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Synthesis of novel nucleos(t)ide analogs as promising lead molecules for the symptomatic treatment of Alzheimer's disease

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Neurodegenerative diseases are a major public health issue of the 21st century. Alzheimer's disease (AD) is the most common neurodegenerative disease for which no cure is available. The current treatment options are symptomatic and target acetylcholinesterase, an enzyme that cleaves the neurotransmitter acetylcholine, whose levels are low in AD patients. The currently used drugs are donepezil, galantamine and rivastigmine. Previous reports from our group showed the potential of nucleoside analogs to inhibit cholinesterases, namely glucuronamide-based purine nucleosides and isonucleosides containing triazole and theobromine moieties. Therefore, motivated by our constant interest in the access and exploitation of the biological potential of novel nucleoside and nucleotide analogs, the work that will be presented in this communication was focused on the synthesis of novel furanosyl nucleoside analogues possessing a triazole or a theobromine unit linked to the anomeric position of a glucofuranuronamide unit or connected to xylofuranose templates at C-5, respectively. Some of the newly synthesized glycosyl triazoles and a theobromine isonucleoside showed selective and potent inhibition of acetylcholinesterase along with low cytotoxicity in human fibroblasts and in a neuronal cell line, rendering them promising lead molecules for AD and motivating further studies. The synthetic work and the results of the bioactivity assessment will be revealed and discussed herein.

Biography

Rita Goncalves-Pereira completed her PhD Degree in 2016 in the research group of Bioorganic Chemistry of Carbohydrates from the University of Seville. She was then awarded a Fellowship under an FCT-funded project to carry out Post-doctoral research under the supervision of Dr. Nuno M Xavier, in the Carbohydrate Chemistry Group, University of Lisbon. Her research interests include the design and synthesis of novel nucleoside and nucleotide analogs and mimetics of biological and therapeutic interest. She has published five papers in reputed journals and has presented her work in various prestigious conferences devoted to carbohydrate science.

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