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Plant Based Nanotechnology – A New Trend in Therapeutic Approaches of Diabetes

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Abstract

Diabetes mellitus (DM) is considered a chronic, lethal, and occasionally deadly disease that affects individuals worldwide. Nanotherapeutics has shown enormous promise in combating chronic illnesses, including diabetes, by improving the overall impact of medications on biological systems. Greenly manufactured nanoparticles (NPs) derived from diverse plant methanolic extracts (NPs) are initially investigated for their anti-diabetic properties and cytotoxicity. Fourier trans-form infrared spectroscopy (FTIR), UV-vis spectroscopy, atomic force microscopy, and X-ray diffraction (XRD) are most used to characterize these NPs (AFM). Before human testing, the NPs are evaluated on several cell lines, such as the Vero cell line (for cytotoxic effects) and then on an animal model. Several investigations have shown the conventional structural and functional characteristics as indicated by various analyses (FTIR and XRD). Many studies have found substantial variations in water consumption, body weight, food intake, urine volume and sugar in rats treated with plant-based NPs aqueous extract. The current study demonstrated the importance of plant-based nanotechnology in diabetes nanotherapeutics.

Introduction

Nanotechnology has currently opened the new door in scientific research. It involves the development or synthesis of minute (nanoscale) particles with a size of 1–100nm, which are very small as compared to other products [1]. Nanotechnology is usually used for delivery purposes, that targets the location where it is required [2]. This technology holds many disciplines as for the fact as it can be used as biological and biosensors agent in developmental tools [3]. They are different methods for nanoparticle production that include physical, chemical, and green methods. Nanotechnology is gaining a lot of importance because it uses bacteria, plants, elements, and other organisms to produce nanoparticles [3,4]. Usually, high temperatures and pressures are used for production of nanoparticles which comes under physical method. While in chemical methods stabilizing and reducing agents are used though they are quite expensive as well as dangerous [5]. One of the advancements in this field is green nanoparticle synthesis which uses plants as base material that include leaves, roots, stems, seeds, bark, flowers, gum, fruits, etc. They come under green synthesis category as they are

environmentally friendly, presence in abundant form, non-toxic and quite economical [6].

Diabetes imposes a serious threat to mankind as it affects globally. Recent studies have reported that overall, 0.39 billion people have been affected globally while many are still undiagnosed [7]. Moreover, the maximum percentage of people lives in middle- and low-income countries and the majority are in between the ages of 40–60 [7]. Diabetes ranks in top five diseases that has very high death rate. Diabetes mellitus is considered a metabolic illness which arises because of glucose intolerance (DM) and hyperglycemia [5]. The World Health Organization (WHO) has reported majority number of 0.42 billion adults are living with this Non-Communicable Diseases (NCD) [4]. Recent studies have also reported that the projected number of these diseases is likely to increase by 25% in 2030 and 51% in 2045 and more in upcoming decades [8].

It has been observed that Asian Indians are more likely to have diabetes and coronary artery disease due to various characteristics, such as increased insulin resistance and increased abdominal obesity [7,9]. Several factors like risks of hypoglycemia, the degree of hyperglycemia, renal functions, the patient's ability to self-monitor their blood sugar level, body mass index, and medication cost, must be considered when choosing and implementing a glucose lowering therapy [7].

Diabetes Mellitus (DM) can be classified into two types. Type-1 DM is distinguished by deficient insulin that is released from cells of pancreas, whereas type-2 diabetes is distinguished by the development of insulin resistance [5]. Type 2 diabetes mellitus affects more than 90% of diabetics worldwide and it is increasing at a frightening rate. DM affects around 0.54 billion individuals worldwide, with 0.033 billion in Pakistan [10]. This disease is also becoming more common in modern lifestyles due to obesity, lack of exercise and physical activity, culture, genetic polymorphism, old age as well as food style [5,10].

Several conventional therapeutics are used to treat type 2 diabetes, including repaglinide and sulfonyl-ureas, which increase the secretion of insulin; troglitazone, which increases the action of insulin in muscle and fat; metformin, which mostly promotes mechanism of insulin in tissue of liver; and miglitol and acarbose, which usually cause hyperglycemia or high blood glucose levels [8,11]. The medications used to treat type-II diabetes have limitations in that they have substantial adverse effects. Other important medication strategies include insulin-sulfonylurea combination therapy, which reduces the insulin requirement per day along with metformin combination therapy (which is approved by the FDA); troglitazone-insulin combination therapy, which efficiently reduced insulin requirement and improved glycemic control; and minimizing gain of weight because of the insulin therapy [5,8]. Persistent hyperglycemia, if left untreated, can lead to metabolic problems in various organs, especially the kidneys. These metabolic related problems may result in tissue damage. Even if a person does not die from diabetes, it can cause secondary complications such as heart, kidney, and liver as well as erectile dysfunction, eye diseases, and loss of sight [12].

Diabetes Mellitus is linked to a multitude of issues for instance, Acute metabolic problems are corelated with mortality that include diabetic ketoacidosis which is caused by coma caused by low blood glucose concentrations (commonly known as hypoglycemia) and extremely high- blood glucose conc. (commonly known as hyperglycemia). The Diabetes complications are classified as "micro-vascular disease" (due to damage to small blood vessels) and "macro- vascular disease" (due to arteries damage). Micro-vascular problems include eye illness, also known as "retinopathy," kidney disease, also known as "nephropathy," and neural injury, also known as "neuropathy" [13].

The fundamental cause of diabetes is oxidative stress caused by reactive oxygen species (ROS), which causes cell dysfunction, poor glucose tolerance, and insulin resistance. ROS is created when glucose and fatty acids are overwhelmed as a result of overeating and inactivity [5]. The apoptotic cell death is also the main cause of pathological and physiological stress on the cells of pancreases [5]. Researchers have also discovered a relationship between pancreatic cell death and oxidative stress, as well as diabetes-related complications. They also claim that hyperglycemia-induced diabetes related issues are produced mostly by an imbalance of ROS, which promotes oxidative stress and apoptosis [4,5]. As a result, these diabetes complications may be successfully controlled by lowering ROS generation. Alteration in diet and lifestyle, as well as oral anti-diabetic medication administration, is crucial in lowering ROS production during diabetes treatment. Whether a person has type-II or type-I diabetes, it is critical to maintain normal glucose levels in blood (70-140 mg/dL) [7,8]. Finding a medication that must work effectively for managing diabetes is a common difficulty. Many anti-diabetic and hypoglycemic drugs, such as sulfonylureas and biguanides, have been introduced for the treatment of diabetes. These drugs, however, do not provide long-term management of blood glucose levels. These treatments are also less well-established because prolonged use causes toxicity and unwanted side effects in the body, such as gastrointestinal pain, hypoglycemia, pancreatic degeneration, and liver damage [14]. Finding innovative hypoglycemia treatments and hypoglycemic medicines with fewer side effects and more efficacy is a valuable goal, and this is the focus of current research to synthesis plant nanoparticles using a green technique [15]. The objective of the present review is to understand diabetes in relation to nano-therapy.

Diabetes Classification

Some of the major types of DM based on insulin deficiency can be divided below:

Insulin Dependent DM (IDDM)

It is also known as type-I or juvenile onset DM and affects almost 10% of people. It is caused by autoimmune destruction of pancreatic cells that are cellular-mediated. The condition can affect people of all group of age, but it most commonly affects children and young adults. A steady supply of insulin injections is required to keep blood glucose levels under control [5,7,11,16].

Idiopathic Diabetes

A small minority of type-II diabetes individuals, usually of African and Asian origin, have no known cause. They are usually prone to ketoacidosis and have chronic deficiency of insulin. Ketoacidosis occurs in episodes, along with the level of insulin insufficiency that fluctuates between these episodes. The Idiopathic DM has a genetic propensity, and the patient's condition determines whether insulin replacement therapy is required [17].

Non-insulin Dependent DM (NIDDM)

It is also known as adult-onset diabetes, and it holds almost 95% of all diabetes cases. Obesity and other major metabolic disorders [18,19], dyslipidaemia, and insulin resistance have led to an epidemic of type-II diabetes [20,21] which can easily be detected by markers as well [21,22].

Gestational Diabetes Mellitus (GDM)

It is described as the level of glucose intolerance during pregnancy that results in hyperglycemia of varying severity [5]. The impaired glucose intolerance, or GDM, is a main kind/type that affects almost 14% of pregnant women, or 0.13 million women each year in the United States and is a risk factor for type-II diabetes in mothers. [8]. The degree of the stated risk varies owing to selection criteria, ethnicity and GDM as well as type-II diabetes testing [5,7,8].

Catamenial diabetic ketoacidosis or *Catamenial* Hyperglycaemia

Diabetic ketoacidosis (DKA) is a disorder caused by infection, insufficient insulin or poor insulin adherence, acute pancreatitis, stroke, medications, metabolic abnormalities inside the body, or medical neglect [8,23]. This type of diabetes is uncontrolled hyperglycemia with DKA that occurs before the period of menstrual cycle in females resulting in up to a fourfold increase in insulin demand [23]. The hormonal changes that occur during the period of menstrual cycle, along with change in food habit, digestion issues, activity levels, may all have a role [24,25].

Diabetes Signaling Pathways

Diabetes pathogenesis is linked to several signaling pathways, including the insulin signaling system, the AMP-activated protein kinase (AMPK) pathway, and the Regulation of peroxisome proliferator-activated receptors (PPAR) regulation and chromatin modification pathways. These signaling pathways have emerged as a key source of prospective new therapeutic targets for the treatment of metabolic disorders including diabetes [8].

Nanotechnology and Diabetes

The production of nanomedical device which is a microcapsule with holes that has shown promise in the medication delivery strategy. These holes are large enough to let tiny molecules like oxygen, glucose, and insulin pass through yet small enough to allow larger immune system molecules like graft-borne virus particles and immunoglobulins to pass through. Microcapsules containing replacement cells of Langerhans, primarily pigs' origin, might be embedded underneath the skin of patients with diabetics. This might temporarily restore the body's sensitive glucose control feedback loop without the need for strong immune suppressants, which can put the patient at danger of infection [26,27].

The nanoparticle targeted drug delivery strategy offers several advantages, including increased drug bioavailability by targeting selected/specific organs, tissues, and tumors, delivering the maximum dosage of medication directly to the marked spot. The scalability of a nanoparticle is one of the most difficult technological difficulties. Manufacturing three- dimensional nanostructures is more difficult than manufacturing nano-surfaces with 2-D layer-shaped have yet to be studied for standardization. Another concern is that nanoparticle exposure might be harmful or dangerous. Concerns regarding the possible negative consequences of manmade nanomaterials such as carbon bucky-balls and nanotubes via inhalation, ingestion, or skin absorption are growing [5,27].

Insulin is required for type-I and type-II advanced diabetes, and conventional insulin delivery methods featured infections, painful administration, and poor patient compliance. Recent micro- and nanotechnologies, however, have eased the insulin administration procedure by regulating insulin delivery, which includes pulmonary, nasal, transdermal, and closed-loop delivery [28-31].

Discussion

Long-term effective techniques with fewer (or less intense) side effects will be necessary using a combined methodology instead of a short-term strategy and a focused way out instead of traditional agriculture procedures, such as nanotechnology [5,18,33]. For example, plant extracts from various species, such as *Cathranthus* roseus, are used in the synthesis of nanoparticles, and their cytotoxicity on Vero cell lines is also tested to determine whether the produced nanoparticles, whether silver, iron, gold, cadmium, or other elements, are effective or not. Plants are often extracted using methanolic solvent, which is also used for phytochemical extractions [5].

In a prior study, methanol was proven to have greater extraction efficiency for phytochemical components from herbal plants [34]. The quantitative phytochemicals analysis of several plant extracts showed that methanolic extract is the optimum solvent for extracting phytochemical components. These findings are consistent with numerous earlier investigations that found a high alkaloid molecule with anti-diabetic action [35,36]. Previous research has shown that alkaloid compounds found in herbal plants have anti-diabetic actions [5].

The utilization of plant extract in the green production of nanoparticles is being researched now [5,37]. Other investigations have found that the addition of phyto-constituents or plant metabolites causes the decrease of metallic ions and the stability of NPs [38]. The SEM and AFM images show that the nanoparticles generated in the investigations are typically spherical in form. Various studies show that the size of the spherical form nanoparticles (silver) generated is typically 35-55nm, which is recognized to be an excellent range for cell permeability [5,39]. The XRD method is also used to determine the material's crystal structure and chemical makeup, with diffraction peaks indicating that nanoparticles are created [5,37]. The interaction of negative group (COO-) or polar

group OH with metal ions (Ag, Fe, Cd, etc.) resulted in the synthesis of NPs, which contributed to the reduction and stability of these ions [40,41]. The application of nanotechnology in the treatment of diabetes has resulted in the development of innovative systems for glucose assessment and insulin administration. Researchers have proved the benefits of glucose monitors and closed-loop insulin administration systems in easing diabetic management in both type-I and type-II diabetes [5,8,26]. More trials and improvements in nanomedicine may result in replacing the conventional way of treating many lethal diseases including diabetes

Conclusion and Recommendations

Diabetes has a rising global impact since it is an expensive illness for emerging nations. Nanotechnology, as a new technology, is the most promising scientific topic of the twenty-first century. As nanotechnology advances, more and more innovative nano materials will be produced and used in medical treatment, promoting the advancement of modern medicine, bringing forth new ideas, and making new contributions to illness prevention and treatment. Nanotechnology has been useful in the treatment of diabetes mellitus by enhancing not only the catalytic capabilities of electrodes but also by expanding the accessible surface area of the sensor-receptor complex.

Nanoparticles have the potential to transform insulin administration through improved oral formulations and islet encapsulation. NPs have received much more attention in recent decades due to their potential applications in fields such as environmental protection and physical health maintenance, so we can say that NPs can be a good substitute for conventional medicine, and many of the side effects of these can be avoided. To isolate, identify, interpret, or validate the efficacy of NPs, research activities are necessary. Further research should be conducted to determine the efficacy of isolated chemicals (NPs) in treating additional human ailments.

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Conflict of Interest

No conflict of interest.

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