Inhibition of pancreatic α-amylase and α-glucosidase as Type II diabetes drug target using cellobiose

Bianca Heyns[1] and Samkelo Malgas[1]

[1]Department of Biochemistry, Faculty of Natural and Agricultural Sciences, University of Pretoria, 0002, South Africa

*Corresponding author. Tel: +27 787 968 447
E-mail address: u21815748@tuks.co.za (B Heyns)

Type II diabetes, a metabolic disorder caused by rapid increase in postprandial blood glucose levels resulting from starch digestion, is currently treated by drugs exhibiting profound side effects. Cellobiose, a cellulose building block, can potentially inhibit amylolytic enzymes, such as pancreatic α-amylase and α-glucosidase, leading to lowered bioavailable sugars for absorption into the bloodstream. However, the mode of inhibition of these enzymes by cellobiose has not been reported. In this study, cellobiose was evaluated for its inhibitory effect on amylolytic enzymes and compared to the commercial drug, acarbose. Acarbose showed a higher inhibitory potential against α-amylase (IC_{50} = 0.003 mM) and α-glucosidase (IC_{50} = 0.35 mM) compared to cellobiose; α-amylase (IC_{50} = 1.2 mM) and α-glucosidase (IC_{50} = 2.4 mM). To identify the mode of inhibition of the amylolytic enzymes by acarbose and cellobiose, enzyme inhibition kinetics and molecular docking was applied. Kinetic parameters of α-amylase in the presence of cellobiose and acarbose showed competitive and uncompetitive type of inhibition, respectively. α-Glucosidase inhibition kinetics showed non-competitive and competitive inhibition with cellobiose and acarbose, respectively. Following both IC_{50} values and the kinetic analysis, cellobiose had a higher binding affinity (-6.6 kJ/mol) towards α-amylase compared to α-glucosidase (-5.7 kJ/mol), although it had lower binding affinities compared to acarbose for both α-amylase (-6.9 kJ/mol) and α-glucosidase (-6.6 kJ/mol). The synergistic potential of acarbose and cellobiose was also investigated, this showed higher inhibition of the α-amylase than when the two compounds were used alone. Combination therapy of cellobiose and acarbose against amylolytic enzymes may show potential as an antidiabetic with reduced side effects.

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