

Supplementary Materials

Innate Immunomodulatory Activity of Cedrol, a Component of Essential Oils Isolated

From *Juniperus* Species

**Gulmira Özek¹, Igor A. Schepetkin², Moldir Yermagambetova^{3,4}, Temel Özek^{1,5}, Liliya N. Kirpotina², Shyryn S. Almerikova^{3,4},
Saule I. Abugalieva^{3,4}, Andrei I. Khlebnikov⁶, and Mark T. Quinn²**

¹*Department of Pharmacognosy, Faculty of Pharmacy, Anadolu University, Eskisehir, 26470, Turkey*

²*Department of Microbiology and Cell Biology, Montana State University, Bozeman, MT 59717, United States*

³*Institute of Plant Biology and Biotechnology, Almaty 050040, Kazakhstan*

⁴*Faculty of Biology and Biotechnology, al-Farabi Kazakh National University, Almaty 050038, Kazakhstan*

⁵*Medicinal Plant, Drug and Scientific Research and Application Center (AUBIBAM), Anadolu University, 26470 Eskişehir, Turkey*

⁶*Kizhner Research Center, Tomsk Polytechnic University, Tomsk 634050, Russia*

Supplemental Table S1. Chemical composition of essential oils (%) isolated from leaves and cones of different *Juniperus* species.

Abbreviations: JH_{Lv}, *J. horizontalis* leaves; JH_{Con}, *J. horizontalis* cones; JS_{Lv}, *J. scopolorum* leaves; JS_{Con}, *J. scopolorum* cones; JC_{Lv}, *J. communis* leaves; JC_{Con}, *J. communis* cones; JSE_{Lv}, *J. seravschanica* leaves; JSE_{Con}, *J. seravschanica* cones; JSA_{Lv}, *J. sabina* leaves; JSA_{Con},

J. sabina cones; JT_{LV}; *J. turkestanica* leaves; JT_{Con}, *J. turkestanica* cones; JPS_{LV}, *J. pseudosabina* leaves; JPS_{Con}, *J. pseudosabina* cones; JSI_{LV}, *J. sibirica* leaves; JSI_{Con}, *J. sibirica* cones.

#	RRI	Compound	JH _{LV}	JH _{Con}	JS _{LV}	JS _{Con}	JCL _V	JCL _{Con}	JSE _{LV}	JSE _{Con}	JSA _{LV}	JSA _{Con}	JT _{LV}	JT _{Con}	JPS _{LV}	JPS _{Con}	JSI _{LV}	JSI _{Con}
1	1014	Tricyclene	0.9					t	0.1	0.1		t	t	t	t	t	0.1	t
2	1032	α-Pinene	1.2	3.0	1.3	4.0	68.7	22.3	45.3	34.4	1.2	4.3	15.2	25.1	30.8	49.3	26.9	44.9
3	1035	α-Thujene	0.5	1.8	1.2	2.3					0.7	1.8	1.1	1.8			1.7	
4	1072	α-Fenchene				t	0.1		0.1	t		t	t	t	t	t	0.1	t
5	1076	Camphene	0.9			0.1	0.4	t	0.3	0.1		0.1	0.1	0.2	0.3	0.3	0.3	0.2
6	1088	Isopropyl isovalerate													t	t	t	
7	1093	Hexanal													t		0.1	t
8	1118	β-Pinene	0.1	0.2	0.1	0.2	3.3	0.6	0.7	0.6	0.1	0.2	1.5	1.6	2.8	3.7	1.8	1.1
9	1132	Sabinene	17.3	77.4	37.6	35.8	0.4	0.2	0.2	0.4	33.2	74.1	39.6	54.2	19.4	20.4	24.3	0.3
10	1133	δ-4-Carene					0.1											
11	1151	<i>p</i> -Xylene					t											
12	1157	<i>m</i> -Xylene					t											
13	1158	Thuja-2,4(10)-diene											t		0.2	t	0.1	
14	1159	δ-3-Carene					2.2	t					0.8	t	0.1		1.3	0.4
15	1174	Myrcene	9.8	5.3	0.9	3.5	3.3	53.2	19.7	19.5	2.7	5.5	3.2	4.8	2.0	4.1	2.6	2.8
16	1176	α-Phellandrene	t	t	t	0.1	0.1	t		t	t	t	t	t	t	t	0.3	0.2
17	1188	α-Terpinene	0.6	0.5	1.2	2.5	t		0.1	0.1	0.3	0.3	1.5	0.3	0.7	0.6	1.3	
18	1202	Sylvestrene					t											
19	1203	Limonene	4.6	1.5					3.2	4.5	1.2	1.2	1	1.2	0.8	1	1.8	
20	1213	1,8-Cineole											1.1					
21	1218	β-Phellandrene		t	0.1	0.3	0.8		0.2	0.1	t	t	t	0.3	0.4	0.9	1.4	
22	1240	p-Mentha-1,3,6-triene													t		t	
23	1225	(Z)-3-Hexenal					0.1	t	t								t	
24	1244	Amyl furan					t											
25	1246	(Z)- β-Ocimene					t	t										
26	1255	γ-Terpinene	1	0.9	2.1	4.8	t	t	0.7	1.0	0.6	0.6	2.6	0.5	1.1	1.0	2.2	t
27	1266	(E)- β-Ocimene	0.1	0.1			t	t	t		0.2	0.1						
28	1266	3-Octanone					t											
29	1280	<i>p</i> -Cymene	t	0.1	1.1	2.5	t	t	0.9	0.2	0.4	0.1	0.2	0.6	0.4	0.2	1.1	t
30	1286	Isoterpinolene					t											
31	1290	Terpinolene	0.8	1.1	0.9	1.9	0.6	0.4	0.5	1.2	0.4	1.1	1.1	0.5	0.3	0.7	1.2	0.4
32	1299	2-Methylbutyl isovalerate					t						t			0.1	t	
33	1348	6-Methyl-5-hepten-2-one													t			
34	1360	Hexanol							0.1									
35	1362	<i>cis</i> -Rose oxide									0.1							

36	1379	3-Methyl-3-butenyl isovalerate					t			t			0.1	0.1	0.3		0.2	
37	1384	α -Pinene oxide							0.1	t				t				
38	1386	Octenyl acetate					t											
39	1393	3-Octanol					t											
40	1398	2-Nonanone									0.2		2.2	0.1	1.0			
41	1400	Nonanal					t				t							
42	1402	(<i>E,Z</i>)-1,3,5-Undecatriene		t			t											
43	1406	α -Fenchone							0.4	t								
44	1408	1,3,8- <i>p</i> -Menthatriene		t			t			t								
45	1418	<i>o</i> -Methylanisol					0.1											
46	1429	Perillene							0.1	t					0.1			
47	1437	α -Thujone	0.2								0.1						0.1	
48	1439	γ -Campholene aldehyde													0.1			t
49	1443	2,5- Dimethylstyrene								t	t						0.1	t
50	1446	1-Octen-3-ol					0.2											
51	1450	<i>trans</i> -Linalool oxide		t				0.1	t		0.1	0.1	t					
52	1451	β -Thujone	2.6	t					0.1		0.9	t	0.1		0.1		0.4	
53	1452	α,p -Dimethylstyrene		t					t				0.1			0.1		
54	1457	Hexyl-3-methyl butyrate							t									
55	1466	α -Cubebene		t			t	t									t	0.2
56	1468	<i>trans</i> -1,2-Limonene epoxide							0.1									
57	1474	<i>trans</i> -Sabinene hydrate		1.3	0.7	0.7	t	0.2		0.1	0.3	0.6	0.4	0.3	0.5	0.1	0.8	t
58	1477	4,8-Epoxyterpinolene									t						t	
59	1479	δ -Elemene		0.1						0.2		t		t		0.2		t
60	1482	<i>cis</i> -Linalool oxide						t				t	t		t			
61	1482	Fenchyl acetate	t	t			t			0.1						t		
62	1487	Citronellal					0.3	0.5			t		0.6				t	
63	1494	(<i>Z</i>)-3-Hexenyl 3-methylbutyrate													0.1			
64	1495	Bicycloelemene																t
65	1497	α -Copaene	t				t	t	t									0.1
66	1499	α -Campholene aldehyde					0.1								0.7		0.3	t
67	1521	2-Nonanol													0.4			
68	1525	α -Funebrene								t								
69	1532	Camphor	0.2							0.4								t
70	1535	β -Bourbonene					t											t
71	1536	Pinocamphone													0.1		0.1	
72	1549	β -Cubebene					t											0.1
73	1551	7- <i>epi</i> -Sesquithujene								0.1	t							

74	1553	Linalool	0.2	0.6	0.1	0.1	0.1	0.6	1.3		1	1.8	3.6	0.1	2.5	0.3	1	
75	1556	<i>cis</i> -Sabinene hydrate		0.7	0.7	0.7				t	0.2	0.4	0.4	0.3	0.6	0.1	0.6	
76	1562	Octanol					t											
77	1565	Linalyl acetate									0.4	0.7		t			t	
78	1565	Methyl citronellate	0.1	0.1	0.2	0.1	0.1	0.7			0.3	t	0.4	0.1	t	t	0.3	0.3
79	1571	<i>trans-p</i> -Menth-2-en-1-ol		0.2	0.6	1.2	t			0.1	0.2	0.1	0.5	0.2	0.3	0.2	0.6	t
80	1574	Acetoxy linalloloxide										t						
81	1577	α -Cedrene							0.3	0.2	0.1	0.1			t			
82	1579	Pregeijerene B	0.1		2.2	0.2												
83	1586	Pinocarvone													0.3		t	
84	1587	1,7-Diepi- β -cedrene							1.7	1.3	0.4				0.2	0.2		0.2
85	1589	β -Ylangene					0.1											
86	1590	Bornyl acetate	26.3	t	0.1	t	0.6	0.3	0.7	1.2	0.1	t	0.1	0.1	t	0.4	0.2	0.4
87	1594	<i>trans</i> - β -Bergamotene							0.1	0.1								
88	1600	β -Elemene		t		t	0.8	0.3		0.2		t		0.1		0.2	0.5	1.6
89	1604	Thymol methyl ether								t	t							
90	1604	2-Undecanone		0.1							0.1	0.1	0.4	0.2	0.2	0.1		
91	1604	Isobornyl acetate	0.5															
92	1608	β -Copaene					t											t
93	1608	Camphene hydrate	t												t			
94	1611	Terpinen-4-ol	3.9	3.1	10.0	23.0	0.1	0.2	0.5	1.3	3.2	1.5	9.5	2.7	4.0	2.7	9.3	0.8
95	1612	β -Caryophyllene					0.2	0.4		t								0.8
96	1613	β -Cedrene							0.3		0.1	t			t	t		
97	1614	2-Methyl-6-methylene-3,7-octadiene-2-ol*													0.1			
98	1614	Sylveterpenyl acetate					0.2											
99	1617	Hexyl hexanoate							0.1									
100	1628	Aromadendrene																t
101	1630	Terpinen-4-yl acetate		t												t	0.3	
102	1638	<i>cis-p</i> -Menth-2-en-1-ol		0.1		0.9	t				0.2	t	0.4	0.1	0.2	0.1	0.4	
103	1644	Widdrene (Thujopsene)							0.4	0.3	0.3				0.2	0.1		
104	1645	<i>cis</i> -Verbenyl acetate					0.2											
105	1648	Myrtenal							t						0.3		0.1	
106	1650	γ -Elemene		t				0.1	0.1	0.3				0.1		0.2	0.1	
107	1629	(Z)-Ocimenyl acetate	0.1															
108	1651	Sabinaketone															0.2	
109	1652	<i>trans</i> -Linalool oxide acetate			t													
110	1658	Sabinyl acetate	16.8		t						30.3	1		t		t		

111	1659	γ -Gurjunene					t											
112	1661	<i>trans</i> -Pinocarvyl acetate					t											
113	1663	<i>cis</i> -Verbenol												0.3				
114	1668	Citronellyl acetate					0.3	0.2										
115	1668	(<i>Z</i>)- β -Farnesene		t			t	0.3	0.4	0.3		0.1		t	0.3	0.1		0.4
116	1670	<i>trans</i> -Pinocarveol					t		0.1	t					1.6		0.5	
117	1677	<i>epi</i> -Zonarene			t		t									t		0.1
118	1680	α -Acoradiene							0.1	0.1								
119	1682	<i>trans</i> -Verbenol										t			3.3	0.2	0.6	
120	1683	Bicyclosesquiphellandrene							0.2									
121	1685	Cadina-3,5-diene	0.1													t		
122	1687	α -Humulene					0.4	0.6									0.6	1.9
123	1689	<i>trans</i> -Piperitol		t	0.2	0.3					0.1		0.2	0.1	0.1			
124	1690	Cryptone													0.1		0.2	
125	1692	(<i>E</i>)-Methyl geranate										0.2	0.3	0.1	0.1			
126	1693	β -Acoradiene							0.2	0.1								
127	1696	γ -Terpinyl acetate					0.4											
128	1700	Limonen-4-ol	t								0.1		0.1					
129	1704	(<i>Z</i>)-Ocimenol			0.4													
130	1704	Myrtenyl acetate															0.3	
131	1704	γ -Curcumene								t								
132	1704	γ -Muurolene	t						0.1	t						0.1		0.6
133	1706	α -Terpineol	0.2			0.9	0.2	0.6	0.2	0.1			0.4	0.1	0.3	0.3		
134	1705	(<i>E</i>)-Methyl geranate		0.1							1.7	0.2						
135	1709	α -Terpinyl acetate		0.2				0.2			0.3	0.4					2.7	0.7
136	1714	β -Alaskene							0.3	0.2		0.1						
137	1715	γ -Terpineol					0.2											
138	1718	Bicyclosesquiphellandrene										t	0.2					
139	1719	Borneol	0.3				t		0.2	0.1			0.3	t	1.2	0.2	0.5	t
140	1720	<i>trans</i> -Sabinol	0.2								1.8		0.1	t	0.2			
141	1720	β -Alaskene					t											
142	1724	β -Himachalene							t									
143	1726	α -Zingiberene								0.1								
144	1726	Germacrene D	0.2	0.6	0.1	0.6	3.9	8.7	0.1	0.9		0.1		0.2		0.4	0.4	16.7
145	1738	<i>p</i> -Mentha-1,5-dien-8-ol													1		0.6	
146	1738	β -Alaskene													0.1	t		
147	1740	α -Muurolene	0.1		0.2	0.2	0.1	0.1	0.1				0.1			0.2		1.4
148	1740	Valencene			0.2													

149	1741	β -Bisabolene					0.4	0.1	0.2	0.2	t	t						
150	1742	Geranial									0.1							
151	1742	β -Selinene							t							t	0.1	0.3
152	1743	α -Cadinene					t						t			0.1		0.3
153	1744	α -Selinene															0.1	0.2
154	1747	<i>trans</i> -Carvyl acetate					t											
155	1748	Piperitone	0.1						t		0.1							
156	1755	Bicyclogermacrene					0.4	0.2								0.1		0.9
157	1755	β -Curcumene							0.2			t	0.1					
158	1758	<i>cis</i> -Piperitol				0.5							0.3	0.1		t	0.2	
159	1759	α -Cuprenene									t							
160	1763	α -Alaskene							0.5	0.6	0.1	0.2				0.1		
161	1765	Geranyl acetate					0.2	0.5										
162	1771	β -Bisabolene					0.2		0.2	0.2		t						
163	1772	Citronellol	0.1	t	0.1		0.3	0.6			0.8		1.3		0.2	t		
164	1773	δ -Cadinene	0.9	0.1	0.8	0.3	0.4	0.7	0.3	0.2	0.1	t	0.7	0.1	0.6	1	0.8	5.8
165	1776	γ -Cadinene	0.1	t	0.1	0.1	0.2	0.2	0.2		t	t	0.1	t	0.2	0.2	0.2	1.4
166	1783	β -Sesquiphellandrene							0.2	0.3	0.1	t						
167	1784	(<i>E</i>)- α -Bisabolene					0.2											
168	1786	<i>ar</i> -Curcumene							0.3	t		t	0.1		0.3			
169	1796	Selina-3,7(11)-diene							0.2									
170	1799	Cadina-1,4-diene																0.1
171	1800	<i>cis</i> -Sabinol											t				0.2	
172	1801	β -Cuprenene								0.1	0.3	t						
173	1802	Hexyl octanoate							0.1									
174	1804	Myrtenol					0.2								0.7		1.3	
175	1805	α -Campholene alcohol					0.1		0.1								0.2	
176	1811	<i>p</i> -Mentha-1,3-dien-7-al									t		t		0.1		0.1	
177	1814	<i>p</i> -Mentha-1,5-dien-7-ol									t				0.3		0.1	
178	1815	2-Tridecanone											0.1			0.1		
179	1823	<i>p</i> -Mentha-1(7),5-dien-2-ol													0.2			
180	1827	(<i>E,E</i>)-2,4-Decadienal					t		0.1		t		t					
181	1845	<i>trans</i> -Carveol											t		0.4		0.2	
182	1849	Cuparene							0.2									
183	1853	<i>cis</i> -Calamenene																0.1
184	1854	Germacrene B		0.1				0.2	0.2	0.8		t	t	0.3		0.5	0.4	0.3
185	1856	<i>m</i> -Cymen-8-ol								0.1		t						
186	1857	Geraniol						0.2			0.1							
187	1864	<i>p</i> -Cymen-8-ol		t					t		0.1		t	0.1	0.3	t	0.6	

188	1870	Hexanoic acid					0.2											
189	1878	2,5-Dimethoxy- <i>p</i> -cymene					t											
190	1882	<i>cis</i> -Carveol												t				
191	1889	Myrtanol					t											
192	1895	Italicene ether												t				
193	1900	<i>epi</i> -Cubebol					t					t		0.1	t	t	0.3	
194	1904	Elema-1,3-dien-6 α -ol		t					0.1				t		0.1			
195	1957	Cubebol			0.1		t			t		t		t	t	t	0.3	
196	1973	Dodecanol					t											
197	2003	(<i>E</i>)-2(3)-Dihydrofarnesal					0.1											
198	2008	Caryophyllene oxide															0.3	
199	2022	Fragranyl pentanoate			0.2													
200	2040	10- <i>epi</i> -Elemol			0.3													
201	2050	(<i>E</i>)-Nerolidol				0.4	0.2	0.5		0.1		t	t	0.1	0.1	0.2		
202	2069	1,6-Germacradien-5 β -ol			0.7		0.5	1.1	0.1	0.2	0.2	0.1	0.7	0.3	0.7	1.4	0.8	4.2
203	2071	Humulene epoxide-II															0.2	t
204	2080	Cubenol	0.1									t			t		0.3	
205	2088	1- <i>epi</i> -Cubenol	0.4									t					0.2	
206	2092	β -Oplophenone			0.2									0.2			t	
207	2095	Salviadienol															t	
208	2096	Elemol	2.1	0.1	14.4	6.0				0.5		2.9	1.3	3.9	1.2	0.7	0.3	
209	2104	Viridiflorol								t								
210	2108	Hedycaryol			0.1													
211	2134	Sesquithuriferol*									0.1							
212	2143	Cedrol							13.1	16.8	12.2	1		t	7.0	3.4		
213	2144	Spathulenol					t					t		0.1		0.1	0.1	
214	2152	α -Acorenol							0.1					0.1	0.1			
215	2157	5- <i>epi</i> -7- <i>epi</i> - α -Eudesmol			0.1							t						
216	2178	Widdrol								t								
217	2184	<i>cis-p</i> -Menth-3-en-1,2-diol			0.1													
218	2185	γ -Eudesmol			1.3	0.8						0.5	0.2					
219	2187	Cedryl acetate						0.2										
220	2187	δ -Cadinol	0.4	t			0.1								0.4	0.3	1.3	
221	2193	Eremoligenol										t						
222	2198	Thymol							0.1									
223	2202	α -Guaiol										t		t				
224	2209	δ -Muurololol	0.4	t	0.6	0.1		t	0.1		t		0.3	0.1	0.2	0.3	0.3	1.5
225	2219	δ -Cadinol	0.1		0.2		t		t		t		0.2			0.1		0.4
226	2219	Dimyrcene II- α						0.4		0.3								

227	2232	α-Bisabolol					0.5											
228	2250	α-Eudesmol	0.1	t	0.9	0.6				0.1			0.3	0.2	0.3	0.2	0.1	
229	2252	Citronellic acid					0.1											
230	2253	(6E)-2,3-Dihydrofarnesol											t					
231	2255	α-Cadinol	1.3	t	1.8		0.1	0.3	0.2	0.1	0.1		0.9	0.2	0.5	0.9	0.8	4
232	2257	β-Eudesmol	0.1	t	0.9					t			0.6	0.3	0.5	0.2	0.1	
233	2259	Guaia-3,9-dien-11-ol											t					
234	2260	Alismol		t						0.1	t		t	0.1		0.1		
235	2269	Dimyrcene II- β						t		0.1								
236	2273	Selin-11-en-4 α -ol																t
237	2279	(2Z,6E)-Farnesal					t											
238	2341	(2Z,6E)-Farnesol					t											
239	2349	Isopimaradiene		t						0.1								
240	2367	Isopimara-8,15-diene								0.4		t						
241	2368	Eudesma-4(15),7-diene-1- β -ol													0.3			
242	2388	Dolabradiene		t														
243	2396	13- <i>epi</i> -Manoyl oxide		t						0.1								
244	2438	Kaur-16-ene								t								
245	2503	Dodecanoic acid													0.4		t	
246	2524	Abietatriene								0.2	t		t	t				0.2
247	2479	8- α -Acetoxyelemol	0.1		11.1	1.0							t	t				
248	2492	8,13-Abietadiene	0.1	0.1		0.4			0.1	3.9	0.2		0.4	0.1	0.4		t	
249	2498	Manool													0.2			
250	2582	Neoabietadiene*								0.3								
251	2830	4- <i>epi</i> -Abietal	0.2							t	t							
252	3049	Abieta-7,13-diene-3-one	0.2							t	0.2							

^aThe data are presented as relative % for each component that was identified in the essential oils. RRI, relative retention index calculated on the basis of retention of n-alkanes; %, calculated from flame ionization detector data. Trace amounts (t) were present at <0.1%. All other compounds were identified by comparison with co-injected standards. Major component compounds (>2%) are indicated in bold.