

MEETING ABSTRACT

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# Antimicrobial activity of antibiotics in urine under different physiological conditions

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## Background

*In vitro* activity of antimicrobials is commonly assessed in well-characterized growth media like Mueller-Hinton broth (MHB); however, such media hardly reflect *in vivo* conditions. We set out to compare activity of selected, mostly novel, antibiotics in MHB and urine, an important compartment for bacterial infections, at different conditions.

## Methods

Urine obtained from healthy volunteers was pooled and sterile filtered. Microdilution tests were performed with *Escherichia coli* ATCC 25922 in MHB and human urine. The pH of urine was adjusted to values ranging from 5 to 8. For simulating different glucose levels in urine of diabetic patients, urine was adjusted to glucose levels of 100 and 1000 mg/dL. Bacterial growth in different media was investigated by growth curves. Results obtained from MIC testing were confirmed by use of bacterial killing curves. *Klebsiella oxytoca* ATCC 700324 was used to investigate transferability of finding to other strains. Each experiment was performed 5 times.

## Results

Growth of bacteria was similar for MHB and adjusted urine. Mean ratios (fold changes) of MICs for *E. coli* at the 6 different conditions simulated in urine compared to MIC-values in standard MHB are presented. Results were confirmed by time-killing curves and were concurrent for *E. coli* and *K. oxytoca*. Fosfomycin activity in urine was in unison higher than in MHB adjusted by glucose-6-phosphate.

## Conclusions

Strong impact on activity was observed at low pH values for fluoroquinolones, trimethoprim, amikacin and tigecycline. Remarkably, all these antimicrobials act intracellularly while impact of pH on cell membrane-active antibiotics like  $\beta$ -lactams and colistin was much lower. Impairment of diffusion into the bacterial cell due to modification of the electric charge of the drug seems likely.

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