Carina Proença et al., Pancreat Disord Ther 2017, 7:4(Suppl)
DOI: 10.4172/2165-7092-C1-008

STRUCTURE-RELATED INHIBITION OF PROTEIN TYROSINE PHOSPHATASE 1B (PTP1B) BY FLAVONOIDS

Carina Proença[a], **Daniela Ribeiro**[a], **Marisa Freitas**[a], **Joana LC Sousa**[a], **Pedro A Fernandes**[a] and **Eduarda Fernandes**[a]
[a]University of Porto, Portugal

Type 2 diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia resulting from inadequate insulin secretion and/or resistance to insulin action. Protein tyrosine phosphatase 1B (PTP1B) is considered a major negative regulator in the insulin signaling pathway, contributing to insulin resistance. Thus, the discovery and development of selective and effective PTP1B inhibitors is a potential therapeutic target for the management of type 2 DM. Some flavonoids have already been shown to inhibit this enzyme, but the literature still lacks in depth structure-activity relationship studies. The main aim of the present work was to test a diversified panel of known and new flavonoids, with different types of substituents (-OH, -OMe and/or -OBn) in different positions, against the PTP1B inhibitory activity. The evaluation of PTP1B activity was performed in vitro by monitoring PTP1B-catalyzed hydrolysis of the substrate p-nitrophenyl phosphate (pNPP) into the product p-nitrophenolate at 405 nm in a microplate reader. The study of the inhibition type of the most active flavonoid was made using the nonlinear regression Michaelis-Menten enzymatic kinetics and the corresponding Lineweaver-Burk plot. Our results suggest that that the presence of -OMe groups at positions 7 and 8 in A ring, together with the presence of -OBn groups at 3' and 4' positions in B ring and a OH group at 3 position in C ring, increases the flavonoids' ability to inhibit PTP1B. The most active flavonoid was 3',4'-dimethoxy-7,8-dibenzoxyflavonol, presenting a mixed type inhibition. In conclusion, some of the tested flavonoids seem to be promising PTP1B inhibitors and potential effective drugs in the management of type 2 DM, increasing insulin sensitivity.

Biography

Carina Proença is a PhD student of Pharmaceutical Sciences at UCIBIO, REQUIMTE, Department of Chemical Sciences, Faculty of Pharmacy of University of Porto. Her actual domain of study involves the in vitro and in silico evaluation of the inhibitory effect of flavonoids against several enzymes intrinsically related with the type 2 diabetes mellitus.

carina.proenca.tas@gmail.com

Notes: