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Triterpenoids from *Momordica balsamina* with a Collateral Sensitivity Effect for Tackling Multidrug Resistance in Cancer Cells.

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Abstract

The collateral sensitivity effect is among the most promising strategies for overcoming multidrug resistance in cancer. In this work, 28 cucurbitane-type triterpenoids (1-28), previously isolated from the African medicinal plant *Momordica balsamina* and its derivatives, were evaluated for their collateral sensitivity effect on three different human cancer entities, gastric (EPG85-257), pancreatic (EPP85-181), and colon (HT-29), each with two different multidrug-resistant variants. One was selected for its resistance to daunorubicin (EPG85-257RDB, EPP85-181RDB, HT-29RDB) and the other was selected for its resistance to mitoxantrone (EPG85-257RNOV, EPP85-181RNOV, HT-29RNOV). On gastric cell lines, the best results were obtained for compounds 3 and 10, which exhibited a collateral sensitivity effect together with high antiproliferative activity. In turn, on colon cancer cell lines, the best multidrug resistance-selective antiproliferative effects were observed for derivatives 11, 13, and 15, which showed collateral sensitivity effects against both resistant variants. Compounds 11 and 3 were also the most selective against the multidrug resistance pancreatic cells lines. Some compounds, such as 6, 10, 11, and 15, were previously found to be strong P-glycoprotein modulators, thus highlighting their potential as promising leads for overcoming multidrug resistance in cancer cells.

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