DIABETES MELLITUS: BIOCHEMICAL MECHANISMS, METABOLIC DISTURBANCES, AND MODERN THERAPEUTIC APPROACHES – A MEDICAL CHEMISTRY PERSPECTIVE

Tolliboyeva Zukhra Abdurasul qizi
zuxratolliboyeva38@gmail.com
Naberayeva Farziya Farkhodovna
farziyanaberayeva@gmail.com
Fayzullayeva Dilbar Botir qizi
dilbarfayzullayeva74@gmail.com
O'ktamova Shakhinabonu Asqar qizi
Oktamovashahinabonu@gmail.com
Students of Samarkand State Medical University

Abstract: *This article is based on the analysis of modern scientific publications devoted to the biochemical basis of diabetes mellitus, its metabolic complications, and current diagnostic and therapeutic strategies. Particular attention is paid to the molecular mechanisms of hyperglycemia, insulin resistance, and diabetic ketoacidosis, as well as the potential application of advanced technologies in the healthcare system of the Republic of Uzbekistan.*

Keywords: *Diabetes mellitus, hyperglycemia, insulin resistance, glucagon, diabetic ketoacidosis, HbA1c, glucose homeostasis, SGLT2 inhibitors, continuous glucose monitoring, medical chemistry.*

Introduction

Part 1. Introduction and Main Directions

Glucose homeostasis is a fundamental concept in medical chemistry and clinical biochemistry. Normal fasting blood glucose levels range from 3.9 to 5.6 mmol/L and are tightly regulated by a complex hormonal network involving insulin, glucagon, cortisol, and epinephrine.

At the molecular level, insulin plays a central role by activating intracellular signaling pathways that promote glucose uptake via GLUT4 transporters in muscle and adipose tissues. In contrast, glucagon stimulates hepatic gluconeogenesis and glycogenolysis, increasing blood glucose levels.

Disturbances in glucose metabolism are classified into two main types. Type 1 diabetes mellitus (T1DM) is characterized by абсолют insulin deficiency due to autoimmune destruction of pancreatic β-cells. Type 2 diabetes mellitus (T2DM) is associated with insulin resistance and relative insulin deficiency.

In addition, metabolic dysregulation involves key biochemical pathways such as glycolysis, gluconeogenesis, and lipid metabolism. Increased hepatic gluconeogenesis and impaired peripheral glucose uptake contribute significantly to chronic hyperglycemia.

Modern technologies—including continuous glucose monitoring systems, biosensors, and nanocarrier-based insulin delivery—represent promising directions for improving diabetes management and modernizing healthcare systems in Uzbekistan.

Part 2. Areas of Application in Medicine

Understanding the biochemistry of diabetes enables early diagnosis and effective management of acute and chronic complications. Diagnostic methods include:

Fasting plasma glucose

Oral glucose tolerance test (OGTT)

HbA1c measurement (glycated hemoglobin)

Blood ketone measurement (β-hydroxybutyrate)

C-peptide levels

Autoantibody testing (GAD, IA-2, ZnT8)

These biochemical approaches are widely applied in:

Endocrinology

Emergency medicine

Cardiology and nephrology

Obstetrics (gestational diabetes)

Pediatrics

Clinical pharmacology

For Uzbekistan, improving diagnostic accuracy and early intervention is essential for reducing morbidity and mortality associated with diabetes.

Results / Main Findings

Part 3. Modern Research Projects

1. Diagnostics and Monitoring: HbA1c and Continuous Glucose Monitoring

HbA1c reflects the average blood glucose level over the previous 2–3 months and is formed through non-enzymatic glycation of hemoglobin. A value ≥6.5% is diagnostic for diabetes.

Continuous glucose monitoring (CGM) systems use glucose oxidase–based electrochemical sensors to measure interstitial glucose levels in real time. These systems allow dynamic monitoring of glycemic variability and early detection of hypo- and hyperglycemia.

2. Diabetic Ketoacidosis: Biochemical Mechanisms and Therapy

Diabetic ketoacidosis (DKA) is a life-threatening condition characterized by hyperglycemia, metabolic acidosis, and ketonemia.

The biochemical mechanism includes:

Increased lipolysis → free fatty acids → hepatic ketogenesis

Elevated glucagon → enhanced gluconeogenesis

Reduced insulin → decreased glucose utilization

Osmotic diuresis → dehydration and electrolyte imbalance

Treatment includes insulin therapy, fluid replacement, and correction of electrolyte disturbances.

3. Hyperosmolar Hyperglycemic State

This condition is characterized by severe hyperglycemia and dehydration with minimal ketosis due to residual insulin activity. It requires intensive rehydration and careful metabolic correction.

4. Chronic Diabetic Complications: Biochemical Pathways

Chronic hyperglycemia leads to complications through several biochemical pathways:

Polyol pathway activation

Formation of advanced glycation end-products (AGEs)

Activation of protein kinase C (PKC)

Hexosamine pathway dysregulation

These mechanisms contribute to vascular damage, inflammation, and organ dysfunction.

5. Nanotechnologies in Diabetes Management

Recent advances include glucose-responsive insulin delivery systems, nanoparticle-based carriers, and microneedle patches. These technologies improve treatment precision and patient compliance.

Conclusion

Understanding the biochemical mechanisms of diabetes mellitus is essential for modern medical practice. Both acute complications (DKA, hyperosmolar state) and chronic complications require early diagnosis and targeted biochemical intervention.

The implementation of modern diagnostic tools and innovative therapeutic approaches in Uzbekistan can significantly improve patient outcomes, reduce complications, and enhance the quality of healthcare services.

Future perspectives include the integration of personalized medicine, artificial intelligence–based glucose monitoring systems, and advanced nanotechnology in diabetes management.

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