



Supplementary Materials: Curcumin Analogues as a Potential Drug against Antibiotic Resistant Protein, β -Lactamases and L, D-Transpeptidase Involved in Toxin Secretion in *Salmonella typhi*: A Computational Approach

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Table S1. The selected ligands.

Serial No	Ligand	Pubchem CID	References
1	(8)-Shogaol	CID_6442560	[1]
2	Desmethoxycurcumin	CID_5469424	[2,3]
3	Tetrahydro curcumin	CID_56965746	[2]
4	6-Dehydrogingerdione	CID_22321203	[4]
5	Difluorinated curcumin	CID_54597187	[5]
6	EAC	CID_8868	[6]
7	DM1	CID_11343137	[7]
8	Chalcone	CID_637760	[8]
9	Cyclovalone	CID_1550234	[9]
10	Curcumin PE	CID_5281767	[10]
11	Salsalate	CID_5161	[11]
12	Go-Y016	CID_1550385	[12]
13	Petasiphenol	CID_6438779	[13]
14	Benzyl ferulate	CID_7766335	[14]
15	Calebin A	CID_637429	[15]
16	ACMC-1AEIO	CID_2889	[16]
17	MFCD00012210	CID_14121	[17]
18	Khi-201	CID_99844	[18]
19	Go-Y032	CID_1714173	[19]
20	3,3'-dimethoxystilbene-4,4'-diol	CID_5280698	[20]
21	AO-002	CID_5318278	[21]
22	phenylethyl-trans-isoferulate	CID_5468215	[22]
23	NSC-43319	CID_5470829	[23]
24	3,4-dimethoxy-4'-hydroxychalcone	CID_5930244	[24]
25	PHSK	CID_6123890	[25]
26	Go-Y022	CID_6474893	[26]
27	BRD-89483	CID_6477637	[23]
28	3,3'-dimethoxy-cis-stilbene-4,4'-diol	CID_9548762	[27]
29	CHEMBL482607	CID_10904292	[28]
30	ZINC100190381	CID_11895692	[29]
31	SCHEMBL18672270	CID_16087306	[30]
32	EI-135	CID_16760039	[30]
33	3,4'-Dimethoxystilbene-4-ol	CID_23652110	[31]
34	BDBM149243	CID_44538441	[30]
35	Go-Y078	CID_46231908	[32]
36	CHEMBL3940632	CID_68556085	[30]
37	CHEMBL494826	CID_71717791	[30]
38	SCHEMBL1374497	CID_86590085	[33]
39	CHEMBL3290186	CID_90644814	[30]
40	BDBM145855	CID_91809442	[30]
41	BDBM145853	CID_91809620	[30]
42	1,5-Bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadien-3-one	CID_131752986	[26]
43	Coniferyl ferulate	CID_6441913	[34]

44	Curcumin sulfate	CID_66645351	[3]
45	Dihydrocurcumin	CID_10429233	[3]
46	Dimethoxycurcumin	CID_9952605	[2]
47	Dimethylcurcumin	CID_6477182	[35]
48	Ethyl curcumin	CID_11474949	[36]
49	Griffithane D	CID_56597215	[37]
50	Monodemethylcurcumin	CID_5469426	[38]
51	Phenylethyl 3-methylcaffeate	CID_5284444	[39]
52	p-Hydroxyphenethyl trans-ferulate	CID_637308	[40]
53	Piperkadsin A	CID_11717379	[41]
54	Shogaol	CID_5281794	[3]
55	Tetrahydrocurcumin	CID_124072	[2]
56	Tetrahydrodemethoxydiferuloylmethane	CID_9906039	[42]
57	Tetramethylcurcumin	CID_11487078	[43]
58	Wallichinine	CID_5315280	[44]
59	6-paradol	94378	[45,46]
60	Bisdemethoxycurcumin	5315472	[2,3]
61	Cassumunin A	10460395	[47]
62	Cassumunin B	10054109	[47]
63	Curcumin	969516	[2,48]
64	Cyclocurcumin	69879809	[49]
65	Dehydrozingerone	5354238	[50]
66	Dibenzoylmethane	8433	[51]
67	6-Gingerol	442793	[3,45]
68	Isoeugenol	853433	[52]
69	Yakuchinone A	133145	[53]
70	Yakuchinone B	6440365	[53]

Table S2. Drug likeliness properties of the ligands.

SL No	Compound Name	MW (g/mol)	miLogP	HBA	HBD	nROTB	TPSA (Å ²)	Lipinski Violation
Rule		<500	≤ 5	< 10	< 5	≤ 10		
01	6-Gingerol	294.39	3.22	4	2	10	66.76	0
02	6-Paradol	278.39	4.60	3	1	9	46.53	0
03	Bisdemethoxycurcumin	276.38	2.67	4	2	6	74.60	0
04	Cassumunin A	558.63	4.96	8	2	13	111.53	1
05	Cassumunin B	588.65	4.77	9	2	14	120.77	1
06	Curcumin	368.38	2.30	6	2	8	93.07	0
07	Cyclocurcumin	368.38	3.03	6	2	5	85.23	0
08	Dehydrozingerone	192.21	1.55	3	1	3	46.53	0
09	Demethoxycurcumin	338.36	2.48	5	2	7	83.83	0
10	Dibenzoylmethane	224.26	2.88	2	0	4	34.14	0
11	Isoeugenol	164.20	2.38	2	1	2	29.46	0
12	Yakuchinone A	312.41	4.24	3	1	9	46.53	0
13	Yakuchinone B	310.39	4.27	3	1	8	46.53	0
14	(8)-Shogaol	304.4	5.36	3	1	11	46.5	1
15	Desmethoxycurcumin	338.4	3.3	5	2	7	83.8	0
16	Tetrahydrocurcumin	372.42	2.24	6	2	10	93.07	0
17	6-Dehydrogingerdione	290.36	3.81	4	2	8	66.76	0
18	Difluorinated curcumin	492.47	4.58	6	2	9	93.07	0
19	EAC	130.14	0.06	3	0	4	43.38	0
20	DM1	738.30	3.45	13	2	8	156.48	2
21	Chalcone	208.26	3.81	1	0	3	17.07	0
22	Cyclovalone	366.41	3.65	5	2	4	76.00	0
23	Curcumin PE	368.38	3.05	6	3	7	96.22	0
24	Salsalate	258.23	3.77	5	2	4	83.83	0
25	Go-Y016	414.45	3.45	7	0	10	72.47	0
26	Petasiphenol	344.32	1.56	7	4	7	124.29	0
27	Benzyl ferulate	284.31	3.46	4	1	6	55.77	0
28	Calebin A	384.38	2.73	7	2	9	102.30	0
29	ACMC-1AEIO	368.38	2.30	6	2	8	93.07	0
30	MFCD00012210	192.21	1.55	3	1	3	46.53	0
31	Khi-201	230.22	1.12	4	1	2	63.60	0

32	Go-Y032	394.47	4.26	5	0	6	54.01	0
33	3,3'-dimethoxystilbene-4,4'-diol	356.37	2.78	6	0	8	71.08	0
34	AO-002	310.39	3.98	3	1	8	46.53	0
35	Phenylethyl-trans isoferulate	298.34	3.67	4	1	7	55.77	0
36	NSC-43319	352.39	3.14	5	2	4	76.00	0
37	3,4-dimethoxy-4'-hydroxychalcone	284.31	3.21	4	1	5	55.77	0
38	PHSK	254.28	3.15	3	1	4	46.53	0
39	Go-Y022	326.35	2.86	5	2	6	76.00	0
40	BRD-89483	352.39	3.14	5	2	4	76.00	0
41	3,3'-dimethoxy-cis-stilbene-4,4'-diol	272.30	3.17	4	2	4	58.92	0
42	CHEMBL482607	352.39	3.38	5	2	7	76.00	0
43	ZINC100190381	372.42	2.99	6	3	9	96.22	0
44	SCHEMBL18672270	428.46	3.92	6	2	11	85.23	1
45	EI-135	368.38	2.30	6	2	8	93.07	0
46	3,4'-Dimethoxystilbene-4-ol	256.30	3.89	3	1	4	38.70	0
47	BDBM149243	372.80	2.91	5	2	7	83.83	0
48	Go-Y078	400.43	3.17	7	1	9	83.47	0
49	CHEMBL3940632	368.38	2.07	6	2	8	93.07	0
50	CHEMBL494826	382.41	3.35	6	2	8	85.23	0
51	SCHEMBL1374497	382.41	2.68	6	2	9	93.07	0
52	CHEMBL3290186	362.33	3.50	5	2	6	76.00	0
53	BDBM145855	406.36	3.77	5	2	8	83.83	0
54	BDBM145853	440.45	2.47	8	1	12	108.38	0
55	1,5-Bis(4-hydroxy-3-methoxyphenyl)- 1,4-pentadien-3-one	326.35	2.86	5	2	6	76.00	0
56	Coniferyl ferulate	356.37	3.56	6	2	8	85.23	0
57	Curcumin sulfate	448.45	-0.14	9	2	10	136.44	0
58	Dihydrocurcumin	370.40	2.27	6	2	9	93.07	0
59	Dimethoxycurcumin	396.44	2.92	6	0	10	71.08	0
60	Dimethylcurcumin	396.44	3.66	6	1	9	74.23	0
61	Ethyl curcumin	396.44	3.06	6	2	10	93.07	0
62	Griffithane D	302.33	1.87	5	1	6	72.84	0
63	Monodemethylcurcumin	354.36	2.00	6	3	7	104.06	0
64	Phenylethyl 3-methylcaffeate	298.34	3.67	4	1	7	55.77	0
65	p-Hydroxyphenethyl trans-ferulate	314.34	3.19	5	2	7	76.00	0
66	Piperkadsin A	356.42	2.51	5	1	7	65.00	0
67	Shogaol	276.38	4.35	3	1	9	46.53	0
68	Tetrahydrocurcumin	372.42	2.24	6	2	10	93.07	0
69	Tetrahydrodemethoxydiferuloylmetha ne	342.39	2.43	5	2	9	83.83	0
70	Tetramethylcurcumin	424.49	3.81	6	0	10	71.08	0
71	Wallichinine	370.44	2.82	5	0	8	54.01	0

(HBA: hydrogen bond acceptors; HBD: hydrogen bond donors; nROTB: number of rotatable bonds; TPSA: topological polar surface area).

Table S3. ADME/T result of controls.

Ligand	Clavulanic Acid	Tazobactam	Carbapenem	Cephalosporin
Human Intestinal Absorption	High	Low	Low	Low
Human Oral Bioavailability	High	High	High	Low
Caco - 2 Permeability	Low	Low	High	Low
P glycoprotein substrate	No	No	Yes	Yes
P glycoprotein inhibitor	No	No	No	No
Blood-Brain-Barrier	No	No	No	No
CYP3A4 substrate	No	Yes	No	No
CYP3C9 substrate	No	No	No	No
CYP2D6 substrate	No	No	No	No
CYP3A4 inhibitor	No	No	No	No
CYP3C9 inhibitor	No	No	No	No
CYP2D6 inhibitor	No	No	No	No
Total Clearance	0.533	0.947	0.352	-0.012
OCT2 substrate	No	No	No	No
AMES Toxicity	No	No	No	No
Hepatotoxicity	yes	Yes	No	Yes
hERG inhibition	No	No	Yes	No

Eye irritation	No	No	Yes	No
Acute oral toxicity	Type III	Type III	Type III	Type III
Carcinogenicity	No	No	No	No

Table S4. ADME/T prediction results

Ligand	Go-Y032	NSC-43319	Salsalate	Petasiphenol	Diffuorinated Curcumin	Cyclocurc Umin	Cyclovalone
Absorption							
Human Intestinal Absorption	High	High	High	High	High	High	High
Human Oral Bioavailability	High	High	High	Low	High	Low	High
Caco - 2 Permeability	High	High	Low	Low	Low	Low	Low
Distribution							
P glycoprotein substrate	No	Yes	No	Yes	Yes	No	Yes
P glycoprotein inhibitor	Yes	Yes	No	No	Yes	Yes	Yes
Blood-Brain-Barrier	Yes	Yes	Yes	No	Yes	No	Yes
Metabolism							
CYP3A4 substrate	Yes	Yes	No	Yes	Yes	Yes	No
CYP3C9 substrate	Yes	No	No	Yes	Yes	Yes	No
CYP2D6 substrate	No	No	No	No	No	No	No
CYP3A4 inhibitor	Yes	Yes	No	No	Yes	No	Yes
CYP3C9 inhibitor	Yes	Yes	No	No	Yes	No	Yes
CYP2D6 inhibitor	No	No	No	No	No	No	No
Excretion							
Total Clearance	0.176	0.039	0.52	−0.012	0.424	0.072	0.047
OCT2 substrate	No	No	No	No	No	No	No
AMES Toxicity	No	No	No	No	No	No	No
Hepatotoxicity	No	No	No	No	Yes	Yes	No
hERG inhibition	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Eye irritation	No	No	Yes	No	No	No	No
Acute oral toxicity	Type III	Type III	Type III	Type III	Type III	Type III	Type III
Carcinogenicity	No	No	No	No	No	No	No

Table S5. Pharmacological activities

Activities	Go-Y032		NSC-43319		Salsalate		Petasiphenol		Diffuorinated Curcumin		Cyclocurcumin		Cyclovalone	
	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
Antibacterial	0.237	0.091	0.312	0.056	0.416	0.026	0.202	0.116	—	—	0.423	0.025	0.298	0.061
Bacterial Efflux Pump Inhibitor	0.154	0.012	0.154	0.011	—	—	—	—	0.181	0.004	0.145	0.02 2	0.149	0.017
Antibiotic	0.105	0.061	—	—	0.109	0.055	—	—	—	—	—	—	0.122	0.037
Anthracycline like	0.118	0.070	0.133	0.055	0.234	0.012	—	—	—	—	—	—	0.128	0.060
Beta-lactamase Inibitor	0.489	0.020	0.544	0.014	—	—	0.282	0.092	0.306	0.077	—	—	0.534	0.015
Anti-micobacterial	—	—	—	—	0.210	0.026	—	—	—	—	0.112	0.071	0.093	0.089

—indicates no activity

Table S6. Biological activities

Activities	Go-Y032	NSC-43319	Salsalate	Petasiphenol	Diffuorinated Curcumin	Cyclocurcumin	Cyclovalone
GPCR ligand	−0.12	−0.26	−0.21	−0.06	−0.10	−0.04	−0.10
Ion channel modulator	−0.27	−0.21	−0.06	−0.17	−0.26	−0.31	−0.25
Kinase inhibitor	−0.32	−0.33	−0.28	−0.31	−0.18	0.28	−0.31
Nuclear receptor ligand	−0.09	0.01	0.05	0.17	−0.05	0.10	−0.02

Protease inhibitor	-0.08	-0.11	-0.29	0.08	-0.14	-0.11	-0.08
Enzyme inhibitor	-0.03	0.02	-0.00	0.08	-0.03	0.09	0.02

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