EUROPEAN GREEN CONFERENCE

LACTONE-BASED DERIVATIVES AS POTENTIAL MODULATORS OF MULTIDRUG RESISTANCE IN K562 CELLS

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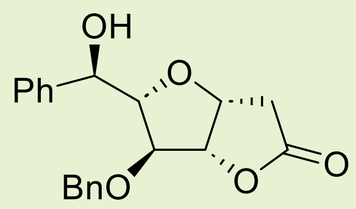
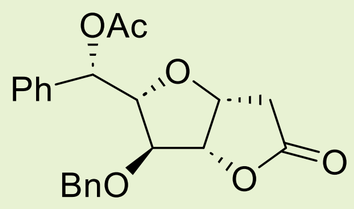
Multidrug resistance represents a major obstacle in cancer therapy, particularly in hematologic malignancies such as chronic myelogenous leukemia. The overexpression of Multidrug Resistance Protein 1 (MRP1) plays an important role in the development of chemotherapy resistance in cancer cells. In this study, we investigated the effect of three lactone-based derivatives on multidrug resistance in cancer cells.



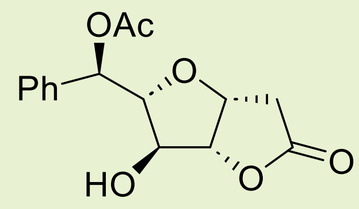
SĐ15

Chemical Formula: $C_{20}H_{20}O_5$
Molecular Weight: 340,38



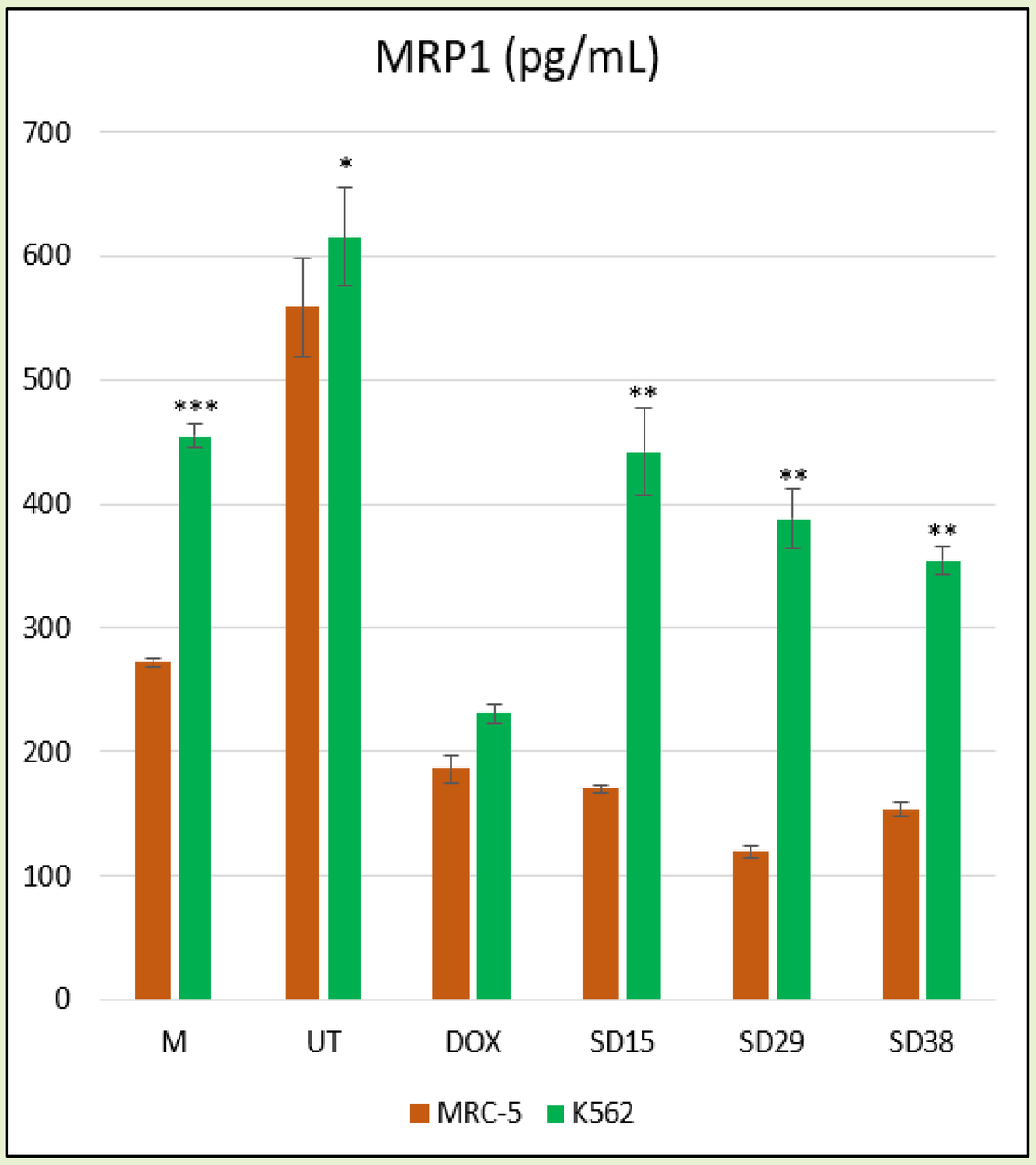
SĐ29

Chemical Formula: $C_{22}H_{22}O_6$
Molecular Weight: 382,41



SĐ38

Chemical Formula: $C_{15}H_{16}O_6$
Molecular Weight: 292,29



Type of cells	DOX IC_{50} (μm)	SĐ15 IC_{50} (μm)	SĐ29 IC_{50} (μm)	SĐ38 IC_{50} (μm)
K562	0.25	8.39	8.33	5.66
MRC-5	0.10	634.66	484.83	258.69

The compounds were tested on human chronic myelogenous leukemia cell line K562 and human fetal lung fibroblast cell line MRC-5 over a 72-hour period. Antiproliferative activity was assessed based on IC_{50} values which were determined using an MTT assay. To explore potential interactions with drug resistance mechanisms, the levels of MRP1 were determined using an ELISA assay. MRC-5 cells were used as a negative control, as prior results indicated no significant cytotoxicity on these cells (M - cells containing growth medium, UT - untreated cells with DMSO solvent, DOX - cells treated with doxorubicin).

The lactone-based derivatives significantly reduced viability of K562 leukemia cells, but did not show notable toxicity in MRC-5 normal lung fibroblasts, indicating selectivity toward malignant cells. The observed increase in MRP1 levels following treatment with the lactone-based compounds, exceeding those induced by doxorubicin, suggests that these agents could be recognized as MRP1 substrates or selective inducers of cellular stress.

The selective cytotoxicity of lactone-based derivates toward K562 cells indicates that they may retain therapeutic efficacy despite elevated MRP1 expression, potentially by engaging alternative, MRP1-independent pathways. Therefore, these results indicate their potential as selective anticancer agents, possibly targeting MRP1-related mechanisms. However, further research is required to confirm their role in modulating drug resistance.