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Diabetes Mellitus: Application in Current Diabetes Management Practices

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Abstract

Nanotechnology is an interdisciplinary scientific field with a great number of applications, which are developed in order to improve the quality of life. Nanomedicine is a specialized branch of medicine that applies the fundamentals of nanotechnology to the prevention, diagnosis and treatment of various diseases, such as cancer, cardiovascular diseases and diabetes. Diabetes mellitus is considered to be among the major afflictions of modern western society. The common approach of this condition is a prescribed insulin replacement therapy, including injections of long acting insulin at mealtimes. Regarding the everyday routine, insulin injections and glucose tests can be painful and time consuming for diabetic patients. Many efforts are given to overcome the drawbacks of injection therapy, but there is the need for new safe and cost effective technologies for diagnosis and treatment. Nanotechnology has obtained increasing importance in the research of diabetes. Nanotechnology based tests can provide more accurate information for the diagnosis of diabetes mellitus. Several therapeutic methods have been proposed for non-invasive monitoring of blood glucose, based on nanotechnology. Some representative achievements include the molecular diagnosis of diabetes, the oral delivery of insulin with the use of nanospheres as biodegradable polymeric carriers, the development of artificial beta cells and artificial pancreas. The aim of this review is to provide insights into the role of nanotechnology in diabetes diagnosis and treatment, shedding light on the potential of nanotechnology in this field and discussing the future prospects.

Keywords: Nanomedicine; Nanotechnology; Diabetes mellitus; Nanomaterials; Diagnosis; Treatment

Introduction

Nanotechnology is a scientific and technological combination, integrating various fields, such as physics, chemistry, biotechnology and engineering. It is considered as the manipulation of matter with at least one dimension sized from 1 nanometer to 100 nanometers. The interesting potential of nanotechnology, due to the special properties of nanomaterials, leads to a great number of applications, which are developed in order to improve the quality of life [1]. Nanomedicine is a specialized branch of medicine that applies the fundamentals of nanotechnology to the prevention and/or the treatment of various diseases. Thus, nanomedicine involves the utilization of nanostructured materials for diagnosis, delivery, detection or actuation purposes in a living organism. There are numerous companies specializing in the fabrication of new forms of nano sized matter, with anticipated applications that include medical therapeutics and diagnostics, energy production, molecular computing and structural materials. Nanotechnology can enhance drug delivery to those areas which were unfavorable for macromolecules to approach [2]. Furthermore, it offers new implantable sensing technologies, providing accurate medical information. Cancer and cardiovascular diseases diagnosis and treatment, dental applications and development of bone implants are among the most famous applications of nanomedicine. In type 1-diabetes, the body cannot produce insulin due to loss of β-cells, as a result of T-cell mediated autoimmune attack. The common approach of this condition is a prescribed insulin replacement therapy, including injections of long acting insulin at mealtimes [3]. An insulin resistance combined with insulin deficiency is found in patients, suffering from type 2-diabetes. Exercise and regulation of the meals is suggested for the initial treatment of type of diabetes. Diabetes can lead to serious long term health complications, such as cardiovascular disease, chronic kidney disease, stroke, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment and is among the top ten leading causes of death worldwide. Regarding the everyday routine, insulin injections and glucose tests can be painful and time consuming for diabetic patients.

Many efforts are given to overcome the drawbacks of injection therapy. Several technologies have been developed, such as continuous glucose monitors and insulin pumps to improve patient compliance. But there is the need for new safe and cost effective technologies for diagnosis and treatment, since there is still risk of patient's infection and scarring due to implanted sensors and cannulas [4]. All the widely used devices must be frequently replaced and maintained with a high cost for the patients and the health systems worldwide. Nanotechnology has obtained increasing importance in the research of diabetes. It can provide more accurate information for the diagnosis of diabetes mellitus. Furthermore, several therapeutic methods have been proposed for non-invasive monitoring of blood glucose, based on nanotechnology [5]. Some representative achievements include the molecular diagnosis of diabetes, the oral delivery of insulin with the use of nanospheres as biodegradable polymeric carriers, the development of artificial beta cells and artificial pancreas. Thus, this review outlines the role of nanotechnology in diabetes diagnosis and treatment, shedding light on the potential of nanotechnology in this field and discussing the future prospects [6].

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Literature Review

Nanotechnology and diabetes diagnosis

Nanotechnology can provide sensing technologies for accurate and medical information, for diagnosis of diabetes. Diabetes blood sugar level tests require autonomous periodical checks by the patients, to avoid the risk of blood glucose decrease to dangerous levels. Sometimes this routine is difficult and painful to be held, particularly for the elderly people and the children. Nanotechnology can offer the opportunity for the development of implantable and wearable sensing technologies, providing continuous and accurate medical information. The most common ways of exploiting nanotechnology in the diagnosis of diabetes is by applying microphysiometer or by using implantable sensor. The microphysiometer is built from multi walled carbon nanotubes, which are electrically conductive. The concentration of insulin in the chamber is directly related to the current at the electrode and thus, the nanotubes are absolutely functionable at pH levels which are characteristic of living cells. The conventional detection methods typically measure insulin production at intervals, by collecting and measuring small samples, periodically. Nanomaterials and diabetes treatment various types of nanomaterials are currently studied for insulin delivery in diabetes treatment. Ceramic nanoparticles, liposomes, dendrimers, polymeric biodegradable nanoparticles and polymeric micelles are the most promising among the proposed ones. Depending on the type of administration each and every one of these categories of nanomaterial gathers some advantages.

Oral administration

Oral insulin administration is considered as the most convenient method for diabetes mellitus maintenance. However, the intestinal epithelium is considered as a major barrier to the absorption of hydrophilic drugs, like insulin, as lipid bilayer cell membranes don't allow the diffusion of these drugs to the bloodstream. Drug delivery systems based on gastric enzymes ensure the transfer and the degradation of the insulin in the stomach. A protective matrix is necessary to embed the active substance, protecting it from the harsh environment inside the stomach. A combination of calcium phosphate polyethylene glycol insulin with casein is indicated as an effective choice. Mansoor, et al., present polymer based nanoparticle strategies for insulin delivery, in various forms. Polymeric nanoparticles are considered quite efficient compared to conventional oral and intravenous administration methods which are widely used. In order to form insulin delivery systems, biodegradable, pH sensitive polymers surrounded by nanoporous membrane are used, allowing controlled release of insulin. In animal studies, the oral delivery of insulin polymeric nanoparticles is achieved through the use of nano pellets loaded with insulin. N-isopropylacrylamide, polyethylenimine and polymethacrylic acid are some of the polymer based nanoparticles which are used for oral insulin administration. Also, co-polymers like N, N-dimethylaminoethyl methacrylatem, polyurethanes, polyacrylic acids, polyanhydrides and polyacrylamide are being under investigation in order to be used as insulin carriers. Hydrogels and microspheres can play a double role, acting both as protease inhibitors by protecting the encapsulated insulin from enzymatic degradation within its matrix as well as permeation enhancers by effectively crossing the epithelial layer post oral administration. Thus, they can effectively carry insulin, providing a promising strategy for oral insulin administration.

Inhalation

The new nanotechnology based insulin system is focusing on inhaling the insulin, instead of injecting it, allowing its controlled release into the bloodstream. Compared to the gastrointestinal route, inhaler systems provide the pros of mild environment, including low enzyme concentrations and neutral pH. Various types of inhaler systems can be used to deliver the active products. Dry powder formulations and solutions are among the most common. The encapsulation of insulin within the nanoparticles, allows the inhalation of the dry powder formulation of insulin into the lungs. Insulin degradation is avoided, ensuring the delivery of insulin to the bloodstream. In order to maximize the efficacy, regular lung function tests are required to be applied to the patients, before the treatment, increasing the cost of this approach. Di J, et al., proposed a controlled insulin delivery system, based on injectable polymeric nanoparticle cross linked network, able to be noninvasively triggered by a focused ultrasound system. As a matrix material biodegradable Poly (Lactic-co-Glycolic Acid) (PLGA) was used. They demonstrated that the resulting FUS activated insulin encapsulated nano network could regulate blood glucose levels of type 1 diabetic mice in a long term. For the treatment of type 2-diabetes, chitosan nanoparticles are considered to be suitable for the development of an inhalation delivery system. Since, insulin is a hydrophilic drug; it is difficult to be diffused through intestinal epithelium. Chitosan can enhance the absorption of insulin. Advanced composite nanomaterials, produced by carboxylated chitosan grafted with poly seem to increase the efficiency of the controlled release of insulin.

Discussion

Nanopump

The nanopump is a powerful device with many medical applications. It is a tiny volumetric pump with a pair of check valves that is integrated into a micro electromechanical systems or a nano electromechanical systems chip. From as structural point of view, the chip is a stack of three layers bonded together. The first one is a Silicon On Insulator (SOI) layer with micromachined pump structures and the two others are Pyrex cover plates. Insulin delivery is the main application of the pump, introduced by Debiotech. The pump can inject insulin to the patient's body in a constant rate, balancing the amount of glucose in the blood. It can also administer small drug doses over a long period of time.

Artificial pancreas

The development of an artificial pancreas system, comprising of a continuous glucose monitor, glucose meter and an insulin infusion pump for the monitor calibration could be the permanent solution for the patients who suffer from diabetes mellitus. The original initial idea was first demonstrated in 1974. The fundamental of this concept includes a sensor electrode which can repeatedly measure the level of blood glucose, with the data feeding into a tiny computer. This process can trigger an infusion pump and the appropriate units of insulin can enter the bloodstream from a small reservoir. The utilization of a tiny silicon box, containing pancreatic beta cells obtained from animals is an alternative approach. This application is used to protect transplanted cells from the immune system. It also allows the sufficient diffusion of glucose, insulin and oxygen. It can be implanted under the skin of diabetes patients.

Conclusion

The impact of nanotechnology on medicine is uncontested. In this manuscript the use of nanotechnology in diabetes diagnosis and treatment was discussed. It was demonstrated that it is very promising in detection of insulin and blood glucose but also in insulin efficient administration and delivery. Nanotechnology based techniques are being helpful in the development of new strategy for the treatment of diabetes, including glucose responsive insulin therapy. Continuous glucose monitoring devices as well as insulin delivery systems like artificial pancreas will be invaluable for diabetic patients. Nanotechnology promised a total absence of lag time between glucose detection and insulin delivery, avoiding dangerous situations, such as hypoglycemia. The next generation nanocomposites mediated insulin in parallel with advanced nanodevices are expected to improve everyday life of diabetic patients in the future.

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