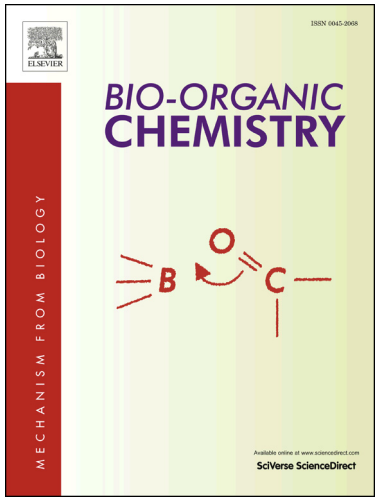

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PII: S0045-2068(16)30222-X
DOI: http://dx.doi.org/10.1016/j.bioorg.2017.03.006
Reference: YBIOO 2033

To appear in: *Bioorganic Chemistry*

Received Date: 23 August 2016
Revised Date: 8 February 2017
Accepted Date: 17 March 2017

Please cite this article as: S.J. Gupta, S. Dutta, R. Gajbhiye, P. Jaisankar, A.K. Sen, Synthesis, *in vitro* evaluation and molecular docking studies of novel amide linked triazolyl glycoconjugates as new inhibitors of α-glucosidase, *Bioorganic Chemistry* (2017), doi: http://dx.doi.org/10.1016/j.bioorg.2017.03.006

Synthesis, *in vitro* evaluation and molecular docking studies of novel amide linked triazolyl glycoconjugates as new inhibitors of α-glucosidase

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Abstract

A series of *N*-substituted amide linked triazolyl β-D-glucopyranoside derivatives (**4a-l**) were synthesized and their *in vitro* inhibitory activity against yeast α-glucosidase enzyme [EC.3.2.1.20] was assessed. Compounds **4e** (IC_{50}=156.06 µM), **4f** (IC_{50}=147.94 µM), **4k** (IC_{50} =127.71 µM) and **4l** (IC_{50} =121.33 µM) were identified as the most potent inhibitors for α-glucosidase as compared to acarbose (IC_{50}=130.98 µM) under the same *in vitro* experimental conditions. Kinetic study showed that both **4e** and **4f** inhibit the enzyme in a competitive manner with *p*-nitrophenyl α-D-glucopyranoside as substrate. Molecular docking studies of **4e, 4f, 4k** and **4l** were also carried out using homology model of α-glucosidase to find out the binding modes responsible for the inhibitory activity. This study revealed that the binding affinity of compounds **4e, 4f, 4k** and **4l** for α-glucosidase were -8.2, -8.6, -8.3 and -8.5 kcal/mol respectively, compared to that of acarbose (-8.9 kcal/mol). The results suggest that the *N*-substituted amide linked triazole glycoconjugates can reasonably mimic the substrates for the yeast α-glucosidase.

Keywords: amide linked glucopyranoside; diabetes; docking studies; α-glucosidase; glycoconjugate; triazole.

1. Introduction

Diabetes mellitus is a group of metabolic disorders where a person has high blood sugar levels. Changes in lifestyle and dietary habits have increased the occurrence of diabetes mellitus [1]. According to the World Health Organization, at least 2.8% of the world population suffered from type-II diabetes mellitus in 2000 and it is estimated that by 2030 this will almost double [2]. The elevated glucose levels in the patients results from the disorder in