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HOMEOSTASIS OF CARBOHYDRATE METABOLISM IN EXPERIMENTAL DIABETES UNDER THE INFLUENCE OF THE BIOPREPARATION SEV-3

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Abstract. *Diabetes mellitus is a major public health issue, characterized by chronic hyperglycemia, complex metabolic dysfunctions, and severe systemic complications. This study investigates the impact of the biopreparation SEV-3 on glucose metabolism homeostasis in experimental diabetes induced in laboratory white rats. The conducted research highlights a hypoglycemic effect and stimulation of insulin secretion, suggesting the potential use of natural biopreparations in improving the metabolic imbalances associated with diabetes mellitus.*

Keywords: Biopreparation, experimental diabetes, homeostasis, glucose metabolism, medicinal plants.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder caused by insufficient insulin production or peripheral insulin resistance, leading to disruption of glucose homeostasis. This condition affects millions of people worldwide and is associated with a wide range of chronic complications, including retinopathy, nephropathy, and diabetic neuropathy [1; 2]. At the core of the disease pathogenesis lies a profound disturbance in carbohydrate metabolism, which, if left untreated, progressively impacts lipid and protein metabolism and, ultimately, the overall homeostasis of the body.

Maintaining glucose metabolism homeostasis—that is, preserving a dynamic balance between glucose intake, storage, and utilization—is essential for the optimal function of all organs, especially those highly sensitive to glycemic fluctuations, such as the brain, liver, and pancreas.

Glucose homeostasis, ensured by complex hormonal and enzymatic mechanisms, plays a critical role in the prevention and control of diabetes-related complications [2]. Under physiological conditions, this balance is maintained

through a complex interplay between insulin secretion by pancreatic β-cells and the peripheral insulin response in muscle, liver, and adipose tissue. In diabetes, this system is impaired, leading to excessive accumulation of glucose in the bloodstream, with long-term detrimental effects. Moreover, oxidative stress and chronic inflammation, frequently associated with diabetes, further contribute to cellular damage and disruption of hormonal regulatory mechanisms [3].

The imbalance in glucose metabolism leads to systemic complications, necessitating effective interventions for glycemic control. Given the limitations and adverse effects of conventional antidiabetic treatments, interest in alternative and complementary therapies has significantly increased over recent decades. Phytotherapy, especially the use of medicinal plant extracts with hypoglycemic action, has emerged as a promising area in diabetes research [4, 5]. Plant-derived biopreparations can positively influence blood glucose levels by increasing insulin sensitivity, stimulating insulin secretion, or through antioxidant activity, thereby reducing oxidative stress on pancreatic cells [6, 7].

In addition to conventional treatments, the use of natural bioactive compounds has become a growing focus in biomedical research, aiming to reduce hyperglycemia and prevent diabetes-associated complications [8, 9]. In modern experimental research, induced diabetes models, such as the alloxan model, have allowed for the evaluation of potential therapeutic effects on carbohydrate metabolism in a controlled and reproducible manner. Alloxan is commonly used in diabetes research due to its ability to selectively induce cytotoxicity in pancreatic β-cells, thereby mimicking the characteristics of diabetes mellitus [10]. These models are essential for understanding the mechanisms of action of antidiabetic compounds and for validating their efficacy prior to clinical application.

In this context, recent studies have been exploring the effectiveness of natural biopreparations, such as SEV-3, which contains standardized plant extracts with antioxidant, anti-inflammatory, and glycemia-regulating properties. This biopreparation shows promising potential in correcting metabolic disturbances associated with diabetes [7]. Due to its rich content of flavonoids, glycosides, alkaloids, and synergistically acting vitamins, SEV-3 may contribute to restoring glycemic balance and alleviating oxidative stress, thus offering an integrative approach to maintaining glucose homeostasis under diabetic conditions. Some of these bioactive substances may positively interact with insulin receptors on target cell membranes, enhancing insulin signal transduction and facilitating glucose uptake via GLUT4 transporter activation, thereby contributing to the normalization of blood glucose levels. This mechanism can directly improve insulin sensitivity in insulin-dependent tissues, such as skeletal muscle and adipose tissue [6]. As a result, these biological products exert pleiotropic effects, enabling them to act simultaneously on multiple pathological mechanisms while reducing the risk of toxic or allergic complications.

Thus, the aim of this study is to evaluate the effects of the SEV-3 biopreparation on glycemic and insulin parameters in an alloxan-induced diabetes model, highlighting its therapeutic potential in maintaining glucose homeostasis.

MATERIALS AND RESEARCH METHODS

The investigations were conducted on laboratory white rats of both sexes, with body weights ranging from 180 to 220 g. A total of 60 rats were used in the study, housed under standard vivarium conditions with free access to food and water for 30 days. Experimental diabetes mellitus was induced by intraperitoneal injection of a 5% alloxan solution at a dose of 200 mg/kg. Blood glucose levels were measured using the "On Call Plus" glucometer, and hormone levels were assessed by the enzyme-linked immunosorbent assay (ELISA) method using the Stat Fax 4700 analyzer. Statistical analysis was performed using GraphPad Prism InStat software (version 10.2.3, GraphPad Software Inc., La Jolla, California, USA).

The biopreparation contains the aerial parts of the following medicinal plants: Vitis vinifera, Equisetum arvense, and *Syringa vulgaris*.



A B C

Figure 1. Dried medicinal plants in the composition of the biopreparation SEV-3

a) Syringa vulgaris b) Equisetum arvense c) Vitis vinifera

The preparation is administered at a dose of 50 mL per rat per 24 hours, prepared by infusing the mixture of the aforementioned plants (6 g per plant in 600 mL of water).

The biopreparation SEV-3 has a complex phytochemical profile with therapeutic potential in regulating carbohydrate metabolism. The major active compounds of these plants are glycosides, flavonoids, alkaloids, vitamins, and other natural antioxidants that act synergistically on multiple mechanisms involved in

maintaining glucose homeostasis [6, 11]. Thus, the flavonoids and glycosides in Vitis vinifera are well-known for their hypoglycemic effects, acting by increasing the sensitivity of peripheral cells to insulin and regulating intestinal glucose absorption [5, 7]. The antioxidants present in *Syringa vulgaris* and *Equisetum arvense* extracts reduce oxidative stress induced by hyperglycemia, thereby protecting pancreatic β-cells against apoptosis [3, 4]. Vitamin C, phenolic compounds, and saponins contribute to neutralizing free radicals, supporting partial regeneration of pancreatic islets [12]. The alkaloids and bitter compounds in the SEV-3 biopreparation may directly stimulate insulin secretion by activating calcium channels in β-cells [6]. This helps maintain a physiological level of insulin in the blood, essential for glucose metabolism. The presence of essential vitamins and phytonutrients aids in stabilizing lipid and protein metabolism, which are often disrupted in the context of diabetes mellitus [7]. This global action supports the general homeostasis of the organism.

Therefore, the biopreparation SEV-3 may contribute to restoring glycemic balance through multiple actions: reducing blood glucose, protecting β-cells, stimulating insulin secretion, and combating oxidative stress. These effects justify its exploration within complementary therapies for diabetes, especially in the early or moderate stages of the disease.

RESULTS AND DISCUSSION

Endocrine pancreatic dysfunction, characteristic of diabetes mellitus, has profound pathological implications, contributing to severe disturbances in the homeostasis of carbohydrate metabolism [2, 3]. This dysfunction is primarily associated with damage to the β-cells of the islets of Langerhans, which are responsible for the synthesis and secretion of insulin—the key hormone regulating blood glucose levels. The loss of functionality or destruction of these cells results in a marked decrease in insulin secretion and, consequently, in the body's inability to maintain plasma glucose concentrations within physiological limits [13].

The dysregulation of this hormonal mechanism leads to significant alterations in carbohydrate metabolism, resulting in persistent hyperglycemia. In the absence of effective glycemic control, the excessive accumulation of glucose in the bloodstream serves as a triggering factor for the onset and progression of both microvascular and macrovascular complications associated with diabetes mellitus [2].

In experimental diabetes, insulin deficiency leads to increased protein catabolism in tissues, elevated amino acid levels in the blood, and increased excretion of ammonia and nitrogen in the urine [10]. These changes correlate directly with the degree of insulin deficiency. Reduced circulating insulin impairs the ability of tissues to absorb glucose, leading to elevated blood glucose levels.

In decompensated diabetes mellitus, insulin—the essential hormone for blood glucose regulation—can no longer effectively exert its functions. As a result, glucose metabolism is severely impaired, with direct consequences for overall homeostasis. Normally, insulin facilitates the uptake of glucose into peripheral tissue cells, such as muscle and liver cells, where it is utilized for energy production. In this form of diabetes, whether due to insufficient insulin or increased insulin resistance, this mechanism becomes dysfunctional, and blood glucose remains elevated [7].

Insulin resistance plays a central role in this process. Under certain conditions, cells become less responsive to insulin, a phenomenon often exacerbated by lipid accumulation in tissues. This impairs glucose transport into cells, resulting in glucose build-up in the blood. In compensation, the pancreas increases insulin secretion. However, over time, this compensatory response becomes inadequate, leading to chronic hyperglycemia.

In addition to insulin imbalance, the liver continues to produce glucose through gluconeogenesis—a metabolic pathway by which glucose is synthesized from non-carbohydrate precursors. Normally, this process is suppressed by insulin, but in poorly controlled diabetes, gluconeogenesis persists, contributing to elevated blood glucose levels. Simultaneously, lipolysis (fat breakdown) is activated, releasing free fatty acids into the bloodstream. While these molecules serve as alternative energy sources, their excess conversion into ketone bodies can lead to ketoacidosis—a life-threatening metabolic disturbance that significantly impairs the body's acid-base balance [2, 3].

At the renal level, hyperglycemia can surpass the kidneys' reabsorptive capacity for glucose, leading to glucosuria and placing additional strain on renal function, thereby contributing over time to the development of diabetic nephropathy. Furthermore, hyperglycemia-induced disturbances in electrolyte balance—such as hypokalemia—may adversely affect cardiovascular function and increase the risk of cardiac arrhythmias [10].

Our study confirmed a significant increase in blood glucose levels in experimental diabetes (16.9 ± 0.84 mmol/L), compared to the control group (5.5 ± 0.27 mmol/L). Administration of the SEV-3 biopreparation reduced blood glucose to 10.5 ± 0.52 mmol/L, demonstrating a clear hypoglycemic effect. Furthermore, insulin levels were significantly reduced in the alloxan-induced group (1.51 ± 0.44 pmol/L), while SEV-3 administration stimulated insulin secretion up to 3.03 ± 0.32 pmol/L, compared to the normal value of 4.02 ± 0.39 pmol/L, indicating the biopreparation's potential to ameliorate metabolic dysfunctions associated with diabetes. These findings are consistent with those reported by Zhang et al. (2020) [13], who demonstrated the antidiabetic effects of plant-derived flavonoids. The differences between groups were statistically significant ($p < 0.05$) for both blood glucose and insulin levels between the diabetic group and the group treated with the

SEV-3 biopreparation.

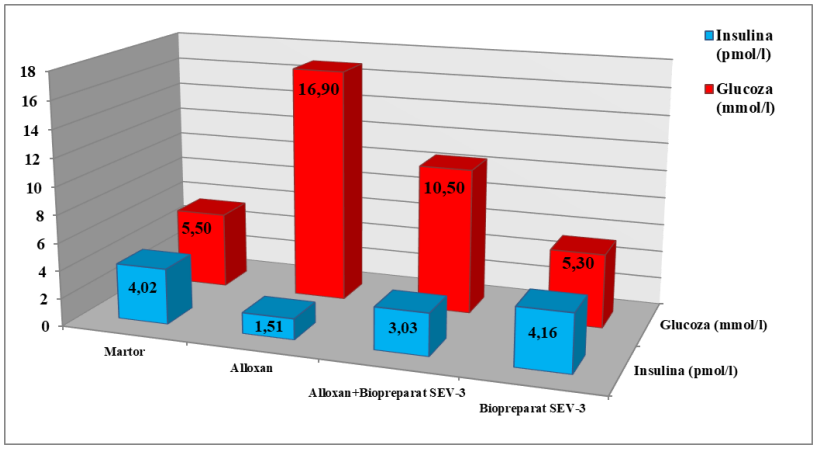


Figure 1. Blood plasma glucose (mmol/l) and insulin (pmol/l) levels following administration of the SEV-3 biopreparation in experimental diabetes.

Insulin plays a central role in the regulation of carbohydrate metabolism. It acts by maintaining blood glucose levels within physiological limits, ensuring the metabolic balance required for optimal organismal function. When blood glucose levels rise, for instance after food intake, the pancreas responds by releasing insulin, which facilitates glucose uptake into cells, where it is utilized as the primary source of energy. Insulin deficiency leads to severe imbalances in glucose metabolism. In the absence of insulin, glucose cannot be efficiently used at the cellular level and accumulates in the bloodstream, resulting in hyperglycemia—a hallmark of diabetes mellitus [2]. In animals, this imbalance can be corrected through the administration of synthetic insulin, a therapeutic approach also widely used in human medicine. Beyond its primary role, insulin also antagonizes the effects of hyperglycemic hormones such as cortisol and adrenaline, which promote glucose release into the bloodstream under stress conditions [3]. Thus, insulin plays a critical role in modulating metabolic responses under both physiological and pathological states.

Preliminary results suggest that administration of SEV-3 may contribute to reducing hyperglycemia and improving metabolic dysfunctions associated with alloxan-induced diabetes. These effects may be attributed to the protection of pancreatic β-cells, attenuation of oxidative stress, and enhancement of glucose utilization in peripheral tissues. This mechanism suggests a beneficial role of SEV-3 in carbohydrate metabolism regulation by promoting glucose uptake and inhibiting excessive endogenous glucose production.

CONCLUSION

Decompensated diabetes mellitus is characterized by a series of metabolic dysfunctions, including insulin resistance, increased hepatic glucose production, disturbances in lipid metabolism, and the development of ketoacidosis. These processes collectively contribute to sustained hyperglycemia and the onset of severe complications associated with the disease. The data obtained support the use of SEV-3 as a phytotherapeutic adjuvant in strategies aimed at preventing and managing hyperglycemia, particularly in the early stages of diabetes. This effect may be attributed to the bioactive compounds present in SEV-3, which play a role in regulating carbohydrate metabolism and maintaining glucose homeostasis. The SEV-3 biopreparation promoted an increase in insulin secretion in experimental diabetes, suggesting a protective effect on pancreatic β-cells. The observed improvements in glycemic and insulin parameters underscore the potential of this biopreparation to ameliorate metabolic dysfunctions associated with diabetes, thereby justifying further investigations to elucidate its mechanisms of action and therapeutic applicability.

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