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Original article

Diosmin ameliorates the effects of oxidative stress in lenses of streptozotocin-induced type 1 diabetic rats

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ABSTRACT

Background: Diabetic cataractogenesis is a complex process connected with hyperglycemia and oxidative stress. Free radicals induce many unfavorable changes in the activity of the antioxidative enzymes and may also lead to oxidative damage. Since diosmin, a plant-derived flavonoid, reveals antioxidative activity, the aim of the study was to investigate if this substance may counteract the oxidative stress in the lenses of diabetic rats.

Methods: The study was conducted on the male Wistar rats with streptozotocin-induced type 1 diabetes. After the administration of diosmin at the doses of 50 and 100 mg/kg for 4 weeks the oxidative stress markers in the lenses of these rats were evaluated. Tested markers included: activity of superoxide dismutase, catalase and glutathione peroxidase, as well as levels of total and soluble protein, level of glutathione, vitamin C, advanced oxidation protein products and malonyldialdehyde.

Results: The obtained results indicate that the administration of diosmin to the diabetic rats counteracted the unfavorable changes induced by diabetes in the lenses.

Conclusion: It can be assumed that diosmin may be a promising compound in prevention or delaying the cataract formation during diabetes.

Introduction

Long-term hyperglycemia is one of the major factors inducing ocular complications including diabetic retinopathy, glaucoma, dry eye disease and cataract [1]. The development of diabetic cataract can be related to the elevated levels of blood sugar and the accelerated aging of the lens. Diabetic patients are 2–5 times more exposed to cataract formation than healthy people. They are also more likely to be affected by the disease earlier than non-diabetic patients [2].

There are many factors responsible for cataract development in diabetes mellitus: oxidative stress, enhanced polyol pathway and nonenzimatic protein glycation. During oxidative stress, high levels of free radicals may lead to the damage of cellular proteins or lipids and, eventually, to the cell death [3]. Free radicals can induce precipitation of soluble proteins of the lens which are responsible for light refraction by oxidation of their –SH groups, as well as the oxidation of polyunsaturated fatty acids in the lens [4]. Even though cataract surgery is considered to be safe, in diabetic patients there is higher risk that surgery-associated complications may occur [5].

Prolonged hyperglycemia may cause mitochondrial overproduction of reactive oxygen species (ROS) [6,7]. As it is well known, in response to the excess of ROS, antioxidative enzymes are activated. However in the diabetic conditions the activity of these enzymes may be changed by nonenzymatic glycation or altered metabolism of their cofactors [8]. What is more, several side pathways related to hyperglycemia, such as polyol pathway, consume coenzymes required to converting oxidized glutathione to its reduced form leading to endogenous antioxidants insufficiency [9]. Therefore, since during diabetes the endogenous antioxidative defense is disturbed, the excess of free radicals may lead to oxidative damages and the development of diabetes-associated complications [3]. To avoid an enhanced oxidative stress expansion and cataract development in diabetic patients, exogenous antioxidants could be supplied. There are many polyphenolic plant-derived compounds with well-known antioxidative activity. Among them, there is diosmin, a citrus flavonoid which shows antioxidative properties resulting from its structure and the ability to formation of intramolecular hydrogen bond [10]. In addition to the antioxidative activity, diosmin demonstrates also

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the protective effect in diabetes. It counteracts the oxidative stress in the plasma, liver and kidneys of diabetic rats, lowers glucose and glycated hemoglobin levels in plasma and shows protective activity against diabetic neuropathy in rats [11–14]. As for now, there is only one *in vitro* study describing the effect of diosmin on sugar-induced cataract formation in goat lenses [15].

Since there is no *in vivo* evidence, the aim of the presented study was to evaluate the effect of diosmin on oxidative stress markers in lenses of streptozotocin-induced type 1 diabetic rats.

Material and methods

Animals and diabetes induction

The experiment was conducted on 3-month old Wistar male rats, provided by the Centre of Experimental Medicine at the Medical University of Silesia. The study was approved by the Local Ethics Commission, Katowice, Poland, approval no. 30/2015. The animals were fed a standard laboratory chow and had unlimited access to the water.

The rats were divided into 4 groups ($n = 8–9$): C – control rats, DM – diabetic rats, Dio50 – diabetic rats treated with diosmin at a dose of 50 mg/kg and Dio100 – diabetic rats treated with diosmin at a dose of 100 mg/kg. Type 1 diabetes mellitus was induced by singular intraperitoneal (*ip*) injection of streptozotocin (STZ) solution in citric buffer at a dose of 60 mg/kg [16,17]. To the further stage of the experiment, the animals were classified as diabetic if the blood glucose level after 2 weeks from STZ injection was over 200 mg/dl. To the Dio50 and Dio100 groups diosmin suspended in water was administered orally (*po*) by the use of intragastric tube for 28 days, once a day. The groups C and DM were vehicle treated with water. The body weight was measured in the day of STZ injection (initial body weight), after 2 weeks from STZ injection (start body weight) and after 4 weeks of diosmin and water administration (final body weight). Body weight gain was estimated based on the difference between final body weight and start body weight. After 4 weeks of diosmin and water administration rats were sacrificed by general anesthesia by the use of ketamine and xylazine mixture (87.5 mg/kg + 12.5 mg/kg), the lenses were collected, weighted and homogenized in PBS buffer, pH 7.4 (10% v/w). Total homogenate was used for the analysis of total protein and malonyldialdehyde, the remaining homogenate was centrifuged at 10,000×g (15 min, +4°C). Assays were measured in Tecan Infinite M200 PRO microplate reader with Magellan 7.2 Software.

Total and soluble protein level estimation

The analysis of total protein (TP) and soluble protein (SP) was conducted according to Lowry's method with the use of Folin-Ciocalteu (FC) reagent. Briefly, the diluted homogenate was transferred into the test-tube, and the mixture of 2% Na_2CO_3 solution in 0.1 M NaOH, 1% $CuSO_4$ and 2% potassium-sodium tartrate was added and incubated for 10 min, then FC reagent was added. After 30 min of incubation, samples were transferred into 96-well microplate and read at 750 nm, BSA was used as a reference [18].

Enzymes activity assays

The activity of the enzymes related with antioxidative response: superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) were tested with commercial kits (Cayman Chemical Company, MI, USA). In the SOD method, the reaction of xhathine oxidase converting the xanthine into uric acid with generation of superoxide radicals. These radicals are bounded by tetrazolium salt with formation of red colored formazan. The main principle of CAT kit is colorimetric measurement of formaldehyde produced by CAT from methanol in the presence of an optimal concentration of hydrogen peroxide. In the GPx assay coupled reaction is used to indirect measurement of the enzyme's activity. In the first step oxidized glutathione (GSSG) is formed by GPx. Afterwards, GSSG, along with NADPH are reduced by glutathione reductase to the reduced form and $NADP^+$. Decrease of absorbance resulting from oxidation of NADPH to $NADP^+$ is proportional to GPx activity.

Oxidative stress markers level estimation

Glutathione (GSH) analysis was carried out according to the method described by Sedlak and Lindsey with the use of Ellman's reagent (DTNB). Briefly, the homogenates were deproteinized by addition of 10% trichloroacetic acid (TCA), then centrifuged. To the obtained supernatants, which were transferred to the 96-well plate, phosphate buffer (pH 8.0) and 0.01 M DTNB were added, then measured at 412 nm, with GSH used as a reference [19,20]. Level of vitamin C (VC) was evaluated according to the procedure described by Jagota and Dani. In this method 10% TCA was added to the homogenates (1:1 TCA and sample ratio) in order to deprotein the samples, then centrifuged. Obtained supernatants were transferred to the microplate, and FC reagent was added. At low pH value FC reagent react specifically with VC. Samples were read at 750 nm, standard curve was prepared with vitamin C [21]. Advanced oxidation protein products (AOPP) assay was conducted based on the protocol described by Witko-Sarsat et al. To the homogenates diluted with 0.01 M PBS, 1.16 M solution of potassium iodide was added. The reaction was stopped with acetic acid and read at 340 nm with chloramine-T used as a reference [22]. The test for malonyldialdehyde (MDA) was carried out according to the method presented by Ohkawa et al. Briefly, to the homogenates 8.1% SDS, 20% acetic acid, and 0.8% TBA were added. The mixture was well mixed, then heated for 60 min in boiling water. After cooling, the mixture of pyridine with n-butanol (1:15) was added, samples were precisely mixed and centrifuged at 4,000×g for 5 min. Supernatants were transferred into the 96-well plate and measured at 532 nm with 1,1,3,3-tetraethoxypropane used as a reference [23].

Statistical analysis

The obtained results were evaluated statistically in Statisctica10 Software by one-way ANOVA followed by Duncan test. The results are presented as mean ± SEM. Differences were considered as statistically significant if p value <0.05: $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$ – statistically significant differences in comparison to the C group, $^{\circ}p < 0.05$; $^{\circ\circ}p < 0.01$; $^{\circ\circ\circ}p < 0.001$ – statistically significant differences between the Dio50 or Dio100 and the DM group.

Results

The effect of diosmin on body weight and lenses weight in diabetic rats

After 2 weeks from STZ injection a decrease of the body weight in the diabetic (DM) rats by 20.0% ($p < 0.001$), diabetic rats treated with diosmin at a dose of 50 mg/kg (Dio50) by 17.5% ($p < 0.001$) and treated with diosmin at a dose of 100 mg/kg (Dio100) by 16.9% ($p < 0.001$) in comparison with the control (C) rats was observed. At the end of the experiment the final body weight of the DM rats was lower by 33.8% ($p < 0.001$), in comparison with the C rats. A 4 weeks administration of diosmin to the diabetic rats at both the doses did not cause statistically significant changes in the final

body weight in comparison with the DM and C group, however, in the Dio100 group there was a tendency to increase the final body weight ($p = 0.09$), when compared to the DM rats. The body weight gain in the DM rats was lower by 168.6% ($p < 0.001$), as compared to that in the C group. No changes in the body weight gain in the Dio50 rats were observed, in comparison with the DM and C rats. In the Dio100 group, there was an increased body weight gain by 58.1% ($p < 0.05$), when compared to the DM group.

In the DM rats, the mean weight of the lenses was lower by 9.0% ($p < 0.001$) in comparison with the C rats. In the Dio50 and Dio100 groups no changes in the mean weight of the lenses were noted in comparison with the DM rats, and the mean weight of the lenses was significantly lower in these groups than in the C rats (Table 1).

Before STZ injection, the blood glucose level in all groups of rats was between 97 and 145 mg/dl (below 200 mg/dl). Two weeks after STZ injection, the blood glucose level in the DM, Dio50 and Dio100 groups exceeded the 200 mg/dl level and even reached values above 600 mg/dl. After 4 weeks of diosmin administration, there were no significant changes with regard to this parameter in the Dio50 and Dio100 groups (data not shown).

The effect of diosmin on the total and soluble protein level in the lenses of the diabetic rats

No significant changes were observed in the total protein (TP) level after diabetes induction in rats, when compared to the C rats. The administration of diosmin at both the doses did not change this parameter, as compared to the C and DM rats. In the DM group, the soluble protein (SP) level was lower by 7.9% ($p < 0.05$) in comparison with the C rats. The administration of diosmin to the diabetic rats resulted in an increase of SP level by 10.8% ($p < 0.01$) in the Dio50 group and by 12.7% ($p < 0.01$) in the Dio100 group when compared to the DM rats, while no changes in this parameter were recorded in comparison with the C group (Table 2).

The effect of diosmin on the enzymes activity in the lenses of the diabetic rats

SOD activity in the lenses of the DM rats was higher by 44.2% ($p < 0.001$), as compared to the C rats. When compared to the C group, in the Dio50 and Dio100 groups activity of SOD was significantly elevated, but administration of diosmin at both the doses led to the decrease in this parameter by 19.5% ($p < 0.001$) and 14.7% ($p < 0.001$) respectively, when compared to the DM group. In comparison with the C rats, in the DM rats an increase of the CAT activity in the lenses by 167.1% ($p < 0.001$) was observed. In the Dio50 and Dio100 groups, there was a decrease of CAT activity by 38.6% ($p < 0.01$) and 42.3% ($p < 0.01$) respectively when compared to the DM rats, no statistically significant changes were observed between Dio50, Dio100 and C groups. The activity of GPx in the lenses was insignificantly higher in the DM rats than in the C rats. The administration of diosmin at both the doses resulted in the decrease of GPx activity by 12.2% ($p < 0.01$) in the Dio50 group and 14.4% ($p < 0.01$) in the Dio100 group, when confronted with the DM group. There was also a significant decrease in this parameter in the Dio50 and Dio100 groups in comparison with the C group (Fig. 1I–III).

The effect of diosmin on oxidative stress markers level in the lenses of the diabetic rats

In the lenses of the DM rats the level of GSH and VC was lower by 82.5% ($p < 0.001$) and 6.3% ($p < 0.001$) respectively, in comparison with the C rats. The administration of diosmin to the diabetic rats did not affect these parameters, when compared to the DM rats, thus they remained significantly lower than in the C group.

In the DM rats AOPP level in the lenses was higher by 26.2% ($p < 0.01$) as compared to the C rats. In comparison with the DM rats, in the Dio50 and Dio100 groups, this parameter was lower by 31.7% ($p < 0.001$) and 37.2% ($p < 0.001$) respectively and in the Dio100 group significantly lower by 20.7% ($p < 0.05$) in comparison with the C group. MDA level was higher by 27.0% ($p < 0.001$) in the lenses of the DM rats than in the C rats. The administration of diosmin to the diabetic rats resulted in a decrease in this parameter by 12.6% ($p < 0.01$) in the Dio50 group and by 14.6% ($p < 0.01$) in the Dio100 group, when confronted with the DM rats. No changes were reported between the Dio50, Dio100 and C groups (Fig. 2I–IV).

Discussion

Diabetic cataractogenesis is a complex process associated with oxidative stress, activation of polyol pathway and protein glycation [2]. Since oxidative stress is one of the major triggers to diabetic cataract development, and cataract surgery may be connected with higher risk of postoperative complications in diabetic patients, there is a need to determine whether there are some antioxidant substances that may delay or prevent the cataract formation. Many plant-derived, polyphenolic substances have proven antioxidative properties.

Diosmin possesses various pharmacological activities including antioxidative ones. There are reports indicating that this flavonoid, administered at the same doses as in our experiment (50 and 100 mg/kg) to the rats with experimentally induced diabetes, reveals antidiabetic effect [13,14]. Since diosmin reveals such properties, we investigated if it may be useful to counteract the oxidative stress induced by diabetes in the lenses of the rats. There is only one *in vitro* report describing the effect of diosmin on sugar-induced cataract [15]. In our study we examined for the first time the effect of diosmin on oxidative stress markers *in vivo* in the lenses of the rats with STZ-induced type 1 diabetes.

Apart from the elevated glucose level, a decreased body weight and an intensified body weight loss are common symptoms in diabetes mellitus. There is a lot of scientific evidence describing the weight loss during diabetes in rats [3,12,24]. Some authors explain

Table 1
Effect of diosmin on body weight and lens weight in diabetic rats.

Parameter/group	C	DM	Dio50	Dio100
Initial body weight (g)	281.2 ± 3.8	283.2 ± 6.2	287.7 ± 6.2	285.2 ± 6.6
Start body weight (g)	312.8 ± 5.9	250.2 ± 8.7***	258.1 ± 8.3***	260.0 ± 8.5***
Final body weight (g)	344.9 ± 5.5	228.2 ± 10.9***	234.7 ± 9.3***	250.8 ± 9.2***
Body weight gain (g)	32.1 ± 2.8	−22.0 ± 5.1***	−23.3 ± 6.3***	−9.2 ± 2.8***°
Lens weight (g)	0.047 ± 0.001	0.043 ± 0.001***	0.043 ± 0.001***	0.043 ± 0.004***

Results were evaluated by one-way ANOVA followed by Duncan test; ***$p < 0.001$ – statistically significant differences in comparison to the C group, °$p < 0.05$ – statistically significant differences between the Dio50 or Dio100 and the DM group.

Table 2
Effect of diosmin on total and soluble protein level in lens of diabetic rats.

Parameter/group	C	DM	Dio50	Dio100
Total protein (mg/g of the lens)	563.2 ± 33.2	536.4 ± 43.7	526.4 ± 25.7	621.5 ± 43.6
Soluble protein (mg/g of the lens)	443.8 ± 8.4	408.5 ± 13.9*	452.8 ± 9.9°°	460.3 ± 10.7°°

Results were evaluated by one-way ANOVA followed by Duncan test; *$p < 0.05$ – statistically significant differences in comparison to the C group, °°$p < 0.01$ – statistically significant differences between the Dio50 or Dio100 and the DM group.

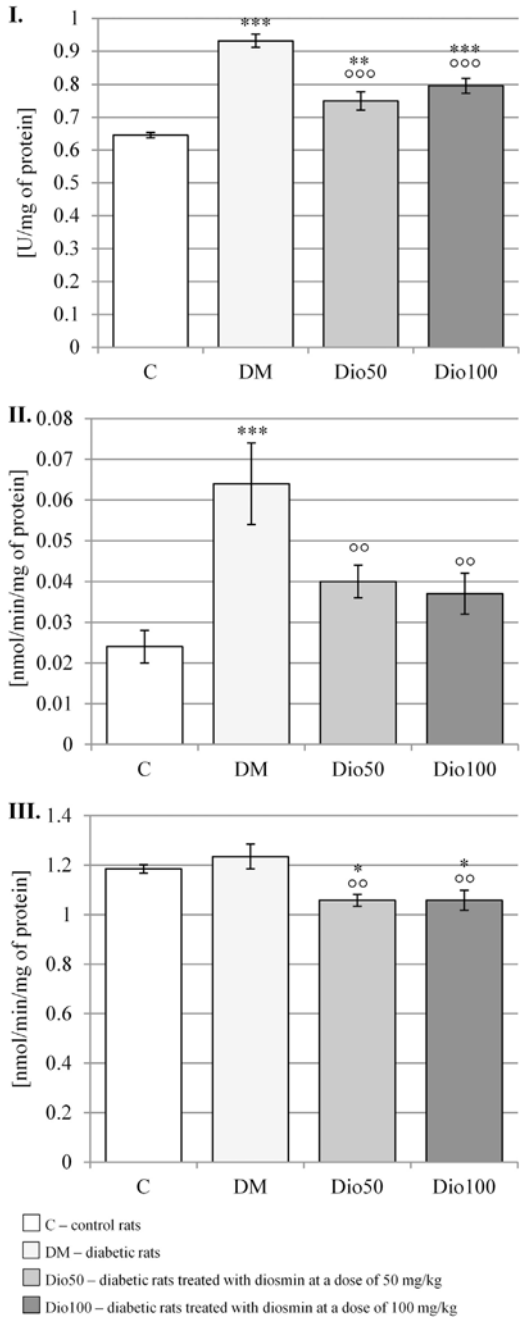

Fig. 1. Effect of diosmin administration on the enzymes activity in the lenses of the diabetic rats: (I) SOD, (II) CAT, (III) GPx. Results were evaluated by one-way ANOVA followed by Duncan test; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ – statistically significant differences in comparison to the C group, °°$p < 0.01$; °°°$p < 0.001$ – statistically significant differences between the Dio50 or Dio100 and the DM group.

that this loss of body weight is caused by the enhanced catabolism of structural proteins and metabolic alterations associated with insulin deficiency [25]. We assume that lower body weight results in lower lens weight. This observation is confirmed in a study conducted by Patil et al. [26]. There were no significant changes in the body weight of the diabetic rats treated with diosmin in comparison with the non-treated rats. However, there was a tendency to the increase in the final body weight after 4 weeks of administration of diosmin at a dose of 100 mg/kg. The body weight gain after 4 weeks of treatment with diosmin at a dose of 100 mg/kg was significantly higher than the one in diabetic rats. This may indicate that the higher dose of diosmin shows protective effect against the diabetes-induced intensified body weight loss. This observation is confirmed by other studies [13,14].

Due to the aggregation of the crystalins in the lenses of diabetic rats, a decrease of soluble protein is observed. Some reports on short-term studies show that only soluble fraction decreases while total fraction remains unchanged [27,28], what corresponds with the results obtained in this study. On the other hand, some long-term studies, where diabetic changes may be more developed, indicate that along with soluble protein level, there is also a total protein level decrease [29–31]. While there were no changes in total protein level in the lenses after diosmin administration to the rats, an increase of the soluble protein was noted, but only when compared to the diabetic rats. Patil et al. in *in vitro* study have shown that incubation of the lenses in the medium containing glucose and 50 μM of diosmin effected in a slight increase of soluble protein in comparison with the lenses cultured in glucose only. The authors, however, do not interpret this result as a significant or positive change [15]. In *in vivo* studies on the lenses in diabetic rats it has been demonstrated that administration of plant-derived substances such as curcumin or tannoids may elevate the level of soluble protein that was reduced in diabetic conditions [30,31]. The increase of soluble protein leads to a better lens transparency, thus obtained results in this study can be interpreted as positive.

Endogenous antioxidative mechanism encompasses enzymatic and nonenzymatic components. To the enzymes involved into defense against free radicals SOD, CAT and GPx are included. Numerous scientific reports indicate that alterations in the activity of these enzymes is one of the major reasons of diabetic catarctogenesis, due to the imbalance between free radicals and antioxidants [29,30]. In our study we observed that in diabetic rats the activity of SOD and CAT was significantly higher than in control rats, and GPx activity tends to be higher than in non-diabetic rats. These results overlap with other studies conducted on the lenses of diabetic rats [26,30,31]. Some authors suggest that an increase in the activity of antioxidant enzymes during diabetes may be a compensatory mechanism to eliminate the oxidative stress [32]. The administration of diosmin to the diabetic rats resulted in the decrease in the activity of all the analyzed enzymes. This may indicate that diosmin reduces the oxidative stress in the lenses of diabetic rats, thus there is no need to synthetize higher amount of these enzymes. Despite the fact that after diosmin administration to the diabetic rats the improvement in the enzymes activity was noted, SOD activity was still significantly higher than in the non-diabetic rats in both the Dio50 and Dio100 groups. It was however observed that CAT activity in both the diosmin-treated groups did not differ significantly from CAT activity in the control group, and

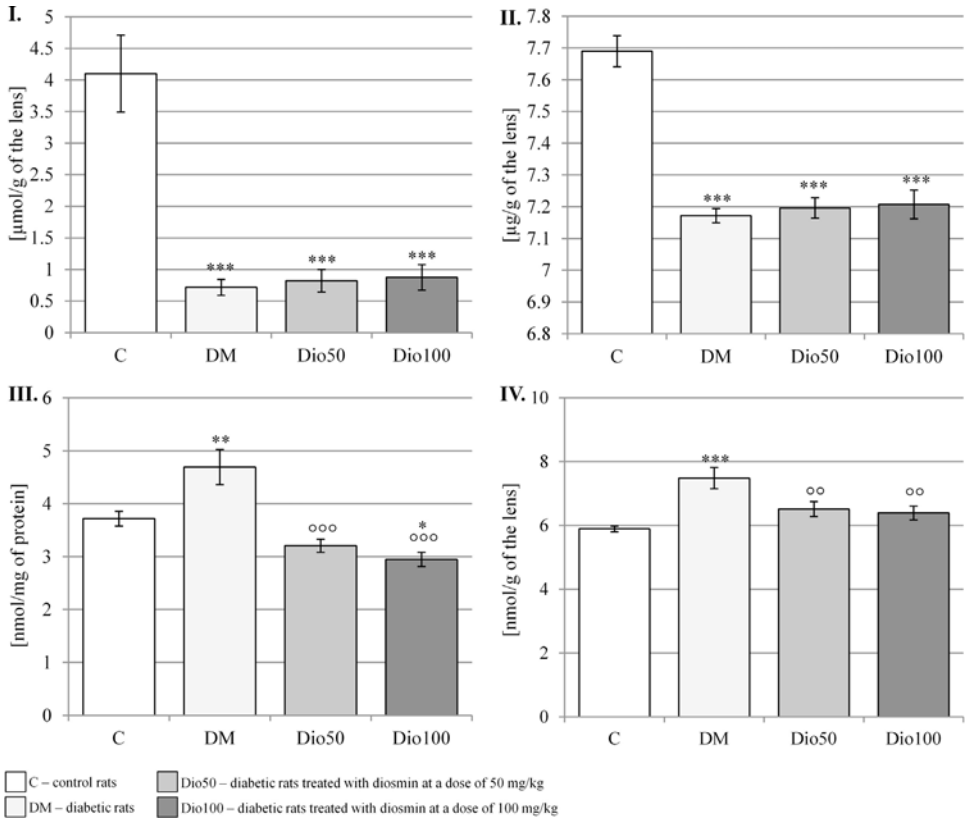

Fig. 2. Effect of diosmin administration on the oxidative stress markers level in the lenses of the diabetic rats: (I) GSH, (II) VC, (III) AOPP, (IV) MDA. Results were evaluated by one-way ANOVA followed by Duncan test; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$ – statistically significant differences in comparison to the C group, $^{\circ\circ}p < 0.01$; $^{\circ\circ\circ}p < 0.001$ – statistically significant differences between the Dio50 or Dio100 and the DM group.

GPx activity was even significantly lower than in the control group. On the basis of this observations it could be speculated, that diosmin may reverse unfavorable oxidative damages resulted from diabetes induction. There are many reports describing the effect of diosmin on antioxidative enzymes in diabetic rats, however, these reports focus on other organs than lenses. In all these studies diosmin administered to the diabetic rats counteracted the activity of SOD, CAT and GPx altered by diabetes. Unlike in the lenses, the activity of SOD, CAT and GPx in the serum, liver or kidney was lower in diabetic rats in comparison with non-diabetic rats, and diosmin treatment effected in the elevation of their activity [12,14]. However, it has been shown that in diabetes the changes in the activity of the antioxidative enzymes may be different in various tissues [33,34], thus there is possibility that in the lenses the response to the oxidative stress is different than in other tissues and organs. This assumption is confirmed by other research conducted on the lenses of diabetic rats. Suryanarayana et al. indicated that curcumin or tannoids administered to the diabetic rats decreased the activity of these enzymes and assumed that this decrease is a positive change [30,31].

Glutathione is an endogenous, nonenzymatic antioxidant, which is one of the main compounds responsible for the redox homeostasis of the organism. In oxidative stress conditions GSH may neutralize free radicals directly through its thiol group or indirectly, as a cofactor for the antioxidative enzymes. In consequence, the level of endogenous GSH decreases [35,36]. In our study we observed that in the lenses of diabetic rats, the level of GSH was significantly reduced. This observations overlap with many other studies [26,30,31]. In rats and other mammals capable of synthesizing vitamin C, this compound is another important antioxidant [37]. It has been shown that during diabetes the level of endogenous vitamin C in the lenses of the rats decreases [38], what corresponds with the results presented in our study. Although there was a beneficial effect of diosmin administration on the antioxidative enzymes activity in the lenses of diabetic rats, there were no changes noted in the levels of endogenous antioxidants (GSH and VC) in the tested organ, and what is more, the values of these parameters still remained significantly lower than in the control rats. Similar effect in the lenses of diabetic rats was observed by Zhao et al. The authors treated diabetic rats with pyruvate, and the GSH level in treated group did not differ significantly from the level recorded in diabetic rats after similar experiment duration time as ours [39].

Witko-Sarsat et al. demonstrated that the imbalance between oxidants and antioxidants leads to the formation of the advanced oxidation protein products, which can be a marker of oxidative stress [22]. In our study the AOPP level in the lenses of diabetic rats was higher than in the control rats. Yildirim et al. in their study showed that there was an increase in this parameter in the lenses of patients with senile diabetic cataract in comparison with the control patients with non-diabetic senile cataract [32]. To the best of our knowledge, there are no other reports on the level of AOPP in the lenses in diabetic subjects. In other studies this marker was useful in the evaluation of oxidative damage in the liver and pancreas of diabetic rats [40,41].

Oxidative stress affects the polyunsaturated fatty acids in the cellular structures and oxidation of the lipids results in MDA formation [4]. Many reports indicate that MDA level in the lenses of diabetic rats and diabetic patients is raised in comparison with non-diabetic subjects [30–32]. These observations correspond with the results obtained in the presented study.

AOPP and MDA levels were significantly lower in the lenses of diabetic rats treated with diosmin at both the doses, than in non-treated rats. A decrease of MDA level in the lenses of diabetic rats

can be interpreted as a beneficial change. What is more there are no significant differences between diosmin-treated groups and the control group, what also indicate the positive response on the flavonoid administration. Other authors investigating the effect of natural compounds on the lenses of diabetic rats obtained similar results [30,31]. There are no reports describing the effect of pharmaceuticals on the AOPP level in the lenses of diabetic subjects. There is, however, a report indicating that elevated AOPP level in the pancreas of diabetic rats can be lowered by a plant extract. The authors of this study concluded that a significant decrease of AOPP level is a favorable effect of the extract administration [42]. Therefore, the result obtained in presented study can be also interpreted as beneficial.

Conclusion

We investigated in the *in vivo* study the effect of diosmin on the oxidative stress markers in the lenses of diabetic rats. The results indicate that this flavonoid shows ameliorative effect on the examined parameters in the lenses of the rats with streptozotocin-induced type 1 diabetes, and it can be a promising compound in the prevention or delaying the cataract formation during diabetes.

Conflict of interests

The authors state that there is no conflict of interests.

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