Effect Of Chalcone Derivatives On Multidrug Resistance Promoted By Pdr5p

Saccharomyces cerevisiae

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Introduction: Nowadays, the multidrug resistance (MDR) is a serious problem for chemotherapy, once the cells become resistant to many chemotherapeutic agents that have no structural or functional similarities. The MDR phenotype is mainly mediated by ABC (ATP-binding cassette) transporters which are capable to promote the drugs efflux, using for this the energy released by hydrolysis of ATP. The Saccharomyces cerevisiae can express several ABC transporters and Pdr5p is one of them. This transporter has been used as a model for the study of MDR phenotype. In the present study we tested the chemosensitization capacity of some synthetic chalcone derivatives against Pdr5p from yeast plasma membrane.

Material and Methods: At first we performed a chemosensitization assay using a mutant strain of S. cerevisiae that overexpresses the Pdr5p. A cell suspension containing 2 x 10^7 cells/mL were plated on YPD solid medium (1% Yeast extract, 2% peptone, 2%dextrose and 2% agar) containing fluconazole at 100 µg/mL using a sterile swab. Then the discs containing 5µL of the compound solutions at 20mM were placed on the inoculated medium surface. The Petri dishes were incubated for 48 hours, at 30°C. If the compound inhibit were capable to reverse the MDR phenotype, it would appear zone of growth inhibition around of the disc. Results and Conclusion: At present moment, two chalcone derivatives appeared to chemosensitize the resistant strain of S. cerevisiae, and now, some confirmatory experiments have been conduct, for the better comprehension of this effect on the Pdr5p, including measure of enzyme activity and rhodamine 6G efflux assay in the presence of those compounds.

Word Keys: Pdr5p, MDR, chalcones

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