3D-QSAR, Docking, ADME/Tox studies on Flavone analogs reveal anticancer activity through Tankyrase inhibition

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Table S1: Comparison of experimental and predicted activities of training data set molecules based on QSAR model.

Sr. No.	Title	Structure (SMILE)	Experimental Activity* (µM)	Predicted activity*(µM)	Distance to model
1.	**FL-1**	O=C1C=C(Oc2ccccc12)c3ccccc3	6.85	6.2	Excellent
2.	**FL-4**	Oc1cccc(C2=CC(=O)c3ccccc3O2)c1	6.5	6	Excellent
3.	**FL-6**	Clc1ccccc1[C@H]2NC(=O)c3ccccc3N2	4.51	4.5	Excellent
4.	**FL-7**	Oc1ccc(C2=CC(=O)c3ccccc3O2)cc1O	6.77	6.6	Excellent
5.	**FL-8**	O=C1c2ccccc2N[C@H](N1)c3ccc(cc3)C	5.57	6	Excellent
6.	**FL-9**	O=C1c2cccnc2N[C@H](N1)c3ccccc3C	4.03	4.3	Excellent
7.	**FL-12**	O=C1c2ccccc2N[C@H](N1)c3ccccc3C	4.04	4.1	Excellent
8.	**FL-13**	O=C1C=C(Oc2cc(O)ccc12)c3cccc(O)c3	6.2	6.1	Excellent
9.	**FL-14**	O=C1C=C(Oc2ccccc12)c3ccc(C(C)C)cc3	7.14	7.4	Excellent
10.	**FL-15**	Clc1ccc(C2=Nc3ccccc3C(=O)N2)cc1	7.27	7.4	Excellent
11.	**FL-16**	Clc1ccccc1[C@@H]2NC(=O)c3cccnc3N2	3.85	4.3	Excellent
12.	**FL-17**	Clc1ccc([C@@H]2NC(=O)c3cccnc3N2)cc1	6.12	6	Excellent
13.	**FL-18**	O=C1C=2COCCC2N=C(N1)c3cscc3	6.87	6.5	Excellent
14.	**FL-19**	O=C1c2cccnc2N[C@@H](N1)c3ccc(cc3)C	5.27	5.5	Excellent
15.	**FL-20**	Brc1ccc(C2=Nc3ccccc3C(=O)N2)cc1	7	7.4	Excellent
16.	**FL-21**	Fc1ccccc1[C@H]2NC(=O)c3cccnc3N2	4.2	3.9	Excellent
17.	**FL-23**	Oc1ccc(C2=CC(=O)c3ccc(O)cc3O2)cc1O	6.06	6	Excellent
18.	**FL-25**	O=C1C=C(Oc2ccccc12)c3ccc([N+]([O-])=O)cc3	6.85	6.4	Excellent
19.	**FL-27**	Oc1cc(O)cc2c1C(=O)C=C(O2)c3ccc(O)cc3	5.53	6	Excellent
20.	**FL-29**	Oc1ccc2C(=O)C=C(Oc2c1)c3ccc(OC)cc3	6.34	6.3	Excellent
21.	**FL-30**	Oc1cccc2C(=O)NC(=Nc12)c3ccc(C)cc3	7.36	7.1	Excellent
22.	**FL-31**	Oc1cc(O)cc2c1C(=O)C=C(O2)c3ccc(O)c(O)c3	5.96	6.3	Excellent
23.	**FL-33**	Clc1ccc(C=2NC(=O)C=3COCCC3N2)cc1	6.83	6.4	Excellent
24.	**FL-34**	O=C1c2cccnc2N[C@H](N1)c3ccc(OC)cc3	5.67	5.8	Excellent
25.	**FL-36**	Brc1ccc(C=2NC(=O)C=3COCCC3N2)cc1	7.09	7.5	Excellent
26.	**FL-37**	O=C1C2=C(N=C(N3CCN(CC3)C)N1)CCCC2	6.52	6.1	Excellent
27.	**FL-38**	Brc1ccc(C2=Nc3c(O)cccc3C(=O)N2)cc1	7.82	7.4	Excellent
28.	**FL-40**	O=C1c2cccnc2N[C@H](N1)c3ccc(C(C)C)cc3	6.45	6	Excellent
29.	**FL-41**	FC(F)(F)c1ccc(C=2NC(=O)C3=C(N2)CCCC3)cc1	6.79	6.9	Excellent
30.	**FL-42**	O=C1c2ccccc2N[C@@H](N1)c3ccc(C(C)(C)C)cc3	6.82	6.6	Excellent
31.	**FL-45**	Fc1ccc(C2=Nc3c(O)cccc3C(=O)N2)cc1	6.58	6.5	Excellent
32.	**FL-46**	O=C1C=2COCCC2N=C(N1)c3ccc(OC)cc3	7.07	7.1	Excellent
33.	**FL-48**	Clc1cc(Cl)ccc1[C@H]2NC(=O)c3cccnc3N2C	4.96	5	Excellent
34.	**FL-51**	Brc1ccc(C=2NC(=O)c3cccc(OC)c3N2)cc1	6.97	7	Excellent
35.	**FL-52**	Clc1ccc(C=2NC(=O)c3cccc(OC)c3N2)cc1	7.21	7.4	Excellent
36.	**FL-54**	Fc1ccc(C=2NC(=O)c3cccc(OC)c3N2)cc1	6.34	6.4	Excellent
37.	**FL-55**	FC(F)(F)Oc1ccc(C=2NC(=O)C=3COCCC3N2)cc1	7.26	6.7	Excellent

38.	**FL-56**	O=C1C=2COCCC2N=C(N1)c3ccc(cc3)C(OC)=O	6.69	7	Excellent
39.	**FL-57**	Oc1cccc2c(O)nc(nc12)-c3ccc(N)cc3	6.66	6.9	Excellent
40.	**FL-59**	Oc1c2cccc(c2nc(n1)-c3ccccc3)C	7.39	7.2	Excellent
41.	**FL-60**	Oc1cccc2c(O)nc(nc12)-c3ccccc3	6.74	6.7	Excellent
42.	**FL-61**	FC(F)(F)c1ccc(cc1)C=2NC(=O)C=3COCCC3N2	7.12	7	Excellent
43.	**FL-63**	Oc1c2cccc(O)c2nc(n1)-c3ccc(O)cc3	7.07	7.5	Excellent
44.	**FL-64**	O=C1C=2COCCC2N=C(N1)c3ccc(N(C)C)cc3	7.39	7.6	Excellent
45.	**FL-65**	Fc1ccc(-c2nc(O)c3ccccc3n2)cc1	5.96	6.8	Excellent
46.	**FL-67**	O=C1c2cccc(c2N=C(N1)c3ccc(CN)cc3)C	7	7.5	Excellent
47.	**FL-69**	O=C1C=2COCCC2N=C(N1)c3ccc(C(O)(C)C)cc3	7.66	7.1	Excellent
48.	**FL-70**	FC(F)(F)c1ccc(-c2cc3c(O)cccc3c(O)n2)cc1	7.6	7.6	Excellent
49.	**FL-73**	Oc1c2cccc(c2nc(n1)-c3ccc(O)cc3)C	8.52	8	Excellent
50.	**FL-74**	FC(F)(F)c1ccc(cc1)-c2nc(O)c3CSCCc3n2	8.3	8	Excellent
51.	**FL-75**	FC(F)(F)c1ccc(C=2NC(=O)[C@@H]3CSC[C@H]3N2)cc1	6.9	7.2	Excellent
52.	**FL-77**	Oc1cccc2c(O)nc(nc12)-c3ccc([N+]([O-])=O)cc3	6.72	7.2	Excellent
53.	**FL-90**	Fc1cccc(-c2ccc3C(C)=CC(=O)Nc3c2)c1	6.82	6.7	Excellent
54.	**FL-94**	FC(F)(F)c1ccc(-c2nc(O)c3cccc(c3n2)C)cc1	8	7.8	Excellent
55.	**FL-98**	Fc1ccc(-c2ccc3C(C)=CC(=O)Nc3c2)cc1	6.51	7	Excellent
56.	**FL-99**	Oc1c2cccc(c2nc(n1)-c3ccc([N+]([O-])=O)cc3)C	7.52	7.2	Excellent
57.	**FL-109**	O=C1c2cccc(c2N=C(N1)c3ccc(CNC(OCc4ccccc4)=O)cc3)C	7.36	7.9	Excellent
58.	**FL-112**	Clc1cc(ccc1-c2ccc3C(C)=CC(=O)Nc3c2)C(O)=O	7.68	7	Excellent
59.	**FL-116**	O=C1C=C(Oc2ccccc12)c3ccc(C)cc3	6.72	7.1	Excellent
60.	**FL-117**	Fc1ccc(C2=CC(=O)c3ccccc3O2)cc1	5.96	6	Excellent
61.	**FL-118**	O=C1c2cccnc2N[C@H](N1)c3ccccc3	4.94	5	Excellent
62.	**FL-120**	Oc1ccc(C2=Nc3ccccc3C(=O)N2)cc1	6.72	6.4	Excellent
63.	**FL-121**	Fc1ccc(C2=Nc3c(cccc3C(=O)N2)C)cc1	7.4	7.3	Excellent
64.	**FL-122**	O=C1C=2COCCC2N=C(N1)c3ccc(cc3)C	7.21	7.4	Excellent
65.	**FL-123**	O=C1c2ccccc2N=C(N1)c3ccc([N+]([O-])=O)cc3	6.59	6.8	Excellent
66.	**FL-124**	O=C1c2ccccc2N[C@H](N1)c3ccc(C(C)C)cc3	6.64	6.9	Excellent
67.	**FL-126**	O=C1c2cccc(OC)c2N=C(N1)c3ccc(C)cc3	6.78	7.1	Excellent
68.	**FL-130**	Oc1c2cccc(c2nc(n1)-c3ccc(N)cc3)C	8.48	8	Excellent
69.	**FL-136**	O=C1C=C(c2ccc(cc2N1)-c3ccccc3)C	6.74	6.7	Excellent

*Experimental and predictive value is in pIC_{50}.

Table S2: Comparison of experimental and predicted activities of test data set molecules based on QSAR model.

Sr. No.	Title	Structure (SMILE)	Experimental Activity (μM)	Predicted activity (μM)	Distance to model
1.	**FL-2**	O=C1c2ccccc2N[C@@H](N1)c3ccccc3	5.26	5.9	Excellent
2.	**FL-3**	Fc1ccccc1[C@H]2NC(=O)c3ccccc3N2	4.82	4.3	Excellent
3.	**FL-5**	O=C1c2ccccc2N=C(c3ccc(cc3)C)C1	6.27	7.1	Excellent
4.	**FL-10**	O=C1c2cccnc2C=C(N1)c3ccccc3	4.97	5.5	Excellent
5.	**FL-11**	Clc1ccc([C@H]2NC(=O)c3ccccc3N2)cc1	6.39	6.5	Excellent
6.	**FL-22**	O=C1c2ccccc2N=C(N1)c3ccc(N)cc3	6.16	6.6	Excellent
7.	**FL-26**	O=C1c2cccc(c2N=C(N1)c3ccc(C)cc3)C	8.17	7.9	Excellent
8.	**FL-32**	Clc1ccc(C2=Nc3c(cccc3C(=O)N2)C)cc1	7.48	7.5	Excellent
9.	**FL-35**	FC(F)(F)c1ccc(C2=Nc3ccccc3C(=O)N2)cc1	6.88	7.1	Excellent
10.	**FL-39**	Brc1ccc(C2=Nc3c(cccc3C(=O)N2)C)cc1	8.26	7.7	Excellent
11.	**FL-43**	Oc1c2ccccc2nc(n1)-c3ccccc3	5.66	6.6	Excellent
12.	**FL-47**	Clc1ccc(C2=Nc3c(O)cccc3C(=O)N2)cc1	7.31	7.3	Excellent
13.	**FL-68**	O=S(=O)(c1ccc(cc1)C=2NC(=O)C=3COCCC3N2)C	7.2	7	Good
14.	**FL-71**	Oc1c2ccccc2nc(n1)-c3ccc(OC)cc3	6.21	7	Excellent
15.	**FL-92**	Oc1c2cccc(c2nc(n1)-c3ccc(OC)cc3)C	7.92	8	Excellent
16.	**FL-103**	Clc1cc(N)ccc1-c2ccc3C(C)=CC(=O)Nc3c2	7.41	6.8	Excellent
17.	**FL-125**	FC(F)(F)c1ccc(C2=NC3=C(SCCC3)C(=O)N2)cc1	7.49	7	Excellent
18.	**FL-143**	O=C1C=C(c2ccc(cc2N1)-c3ccccc3OC)C	5.86	6.6	Excellent

*Experimental and predictive value is in pIC_{50}.

Table S3: 3D-QSAR model statistics.

Component	R^2	Q^2	Test R^2
Component 1	0.542	0.441	0.16
Component 2	0.718	0.57	0.519
Component 3	0.814	0.633	0.623
Component 4	0.862	0.653	0.678
Component 5	0.886	0.666	0.75
Component 6	0.919	0.645	0.732
Component 7	0.938	0.638	0.773
Component 8	0.953	0.631	0.798
Component 9	0.96	0.631	0.796
Component 10	0.968	0.606	0.771
Component 11	0.974	0.61	0.761
Component 12	0.98	0.597	0.781
Component 13	0.984	0.594	0.764
Component 14	0.988	0.582	0.747
Component 15	0.99	0.587	0.724
Component 16	0.992	0.58	0.702
Component 17	0.994	0.57	0.675
Component 18	0.995	0.566	0.677
Component 19	0.996	0.558	0.679
Component 20	0.997	0.546	0.689

Table S4: ADMET Risk screening of query set compounds.

Sr. No.	Compound Name	ADMET_ Risk	Absn_ Risk	RuleOf5	CYP_ Risk	MUT Risk	MUT Code	TOX Risk
1.	**F1**	0	0	0	0	1	m1	0
2.	**F2**	0	0	0	0	1	S1	0
3.	**F3**	0	0	0	0	0	Nil	0
4.	**F4**	0	0	0	0	1	S1	0
5.	**F5**	0	0	0	0	1	S1	0
6.	**F6**	0	0	0	0	1	m1	0
7.	**F7**	0	0	0	0	1	S1	0
8.	**F8**	0	0	0	0	1	m1	0
9.	**F9**	0	0	0	0	1	S1	0
10.	**F10**	0	0	0	0	1	m1	0
11.	**F11**	0	0	0	0	0	Nil	0
12.	**F12**	0	0	0	0	1	m1	0
13.	**F13**	0	0	0	0	1	m1	0
14.	**F14**	0	0	0	0	1	m1	0
15.	**F15**	0	0	0	0	0	Nil	0
16.	**F16**	0	0	0	0	1	S1	0
17.	**F17**	0	0	0	0	1	m1	0
18.	**F18**	0	0	0	0	1	m1	0
19.	**F19**	0	0	0	0	1	m1	0
20.	**F20**	0	0	0	0	0	Nil	0
21.	**F21**	0	0	0	0	0	Nil	0
22.	**F22**	0	0	0	0	1	m1	0
23.	**F23**	0	0	0	0	1	m1	0
24.	**F24**	0	0	0	0	1	m1	0

25.	**F25**	0	0	0	0	0	Nil	0

Table S5: Bio-physicochemical properties of the candidate compound.

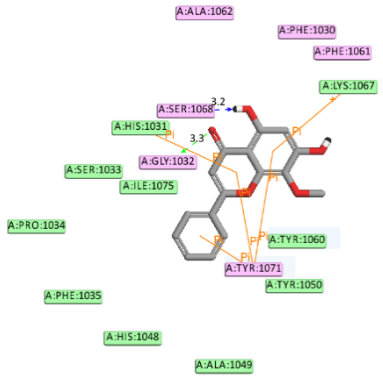
Identifier	F2	F3	F8	F11	F13	F20	F21	F25
S+Acidic_pKa	11.52	9.48	9.82	9.67	9.70	9.81	9.75	8.3
DiffCoef	0.83	0.87	0.78	0.83	0.83	0.86	0.82	0.76
MlogP	1.55	2.24	1.02	2.49	1.55	1.45	1.70	2.46
S+logP	2.86	3.09	2.40	3.32	2.9	2.42	2.67	3.51
S+logD	2.67	2.78	2.38	3.03	2.82	2.10	2.28	3.46
logHLC	-10.37	-10.86	-10.56	-10.57	-11.00	-12.06	-11.81	-8.71
S+Peff	5.17	4.94	5.06	5.33	5.56	2.99	3.22	4.78
S+MDCK	581.73	338.72	699.35	480.63	600.54	137.34	189.57	811.91
Perm_Cornea	151.4	123.50	102.9	130.61	154.71	59.78	65.81	138.93
Perm_Skin	11.53	14.20	5.26	11.92	10.44	5.05	4.02	8.87
S+Sw	0.01	0.11	0.09	0.11	0.02	0.15	0.15	0.03
S+pH_Satd	5.98	5.39	6.09	5.41	6.11	5.32	5.27	6.15
S+S_Intrins	0.01	0.11	0.09	0.11	0.02	0.15	0.15	0.03
SolFactor	751.45	217.63	268.55	222.10	611.53	184.3	192.47	507.45
S+S_pH	0.02	0.21	0.1	0.21	0.02	0.31	0.36	0.03
S+FaSSGF	0.08	0.07	0.05	0.05	0.04	0.12	0.09	0.04
S+FaSSIF	0.18	0.16	0.19	0.14	0.12	0.35	0.38	0.04
S+FeSSIF	0.34	0.44	0.26	0.39	0.25	0.47	0.48	0.17
SupSatn	SupSat	SupSat	SupSat	SupSat	SupSat	SupSat	SupSat	SupSat
BBB_Filter	Low	Low	Low	Low	Low	Low	Low	Low
LogBB	-0.39	-0.29	-0.47	-0.35	-0.49	-0.39	-0.52	-0.21
PrUnbnd	3.16	2.83	7.1	2.31	4.33	4.51	3.21	3.59
Vd	0.58	0.45	1.05	0.5	1.4	0.38	0.37	1.35
RBP	0.53	1.08	0.54	0.87	0.73	1.06	0.85	0.87
S+fumic	0.62	0.57	0.70	0.51	0.59	0.74	0.7	0.4
Pgp_Substr	No	No	No	No	No	No	No	No
Pgp_Inh	Yes	No	No	No	No	No	No	No
OATP1B1_Inh	No	No	No	No	No	No	No	No
HIVI-ST	4.37	4.03	4.97	4.16	4.65	4.09	4.32	4.17
HIVI-TC	4.32	3.75	4.46	3.81	4.27	3.98	3.99	3.81
Absn_Risk	0	0	0	0	0	0	0	0
RuleOf5	0	0	0	0	0	0	0	0

Table S6: Metabolism study of the candidate compound.

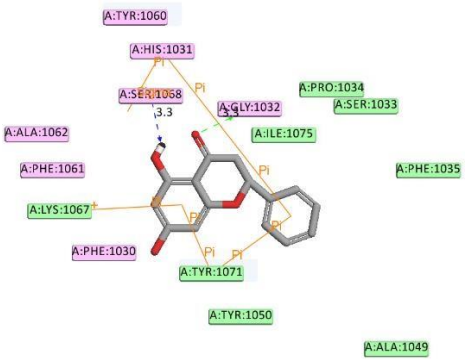
Identifier	F2	F3	F8	F11	F13	F20	F21	F25
CYP1A2_Inh	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CYP1A2_Substr	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
CYP1A2_Sites	C14(933); C13(767); C15(767)	C2(920); C6(560)	C23(944); C21(648); C15(585)	C2(862)	C21(970); C2(840); C15(628)	C2(917)	C15(388); C13(388); C6(236); C8(226)	Non-Substrate
CYP1A2_Km	28.53	33.79	18.55	16.59	7.42	158.31	49.91	Non-Substrate
CYP1A2_Vmax	1.76	4.22	5.34	1.18	1.99	5.19	8.04	Non-Substrate
CYP1A2_CLint	3.21	6.49	14.96	3.69	13.92	1.70	8.37	Non-Substrate
CYP2A6_Substr	No	No	No	No	No	No	No	No
CYP2A6_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2B6_Substr	No	No	No	No	No	No	No	Yes
CYP2B6_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	C22(799); C8(731)
CYP2C8_Substr	Yes	No	No	No	No	No	No	No

CYP2C8_Sites	C21(921)	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2C9_Inh	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CYP2C9_Substr	Yes	Yes	No	Yes	No	Yes	Yes	No
CYP2C9_Sites	C14(889); C21(872)	C2(851)	Non-Substrate	C2(800)	Non-Substrate	C2(871)	C21(655)	Non-Substrate
CYP2C9_Km	3.43	5.38	Non-Substrate	3.81	Non-Substrate	3.59	37.40	Non-Substrate
CYP2C9_Vmax	0.38	0.35	Non-Substrate	0.24	Non-Substrate	0.49	4.95	Non-Substrate
CYP2C9_CLint	8.14	4.8	Non-Substrate	4.61	Non-Substrate	9.97	9.67	Non-Substrate
CYP2C19_Inh	No	No	No	No	No	No	No	No
CYP2C19_Substr	No	No	No	No	Yes	No	No	No
CYP2C19_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	C21(984); C15(858); C2(767)	Non-Substrate	Non-Substrate	Non-Substrate
CYP2C19_K_m	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	61.866	Non-Substrate	Non-Substrate	Non-Substrate
CYP2C19_V_{max}	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	2.35	Non-Substrate	Non-Substrate	Non-Substrate
CYP2C19_C_{Lint}	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	0.53	Non-Substrate	Non-Substrate	Non-Substrate
CYP2D6_Inh	No	Yes	Yes	Yes	No	Yes	Yes	Yes
CYP2D6_Substr	No	No	No	No	No	No	No	No
CYP2D6_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2D6_Km	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2D6_Vmax	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2D6_CLint	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP2E1_Substr	No	No	No	No	No	No	No	No
CYP2E1_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate
CYP3A4_Inh	Yes	No	Yes	No	Yes	No	No	No
CYP3A4_Substr	No	No	No	No	No	No	No	Yes
CYP3A4_Sites	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	C22(856); C20(846); C9(710);C19(605)
CYP3A4_Km	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	46.37
CYP3A4_Vmax	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	6.36
CYP3A4_CLint	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	15.23
CYP3A4_HLM_Km	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	1055.87
CYP3A4_HLM_V_{max}	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	1.25
CYP3A4_HLM_C_{Lint}	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	Non-Substrate	1.19
CYP_HLM_C_{Lint}	19.5	12.63	17.30	13.97	17.58	7.72	7.3	20.34
CYP3A4_Inh_midaz	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CYP3A4_Inh_testo	No	No	No	No	No	No	No	No
CYP3A4_Ki_midaz	63.13	14.75	28.07	14.3	28.42	14.89	14.64	16.87
CYP3A4_Ki_testo	4.36	2.33	4.24	3.89	3.20	1.9	3.01	8.18
UGT1A1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
UGT1A3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
UGT1A4	No	No	No	No	No	No	No	Yes
UGT1A6	No	No	No	No	No	No	No	No
UGT1A8	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
UGT1A9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
UGT1A10	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

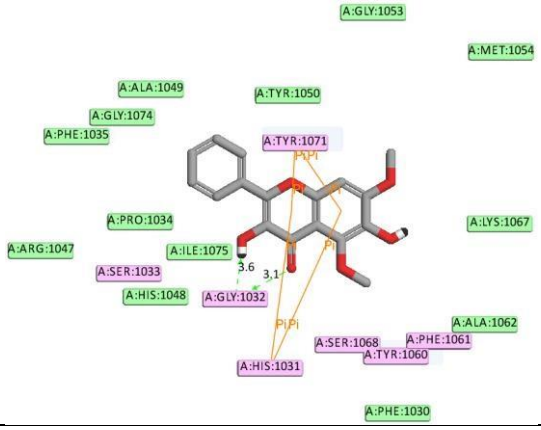
UGT2B7	Yes	No	No	No	No	No	No	No
UGT2B15	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes



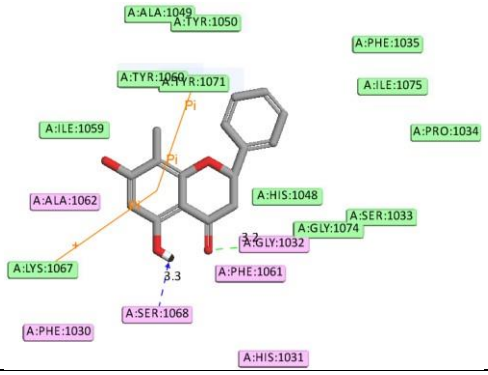
Compound F2



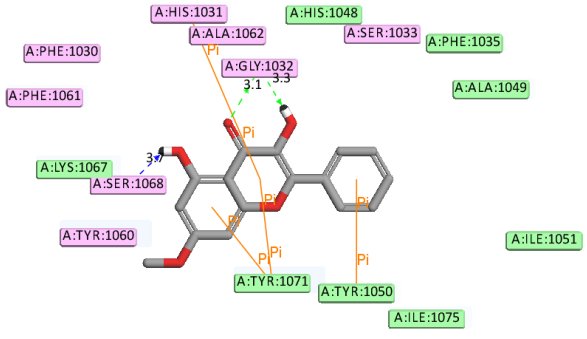
Compound F3



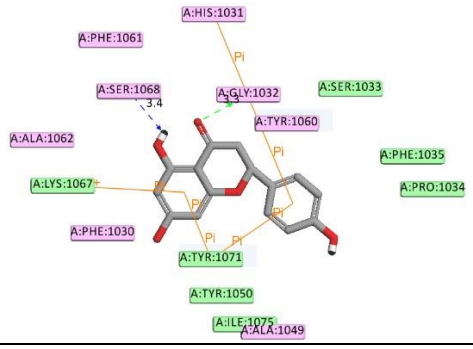
Compound F8



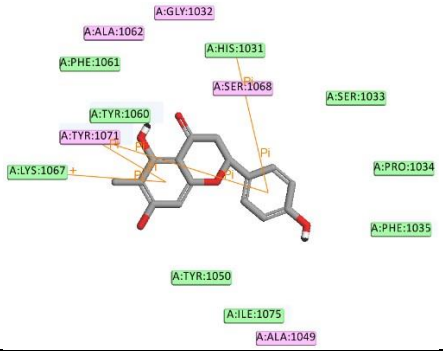
Compound F11



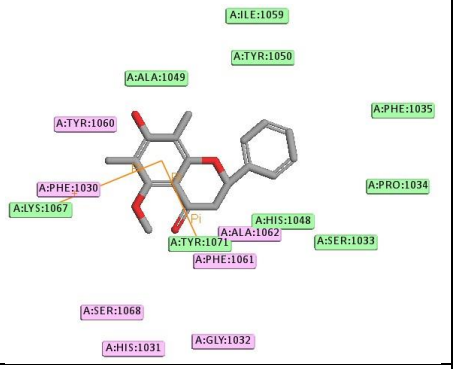
Compound F13



Compound F20



Compound F21



Compound F25

Figure S1: Two-dimensional diagrams illustrating protein-ligand interactions between candidate compounds and target receptor. Broken arrow represents the hydrogen bonding, and orange line represents the pi-interactions with length in Å.

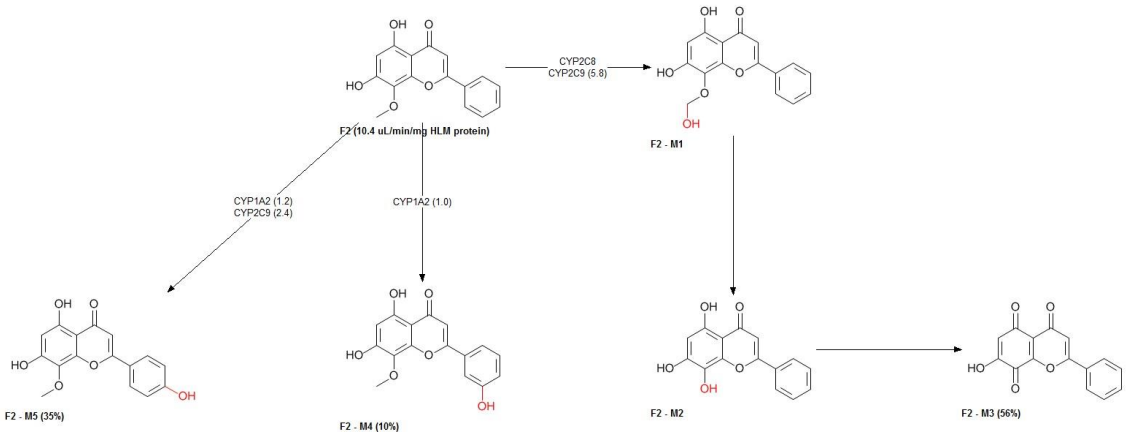


Figure S4.6.2a: The predictive metabolites and sites of metabolism of candidate compound F2**.**

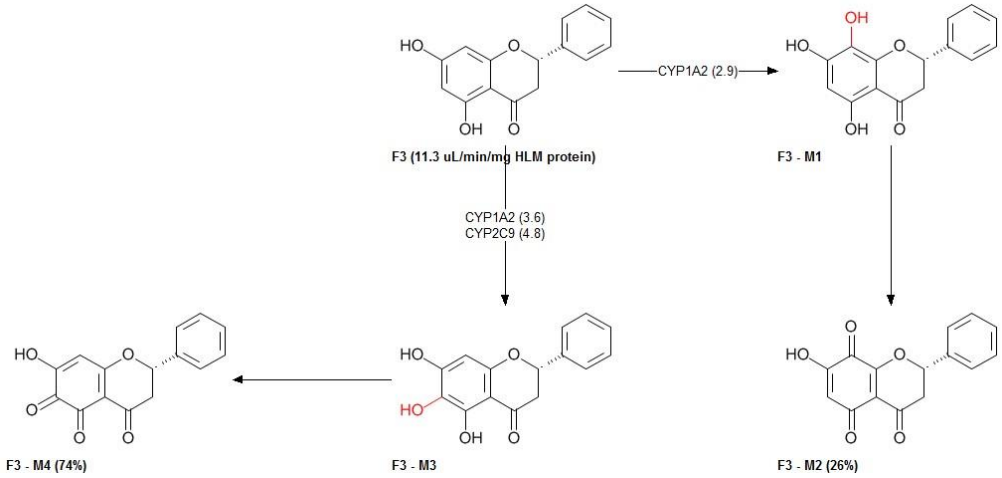


Figure S4.6.2b: The predictive metabolites and sites of metabolism of candidate compound F3.

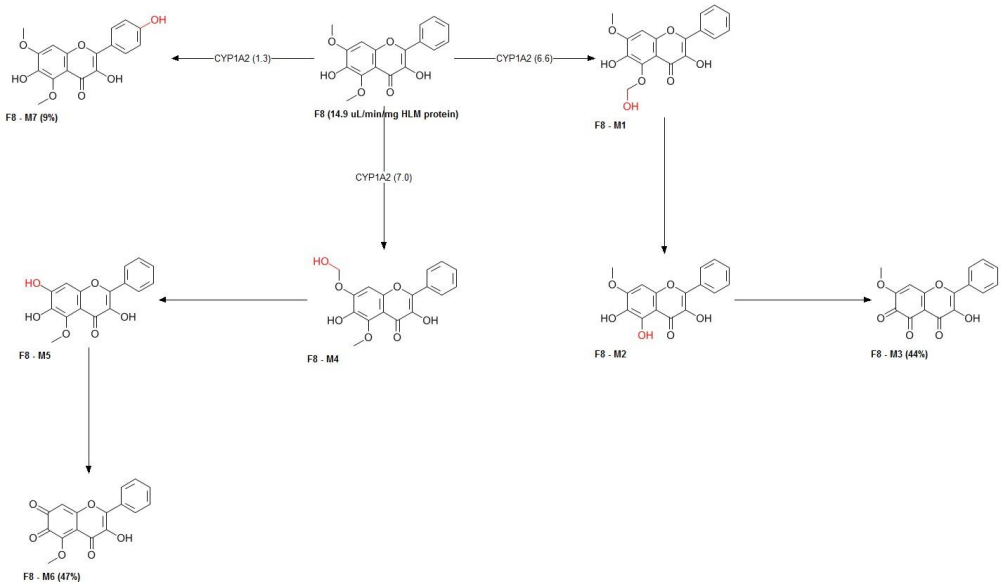


Figure S2c: The predictive metabolites and sites of metabolism of candidate compound F8.

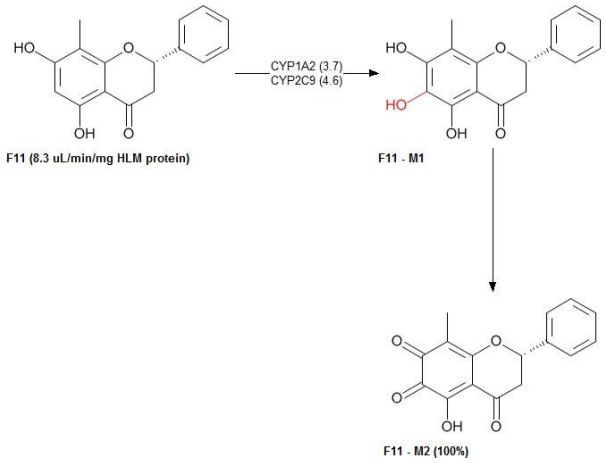


Figure Sd: The predictive metabolites and sites of metabolism of candidate compound F11.

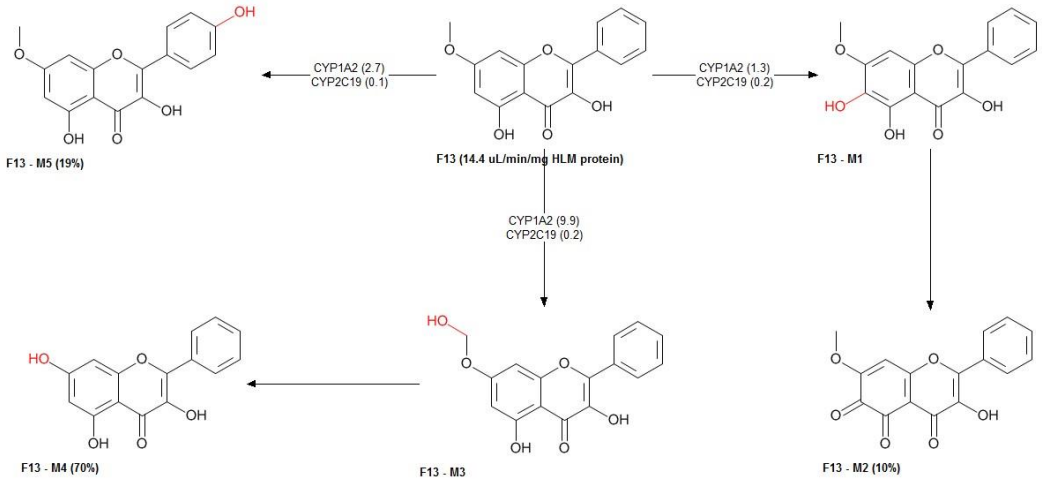


Figure S2e: The predictive metabolites and sites of metabolism of candidate compound F13.

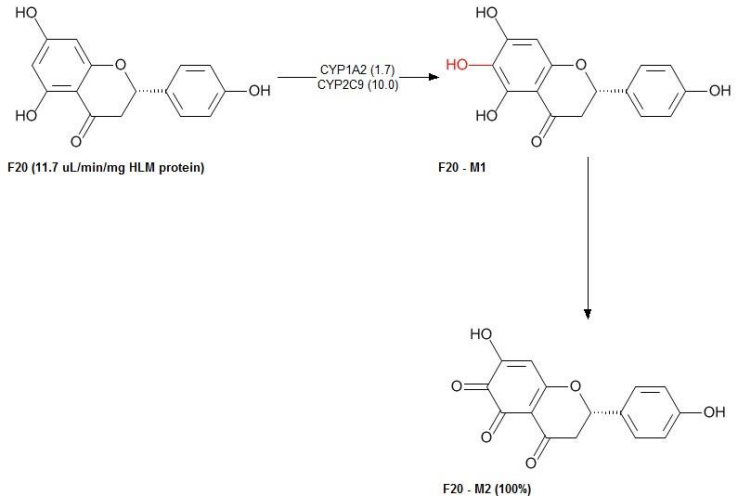


Figure S2f: The predictive metabolites and sites of metabolism of candidate compound F20.

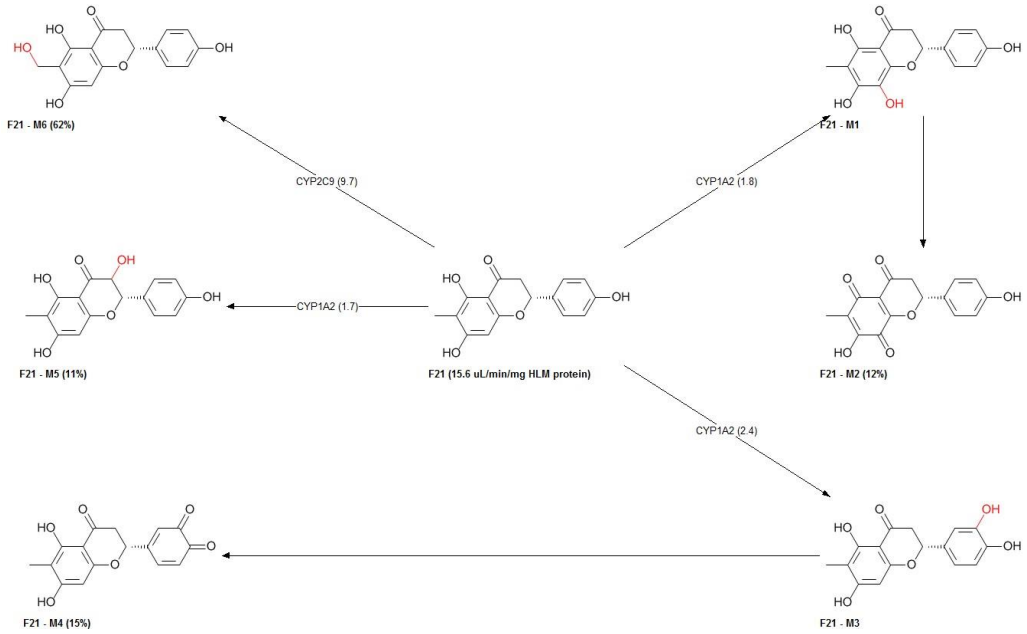


Figure S2g: The predictive metabolites and sites of metabolism of candidate compound F21**.**

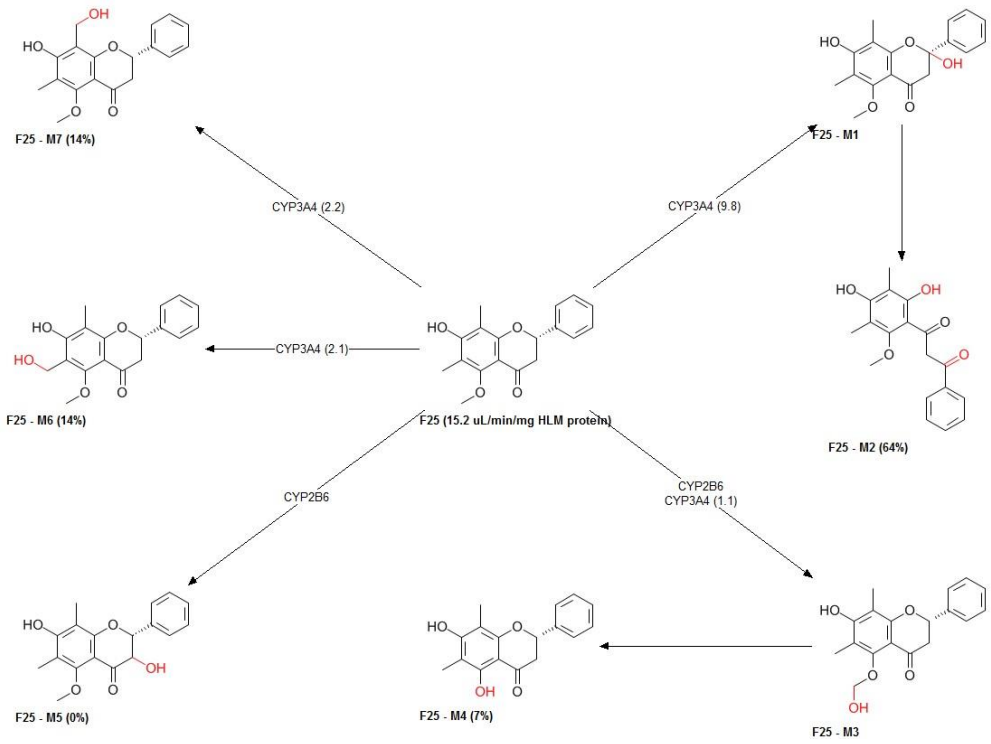


Figure S2h: The predictive metabolites and sites of metabolism of candidate compound F25.