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## Review

# Nanotechnology based approaches for anti-diabetic drugs delivery



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## ABSTRACT

Nanotechnology science has been diverged its application in several fields with the advantages to operate with nanometric range of objects. Emerging field of nanotechnology has been also being approached and applied in medical biology for improved efficacy and safety. Increased success in therapeutic field has focused several approaches in the treatment of the common metabolic disorder, diabetes. The development of nanocarriers for improved delivery of different oral hypoglycemic agents compared to conventional therapies includes nanoparticles (NPs), liposomes, dendrimer, niosomes and micelles, which produces great control over the increased blood glucose level and thus becoming an eye catching and most promising technology now-a-days. Besides, embellishment of nanocarriers with several ligands makes it more targeted delivery with the protection of entrapped hypoglycaemic agents against degradation, thereby optimizing prolonged blood glucose lowering effect. Thus, nanocarriers of hypoglycemic agents provide the aim towards improved diabetes management with minimized risk of acute and chronic complications. In this review, we provide an overview on distinctive features of each nano-based drug delivery system for diabetic treatment and current NPs applications in diabetes management.

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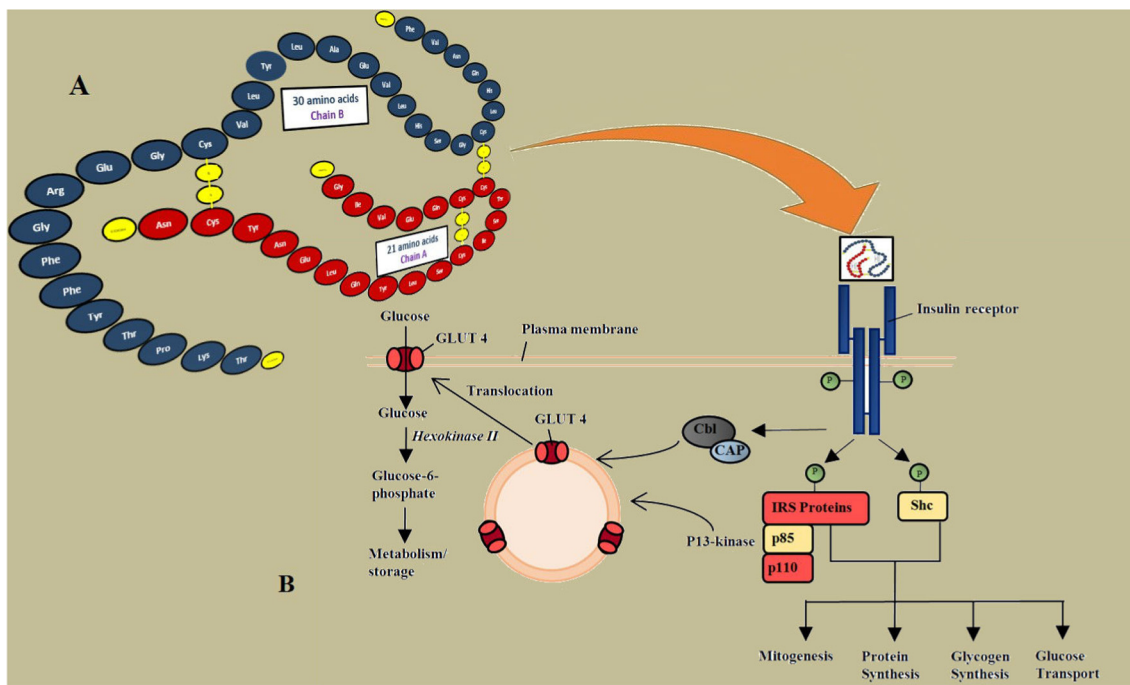
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## 1. Introduction

Diabetes mellitus (DM) is a chronic lifelong metabolic disorder that alters the life of billions of people throughout the world [1,2]. It can be classified into two major forms, namely Type 1 DM (T1DM) and Type 2 DM (T2DM) [1,3–6]. In DM, constant hyperglycemia may result in chronic micro- and macrovascular effects such as nephropathy, retinopathy, neuropathy, stroke and cardiovascular disease [1,3,5,7,8]. The number of diabetic patients are increasing tremendously worldwide, where a recent report has indicated the increase of 422 million patients in 2014 from 171 million in 2000, showing the sharp increase in the sufferers [9]. Adaptation of sedentary lifestyle and increasing in demographics with the age of >65 years suggesting this increased incidences of diabetes may be doubled, approximately 366 million in 2030 [10,11]. Therefore, management is needed to control diabetes conditions and consequence complications. Monitoring programmes make people aware for effective management diabetic through adaptation of proper low carbohydrate diet, regular physical exercise, and adherence to medication therapy, if needed [1,8,12–14]. The conventional medications used now-a-days to control hyperglycemic condition in DM are oral hypoglycemic agents (OHA) and parenteral preparations of

insulin and glucagon-like Peptide-1 (GLP-1) receptor agonists [1,8,12,15–17].

Insulin, is a polypeptide hormone consists of 51 amino acids in two chains (A chain, 21 amino acids; B chain, 30 amino acid), joined together by two disulfide bonds (–S–S–) (Fig. 1A), that helps in regulating the uptake and storage of glucose in the liver and muscles [6,18]. It is produced by  $\beta$ -cells of pancreas and released via exocytosis process into the blood stream to help in utilization of peripheral glucose for generation of energy [6,18]. The coordinated responses which stimulate glucose oxidation and inhibit gluconeogenesis simultaneously led to the hypoglycaemic action of insulin. The plasma glucose concentration decrease when insulin directs the glucose transporters (GLUT 4) into the cell membranes and increases glucose transport into target cells (Fig. 1B) [10,19]. The aim of insulin therapy is to provide insulin replacement as close as possible in all patients. However, insulin resistance sometimes may happen during insulin therapy for the management of diabetic conditions [20,18]. Therefore, nanosize particles have comes out as for a more convenient, safe and non-invasive route for insulin delivery in order to overcome such limitations in diabetes management [2].



**Fig. 1 – A. Chemical structure of insulin consists of A chain (20 amino acids) and B chain (31 amino acids) are linked together by two disulfide linkages; B. Mechanism of action of insulin-activation through phosphatidylinositol-3'-kinase pathway, stimulation of translocation of glucose transporter (GLUT 4) on the cell surface.**

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