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Review article

Applications of nanotechnology in diabetes: A review

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ABSTRACT

Nanotechnology is an emerging field in the area of interdisciplinary research, especially in biotechnology. Nanotechnology trying to construct objects atom by atom, the way that the nature does. Nanomedicine is a sub discipline of nanotechnology, an emerging field. Nanotechnology offers some new methods in treating diabetes mellitus. Such as Boxes with nano pores that protect transplanted beta cells from the immune system attack, artificial pancreas and artificial beta cell, nanospheres as biodegradable polymeric carrier for oral delivery of insulin. This also offers new implantable and/or wearable sensing technologies that provide continuous and extremely accurate medical information about the blood glucose level of patient especially for the children and older patients. The aim of present review is to offers more information on the recent advaces and impact of nanotechnology to cure diabetes.

Keywords: Nanomedicine, Diabetes, Nanotechnology, Pancreas, insulin, Photodynamic therapy.

INTRODUCTION

The development of reliable technology to produce nano particles is an important aspect of nanotechnology. From the past few decades, there has been a considerable research interest in the area of drug delivery using particulate system like Nan particles. Biological synthesis process provides a wide range of environmentally acceptable methodology. The impact of nanotechnology on medicine is growing every day. Nanotechnology is to build with molecule by molecule in short, the way nature does. A human fetus begins life as a single cell and then divides to become two cells, then four, then eight and so on. Nanotechnology aims to build in a similar way, constructing objects out of their most basic component and assembling products out of bulk materials. Building objects molecule by molecule offers an unprecedented degree of precision and control over the final product. This all started in 1989, when a group of engineers at IBM Company managed to create the smallest ever company logo. They spelled IBM letters out of individual atoms. Since then nanotechnology has become a part of our world. Medical nanomaterials may also include smart drugs that become active only in specific circumstances.

Yoshihisa Suzuki from Kyoto University has designed a novel drug molecule that release antibiotics only in the presence of an infection. Suzuki bound the molecule of gentamycin to a hydrogel using a newly developed peptide linker. The linker can be cleaved by a proteinase enzyme produced by Pseudomonas aeruginosa. Tests on rats have shown that the antibiotic is not released if no pseudomonas aeruginosa bacteria are present. If any bacteria of this type are present, the enzyme produced by the microbes cleaves the linker and gentamicin is released to kill the bacteria. This is highly desirables because the indiscriminate prophylactic use of antibiotics is associated with the emergence of drug- resistant bacterial strains.

Diabetes is rapidly rising all over the globe at an alarming rate. Over the past 30 year, 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. Type-2 diabetes represents approximately 90 % of individuals with diabetes in the United States, while most of the remainder has type-1 diabetes. 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 population.

The application of nanotechnology for the treatment of diabetes is by Novel drug delivery to achieve increased therapeutic value as well as reducing toxicity. It was achieved by making a drug to its atomic size approximately 1–100 nanometer range. 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) Diabetes mellitus is a common and very prevalent disease affecting the citizens of both developed and developing countries. It is estimated that 25% of the world population is affected by this disease.

Diabetes mellitus is caused by the abnormality of carbohydrate, fat and protein metabolism or usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels (hyperglycemia) which is linked to low blood insulin level or insensitivity of target organs to insulin [2].

There are two major forms of diabetes

Type-1 diabetes, formerly called juvenile diabetes, is usually first diagnosed in children, teenagers, and young adults. In this form of diabetes, the pancreas no longer makes insulin because the body's immune system has attacked and destroyed the pancreatic cells specialized to make insulin. These insulin-producing cells are called beta cells.

Type-2 diabetes is commonly linked to obesity, which promotes insulin resistance. 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. In approximately one third of obese individuals, there is a decreased cell mass caused by a marked increase in cell apoptosis, rendering these individuals in capable 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 (8-10). 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.

Application of Nanotechnology

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

Micro Physiometer

The microphysiometer is built from multi walled carbon nano tubes, which are like several flat sheets of carbon atoms stacked and rolled into very small tubes. The nano tubes 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.

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. 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 [3].

Use of Nanotechnology in the treatment of diabetes

The patients control their blood-sugar levels by 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). 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. 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. 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. Therefore, attention has been given to improving the para cellular transport of hydrophilic drugs. A variety of intestinal permeation enhancers including chitosan have been used for the assistance of the absorption of hydrophilic macromolecules. Therefore, a carrier system is needed to protect protein drugs from the acidic environment in the stomach and small intestine, if given orally additionally; chitosan nanoparticles enhanced the intestinal absorption of protein molecules to a greater extent than aqueous solutions of chitosan in vivo. he insulin loaded Nanoparticles coated with muco-adhesive chitosan 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 para cellular pathway to the bloodstream, its ultimate destination [4].

Nanosphere 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 by enzymatic degradation within its matrix and as permeation enhancers by effectively crossing the epithelial layer after oral administration. Radwant M.A. and Aboul- Enein H.Y. from Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, used polyethyl cyanoacrylate (PECA) nanospheres as biodegradable polymeric carriers for oral delivery of insulin. The administration to streptozotocin-induced diabetic rats showed a very good hypoglycemic effect. Should the effect be proven in human research, it might significantly improve patient compliance.

Artificial Pancreas

Artificial pancreas could be the permanent solution for diabetic patients. The concept of its work is based on a sensor electrode repeatedly measures the level of blood glucose and 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. Since this reservoir we called Nano robot 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. The progressive development toward the therapeutic use of nanorobots based on nanobioelectronics is possible through a computational approach with the application of medical nanorobotics. In the proposed 3D prototyping, a physician can help the patient to avoid hyperglycemia by means of a handheld device, like a cell phone enclosed with cloth that is used as a smart portable device to communicate with nanorobots. Therefore, this architecture provides a suitable choice to establish a practical medical nanorobotics platform for in vivo health monitoring.

The Computational nanotechnology has proven his importance as a power tool for the purpose of designing device at nanoscale. Simulation can anticipate performance and help in new device design. Manufacturing investigation nano mechatronics contrl analysis and hardware implemention. The nanorobots design includes integrated nanoelectronics, As a valuable tool for automatically monitoring glucose level and the exterior consis of carbon metal nanocomposites, which are a diamod-like carbon thin film and posses atomic smoothness, chemical inertness and hardness properties close to those of diamond. It has an artificial glycocalyx surface. This minimizes adsorption and bioactivity in relation to fibrinogen as well as other blood proteins, ensuring sufficient biocompatibility to avoid immune system attack. 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 for 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.

Another approach is to insert new genes into naturally occurring cells. The cells can be genetically altered so that they could not only produce insulin, but could also respond to the rise and fall of blood glucose, just as normal pancreatic beta cells do. Illani Atwater, from Sansum Medical Research Institute, Santa Barbara, CA, is working on inserting the proinsulin gene into a keratinocyte cell line attached to a glucose sensitive promoter gene, as well as the genes for GLUT2 glucose transporters and glucokinase phosphorylation enzymes. No matter which way leads toward the solution, the result will be the same, i.e. artificial beta cell that will produce insulin in response to the rise of blood glucose, and no target for the immune system. So, without immunosuppression, cell a better solution than pancreas transplantation [5].

The Nano pump

The nano pump is a powerful device and has many possible applications in the medical field. The first application of the pump introduced by De biotech, in 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. The pump is composed of nanotech silicon membranes with mesopores that would allow insulin proteins out, but would be too small to allow in cells that would attack the implanted beta cells. This would allow the pump to continuosly produce insulin.

Implantable pumps allow patients to participate in activities, such as swimming and contact sports that other insulin pump devices would not allow. A nanoinsulin pump would be much smaller than existing implantable insulin pumps and would be much longer lasting and easier to insert into the patient. These attributes would reduce the need for and number of invasive procedures such is the case with other implantable nanopumps. The pumps could be easily installed and replaced in an outpatient setting, creating little inconvenience or risk for the patient.

Smart Cell

Todd Zion from Nanostructure Materials Research Laboratory has developed technology for diabetes treatment called Smart Cell. When glucose rises in the bloodstream, it will eat away Smart Cell's structure. As the Smart Cell protein matrix breaks down, insulin is released. The more glucose is present, the faster matrix will erode. Smart Cell technology means that diabetics could stop endlessly checking and rechecking their glucose levels, injecting more insulin as needed, because the drug will handle the chore. An injection a day is all that diabetics will need. No blood testing, no multiple shots. Early round of experiments with lab rats has begun, and the preliminary results are promising [6].

CONCLUSION

Nanotechnology has great potential in the field of medicine today, so it is not hard to imagine that nanotechnology will become an important part of our lives tomorrow.

Diabetic patients are able to survive for long time as equivalent to normal persons. The different Researchers, Scientists and governments around the world have recognized the possibilities of nanotechnology, and continue effort is made to develop new methods of nanotechnology for the treatment of disease like diabetes Mellitus. The present review work reveal that how different approaches of Nanotechnology is applied for common goal i.e. treatment of diabetes millitus. These applications take advantage of the unique properties of nano particles 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 new kind of treatment may help in making the everyday lives of millions of diabetes patients more tolerable.device.

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