

# Synthesis, characterization, antibacterial and mutagenic activities, and release capacity in bacterial cellulose membranes of a new Ag(I) complex with chlorthalidone

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Silver complexes have demonstrated antimicrobial activity against Gram-positive and negative pathogens.<sup>1</sup> Silver-sulfadiazine can be considered one of the best examples of an Ag(I) compound used in the clinics in the treatment of skin infections caused by bacterial strains. In this case, silver ions are responsible for the antibacterial action of the compound, while sulfadiazine, a well known sulfonamide, acts only as a silver carrier. Bacterial cellulose membranes (BC) have been explored as new nanostructured transdermal delivery systems for antimicrobial compounds.<sup>2</sup> However, the use of BC as a support for retention and release of metal complexes is rare. In this work, we describe the synthesis, antibacterial activities and the use of BC for the controlled release of a Ag(I) complex with the sulfonamide chlorthalidone (Ag-CLR). The Ag-CLR complex was synthesized by the reaction of an aqueous solution of AgNO<sub>3</sub> with a methanolic solution of chlorthalidone (CLR). The pH was adjusted to 10 with a dilute solution of KOH. After one hour of constant stirring, a white precipitate was obtained. The solid was collected by filtration, washed with water and dried. Infrared spectra indicate loss of the hydrogen atom of the isoindolinyl group present in the structure of the ligand and nitrogen coordination to silver. The Ames test indicated that the complex has no mutagenic activities. The ability of BC produced in glucose/sucrose medium (BC<sub>GS</sub>) to act as a support for retention capacity release of the complex was also investigated. BC<sub>GS</sub> discs of 10 mm diameter were aseptically impregnated with 2.0 mg of Ag-CLR and identified as BC<sub>GS</sub>-Ag-CLR. First, one sample of the discs was immediately placed on the surface of the solid Muller Hinton (MH), with an inoculum of *Staphylococcus aureus* (ATCC 25923). To evaluate the retention capacity and sustained release of the complex, the diameter of the inhibition zones was measured after 24 hours and then the discs were transferred to another MH plate inoculated with *S. aureus*. This procedure was repeated every 24 hours until no longer inhibition zones of bacterial growth were detected. The results are observed in table 1. The observed data allowed the determination of holding capacity and sustained release of the BC<sub>GS</sub>-Ag-CLR system. The BC impregnated with free CLR did not show antibacterial activity. Experiments were performed in triplicate.

Table 1 - Inhibition zone diameters (mm) produced by BC<sub>GS</sub>-Ag-CLR

Samples \ Time (h)	0	24	48	72	96	120	144	168
BC <sub>GS</sub> -Ag-CLR (mm)	18	15	15	15	14	14	14	12

The BC<sub>GS</sub>-Ag-CLR complex has shown to possess significant stability air/light exposure and a sustained *in vitro* antibacterial activity against Gram-positive *S. aureus* (ATCC 25923) for 168 hours. The observed results reinforce the possible application of BC as a support for controlled sustained and release of the Ag-CLR complex.

1. Nunes, J.H.B.; dePaiva, R.E.F.; Cuin, A.; Lustri, W.R.; Corbi, P.P.; *Polyhedron*. **2015**, 437–444.
2. Lazarini, S.C.; Aquino, R.; Amaral, A.C.; Corbi, F.C.A.; Corbi, P.P.; Barud, H.S.; Lustri, W.R.; *Cellulose*. **2016**, 737-748.

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