Effects of alkaloids extracted from Solenopsis invicta venom reversing the multidrug resistance phenotype in yeast

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INTRODUCTION: The multidrug resistance (MDR) phenotype is found in microorganisms such as fungi and it is responsible for failure in chemotherapy. The main mechanism of MDR is the overexpression of efflux pumps such as Pdr5p from Saccharomyces cerevisiae, a protein member of superfamily of ABC transporters. The search for inhibitors is important because they can be used to reverse the MDR phenotype. Solenopsin is an alkaloid found in the venom of the Solenopsis invicta ant which is known for its antimicrobial effect. The present study aimed to evaluate if solenopsin could reverse the MDR phenotype mediated by the ABC transporters in yeast cells.

MATERIAL & METHODS: The reversing test consist of (1) measuring ATPase activity using the enriched yeast plasma membrane, (2) chemosensibilization assay in solid agar medium and (3) Rodamine 6G (a fluorescent probe which is a substrate for ABC transporters) in uptake and efflux assays. An assay to determine the minimum inhibitory concentration of venom will also be performed, in order to evaluate its fungicide effect. Cytotoxicity assays will be performed on erythrocytes in order to evaluate the hemolytic effect of solenopsin.

RESULTS & DISCUSSION: Parcial results show that solenopsin, in association with fluconazole is capable of reversing the multiple drug resistance phenotype in S. cerevisiae strains. Furthermore, citotoxicity assays on erythrocytes shows that the hemolitic effect associated with solenopsin occurs in a concentration higher than was able to reverse the resistance.

CONCLUSION: The results show that solenopsin has a strong potential as a MDR phenotype reverser. A low hemolitic effect in the presence of the compound was observed. Other tests with mammalian cells will be performed to evaluate the toxicity of solenopsin and the possible use of this molecule in association with conventional drugs in combat of human fungal infections.

Key words: MDR, yeast, alkaloids

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