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FIC Index Determination of CXA-101 (CXA)/Tazobactam (TAZ) in Combination with Amikacin (AMK), Aztreonam (ATM), Meropenem (MEM), Levofloxacin (LVX), and Tigecycline (TGC) against *Escherichia coli* (EC), *Klebsiella pneumoniae* (KP), and *Pseudomonas aeruginosa* (PA) Strains

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Background: CXA is a novel parenteral cephalosporin with potent in vitro activity against EC and KP (including extended-spectrum β-lactamase (ESBL)-producer) as well as PA (including multi-resistant strains). The aim of this work was to evaluate the in vitro activity of CXA/TAZ in combination with AMK, ATM, MEM, LVX, and TGC against EC, KP, and PA strains.

Methods: 4 EC (2 ESBL+), 4 KP (2 ESBL+), and 6 PA strains (exhibiting different resistance phenotypes to ceftazidime (CAZ) and imipenem (IMP)) were studied. CXA and partner drugs were studied from 1/8xMIC to 8xMIC and dispensed in a checkerboard fashion. TAZ was used at a fixed concentration of 4 mg/L. Readings were performed and the FIC index was determined for each combination and each strain.

Results:

				FIC index				
Bacterial strains			CXA/TAZ MIC (mg/L)	ATM	MEM	AMK	LVX	TGC
EC	ESBL -	1	0.25	1.0 / AD	0.75 / AD	1.25 / I	0.75 / AD	0.75 / AD
		2	0.25	0.75 / AD	0.75 / AD	0.75 / AD	1.0 / AD	0.75 / AD
	ESBL +	3	0.25	<0.5 / S	0.62 / AD	0.62 / AD	1.0 / AD	1.0 / AD
		4	1	<0.5 / S	0.75 / AD	0.5 / S	1.0 / AD	0.52 / AD
KP	ESBL -	5	0.25	0.62 / AD	1.0 / AD	0.75 / AD	0.75 / AD	0.62 / AD
		6	0.25	0.75 / AD	0.75 / AD	0.62 / AD	1.12 / I	0.5 / S
	ESBL +	7	0.5	<0.5 / S	0.32 / S	0.28 / S	0.75 / AD	0.53 / AD
		8	1	<0.5 / S	0.37 / S	0.75 / AD	0.56 / AD	0.75 / AD
PA	CAZ-S	9	0.25	0.53 / AD	1.0 / AD	0.32 / S	0.75 / AD	1.0 / AD
		10	0.5	0.75 / AD	0.62 / AD	0.5 / S	0.75 / AD	1.0 / AD

		11	2	1.0 / AD	0.75 / AD	0.56 / AD	0.5 / S	0.37 / S
	CAZ-R	12	2	0.75 / AD	1.0 / AD	1.0 / AD	0.62 / AD	0.5 / S
		13	0.5	1.0 / AD	0.56 / AD	1.0 / AD	1.0 / AD	1.0 / AD
	IMP-R	14	0.5	0.62 / AD	0.62 / AD	0.62 / AD	0.62 / AD	0.31 / S
S: synergism; AD: additivity; I: indifference.								

Conclusions: (1) No antagonism was detected with CXA/TAZ in combination with AMK, ATM, MEM, LVX, and TGC. (2) Additivity was the main interaction observed between CXA/TAZ and studied partner drugs. (3) Synergy was observed with the addition of ATM to CXA/TAZ against ESBL-producing strains due to the inhibition of ESBL by the β-lactamase inhibitor. (4) MEM combined with CXA exhibited a synergistic interaction against ESBL+ KP strains. (5) The combination of CXA/TAZ with TGC appears to be synergistic against 3 PA strains, including CAZ-R isolates. Further studies are needed to explore these positive interactions between CXA/TAZ and partner drugs.