Exploring the synthesis and the biological profile of Novel D-Glucopyranuronamide-base Nucleosides

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Synthetic nucleos(t)ides are important groups of molecules in medicinal chemistry, due to their ability to interfere with nucleos(t)ide-dependent biological events and act as anticancer and antiviral agents. [1] Their antimicrobial potential is also well reported. [2] However, some limitations are associated with their clinical use, such as low oral bioavailability and chemotherapeutic resistance.[1] Therefore, the development of bioactive nucleos(t)ides-like structures that may overcome such issues and act through alternative mechanisms of action is of significant interest.

In this context, the synthesis and biological evaluation of novel nucleosides based on D-glucuronamide units will be presented. The inclusion of this glycosyl moiety was motivated by the known biological profile of D-glucuronamide derivatives.[3] Moreover, it allows structural variations in a *gluco*-configured template at C-6 via N-substitution, which can be tuned for attaining better bioactivities.

Differently *N*-substituted glucuronamide-based purine and uracil nucleosides were accessed as well as nucleotide sugar mimetics based on a pseudodisaccharidic skeleton and containing a (triazolyl)methyl amide linkage as a potential neutral and rather stable surrogate of a diphosphate group.

The biological evaluation of the compounds included the study of their antiproliferative activities in cancer cells and of their antibacterial effects. Some molecules showed a potent anticancer activity with GI_{50} values similar or lower than those of standard drugs, turning them prospective lead molecules for further studies.

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