APPLICATIONS OF NANOTECHNOLOGY IN DIABETES

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Abstract

Nanotechnology offers sensing technologies that provide more accurate and timely medical information for diagnosing disease, and miniature devices that can administer treatment automatically if required. Some tests such as diabetes blood sugar levels require patients to administer the test themselves to avoid the risk of their blood glucose falling to dangerous levels. Certain users such as children and the elderly may not be able to perform the test properly, timely or without considerable pain. Nanotechnology can now offers new implantable and/or wearable sensing technologies that provide continuous and extremely accurate medical information.The purpose of this review is to throw more light on the recent advances and impact of nanotechnology on biomedical sciences to cure diabetes.

Keywords: Diabetes, Nanotechnology, Insulin, Pancreas, Blood

1. Introduction

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate (1). Over the past 30 yr, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. It is important to note that the rise in prevalence is seen in all six inhabited continents of the globe (2**)**. Type 2 diabetes represents approximately 90% of individuals with diabetes in the United States, while most of the remainder has type 1 diabetes (3). According to statistics from the Centre for Disease Control (CDC) diabetes is the sixth leading cause of death due to disease in the U.S., and the third leading cause among some ethnic populations.
The application of nanotechnology to medicine is called nanomedicine, it is defined as:
" Research and technology development at the atomic, molecular and macromolecular levels in the length scale of approximately 1 – 100 nanometer range, to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size." The size domains of components involved with nanotechnology are similar to that of biological structures. For example, a quantum dot is about the same size as a small protein (<10nm) and drug-carrying nanostructures are the same size as some viruses (<100 nm). Because of this similarity in scale and certain functional properties, nanotechnology is a natural progression of many areas of health-related research such as synthetic and hybrid nanostructures that can sense and repair biological lesions and damages just as biological nanostructures (e.g. white-blood cells and wound-healing molecules) (4).

2. Diabetes mellitus

Diabetes mellitus often referred to simply as diabetes is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels (hyperglycemia). There are two major forms of diabetes: Type 2 diabetes is commonly linked to obesity, which promotes insulin resistance (3). In many obese individuals, insulin resistance is compensated for by increased insulin production, which can occur if there is an increase in β cell mass (5). In approximately one third of obese individuals, there is a decreased cell mass caused by a marked increase in cell apoptosis, rendering these individuals incapable of compensating for the insulin-resistant state. Similarly, type 1 diabetes is associated with a loss of beta cell mass, typically caused by autoimmune-induced inflammation and apoptosis (6). Thus, both type 1 and type 2 diabetes are negatively affected by the death of beta cells in the pancreas, resulting in inadequate insulin production.
Metabolic disturbances associated with diabetes can lead to: (1) activation of the polyol Pathway; (2) high levels of the cytokine, TNF-α (3) the formation of advanced glycation end-products (AGEs); (4) high levels of protein kinase C activation; and (5) enhanced oxidative stress (7, 8, 9, 10). The activation of these pathways may be especially important in initiating events linked to inflammation and apoptosis (11, 12,13). Long-term manifestations of diabetes include retinopathy, neuropathy, nephropathy, angiopathy, atherosclerosis, periodontitis, and other diabetic complications, such as impaired wound-healing.

3. Use of nanotechnology in the detection of insulin and blood sugar:

A new method that uses nanotechnology to rapidly measure minute amounts of insulin and blood sugar level is a major step toward developing the ability to assess the health of the body's insulin-producing cells. It can be achieved by following ways-

By microphysiometer:
The microphysiometer is built from multiwalled carbon nanotubes, which are like several flat sheets of carbon atoms stacked and rolled into very small tubes. The nanotubes are electrically conductive and the concentration of insulin in the chamber can be directly related to the current at the electrode and the nanotubes operate reliably at pH levels characteristic of living cells. Current detection methods measure insulin production at intervals by periodically collecting small samples and measuring their insulin levels. The new sensor detects insulin levels continuously by measuring the transfer of electrons produced when insulin molecules oxidize in the presence of glucose. When the cells produce more insulin molecules, the current in the sensor increases and vice versa, allowing monitoring insulin concentrations in real time (14).

By implantable sensor:
Use of polyethylene glycol beads coated with fluorescent molecules to monitor diabetes blood sugar levels is very effective in this method the beads are injected under the skin and stay in the interstitial fluid. When glucose in the interstitial fluid drops to dangerous levels, glucose displaces the fluorescent molecules and creates a glow. This glow is seen on a tattoo placed on the arm (4).

Sensor microchips are also being developed to continuously monitor key body parameters including pulse, temperature and blood glucose. A chip would be implanted under the skin and transmit a signal that could be monitored continuously.

4. Use of Nanotechnology in the treatment of diabetes:

Diabetes is considered to be one of the major afflictions of modern western society. To date, diabetic patients control their blood-sugar levels via insulin introduced directly into the bloodstream using injections. This unpleasant method is required since stomach acid destroys protein-based substances such as Insulin, making oral insulin consumption useless. The new system is based on inhaling the insulin (instead of injecting it) and on a controlled release of insulin into the bloodstream (instead of manually controlling the amount of insulin injected) (15).
The treatment of diabetes includes the proper delivery of insulin in the blood stream which can be achieved by nanotechnology in the following ways:

Development of oral insulin:

Production of pharmaceutically active proteins, such as insulin, in large quantities has become feasible (16, 17). The oral route is considered to be the most convenient and comfortable means for administration of insulin for less invasive and painless diabetes management, leading to a higher patient compliance (18). Nevertheless, the intestinal epithelium is a major barrier to the absorption of hydrophilic drugs, as they cannot diffuse across epithelial cells through lipid-bilayer cell membranes to the bloodstream (19). Therefore, attention has been given to improving the paracellular transport of hydrophilic drugs (20, 21). A variety of intestinal permeation enhancers including chitosan(CS) have been used for the assistance of the absorption of hydrophilic macromolecules (22). Therefore, a carrier system is needed to protect protein drugs from the harsh environment in the stomach and small intestine, if given orally (23). Additionally, CS nanoparticles (NPs) enhanced the intestinal absorption of protein molecules to a greater extent than aqueous solutions of CS in vivo (24).
The insulin loaded NPs coated with mucoadhesive CS may prolong their residence in the small intestine, infiltrate into the mucus layer and subsequently mediate transiently opening the tight junctions between epithelial cells while becoming unstable and broken apart due to their pH sensitivity and/or degradability. The insulin released from the broken-apart NPs could then permeate through the paracellular pathway to the bloodstream, its ultimate destination.

Microsphere for oral insulin production:

The most promising strategy to achieve oral insulin is the use of a microsphere system which is inherently a combination strategy. Microspheres act both as protease inhibitors by protecting the encapsulated insulin from enzymatic degradation within its matrix and as permeation enhancers by effectively crossing the epithelial layer after oral administration (25).

Artificial Pancreas:

Development of artificial pancreas could be the permanent solution for diabetic patients . The original idea was first described in 1974. The concept of its work is simple: a sensor electrode repeatedly

measures the level of blood glucose; this information feeds into a small computer that energizes an infusion pump, and the needed units of insulin enter the bloodstream from a small reservoir (26).
Another way to restore body glucose is the use of a tiny silicon box that contains pancreatic beta cells taken from animals. The box is surrounded by a material with a very specific nanopore size (about 20 nanometers in diameter). These pores are big enough to allow for glucose and insulin to pass through them, but small enough to impede the passage of much larger immune system molecules. These boxes can be implanted under the skin of diabetes patients. This could temporarily restore the body's delicate glucose control feedback loop without the need of powerful immunosuppressant that can leave the patient at a serious risk of infection (27). Scientists are also trying to create a nanorobot which would have insulin departed in inner chambers, and glucose-level sensors on the surface. When blood glucose levels increase, the sensors on the surface would record it and insulin would be released. Yet, this kind of nano-artificial pancreas is still only a theory (28).

The Nanopump:
The nanopump is a powerful device and has many possible applications in the medical field. The first application of the pump, introduced by Debiotech, is Insulin delivery. The pump injects Insulin to the patient's body in a constant rate, balancing the amount of sugars in his or her blood. The pump can also administer small drug doses over a long period of time (29).

1. Conclusion

In the foreseeable future, the most important clinical application of nanotechnology will probably be in pharmaceutical development. These applications take advantage of the unique properties of nanoparticles as drugs or constituents of drugs or are designed for new strategies to controlled release, drug targeting, and salvage of drugs with low bioavailability. Hopefully, the 224 new kind of treatment may help in making the everyday lives of millions of diabetes patients more tolerable.

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