

TITLE: ANTIBACTERIAL ACTIVITY OF UNLOADED AND LOADED Ag (I) COORDINATION COMPOUNDS IN THE NANOTECHNOLOGICAL DRUG DELIVERY SYSTEMS

AUTHORS: CAMARGO, B. A. F.¹; FORTUNATO, G. C.¹; SILVA, D. E. S.²; SILVA, P. B.³; CHORILLI, M.¹; NETTO, A. V. G.²; BAUAB, T. M.¹.

INSTITUTION: ¹SCHOOL OF PHARMACEUTICAL SCIENCES, SÃO PAULO STATE UNIVERSITY-UNESP (RODOVIA ARARAQUARA-JAÚ, KM 1, ZIP CODE 14801903, ARARAQUARA - SP, BRAZIL).

²CHEMISTRY INSTITUTE, SÃO PAULO STATE UNIVERSITY-UNESP (RUA PROF. FRANCISCO DEGNI, 55 – QUITANDINHA – ZIP CODE 14800060, ARARAQUARA - SP, BRAZIL).

³UNIVERSITY OF BRASÍLIA-UnB, DISTRITO FEDERAL (QUADRA SQN 303 BLOCO J ASA NORTE, CODE 70735100, BRASÍLIA, DISTRITO FEDERAL, BRAZIL).

ABSTRACT

Classified as a public health problem, death from infectious diseases is still a worldwide concern, mainly due to the growing number of microbial strains resistant to various drugs. Metallic ions, such as silver, have demonstrated antimicrobial properties and has the capacity to form complexes, which attract interest in providing new drug approaches. The drug delivery systems present as a strategy to improve the antimicrobial activity of metallic compounds, as well as to enable a better solubilization and release. Thereby, this study aimed to evaluate the *in vitro* antibacterial potential of the compounds [Ag(PCAPhTSC)₂]₂NO₃ (1), [Ag(PCAhTSC)₂]₂NO₃ (2), [AgCl(PCAPhTSC)₂] (3) e [AgCl(PCAhTSC)₂] (4), unloaded and loaded in a nanostructured drug delivery system (polymeric nanoparticle) against *Staphylococcus aureus* and *Escherichia coli*. Polymeric nanoparticles consisting of polymer (polycaprolactone), a surfactant (poloxamer 407) and an aqueous phase (phosphate buffered pH 7.4). The system was prepared by nanoprecipitation. The minimal inhibitory concentration (MIC) was determined by microdilution assay according to the protocol described by CLSI for aerobic bacteria against *S. aureus* ATCC 25923 and *E. coli* ATCC 25922. Unloaded and loaded compounds 1 and 2 showed MIC values of 15.62 µg mL⁻¹ and 6.25 µg mL⁻¹, respectively, against *S. aureus*. Unloaded and loaded compound 3 showed MIC of 31.25 µg mL⁻¹ and 1.56 µg mL⁻¹ against *S. aureus*. Unloaded and loaded compound 4 inhibited *S. aureus* with MIC of 15.62 µg mL⁻¹ and 3.12 µg mL⁻¹, respectively. The use of nanotechnology improved the antibacterial activity against *S. aureus*. The compounds 1, 2, 3 and 4 presented MIC of 500 µg mL⁻¹, 7.81 µg mL⁻¹, 250 µg mL⁻¹ and 3.90 µg mL⁻¹, respectively, against *E. coli*. Loaded compounds 1, 2 and 3 showed MIC values of >100 µg mL⁻¹ against *E. coli*. Loaded compound 4 inhibited *E. coli* with MIC of 12.50 µg mL⁻¹. Silver (I) coordination compounds showed relevant antibacterial activity and the use of nanotechnology can be a promising alternative to the control infections caused by *S. aureus* and *E. coli*.

Keywords: *Staphylococcus aureus*; *Escherichia coli*; metal complex, silver; polymeric nanoparticle

Development Agency: We thank National Council for Scientific and Technological Development, Brazil (Process number: 134170/2018-0); This study was financed in part by the Coordenação de Aperfeiçoamento Pessoal de nível Superior- Brasil (CAPES) – Finance Code 001