Effects of different groups of chalcones on ABCG2-overexpressing cells through mitoxantrone accumulation

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Multidrug resistance (MDR) is one of the most preoccupying phenomena in chemotherapy nowadays. It is generally conferred by membrane proteins which are able to pump drugs out of the cell, leading to treatment failure. Tumor cells express several types of transporters, among which is ABCG2/BCRP (Breast Cancer Resistance Protein). In this work, we have evaluated the effect of 58 chalcones belonging to three different series on the accumulation, by human wild-type (R482) ABCG2-transfected HEK-293 cells, of its fluorescent substrate mitoxantrone using flow cytometry. These different series of chalcones are composed by the derivatives of 3,4-methilenodioxy-acetophenone, 2-naphtylacetophenone and some hydroxychalcones. At a 10µM concentration, some of these compounds were found to increase mitoxantrone accumulation to a greater extent than a reference ABCG2 inhibitor, GF120918. The best compounds showed very low IC_{50} values, in the range of 0.1 µM. Additionally, these chalcones had no effect on mitoxantrone accumulation in P-glycoprotein-overexpressing HEK-293 cells. These results indicate that these compounds are potent and specific inhibitors of BCRP; their mode of action is still being further investigated.

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