

Outlook on Chronic Venous Disease Treatment: Phytochemical Screening, In Vitro Antioxidant Activity and In Silico Studies for Three Vegetal Extracts

Supplementary Materials

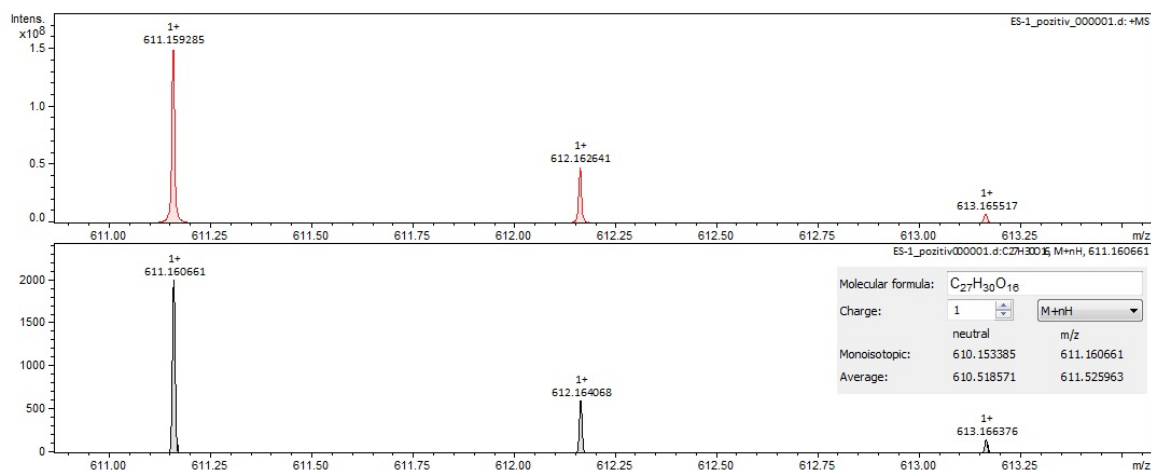


Figure S1. Rutin – *Sophorae flos* extract spectrogram ESI+, water sample.

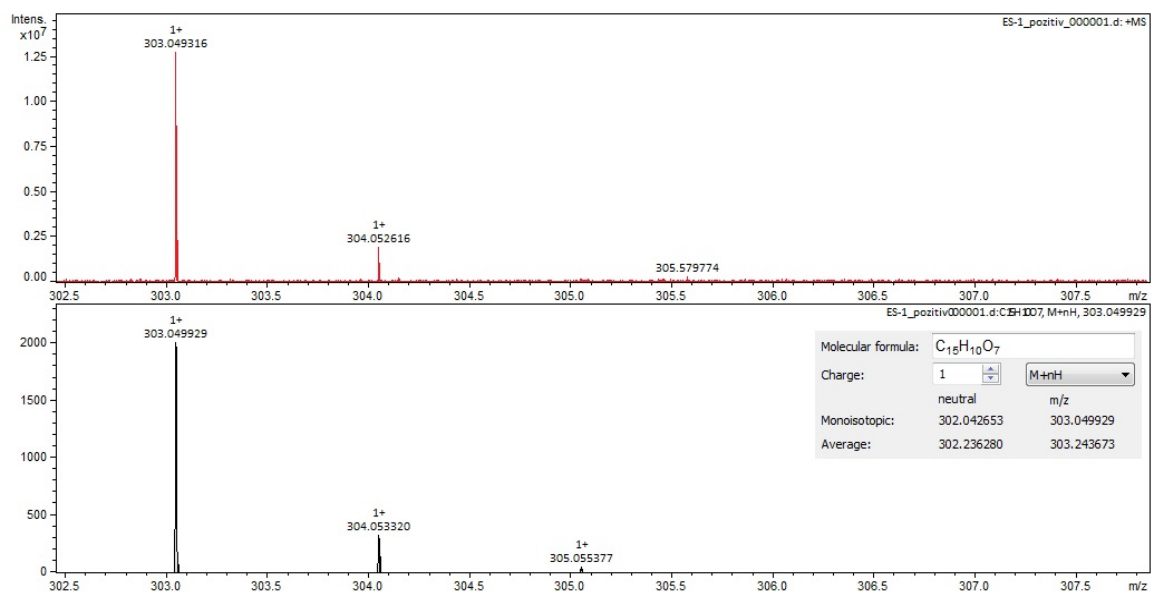


Figure S2. Quercetin – *Sophorae flos* extract spectrogram ESI+, water sample.

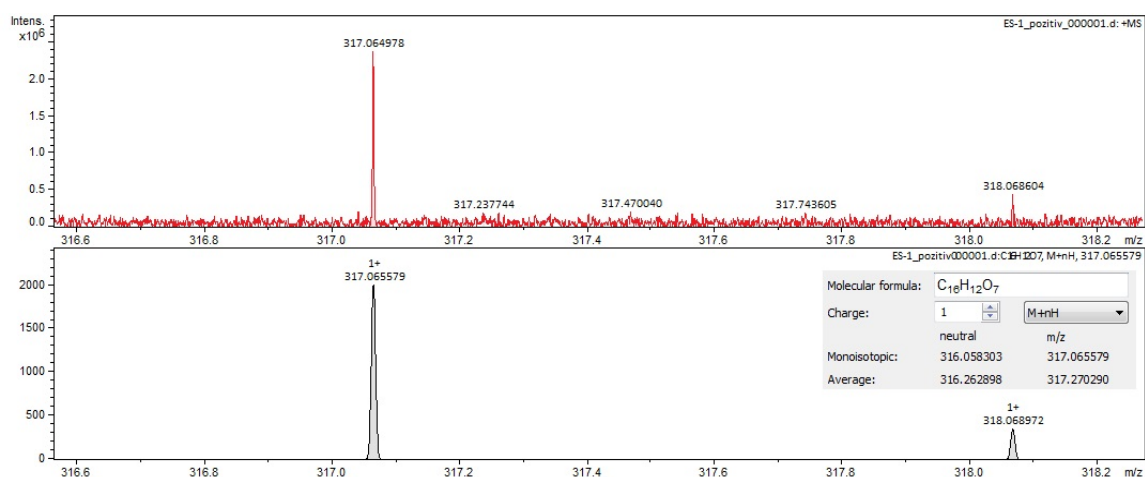


Figure S3. Isorhamnetin – *Sophorae flos* extract spectrogram ESI+, water sample.

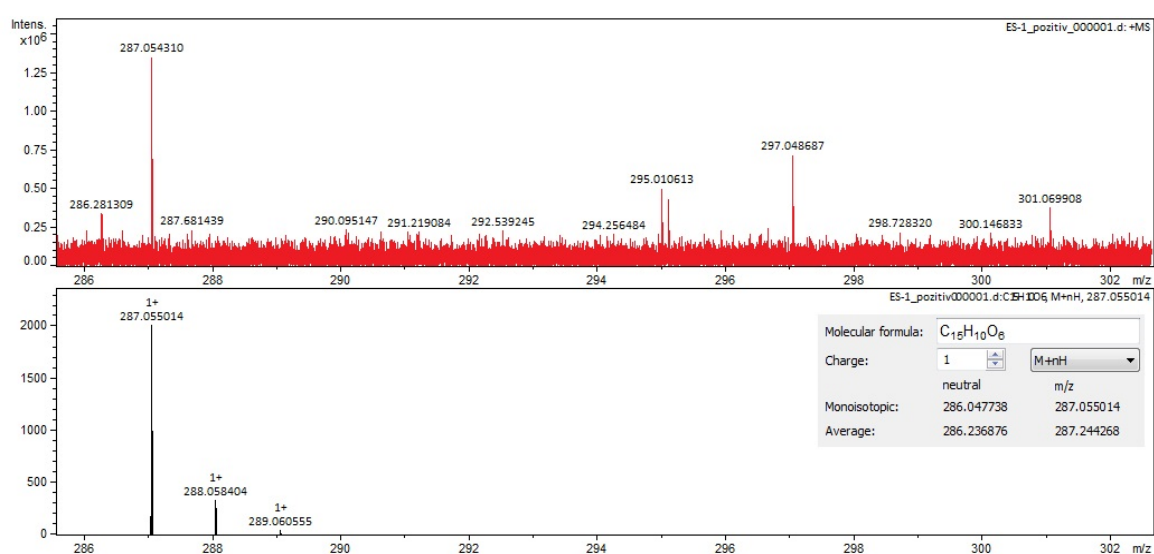


Figure S4. Kaempferol/fisetin– *Sophorae flos* extract spectrogram ESI+, water sample.

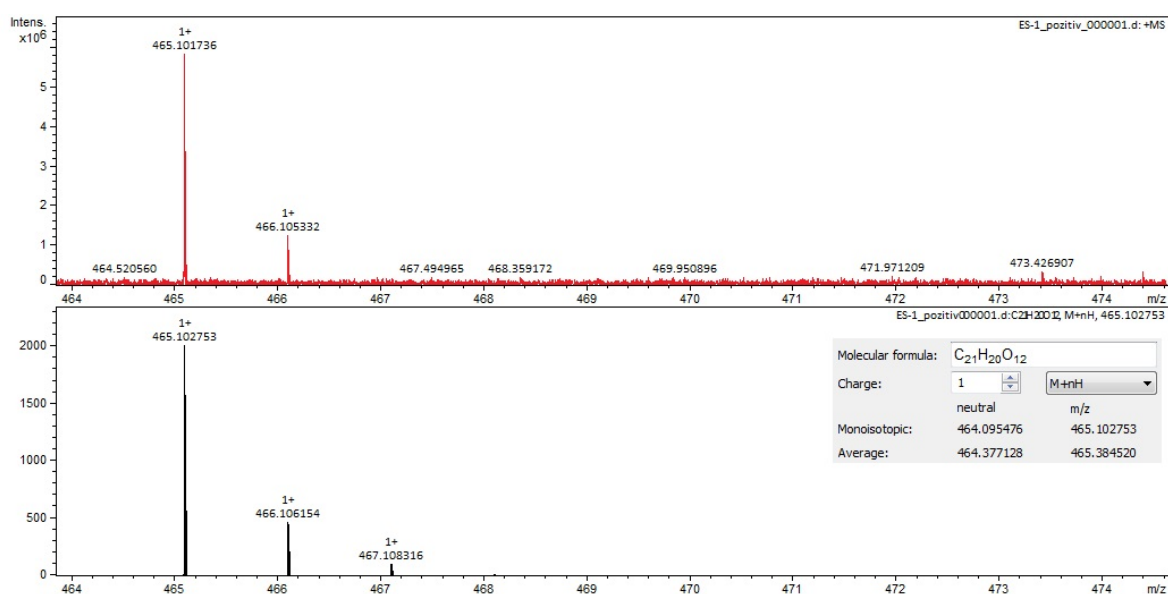


Figure S5. Isoquercetin – *Sophorae flos* extract spectrogram ESI+, water sample.

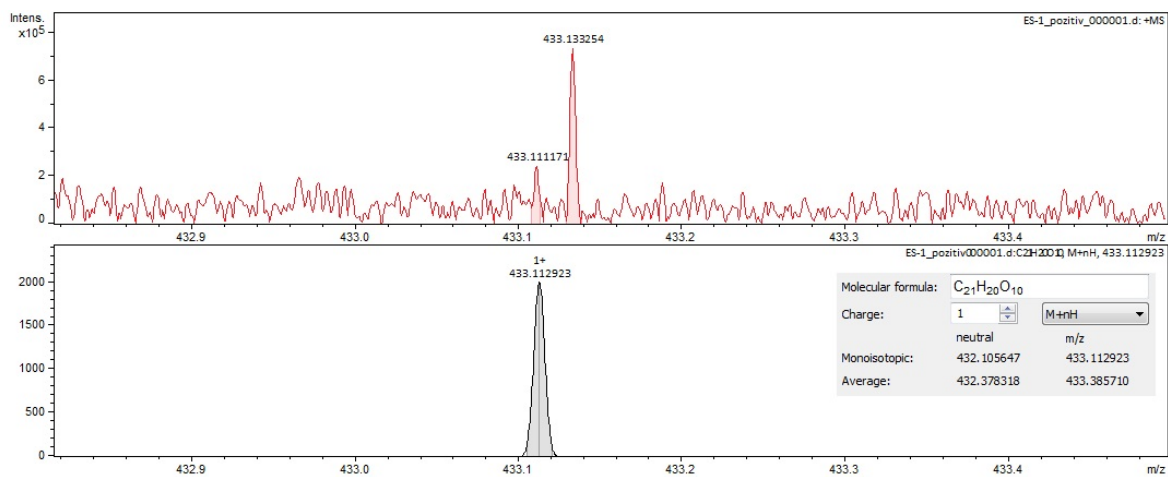


Figure S6. Sophoricoside – *Sophorae flos* extract spectrogram ESI+, water sample.

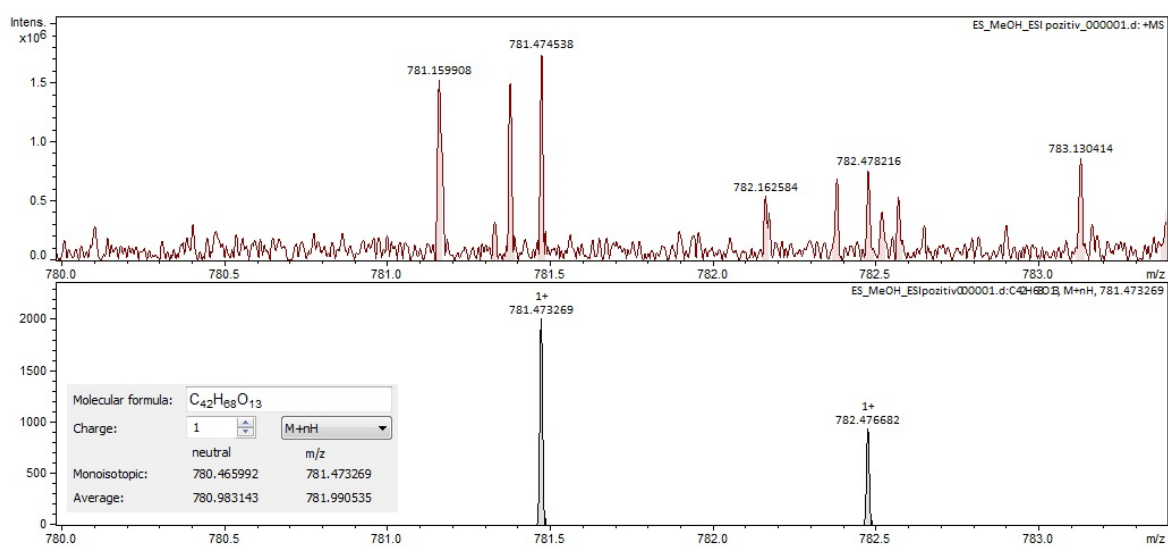


Figure S7. Kaikasaponin I – *Sophorae flos* extract spectrogram ESI+, methanol sample.

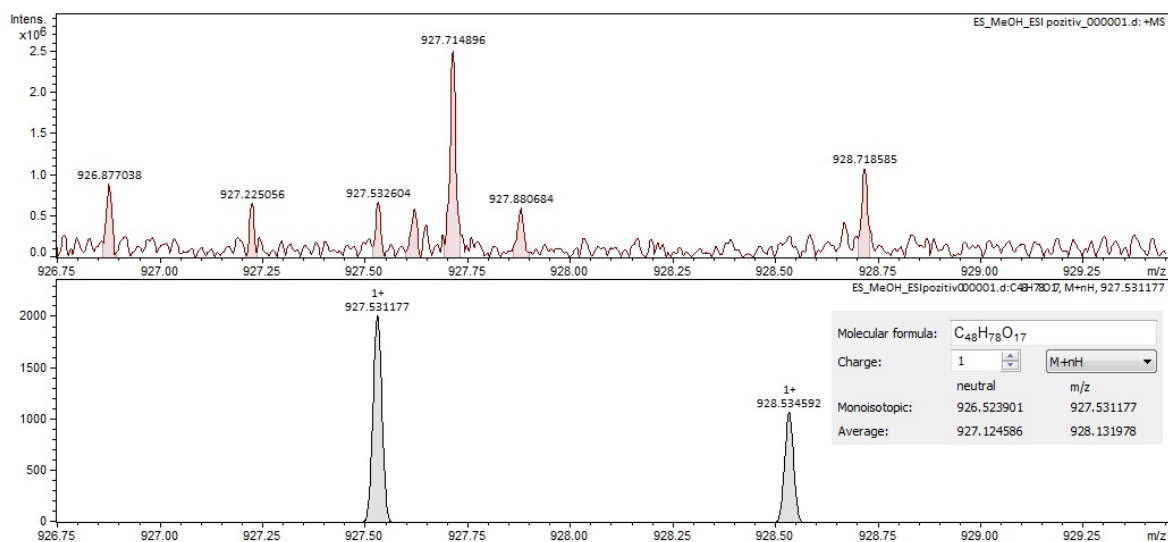


Figure S8. Kaikasaponin III – *Sophorae flos* extract spectrogram ESI+, methanol sample.

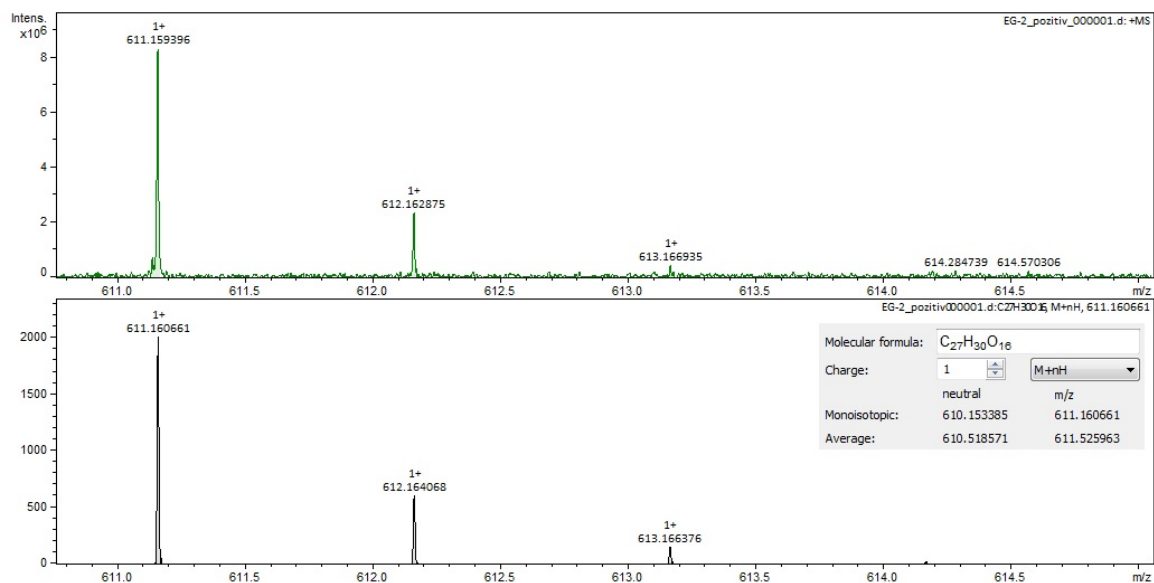


Figure S9. Rutin – *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

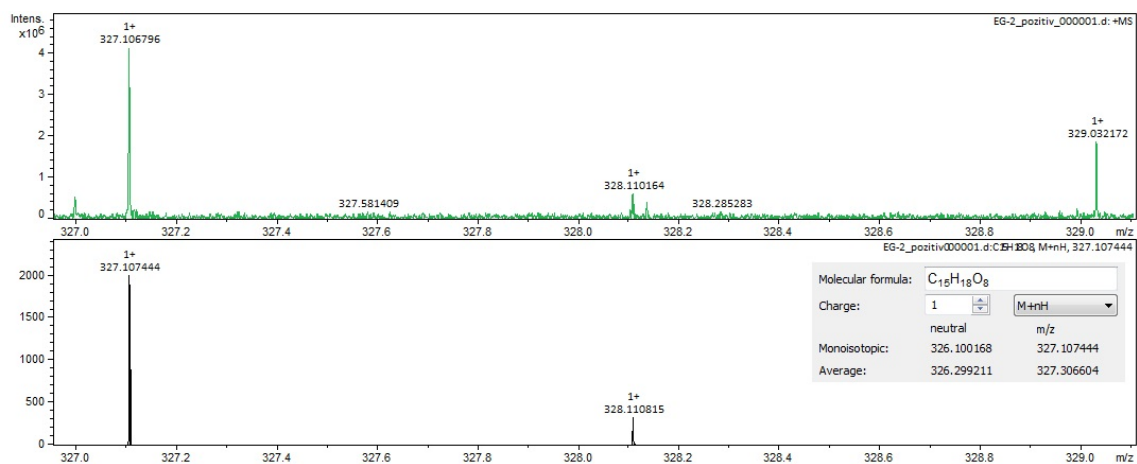


Figure S10. Bilobalide – *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

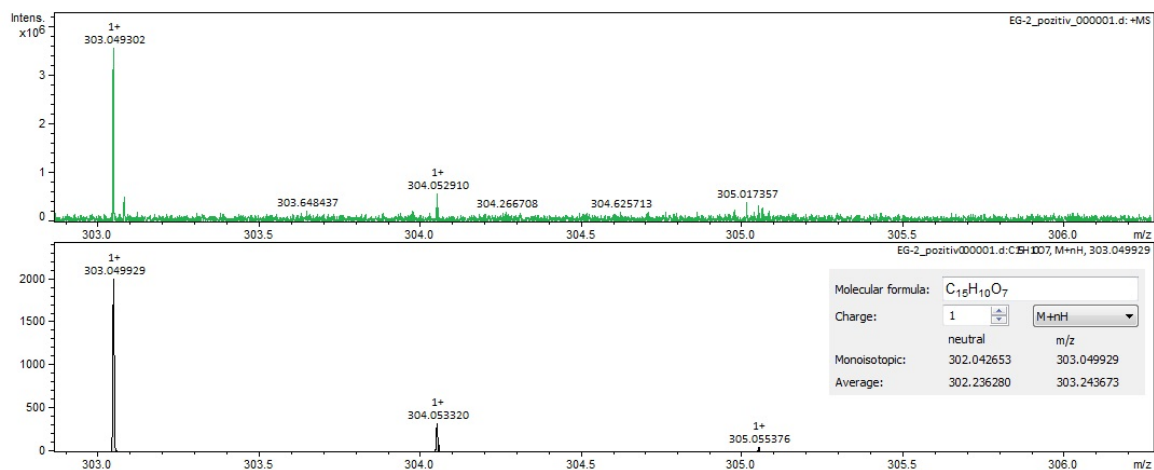


Figure S11. Quercetin – *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

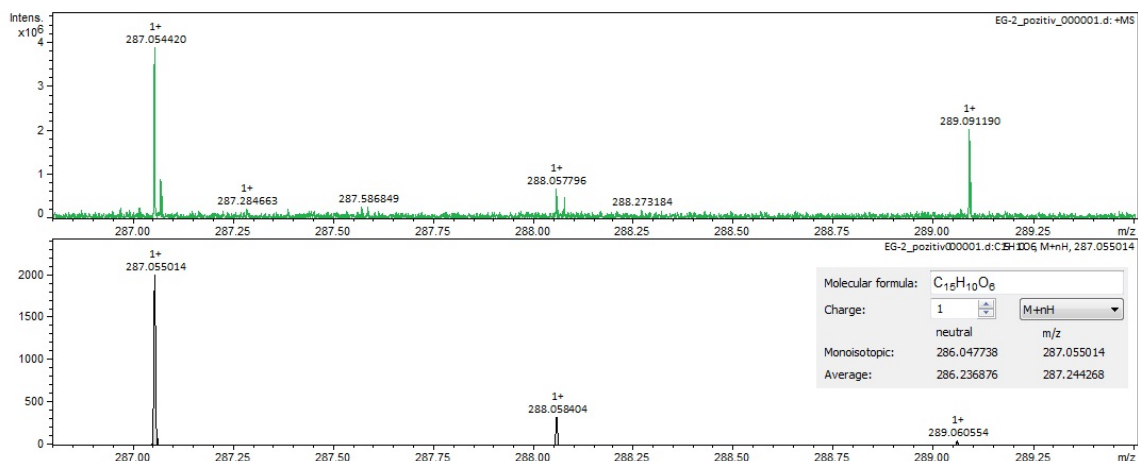


Figure S12. Kaempferol – *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

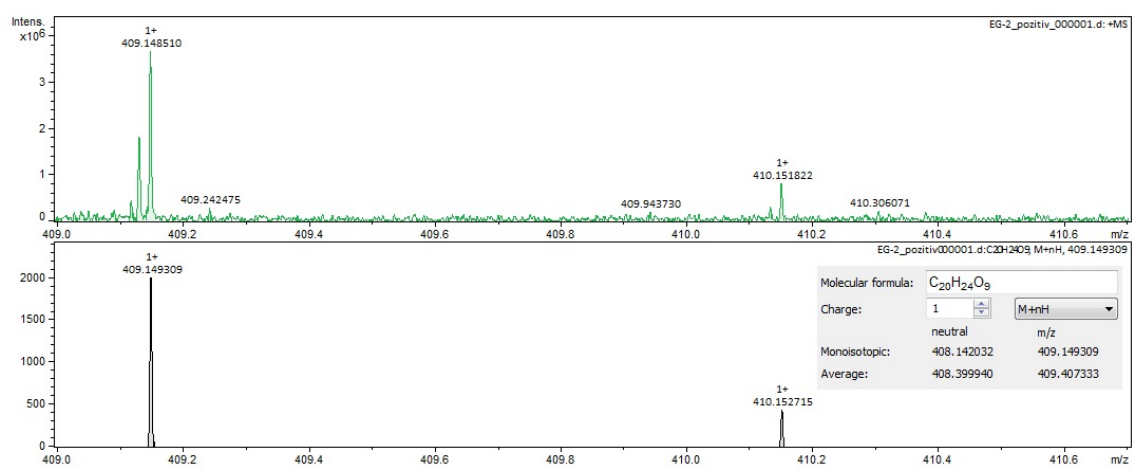


Figure S13. Ginkgolide A - *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

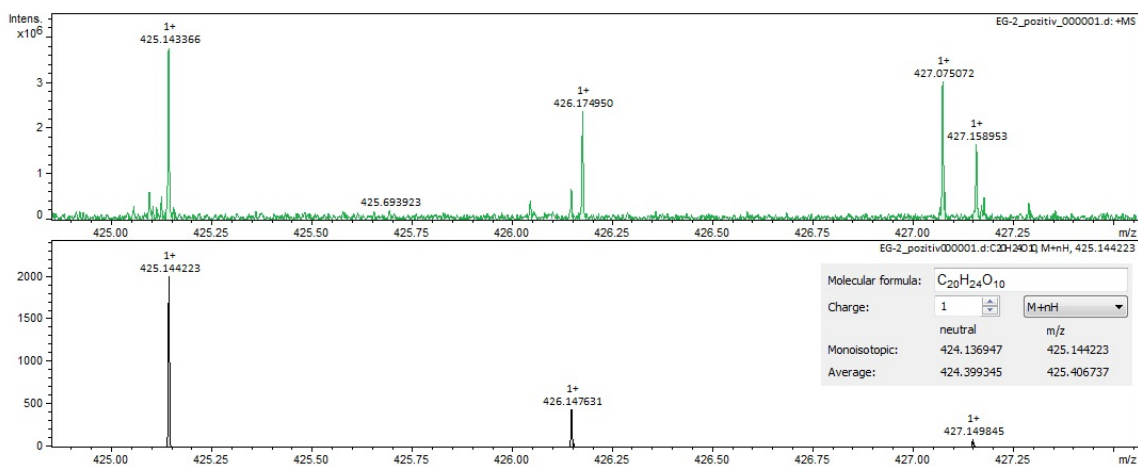


Figure S14. Ginkgolide B - *Ginkgo biloba* folium extract spectrogram ESI+, water sample.

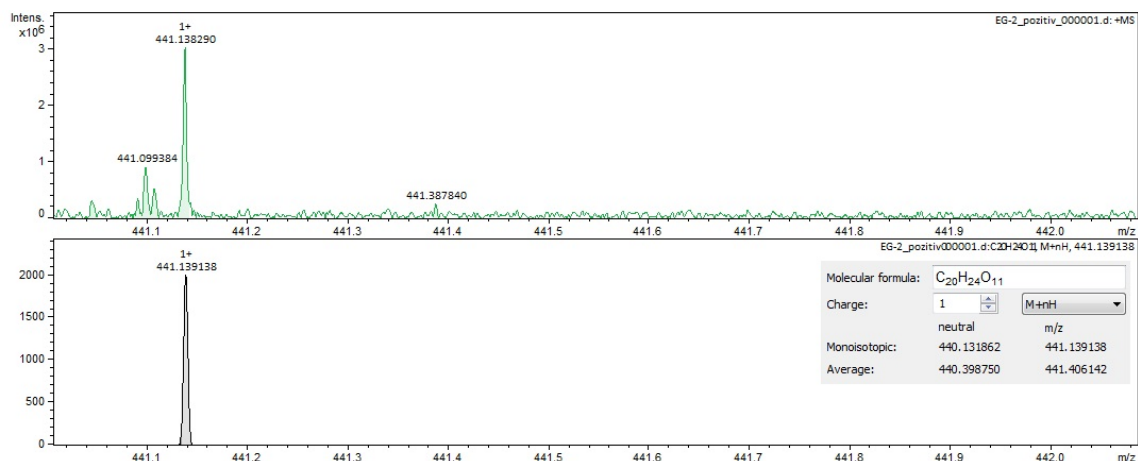


Figure S15. Ginkgolide C – *Ginkgo bilobae folium* extract spectrogram ESI+, water sample.

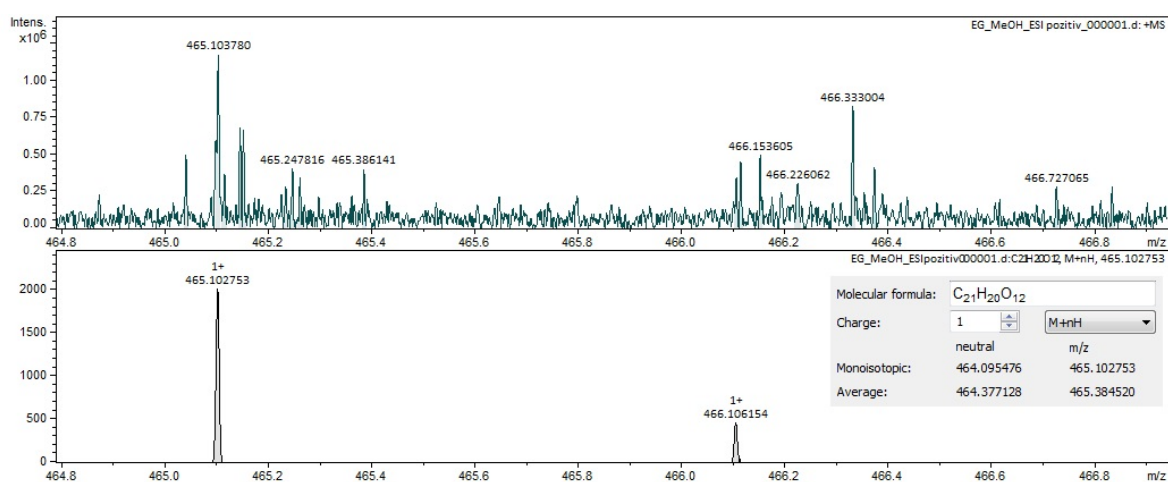


Figure S16. Isoquercitrin – *Ginkgo bilobae folium* extract spectrogram ESI+, methanol sample.

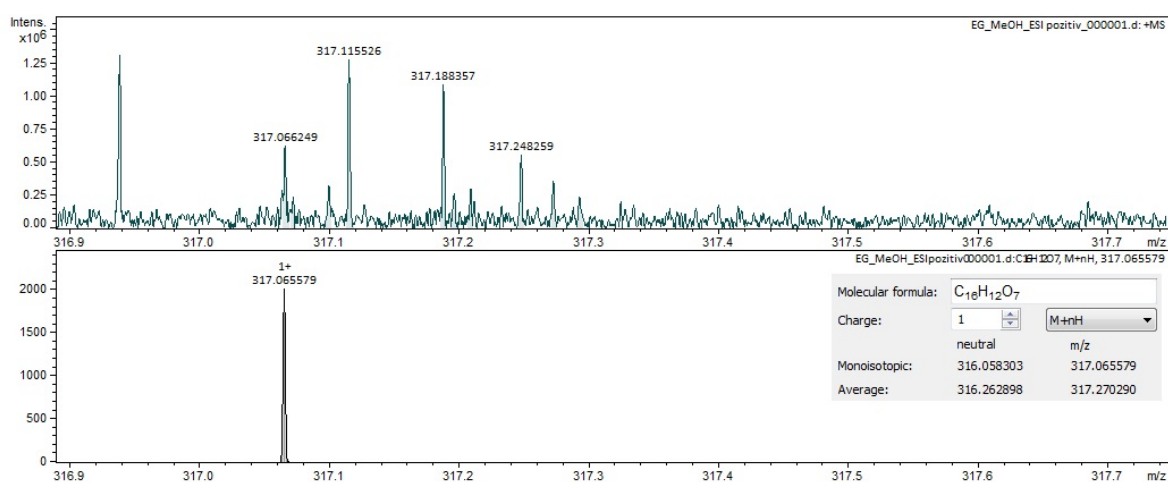


Figure S17. Isorhamnetin – *Ginkgo bilobae folium* extract spectrogram ESI+, methanol sample.

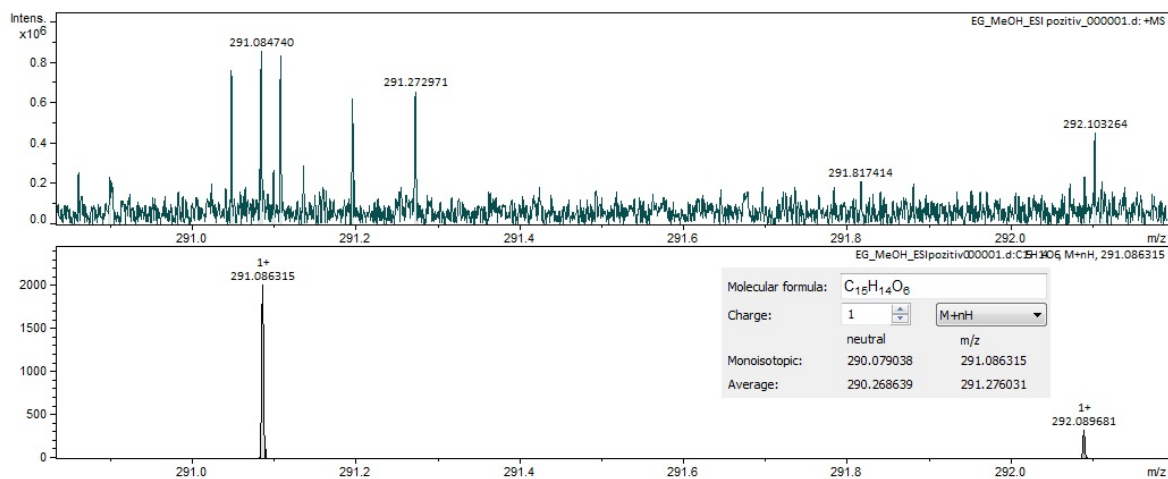


Figure S18. Catechin – *Ginkgo bilobae folium* extract spectrogram ESI+, methanol sample.

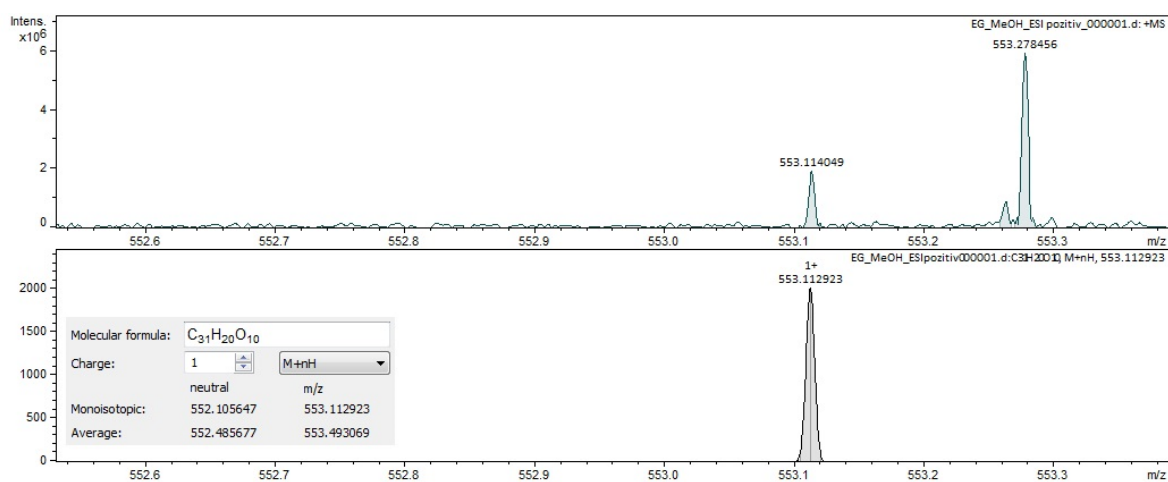


Figure S19. Bilobetin – *Ginkgo bilobae folium* extract spectrogram, ESI+, methanol sample.

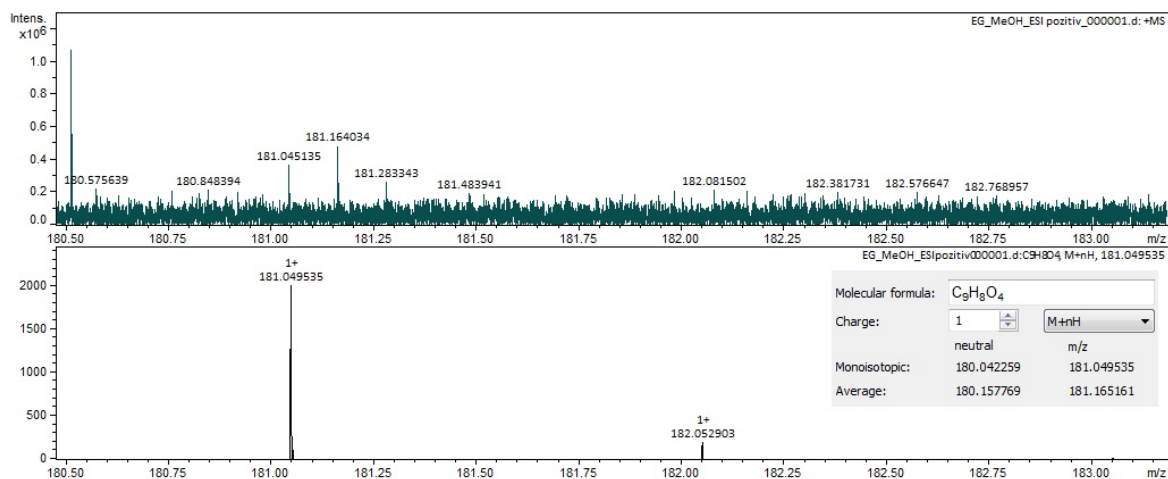


Figure S20. Caffeic acid – *Ginkgo bilobae folium* extract spectrogram, ESI+, methanol sample.

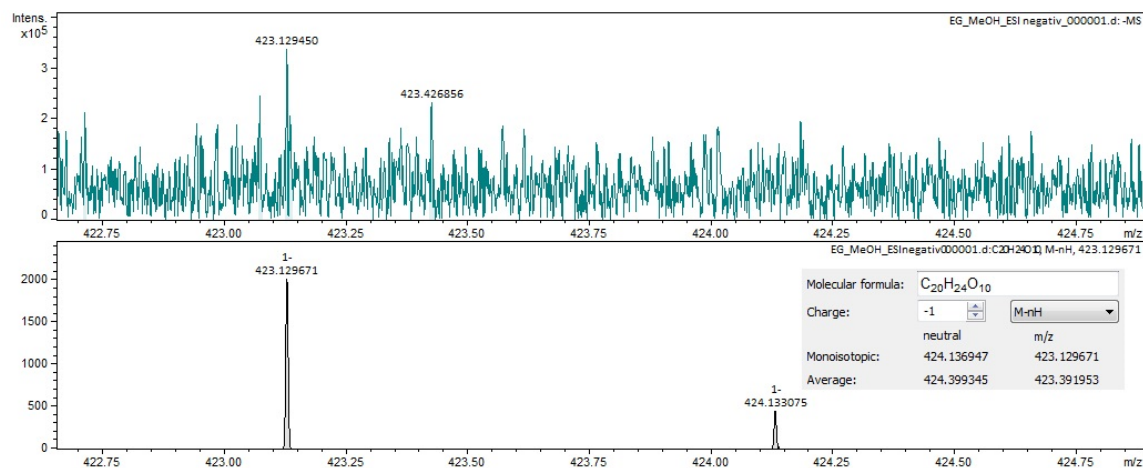


Figure S21. Ginkgolide B – *Ginkgo bilobae folium* extract spectrogram, ESI–, methanol sample.

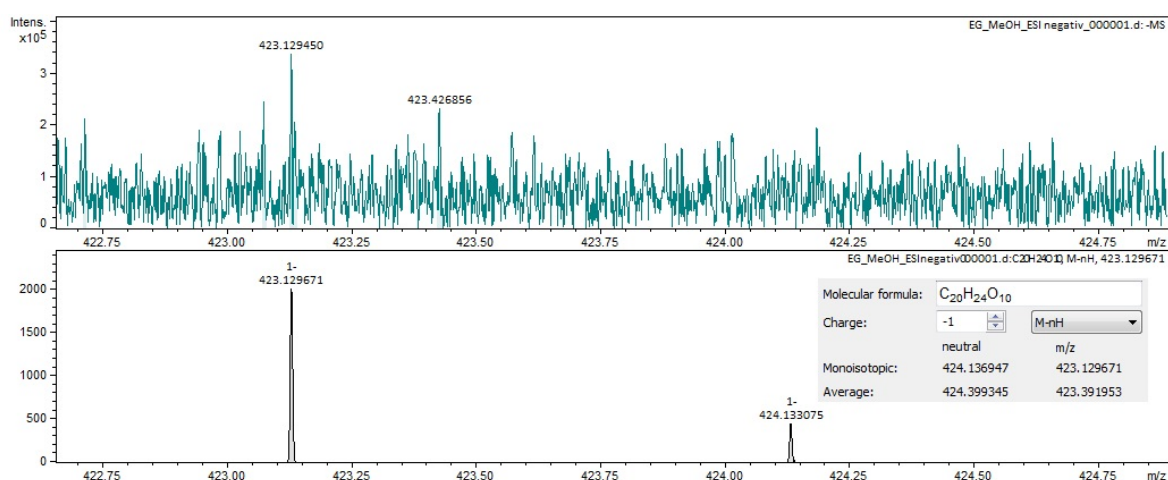


Figure S22. Bilobalide – *Ginkgo bilobae folium* extract spectrogram, ESI–, methanol sample.

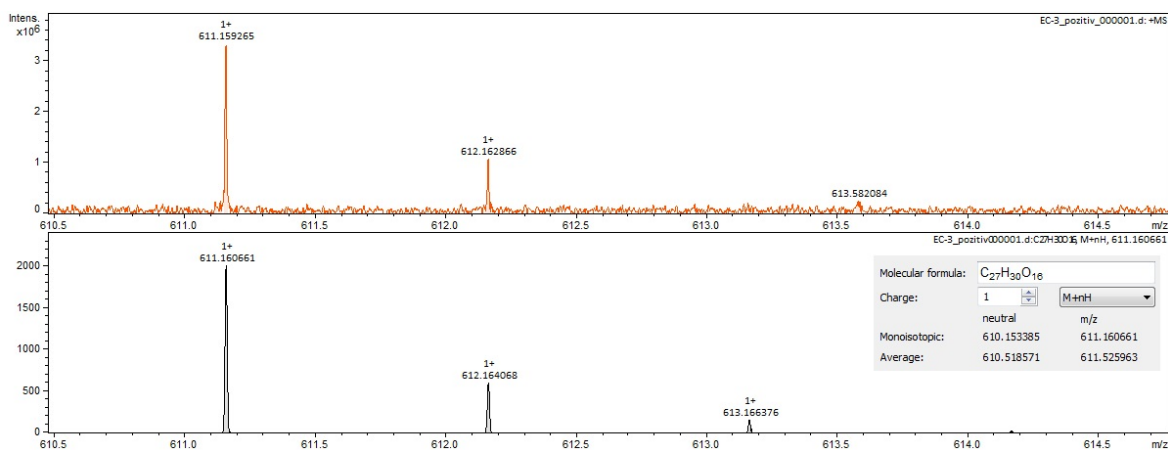


Figure S23. Rutin – *Calendulae flos* extract spectrogram, ESI+, water sample.

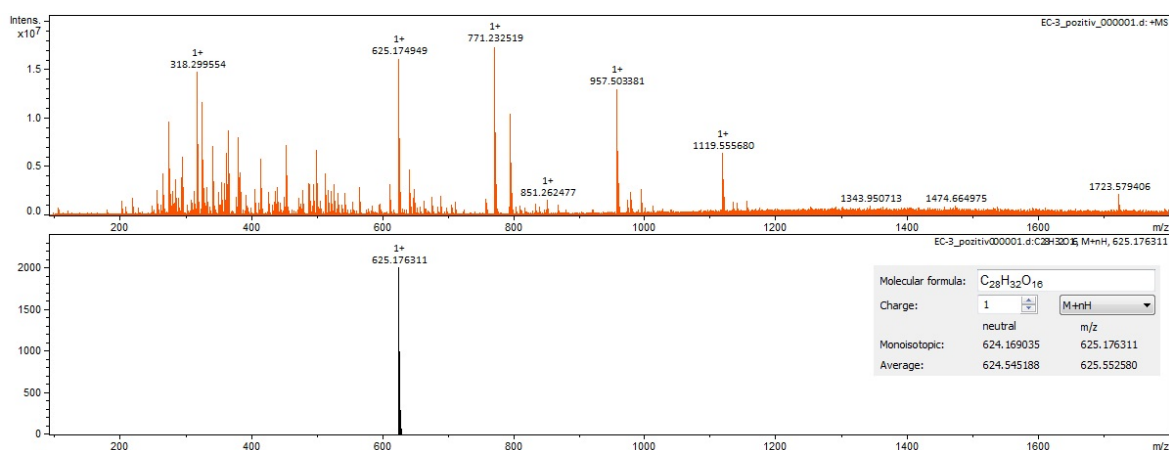


Figure S24. Calendoflavoside/narcissin – *Calendulae flos* extract spectrogram, ESI+, water sample.

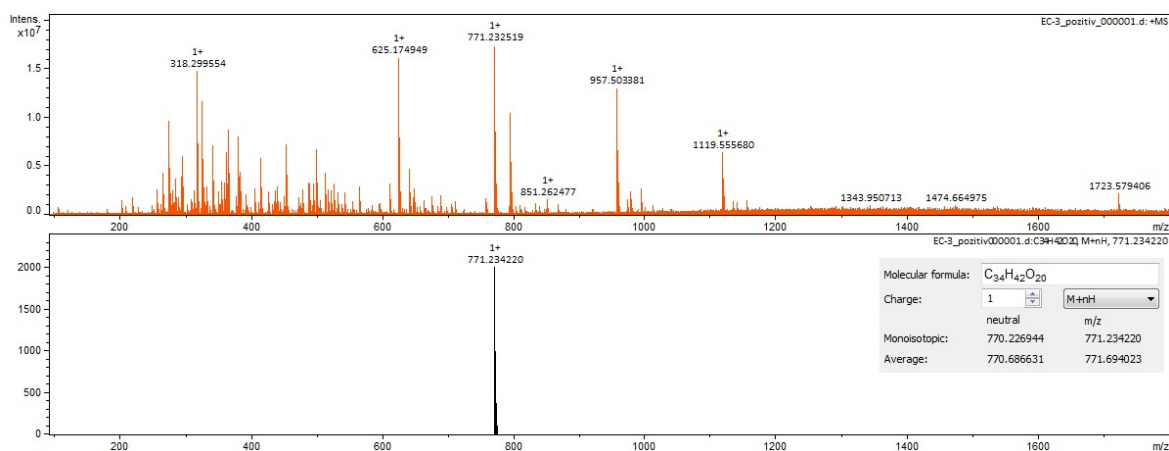


Figure S25. Thyphaneoside – *Calendulae flos* extract spectrogram, ESI+, water sample.

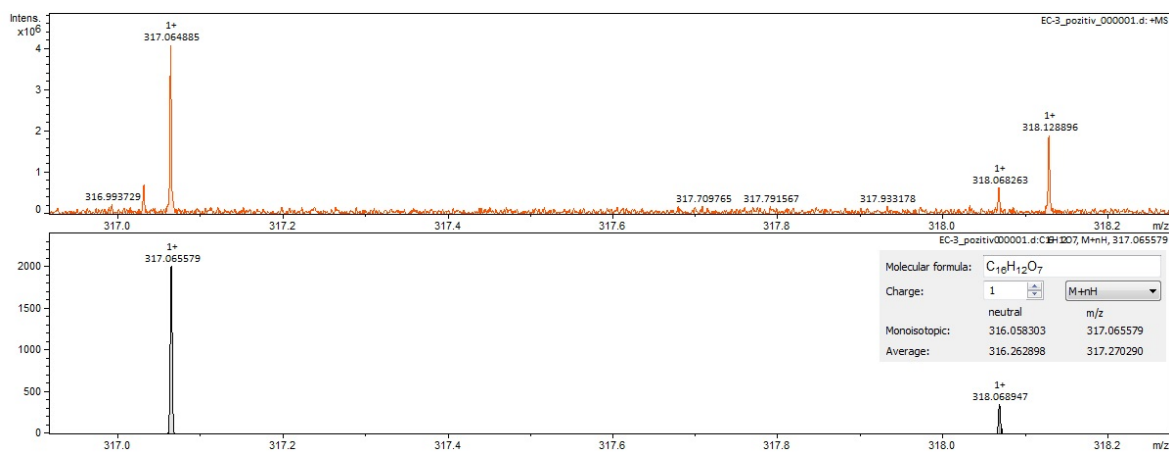


Figure S26. Isorhamnetin – *Calendulae flos* extract spectrogram, ESI+, water sample.

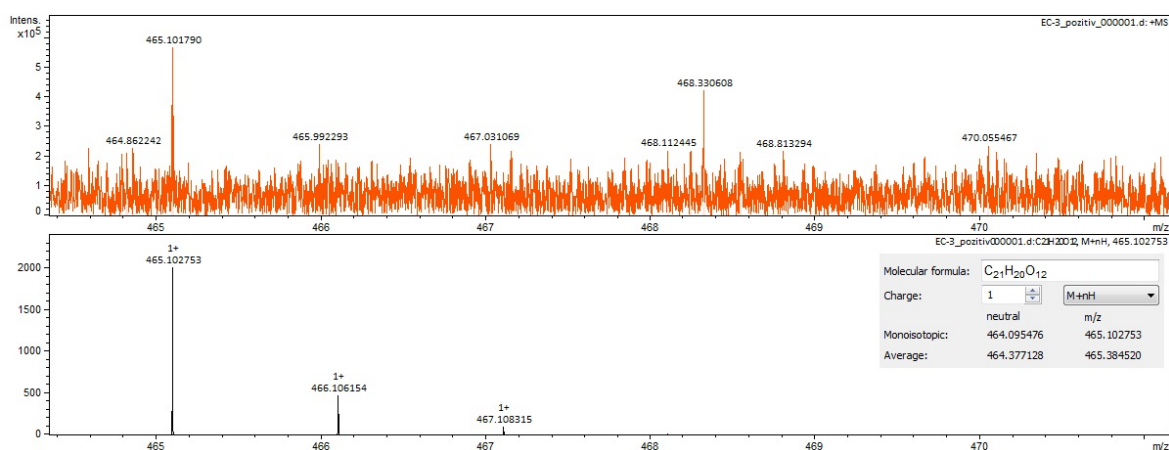


Figure S27. Isoquercitrin – *Calendulae flos* extract spectrogram, ESI+, water sample.

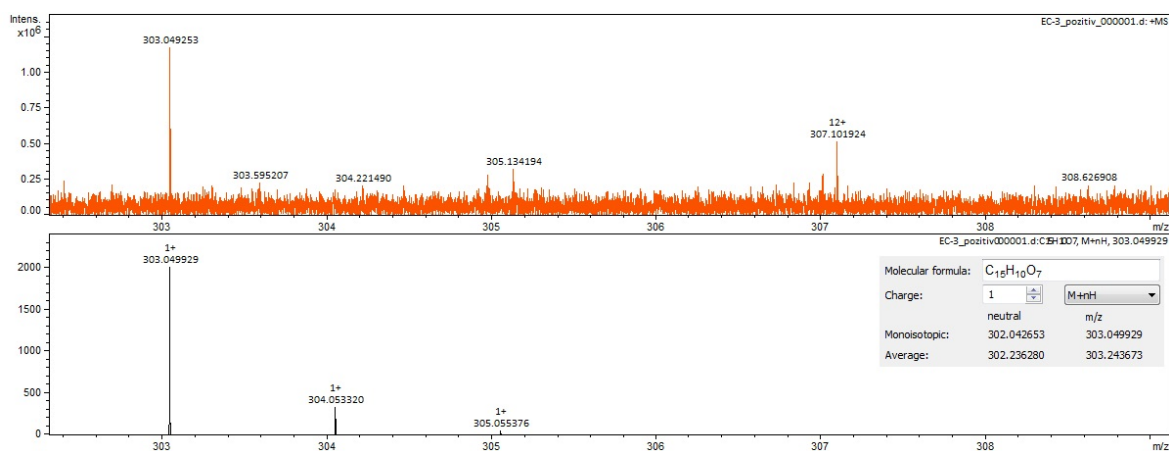


Figure S28. Quercetin – *Calendulae flos* extract spectrogram, ESI+, water sample.

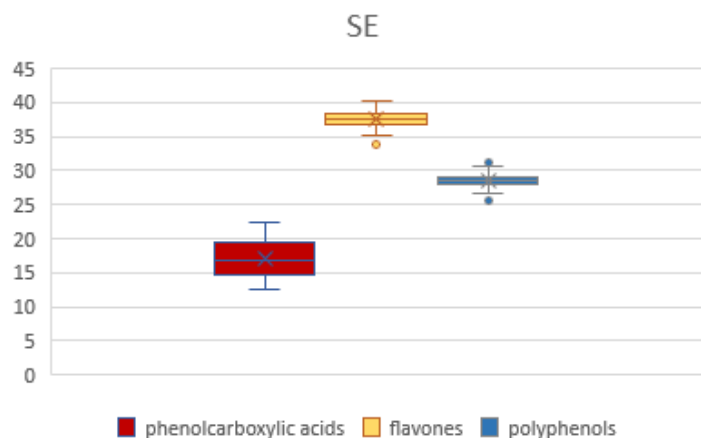


Figure S29. Quantitative spectrophotometric analysis – boxplot for *Sophorae flos* extract.

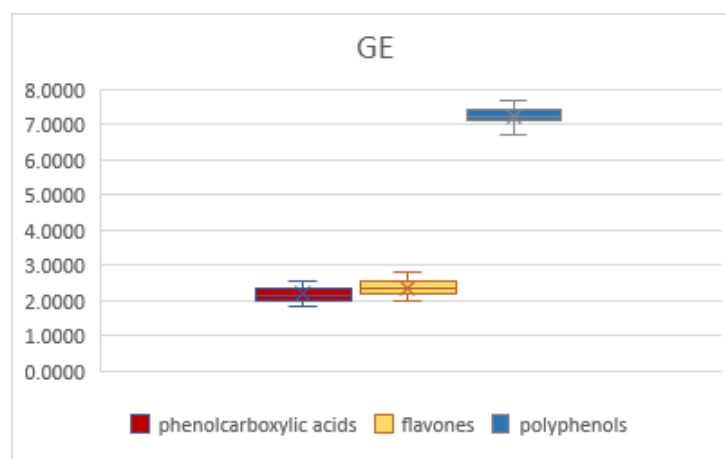


Figure S30. Quantitative spectrophotometric analysis – boxplot for *Ginkgo biloba folium* extract.

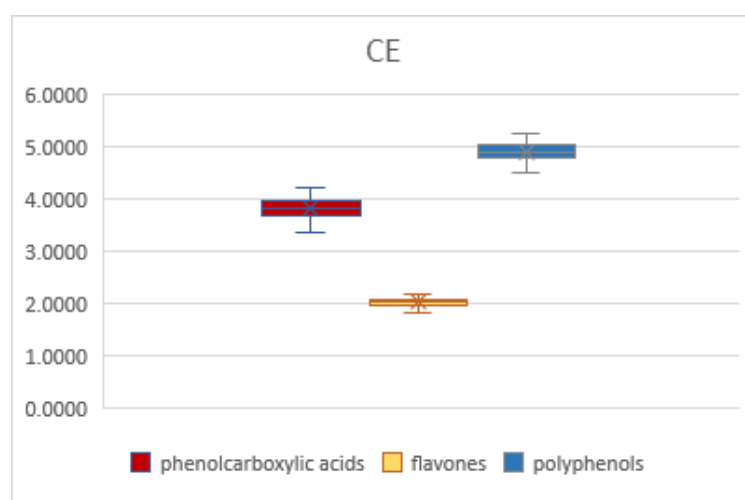


Figure S31. Quantitative spectrophotometric analysis – boxplot for *Calendulae flos* extract.

Table S1. UHPLC-HRMS/MS general screening.

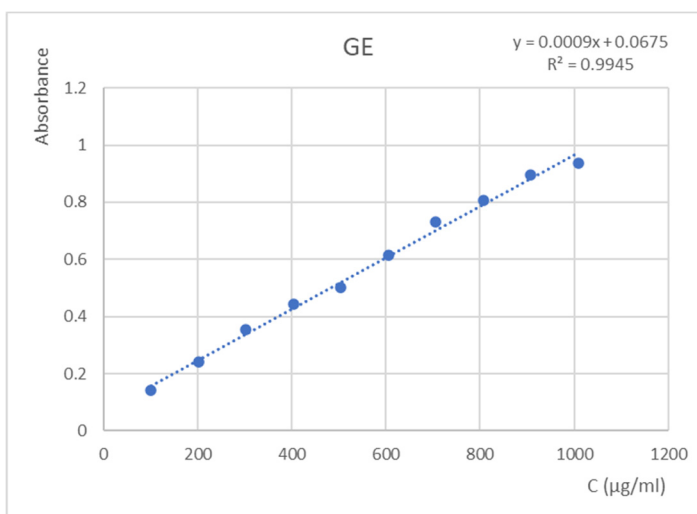
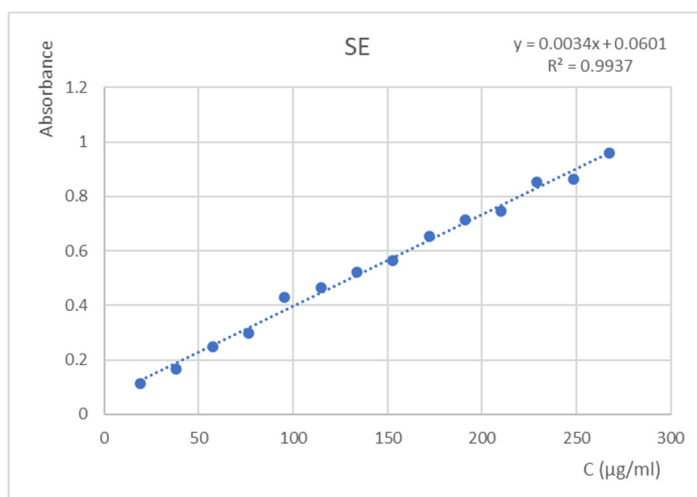
Nr.	Phytochemical class	Compound	Molecular formula	Adduct Ion (m/z) Monitored Negative Ion	Retention time (min)		
					SE	GE	CE
1	carboxylic acids	folinic acid	C ₂₀ H ₂₃ N ₇ O ₇	472.15864	/	/	/
2	cyclohexancarboxylic acids	quinic acid	C ₇ H ₁₂ O ₆	191.05611	0.66	0.66	0.66
3	Cyclohexencarboxylic acids	perillic acid	C ₁₀ H ₁₄ O ₂	165.09210	/	/	/
4	dicarboxylic acids	azelaic acid	C ₉ H ₁₆ O ₄	187.09761	14.13	14.12	14.1
5	dicarboxylic acids	malic acid	C ₄ H ₆ O ₅	133.01427	/	/	/
6	phenolcarboxylic acids	dihydro-o-coumaric acid	C ₉ H ₁₀ O ₃	165.05574	/	/	/
7	phenolcarboxylic acids	gallic acid	C ₇ H ₆ O ₅	169.01427	/	19.66	/
8	phenolcarboxylic acids	chlorogenic acid	C ₁₆ H ₁₈ O ₉	353.08783	6.25	6.23	/
9	phenolcarboxylic acids	caffeic acid	C ₉ H ₈ O ₄	179.03501	6.88	/	/

Nr.	Phytochemical class	Compound	Molecular formula	Adduct Ion (<i>m/z</i>) Monitored Negative Ion	Retention time (min)		
				SE	GE	CE	
10	phenolcarboxylic acids	ferulic acid	C ₁₀ H ₁₀ O ₄	193.05066	10.22	/	/
11	phenolcarboxylic acids	ellagic acid	C ₁₄ H ₆ O ₈	300.99899	/	/	/
12	phenolcarboxylic acids	p-coumaric acid	C ₉ H ₈ O ₃	163.03954	9.13	9.09	9.09
13	phenolcarboxylic acids	syringic acid	C ₉ H ₁₀ O ₅	197.04555	9.09	8.86	8.86
14	phenolcarboxylic acids	cynarin (1,5-di-O-caffeoylquinic acid)	C ₂₅ H ₂₄ O ₁₂	515.11950	12.42/13.72	12.37	/
15	phenolcarboxylic acids	rosmarinic acid	C ₁₈ H ₁₆ O ₈	359.07727	/	/	/
16	phenolcarboxylic acids	carnosic acid	C ₂₀ H ₂₈ O ₄	331.19151	/	/	/
17	phenolcarboxylic acids	neochlorogenic acid	C ₁₆ H ₁₈ O ₉	353.08783	/	/	/
18	phenolcarboxylic acids	salvianolic acid B	C ₃₆ H ₃₀ O ₁₆	717.14611	/	/	/
19	phenolcarboxylic acids	caftaric acid	C ₁₃ H ₁₂ O ₉	311.04085	/	/	/
20	phenolcarboxylic acids	cichoric acid	C ₂₂ H ₁₈ O ₁₂	473.07257	/	/	/
21	phenolcarboxylic acids	coumanoylquinic acid/ isomers	C ₁₆ H ₁₈ O ₈	337.09292	8.18/1.04	/	/
22	phenolcarboxylic acids	anisic acid (4-methoxybenzoic acid)	C ₈ H ₈ O ₃	151.04009	/	/	/
23	phenolcarboxylic acids	sinapic acid	C ₁₁ H ₁₂ O ₅	223.06122	7.45	/	/
24	phenolcarboxylic acids	hydroxyferulic acid	C ₁₆ H ₂₀ O ₁₀	371.09839	/	6.79	6.77
25	phenolcarboxylic acids	caffeoylshikimic acid	C ₁₀ H ₁₅ O ₉	278.06435	7.72	7.7	7.65
26	carotenoids	violaxantin	C ₄₀ H ₅₆ O ₄	599.41061	/	/	/
27	carotenoids	taraxantin	C ₄₀ H ₅₆ O ₃	583.41569	/	/	/
28	coumarins	cichorin	C ₁₅ H ₁₆ O ₉	339.07218	5.18	/	/
29	coumarins	aesculetin/isomers	C ₉ H ₆ O ₄	177.01936	/	/	/
30	coumarins	scopoletin	C ₁₀ H ₈ O ₄	191.03501	/	/	/
31	coumarins	esculetin-7-hexoside	C ₁₅ H ₁₆ O ₉	339.07218	/	/	/
32	coumarins	coumarin	C ₉ H ₆ O ₂	145.02953	/	/	/
33	coumarins	dihydrocoumarin	C ₉ H ₈ O ₂	147.04518	/	/	/
34	coumarins	7-hydroxycoumarin	C ₉ H ₆ O ₃	161.02444	/	/	/
35	diterpenes	carnasol	C ₂₀ H ₂₆ O ₄	329.17586	18.89	/	/
36	diterpenes	rosmanol/epirosmanol	C ₂₀ H ₂₆ O ₅	345.17077	/	/	/
37	diterpenes	rosmadial/isomers	C ₂₀ H ₂₄ O ₅	343.15510	/	/	/
38	diterpenes	rosmaridiphenol	C ₂₀ H ₂₈ O ₃	315.19657	/	/	/
39	diterpenes	rosmanol methyl ether	C ₂₁ H ₂₈ O ₅	359.18640	/	/	/
40	diterpenes	carnasic acid quinone	C ₂₀ H ₂₅ O ₄	328.16803	/	/	/
41	esters	coniferyl ferulate	C ₂₀ H ₂₀ O ₆	355.11874	/	/	/
42	phenols	coniferyl	C ₁₀ H ₁₂ O ₃	179.07139	/	/	/
43	flavonoids	catechin	C ₁₅ H ₁₄ O ₆	289.07176	/	/	/
44	flavonoids	epicatechin	C ₁₅ H ₁₄ O ₆	289.07176	/	8.01	/
45	flavonoids	quercetin	C ₁₅ H ₁₀ O ₇	301.03540	15.2	15.22	15.15
46	flavonoids	rutin (quercetin-3-rutinoside)	C ₂₇ H ₃₀ O ₁₆	609.14613	12.56	12.6	12.58
47	flavonoids	apigenin	C ₁₅ H ₁₀ O ₅	269.04502	16.88	16.86	16.83
48	flavonoids	kaempferol	C ₁₅ H ₁₀ O ₆	285.04049	/	16.67	16.62
49	flavonoids	6-methoxyluteolin	C ₁₆ H ₁₂ O ₇	315.05105	/	16.86	16.85
50	flavonoids	naringenin	C ₁₅ H ₁₂ O ₅	271.06122	15.6	15.65	15.63

Nr. Phytochemical class		Compound	Molecular formula	Adduct Ion	Retention time (min)		
				(<i>m/z</i>) Monitored Negative Ion	SE	GE	CE
51	flavonoids	naringin	C ₂₇ H ₃₂ O ₁₄	579.17185	/	12.93	13
52	flavonoids	hesperitin	C ₁₆ H ₁₄ O ₆	301.07179	/	/	15.71
53	flavonoids	pinostrobin	C ₁₆ H ₁₄ O ₄	269.08196	/	/	/
54	flavonoids	pinocembrin	C ₁₅ H ₁₂ O ₄	255.06631	/	/	/
55	flavonoids	chrysin	C ₁₅ H ₁₀ O ₄	253.05066	/	/	/
56	flavonoids	myricetin	C ₁₅ H ₁₀ O ₈	317.03032	/	/	7.82
57	flavonoids	galangin	C ₁₅ H ₁₀ O ₅	269.04557	/	/	/
58	flavonoids	hyperoside (quercetin-3-hexoside)	C ₂₁ H ₂₀ O ₁₂	463.08768	9.61	9.64	9.63
59	flavonoids	genistin	C ₂₁ H ₂₀ O ₁₀	431.09837	/	/	12.96
60	flavonoids	genistein	C ₁₅ H ₁₀ O ₅	269.04502	/	/	/
61	flavonoids	daidzin	C ₂₁ H ₂₀ O ₉	415.10348	/	/	/
62	flavonoids	daidzein	C ₁₅ H ₁₀ O ₄	253.05066	/	/	/
63	flavonoids	2',6-dihydroxyflavone	C ₁₅ H ₁₀ O ₄	253.05066	/	14.67	/
64	flavonoids	ononin	C ₂₂ H ₂₂ O ₉	429.11913	/	/	/
65	flavonoids	formononetin	C ₁₆ H ₁₂ O ₄	267.06631	/	/	17.51
66	flavonoids	glycitein	C ₁₆ H ₁₂ O ₅	283.06122	/	19.66	19.65
67	flavonoids	coumestrol	C ₁₅ H ₈ O ₅	267.02990	/	/	/
68	flavonoids	coumestrol-3-O-hexoside	C ₂₁ H ₁₈ O ₁₀	429.08274	/	/	/
69	flavonoids	biochanin A	C ₁₆ H ₁₂ O ₅	283.06122	/	/	/
70	flavonoids	sissotrin (biochanin A7-O-β-D-hexoside)	C ₂₂ H ₂₂ O ₁₀	445.11404	/	/	12.50/15.91
71	flavonoids	5,7-dihydroxy-2'-methoxyflavone	C ₂₂ H ₁₂ O ₅	283.06122	/	/	/
72	flavonoids	calycosin (3'-hydroxy-formononetin)	C ₁₆ H ₁₂ O ₅	283.06122	/	/	/
73	flavonoids	irilone	C ₁₆ H ₁₀ O ₆	297.04049	/	/	/
74	flavonoids	baptigenin	C ₁₅ H ₁₀ O ₆	285.04046	/	15.71	/
75	flavonoids	pseudobaptigenin	C ₁₆ H ₁₀ O ₅	281.04557	/	/	17.36
76	flavonoids	pratensein	C ₁₆ H ₁₂ O ₆	299.05614	/	/	/
77	flavonoids	afroformosin	C ₁₇ H ₁₄ O ₅	297.07687	/	/	16.39
78	flavonoids	tectorigenin	C ₁₆ H ₁₂ O ₆	299.05611	/	/	/
79	flavonoids	alfalone	C ₁₇ H ₁₄ O ₅	297.07687	/	/	/
80	flavonoids	irisolidone	C ₁₇ H ₁₄ O ₆	313.07179	/	/	/
81	flavonoids	medicarpin	C ₁₆ H ₁₄ O ₄	269.08196	/	/	/
82	flavonoids	liquiritigenin/isoliquiritigenin	C ₁₅ H ₁₂ O ₄	255.06631	/	/	/
83	flavonoids	kaempferol-3-O- rutinoside	C ₂₇ H ₃₀ O ₁₅	593.15122	12.7	/	/
84	flavonoids	kaempferol (or luteolin)-O-hexoside/ isomers	C ₂₁ H ₂₀ O ₁₁	447.09331	13.8/14.56	13.76/14.66	13.75
85	flavonoids	isorhamnetin-3-O-hexoside	C ₂₂ H ₂₂ O ₁₂	477.10381	/	5.69	/
86	flavonoids	vitexin (apigenin-8- C-hexoside)/isovitexin	C ₂₁ H ₂₀ O ₁₀	431.09839	/	13.51/14.89	/
87	flavonoids	apigetrin (apigenin -7-hexoside)	C ₂₁ H ₂₀ O ₁₀	431.09839	/	/	/
88	flavonoids	chrysoeriol	C ₁₆ H ₁₂ O ₆	299.05614	/	/	/
89	flavonoids	chrysoeriol-7-hexoside	C ₂₂ H ₂₂ O ₁₁	461.10893	13.38	13.33/14.96	13.4
90	flavonoids	tricin	C ₁₇ H ₁₄ O ₇	329.06668	/	17.39/17.69	/
91	flavonoids	cynaroside (luteolin-7-hexoside)	C ₂₁ H ₂₀ O ₁₁	447.09328	13.8	13.79	13.75
92	flavonoids	apigenin-7-O-glucosylhexoside	C ₂₇ H ₃₀ O ₁₅	593.15122	13.85	13.82	13.8
93	flavonoids	diosmetin-7-O-rutinoside (diosmin)	C ₂₈ H ₃₂ O ₁₅	607.16684	/	/	/
94	flavonoids	cirsimarín	C ₂₃ H ₂₄ O ₁₁	475.12461	/	/	/
95	flavonoids	hispidulin-7-rutinoside/isomers	C ₂₈ H ₃₂ O ₁₅	607.16684	/	/	13.82

Nr.	Phytochemical class	Compound	Molecular formula	Adduct Ion (<i>m/z</i>) Monitored Negative Ion	Retention time (min)		
					SE	GE	CE
96	flavonoids	hispidulin- <i>O</i> -hexoside/ isomers	C ₂₂ H ₂₂ O ₁₁	461.10893	14.98	13.63/14.96	13.64
97	flavonoids	hispidulin	C ₁₆ H ₁₂ O ₆	299.05614	/	/	/
98	flavonoids	gallocatechin/epigallocatechin	C ₁₅ H ₁₄ O ₇	305.06668	/	5.47	15.73
99	flavonoids	luteolin	C ₁₅ H ₁₀ O ₆	285.04049	/	/	/
100	flavonoids	quercetin-3- <i>O</i> glucuronid	C ₂₁ H ₁₈ O ₁₃	477.06749	/	/	/
101	flavonoids	apigenin-7-rutinoside	C ₂₇ H ₃₀ O ₁₄	577.15630	/	/	13.49
102	flavonoids	narirutin (naringenin-7- <i>O</i> rutinoside)	C ₂₇ H ₃₂ O ₁₄	579.17195	/	12.24	/
103	flavonoids	apigenin-7- <i>O</i> -glucuronide	C ₂₁ H ₁₈ O ₁₁	445.07763	/	/	/
104	flavonoids	procyanidine B1/B2	C ₃₀ H ₂₆ O ₁₂	577.13515	/	/	/
105	flavonoids	procyanidine	C ₃₀ H ₂₆ O ₁₃	593.13006	16	/	/
106	flavonoids	diosmetin	C ₁₆ H ₁₂ O ₆	299.05611	/	16.93	16.92
107	flavonoids	isoquercitrin/quercitrin (quercetin-3-rhamnoside)	C ₂₁ H ₂₀ O ₁₁	447.09331	13.8	13.76/14.66	13.75
108	flavonoids	quercetin-3- <i>O</i> rutinoside	C ₃₃ H ₄₀ O ₂₁	771.19896	/	10.25	10.37
109	flavonoids	isorhamnetin-3- <i>O</i> -rutinosid	C ₂₈ H ₃₂ O ₁₆	623.16178	14	14	13.96
110	flavonoids	isorhamnetin-3- <i>O</i> -hexoside	C ₂₂ H ₂₂ O ₁₂	477.10387	13.9	13.87	11.97/13.86
111	flavonoids	quercetin-acetyl-hexoside	C ₂₃ H ₂₂ O ₃	345.14964	/	/	/
112	flavonoids	epigallocatechin gallate	C ₂₂ H ₁₈ O ₁₁	457.07766	/	/	/
113	flavonoids	amentoflavone	C ₃₀ H ₁₈ O ₁₀	537.08274	/	18.77	/
114	flavonoids	quercetin-3-(6-malonyl)- hexoside	C ₂₄ H ₂₂ O ₁₅	549.08862	13.09	/	/
115	flavonoids	quercetagenin (6- hydroxyquercetin)	C ₁₅ H ₁₀ O ₈	317.03032	/	/	7.82
116	flavonoids	phlorizin	C ₂₁ H ₂₄ O ₁₀	435.12969	/	/	10.27
117	flavonoids	chalcone	C ₁₅ H ₁₂ O	207.08156	/	/	/
118	flavonoids	robinin	C ₃₃ H ₄₀ O ₁₉	739.20913	12.42	12.39	12.67
119	flavonoids	tomentosanol E	C ₃₀ H ₃₆ O ₇	507.23885	/	/	/
120	flavonoids	tomentosanol D	C ₂₀ H ₂₀ O ₆	355.11874	/	/	/
121	flavonoids	vitexin-2- <i>O</i> -rhamnoside	C ₂₇ H ₃₀ O ₁₄	577.15630	/	/	14.29
122	flavonoids	sophoraflavanone G/ isomers	C ₂₅ H ₂₈ O ₆	423.18134	/	19.48	24.22
123	flavonoids	leachianone A	C ₂₆ H ₃₀ O ₆	437.19699	/	/	/
124	flavonoids	lehmannin	C ₂₅ H ₂₈ O ₅	407.18642	/	/	/
125	flavonoids	kushenol/ leachianone isomers	C ₂₅ H ₂₈ O ₅	407.18642	/	/	/
126	flavonoids	prostatrol F	C ₂₅ H ₂₈ O ₄	391.19151	/	/	/
127	flavonoids	prostatrol C	C ₂₁ H ₂₂ O ₅	353.13947	/	/	/
128	flavonoids	alopecurone A	C ₃₉ H ₃₈ O ₉	649.24433	/	/	/
129	flavonoids	sophoronol A	C ₂₀ H ₁₈ O ₇	369.09800	/	/	/
130	flavonoids	sophoronol B	C ₂₁ H ₂₀ O ₈	399.10857	/	/	/
131	flavonoids	2'-hydroxygenistein	C ₁₅ H ₁₀ O ₆	285.04049	/	/	/
132	flavonoids	ginkgetin	C ₃₂ H ₂₂ O ₁₀	565.11404	/	21.39	21.37
133	flavonoids	daphnin	C ₁₅ H ₁₆ O ₉	339.072155	5.16	5.18	/
134	flavonoids	morachalcone	C ₂₀ H ₂₀ O ₅	339.1237966	/	/	/
135	flavonoids	cyanidin-3- <i>O</i> -hexoside	C ₂₁ H ₂₁ ClO ₁₁	483.0699619	/	/	/
136	monoterpenes	albiflorin	C ₂₃ H ₂₈ O ₁₁	479.15591	/	/	/
137	polyholosides	inulin	C ₁₈ H ₃₄ O ₁₇	521.17235	/	/	/
138	sesquiterpenes	abscisic acid	C ₁₅ H ₂₀ O ₄	263.12891	14.87	/	14.84
139	sesquiterpenes	cynaropicrin	C ₁₉ H ₂₂ O ₆	345.13439	/	11.5	/
140	sesquiterpenes	lactucopicrin	C ₂₃ H ₂₂ O ₇	409.12930	7.67	/	/
141	sesquiterpenes	lactucin	C ₁₅ H ₁₆ O ₅	275.09252	/	/	/
142	sesquiterpenes	valerenic acid	C ₁₅ H ₂₂ O ₂	233.15473	/	/	/
143	triterpenes	betulin	C ₃₀ H ₅₀ O ₂	441.37383	/	/	/
144	triterpenes	oleanolic acid	C ₃₀ H ₄₈ O ₃	455.35309	/	/	/
145	triterpenes	ursolic acid	C ₃₀ H ₄₈ O ₃	455.35307	/	/	/
146	triterpenes	taraxasterol	C ₃₀ H ₄₈ O	423.36326	/	/	/

Nr.	Phytochemical class	Compound	Molecular formula	Adduct Ion (<i>m/z</i>) Monitored Negative Ion	Retention time (min)		
					SE	GE	CE
147	triterpenes	taraxerol	C ₃₀ H ₅₀ O	425.37889	/	/	/
148	triterpenes	spicoside A	C ₃₀ H ₂₆ O ₁₅	625.11992	/	/	/
149	triterpenes	taraxerone	C ₃₀ H ₄₈ O	423.36324	/	/	/
150	triterpenes	calenduloside G/isomers	C ₄₂ H ₆₆ O ₁₄	793.43800	21.02/23.03	/	22.99
151	triterpenes	calenduloside E/isomers	C ₃₆ H ₅₆ O ₉	631.38518	23.47	/	/
152	triterpenes	calenduloside F/isomers	C ₄₂ H ₆₆ O ₁₄	793.43800	/	/	/



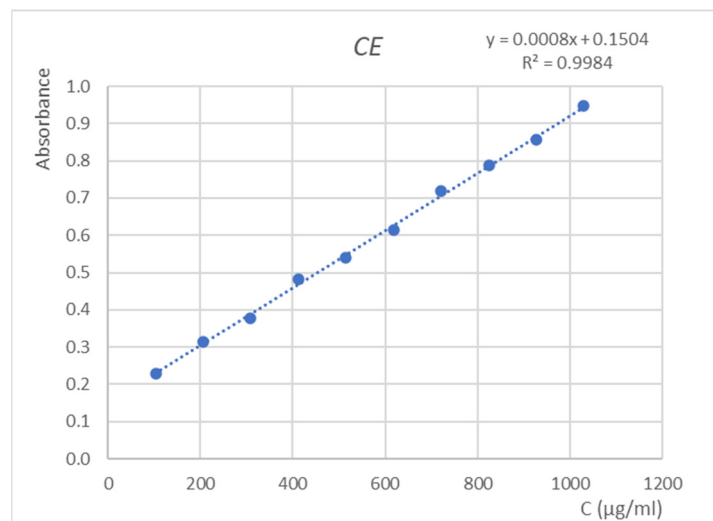
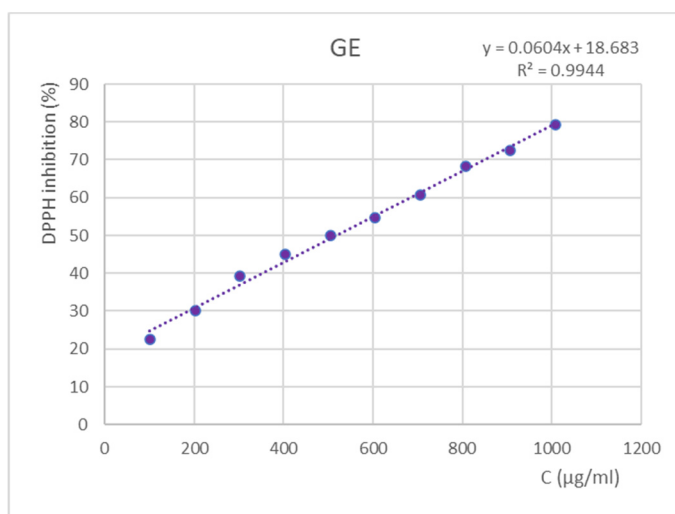
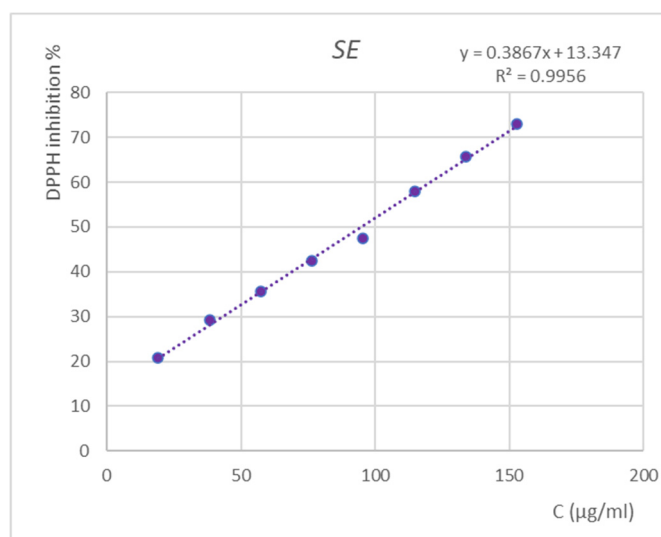


Figure S32. Regression trendlines and equations – FRAP assay (SE = *Sophorae flos* extract; GE = *Ginkgo bilobae folium* extract; CE = *Calendulae flos* extract).



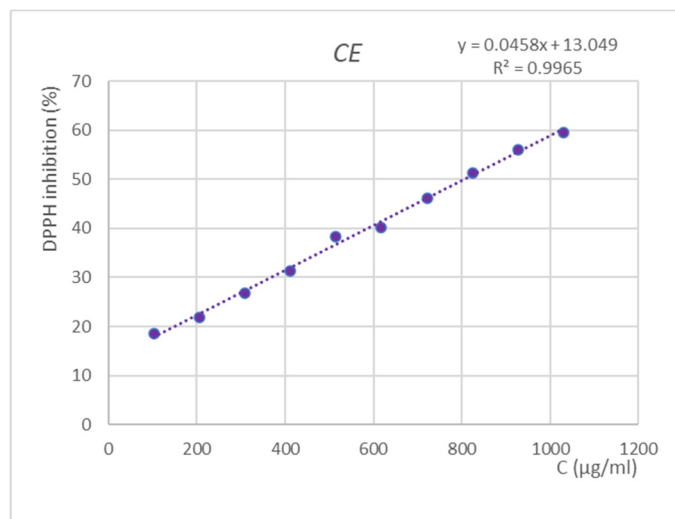
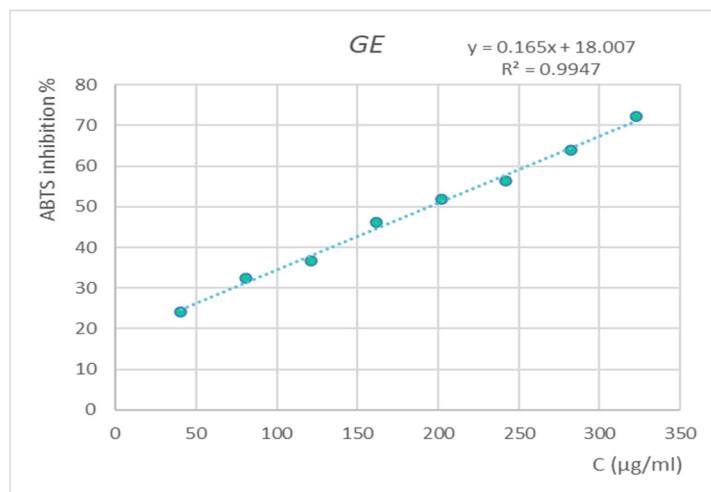
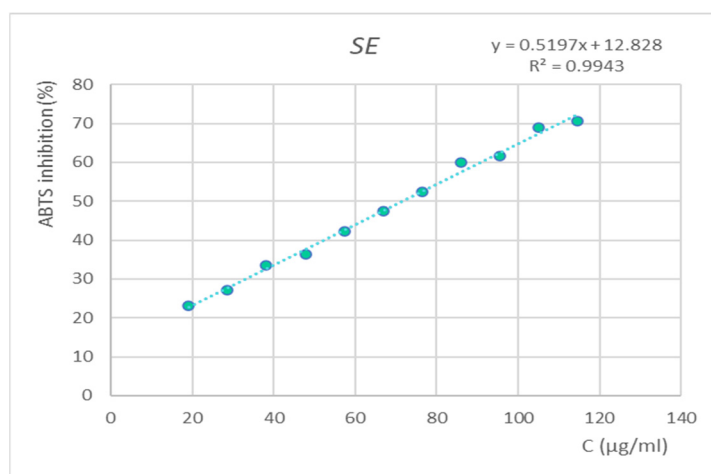


Figure S33. Regression trendlines and equations – DPPH assay (SE = *Sophorae flos* extract; GE = *Ginkgo bilobae folium* extract; CE = *Calendulae flos* extract).



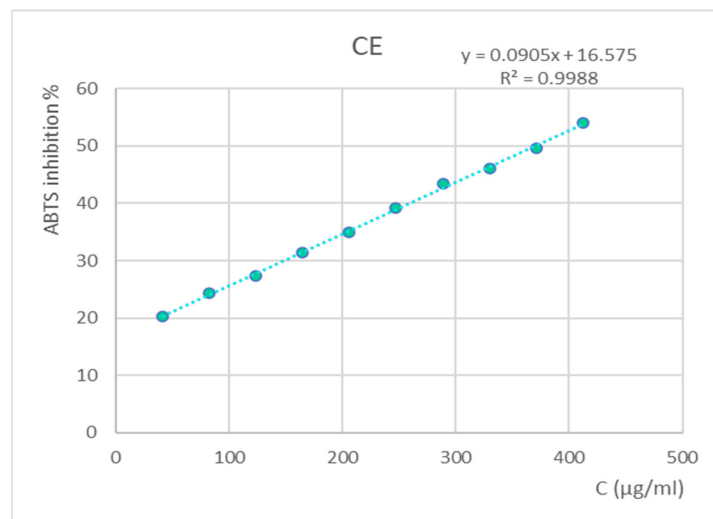


Figure S34. Regression trendlines and equations – ABTS assay (SE = *Sophorae flos* extract; GE = *Ginkgo bilobae folium* extract; CE = *Calendulae flos* extract).

Table S2. Correlation between flavonoid content (FLV) and antioxidant methods.

		ABTS (log₁₀)	DPPH(log₁₀)	FRAP(log₁₀)	FLV
ABTS (log₁₀)	Pearson correlation	1.000	0.979	0.894	0.924
	Sig.(2-tailed)	/	0.129	0.296	0.249
DPPH (log₁₀)	Pearson correlation	0.979	1.000	0.966	0.982
	Sig.(2-tailed)	0.129	/	0.167	0.120
FRAP (log₁₀)	Pearson correlation	0.894	0.966	1.000	0.997
	Sig.(2-tailed)	0.296	0.167	/	0.047*
FLV	Pearson correlation	0.924	0.982	0.997	1.000
	Sig.(2-tailed)	0.249	0.120	0.047*	/

*significant at 0.05 level

Table S3. Correlation between phenolcarboxylic acids content (PCA) and antioxidant methods.

		ABTS (log₁₀)	DPPH(log₁₀)	FRAP(log₁₀)	PCA
ABTS (log₁₀)	Pearson correlation	1.000	0.979	0.894	0.878
	Sig.(2-tailed)	/	0.129	0.296	0.318
DPPH (log₁₀)	Pearson correlation	0.979	1.000	0.966	0.956
	Sig.(2-tailed)	0.129	/	0.167	0.189
FRAP (log₁₀)	Pearson correlation	0.894	0.966	1.000	0.999
	Sig.(2-tailed)	0.296	0.167	/	0.022
PCA	Pearson correlation	0.878	0.956	0.999*	1.000
	Sig.(2-tailed)	0.318	0.189	0.022	/

*significant at 0.05 level

Table S4. Correlation between polyphenolic content (PPC) and antioxidant methods.

		ABTS (log₁₀)	DPPH(log₁₀)	FRAP(log₁₀)	PPC
ABTS (log₁₀)	Pearson correlation	1.000	0.979	0.894	0.952
	Sig.(2-tailed)	/	0.129	0.296	0.198
DPPH (log₁₀)	Pearson correlation	0.979	1.000	0.966	0.994
	Sig.(2-tailed)	0.129	/	0.167	0.068
FRAP (log₁₀)	Pearson correlation	0.894	0.966	1.000	0.988
	Sig.(2-tailed)	0.296	0.167	/	0.099
PPC	Pearson correlation	0.952	0.994	0.988	1.000
	Sig.(2-tailed)	0.198	0.068	0.099	/

* significant at 0.05 level

Table S5. Correlation between UHPLC-HRMS/MS method (QHPLC), antioxidant methods and spectrophotometric methods.

		QHPLC
ABTS (log₁₀)	Pearson correlation	0.896
	Sig.(2-tailed)	0.292
DPPH (log₁₀)	Pearson correlation	0.967
	Sig.(2-tailed)	0.163
FRAP (log₁₀)	Pearson correlation	1.000
	Sig.(2-tailed)	0.004*
PPC	Pearson correlation	0.989
	Sig.(2-tailed)	0.095
PCA	Pearson correlation	0.999
	Sig.(2-tailed)	0.026*

		QHPLC
FLV	Pearson correlation	0.998
	Sig.(2-tailed)	0.043*
QHPLC	Pearson correlation	1.000
	Sig.(2-tailed)	/

* significant at 0.05 level

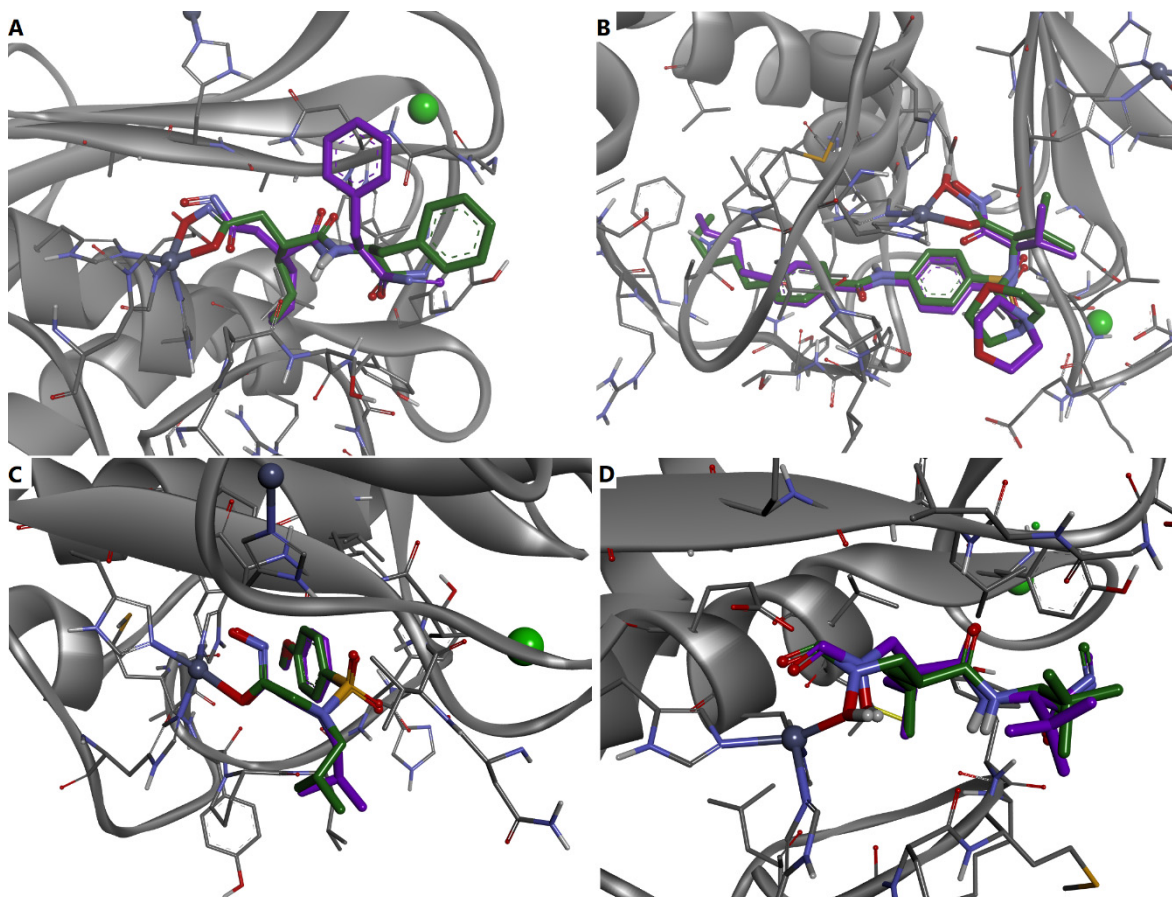


Figure S35. Superposition of predicted conformations for MMPs inhibitors on experimentally determined conformations. A – MMP1 inhibitor PLH, B – MMP2 inhibitor SC-74020; C – MMP3 inhibitor NGH; D – MMP9 inhibitor NFH.

Table S6. Molecular docking results after screening the selected phytochemicals.

Compound	MMP1		MMP2		MMP3		MMP9	
	ΔG (kcal/mol)	LE	ΔG (kcal/mol)	LE	ΔG (kcal/mol)	LE	ΔG (kcal/mol)	LE
bilobalide	-6.076	0.264 2	-7.183	0.312 3	-6.522	0.283 6	-5.844	0.254 1
bilobetin	-9.194	0.224 2	-9.645	0.235 2	-9.334	0.227 7	-9.347	0.228 0
caffeic acid	-7.677	0.590 5	-7.303	0.561 8	-7.256	0.558 2	-8.245	0.634 2
calendoflavoside	-8.576*	0.194 9	-7.401*	0.168 2	-7.860	0.178 6	-7.629*	0.173 4
calenduloside E	-7.911	0.175 8	-9.330	0.207 3	-7.574*	0.168 3	-7.771*	0.172 7

calenduloside F	-7.688	0.137 3	-8.626	0.154 0	-7.513*	0.134 2	-7.467*	0.133 3
calenduloside G	-8.383*	0.149 7	-9.923*	0.177 2	-8.384*	0.149 7	-9.655*	0.172 4
calenduloside H	-7.565	0.112 9	-8.852*	0.132 1	-8.367	0.124 9	-8.395	0.125 3
catechin	-8.679	0.413 3	-7.853	0.374 0	-7.864*	0.374 5	-9.748	0.464 2
chlorogenic acid	-8.912*	0.356 5	-9.512	0.380 5	-8.807	0.352 3	-10.665	0.426 6
fisetin	-9.189	0.437 6	-8.756	0.417 0	-8.403	0.400 1	-9.103	0.433 5
ginkgolide A	-7.329	0.252 7	-7.579	0.261 3	-8.244	0.284 3	-7.362*	0.253 9
ginkgolide B	-6.495	0.216 5	-7.667*	0.255 6	-7.105	0.236 8	-6.818*	0.227 3
ginkgolide C	-6.360	0.205 2	-8.121	0.262 0	-7.097*	0.228 9	-6.953*	0.224 3
isoquercitrin	-8.529*	0.258 5	-8.215	0.248 9	-8.060*	0.244 2	-8.760	0.265 5
isorhamnetin	-8.303	0.361 0	-7.356	0.319 8	-7.881	0.342 7	-8.680	0.377 4
kaempferol	-8.342	0.397 2	-8.288	0.394 7	-8.001	0.381 0	-8.627	0.410 8
kaikasaponin I	-8.541	0.155 3	-8.625	0.156 8	-8.884	0.161 5	-7.896*	0.143 6
kaikasaponin III	-8.400*	0.129 2	-9.848*	0.151 5	-8.615*	0.132 5	-8.162	0.125 6
narcissin	-8.975*	0.204 0	-7.919*	0.180 0	-8.865*	0.201 5	-8.294*	0.188 5
quercetin	-9.280	0.421 8	-8.694	0.395 2	-8.508	0.386 7	-8.944	0.406 5
rhamnetin	-9.470	0.411 7	-8.275	0.359 8	-8.642	0.375 7	-9.184	0.399 3
rutin	-8.164	0.189 9	-8.054*	0.187 3	-9.406*	0.218 7	-8.730*	0.203 0
sophoricoside	-7.801*	0.251 6	-10.655	0.343 7	-9.547	0.308 0	-11.492*	0.370 7
typhaneoside	-8.619	0.159 6	-8.506	0.157 5	-9.445*	0.174 9	-7.595*	0.140 6
PLH	-6.467*	0.258 7	-	-	-	-	-	-
SC-74020	-	-	-9.306*	0.232 7	-	-	-	-
NGH	-	-	-	-	-7.509*	0.357 6	-	-
NFH	-	-	-	-	-	-	-6.913*	0.314 2

ΔG – binding energy, LE – ligand efficiency, * - presence of metal bonds between the docked compound and catalytic zinc.

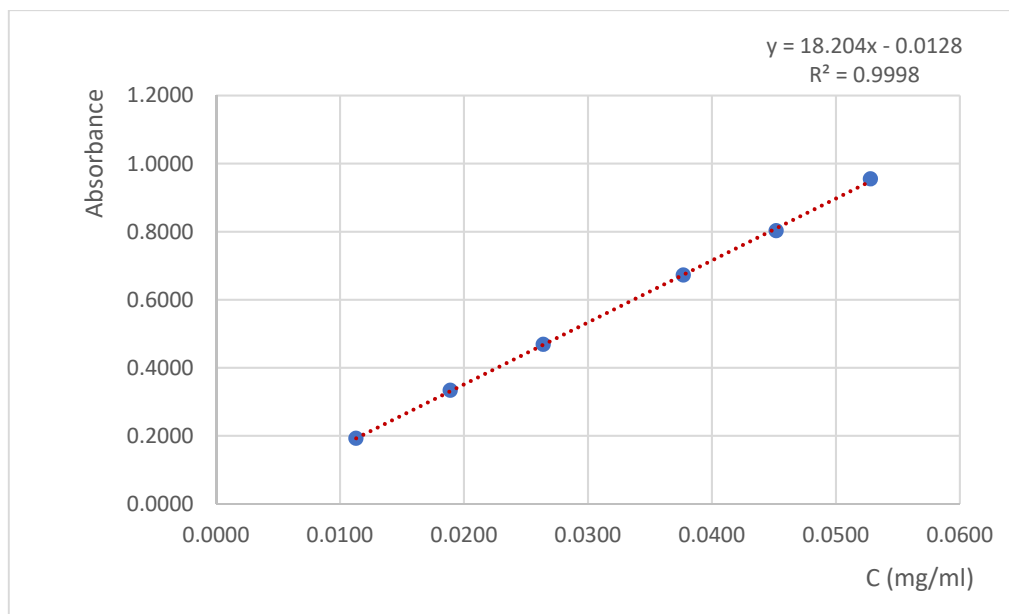


Figure S36. Chlorogenic acid standard curve.

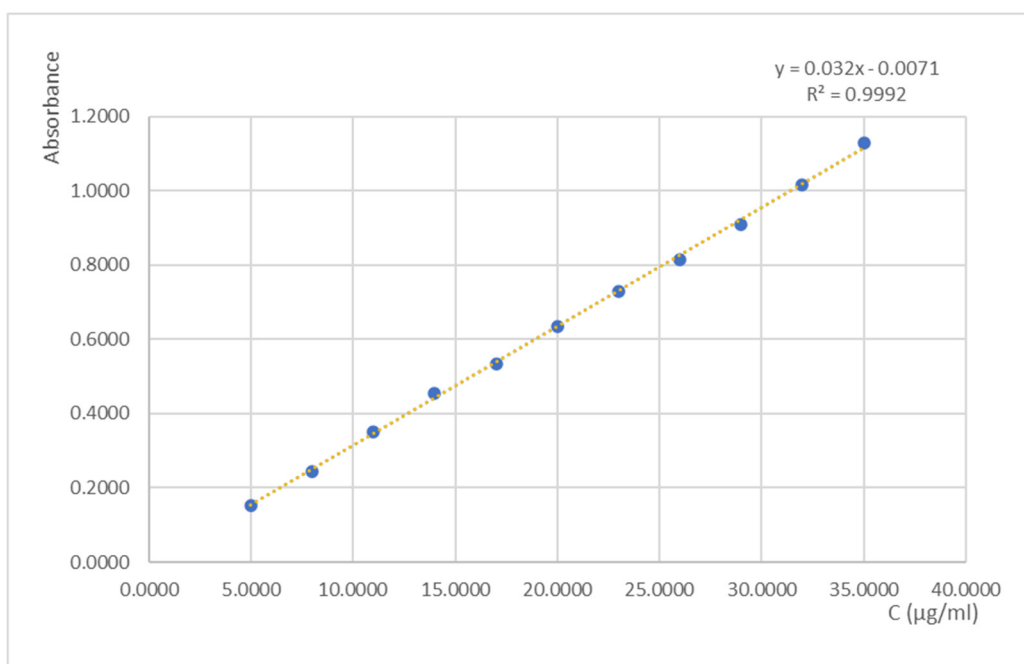


Figure S37. Rutin standard curve.

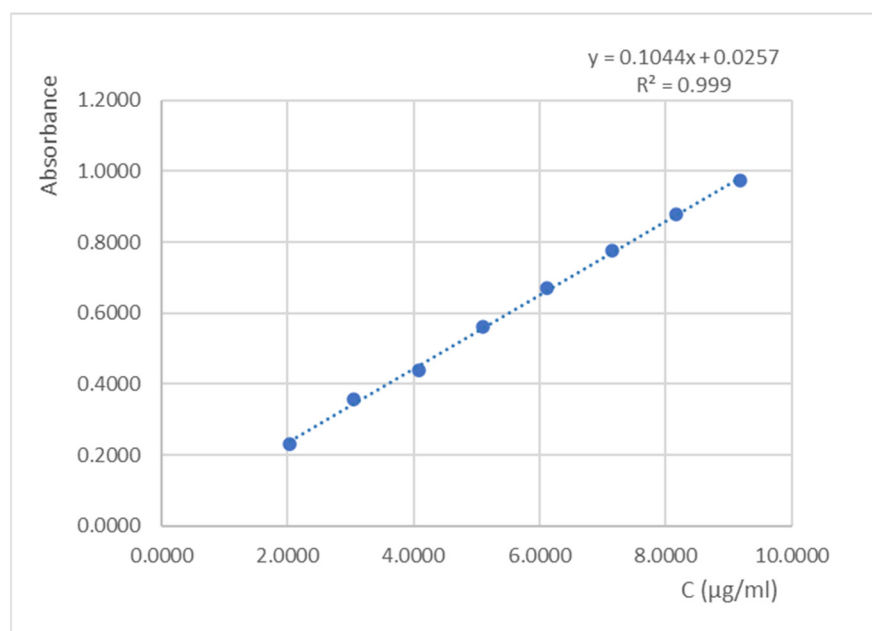


Figure S38. Tannic acid standard curve.