Title: Antimicrobial activity of a Shiff base against *Acinetobacter baumannii* multidrug-resistant strains and its cytotoxicity to Vero cells

Authors: Costa, P. S.[1], Souza-Fagundes, E. M.[1], França, R. O.[1],Nobre, V. [1] de Fátima, A.[1], Santos, S.G.[1]

[1] UFMG - Universidade Federal de Minas Gerais- (Avenida Presidente Antônio Carlos, 6627 - Pampulha, Belo Horizonte – MG, Brasil)

Abstract:

Antimicrobial resistance is one ofthe most important problem worldwide public health. In recent years, *Acinetobacter baumannii* has been standing out as relevance nosocomial pathogen due to its multi-drug resistance emergency.Thus, the need for new antimicrobial agents is increasing, especially against this bacterial specie. The Schiff bases, known by their biological activities against different microorganisms, are currently a functional group that shows potential for the development of new antimicrobial substances. The aim of this study was to evaluate the antimicrobial activity of a Schiff base derived from the nitro-furfural (3F10), previously selected, against the reference strain *A. baumannii* ATCC 19606 and 16 clinical *A. baumannii* multidrug-resistant strains. In addition, the cytotoxic activity of this substance to the Vero cells was evaluated. The determination of the minimum inhibitory concentration (MIC) of the substance 3F10 was carried out by microdilution method in 96-well plates, ranging concentrations from 2 to 128µg/mL, varying in log scale on the base 2. The cytotoxic activicty was investigated in Vero cells (ATCC-CCL-81), which were cultured in media culture DEMEM containing gentamicin, maintained at 37°C and in an atmosphere containing CO_2 (5%). After 24 hours, eight concentrations of this compound (0.001 to 100 uM) were added in triplicata.Tetrazolium salt (MTT- [3- (4,5-dimethylthiazol-2-yl) -2,5-diphenyl tetrazolium bromide]), was added in the culture after 48h of incubation, which aims to quantify the viable kidney cells that are able to metabolize it to a compound named formazan, and thus information about cytotoxicity.The clinical *A. baummanni* strains were resistant to carbapenens and polimixina B, besides expressing important genes for their pathogenicity, such as bla_{OXA23} and *omp*A, evaluated in previous studies.The dose which inhibits 50% of cell growth (IC50) was determined graphically for a program selected for analysis data. The substance was active against all clinical samples tested and showed bacteriostatic activity. The MIC obtained for the reference strain, *A. baumannii* ATCC 19606 and for the clinical strains were 4µg/mL and 8µg/mL, respectively. The substance showed IC50 values for Vero cells of 9,7µg/mL. Although the results of the antimicrobial activity obtained in this study confirm the therapeutic potential of this class of compounds, their cellular cytotoxicity should be further investigated. The importance of more studies in this area is needed, since the spread of resistance is large on the world stage and the availability of new drugs is limited.

Key words: Schiff bases*, Acinetobacter baumannii*, Antimicrobial activity,Cytotoxic activity.

Funding agencies: CNPq, FAPEMIG, CAPES, PRPq/UFMG