Metal Salts and Metal Complexes as Promising Efflux Pump Inhibitors to Combat Multidrug-Resistant Bacteria

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Outline

I. Introduction

II. Zinc sulfate acts as an efflux pump inhibitor on *Pseudomonas aeruginosa* clinical isolates

III. Effect of palladium (II) complexes on NorA efflux pump inhibition and resensitization of fluoroquinolone-resistant *Staphylococcus aureus*: in vitro and in silico approach

IV. Conclusion

Abstract

The rapid emergence of multidrug-resistant (MDR) bacteria poses a major challenge to clinical treatment, largely driven by efflux pump overexpression and biofilm formation. Metal salts and complexes have recently gained attention as novel antibacterial strategies. Zinc sulfate demonstrated strong efflux pump inhibition against *Pseudomonas aeruginosa* clinical isolates, reducing MDR phenotypes even at sub-inhibitory concentrations and showing synergism with multiple antibiotics. Likewise, α-picolinic acid-derived palladium (II) complexes, especially QSL_Pd5A, inhibited the NorA efflux pump in *Staphylococcus aureus*, disrupted biofilm formation, and enhanced fluoroquinolone activity. Notably, QSL_Pd5A retained potency at low concentrations without significant cytotoxicity, while molecular docking confirmed its high affinity for the NorA protein through extensive hydrophobic interactions. Collectively, these findings underscore the promise of metal salts and palladium complexes in sensitizing resistant pathogens to antibiotics and suppressing resistance mechanisms, offering a potential foundation for next-generation antimicrobial development.

參考文獻

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Shobana, R., Thahirunnisa, J. H., Sivaprakash, S., Amali, A. J., Solomon, A. P., & Suresh, D. (2024). Effect of palladium(II) complexes on NorA efflux pump inhibition and resensitization of fluoroquinolone-resistant Staphylococcus aureus: in vitro and in silico approach. *Frontiers in Cellular and Infection Microbiology, 13*. https://doi.org/10.3389/fcimb.2023.1340135.