

Publication

2-Deoxyglycosylation towards more effective and bioavailable neuroprotective molecules inspired by nature

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**ID** 4601701**Author(s)** Dias, Catarina; Matos, Ana M.; Blasquez-Sanchez, Maria T.; Calado, Patricia; Martins, Alice; Daetwyler, Philipp; Ernst, Beat; Macedo, M. Paula; Colabufo, Nicola; Rauter, Amelia**Author(s) at UniBasel** Ernst, Beat ; Dätwyler, Philipp ;**Year** 2019**Title** 2-Deoxyglycosylation towards more effective and bioavailable neuroprotective molecules inspired by nature**Journal** Pure and applied chemistry**Volume** 91**Number** 7**Pages / Article-Number** 1209-1221**Keywords** bioactive molecules; biomolecular chemistry; caffeic acid ester; cytotoxicity; deoxyglycoside; ICS-29; lipophilicity; medicinal chemistry; neuroprotection; organic synthesis; resveratrol

The neuroprotective role of natural polyphenols is well established but phenolics poor water solubility affects their bioavailability and bioactivity. Aiming to overcome this issue, we were encouraged to investigate the 2-deoxyglycosylation of natural or nature inspired neuroprotective molecules, using glycals as easily accessed glycosyl donors. This robust methodology allowed the generation of a set of new resveratrol and caffeic acid ester glycosides, envisioning more effective and bioavailable compounds. Resveratrol 2-deoxyglycosides were more effective at protecting the neuronal cells from peroxide-induced cytotoxicity than resveratrol itself, while the caffeic acid ester glycoside also showed extraordinary neuroprotection activity. Coefficient partition measurements demonstrated the moderate lipophilicity of resveratrol glycosides, which Log D values are typical of a central nervous system (CNS) drug and ideal for blood-brain barrier (BBB) penetration. Passive permeation assessed by the parallel artificial membrane permeability assay (PAMPA) revealed that 2,6-dideoxy- l - arabino -hexopyranosides were more effective than 2-deoxy- d - arabino -hexopyranosides. The lack of toxicity of the neuroprotective glycosides and their promising physicochemical properties revealed the usefulness of sugar coupling towards the modulation of natural product properties and bioactivity.

Publisher de Gruyter**ISSN/ISBN** 0033-4545 ; 1365-3075**edoc-URL** <https://edoc.unibas.ch/78085/>**Full Text on edoc** No;**Digital Object Identifier DOI** 10.1515/pac-2019-0303**ISI-Number** WOS:000475296300010**Document type (ISI)** ArticleProceedings Paper