

# ***Sideritis scardica* extracts demonstrate neuroprotective activity against A $\beta$ <sub>25-35</sub> toxicity**

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## **Supplementary Material**

**Table S1:** Multiple Reaction Monitoring conditions for polyphenolic acids and flavonoids in UPLC-MS/MS analysis

Polyphenolic compound	Chemical formula	Molecular weight	[M-H] <sup>±</sup> (m/z)	MS <sup>2</sup> fragments (m/z)	Cone voltage (V)	Collision energy (eV)	Retention time (R <sub>t</sub> )
4-hydroxybenzoic acid	C <sub>7</sub> H <sub>6</sub> O <sub>3</sub>	138.12	136.95	65.0 93.0	23	25 13	1.88
Protocatechuic acid	C <sub>7</sub> H <sub>6</sub> O <sub>4</sub>	154.12	152.95	108.95	25	13	1.64
Gallic acid	C <sub>7</sub> H <sub>6</sub> O <sub>5</sub>	170.12	168.95	78.98 124.95	23	22 15	1.37
Vanillin	C <sub>8</sub> H <sub>8</sub> O <sub>3</sub>	152.15	151.0	92.2 136.0	22	20 15	2.23
Syringic acid	C <sub>9</sub> H <sub>10</sub> O <sub>5</sub>	198.17	197.0	122.95 182.0	27	23 13	1.93
p-coumaric acid	C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>	164.16	163.0	119.0	15	13	2.13
Caffeic acid	C <sub>9</sub> H <sub>8</sub> O <sub>4</sub>	180.16	178.95	134.95 134.0	25 26	13 25	1.89
Ferulic acid	C <sub>10</sub> H <sub>10</sub> O <sub>4</sub>	194.18	192.95	178.0	26	12	2.20
Rosmarinic acid	C <sub>18</sub> H <sub>16</sub> O	360.32	359.2	161.0 197.0	10	15 15	2.26
Chlorogenic acid	C <sub>16</sub> H <sub>18</sub> O <sub>9</sub>	354.31	353.1	84.0 191.02	22	14 14	1.70
Forsythoside A	C <sub>29</sub> H <sub>36</sub> O <sub>15</sub>	624.59	623.65	160.90	35	27	4.48
Verbascoside	C <sub>29</sub> H <sub>36</sub> O <sub>15</sub>	624.59	623.00	191.0	35	28	3.29
Ellagic acid	C <sub>14</sub> H <sub>6</sub> O <sub>8</sub>	302.19	301	145.0 173.0	35	34 36	2.00
2'-hydroxyflavanone	C <sub>15</sub> H <sub>12</sub> O <sub>3</sub>	240.27	239	119.3 93.1	40	25 16	3.42
7-hydroxyflavanone	C <sub>15</sub> H <sub>12</sub> O <sub>3</sub>	240.27	239.05	135.2 91.15	41	25 23	3.52
4'-methoxyflavanone	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub>	254.29	255.15	240 161.3	31	17 22	3.78
5-methoxyflavanone	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub>	254.29	255.15	151.3	34	22	3.49
Apigenin	C <sub>15</sub> H <sub>10</sub> O <sub>5</sub>	270.05	269.95	125	29	23	2.35
Apigenin-7-O-glucoside	C <sub>21</sub> H <sub>20</sub> O <sub>10</sub>	432.38	431.15	268.35	35	22	2.15
Luteolin-7-O-glucoside	C <sub>21</sub> H <sub>20</sub> O <sub>11</sub>	448.38	449.15	287.1	34	31	2.01

Isorhamnetin	$C_{16}H_{12}O_7$	316.28	315	151.0 300.2	43	30 20	2.86
Quercetin-3-O-rhamnoside	$C_{21}H_{20}O_{11}$	448.38	447.01	271.0 300.0	43	47 28	2.14
Quercetin-3-O-rutinoside	$C_{27}H_{30}O_{16}$	610.53	609.1	300.0 271	47	39 65	1.92
Quercetin-3-O-galactoside	$C_{21}H_{20}O_{12}$	464.38	463.3	300.0 271.15	47	24 44	1.99
Myricetin-3-O-galactoside	$C_{21}H_{20}O_{13}$	480.38	479.05	271.1 287.1	48	39 44	1.87
Kaempferol-3-O-rhamnoside	$C_{21}H_{20}O_{10}$	432.39	431.05	255.3 284.2	45	42 28	2.27

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**Table S2:** The limit of detection (LOD), quantification (LOQ), linearity, precision, and accuracy results for the screened polyphenolic compounds. The calibration equations represent the peak area as a function of concentration in ppb. The intra- and interday experimental data concern data that have been collected from a six days experiment, whereas the %recovery data are the means of three independent experiments.

Compound	Linear range (ppb)	LOD (ppb)	LOQ (ppb)	Calibration equation <sup>a</sup>	Correlation coefficient (r <sup>2</sup> )	%RSD		%REC <sup>d</sup>
						(intra-day) <sup>b</sup>	(inter-day) <sup>c</sup>	
POLYPHENOLIC COMPOUNDS								
4-hydroxybenzoic acid	3.01-499.50	3.01	14.20	y=36.87x-62.07	0.9991	1.15	2.21	98.8
Protocatechuic acid	0.66-504.50	0.66	14.70	y=34.24x-69.4	0.9995	1.25	2.65	86.3
Gallic acid	53.20-513.20	53.20	105.20	y=0.67x-1.5	0.9996	0.46	0.21	99.9
Vanillin	2.87-335.00	2.87	5.62	y=0.67x-0.1	0.9999	0.98	0.95	100.4
Syringic acid	2.01-501.60	2.01	2.86	y=7.28x-2.7	0.9996	1.36	1.01	96.6
p-coumaric acid	0.65-497.30	0.65	1.55	y=52.84x+36.9	0.9997	1.7	1.94	93.2
Caffeic acid	1.21-500	1.21	1.25	y=92.95x-344.4	0.9995	1.01	2.21	100.1
Ferulic acid	2.10-505.60	2.10	12.17	y=19.02x-68.4	0.9992	0.7	2.45	102.6
Rosmarinic acid	2.32-499.50	2.32	2.56	y=7.03x+12.34	0.9996	1.3	3.02	86.9
Chlorogenic acid	3.48-495.60	3.48	4.76	y=25.02x+60.3	0.9991	1.35	1.98	87.4
Forsythoside-A	0.56-499.99	0.56	4.15	y=26.08x-1.36	0.9995	1.11	2.00	89.9
Verbascoside	0.62-486.86	0.62	11.62	y=16.789x-62.21	0.9999	1.06	4.15	94.3
Ellagic acid	5.53-499.10	5.53	75.60	y=2.18x+7.4	0.9995	1.32	3.05	89.9
2'-hydroxyflavanone	19.50-250.00	19.50	20.12	y=38.69x+22.5	0.9998	2.7	4.32	99.5
7-hydroxyflavanone	1.97-249.90	1.97	2.21	y=51.17x-73.6	1	2.63	1.42	98.9
4'-methoxyflavanone	2.21-250.00	2.21	3.89	y=83.54x+60.3	0.9999	2.89	1.87	93.6
5-methoxyflavanone	6.47-248.50	6.47	8.52	y=195.14x-493.9	0.9992	3.21	2.69	94.7
Apigenin	0.59-249.99	0.59	7.98	y=45.12x+3.21	0.9994	0.38	1.87	96.6
Apigenin-7-O-glucoside	1.87-125.30	1.87	4.42	y=6.17x+3.8	0.9998	3.48	2.54	95.8
Luteolin-7-O-glucoside	2.21-250.10	2.21	2.22	y=51.52x-89.9	0.9998	3.64	3.22	89.2

Isorhamnetin	14.01-251.1	14.01	2.31	$y=6.08x-15.4$	0.9992	2.48	1.18	100.1
Quercetin-3-O-rhamnoside	1.02-250.60	1.02	4.21	$y=60.83x-38.6$	0.9999	2.21	3.01	99.8
Quercetin-3-O-rutinoside	1.40-251.30	1.40	4.32	$y=97.74x+109.7$	0.9999	1.35	1.89	87.4
Quercetin-3-O-galactoside	6.32-249.90	6.32	3.21	$y=3.97x+0.5$	0.9998	2.14	1.37	96.3
Myricetin-3-galactoside	0.85-251.20	0.85	2.12	$y=26.38x-31.8$	0.9997	1.78	1.65	100.2
Kaempferol-3-O-rutinoside	0.76-250.00	0.76	1.21	$y=25.73x+73.7$	0.9997	1.36	2.21	91.2
Naringin	3.01-250.60	3.01	1.21	$y=22.88x-43.3$	0.9997	2.22	4.02	95.4

<sup>a</sup> Chromatographic peak area (y) as a function of ppb concentration (x)

<sup>b</sup> Values are means of intra-day assays ( $n=6$ )

<sup>c</sup> Values are means of inter-day assays ( $n=6$ )

<sup>d</sup> ( $n=3$ )