)	Homotypic Names: <i>Sclarea</i> <i>candidissima</i> (Vahl) Soják, Cas. Nár. Mus., Odd. Prír. 152: 21 (1983).	aerial parts	2.5% of the es- sential oil	1.8% of the es- sential oil		[8]	
<i>Salvia cassia</i> Sam. ex Rech.f., Ark. Bot., a.s., 1: 320 (1950)	-	aerial parts	ND	2.1% of the es- sential oil		[9]	
<i>Salvia chrys-</i> <i>ophylla</i> Stapf, Denkschr. Kaiserl. Akad. Wiss., Wien. Math.Naturw iss. Kl. 50: 96 (1885)	Heterotypic Synonyms: <i>Sal-</i> <i>via bourgeana</i> Barbey, Bull. Soc. Vaud. Sci. Nat. 21: 96 (1885).	aerial parts	NQ	1.12% of the essential oil	1.37% of the essential oil		[10]
<i>Salvia</i> <i>desoleana</i> Atzei & V.Picci, Webbia 36: 72 (1982)	-	aerial parts	ND	2.8% of the es- sential oil			[12]
<i>Salvia</i> <i>dominica</i> L., Sp. Pl.: 25 (1753)	Heterotypic Synonyms: <i>Sal-</i> <i>via graveolens</i> Vahl, Enum. Pl. Obs. 1: 273 (1804). <i>Salvia com-</i> <i>mutata</i> Benth., Labiat. Gen. Spec.: 222 (1833). <i>Salvia syri-</i> <i>aca</i> Gouan ex Benth. in A.P.de Candolle, Prodr. 12: 279 (1848).	whole plant	NQ	ND			[13]
<i>Salvia</i> <i>fruticosa</i> Mill., Gard. Dict. ed. 8: n. <sup>o</sup> 5 (1768)	Heterotypic Synonyms: <i>Salvia baccifera</i> Etl., Salv.: 18 (1777); <i>Salvia incarnata</i> Etl., Salv.: 25 (1777); <i>Salvia triloba</i> L.f., Suppl. Pl.: 88 (1782); <i>Sal-</i> <i>via sypylea</i> Lam., Tabl. Encycl. 1: 68 (1791); <i>Salvia sypilea</i> Lam., Tabl. Encycl. 1: 68 (1791); <i>Salvia clusii</i> Jacq., Pl. Hort. Schoenbr. 2: 37 (1797); <i>Salvia marrubiooides</i> Vahl, Enum. Pl. Obs. 1: 223 (1804); <i>Salvia ovata</i> F.Dietr., Nachtr. Vollst. Lex. Gärtn. 7: 465	whole plant	ND	NQ			[14]
		aerial parts	ND	0.2-4% of the essential oil			[15]
		leaves	ND	NQ			[16]

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	(1821); <i>Salvia subtriloba</i> Schrink, Syll. Pl. Nov. 2: 58 (1826); <i>Sclarea triloba</i> (L.f.) Raf., Fl. Tellur. 3: 94 (1837); <i>Salvia libanotica</i> Boiss. & Gaill. in P.E.Boissier, Diagn. Pl. Orient., ser. 2, 4: 16 (1859); <i>Salvia cypria</i> Unger & Kotschy, Ins. Cypern: 266 (1865); <i>Salvia triloba</i> var. <i>calpeana</i> Dautez & Debeaux in J.O. Debeaux, Syn. Fl. Gibraltar: 161 (1889); <i>Salvia</i> <i>lobryana</i> Azn., Magyar Bot. Lapok 1: 195 (1902); <i>Salvia</i> <i>triloba</i> var. <i>subhastata</i> H.Lindb., Öfvers. Finska Vetensk.-Soc. Förh. 48(13): 94 (1906); <i>Salvia fruticosa</i> subsp. <i>cypria</i> (Unger & Kotschy) Holmboe, Stud. Veg. Cyprus: 158 (1914); <i>Salvia</i> <i>triloba</i> subsp. <i>cypria</i> (Kotschy) Holmboe, Stud. Veg. Cyprus: 158 (1914); <i>Salvia triloba</i> subsp. <i>libanotica</i> (Boiss. & Gaill.) Holmboe, Stud. Veg. Cyprus: 158 (1914); <i>Salvia thomasii</i> Lacaita, Nuovo Giorn. Bot. Ital., n.s., 29: 186 (1922 publ. 1923); <i>Salvia triloba</i> subsp. <i>calpeana</i> (Dautez & Debeaux) P.Silva, Agron. Lusit. 20: 237 (1958); <i>Salvia fruticosa</i> subsp. <i>thomasii</i> (Lacaita) Brullo, Guglielmo, Pavone & Terrasi, Inform. Bot. Ital. 26: 211 (1994 publ. 1995). Homotypic Names: <i>Sclarea</i> <i>glutinosa</i> (L.) Mill., Gard. Dict. ed. 8: n.º 11 (1768). <i>Salvia glutinosa</i> L., <i>Glutinaria glutinosa</i> (L.) Raf., Sp. Pl.: 26 Fl. Tellur. 3: 93 (1837). aerial 11.9% of the 6.8% of the es- (1753) <i>Drymosphace glutinosa</i> (L.) parts essential oil ential oil [8] Opiz, Seznam: 38 (1852). Heterotypic Synonyms: <i>Glutinaria acuminata</i> Raf., Autik. Bot.: 122 (1840). <i>Salvia hypoleuca</i> Benth.. - roots ND NQ [17]				
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A.P.de Candolle, Prodr. 12: 279 (1848) <i>Salvia juda- ica</i> Boiss., Diagn. Pl. Orient. 12: 61 (1853)	-	leaf	7.01% of the essential oil	ND	[18]
Homotypic Names: <i>Salvia verbenaca</i> subsp. <i>lanigera</i>					
<i>Salvia lanigera</i> Poir. (Poir.) Batt. in J.A.Battandier J.B.A.M.de & L.C.Trabut, Fl. Algérie, Di- Lamarck, cot.: 688 (1890). Heterotypic leaves Encycl., Synonyms: <i>Salvia rugosissima</i>		14.44% of eth- anol extract		ND	[19]
Suppl. 5: 49 Zucc., Abh. Math.-Phys. Cl. (1817) Königl. Bayer. Akad. Wiss. 3: 244 (1843).					
Heterotypic Synonyms: <i>Sal- via flexuosa</i> Schrank, Syll. Pl. <i>Salvia limbata</i> Nov. 2: 57 (1826), provision- ally listed as a synonym; <i>Sal- via polyadenia</i> Boiss. & Heldr. aerial Verz. Pfl. in P.E.Boissier, Diagn. Pl. Casp. Meer.: Orient. 5: 7 (1844); <i>Salvia chrysadenia</i> Freyn, Bull. Herb. Boissier, sér. 2, 1: 279 (1901)	parts	NQ	NQ		[20]
<i>Salvia maj- dae</i> (Rech.f.) & Wen- delbo) Homotypic Names: <i>Zhumeria majdae</i> Rech.f. & Wendelbo, Sytsma, Nytt Mag. Bot. 14: 39 (1967).	roots	ND	NQ		[21]
Taxon 66: 142 (2017)		ND	NQ		[22]
Heterotypic Synonyms: <i>Sal- via kotschyi</i> Boiss., Diagn. Pl. Orient. 7: 46 (1846); <i>Salvia macrosiphon</i> var. <i>cabulica</i> Benth. in A.P.de Candolle, Prodr. 12: 282 (1848); <i>Salvia macrosiphon</i> var. <i>kotschyi</i>	aerial parts	ND	37.1% of es- ential oil		[23]
<i>Salvia macrosiphon</i> (Boiss.) Boiss., Fl. Orient. 4: Boiss., Di- 615 (1879); <i>Salvia macrosiphon-</i> agn. Pl. Ori- <i>nia</i> St.-Lag., Ann. Soc. Bot. aerial ent. 5: 11 Lyon 7: 134 (1880); <i>Salvia cus- (1844) <i>pidatissima</i> Pau, Trab. Mus.</i>	parts	15.76 % of es- ential oil	2.10% of es- ential oil		[24]
Ci. Nat., Ser. Bot. 14: 33 (1918); <i>Salvia albifrons</i> Nábelek, Spisy Prír. Fak. Ma- sarykovy Univ. 70: 49 (1926); <i>Salvia macrosiphon</i> var. <i>brach- ycalycina</i> Bornm., Bot. Jahrb.		8.6% % of es- ential oil	ND		[6]

Syst. 62: 238 (1934); *Salvia macrosiphon* var. *glandulosis-sima* Bornm., Bot. Jahrb. Syst. 62: 238 (1934); *Salvia na-chiczevanica* Pobed. in V.L.Komarov, Fl. URSS 21: 657 (1954)

*Salvia mont-bretii* Benth.

Ann. Sci. Nat., Bot., sér. 2, 6: 42 (1836)

aerial parts ND 0.3 % of essential oil [25]

&lt;/

			(stem) of etha-	
			nol extract	
	Heterotypic Synonyms:			
	<i>Salvia sinaica</i> Delile ex Benth.,			
<i>Salvia</i>	Labiat. Gen. Spec.: 718	Aerial parts	ND	Non spe-
<i>oligophylla</i> (1835); <i>Salvia lorentii</i> Hochst.				ficata
<i>Aucher ex</i> in J.A.Lorent, Wanderungen:				
<b>Benth.</b> , 333 (1845); <i>Salvia sieberi</i> aerial				
A.P.de C.Presl, Abh. Königl. Böhm. parts	ND	3.99% of es-		
Candolle, Ges. Wiss., ser. 5, 3: 530		sential oil	[6]	
Prodri. 12: (1845); <i>Salvia rassamii</i> Boiss.,				
279 (1848) Fl. Orient. 4: 615 (1879);				
<i>Salvia alliaria</i> Parsa, Kew				
Bull. 3: 224 (1948).				
Heterotypic Synonyms:				
<i>Salvia sinaica</i> Delile ex Benth.,				
Labiat. Gen. Spec.: 718				
<i>Salvia</i> (1835); <i>Salvia lorentii</i> Hochst.	Aerial parts	ND	Non spe-	
<i>palaestina</i> in J.A.Lorent, Wanderungen:				ficata
<b>Benth.</b> , 333 (1845); <i>Salvia sieberi</i> leaves	NQ	ND		
Labiat. Gen.C.Presl, Abh. Königl. Böhm. Spec.: 718 Ges. Wiss., ser. 5, 3: 530				
(1835) (1845); <i>Salvia rassamii</i> Boiss., Fl. Orient. 4: 615 (1879);				
<i>Salvia alliaria</i> Parsa, Kew Bull. 3: 224 (1948).				
Heterotypic Synonyms:				
<i>Salvia grandiflora</i> Née ex Cav., Icon. 5: 33 (1799), nom. illeg. <i>Salvia spectabilis</i> Kunth in F.W.H.von Humboldt,				
A.J.A.Bonpland & C.S.Kunth, Nov. Gen. Sp. 2: 304 (1818). <i>Salvia macrantha</i> Schldl., Allg. Gartenzeitung 6: 314 (1838). <i>Salvia decipiens</i> whole plant 4.85% of es-				
<i>Salvia patens</i> Cav., Icon. 5: 33 (1799)	M.Martens & Galeotti, Bull. Acad. Roy. Sci. Bruxelles 11(2): 64 (1844). <i>Salvia staminea</i> M.Martens & Galeotti, Bull. Acad. Roy. Sci. Bruxelles 11(2): 65 (1844), nom. illeg. <i>Salvia mendax</i> Epling, Repert. Spec. Nov. Regni Veg. Beih. 110: 96 (1938).	ND		
<i>Salvia persepolitan</i> a Boiss., Diagn. Pl. Orient. 12: 60 (1853)	aerial parts	0.5% of essential oil	37.3% of essential oil	[33]

<i>Salvia</i>						
<i>poculata</i>	Heterotypic Synonyms: <i>Salvia brevidens</i> Hedge & Hub.-Mor., Notes Roy. Bot. Gard. Edinburgh 22: 183	aerial parts	NQ	ND	[34]	
<b>Nábelek,</b> Spisy Prír. Fak. Masa- rykovy Univ. 70: 50 (1926)	(1957).					
<i>Salvia</i> <i>reuteriana</i>		0.77 - 7.88% of essential oil	ND	[35]		
<b>Boiss.,</b> Diagn. Pl. Orient. 5: 10 (1844)	-	aerial parts	2% of essential oil	ND	[36]	
			NQ	ND	[37]	
<i>Salvia</i> <i>runcinata</i> L.f., Suppl. Pl.: 89 (1782)	Heterotypic Synonyms: <i>Salvia monticola</i> Benth. in E.H.F.Meyer, Comm. Pl. Afr. Austr.: 238 (1838). <i>Salvia</i> <i>runcinata</i> var. <i>major</i> Benth. in A.P.de Candolle, Prodr. 12: 352 (1848). <i>Salvia runcinata</i> var. <i>grandiflora</i> Skan in W.H.Harvey & auct. suc. (eds.), Fl. Cap. 5(1): 327 (1910). <i>Salvia runcinata</i> var. <i>nana</i> Skan in W.H.Harvey & auct. suc. (eds.), Fl. Cap. 5(1): 327 (1910). <i>Salvia sisymbifolia</i> Skan in W.H.Harvey & auct. suc. (eds.), Fl. Cap. 5(1): 328 (1910).	aerial parts	ND	6.4% of essential oil	[38]	
<i>Salvia</i> <i>sahendica</i> Boiss. & Buhse, Nouv. Mém. Soc. Imp. Na- turalistes Moscou 12: 172 (1860)			NQ	ND	[39]	
<i>Salvia</i> <i>santolinifoli</i>	Homotypic Names: <i>Pleudia</i> <i>a Boiss.</i> , <i>santolinifolia</i> (Boiss.) M.Will, Diagn. Pl. N.Schmalz & Class.-Bockh., Orient. 5: 13 Turkish J. Bot. 39: 703 (2015). (1844)	aerial parts	NQ	ND	[40]	
<i>Salvia</i> <i>sclarea</i> L., Sp. Pl.: 27 (1753)	Homotypic Names: <i>Sclarea</i> <i>vulgaris</i> Mill., Gard. Dict. ed.8: n°1 (1768); <i>Aethiopis</i> <i>sclarea</i> (L.) Opiz, Seznam: 11 (1852). Heterotypic Names: <i>Salvia haematodes</i> Scop., Fl. Carniol., ed.2, 1: 29 (1771),	whole plant	NQ	NQ	[41]	
		aerial parts	5.3% of essential oil	ND	[42]	
					[43]	
					[6]	

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	nom. illeg.; <i>Salvia coarctata</i> Vahl, Enum. Pl. Obs. 1: 253 (1804); <i>Salvia simsiana</i> Schult., Mant. 1: 210 (1822); <i>Salvia calostachya</i> Gand., Fl. Lyon.: 171 (1875); <i>Salvia</i> <i>sclarea</i> var. <i>calostachya</i> (Gand.) Nyman, Consp. Fl. Eur.: 569 (1881); <i>Salvia turke-</i> <i>stanica</i> Noter, Rev. Hort. (Paris) 77: 502 (1905); <i>Salvia</i> <i>sclarea</i> var. <i>turkestaniana</i> Mottet, Rev. Hort. (Paris) 79: 135 (1907); <i>Salvia lucana</i> Cavara & Grande, Bull. Orto Bot. Regia Univ. Napoli 3: 436 (1913); <i>Salvia pamirica</i> Gand., Bull. Soc. Bot. France 60: 26 (1913); <i>Salvia altilabrosa</i> Pan, Trab. Mus. Ci. Nat., Ser. Bot. 14: 33 (1918). Homotypic Names: <i>Salvia</i> <i>pratensis</i> var. <i>sclareoides</i> (Brot.) Briq., Lab. Alp. Mar.: 532 (1895). Heterotypic Syno- nyms: <i>Sclarea lusitanica</i> Mill., Gard. Dict. ed. 8: n.º 3 (1768). <i>Salvia bullata</i> Vahl, Enum. Pl. Obs. 1: 265 (1804), nom. illeg. <i>Salvia lusitanica</i> Poir. in J.B.A.M.de Lamarck, Encycl. <i>Salvia</i> 6: 606 (1805). <i>Salvia elongata</i> <i>sclareoides</i> Spreng., Pl. Min. Cogn. Pug. <i>Brot.</i> , Fl. Lu- 1: 3 (1813), nom. illeg. <i>Salvia</i> sit. 1: 17 <i>lusitanica</i> J.Jacq., Ecl. Pl. Rar. (1804) 1: 47 (1813), sensu auct. <i>Salvia baetica</i> Boiss., Elench. Pl. Nov.: 73 (1838). <i>Salvia</i> <i>pratensis</i> var. <i>bullata</i> Briq., Lab. Alp. Mar.: 531 (1895). <i>Salvia pratensis</i> var. <i>lusitanica</i> Briq., Lab. Alp. Mar.: 532 (1895). <i>Salvia sclareoides</i> var. <i>baetica</i> (Boiss.) Figuerola, Collect. Bot. (Barcelona) 17: 309 (1988 publ. 1989).	aerial parts	0.3% of essential oil	ND	[44]
<i>Salvia shari-</i> <i>ffi Rech.f. &amp;</i> <i>Esfand.</i> , Oes- terr. Bot. Z. 99: 55 (1952)	-	seeds	21.9% of es- sential oil	ND	[45]

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	Heterotypic Synonyms:				
	<i>Salvia calvertii</i> Boiss., Fl.				
	Orient. 4: 626 (1879). <i>Salvia</i>				
	<i>staminea</i> subsp. <i>armeniaca</i>				
<i>Salvia</i>	Bordz., Trudy Bot. Sada Imp.				
<i>staminea</i>	Yur'evsk. Univ. 13: 22 (1912).				
<b>Montbret &amp;</b>	<i>Salvia armeniaca</i> (Bordz.)				
<b>Aucher ex</b>	Grossh., Beih. Bot. Centralbl.	aerial	da 0.01 a 3.1%	ND	[46]
<b>Benth., Ann.</b>	44(2): 237 (1927). <i>Salvia</i>	parts	of essential oil		
Sci. Nat.,	<i>kudjurica</i> Rech.f., Oesterr.				
Bot., sér. 2, 6:	Bot. Z. 99: 56 (1952). <i>Salvia</i>				
41 (1836)	<i>transcaucasica</i> Pobed., Bot.				
	Mater. Gerb. Bot. Inst.				
	Komarova Akad. Nauk				
	S.S.S.R. 21: 321 (1961).				
	Heterotypic Synonyms: <i>Sal-</i>				
	<i>via chlorophylla</i> Briq., Bull.				
	Herb. Boissier, sér. 2, 3: 1080				
<i>Salvia steno-</i>	(1903). <i>Salvia xerobia</i> Briq.,				
<i>phylla</i>	Bull. Herb. Boissier, sér. 2, 3:				
<b>Burch. ex</b>	1076 (1903). <i>Salvia stenophylla</i>	aerial			
<b>Benth., La-</b>	var. <i>subintegra</i> Skan in	ND			
<b>biat. Gen.</b>	W.H.Harvey & auct. suc.	parts	3.2 -12.7% of		
<b>Spec.: 306</b>	(eds.), Fl. Cap. 5(1): 326		essential oil		
<b>(1833)</b>	(1910). <i>Salvia pallida</i> Dinter,				
	Repert. Spec. Nov. Regni				
	Veg. 23: 227 (1926), nom.				
	nud.				
	Homotypic Names: <i>Hormi-</i>				
	<i>num verticillatum</i> (L.) Mill.,				
	Gard. Dict. ed. 8: n. <sup>o</sup> 3 (1768);				
<i>Salvia</i>	<i>Covola verticillata</i> (L.) Medik.,				
<i>verticillata</i>	Philos. Bot. 2: 67 (1791);				
<b>L., Sp. Pl.: 26</b>	<i>Hemisphace verticillata</i> (L.)	roots		NQ	
<b>(1753)</b>	Opiz, Seznam: 50 (1852);				
	<i>Sphacopsis verticillata</i> (L.)				
	Briq., Lab. Alp. Mar.: 184				
	(1891)				

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<sup>a</sup> ND: not detected; NQ: isolated, but quantification non reported.

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## References

1. Govaerts, R. World Checklist of Selected Plant Families. **2019**.
2. Veličković, D.; Randelović, N.; Ristić, M.; Šmelcerović, A.; Veličković, A.S. Chemical composition and antimicrobial action of the ethanol extracts of *Salvia pratensis* L., *Salvia glutinosa* L. and *Salvia aethiopis* L. *J. Serb. Chem. Soc.* **2002**, *67*, 639-646.
3. Morteza-Semnani, K.; Moshiri, K.; Akbarzadeh, M. The Essential Oil Composition of *Salvia multicaulis* Vahl. *J. Essent. Oil Bear. Pl.* **2005**, *8*, 6-10, doi:10.1080/0972060X.2005.10643412.
4. Couladis, M.; Tzakou, O.; Stojanovic, D.; Mimica-Dukic, N.; Jancic, R. The essential oil composition of *Salvia argentea* L. *Flavour Fragrance J.* **2001**, *16*, 227-229, doi:<https://doi.org/10.1002/ffj.989>.
5. Mirza, M.; Ahmadi, L. Composition of the Essential Oil of *Salvia atropatana* Bunge. *J. Essent. Oil Res.* **2000**, *12*, 575-576, doi:10.1080/10412905.2000.9712162.
6. Salimpour, F.; Mazooji, A.; Akhoondi, S. Chemotaxonomy of six *Salvia* species using essential oil composition markers. *J. Med. Plant. Res.* **2011**, *5*, 1795-1805.
7. Ulubelen, A.; Tan, N.; Topcu, G. Terpenoids from *Salvia candidissima* subsp. *candidissima*. *Phytochemistry* **1997**, *45*, 1221-1223.
8. Pitarokili, D.; Tzakou, O.; Loukis, A. Essential oil composition of *Salvia verticillata*, *S. verbenaca*, *S. glutinosa* and *S. candidissima* growing wild in Greece. *Flavour Fragrance J.* **2006**, *21*, 670-673, doi:<https://doi.org/10.1002/ffj.1647>.
9. Şen Utsukarci, B.; Gurda, B.; Bilgin, M.; Satana, D.; Demirci, B.; Tan, N.; Mat, A. Biological Activities of Various Extracts from *Salvia cassia* Sam. ex Rech.f. and Chemical Composition of Its Most Active Extract. *Rec. Nat. Prod.* **2019**, *13*, 24-36, doi:10.25135/rnp.68.18.02.090.
10. Duru, M.; Tel Çayan, G.; Öztürk, M.; Harmandar, M. Chemical Composition, Antioxidant and Anticholinesterase Activities of the Essential Oil of *Salvia chrysophylla* Staph. *Rec. Nat. Prod.* **2012**, *6*, 175.
11. Çulhaoglu, B.; Yapar, G.; Dirmenci, T.; Topcu, G. Bioactive constituents of *Salvia chrysophylla* Stapf. *Nat. Prod. Res.* **2013**, *27*, 438-447, doi:10.1080/14786419.2012.734820.
12. Marongiu, B.; Porcedda, S.; Porta, G.D.; Reverchon, E. Extraction and isolation of *Salvia desoleana* and *Mentha spicata* subsp. *insularis* essential oils by supercritical CO<sub>2</sub>. *Flavour Fragrance J.* **2001**, *16*, 384-388, doi:<https://doi.org/10.1002/ffj.1021>.
13. Hasan, M.; Al-Jaber, H.; Al-Qudah, M.; Zarga, M. New sesterterpenoids and other constituents from *Salvia dominica* growing wild in Jordan. *Phytochem. Lett.* **2016**, *16*, 12-17, doi:10.1016/j.phytol.2016.02.009.
14. Topcu, G.; Öztürk, M.; Kuşman, T. Terpenoids, essential oil composition, fatty acid profile, and biological activities of Anatolian *Salvia fruticosa* Mill. *Turk. J. Chem.* **2013**, *37*, 619-632.
15. Pitarokili, D.; Tzakou, O.; Loukis, A.; Harvala, C. Volatile metabolites from *Salvia fruticosa* as antifungal agents in soilborne pathogens. *Journal of Agricultural and Food Chemistry* **2003**, *51*, 3294-3301, doi:10.1021/jf0211534.
16. Abou-Jawdah, Y.; Sobh, H.; Salameh, A. Antimycotic activities of selected plant flora, growing wild in Lebanon, against phytopathogenic fungi. *Journal of Agricultural and Food Chemistry* **2002**, *50*, 3208-3213, doi:10.1021/jf0115490.
17. Saeidnia, S.; Ghamarinia, M.; Gohari, A.R.; Shakeri, A. Terpenes From the Root of *Salvia hypoleuca* Benth. *Daru* **2012**, *20*, 66, doi:10.1186/2008-2231-20-66.
18. Böszörmenyi, A.; Héthelyi, E.; Farkas, A.; Horváth, G.; Papp, N.; Lemberkovics, E.; Szoke, E. Chemical and genetic relationships among sage (*Salvia officinalis* L.) cultivars and Judean sage (*Salvia judaica* Boiss.). *Journal of Agricultural and Food Chemistry* **2009**, *57*, 4663-4667, doi:10.1021/jf9005092.
19. Alonazi, M.A.; Jemel, I.; Moubayed, N.; Alwhibi, M.; El-Sayed, N.N.E.; Ben Bacha, A. Evaluation of the in vitro anti-inflammatory and cytotoxic potential of ethanolic and aqueous extracts of *Origanum syriacum* and *Salvia lanigera* leaves. *Environ. Sci. Pollut. Res. Int.* **2021**, *28*, 19890-19900, doi:10.1007/s11356-020-11961-z.
20. Ulubelen, A.; Topcu, G.; Sonmez, U.; Eris, C.; Ozgen, U. Norsesterterpenes and Diterpenes from the Aerial Parts of *Salvia limbata*. *Phytochemistry* **1996**, *43*, 431-434.
21. Rustaiyan, A.; Samadizadeh, M.; Habibi, Z.; Jakupovic, J. Two diterpenes with rearranged abietane skeletons from *Zhumeria majdae*. *Phytochemistry* **1995**, *39*, 163-165, doi:[https://doi.org/10.1016/0031-9422\(94\)00692-M](https://doi.org/10.1016/0031-9422(94)00692-M).
22. Zadali, R.; Nejad-Ebrahimi, S.; Hadjiakhoondi, A.; Fiengo, L.; D'Ambola, M.; De Vita, S.; Tofighi, Z.; Chini, M.G.; Bifulco, G.; De Tommasi, N. Diterpenoids from *Zhumeria majdae* roots as potential heat shock protein 90 (HSP90) modulators. *Phytochemistry* **2021**, *185*, 112685, doi:<https://doi.org/10.1016/j.phytochem.2021.112685>.
23. Javidnia, K.; Moein, M.R.; Ayatollahi, M.; Moein, S.; Amoozegar, Z.; Rustaiyan, A. Constituents of Stem Oil of *Zhumeria majdae* Rech. from Iran. *J. Essent. Oil Res.* **2006**, *18*, 91-92, doi:10.1080/10412905.2006.9699395.
24. Sefidkon, F.; Mirza, M.; Javidtash, I. Essential oil Composition of *Salvia macrosiphon* Boiss. from Iran. *J. Essent. Oil Bear. Pl.* **2005**, *8*, 126-129, doi:10.1080/0972060X.2005.10643431.
25. Abak, F.; Yıldız, G.; Atamov, V.; Kurkcuglu, M. Composition of the Essential Oil of *Salvia montbretii* Benth. from Turkey. *Rec. Nat. Prod.* **2018**, *12*, 426-431, doi:<http://dx.doi.org/10.25135/rnp.51.17.12.080>.
26. Ulubelen, A.; Topcu, G.; Johansson, C.B. Norditerpenoids and diterpenoids from *Salvia multicaulis* with antituberculous activity. *Journal of Natural Products* **1997**, *60*, 1275-1280, doi:10.1021/np9700681.
27. Christensen, K.B.; Jørgensen, M.; Kotowska, D.; Petersen, R.K.; Kristiansen, K.; Christensen, L.P. Activation of the nuclear receptor PPAR $\gamma$  by metabolites isolated from sage (*Salvia officinalis* L.). *J. Ethnopharmacol.* **2010**, *132*, 127-133, doi:10.1016/j.jep.2010.07.054.

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28. Moreira, M.R.; Souza, A.B.; Moreira, M.A.; Bianchi, T.C.; Carneiro, L.J.; Estrela, F.T.; dos Santos, R.A.; Januário, A.H.; Martins, C.H.G.; Ambrosio, S.R.; et al. RP-HPLC analysis of manool-rich *Salvia officinalis* extract and its antimicrobial activity against bacteria associated with dental caries. *Rev. Bras. Farma.* **2013**, *23*, 870-876, doi:<https://doi.org/10.1590/S0102-695X2013000600003>.
29. Nicolella, H.D.; de Oliveira, P.F.; Munari, C.C.; Costa, G.F.; Moreira, M.R.; Veneziani, R.C.; Tavares, D.C. Differential effect of manool -a diterpene from *Salvia officinalis*, on genotoxicity induced by methyl methanesulfonate in V79 and HepG2 cells. *Food Chem. Toxicol.* **2014**, *72*, 8-12, doi:10.1016/j.fct.2014.06.025.
30. Veličković, T.; Randjelović, V.; Ristić, S.; Veličković, S.; Šmelcerović, A. Chemical constituents and antimicrobial activity of the ethanol extracts obtained from the flower, leaf and stem of *Salvia officinalis* L. *J. Serb. Chem. Soc.* **2003**, *68*, 17-24.
31. Ulubelen, A. Terpenoids from *Salvia palaeistica*. *Phytochemistry* **1985**, *24*, 1386-1387.
32. Ulaş Çolak, N.; Yıldırım, S.; Bozdeveci, A.; Yaylı, N.; Coskuncelebi, K.; Fandaklı, S.; Yaşar, A. Essential Oil Composition, Antimicrobial and Antioxidant Activities of *Salvia staminea*. *Rec. Nat. Prod.* **2017**, *12*, 86-94, doi:10.25135/rnp.08.17.03.013.
33. Habibi, Z.; Yousefi, M.; Aghaie, H.R.; Salehi, P.; Masoudi, S.; Rustaiyan, A. Chemical Composition of Essential Oil of *Salvia persepoltana* Boiss. and *Salvia rhytidia* Benth. from Iran. *J. Essent. Oil Res.* **2008**, *20*, 1-3, doi:10.1080/10412905.2008.9699405.
34. Kolak, U.; Hacıbekir lu, I.; Öztürk, M.; Özgökçe, F.; Topçu, G.; Ulubelen, A. Antioxidant and anticholinesterase constituents of *Salvia poculata*. *Turk. J. Chem.* **2009**, *33*, 813-823.
35. Fattahi, B.; Nazeri, V.; Kalantari, S.; Bonfill, M.; Fattahi, M. Essential oil variation in wild-growing populations of *Salvia reuterana* Boiss. collected from Iran: Using GC-MS and multivariate analysis. *Ind. Crop. Prod.* **2016**, *81*, 180-190, doi:<https://doi.org/10.1016/j.indcrop.2015.11.061>.
36. Karamian, R.; Asadbegy, M.; Pakzad, R.; Ranjbar, M. Essential oil compositions and in vitro antioxidant and antibacterial activities of the methanol extracts of two *Salvia* species (Lamiaceae) from Iran. *International Journal of Agriculture and Crop Sciences (IJACS)* **2013**, *5*.
37. Farimani, M.M.; Miran, M. Labdane diterpenoids from *Salvia reuterana*. *Phytochemistry* **2014**, *108*, 264-269, doi:10.1016/j.phytochem.2014.08.024.
38. Viljoen, A.M.; Gono-Bwalya, A.; Kamatou, G.P.P.; Bašer, K.H.C.; Demirci, B. The Essential Oil Composition and Chemotaxonomy of *Salvia stenophylla* and its Allies *S. repens* and *S. runcinata*. *J. Essent. Oil Res.* **2006**, *18*, 37-45, doi:10.1080/10412905.2006.12067117.
39. Moghaddam, F.M.; Zaynizadeh, B.; Ruedi, P. Salvileucolide methylester, a sesterterpene from *Salvia Sahendica*. *Phytochemistry* **1995**, *39*, 715-716.
40. Mofidi Tabatabaei, S.; Salehi, P.; Moridi Farimani, M.; Neuburger, M.; De Mieri, M.; Hamburger, M.; Nejad-Ebrahimi, S. A nor-diterpene from *Salvia sahendica* leaves. *Nat. Prod. Res.* **2017**, *31*, 1758-1765, doi:10.1080/14786419.2017.1290619.
41. Nadir, M.; Rasheed, M.; Sherwani, S.K.; Kazmi, S.U.; Ahmad, V.U. Chemical and antimicrobial studies on the essential oil from *Salvia santolinifolia* Boiss. *Pak. J. Pharm. Sci.* **2013**, *26*, 39-52.
42. Ulubelen, A.; Topcu, G.; Eriş, C.; Sönmez, U.; Kartal, M.; Kurucu, S.; Bozok-Johansson, C. Terpenoids from *Salvia sclarea*. *Phytochemistry* **1994**, *36*, 971-974, doi:10.1016/s0031-9422(00)90474-6.
43. Noori, S.; Hassan, Z.M.; Mohammadi, M.; Habibi, Z.; Sohrabi, N.; Bayanolagh, S. Sclareol modulates the Treg intra-tumoral infiltrated cell and inhibits tumor growth in vivo. *Cell. Immunol.* **2010**, *263*, 148-153, doi:10.1016/j.cellimm.2010.02.009.
44. Sepahvand, R.; Delfan, B.; Ghanbarzadeh, S.; Rashidipour, M.; Veiskarami, G.H.; Ghasemian-Yadegari, J. Chemical composition, antioxidant activity and antibacterial effect of essential oil of the aerial parts of *Salvia sclareoides*. *Asian Pac. J. Trop. Med.* **2014**, *7s1*, S491-S496, doi:10.1016/s1995-7645(14)60280-7.
45. Alipour-Gougeh, S.; Asgarpanah, J. Essential and fixed oil chemical compositions of the seeds from the endemic species *Salvia sharifii* Rech. F. & Esfand. *J. Chil. Chem. Soc* **2015**, *60*, 2695-2697, doi:10.4067/S0717-97072015000400012.
46. Samadi, S.; fattahi, B. Study of Compounds of essential oil diversity of some populations of *Salvia staminea* Monthr et Auch. ex Benth in Iran. *TACL* **2014**, *4*, 50-56, doi:10.1080/22297928.2013.770673.
47. Sonmez, U.; Topcu, G.; Ulubelen, A. Constituents of *Salvia verticillata*. *Turk. J. Chem.* **1997**, *21*, 376-382.