

# Influence of natural anthocyanins derived from chokeberry (*Aronia melanocarpa*) extract on glycosylated hemoglobin level in pregnant women with insulin-dependent diabetes mellitus

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**Key words:** natural anthocyanins, *Aronia melanocarpa*, glycosylated hemoglobin, diabetes, pregnancy

## Abstract

The aim of the study was to assess the influence of anthocyanins derived from *Aronia melanocarpa* extract on glycosylated hemoglobin serum levels in pregnancy complicated by mother's insulin-dependent diabetes. Diabetes is a serious emergency for pregnancy development and increase of complications risk. 84 pregnant women in II and III trimester were included in this study. Pregnant women were divided into two groups: I group (n=46) - women with controlled insulin-dependent diabetes and II group (n=38) - women with uncontrolled diabetes. In both groups during 8 weeks anthocyanins in daily dose 300 mg were orally administered. Glycosylated hemoglobin (HbA1c) serum levels in pregnant women were measured before therapy and after 4 and 8 weeks of this treatment. In the I group mean HbA1c level did not undergo statistically significant changes: before treatment it was 6.2±0.3%, after 4 weeks - 6.1±0.4%, and

after 8 weeks - 5.9±0.6%;  $p>0.05$ . In the II group HbA1c levels decrease was noted during anthocyanins therapy: from 8.3±0.4% before treatment to 6.9±0.3% after 4 weeks and 6.2±0.4% after 8 weeks of treatment;  $p<0.01$ . Our results indicate that anthocyanins derived from *Aronia melanocarpa* extract help to normalize carbohydrate metabolism in pregnant women with uncontrolled insulin-dependent diabetes.

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## Introduction

Diabetes is a complex of various genetically determined and acquired metabolic disorders. Their common feature is glucose intolerance and hyperglycaemia and appearance of complaints and clinical symptoms concerned with them. It is caused by hypoinsulinaemia which leads to disorders in metabolism of carbohydrates, proteins, fats and disorders in electrolyte equilibrium and water balance. As

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Tab. 1. Glycosylated hemoglobin levels [HbA<sub>1c</sub> (%)] during anthocyanins treatment

	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>
Pregnant women with controlled IDDM	6.2±0.3	6.1±0.4	5.9±0.6
Pregnant women with uncontrolled IDDM	8.3±0.4	6.9±0.3*	6.2±0.4*

T<sub>0</sub> - before treatment; T<sub>1</sub> - after 4 weeks of treatment; T<sub>2</sub> - after 8 weeks of treatment; \*p<0.01

a consequence, chronic complications of diabetes appeared as a vascular disease, pathological changes in the nervous system and specific organ pathological changes [1].

Diabetes is a serious emergency for pregnancy development and increases complications risk. Main pregnancy complications concerned with diabetes are divided into the following groups: higher prevalence of abortions and preterm labours, intrauterine fetal deaths, congenital malformations, fetal macrosomy, increase of incidence of neonatal diseases and increase of perinatal mortality of neonates [2-6].

These complications prevalence can be decreased by precision control of glycaemia, intensive insulinotherapy, modern methods of fetal distress monitoring and modern neonatal care [4, 5, 7, 8].

The most serious outcome of diabetic mother's harmful metabolic environment influence on her fetus is intrauterine fetal death. Intrauterine fetal death occurs most frequently in last weeks of pregnancy. It happens in mothers with poor glycaemia control with associated ketoacidosis, in pregnancy complicated by gestosis, hydramnion, fetal hyper- or hypotrophy. The most likely cause of fetal death is prolonged fetal hyperglycaemia, maternal hypoglycaemia (lower than 50 mg%) and chronic intrauterine asphyxia [7, 8]. Many authors indicate that fetal asphyxia is caused by vascular pathological changes concerned with thickening of basement membrane of placental blood vessels, which leads to blood flow disturbances and decreased oxygenation of fetal tissues. Diminished oxygen concentration in tissues stimulates anaerobic glycolysis leading to lactic acid increase. In extreme cases metabolic acidosis and fetal death occur. That is why fetal acidosis is considered as the main cause of intrauterine fetal death. Some authors

report that prenatal mortality in cases of fetal acidosis is 84%. This emergency mostly occurs in III trimester, that is why fetal biophysical monitoring is so important [7, 8].

## Material and methods

84 pregnant women in II and III trimester were included in this study. Pregnant women were divided into two groups: I group (n=46) - women with controlled diabetes - fasting blood glucose levels less than 100 mg/dl, 1.5 hour after meal - less than 140 mg/dl.; II group (n=38) - women with uncontrolled diabetes - glucose levels over the values above. In both groups during 8 weeks (minimum) anthocyanins in daily dose 300 mg (3 x 100 mg) were orally administered.

Glycosylated hemoglobin (HbA<sub>1c</sub>) serum levels in pregnant women were measured before therapy and after 4 and 8 weeks of this treatment.

For statistical analysis of obtained results Fisher exact test was used.

The study was performed by order of Agropharm S.A., Tuszyn, Starościanańska 33, Poland.

## Results

In the I group (pregnant women with controlled IDDM) mean HbA<sub>1c</sub> level did not undergo statistically significant changes: before treatment it was 6.2±0.3%, after 4 weeks - 6.1±0.4%, and after 8 weeks - 5.9±0.6%; p>0.05. In the II group (pregnant women with uncontrolled IDDM) HbA<sub>1c</sub> levels decrease was noted during anthocyanins therapy: from 8.3±0.4% before treatment to 6.9±0.3%\* after 4 weeks and 6.2±0.4%\* after 8 weeks of treatment; \*p<0.01. The obtained results were shown in Table 1.

## Discussion

One of the methods to evaluate insulin dependent diabetes metabolic control is glycosylated hemoglobin HbA<sub>1c</sub> serum levels measurement every 6 weeks.

In hyperglycaemic environment hemoglobin undergoes glycation process. Elevated HbA<sub>1c</sub> are noted in pregnancies with uncontrolled diabetes [7, 8]. During hyperglycaemia in pregnant women with uncontrolled diabetes oxidative stress developed, concerned with increased concentration of reactive oxygen intermediates, which leads among others to lipids peroxidation [9, 10]. Natural vegetable antioxidants administration, such as anthocyanins derived from *Aronia melanocarpa* extract, causes peroxidation level decrease, which leads to HbA<sub>1c</sub> levels normalization and reactive oxygen intermediates levels decrease [11-13].

Reactive oxygen intermediates (ROI) are ones of an embryo cells damaging factors. Their production increase in hyperglycaemia environment and D-glucose is responsible for this process. Reactive oxygen intermediates toxicity mechanism is concerned with their influence on lipoproteins of cell membranes. Oxidation of lipoproteins of cell membranes leads to their integrity loss and permeability increase. Direct cytotoxic activity effect of ROI is damage of the following structures: trophoblasts, placental macrophages and blood vessels endothelium. Cell metabolism disturbances are concerned with synthesis of proteins, fats, carbohydrates and nucleic acids. ROI are extremely active molecules and that is why they react with first substances they meet, which are mostly lipid components of a cell: membrane and cell organelles. In lipids metabolism ROI initiate chain reaction of polyunsaturated and estrified fatty acids [2, 3, 9, 14-17].

Our studies demonstrated a statistically significant increase of glycosylated hemoglobin levels in pregnant women with uncontrolled insulin-dependent diabetes during anthocyanins therapy. This treatment was not observed to influence HbA<sub>1c</sub> levels in metabolic controlled diabetes.

## Conclusion

Anthocyanins derived from *Aronia melanocarpa* extract help to normalize carbohydrate metabolism in pregnant women with uncontrolled insulin-dependent diabetes.

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