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Caracterização farmacológica das gliflozinas em plaquetas humanas isoladas: avaliação in vitro.

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Abstract

Gliflozins are relatively recent drugs, and have been incorporated into the arsenal of the treatment of diabetics. To these, a favorable cardiovascular effect was attributed to clinical data from diabetic patients treated with similar therapies compared to glyphlozines. The project sought to investigate the performance of these drugs in platelets, since they are emblematic figures in the main pathophysiology of the disease that has the highest cause of death in the world: Coronary artery disease.

Key words:

gliflozin, platelet aggregation, platelets.

Introduction

Recent clinical studies have shown that diabetic patients who received canagliflozine or dapagliflozin, drugs approved for the treatment of type II diabetes, had improvements in cardiovascular outcomes assessed as death from cardiovascular causes and fewer hospitalizations for congestive heart failure compared to patients who did not received canagliflozin or dapagliflozin. Arterial thrombosis and atherosclerosis are regulated by complex interactions involving several families of molecules present in platelets. Thus, the main objective of this project was to evaluate the in vitro effects of canagliflozin, dapagliflozin and empagliflozin on platelet-rich plasma and isolated platelets obtained from healthy volunteers and their effects on calcium mobilization, cyclic nucleotide levels and time activated partial thromboplastin (aPTT).

Results and Discussion

Gliflozins were able to inhibit platelet aggregation against the collagen agonist, ADP, thrombin and U-46619, a stable analogue of thromboxane A2. The results were better in the presence of the endothelial mediators against the collagen agonist. The mobilization of intracellular calcium in platelets was lower in the presence of canagliflozin and dapagliflozin. On the other hand, the glyphlozins did not significantly influence the levels of the cAMP and cGMP nucleotides and the APTT were not affected by the glyphlozins.

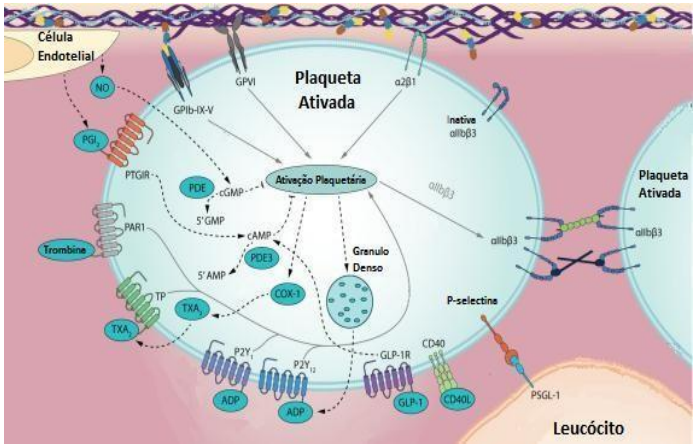

Figure 1. Platelet aggregation mechanism[4]

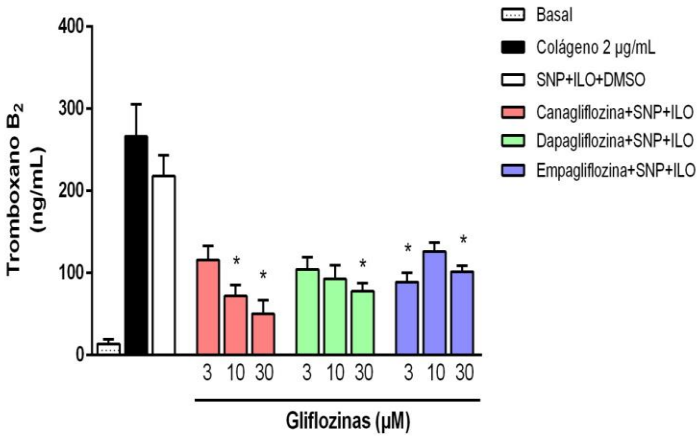

Figure 2. The columns show an indirect reduction by measuring the stable metabolite of the platelet thromboxane A2 molecule. As concentrations of the glyphlozins added to the platelet rich plasma are increased, a trend towards a reduction in thromboxane B2 concentration is seen.

Conclusions

The favorable results lead to a partial clarification of the mechanism of action of these drugs in the platelet, directing the new steps of this investigation.

Acknowledgement

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1. Abdul-Ghani, M.A., Norton, L., and Defronzo, R.A. (2011). Role of sodium-glucose cotransporter 2 (SGLT 2) inhibitors in the treatment of type 2 diabetes. Endocrine reviews 32, 515-531.
2. Davì, G., and Patrono, C. (2007). Platelet activation and atherothrombosis. New England Journal of Medicine 357, 2482-2494.
3. Inzucchi, S.E., Zinman, B., Wanner, C., Ferrari, R., Fitchett, D., Hantel, S., Espadero, R.-M., Woerle, H.-J., Broedl, U.C., and Johansen, O.E. (2015). SGLT-2 inhibitors and cardiovascular risk: proposed pathways and review of ongoing outcome trials. Diabetes and vascular disease Research 12, 90-100.
4. Ruggeri, Z.M. Platelets in atherothrombosis. *Nature medicine* **8**, 1227-1234 (2002).

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