Supplementary information

Figures

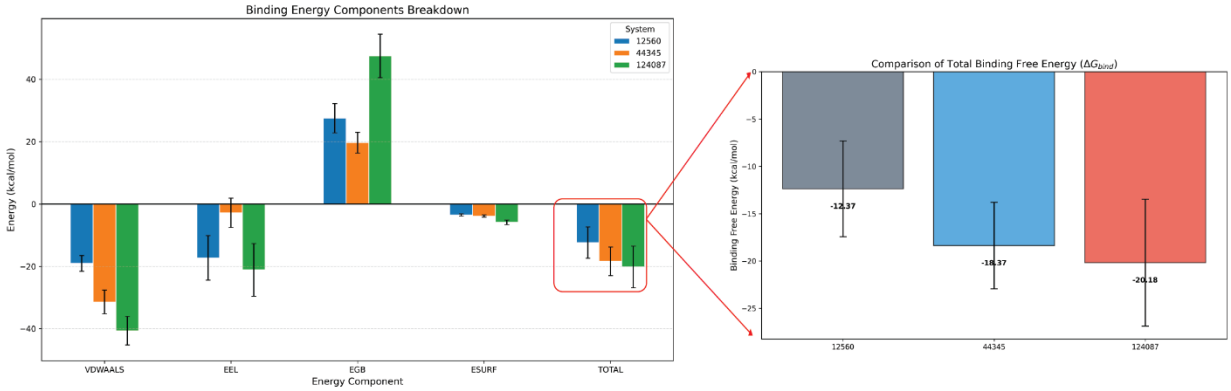

Figure S1. Binding free energy analysis of protein (7M4P) with desloratadine (CID 124087), zinc gluconate (CID 443445), and the control, erythromycin (CID 12560)

Tables

Table S1. Antibacterial activities (zone of inhibition in mm) of non-ABs alone, Obsolete ABs, and their combination against pathogens. Here, the effect of combinations was interpreted based on the increase or decrease in ZOI compared with ABs alone: an increase of <2 mm was considered slightly or weak synergistic (*), 3-5 mm as moderately synergistic (**), and >5 mm indicates highly synergistic (***). Also, 'A' indicates that the antagonistic effect, and 'N' indicates no effect**.**

Zone of Inhibition (ZOI) Values in mm : Combination of ABs with Non-ABs										
Pathogens	**Selected non-ABs**		**Ambroxol**		**Cetirizine**		**Zinc Gluconate**		**Desloratadine**	
	Selected ABs	**Alone (ABs)**	**Zone**	**Effect**	**Zone**	**Effect**	**Zone**	**Effect**	**Zone**	**Effect**
Acinetobacter Baumannii (NCTC-12156)	**Non-AB (Alone)**		8		7		9		8	
	Oxytetracycline	**21**	21	N	23	*	24	**	28	***
	Gentamycin	**16**	20	**	20	**	18	*	22	***
	Chloramphenicol	**12**	15	**	16	**	17	**	17	**

	Erythromycin	**16**	20	**	20	**	18	*	22	***
	Azithromycin	**12**	13	*	13	*	14	*	15	**
	Levofloxacin	**28**	28	N	29	*	29	*	30	*
Escherichia coli (ATCC-25922)	**Non-AB (Alone)**		9		8		10		9	
	Oxytetracycline	**21**	27	***	25	**	27	***	29	***
	Gentamycin	**20**	21	*	25	**	21	*	26	***
	Chloramphenicol	**16**	18	*	16	N	21	**	20	**
	Erythromycin	**16**	19	**	19	**	20	**	21	**
	Azithromycin	**21**	23	*	23	*	24	**	24	**
	Levofloxacin	**32**	31	*	31	A	34	*	29	A
Pseudomonas aeruginosa (ATCC-27853)	**Non-AB (Alone)**		7		0		0		8	
	Oxytetracycline	**20**	24	**	23	**	20	N	18	A
	Gentamycin	**22**	26	**	25	**	23	*	27	**
	Chloramphenicol	**17**	16	*	15	A	12	A	9	A
	Erythromycin	**8**	12	**	8	N	9	*	8	N
	Azithromycin	**18**	20	*	19	*	20	*	20	*
	Levofloxacin	**33**	32	A	36	**	34	*	31	A
Staphylococcus aureus (ATCC 25923)	**Non-AB (Alone)**		0		0		8		8	
	Oxytetracycline	**32**	33	*	30	A	31	A	34	*
	Gentamycin	**22**	22	N	18	A	21	A	23	*
	Chloramphenicol	**30**	26	A	32	*	31	*	32	*
	Erythromycin	**35**	37	*	37	*	39	**	37	*
	Azithromycin	**30**	32	*	31	*	34	**	32	*
	Levofloxacin	**33**	32	A	34	*	33	N	34	*

Group	Control	Disease	Erythromycin (Alone)	Ery + ZnG	Ery + Des
Day1	34.80±1.38	33.68±0.74	33.23±0.75	33.51±0.54	32.81±0.75
Day2	34.94±1.45	32.70±0.71	32.31±0.71	32.38±0.63	31.91±0.60
Day3	35.23±1.40	32.69±0.61	32.36±0.68	32.70±0.73	32.11±0.69
Day4	35.85±1.38	32.76±0.66	32.48±0.75	33.10±0.84	32.39±0.81

Day5	36.54±1.28	32.97±0.60	32.81±0.72	33.49±0.70	32.95±0.93

Table S2. Impact of body weight (gm) changes after administering a combination of erythromycin and non-antibiotics. Here, Ery= Erythromycin, ZnG = Zinc gluconate, Des= Desloratadine.

Table S3. Summarizes the predicted resistance genes. For each ORF, key genomic and functional attributes are presented, including orientation, detection cut-off, bit score metrics, best-hit ARO (Antibiotic Resistance Ontology), predicted drug class, underlying resistance mechanism, and the corresponding AMR gene family.

ORF_ID	Orientation	Cut Off	Pass Bitscore	Bitscore	Resistant genes	Best Identities	ARO	Drug Class	Resistance Mechanism	AMR Gene Family
ENA_UFRW01000002_UFRW01000002_1_686 # 735827 # 737281 # -1 # ID=2_686;partial=00;start_type=ATG;rbs_motif=AGGAG/GGAGG;rbs_spacer=11-12bp;gc_cont=0.418	-	Perfect	950	974.926	**adeK**	100	3000782	macrolide; fluoroquinolone ; lincosamide; carbapenem; cephalosporin; tetracycline; rifamycin ;	antibiotic efflux	RND antibiotic efflux pump
ENA_UFRW01000002_UFRW01000002_1_687 # 737281 # 740457 # -1 # ID=2_687;partial=00;start_type=ATG;rbs_motif=GGA/GAG/AGG;rbs_spacer=5-10bp;gc_cont=0.422	-	Strict	2000	**2149.4**	**adeJ**	99.91	3000781	**macrolide**; fluoroquinolone ; lincosamide; carbapenem; cephalosporin; tetracycline; rifamycin; diaminopyrimidine; chloramphenicol; penem	antibiotic efflux	RND antibiotic efflux pump
ENA_UFRW01000002_UFRW01000002_1_688 # 740470 # 741720 # -1 # ID=2_688;partial=00;start_type=ATG;rbs_motif=GGAG/GAGG;rbs_spacer=5-10bp;gc_cont=0.429	-	Perfect	800	832.787	**adeI**	100	3000780	macrolide; fluoroquinolone ; lincosamide ; carbapenem; cephalosporin; tetracycline ; rifamycin ; diaminopyrimidine ; phenicol ; penem	antibiotic efflux	RND antibiotic efflux pump

ENA_UFRW01000002_UFRW0100 0002_1_1147 # 1251553 # 1251882 # -1 # ID=2_1147;partial=00;start_type=A TG;rbs_motif=None;rbs_spacer=Non e;gc_cont=0.361	-	Strict	175	208.379	**abeS**	99.08	3000768	macrolide ; aminocoumarin	antibiotic efflux	SMR antibiotic efflux pump
ENA_UFRW01000002_UFRW0100 0002_1_1409 # 1524443 # 1525921 # 1 # ID=2_1409;partial=00;start_type=A TG;rbs_motif=GGA/GAG/AGG;rbs_ spacer=3-4bp;gc_cont=0.408	+	Strict	600	964.14	**AmvA**	98.98	3004577	macrolide ; disinfecting agents and antiseptics	antibiotic efflux	MFS antibiotic efflux pump
ENA_UFRW01000002_UFRW0100 0002_1_1463 # 1579989 # 1580642 # -1 # ID=2_1463;partial=00;start_type=A TG;rbs_motif=None;rbs_spacer=Non e;gc_cont=0.356	-	Strict	420	446.432	**adeN**	98.62	3000559	macrolide ; fluoroquinolone ; lincosamide ; carbapenem; cephalosporin; tetracycline ; phenicol ; penem	antibiotic efflux	RND antibiotic efflux pump

Table S4. Analysis of docking and ligand efficiency of 7M4P protein with ligands desloratadine, zinc gluconate, and 7M4P protein with erythromycin as a control.

Complexes	Binding energy (kcal/mol)	Amino acid residues	Bond types	Distance (Å)
7M4P + Desloratadine	**-9.9**	Phe136	Pi-Alkyl	5.56
		Val139	Alkyl	5.37
			Pi-Alkyl	6.39
		Ala326	Alkyl	4.8
		Try327	Pi-Pi T-shaped	5.01
		Phe611	Pi-Alkyl	4.3
		Phe629	Pi-Alkyl	4.3
			Pi-Pi Stacked	5.18
			Pi-Alkyl	6.2
7M4P + Zinc Gluconate	**-5.6**	Try35	Hydrogen	5.31
		Ser135	Hydrogen	2.92
			Hydrogen	3.61
		Phe136	Hydrogen	6.42
		Thr329	Hydrogen	4.25
7M4P + Erythromycin (control)	**-10.2**	Ser79	Unfavorable Donor	4.11
		Asn81	Hydrogen	4.21
		Gln91	Hydrogen	4.95
			Unfavorable Acceptor	4.95

		Phe616	Pi-Alkyl	6.23
		Phe618	Pi-Alkyl	4.09
		Glu675	Hydrogen	4.6

Table S5. The experimental design outlines the distinct groups of mice receiving treatments with ABs and their combinations with adjuvants. Here, Ery= Erythromycin, ZnG = Zinc gluconate, Des= Desloratadine

Experimental group	**Information**
Control group	Normal controls received only a normal diet for 5 days.
Disease group	Received only vehicles fed with a normal diet for 5 days without treatment.
Ery Group	Received erythromycin (100 mg/kg of BW) intraperitoneally twice a day
Ery + ZnG group	Received erythromycin (100 mg/kg of BW) and desloratadine (0.777 mg/kg of BW) intraperitoneally twice a day.
Ery + Des group	Received erythromycin (100 mg/kg of BW) and zinc gluconate (31 mg/kg of BW) intraperitoneally twice a day.**[1]**

Reference:

1. Nair A, Jacob S. A simple practice guide for dose conversion between animals and human. *J Basic Clin Pharm* 2016;**7**(2):27. https://doi.org/10.4103/0976-0105.177703.