American Journal of Biomedicine and Pharmacy
https://biojournals.us/index.php/AJBP
ISSN: 2997-7177

Biochemical Analysis of Antioxidant System Enzymes in Type 2 Diabetes

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Received: 2024, 15, Mar
Accepted: 2025, 21, Apr
Published: 2025, 03, May

Annotation: The study of lipid peroxidation (LPO) processes has been studied in depth since the late 1970s. In the works of a number of authors, it has been shown that in patients with experimental diabetes and diabetes mellitus, the level of lipid peroxidation products in blood plasma increases and the activity of antioxidant defense enzymes decreases.

It is known that the induction of lipid peroxidation in biological membranes can be carried out by anion radicals and other active forms of oxygen, which triggers a whole cascade of free radical oxidation reactions, the products of which have a toxic effect on the cell and may be one of the pathogenetic factors of the specific development of insulin-dependent diabetes mellitus.

Since the primary and secondary products of lipid peroxidation have a detrimental effect on the cell, the body has regulatory mechanisms that limit the accumulation of highly toxic products, which is called antioxidant defense. Enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GLP), and glutathione reductase play a leading role in the regulation of lipid peroxidation.

There are conflicting opinions in the literature about the nature of changes in the activity of antioxidant enzymes in diabetes mellitus in children. Therefore, the aim of our

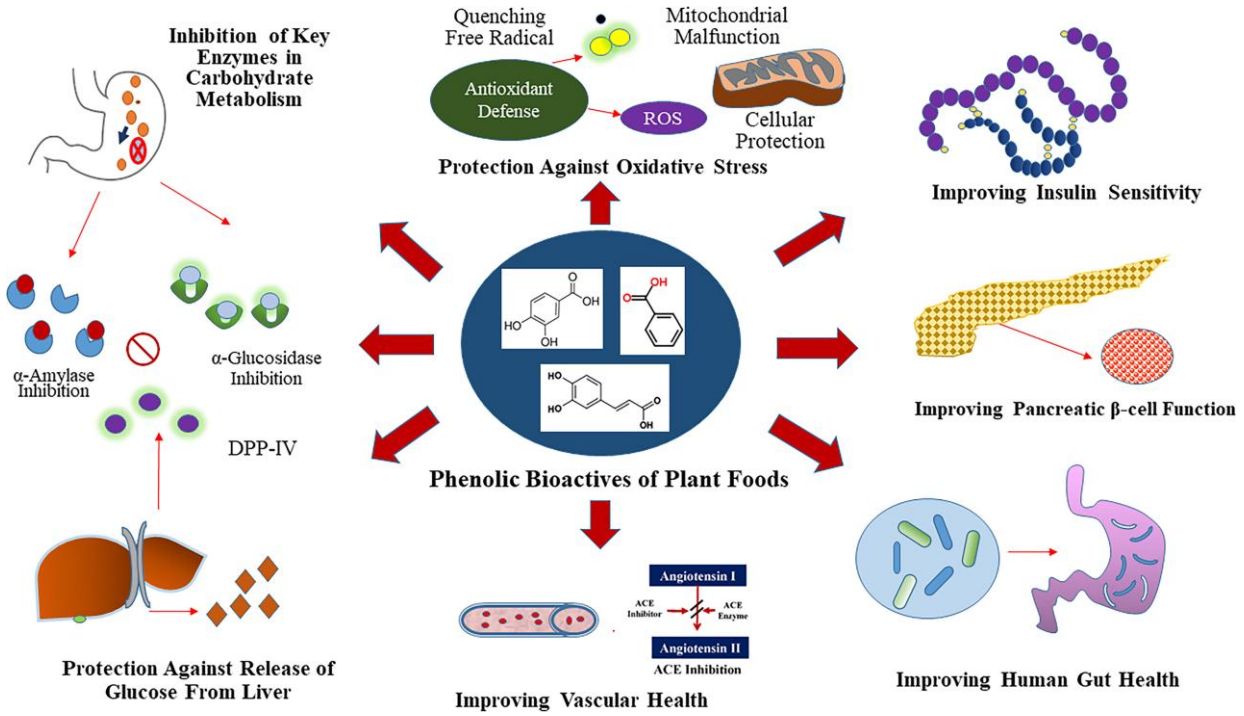
study was to show how the activity of antioxidant enzymes in children changes depending on the degree of compensation and duration of the disease.

Keywords: Diabetes, Antioxidants, Lipid peroxidation.

Introduction: Lipid peroxidation (LPO) processes have been studied in depth since the late 1970s. Studies by a number of authors [1, 3, 7] have shown that in experimental diabetes mellitus and diabetic patients, the level of lipid peroxidation products in blood plasma is increased and the activity of antioxidant defense enzymes is reduced.

It is known that the induction of lipid peroxidation in biological membranes can be carried out by the anion radical O2 and other active forms of oxygen, which trigger a whole cascade of free radical oxidation reactions, the products of which have a toxic effect on the cell and may be one of the pathogenetic factors of the specific development of diabetes.

Since the primary and secondary products of lipid peroxidation have a detrimental effect on the cell, the body has regulatory mechanisms that limit the accumulation of highly toxic products, which is called antioxidant defense. Enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GLP), and glutathione reductase play a leading role in the regulation of lipid peroxidation.



There are conflicting opinions in the literature about the nature of changes in the activity of antioxidant enzymes in diabetes mellitus in children. Therefore, the aim of our study was to show how the activity of antioxidant enzymes in children changes depending on the degree of compensation and duration of the disease.

Materials and methods

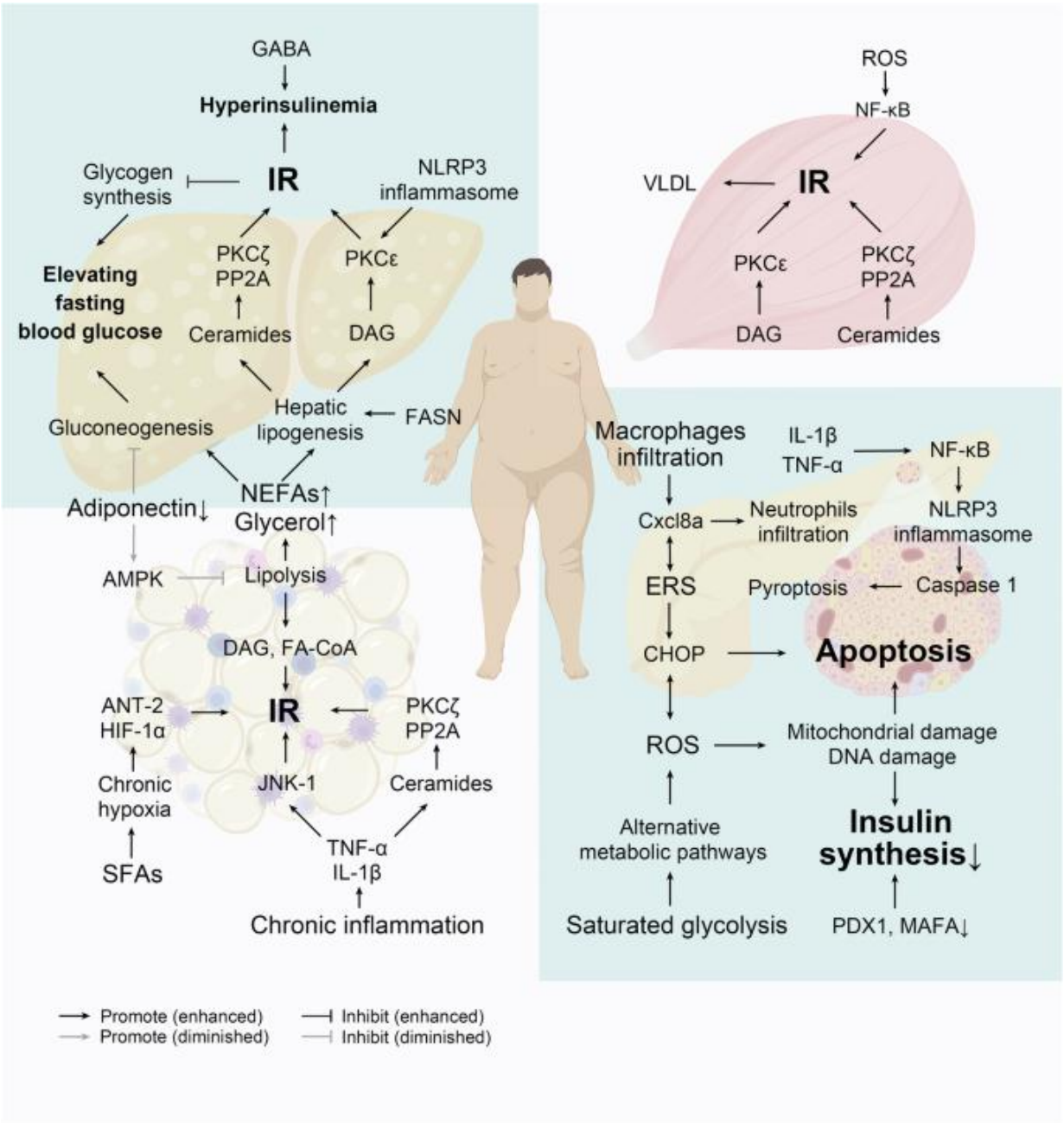
A total of 60 children (43 girls and 17 boys) aged 5 to 15 years with IDDM were examined. All patients were hospitalized and received insulin therapy.

The control group consisted of 10 healthy siblings of the probands with diabetes, aged 7 to 15

years.

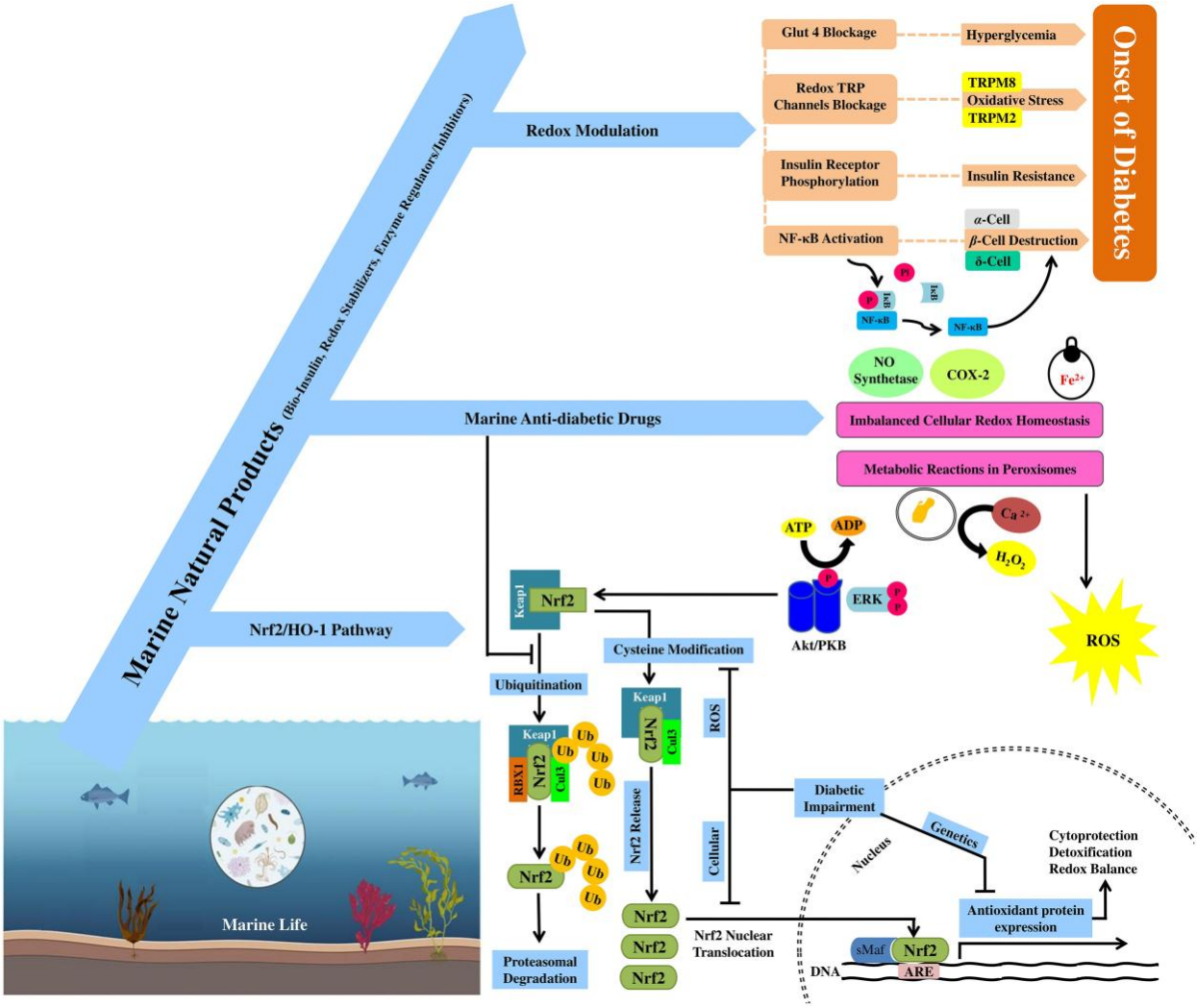
The degree of diabetes compensation was assessed by the level of glycated hemoglobin (HbA1) determined using Boehringer Mannheim kits. An HbA1 level of less than 10% indicates satisfactory compensation, and a level above 10% indicates a decompensated state.

Of the 60 children examined, 16 had a disease duration of more than 7 years (a group of children with long-term disease).

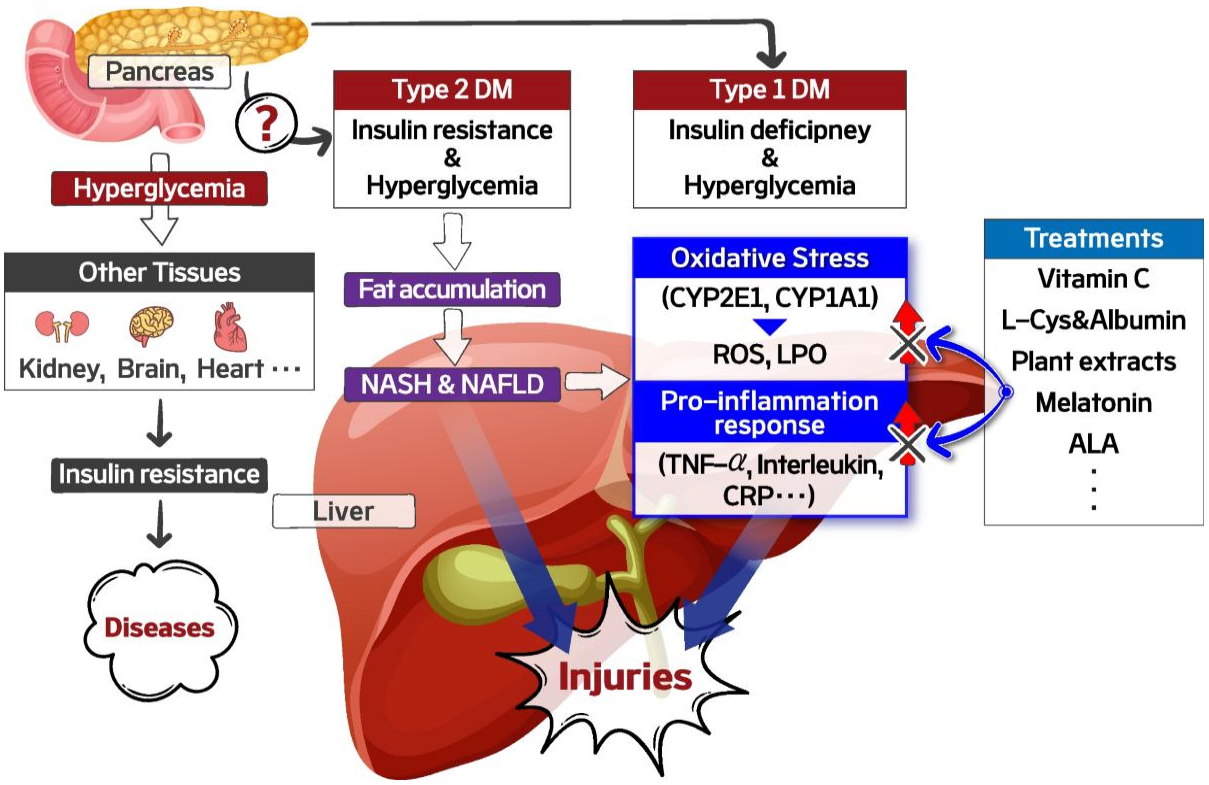


The activity of antioxidant defense enzymes and the level of lipid peroxidation products were assessed both in the general group of children with IDDM and depending on the degree of diabetes compensation and its duration.

For the study, blood was taken from the cubital vein on an empty stomach. EDTA (1 mg/ml) was used as an anticoagulant. The blood was centrifuged at 3000 rpm. The activity of lipid peroxidation processes was assessed by the content of hydroperoxides (HP) and malonaldehyde (MDA) in blood plasma [2].



Enzyme activity was measured in erythrocytes previously washed with 0.9% NaCl from plasma. SOD was determined using a method proposed by N. Nishikimi and described by S. Chevari et al. [9]. The method is based on the ability of SOD to compete with nitroblue tetrazolium (NBT) for superoxide anions formed by the aerobic interaction of the reduced form of NADH and phenazine metasulfate (PMS). As a result of this reaction, HCT is reduced to form hydrazine tetrazolium and is recorded at 540 nm. The percentage recovery of NST in the presence of SOD is reduced. One unit of activity was taken as 50% inhibition of the NST reduction reaction; enzyme activity was expressed in conventional units for 1 ml of erythrocytes. GLP was determined using the method described by VM Moin [6]. The measure of enzyme activity was the rate of glutathione oxidation in the presence of tertiary butyl GP. The concentration of reduced glutathione before and after starting with the enzyme was determined colorimetrically. Enzyme activity was expressed in μm/min per 1 g of hemoglobin.



Hemoglobin was determined by the hemoglobin cyanide method using standard kits.

The obtained data were processed using the Student's t-variance statistical method and correlation analysis was performed.

Results and discussion

Analysis of the results showed that lipid peroxidation processes are enhanced in children with IDDM. As can be seen from Table. 1, the level of GP and MDA in the serum of patients is significantly higher ($p< 0.001$) than in the control group (healthy siblings of patients with diabetes). It should be noted that

MDA levels increased significantly compared to GP levels. It is known that MDA is the most toxic substance that has a detrimental effect on cell membranes.

Of the currently known enzymes of the body's antioxidant defense, we studied the activity of SOD and GLP. SOD is the only enzyme that catalyzes the enzymatic dismutation of oxygen superoxide. The action of another enzyme, GLP, is aimed at eliminating both peroxides and lipid peroxide compounds.

In the overall group of children with IDDM (see Table 1), SOD activity was significantly higher ($p < 0.001$) and GLP activity was significantly lower ($p < 0.001$) than in controls. In the group of adult patients with IDDM that we previously studied, SOD activity was always lower than control values, regardless of the severity of diabetes [7].

Therefore, it can be assumed that increased SOD activity in children with IDDM is probably a compensatory reaction of the developing organism.

According to a number of authors, the degree of diabetes compensation, determined by glycemia and glucosuria indicators, does not affect the level of primary and secondary peroxides [8].

Our studies have shown (Table 2) that in children with IDDM in a decompensated state (Hb Aj 13.3 + 0.38%) the level of GP and MDA in the blood serum was significantly higher than in compensated patients (Hb Aj 9.03 + 0.36%). However, during the compensation of diabetes mellitus, the level of GP and MDA did not decrease to normal values and remained significantly higher than in controls. An increase in the level of primary and secondary lipid peroxides in

children in a compensated state can be considered as one of the triggers for the development of late specific complications of diabetes mellitus.

The increase in SOD activity under compensatory conditions in children was unreliable, while GLP activity decreased significantly ($p < 0.001$), as in the total group examined.

Thus, the glutathione peroxidase system is an effective antioxidant defense system of the body and is altered to a greater extent than the superoxide dismutase system in children with IDDM.

The duration of the disease did not affect the levels of primary and secondary lipid peroxides. GP and MDA levels remained elevated.

in both groups compared to the control group ($p < 0.001$). Decreased SOD and GLP activity was noted in children with long-term (over 7 years) IDDM.

Conclusion

In children with IDDM, an increase in the level of GP and MDA in the blood plasma is accompanied by a significant decrease in the level of GLP and an increase in SOD activity. The increase in SOD activity, apparently, is of a compensatory nature. The decrease in GLP activity is more pronounced in decompensated patients.

Determination of GLP activity in children with IDDM is the most informative indicator of the state of the antioxidant defense system.

The duration of diabetes does not significantly affect the activity of antioxidant defense enzymes:

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