

Diabetes Management: Insights of Current and Future Trends

M. Sayyed^{1*}, S. Yadav¹, F. Ansari¹, V. Netke¹, N. Sinha¹, V. Sarode¹ and A. Ali²

¹Department of Pharmacology, Oriental College of Pharmacy, Navi Mumbai 400705, India

²Department of Quality Assurance, Oriental College of Pharmacy, Navi Mumbai 400705, India

*Corresponding author: M. Sayyed, Department of Pharmacology, Oriental College of Pharmacy, Navi Mumbai 400705, India, E-mail: mateen.sayyed@ocp.edu.in

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Abstract

There is large diversity of methodologies to treat the Type 2 Diabetes Mellitus (T2DM). When nutrition and physical exercise neglect to control diabetes, the individuals are compelled to start the treatment with antidiabetic specialists by using the newly discovered antidiabetic agents with the help of various recent advance technologies. However, these medications present a few disadvantages that can influence the therapy regimen. The primary demerits of existing oral modalities for the treatment of diabetes are the insufficient bioavailability and immediate release of the medication, which necessitates an increase in dose frequency. Diabetes Mellitus (DM) is a growing pandemic that imposes a significant socioeconomic impact on governments worldwide. Different therapy options for diabetes control are fast emerging since traditional methods of treatment have not addressed the root causes of the condition and are fraught with serious side effects. This review investigates several therapy regimens for diabetes control. A literature survey for published studies on popular recent breakthroughs in diabetes treatment was conducted using search engines such as Web of Science, PubMed/Medline, Scholar, with keywords such as diabetes, gene therapy, diabetes management. Our findings show that significant advancement has been achieved in the management of diabetes, diabetes, with promising outcomes employing various treatment therapy such as nanotechnology, gene therapy, stem cell, medical nutrition therapy, and lifestyle modification. However, using these techniques has several numbers of challenges, including their enhancement to make sure optimum glycemic, lipid, and proper control of blood pressure to reduce problems, enhancement of patients' lifestyle compliance to lifestyle and pharmacological treatments, prevention, ethical issues, and a reliable delivery method, among other things. In conclusion, management of one's lifestyle in addition to pharmacological methods and the advancement of these techniques is crucial for a successful efficient and secure clinical diagnosis plan.

Keywords: Diabetes mellitus; Nanotechnology; Stem cell; Nanomedicine; Hyperglycemia

Introduction

Diabetes is a severe public health issue that affects people all over the world. In 2013, 382 million individuals worldwide have diabetes, with 50% going undiagnosed. According to the most recent diabetes categorization criteria, diabetes is divided into juvenile diabetes or insulin dependent diabetes which is also called as type 1 and type 2 which is diabetes mellitus. There are various specific kinds of diabetes, and gestational diabetes [1]. About 90% of diabetes cases are of diabetes mellitus. Type 1 diabetes is prompted by a complete lack of hypoglycemic hormone insulin due to the insufficiency of its secretion and/or use. Diabetes patients may develop ketosis-prone diabetes, other infections other severe complications brought on by long-term problems with protein, lipid, and carbohydrates metabolism, including diabetic nephropathy, diabetic retinopathy, diabetic foot, and numerous other persistent problems [2]. There are several technologies to treat the retinopathy and nephropathy and other complexes. These technologies are used to regenerate the damages cells. A physiological and pathological process is referred to as regeneration, physiological regeneration, also called as endogenous regeneration that describe to some organs and tissues that renew as a result of continuing ageing and used by new cells. Regeneration of full or portions of organs as a result of external force injury and partial loss is known as pathological regeneration pathologic regeneration is the whole or partial destruction of an organ caused by external force in order to maintain the original structure and cell transplantation, tissue engineering and in addition to pharmacological stimulation of bodily regeneration function [3]. And therapeutic cloning are regenerative medicine's therapeutic technologies. It is currently being expanded to incorporate tissue engineering, stem cell gene therapy and etc. diabetic regenerative technologies are to restore islets of Langerhans, damaged retinal tissue and nerve tissue and the diagnosis of diabetes.

Nanotechnology incorporates the investigation of material characteristics and applications. When a material approaches the Nanoscale level, its characteristics alter and new properties emerge. The proportionate increase in surface area is the main difference between nanomaterials and agglomerates. that is, a

ladder-like pattern covers the surfaces of fine particulate matter, symbolizing the atoms high surface thermal conductivity and restless motion. Because of their small particle sizes. The ions produce big, surface-active atoms that may form bonds to other atoms. Its medical uses include simple-to-detect drug delivery systems and a fresh meth [4]. As a result, nanotechnology is essential for regenerative technology.

Literature Review

Engineering and cutting-edge technologies can help to manage diabetes more effectively than the conventional methods

Where is the need for chemical engineering and cutting-edge technologies to manage the diabetes? The prevention of unfavorable sequelae in diabetes patients, such as eye and kidney illnesses, cardiovascular issues, and other difficulties, still depends on maintaining proper and, if at all possible, continuous glucose management [5]. Through the use of wearable and contemporary diagnostic gadgets built on cutting-edge technological principles, continuous glucose monitoring is made possible [6,7]. Recently, closed-loop solutions that combine triggered insulin delivery *via* insulin pumps and continuous glucose monitoring devices have been launched. There are various limitations to the use of insulin pumps, including insulin loading and unique software interface needs. Although this approach represents a significant advancement, maintaining glucose levels within a tolerable range is still difficult. A recent example of how cutting-edge technology might aid in the management of diabetes is the invention of implanted nano sensors for continual glucose monitoring, which can speed up online diagnosis. Numerous advancements have been proposed, including a sweatband around the wrist for constant glucose monitoring, ideas for soft contact lenses, installed glucometers that read through wireless monitoring and equally implanted mouth strips for saliva glucose monitoring. Abbott sells biosensor which can offer continuous up to 10 days of continuous glucose monitoring. The above mentioned subcutaneously implanted amperometric sensors measure to keep track of a relationship between an electrical current and blood glucose level. Based on carbon nanomaterial. Based on carbon nanomaterial, carbon quantum dots and the nanocomposites with grapheme have demonstrated to be of significant promise for enhancing the efficiency and accuracy glucose monitoring [8]. These resources are designed by chemical substances by using chemical technology. Their characterization is made feasible by the availability of sophisticated characterization instruments for nanotechnology. Innovative biomimetics and supramolecular chemistry techniques for designing nanocarriers for medication administration, as well as the production of nanoparticles, including magnetic entities which is enabled for the quantification of relatively small differences in beta cell masses which facilitate the early treatment and its diagnosis [9]. In addition to have the implanted glucose monitors, other high-tech insulin delivery techniques are being investigated as innovative treatments. Insulin distribution using non-invasive

means may help with noncompliance problems. Using thermal skin ablation techniques and micro needle-based insulin patches have been documented [10,11]. To address problems with insulin administration, injectable insulin Nano gels might be viewed as a more traditional technical improvement. Furthermore, nanofiber-based polymer scaffolds have been used to create better methods for converting induced pluripotent stem cells into cells that produce insulin [12].

Newer technologies for management of diabetes

Management by gene therapy: In order to create novel gene related treatments, nucleic acids such as plasmid DNA (pDNA), complementary RNA, microRNA (miRNA), small hairpin RNA (shRNA), and small interfering RNA (siRNA) should be introduced systemically in order to produce innovative gene therapy [13]. In an aqueous solution, most of the methods for delivering nucleic acids are created by the assembly of nucleic acid molecules with cationic polymers [14,15]. The use of lipid-based nanoparticles as systemic gene delivery vehicles has been investigated. In the first technique, cationic lipid/DNA complexes were created using mixes of DNA and cationic liposomes. The strong cationic charge of these compounds renders them effective delivery vehicles *in vitro*. However, it has very low gene transfer efficiency and fast clearing from the reticular endothelial system. Due to this delivery of gene *in vivo* system fails [16,17]. It is possible to create stable DNA-containing particles utilizing conventional liposome-based technologies. Because of protamine condensation DNA forms a virus like structure. A formulation of lipid-protamine-DNA was formulated for gene transfer in *in vivo* system which provide better protection for plasmid DNA [18,19]. In this regard, attempts have been made to facilitate the cationic lipid-DNA combination stability. The particles of lipid plasmid had longer duration of circulation that reaches to the target of cell through the improved porosity and effective absorption. Which results in better expression of genes than the lipoplex. The combination of amines and triazinetrione are being used to create novel lipidoid nanomaterials with the PEG-lipids, cholesterol and phospholipids. pDNA and siRNA were effectively administered in combination, both *in vitro* and *in vivo*. Therefore, a promising approach to combat several genes implicated in autoimmune disorders like diabetes from malfunctioning is simultaneous gene expression and silencing treatment. Hyperglycemia results from system of immune cell that destroy the beta cells of pancreases which is responsible for production of insulin in Type1 Diabetes (T1D). Patients with T2D have a rise in blood glucose levels as a result of low blood insulin levels brought on by release of insulin due to insufficient pancreatic b-cell. Several techniques have been invented to prevent b-cells from being destroyed by the immune system or to limit the insulin release from patients own pancreatic β -cells.

- Gene therapy for insulin.
- Development of stem cells.
- Implantation of islets.
- Proliferation of β -cells.

Insulin gene therapy may assist the production of body insulin again with the aid of foreign genes. The carrier choice and administration modes are critical I factors in determining the

outcome of treatment. A plasmid encoding the human insulin gene encapsulated in chitosan nanoparticles was delivered to diabetic rats which encourages the use of chitosan as a non-viral delivery method. Similarly, the plasmid DNA which is encoded with the insulin for the hyperglycemic mice was tested for the sake of animal's protection from diabetes for over ten days. Chitosan is covalently designed with cationic polymer (polyethyleneimine, PEI) which is then condensed with human pDNA-insulin. This improves the stability against gastrointestinal tract and lever transgenic expression. After three repeated doses every 24 hours orally administered pDNA-insulin shows reduced blood glucose in type 1 diabetes mice for 36 hour period. The coated PEG-functionalized lipoplexes stimulate the reduction in their capture by gastro intestinal tract mucus and allows for greater effective transfection. The stem cells which are obtained from beta cells is seen as best substitute for the transplantation of islet cells. And hence is regarded as ultimate hope for improvement t of type 1 diabetic therapies.

They provide some assistant help to the incretin hormone GLP1 which increase the secretion of insulin by combining of siRNA to specific to dipeptidyl peptidase-4 with GLP1 in polymeric permeable micro particles or in particular chitosan NPs using GLP1 agonists sensitive to DPP-4.

Wearable devices for diabetes prevention

Due to their accessibility, the monitors which shows wearable activity are the most form of wearable gadget utilized in technical therapies addressing the risk factors of diabetes. Cost effectiveness and capacity to use successful, evidence-based behavior modification strategies, evidence-based behavior modification strategies (e.g., self-monitoring, feedback, setting of goal). These gadgets offer daily/weekly feedback and real-time measurements of physical activity *via* a monitor display, an associated app, an email or text message. Various activity monitors have been tested as management tools to help people for management of their weight, physical exercise time increment and sedentary time decrease. Despite the fact that no studies on wearable activity monitors have yet examined the relationship between device use and diabetes outcomes. In one study, sedentary time was addressed by giving overweight women a Fit bit® activity tracker and sending an awareness alert when sedentary time exceeded d a predetermined time limit. Preliminary data from the study in question and others suggests that the use of wearable activity monitors in behavioral interventions, particularly those based on behavior change theory, may enhance physical activity, reduce inactive time, and aid in short-term weight loss. However, there is not enough evidence to support the use of wearable activity monitors as a stand-alone intervention strategy to lower the risk of diabetes. Despite the fact that participant engagement is a crucial component of the success of physical activity and weight reduction interventions, data on user engagement are scarce. In addition, most simply evaluate usability during the implementation phase rather than involving users throughout the entire intervention development and implementation process, as was shown by Yingling in an environment which was based on community.

Discussion

Wearable technology to manage diabetes

Non-invasive medical devices: Self-observing of blood sugar is crucial for enhancing glycemic control since it directs long-term care and enables essential insulin dose adjustments between doctor appointments. The goal of non-invasive glucose monitoring is to make self-monitoring less uncomfortable and painful. There have been investigations on many non-invasive techniques (e.g., spectroscopy by near infrared, reverse iontophoresis). Despite the FDA's approval of non-invasive devices in 2001, there is no glucose sensitive devices of non-invasive type devices are currently on the market because of issues with inaccurate readings, sensitivity toward skin, and sizable delay between the observed value and true blood sugar amounts. For instance, the use of contact lenses as a mean for measuring blood sugar has recently been investigated. These instruments assess glucose levels in tears using fluorescence, however they still struggle with issues such variable glucose levels between the eyes, irritability, erroneous depictions of blood glucose and unpredictable sources of energy.

Medical devices of invasive type: Regularly Glucose Assessing (RGA) with invasive technology provides a number of commercially available solutions Devices by Animas and by Medtronic Diabetes were available in 2015; this technology was first presented in 1999. These gadgets join blood glucose detector (Centered into the subcutaneous skin fat) with the help of a gadget that shows the reading and record it. Several times per minute, the sensor analyses the interstitial fluid's glucose levels and sends an estimate of those measurements Receiver device for each few minutes. Regularly glucose assessing was linked to lower HbA1c levels, more time spent in the normal glycemic zone, and fewer hypoglycemia episodes in a number of short-term investigations in type 2 diabetic patients. Randomized clinical trial compares the benefit of real-time Regularly glucose assessing and blood glucose assessing system found that Regularly glucose assessing reduced HbA1c in the beginning of first six months but the effect was not last for next six months. However, the calibration frequency, invasiveness and shortened sensor lifespan have confined the popularity of Regularly Glucose Assessing (RGA), standard of care recommendations are starting to take into account which patients would benefit most from it.

Application of nanotechnology for the rejuvenation of insulin producing cells

The replacement of islets from cadavers or cells produced from induced Pluripotent Cell (iPSC) or embryonic cells or the activation of endogenous proliferation are two alternative strategies to supplement islet cells due to the lack of insulin release by islets activity. In other words, it happens as a result of progenitor differentiation or trans differentiation of differentiated cell types (neogenesis). Meanwhile, research using pluripotent precursor cells and inductive e pluripotent cells and allogeneic pancreatic islets, particularly islets of porcine s, have been prompted by immunological rejection and

a lack of donors for islet organs. In order to create a nano-controlled medication system, nanotechnology offers precise targeted for implantation of the cells that has high cytocompatibility and it utilizes biodegradable made of biopolymers as the carrier for drug molecules. It can enhance the survival period of the stem cells, proliferation and insertion when combined with stem cells. The advancement of regenerative medicine is aided by the use of nanomedicine, nanomedicine carriers, nanocontrast agents, and nanosensors. For the achieving the goal of indefinitely curing of hyperglycemic condition. Transplantation of islets cells are the endless growth potential of stem cells to generate the insulin by generation of insulin like p-polymers. At this stage efficient encapsulation transportation can safeguard these cells from dispersal, devastation and suppression of immune system has accomplished long-term existence. For subcutaneous transplantation, poly-lactic acid nanoparticles. A nanoparticles were used because of their high biocompatibility, prolonged half-life, lack of toxic effects and ease of islets cells biodegradation. The main immunosuppressive factors that affect islet cells after transplantation into the body are interleukin-1, Interferon (INF) and T-Necrosis Factors (TNF). Agarose and Alginate is employable as a hydrogel encapsulates and their produced a perm selective membrane can be utilized to shield islet cells that were implanted from the immunological system of the host. Additionally, the convenient nanoparticle scaffolds with extracellular matrix-like constructs can offer a significant contact area for interactions between cell scaffolds and adhesion as well as effective exchange of oxygen and nutrients. Nano scaffolds proteins in the extracellular environment matrix, proliferative factors and nanomolecules can help tissue-like structures form in tissue engineered implants and transplants. Studies have demonstrated that pancreatic cells differentiation human pluripotent precursor cells cannot be improved by chips in a gradient pattern with polystyrene substrate features of various dimensions and structure. The optimum aperture to produce producing pancreatic endocrine progenitor clusters (PDX1+ and NGN3+) is a chip which have gradient of nanometer pore size (Po-1,100-200). Clinical issues now include the accurate and accurate recognition of islets activity following implantation. In addition, the use of nanotechnology has raised expectations for the resolution of this issue. In addition, Nanoparticles can alter their surface groups in ways like methylation and polyethylene oxidation which allows them to prevent the being removed by immune cells to remain constant in the body while being monitored. Due to small molecular mass of nanoparticles, it carries meds and scanning agents through the different barriers and to be implanted into the tissue replenished pancreatic cell responsible for insulin secretion or tissue to accomplish precise and clear images. In order to track the survival of convenient tissue implantation, transplantation, systemic dispersion of human tissues which are iPSC derived as well as the ensuing renewal procedures in early porcine genetic hyperglycemia studies. NanoBIT, a type of project that is committed to develop extremely sensitive scanning techniques. In order to monitor the activity of transplanted cells and tissues, multifunctional Nanoparticles (NPs), which are based on biopolymers, are developed as particular nano tools. Their primary target is the cell membrane-expressed receptor for

Glucagon-Like Peptide 1 (GLP-1R). One natural ligand for the GLP-1R is the GLP-1. They are quite affine. However, because of its brief half-life in tissues, it is unable to accomplish precise blood sugar level management. Therefore, GLP-1 simulations are used in the current therapy. The most well-known is exenatide, a mixture of chitosan-PGA nanomaterials and detecting substances for photo acoustic tomography (MSOT), magnetic resonance imaging, Single-Photon Emission Computed Tomography (SPECT) for amplified multimodal picturing. Exenatide is derived from natural protein exendin-4 (ex4). Ex4 peptides have been used to functionalize the imaging NP. Consequently, we are able to mark a cell population specifically.

Diabetic neuropathy and retinal tissue regeneration

Diabetic neuropathy is the most difficult and severe consequence of diabetes. Such as peripheral autonomic dysfunction known as neuropathy, primary neuropathy and autonomic type of neuropathy. One of most prominent type is distally homogeneous polyneuropathy. The nanoparticles which are made up of copolymers of lactic acid and glycolic acid possessing curcumin that stimulating neuropathy symptoms and change proliferation growth *in vitro* via stimulation of Wnt/-Catenin cascade signaling pathway. Spiral ganglion neurons are supported in their ability to survive *in vitro* by loaded BDNF silica nanoparticles. Similar to how iron oxide nanoparticles conjugation is superior than free neurotropic component a ventral stem ganglion. In addition to being stable, the neurotropic factor which are derived from glial cell and Fibroblast Growth Factor (FGF-2) have increased nerve regeneration. In order to increase mechanical quality of cell engineered materials for the regrowth of nerve tissue n and successfully stimulate the regeneration of nerve tissue Aydemir et al. employed electro spinning nanofibers which is hexyl lactone with regeneration of iron. The bi-directionally induced silica-DNA combination effectively stimulates the FGF receptor 1 signaling pathway to cause neurogenesis in neural stem/progenitor cells. However, local injection is the main technique of delivering nanoparticles due to having less permeability of blood brain barrier. Depletion of nanoparticles is the primary drawback of the injection introduced locally brought on by the reflux of the fluid. Recently, combine 3D printing technology and recently released hydrogels has emerged as significant scientific proof in the advancement desirable tissue engineering. Nano peptides assemble can also replicate the surroundings of the extracellular matrix for the regeneration of nerve cell.

Stem cell therapy in diabetes

The traditional methods for treating DM are fraught with drawbacks and do not address the disease's root causes. Consequently, there is a search for an ideal new therapeutic regimen. The cellular-based treatment approach now used in the therapy of DM is based on the revival of beta cells for insulin secretion through pancreatic or islet cell transplantation. The scarcity of organ donors limits this method. These challenges prompt an investigation into the viability of synthesizing pancreatic islet cells from embryonic stem cells. Embryonic stem cells' unusual ability to regenerate tissue may be a crucial tool in

the treatment of Diabetes Mellitus (DM). The existing supply and demand concerns regarding pancreatic islet cell transplant could be resolved by synthesizing renewable pancreatic islets through embryonic stem cells thereby providing diabetic patients with a constant supply of pancreatic islet cells facilitating insulin release. Consequently, stem cell research has emerged as a possible strategy for treating diabetes mellitus. The goal of the stem cell DM therapy is to replace damaged or employing embryonic or hematopoietic stem cells to treat malfunctioning cells of the pancreas. This approach has been employed to evaluate the potential of numerous types of stem cells, such as induced Pluripotent Stem Cells (iPSCs), Embryonic Stem Cells (ESCs), as well as somatic stem cells, in producing substitute pancreatic islet cells or restore the physiological function of the pancreatic islet cell. Technological advancements have revolutionized the process of producing totipotent stem cells though a variety of sources derived from body tissues, incorporating myeloid tissue, naval string blood, periosteum, endodontia, and adipose tissue. Usually, pancreas serves as the first part of the body considered when seeking out promising totipotent stem cells. A modest amount of pancreatic tissue, if accessible, has been shown in studies using animal models to be able to restore the ideal pancreatic beta-cell mass. This occurred as a consequence of the proliferation and reverse development that differentiated islet cells of the pancreatic duct underwent, which generated pluripotent stem cells, which in turn produced more pancreatic islet cells. According to another research, these ductal cell populations might be grown in a lab and programmed to form clusters that synthesize insulin. Furthermore, both haemopoietic somatic stem cells and multipotent stem cells possess the ability for transdifferentiating over to a range of cell origins, such as those from hepatic, respiratory, and gastrointestinal system.

Conclusion

Diabetes mellitus management solutions are getting increasingly important as time passes. The majority of current diabetes medications work by increasing either insulin release or glucose absorption in certain peripheral tissues. Many current medications frequently fail to control or even postpone hyperglycemia, and insulin treatment is eventually required. Many therapy regimens have demonstrated promising outcomes in the treatment of diabetes. Nonetheless, despite the promise of these massive treatment schemes, diabetes remains a severe concern that may continue to endanger public health. DM is still a significant problem that might pose a hazard to public health, notwithstanding the promise of the expansive treatment regimens. Therefore, it is necessary to address the issues with each of these technologies in order to develop a solid, effective, and secure clinical care strategy. The objectives of diabetes treatment are to increase patients' quality of life, stop or postpone the onset of disease complications. The improvement of nutrition, increased physical activity, and weight loss are necessary for the metabolic control of glucose, blood pressure, and body weight to function well. An emphasis on public policies to support health care access and resources, the promotion of a patient-centered care approach, and health-promoting

infrastructures at the environmental level are necessary to effectively and successfully manage the control of this condition.

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