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BOOK OF ABSTRACTS

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Small molecule crystallography aiding the search for novel antimicrobial agents. Design, characterization and QSAR studies of adamantane containing complexes.

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Antimicrobial resistance has been deemed as one of the top global public health concerns by the World Health Organization. One of the ways we can contribute to its resolution is by developing new and more effective antimicrobial treatments. Medicinal Inorganic Chemistry offers diverse strategies for this purpose, for instance, through the design of metal-based drugs. In our work we coordinate bioactive organic molecules to metal centers, looking to modulate the physicochemical properties of the obtained metallodrug, its biological activity and even altering its mechanism of action when compared to the free ligand. In recent years, we have explored the development of potential antitumor and antimicrobial metallodrugs using essential metals such as copper(II) and zinc(II), or the less studied diorganotin(IV) moiety with promising results. In this work, we report advances on Zn(II) and dimethyltin(IV) complexes with carbothiamide ligands containing an adamantane moiety. Zn(II) complexes presented an unexpected structural diversity with dinuclear and 1D extended chains depending on the substituent in the ligand. Whereas the dimethyltin(IV) complexes yielded mononuclear compounds with modulated physicochemical and biological properties. Several crystal structures were determined and their supramolecular arrangements explored using Hirshfeld Surface Analysis. The mononuclear dimethyltin(IV) complexes were studied in solution and their antimicrobial activity was evaluated against *Acinetobacter baumannii* and *Staphylococcus aureus*. These studies confirmed that the incorporation of the dimethyltin(IV) center led to a marked decrease in viability in both microorganisms. The compounds exhibited greater effectiveness against *S. aureus* than against *A. baumannii*. To rationalize the influence of ligand modifications on antimicrobial performance, gas-phase DFT optimizations were performed. Molecular descriptors obtained from Gaussian and calculated using MOE were subjected to statistical analysis using the DEMOVA package in R. This led to the development of a robust QSAR model for predicting activity against *S. aureus*. The most accurate model (adjusted R^2 = 0.98) included descriptors such as metal presence, HOMO-LUMO energy gap, donor-acceptor surface area, number of rotatable bonds, KierFlex, and octanol-water partition coefficient (logP). This successful QSAR model provides a powerful tool for the rational design of novel adamantane-based ligands, guiding the development of more potent dimethyltin(IV) antimicrobial agents.

Keywords: antimicrobial; metallopharmaceuticals; organotin(IV)

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