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Short communication

Antioxidant potential of *Hypericum perforatum* L. hairy roots extracts in the kidney of STZ-induced diabetic rats

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Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia, which further generates reactive oxygen species (ROS) and increased oxidative stress in the organism. This hyperglycemia-induced oxidative stress in diabetes mellitus causes several adverse effects on the cellular physiology, associated with dysfunction of normal functioning of various tissues, including kidneys (Jha et al., 2016).

Hypericum perforatum L. is one of the most important medicinal plants widely used in herbal medicine as a source of bioactive metabolites (Nahrstedt and Butterweck, 2010), related to its antidepressant, antioxidant, analgesic, anti-inflammatory, cytotoxic and antidiabetic effects (Nahrstedt and Butterweck, 2010; Arokiyaraj et al., 2011, Rafailovska et al., 2021).

In order to increase the production of phenolic compounds in *H. perforatum*, models of genetic transformation using *Agrobacterium rhizogenes* are employed (Tusevski et al., 2013). Among these, predominant phenolic compounds in the HR cultures are xanthones (Tusevski et al., 2013). We have previously reported the antihyperglycemic effects of *Hypericum perforatum* hairy roots extracts (HR) in STZ - induced diabetic rats (Rafailovska et al, 2021).

The kidney is an organ that is very sensitive to damage caused by ROS, probably due to the abundance of polyunsaturated fatty acids in the renal composition (Jha et al., 2016). Thus, the aim of this study was to investigate the antioxidant activity of both wild growing Hyperici herba (HH) and transgenic hairy roots (HR) extracts form *H. perforatum* in the kidney of STZ-diabetic rats.

Materials and Methods

We used adult male Wistar rats (200 - 250 g) for the experimental purposes. Experimental diabetes was induced by single intraperitoneal injection of streptozotocitn (45 mg/kg) freshly dissolved in citrate buffer (pH 4.5). The rats were divided into healthy (control) and diabetic groups, which were further treated with both HH and HR extracts. For the extraction of the bioactive compounds from HH and HR powder, 80% (v/v) CH_3OH was used (Gadzovska et al., 2005). The obtained dry HH and HR extracts were dissolved in 0.3% CMC and administrated via feeding needle, daily as a single dose (200 mg/kg/b.w.), in a 14 days treatment. Standard hypoglycemic drug Glibenclamide was used as positive control.

We estimated the activity of antioxidative enzymes superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx) as well as total glutathione (GSH) and malondialdehyde (MDA) concertation in the kidney tissue homogenate.

Results and discussion

Our results show that experimental diabetes caused a significant decrease in GSH concentration, CAT and SOD activity in the kidney. This reduction is an indicator of tissue degeneration (Andersen, 2004). On the other hand, our results showed that the experimental diabetes caused significant increase in GR and GPx activity. Increased GR activity indicates that intensive reduction of oxidized glutathione occurs in the kidney of diabetic rats, which in

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turn indicates that intensive consumption of reduced glutathione occurs at the same time. Namely, the increased activity of GPx confirms that diabetic state induce oxidative stress in the kidneys of diabetic animals, followed by overproduction of free radicals. Furthermore, there was significant increase in renal MDA concentration, which indicates intensive lipid peroxidation, resulting from overproduction of ROS in hyperglycemic conditions.

The treatment of diabetic animals with HH and HR caused normalization of the estimated parameters. Namely, both HH and HR extracts increased the GSH concentration. Additionally, both treatments caused significant increase and normalization of CAT and SOD activity. Both treatments with HH and HR extracts caused significant decrease and normalization of GR activity and MDA content in the kidney. According to Silva et al. (2008), the antioxidant action of *H. perforatum* extract is due to the high content of polyphenolic compounds, primarily flavonoids and phenolic acids. Flavonoids are particularly interesting because of their antioxidant properties, and their excellent ability to scavenge free radicals, as well as their antidiabetic potential (Coskun et al., 2005). This finally which leads to a significant improvement in antioxidant defense and reduction in oxidative stress in the kidney of STZ-diabetic rats.

Concerning effects of hairy roots extracts, to the best of our knowledge there are no data about the antioxidant properties of HR extracts *in vivo*. However, aaccording to a study by Gondi and Rao (2015), ethanoic extract of *Mangifera indica* and its active component mangiferin increases the activity of SOD, CAT, and GR in the kidney, liver, and serum of STZ-diabetic rats. This is probably due to the extract's ability to neutralize free radicals, which further improves the activities of antioxidant enzymes and the diabetic condition of rats. In the study of Mahendran et al. (2014), the authors found that the extract of *Swertia corymbosa* (rich in xanthones), leads to an increase and normalization of the concentration of GSH in the kidney and liver of STZ-diabetic rats. Our assumption is that the increased GSH concentrations and normalization of GR activity are clear indications that xanthones present in HR extract might have stabilized the renal glutathione redox cycle in STZ-diabetic animals, indicating a general improvement in redox potential in diabetic animal's kidney.

Conclusion

Based on the obtained results, the general conclusion is that both extracts regulate and normalize the activity of endogenous antioxidant enzymes and substrates, which generally reduce the oxidative stress in renal tissue caused by the diabetic condition. HR extract has more pronounced antioxidant effects in kidney of diabetic rats.

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