Macedonian Pharmaceutical Bulletin, 66 (Suppl 1) 41 - 42 (2020)
Online ISSN 1857 - 8969
UDC: 615.322:582.684.1-192]:612.173
DOI: 10.33320/maced.pharm.bull.2020.66.04.020
Short communication

The effects of transgenic root extracts of *Hypericum perforatum* L. on carbohydrate metabolism in heart of diabetic rats

Kristiana Shijakova, Elena Rafailovska, Oliver Tushevski, Sonja Gadzovska-Simic, Suzana Dinevska-Kjovkarovska, Biljana Miova*

Institute of Biology, Faculty of Natural Sciences and Mathematics,
Ss. Cyril and Methodius University, Arhimedova 3, 1000 Skopje, R.N. Macedonia

Introduction

Hypericum perforatum L. (St. John's wort) is still one of the most important medicinal plants widely used in herbal medicine as a source of bioactive metabolites. Among the many biological activities of the plant (antidepressant, anti-inflammatory, antiviral, anti-cancer, antibacterial and antihyperglicemic) (Asgarpanah, 2012), *H. perforatum* extracts were found to be endowed with the ability to modulate the activity of key enzymes from the carbohydrate metabolism in diabetic rats (Arokiyaraj et al., 2011). Among the phenolic compounds present in the species are xanthones, a class of secondary metabolites that are known as the most potent antidiabetic agents with powerful antioxidant activities (Vladimirovna and Chi, 2016).

The downside is that this class of compounds occurs in traces in the field-grown plants (hyperici herba - HH) and are mainly accumulated in the roots. However**,** *H. perforatum* transgenic roots cultures (HR) are characterized with the strong capacity for xanthone accumulation (Tusevski et al., 2013). Based on the above knowledge, in this study we investigated the effect of HH and HR extracts on the heart carbohydrate-related key enzymes and substrates in control and diabetic rats, as well as markers of tissue damage in the blood.

Materials and methods

For the experimental purposes, adult male Wistar rats (200 - 250 g) were used. We estimated the effect of hyperici herba (HH, and hairy roots (HR) extracts in healthy and streptozotocin induced-diabetic rats. The extraction of bioactive compounds from HH and HR powder was made using 80% (v/v) CH_3OH (Gadzovska et al., 2005). The obtained dry HH and HR extracts were dissolved in 0.3% CMC and administrated daily as a single dose (200 mg/kg bw), in a 14 days' treatment. Glibenclamide (Glb) was used as a positive control. Key carbohydrate enzymes and substrates were assessed in heart tissues homogenate by appropriate enzymatic methods, as well as plasma enzyme profile were determined by colorimetric methods.

Results and discussion

Our results show that experimental diabetes caused a significant increase of heart Glu concentration and HK activity, which resulted with increased Glc. On the other side, there was decrease of GP*a* activity and G6P concentration in the heart. Namely, the shift of cardiac energy substrate utilization from carbohydrate to lipids increases the intracellular Glc pool, probably through augmented Glk synthesis, or impaired glycogenolysis, or a combination of both processes (Montanari et al.,

* bmiova@pmf.ukim.mk

2005). Some studies indicated that transmembrane Glc gradient is determined by the interstitial and intracellular free Glc concentration, which in hyperglycemia, accompanying STZ-induced diabetes are helping to compensate for the decreased capacity for sarcolemmal Glc transport as a result of decreased GLUT transporters (Stanley et al., 1997). Therefore, taking in consideration these changes, the increased HK activity that we found in the heart of diabetic animals, is probably important mechanism that facilitates Glc input into the cell and regulates intracellular Glc content.

Both HH and HR treatment of diabetic rats' reverses and even normalizes the Glc content up to control values. Still, concerning heart Glu content, there was even more evident increase by both HH and HR compared to diabetic rats. These changes were accompanied with still elevated HK activity in DHH and DHR animals. Compared to diabetic animals, HH and HR treatment did not cause significant changes in GP*a* activity and G6P content. Finally, both HH and HR caused increase of Glc content, decrease of Glu and G6P content, decreased GPa and increased HK activity.

The main two active ingredients of *H. perforatum* extract appear to be complementary in inhibiting inflammatory signaling in pancreatic beta cells and improving insulin sensitivity in peripheral tissues. In this sense, Tian et al. (2015) suggests that *H. perforatum*, and in particular its naphthodianthrone components, facilitates insulin-dependent glucose uptake in skeletal muscle. As to our knowledge, no data were found for effects of *H. perforatum* over cardiac muscle in diabetic state.

AST and ALT are intracellular enzymes, which have been widely used in clinical practice to evaluate extent of liver injury or myocardial injury. Namely, increased serum activity of these enzymes due to their leakage in the blood indicates tissue damage (McGill, 2016). Our results show that STZ causes significant increase of ALT activity, but did not affect the activity of AST. Glb treatment had no significant effect on any of the parameters. Administration of HH and HR extracts significantly reduced the activity of ALT, but did affect the activity of AST in diabetic animals. Also, both extracts show non-significant effect on these parameters in healthy animals. Arokiyaraj et al. (2011) showed similar effects of HH extracts in the study.

Conclusion

Our findings indicate that HH and HR treatments manifested only moderate improvement of the carbohydrate-related enzymes in the heart of diabetic animals. Also, there was moderate tissue damage in this model of STZ-induced diabetes and both HH and HR extracts tended to reverse the markers of tissue damage.

References

Arokiyaraj, S., Balamurugan, R., Augustian, P., 2011. Antihyperglycemic effect of *Hypericum perforatum* ethyl acetate extract on streptozotocin–induced diabetic rats. Asian Pacific J. of Tropical Biomedicine 1(5), 386-390.

Asgarpanah, J., 2012. Phytochemistry, pharmacology and medicinal properties of *Hypericum perforatum* L. African Journal of Pharmacy and Pharmacology 6(19), 1387-1394.

Gadzovska, S., Maury, S., Ounnar, S., Righezza, M., Kascakova, S., Refregiers, M., Spasenoski, M., Joseph, C. and Hagège. D., 2005. Identification and quantification of hypericin and pseudohypericin in different *Hypericum perforatum* L. in vitro cultures. Plant Physiology and Biochemistry 43(6), 591-601.

McGill, M. R., 2016. The past and present of serum aminotransferases and the future of liver injury biomarkers. EXCLI journal 15, 817.

Montanari, D., Yin, H., Dobrzynski, E., Agata, J., Yoshida, H., Chao, J., and Chao L., 2005. Kallikrein gene delivery improves serum glucose and lipid profiles and cardiac function in streptozotocin-induced diabetic rats. Diabetes 54, 1573-1580.

Tian, J-Y., Tao, R-Y., Zhang, X-L., Liu, Q., He, Y-B., Su, Y-L., Ji, T-F. and Ye, F. 2015. Effect of *Hypericum perforatum* L. extract on insulin resistance and lipid metabolic disorder in high-fat-diet induced obese mice. Phytother. Res. 29, 86-92.

Tusevski, O., Stanoeva, J. P., Stefova, M., Kungulovski, Dz., Pancevska, N., Sekulovski, N., Panov, S. and Simic S., 2013. Hairy roots of *Hypericum perforatum* L.: a promising system for xanthone production. Central European Journal of Biology 8(10), 1010-1022.