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Ursolic acid inhibits colistin efflux and curtails colistin resistant *Enterobacteriaceae*

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Table S1: Antimicrobial profiling of *Klebsiella pneumoniae* and *Escherichia coli* clinical isolates

Minimum Inhibitory Concentration (µg/ml)											
Antibiotic/ Compound	MTC C KP	KP BC1994	KP BC2412	KP U3866	KP U2016	KP BC1415	KP U2192	KP E474	KP BC936	<i>E. coli</i> U3176	<i>E. coli</i> U3790
Ceftriaxone	<1	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128
Meropenem	0.5	>32	>32	>32	32	16	>128	16	16	>32	>32
Ciprofloxacin	4	32	16	128	16	16	32	32	16	64	256
Levofloxacin	1	8	16	64	32	32	64	32	32	32	32
Norfloxacin	<2	64	16	128	64	>128	64	128	64	>128	>128
Amikacin	<2	4	16	>128	>128	>128	>128	>128	>128	>128	8
Gentamicin	<4	256	<4	>256	>128	>128	>128	>128	>128	>256	256
Tobramycin	16	64	64	>256	>128	>128	>128	>128	>128	>256	128
Erythromycin	64	256	64	256	>128	>128	>128	>128	>128	>256	256
Tetracycline	>128	<2	4	16	8	>128	>128	>128	>128	<2	128
Tigecycline	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128
Colistin	2	2	1	1	8	8	8	<2	32	1	32
Rifampicin	4	64	32	>128	>128	>128	>128	>128	>128	4	16
Streptomycin	64	128	32	4	32	32	32	32	32	32	16
Kanamycin	>256	>256	>256	>256	>128	>128	>128	>128	>128	>256	>256

Table S2: MIC of plant metabolites against XDR strains of *Klebsiella pneumoniae* and *Escherichia coli*

Compounds	Minimum Inhibitory Concentration (µg/ml)	
	<i>K. pneumoniae</i> BC936	<i>E. coli</i> U3790
Arjunolic Acid (AJ)	128	256
Acetyl Shikonin (AS)	512	256
B-Dimethyl acetyl shikonin (BD)	512	256
Caffeic Acid (CA)	128	512
Chrysin (CH)	512	1024
Crysophenol (CR)	512	512
Emoidin (EM)	512	512
Naringenin (NIN)	512	256
Naringin (NG)	64	256
Physicion (PH)	512	512
Ursolic acid (UR)	512	256
Ventilone A (VA)	512	256
Ventiloquinone (VQ)	512	512

Fig S1: Membrane permeability of colistin resistant *Escherichia coli* and *Klebsiella pneumoniae* is enhanced by ursolic acid treatment. Mid-log cells of *E.coli* U3790 and *K. pneumoniae* BC936 were treated with either colistin (Col) or ursolic acid (UR) or in combination (Col+UR) along with fluorescent dye N-Phenyl 1-Naphthylamine (NPN) and fluorescence intensity was measured using a spectrofluorimeter. NPN uptake factor was calculated as the ratio of background subtracted fluorescence of different groups to that of buffer.

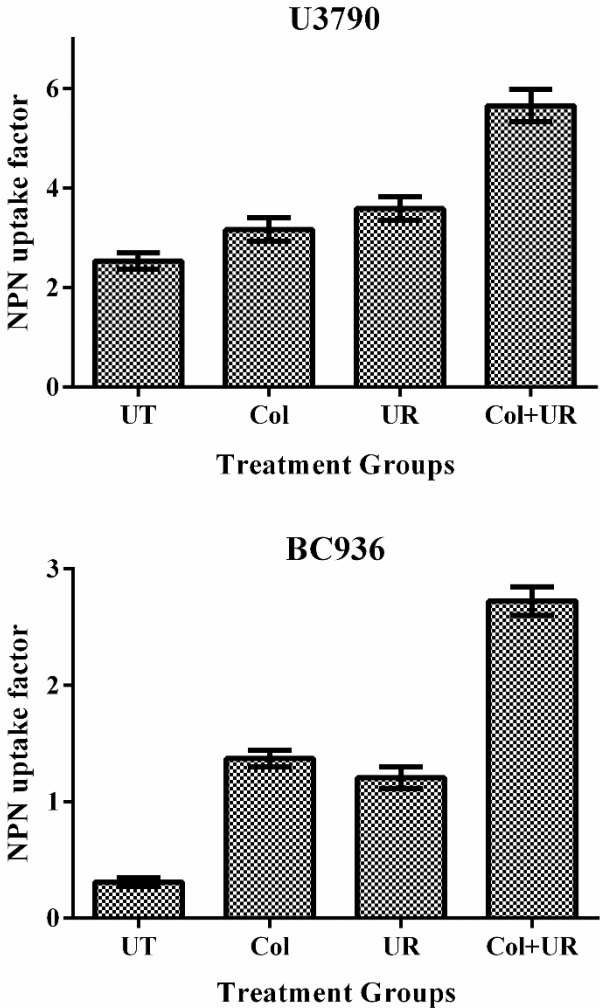


Fig S2: Ursolic acid reduced ROS generation by colistin. Mid-log cells of *E. coli* U3790 and *K. pneumoniae* BC936 were challenged with treatments comprising colistin (Col), ursolic acid (UR) and colistin+ ursolic acid (Col+UR). H₂O₂ was used as a positive control in the assay. DCFH-DA was used as fluorophore to detect the amount of ROS generated in each of the treatments. The fluorescence intensity was quantified in a spectrofluorimeter.

