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New approaches for management of diabetes mellitus: A review

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Abstract

Diabetes mellitus is a multifaceted, non-communicable endocrine condition marked by persistent hyperglycaemia and related complications that impact multiple organs. The incidence of DM is on the rise, with estimates predicting over 640 million cases worldwide by 2040. This review explores innovative strategies for diabetes management, highlighting advancements in nanotechnology, statin therapies, stem cell treatments, gene therapy, and herbal remedies. Each strategy offers distinct advantages and challenges, ranging from nanotechnology's capability for continuous glucose monitoring and targeted drug delivery to the role of statins in mitigating cardiovascular risks among diabetic patients. Furthermore, stem cell methods and gene therapy present promising prospects for creating insulin-producing cells and providing immunological interventions, while herbal treatments serve as effective adjuncts with minimal side effects. Despite these advancements, a definitive cure for DM remains elusive, emphasizing the necessity for comprehensive management strategies. The review underscores the significance of achieving optimal metabolic control and advocating for public health initiatives that enhance healthcare accessibility and foster patient-centered care. Ultimately, a holistic approach that integrates these emerging technologies and therapies could lead to improved therapy of diabetes and its related complications.

Keywords: Hyperglycemia; Complications; Glycemic control; Pharmacotherapy

1. Introduction

Diabetes mellitus is a long-standing, intricate, and non-transmissible endocrinal disease that is hastily expanding worldwide clinical practice, frequently tied to complex metabolic developments. Marked by high blood glucose and lipid levels, along with oxidative stress, DM results in chronic complications that affect various organs. According to the World Health Organization (WHO), DM is a high-morbidity and high-mortality epidemic affecting approximately 387 million people globally, with projections surpassing 640 million by 2040 [1]. T2DM is categorized by hyperglycaemia and complications such as renal failure, loss of sight, stroke, and lower limb injured. Epidemiological studies show that T2DM is triggered by the genetic and environmental factors [2]. In spite of the prevalence of obesity-related T2DM, the incidence of Type I diabetes mellitus is increasing [3]. Most10 percent of diabetes patients have Type 1 Diabetes Mellitus, and both types are linked to prolonged circulatory system complications and the risk of hypoglycaemia [4]. Achieving normoglycemia can reduce DM-related complications, but hypoglycaemia episodes hinder achieving near-normoglycemia in T1DM patients [5]. Those unaware of their hypoglycaemic status face significant clinical challenges, particularly hypoglycaemic unawareness. Advances in gene therapy offer promising prospects for DM treatment [6]. Current T2DM treatments include insulin injections and oral hypoglycaemic agents, which, despite their importance, have side effects [7]. Insulin has been crucial for managing insulin-deficient DM since its discovery, yet the severe beta-cell deficiency necessitates exogenous insulin for survival. Despite advancements in understanding DM and developing

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insulin analogues, finding alternatives or additional treatments to achieve tight control of blood sugar levels without causing issues like low blood sugar or weight gain continues to be difficult, emphasizing the need for different approaches. This review examines alternative therapeutic strategies for managing DM, such as nanotechnology, statin techniques, stem cell therapy, gene therapy, and herbal therapy, and the challenges linked to these methods [8].

2. Classification of diabetes

2.1. Type 1 diabetes mellitus

Type 1 DM, also known as reaction diabetes, was previously referred to as juvenile-onset or ketosis-prone diabetes. Individuals with Type I diabetes may also have other autoimmune disorders like Graves' disease, Hashimoto's thyroiditis, and Addison's disease [9]. Type I diabetes, also known as insulin-dependent diabetes (IDDM), primarily affects children and young adults, with its onset often sudden and potentially life-threatening. This type of diabetes is linked to autoimmune processes that destroy beta cells in the pancreas, leading to a lack of insulin production. Treatment typically involves insulin injections due to the severe deficiency or absence of insulin secretion caused by beta-cell destruction. The rate at which beta cells are destroyed can vary from person to person, occurring rapidly in some and slowly in others. Biomarkers such as islet cell auto-antibodies and insulin auto-antibodies are indicative of immune destruction in Type I diabetes, insulin auto-antibodies, Around 85-90% of people with type I diabetes show the presence of auto-antibodies to glutamic acid decarboxylase (GAD) when their fasting hyperglycaemia is detected. The cause of diabetes is still not fully understood, but there is evidence suggesting an autoimmune process where these auto-antibodies attack and destroy the beta-islet cells in the majority of cases [10,11].

2.2. Type 2 diabetes mellitus

Type 2 DM is also called as ketosis-resistant diabetes. It is characterized by a progressive insulin secretion defect against of insulin resistance [12]. Both types of diabetes can affect the blood vessels, renal, eyes, and nerves are leads to illness and death rate. The major predisposing factors are weight gain, inactive lifestyle, elders, and genetic factors (Ross and Wilson, 2010). Patients with type 2 DM are mostly emerging the issues are macro and microvascular [13,14].

2.3. Gestational diabetes

Gestational Diabetes Mellitus is a form of diabetes that occurs during pregnancy. It includes women who develop Type 1 Diabetes during pregnancy or those with undiagnosed type 2 diabetes discovered during pregnancy [15]. GDM is diabetes diagnosed during pregnancy that is not clearly over diabetes, often disappearing after delivery. Children born to mothers with GDM are at a greater risk of weight gain and type 2 DM in the future due to the effects of exposure to high blood sugar levels in the womb [16].

3. New strategies for treating diabetes mellitus

3.1. Using nanotechnology to treat diabetes mellitus

Recent advances in diabetes research have been leveraged by nanotechnology to develop cutting-edge glucose measurement and insulin delivery techniques with the potential to significantly enhance the well-being of diabetes patients. This analysis delves into the intersection of nanotechnology and diabetes research, specifically focusing on the developmental of glucose sensors utilizing nanoscale elements like metal nanoparticles and carbon nanostructures. These tiny components have been proven to enhance the sensitivity and response time of glucose sensors, enabling continuous monitoring of glucose levels within the body. Additionally, the review delves into the nanoscale strategies for creating “closed-loop” insulin delivery systems that automatically adjust insulin release based on blood glucose changes. By integrating blood glucose measurements with insulin administration, these systems aim to reduce the need for patient intervention, ultimately leading to improved health outcomes and overall quality of life for individuals with diabetes mellitus [17].

3.2. The use of nanoparticles in biology for treating diabetes mellitus

Nanotechnology has emerged as a valuable tool for a range of biomedical uses in recent years. Nanoparticles, which are materials with sizes smaller than 100 nm in at least one dimension, have distinct characteristics that change when scaled down to the nanoscale. This enables them to interact with cellular biomolecules in a specific manner. NPs engineered for precise cell delivery carry therapeutic substances [18]. Moreover, metal nanoparticles are perceived as being less harmful than mineral salts and provide numerous advantages to the body [19].

3.2.1. Zinc oxide NPs

ZnO nanoparticles (NPs) find uses in a range of biomedical applications, including treating diabetes, fighting bacteria, combating cancer and fungal infections, delivering drugs, and reducing inflammation [20]. Zinc is crucial for the biosynthesis, secretion, and storage of insulin, with zinc transporters like zinc transporter-8 being vital for insulin release from pancreatic beta cells [21]. ZnO NPs can boost insulin signaling by enhancing insulin receptor phosphorylation and phosphoinositide 3-kinase activity [22]. Research indicates that ZnO NPs can repair pancreatic tissue damaged by diabetes, improving blood sugar and serum insulin levels. Studies comparing ZnO NPs with standard antidiabetic drugs like Vildagliptin show that ZnO NPs are effective in treating type 2 diabetes [23]. ZnO NPs have shown notable antidiabetic activity in various animal models, often surpassing other treatments. They also have powerful biological effects, such as acting as antioxidants and reducing inflammation, which makes them potential candidates for treating diabetes and its related complications [24].

3.2.2. Magnesium NPs

Magnesium (Mg) is essential for glucose homeostasis and insulin secretion, Contribution to the process of adding phosphate groups to molecules and regulating the breakdown of glucose through a variety of enzymes [19]. Mg deficiency can result in insulin resistance, dyslipidemia, and complications in diabetic mice [25]. A study by Kei et al. (2020) demonstrated that MgO nanoparticles can help reduce blood sugar levels, improve insulin sensitivity, and regulate lipid levels in diabetic mice. The study found that using the polymer-directed aptamer (DPAP) system efficiently delivered MgO NPs to diabetic target cells, leading to reduced sugar oxidation. This suggests that magnesium, particularly in the form of MgO NPs, may be a promising treatment for type II diabetes [26].

3.2.3. Cerium oxide NPs

The rare earth element cerium, found in the lanthanide series, forms CeO2 nanoparticles (NPs) that have shown potential in treating oxidative disorders and brain injuries. Research indicates that CeO2 NPs could serve as a regenerative agent, preventing nerve damage caused by diabetes and treating diabetic neuropathy [27]. Additionally, CeO2 NPs may help reduce complications from gestational diabetes. However, further research is needed to validate these findings [28].

3.2.4. Copper NPs

Copper is a crucial transitional element involved in various biochemical processes. Copper nanoparticles (Cu NPs) are effective in treating Type 2 diabetes due to their superior antioxidant properties and their ability to inhibit alpha-amylase and alpha-glucosidase [29]. Additionally, Cu NPs have been shown to significantly prevent cardiovascular defects in diabetic individuals by enhancing nitric oxide availability in the vascular endothelium and reducing oxidative stress. Research indicates that Cu NPs also aid in wound healing in diabetic mice, accelerating recovery and controlling bacterial infections. Overall, Cu NPs show potential benefits for diabetes patients [30].

3.2.5. Selenium NPs

Selenium is a vital trace element found in many plants, and its deficit can result in health issues like diabetes [31]. Selenium nanoparticles (Se NPs) are less toxic and have antioxidant properties that help scavenge peroxides and protect cellular macromolecules. Studies indicate that Se NPs can assist in managing T2DM by preserving the authenticity of pancreatic β-cells, boosting insulin secretion, and reducing glucose levels. Additionally, they enhance liver function and lower inflammatory markers. Overall, Se NPs hold promise as a treatment for diabetes and insulin resistance, effectively mitigating related complications while maintaining a balance between oxidative and antioxidant processes [32].

3.3. Statin techniques for diabetes mellitus

Statins work by inhibiting the enzyme HMG-CoA reductase, which is necessary for the liver to make LDL cholesterol. By blocking this enzyme, statins lower LDL cholesterol levels in the blood and improve the health of the blood vessel lining. Because diabetes increases the risk of cardiovascular issues, statins are a crucial treatment option for reducing this risk in individuals with type 2 diabetes [33]. These medications that lower lipids work by targeting and temporarily stopping the action of HMG-CoA reductase, an enzyme crucial in the synthesis of cholesterol. Studies have shown that statins are more effective than supplements in reducing cholesterol levels. Clinical research demonstrates that statin treatment can notably decrease LDL cholesterol, which in turn lowers the risk of coronary artery disease. Guidelines from NICE and SIGN recommend lipid-lowering therapy for individuals over 40 with type 2 diabetes (Grade A recommendation) and suggest it for those with type 1 diabetes as well (Grade B recommendation). However, recent studies indicate that many patients with type 2 diabetes in the United States may not be receiving adequate statin treatment [34]. While statins are effective, they do come with potential side effects, including muscle disorders ranging from myositis to

rhabdomyolysis, as well as rare instances of liver dysfunction. Studies have shown that younger patients and those without existing cardiovascular disease tend to have lower adherence to statin therapy. As a result, treatment should prioritize older patients and those with significant cardiovascular risk factors. Furthermore, concerns have been raised that statins may slightly increase blood glucose levels, potentially leading to the onset of diabetes mellitus. Nonetheless, they are generally well-tolerated and associated with fewer adverse effects in patients with type 2 diabetes [35].

3.4. Stem cell techniques for diabetes mellitus

By altering culture conditions, embryonic stem cells (ESCs) can be transformed into insulin-producing cells. In the laboratory setting, mouse ESCs can be induced to form embryoid bodies through in-vitro differentiation. Following the selection of nestin-expressing ESCs, these cells were encouraged to mature into a phenotype similar to β-cells. [36]. Adding phosphoinositide kinase inhibitors enhanced the differentiation of more ESCs into efficient beta cells [37]. Altering embryonic stem cell culture circumstances can generate cells with characteristics of β-cells. By incorporating transcription factors such as pax4 or pdx-1, which are linked to β-cell lineage, and fine-tuning the culture environment, encouraging outcomes have been observed [38]. There is doubt surrounding whether ESC differentiation techniques actually generate insulin-secreting cells or simply cells that absorb insulin. It is crucial for these cells to actively produce and release insulin to be effective. Certain molecular elements and insulin-containing vesicles are indicative of a beta-cell phenotype. Studies show that transplanting ESC-derived insulin-producing cells into rodents with diabetes successfully reverses the condition, proving their ability to produce and release insulin. It is suggested that a controlled introduction of transcription factors during in-vitro differentiation could yield better results compared to an early, uncontrolled approach. Injecting ESCs selected for insulin expression into diabetic rats has shown improvement in glucose control. Human ESCs have also been found to produce insulin under various culture conditions. New methods that eliminate the need for mouse feeder cells make single-species ESC propagation viable and reduce the risk of zoonotic infections for clinical use. However, challenges persist in controlling differentiation and preventing teratoma formation from ESC-derived insulin-producing cells. Additionally, ethical concerns regarding the use of ESCs must be addressed given the enormous potential of this technology [39].

3.5. Gene therapy technique for diabetes mellitus

T1DM is a widespread epidemic impacting many patients worldwide. The main objective of T1DM management is to keep blood glucose levels close to normal, with gene therapy playing a vital role in achieving this safely, effectively, and with precision. Genetic engineering is vital for incorporating genes into cells and developing new techniques. The review also examines the transplantation of cells expressing genes for T1DM, discussing the benefits and drawbacks of various stem cell types. Genetic vaccination holds promise for T1DM treatment, offering flexibility in managing T-cell responses. DNA vaccination strategies include plasmid DNA and viral-vector-based vaccinations, both showing positive results in preventing or reversing Type 1 Diabetes Mellitus. Non-viral vectors are less antigenic and safer for human use, but more research is needed to improve their transfection efficiency. Additionally, further studies are required to enhance the glucose sensitivity of stem cells and to identify effective DNA vaccine combinations. Comprehensive research on combined immunological interventions and the cytokine biology related to T1DM is crucial for developing safe and effective immunotherapies. Finally, discovering potential genes and proteins to minimize ADR is essential for creating innovative treatments for T1DM [40].

3.6. Herbal therapy for diabetes mellitus

Herbal remedies are becoming more popular for their ability to reduce blood sugar levels in diabetic individuals with fewer side effects and longer-term use. Traditional herbal practices have evolved to create various formulations, such as Qishen and Jin-Yi from China, and combinations of nettle, galega, dandelion, beans, and cranberry in Russia and Ukraine. In India, Glucobeet from Syzygium cumini has shown promise in treating diabetes. Research indicates that active compounds like glycosides, polysaccharides, and flavonoids play a significant role in regulating blood sugar levels. In Iran, herbal antidiabetic products like B-Glocorex and Galega tablets are available, showing positive results in managing type 2 diabetes. Glycogol, made from Salvia officinalis L., is another popular option in Iran. As interest in herbal medicine grows, these natural remedies are believed to play an essential role in managing diabetes and other health conditions, with ongoing research likely to further enhance their place in modern medicine [41,42,43].

3.7. Conclusion

Diabetes mellitus (DM) is a significant public health issue that is on the rise and shows no signs of slowing down. While there is no cure for DM at the moment, various treatments have shown promise in controlling the condition. However, DM still poses a serious threat to public health, highlighting the need for a comprehensive and safe management strategy. Proper education, support, and lifestyle changes such as improving diet, increasing physical activity, and weight loss are crucial for optimal management of blood sugar levels, blood pressure, and body weight. To effectively

tackle this disease, it is important to focus on public policies that improve access to healthcare, prioritize patient-centered care, and create environments that promote overall health.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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