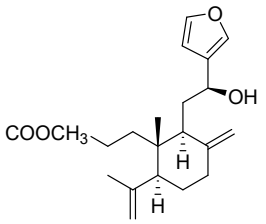
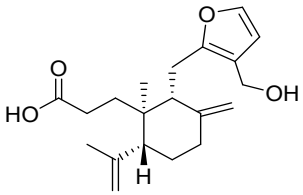
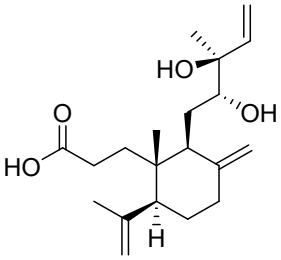
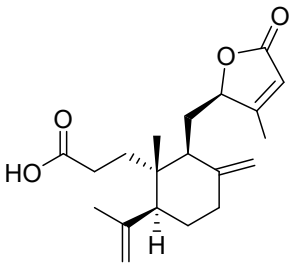
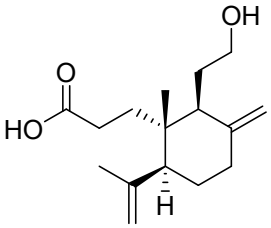
Supplementary Material

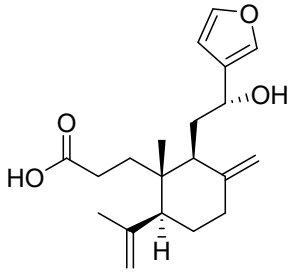
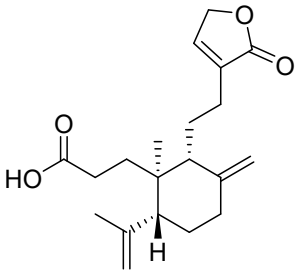
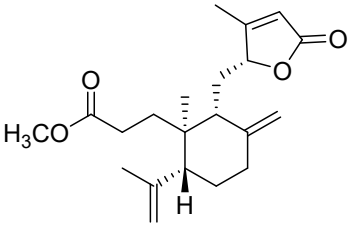
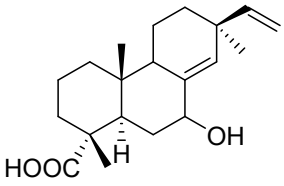
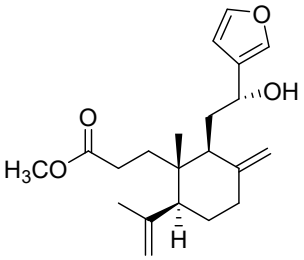
1 Supplementary Tables

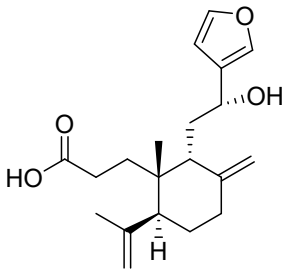
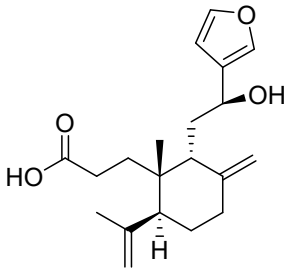
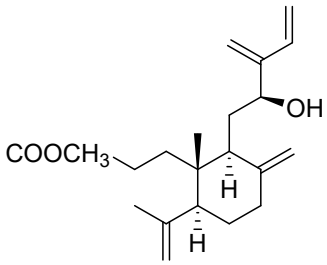
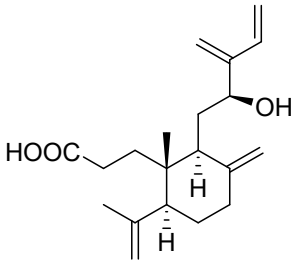
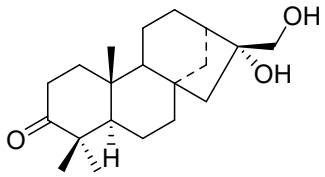
Supplementary Table 1. 26 active compounds screened by ADMET.

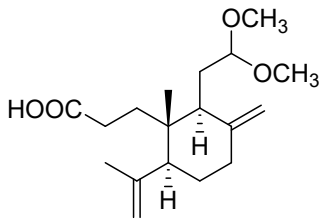
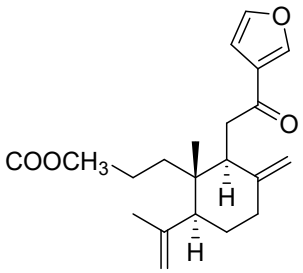
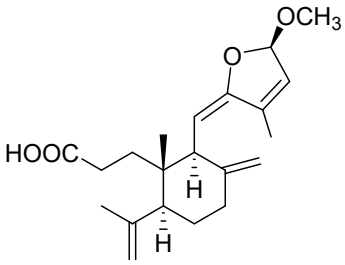
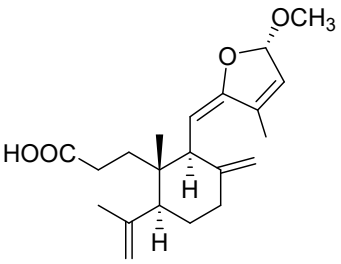
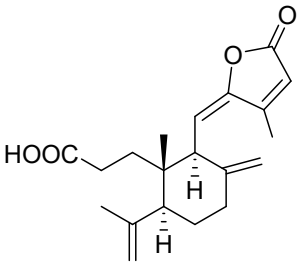
Name	HIA_Level	Solubility_Level	BBB_Level	Hepatotoxic#MDpvalue	PPB#MDpvalue
Call.01	6.1261	-2.66647	0.92298	0.0236195	0.188386
Call.02	6.351489	-3.249539	0.92298	0.0736195	0.188386
Call.03	7.461447	-3.0706032	0.7414	1.13E-02	4.14E-01
Call.04	8.621673	-2.351489	0.792298	0.0407989	0.840937
Call.05	9.314668	-1.0461447	0.892298	6.91E-02	0.18738
Call.06	10.963553	-3.0621673	0.96977	3.48E-02	0.171421
Call.07	9.0054175	-2.314668	0.96977	0.0176202	0.958889
Call.08	7.70502	-1.963553	0.96977	0.174918	0.184752
Call.09	6.8858	-2.0954175	0.96977	6.91E-02	1.92E-01
Call.10	6.92212	-1.0770502	0.725769	3.48E-02	0.262356
Call.11	7.0179	-3.368858	0.8450619	0.0176518	0.302343
Call.12	6.18676	-2.0126922	0.9498591	2.27E-02	0.192752
Call.13	6.14747	-1.00170179	0.8174143	2.27E-02	0.192752
Call.14	6.590082	-0.000618676	0.881956	0.0933375	0.3533643
Call.15	6.144284	-6.14747E-05	0.934849	0.0560181	0.781068
Call.16	6.14747	-3.00590082	0.734849	0.0560181	0.781068
Call.17	7.203918	-1.0144284	0.964959	0.0560181	0.781068
Call.18	7.88545	-6.14747E-05	0.884849	0.0407773	0.333518
Call.19	8.144905	-0.0203918	0.934994	0.195732	0.316632
Call.20	9.216313	-0.000788545	0.986859	0.17015	0.166551
Call.21	9.63553	-0.00144905	0.870969	0.775741	0.400007
Call.22	9.54175	-0.00216313	0.804049	0.790305	0.441486
Call.23	7.70502	-0.00273525	0.88863	1.41E-02	1.83E-01
Call.24	6.368858	-0.249539	0.954849	3.48E-02	0.201421
Call.25	6.126922	-0.99715	0.82484	0.0407989	0.282328
Call.26	6.170179	-0.174298	0.835969	0.0162439	0.156471

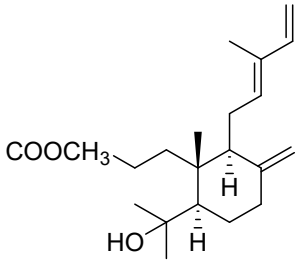
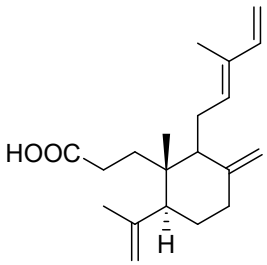
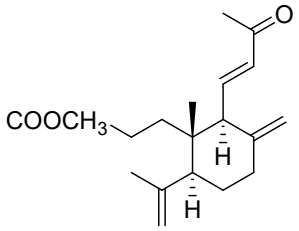
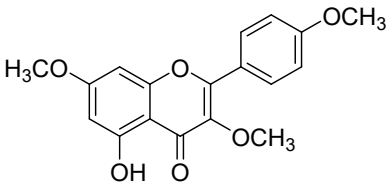
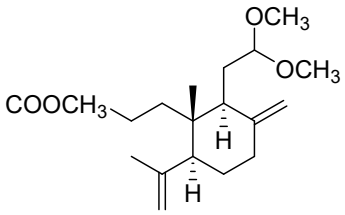
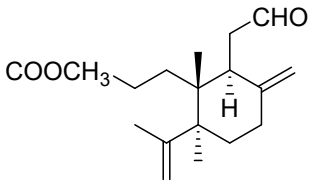
Supplementary Table 2.The information of the potential active compounds in CN

No.	Molecular Name	Molecular Formula	MolecularWeight	Structure
Call.1	Nudiflflopenes C	C21H30O4	346.21	
Call.2	Ent-3,4-seco-16-hydroxy-12,15-epoxy-4(18),8 (17),12,14-labdatetraen-3-oic acid	C20H28O4	332.20	
Call.3	3,4-Seco-12R,13S-dihydroxy-4(18),8(17),14 (15)-labdatrien-3-oic acid	C20H32O4	336.23	
Call.4	Callicarpaolide	C20H28O4	332.20	
Call.5	Callicarpic acid	C20H28O4	266.19	

Call.6	Callicarpic acid A	C20H28O4	332.20	
Call.7	Ent-3,4-seco-14-carbonyl-15,16-epoxy-4(18),8(17),13 (14)-labdatrien-3-oic acid	C20H28O4	332.20	
Call.8	Ent-3,4-seco-12R,15-epoxy-4(18),8(17),13-labdatrien-3-oic acid	C21H30O4	346.21	
Call.9	7α-Hydroxy sandaracopimaric acid	C20H30O3	318.22	
Call.10	Methylcallicarpate	C21H30O4	346.21	

Call.11	Syn-3,4-seco-12R-hydroxy-15,16-epoxy-4(18),8(17),13(16),14(15)-labdatetraen-3-oic acid	C20H28O4	332.20	
Call.12	Syn-3,4-seco-12S-hydroxy-15,16-epoxy-4(18),8(17),13(16),14(15)-labdatetraen-3-oic acid	C20H28O4	332.20	
Call.13	Nudiflflopenes A	C21H32O3	332.24	
Call.14	Nudiflflopenes B	C20H30O3	318.22	
Call.15	16,17-Dihydroxy-3-O-phyllocladane	C20H32O3	320.24	

Call.16	Nudiflflopenes D	C18H30O4	310.21	
Call.17	Nudiflopenes M	C21H28O4	344.20	
Call.18	Nudiflflopenes F	C21H30O4	346.21	
Call.19	Nudiflflopenes G	C21H30O4	346.21	
Call.20	Nudiflflopenes H	C20H26O4	330.18	

Call.21	Nudiflflopenes I	C21H34O3	334.25	
Call.22	Maravuic acid	C20H30O2	302.22	
Call.23	Nudiflopenes J	C19H28O3	304.20	
Call.24	5-Hydroxy-3,7,4′-trimethoxyflavone	C18H16O6	328.09	
Call.25	Nudiflflopenes E	C19H32O4	324.23	
Call.26	Nudiflopenes L	C18H28O3	292.20	

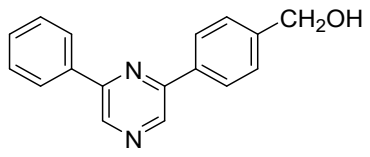
Supplementary Table 3. Matching degree of the test set compounds predicted by the 10 pharmacophore models.

Cormpound NO	01	02	03	04	05	06	07	08	09	10
Int-01	3.9625	0.65945	1.18796	3.91613	3.19639	0.25925	1.2866	3.82654	0.43834	3.98766
Int-02	3.76901	1.67219	2.2906	3.93413	2.239	2.20579	1.2296	2.12656	2.25124	2.33345
Int-03	3.98766	1.44859	2.03972	3.80143	1.98309	2.17139	1.10379	1.91912	2.39457	2.28772
Int-04	2.30598	1.37146	0.102987	3.12501	2.33882	2.24423	3.24954	1.32004	0.977881	0.571884
Int-05	0.71122	3.40324	3.592	1.54423	2.79911	2.68718	0.42824	3.38519	2.43606	2.55252
Int-06	1.82858	0.49892	3.14941	3.85981	2.0913	2.5317	1.37478	3.28597	3.18324	2.92272
Int-07	1.72381	3.41422	2.62755	1.04385	1.23636	2.6167	1.73441	1.30561	3.92842	3.03839
Int-08	3.57653	2.41422	0.88855	1.74395	1.76555	2.3085	1.97925	2.20982	3.92842	2.12939
Int-09	0.90094	1.42402	2.62766	2.94485	2.05132	1.80937	2.33539	1.00561	0.82832	1.11837
Int-10	2.40709	1.80078	2.75906	3.19004	2.81573	2.67785	2.31056	3.1489	3.33791	3.4629
Int-11	3.16004	1.80112	3.15906	2.91195	2.1356	2.58894	2.23714	2.52124	2.99339	3.24629
Int-12	0.12409	1.57653	3.11555	2.72395	2.1728	2.38998	1.4288	2.84429	3.50444	3.15449
Int-13	3.11315	1.90094	3.21516	3.03933	2.53714	2.64252	3.01965	2.35095	3.43486	3.60293
Int-14	2.95962	1.78932	3.04463	3.21488	1.97068	2.18611	2.00125	1.16105	3.65769	3.41952
Int-15	3.79196	2.00706	2.90067	2.72521	3.11684	2.55888	2.94044	1.37123	2.75737	2.94364
Int-16	3.90969	3.35443	3.57514	3.64667	2.37883	2.60261	2.27789	3.38256	3.83756	3.6764
Int-17	1.61287	0.734	2.2414	2.46882	1.74164	2.28845	2.09611	1.10532	3.68493	2.08422
Int-18	1.93824	1.02205	1.33054	0.640566	2.34411	2.62902	2.31717	3.22565	3.50321	0.669873
Int-19	2.22125	0.778	2.12968	2.01839	1.86682	1.28808	2.01914	0.11238	1.9591	1.87823
Int-20	1.53505	1.129	1.32367	1.6572	2.6538	3.89412	0.8565	2.14176	3.56622	3.39215
Int-21	3.33508	3.47246	3.1939	2.22511	3.43879	3.34423	1.25054	2.39119	2.98892	1.5819
Int-22	3.40324	2.68718	0.42824	3.38519	2.43606	2.55252	2.71122	3.28597	1.54423	2.79911
Int-23	1.49892	2.5317	1.74478	3.592	3.18324	2.92272	1.82858	1.32004	3.85981	2.0913
Int-24	1.37146	2.24423	3.24954	3.1941	1.977881	0.57188	2.30598	3.38519	2.32501	3.93882
Int-25	3.40324	2.68718	0.42824	0.102987	2.43606	2.55252	0.71932	3.28597	1.54423	2.79911
Int-26	0.49892	2.5317	1.37478	3.592	3.18324	2.92272	3.82858	3.38519	3.85981	2.2313

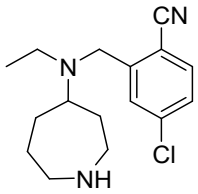
Supplementary Table 4. Molecular docking results.

Compound	Protein	Libdock score	Binding energy (kcal/mol)	Ligand energy (kcal/mol)	Protein energy (kcal/mol)	Complex energy (kcal/mol)
ent 3,4-seco-16-hydroxy-12,15-epoxy4(18),8(17),12,14-Labdatetraen-3-oic acid	interleukin-6(6CQ5)	94.7441	-9.64	39.5681	-19026.6085	-19156.8426
Nudiflflopenes C	interleukin-6(6CQ5)	96.3626	-9.84	34.2619	-19026.6085	-19346.6810
5-hydroxy-3,7,4'-trimethoxyflavone	interleukin-6(6CQ5)	96.9272	-11.64	49.6250	-19026.6085	-19415.2729
NudiflflopenesM	interleukin-6(6CQ5)	95.9583	-3.27	62.3906	-19026.6085	-19156.6197

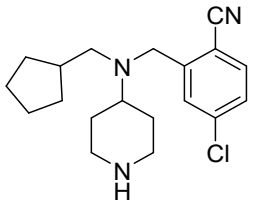
Supplementary Figures 1. Structural formulae of 26 training set compounds.



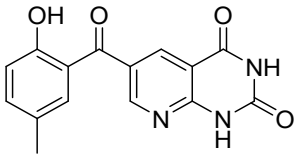
Int-1 IC50=68μM



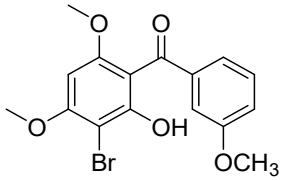
Int-2(IC50=660nM)



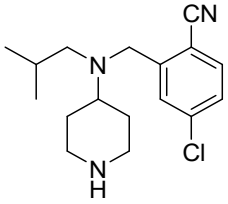
Int-3(IC50=1500nM)



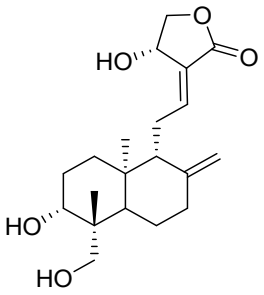
Int-4 IC50=0.16μM



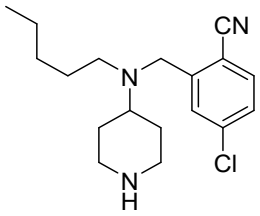
Int-5 IC50=82μM



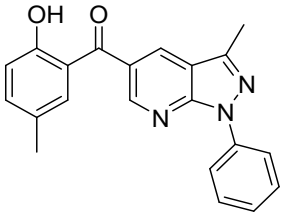
Int-6 (IC50=32nM)



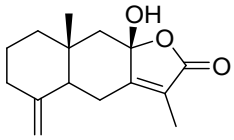
Int-7 IC50=56μM



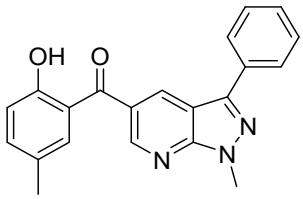
Int-8(IC50=570nM)



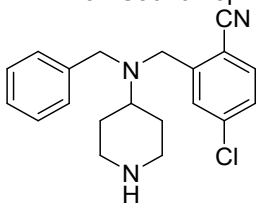
Int-9 IC50=0.16μM



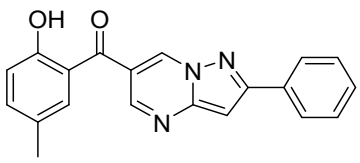
Int-10 IC50=2μM



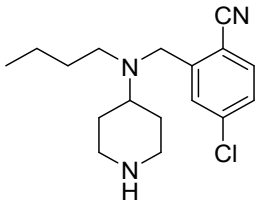
Int-11 IC50=0.16μM



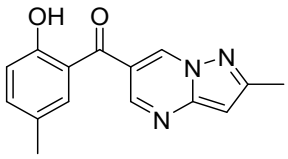
Int-12(IC50=660nM)



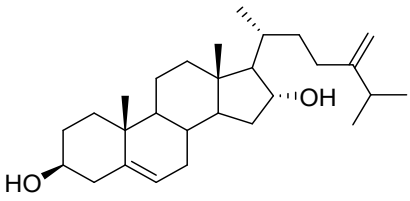
Int-13 IC50=0.16μM



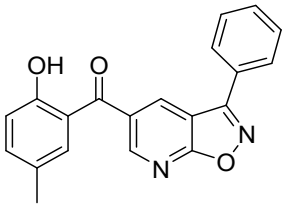
Int-14(IC50=130nM)



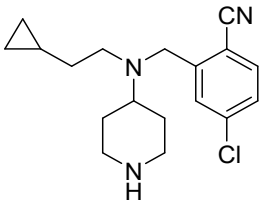
Int-15 IC50=0.16μM



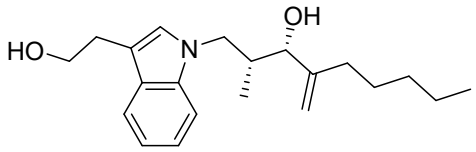
Int-16 IC50=5.2μM



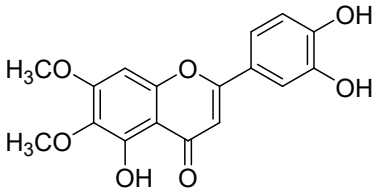
Int-17 IC50=0.16μM



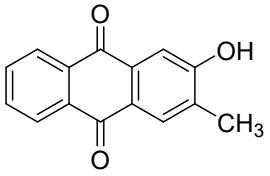
Int-18(IC50=160nM)



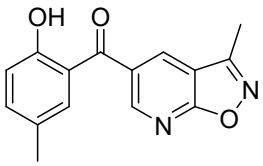
Int-19 IC50=6.83μM



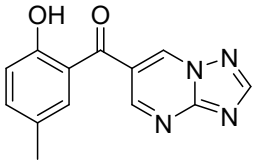
Int-20 IC50=80μM



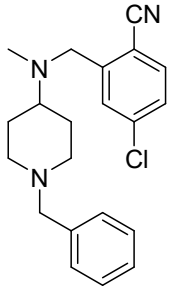
Int-21 IC50=60μM



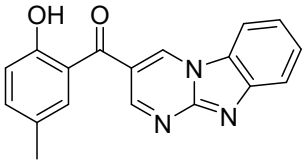
Int-22 IC50=0.16μM



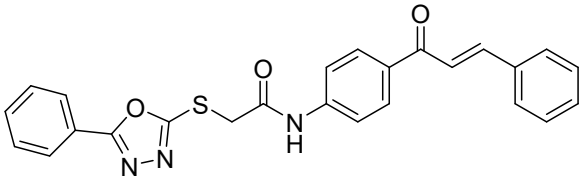
Int-23 IC50=0.16μM



Int-24(IC50=270nM)

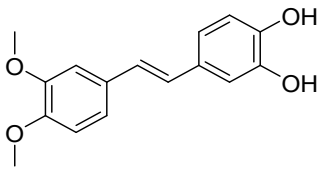


Int-25 IC50=0.16μM

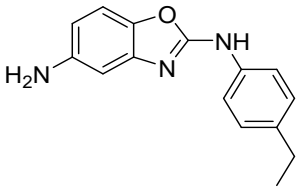


Int-26 IC50=82μM

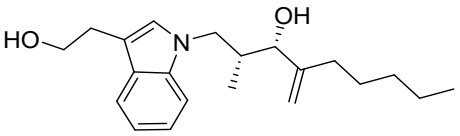
Supplementary Figures 2. Structural formulae of 26 test set compounds.



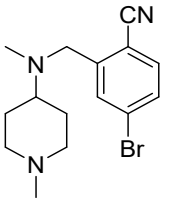
Nit-1(IC50=80nM)



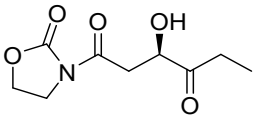
Nit-2(IC50=18.9nM)



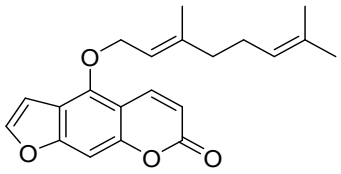
Nit-3(IC50=6.83μM)



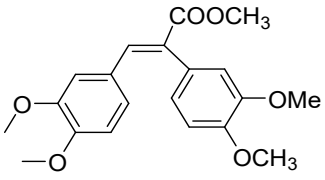
Nit-4(IC50=210nM)



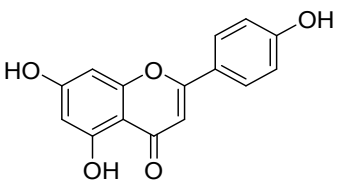
Nit-5(IC_{50}=100μM)



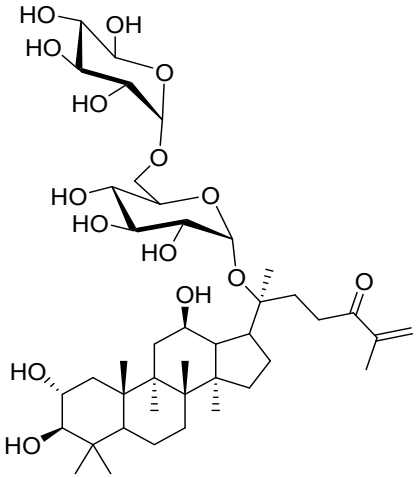
Nit-6(IC_{50}=1400nM)



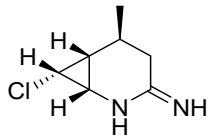
Nit-7(IC_{50}=5050nM)



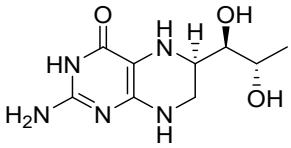
Nit-8(IC_{50}=6860nM)



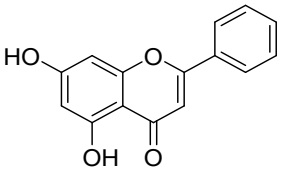
Nit-11(IC_{50}=270nM)



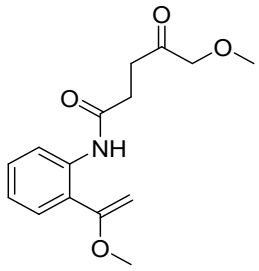
Nit-9(IC_{50}=2300nM)



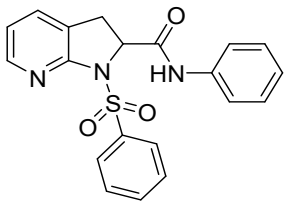
Nit-10(IC_{50}=250nM)



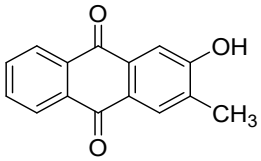
Nit-12 IC50=56μM



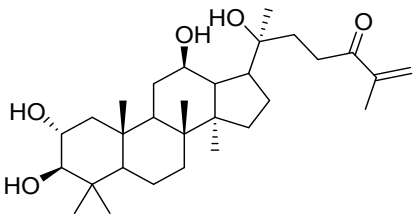
Nit-13 IC50=10μM



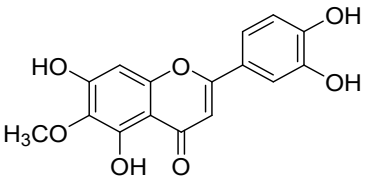
Nit-14(IC_{50}=100nM)



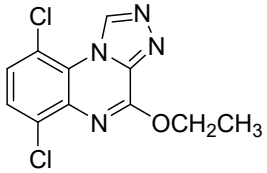
Nit-15 IC50=73.8μM



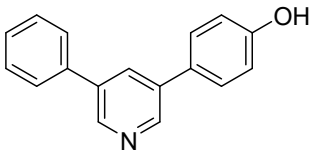
Nit-16 IC50=0.59μM



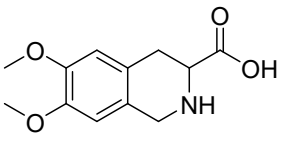
Nit-17 IC50=68.8μM



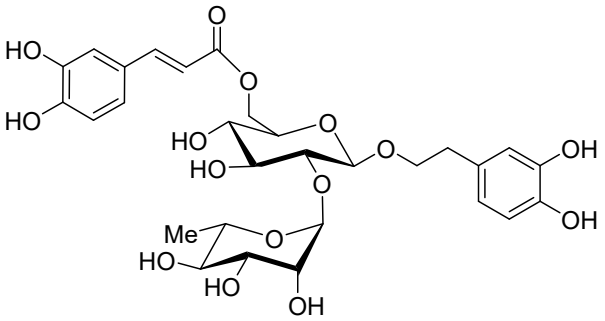
Nit-18 IC50=46.4μM



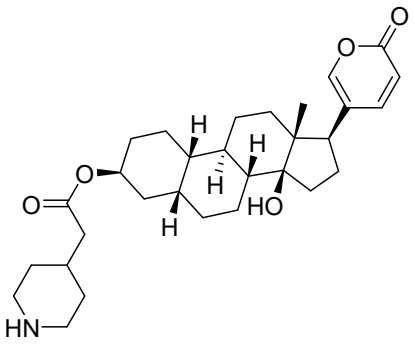
Nit-19 IC50=73μM



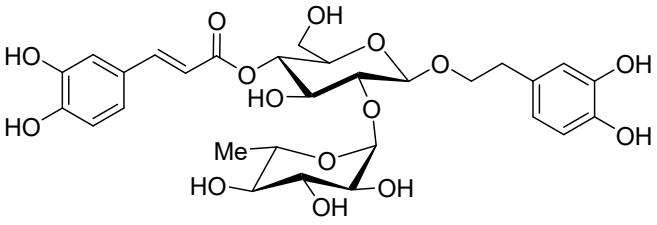
Nit-20 IC50=10μM



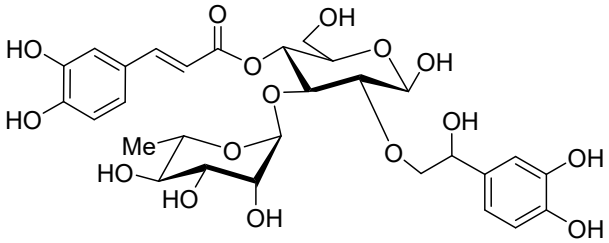
Nit-22



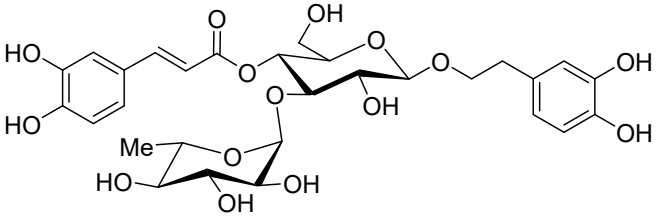
Nit-21 IC50=82μM



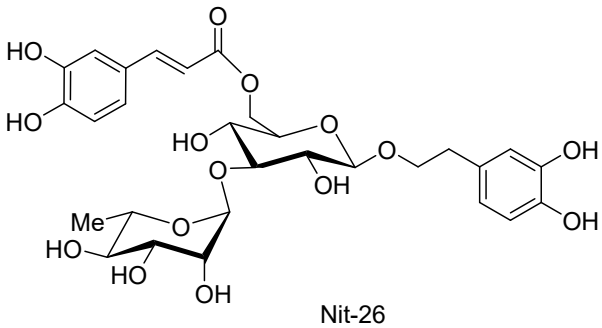
Nit-23



Nit-24



Nit-25



Nit-26