

Agar dilution (mcg/ml)	32 (16-128)	>512 (>512)	64 (32-256)	4 (0.5-16)	1 (0.25-4)
Broth microdilution (mcg/ml)	64 (16-128)	512 (128->512)	64 (16-256)	0.5 (<0.03-2)	0.06 (<0.03-0.5)

Time kill assays demonstrated approximately 10^4 to 10^7 -fold microbicidal activity of CAZ-AVI + ATM at 24 hrs versus growth control, CAZ, and ATM. **Conclusions:** The combination of ceftazidime-avibactam plus aztreonam is microbicidal *in vitro* against bloodstream isolates of *Stenotrophomonas maltophilia* through a mechanism of simultaneous inhibition of beta-lactamases encoded by L1 and L2.

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Abstract Title:

Antimicrobial Photodynamic Therapy Challenges Microbial Drug-Resistance

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Abstract Body:

Background: The rising challenge of microbial resistance to chemotherapy demands immediate implementation of global policies and therapeutic alternatives. Antimicrobial photodynamic therapy (APDT) combines the administration of a photosensitizer (PS) compound with low-intensity monochromatic light to induce photochemical reactions that yield high amounts of reactive oxygen species (ROS). Since some PS molecular frameworks can be selectively incorporated by pathogens and ROS react with virtually all biomolecules, APDT offers a powerful strategy to challenge microbial resistance of local infections. **Methods:** In this study we assayed the APDT efficacy, using methylene blue (MB) as PS and red light provided by LED, against planktonic suspensions of high-risk representative fungal and bacterial species. The species tested include *A. baumannii* (OXA-23 and 143), *E. aerogenes* (NDM-1), *E. faecalis* (VAN-B), *E. faecium* (VAN-A), *E. coli* (MCR-1, CTX-M8 and 15), *K. pneumoniae* (KPC-2, IMP-1, OXA-48), *S. aureus* (MRSA, VISA), *P. aeruginosa* (VIM-1, SPM-1, GES-5), *C. albicans* and *C. neoformans*. For all species, we tested standard control strains compared to azole-resistant yeast, or bacteria resistant to nearly all commercially available antimicrobials, in attempt to observe any cross-resistance in between APDT and standard chemotherapy. **Results:** More than $5\log_{10}$ reduction was observed within less than a minute of illumination for non-capsulated bacteria and within less than 5 minutes for yeast and capsulated bacteria. Regardless of resistance phenotype MB-APDT presented species-specific dose-response kinetics suggesting that similar therapeutic protocols may bring successful outcomes in clinical practice. **Conclusions:** Our study proposes that MB-APDT can efficiently inactivate a broad-spectrum of drug-resistant microorganisms and impair drug-resistance genes selection and dissemination.