SUPPORTING INFORMATION

Identification of prochlorperazine dimaleate as a Sortase A inhibitor from FDA libraries for MRSA infection treatment

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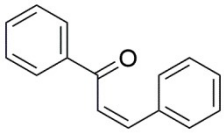
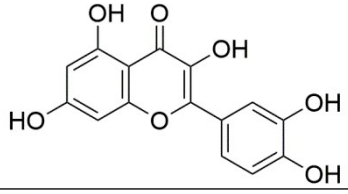
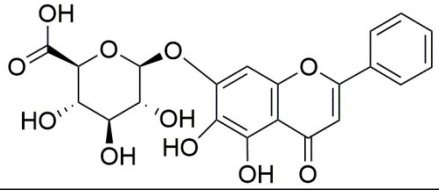
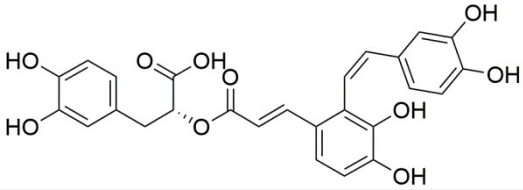
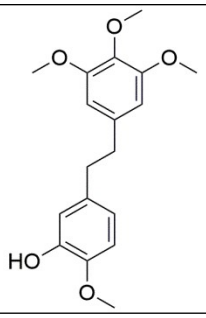
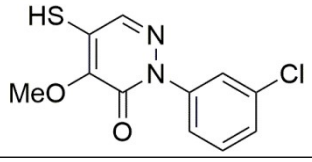
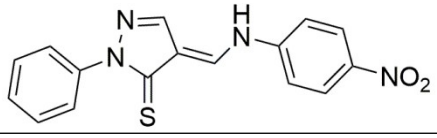
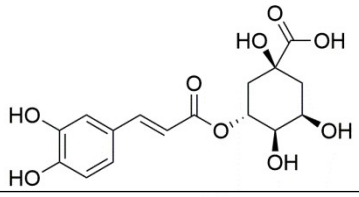
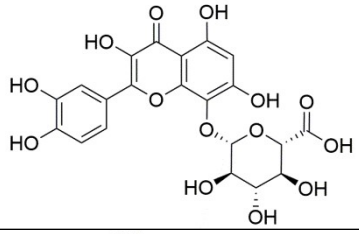
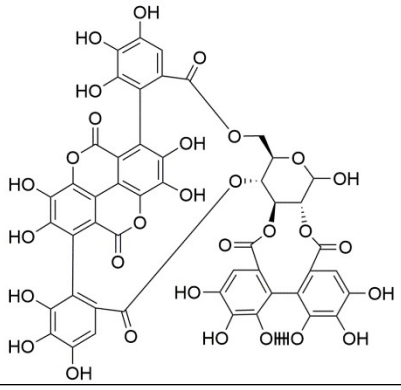
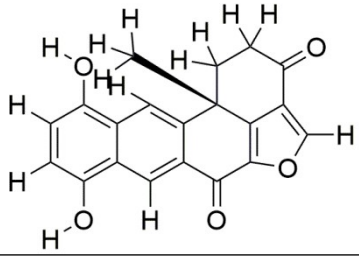
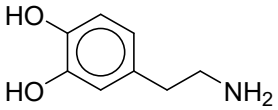
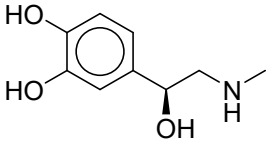
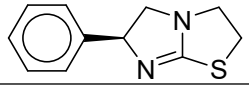
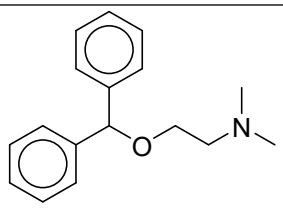
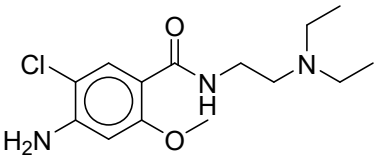
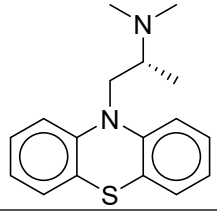
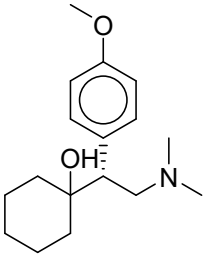
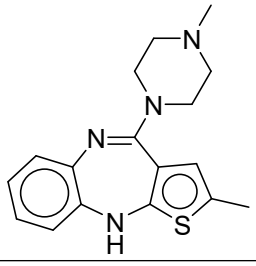
Table S1. Chemical structures and their biological activity against Sortase A in *S. aureus*

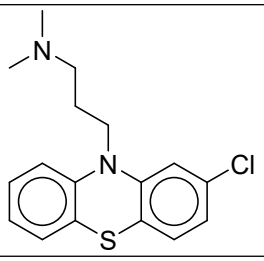
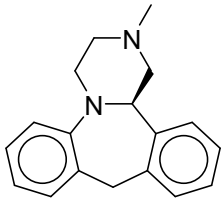
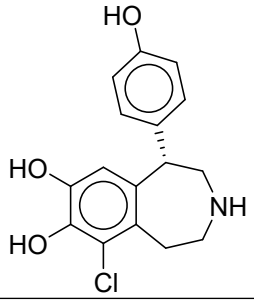
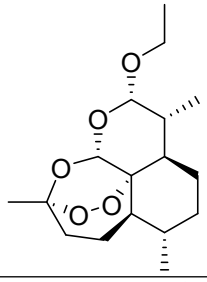
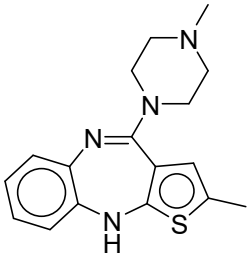
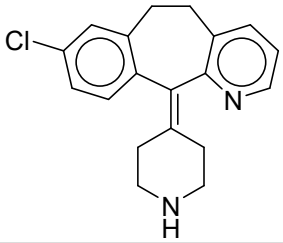
Compounds	Structure	IC_{50}	MIC	Ref
Chalcone		53.15 µM	>4864 µM	1
Quercetin		157 µM	>128 µg/mL	2
Baicalin		NA	>1024 µg/mL	3
Salvianolic acid A		5.75 µg/mL	NA	4

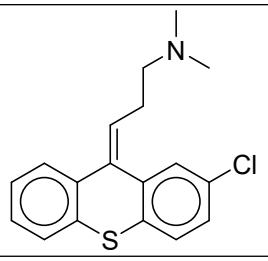
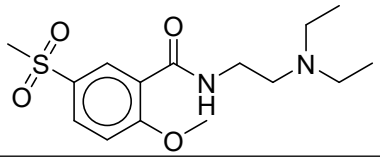
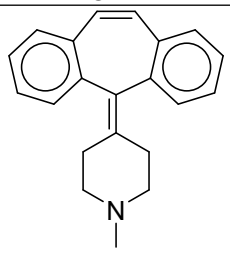
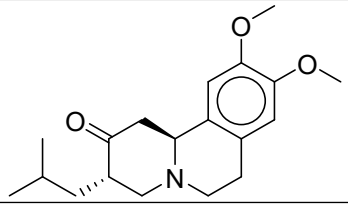
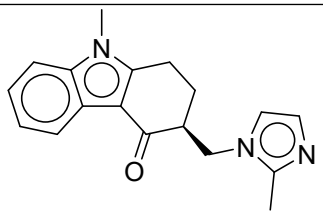
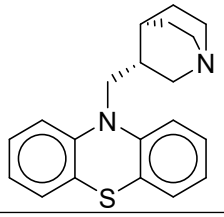
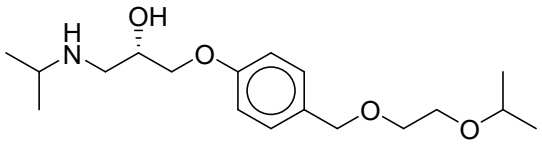
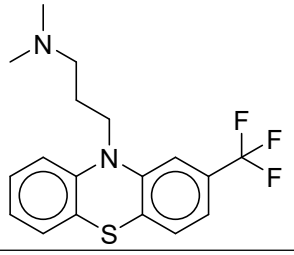
Erianin		20.91 µg/mL	512 µg/mL	[5]
Pyridazinone		4.5 µM	3.74–8.92 µM	[6]
Pyrazolethione		5.2 µM	25 µg/mL	[7]
Chlorogenic acid		33.86 µg/mL	NA	[8]
Hibifolin		31.20 µg/mL	512 µg/mL	[9]
Punicalagin		4.23 µg/mL	250 µg/mL	[10]
Halenaquinol		13.94 µM	>128 µg/mL	[2]

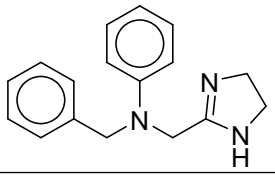
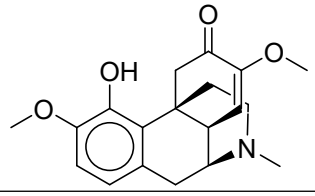
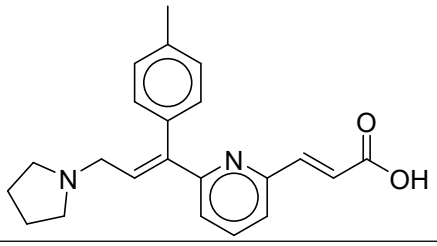
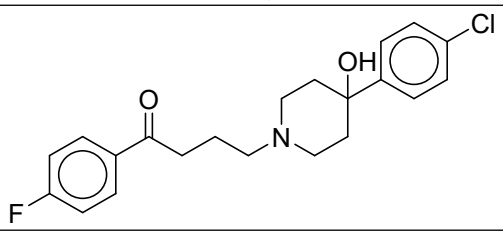
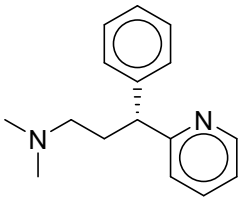
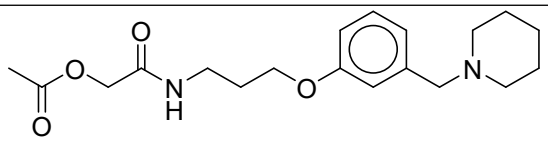
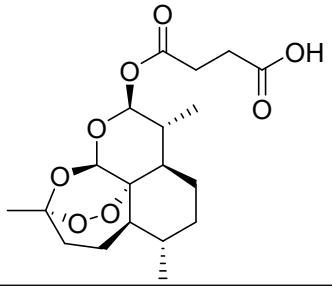
NA: Not available

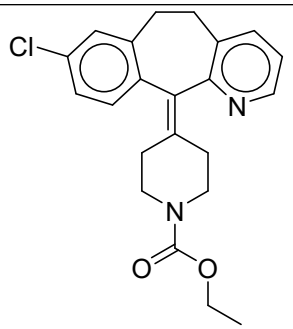
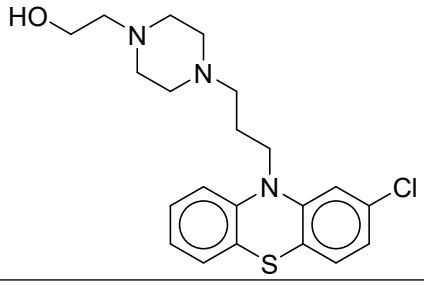
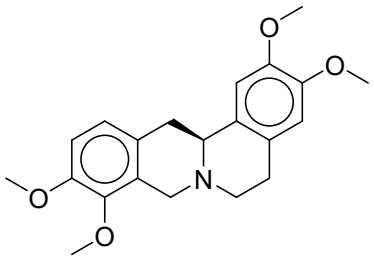
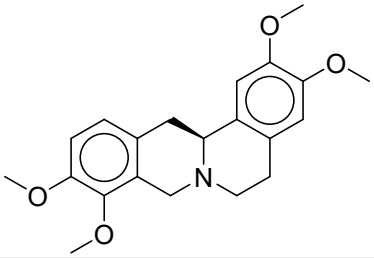
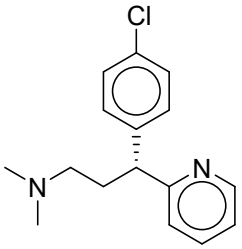
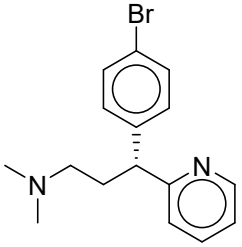
Table S2. Chemical structures of hits evaluated for antimicrobial activity against MRSA

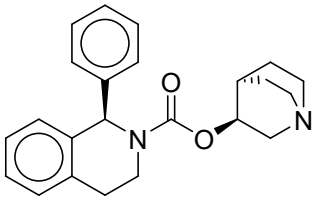
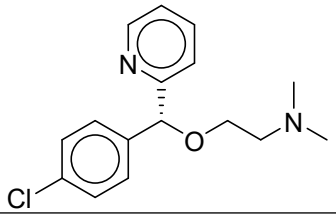
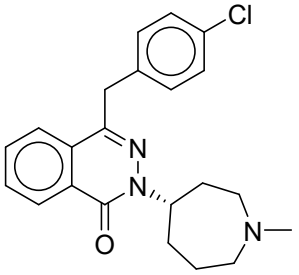
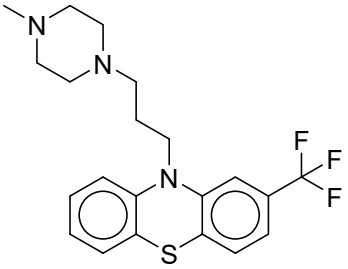
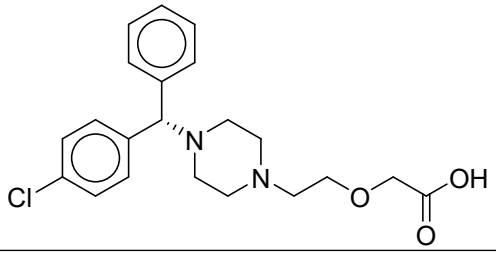
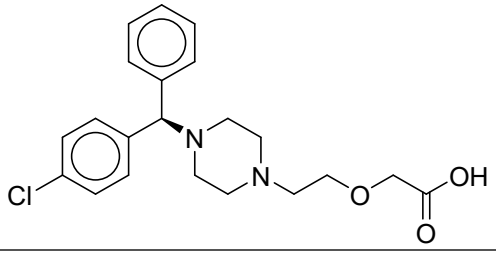
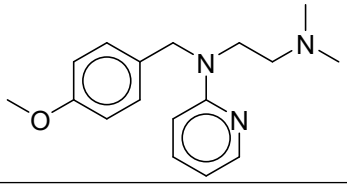
Sr. No.	Smiles	Structure
1	Cl.NCCC1=CC(=C(O)C=C1)O_D	
2	Cl.CNCC(O)C1=CC=C(O)C(=C1)O_D	
3	Cl.C1CN2CC(N=C2S1)C3=CC=CC=C3_D (1)	
4	Cl.CN(C)CCOC(C1=CC=CC=C1)C2=CC=CC=C2_D	
5	Cl.CCN(CC)CCNC(=O)C1=CC(=C(N)C=C1OC)Cl_D	
6	Cl.CC(CN1C2=CC=CC=C2SC3=C1C=CC=C3)N(C)C_D	
7	Cl.COC1=CC=C(C=C1)C(CN(C)C)C2(O)CCCCC2_D	
8	Cl.CN(C)CCOC(C1=CC=CC=C1)C2=CC=CC=C2C_D	

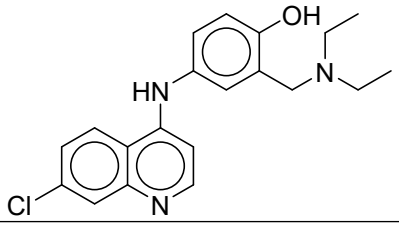
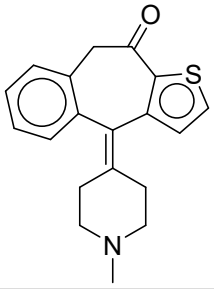
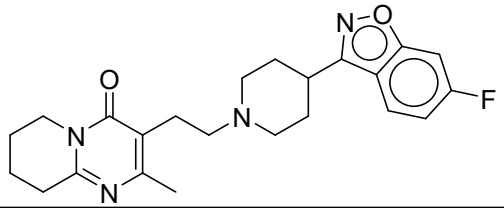
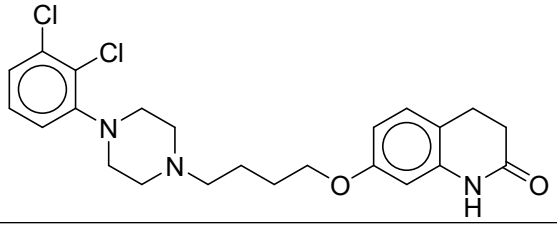
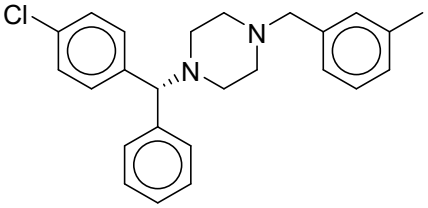
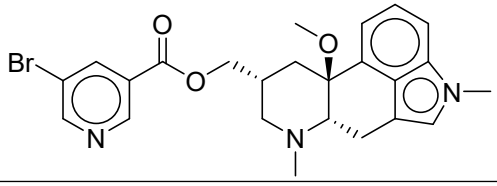
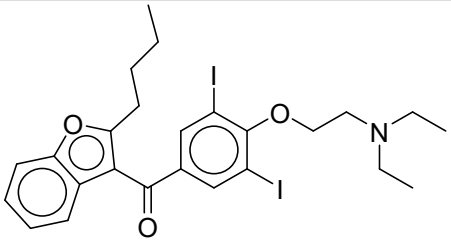
9	CN(C)CCCN1C2=C(SC3=C1C=C(Cl)C=C3)C=CC=C2_D	
10	Cl.CN1CCN2C(C1)C3=C(CC4=C2C=CC=C4)C=CC=C3_D	
11	OC1=CC=C(C=C1)C2CNCCC3=C(Cl)C(=C(O)C=C23)O_D	
12	CCOC1OC2OC3(C)CCC4C(C)CCC(C1C)C24OO3_D	
13	CN1CCN(CC1)C2=NC3=C(NC4=C2C=C(C)S4)C=CC=C3_D	
14	ClC1=CC2=C(C=C1)C(=C3CCNCC3)C4=C(CC2)C=CC=N4_D	

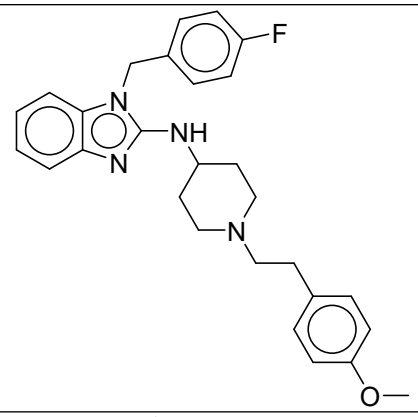
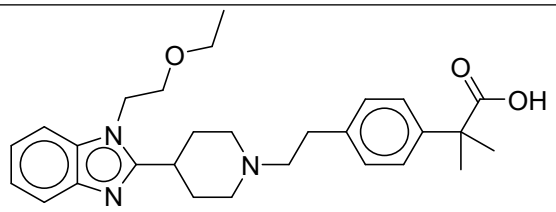
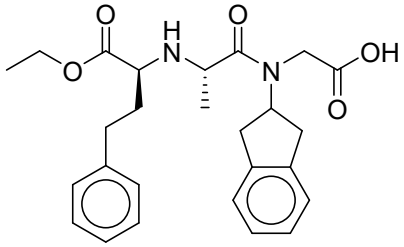
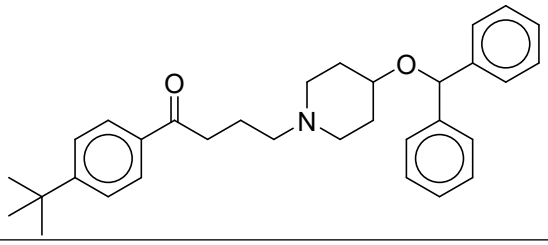
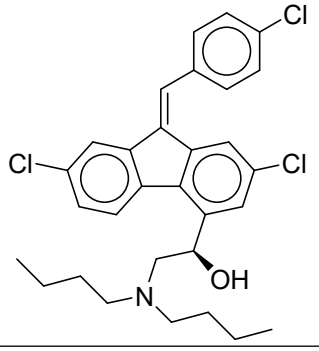
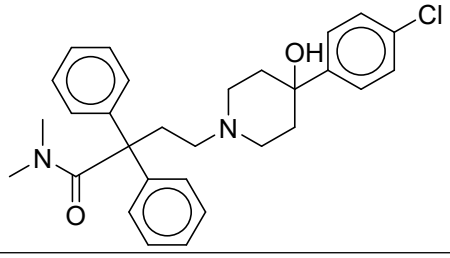
15	Cl.CN(C)CC\C=C/1C2=C(SC3=C1C=C(Cl)C=C3)C=CC=C2_D	
16	Cl.CCN(CC)CCNC(=O)C1=CC(=CC=C1OC)[S](C)(=O)=O_D	
17	Cl.CN1CCC(CC1)=C2C3=C(C=CC=C3)C=CC4=C2C=CC=C4_D	
18	COC1=CC2=C(C=C1OC)C3CC(=O)C(CC(C)C)CN3CC2_D	
19	Cl.C[N]1C2=C(C(=O)C(CC2)C[N]3C=CN=C3C)C4=CC=CC=C14_D	
20	C1CN2CCC1C(C2)CN3C4=C(SC5=C3C=CC=C5)C=CC=C4_D	
21	CC(C)NCC(O)COC1=CC=C(COCCOC(C)C)C=C1_D	
22	Cl.CN(C)CCCN1C2=C(SC3=CC=C(C=C13)C(F)(F)F)C=CC=C2_D	

23	O[P](O)(O)=O.C1CN=C(CN(CC2=CC=CC=C2)C3=CC=CC=C3)N1_D	
24	Cl.COC1=C(O)C2=C(CC3C4C=C(OC)C(=O)CC24CCN3C)C=C1_D	
25	CC1=CC=C(C=C1)C(=C\CN2CCCC2)/C3=CC=CC(=N3)\C=C\C(O)=O_D	
26	OC1(CCN(CCCC(=O)C2=CC=C(F)C=C2)CC1)C3=CC=C(Cl)C=C3_D	
27	CN(C)CCC(C1=CC=CC=C1)C2=NC=CC=C2.OC(=O)\C=C/C(O)=O_D	
28	Cl.CC(=O)OCC(=O)NCCCOC1=CC=CC(=C1)CN2CCCCC2_D	
29	CC1CCC2C(C)C(OC3OC4(C)CCC1C23OO4)OC(=O)CCC(O)=O_D	

30	CCOC(=O)N1CCC(CC1)=C2C3=C(CCC4=C2N=CC=C4)C=C(Cl)C=C3_D	
31	OCCN1CCN(CCCN2C3=CC=CC=C3SC4=C2C=C(Cl)C=C4)CC1_D	
32	Cl.COC1=C(OC)C2=C(CC3N(CCC4=C3C=C(OC)C(=C4)OC)C2)C=C1_D	
33	Cl.COC1=C(OC)C2=C(CC3N(CCC4=C3C=C(OC)C(=C4)OC)C2)C=C1_D	
34	CN(C)CCC(C1=CC=C(Cl)C=C1)C2=NC=CC=C2.OC(=O)\C=C/C(O)=O_D	
35	CN(C)CCC(C1=CC=C(Br)C=C1)C2=CC=CC=N2.OC(=O)\C=C/C(O)=O_D	

36	O=C(OC1CN2CCC1CC2)N3CCC4=C(C=CC=C4)C3C5=CC=CC=C5_D	
37	CN(C)CCOC(C1=CC=C(Cl)C=C1)C2=NC=CC=C2.OC(=O)\C=C/C(O)=O_D	
38	Cl.CN1CCCC(CC1)N2N=C(CC3=CC=C(Cl)C=C3)C4=CC=CC=C4C2=O_D	
39	CN1CCN(CCCN2C3=C(SC4=C2C=C(C=C4)C(F)(F)F)C=CC=C3)CC1_D	
40	Cl.Cl.OC(=O)COCCN1CCN(CC1)C(C2=CC=CC=C2)C3=CC=C(Cl)C=C3_D	
41	Cl.Cl.OC(=O)COCCN1CCN(CC1)C(C2=CC=CC=C2)C3=CC=C(Cl)C=C3_D (1)	
42	COC1=CC=C(CN(CCN(C)C)C2=CC=CC=N2)C=C1.OC(=O)\C=C/C(O)=O_D	

43	O.O.Cl.Cl.CCN(CC)CC1=CC(=CC=C1O)NC2=C3C=CC(=CC3=NC=C2)Cl_D	
44	CN1CCC(CC1)=C2C3=C(CC(=O)C4=C2C=CS4)C=CC=C3.OC(=O)\C=C\C(O)=O_D	
45	CC1=C(CCN2CCC(CC2)C3=NOC4=C3C=CC(=C4)F)C(=O)N5CCCCC5=N1_D	
46	ClC1=CC=CC(=C1Cl)N2CCN(CCCCOC3=CC=C4CCC(=O)NC4=C3)CC2_D	
47	Cl.Cl.CC1=CC(=CC=C1)CN2CCN(CC2)C(C3=CC=CC=C3)C4=CC=C(Cl)C=C4_D	
48	COC12CC(COC(=O)C3=CN=CC(=C3)Br)CN(C)C1CC4=C[N](C)C5=CC=CC2=C45_D	
49	Cl.CCCCC1=C(C(=O)C2=CC(=C(OCCN(CC)CC)C(=C2)I)I)C3=C(O1)C=CC=C3_D	

50	COC1=CC=C(CCN2CCC(CC2)NC3=NC4=CC=CC=C4[N]3CC5=CC=C(F)C=C5)C=C1_D	
51	CCOCC[N]1C(=NC2=C1C=CC=C2)C3CCN(CC3)CCC4=CC=C(C=C4)C(C)(C)C(O)=O_D	
52	Cl.CCOC(=O)C(CCC1=CC=CC=C1)NC(C)C(=O)N(CC(O)=O)C2CC3=C(C2)C=CC=C3_D	
53	CC(C)(C)C1=CC=C(C=C1)C(=O)CCCN2CCC(CC2)OC(C3=CC=CC=C3)C4=CC=CC=C4_D	
54	CCCCN(CCCC)CC(O)C1=CC(=CC\2=C1C3=C(C=C(Cl)C=C3)C2=C/C4=CC=C(Cl)C=C4)Cl_D	
55	Cl.CN(C)C(=O)C(CCN1CCC(O)(CC1)C2=CC=C(Cl)C=C2)(C3=CC=CC=C3)C4=CC=CC=C4_D	

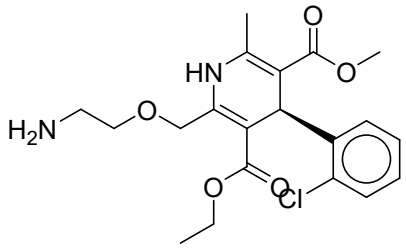
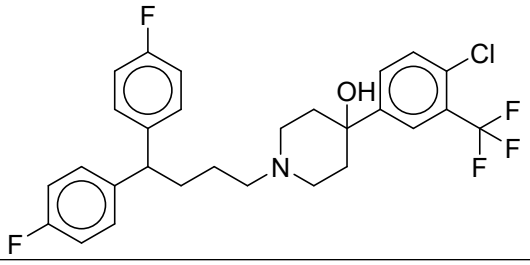
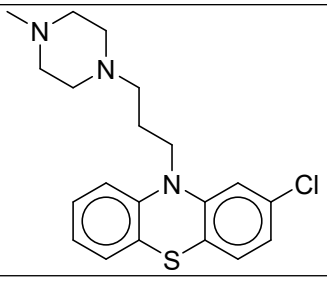
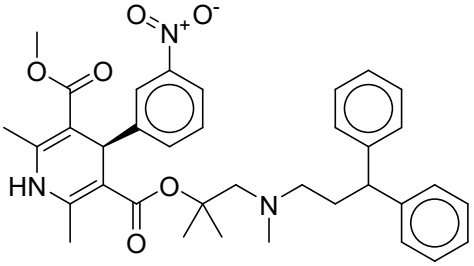
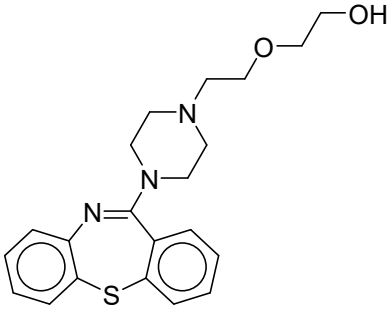
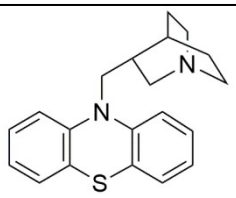
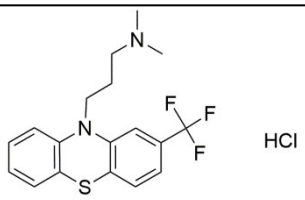
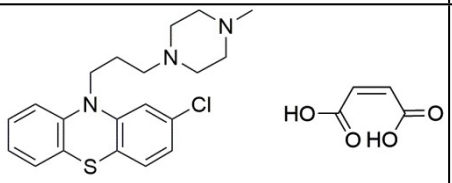
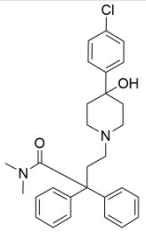
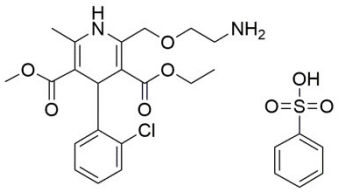
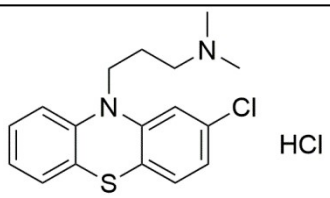
56	CCOC(=O)C1=C(COCCN)NC(=C(C1C2=CC=CC=C2Cl)C(=O)OC)C.OC(=O)\C=C/C(O)=O_D	
57	OC1(CCN(CCCC(C2=CC=C(F)C=C2)C3=CC=C(F)C=C3)CC1)C4=CC(=C(Cl)C=C4)C(F)(F)F	
58	CN1CCN(CCCN2C3=C(SC4=C2C=C(Cl)C=C4)C=CC=C3)CC1.OC(=O)\C=C/C(O)=O.OC(=O)\	
59	Cl.COC(=O)C1=C(C)NC(=C(C1C2=CC=CC(=C2)[N+]([O-])=O)C(=O)OC(C)(C)CN(C)CCC	
60	Cl.COC(=O)C1=C(C)NC(=C(C1C2=CC=CC(=C2)[N+]([O-])=O)C(=O)OC(C)(C)CN(C)CCC	

Table S3. Docking score of hit molecules and their respective binding interactions with Sortase A protein

Drug Name	Structure	Docking Score (kcal/mol)	Hydrogen Bonds	Hydrophobic Interactions
Mequitazine		-6.24	-	Ala34, Pro36, Leu39, Ala60, Cys126, Tyr129
Triflupromazine-HCL		-5.97	Val108, Glu113, Arg139	Val108, Val110, Leu111
Prochlorperazine dimaleate		-7.24	Val108, Asp112, Arg139	Val110, Glu113, Ile124, Ile141
Loperamide		-7.67	Val108, Glu113, Arg139, Trp136	Val108, Val110, Leu111, Ile124, Cys126, Trp136

Amlodipine besylate		-6.65	Val108, Asp112, Gln114, Arg139	Glu113, Ile141, Leu111, Val110
Chlorpromazine-HCL		-6.96	Val108	Leu111, Glu113

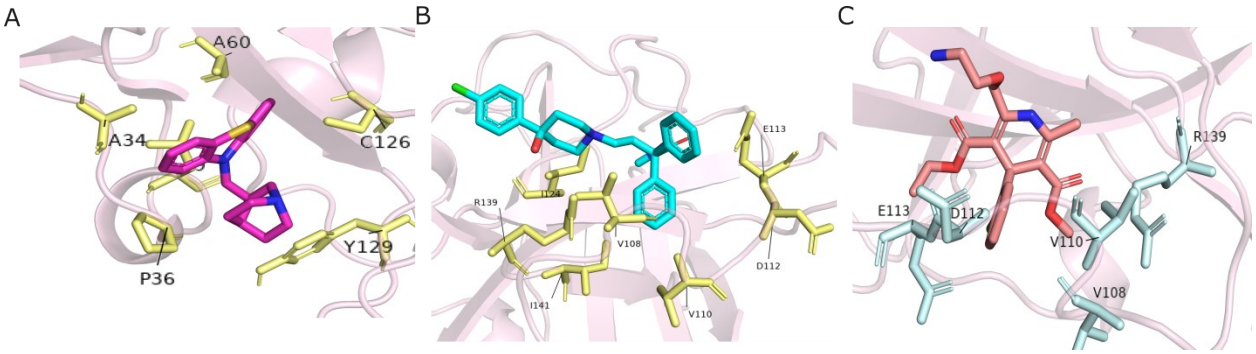


Figure S1. The three-dimensional visualization of protein-ligand interactions illustrates the spatial arrangement of key amino acids involved in hydrogen bonding and hydrophobic interactions with the compounds. (A) Mequitizine, (B) Loperamide, and (C) Amlodipine.

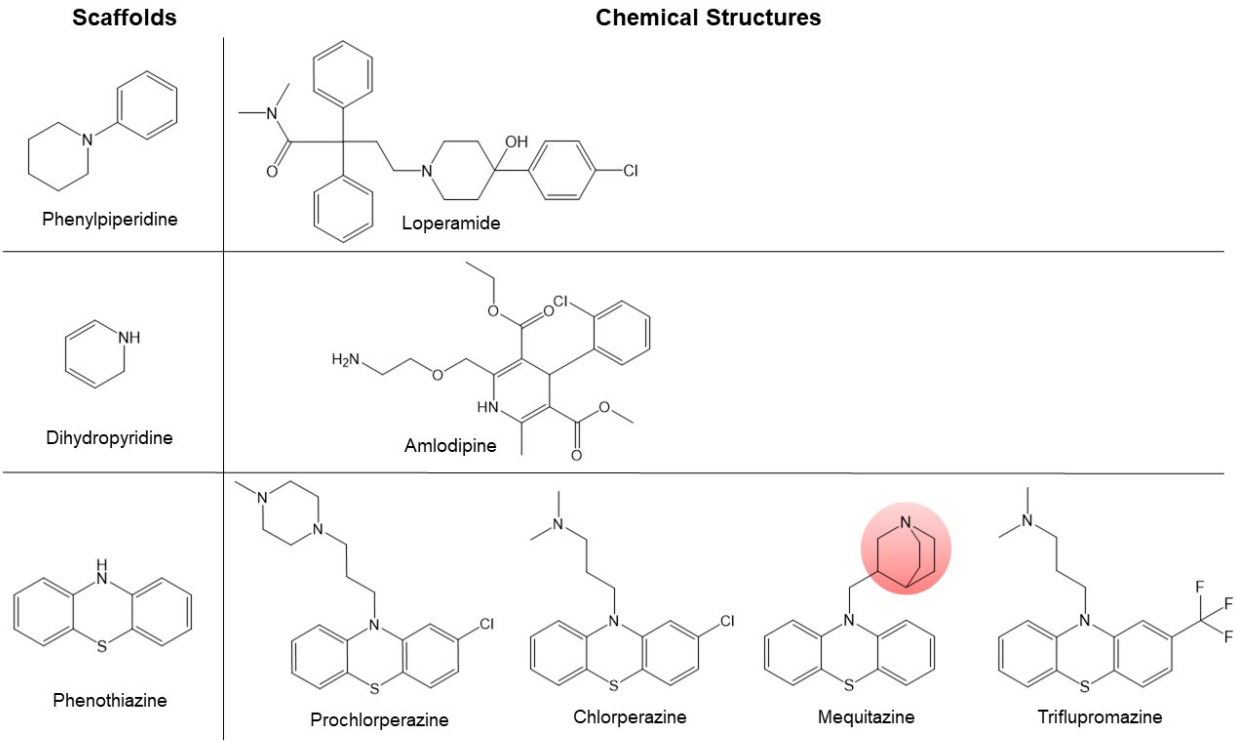


Figure S2. Chemical structures of hit molecules.

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