Supporting Information

Structure-Based Identification of Potent Natural Product Chemotypes as Cannabinoid Receptor 1 Inverse Agonists

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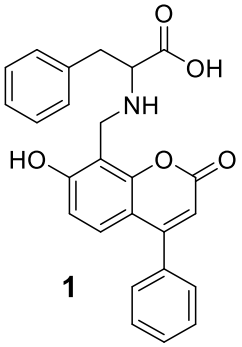

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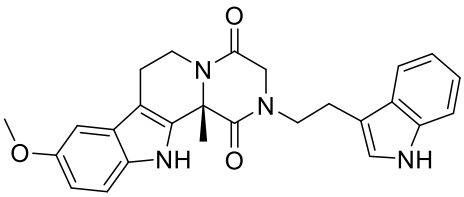

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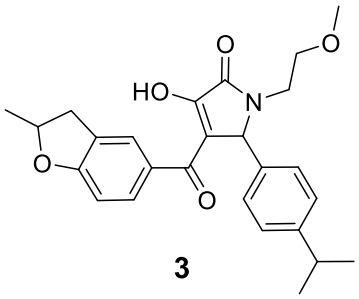

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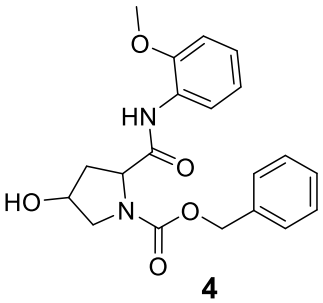

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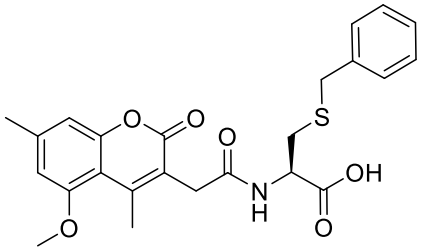

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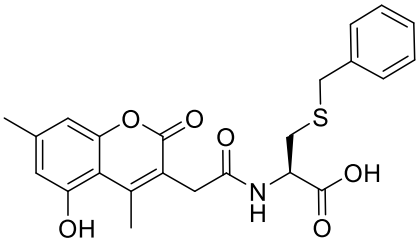

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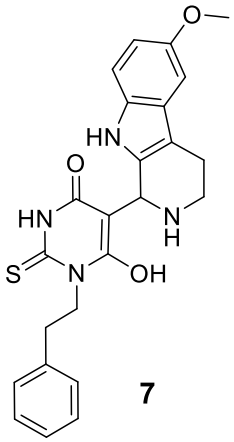

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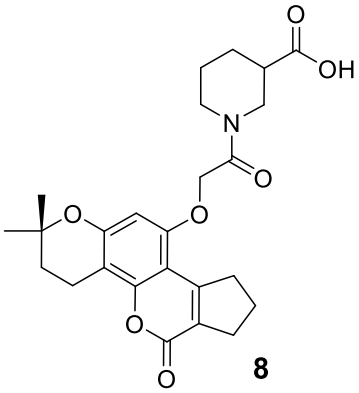

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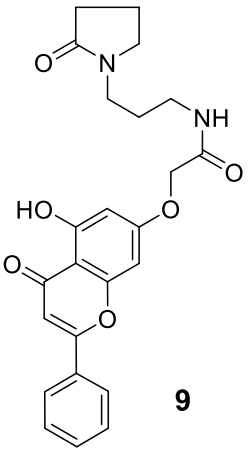

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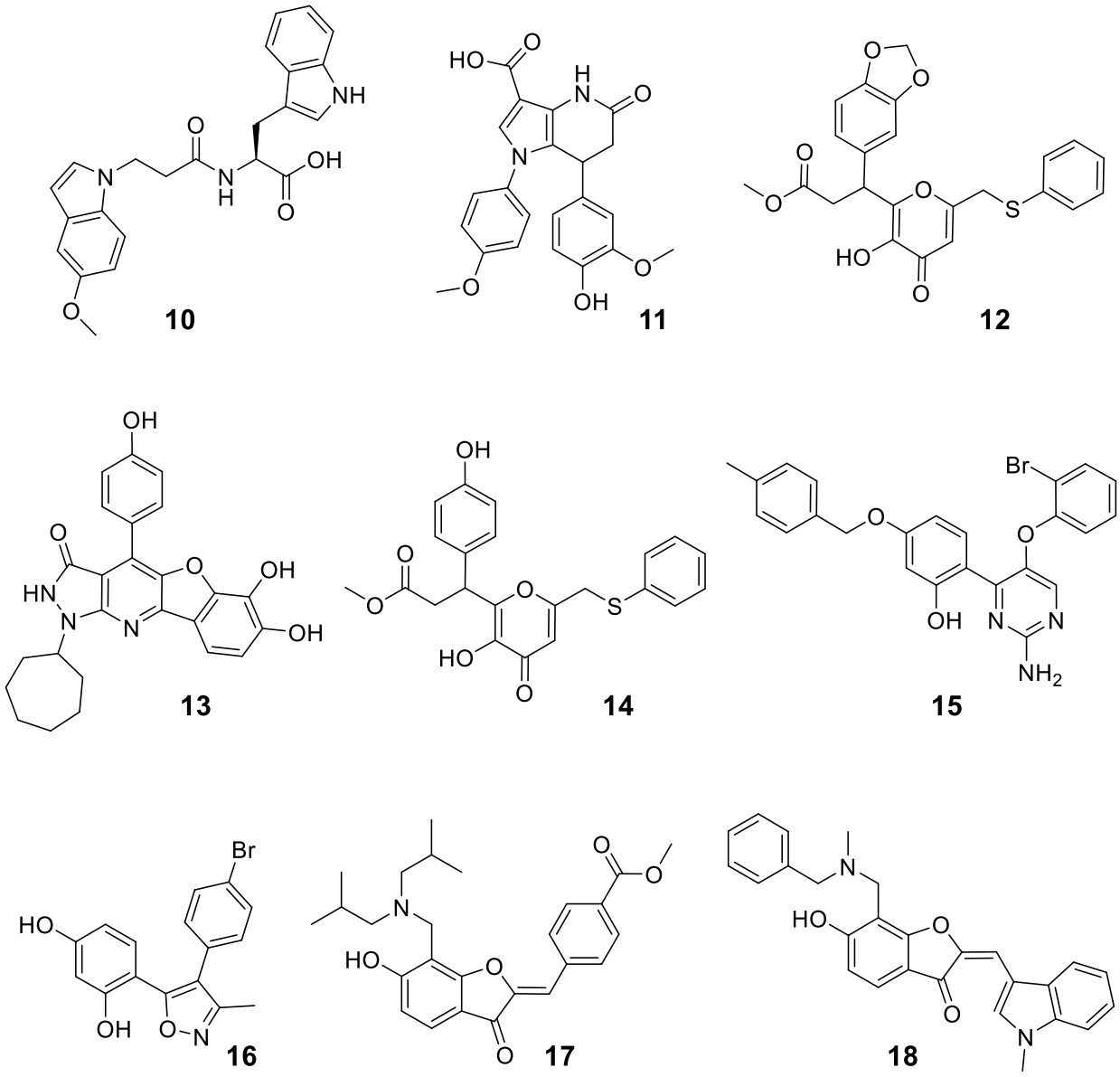

Figure S1. Chemical structures of the eighteen selected hits used for *in vitro* study.

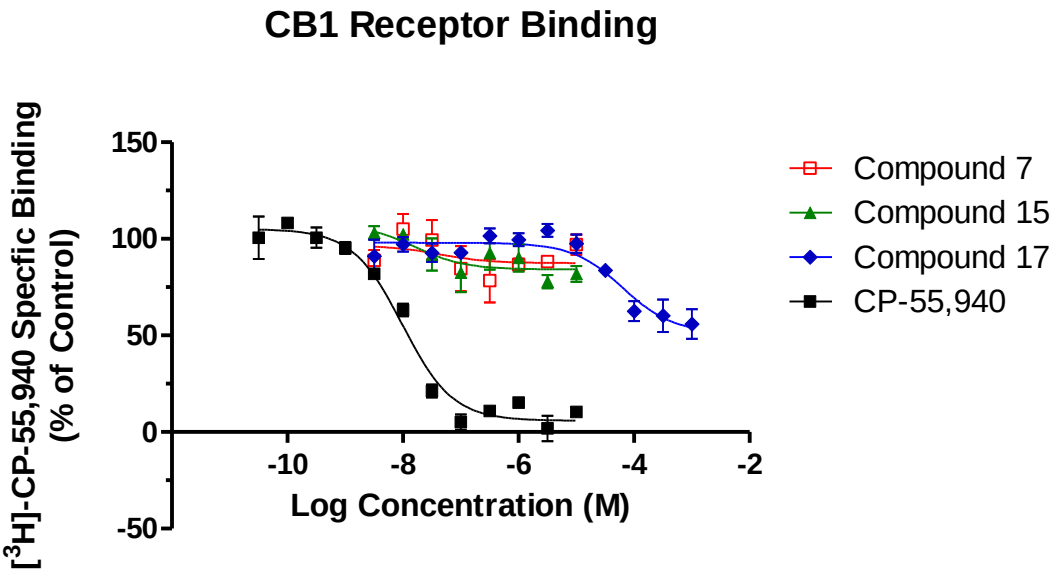

Figure S2. The displacement binding curves for compounds **7**, **15** and **17** obtained from the radioligand competitive binding assay. CP55,940 was used as a positive control.

Table S1. The percentage (%) displacement of radioligand at CB1 and CB2 receptors for all eighteen screened compounds.

Compound number	Sample name	ZINC code	Docking score ‡	% displacement at 10 μM	
				CB1	CB2
1*	STOCK1N-06857	ZINC00940539	−10.153	14.1	-
2	STOCK1N-34850	ZINC09033729	−9.975	81.8	67.2
3*	STOCK1N-43108	ZINC09374751	−9.74	-	51
4*	STOCK1N-43876	ZINC00861983	−9.60	13.9	-
5	STOCK1N-51636	ZINC02118939	−11.119	14	15.5
6	STOCK1N-53876	ZINC02123699	−11.517	28	26.7
7*	STOCK1N-62719	ZINC20755817	−12.295	49.7	15.7
8*	STOCK1N-68672	ZINC08879802	−9.777	30.5	7
9	STOCK1N-69353	ZINC12896219	−9.804	28.6	30.2
10	STOCK1N-73177	ZINC20763677	−9.014	30.2	17.3
11*	STOCK1N-75513	ZINC40313209	−10.73	37.6	13.1
12*	STOCK1N-79387	ZINC85875400	−11.723	69.9	63
13	STOCK1N-79693	ZINC85877048	−9.638	23.1	37.4
14*	STOCK1N-80140	ZINC85879663	−9.967	18.7	30
15	STOCK5S-41625	ZINC02229040	−10.459	57.6	35.5
16	STOCK6S-13543	ZINC06757795	−9.378	61.8	40.2
17	STOCK6S-34022	ZINC08823658	−9.818	50.4	35
18	STOCK6S-39252	ZINC28182437	−10.436	69	61.2

‡ Kcal/mol; * Racemic

Table S2. Physicochemical and other selected properties related to drug-likeness for all eighteen tested hits.

Compound number	MW	QPLogP	#HBA [a]	#HBD [b]	PSA [c]	#RB [d]
1 [e]	415.45	1.710	7	3	117.402	8
2	442.52	3.886	6	1	87.903	4
3 [e]	435.519	4.406	7.2	0	91.620	7
4 [e]	370.404	3.233	7.45	2	98.812	6
5	455.525	4.160	7.5	1.25	123.966	9
6	441.498	3.403	7.5	2.25	137.364	9
7 [e]	448.539	4.696	4.25	3	103.898	5
8 [e]	455.507	2.872	9	1	126.134	4
9	436.463	2.170	8	1	132.713	8
10	405.45	4.572	4.5	2.25	107.384	8
11 [e]	408.410	3.121	5.75	2	129.267	4
12 [e]	440.47	3.924	7.25	1	109.649	8
13	445.474	3.789	4.75	4	123.602	5
14 [e]	412.456	3.350	6.5	2	113.379	9
15	478.344	4.918	4.5	3	83.400	8
16	346.18	3.153	3	2	69.421	2
17	437.535	3.971	7.25	1	94.545	10
18	424.5	4.597	5.25	1	65.049	7

[a] Number of Hydrogen Bond Acceptors; [b] Number of Hydrogen Bond Donor; [c] Polar Surface Area; [d] Number of Rotatable Bonds; [e] Racemic.