

Antimicrobial Activity of Antibiotics in Combination with Natural Flavonoids against Clinical Extended-Spectrum β -Lactamase (ESBL)-producing *Klebsiella pneumoniae*

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Abstract

Extended-spectrum beta-lactamases (ESBLs) are plasmid-mediated class A enzymes commonly found in the family Enterobacteriaceae, mainly in *Klebsiella pneumoniae*. Flavonoids have also been reported to possess antimicrobial activity. In this study, the in vitro activities of 18 antibiotics and 12 flavonoids against 20 ESBL-producing *K. pneumoniae* isolates were evaluated. All of these isolates were susceptible to imipenem and cefmetazole, but were resistant to ampicillin, ampicillin/sulbactam, aztreonam, cefazolin, cefoperazone, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, piperacillin and ticarcillin. Susceptibilities to amikacin, amoxicillin/clavulanate, ceftiofuran, ciprofloxacin and gentamicin were variable. Myricetin, a flavonol, inhibited ESBL-producing *K. pneumoniae* isolates at a high minimum inhibitory concentration (MIC) (MIC₉₀) value 256 mg/mL, but exhibited significant synergic activity against ESBL-producing *K. pneumoniae* in separate combination with amoxicillin/clavulanate, ampicillin/sulbactam and ceftiofuran. Because of the low-toxic nature of flavonoids, the combination of antibiotics and flavonoids is a potential new strategy for developing therapies for infections caused by ESBL-producing bacteria in the future.