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DIABETES AND NANOMATERIALS

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About 150 million people suffer from diabetes in the world and it has been predicted that this number will be doubled within 15 years. Type 2 diabetes accounts for about 85% of all cases with diabetes. Type 2 diabetes is considered a paradigm for a multifactorial polygenic disease where common variations in several genes interact to cause the disease when exposed to the affluent environment of too much food and too little exercise. Recently many scientists focused their research on nanomedicine and nanodiagnostics for many diseases, like diabetes, cancer, spinal card injury etc. For the scientists to synthesize the nanomedicine (hypoglycemic drugs) for diabetics is on the top priority to reduce the cost and pain of the patients. This article is an attempt to illustrate the diabetes and the use of nanomaterials for benefit of diabetic patients.

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1. Introduction

People with diabetes mellitus have five times more risk of having heart disease as people without diabetes. More than 60% of people with end-stage renal disease are people with diabetes. Diabetes is the leading cause of blindness in the United States. Till date our understanding of its patho-physiology and management is incomplete. The WHO estimates that by 2025 as many as 200–300 million people worldwide will have developed type 2 diabetes. South East Asian countries have the highest burden of diabetes, and the projections of the International Diabetes Federation on the prevalence of diabetes mellitus and impaired glucose tolerance (IGT) for the year 2005 is, respectively, 7.5 and 13.5% [1, 2, 3].

Nanomedicine is defined as the application of nanotechnology to health. It exploits the improved and novel physical, chemical and biological properties of materials at the nanometric scale. Nanomedicine has potential impact on the prevention, early and reliable diagnosis and treatment of disease. The objective of drug delivery systems is to target selected cells or receptors within the body. This technique is driven by the need on one hand to more effectively target drugs to the site of disease, to increase patient acceptability and reduce healthcare costs; and on the other hand to deliver new class of pharmaceuticals that cannot be effectively delivered by conventional means [4].

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2. Diabetes

The World Health Organization recognizes three main forms of diabetes: type 1, type 2, and gestational diabetes (or type 3, occurring during pregnancy), although these share signs and symptoms but have different causes and population distributions. They are not a single disease or condition. Type 1 is generally due to autoimmune destruction of the insulin-producing cells - pancreatic beta cells, while type 2 is characterized by tissue wide insulin resistance and varies widely. Gestational diabetes is due to a poorly understood interaction between fetal needs and maternal metabolic controls [5].

The term "type 1 diabetes" has universally replaced several former terms, including childhood-onset diabetes, juvenile diabetes, and insulin-dependent diabetes. "Type 2 diabetes" has also replaced several older terms, including adult-onset diabetes, obesity-related diabetes, and non-insulin-dependent diabetes. Beyond these numbers, there is no standard, so a type 2 who has become insulin dependent has sometimes been called type 3, while the same term is also used for gestational diabetes in some cases [5].

About 150 million people suffer from diabetes in the world today and it has been predicted that this number will be doubled within 15 years [6]. Current estimates of the prevalence of diabetes in the United States and Canada reveal that one person in 14 either has or will develop the disease. There are large ethnic and geographic variations in the prevalence of type 2 diabetes. In Scandinavia, where type 1 diabetes is common, type 2 diabetes accounts for about 85% of all cases with diabetes. As many as 60% of the adult population of certain groups (Pima Indians) have the disease. Diabetes mellitus is among the top 10 causes of death either directly or indirectly, yet our understanding of its pathophysiology and management is incomplete.

Aside from acute glucose level abnormalities, the main risks to health are the characteristic long-term complications. These include cardiovascular disease (doubled risk), chronic renal failure (the main cause of dialysis in developed world adults), retinal damage (which can lead to blindness and is the most significant cause of adult blindness in the non-elderly in the developed world), nerve damage (of several kinds), and microvascular damage (including erectile dysfunction (impotence) and poor healing which can lead to gangrene and even amputation - the leading cause of non-traumatic amputation in developed world adults.

The prevalence of type 2 diabetes is increasing in epidemic proportions worldwide. Furthermore, the long-term complications associated with diabetes are major causes of morbidity and mortality, imposing a high financial burden on health care costs [7]. Type 2 diabetes will certainly be one of the major diseases of the 21st century and should be recognized as a priority. It is now well established that the development of type 2 diabetes results from the interaction between the genetic makeup of the individuals and their environment [8]. The development of obesity seems to be an important factor in the development of insulin resistance [9]. If this insulin resistance occurs in the presence of a genetically determined propensity to β-cell dysfunction, glucose intolerance can occur. Although there is still disagreement over the relative contribution in the alterations in insulin sensitivity versus β-cell function in the development of diabetes, it is becoming clear that reductions in both processes have already occurred by the time hyperglycemia develops. The concept for the prevention of diabetes developed on the basis of a better understanding of the pathophysiology of glucose intolerance and stimulated by the ever-increasing burden of the disease. It has now been demonstrated that diabetes can be prevented, or at least delayed, by non pharmacological interventions, such as lifestyle modification including diet and exercise[10], and by pharmacological intervention, including metformin, acarbose and troglitazone [11].

Clinical type 1 diabetes represents end-stage insulitis, and it has been estimated that at the time of diagnosis, only 10–20% of the insulin-producing β-cells are still functioning. Environmental factors have been implicated in the pathogenesis of type 1 diabetes both as triggers and potentiators of β-cell destruction [12], although the contribution of any individual exogenous factor has not yet been definitely proven. Type 1 diabetes is considered to be a chronic immune-mediated disease with a subclinical prodrome of variable duration. It is characterized by selective loss of insulin-producing β-cells in the pancreatic islets in genetically susceptible subjects. The

most important genes contributing to disease susceptibility are located in the HLA class II locus on the short arm of chromosome 6 [13]. Nevertheless, only a relatively small proportion, i.e.,>10%, of genetically susceptible individuals progress to clinical disease.

3. Role of Nanomaterials in Diabetes:

Nanotechnology has achieved the status as one of the critical research endeavors of the early 21st century, as scientists harness the unique properties of atomic and molecular assemblages built at the nanometer scale. Our ability to manipulate the physical, chemical, and biological properties of these particles affords researchers the capability to rationally design and use nanoparticles for drug delivery, as image contrast agents, and for diagnostic purposes [14].

The application of nanomaterials in management of diabetes has been primarily confined to the following areas:

1. Sterile needles, including lancets, are required in clinical and medical settings, and their use in self-monitoring of blood glucose (SMBG) is increasing due to the rise in diabetes [15]. In the development of needles, both low piercing resistance and low-cost, safe sterilizing methods are required. In a conventional method to reduce piercing resistance, a silicone compound was applied to a metal surface in the form of an adhesive coating material comprising a siloxane unit with an amino group and an organosiloxane unit. Hideaki Nakamura et al. applied uniform nano-layer of TiO2 onto the surface of lancets by sputtering. They developed Photocatalytic, velvety lancets with antibacterial properties and low lancing resistance for use in SMBG. The lancet coated with a crystallized, velvety nano-layer of TiO2 obtained by annealing had antibacterial properties and a similar lancing resistance compared with the bare lancet, and showed potential for application in monitoring blood glucose in diabetes [16].

2. The oral route is the preferred route of drug administration for patients on chronic therapy. However, the oral delivery of many therapeutic peptides and proteins remain an unresolved challenge mainly because of the large size, hydrophilicity, and instability of these macromolecules [17]. Zengshuan Ma et al. proposed to use chitosan nanoparticles as a carrier for the oral delivery of insulin [18]. As chitosan is a mucoadhesive, polycationic polymer that can facilitate drug absorption by localizing drug concentration around absorptive cells and prolonging drug residence in the gut [19]. It is also an effective permeability enhancer because of its depolymerizing action on cellular F-actin and the tight junction protein ZO-1 [20]. Co-administered chitosan has been shown to enhance the transport of 14 C-mannitol [21], buserelin, vasopressin and insulin across the Caco-2 monolayers [22]. Chitosan, in the form of glutamate solution and nanoparticles, is also reported to promote the transport of insulin through the nasal epithelium of sheep and rabbits, respectively [23]. Oral delivery of insulin via polymer nanoparticles has also met with some success. The first report in 1988 suggested that insulin encapsulated in poly (isobutylcyanoacrylate) (PIBCA) nanocapsules had a long-term (up to 20 days) hypoglycemic effect in diabetic rats after oral administration [24]. Peroral administration of insulin-loaded nanoparticles of poly (lactide-co-glycolide) and poly(fumaric-cosebacic) anhydride also controlled the plasma glucose levels of rats against an initial glucose load. A recent study has shown that peroral chitosan– insulin nanoparticles could significantly lower the serum glucose levels of alloxan-induced diabetic rats [25,26,27]. Insulin association to chitosan nanoparticles at pH 5.3 was 50% less efficient than that at pH 6.1. However, the insulin association at pH 5.3 was stronger, where more than 75% of the associated insulin remained intact in vitro release studies. In contrast, insulin association at pH 6.1 was highly labile, the insulin rapidly and completely dissociating when the chitosan nanoparticles were diluted with aqueous media. These differences between the pH 5.3 and 6.1 formulations could have an impact on the in vivo pharmacological activity of the chitosan–insulin nanoparticles [18].

3. Despite the attractive features of nanoparticles in enhancing insulin delivery, the usual mechanism of sustained release is independent of physiological blood sugar concentration. The best way to treat diabetes, however, is to provide exogenous insulin proportional to the varying blood glucose level in the patients [28]. Toward such an end, several researchers have attempted to develop glucose-responsive materials. In particular, those based on competitive binding have

received considerable attention [29]. In one such system, a polymer comprising covalently bound sugar is crosslinked using a multifunctional glucose-binding protein such as one of the plant lectins [30]. When the matrix comes in contact with free glucose in solution, the protein releases polymeric glucose and binds to free glucose molecules, causing the hydrogel to disintegrate. Nanoparticles constructed from such glucose responsive materials might then not only improve the means of insulin delivery as outlined above but also provide a more desirable release profile once administered. Todd C. Zion et al. developed a reverse microemulsion (RM) synthesis of inorganic nanoparticles for catalytic applications and apply the technique to the synthesis of polymer nanoparticles for controlled drug delivery [31, 32].

4. Conclusions

This article was an attempt to review the metabolic disorder diabetes mellitus and the use of nanomaterials for drug administration and the management. The scientists are also focusing the use of nanomaterials in diagnostics of diabetes and in wound healing. Further research is going on very quickly in this field and may be possibly we will get some fruitful results in drug administration and diagnostics for use of the patients suffering with diabetes.

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