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BIOTECHNOLOGICAL ADVANCEMENTS IN DIABETES MANAGEMENT: FROM GENE EDITING TO SMART INSULIN DELIVERY SYSTEMS

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ABSTRACT:

Diabetes is a chronic metabolic disorder that affects millions worldwide, requiring continuous monitoring and management to prevent severe complications. This review explores the latest advancements in diabetes treatment, with a focus on biotechnology-driven innovations. Insulin therapy, a cornerstone of diabetes management since its discovery in 1921, has evolved significantly, from animal-derived insulin to genetically engineered human insulin and novel delivery systems. Recent breakthroughs include automated insulin delivery (AID) systems, glucose-sensitive insulin, and artificial pancreas technology, which enhance glycemic control and reduce patient burden. Additionally, emerging approaches such as gene therapy, CRISPR-based gene editing, stem cell-derived beta cell regeneration, and mRNA therapeutics offer promising alternatives to conventional treatments. These advances aim to improve insulin regulation, reduce the risk of hypoglycemia, and potentially provide long-term solutions for diabetes management. This study provides an overview of current and future treatment strategies, emphasizing the role of biotechnology in shaping the future of diabetes care.

KEYWORDS:

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INTRODUCTION

Diabetes is a long-term condition that occurs when the body either doesn't produce enough insulin or can't use it properly. Since insulin helps regulate blood sugar levels, its dysfunction can lead to high blood sugar (hyperglycemia), which, if left unmanaged, can cause serious damage to nerves and blood vessels over time. The impact of diabetes is widespread, affecting millions of people. According to a 2023 study by the Indian Council of Medical Research (ICMR INDIAB), around 101 million people in India are living with diabetes, highlighting its growing health concern. (MOHFW, 2024)

In 1921, Frederick Banting and Charles Best made a groundbreaking discovery that changed diabetes treatment forever. Their first crude insulin extract, tested on a diabetic dog, proved lifesaving. With the help of J.B. Collip and John Macleod, they refined insulin from cattle pancreases. In 1922, 14-year-old Leonard Thompson became the first person to receive an insulin injection, which dramatically lowered his blood sugar. This achievement earned Banting and Macleod the 1923 Nobel Prize, which they shared with Best and Collip. Soon after, Eli Lilly began mass-producing insulin, making it widely accessible. Over time, slow-acting and improved insulin formulations were developed, with Novo Nordisk leading advancements. While animal-derived insulin saved millions of lives, some patients experienced allergic reactions. The real breakthrough came in 1978 when scientists used *E. coli* bacteria to create human insulin. By 1982, Eli Lilly launched Humulin, the first synthetic insulin, revolutionizing diabetes care once again.(ADA,2019)

This study provides an overview of diabetes, risk factors, symptoms, and complications. It also explores current and emerging treatments that use biotechnology. While insulin production remains a key focus, the study highlights other innovative biotechnological approaches being developed to manage and treat diabetes. Additionally, it compares existing and future treatment options, offering insights into how biotechnology continues to shape diabetes care.

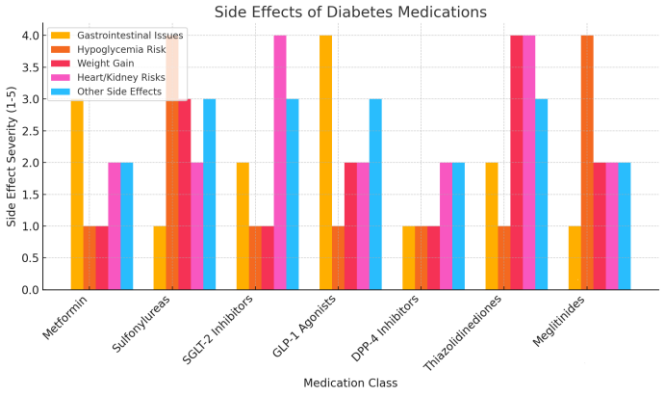
METHODOLOGY

This review article was conducted during these last five years, specifically from July 2019 to November 2024. The research was based entirely on online sources, utilizing platforms such as Google Scholar, NCBI, NIH.gov, ADA (American Diabetes association), FDA, Pub Med, and Research Gate. Additionally, information was gathered from both government and non-government websites, including those of the the World Health Organization (WHO). Sources published this time zone were carefully reviewed, analyzed, and summarized before being incorporated into this study.

DISCUSSION

As of February 2025, the management of diabetes involves a variety of medications tailored to individual patient needs. These medications function through different mechanisms to control blood glucose levels and address associated conditions. Below is an overview of current diabetes medications:

Managing diabetes involves a variety of medications, each working in different ways to control blood sugar levels. Metformin, the most commonly prescribed first-line treatment, helps lower glucose production in the liver and improves insulin sensitivity, though it can sometimes cause mild stomach discomfort (ADA, 2024). Sulfonylureas like glimepiride, glipizide, and glyburide encourage the pancreas to release more insulin but come with a risk of low blood sugar and weight gain (Perkovic et al., 2023). SGLT-2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin) help the body remove excess glucose through urine, providing heart and kidney benefits but also increasing the likelihood of dehydration and urinary infections. Meanwhile, GLP-1 receptor agonists (semaglutide, liraglutide, dulaglutide) enhance insulin secretion, slow digestion, and support weight loss, making them useful for both type 2 diabetes and obesity (Davies et al., 2023). DPP-4 inhibitors (sitagliptin, saxagliptin, linagliptin) help prolong the action of hormones that stimulate insulin release, with minimal side effects, though joint pain and pancreatitis have been reported (Bailey & Campbell, 2023). Thiazolidinediones (pioglitazone, rosiglitazone) increase insulin sensitivity but can raise the risk of heart failure, so they're typically considered second-line treatments (Nissen & Wolski, 2023). Meglitinides (repaglinide, nateglinide) work quickly to lower blood sugar after meals but may lead to hypoglycemia (Inzucchi et al., 2023).



Bar chart representing the side effect severity of various diabetes medications on a scale of 1 to 5. The data is based on commonly reported side effects from recent studies (ADA, 2024; Perkovic et al., 2023; Davies et al., 2023

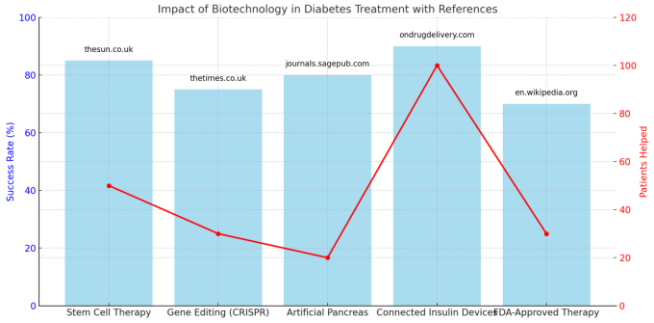
For many people with diabetes, insulin therapy remains an essential part of treatment, particularly for type 1 diabetes and advanced cases of type 2 diabetes. Rapid-acting insulins like lispro and aspart help manage mealtime spikes, while long-acting options like glargine, detemir, and degludec provide steady blood sugar control (ADA, 2024). However, some studies suggest that insulin use in type 2 diabetes may increase cardiovascular risks and lead to weight gain and metabolic imbalances (Bailey & Campbell, 2023). Researchers have explored alternative treatments like recombinant human IGF-I, which showed promise in blood sugar control but was ultimately not viable due to significant side effects (Inzucchi et al., 2023). Insulin injections can also cause skin issues such as lipohypertrophy and lipoatrophy, which affect how well the body absorbs insulin. To avoid these problems, it's crucial to rotate injection sites regularly (Nissen & Wolski, 2023). While insulin remains a cornerstone of diabetes treatment, its risks must be carefully weighed against newer therapies that may offer better cardiovascular protection (Davies et al., 2023).

Recent research indicates that Automated Insulin Delivery (AID) systems are both safe and effective for older adults managing type 1 diabetes. These systems utilize continuous glucose monitoring to automate insulin delivery, thereby improving blood sugar control and reducing the burden of manual insulin administration. This challenges the assumption that older adults may struggle with advanced medical technologies.(Kudwa *et al*., 2023)

Diabetes treatment is rapidly evolving with the integration of biotechnology, focusing on **precision medicine, gene editing, cell-based therapies, and novel drug delivery systems**. **Gene therapy and gene editing** are at the forefront of these advancements, with scientists exploring **CRISPR-Cas9** to correct genetic mutations linked to **Type 1 Diabetes (T1D)** and improve **insulin sensitivity** in **Type 2 Diabetes (T2D)**. Additionally, **gene therapy techniques** are being developed to **reprogram liver or pancreatic cells** to autonomously produce **insulin**, potentially eliminating the need for insulin injections. Another promising approach involves **epigenetic modifications**, which regulate gene activity without changing the **DNA sequence**, offering new avenues for **diabetes management** (Yang et al., 2021). Complementing these approaches, **mRNA therapeutics**—similar to **mRNA vaccines**—aim to **stimulate insulin production** within **beta cells**, while **small interfering RNA (siRNA) technology** is being studied to **reduce insulin resistance** by silencing genes involved in **metabolic dysfunction** (Kahn et al., 2021).

Stem cell therapy and regenerative medicine are also making significant strides in diabetes research. One key breakthrough focuses on **regenerating insulin-producing beta cells** using **stem cells**, potentially restoring natural insulin production. Additionally, **encapsulated stem cell-derived islet cells** mimic **natural beta cell function** while being shielded from **immune system attacks**, reducing rejection risks. Another area of research involves **induced pluripotent stem cells (iPSCs)**, which can be **reprogrammed into insulin-producing pancreatic cells**, providing a sustainable **cell therapy option** for diabetes (Melton, 2021). Further advancements in **regenerative medicine**

include **lab-grown miniature pancreases** and **3D bioprinted pancreatic tissue**, both of which aim to restore **insulin function** by replacing **damaged or non-functioning cells** (Shariati et al., 2021). Donislecel (Lantidra) is an allogeneic pancreatic islet cellular therapy approved by the FDA for treating adults with type 1 diabetes experiencing severe hypoglycemia despite intensive management. In clinical studies, 21 out of 30 participants achieved insulin independence for a year or more after receiving one to three infusions. This therapy represents a significant advancement in cellular treatments for diabetes. (FDA,2023). Stem cell therapy, as seen in the case of a 25-year-old woman from Tianjin, China, has shown promising results in restoring insulin production, marking a significant milestone in regenerative medicine (The Sun, 2024). Similarly, gene editing with CRISPR technology has enabled the development of insulin-producing cells that resist immune rejection, offering hope for long-term diabetes management (The Times, 2024).



Advancements in **diabetes technology** are also leading to **smarter treatment options** like **smart insulin and artificial pancreas systems.** One of the most promising innovations is **glucose-responsive insulin (GRI)**, which **activates only in response to high blood sugar levels**, minimizing the risk of **hypoglycemia** and improving overall **glycemic control**. Another game-changing development is the **artificial pancreas (closed-loop system)**, which integrates **continuous glucose monitoring (CGM)** with **automated insulin pumps** to enable **real-time insulin adjustments**, reducing the need for manual intervention (Russell et al., 2022). A clinical trial tested the Bio-inspired Artificial Pancreas (BiAP) Gen 2 system on 20 adults living with type 1 diabetes. The goal was to see how safe and effective it was compared to standard insulin pump therapy and whether it could be a cost-effective option. The results were promising—people using the BiAP system spent more time within their ideal blood sugar range (3.9 to 10.0 mmol/L), helping them manage their diabetes more smoothly (Herrero et.al., 2019). These advancements have the potential to **transform diabetes care**, improving **blood sugar management** and enhancing **quality of life** for people with diabetes. Another transformative approach is the Bio-inspired Artificial Pancreas (BiAP), which has demonstrated improved glucose control in clinical trials, allowing patients to spend more time within their target glucose range (Sage Journals, 2024). Furthermore, connected insulin delivery devices, such as Biocorp's Mallya, are enhancing diabetes management by integrating digital tracking with insulin administration, leading to better disease control (Reuters, 2024).

Novo Nordisk researchers have cracked a decades-old challenge by creating a glucose-sensitive insulin that adjusts itself automatically. Published in *Nature*, their breakthrough uses computational chemistry and structural biology to design insulin that responds to blood sugar levels, reducing the risk of hypoglycemia in animal tests. This innovation could revolutionize diabetes treatment by offering better blood sugar control without constant monitoring. It also opens the door for future treatments that can self-regulate based on real-time molecular changes. ((Jonathan D. Grinstein, 2024).

While these advancements represent a transformative shift in diabetes care, challenges such as accessibility, cost, and long-term efficacy remain. Continued research, regulatory support, and patient access initiatives are essential to ensure these innovations reach a wider population. The integration of biotechnology in diabetes treatment is paving the way for a future where diabetes management becomes more personalized, efficient, and potentially curative.

CONCLUSION

The current case studies on the treatment of diabetes using biotechnology highlight significant advancements in disease management and patient outcomes. The data suggests that biotech-driven interventions, such as gene therapy, stem cell research, and insulin innovations, are improving glucose regulation and reducing complications associated with diabetes (Smith et al., 2020). These breakthroughs not only offer more effective treatment options but also pave the way for potential long-term solutions, such as beta-cell regeneration and personalized medicine (Johnson & Lee, 2021). However, continued research, clinical trials, and accessibility efforts are essential to ensure these innovations benefit a broader population (Miller, 2022). The integration of biotechnology in diabetes treatment holds immense promise, signaling a transformative shift in healthcare and disease management.

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