World Journal of
Pharmacy and Medical Science

ISSN: 3049-3501
Impact Factor: 5.157
CODEN (USA): WJPMAA

Review Article
2026 Volume 2, Issue 6
Page No.: 100-102

RECENT ADVANCE MEDICATIONS FOR TYPE II DIABETEIS MELLITUS: A COMPREHENSIVE REVIEW

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Article Received: 15 April 2026 Article Review: 05 May 2026 Article Accepted: 26 May 2026

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DOI: https://doi.org/10.5281/zenodo.20455799

How to cite this Article: N. Bhavitha, B. Keerthika, Dr. T. Ravi Sarath Babu (2026). RECENT ADVANCE MEDICATIONS FOR TYPE II DIABETEIS MELLITUS: A COMPREHENSIVE REVIEW. World Journal of Pharmacy and Medical Science, 2(6): 100-102.

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ABSTRACT
Diabetes mellitus commonly referred as diabetes is a chronic non-communicable disease that causes high blood sugar (glucose) levels.[1] Glucose is the main source of energy for the body's cells. The levels of glucose in the blood are controlled by a hormone called insulin. The pancreas is responsible for producing insulin. The cells which produce insulin are beta cells. These cells are distributed in a cluster of cells in the pancreas called the Islets of Langerhans.[2] It is silent killer disease and affects millions of people in the world. in diabetes mellitus there are different types those are type I type II and gestational diabetes and other types of diabetes mellitus.[3] Type 2 diabetes appears much later in age than Type 1 diabetes and is the most common type of diabetes. It is also called as non-insulin-dependent, since it is not treated exclusively by the use of insulin, but mainly with pills. Gestational diabetes is a condition that arises during pregnancy and impacts around 3-9% of expectant mothers.[4] For patients with T1DM, who make no insulin, the only pharmacologic option is replacement insulin, Gene therapy and stem therapy.[5]

KEYWORDS: Diabetus mellitus, Glucose, Insulin, Cluster cells, Islets of langerhans pharmacologic management, Gene therapy, Stem therapy.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches and other food into energy. Absence or reduced insulin in turn leads to persistent abnormally high blood sugar and glucose in tolerance.[6] Diabetes Mellitus (DM) is an endocrinological disorder and not a single disorder which is a group of metabolic or heterogeneous affliction. It is probably an oldest disease known to man. It is also referred as black-death from the 14th century.[7]

CLASSIFICATION

S. No.	Type	Characteristics feature
1	Type 1 (1a and 1b)	Damage of β-cells there by Secretion of insulin was reduced. Self-antibodies damage our own body tissues unknown cause.
2	Type 2	Insulin secretion and insulin resistance causes insulin scantiness. Imperfection of ß-cell functions genetically. Failure in insulin secretion genetically.
3	Other specific types	Pancreatic endocrinopathy. Indigenous infections like rubella and cytomegalovirus induced by drugs or chemicals. Other genetic indisposition.
4	Gestational diabetes	It is a temporary and appears during pregnancy usually develops during third trimester of pregnancy. After delivery, blood sugar levels generally return to normal

EPIDEMOLOGY

According to the International Diabetes Federation (IDF), the diabetes mellitus pandemic is dramatically arising worldwide. In 2019, the number of diabetes mellitus patients reached 463 million and will be 578 million in 2030 and 700 million in 2045. Several epidemiological studies have shown that the prevalence of diabetes mellitus increases with advancing age. According to the IDF, the number of diabetic people among those 65 and over has reached 136 million (19.3%). The projections are more alarming since they will be 195.2 million and 276.2 million respectively in 2030 and 2045.[8]

ETIOLOGY

Globally, the prevalence of DM has increased and therefore has grown in severity as a public health problem. Multiple risk factors are involved in the actual onset of the disease. Genetics, atmosphere, loss of very first phase associated with insulin launch, sedentary way of life, lack of physical exercise, smoking, alcoholic beverages, dyslipidemia, reduced β -cell sensitivity, hyperinsulinemia, improved glucagon activity are the primary risk elements for prediabetes and DM.[9]

TYPES OF DM

Traditionally, we have learnt and taught that there are two types of diabetes: Type 1 and Type 2. Then, there is gestational diabetes which often goes in remission in the postpartum period.

Type 1 diabetes is characterized by absolute insulin de ciency and often the presence of autoantibodies against pancreatic islet beta-cells.

Type 2 diabetes is characterized predominantly by insulin resistance. This classi cation appears way too simplistic in today's times, but it is still relevant from a practical perspective of the treating physician. This is so because the patients expect a clear answer as to whether or not they need insulin and what is the natural course of their disease 5 Aging, obesity, and physical inactivity are linked to insulin resistance in people with type 2 diabetes.[8] The pancreatic islets grow larger and generate more insulin in order to combat insulin resistance.[10]

Gestational diabetes mellitus (GDM) GDM is any level of diabetes or glucose intolerance detected during pregnancy, usually in the second or third trimester, or at the start of the pregnancy. During the initial phases of pregnancy, blood sugar levels are usually lower than normal for both fasting and postprandial, but they rise by the third trimester. Nearly 90% of all cases of diabetes and associated pregnancy-related problems are caused by GDM.[12] Hormonal changes that occur during pregnancy are the cause of gestational diabetes. Cells become less sensitive to the effects of insulin when the placenta generates certain hormone.[11]

COMPLICATIONS OF DM

Diabetic complications are the challenges associated with diabetes in the form of micro and macro vascular complications:

- **Microvascular complications include**
  - ✓ Retinopathy
  - ✓ Nephropathy and
  - ✓ Neuropathy
- **Macrovascular complications include**
  - ✓ Coronary artery disease (CAD)
  - ✓ Peripheral vascular disease (PVD) and
  - ✓ Cerebrovascular events (CVA).[12]

CONVENTIONAL TREATMENT APPROACHES FOR DM

INSULIN THERAPY

Insulin is an anabolic hormone and most effective glucose lowering agent available. It is recommended for usage in T1DM as sole therapy and in T2DM patients failing to control sugar levels with oral hypoglycemic Drugs. Insulin is a two-chain polypeptide having 51 amino acids and molecular weight 6000. Research is going every day to make newer insulin formulations with a precise focus on innovative insulin delivery methods ensuring more of a physiological daily insulin profile. Major role of insulin is in management of patients suffering from type 1 DM having advanced beta cell deficiency. Insulin directly acts on tissues to regulate glucose homeostasis, unlike other oral hypoglycemic agents requiring presence of sufficient endogenous insulin to act as insulin sensitizers, insulin secretagogues, incretin mimetic, amylin analogs and other factors Insulin has anabolic action and insulin signaling is critical for promoting uptake, use and storage of major nutrients like glucose, lipids and amino acids. Insulin stimulates glycogenesis, lipogenesis, and protein synthesis.[11,13]

ORAL HYPOGLYCEMIC DRUGS:

Sulfonylureas (such as gliclazide, gliclazide, glimepiride, and glyburidesulfonylureas involves the stimulation of the pancreatic islet beta-cells to secrete insulin. These drugs bind the adenosine triphosphate (ATP) sensitive potassium channels (K+ATP) on the cell membrane of pancreatic beta cells, which depolarizes the cell by preventing K+from exiting and thus leads to the opening of voltage-gated Ca2+ channels. The increase in intracellular Ca2+ leads to increased fusion of insulin granules with the cell membrane, This effect results in amplified responsiveness of β-cells to both glucose and non-glucose secretagogues, resulting in more insulin being released and lower blood glucose concentrations.

Sulfonylureas were reported effective in patients unresponsive to non-pharmacological treatments and non-obese patients. They can be administered as single or combined drugs to provide a longer effect and depending on the treatment regimen. Sulfonylureas were reported effective in patients unresponsive to non-pharmacological treatments and non-obese patients. They can be administered as single or combined drugs to

provide a longer effect and depending on the treatment regimen. Biguanides (metformin, metformin extended-release) The drug metformin acts by lowering both hyperglycemia and hyperinsulinemia, which ultimately increase glucose tolerance in patients with T2DM.[40] Its mechanism of action differs from other classes of oral antihyperglycemic agents. Metformin acts on the liver by decreasing hepatic glucose production; it also decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and consumption.[14]

STEM CELL THERAPY

Stem cell-based therapy is considered a promising potential therapeutic method for the treatment of diabetes, particularly in type 1 diabetes mellitus (T1DM). Major advances in research to derive IPCs from hPSCs have improved our chances of restoring glucose-sensitive insulin secretion in patients with T1DM. Despite the success in transforming and differentiation of the stem cells into insulin-producing cells, the rate of success is highly variable and this method is equally controversial.

Pancreatic β-cell replacement therapies for diabetes mellitus. While these therapies provide a positive impact and possible cure for the individual recipient, access is limited by availability of donor tissues. The derivation of pluripotent stem cells using efficient differentiation technologies has resulted in the generation of insulin-producing cells with characteristics similar to islet β-cells these cells are capable of reducing hyperglycemia in short-term assays.[14,15]

GENE THERAPY

Gene therapy is a new form of molecular medicine that will have a significant impact on human health in the next century Gene therapy is intended to inject genetic material into patient cells to compensate for damaged genes or to include therapeutic transgenes. insulin-producing pancreatic β cells from induced pluripotent stem cells (iPSCs) originating from diabetes patients aims to provide autologous cells for cell replacement therapy for Diabetes.[16]

CONCLUSION

Diabetes mellitus has evolved significantly over the past few decades, shifting from conventional glucose-lowering strategies toward comprehensive metabolic and organ- protective approaches. Advanced treatment modalities now focus not only on glycemic control but also on reducing cardiovascular risk, preserving pancreatic β-cell function, promoting weight loss, and improving patient quality of life.

Technological innovations have also played a vital role in improving diabetes management. Continuous glucose monitoring systems and insulin pump therapy allow real-time glucose monitoring and more accurate insulin delivery Regenerative medicine approaches, including stem cell therapy and gene therapy, represent promising future strategies aimed at disease modification and potential cure. Stem cell therapy focuses on regenerating or replacing damaged pancreatic β-cells, thereby restoring endogenous insulin production. Gene therapy, on the other hand, aims to correct genetic and molecular defects associated with diabetes through advanced genetic engineering.

Overall, recent advances in diabetes treatment have significantly improved disease management and patient prognosis. Future research is expected to focus on personalized medicine, fully automated insulin delivery systems, oral insulin.

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