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ANTIMICROBIAL AND ANTIFUNGAL ACTIVITY OF CU(II) AND BI(III) COMPLEXES BASED ON AMINOPOLYCARBOXYLATE IONS AND 2-FORMYL AND 2-ACETYLPYRIDINE THIO-SEMICARBAZONES

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Introduction. The biological properties of thiosemicarbazones are often related to metal coordination, which as result affects lipophilicity that controls the rate of entry into the cell. Metal complexes are generally more active than the free ligand, or the metal complex can be a vehicle for activation of the ligand as the cytotoxic agent. Among biologically active metal compounds, copper (II) complexes with 2-formyl and 2-acetylpyridine thiosemicarbazones proved to be among the most potent antiviral, antitumor and anti-inflammatory agents. Bismuth compounds have been widely used in medicine for more than two centuries due to their high effectiveness and low toxicity. In the antimicrobial realm, applications have been widespread, due to bismuth antiseptic, astringent, protective, antacid, antisecretory and local gastrointestinal properties.

Material and methods. The research is focused on the synthesis and biological activity investigation of homometallic and heterometallic coordination compounds with 2-formyl (HFopytsc) and 2-acetylpyridine (HAcpytsc) thiosemicarbazones of general formulas $\{Cu(Fo/Acpytsc)\}_2Cu(APC)\cdot nH_2O$, $Cu(HFo/Acpytsc)Cu(APC)\cdot nH_2O$ and $Bi(HAPC)(HAcpytsc)_m\cdot nH_2O$. Targeting at getting synergistic biological effect, three series of heterometallic coordination compounds of general formula $\{Cu(Fo/Acpytsc)\}Bi(APC)\cdot nH_2O$ with aminopolycarboxylate (APC) ions have been synthesized (n=1-9; m=1 or 2; APC=ethylenediaminetetraacetate ($edta^{4-}$), 1,2-cyclohexanediaminetetraacetate ($cdta^{4-}$) and diethylenetriaminepentaacetate ($dtpa^{5-}$). The composition and structures of the complexes have been determined by means of elemental analysis, IR spectroscopy and single crystal X-ray diffraction study.

Results. The antimicrobial activity of the complexes was evaluated against three bacterial strains, *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Acinetobacter baumannii* (BAA-747) Determination of the MIC (minimum inhibitory concentration, mg/mL) and MBC (minimum bactericidal concentration, mg/mL) was carried out by using serial dilutions in liquid broth method.

The results demonstrated that *Staphylococcus aureus* was the most susceptible to the considered compounds. In this case, the values of MIC and MBC vary, ranging from 0.001 to 0.5 mg/mL, indicating high to moderate activity of the compounds.

Conclusions. Generally, complexes based on 2-acetylpyridine thiosemicarbazone and $edta^{4-}$ ion, both homo and heterometallic, are more active than the analogues with other APC ligands. The highest antimicrobial activity was displayed by Cu (II) homometallic complex based on 2-acetylpyridine thiosemicarbazone (0.001 mg/mL), followed by its heterometallic Cu (II)-Bi (III) analogue with $edta^{4-}$ ion. Among the complexes with 2-formylpyridine thiosemicarbazone, the derivative of Cu (II) with 4-phenylthiosemicarbazone and $edta^{4-}$ ions displays an activity close to the one displayed by the 2-acetylpyridine representatives.