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# RECENT ADVANCE IN DIABETES: INNOVATION, CHALLENGES AND FUTURE DIRECTION

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**Abstract:**
Diabetes remains a significant global health challenge, characterized by rising prevalence, complex management needs, and a substantial burden on healthcare systems. Recent advances in diabetes research have introduced innovative approaches aimed at improving patient outcomes, yet numerous challenges persist. This review explores these advancements, focusing on the latest innovations in pharmacotherapy, technological interventions, and personalized care strategies. Notable developments include the introduction of SGLT-2 inhibitors and GLP-1 receptor agonists, which have shown promise in not only managing blood glucose levels but also reducing cardiovascular risks in patients with type 2 diabetes. Additionally, advancements in continuous glucose monitoring (CGM) and insulin delivery systems, including artificial pancreas technologies, have significantly improved glycemic control and quality of life for patients. However, these innovations come with challenges such as high costs, limited access in low-resource settings, and the need for widespread education and training. The review also addresses the integration of digital health solutions, including mobile health applications and telemedicine, which have the potential to enhance patient engagement and adherence to treatment. Looking to the future, the focus will likely shift towards the implementation of precision medicine, leveraging advances in genomics and bioinformatics to create tailored treatment plans that account for individual variability. Overcoming existing barriers, such as ensuring equitable access to these new technologies and addressing socioeconomic disparities, will be critical to realizing the full potential of these innovations. This article provides a critical overview of the recent advances, ongoing challenges, and future directions in diabetes research and care.

**Keywords:** Diabetes Management, Insulin Delivery systems, Gene theraphy, continuous Glucose Monitoring(CGM)

## INTRODUCTION:

Diabetes is a common disease that affects millions of people around the world. Diabetes is a most established issue it found by the Egypt doctor around multi year ago. Diabetes is a disease that occurs when your blood glucose, also called blood sugar, is too high. It happens when the body cannot properly use sugar from food, leading to high levels of sugar in the blood.
There are three type of diabetes:

1. Type 1 Diabetes
2. Type 2 Diabetes
3. Gestational diabetes mellitus

The year 2021 marks the 100th anniversary of the discovery of insulin, which has greatly changed the lives of people with diabetes. Although polyuric states resembling diabetes mellitus have been known for over 3,500 years since the initial description in an Egyptian papyrus (1550 BC), it was only after the discovery of insulin that meaningful treatment of diabetes was possible. [1] A major public health concern today is the diabetes epidemic of the late 20th and early 21st centuries, which is linked to a confluence of genetic, behavioural, social, and prenatal variables. Less than 5% of US diabetes patients have type 1 diabetes, despite a gradual rise in its occurrence. The majority of occurrences of diabetes globally are type 2. In the US, 28 million individuals have type 2 diabetes, and over 80 million are thought to be at high risk of getting the disease, a condition known as prediabetes. [2] It is estimated that type 2 diabetes affects more than 350 million people worldwide.[3] Diabetes, a chronic degenerative illness, has relatively specific long-term consequences that affect the eyes, kidneys, and peripheral and autonomic nerve systems.[4] Accounting for more adult cases of vision loss, end-stage kidney failure, and amputations than any other disease.[5] Furthermore, type 1 and type 2 diabetes raise the risk of cardiovascular disease (CVD) by a factor of two to five.[6]Over the last decade, the usual vascular problems of diabetes have been joined by an increased risk of several malignancies, including pancreatic, liver, colorectal, endometrial, and braes.[7] The economic burden of diabetes and prediabetes is estimated in the United States to be $322 billion per year8, with complications accounting for the majority of overall expenses. However, pharmaceutical and monitoring costs have recently contributed an increasing proportion of total costs. [8] Smaller and more accurate glucose monitoring systems are now available, allowing patients with T1Ds to see their glucose readings every 1-5 minutes [9]. Despite advancements, individuals with type 1 diabetes continue to have a lower life expectancy, higher risk of macro- and microvascular problems, and lower quality of life compared to non-diabetics. To improve diabetes control, three areas have been studied: pharmaceutical, technological, and biological techniques. New insulin formulations offer improved efficacy, safety, and flexibility in diabetes care. Advancements in technology have made insulin pumps, sensors, and glucometers more efficient and effective. [10]

**Types of Diabetes:**

1. Type 1 diabetes: Type 1 diabetes is a metabolic disorder that results from the progressive destruction of insulin-secreting β-cells in the islets of Langerhans of the pancreas, leading to insulin insufficiency and hyperglycemia [11]. People with type 1 diabetes are dependent on insulin for the rest of their life. But insulin is not a cure, and people with diabetes are at significant risk for a wide range of serious complications, including heart and kidney diseases and blindness.[12]To avoid the variations in blood glucose levels in those with type 1 diabetes, and to reduce the chance of long-term complications, it would be helpful for new β-cells to be produced. Ideally, new β-cells should be derived from cell sources already existing within the person with diabetes so avoiding immune suppression. [13]
2. Type II Diabetes: Type II Diabetes is Alternatively exogenous sources of surrogate β-cells have also been described, including adult human pancreases donated after death, fetal pancreas, pluripotent and multipotent stem cells, and cells that reside in the liver. Whilst most of these exogenous sources are heterologous to the recipient; some are autologous such as cord blood stem cells and pluripotent stem cells induced from fibroblasts derived from skin. [14] In insulin-resistant individuals, a gradual decrease in β-cell compensation leads to hyperglycemia.
3. Gestational diabetes mellitus: Gestational diabetes mellitus (GDM) is a state of hyperglycemia (fasting plasma glucose ≥ 5.1 mmol/L, 1 h ≥ 10 mmol/L, 2 h ≥ 8.5 mmol/L during a 75 g oral glucose tolerance test according to IADPSG/WHO criteria) that is first diagnosed during pregnancy.GDM is one of the most common medical complications of pregnancy, and its inadequate treatment can lead to serious adverse health effects for the mother and child.[15,16]

**Traditional and Modern Strategies for Addressing Diabetic Symptoms:**
Together with the discovery of new antidiabetic drugs with the least side effects but with highest efficiency, different administration approaches are being relentlessly searched for (Fig. 1a) including next to the most common oral approach, nasal, buccal, pulmonary and subcutaneous administration routes.[17-19]The administration method is largely dependent on the size and physico-chemical character of the antidiabetic drug to be delivered. As treatment of T2D occurs mainly with small organic molecules, therapeutic peptides such as insulin and amylin are mostly considered for T1D.[20,21]

**(i) Oral drug delivery:**
The oral delivery remains a preferential drug administration route as it is a non-invasive, on-demand approach.(a) List or currently investigated antidiabetic drug administration routes ranging from oral delivery of small organic T2D drugs (metformin, repaglidine, glibenclamide) to subcutaneous delivery of T1D therapeutics such as insulin and amylin.[22] Their advantages and limitations are listed in addition. (b) Chemical structures of common T2D antidiabetic drugs as well as insulin, the main T1D therapeutic. The region of the insulin molecule not critical for insulin receptor recognition is labelled as B26–B30. It is in this region that amino acids are generally substituted. These insulin analogues are still recognized by and bind to the insulin receptor.[23-26]

**(ii) Subcutaneous drug delivery:**
For class III drugs such as peptides (insulin), subcutaneous drug delivery is required. These drugs can be oxidized and denatured in the acid environment of the gastrointestinal (GI) tract, losing their therapeutic activity. Next to the low pH, gastric enzymes are major barriers for antidiabetic drugs such as insulin when administered orally.[27-29] A typical absorption-enhancing excipient is sodium N-[8-(2-hydroxybenzoyl)aminocaprylate], which protects against enzymatic degradation via local buffering actions and transiently enhances absorption. While the need of higher doses to compensate the elevated level of unabsorbed drug and the associated increase in costs are considered less problematic nowadays owing to the significant decrease of the cost of peptide synthesis over the past years, the main drawback associated with oral delivery is the high inter-subject variability, which makes it often difficult to create robust methodology to define a safety margin, in particular for peptide/protein-based antidiabetic drugs. Other routes have been considered in diabetes treatment such as nasal, pulmonary, buccal , and trans dermal approaches. [30]

**(iii) Pulmonary delivery:**
Human lungs (Fig. 1b) have a combined surface area of 50–100 m2 , 1000-fold larger than that of the nasal cavity and several times larger compared to the 2 m2 of skin. Both lungs contain about 274–790 million alveoli involved in gas and liquid exchange and transport of liquids delivered from alveoli to the blood.102 Its alveolar epithelium has a thickness of 0.1–0.2 mm with minimal mucociliary clearance and presents high permeability as well as abundant vasculatures, allowing rapid drug absorption. This makes alveoli and the associated vascular network a sought-after method for delivering antidiabetic drugs to the systemic circulation. However, while corticosteroids and other drugs might be delivered effectively, hydrophilic macromolecules such as insulin have limited permeation through the mucus layer (1–10 mm thickness) that covers the pulmonary epithelium. Furthermore, 90% of inhaled insulin is lost in its passage to alveoli to enter the blood stream. The other barriers to overcome for insulin absorption include pulmonary enzymes and macrophages. Most proteins are subjected to degradation by proteases or clearance by macrophages.

**(iv) Buccal delivery:**
In the recent years, buccal mucosa has emerged as a promising delivery site for antidiabetic drugs such as insulin.103 Buccal mucosa offers a rich vasculature (Fig. 1c). The buccal route owns a series of advantages as it avoids pre-systemic metabolism of insulin via low enzymatic activity and

ease of accessibility of buccal absorption site. Salivary scavenging as well as the barrier properties of mucosa and small area available for drug absorption are intrinsic limitations of this approach.

Management of diabetes involves a combination of lifestyle modifications, medication, and regular monitoring of blood glucose levels. Key strategies include maintaining a balanced diet, engaging in regular physical activity, and adhering to prescribed medications like insulin or oral hypoglycemic agents. Effective management also requires regular monitoring for potential complications and adjustments to the treatment plan as needed to maintain optimal blood sugar levels.

The management of diabetes is challenging for both patients and professionals find it difficult to control diabetes mellitus. Patients with strong levels of health literacy and numeracy are better able to self-manage their food, exercise, medications, and insulin dosages. Clinicians frequently urge behaviour change, assess blood glucose patterns, and modify medication doses during brief clinic appointments, sometimes working with patients who have a limited awareness of their diagnosis or treatment plan.

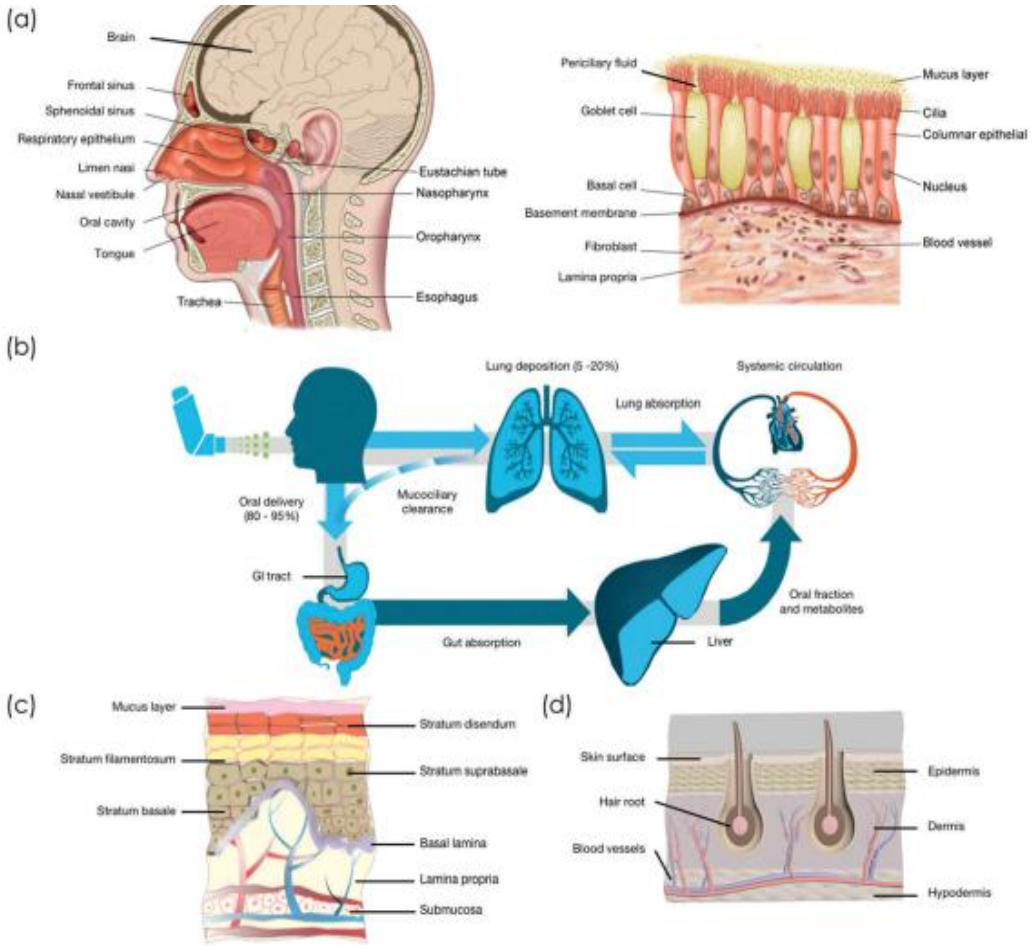


Figure : 1 Antidiabetic delivery pathways. (a) Nasal drug administration. (b) Pulmonary delivery where, in general, 420% of the drug is deposited in the lung, with the rest being swallowed orally. Deposited compounds in the lung are also cleared by mucociliary clearance and systemic absorption through lung. (c) Buccal administration. (d) Transcellular and intercellular routes of drug delivery via the skin[31]

**Recent Innovation in Diabetes Management:**

| Sr. No. | Drug Name | Drug Class | Use | Route of Administration | Dosage Form |
|---|---|---|---|---|---|
| 1. | Bexagliflozin[32] | sodium-glucose co-transporter 2 (SGLT2) inhibitors | used in the treatment of type 2 diabetes mellitus. | Administration by orally | Tablet |
| 2. | Teplizumab[33] | Anti-CD3 monoclonal antibody | Delays the onset of Type 1 Diabetes in At-risk individuals. | Intravenous(IV) | Injection |
| 3. | Tirzepatide[34] | GIP\GLP-1 receptor agonist | Type 2 diabetes management. | Subcutaneous | Injection |
| 4. | Finerenone[35] | Nonsteroidal mineralocorticoid receptor antagonist. | Reduces the risk of kidney failure and cardiovascular events in patients with chronic kidney disease associated with Type 2 diabetes. | Administered by orally | Tablet |
| 5. | Imeglimin[36] | Glimins | Type 2 diabetes management. | Administered orally | Tablet |
| 6. | Linagliptin[37] | Dipeptidyl Peptidase-4 (DPP-4) Inhibitor | used primarily in the management of type 2 diabetes. | Administered by orally | Tablet |
| 7. | Qternmet XR[38] | Dapagliflozin - SGLT2 inhibitor (Sodium-glucose co-transporter 2 inhibitor) Saxagliptin - DPP-4 inhibitor (Dipeptidyl peptidase-4 inhibitor) Metformin - Biguanide | **Dapagliflozin:** SGLT2 inhibitor (Sodium-glucose co-transporter 2 inhibitor). **Saxagliptin:** DPP-4 inhibitor (Dipeptidyl peptidase-4 inhibitor). **Metformin:** Biguanide, which decreases hepatic glucose production and improves insulin sensitivity. | Administered by orally | Tablet |
| 8. | Semaglutide[39] | GLP-1 Receptor Agonist | used to improve blood sugar control in adults | Administred by oral and Subcutaneous | Injection, Tablet |

| | | | | | |
|---|---|---|---|---|---|
| | | | with type 2 diabetes | injection | |
| 9. | Albiglutide[40] | GLP-1 receptor agonist | It is typically used when other oral medications for diabetes are not providing adequate blood glucose control. | Subcutaneous injection | Injectable solution or pre-filled pen |
| 10. | Lixisenatide [41] | GLP-1 Receptor Agonist | used to improve glycemic control in adults with type 2 diabetes | Subcutaneous Injection | Injection |

**Challenges and its management in diabetes:**

A diabetes diagnosis in youth or adolescent has significant ramifications. The majority of diabetic complications are linked to both the length of the disease and glycemic management. A young person diagnosed with diabetes will almost certainly experience hyperglycemia for many years, which will increase their chance of developing complications from their diabetes. In the prime of their productive life, these patients are also susceptible to morbidity and incapacity as a result of complications from diabetes. The effects of various forms of diabetes in young people. [42]

Furthermore, research has demonstrated that T2D with an early onset progresses more quickly than T2D with a late-life onset . Compared to people with later-onset disease, these people have more difficulty controlling their blood sugar, more frequent comorbidities, and a higher risk of complications. It is crucial to guarantee ideal management of diabetes from the moment of diagnosis.[43,44]

All patients with diabetes mellitus with a juvenile onset should have a high index of suspicion for the emergence of chronic problems. It is not necessary to screen for retinopathy and nephropathy in the first five years following the onset of T1D because these complications are uncommon during this period. Due to the likelihood of long-term diabetes going untreated, individuals with all other forms of diabetes should have screenings for complications performed at the time of diagnosis.

The two medications that have been licensed for the treatment of T2D in children and adolescents are insulin and metformin These kids also frequently have other cardiovascular risk factors, like hypertension and abnormal lipid profiles, which require age-appropriate treatment. It is imperative to make lifelong lifestyle changes in order to stop gaining weight and lose extra weight.[45]

**Technology Innovation:**

The treatment of diabetes has undergone a technological revolution in recent years. This is due to the use of insulin pumps and sensors for continuous glucose monitoring, as well as the ability to integrate these two systems to create a device that can autonomously adjust insulin administration based on sensor values, resulting in the creation of a closed-loop system, also known as an artificial pancreas.[46]

**Further Role of Technology:**

Technology can simplify the management of diabetes: as an example, smart insulin pens with memory functions could record the insulin doses administered and transfer data via Bluetooth to dedicated apps.[47] Several smart phone apps for diabetes management have been developed, with the aim of help T1Ds to calculate insulin bolus, registered glucose data, track carbohydrate intake, or physical activity, with the possibility of sharing data on glycemic trends with clinicians. Also, CGM data could be managed with a smart phone app and shared in a cloud system, thus allowing also clinicians to visualize glucose values.[48] This leads to the development aof telemedicine methods which are tremendously useful when subjects can't access the clinic, as recently occurred

during Covid 19 pandemic. Similarly, data could be shared between T1Ds and caregivers, especially for example for children with T1D.[49,50]

## COUNCLUSION:

Recent advances in diabetes research have significantly improved our understanding and management of this complex disease. Innovations such as continuous glucose monitoring systems, closed-loop insulin delivery, and the development of GLP-1 receptor agonists have enhanced patient outcomes and quality of life. However, challenges remain, including addressing the rising prevalence of diabetes, ensuring equitable access to new therapies, and managing complications associated with long-term diabetes. Furthermore, the integration of artificial intelligence and precision medicine holds great promise for individualized treatment strategies, but also presents ethical and logistical challenges. Future directions should focus on combining technological innovation with public health initiatives, aiming for more accessible, cost-effective, and personalized care. Continued investment in research, particularly in understanding the genetic and environmental factors contributing to diabetes, will be crucial in overcoming current barriers and moving towards a future where diabetes is better managed and potentially curable. Collaborative efforts across disciplines and sectors are essential to address these challenges and capitalize on the opportunities presented by recent ad vancements in diabetes care.

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