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Novel types of nucleosides with therapeutic potential

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Nucleosides, nucleotides and analogs are among the most relevant carbohydrate-containing molecules in drug research due to their biological profile, which include anticancer, antiviral or antimicrobial properties. Some synthetic derivatives have reached clinical application against cancer or viral infections, interfering with nucleic acid synthesis by mimicking their physiological counterparts and being recognized by polymerases. Acquisition of resistance of cancer cells and some virus towards nucleos(t)ide analogs and low bioavailability are major weaknesses of their use in clinics. Therefore, research on nucleos(t)ide-based structures that may circumvent these drawbacks as well as the focus on other and less studied potential therapeutic uses for these types of compounds remain of interest. In this context, in this communication, the development of new types of nucleoside lead molecules for cancer and Alzheimer's disease will be presented. The groups of compounds, whose synthesis, bioactivity screening and structural optimization will be disclosed, consist of 5'/6'-azido nucleosides, glucuronamide-based nucleosides, isonucleosides and N-glycosyltriazole analogs. The methodologies towards their synthesis involved N-glycosylation, Mitsunobu coupling, anomeric azidation and "click" 1, 3-dipolar cycloaddition as key steps. Biological evaluation revealed some molecules displaying potent anticancer efficacy or exhibiting effective inhibition of acetylcholinesterase, with activities in the micromolar concentration range, in some cases similar or close to those of standard drugs.

Biography

Nuno Manuel Xavier obtained a dual PhD Degree from the University of Lisbon and from the National Institute of Applied Sciences of Lyon in 2011. He carried out Post-doctoral Research periods at the University of Natural Resources and Life Sciences, Vienna and at the University of Lisbon. Since 2014, he is Researcher (FCT Investigator) at the Faculty of Sciences, University of Lisbon. His research activities, reported in ca. 30 publications and frequently presented in reputed international conferences, are devoted to the design and synthesis of original bioactive carbohydrate derivatives and nucleos(t)ide analogs. He is also a Member of IUPAC.

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