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Master Thesis Defense

Entitled

The Effect of Licogliflozin (SGLT1/2 inhibitor) on Diabetes and Cardiac Complications

by

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Date & Venue

13:00 h
Thursday - November 24, 2022
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Abstract:

Diabetes mellitus (DM) is a chronic endocrine disease affecting millions of people worldwide. In spite of the advances made in the management of DM, poor glycemic control and diabetes complications are still very common. There is a continuous search for new and more effective drugs to treat DM. One of the drugs currently in clinical trials for the treatment of DM is licogliflozin (LIK066), a dual SGLT1/2 inhibitor, which can be used to treat obesity and diabetes. LIK066 inhibits glucose reabsorption in the kidney and small intestine, thereby reducing hyperglycemia. The aim of this study was to investigate the efficacy of licogliflozin on diabetes and cardiac complications in a rodent model of experimental diabetes. DM was induced by streptozotocin in male Wistar rats. This was followed by the administration of LIK066 at a dose of 0.588 mg/Kg given intraperitoneally for 4 weeks. Immunofluorescence technique was used to determine whether SGLT1/2 is found in the pancreas and to determine if it co-localizes with insulin in pancreatic islet cells. Markers of cardiomyopathy (Collage 3, TIMP4, Keap1, fibronectin) and oxidative stress (catalase, superoxide dismutase, glutathione reductase) were also examined using immunofluorescence and Masson staining and enzyme immunoabsorbent essay in heart homogenates and the serum. Moreover, oxidative stress markers were also studied in the pancreas using immunofluorescence techniques and in serum by colorimetric analysis. LIK066 causes slight weight reduction in diabetic rats. SGLT1 and SGLT2 are expressed in pancreatic islet cells, where they co-localize with insulin in normal and diabetic rats. TIMP4 result shows a significant elevation in LIK066-treated diabetic rats compared to diabetic untreated causing improvement in diabetic cardiomyopathy. In the pancreas, LIK066 caused significant elevation in glutathione (GSH) compared to untreated DM rats. Heart muscle catalase level shows a significant increase in diabetic rats after treatment with LIK066 when compared to diabetic untreated rats. Moreover, GSH reductase was significantly increased in diabetic rats treated with LIK066. In conclusion, LIK066 may exert its beneficial effects by increasing the endogenous pool of antioxidants.

Keywords: Diabetes mellitus, Pancreas, Cardiovascular disease, Licogliflozin, Immunohistochemistry, Dual SGLT1/2 inhibitors, Oxidative stress.