Supplementary information

Structure-based methoxyflavone derivatives with potent inhibitory activity against various influenza neuraminidases

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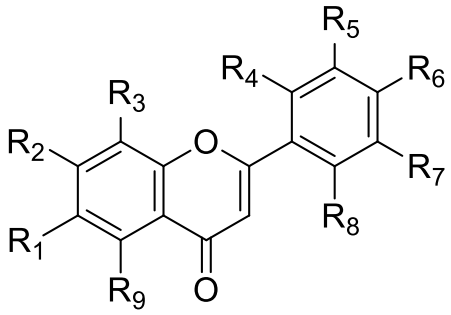
Table S1. Chemical structures of the compounds used in this study



	R1	R2	R3	R4	R5	R6	R7	R8	R9
1	-H	-OH	-OMe	-H	-H	-OH	-H	-H	-OH
2	-H	-OH	-COOH	-H	-H	-OH	-H	-H	-OH
3	-H	-COOH	-OMe	-H	-H	-OH	-H	-H	-OH
4	-H	-OH	-OMe	-H	-H	-OH	-H	-H	-NHAc
5	-H	-OH	-OMe	-H	-H	-OH	-H	-H	$-N=C(NH_2)_2$
6	-H	-OH	-COOH	-H	-H	-OH	-H	-H	-NHAc
7	-H	-OH	-COOH	-H	-H	-OH	-H	-H	$-N=C(NH_2)_2$
8	-H	-COOH	-OMe	-H	-H	-OH	-H	-H	-NHAc
9	-H	-COOH	-OMe	-H	-H	-OH	-H	-H	$-N=C(NH_2)_2$
10	- OMe	-OMe	- OMe	-OH	-H	-H	-H	-H	-OH
11	- OMe	-OH	-H	-H	-H	-H	-H	-H	-OH
12	- OMe	- OMe	- OMe	-OH	-H	-H	-H	- OMe	-OH
13	-H	-OH	-H	-H	-H	-H	-H	-H	-OH
14	- OMe	-OH	- OMe	-H	-H	-H	-H	-H	-OH
15	-H	-OH	- OMe	-H	-H	-H	-H	-H	-OH
16	-H	- OMe	- OMe	-OH	-H	-H	-H	- OMe	-OH
17	-OH	-OH	-H	-H	-H	-H	-H	-H	-OH

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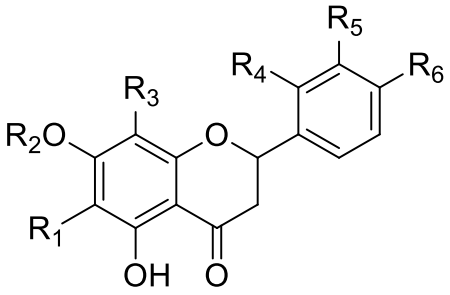
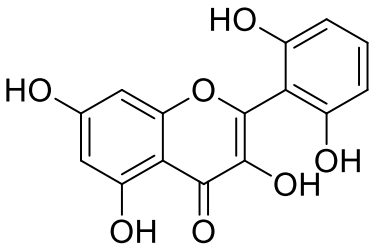
18	-H	-OH	-OH	-H	-H	-H	-H	-H	-OH
19	-H	-OGlu acid	-H	- OMe	-H	-H	-H	-H	-OH
20	- OMe	-OGlu acid	- OMe	-H	-H	-H	-H	-H	-OH
21	-H	-OGlu acid	- OMe	-H	-H	-H	-H	-H	-OH
22	-OGlu acid	-OH	-H	-H	-H	-H	-H	-H	-OH
23	-OH	-OGlu acid	- OMe	-H	-H	-H	-H	-H	-OH
24	-H	-OGlu acid	-H	-H	-H	-H	-H	-H	-OH
25	- OMe	-OGlu acid	-H	-H	-H	-H	-H	-H	-OH
26	-H	-OGlu	- OMe	-H	-H	-H	-H	-H	-OH
27	- OMe	-OGlu acid	-OH	-H	-H	-H	-H	-H	-OH
28	-H	-OGlu acid	-OH	-H	-H	-H	-H	-H	-OH
29	- OMe	-OGlu	-H	-H	-H	-H	-H	-H	-OH
30	-H	-OH	- OMe	-OH	-H	-H	-OH	- OMe	-OH
31	-OH	-OGlu acid	-H	-H	-H	-H	-H	-H	-OH
32	-OH	-OGlu	-H	-H	-H	-H	-H	-H	-OH
33	- OMe	-OGlu acid	-H	-OH	-H	-H	-H	-H	-OH
34	-OH	-OGlu acid	-H	-H	-H	-OH	-H	-H	-OH
35	-Glu	-OGlu	-Ara	-H	-H	-H	-H	-H	-OH
36	Ara	-OGlu	-Glu	-H	-H	-H	-H	-H	-OH
37	-Glu	-OH	-Ara	-H	-H	-OH	-H	-H	-OH
38	-OH	-OGlu acid	-H	-H	-OH	-OH	-H	-H	-OH
39	-H	-OGlu acid	-OH	-H	-H	-OH	-H	-H	-OH
40	-H	-OGlu acid	-H	-H	-H	-OH	-H	-H	-OH
41	-H	-OH	-OGlu acid	-H	-H	-OH	-H	-H	-OH
42	-H	-OH	-H	-H	-OH	-OH	-H	-H	-OH
43	-H	-OH	-H	-H	-H	-OH	-H	-H	-OH



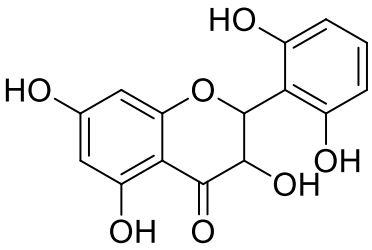
	R1	**R2**	**R3**	**R4**	**R5**	**R6**
44	-H	-Glu acid	-H	- OMe	-H	-H
45	-OH	-Glu acid	-H	-H	-H	-H
46	-OH	-Glu acid	-H	-H	-OH	-OH
47	-H	-Glu acid	-OH	-H	-OH	-OH
48	-OH	-Glu acid	-H	-H	-H	-OH
49	-H	-Glu acid	-OH	-H	-H	-OH
50	-H	-Glu acid	-H	-H	-H	-OH
51	-H	-Glu acid	-H	-H	-H	-H

52	-H	-H	-H	-H	-H	-H



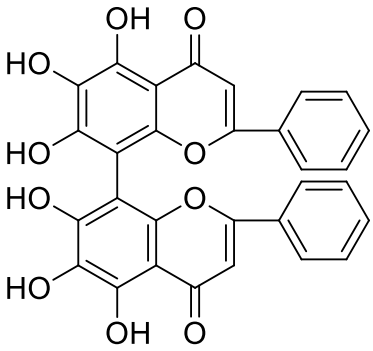
53

Flavonol



54

Flavanonol



55

Biflavone

Table S2. The cDocker energy (E_{total}) and cDocker interaction energy (E_{int}) between compounds and various proteins [a]

	N1^{open}		**N1^{closed}**		**N2**		**N9**		**B**	
Compound [b]	E_{total}	E_{int}	E_{total}	E_{int}	E_{total}	E_{int}	E_{total}	E_{int}	E_{total}	E_{int}
1	-26.07	-38.36	-28.43	-36.43	-25.44	-36.39	-25.39	-40.42	-26.20	-35.56
2	-32.97	-40.16	-33.81	-39.45	-37.57	-45.31	-36.98	-43.07	-36.84	-42.99
3	-32.33	-43.44	-34.74	-46.06	-34.03	-47.95	-34.80	-45.48	-30.30	-41.93
4	—	—	—	—	-25.17	-39.83	-30.45	-45.39	-29.52	-43.20
5	—	—	—	—	-24.57	-49.64	-24.44	-49.32	-29.29	-50.66
6	—	—	-17.09	-25.86	-37.80	-50.10	-38.15	-48.70	-36.86	-53.81
7	-30.87	-44.81	-13.15	-30.88	-40.45	-56.45	-40.35	-55.12	-50.72	-65.42
8	-15.34	-32.02	-16.77	-30.61	-32.21	-49.68	-34.19	-49.05	-32.91	-48.90
9	-20.71	-40.49	-10.23	-40.03	-37.78	-56.74	-37.02	-57.95	-41.14	-62.04
10	-8.90	-31.43	-10.99	-32.86	-18.71	-42.18	-19.65	-42.01	-19.24	-42.57
11	-21.03	-33.22	-27.28	-42.11	-22.92	-33.28	-25.10	-33.64	-22.72	-32.36
12	—	—	—	—	-13.82	-41.69	-15.68	-42.82	-18.23	-45.64
13	-22.68	-28.43	-27.16	-34.54	-23.94	-29.92	-27.13	-33.38	-27.18	-32.95
14	-21.64	-36.89	-12.91	-28.69	-21.89	-36.48	-23.03	-36.45	-20.16	-36.11
15	-22.19	-30.72	-21.03	-32.70	-21.87	-32.94	-24.78	-32.56	-26.39	-35.24

16	—	—	-23.15	-40.36	-21.48	-41.42	-22.93	-48.60	-21.61	-39.99
17	-28.61	-38.55	-33.14	-39.10	-30.37	-33.46	-32.01	-36.82	-28.70	-32.59
18	-28.34	-30.26	-29.72	-31.40	-28.72	-32.24	-31.93	-34.49	-27.16	-31.13
19	—	—	—	—	-18.05	-55.50	-18.67	-56.45	-18.34	-52.59
20	—	—	—	—	-11.55	-48.62	-7.35	-52.87	-17.85	-54.43
21	—	—	—	—	-14.77	-47.70	-21.06	-49.65	-20.74	-51.96
22	—	—	—	—	-22.94	-58.05	-23.74	-52.38	-24.25	-52.24
23	—	—	—	—	-20.21	-53.79	-23.12	-58.07	-22.46	-54.04
24	—	—	—	—	-24.30	-50.43	-25.94	-52.64	-20.78	-56.28
25	—	—	—	—	-9.06	-46.65	-1.20	-53.22	-3.40	-60.48
26	—	—	—	—	-11.84	-52.17	-11.83	-53.61	-13.33	-49.69
27	—	—	—	—	-14.32	-43.10	-11.74	-47.12	-22.70	-53.22
28	—	—	—	—	-22.69	-52.56	-25.40	-55.54	-25.43	-51.55
29	—	—	—	—	-13.28	-49.34	-9.91	-55.84	-11.00	-50.33
30	—	—	-24.99	-36.98	-24.46	-42.33	-26.78	-46.12	-34.02	-47.09
31	—	—	—	—	-22.03	-50.31	-27.62	-56.50	-24.73	-53.16
32	—	—	—	—	-13.55	-47.29	-17.83	-57.21	-16.54	-51.73
33	—	—	—	—	-17.95	-55.52	-11.52	-45.56	-18.15	-60.09
34	—	—	—	—	-23.85	-55.94	-32.49	-59.29	-28.55	-59.06
35	—	—	—	—	—	—	—	—	—	—

36	—	—	—	—	—	—	—	—	—	—
37	—	—	—	—	-5.37	-49.89	—	—	-1.58	-58.67
38	—	—	—	—	-31.79	-58.70	-26.73	-51.68	-27.99	-59.57
39	—	—	—	—	-27.48	-58.96	-25.88	-57.64	-22.75	-50.22
40	-5.30	-29.19	—	—	-21.99	-51.76	-22.94	-51.07	-27.34	-54.53
41	—	—	—	—	-23.50	-49.42	-24.61	-53.69	-25.05	-53.83
42	-31.52	-35.44	-31.89	-35.61	-30.75	-35.11	-35.84	-40.11	-31.87	-37.00
43	-28.84	-35.07	-26.77	-32.40	-25.88	-31.95	-29.65	-35.48	-26.94	-33.03
44	—	—	—	—	-14.53	-42.40	-12.29	-40.57	-15.39	-50.01
45	—	—	—	—	-26.70	-58.58	-26.53	-56.89	-23.88	-53.94
46	—	—	—	—	-33.42	-59.90	-26.54	-53.99	-31.35	-58.99
47	—	—	—	—	-35.50	-62.12	-28.63	-52.46	-31.43	-57.30
48	—	—	—	—	-31.65	-56.84	-24.59	-48.29	-28.15	-52.01
49	—	—	—	—	-34.11	-63.16	-29.81	-58.36	-25.94	-59.13
50	—	—	—	—	-26.46	-57.60	-28.75	-60.67	-24.73	-56.75
51	—	—	—	—	-21.87	-53.01	-21.75	-51.83	-24.76	-53.56
52	-23.83	-30.85	-24.49	-31.36	-25.10	-31.43	-27.97	-34.61	-28.21	-34.58
53	-28.94	-34.39	-32.60	-39.24	-29.64	-39.27	-32.84	-39.72	-32.16	-39.35
54	-26.66	-36.87	-30.36	-39.91	-29.05	-45.01	-29.85	-42.14	-28.91	-36.41
55	—	—	—	—	-29.07	-24.18	—	—	-26.63	-44.70

[a] Energy units in kcal mol^{-1};

[b] Chemical structures can be found in Table S1.