Supplementary Materials

Rational Design of Multifunctional Ferulic Acid Derivatives Aimed for Alzheimer's and Parkinson's diseases

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Contents

Table S1. Ferulic acid (FA) derivatives designed in this work.

	R_1	R_2	R_3	R_4	R_5
FA	H	H	H	H	H
FA-1	H	H	H	COOH	COOH
FA-2	H	H	H	COOH	NH2
FA-3	H	H	H	COOH	OH
FA-4	H	H	H	COOH	SH
FA-5	H	H	H	NH2	COOH
FA-6	H	H	H	NH2	NH2
FA-7	H	H	H	NH2	OH
FA-8	H	H	H	NH2	SH
FA-9	H	H	H	OH	COOH
FA-10	H	H	H	OH	NH2
FA-11	H	H	H	OH	OH
FA-12	H	H	H	OH	SH
FA-13	H	H	H	SH	COOH
FA-14	H	H	H	SH	NH2
FA-15	H	H	H	SH	OH
FA-16	H	H	H	SH	SH
FA-17	COOH	H	H	H	COOH
FA-18	COOH	H	H	H	NH2
FA-19	COOH	H	H	H	OH
FA-20	COOH	H	H	H	SH
FA-21	NH2	H	H	H	COOH
FA-22	NH2	H	H	H	NH2
FA-23	NH2	H	H	H	OH
FA-24	NH2	H	H	H	SH
FA-25	OH	H	H	H	COOH
FA-26	OH	H	H	H	NH2
FA-27	OH	H	H	H	OH
FA-28	OH	H	H	H	SH
FA-29	SH	H	H	H	COOH
FA-30	SH	H	H	H	NH2
FA-31	SH	H	H	H	OH
FA-32	SH	H	H	H	SH
FA-33	H	COOH	H	H	COOH
FA-34	H	COOH	H	H	NH2
FA-35	H	COOH	H	H	OH
FA-36	H	COOH	H	H	SH
FA-37	H	NH2	H	H	COOH
FA-38	H	NH2	H	H	NH2
FA-39	H	NH2	H	H	OH

FA-40	H	NH2	H	H	SH
FA-41	H	OH	H	H	COOH
FA-42	H	OH	H	H	NH2
FA-43	H	OH	H	H	OH
FA-44	H	OH	H	H	SH
FA-45	H	SH	H	H	COOH
FA-46	H	SH	H	H	NH2
FA-47	H	SH	H	H	OH
FA-48	H	SH	H	H	SH
FA-49	H	H	COOH	H	COOH
FA-50	H	H	COOH	H	NH2
FA-51	H	H	COOH	H	OH
FA-52	H	H	COOH	H	SH
FA-53	H	H	NH2	H	COOH
FA-54	H	H	NH2	H	NH2
FA-55	H	H	NH2	H	OH
FA-56	H	H	NH2	H	SH
FA-57	H	H	OH	H	COOH
FA-58	H	H	OH	H	NH2
FA-59	H	H	OH	H	OH
FA-60	H	H	OH	H	SH
FA-61	H	H	SH	H	COOH
FA-62	H	H	SH	H	NH2
FA-63	H	H	SH	H	OH
FA-64	H	H	SH	H	SH
FA-65	H	H	H	H	COOH
FA-66	H	H	H	H	NH2
FA-67	H	H	H	H	OH
FA-68	H	H	H	H	SH
FA-69	COOH	H	H	COOH	H
FA-70	COOH	H	H	NH2	H
FA-71	COOH	H	H	OH	H
FA-72	COOH	H	H	SH	H
FA-73	NH2	H	H	COOH	H
FA-74	NH2	H	H	NH2	H
FA-75	NH2	H	H	OH	H
FA-76	NH2	H	H	SH	H
FA-77	OH	H	H	COOH	H
FA-78	OH	H	H	NH2	H
FA-79	OH	H	H	OH	H
FA-80	OH	H	H	SH	H
FA-81	SH	H	H	COOH	H
FA-82	SH	H	H	NH2	H

FA-83	SH	H	H	OH	H
FA-84	SH	H	H	SH	H
FA-85	H	COOH	H	COOH	H
FA-86	H	NH2	H	COOH	H
FA-87	H	OH	H	COOH	H
FA-88	H	SH	H	COOH	H
FA-89	H	H	COOH	COOH	H
FA-90	H	H	NH2	COOH	H
FA-91	H	H	OH	COOH	H
FA-92	H	H	SH	COOH	H
FA-93	H	H	H	COOH	H
FA-94	H	COOH	H	NH2	H
FA-95	H	NH2	H	NH2	H
FA-96	H	OH	H	NH2	H
FA-97	H	SH	H	NH2	H
FA-98	H	H	COOH	NH2	H
FA-99	H	H	NH2	NH2	H
FA-100	H	H	OH	NH2	H
FA-101	H	H	SH	NH2	H
FA-102	H	H	H	NH2	H
FA-103	H	COOH	H	OH	H
FA-104	H	NH2	H	OH	H
FA-105	H	OH	H	OH	H
FA-106	H	SH	H	OH	H
FA-107	H	H	COOH	OH	H
FA-108	H	H	NH2	OH	H
FA-109	H	H	OH	OH	H
FA-110	H	H	SH	OH	H
FA-111	H	H	H	OH	H
FA-112	H	COOH	H	SH	H
FA-113	H	NH2	H	SH	H
FA-114	H	OH	H	SH	H
FA-115	H	SH	H	SH	H
FA-116	H	H	COOH	SH	H
FA-117	H	H	NH2	SH	H
FA-118	H	H	OH	SH	H
FA-119	H	H	SH	SH	H
FA-120	H	H	H	SH	H
FA-121	COOH	COOH	H	H	H
FA-122	COOH	NH2	H	H	H
FA-123	COOH	OH	H	H	H
FA-124	COOH	SH	H	H	H
FA-125	COOH	H	COOH	H	H

FA-126	COOH	H	NH2	H	H
FA-127	COOH	H	OH	H	H
FA-128	COOH	H	SH	H	H
FA-129	COOH	H	H	H	H
FA-130	NH2	COOH	H	H	H
FA-131	NH2	NH2	H	H	H
FA-132	NH2	OH	H	H	H
FA-133	NH2	SH	H	H	H
FA-134	NH2	H	COOH	H	H
FA-135	NH2	H	NH2	H	H
FA-136	NH2	H	OH	H	H
FA-137	NH2	H	SH	H	H
FA-138	NH2	H	H	H	H
FA-139	OH	COOH	H	H	H
FA-140	OH	NH2	H	H	H
FA-141	OH	OH	H	H	H
FA-142	OH	SH	H	H	H
FA-143	OH	H	COOH	H	H
FA-144	OH	H	NH2	H	H
FA-145	OH	H	OH	H	H
FA-146	OH	H	SH	H	H
FA-147	OH	H	H	H	H
FA-148	SH	COOH	H	H	H
FA-149	SH	NH2	H	H	H
FA-150	SH	OH	H	H	H
FA-151	SH	SH	H	H	H
FA-152	SH	H	COOH	H	H
FA-153	SH	H	NH2	H	H
FA-154	SH	H	OH	H	H
FA-155	SH	H	SH	H	H
FA-156	SH	H	H	H	H
FA-157	H	COOH	COOH	H	H
FA-158	H	NH2	COOH	H	H
FA-159	H	OH	COOH	H	H
FA-160	H	SH	COOH	H	H
FA-161	H	COOH	NH2	H	H
FA-162	H	NH2	NH2	H	H
FA-163	H	OH	NH2	H	H
FA-164	H	SH	NH2	H	H
FA-165	H	COOH	OH	H	H
FA-166	H	NH2	OH	H	H
FA-167	H	OH	OH	H	H
FA-168	H	SH	OH	H	H

FA-169	H	COOH	SH	H	H
FA-170	H	NH2	SH	H	H
FA-171	H	OH	SH	H	H
FA-172	H	SH	SH	H	H
FA-173	H	COOH	H	H	H
FA-174	H	NH2	H	H	H
FA-175	H	OH	H	H	H
FA-176	H	SH	H	H	H
FA-177	H	H	COOH	H	H
FA-178	H	H	NH2	H	H
FA-179	H	H	OH	H	H
FA-180	H	H	SH	H	H

Table S2. Values of the ADME properties: water/octanol partition coefficient (logP), topological polar surface area (PSA), number of heavy atoms (^{X}At), molecular weight (MW), number of H-bond acceptors (HBA), number of H-bond donors (HBD), rotatable bonds (RB), and molar refractivity (MR); toxicity descriptors: oral rat 50 percent lethal dose (LD50); Ames' mutagenicity (M); the synthetic accessibility (SA); and selection score (S^{S}).

	logP	PSA	^{x}At	MW	HB^{A}	HB^{D}	RB	^{M}R	LD_{50}	M	SA	S^{S}
FA	1.25	66.76	14	194.19	4	2	3	51.33	4742.73	0.22	2.13	3.77
FA-1	-0.30	141.36	20	282.20	8	4	5	64.87	1672.76	0.52	3.72	2.99
FA-2	-0.39	130.08	18	253.21	7	5	4	62.32	2289.44	0.33	3.30	3.34
FA-3	-0.10	124.29	18	254.19	7	4	4	59.57	1181.06	0.28	3.26	3.23
FA-4	0.35	104.06	18	270.26	6	3	4	65.16	1003.90	0.16	3.32	3.31
FA-5	-0.15	130.08	18	253.21	7	5	4	61.42	3936.05	0.18	3.51	3.56
FA-6	-0.24	118.81	16	224.22	6	6	3	58.87	2458.08	0.41	3.12	3.20
FA-7	0.06	113.01	16	225.20	6	5	3	56.12	1117.37	0.18	3.09	3.34
FA-8	0.51	92.78	16	241.27	5	4	3	61.71	1911.70	0.04	3.15	3.78
FA-9	1.21	124.29	18	254.19	7	4	4	59.86	3182.26	0.59	3.41	3.27
FA-10	1.12	113.01	16	225.20	6	5	3	57.31	1101.01	0.14	3.01	3.40
FA-11	1.41	107.22	16	226.18	6	4	3	54.57	1964.96	0.33	2.98	3.35
FA-12	1.86	86.99	16	242.25	5	3	3	60.15	2424.68	0.04	3.03	3.85
FA-13	0.76	104.06	18	270.26	6	3	4	66.22	1213.44	0.29	3.51	3.20
FA-14	0.67	92.78	16	241.27	5	4	3	63.67	1358.57	0.21	3.13	3.35
FA-15	0.97	86.99	16	242.25	5	3	3	60.92	2485.60	0.23	3.09	3.46
FA-16	1.42	66.76	16	258.32	4	2	3	66.51	2034.75	0.28	3.15	3.37
FA-17	-0.05	141.36	20	282.20	8	4	5	64.87	3249.58	0.43	3.63	3.19
FA-18	-0.14	130.08	18	253.21	7	5	4	62.32	1928.03	0.64	3.23	3.16
FA-19	0.16	124.29	18	254.19	7	4	4	59.57	2351.06	0.27	3.15	3.41
FA-21	0.29	130.08	18	253.21	7	5	4	61.42	4091.49	0.25	3.48	3.50
FA-22	0.20	118.81	16	224.22	6	6	3	58.87	3023.67	0.19	3.09	3.42
FA-23	0.49	113.01	16	225.20	6	5	3	56.12	2352.39	0.25	3.06	3.44

FA-24	0.94	92.78	16	241.27	5	4	3	61.71	1979.75	0.08	3.12	3.64
FA-25	0.43	124.29	18	254.19	7	4	4	59.86	3493.74	0.36	3.48	3.39
FA-26	0.34	113.01	16	225.20	6	5	3	57.31	3635.20	0.11	3.09	3.70
FA-27	0.64	107.22	16	226.18	6	4	3	54.57	3011.62	0.20	3.05	3.54
FA-28	1.09	86.99	16	242.25	5	3	3	60.15	1506.13	0.07	3.12	3.61
FA-29	0.82	104.06	18	270.26	6	3	4	66.22	3312.19	0.30	3.48	3.41
FA-30	0.73	92.78	16	241.27	5	4	3	63.67	3573.17	0.48	3.09	3.38
FA-31	1.03	86.99	16	242.25	5	3	3	60.92	1807.44	0.56	3.06	3.20
FA-32	1.47	66.76	16	258.32	4	2	3	66.51	1312.43	0.25	3.12	3.30
FA-33	0.27	141.36	20	282.20	8	4	5	65.25	3646.68	0.07	3.68	3.60
FA-34	0.18	130.08	18	253.21	7	5	4	62.70	3807.34	0.19	3.42	3.55
FA-35	0.48	124.29	18	254.19	7	4	4	59.95	3903.17	0.22	3.37	3.53
FA-36	0.92	104.06	18	270.26	6	3	4	65.54	2349.00	0.24	3.43	3.39
FA-37	0.18	130.08	18	253.21	7	5	4	62.70	3599.69	0.35	3.42	3.41
FA-38	0.09	118.81	16	224.22	6	6	3	60.15	1349.50	0.35	3.02	3.12
FA-39	0.39	113.01	16	225.20	6	5	3	57.41	3193.72	0.21	3.01	3.55
FA-40	0.84	92.78	16	241.27	5	4	3	62.99	2361.13	0.14	3.04	3.57
FA-41	0.68	124.29	18	254.19	7	4	4	59.95	3185.60	0.04	3.40	3.85
FA-42	0.59	113.01	16	225.20	6	5	3	57.41	3124.48	0.25	3.01	3.51
FA-43	0.89	107.22	16	226.18	6	4	3	54.66	2148.21	0.16	2.99	3.52
FA-44	1.34	86.99	16	242.25	5	3	3	60.25	1950.51	0.34	3.02	3.33
FA-46	0.84	92.78	16	241.27	5	4	3	62.99	2671.60	0.31	3.05	3.42
FA-47	1.13	86.99	16	242.25	5	3	3	60.25	1623.64	0.41	3.03	3.25
FA-49	0.92	141.36	20	282.20	8	4	5	65.25	3698.65	0.27	3.70	3.31
FA-50	0.83	130.08	18	253.21	7	5	4	62.70	4869.38	0.13	3.38	3.69
FA-51	1.13	124.29	18	254.19	7	4	4	59.95	3990.69	0.35	3.36	3.44
FA-53	0.41	130.08	18	253.21	7	5	4	62.70	3442.03	0.22	3.42	3.50
FA-54	0.32	118.81	16	224.22	6	6	3	60.15	1620.47	0.34	3.02	3.17
FA-55	0.62	113.01	16	225.20	6	5	3	57.41	2973.63	0.26	3.01	3.49

FA-58	0.39	113.01	16	225.20	6	5	3	57.41	2788.03	0.31	2.96	3.44
FA-59	0.68	107.22	16	226.18	6	4	3	54.66	2396.38	0.24	2.99	3.46
FA-62	1.06	92.78	16	241.27	5	4	3	62.99	1542.31	0.27	3.05	3.33
FA-63	1.36	86.99	16	242.25	5	3	3	60.25	1553.81	0.46	3.03	3.22
FA-65	0.77	104.06	17	238.20	6	3	4	58.29	4344.40	0.17	3.31	3.62
FA-66	0.68	92.78	15	209.20	5	4	3	55.74	4961.04	0.27	2.90	3.60
FA-67	0.98	86.99	15	210.19	5	3	3	52.99	4195.81	0.27	2.83	3.58
FA-69	-0.82	141.36	20	282.20	8	4	5	64.49	1688.65	0.38	3.47	2.97
FA-70	-0.67	130.08	18	253.21	7	5	4	61.04	2959.29	0.49	3.26	3.19
FA-71	0.69	124.29	18	254.19	7	4	4	59.48	1781.70	0.41	3.13	3.26
FA-72	0.25	104.06	18	270.26	6	3	4	65.84	1747.36	0.28	3.26	3.32
FA-73	-0.48	130.08	18	253.21	7	5	4	61.04	2226.10	0.33	3.30	3.21
FA-74	-0.33	118.81	16	224.22	6	6	3	57.59	3364.27	0.19	3.16	3.43
FA-75	1.03	113.01	16	225.20	6	5	3	56.03	2291.55	0.28	2.99	3.42
FA-76	0.58	92.78	16	241.27	5	4	3	62.39	1506.03	0.36	3.17	3.24
FA-77	-0.34	124.29	18	254.19	7	4	4	59.48	1566.95	0.39	3.28	3.22
FA-78	-0.18	113.01	16	225.20	6	5	3	56.03	1579.79	0.26	3.13	3.33
FA-79	1.17	107.22	16	226.18	6	4	3	54.47	2073.78	0.36	2.98	3.34
FA-80	0.73	86.99	16	242.25	5	3	3	60.83	1802.60	0.15	3.13	3.48
FA-81	0.05	104.06	18	270.26	6	3	4	65.84	1641.82	0.27	3.30	3.31
FA-82	0.20	92.78	16	241.27	5	4	3	62.39	2934.47	0.12	3.17	3.63
FA-83	1.56	86.99	16	242.25	5	3	3	60.83	5133.66	0.33	3.00	3.55
FA-84	1.11	66.76	16	258.32	4	2	3	67.19	1258.31	0.15	3.16	3.40
FA-85	-0.50	141.36	20	282.20	8	4	5	64.87	1309.65	0.39	3.63	2.89
FA-86	-0.59	130.08	18	253.21	7	5	4	62.32	2489.84	0.33	3.24	3.24
FA-87	-0.09	124.29	18	254.19	7	4	4	59.57	1218.06	0.28	3.22	3.25
FA-88	0.16	104.06	18	270.26	6	3	4	65.16	510.09	0.01	3.28	3.77
FA-89	0.15	141.36	20	282.20	8	4	5	64.87	2452.13	0.41	3.57	3.15
FA-90	-0.36	130.08	18	253.21	7	5	4	62.32	2090.73	0.33	3.22	3.33

FA-91	-0.29	124.29	18	254.19	7	4	4	59.57	1694.60	0.54	3.16	3.18
FA-92	0.39	104.06	18	270.26	6	3	4	65.16	1232.70	0.10	3.24	3.47
FA-93	0.00	104.06	17	238.20	6	3	4	57.91	1988.85	0.19	3.10	3.45
FA-94	-0.35	130.08	18	253.21	7	5	4	61.42	1778.62	0.49	3.42	3.18
FA-95	-0.44	118.81	16	224.22	6	6	3	58.87	2377.73	0.77	3.05	2.94
FA-96	0.07	113.01	16	225.20	6	5	3	56.12	1340.74	0.23	3.04	3.33
FA-98	0.30	130.08	18	253.21	7	5	4	61.42	2462.27	0.21	3.40	3.44
FA-99	-0.21	118.81	16	224.22	6	6	3	58.87	2551.25	0.36	3.05	3.25
FA-100	-0.14	113.01	16	225.20	6	5	3	56.12	1229.27	0.39	3.00	3.21
FA-101	0.54	92.78	16	241.27	5	4	3	61.71	558.39	0.45	3.07	2.99
FA-102	0.15	92.78	15	209.20	5	4	3	54.46	3063.91	0.20	2.94	3.56
FA-103	1.01	124.29	18	254.19	7	4	4	59.86	2566.85	0.46	3.34	3.28
FA-104	0.92	113.01	16	225.20	6	5	3	57.31	2624.82	0.27	2.97	3.46
FA-105	1.42	107.22	16	226.18	6	4	3	54.57	1630.44	0.36	2.96	3.29
FA-106	1.66	86.99	16	242.25	5	3	3	60.15	1014.35	0.01	2.99	3.96
FA-107	1.66	124.29	18	254.19	7	4	4	59.86	3704.29	0.22	3.29	3.53
FA-108	1.15	113.01	16	225.20	6	5	3	57.31	2381.79	0.10	2.94	3.66
FA-109	1.22	107.22	16	226.18	6	4	3	54.57	1587.16	0.23	2.89	3.39
FA-110	1.89	86.99	16	242.25	5	3	3	60.15	1292.67	0.11	2.95	3.50
FA-111	1.51	86.99	15	210.19	5	3	3	52.90	2167.98	0.15	2.79	3.57
FA-112	0.56	104.06	18	270.26	6	3	4	66.22	508.88	0.28	3.42	3.03
FA-113	0.47	92.78	16	241.27	5	4	3	63.67	988.86	0.36	3.06	3.17
FA-114	0.98	86.99	16	242.25	5	3	3	60.92	3122.98	0.27	3.04	3.48
FA-115	1.22	66.76	16	258.32	4	2	3	66.51	1461.59	0.01	3.10	4.03
FA-116	1.21	104.06	18	270.26	6	3	4	66.22	4240.07	0.26	3.40	3.51
FA-117	0.70	92.78	16	241.27	5	4	3	63.67	1996.09	0.19	3.05	3.46
FA-118	0.77	86.99	16	242.25	5	3	3	60.92	2113.27	0.06	3.00	3.73
FA-119	1.45	66.76	16	258.32	4	2	3	66.51	1550.35	0.17	3.07	3.43
FA-120	1.06	66.76	15	226.25	4	2	3	59.26	3912.04	0.20	2.94	3.61

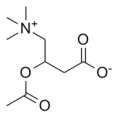
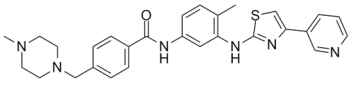
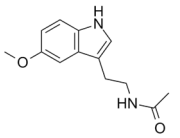
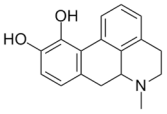
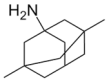
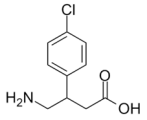
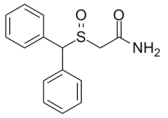
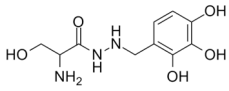
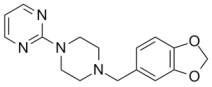
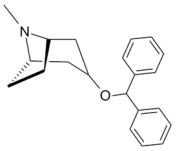
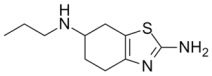
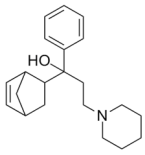
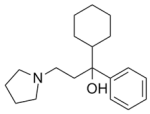
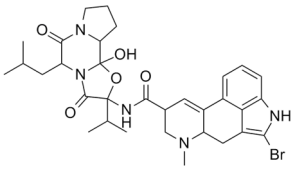
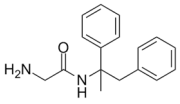
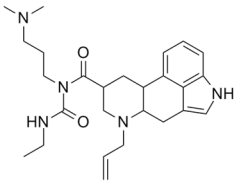
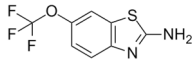
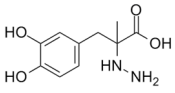
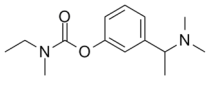
FA-121	-0.25	141.36	20	282.20	8	4	5	64.87	2228.35	0.49	3.56	3.09
FA-122	-0.34	130.08	18	253.21	7	5	4	62.32	1655.03	0.52	3.18	3.18
FA-123	0.17	124.29	18	254.19	7	4	4	59.57	1872.80	0.28	3.09	3.36
FA-125	0.58	141.36	20	282.20	8	4	5	64.87	3916.41	0.36	3.52	3.28
FA-126	0.07	130.08	18	253.21	7	5	4	62.32	1813.57	0.47	3.16	3.23
FA-127	0.14	124.29	18	254.19	7	4	4	59.57	3017.85	0.29	3.11	3.45
FA-129	0.43	104.06	17	238.20	6	3	4	57.91	2030.14	0.13	2.98	3.56
FA-130	0.09	130.08	18	253.21	7	5	4	61.42	3957.12	0.28	3.40	3.48
FA-131	0.00	118.81	16	224.22	6	6	3	58.87	2643.05	0.26	3.04	3.33
FA-132	0.50	113.01	16	225.20	6	5	3	56.12	2740.56	0.23	3.03	3.49
FA-134	0.92	130.08	18	253.21	7	5	4	61.42	4520.59	0.32	3.37	3.48
FA-135	0.41	118.81	16	224.22	6	6	3	58.87	3348.67	0.21	3.01	3.43
FA-136	0.48	113.01	16	225.20	6	5	3	56.12	4228.28	0.21	2.86	3.63
FA-137	1.15	92.78	16	241.27	5	4	3	61.71	2165.76	0.18	3.04	3.49
FA-138	0.77	92.78	15	209.20	5	4	3	54.46	3022.97	0.05	2.74	3.89
FA-139	0.24	124.29	18	254.19	7	4	4	59.86	3721.68	0.28	3.40	3.47
FA-140	0.15	113.01	16	225.20	6	5	3	57.31	2574.85	0.24	3.04	3.47
FA-141	0.65	107.22	16	226.18	6	4	3	54.57	2163.28	0.17	3.02	3.51
FA-142	0.89	86.99	16	242.25	5	3	3	60.15	1780.92	0.01	3.08	4.07
FA-143	1.06	124.29	18	254.19	7	4	4	59.86	4175.83	0.28	3.37	3.49
FA-144	0.56	113.01	16	225.20	6	5	3	57.31	2283.22	0.30	3.01	3.40
FA-145	0.62	107.22	16	226.18	6	4	3	54.57	3310.89	0.19	2.96	3.58
FA-147	0.92	86.99	15	210.19	5	3	3	52.90	6133.62	0.37	2.86	3.59
FA-148	0.62	104.06	18	270.26	6	3	4	66.22	3014.87	0.34	3.40	3.38
FA-149	0.53	92.78	16	241.27	5	4	3	63.67	4122.82	0.39	3.04	3.46
FA-150	1.04	86.99	16	242.25	5	3	3	60.92	2156.74	0.39	3.03	3.33
FA-151	1.28	66.76	16	258.32	4	2	3	66.51	662.14	0.06	3.08	3.47
FA-152	1.45	104.06	18	270.26	6	3	4	66.22	2630.16	0.21	3.37	3.46
FA-153	0.94	92.78	16	241.27	5	4	3	63.67	1610.40	0.33	3.02	3.30

FA-154	1.01	86.99	16	242.25	5	3	3	60.92	1902.78	0.31	2.97	3.36
FA-155	1.69	66.76	16	258.32	4	2	3	66.51	887.05	0.04	3.04	3.63
FA-156	1.30	66.76	15	226.25	4	2	3	59.26	1492.20	0.12	2.86	3.53
FA-157	0.30	141.36	20	282.20	8	4	5	65.25	3254.06	0.24	3.69	3.31
FA-158	0.21	130.08	18	253.21	7	5	4	62.70	3835.71	0.28	3.38	3.47
FA-159	0.51	124.29	18	254.19	7	4	4	59.95	3404.81	0.29	3.36	3.44
FA-161	0.21	130.08	18	253.21	7	5	4	62.70	3591.72	0.22	3.42	3.51
FA-162	0.12	118.81	16	224.22	6	6	3	60.15	1787.02	0.49	3.02	3.11
FA-163	0.42	113.01	16	225.20	6	5	3	57.41	3262.29	0.25	3.01	3.51
FA-165	0.51	124.29	18	254.19	7	4	4	59.95	4618.86	0.23	3.37	3.56
FA-166	0.42	113.01	16	225.20	6	5	3	57.41	2936.62	0.13	2.96	3.64
FA-167	0.72	107.22	16	226.18	6	4	3	54.66	2543.00	0.31	3.00	3.42
FA-169	0.96	104.06	18	270.26	6	3	4	65.54	1911.54	0.30	3.43	3.30
FA-170	0.87	92.78	16	241.27	5	4	3	62.99	4026.98	0.28	3.04	3.53
FA-171	1.16	86.99	16	242.25	5	3	3	60.25	1726.80	0.63	3.02	3.17
FA-173	0.57	104.06	17	238.20	6	3	4	58.29	4471.90	0.13	3.22	3.70
FA-174	0.48	92.78	15	209.20	5	4	3	55.74	3391.37	0.44	2.78	3.43
FA-175	0.99	86.99	15	210.19	5	3	3	52.99	4040.74	0.03	2.76	4.06
FA-177	1.40	104.06	17	238.20	6	3	4	58.29	3837.04	0.14	3.18	3.65
FA-178	0.89	92.78	15	209.20	5	4	3	55.74	4841.39	0.36	2.80	3.55
FA-179	0.96	86.99	15	210.19	5	3	3	52.99	4863.77	0.21	2.70	3.69
FA-181	0.83	107.22	17	258.25	6	4	3	61.82	1454.07	0.29	3.22	3.28
FA-182	0.72	107.22	16	226.18	6	4	3	54.66	2543.00	0.31	3.00	3.42
FA-184	1.60	107.22	17	258.25	6	4	3	61.82	1675.77	0.11	3.15	3.53
FA-185	0.48	113.01	16	225.20	6	5	3	56.12	4228.28	0.21	2.86	3.63

Table S3. Elimination scores for the subset of ferulic acid derivatives chosen as the most promising, according to S^S.

	$S^{E,ADME2}$	$S^{E,ADME8}$	$S^{E,ADMET}$	$S^{E,ADMETSA}$
FA	1.33	4.12	9.28	11.13
FA-8	1.18	5.30	7.67	8.59
FA-12	0.56	4.01	6.99	8.03
FA-26	1.42	7.34	11.54	12.52
FA-41	0.97	6.21	10.11	10.80
FA-88	1.04	4.48	6.35	7.16
FA-106	0.65	4.09	5.50	6.56
FA-115	0.68	2.59	4.53	5.50
FA-118	1.05	4.50	7.04	8.11
FA-138	1.40	5.95	9.62	10.92
FA-142	1.00	4.44	6.76	7.74
FA-173	1.18	5.06	10.20	11.06
FA-175	1.29	5.17	10.12	11.40
Average	1.06	4.86	8.13	9.19

Table S4. Reference set of molecules, with some neuroprotective effects.

Compound (CAS)	Structure	Compound (CAS)	Structure
Acetylcarnitine (3040-38-8)		Masitinib (790299-79-5)	
Amantadine (768-94-5)		Melatonin (73-31-4)	
Apomorphine (58-00-4)		Memantine (19982-08-2)	
Baclofen (1134-47-0)		Modafinil (68693-11-8)	
Benserazide (14919-77-8)		Piribedil (3605-01-4)	
Benztropine (86-13-5)		Pramipexole (104632-26-0)	
Biperiden (514-65-8)		Procyclidine (77-37-2)	
Bromocriptine (25614-03-3)		Remacemide (128298-28-2)	
Cabergoline (81409-90-7)		Riluzole (1744-22-5)	
Carbidopa (28860-95-9)		Rivastigmine (123441-03-2)	

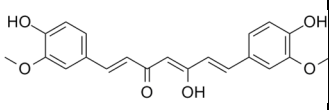
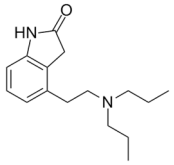
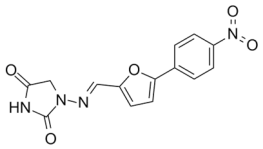
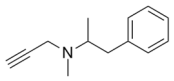
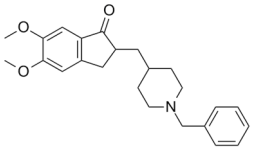
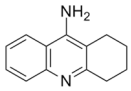
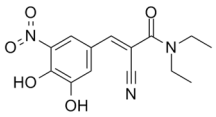
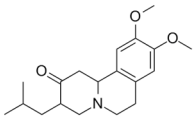
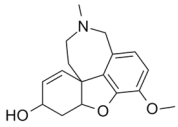
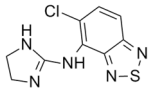
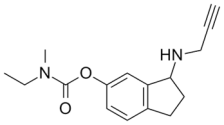
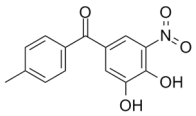
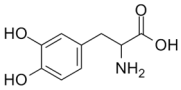
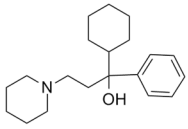
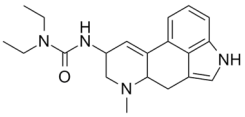
Curcumin (458-37-7)		Ropinirole (91374-21-9)	
Dantrolene (7261-97-4)		Selegiline (14611-51-9)	
Donepezil (120014-06-4)		Tacrine (321-64-2)	
Entacapone (130929-57-6)		Tetrabenazine (58-46-8)	
Galantamine (357-70-0)		Tizanidine (51322-75-9)	
Ladostigil (209349-27-4)		Tolcapone (134308-13-7)	
L-DOPA (59-92-7)		Trihexyphenidyl (144-11-6)	
Lisuride (18016-80-3)			

Table S5. Pole strength (PS) values for the EPT approximation (P3) used to calculated ionization energies and electron affinities.

	PS (IE)	PS (EA)
q= +1		
FA-138	0.875	0.953
q= 0		
FA	0.879	0.913
FA-8	0.881	0.968
FA-26	0.879	0.970
FA-118	0.879	0.976
FA-138	0.877	0.968
FA-175	0.879	0.906
q= -1		
FA	0.881	0.973
FA-8	0.880	0.978
FA-26	0.883	0.980
FA-118	0.886	0.981
FA-138	0.883	0.982
FA-175	0.881	0.979
q= -2		
FA	0.876	0.983
FA-8	0.886	0.980
FA-26	0.877	0.983
FA-118	0.889	0.983
FA-138	0.878	0.984
FA-175	0.872	0.982
q= -3		
FA-118	0.875	0.985

Table S6. Equations concerning S^S construction.

$$S^S = S^{ADME} + S^T + S^{SA}$$

where

$$S^{ADME} = \frac{S^{logP} + S^{HB^D} + S^{HB^A} + S^{MW} + S^{^M R} + S^{^X A} + S^{RB} + S^{PSA}}{8}$$

$$S^T = \frac{S^{LD_{50}} + S^M}{2}$$

with

$$S^{logP} = \begin{cases} 1, & \text{if } -0.4 \le logP \le 5.0 \\ 0, & \text{otherwise} \end{cases} \qquad S^{HB^D} = \begin{cases} 1, & \text{if } HB^D \le 5 \\ 0, & \text{otherwise} \end{cases}$$

$$S^{HB^A} = \begin{cases} 1, & \text{if } HB^A \le 10 \\ 0, & \text{otherwise} \end{cases} \qquad S^{MW} = \begin{cases} 1, & \text{if } 160 \le MW \le 480 \\ 0, & \text{otherwise} \end{cases}$$

$$S^{^M R} = \begin{cases} 1, & \text{if } 40 \le {}^M R \le 130 \\ 0, & \text{otherwise} \end{cases} \qquad S^{^X A} = \begin{cases} 1, & \text{if } {}^X A \le 70 \\ 0, & \text{otherwise} \end{cases}$$

$$S^{RB} = \begin{cases} 1, & \text{if } RB \le 10 \\ 0, & \text{otherwise} \end{cases} \qquad S^{PSA} = \begin{cases} 1, & \text{if } PSA \le 140 \\ 0, & \text{otherwise} \end{cases}$$

$$S^{LD_{50}} = 1 + \log\left(\frac{LD_{50}{}^{dM}}{LD_{50}{}^{\overline{RefSet}}} \right) \qquad S^M = 1 + \log\left(\frac{M^{\overline{RefSet}}}{M^{dM}} \right) \qquad S^{SA} = 1 + \log\left(\frac{SA^{\overline{RefSet}}}{SA^{dM}} \right)$$

Table S7. Exclusion scores (S^E) equations.

$$S^{E,ADME2} = \left| \frac{\log P_{\overline{RefSet}} - \log P_{dM}}{SD_{\log P}} \right| + \left| \frac{MW_{\overline{RefSet}} - MW_{dM}}{SD_{MW}} \right|$$

$$S^{E,ADME8} = S^{E,ADME2} + \left| \frac{PSA_{\overline{RefSet}} - PSA_{dM}}{SD_{PSA}} \right| + \left| \frac{{}^{X}A_{\overline{RefSet}} - {}^{X}A_{dM}}{SD_{{}^{X}A}} \right| + \left| \frac{HB^{A}{}_{\overline{RefSet}} - HB^{A}{}_{dM}}{SD_{HB^{A}}} \right| + \left| \frac{HB^{D}{}_{\overline{RefSet}} - HB^{D}{}_{dM}}{SD_{HB^{D}}} \right| + \left| \frac{RB_{\overline{RefSet}} - RB_{dM}}{SD_{RB}} \right| + \left| \frac{{}^{M}R_{\overline{RefSet}} - {}^{M}R_{dM}}{SD_{{}^{M}R}} \right|$$

$$S^{E,ADMET} = S^{E,ADME8} + \left| \frac{LD_{50\,\overline{RefSet}} - LD_{50\,dM}}{SD_{LD_{50}}} \right| + \left| \frac{M_{\overline{RefSet}} - M_{dM}}{SD_{M}} \right|$$

$$S^{E,ADMETSA} = S^{E,ADMET} + \left| \frac{SA_{\overline{RefSet}} - SA_{dM}}{SD_{SA}} \right|$$

Table S8. Zero-point bond dissociation energies (BDE, in kcal/mol) for ferulic acid and its derivatives. Only the species with molar fractions $\geq 10^{-4}$ are included.

FA	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	---	98.09	97.94	96.96	---
Site b	---	85.15	82.48	---	---
FA-8	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	---	98.45	189.16	97.23	---
Site b	---	88.78	87.79	82.04	---
Site R5 (SH)	---	80.24	77.44	---	---
FA-26	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	---	98.93	97.79	96.98	---
Site b	---	85.12	81.89	71.30	---
Site R1 (OH)	---	83.06	77.29	---	---
FA-118	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	---	99.15	99.34	98.93	97.20
Site b	---	80.18	78.79	74.87	71.01
Site R3 (OH)	---	85.29	84.35	75.99	---
Site R4 (SH)	---	80.33	79.56	---	---
FA-138	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	100.02	98.90	98.62	97.02	---
Site b	89.30	83.97	74.88	---	---
FA-175	**q=+1**	**q=0**	**q=-1**	**q=-2**	**q=-3**
Site a	---	97.56	97.49	97.55	---
Site b	---	80.82	78.54	75.90	---
Site R2 (OH)	---	80.09	78.60	---	---

Table S9. Binding energies (ΔG_B, kcal/mol) for acid-base species of ferulic acid and its derivatives.

Compound	q= +1	q= 0	q= -1	q= -2	q= -3
COMT					
Ferulic acid	---	-5.49	-5.28	-5.31	---
FA-8	---	-5.03	-5.14	-4.93	---
FA-26	---	-4.98	-5.09	-4.8	---
FA-118	---	-5.46	-5.88	-6.09	-5.71
FA-138	-5.25	-5.1	-5.14	-5.2	---
FA-175	---	-5.35	-5.42	-5.49	---
MAO-B					
Ferulic acid	---	-7.32	-7.19	-6.98	---
FA-8	---	-6.88	-6.91	-6.75	---
FA-26	---	-7.37	-7.63	-7.31	---
FA-118	---	-6.35	-7.08	-7.24	-6.62
FA-138	-6.96	-7.02	-7.4	-7.1	---
FA-175	---	-6.96	-7.02	-6.92	---
AChE					
Ferulic acid	---	-7.25	-7.37	-7.51	---
FA-8	---	-6.45	-6.43	-6.42	---
FA-26	---	-7.93	-7.88	-8.08	---
FA-118	---	-6.82	-6.95	-6.94	-7.09
FA-138	-7.36	-7.39	-7.41	-7.67	---
FA-175	---	-6.81	-7.01	-7.02	---

Table S10. Complete set of weighted binding energies (ΔG^{w}_{B}, kcal/mol) for FA and its derivatives.

Compound	ΔG^{W}_{B} (Kcal/mol)			S_P
	COMT	MAO	AChE	
Ferulic acid	-5.28	-7.19	-7.37	3.78
FA-8	-5.14	-6.91	-6.43	3.50
FA-12	-4.97	-7.33	-4.38	3.09
FA-26	-5.09	-7.63	-7.88	3.93
FA-41	-5.23	-5.61	-6.59	3.34
FA-88	-4.84	-6.91	-3.79	2.87
FA-106	-5.25	-6.86	-4.44	3.08
FA-115	-4.67	-6.59	-4.30	2.90
FA-118	-5.90	-7.09	-6.95	3.79
FA-138	-5.12	-7.17	-7.40	3.76
FA-142	-5.31	-5.47	-5.83	3.17
FA-173	-5.23	-6.94	-7.35	3.73
FA-175	-5.42	-7.02	-7.01	3.70

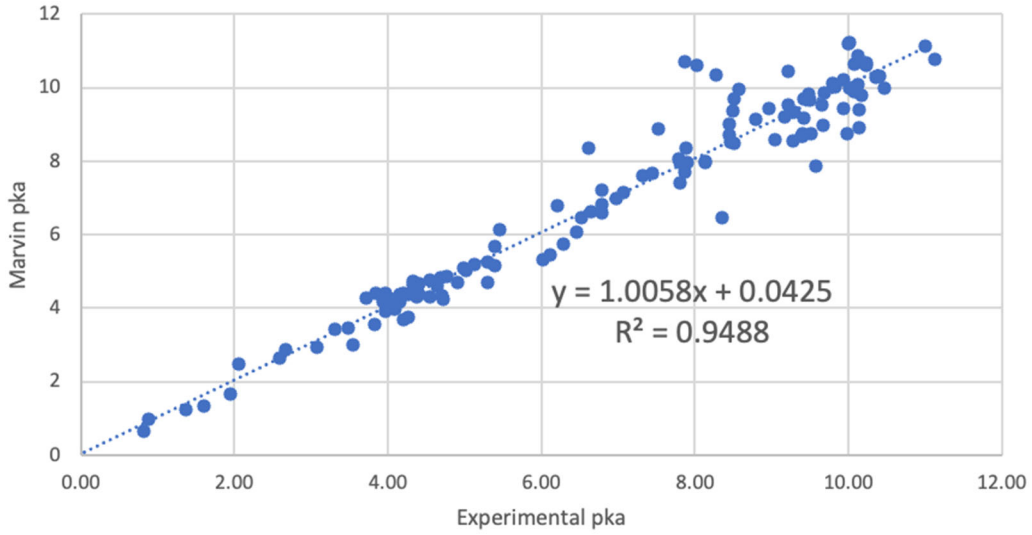


Figure S1. Correlation between pKa values estimated with Marvin software vs experimentally pKa values.

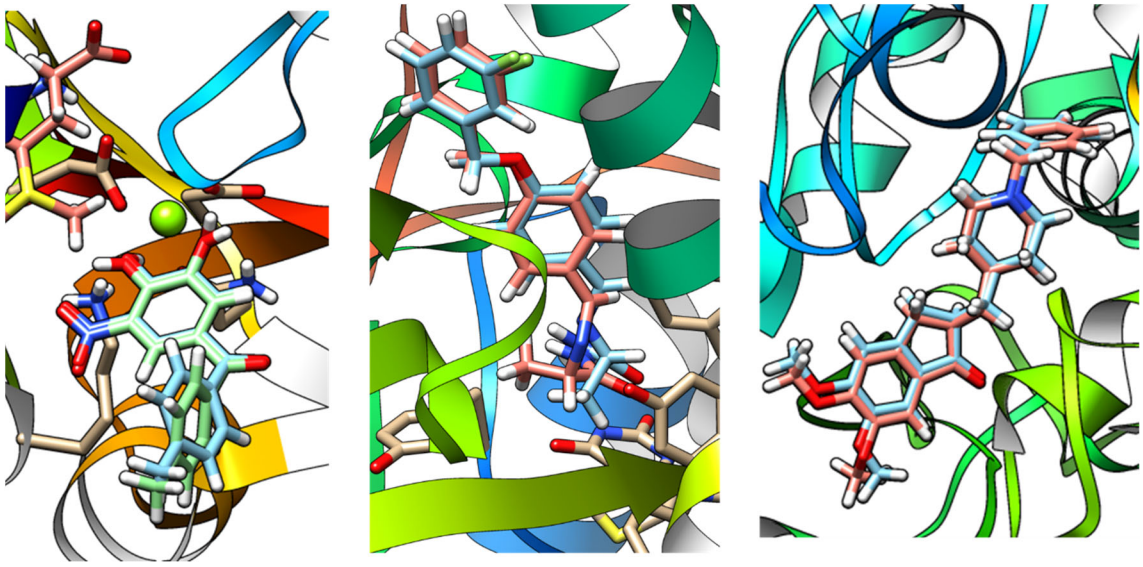


Figure S2. Redocking simulations of tolcapone in comt (left), Safrinamide in MAO-B (center) and Donopezil in AChE (right).

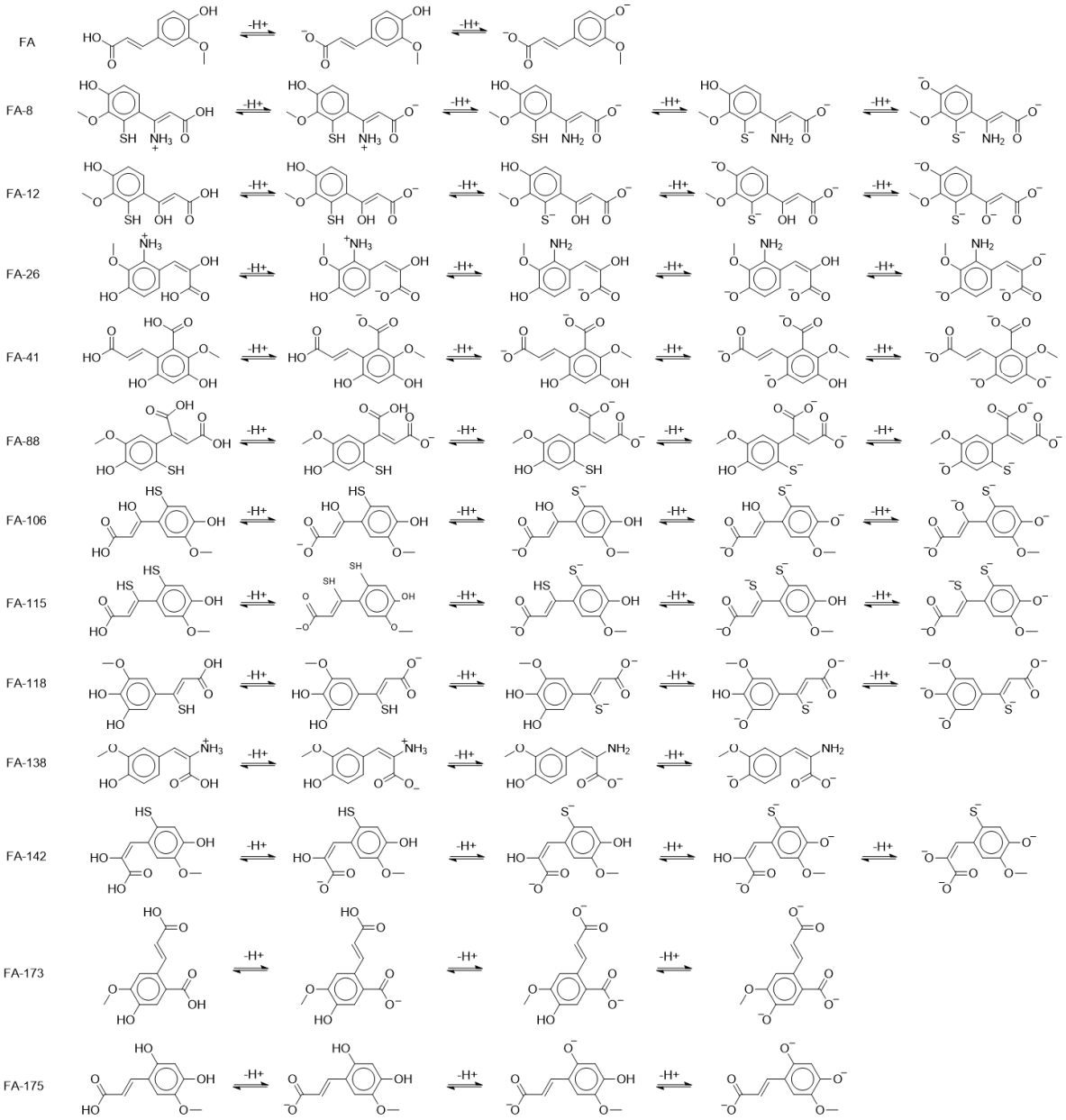


Figure S3. Deprotonation routes for the subset of ferulic acid derivatives chosen as the most promising, from their drug-like behavior.

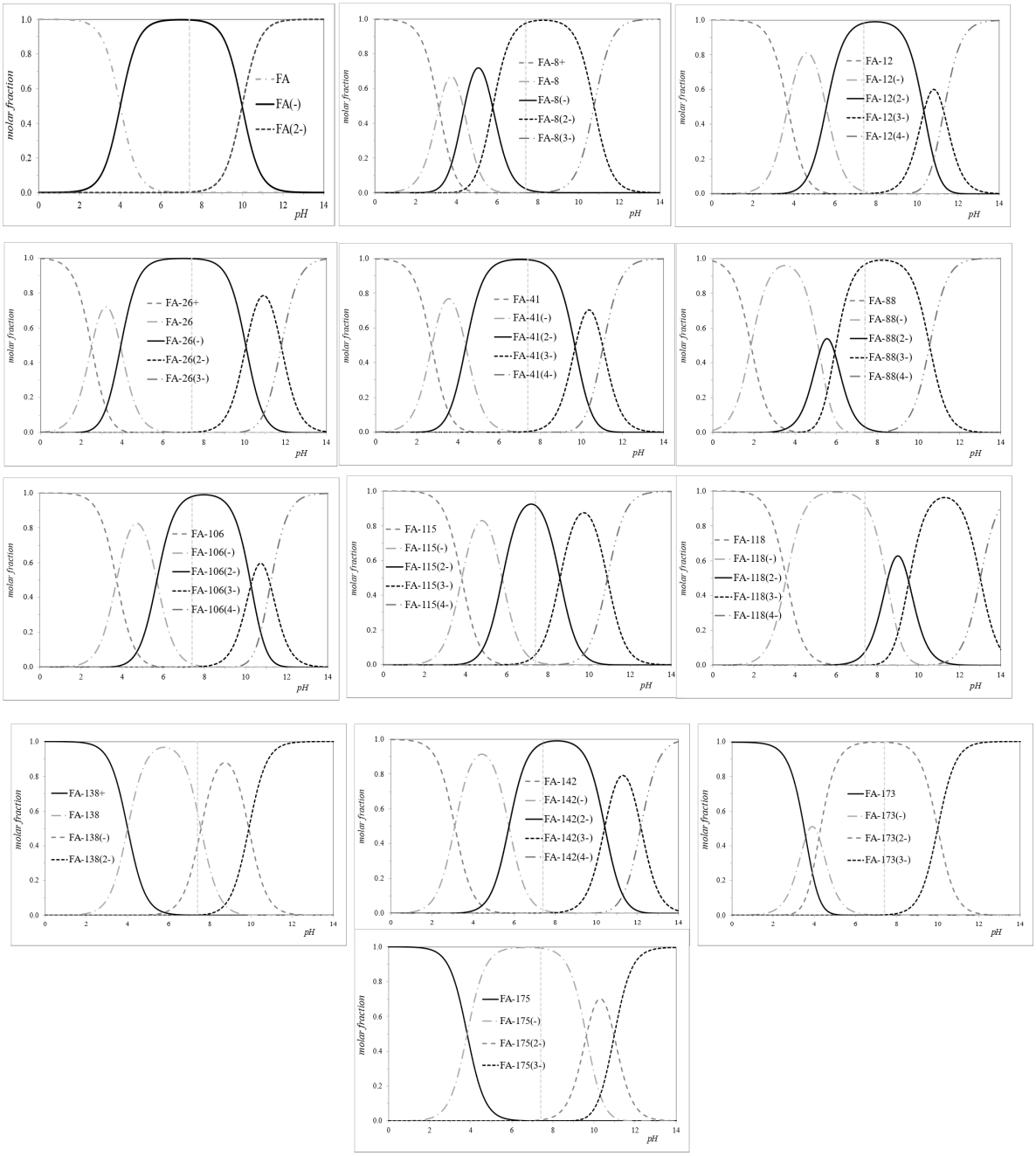


Figure S4. Distribution diagram of the acid-base species of ferulic acid derivatives. The vertical line landmarks the physiological pH (pH=7.4).