Anti-proliferative effects of compounds derived from glucopyranuronamide

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Chemotherapy is a major cancer treatment option. The synthesis of new compounds with better anti-proliferative properties and higher specificity is a current challenge in *drug discovery* today. Our goal with this work was to develop compounds derived from D-glucuronic acid and to evaluate their anti-proliferative properties. We have synthetized a library of hydroxyamide derivatives of D-glucuronic acid using amines and aminoalcohols. The synthesis of these compounds were based on the work of El-Nezhawy's group, who have designed some novel D-glucuronic acid acetylated and deacetylated derivatives, which showed interesting results with breast cancer cell lines.

Anti-proliferative activity of the newly synthesized compounds was examined against human breast adenocarcinoma (MCF-7) and human colon carcinoma (MDST8) cell lines. Cell growth and viability was analysed by the Cell Counting Kit-8 method. The chemotherapeutic agent 5-fluoroacil was used as a positive control, allowing one to estimate the maximal anti-proliferative action expected in both carcinoma cell lines. All the compounds were studied in the 10^{-9}-10^{-5}M range.

The compound *N*-(ethanol)-α/β D-glucopyranuronamide presented the best anti-proliferative potential with an IC_{50} (concentration of the compound causing 50% decrease in net cell growth) of $1.4x10^{-7}$M in MCF-7 cells. The 1-pheny-l-2-hydroxy-ethane-2-yl and the 1-propanol derivatives evoked weak anti-proliferative effects in MCF-7, with slight growth inhibition of 37% and 35%, respectively, for the highest concentration used (10^{-5}M). On the contrary, the MDST-8 cell growth was not affected by these compounds. On the contrary, the 1-hydroxy-2-isopropyl-ethane-2-yl and 3-phenyl-1-hydroxy-propane-2-yl derivatives, exhibited weak anti-proliferative effects (22% and 40%, respectively) at 10^{-5}M, in the MDST8 cell line, without affecting MCF-7 cell growth. None of the compounds exihibited toxic effects, at least up to 72h exposure, in the concentration range studied.

These results show that the ethyl substituent was the most effective *N*-substituent for glucopyranuronamide for anti-proliferative actions in MCF-7 cell line, whilst in the case of the MDST8 cells, 3-phenyl-1-hydroxy-propane-2-yl was the most effective *N*-substituent. Moreover, all the glucopyranonamide compounds studied presented selective anti-proliferative effects for the different carcinoma cell lines used.

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