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In vitro evaluation of the antiproliferative effect of novel ursolic acid derivatives

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Introduction: The incidence of melanoma, the most aggressive skin cancer, is continuously increasing, and its treatment is difficult due to chemoresistance and severe side effects. Various natural products have been shown to be effective in cancer management. Among them, ursolic acid (UA), a pentacyclic triterpenoid, has been tested *in vitro* against several cancer cell lines, including human and murine melanoma (WM-244-6 and B16), with promising results [1, 2]. However, due to low solubility and cell penetration capacity, it is necessary to obtain semisynthetic derivatives of UA with superior properties. It was already stated that the transformation of C17-COOH into esters or amides improves the antiproliferative activity of the parent compound [3]. **Aim:** The current study is designed to evaluate the antiproliferative potential (B164A5 murine melanoma cell line) of novel UA and ursonic acid (UoA) derivatives (UP, UPm, UoP, UoPm). **Materials and methods:** The antiproliferative of UA derivatives was evaluated using the MTT assay (72 h of incubation) and the cytotoxic activity was assessed using the LDH assay (72 h of incubation). **Results:** Within the MTT assay, UA derivatives showed a weaker antiproliferative effect than the parent compound, while UoA derivatives had a stronger effect than UoA. In addition, at 75 µM, UP (IC50 = 47.95 µM) and UoP (IC_{50} = 70.36 µM) caused a more significant reduction in cell viability compared to (IC_{50} = 59.09 µM), respectively UoPm (IC_{50} = 142.5 µM). Regarding the LDH assay, UA exhibited a cytotoxicity of 54.2% against the melanoma cell line, which was higher that of its derivatives. **Conclusions:** The derivatization process did not increase the antiproliferative and cytotoxic potential of UA. UA derivatives exhibited a stronger antiproliferative effect compared to their counterparts derived from UoA.

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