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FP13

1,2,4-Oxadiazole Salts for Antimicrobial Applications: Synthesis and Biological Evaluation

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The emergence of resistant bacteria poses a significant global threat, primarily due to the widespread overuse of antibiotics and the shortage of new antibacterial drugs. This problem is further exacerbated by the continued emergence of bacteria resistant to multiple antibiotics, which significantly reduces their effectiveness in treating infections.^[1] This phenomenon is not limited to specific clinical settings, but is a systematic problem, with repercussions in surgery, oncology and installation of medical implants.^[2] For this purpose, a series of novel 1,2,4-oxadiazole pyridinium salts with antibacterial properties have been synthesized, taking inspiration from a previously published work.^[3] 34 compounds have been tested in vitro against Gram-negative (*K. pneumoniae* and *E. coli*) and Gram-positive (*S. aureus*, *S. haemolyticus* and *E. faecium*) strains and 5 of them against resistant strains with dilution and minimal inhibition concentration (MIC) methods. Compounds with electron donating group (-OCH₃) on the phenyl ring, compared with an electron withdrawing group (-NO₂ and -F), show better antibacterial activity. Five compounds with MIC values between 0.5 µg/mL and 4 µg/mL have been incorporated into PVC films and tested as gelators for glycerol-based gels.

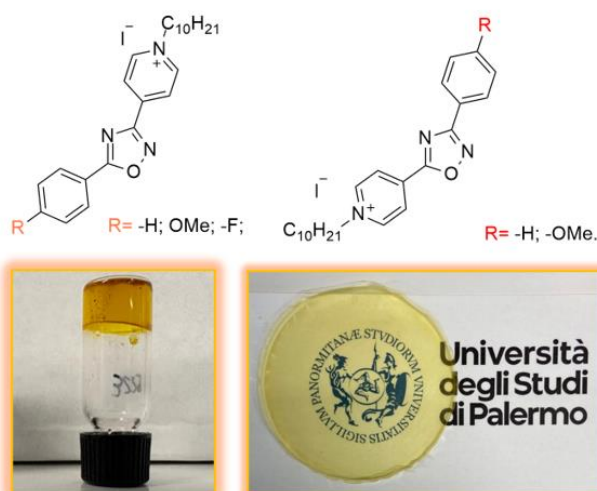


Figure 2: General structures of salts synthesized, example of derived glycerol-based gel (left) and PVC film (right).



The tested materials showed antimicrobial activity against *Staphylococcus aureus* ATCC 25923. The gels produced ZOI of 30–35 mm, while PVC films had a more limited effect with ZOI of 8–10 mm. Broth diffusion tests showed a bacterial growth reduction of up to 10^7 CFU/mL for the more active film and 10^2 CFU/mL for the less active one, confirming the antimicrobial potential of the materials. This study represents a starting point for the development of potential antibacterial materials for coating medical implants.

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- [1] Tang KWK, Millar BC, Moore JE. *Antimicrobial Resistance (AMR)* **2023**, Br J Biomed Sci, 80:11387.
 - [2] E. Avershina, V. Shapovalova, G. Shipulin, *Fighting Antibiotic Resistance in Hospital-Acquired Infections: Current State and Emerging Technologies in Disease Prevention, Diagnostics and Therapy*, **2021**, Frontiers in Microbiology, 12.
 - [3] S. Amata, C. Calà, C. Rizzo, I. Pibiri, M. Pizzo, S. Buscemi, A. Palumbo Piccionello, *Synthesis and Antibacterial Activity of Mono- and Bi-Cationic Pyridinium 1,2,4-Oxadiazoles and Triazoles*, **2024**, International Journal of Molecular Science, 25, 377.