

ABSTRACT

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Biological and Medical Sciences

Title of Diploma Thesis: Effect of dapagliflozin on the expression and function of endoglin and related biomarkers of endothelial dysfunction in human diabetic coronary artery endothelial cells

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Aim: The aim of this thesis was to investigate how dapagliflozin affects the expression and function of endoglin (Eng) and related biomarkers of endothelial dysfunction at different times and concentrations in human diabetic cells.

Methods: In this thesis, we worked with human diabetic coronary endothelial cells. We premedicated these with dapagliflozin at different times and concentrations, and dimethyl sulfoxide was used as a control. We measured protein expression of Eng and biomarkers of endothelial dysfunction using flow cytometry. We also used flow cytometry to measure the rate of monocyte adhesion to endothelial. Using ELISA, we detected soluble endoglin (sEng) levels.

Results: We demonstrated that a 1nM concentration of dapagliflozin during a 12-hour premedication period led to a decrease in protein expression of adhesion molecules. We further showed that protein expression of Eng was also significantly reduced with low concentrations of dapagliflozin. At the times and concentrations examined, dapagliflozin had no significant effect on monocyte adhesion or on sEng formation.

Conclusion: In conclusion, low concentrations of dapagliflozin may lead to decreased protein expression of Eng and adhesion molecules. However, protein expression of Eng was not reduced sufficiently to have a significant effect on monocyte adhesion to endothelial cells, nor on soluble endoglin formation.

Keywords: endoglin, endothelial dysfunction, diabetes mellitus, dapagliflozin