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Dinuclear silver(I) complexes with a pyridine-based macrocyclic type of ligand as antimicrobial agents against clinically relevant species: the influence of the counteranion on the structure diversification of the complexes†

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New dinuclear silver(I) complexes with *N*,*N*′,*N*″,*N*‴-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc), $[Ag_2(NO_3)(tpmc)]NO_3{\cdot}1.7H_2O$ (**1**), $[Ag_2(CF_3SO_3)_2(tpmc)]$ (**2**), and $[Ag_2(tpmc)](BF_4)_2$ (**3**) were synthesized and characterized by NMR (^1H and ^{13}C), IR and UV-Vis spectroscopy, cyclic voltammetry and molar conductivity measurements. The molecular structures of the complexes were determined by single-crystal X-ray diffraction analysis. The spectroscopic and crystallographic data showed that the structure of the complexes strongly depends on the nature of the counteranion of silver(I) salt used for their synthesis. The antimicrobial activity of complexes **1–3** was examined against Gram-positive and Gram-negative bacteria and different species of unicellular fungus *Candida* spp. The ability of these complexes to inhibit the formation of *Candida* biofilms and to eradicate the already formed biofilms was tested in the standard microtiter plate-based assay. In addition, a bioelectrochemical testing of the antimicrobial activity of complex **1** against early biofilm was also performed. The obtained results indicated that complexes **1–3** showed increased activity toward Gram-negative bacteria and *Candida* spp. and could inhibit the formation of biofilms. In most cases, these complexes had positive selectivity indices and showed similar or even better activity with respect to the clinically used silver(I) sulfadiazine (AgSD). The values of the binding constants for complexes **1–3** to bovine serum albumin (BSA) were found to be high enough to indicate their binding to this biomolecule, but not so high as to prevent their release upon arrival at the target site. Moreover, the positive values of partition coefficients for these complexes indicated their ability to be transported through the cell membrane. Once inside the cell, complexes **1–3** could induce the formation of the reactive oxygen species (ROS) in *C. albicans* cells and/or interact with DNA. Taken together, silver(I) complexes with the tpmc ligand could be considered as novel antimicrobial compounds with favourable pharmacological properties, being safer than AgSD.

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