

Article

A Cell-Free Screen for Bacterial Membrane Disruptors Identifies Mefloquine as a Novel Antibiotic Adjuvant

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Table S1. Complete list of HTS compounds yielding a lytic ratio greater than 1.15.

Compound Name	SMILES	Lytic Ratio (PGCL/PC)	P-value
2-[[2-(3-chloroanilino)-2-oxoethyl]thio]-4-(dimethoxymethyl)pyrimidine-5-carboxylic acid	<chem>COC(OC)c1nc(SCC(=O)Nc2cccc(Cl)c2)ncc1C(=O)O</chem>	1.246	5.26021E-42
N-(6-chloro-1,3-benzothiazol-2-yl)-4-(trifluoromethyl)benzamide	<chem>FC(F)(F)c1ccc(cc1)C(=O)Nc2nc3ccc(Cl)cc3s2</chem>	1.165	0.001103355
ethyl 1-[4-(2,5-dioxotetrahydro-1H-pyrrol-1-yl)phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxylate	<chem>CCOC(=O)c1c(C)nn(c1C)c2ccc(c2)N3C(=O)CCC3=O</chem>	1.264	0.191297999
N,N-dimethyl-N'-(3-phenyl[1,2,4]triazolo[4,3-b]pyridazin-6-yl)iminoformamide	<chem>CN(C)C=Nc1ccc2nnc(c3ccccc3)n2n1</chem>	1.211	0.00021766
2,8-di(trifluoromethyl)quinoline	<chem>FC(F)(F)c1ccc2cccc(c2n1)C(F)(F)F</chem>	1.154	7.18846E-16
2-(2,6-dichlorobenzyl)-6-(methoxymethyl)pyrimidin-4-ol	<chem>COCc1cc(O)nc(Cc2c(Cl)cccc2Cl)n1</chem>	1.185	6.24666E-26
N-benzyl-N'-ethyl-N-(pyridin-3-ylmethyl)urea	<chem>CCNC(=O)N(Cc1cccc1)Cc2cccn2</chem>	1.174	0.001152631
2-amino-N'-(2-furylcarbonyl)-5-nitrobenzohydrazide	<chem>Nc1ccc(cc1C(=O)NNC(=O)c2ccc(O2)N(=O)=O</chem>	1.174	0.001969053
6,8-dichloro-4-hydroxy-3-methyl-1,2-dihydroquinolin-2-one	<chem>Cc1c(O)c2cc(Cl)cc(Cl)c2[nH]c1=O</chem>	1.179	2.20868E-11
(5-nitro-2-furyl)methyl thiocyanate	<chem>O=N(=O)c1ccc(CSC#N)o1</chem>	1.154	2.25142E-18
2,3-dihydro-1H-inden-2-yl(morpholino)methanone	<chem>O=C(C1Cc2ccccc2C1)N3CCOCC3</chem>	1.25	0.087916416
5-methyl-N-phenyl-3-isoxazolecarboxamide	<chem>Cc1cc(no1)C(=O)Nc2ccccc2</chem>	1.163	4.32613E-11
2-(2-furyl)-1,3-thiazole	<chem>c1coc(c1)c2nccs2</chem>	1.18	4.24788E-20
methyl 2-cyano-2-(2-oxo-2,3-dihydro-1H-indol-3-yliden)acetate	<chem>COC(=O)C(=C1C(=O)Nc2cccc12)C#N</chem>	1.177	0.001390214
11-(1-methylethylidene)tricyclo[6.2.1.0~2,7~]undec-2(7),3,5,9-tetraene	<chem>CC(=C1C2C=CC1c3ccccc23)C</chem>	1.155	0.00534184
2-amino-4-methylthiophene-3-carbonitrile	<chem>S1C(=C(C(=C1)C)C#N)N</chem>	1.169	3.08592E-05
1-(1-adamantyl)-3-(dimethylamino)prop-2-en-1-one	<chem>CN(C)C=CC(=O)C1(CC2CC3CC(C2)C1)C3</chem>	1.175	2.28729E-06

N1-[5-chloro-2-(methylthio)phenyl]-2,2,2-trifluoroacetamide	<chem>CSc1ccc(Cl)cc1NC(=O)C(F)(F)F</chem>	1.189	1.72153E-05
4-(2,6-dichlorophenoxy)-3-nitrobenzene-1-sulfonamide	<chem>NS(=O)(=O)c1ccc(Oc2c(Cl)cccc2Cl)c(c1)N(=O)=O</chem>	1.194	0.007518639
4-[4-(9H-fluoren-9-yl)piperazino]-4-oxobutanoic acid	<chem>OC(=O)CCC(=O)N1CCN(CC1)C2c3cccc3-c4cccc24</chem>	1.172	1.97902E-05
2-hydroxy-4-methoxybicyclo[2.2.2]octane-2-carbonitrile	<chem>COC1(CCC2CC1)CC2(O)C#N</chem>	1.19	0.000801939
3-(1,4-thiazinan-4-yl)-4,5-dihydro-1H-1,2,4-triazol-5-one	<chem>O=c1[nH]nc([nH]1)N2CCSCC2</chem>	1.16	4.5185E-31
tert-butyl N-[1-(aminocarbonyl)-3-methylbutyl]carbamate	<chem>CC(C)CC(NC(=O)OC(C)(C)C(=O)N</chem>	1.15	5.64038E-33
Alfuzosin hydrochloride	<chem>CN(CCCNC(=O)C1CCCCO1)C2=NC3=CC(=C(C=C3C(=N2)N)OC</chem>	1.162	0.002251788
Amlodipine	<chem>CCOC(=O)C1=C(NC(=C(C1C2=CC=CC=C2Cl)C(=O)OC)C)COC</chem>	1.165	3.35398E-08
Cyclosporin A	<chem>CCC1C(=O)N(CC(=O)N(C(C(=O)NC(C(=O)N(C(C(=O)NC(C(=O)N(C(C(=O)N(C(C(=O)N1)C(C(C)CC=CC)O)C)C(C)C)CC(C)C)CC(C)C)C)CC(C)C)C)CC(C)C)C</chem>	1.168	0.001001536
Piperacillin sodium salt	<chem>CCN1CCN(C(=O)C1=O)C(=O)NC(C2=CC=CC=C2)C(=O)NC3C4N(C3=O)C(C(S4)(C)C)C(=O)[O-]</chem>	1.211	0.000157617
Merbromin	<chem>C1=CC=C2C(=C1)C(=O)OC23C4=CC(=C(C=C4OC5=C(C(=C(C=C35)Br)[O-])[Hg])[O-])Br.O.[Na+].[Na+]</chem>	1.312	9.51249E-17
Mecamylamine hydrochloride	<chem>CC1(C2CCC(C2)C1(C)NC)C.Cl</chem>	1.166	1.06786E-05
Flavoxate hydrochloride	<chem>CC1=C(OC2=C(C1=O)C=CC=C2C(=O)OCCN3CCCCC3)C4=CC=CC=C4.Cl</chem>	1.174	4.88174E-07
Troleandomycin	<chem>CC1CC(C(C(O1)OC2C(CC3(CO3)C(=O)C(C(C(C(OC(=O)C(C(C2)OC4CC(C(C(O4)C)OC(=O)C)OC)C)C)OC(=O)C)C)OC(=O)C)N(C)C</chem>	1.158	3.1166E-06
Pentoxifylline	<chem>CC(=O)CCCCN1C(=O)C2=C(N=CN2C)N(C1=O)C</chem>	1.192	7.85643E-08
Quinidine hydrochloride monohydrate	<chem>COC1=CC2=C(C=CN=C2C=C1)C(C3CC4CCN3CC4C=C)O.O.Cl</chem>	1.249	1.1409E-10
Mefloquine hydrochloride	<chem>C1CCNC(C1)C(C2=CC(=NC3=C2C=CC=C3C(F)(F)F)C(F)(F)F)O.Cl</chem>	1.201	2.46024E-08
Neomycin sulfate	<chem>C1C(C(C(C(C1N)OC2C(C(C(C(O2)CN)O)O)N)OC3C(C(C(O3)C)O)OC4C(C(C(C(O4)CN)O)O)N)O)O)N.OS(=O)(=O)O</chem>	1.246	7.11226E-09

Table 2. Oxacillin potentiation with melittin in *S. Aureus* .

Strain	Oxacillin (µg/ml)	Oxacillin (µg/ml) + ¼ MIC Melittin	Fold potentiation
MSSA ATCC 25923	0.25	0.125	2
MSSA NCTC 8325	0.25	0.126	2
MRSA252	512	64	4
MRSA ATCC 33592	128	<2	>64