

SUPPLEMENTARY: Identification of Potential Antimalarial Drug Candidates Targeting Falcipain-2 Protein of Malaria Parasite – A Computational Strategy

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Table S1: Pharmacokinetic parameters for oral bioavailability evaluation of different lead molecules

S. No	Compounds Name	miLogP	MW	nON	nOHNH	nviolations
Ref.	Artemisinin	3.32	282.34	5	0	0
1	Nicotine	1.09	162.24	2	0	0
2	Caffeine	0.06	194.19	6	0	0
3	Reserpine	5.01	608.69	11	1	3
4	Trospium	-0.61	392.52	4	1	0
5	Benzatropine	4.27	307.44	2	0	0
6	Methysergide	1.97	353.47	5	2	0
7	Cabergoline	3.44	451.62	7	2	0
8	Theophylline	-0.01	180.17	6	1	0
9	Morphine	1.1	285.34	4	2	0
10	Vindesine	3.73	753.94	12	6	3
11	Codeine	1.41	299.37	4	1	0
12	Dihydroergotamine	2.09	583.69	10	3	1
13	Hydromorphone	1.42	285.34	4	1	0
14	Ipratropium	-1.47	332.46	4	1	0
15	Methylergometrine	1.9	339.44	4	3	0
16	Vinorelbine	5.92	778.95	12	2	3
17	Metocurine iodide	-1.41	652.83	8	0	1
18	Miglustat	-0.72	219.28	5	4	0
19	Hyoscyamine	1.77	289.38	4	1	0
20	Quinine	3.06	324.42	4	1	0
21	Miglitol	-2.79	207.23	5	6	0
22	Oxycodone	0.79	315.37	5	1	0
23	Levallorphan	4.04	283.42	2	1	0
24	Dextromethorphan	3.94	271.4	2	0	0
25	Anisotropinemethylbromide	0.24	282.45	3	0	0
26	Vincristine	4.95	824.97	14	3	2
27	Cisatracurium	-1.59	929.16	14	0	2

28	Vinblastine	5.56	810.99	13	3	3
29	Atropine	1.77	289.38	4	1	0
30	Lisuride	3.16	338.45	5	2	0
31	Butorphanol	3.5	327.47	3	2	0
32	Dyphylline	-1.21	254.25	8	2	0
33	Pentazocine	4.59	285.43	2	1	0
34	Galantamine	1.54	287.36	4	1	0
35	Ergotamine	2.08	581.67	10	3	1
36	Nicergoline	3.85	484.39	6	0	0
37	Naltrexone	1.35	341.41	5	2	0
38	Apomorphine	2.89	267.33	3	2	0
39	Homatropinemethylbromide	-2.19	290.38	4	1	0
40	Atracuriumbesylate	-1.59	929.16	14	0	2
41	Scopolamine	1.05	303.36	5	1	0
42	Irinotecan	4.1	586.69	10	1	1
43	Pentoxifylline	0.65	278.31	7	0	0
44	Enprofylline	-0.14	194.19	6	2	0
45	Nalbuphine	1.71	357.45	5	3	0
46	Levorphanol	3.4	257.38	2	1	0
47	Cocaine	2.17	303.36	5	0	0
48	Quinidine	3.06	324.42	4	1	0
49	Buprenorphine	4.87	467.65	5	2	0
50	Hydrocodone	1.73	299.37	4	0	0
51	Physostigmine	1.94	275.35	5	1	0
52	Dimenhydrinate	3.5	255.36	2	0	0
53	Topotecan	2.03	421.45	8	2	0
54	Ergoloidmesylate	2.83	611.74	10	3	1
55	Pilocarpine	-0.24	208.26	4	0	0
56	Deserpidine	4.98	578.66	10	1	1
57	Papaverine	3.52	339.39	5	0	0
58	Rescinnamine	5.43	634.73	11	1	3
59	Naloxone	1.12	327.38	5	2	0
60	Pergolide	3.97	314.5	2	1	0
61	Oxymorphone	0.48	301.34	5	2	0
62	Tubocurarine	1.99	609.74	8	2	1
63	Bromocriptine	3.6	654.61	10	3	1
64	Aminophylline	-0.01	180.17	6	1	0
65	Ergometrine	1.36	325.41	5	3	0
66	Oxtriphylline	-3.55	179.16	6	0	0
67	Metocurine	-1.41	652.83	8	0	1

68	Yohimbine	3.22	354.45	5	2	0
69	Colchicine	1.1	399.44	7	1	0
70	Tiotropium	-1.94	392.52	5	1	0
71	Theobromine	-0.95	180.17	6	1	0
72	Ajmaline	2.56	326.44	4	2	0
73	5-Methoxy-N,N-diisopropyltryptamine	3.68	274.41	3	1	0
74	Dihydroetorphine	3.74	413.56	5	2	0
75	Diamorphine	1.61	369.42	6	0	0
76	Ethylmorphine	1.79	313.4	4	1	0
77	Cyprenorphine	3.52	423.55	5	2	0
78	Fenethylline	1.98	341.42	7	1	0
79	Etorphine	3.71	411.54	5	2	0
80	Benzoylcegonine	2.25	289.33	5	1	0
81	Ecgonine	-0.18	185.22	4	2	0
82	Desomorphine	2.76	271.36	3	1	0
83	Drotebanol	1.39	333.43	5	2	0
84	Diprenorphine	3.55	425.57	5	2	0
85	Dihydrocodeine	1.92	301.39	4	1	0
86	Dihydromorphine	1.61	287.36	4	2	0
87	Tropinone	0.29	139.2	2	0	0
88	8-azaxanthine	-1.23	153.1	7	3	0
89	7-Hydroxystaurosporine	3.42	482.54	8	3	0
90	Staurosporine	3.88	466.54	7	2	0
91	Xanthine	-1.09	152.11	6	3	0
92	K-252a	3.43	476.48	8	2	0
93	Duvoglustat	-2.4	163.17	5	5	0
94	Pseudotropine	0.48	141.21	2	1	0
95	Berberine	0.2	336.37	5	0	0
96	Arecoline	0.79	155.2	3	0	0
97	Methylecgonine	0.44	199.25	4	1	0
98	Camptothecin	2.03	348.36	6	1	0
99	Lysergic acid diethylamide	2.66	323.44	4	1	0
100	Omacetaxinermepesuccinate	1.96	545.63	10	2	1
101	Voacamine	7.71	704.91	9	2	2
102	Phenserine	3.64	337.42	5	1	0
103	Altropane	4.5	429.27	3	0	0
104	Migalastat	-2.4	163.17	5	5	0
105	Lobeline	3.73	337.46	3	1	0
106	Vintafolide	-5.01	1917.07	47	25	3
107	NS-2359	4.56	314.26	2	0	0

108	Cositecan	4.75	448.6	6	1	0
109	Rivanicline	1.3	162.24	2	1	0
110	Rubitecan	2.24	393.36	9	1	0
111	Nalmefene	2.76	339.44	4	2	0
112	Naxifylline	2.65	344.42	7	1	0
113	Propentofylline	1.53	306.37	7	0	0
114	Midostaurin	4.69	570.65	8	1	1
115	Gimatecan	3.24	447.49	8	1	0
116	Sparteine	2.9	234.39	2	0	0
117	Drotaverine	4.54	397.51	5	1	0
118	Capsaicin	3.1	305.42	4	2	0
119	Methylnaltrexone	-2.63	356.44	5	2	0
120	3-isobutyl-1-methyl-7H-xanthine	1.12	222.25	6	1	0
121	Ioflupane I-123	4.8	431.29	3	0	0
122	Uric acid	-1.44	168.11	7	4	0
123	Acridinium	0.59	484.66	5	1	0
124	Fentonium	0.73	484.62	5	1	0
125	Naloxegol	0.5	651.79	12	2	2
126	Xanthinol	-1.18	311.34	9	2	0
127	Zucapsaicin	3.1	305.42	4	2	0
128	Pholcodine	1.29	398.5	6	1	0
129	Cimetropium	-2.06	358.46	5	1	0
130	Doxofylline	-0.13	266.26	8	0	0
131	Butylscopolamine	-1.49	360.47	5	1	0
132	Homatropine	1.78	275.35	4	1	0
133	Dihydroergocornine	2.15	563.7	10	3	1
134	Epicriptine	2.65	577.73	10	3	1
135	Methscopolamine	-2.93	318.39	5	1	0
136	Nonivamide	4.12	293.41	4	2	0
137	Nalorphine	1.75	311.38	4	2	0
138	Metoserpate	3.57	428.53	7	1	0
139	Bicuculline	2.88	367.36	7	0	0
140	Thiocolchicoside	-0.16	563.62	11	5	2
141	Vinflunine	6.24	816.94	12	2	3
142	Psilocybin	1.02	284.25	6	3	0
143	Anisodamine	0.85	305.37	5	2	0
144	Axelopran	2.35	457.62	7	4	0
145	Oxitropium	-2.56	332.42	5	1	0
146	Tetrahydropalmatine	2.75	355.43	5	0	0
147	Namitecan	0.86	434.45	9	3	0

148	Vinpocetine	4.12	350.46	4	0	0
149	Exatecan	0.75	435.45	7	3	0
150	Lurtotecan	1.44	518.57	10	1	1
151	Moxaverine	4.88	307.39	3	0	0
152	AR-67	4.556	478.62	7	2	0
153	10-hydroxycamptothecin	1.52	364.36	7	2	0
154	Lisofylline	0.84	280.33	7	1	0
155	Zalypsis	4.87	709.72	11	3	2
156	Belotecan	2.9	433.51	7	2	0
157	9-aminocamptothecin	1.77	363.37	7	3	0
158	Samidorphan	1.31	370.45	6	4	0
159	Tonapofylline	3.1	416.52	8	2	0
160	Patidegib	5.73	504.78	5	2	2
161	Rolofylline	3.95	356.47	4	1	0
162	Solamargine	2.41	868.07	16	9	3
163	Pegamotecan	3.38	980.98	20	2	2
164	Reproterol	-0.45	389.41	10	4	0
165	Sacituzumabgovitecan	-3.19	1601.8	36	10	3
166	Cafedrine	0.99	357.41	8	2	0
167	Theodrenaline	-0.66	375.38	10	4	0
168	8-cyclopentyl-1,3-dipropylxanthine	3.24	304.39	6	1	0
169	CT-2584	7.9	533.8	8	2	2
170	Ambroxolacefyllinate	2.74	378.11	3	4	0
171	Bamifylline	1.9	385.47	8	1	0
172	Atracurium	-1.59	929.16	14	0	2
173	Demecolcine	1.74	371.43	6	1	0
174	Dihydroergocristine	2.83	611.74	10	3	1
175	Vincamine	3.18	354.45	5	1	0
176	Dihydroergocryptine	2.68	577.73	10	3	1
177	Emetine	3.64	480.65	6	1	0
178	Terguride	3.17	340.47	5	2	0
179	Proxiphylline	-0.21	238.25	7	1	0
180	Nicomorphine	2.5	495.54	8	0	0
181	Etybenzatropine	4.65	321.46	2	0	0
182	Nalfurafine	2.63	476.57	7	2	0
183	Metergoline	3.87	403.53	5	1	0
184	Prajmaline	-0.54	369.53	4	2	0
185	Acefylline	-0.69	238.2	8	1	0
186	Bietaserpine	5.86	707.87	12	0	3
187	Etamiphylline	0.84	279.34	7	0	0

188	Phenazocine	4.72	321.46	2	1	0
189	Pentifylline	2.51	264.33	6	0	0
190	Alcuronium	-2.45	666.91	6	2	1
191	Lorajmine	3.66	402.92	5	1	0
192	Tretoquinol	2.12	345.339	6	3	0
193	Hydroquinine	3.29	326.44	4	1	0
194	Vinburnine	3.78	294.4	3	0	0
195	Dimemorfan	4.33	255.41	1	0	0
196	Buftylline	-0.01	180.17	6	1	0
197	Methylatropine	-2.21	304.41	4	1	0
198	Dehydroemetine	3.3	478.63	6	1	0
199	Harmaline	2.68	214.27	3	1	0
200	Bromotheophylline	1.12	259.06	6	1	0
201	Furafylline	0.94	260.25	7	1	0
202	Tetrandrine	6.55	622.76	8	0	2
203	8-chlorotheophylline	0.99	214.61	6	1	0
204	Dextrorphan	3.4	257.38	2	1	0
205	7-ethyl-10-hydroxycamptothecin	2.67	392.41	7	2	0
206	Rauwolfiaserpentina root	3.41	352.43	5	1	0
207	Almitrine	6.14	477.56	7	2	1
208	Morphine glucuronide	-0.73	461.47	10	5	0
209	Firtecانpegol	7.22	2300.32	49	8	4
210	18-methoxycoronaridine	3.55	368.48	5	1	0
211	Hydroquinidine	3.29	326.44	4	1	0
212	Posiphen	3.64	337.42	5	1	0
213	Dihydrocapsiate	4.74	308.42	4	1	0
214	Naldemedine	3.65	570.65	10	4	1
215	Deptropine	4.39	333.48	2	0	0
216	Tenidap	3.34	320.76	5	3	0
217	Loxicodegol	0.36	595.73	11	1	2
218	Lucerastat	-0.72	219.28	5	4	0
219	PCS-499	0.84	280.337	7	1	0
220	Colchiceine	0.83	385.42	7	2	0
221	Variolin B	-0.15	293.29	8	5	0
222	Deacetoxyvinzolidine	6.21	826.43	12	2	3
223	Harmine	2.63	212.25	3	1	0
224	Raubasine	2.83	611.74	10	3	1
225	Strychnine	1.84	334.42	4	0	0
226	Butropium	0.88	452.62	5	1	0
227	Diflomotecan	1.25	398.37	6	1	0

228	Nazartinib	3.28	495.03	8	1	0
229	Dihydroergotoxine	2.09	583.69	10	3	1
230	3,5'-dihydroxythalifaboramine	5.9	684.79	11	3	3
231	3-hydroxy-6'-desmethyl-9-O-methylthalifaboramine	5.96	668.79	10	2	2
232	3-hydroxythalifaboramine	5.99	668.79	10	2	2
233	5'-hydroxythalifaboramine	5.99	668.79	10	2	2
234	6'-desmethylthalifaboramine	5.78	638.76	9	2	2
235	Alpha-tomatine	-0.92	1034.2	22	13	3
236	Berberine	6.24	608.74	8	1	2
237	Berberine	0.2	336.37	5	0	0
238	Betanin	-6.03	550.47	15	8	3
239	Brucine	1.46	394.47	6	0	0
240	Brucine N-oxide	1.42	410.47	7	0	0
241	Camptothecin	2.03	348.36	6	1	0
242	Chelerythrine	0.75	348.38	5	0	0
243	Cis-Zeatin	1.04	219.25	6	3	0
244	Cryptolepine	3.86	232.29	2	0	0
245	Dehydrotomatine	-1.1	1032.18	22	13	3
246	Emarginatine F	3.64	918.9	20	2	2
247	Emarginatine G	3.3	924.91	21	1	2
248	Fangchinoline	6.27	608.74	8	1	2
249	Harmaline	6.54	409.19	3	0	1
250	Harmalol	3.02	323.35	6	2	0
251	Harmane	2.59	182.23	2	1	0
252	Harmine	2.63	212.25	3	1	0
253	Harmol	1.89	198.22	3	2	0
254	Homoharringtonine	1.96	545.63	10	2	1
255	Hydrastine	2.83	383.4	7	0	0
256	Isostrychnine	1.46	334.42	4	1	0
257	Lycoricidinol	-1.12	307.26	8	5	0
258	Lycorine	0.54	287.31	5	2	0
259	Mahanimbicine	7.15	331.46	2	1	1
260	Mahanimbine	7.1	331.46	2	1	1
261	Mahanine	6.15	333.43	3	2	1
262	Marcanines A	1.92	239.23	4	1	0
263	Matrine	1.98	248.37	3	0	0
264	N-(4-hydroxyundecanoyl)anabasine	4.27	346.51	4	1	0
265	Neocryptolepine	3.86	232.29	2	0	0
266	N-n-octanoylnornicotine	3.87	274.41	3	0	0

267	Noscapine	2.81	413.43	8	0	0
268	Papaverine	3.52	339.39	5	0	0
269	Physostigmine	1.94	275.35	5	1	0
270	Reserpine acid	2.33	400.48	7	3	0
271	Rhyncophylline	2.83	384.48	6	1	0
272	Rohitukine	1.13	305.33	6	3	0
273	Sanguinarine	0.8	332.33	5	0	0
274	Solamargine	2.41	868.07	16	9	3
275	Strychnine	1.84	334.42	4	0	0
276	Tetrandrine	6.55	622.76	8	0	2
277	Tomatidenol	5.73	413.65	3	2	1
278	Tomatidine	5.92	415.66	3	2	1
279	Vinblastine	5.56	810.99	13	3	3
280	Vincamine	3.18	354.45	5	1	0
281	Vincristine	4.95	824.97	14	3	2
282	(-)-anonnaine	3.25	265.31	3	1	0
283	(+)-tylophorinidine	2.75	365.43	5	2	0
284	(R)-antofine	4.05	363.46	4	0	0
285	(R)-cryptopleurine	4.55	377.48	4	0	0
286	(R)-tylophorine	3.64	393.48	5	0	0
287	(S)-tyloindicine I	2.93	409.48	6	1	0
288	11-beta-hydroxycephalotaxine beta-N-oxide	-0.04	347.37	7	2	0
289	5alpha-O-(3'-dimethylamino-3'- phenylpropionyl) taxinine M	4.78	861.94	16	1	2
290	9-Aminocamptothecin	1.77	363.37	7	3	0
291	9-methoxycanthin-6-one	2.72	250.26	4	0	0
292	9-methoxycanthin-6-one 3N-oxide	1.31	266.26	5	0	0
293	Antofine	4.05	363.46	4	0	0
294	beta-carboline-1-propionic acid	2.31	240.26	4	2	0
295	canthin-6-one	2.69	220.23	3	0	0
296	canthin-6-one 9-O-beta- glucopyranoside	0.4	398.37	9	4	0
297	Capsaicin	3.1	305.42	4	2	0
298	Cephalotaxine alpha-N-oxide	0.95	331.37	6	1	0
299	Cephalotaxine beta-N-oxide	0.95	331.37	6	1	0
300	Cepharanthine	6.59	606.72	8	0	2
301	Corydaline	3.08	369.46	5	0	0
302	Cycleanine	6.75	622.76	8	0	2
303	Ellipticine	4.28	246.31	2	1	0
304	Evodiamine	2.82	303.37	4	1	0
305	Holacurtine	4.04	491.71	6	2	0

306	Holacurtinol	2.04	491.67	7	4	0
307	Holamine	3.5	315.5	2	2	0
308	Isocephalotaxine	1	315.37	5	1	0
309	Isotetrandrine	6.55	622.76	8	0	2
310	liriodenine	3.3	275.26	4	0	0
311	Psychotrine	4.71	478.63	6	0	0
312	Secoantofine	3.76	365.47	4	0	0
313	Tubulosine	4.86	475.63	6	3	0
314	Tylocrebrine	3.84	393.48	5	0	0
315	tyloindicine F	3.65	381.47	5	1	0
316	tyloindicine G	2.65	409.48	6	1	0
317	tylophoridicine C	2.71	381.43	6	2	0
318	tylophoridicine F	3.02	395.45	6	1	0
319	Vincristine sulfate	4.95	824.97	14	3	2
320	(S)-tylophorine	3.64	393.48	5	0	0
321	6-O-desmethylanantofine	3.51	349.43	4	1	0
322	13(R)-antofine-N-oxide	4.01	379.46	5	0	0
323	13(R)-14(R)-hydroxyantofine-N-oxide	3.02	395.45	6	1	0
324	7-methoxy-beta-carboline-1-propionic acid	2.34	270.29	5	2	0
325	4-methoxycarbonyl-5,10-benzogquinolinequinone	2.08	267.24	5	0	0
326	6-O-desmethy secoantofine	3.22	351.45	4	1	0
327	Saprosmine A	2.37	285.3	5	1	0
328	Saprosmine B	2.75	299.33	5	1	0
329	2-alpha-acetoxy-2'beta-deacetylaustrospicatin	5.89	783.91	14	1	3
330	9-hydroxycanthin-6-one	1.99	236.23	4	1	0
331	15-alpha-Hydroxyholamine	2.58	331.5	3	3	0
332	17-epi-Holacurtine	4.04	491.71	6	2	0
333	3-alpha-Amino-14-beta-hydroxypregnan-20-one	2.74	333.52	3	3	0
334	17-epi-N-Demethylholacurtine	3.13	477.69	6	3	0
335	N-Demethylholacurtine	3.13	477.69	6	3	0
336	(S)-isotylocrebrine	3.84	393.48	5	0	0
337	Isotylocrebrine	3.84	393.48	5	0	0
338	7-desmethyltylophorine	3.33	379.46	5	1	0
339	1',2',3',4'-tetrahydrotubulosine	5.26	471.6	6	2	1
340	Reticuline	2.38	329.4	5	2	0

Note: Bold entries were taken for further analysis

Table S2: Drug-likeness and Toxicity risk assessment of Artemisinin and alkaloids

S. No.	Compounds Name	Druglikeness	Mutagenic	Tumorigenic	Reproductive Effective	Irritant
Ref	Artemisinin	-1.97	None	None	High	High
1	Uric acid	2.923	high	none	high	none
2	Xanthine	3.2262	none	none	none	none
3	8-cyclopentyl-1,3-dipropylxanthine	2.6064	none	none	none	none
4	Enprofylline	5.7339	high	none	none	none
5	Theophylline	2.5134	high	high	high	none
6	Arecoline	3.0974	high	high	none	none
7	Berberine	-2.2467	none	none	none	none
8	Caffeine	2.5858	high	high	high	none
9	Nonivamide	-19.466	none	none	none	none
10	Dyphylline	4.4457	none	none	none	none
11	Furafylline	4.374	none	none	none	none
12	Harmaline	2.0945	none	none	high	none
13	3-isobutyl-1-methyl-7H-xanthine	-1.4031	high	none	none	none
14	Papaverine	-1.7454	none	none	none	none
15	Pentoxifylline	-1.5832	high	none	high	high
16	Propentofylline	-1.6163	none	none	none	high
17	Proxiphylline	2.7251	low	high	none	none
18	Tetrahydropalmatine	2.9203	none	none	low	none
19	Theobromine	3.421	high	high	high	none
20	Lysergic acid diethylamide	7.8391	none	none	high	none

21	Pilocarpine	4.1824	none	none	none	none
22	Physostigmine	1.9297	none	none	none	none
23	Apomorphine	4.7822	none	none	none	none
24	Colchicine	1.024	none	none	high	none
25	Methylergometrine	8.0208	none	none	high	high
26	Pseudotropine	1.8332	none	none	none	none
27	Yohimbine	1.5035	none	none	none	none
28	Aminophylline	2.5134	high	high	high	none
29	Galantamine	5.3857	none	none	none	none
30	Methysergide	8.0208	high	none	high	high
31	Xanthinol	6.0082	none	none	none	none
32	Emetine	3.8313	none	high	none	high
33	Psilocybin	-14.96	high	none	none	none
34	Dimenhydrinate	4.6945	high	none	high	none
35	8-chlorotheophylline	2.5231	none	none	none	none
36	Bromotheophylline	0.68159	none	none	none	none
37	Phenazocine	3.329	none	none	high	none
38	Vincamine	1.8025	none	none	none	none
39	Bamifylline	5.8382	none	none	none	none
40	Fenethylline	7.1692	none	none	high	none
41	Dehydroemetine	3.8992	none	high	none	high
42	Bufoylline	2.5134	high	high	high	none
43	Camptothecin	5.3292	none	none	none	none
44	Reproterol	5.7176	none	none	high	none
45	Etamiphylline	6.8977	none	none	none	high

46	Metergoline	-7.3817	none	none	high	none
47	Lisuride	7.3646	none	none	high	none
48	Duvoglustat	3.055	none	none	none	none
49	Nicergoline	2.5093	none	none	high	none
50	Staurosporine	4.7259	none	none	none	none
51	Pergolide	4.1164	none	none	high	none
52	Doxofylline	-2.5282	none	none	none	none
53	Miglustat	2.5386	none	none	none	none
54	Cabergoline	6.1842	none	none	high	none
55	Topotecan	6.6593	none	none	none	none
56	Tenidap	5.0482	none	high	none	high
57	Rolofylline	5.4469	none	none	none	none
58	Tretoquinol	1.2531	none	none	none	none
59	Metoserpate	2.1823	none	none	high	none
60	Acefylline	-2.1888	none	none	none	none
61	Pentifylline	-5.5075	none	none	none	none
62	Moxaverine	-2.0047	none	none	none	none
63	Methscopolamine	1.9941	none	none	none	none
64	Vinburnine	3.4076	none	none	none	none
65	Cafedrine	6.7504	none	none	low	none
66	Theodrenaline	5.6468	none	none	none	none
67	7-Hydroxystaurosporine	5.0622	none	none	none	none
68	9-aminocamptothecin	5.3457	high	low	none	none
69	Tropinone	1.4196	none	none	none	none
70	Nicotine	4.4595	none	none	none	none

71	Ecgonine	1.8158	none	none	none	none
72	Hydroquinidine	1.038	none	none	none	high
73	10-hydroxycamptothecin	5.3292	none	none	none	none
74	Lobeline	-0.2215	none	none	none	none
75	7-ethyl-10-hydroxycamptothecin	5.3292	none	none	none	none
76	Dihydroetorphine	3.265	none	none	none	high
77	Hydroquinine	1.038	none	none	none	high
78	Cositecan	-68.377	none	none	none	high
79	Exatecan	3.0211	none	none	none	none
80	5-Methoxy-N,N-diisopropyltryptamine	3.0812	none	none	none	none
81	Hyoscyamine	3.0135	none	none	none	none
82	Butylscopolamine	-0.38167	none	none	none	none
83	Atropine	3.0135	none	none	none	none
84	Migalastat	3.055	none	none	none	none
85	Ambroxolacefyllinate	-1.2867	none	none	none	none
86	Phenserine	-3.6765	none	none	none	none
87	Deptropine	2.1325	none	none	none	none
88	Tonapofylline	4.1019	none	none	none	none
89	Diflomotecan	2.7696	none	none	none	none
90	Demecolcine	1.837	none	none	high	none
91	Colchicine	1.1911	high	none	high	none
92	Methylecgonine	-0.18672	none	none	none	none
93	Noscapine	4.3358	none	none	none	none
94	Strychnine	4.5843	none	none	none	none
95	Quinidine	0.87864	none	none	none	none

96	Pentazocine	3.3217	none	none	high	none
97	Miglitol	4.2706	none	none	none	none
98	Rauwolfiaserpentina root	2.6043	none	none	none	none
99	Diprenorphine	2.5267	none	none	none	none
100	Ergometrine	6.2554	none	none	high	none
101	Terguride	7.3416	none	none	high	none
102	Vinpocetine	-0.26904	none	none	none	none
103	Cocaine	-0.52972	none	none	high	high
104	Benzoylcegonine	1.4683	none	none	none	none
105	Rubitecan	0.38166	none	none	none	none
106	Lisofylline	-3.3518	none	none	none	none
107	Lucerastat	2.5386	none	none	none	none
108	Sparteine	1.4482	none	none	none	none
109	Buprenorphine	2.5141	none	none	none	none
110	Etorphine	4.4752	none	none	none	high
111	Butropium	-3.2621	none	none	none	high
112	Methylatropine	3.4926	none	none	none	none
113	Oxtriphylline	1.7125	none	none	none	none
114	Anisotropinemethylbromide	1.7176	none	none	none	none
115	Ipratropium	1.8233	none	none	none	none
116	Benzatropine	2.1325	none	none	none	none
117	Zucapsaicin	-10.379	none	none	none	none
118	Capsaicin	-10.379	none	none	none	none
119	Drotaverine	-0.30443	none	none	high	none
120	Scopolamine	2.875	none	none	none	none

121	Quinine	0.87864	none	none	none	none
122	K-252a	1.9148	none	none	none	none
123	Dimemorfan	-0.22762	none	none	none	none
124	Ioflupane I-123	-1.1542	none	none	none	none
125	Harmine	-0.92948	low	none	none	none
126	Homatropine	1.1497	none	none	none	high
127	Codeine	5.1305	none	none	none	none
128	Dihydrocodeine	4.2758	none	none	none	none
129	Hydrocodone	4.2643	none	none	none	none
130	Hydromorphone	4.2337	none	none	none	none
131	Nalmefene	1.35	none	none	none	none
132	Nalorphine	0.91284	none	none	none	none
133	Naloxone	0.78037	none	none	none	none
134	Oxycodone	4.9034	none	none	none	none
135	Oxymorphone	4.8562	none	none	none	none
136	Trospium	-0.46271	none	none	none	none
137	Morphine	5.0881	none	none	none	none
138	Rivanicline	-0.28957	none	high	none	none
139	Nalbuphine	3.6567	none	none	none	none
140	Bicuculine	0.12	None	None	None	None
141	Pholcodine	5.8282	none	none	none	none
142	Ethylmorphine	3.6915	none	none	none	none
143	Levorphanol	-0.25467	none	none	low	none
144	Levallorphan	-4.6071	none	none	none	none
145	Dihydromorphone	4.2386	none	none	none	none

146	Naltrexone	4.6068	none	none	none	none
147	Morphine glucuronide	3.962	none	none	none	none
148	Dextromethorphan	-0.33388	none	none	none	none
149	Dextrophan	-0.25467	none	none	low	none
150	Butorphanol	-0.62733	none	none	none	none
151	Methylnaltrexone	0.63257	none	none	none	none
152	Desomorphine	2.0446	none	none	none	none
153	Nicomorphine	4.7938	none	none	none	none
154	Diamorphine	4.8851	none	none	none	none
155	Drotebanol	4.6517	none	none	none	none
156	Tiotropium	4.8619	none	none	none	none
157	Ajmaline	3.4513	none	none	none	none
158	Altropane	-1.3287	none	none	none	none
159	Nalfurafine	4.4373	none	none	none	none
160	Belotecan	7.6567	none	none	none	none
161	AR-67	-52.664	none	none	none	high
162	Oxitropium	1.9563	none	none	none	none
163	Anisodamine	3.4327	none	none	none	none
164	Gimatecan	-2.2795	none	none	none	none
165	Variolin B	3.1147	none	none	none	none
166	Naxifylline	5.639	none	none	none	none
167	Dihydrocapsiate	-15.31	none	none	none	none
168	Fentonium	1.9364	none	none	none	none
169	Homatropinemethylbromide	1.3761	none	none	none	high
170	Namitecan	5.1799	none	none	none	none

171	Posiphen	-3.6765	none	none	none	none
172	Aclidinium	3.1287	none	none	none	none
173	Samidorphan	4.4951	none	none	none	none
174	18-methoxycoronaridine	1.6643	none	none	none	none
175	Cimetropium	2.22	none	none	none	none
176	Cyprenorphine	3.7547	none	none	none	none
177	Etybenzatropine	1.0379	none	none	none	none
178	PCS-499	3.9575	none	none	none	none
179	Axelopran	0.25891	none	none	none	none
180	NS-2359	0.98602	none	none	none	none
181	Nazartinib	2.8132	none	high	high	none
182	Lorajmine	2.1446	high	high	high	high
183	Prajmaline	2.3465	none	none	none	none
184	8-azaxanthine	4.4521	none	none	none	none
185	N-n-octanoylnornicotine	-16.26	none	none	none	none
186	N-(4-hydroxyundecanoyl)anabasine	-13.509	none	none	none	none
187	Capsaicin	-10.379	none	none	none	none
188	Harmalol	-8.933	high	none	none	none
189	Saprosmine A	-8.7616	none	none	none	none
190	Saprosmine B	-6.8486	none	none	none	none
191	13(R)-antofine-N-oxide	-4.8761	low	high	none	none
192	tylophoridicine F	-3.97	low	high	none	none
193	tylophoridicine C	-3.97	low	high	none	none
194	13(R)-14(R)-hydroxyantofine-N-oxide	-3.97	low	high	none	none
195	canthin-6-one 9-O-beta-glucopyranoside	-3.2891	low	none	none	none

196	Cephalotaxine beta-N-oxide	-3.2562	none	none	none	none
197	Cephalotaxine alpha-N-oxide	-3.2562	none	none	none	none
198	4-methoxycarbonyl-5,10-benzogquinolinequinone	-3.0999	high	none	none	none
199	Sanguinarine	-2.4707	none	none	none	none
200	Berberine	-2.2467	none	none	none	none
201	Chelerythrine	-2.1842	none	none	none	none
202	beta-carboline-1-propionic acid	-1.9151	low	none	none	none
203	Papaverine	-1.7454	none	none	none	none
204	7-methoxy-beta-carboline-1-propionic acid	-1.706	low	none	none	none
205	9-methoxycanthin-6-one 3N-oxide<NL>	-0.99092	none	none	none	none
206	Harmame	-0.96557	high	none	none	none
207	Ellipticine	-0.96557	high	none	none	none
208	Harmine	-0.92948	low	none	none	none
209	liriodenine	-0.92304	none	none	none	none
210	Cis-Zeatin	-0.51868	high	high	low	high
211	Rohitukine	-0.1543	none	none	none	none
212	Holamine	-0.066098	none	none	high	none
213	Marcanines A	0.016126	none	none	none	none
214	Matrine	0.2541	none	none	none	none
215	Brucine N-oxide	0.26167	none	low	none	none
216	canthin-6-one	0.35032	low	none	none	none
217	(R)-cryptopleurine	0.52242	low	high	none	none
218	(-)-anonnaine	0.61	none	none	none	none
219	15-alpha-Hydroxyholamine	0.635	none	none	high	none

220	3-alpha-Amino-14-beta-hydroxypregnan-20-one	0.82077	none	none	high	none
221	9-methoxycanthin-6-one	1.24	high	none	none	none
222	Lycoricidinol	1.313	none	none	high	none
223	17-epi-N-Demethylholacurtine	1.5367	none	none	high	none
224	N-Demethylholacurtine	1.5367	none	none	high	none
225	Vincamine	1.8025	none	none	none	none
226	Physostigmine	1.9297	none	none	none	none
227	9-hydroxycanthin-6-one	2.1077	none	none	none	none
228	Holacurtinol	2.1445	none	none	high	none
229	Neocryptolepine	2.3562	none	none	high	none
230	Harmol	2.6265	none	none	none	none
231	Cryptolepine	2.9343	none	none	none	none
232	Corydaline	3.1151	none	none	none	none
233	7-desmethyltylophorine	3.1309	low	high	none	none
234	6-O-desmethylanofine	3.1309	low	high	none	none
235	Isocephalotaxine	3.1454	none	none	high	none
236	Tylocrebrine	3.1505	low	high	none	none
237	Isotylocrebrine	3.1505	low	high	none	none
238	Antofine	3.1505	low	high	none	none
239	(S)-tylophorine	3.1505	low	high	none	none
240	(S)-isotylocrebrine	3.1505	low	high	none	none
241	(R)-tylophorine	3.1505	low	high	none	none
242	(R)-antofine	3.1505	low	high	none	none
243	11-beta-hydroxycephalotaxine beta-N-oxide	3.1505	low	high	none	none
244	Lycorine	3.1877	none	none	none	none

245	Rhyncophylline	3.3474	none	none	none	none
246	(S)-tyloindicine I	3.3476	none	none	high	none
247	(+)-tylophorinidine	3.5386	low	high	none	none
248	6-O-desmethylsecoantofine	3.6885	none	none	high	none
249	Secoantofine	3.7051	none	none	high	none
250	Psychotrine	3.9783	none	high	none	high
251	Tubulosine	4.1737	none	high	none	high
252	tyloindicine G	4.3085	none	none	high	high
253	tyloindicine F	4.3085	none	none	high	none
254	Hydrastine	4.3358	none	none	none	none
255	Holacurtine	4.3905	none	none	high	none
256	17-epi-Holacurtine	4.3905	none	none	high	none
257	Isostrychnine	4.5247	none	none	none	none
258	Strychnine	4.5843	none	none	none	none
259	Brucine	4.6438	none	low	none	none
260	Reserpine acid	4.7169	none	none	high	none
261	Evodiamine	5.1076	none	none	none	none
262	Camptothecin	5.3292	none	none	none	none
263	9-Aminocamptothecin	5.3457	high	low	none	none
264	Reticuline	5.29	None	None	None	None

Note: Bold entries were taken for further screening

Table S3:Docking results of iGEMDOCK algorithm

S. No.	Compounds	iGEMDOCK (kcal/mol)
Ref	Artemisinin	-91.3722
1	Axelopran	-125.326
2	Nicomorphine	-122.544
3	Fentonium	-121.709
4	Namitecan	-121.464
5	Morphine glucuronide	-119.945
6	Rubitecan	-119.292
7	Aclidinium	-116.089
8	K-252a	-115.782
9	7-ethyl-10-hydroxycamptothecin	-115.559
10	Tonapofylline	-113.324
11	Oxitropium	-112.543
12	Topotecan	-110.615
13	Hydrastine	-110.116
14	Tretoquinol	-110.106
15	Theodrenaline	-109.685
16	Bicuculline	-109.455
17	Belotecan	-108.553
18	10-hydroxycamptothecin	-108.289
19	Bamifylline	-107.61
20	Xanthinol	-107.509
21	Nalfurafine	-106.569
22	Naxifylline	-106.121
23	Variolin B	-104.742
24	Diflomotecan	-103.702
25	Ipratropium	-103.666
26	Lycorine	-102.344
27	Methscopolamine	-102.245
28	Hyoscyamine	-101.993

29	Camptothecin	-101.781
30	Rhyncophylline	-101.492
31	Noscapine	-101.414
32	Tiotropium	-101.042
33	7-Hydroxystaurosporine	-100.894
34	Benzoylecgonine	-99.9005
35	Furafylline	-99.4678
36	Quinine	-99.0127
37	18-methoxycoronaridine	-98.5351
38	Dyphylline	-98.2116
39	PCS-499	-97.0292
40	Vincamine	-96.9741
41	Buprenorphine	-96.7721
42	Praijmaline	-96.477
43	Evodiamine	-96.2743
44	Staurosporine	-96.2402
45	Atropine	-96.1418
46	Rolofylline	-95.7426
47	Reticuline	-95.6594
48	Anisodamine	-95.0347
49	Exatecan	-95.0082
50	8-cyclopentyl-1,3-dipropylxanthine	-94.2662
51	Cimetropium	-94.0635
52	Methylatropine	-94.0079
53	Samidorphan	-93.6762
54	Yohimbine	-93.6743
55	Cyprenorphine	-93.4031
56	Rauwolfia serpentina root	-93.2392
57	Methylnaltrexone	-93.142
58	Etybenzatropine	-93.0622
59	Deptropine	-92.8259
60	Isostrychnine	-92.619

61	Lucerastat	-91.9422
62	Diprenorphine	-91.803
63	Ajmaline	-90.9876
64	Vinburnine	-90.284
65	Pholcodine	-90.2835
66	Benzatropine	-90.1175
67	Corydaline	-90.0204
68	Nalbuphine	-89.9547
69	5-Methoxy-N,N-diisopropyltryptamine	-89.7153
70	Scopolamine	-89.7064
71	Quinidine	-89.5134
72	Naltrexone	-88.9509
73	Apomorphine	-88.6905
74	Physostigmine	-88.5954
75	(-)-anone	-87.93
76	Ioflupane I-123	-87.9
77	Strychnine	-87.4441
78	Naloxone	-87.2566
79	Anisotropin methyl bromide	-87.1993
80	Oxymorphone	-85.8151
81	Cryptolepine	-85.7146
82	Nalorphine	-85.5843
83	Diamorphine	-85.4754
84	Miglustat	-85.0007
85	Miglitol	-84.7194
86	Marcaines A	-84.5263
87	9-hydroxycanthin-6-one	-83.946
88	Nalmefene	-83.6774
89	Oxtriphylline	-83.6001
90	Hydromorphone	-83.5136
91	Morphine	-83.4119
92	Harmol	-81.6226

93	Dihydromorphine	-80.9058
94	Pilocarpine	-80.8781
95	NS-2359	-79.9321
96	Galantamine	-79.591
97	Matrine	-78.9337
98	Hydrocodone	-78.6178
99	Migalastat	-78.5602
100	Codeine	-77.95
101	Oxycodone	-76.3101
102	Desomorphine	-75.1219
103	8-azaxanthine	-74.939
104	Drotebanol	-74.8465
105	Duvoglustat	-74.3026
106	Bromotheophylline	-73.0872
107	8-chlorotheophylline	-72.7254
108	Ecgonine	-72.404
109	Xanthine	-71.5821
110	Ethylmorphine	-71.4814
111	Dihydrocodeine	-71.3592
112	Sparteine	-68.1736
113	Nicotine	-65.4694
114	Pseudotropine	-57.0935
115	Tropinone	-51.787

Note: Bold entries were taken for further analysis

Table S4: Computational estimation of oral toxicity (LD50) and oral absorption availability (clogS)

S. No.	Compounds	AMES toxicity	Oral Rat Acute Toxicity (LD50) mol/kg	Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day)	Hepatotoxicity
Ref.	Artemisinin	Yes	2.459	1	No
1	Exatecan	No	3.06	1.323	Yes
2	10-hydroxycamptothecin	No	2.418	1.738	Yes
3	Fentonium	No	2.883	1.411	Yes
4	7-ethyl-10-hydroxycamptothecin	No	2.444	1.551	Yes
5	Diflomotecan	No	2.551	1.324	Yes
6	Camptothecin	No	2.565	1.756	Yes
7	Morphine glucuronide	No	2.312	3.346	Yes
8	Rubitecan	Yes	2.789	1.494	Yes
9	Nicomorphine	No	3.172	2.149	Yes
10	Rauwolfia serpentina root	No	2.974	0.431	Yes
11	Belotecan	No	3.03	1.994	Yes
12	Yohimbine	No	2.942	0.687	No
13	Deptropine	No	2.711	0.414	Yes
14	Axelopran	No	2.278	2.09	Yes
15	Hydrastine	No	2.893	2.319	No
16	Lycorine	Yes	2.545	0.912	Yes
17	Evodiamine	Yes	2.542	1.006	Yes
18	Tretoquinol	No	2.886	1.843	No

19	Nalfurafine	No	3.285	0.278	Yes
20	Vincamine	No	3	0.613	No
21	Aclidinium	No	2.301	1.028	No
22	Reticuline	No	2.296	1.542	No
23	Isostrychnine	No	3.087	2.097	No
24	Diprenorphine	No	2.858	0.575	Yes
25	Naxifylline	Yes	2.618	0.239	Yes
26	Variolin B	No	2.355	2.099	Yes
27	Noscapine	No	2.91	2.313	No
28	Rolofylline	No	2.751	0.411	No
29	Cyprenorphine	No	2.847	0.609	Yes
30	Tonapofylline	No	2.638	1.103	Yes
31	Theodrenaline	Yes	2.184	2.271	No
32	Quinine	Yes	2.728	0.635	Yes
33	Namitecan	Yes	2.727	2.078	Yes
34	Benzoylecgonine	No	1.787	2.051	No
35	18-methoxycoronaridine	Yes	3.464	0.793	Yes
36	8-cyclopentyl-1,3-dipropylxanthine	Yes	2.835	0.457	Yes
37	Methylatropine	No	2.624	2.624	No
38	Samidorphan	No	2.143	2.317	Yes

Note: Bold entries were taken for analysis

Table S5:3D pharmacophore analysis using PharmaGist

S. No.	Compounds	Best Pairwise Alignment Scores
1	Noscapine	6.64027
2	Reticuline	6.6333
3	Acridinium	6.3347
4	Benzoylcegonine	6.32994
5	Vincamine	6.329
6	Tretoquinol	6.32673
7	Yohimbine	5.433
8	Hydrastine	5.13019
9	Rolofylline	4.818
10	Methylatropine	4.52976
11	Isostrychnine	3.926

Note: Bold entries (top 3) were taken for MSD analysis

Table S6: Binding Free Energy calculations using MMPBSA

Complex	Van der Waal energy (kJ/mol)	Electrostatic energy (kJ/mol)	Polar solvation energy (kJ/mol)	Binding energy (kJ/mol)
FP2-Artemisinin (Reference)	-82.58 +/- 9.13	-7.53 +/- 8.79	33.10 +/- 11.41	-64.76 +/- 10.39
FP2-Acridinium	-276.00 +/- 11.02	-25.11 +/- 6.27	122.14 +/- 9.33	-204.23 +/- 12.37
FP2-Noscapine	-145.10 +/- 14.16	-30.27 +/-12.09	85.36 +/-18.48	-104.44 +/- 13.80
FP2-Reticuline	-207.69 +/- 9.30	0.04 +/- 2.224	42.910 +/- 8.22	-183.37 +/- 10.88

Table S7: Detail of the top compounds with interacting residues, types of bond and bond distance

Compound	Interacting residues	Types of bond with distance
Artemisinin (Reference)	ALA 157	3.78, 4.99 (pi-alkyl)
	TRP 206	4.22 (pi-alkyl), 4.13 (pi-alkyl), 4.88 (pi-alkyl and alkyl), 5.09 (pi-alkyl), 2.39 (pi-sigma)
	TRP 210	4.67, 5.41 (pi-alkyl)
Noscapine	TRP 206	2.99 (carbon hydrogen), 4.02 (pi-pi stacked), 4.13 (pi-pi stacked)
	ALA 157	5.15 (pi-alkyl)
	SER 153	2.67 (carbon-hydrogen)
Reticuline	ALA 157	3.93, 4.96 (pi-alkyl),
	TRP 206	3.64 (pi-pi stacked)
	ASP 154	3.74 (carbon-hydrogen)
	VAL 152	5.46 (alkyl), 3.37 (carbon hydrogen)
	ASN 173	2.45 (hydrogen bond)
Aclidinium	GLN 36	2.32 (hydrogen bond)
	ASN 173	2.38, 2.54 (carbon hydrogen)
	HIS 174	2.53 (carbon hydrogen)
	GLY 40	2.27 (carbon hydrogen)
	ALA 175	4.78 (pi-alkyl)
	LEU 84	4.76 (pi-alkyl)