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A new aziridine compound with highly selective anticancer activity

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Despite recent advances in cancer research, the survival of patients with metastatic disease continues to be very low, mainly because the anticancer drugs used in these patients have low selectivity for cancer cells. In this work, the possible selective anticancer activity of a new series of compounds with an aziridine group in their structure has been evaluated in a panel of cancer and normal cells using the MTT assay. A549 lung cancer cells and MRC5 non-malignant lung cells were exposed for 48 h to all compounds at a concentration range between 0,01 and 1 mM. The compound (2-methyl-1-tosylaziridin-2-yl)methyl-2,3-di-O-benzyl-4,6-O-(S)-benzylidene- β -D-galactopyranoside showed the highest selectivity for the cancer cell line and was selected for further studies. This compound showed selective cytotoxic activity against breast cancer cells (MCF7) and melanoma cells (UACC62) versus non-malignant breast cells (MCF10) and skin cells (VH10). It is worth noting that the concentration of this aziridine needed to kill breast cancer cells by 50% was over 50-fold lower than that required to kill non-malignant breast cells; the IC₅₀ value ($\mu\text{M} \pm \text{SEM}$) was 583.06 ± 79.32 for MCF10 and 11.66 ± 2.04 for MCF7; $p=0,03$ (paired, two-tailed t-test). We next explored three possible mechanisms of action involved in the selective anticancer activity of this new compound: generation of reactive oxygen species, inhibition of glycolysis, and induction of DNA damage. To test whether the anticancer activity was due to the generation of ROS, the cytotoxicity of this aziridine was measured with the MTT assay in the presence or absence of two antioxidants: N-acetylcysteine and Mn (III) tetrakis (1-methyl-4-pyridyl)porphyrin. Inhibition of glycolysis was evaluated by measuring lactate and glucose levels after drug treatment. The induction of DNA damage was studied by the immunofluorescence γ -H2AX focus assay. Our preliminary results show that the pro-oxidant activity of this aziridine along with its ability to induce specific types of DNA damage may play a role in its highly selective anticancer activity. Animal studies are warranted to assess the potential anticancer effects of this novel compound in vivo.