Supplementary materials:

In silico screening and validation of natural compounds with fabrication and characterization of lead compound loaded chitosome for targeting lung fibrosis

Ajay Kakati[a,b], Amartya Banerjee[a], Parikshit Das[a], GouravRakshit[c], Rahul Ghosh[c], Reshmi Chakraborty[a], Buddhadeb Saha[a], Danswrang Goyary[a], Yangchen D Bhutia[a], Sanjeev Karmakar[a], Sumit Kishor[a], Bhaskar Mazumder[b], Pronobesh Chattopadhyay[a*]

[a]Division of Pharmaceutical Technology, Defence Research Laboratory, Tezpur, Assam-784001, India

[b]Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, Assam-786004, India

[c]Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra, Ranchi-835215, Jharkhand India

***Corresponding author**

Dr. Pronobesh Chattopadhyay

Defence Research Laboratory (DRL), DRDO,

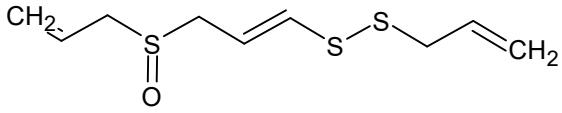
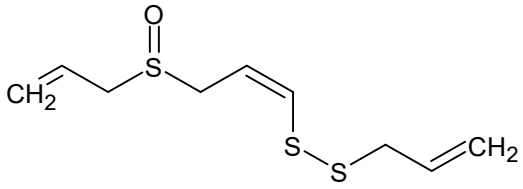
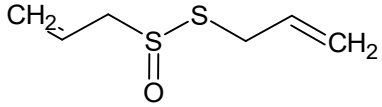
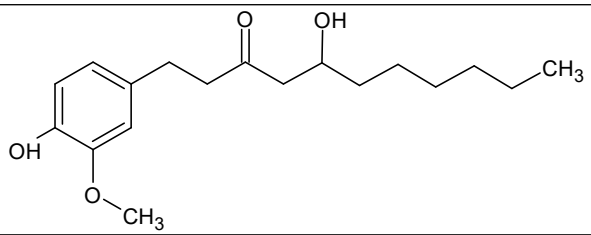
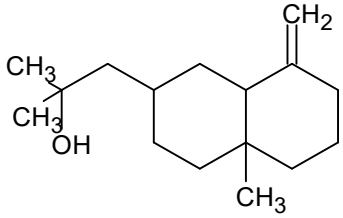
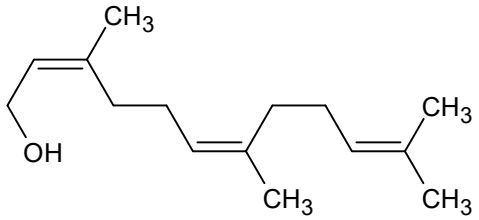
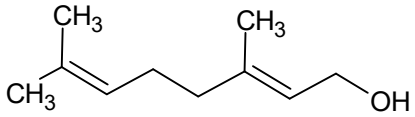
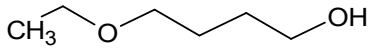
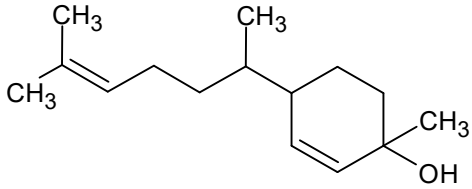
Tezpur, Assam-784001, India

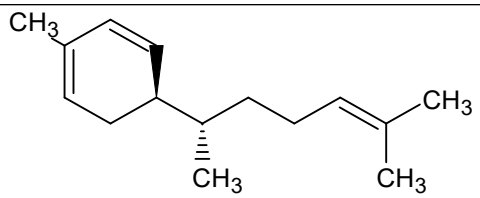
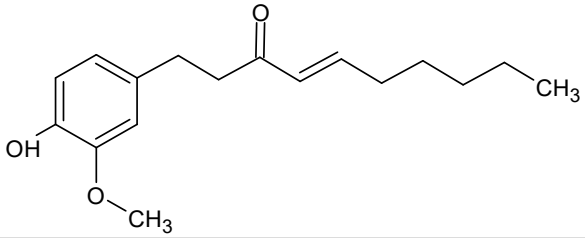
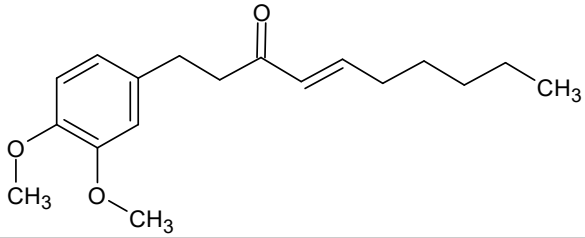
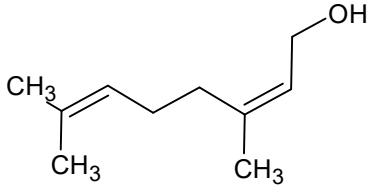
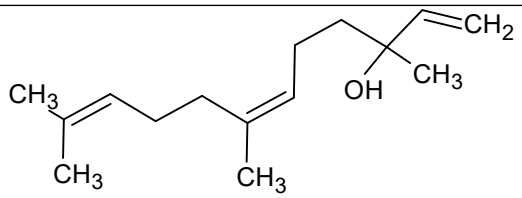
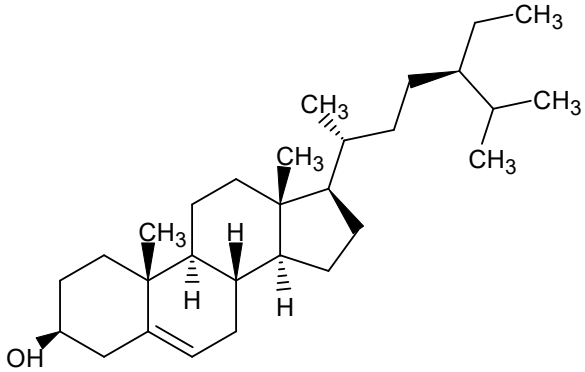
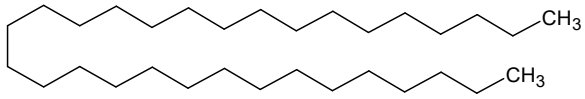
Tel: +91-3712258836/258508

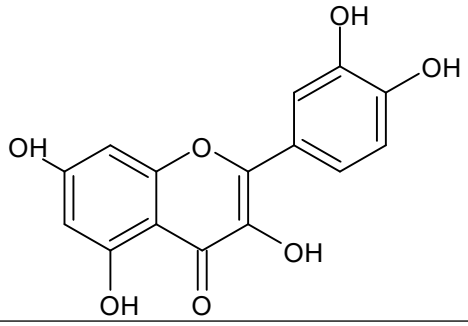
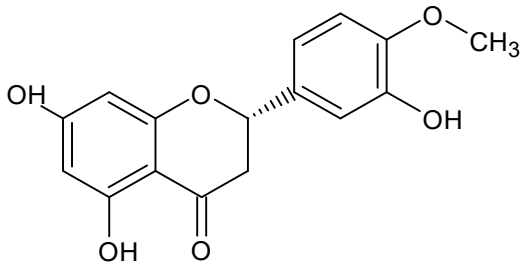
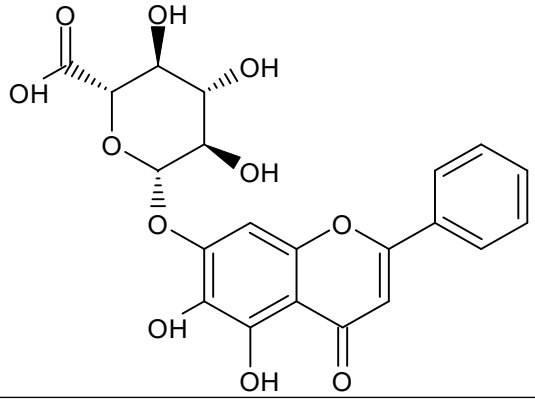
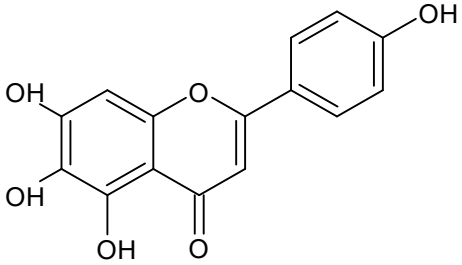
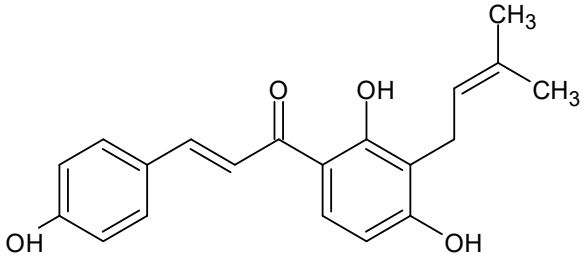
Fax: +91-3712258534

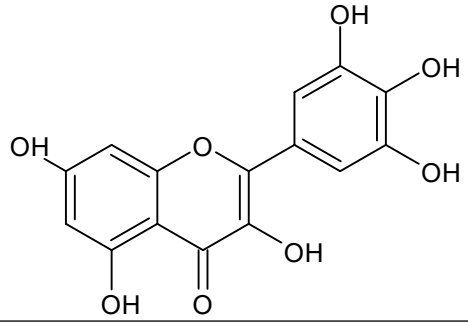
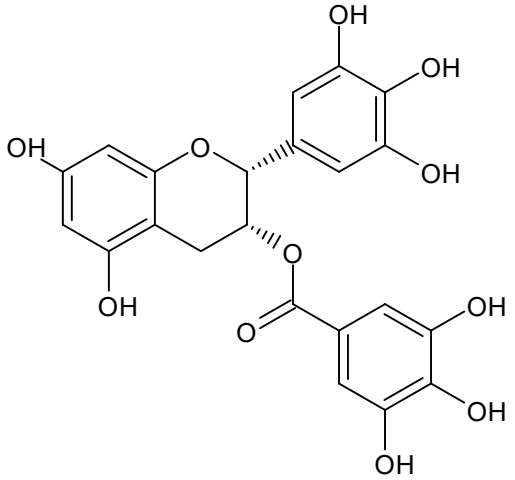
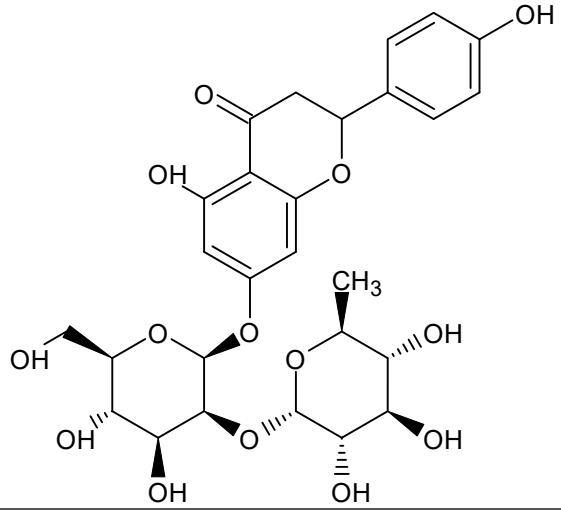
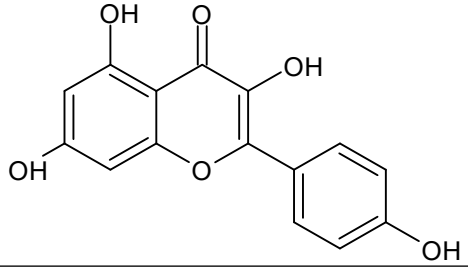
Email: chattopadhyay.drl@gmail.com

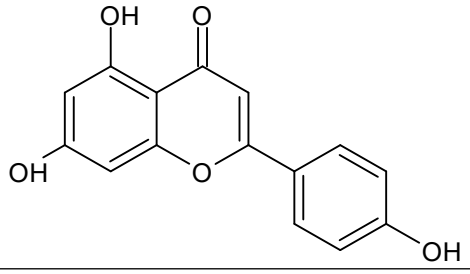
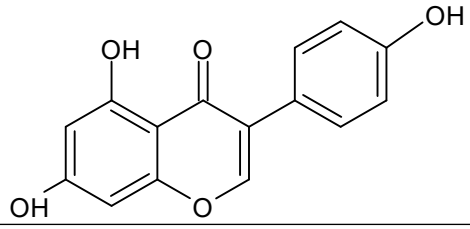
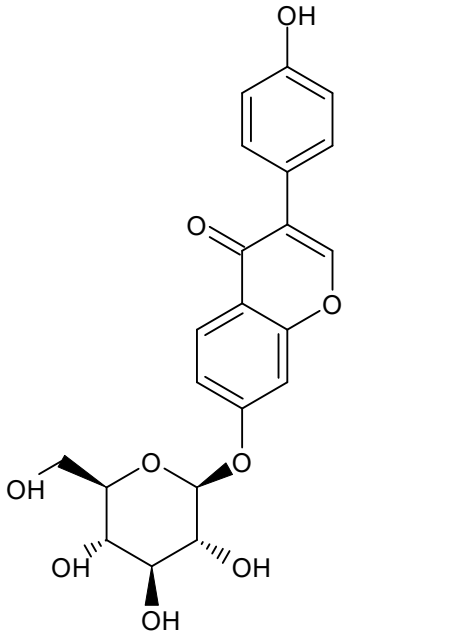
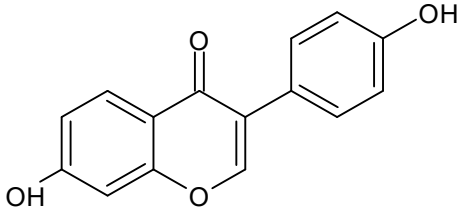
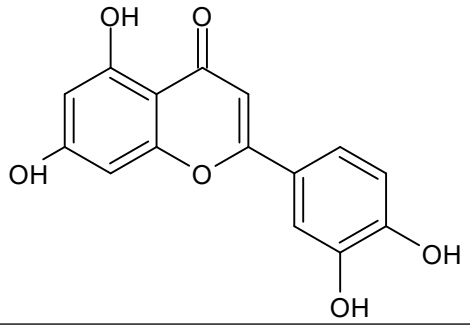
Table.S1. List of selected natural compounds

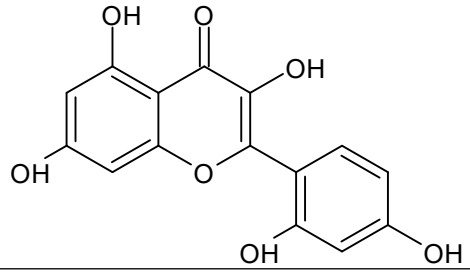
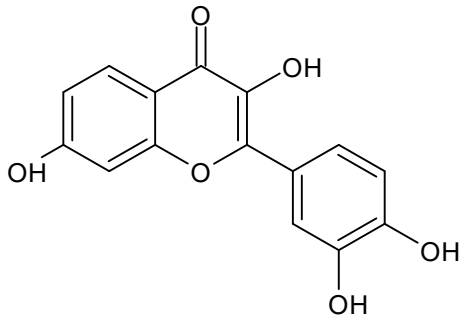
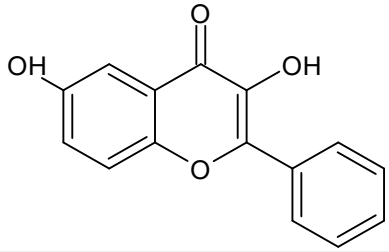
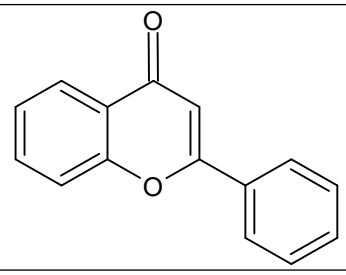
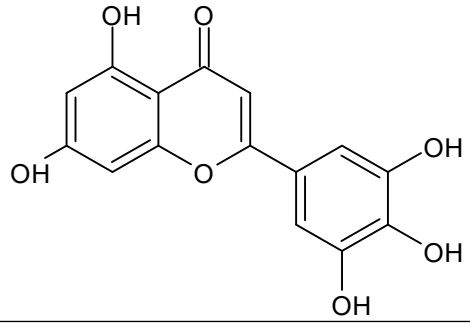
S.No.	Name	Structure	Smiles
1	**E-Ajoene**		O=S(C\C=C\SSCC=C)CC=C
2	**Z-Ajoene**		O=S(C\C=C/SSCC=C)CC=C
3	**Allicin**		C=CCS(=O)SCC=C
4	**6-Gingerol**		Oc1ccc(cc1OC)CCC(=O)CC(O)CCCCCC
5	**Zingiberol**		CC(C)(O)CC1CCC2(C)CCCC(=C)C2C1
6	**Farnesol**		C/C(C)=C\CCC(/C)=C\CCC(/C)=C\CO
7	**Geraniol**		C\C(C)=C\CCC(\C)=C\CO
8	4-Ethoxybulanol		CCOCCCCO
9	Zingiberenol		CC1(O)C=CC(CC1)C(C)CC\C=C(/C)C

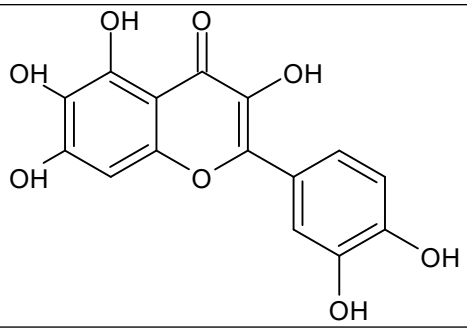
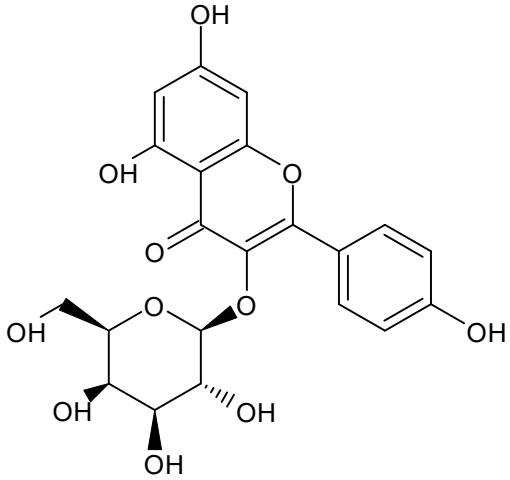
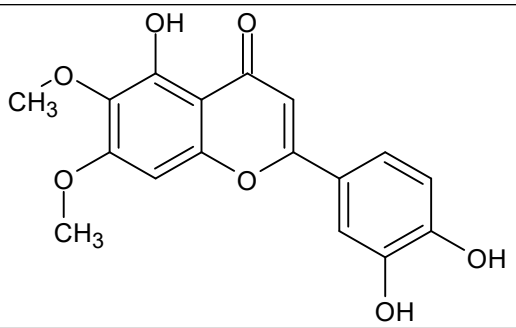
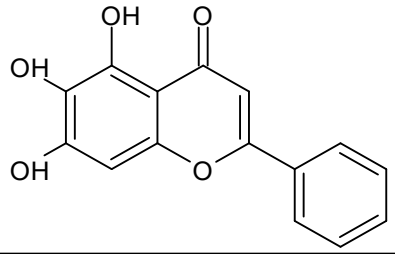
10	Zingiberene		C/C(C)=C\CC[C@H](C)[C@@H]1C=CC(C)=CC1
11	6-Shogaol		Oc1ccc(cc1OC)CCC(=O)\C=C\CCCCC
12	Methyl-6-shogaol		COc1cc(ccc1OC)CCC(=O)\C=C\CCCCC
13	Nerol		C\C(C)=C\CCC(/C)=C\CO
14	Nerdiol		C/C(C)=C\CCC(/C)=C\CCC(C)(O)C=C
15	b-Sitosterol		CC(C)[C@H](CC)CC[C@@H](C)[C@H]1CC[C@H]2[C@@H]3CC=C4C[C@@H](O)CC[C@]4(C)[C@H]3CC[C@]12C
16	Hentriacontane		CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC

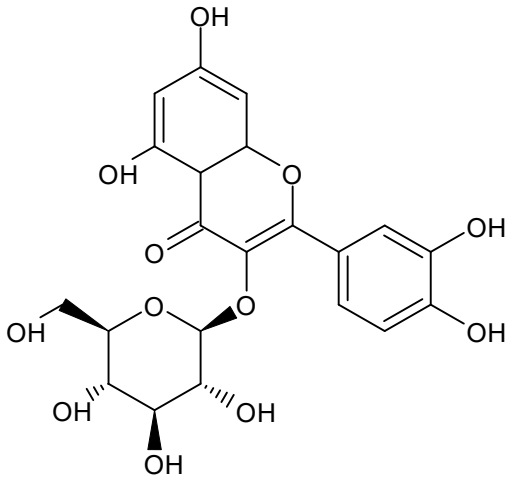
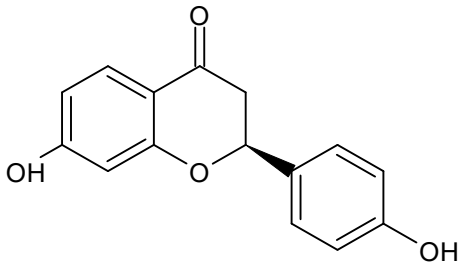
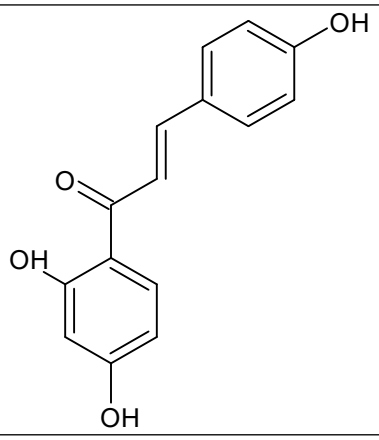
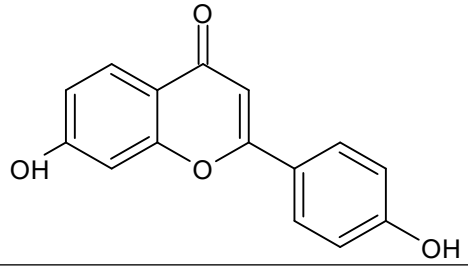
17	**Quercetin**		Oc1ccc(cc1O)C=1Oc2cc(O)cc(O)c2C(=O)C=1O
18	Hesperetin		COc1ccc(cc1O)[C@@H]1CC(=O)c2c(cc(O)cc2O)O1
19	Baicalin		C1=CC=C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3O2)OC4C(C(C(C(O4)C(=O)O)O)O)O)O)O
20	Scutellarin		Oc1ccc(cc1)C1=CC(=O)c2c(O)c(O)c(O)cc2O1
21	Isobavachalcone		Oc1c(ccc(O)c1C\C=C(/C)C)C(=O)/C=C/c1ccc(O)cc1

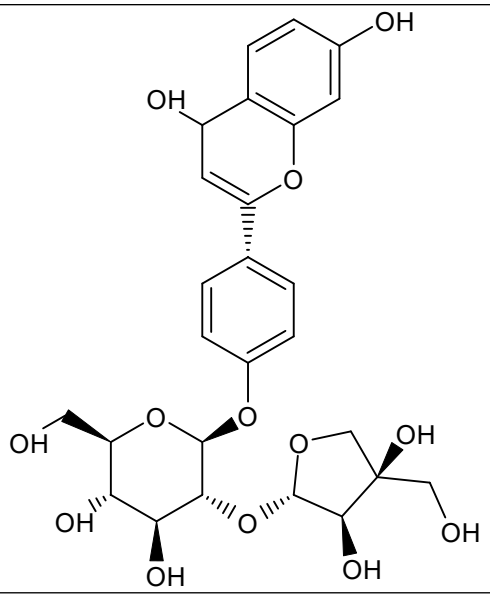
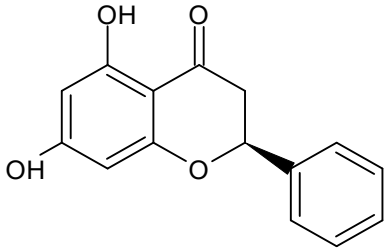
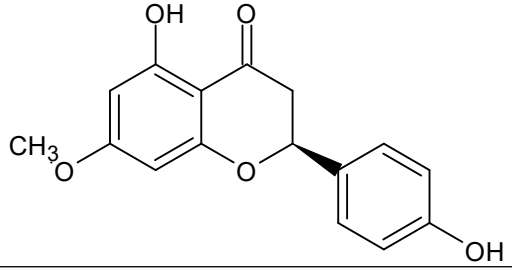
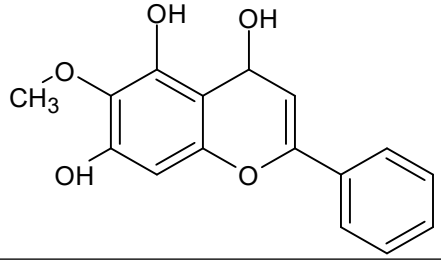
22	Myricetin		Oc1cc(cc(O)c1O)C=1Oc2cc(O)cc(O)c2C(=O)C=1O
23	EGCG		Oc1cc(cc(O)c1O)C(=O)O[C@@H]1Cc2c(cc(O)cc2O)O[C@@H]1c1cc(O)c(O)c(O)c1
24	Naringin		Oc1ccc(cc1)C1CC(=O)c2c(O)cc(cc2O1)O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@@H]1O[C@@H]1O[C@@H](C)[C@H](O)[C@@H](O)[C@@H]1O
25	Kaempferol		Oc1ccc(cc1)C=1Oc2cc(O)cc(O)c2C(=O)C=1O

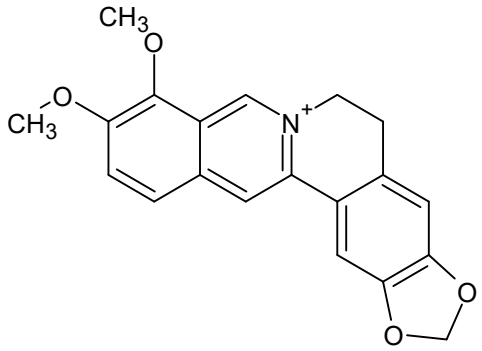
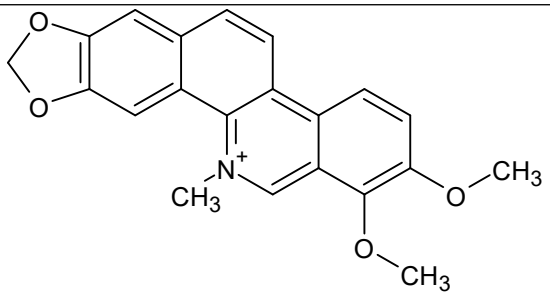
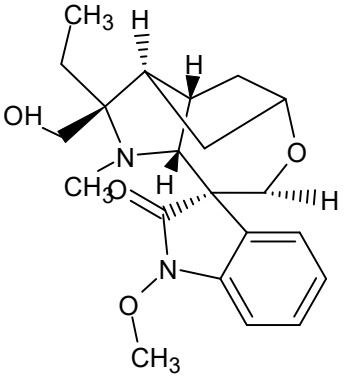
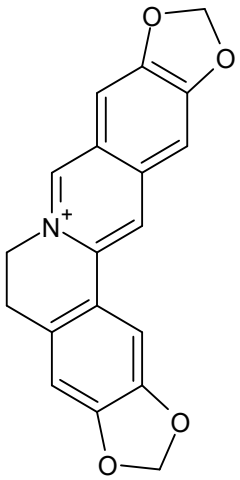
26	Apigenin		Oc1ccc(cc1)C1=CC(=O)c2c(cc(O)cc2O)O1
27	Genistein		Oc1ccc(cc1)C1=COc2cc(O)cc(O)c2C1=O
28	Daidzin		Oc1ccc(cc1)C1=COc2cc(O[C@@H]3O[C@H](CO)[C@@H](O)[C@H](O)[C@H]3O)ccc2C1=O
29	Daidzein		Oc1ccc(cc1)C1=COc2cc(O)ccc2C1=O
30	Luteolin		Oc1ccc(cc1O)C1=CC(=O)c2c(cc(O)cc2O)O1

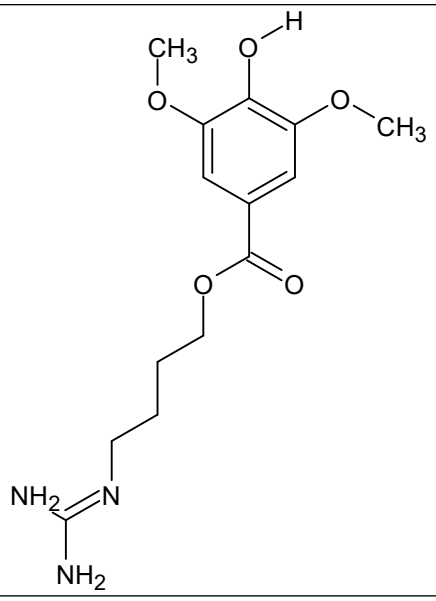
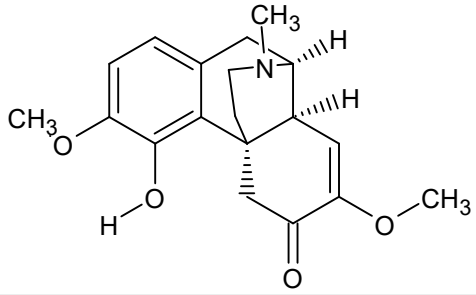
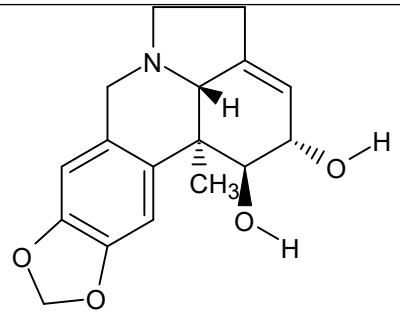
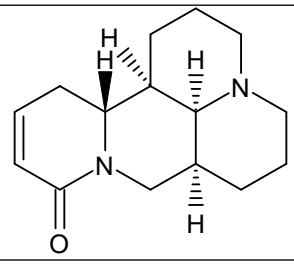
31	Morin		Oc1ccc(C=2Oc3cc(O)cc(O)c3C(=O)C=2O)c(O)c1
32	Fisetin		Oc1ccc(cc1O)C=1Oc2cc(O)ccc2C(=O)C=1O
33	3,6-Dihydroxyflavone		Oc1ccc2OC(=C(O)C(=O)c2c1)c1ccccc1
34	Flavone		O=C1C=C(Oc2ccccc21)c1ccccc1
35	Tricetin		Oc1cc(cc(O)c1O)C1=CC(=O)c2c(cc(O)cc2O)O1

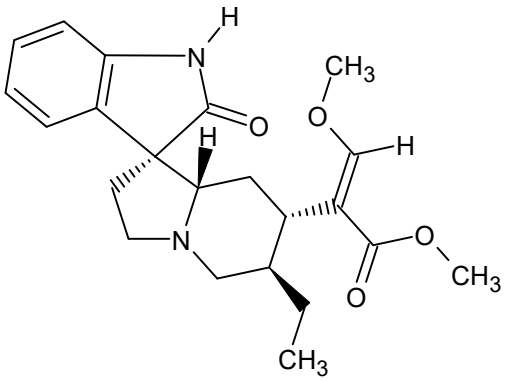
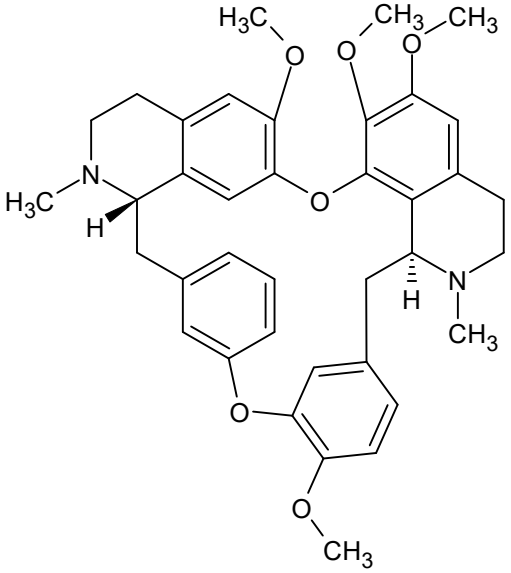
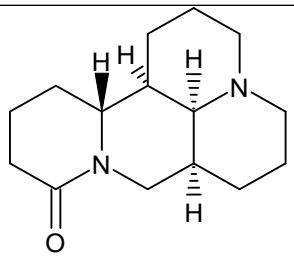
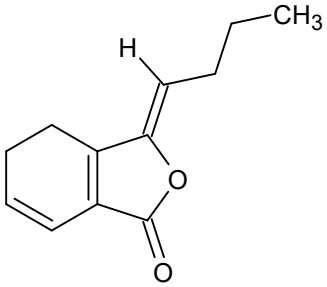
36	Quercetagetin		Oc1ccc(cc1O)C=1Oc2cc(O)c(O)c(O)c2C(=O)C=1O
37	Kempferol-3-O-galactoside		Oc1ccc(cc1)C=1Oc2cc(O)cc(O)c2C(=O)C=1O[C@@H]1O[C@H](CO)[C@H](O)[C@H](O)[C@H]1O
38	Cirsiliol		Oc1ccc(cc1O)C1=CC(=O)c2c(O)c(OC)c(cc2O1)OC
39	Baicalein		Oc1cc2OC(=CC(=O)c2c(O)c1O)c1ccccc1

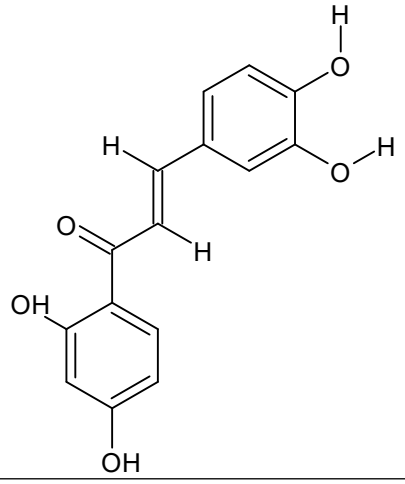
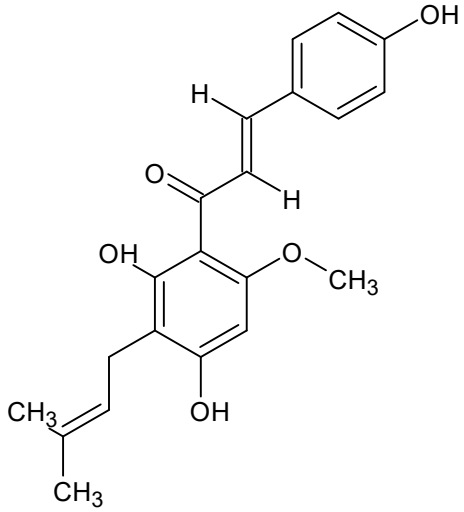
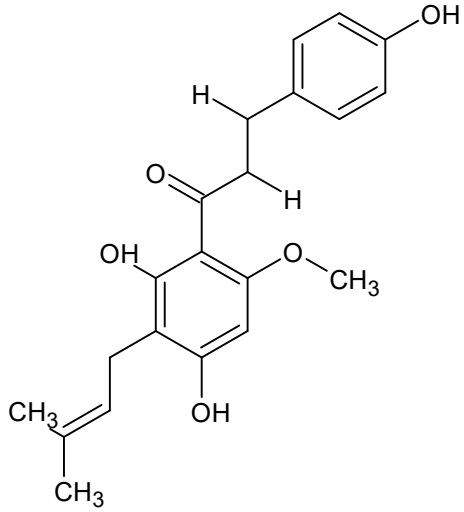
40	Isoquercetin		Oc1ccc(cc1O)C=1OC2C=C(O)C=C(O)C2C(=O)C=1O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O
41	Liquiritigenin		Oc1ccc(cc1)[C@@H]1CC(=O)c2ccc(O)cc2O1
42	Isoliquiritigenin		O=C(/C=C/c1ccc(O)cc1)c1ccc(O)cc1O
43	7,4'-Dihydroxyflavone		Oc1ccc(cc1)C1=CC(=O)c2ccc(O)cc2O1

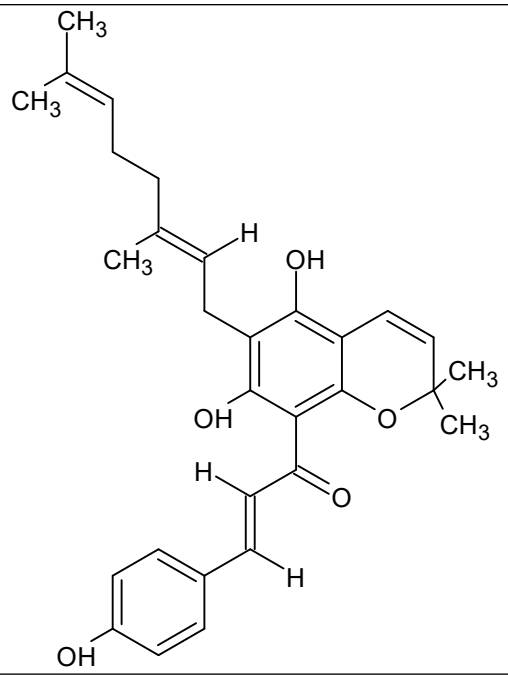
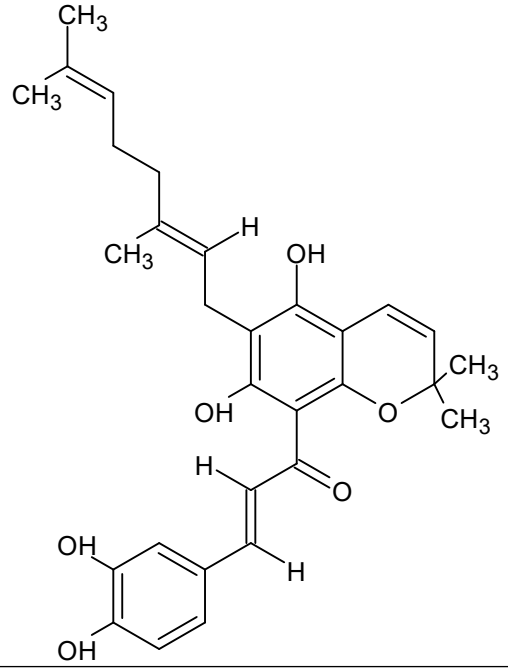
44	Liquiritinapioside		Oc1ccc2C(O)C=C(Oc2c1)c1ccc(cc1)O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O[C@@H]1OC[C@](O)(CO)[C@H]1O
45	Pinocembrin		Oc1cc(O)cc2O[C@@H](CC(=O)c21)c1ccccc1
46	Sakuranetin		Oc1ccc(cc1)[C@@H]1CC(=O)c2c(cc(cc2O)OC)O1
47	Oroxylin A		Oc1cc2OC(=CC(O)c2c(O)c1OC)c1ccccc1

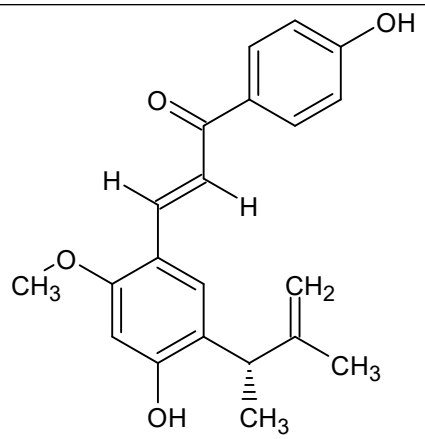
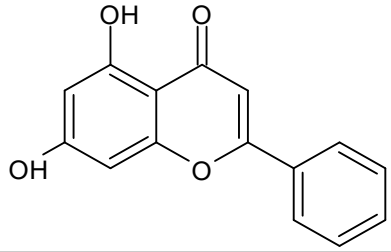
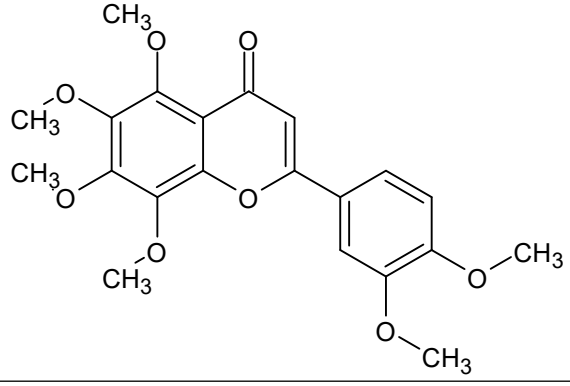
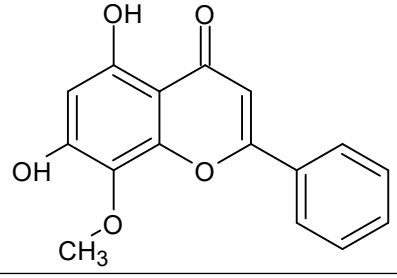
48	Berberine		COc1ccc2cc3c4cc5O COc5cc4CC[n+]3cc2 c1OC
49	Chelerythrine		C[n+]1cc2c(OC)c(OC)ccc2c2ccc3cc4OCOc 4cc3c12
50	Gelselegine		CON1c2ccccc2[C@ @]2(COC3C[C@H]4 [C@@H](C3)[C@](C C)(CO)N(C)[C@H]4 2)C1=O
51	Pseudocoptisine		c1[n+]2CCc3cc4OCO c4cc3c2cc2cc3OCOc 3cc12

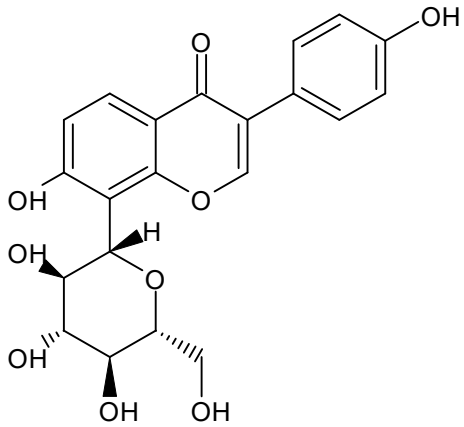
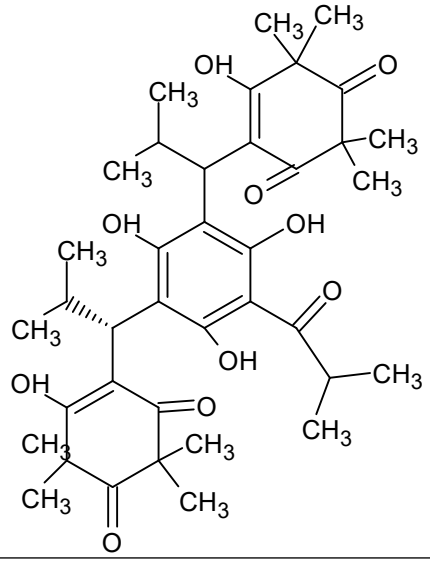
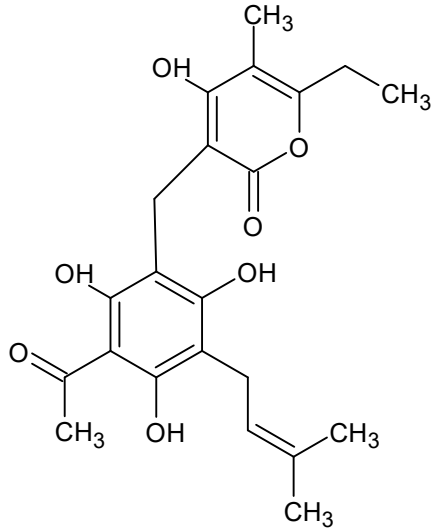
52	Leonurine		COc1cc(cc(OC)c1O)C(=O)OCCCC\N=C(/N)N
53	Sinomenine		COC1=C[C@@H]2[C@H]3Cc4ccc(OC)c(O)c4[C@]2(CCN3C)CC1=O
54	Lycorine		O[C@H]1C=C2CCN3Cc4cc5OCOc5cc4[C@](C)([C@@H]1O)[C@H]32
55	Sophocarpine		O=C1C=CC[C@@H]2[C@H]3CCCN4CCC[C@@H](CN21)[C@@H]34

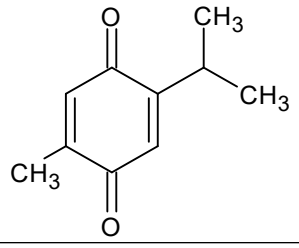
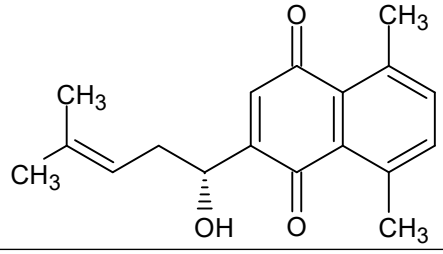
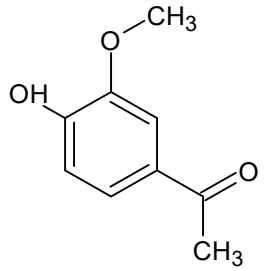
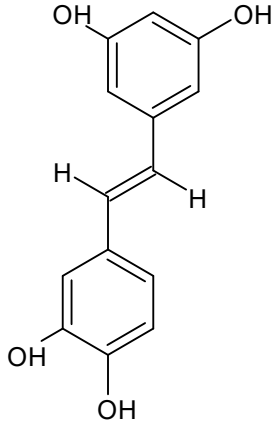
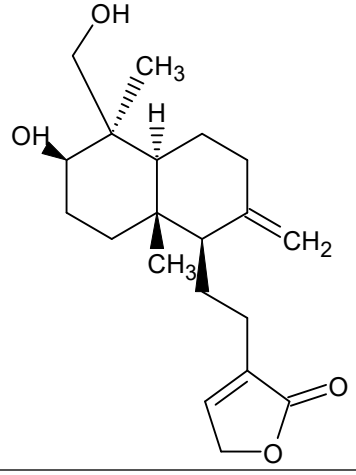
56	Rhynchophylline		O=C(OC)C(=C\OC)\[C@H]1C[C@@H]2N(CC[C@@]22c3ccccc3NC2=O)C[C@@H]1CC
57	Tetrandrine		COc1c(OC)cc2CCN(C)[C@H]3Cc4ccc(OC)c(c4)Oc4cccc(c4)C[C@H]4c5cc(Oc1c32)c(OC)cc5CCN4C
58	Matrine		O=C1CCC[C@@H]2[C@H]3CCCN4CCC[C@@H](CN21)[C@@H]34
59	Ligustilide		CCC\C=C1/OC(=O)C=2C=CCCC1=2

60	Butein		Oc1ccc(/C=C/C(=O)c2ccc(O)cc2O)cc1O
61	Xanthohumol		Oc1c(c(cc(O)c1C\C=C(/C)C)OC)C(=O)/C=C/c1ccc(O)cc1
62	Dihydroxanthohumol		Oc1c(c(cc(O)c1C\C=C(/C)C)OC)C(=O)CCc1ccc(O)cc1

63	Mallotophilippen C		Oc1ccc(cc1)/C=C/C(=O)c1c(O)c(C\C=C(/C)CC\C=C(/C)C)c(O)c2C=CC(C)(C)Oc12
64	Mallotophilippen D		Oc1ccc(cc1O)/C=C/C(=O)c1c(O)c(C\C=C(/C)CC\C=C(/C)C)c(O)c2C=CC(C)(C)Oc12

65	Licochalcone E		COc1cc(O)c(cc1/C=C/C(=O)c1ccc(O)cc1)[C@@H](C)C(=C)C
66	Chrysin		Oc1cc(O)cc2OC(=CC(=O)c21)c1ccccc1
67	Nobiletin		COc1ccc(cc1OC)C1=CC(=O)c2c(O1)c(OC)c(OC)c(OC)c2OC
68	Wogonin		Oc1cc(O)c(OC)c2OC(=CC(=O)c21)c1ccccc1

69	Puerarin		O[C@H]1[C@H](O)[C@@H](O)[C@@H](O[C@@H]1CO)c1c(O)ccc2C(=O)C(=COc21)c1ccc(O)cc1
70	Myrtucommulone A		O=C1C(C)(C)C(O)=C(C(=O)C1(C)C)[C@@H](c1c(O)c(C(=O)C(C)C)c(O)c(C(C2=C(O)C(C)(C)C(=O)C(C)(C)C2=O)C(C)C)c1O)C(C)C
71	Arzanol		O=C1OC(CC)=C(C)C(O)=C1Cc1c(O)c(C(C)=O)c(O)c(C\C=C(/C)C)c1O

72	Thymoquinone		CC(C)C1=CC(=O)C(C)=CC1=O
73	Shikonin		C/C(C)=C\C[C@@H](O)C1=CC(=O)c2c(cC)ccc2C)C1=O
74	Acetovanillone		Oc1ccc(cc1OC)C(C)=O
75	Piceatannol		Oc1ccc(/C=C/c2cc(O)cc(O)c2)cc1O
76	14-Deoxyandrographolide		C=C1CC[C@H]2[C@@](C)(CC[C@@H](O)[C@@]2(C)CO)[C@@H]1CCC1=CCOC1=O

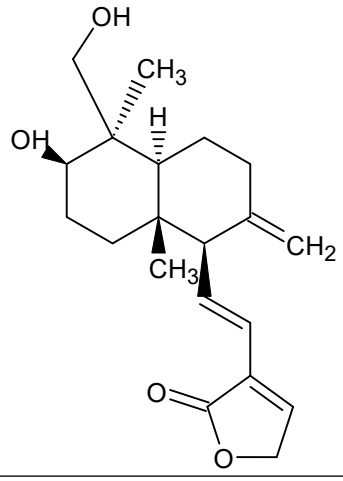
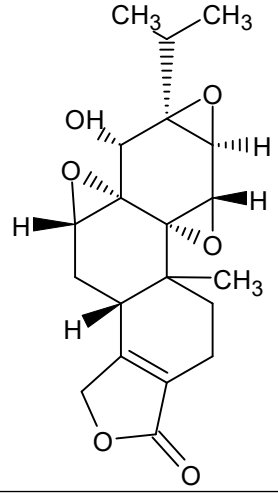
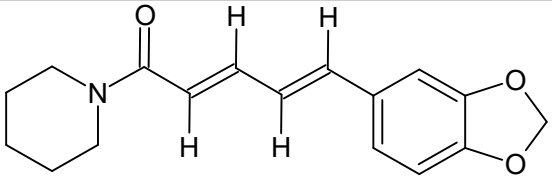
77	14-Deoxy-11,12-didehydroandrographolide		C=C1CC[C@H]2[C@@](C)(CC[C@@H](O)[C@@]2(C)CO)[C@@H]1/C=C/C1=CCOC1=O
78	Triptolide		CC(C)[C@]12O[C@H]1[C@@H]1O[C@]11[C@]3(O[C@H]3C[C@H]3C=4COC(=O)C=4CCC31C)[C@@H]2O
79	Piperine		O=C(/C=C/C=C/c1ccc2OCOc2c1)N1CCCCC1

Table.S2. Result of molecular docking simulation study of 79 compounds in the active site of proteins with PDB IDs: 2FAP, 3CQU, 3DK9, 3HNG, and 6B8Y arranged in order of highest negative binding energies.

Protein ID: 2FAP		**Protein ID: 3CQU**		**Protein ID: 3DK9**		**Protein ID: 3HNG**		**Protein ID: 6B8Y**	
Ligand code	**Dock score**	**Ligand code**	**Dock score**	**Ligand code**	**Dock score**	**Ligand code**	**Dock score**	**Ligand code**	**Dock score**
64	-9.425	40	-6.935	24	-9.707	4	-11.805	17	-14.725
63	-9.388	24	-6.394	40	-9.353	28	-11.478	22	-14.179
44	-7.682	19	-5.740	19	-9.213	60	-10.262	32	-13.718
73	-7.598	64	-5.624	44	-8.990	75	-9.925	30	-13.708
57	-7.294	54	-5.428	69	-8.684	18	-9.764	18	-13.653
23	-7.260	35	-5.425	22	-8.173	42	-9.761	35	-13.504
79	-7.242	52	-5.382	36	-8.116	40	-9.258	40	-13.154
40	-7.239	73	-5.259	37	-7.889	34	-9.110	44	-12.525
32	-7.180	17	-5.143	23	-7.197	12	-8.857	75	-11.884
62	-7.175	36	-5.038	71	-7.175	19	-8.767	60	-11.873
49	-7.129	22	-5.005	52	-7.078	59	-8.256	24	-11.743
15	-6.992	57	-4.679	17	-7.004	29	-8.113	69	-11.472
21	-6.952	75	-4.592	38	-6.912	37	-8.040	38	-11.182
51	-6.925	38	-4.472	73	-6.640	64	-8.005	28	-10.636
69	-6.873	29	-4.444	4	-6.603	22	-7.861	19	-10.447
24	-6.816	37	-4.094	64	-6.588	73	-7.809	36	-10.418
61	-6.729	18	-4.091	31	-6.584	6	-7.733	31	-10.263
37	-6.692	30	-4.009	20	-6.468	43	-7.720	42	-10.230
28	-6.586	4	-3.976	30	-6.456	68	-7.562	25	-10.177
72	-6.568	28	-3.959	35	-6.365	72	-7.551	45	-10.160
26	-6.484	47	-3.926	68	-6.263	30	-7.479	64	-10.048
54	-6.468	32	-3.912	42	-6.151	11	-7.386	66	-9.926
59	-6.462	25	-3.903	32	-6.064	36	-7.379	39	-9.520
18	-6.429	68	-3.899	18	-6.021	74	-7.324	65	-9.421
78	-6.400	26	-3.887	28	-6.006	39	-7.310	20	-9.416

4	-6.392	44	-3.856	25	-5.952	20	-7.230	43	-9.391
50	-6.365	55	-3.840	21	-5.950	21	-7.191	26	-9.363
66	-6.358	45	-3.838	75	-5.902	44	-7.170	59	-8.930
55	-6.340	42	-3.836	39	-5.864	46	-7.159	23	-8.578
30	-6.332	66	-3.751	63	-5.821	52	-7.099	76	-8.514
58	-6.283	39	-3.639	54	-5.820	17	-6.960	33	-8.466
17	-6.266	31	-3.626	60	-5.803	35	-6.943	37	-8.443
19	-6.251	20	-3.620	27	-5.689	32	-6.940	68	-8.395
29	-6.234	56	-3.571	76	-5.633	38	-6.750	73	-8.390
27	-6.197	43	-3.509	43	-5.501	69	-6.720	62	-8.304
39	-6.188	74	-3.495	47	-5.473	24	-6.681	74	-8.284
20	-6.156	62	-3.462	65	-5.434	61	-6.603	41	-8.191
71	-6.147	53	-3.437	45	-5.413	10	-6.552	47	-7.943
34	-6.144	27	-3.401	77	-5.367	25	-6.546	79	-7.886
74	-6.079	41	-3.380	26	-5.355	62	-6.521	27	-7.796
68	-6.075	49	-3.337	58	-5.350	8	-6.506	71	-7.638
45	-6.026	48	-3.335	55	-5.287	66	-6.383	29	-7.633
48	-5.992	50	-3.299	29	-5.250	67	-6.282	21	-7.510
65	-5.975	78	-3.297	46	-5.208	79	-6.195	72	-7.483
47	-5.934	33	-3.239	66	-5.124	41	-6.122	34	-7.407
38	-5.865	58	-3.199	74	-4.978	31	-6.029	11	-7.348
43	-5.848	63	-3.178	41	-4.856	33	-6.029	77	-7.187
36	-5.722	70	-3.094	34	-4.832	65	-5.992	46	-7.174
42	-5.714	61	-3.008	5	-4.822	9	-5.959	52	-7.054
41	-5.579	76	-2.996	33	-4.810	13	-5.827	63	-6.985
35	-5.501	60	-2.983	79	-4.808	47	-5.719	12	-6.920
31	-5.442	69	-2.965	51	-4.788	27	-5.630	4	-6.518
33	-5.431	46	-2.888	53	-4.785	77	-5.462	61	-6.494
56	-5.428	51	-2.845	62	-4.757	76	-5.331	67	-6.395
60	-5.423	59	-2.749	49	-4.699	63	-5.285	16	-6.159

5	-5.402	77	-2.672	12	-4.665	51	-5.009	57	-5.982
22	-5.394	11	-2.536	15	-4.492	1	-5.005	53	-5.639
25	-5.393	71	-2.529	56	-4.238	45	-4.901	7	-5.591
77	-5.362	67	-2.498	67	-4.111	2	-4.833	49	-5.485
46	-5.266	21	-2.439	57	-3.887	54	-4.786	5	-5.113
9	-5.183	34	-2.388	78	-3.861	26	-4.726	51	-5.056
75	-5.144	79	-2.356	59	-3.808	3	-4.699	48	-5.034
76	-5.094	72	-2.342	61	-3.747	14	-4.580	13	-5.016
53	-5.085	5	-1.898	72	-3.670	5	-4.385	9	-4.931
52	-4.938	9	-1.830	50	-3.639	71	-4.301	15	-4.873
70	-4.889	65	-1.792	70	-3.636	16	-4.211	78	-4.817
10	-4.875	13	-1.552	7	-3.455	49	-4.150	10	-4.772
67	-4.413	15	-1.530	48	-3.305	70	-3.959	3	-4.693
7	-4.251	23	-1.517	9	-2.928	53	-3.784	58	-4.519
11	-4.017	7	-1.457	3	-2.889	7	-3.738	14	-4.412
13	-3.769	8	-1.003	13	-2.853	50	-3.262	55	-4.401
3	-3.753	10	-0.969	10	-2.611	23	-3.211	70	-4.327
12	-3.655	14	-0.933	6	-2.493	78	-3.079	56	-4.119
16	-3.260	6	-0.923	2	-2.482	56	-2.915	50	-4.029
6	-2.607	16	-0.713	1	-2.345	58	-1.924	6	-3.951
1	-2.437	2	-0.631	8	-2.290	55	-1.884	1	-3.936
14	-2.120	1	-0.390	16	-2.058	15	-1.652	2	-3.859
2	-1.974	12	-0.062	14	-1.535	57	-1.006	54	-3.601
8	-1.260	3	-0.028	11	-1.014	48	1.014	8	-3.181

all units are in Kcal/mol

Table.S3. Release kinetics of the optimized formulation in different mathematical models.

Replicates	Optimum condition			r^2 values of Kinetic Models (0 – 2 h)			
	LEC: CHO (%)	Chitosan concentration (%)	Sonication time (min)	Zero	First	Higuchi	Korsmeyer peppas
R1	**7.00**	**0.30**	**15.00**	0.994	**0.998**	0.707	0.136
R2				0.986	**0.995**	0.676	0.094
R3				0.998	**0.999**	0.926	0.129
Replicates	**Optimum condition**			**r^2 values of Kinetic Models (0 – 24 h)**			
R1	**7.00**	**0.30**	**15.00**	0.823	0.929	**0.970**	0.630
R2				0.810	0.919	**0.971**	0.608
R3				0.820	0.926	**0.966**	0.628