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Review Article

Nanoparticles and the new era in diabetes management

Minyahil A. Woldu*, Jimma L. Lenjisa

Department of Clinical Pharmacy, Ambo University, College of Medicine and Health Sciences, Ambo, Ethiopia

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***Correspondence to:**
Minyahil A. Woldu,
Email: minwoldu@gmail.com

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ABSTRACT

Diabetes mellitus (DM) has been known to mankind for more than 2000 years. DM is a group of metabolic disorder characterized by a complete lack of insulin, a relative lack of insulin, or insulin resistance. The increase in prevalence of DM is due to three influences: lifestyle, ethnicity, and age. Current challenges in diabetes management include: optimizing the use of the already available therapies to ensure adequate glycemic, blood pressure, and lipid control and to reduce complications. At present several researches have been focusing on new management options for diabetes. Among these options the use of nanomedicine is becoming an eye catching and most promising. The aim of the present review is to provide brief overview of the applications of nanoparticles (NPs) in diabetes management. The development of improved oral insulin administration is very essential for the treatment of DM to overcome the problem of daily subcutaneous injections. In diabetic patients oral administration of insulin can be beneficial not only to alleviate the pain and trauma caused by injections, but it can also mimic the physiological fate of insulin as well. It has been found that NPs of chitosan, calcium pectinate zinc oxide, alginate, casein and different polymers have been used as a carrier for oral insulin delivery. Buccal administration of insulin with absorption enhancers showed a maximum 12% pharmacological activity. Biodegradable Polymeric NPs for parenteral insulin delivery have also been used, where the insulin matrix surrounded by the nanoporous membrane containing grafted glucose oxidase. A rise in blood glucose level triggers a change in the surrounding nanoporous membrane, resulting in biodegradation and subsequent insulin delivery. Inhalable, polymeric NP-based drug delivery systems have also been tried earlier for the treatment of tuberculosis and cardiovascular disease treatment. Such approaches can be directed toward insulin delivery through inhalable NPs. All previous studies resulted in post treatment accumulation of the NPs in skin and eyes. These drug delivery technologies are in various stages of research and development. The medical applications for nanotechnology are enormous and could give medicine, including the treatment of diabetes, an entirely new outlook.

Keywords: Diabetes Mellitus, Nanoparticles, Nanomedicine, Nanotechnology

INTRODUCTION

Diabetes mellitus (DM) has been known to mankind for more than 2000 years.[1] It is likely to become one of the most prevalent and economically important diseases of the 21st century in both the developed and developing nations.[2] DM is a group of metabolic disorder characterized by a complete lack of insulin, a relative lack of insulin, or insulin resistance, which then results in hyperglycemia.[2,3] DM has reached epidemic proportions in many countries.[4] The prevalence of type 2 DM (T2DM) is predicted to increase dramatically over the coming years.[5] Worldwide, the number of people with DM is expected to rise to 35% by the year 2025.[3] The increase in prevalence of DM is due to three influences: lifestyle, ethnicity, and age.[3] A number of developments has been tried to counteract the resulting impact on morbidity and mortality.[5] The hallmarks of DM are long latency, chronicity, multi-organ involvement and need for long-term care make the management of chronic conditions difficult.[6]

One of the challenges in clinical diabetology today is to develop and implement diabetes prevention management programs for clinical practice. Recent studies have convincingly demonstrated that lifestyle intervention, addressing diet and exercise as well as pharmacologic preventive strategies reduced the risk of progressing from impaired glucose tolerance to diabetes.[7] Despite the known benefits of lifestyle modification, many individuals still find it harder to maintain a healthier life because of the higher possibilities of sedentary behavior and overeating in the modern world.[5]

Current challenges in diabetes management include: optimizing the use of currently available therapies to ensure adequate glycemic, blood pressure, and lipid control and to reduce complications; educating patients on diabetes self-management; improving patient adherence to lifestyle and pharmacologic interventions; reducing barriers to the early use of insulin; and improving the delivery of health care to people with chronic conditions.[8] Furthermore, the management of DM using insulin limited by insulin resistance and in chronic treatment by anaeroxia nervosa, brain atrophy and fatty liver.[9]

Nanotechnology can be defined as the monitoring, repairing, construction and control of human biological systems at the cellular level by using materials and structures engineered at the molecular level.[10] Nanomedicine is then the integration of nanotechnology in medicine for the better human health care.[9] Nanomedicine utilizes components as tiny as 1/80,000th of the diameter of a human hair. At the scale of 1 nanometer (or 10 times the diameter of a hydrogen atom), materials and devices can interact with cells and biological molecules in a unique way.[11]

The applications of nanomedicine include the detection of molecules such as proteins or DNA, imaging enhancers and targeting specific tissues to deliver therapeutic agents.[12] The possibilities of nanomedicine include nano-formulations for efficient drug delivery, smart drugs which only activate when needed, engineered microbes which produce human hormones, and even "nanorobots", which would move autonomously around the body acting as a boost, or a replacement, for our immune system, red blood cells, or many other biological systems.[13] Therefore, the aim of the present review is to provide brief overview of the applications of NPs in diabetes management.

APPLICATIONS OF NANOTECHNOLOGY FOR DIABETES MANAGEMENT

Buccal insulin

The buccal delivery system for insulin delivers insulin through anaerosol spray into the oral cavity and hence differs from inhalers. The insulin is absorbed through the inside of the cheeks and in the back of the mouth instead of the lungs.[14] Buccal administration of insulin with absorption enhancers showed a maximum 12% pharmacological activity. Recently buccal mucosal delivery of insulin using bioadhesive formulation has been successfully tried and researchers have investigated a variety of bucco-adhesive formulations including nanoparticles.[15] Generex Biotechnology Corporation is developing a buccal insulin formulation based on RapidMist™. Oral-lyn™ is a liquid formulation of human regular insulin with a spray propellant for prandial insulin therapy. The formulation results in an aerosol with relatively large micelles where the majority of the particles have a mean size >10 μm and therefore cannot go into the lungs. Each puff is claimed to deliver 10 U of insulin. The absorption rate of administered insulin as a puff is 10%, and that corresponds to 1 U when 1 puff of 10 U is delivered, which means 10 puffs will deliver 10 U insulin for a meal.[16]

Oral insulin

New approaches for oral administration of insulin are strongly related to novel insulin carriers.[17] Oral route would be the most convenient and preferred route if it is available.[18] The development of improved oral insulin administration is very essential for the treatment of DM to overcome the problem of daily subcutaneous injections. Insulin, when administered orally, undergoes degradation in the stomach due to gastric enzymes.[19] Beside, nanoencapsulated insulin has been found bioactive, as demonstrated through both *in vivo* and *in vitro* bioassays.[20]

In diabetic patients oral administration of insulin can be beneficial not only to alleviate the pain and trauma caused by injections, but it can mimic the physiological fate of insulin as well.[9,21] The nanomedicine technologies that may be employed for oral insulin delivery include pro-drugs (insulin-polymer conjugation), micelles, liposomes solid lipid nanoparticles (NPs) and NPs of biodegradable polymers.[9,22]

Among the natural polymers used for oral insulin delivery, chitosan (a derivative of chitin, a natural structural polymer found in crustaceans and fungi) is widely explored owing to its ease of chemical modification and favorable biological properties.[18] It has been found that chitosan can protects the insulin from digestive juices, and allows the insulin to be absorbed into the blood stream much more effectively.[13,18] The chitosan-coated NPs have also a higher transport potential over both free drug and unmodified particles. The delivery of oral insulin with such type of polymeric NPs has progressed to a greater extent in the recent years. Therefore, nano-sized polymeric particles are highly promising for oral insulin delivery.[23-25]

Calcium pectinate-insulin NPs formed from a mixture of pectin-insulin at pH 3 were associated with a release of 12.6% ± 3.2% and 21.7% ± 8.7% insulin at 8 and 24 h of dissolution in simulated intestinal medium due to the sustained-release characteristics effect of pectin-insulin interaction.[26] Oral administration of zinc oxide NPs [Figure 1] also resulted in significant antidiabetic effects - with improved glucose tolerance, higher serum insulin (70%), reduced blood glucose (29%), reduced non-esterified fatty acids (40%) and reduced triglycerides (48%).[27]

Insulin should be enveloped in a matrix-like system to protect it from gastric enzymes. This can be achieved by encapsulating the insulin molecules in polymeric nanoparticles (PNPs) [Figure 2]. In one such study, insulin-loaded PNPs were used in the form of pellets for oral delivery

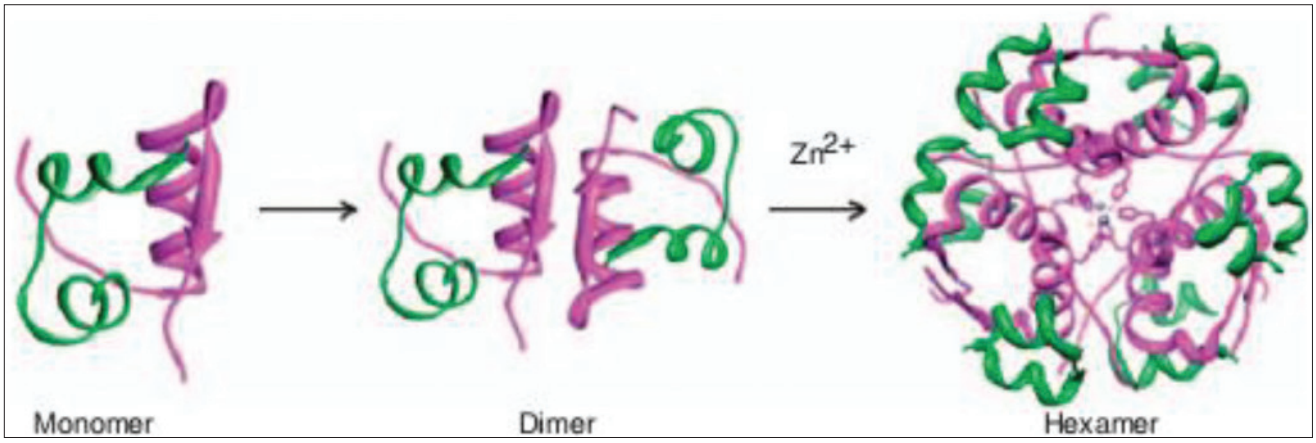


Figure 1: The pattern of assembly of insulin monomer, dimer, and hexamer. In the presence of zinc ions, insulin dimmers associate into hexamers with greater stability. Source: From Ref.[17]

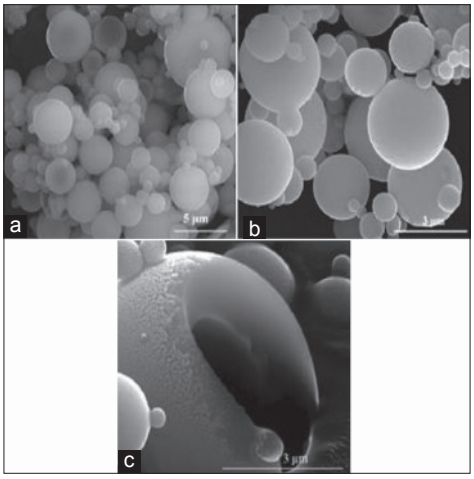


Figure 2: Surface morphology of insulin loaded zinc-silica microspheres according to scanning electron microscopy images taken at different magnifications. Source: From Ref.[17]

of insulin in diabetic rats. The results showed a significant decrease in blood sugar level following the administration of insulin through the buccal route. Temperature-sensitive nanospheres made from poly(N-isopropylacrylamide) and poly(ethylene glycol) dimethacrylate were shown to protect the loaded insulin from high temperature and high shear stress; such a polymeric system can be an effective carrier for insulin.[23] Similarly insulin loaded copolymer poly(N-isopropylacrylamide [NIPAM]-acrylamide [AAm]-2-aminomethyl-5-fluorophenylboronic acid [FPBA]) represented a good smart-release behavior in different pH, and act as a stimuli for stomach, and intestine pH.[28] Alginate-dextran particles suppressed insulin release in acidic media and promoted a sustained release at near neutral conditions.[20] Therefore, Alginate NPs can also be used as oral insulin carrier or glucose binder in the treatment of diabetes as a function of its chemical composition.[29]

In another study, calcium phosphate-poly(ethylene glycol)-insulin combination was combined with casein (a milk protein). The casein coating protects the insulin from the gastric enzymes [Figure 3]. Due to casein's mucoadhesive property, the formulation remained concentrated in the small intestine for a longer period, resulting in slower absorption and longer availability in the bloodstream.[23] Dextran NPs with vitamin B12 combination has also been tested to overcome the gastrointestinal degradation of vita-min B12-peptide-protein drug conjugates. These NPs were found to protect the entrapped insulin against gut proteases and showed a release profile that was suitable for oral delivery systems of insulin.[23]

Evaluation of pH-sensitive oral insulin-loaded with poly (lactic-co-glycolicacid) NPs (PINPs) were administered orally to DM -induced rats and the response of blood glucose and insulin levels was estimated. The rate of insulin release was found to be slower in acidic pH; about 90% of insulin was released in 11 days at pH 1.0. In alkaline conditions, the release was faster; about 90% release was observed to occur within 3 days at pH 7.8. These experiment indicated that oral PINPs are able to deliver insulin effectively and decrease animal blood sugar; and this may be a promising delivery system for the treatment of diabetes.[30]

PNPs for parenteral insulin administration

Polymeric materials have been used in a range of pharmaceutical and biotechnology products for more than 40 years.[31] PNPs are solid, colloidal particles consist of macromolecular substances that vary in size from 10 nm to 1000 nm.[32] Depending on the methods of preparation NPs can be of two types, nanosphere or nanocapsule.[33]

Controlled release systems generally refer to technologies or biomaterials that can be engineered to release drugs at predetermined and/or tuneable rates, or in response to external stimuli and triggers. Polymeric materials have emerged as a major class of controlled release systems since their unique physico-chemical, synthetic, biocompatibility, and degradation properties can be readily manipulated using well-established techniques.[31]

PNPs, either natural or synthetic have been used as matrices for insulin delivery. Natural polymers are of particular interest due to their nontoxic, biocompatible, biodegradable and hydrophilic nature.[18] Today, the most commonly used polymers for controlled drug release applications include poly(D,L-lactide-co-glycolide) (PLGA), poly(lactic acid) (PLA), poly(glutamic acid) (PGA), poly(caprolactone) (PCL), N-(2-hydroxypropyl)-methacrylate copolymers (HPMA), and poly(amino acids). In particular, PLGA, PGA and PLA have been widely used in an impressive number of controlled release products, particularly due to their favourable biocompatibility and biodegradability properties.[31,34]

Biodegradable PNPs have been used as carriers of insulin, where the insulin matrix surrounded by the nanoporous membrane containing grafted glucose oxidase. A rise in blood glucose level triggers a change in the surrounding nanoporous membrane, resulting in biodegradation and subsequent insulin delivery. The glucose/glucose oxidase reaction causes a lowering of the pH in the delivery system's microenvironment. This can cause an increase in the swelling of the polymer system, leading to an increased release of insulin.[23] Such type smart cell drug delivery study was first reported in 2003.[35,36] Study on insulin-loaded poly(epsilon-caprolactone) NPs prepared by water-in-oil-in-water emulsion method showed that it was biocompatible, efficient and safe insulin-delivering system with controlled insulin release.[37]

Other polymer systems investigated for such applications include copolymers such as N,N-dimethylaminoethyl methacrylate and polyacrylamide. This "molecular gate" system is composed of an insulin reservoir and a delivery rate–controlling membrane made of poly [methacrylic acid-g-poly(ethylene glycol)] copolymer. The polymer swells in size at normal body pH (pH=7.4) and closes the gates. It shrinks at low pH (pH=4) when the blood glucose level increases, thus opening the gates and releasing the insulin from the NPs. These systems release insulin by swelling caused due to changes in blood pH. The control of the insulin delivery depends on the size of the gates, the concentration of insulin, and the rate of gates' opening or closing (response rate).[23]

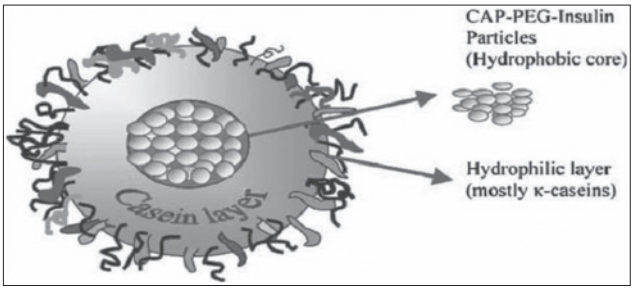


Figure 3: Schematic of a calcium phosphate-PEG-insulin-casein oral insulin delivery system. Abbreviations: CAP, calcium phosphate; PEG, poly(ethylene glycol). Source: From Ref.[23]

In another study, the Zinc oxide poly(NIPAM-AAm-FPBA) hybrid nanogels can sensitively and selectively detect glucose in highly reproducible fluorescent signals over the clinically relevant glucose concentration range of 18-540 mg/dl. The insulin release from the nanogels exhibits the slowest rate (~5% released in 76 hrs) at a normal glucose level (108.0 mg/dl) but becomes quicker and quicker as the glucose increases to higher and higher levels.[38]

Insulin delivery through inhalable nanoparticles

The nanotechnology has reignited interest in the lungs as a main route of drug delivery for both systemic and local treatments. The large alveolar surface area of lung coupled with the thin epithelial barrier and extensive vascularization might enhance drug transport and uptake.[39] The sizes of particles which are used for inhalation therapy are usually expressed in terms of the mass median aerodynamic diameter.[40] If the formulations are manufactured in the correct size range, inhaled insulin formulations have met with more success.[41]

The inhaled products fall into two main groups: dry powder formulations and solution, which are delivered through different inhaler systems. Therefore, the insulin molecules can be encapsulated within the NPs and can be administered into the lungs by inhaling the dry powder formulation of insulin [Figure 4]. Exubera®, containing rapid-acting insulin in powder form, was studied in patients with type 1 and T2DM.[14] Results from phase III clinical trials with insulin administered by the dry-powder inhaler system of Exubera indicate that inhaled insulin formulation given before meals is as effective as mealtime insulin injections.[16]

Inhalable, PNP-based drug delivery systems have also been tried earlier for the treatment of tuberculosis and cardiovascular disease treatment. Such approaches can be directed toward insulin delivery through inhalable NPs. The NPs should be small enough to avoid clogging up the lungs but large enough to avoid being exhaled. Such a method of administration allows the direct delivery of insulin molecules to the bloodstream without undergoing degradation.[23,42] Insulin-loaded polybutylcyanoacrylate (PBCA) NPs were studied and it was demonstrated that the pulmonary administration of these NPs could significantly

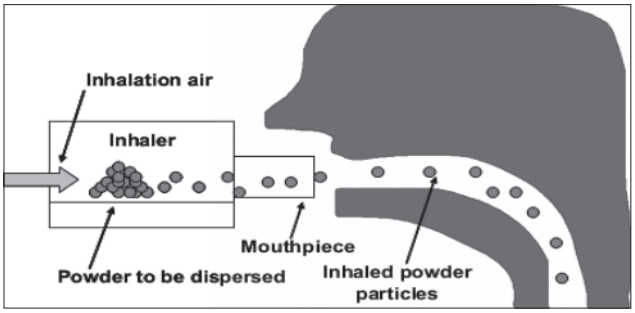


Figure 4: Diagram of a generalized dry powder inhaler in action. Source: From Ref.[42]

prolong the hypoglycemic effect of insulin.[43] Insulin-loaded PBCA NPs when delivered to the lungs of rats were shown to extend the duration of hypoglycemic effect over 20 hrs when compared with pulmonary administration of insulin solution.[44] Preclinical studies in guinea pig lungs with insulin-loaded poly(lactide-co-glycolide) nanospheres demonstrated a significant reduction in blood glucose level with a prolonged effect over 48 hrs when compared with insulin solution.[44]

Inhalable glycol chitosan-coated PLGA NPs containing palmitic acid-modified exendin-4 (Pal-Ex4) and chitosan-modified exendin-4 (chitosan-Ex4) NPs were prepared and it was found that chitosan Pal-Ex4 PLGA NPs have considerable potential to be long-acting inhalation delivery system for the treatment of type 2 diabetes.[45] It was also reported that the bioavailability of insulin NPs was relatively higher than that of solution when administered by pulmonary route to normal rats, but when NPs were administered subcutaneously the bioavailability was comparatively lower compared to solution administered the same way.[43]

Limitations of inhaled NPs: estimating the dose of inhaled particles (dosimetry) requires the knowledge of several mechanisms including regional deposition, retention, solubility, redistribution, translocation into the circulation, metabolism, accumulation in certain organs and the excretion pathways via urine and faeces. The factors that control or affect particle deposition include the particle characteristics themselves, the respiratory tract geometry and individual features of ventilation such as the mode of breathing.[46]

Intranasal insulin delivery

Study showed that nasal administration of insulin-loaded, chitosan-reduced gold nanoparicles (GNPs) improved pharmacodynamic activity of insulin.[47] The major factors limiting the bioavailability of nasally administered insulin include poor permeability across the mucosal membrane and rapid mucociliary clearance mechanism that removes the non-mucoadhesive formulations from the absorption site. To overcome these limitations, mucoadhesive NPs made of chitosan/tripolyphosphate[48] and starch have been evaluated. These NPs showed good insulin-loading capacity, providing the release of 75% to 80% insulin within 15 min after administration.[23]

Transdermal insulin

Transdermal insulin delivery is a needle-free alternative and avoids the disadvantages associated with other alternative routes such as the pulmonary and nasal routes. The stratum corneum, the outermost layer of the skin, constitutes the major barrier for insulin permeation to reach useful levels. Microneedles have also been reported as effective transdermal systems for insulin delivery. Permeation of compounds is limited to small, lipophilic molecules. Several chemical and physical enhancement techniques such as iontophoresis, ultra-sound/sonophoresis, micro-needles, electroporation, laser ablation, and chemical enhancers have been explored to overcome the stratum corneum barrier to increase skin permeability of insulin.[16,49,50]

It is possible to engineer fluorescent micro/nanoscale devices for glucose sensing. Exploitation of micro/NPs in the dermis may allow transdermal monitoring of glucose changes in interstitial fluid.[51]

Biological micro electro mechanical systems for insulin delivery

Implantable biological micro electro mechanical systems (BioMEMS) can be used as insulin pumps for controlled release of insulin when there is an increase in blood glucose level. Interest in BioMEMS is growing rapidly, with opportunities in areas such as biosensors, pacemakers, immunoisolation capsules, and drug delivery.[52] BioMEMS device has a drug reservoir compartment filled with insulin molecules. Biosensors and nonporous membranes with pores of 6-nm diameter are located in the exterior to detect the changes in blood glucose level and for insulin release.[23] The small size scale of MEMS, therefore, offers a unique opportunity to take advantage of the capabilities of responsive hydrogels in sensing and valving applications. Hydrogels that swell in response to changes in osmotic pressure, pH, or temperature or analyte concentration could be quite useful for sensing applications *in vivo*.[53]

The concept of an assembled biocapsule consisting of two micro-machined membranes bonded together to form a cell-containing cavity bound by membranes with nanopores was reported earlier. Microfabricated membranes with 18-nm pore size were shown to be sufficiently permeable to small biomolecules, such as oxygen, glucose, and insulin. While the nanopores were designed to be permeable to glucose, insulin, and other metabolically active products, the pores were small enough to prevent the passage of larger cytotoxic cells, macrophages, antibodies, and complement.[23,54] Such biocapsules can be incorporated into BioMEMS devices for insulin delivery and diabetes treatment.[23]

Study on the integration of an injectable insulin-encapsulated nano-network with a focused ultrasound system (FUS) also identified and such integration can remotely regulate insulin release both *in vitro* and *in vivo*. A single subcutaneous injection of the nano-network with intermittent FUS administration facilitated reduction of the blood glucose levels in type 1 diabetic mice for up to 10 days.[55]

Glucose nanosensors

Fluorescence glucose sensors can provide a continuous glucose reading by being embedded into removable wire-shaped subcutaneous or intravenous catheters as

well as other types of implanted structures, such as capsules, microcapsules, microbeads, nano-optodes, or capillary tubes.[56] Nanosensor-expressing plants can also be used to assess glucose flux differences between cells, invertase-mediated sucrose hydrolysis *in vivo*, delivery of assimilates to roots, and glucose flux in mutants affected in sugartransport, metabolism, and signaling.[57]

Fluorescence glucose-sensing methods, which are under development, offer four potential advantages over commercially used continuous glucose monitoring technologies: (1) Greater sensitivity to low concentrations of glucose, (2) the possibility of constructing sensors that operate most accurately in the hypoglycemic range by using binding proteins with disassociation constants in this range, (3) less need to recalibrate in response to local tissue reactions around the sensor, and (4) no need to implant either a transmitter or a power source for wireless communication of glucose data.[56]

Other nanoparticulate systems for insulin delivery and diabetes management

Diabetes causes a lot of systemic complications. The associated conditions are inflammatory diseases of skin and gums, diabetic retinopathy (eyes), diabetic neuropathy (nervous system), heart diseases, kidney diseases, delayed wound healing, and many more.[23] Nanoparticle-based ocular drug delivery systems have been already described in the past decade. The recent years have seen the advancement in applications of NPs made of polyacrylic acid, polylactide, and chitosan for ophthalmic drug delivery.[23] Chitosan reduced GNPs loaded with insulin prove to be promising in controlling the postprandial hyperglycemia.[58]

The scientific community is working toward utilizing nanoparticle-based drug delivery systems for the treatment of diabetes-associated complications.[23] Other than the ceramic and PNPs, GNPs have also been tested as insulin carriers.[23] Oral and nasal administration of insulin-loaded, chitosan-reduced GNPs improved pharmacodynamic activity of insulin.[23] Insulin-conjugated GNPs had a better drug influence than even direct conventional insulin solution, due to the enhanced permeation and retention effect [Figure 5].[59]

Implantable nanomedical device, which contains pancreatic beta cells from animals, has been promising. The intention of this device is the temporary restoration of the body's delicate glucose control feedback loop without the need of powerful immunosuppressants.[11]

LIMITATIONS OF NANOPARTICLES

The science and knowledge that the scientific community has today about nanotechnology and its potential versatile applications are majorly based on the research work done in the laboratories.[60,61] Therefore, the scientific community has not yet understood completely how the human body would react to these NPs and nanosystems, which are acting as drug carriers. Hence, these research studies are being conducted to understand how matter behaves at the nanoscale level.[61] Factors and conditions governing the behavior of macrosystems do not really apply to the nanosystems. The major limitations and technological hurdles faced by nanotechnology and its applications in the field of drug delivery should be addressed.[60]

NPs have larger surface area when compared to their volume. Friction and clumping of the NPs into a larger structure is inevitable, which may affect their function as a drug delivery system. Due to their minute size, these drug carriers can be cleared away from the body by the body's excretory pathways. When these are not excreted, larger NPs can accumulate in vital organs, causing toxicity leading to organ failure. Recent study in mice revealed that tissue distribution of GNPs is size dependent, with the smallest NPs (15-50 nm)

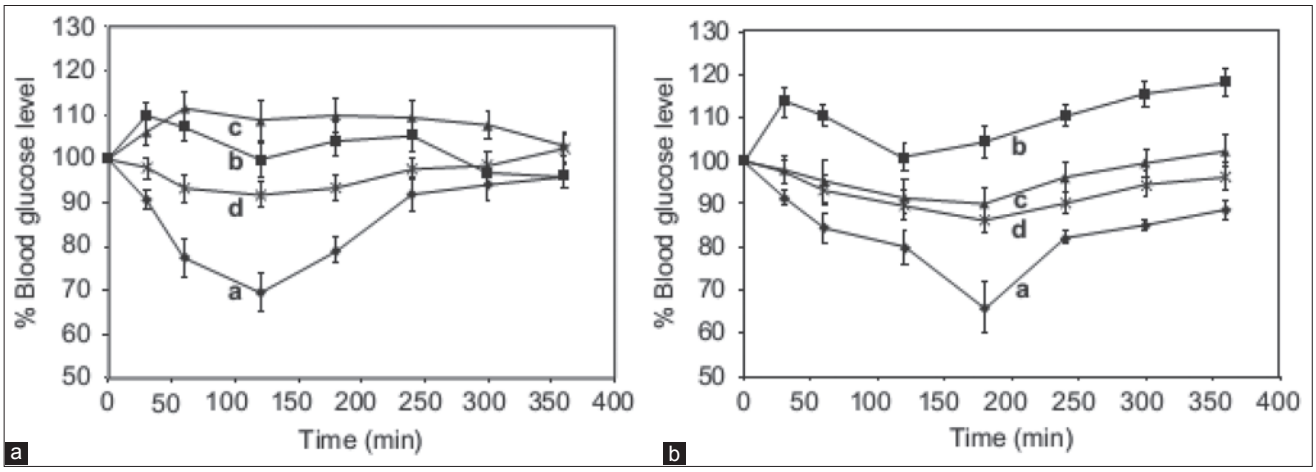


Figure 5: (a) Percentage reduction in blood glucose level after oral administration (dose 50 IU/kg, *n*=6). (b) Percentage reduction in blood glucose level after nasal administration (dose 10 IU/kg, *n*=6); a, insulin-loaded chitosan-reduced gold nanoparticles; b, blank chitosan-reduced nanoparticles; c, insulin solution; and d, insulin in chitosan solution. Source: From Ref.[59]

showing the most widespread organ distribution including blood, liver, lung, spleen, kidney, brain, heart, and stomach.[61]

Liposomes have certain drawbacks, such as being captured by the human body's defense system. The drug-loading capacity of liposomes is being tested by researchers and still remains inconclusive. All previous studies resulted in post treatment accumulation of the NPs in skin and eyes. GNPs tend to accumulate in bone joints and organs. Once the NPs are administered into the human body, they should be controlled by an external control, preventing them from causing adverse effects. These drug delivery technologies are in various stages of research and development. It is expected that these limitations can be overcome and the discoveries to come into practical use within the next 5 to 10 years.[23]

One mechanism of toxicity of NPs is likely to be induction of reactive oxygen species and the consequential oxidative stress in cells and organs. Testing for interaction of NPs with proteins and various cell types should be considered as part of the toxicological evaluation. Nanoparticle translocation and uptake by the body occurs after inhalation exposure (neuronal uptake, translocation across lung epithelium, and ingestion), oral exposure (ingestion), and dermal exposure depending on the characteristics of the nanoparticle under investigation. With the exception of airborne particles delivered to the lung, information on the biological fate of NPs including distribution, accumulation, metabolism, and organ specific toxicity is still minimal.[46]

CONCLUSION

The impact of nanotechnology on medicine is growing with each passing day. Although the science of nanomedicine is still in its infancy, it has major potential applications in treating diabetes. Oral insulin in particular could prove to be promising, especially since as a therapy it seems to have progressed with nanotechnology research, allowing for several types of encapsulations to bypass the gastric acidic environment. The medical applications for nanotechnology are enormous and could give medicine, including the treatment of diabetes, an entirely new outlook.

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