





Belo Horizonte, September 12 - 15th 2024

Metal complexes containing nucleotide analogs: a proposal for the treatment of skin lesions

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Thematic Area: Biological Inorganic Chemistry

Keywords: metal complexes, squamous cell carcinoma and nucleotide analog.

There are known more than 1000 skin-related diseases that have an important impact in human life^[1]. In special, skin infections caused by burns are linked to several pathogens as Gram-negative *Pseudomonas aeruginosa* and Gram-positive methicillin-resistant *Staphylococcus aureus* (MRSA). In addition, skin tumors can cause severe impacts in health of patients. Squamous cell carcinoma (SCC) is one of the most prevalent skin tumors in humans and the second most common type of skin cancer^[2]. In this study, the nucleotide

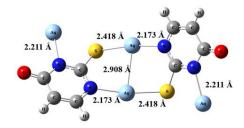


Figure 1: Proposed Ag-2tu structure

analog 2-thiouracil (2tu) was selected for the synthesis of a new Ag(I) complex that has been considered for the treatment of skin lesions. The Ag-2tu complex was synthesized by the reaction of an aqueous solution of silver nitrate (0.60 mmol) with an aqueous solution of 2tu (0.30 mmol) in alkaline medium, under stirring at room temperature for 1 hour. A brown precipitate, with a yield of 95.8%, was obtained. The Ag-2tu complex was characterized by elemental, FT-IR, Raman and solid-state NMR analyses. The composition found for this complex was Ag₂C₄N₂H₂OS. Calculated(%): C, 14.05; H, 0.59; N, 8.19. Found(%): C, 13.52; H, 0.46; N 7.7. FT-IR, Raman and solid-state NMR spectroscopies indicated coordination of 2tu to silver by nitrogen and sulfur atoms forming a polymeric structural arrangement. Molecular modeling studies reinforced polymeric structure (Figure 1) as the most likely to be formed. The antimicrobial activity of the complex was tested over four ATCC bacterial strains by the MIC assay^[3]. The compound was active over Gram-positive *S. aureus* and *Bacillus cereus*, and Gram-negative *P. aeruginosa* and *Escherichia coli* strains with MIC values in the range 3.65-1.85 mmol L⁻¹, being close to the MIC values of silver sulfadiazine used in the clinics^[4].

Acknowledgments: CAPES, FAPESP (grant # 2021/08717-8, 2023/11857-1 and # 2021/10265-8 Cancer Theranostics Innovation Center CancerThera-CEPID), FAEPEX and CNPq (309800/2021-8).

References

- [1] Xue Y. et al. Front Med, 9, 861115 (2022).
- [2] Sung H. et al., CA Cancer J Clin, 71(3), 209-249 (2021).
- [3] Wayne P.A. Clinical and Laboratory Standards Institute Performance standards for antimicrobial susceptibility testing: twenty-sixth informational supplement M100- S26, Clinic. Lab. Stand. Inst. (CLSI) 34 (1) (2016).
- [4] Nunes, J.H.B et al., Coord. Chem. Rev. 490, 215228 (2023)