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REVIEW ARTICLE **OPEN ACCESS**

Nanoparticle based Drug Delivery System for Diabetes Mellitus: A Short Review

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ABSTRACT
Diabetes mellitus is one of the chronic metabolic disorder and is a major threat worldwide. At present, treatments of diabetes mellitus have brought complications to humans, therefore the prevention has been slow. It is fast growing global problem with physical, mental and economic consequences. In recent days, nanotechnology has emerged as one of the leading technology for the diagnosis, treatment and research of diabetes mellitus. Nanoparticles are produced on nanoscale level and are very safe to introduce into the patient body without using any syringes. It increases the efficiency of drug delivery to those areas where macromolecules are not so effective. The current review reflected the scope of nanotechnology in diabetes therapy through novel approaches for the delivery of insulin to specific transporter site. It holds therapeutic potential to make quality of life among diabetic patients.
Keynotes: Diabetes mellitus; Insulin; Nanotechnology; Drug delivery system; Hyperglycaemia

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INTRODUCTION

Diabetes is a chronic metabolic disorder which affects millions of people in India and worldwide[1],According to CDC (Centers for Disease Control and Prevention), there was almost triple rise of diabetic patients between 1920 and 2010. Diabetes mellitus is the 3rd leading cause of deaths worldwide [2].Stokes &Preston, estimated that 2.2 million deaths were caused by high blood glucose in 2012 and 1.5 million deaths were due to diabetes mellitus [3]. It is also estimated that the total number of diabetes would reach 578 million by 2040 and 700 million by 2045[4]. One person among five is diabetic patient in the age group of 65 in about 136 million people and one among the six live births i.e. about 20 million babies are affected by hyperglycaemia during pregnancy, Over 1.1 million children and adolescents that is below the age of 20 years have type 1 diabetes mellitus. One in the thirteen adults of age 20-79 years old has the problem of glucose intolerance[5]. There are so many people that live with undiagnosed diabetes. The survey report of Diabetic mellitus is represented in Figure 1.

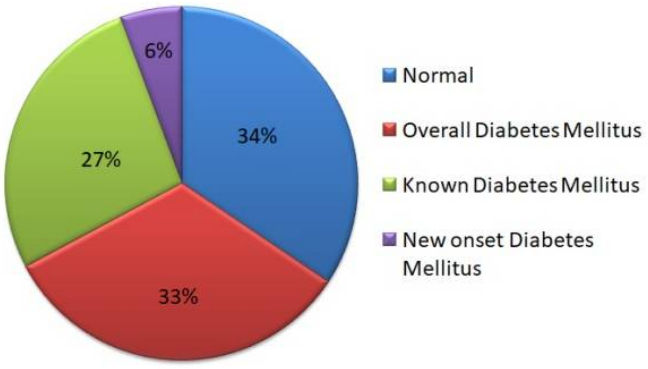

Fig.1. The survey analysis for onset of Diabetes mellitus.

Nanotechnology has aided the development of innovative glucose testing and insulin administration mechanisms in diabetes research, which has the potential to significantly improve the quality of life for diabetics. The application of nanotechnology to medicine also holds many possible advantages, such as access to small and clinically relevant areas of cells and analysis of small volumes of analytes. The current review looks at many elements of nanoparticles as well as recent advancements relating to diabetic control using nanotechnology.

Role of nanoparticles

There is use of insulin injections and oral insulin formulation for the treatment of diabetes but the main drawbacks are, multiple daily insulin injections cause local infection, hypertrophy, pain, dis-comfort and fat deposits at injection site [6]. In oral insulin, the drugs don't reach at desired site or in required amount [7]. In 1922, first results on oral insulin were obtained which was found unsuccessful [8-9] It has physiological barriers, so to overcome the barriers and to enhance patient ability to fight against diabetes, non-invasive and sustained release alternatives that increases the drug contact time with tissue and also increase its bioavailability has been proposed [10]. So we use of nanoparticles that increase the cellular absorption of drugs, increase the residence time and increase bioavailability, prolonged circulation time, increase mean residence time (MRT) and reduce the clearance [11]. Nanomedicines are used to increase absorption of drugs as the positively charged nanoparticles interact with mucus membrane which is negatively charged that limits their absorption [12]. Nowadays, nanoformulations have an established history to overcome the issue related to the conventional drug usage in diabetic patients [13]. Nanoformulations boost the drug solubility and it has many more advantages like reduced dosage, rapid onset of action, controlled drug release profile, approximately zero side effects, optimized drug delivery, half-life of drug extended, minimized patient variability, enhanced the bioavailability of drug and can resolve several drawbacks of anti-diabetic drug [14].

In oral medication, drug has to overcome or pass from four layers of stomach and gastric fluids, due to this complete amount of drug was not able to reach at a specific site leading poor absorption and low drug bioavailability [11]. Insulin has to be in its tertiary structure when loaded in nanoparticles can easily survive at the pH of stomach and passes all the barriers [15]. Some of the nanoparticles are having unique properties that enable them to be directly used in therapies. Magnetic nanoparticles induce heating of Microfold (M) cells without affecting any surrounding cells [16]. Some examples of nanoparticles like silver NPs and zinc oxide NPs show antimicrobial activity and they become alternatives to antibiotics [17].

NANOPARTICLES AS DRUG DELIVERY SYSTEM

Nanoparticles are small particles that range between 1 to 100 nanometers in size [18]. Nanoparticles and nanostructured materials are used in drug delivery system [19], gas sensing [20-21], chemical and biological sensing [22]. Nanoparticles are also used for loading of antidiabetic drugs and show best results to manage the blood sugar level [23]. Nanoparticles are classified into various categories which are now been generally used as a vehicle for targeted delivery of insulin [Figure 2].

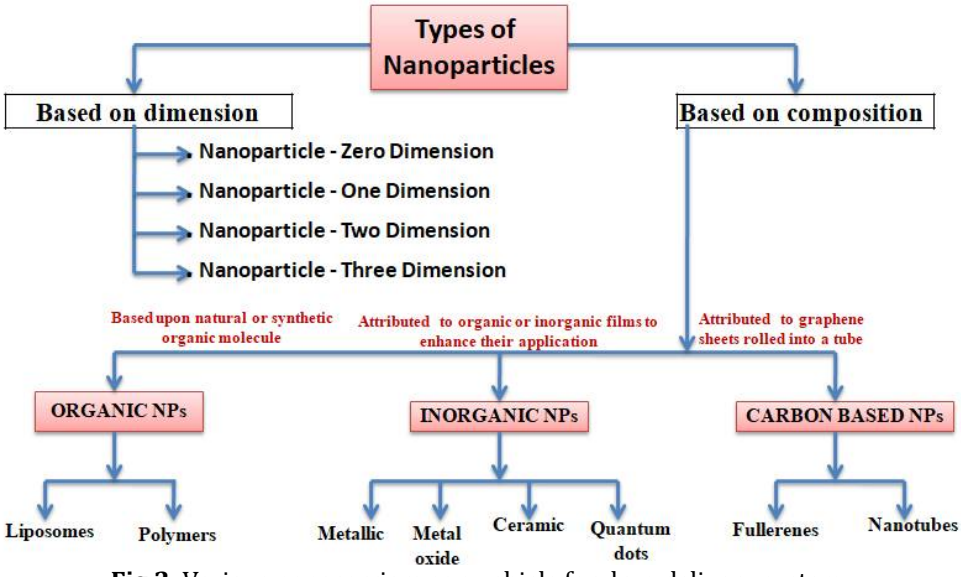

Fig.2. Various nanocarriers as a vehicle for drug delivery system.

CLASSIFICATION OF NANOPARTICLES

1. Lipid based nanoparticles - They are spherical in shape having diameter ranges between 10-1000 nm. They are biodegradable, biocompatible and have low toxicity. They possess a solid core and matrix. The solid core is made up of lipid and matrix has soluble lipophilic molecules. The external surface of core is stabilized by emulsifiers and surfactants [24]. They act as drug carrier and deliver the insulin to specific site [25]. Lipid based nano-delivery system are composed of lipid constituents which is biocompactible and biodegradable in nature. Lipid can enhance oral bioavailability of poor water soluble drugs. It is excellent drug delivery vehicle [26].
2. Polymers - They are organic based nanoparticles having diameter ranging from 10nm to 1000nm, spherical in shape or having capsule like structure. The nanospheres are matrix particles which are solid in nature and the nanocapsules are adsorbed at the outer boundary of surface [27]. They are pH sensitive. They show ideal properties like biocompatibility, biodegradability, non-toxic, mucoadhesive, permeation enhancing effect [28].
3. Metallic nanoparticles - Metal nanoparticles are the pure form of metal (Silver, Titanium, Zinc, Gold and Platinum) based nanoparticles [29]. The noble metal particles i.e. gold, silver, platinum are used as nanoparticles as they have photothermal and optical properties [30]. Gold nanoparticles are mainly used due to their low toxicity, easy to prepare and easily attach with biological molecules [31]. They appear very promising way for the treatment of type 2 diabetes mellitus. The formation of metallic nanoparticles by medicinal plants has obtained wide attention as it overcomes the disadvantage of using chemicals for the biosynthesis of metallic nanoparticles [32].
4. Metal oxide nanoparticles - They are formed from pure metallic precursors. They can adopt different type of structures [33]. Some examples of metal oxide nanoparticles are iron oxide, Cesium oxide, ZnO, MgO, AlO and many more. They have bactericidal properties, used in drug delivery, bioimaging, antimicrobial activities, biosensing and applications of electronics, optical and detection [34].
5. Ceramic nanoparticles - Ceramic nanoparticles are small and these are permeable in nature for example hydroxyapatite, zirconia etc. Ceramic nanoparticles help to improve physiochemical properties by reducing toxicity, increasing stability and easily incorporated [35].
6. Quantum Dots - It is also called graphene quantum dots (GQDs) as graphene is a promised material because of its excellent features. They show photoluminescence, biosensing, tissue engineering and many more other properties. [36-37] These nanoparticles have large band gaps and due to these beneficial shifts in their properties with band gaps tunings, they are considered as one of the important nanocarriers for drug to be delivered [38].
7. Fullerenes - It contains nanomaterials that are made up of globular hollow cage like allotropic form of carbon. Due to electrical conductivity, high strength, adaptability they generate commercial attentiveness and used to diagnose diabetes. C60 fullerenes is used with drug to treat diabetes [39].
8. Nanotubes - They are elongated, tubular structures having diameter 1-2 nm [40]. They resemble to graphite sheet rolling upon itself. It can be single, double or multi walled nanotubes. They are synthesized via chemical vapour deposition technique [41].

MECHANISTIC APPROACH OF NANOPARTICLES

Insulin is very important molecule that helps to regulate the intracellular transport of glucose into the tissues like skeletal muscles, liver tissues and adipose tissues that utilize glucose. Insulin binded nanoparticles bind to specific membrane bound insulin receptor i.e Receptor tyrosine kinase (consisting of two extracellular alpha and two transmembrane beta subunits linked together by disulfide bonds) present on the target cell which results in activation of metabolic process in that cell and that cell utilize glucose by gluconeogenesis, lipolysis and take up by skeletal muscles [42]. This nanoparticle based insulin transport provide ideal target for drug delivery to increase uptake of drug at specific site. When insulin binded nanoparticle attach to membrane receptor, endocytosis occur and the drug enter the cell. There is dissolution of surface of nanoparticle and release the drug inside the cell and perform the metabolic activity [43-44] The mechanistic action of nanoparticle transport facilitated using ligand binding to transporter region has been explained through Figure 3.

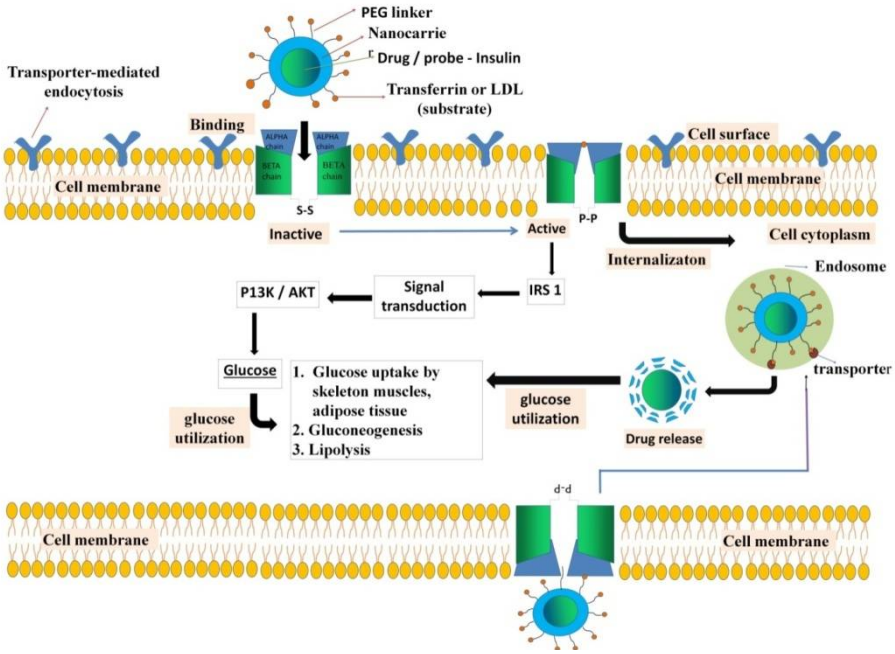

Fig. 3. Nano-based drug delivery systems used as vehicles to enhance active signal transduction for therapeutic effect for Diabetes mellitus treatment.

CONCLUSIONS

Diabetes is a metabolic disorder and it affects so many people worldwide mainly, the people aged between 40 and70. There are three types of diabetes, out of which type 2 diabetes mellitus is the most common. About 95% people are affected with type 2 diabetes mellitus. Increased thirst, frequently urination, hunger, weight loss, fatigue are the common symptoms. To treat diabetes, injections of insulin are subcutaneously given to the patients. Due to uneasiness, suffering with pain and risk of getting local infection, we use non- invasive administration route of drugs i.e. insulin or sugar lowering drugs are used with nanoparticles. Nanoparticles based drugs are used because these drugs reached at specific site, the dose used would be less, there is no need to cross barrier. Insulin enters the target cell which result in activation of metabolic activities in the cell that help to lower the level of glucose and attain normal level. Even material from natural sources is employed as nanocarriers. More and more excellent oral nanodrug delivery will be employed to treat diabetes and other diseases. Insulin uptake in gastrointestinal tract, different targeting ligands are searched and studied for better future.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS CDC: Centers for Disease Control and Prevention; MRT: Mean residence time; GQDs: Graphene quantum dots.

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