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# Diabetes Mellitus: A Comprehensive Review

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**Abstract**
Diabetes mellitus (DM) is a chronic and heterogeneous metabolic disorder characterized by sustained hyperglycemia arising from defects in insulin secretion, insulin action, or both. The rapidly increasing global prevalence of diabetes has made it a critical public health challenge. Persistent hyperglycemia is associated with progressive damage and dysfunction of multiple organ systems, including the eyes, kidneys, nerves, and cardiovascular system. This review critically summarizes current knowledge on the classification, pathophysiology, risk factors, clinical features, diagnostic criteria, complications, and contemporary pharmacological management of diabetes mellitus, with emphasis on mechanisms of action of antidiabetic agents and recent therapeutic advances, making it suitable for M.Pharm academic and research applications.This review highlights recent advances in antidiabetic pharmacotherapy and emphasizes the role of newer agents in improving long-term outcomes.

**Keywords**
Antidiabetic drugs, Diabetes mellitus,
Hyperglycemia, Insulin resistance, Type 1 diabetes,
Type 2 diabetes,

## I. INTRODUCTION

Diabetes mellitus represents a group of metabolic disorders with shared features of chronic hyperglycemia and impaired regulation of carbohydrate, lipid, and protein metabolism. The incidence of diabetes has increased substantially due to urbanization, sedentary lifestyles, dietary changes, and population aging. From a pharmacological perspective, diabetes is of particular importance because long-term glycemic dysregulation necessitates lifelong drug therapy and careful monitoring. Advances in molecular biology and pharmacotherapy have significantly improved disease outcomes; however, diabetes continues to impose a major economic and healthcare burden worldwide, highlighting the need for optimized therapeutic strategies and continuous research.According to recent estimates, diabetes affects over 537 million adults worldwide, with a significant burden in developing countries.

Classification of Diabetes Mellitus

Diabetes mellitus is broadly classified into the following categories:

1.Type 1 Diabetes Mellitus (T1DM)

Type 1 diabetes is an autoimmune disorder characterized by the destruction of pancreatic β-cells, leading to absolute insulin deficiency. It commonly presents in childhood or adolescence but may occur at any age.

2. Type 2 Diabetes Mellitus (T2DM)

Type 2 diabetes is the most common form of diabetes and is characterized by insulin resistance combined with relative insulin deficiency. Genetic predisposition, obesity, sedentary lifestyle, and dietary factors play a crucial role in its development.

3. Gestational Diabetes Mellitus (GDM)

Gestational diabetes occurs during pregnancy and is associated with increased risk of maternal and fetal complications. Women with GDM have a higher risk of developing type 2 diabetes later in life.

4. Other Specific Types

These include diabetes due to genetic defects of β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas, endocrinopathies, drug- or chemical-induced diabetes, and infections.

## PATHOPHYSIOLOGY

The fundamental mechanism underlying diabetes mellitus is hyperglycemia. In type 1 diabetes, autoimmune-mediated β-cell destruction leads to insulin deficiency. In type 2 diabetes, insulin resistance in peripheral tissues such as muscle, liver, and adipose tissue is accompanied by impaired insulin secretion. Chronic hyperglycemia results in oxidative stress, inflammation, and activation of various metabolic pathways that contribute to diabetic complications.

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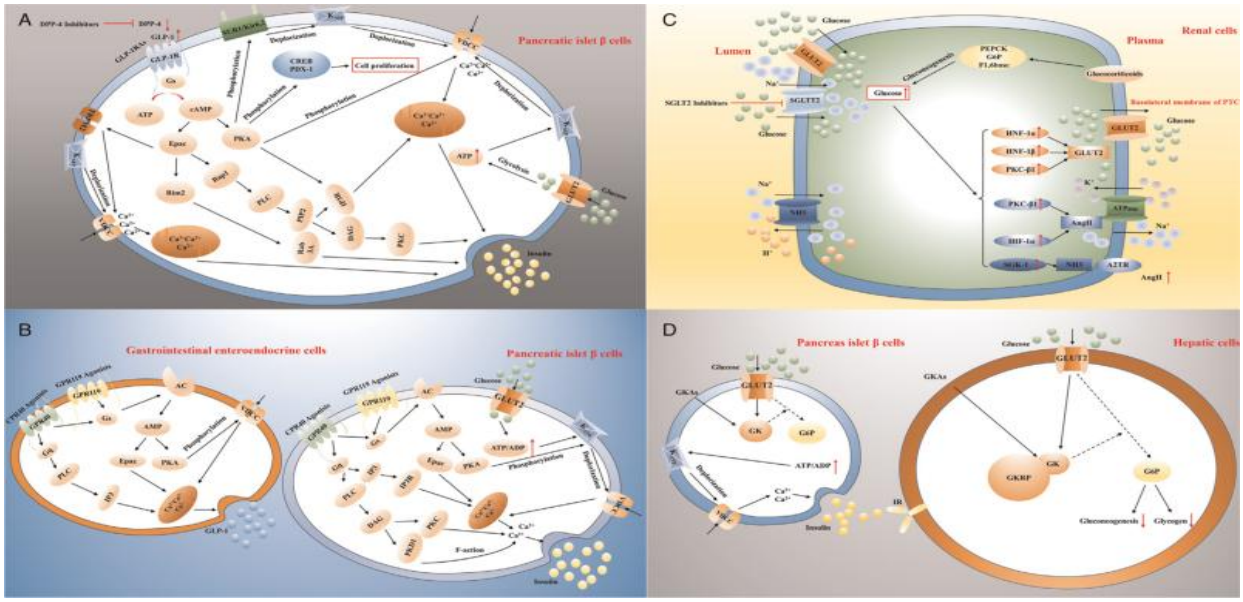


***Figure 1. Pathophysiological mechanisms involved predominantly in Type 2 diabetes mellitus.(adapted fromDeFronzo RA et al., Nat Rev Dis Primers, 2015, under CC BY-NC 4.0 license)***

Schematic representation showing insulin deficiency and insulin resistance leading to hyperglycemia, increased hepatic glucose production, reduced peripheral glucose uptake, and development of chronic complications.

Risk Factors

Major risk factors associated with diabetes mellitus include:

- Genetic predisposition
- Obesity and central adiposity
- Physical inactivity
- Unhealthy diet
- Advancing age
- History of gestational diabetes
- Hypertension and dyslipidemia

Clinical Manifestations

Common clinical features of diabetes mellitus include:

- Polyuria
- Polydipsia
- Polyphagia
- Unexplained weight loss
- Fatigue
- Blurred vision
- Recurrent infections

Diagnosis

The diagnosis of diabetes mellitus is based on the following laboratory criteria:

- Fasting plasma glucose (FPG) ≥ 126 mg/dL
- 2-hour plasma glucose ≥ 200 mg/dL during oral glucose tolerance test (OGTT)
- Glycated hemoglobin (HbA1c) ≥ 6.5%
- Random plasma glucose ≥ 200 mg/dL in the presence of symptoms

Complications of Diabetes Mellitus

❖ Acute Complications

- Diabetic ketoacidosis (DKA)
- Hyperosmolar hyperglycemic state (HHS)
- Hypoglycemia

❖ Chronic Complications

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy
- Cardiovascular diseases

Microvascular: Retinopathy, Nephropathy, Neuropathy

Macrovascular: CAD, Stroke, PVD

**MANAGEMENTOF DISEASE**

Management of diabetes involves a multifaceted approach including lifestyle modification, pharmacotherapy, and regular monitoring.

❖ Lifestyle Modification

- Balanced diet with controlled carbohydrate intake
- Regular physical activity
- Weight management
- Smoking cessation

❖ Pharmacological Treatment (Advanced Pharmacology)

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Pharmacological management of diabetes mellitus aims to achieve and maintain optimal glycemic control while minimizing adverse effects.

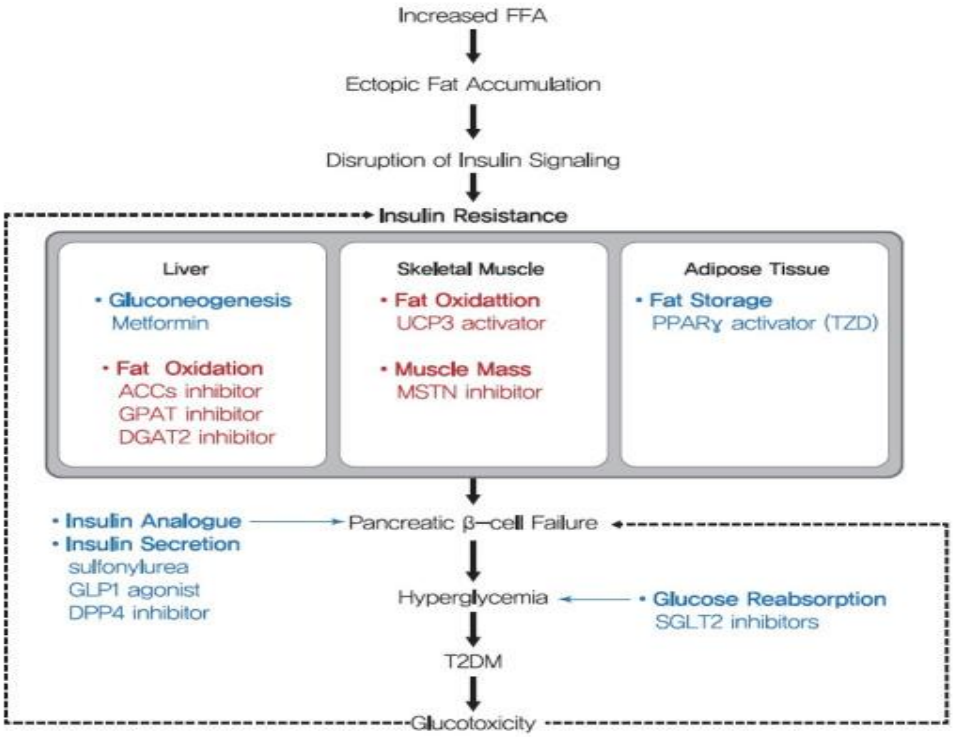


***Figure 2. Mechanism of Action of Major Antidiabetic Drugs (adapted from* Kim MK et al., Diabetes Metab J, 2021*)***

The major classes of antidiabetic drugs are discussed below:

1. Insulin and Insulin Analogues

Insulin therapy is mandatory in Type 1 diabetes and is also used in advanced Type 2 diabetes. Preparations include rapid-acting (insulin lispro, aspart), short-acting (regular insulin), intermediate-acting (NPH), and long-acting analogues (glargine, detemir, degludec). Insulin binds to insulin receptors and activates tyrosine kinase signaling, promoting glucose uptake and inhibiting hepatic glucose output.

2. Biguanides

Metformin is the first-line agent for Type 2 diabetes mellitus. It decreases hepatic gluconeogenesis, improves peripheral insulin sensitivity, and enhances glucose utilization. It has favorable effects on body weight and cardiovascular risk.

3. Sulfonylureas

Sulfonylureas (glibenclamide, glipizide, gliclazide) stimulate insulin release by closing ATP-sensitive potassium channels in pancreatic β-cells. Their use is limited by hypoglycemia and weight gain.

4.Meglitinides

Meglitinides (repaglinide, nateglinide) stimulate rapid and short-duration insulin secretion, mainly targeting postprandial hyperglycemia.

5.Thiazolidinediones

Thiazolidinediones such as pioglitazone activate PPAR-γ receptors, improving insulin sensitivity in peripheral tissues. Adverse effects include weight gain, edema, and heart failure risk.

6.α-Glucosidase Inhibitors

Acarbose and miglitol inhibit intestinal alpha-glucosidases, delaying carbohydrate absorption and reducing postprandial glucose levels.

7. DPP-4 Inhibitors

DPP-4 inhibitors (sitagliptin, linagliptin) enhance incretin activity, leading to glucose-dependent insulin secretion and reduced glucagon release.

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8.GLP-1 Receptor Agonists
GLP-1 receptor agonists (exenatide, liraglutide, semaglutide) improve glycemic control, promote weight loss, and show cardiovascular benefits.

9. SGLT2 Inhibitors
SGLT2 inhibitors (dapagliflozin, empagliflozin) reduce renal glucose reabsorption and provide significant cardiovascular and renal protection.

❖ Emerging and Advanced Therapies
- Dual GLP-1/GIP receptor agonists
- Stem cell–based β-cell regeneration
- Gene therapy
- Nanotechnology-based drug delivery systems
- Novel drug delivery systems

Role of Pharmacist in Diabetes Management
Pharmacists play a vital role in patient education, medication adherence, monitoring of adverse drug reactions, and promotion of lifestyle changes. Their involvement significantly improves therapeutic outcomes and quality of life in diabetic patients.

## II. CONCLUSION

Diabetes mellitus remains a significant global health challenge due to its increasing prevalence and associated complications. Early diagnosis, effective glycemic control, and comprehensive management strategies are essential to reduce disease burden.Pharmacists and healthcare professionals play a crucial role in translating these advances into effective patient care. Continuous research and innovation in pharmacotherapy and drug delivery systems hold promise for improved diabetes care in the future.

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