

## NANOPARTICLES USED FOR THE TREATMENT OF DIABETES

SURBHI SRIDHAR<sup>1\*</sup>, AJEET PAL SINGH<sup>2</sup>, AMAR PAL SINGH<sup>2</sup>

<sup>1</sup>Department of Pharmaceutics, St. Soldier Institute of Pharmacy, Lidhran Campus, Behind NIT (R. E. C.), Jalandhar-Amritsar by pass, NH-1, Jalandhar-144011, Punjab, India. <sup>2</sup>Department of Pharmacology, St. Soldier Institute of Pharmacy, Lidhran Campus, Behind NIT (R. E. C.), Jalandhar-Amritsar by pass, NH-1, Jalandhar-144011, Punjab, India

\*Corresponding author: Surbhi Sridhar; \*Email: [surbhisridhar02@gmail.com](mailto:surbhisridhar02@gmail.com)

Received: 05 Oct 2025, Revised and Accepted: 25 Nov 2025

### ABSTRACT

The worldwide health crisis caused by diabetes mellitus calls for novel therapeutic solutions because traditional treatments have shown their limitations. The review conducts an in-depth evaluation of nanoparticle-based technologies within diabetes care. For this, their functions in drug transport optimization and enhanced substance distribution, along with prolonged blood sugar stabilization capabilities, are examined and investigated. Different types of nanoparticle platforms, which include polymeric, lipid-based, inorganic, and natural nanoparticles, have shown excellent achievements in both preclinical research and clinical practice by delivering targeted drugs while minimizing adverse effects alongside glucose-triggered insulin release. The review explains how smart insulin delivery methods, along with anti-inflammatory care and personalized nanomedicine solutions, have progressed; however, it details the barriers that exist for biocompatibility and regulatory requirements and large-scale production. Laboratory research shows that nanotechnology has great potential for diabetes treatment through independent glucose control systems and simplified drug delivery processes, leading to better healthcare results. Nanoparticles offer promise to achieve disease modification rather than symptom management, even though their production requires solutions, and their long-term effects need further investigation. Nanomedical research should concentrate on maximizing smart nanoparticulate development while creating scalable manufacturing processes and developing patient-customized therapy models to establish nanomaterials fully in diabetes treatment practice.

**Keywords:** Nanoparticles, Diabetes mellitus, Insulin delivery, Glucose-responsive nanomedicine, Polymeric nanoparticles, Lipid-based carriers, Targeted drug delivery, Smart insulin, Preclinical studies, Clinical applications

© 2026 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>) DOI: <https://dx.doi.org/10.22159/ijcpr.2026v18i1.7075> Journal homepage: <https://innovareacademics.in/journals/index.php/ijcpr>

### INTRODUCTION

Diabetes mellitus exists as a long-lasting metabolic condition that causes elevated blood sugar because patients demonstrate reduced insulin secretion and/or insulin resistance in their bodies. The uncontrolled condition progresses into multiple severe health complications that affect cardiovascular health and kidneys, nerves and eyesight [1]. The increasing number of diabetes cases around the world requires better treatment approaches which focus on improved drug administration methods alongside diminished adverse effects. Researchers have developed nanoparticle-based therapeutic methods that provide engineered glucose control abilities. The capabilities also strengthen drug durability and controlled drug delivery without the problems of traditional treatment options [2].

#### Background of diabetes mellitus

Diabetes exists as a worldwide health problem that affects millions of individuals globally. The prevalence of adult diabetes cases keeps increasing rapidly in current times, and doctors predict similar or higher numbers will persist during the coming decades. Experts link this rising trend to multiple causes, which include inactive behaviours and unhealthy food choices and weight-related problems and family history of disease [3]. Most people suffer from type 2 diabetes, but the rarer form of type 1 diabetes necessitates patients to depend on insulin therapy for their entire lives. Healthcare systems allocate large financial resources each year to treat and manage diabetes since there is an immediate necessity for better solutions that operate both effectively and with reduced costs [4]. Recent treatment developments for diabetes have not resolved the many persistent difficulties that therapy faces. The pharmaceutical agent's metformin and SGLT-2 inhibitors show reduced availability in the body while also causing adverse effects on digestion. Type 1 diabetes patients depend on daily insulin injections, but their effectiveness requires close medical supervision because mismanagement may cause dangerous hypoglycemic events [5]. Recent drug delivery systems cannot replicate insulin release patterns like the human body

does, which affects poor blood sugar management. The present challenges identify why new solutions need to be developed to achieve better therapeutic results [6, 7].

#### Role of nanotechnology in medicine

Modern medicine has experienced a revolution through nanotechnology, which allows customised medication delivery and good control over drug release durations while increasing therapeutic outcomes. The drug delivery system known as nanoparticles exists between 1 and 100 nanometers in dimension and functions by protecting drugs and proteins along with genetic material while enhancing their ability to move throughout the body properly [8]. Research specialists have investigated polymeric lipid-based and inorganic nanoparticles for diabetes treatment applications because of their adjustable characteristics and exclusive properties. Nanocarriers possess the ability to react to biological triggers which including glucose levels, to deliver smart insulin therapy that functions like human insulin production [9, 10].

Nanoparticles surpass traditional drugs by providing multiple medical benefits, which include reduced medication schedules and lessened adverse effects and more stable pharmaceutical substances. Nanoparticles containing oral insulin operate successfully through the digestive system, thus improving both drug absorption and bioavailability. The insulin release function of glucose-sensitive nanoparticles enables precise drug delivery to lower the chances of insulin-related low blood sugar events. Nanotechnology provides the capability for delivering multiple treatment medications at once to treat diabetes, along with its associated complications. There is strong promise that nanomedicine will establish itself as a leading technology for treating diabetes [11].

#### Literature selection criteria

##### Search strategy

A systematic search strategy involving various high-impact databases was put into practice to perform a complete, unbiased

review of existing literature. Four primary databases used for this review were PubMed, together with both Scopus and Web of Science and ScienceDirect because they cover the Biomedical and Nanotechnology fields extensively. Google Scholar helped locate other types of grey literature, which included preprint articles, conference proceedings. Journals that conducted peer reviews formed the basis of the search to guarantee both academic strength and reliability [12].

The selected keywords specifically targeted every possible research related to diabetes treatment using nanoparticles. The research strategy combined both Medical Subject Headings (Mesh) terminology with free-text keywords, which consisted of "nanoparticles," "nanomedicine," "diabetes treatment," "insulin delivery," "glucose-responsive nanoparticles," and "polymeric nanocarriers." Boolean operators (AND, OR) operate sequentially in the search to optimise the accuracy ratio between inclusive results and specific criteria. The PubMed database utilised the search string ("nanoparticles" OR "nanocarriers") AND ("diabetes" OR "hyperglycemia") AND ("drug delivery" OR "insulin therapy"). The inquiry produced numerous articles that researchers evaluated for suitability.

A selection process streamlining approach based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was employed. After importing the search results to reference management software (EndNote or Zotero), duplicate materials were removed from the system. The screening process was conducted in two stages, starting with title and abstract evaluation, followed by complete document assessment [13].

### Inclusion and exclusion criteria

The selection criteria established requirements for studies that investigated nanoparticle applications in diabetes medical treatments specifically. The research evaluated only original studies that conducted experiments *in vitro* or *in vivo* or performed clinical trials while using empirical evidence to establish their findings. This review omitted review articles and non-English publications except for cases in which they supplied essential background information. The research evaluation excluded investigations that produced nanoparticles yet lacked proof of their therapeutic utility in diabetic treatment [14].

The researchers applied a strict period from 2015 to 2025 because nanotechnology has developed quickly throughout this recent era. Essential research from earlier than 2015 received consideration when it introduced baseline concepts such as the initial glucose-sensitive insulin delivery methods [15]. The study only included English-language articles as a language restriction measure to prevent translation mistakes. Scientific validity was the basis for excluding studies which either omitted proper control groups or presented insufficient methodological detail.

Study authors applied additional refinement to their inclusion and exclusion standards according to research design and outcome measures. *In vitro* studies included in the review would incorporate nanoparticle-drug interaction mechanism understanding as their main criterion, while *in vivo* studies needed to show therapeutic effects within diabetic animal models. Clinical trials received priority status when they presented information about human participant safety as well as pharmacokinetics and glycemic control [16]. The following table presents the exact evaluation standards:

**Table 1: Inclusion and exclusion criteria**

Category	Inclusion criteria	Exclusion criteria
Study type	Original research ( <i>in vitro</i> , <i>in vivo</i> , clinical trials), peer-reviewed articles	Reviews, editorials, non-research articles
Time frame	2015–2025 (except for landmark studies)	Studies published before 2015 without novel contributions
Language	English	Non-English publications without official translations
Relevance	Direct focus on nanoparticles for diabetes treatment	Nanoparticles unrelated to diabetes or drug delivery
Methodology	Clear experimental design, appropriate controls, and statistical analysis	Poorly described methods, lack of controls

The stringent selection procedure validated that the reviewed literature consisted of premium-quality research, leading to an organized examination of nanoparticles serving diabetes treatment purposes [17].

### Literature review

#### Types of nanoparticles used in diabetes treatment

The research conducted by Javed *et al.* (2021) outlined the delivery of drugs through polymeric nanoparticles stands out as a top therapeutic platform for diabetes treatment, thanks to their good biodegradability, together with their biocompatible nature, alongside their ability to manage drug release profiles. The FDA-approved polymers PLGA and chitosan create nanoparticles which function to protect the therapy drugs insulin and oral hypoglycemics by defending them against degradation within the harsh stomach conditions. Drug delivery nanoparticles become more effective by integrating targeting ligands such as lectins or transferrin, since these ligands direct the nanoparticles toward specific absorption sites or pancreatic  $\beta$ -cells [18]. The gradual breakdown characteristics of these polymers create specific drug delivery control mechanisms which preserve therapeutic drug amounts throughout periods and reduce the necessary dosing schedules. Modern research indicates that polymeric nanoparticles demonstrate oral delivery capabilities which result in insulin bioavailability levels almost reaching 15-20%, marking significant progress since traditional oral delivery methods [19].

Furthermore, Wang *et al.* (2022) outlined that the diabetes therapy benefits from lipid-based nanoparticle systems such as liposomes and solid lipid nanoparticles (SLNS) because they exhibit both excellent biocompatibility and dual hydrophobic and hydrophilic therapeutic agent encapsulation capabilities. The oral, pulmonary, and

transdermal drug routes employ liposomes as a delivery system because they consist of bilayer vesicles made from natural or synthetic phospholipids [20]. Enhanced stability aspects from solid lipid nanoparticles supported by surfactants surrounding solid lipid cores have demonstrated effective improvements for the oral bioavailability of poorly soluble drugs, metformin and glibenclamide. Because of their lipidic composition, these carriers demonstrate natural membrane fusion properties, which lead to enhanced cell entry and delivery within cells [21]. Drugs presented with bile salts and permeation enhancers show recent progress in intestinal absorption that leads to substantial drug bioavailability improvement, totalling a 10-fold boost compared to typical dosage forms [22, 23].

On the other hand, Ponnanikamideen *et al.* (2019) argued that diabetes treatment utilizes three types of inorganic nanoparticles, which include gold nanoparticles alongside silver nanoparticles and mesoporous silica nanoparticles, because of their unique characteristics. Engineers designed gold nanomaterials for insulin delivery based on the functional integration of glucose oxidase and insulin molecules over their surfaces, which triggers insulin release under hyperglycemia conditions. The pore structures of mesoporous silica nanoparticles provide excellent drug storage capabilities and fine-grained control for drug delivery because they possess organized structures together with vast surface areas. The diagnostic features built into these inorganic carriers allow them to support combined treatment and diagnostic functions known as the agnostic. The study of surface modification technologies emerged to increase the compatibility and ease of breakdown of these materials because researchers expressed worries about their accumulation within body organs. Scientific studies demonstrate that controlling nanoparticle size together with shape characteristics and surface modifications enables substantial improvement of safety standards without compromising therapeutic strength [24].

The authors Rabiee *et al.* (2022) said that the emerging field of diabetes nanomedicine focuses primarily on natural nanoparticle technology that includes exosomes alongside plant-derived extracellular vesicles. Exosomes function as naturally secreted nanoscale vesicles from cells because they display native targeting functions alongside minimal immunological responses that qualify them for drug delivery purposes. Researchers have shown tissue-homing properties of these biological nanoparticles in their preclinical research after loading them with insulin and GLP-1 analogues or nucleic acids as therapeutic agents [25]. The drug delivery capacity of plant-derived nanoparticles produced from edible plants such as grapes and ginger demonstrates antidiabetic properties by letting them serve as active antioxidants and anti-inflammatory agents simultaneously. The natural nature of these nanoparticles helps lessen toxicity risks; yet, more work needs to be done regarding large-scale production and quality consistency for regulatory approval. Modern advancements in isolation methods and loading procedure optimization enhance the drug cargo capacity, together with stability of natural nanocarriers, thus making them near clinical readiness.

### Mechanisms of action

The nanoparticle-based delivery approach for insulin therapy uses complex processes to provide solutions for current insulin treatment difficulties. The delivery system shields insulin from gastrointestinal enzymes until it reaches the intestinal epithelial membranes, where it moves through transcellular or paracellular trafficking paths. Modern formulations of oral insulin contain mucoadhesive polymers, which extend drug stay time in critical absorption areas, and permeation enhancers, which briefly damage tight junctions to boost drug absorption. Engineers design these nanoparticles to react through the detection of biological pH and enzymatic activities for gradual drug delivery, which follows natural insulin secretion patterns. The insulin delivery method through intranasal administration provides better physiological glucose control, together with a lower risk of unwanted hypoglycemic episodes than standard subcutaneous insulin injections. The recent advancement of oral insulin nanoparticles has achieved pharmacological availability greater than 20% in animal tests, leading to clinical trial evaluations of these formulations [26].

In a similar manner, research has shown that the development of glucose-responsive nanoparticle systems provides essential progress for establishing automated insulin delivery systems which do not require external monitoring. The smart systems function by utilizing one of three core methods, which include glucose oxidase-based systems generating acidic substances which activate pH-sensitive release, along with phenylboronic acid-containing polymers that alter their structure when they bind to glucose or competitive displacement mechanisms that enable insulin to bind to glucose [27]. The highest-performing glucose-responsive systems demonstrate physiological response times through mechanisms that verify changes in glucose concentration at speeds as quick as 20-30 min in preclinical models. Modern research aims at enhancing system response sensitivity and achieving stable responses that last week's inside the body, and maintaining reversibility. The therapeutic options show significant potential to assist with type 1 diabetes care by potentially doing away with regular glucose measurements and insulin delivery [28].

Anti-inflammatory properties observed in specific nanoparticle formulations provide significant benefits to diabetes pathophysiology because they address inflammatory processes that promote insulin resistance, together with  $\beta$ -cell dysfunction in patients with type 2 diabetes. Anti-inflammatory agents, including curcumin and resveratrol, together with cytokine inhibitors, are delivered through various nanoparticle structures directly to affected tissues while preventing their systemic spread [29, 30]. Nanoparticles demonstrate native anti-inflammatory properties which become activated by their building materials and surface structure while not requiring any drug contents. The delivery systems offer targeted inhibition of diabetes-related pathways, such as NF- $\kappa$ B signaling, by avoiding essential immune responses. Modern research shows therapeutic nanoparticles help patients achieve better glucose management and demonstrate the ability to

stop or reverse neuropathy and nephropathy symptoms in animals during recent trials [31].

Antioxidant nanoparticles prevent oxidative stress, which functions as both a cause and a developmental factor for diabetes. Modern nanotechnology creates nanoparticles which either include traditional antioxidant agents, such as  $\alpha$ -lipoic acid, or utilise new nanomaterial antioxidants like cerium oxide nanoparticles, which replicate endogenous antioxidants [32]. The use of nanoparticles as antioxidants presents various benefits versus ordinary antioxidants, which include defense against degradation, together with site-specific delivery capabilities as well as extended release duration. Some antioxidant formulations operate according to oxidative stress levels to activate their activity depending on reactive oxygen species concentrations in the environment. The targeted method enables the effective destruction of oxidants that cause damage but prevents unwanted disruption to essential cellular signaling mechanisms [34].

### Applications in different diabetes types

Nanoparticle-based therapies for type 1 diabetes concentrate on two major aspects, which include enhanced insulin replacement methods together with management of the autoimmune components of the disease. Preclinical studies indicate that insulin-loaded nanoparticles show equal blood glucose management to subcutaneous delivery without requiring invasive needle injections because of their effective design. Sophisticated absorption-enhancing strategies that employ either mucus-penetrating designs provide additional functionality [34]. The development of immunomodulatory nanoparticles focuses on blocking the autoimmune attack against pancreatic  $\beta$ -cells. The formulations include antigens and immune-modulating drugs which support  $\beta$ -cell tolerance to immune acceptance while preserving typical immune operation [35]. The combination therapy delivering insulin and immunomodulators holds specific promise for keeping remaining  $\beta$ -cell functions intact in patients who have just received their diagnosis [36]. The latest discoveries in medicine have demonstrated glucose-responsive immunomodulatory nanoparticles which activate or deactivate their functions through monitoring blood glucose amounts for combined autoimmune management and metabolic control in one product.

The applications of nanoparticles in type 2 diabetes treatment involve more diverse therapeutic strategies, which align with the multiple factors affecting the disease pathophysiology. The delivery of oral hypoglycemic drugs gets improved through metformin and sulfonylureas, and thiazolidinediones nanoparticle formulations, which increase their bioavailability while decreasing their side effects. Researchers have developed nanoparticles which attack multiple diabetic pathways simultaneously through the merger of insulin sensitizers together with GLP-1 receptor agonists and other pathways. Scientific research explores liver-targeted nanoparticles which supply drugs to hepatocytes as a method to control glucose production, together with lipid metabolism regulation [37-38]. The field has introduced research about nanoparticles aimed at the intestine, which modify microorganism activity together with incretin mimetic medications directed toward intestinal L-cells while leveraging the pancreatic-enteric connection. Multifunctional nanoparticles stand out as the most promising innovation because they manage blood glucose levels and defend against diabetic complications by carrying dual antidiabetic drugs and nephroprotective agents for diabetic kidney disease therapy.

### Challenges and limitations

The implementation of diabetes treatments based on nanoparticles faces substantial hurdles before becoming clinically available. The safety issues pose the greatest challenge, especially since they focus on nanoparticle side effects that appear after patients receive continuous treatment. A majority of investigative materials qualify as biocompatible, but researchers continue to analyse potential build-up in the liver and spleen organs and recurrent injection-induced inflammatory reactions [39]. Scientific researchers need to study nanoparticle materials to determine how these components and their decay products break down and affect the body, especially for synthetic polymers and inorganic substances. Immunological

aspects must be understood well for diabetic patients because their condition changes immune responses and affects how the body removes foreign substances. Recent medical research focuses on expanding toxicology evaluation through assessments of long-lasting exposure scenarios, together with the effects of successive generations and diabetic condition interactions. A major obstacle to clinical translation exists due to production difficulties and scalability issues. The production methods for many nanoparticle formulations become complicated when developers must integrate numerous manufacturing stages that prevent successful mass production and consistent batch outcomes. Nanoscale pharmaceutical systems make the quality control process challenging since performance depends heavily on size-related and surface charge effects, together with drug loading requirements. A thorough evaluation needs to address stability problems, such as drug release before and during storage, for every formulation. Complex nanoparticle development presents both affordability challenges as well as financial barriers that limit their implementation in low-income communities showing rapid diabetes growth [40]. The developing nature of nanomedicine product regulatory pathways creates uncertainties that present barriers to their development process. The existing regulatory frameworks intended for other purposes than nanoparticle therapies create approval uncertainties due to their inadequate design for these substances. The development of nanomedicine faces three main regulatory questions about safe product development characteristics, alongside adequate proof of effectiveness and robust quality standards. The behavioral patterns of nanoparticles within biological systems, together with their numerous possible interactions with living organisms, make it difficult to conduct traditional pharmacokinetic and pharmacodynamic evaluations. The worldwide development of nanomedicine product guidelines requires the need for careful evaluation from regulatory agencies, but takes an extensive amount of time. Despite the good preclinical data, nanoparticle treatments face delays in clinical translation since regulatory ambiguity causes potential investors to hold back their support. The below mentioned diagram represents the process of using nanoparticles for diabetes diagnosis [41].

One must pay attention to how diabetes itself alters nanoparticle performance because it represents a biological challenge affecting products in diabetic conditions. Physiological changes caused by diabetes affect the behavior of nanoparticles because they alter gastrointestinal motility and impact vascular permeability and modify immune system responses when compared to standard healthy animal preclinical research. The therapeutic response to nanoparticle therapy should involve personalized strategies because each individual possesses distinct variations in gut microbiota composition and metabolic status, and complication status [42]. Development of reliable biomarkers must occur to predict how individuals will respond to nanoparticle treatments because this will lead to optimized treatment results. A systematic evaluation must occur to determine the safe application of nanoparticle therapies with conventional diabetes drugs and medication for complications.

The current field needs to solve multiple practical issues as they relate to how patients accept treatment methods and how these methods can be effectively implemented in everyday healthcare

settings. Patients alongside healthcare providers express hesitance toward using novel nanoparticle-based therapies mainly because of their unfamiliar nature. The public needs to become aware of nanomedicine safety alongside its advantages, while developers must create easy-to-use delivery methods suitable for self-administration during necessary times. Cost-effectiveness analyses will play a critical role in displaying the valuable proposition behind therapies which normally cost more than standard treatment modalities. The inclusion of nanoparticle-based therapies into current diabetes care protocols demands meticulous preparation and possibly needs additional monitoring systems [43].

Active research and development of nanoparticle-based diabetes therapies persist since their potential therapeutic benefits remain compelling factors. Enhanced technological developments are helping to reduce current barriers that stand in the way of achieving top performance for nanomedicine in diabetes therapies. Progress in diabetes nanoparticle therapy will continue in the following years by tackling safety issues and enhancing production methods and regulatory requirements for diabetic patient solutions. The solution of existing challenges will enable nanoparticle-based therapies to revolutionise diabetes management by providing more efficient and custom-made treatment solutions for better systemic control and lifestyle quality of patients who have diabetes [44, 45].

## RESULTS AND DISCUSSION

### Efficacy of nanoparticles in preclinical studies

Studies on nanoparticles in diabetic patients have shown outstanding potential for treating diabetes because multiple formulations outperform traditional therapy approaches. Laboratory tests show that insulin-containing polymeric nanoparticles delivered orally can maintain stable blood sugar for 24 continuous hours while lowering blood glucose effectively without hypoglycemic side effects. Research demonstrates that nanoparticles made from lipids improve GLP-1 analogue delivery so they stay in the bloodstream longer, thus triggering enhanced insulin response and  $\beta$ -cell protection in diabetic rodent subjects. Experimental tests involving cultured cells demonstrate that nanoparticles which respond to glucose reveal quick insulin release in high-glucose solutions but maintain stability under regular conditions [46].

The preclinical sector uses gold nanoparticles together with silica-based systems because these inorganic nanoparticles show distinct advantages in research. A single dose of insulin-releasing gold nanoparticles containing glucose oxidase released insulin to high-glucose conditions after thirty minutes, exactly like human insulin signaling does. Laboratory tests revealed that oral antidiabetic drugs contained within mesoporous silica nanoparticles absorbed into the intestine at heightened levels of 3-5 times superior to existing pharmaceutical forms. Dose-dependent toxicity in liver and kidney tissues has been observed during inorganic nanoparticle testing, although researchers need to optimize their dosage levels better (Debele and Park, 2022).

The table below summarizes key findings from recent preclinical studies:

**Table 2: Summary of preclinical studies on nanoparticles for diabetes treatment**

Nanoparticle type	Model system	Key findings
PLGA-Insulin NPs	Type 1 diabetic rats	18-24h glycemic control after a single oral dose
GLP-1 liposomes	db/db mice	Improved $\beta$ -cell function, reduced HbA1c by 2.1%
Glucose-responsive AuNPs	<i>In vitro</i> glucose challenge	Insulin release within 30 min of hyperglycemia
Metformin-Silica NPs	Caco-2 cell monolayer	5 $\times$ increased permeability vs. free metformin

### Clinical trials and human applications

The shift from laboratory research success into medical practice delivery has shown both positive and negative results. Multiple phase I/II clinical trials investigated oral insulin nanoparticles and produced statistically meaningful evidence that type 1 diabetes

participants showed decreased night-time blood glucose levels using ORMD-0801. The exenatide nanoparticles in this study released the drug for continuous 7 days, which decreased injection requirements while preserving blood sugar management. The absorption rates differ between patients because of their distinct gastrointestinal physiological characteristics in various trials focusing on oral insulin

nanoparticles. Trials that have been completed demonstrate most nanoparticle formulations deliver good safety outcomes since their adverse effects remain consistent with standard treatment side effects. The success rates differ between platforms although glucose-responsive systems performed best in a certain trial where this innovation reached 75% target glycemic control level with a smart insulin patch. Patient feedback demonstrates better quality of life because people experience fewer doses and no more injection discomfort and concerns about needles. Phase III trials currently test large-scale production processes and long-term safety.

#### Comparative analysis with conventional therapies

Disease management through nanoparticle-based therapeutic approaches provides better results than traditional diabetes treatment methods. The specific drug delivery systems enhance medication concentration within targeted treatment areas and minimise contact with systemic components, thus reducing

undesirable side effects from hypoglycemia and gastrointestinal issues [47]. Controlled release formulations extend the duration of therapeutic drug levels, so patients need to take their medication less frequently and can use weekly instead of daily dosing as their method. The drug delivery system using nanoparticles shows potential for reversing insulin resistance, combined with preserving  $\beta$ -cell mass, which is not easily achieved through currently available medications.

Nanoparticle therapies encounter different obstacles which constrain their universal acceptance. The creation of nanoparticle formulations is at least five times more expensive than traditional preparations, making them both hard to afford and challenging to cover through insurance. A few nanoparticle formulations need specific storage conditions, which makes distribution and patient use processes more complex. A direct comparison between nanoparticle drugs and conventional medications appears in this table.

**Table 3: Nanoparticle vs. conventional diabetes therapies**

Parameter	Nanoparticle therapies	Conventional therapies
Dosing frequency	Weekly/Monthly	Daily/Multiple daily
Side effect profile	Generally reduced	More frequent
Production cost	5-10 $\times$ higher	Lower
Stability	Often requires special handling	Generally stable
Therapeutic effects	Potential disease modification	Primarily symptomatic relief

#### Future perspectives

Smart insulin delivery nanoparticles of the following generation strive to achieve self-operating glucose control, while multiple development groups create systems that monitor blood glucose and execute real-time insulin delivery autonomously. The "artificial pancreas" nanoparticles represent a potential breakthrough for type 1 diabetes management since they can remove the current requirement for continuous glucose monitoring and manual insulin control. The initial animal-based testing indicated that beta-cell performance levels can be achieved within 15 min response times using these prototypes. The development of personalized nanomedicine represents an effective solution for dealing with differences between patients in therapeutic reactions. Researchers continue to develop biomarker profiling and nanoparticle improvement approaches for personalized medicine solutions based on individual biological characteristics and medical conditions. Theragnostic systems based on single nanoparticles allow for continuous treatment monitoring and automatic adjustment through the combination of diagnosis and therapeutic functions. These treatment methods show special advantages in the management of patients who have brittle diabetes or complications from their condition.

#### CONCLUSION

The extensive review showcases the radical potential of nanoparticle-based treatments for diabetic medical care. Studies both before clinical trials and within clinical settings show that nanoparticle-based approaches lead to enhanced bioavailability and targeted delivery methods and fewer side effects as well and possibly disease-altering outcomes. The pathophysiology of diabetes receives targeted treatment through different nanoparticle platforms that include polymers, lipids, inorganic and natural materials. Researchers focus on designing glucose-responsive systems which provide great potential for autonomous insulin delivery through closed-loop technology.

These technologies possess significant clinical potential by transitioning diabetes care from symptom treatment to disease transformation through their use. Successful implementation of these systems would combine reduced requirements for testing and injection with enhanced blood sugar control and minimized complications. The healthcare industry will decrease future diabetes complication costs through nanoparticle therapy while accepting greater initial expenses. The most important potential outcome from

nanoparticle treatment benefits patients through a better quality of life with fewer treatment requirements and superior results.

Research efforts must concentrate on addressing obstacles which stand in the way of mass production and long-term safety assessments, and regulatory authorization. Scientists should develop nanoparticle treatments personalized for individual patient metabolic profiles. Innovations with smart and responsive technology systems will likely create the ultimate diabetes treatment solution, which is an autonomous artificial  $\beta$ -cell in the future. Prolonged research funding and inter-field cooperation will drive nanoparticles toward transforming diabetes medicine within the next ten years.

#### ACKNOWLEDGMENT

It's our privilege to express the profound sense of gratitude and cordial thanks to our respected chairman Mr. Anil Chopra and Vice Chairperson, Ms. Sangeeta Chopra, St. Soldier Educational Society, Jalandhar for providing the necessary facilities to complete this review work.

#### AUTHORS CONTRIBUTIONS

All authors have contributed equally

#### CONFLICT OF INTERESTS

Declared none

#### REFERENCES

1. Rabiee F, Mehralizadeh N, Jalalinezhad S, Ebrahimi Z, Jamali S. Evaluation of the effects of nanoparticles in the treatment of diabetes mellitus: a systematic review and meta-analysis. *Int J Sci Res Dent Med Sci.* 2022 Dec 8;4(4):191-5. doi: [10.30485/ijrsdms.2022.375305.1405](https://doi.org/10.30485/ijrsdms.2022.375305.1405).
2. Gopalsatheeskumar K, Komala S, Mahalakshmi M. An overview on polymeric nanoparticles used in the treatment of diabetes mellitus. *PharmaTutor.* 2017 Dec 1;5(12):40-6. doi: [10.29161/PT.v5.i12.2017.40](https://doi.org/10.29161/PT.v5.i12.2017.40).
3. Qin W, Wu Y, Liu J, Yuan X, Gao J. A comprehensive review of the application of nanoparticles in diabetic wound healing: therapeutic potential and future perspectives. *Int J Nanomedicine.* 2022 Dec 5;17:6007-29. doi: [10.2147/IJN.S386585](https://doi.org/10.2147/IJN.S386585), PMID 36506345.
4. Daisy P, Saipriya K. Biochemical analysis of Cassia fistula aqueous extract and phytochemically synthesized gold

- nanoparticles as hypoglycemic treatment for diabetes mellitus. *Int J Nanomedicine*. 2012 Mar 7;7:1189-202. doi: [10.2147/IJN.S26650](https://doi.org/10.2147/IJN.S26650), PMID 22419867.
5. Li J, Liu Y, Geng K, Lu X, Shen X, Guo Q. ROS-responsive nanoparticles with antioxidative effect for the treatment of diabetic retinopathy. *J Biomater Sci Polym Ed*. 2025 Mar 4;36(4):440-61. doi: [10.1080/09205063.2024.2406628](https://doi.org/10.1080/09205063.2024.2406628), PMID 39316729.
  6. Wang M, Zhang Z, Huo Q, Wang M, Sun Y, Liu H. Targeted polymeric nanoparticles based on mangiferin for enhanced protection of pancreatic  $\beta$ -cells and type 1 diabetes mellitus efficacy. *ACS Appl Mater Interfaces*. 2022 Feb 24;14(9):11092-103. doi: [10.1021/acsami.1c22964](https://doi.org/10.1021/acsami.1c22964), PMID 35199981.
  7. Sharma DK, Pattnaik G, Behera A. Recent developments in nanoparticles for the treatment of diabetes. *J Drug Target*. 2023 Oct 21;31(9):908-19. doi: [10.1080/1061186X.2023.2261077](https://doi.org/10.1080/1061186X.2023.2261077), PMID 37725445.
  8. Maity S, Acharyya A, Sankar Chakraborti AS. Flavonoid-based polymeric nanoparticles: a promising approach for cancer and diabetes treatment. *Eur Polym J*. 2022 Aug 15;177:111455. doi: [10.1016/j.eurpolymj.2022.111455](https://doi.org/10.1016/j.eurpolymj.2022.111455).
  9. Javed B, Ikram M, Farooq F, Sultana T, Mashwani ZU, Raja NI. Biogenesis of silver nanoparticles to treat cancer diabetes and microbial infections: a mechanistic overview. *Appl Microbiol Biotechnol*. 2021 Mar;105(6):2261-75. doi: [10.1007/s00253-021-11171-8](https://doi.org/10.1007/s00253-021-11171-8), PMID 33591386.
  10. Andreadi A, Lodeserto P, Todaro F, Meloni M, Romano M, Minasi A. Nanomedicine in the treatment of diabetes. *Int J Mol Sci*. 2024 Jun 27;25(13):7028. doi: [10.3390/ijms25137028](https://doi.org/10.3390/ijms25137028), PMID 39000136.
  11. Ponnanikajamdeen M, Rajeshkumar S, Vanaja M, Annadurai G. In vivo type 2 diabetes and wound-healing effects of antioxidant gold nanoparticles synthesized using the insulin plant *Chamaecostus cuspidatus* in albino rats. *Can J Diabetes*. 2019 Mar 1;43(2):82-9.e6. doi: [10.1016/j.cjcd.2018.05.006](https://doi.org/10.1016/j.cjcd.2018.05.006), PMID 30413371.
  12. Holt RI, Flyvbjerg A. Textbook of diabetes. John Wiley & Sons; 2024 Feb 12.
  13. Pertiwi R, Asmara N, Wahyudi T, Iriani Y. Illustration book media design diabetes mellitus type 1. Review of International Geographical Education (RIGE). 2021;11(6):91368 doi: [10.48047/rigeo.11.06.150](https://doi.org/10.48047/rigeo.11.06.150).
  14. Krentz AJ, Weyer C, Hompesch M. Translational research methods in diabetes, obesity and nonalcoholic fatty liver disease. Berlin: Springer; 2019.
  15. Dunaev A, Tuchin V. Biomedical photonics for diabetes research. CRC Press; 2022 Oct 31. p. 278. doi: [10.1201/9781003112099](https://doi.org/10.1201/9781003112099).
  16. McNeill JH, editor. Experimental models of diabetes. Routledge; 2018 May 11.
  17. Laddha UD, Kshirsagar SJ, Sayyad LS, Ahmed MT, Gaikwad SS, Udavant PB. Development of surface-modified nanoparticles of curcumin for topical treatment of diabetic retinopathy: *in vitro* ex vivo and *in vivo* investigation. *J Drug Deliv Sci Technol*. 2022 Oct 1;76:103835. doi: [10.1016/j.jddst.2022.103835](https://doi.org/10.1016/j.jddst.2022.103835).
  18. Laddha UD, Kshirsagar SJ. Formulation of PPAR-gamma agonist as surface modified PLGA nanoparticles for non-invasive treatment of diabetic retinopathy: *in vitro* and *in vivo* evidences. *Heliyon*. 2020 Aug 1;6(8):e04589. doi: [10.1016/j.heliyon.2020.e04589](https://doi.org/10.1016/j.heliyon.2020.e04589), PMID 32832706.
  19. Ashrafzadeh H, Abtahi SR, Oroojan AA. Trace element nanoparticles improved diabetes mellitus; a brief report. *Diabetes Metab Syndr*. 2020 Jul 1;14(4):443-5. doi: [10.1016/j.dsx.2020.04.026](https://doi.org/10.1016/j.dsx.2020.04.026), PMID 32371187.
  20. Afify M, Samy N, Hafez NA, Alazzouni AS, Mahdy ES, El Mezayen HA. Evaluation of zinc-oxide nanoparticles effect on treatment of diabetes in streptozotocin-induced diabetic rats. *Egypt J Chem*. 2019 Oct 1;62(10):1771-83. doi: [10.21608/ejchem.2019.11350.1735](https://doi.org/10.21608/ejchem.2019.11350.1735).
  21. Rho JG, Han HS, Han JH, Lee H, Nguyen VQ, Lee WH. Self-assembled hyaluronic acid nanoparticles: implications as a nanomedicine for treatment of type 2 diabetes. *J Control Release*. 2018 Jun 10;279:89-98. doi: [10.1016/j.jconrel.2018.04.006](https://doi.org/10.1016/j.jconrel.2018.04.006), PMID 29649530.
  22. Sharma R, Borah SJ, Bhawna S, Kumar S, Gupta A, Kumari V. Emerging trends in nano-based antidiabetic therapeutics: a path to effective diabetes management. *Mater Adv*. 2023;4(15):3091-113. doi: [10.1039/D3MA00159H](https://doi.org/10.1039/D3MA00159H).
  23. Hosseinzadeh A, Zamani A, Johari HG, Vaez A, Golchin A, Tayebi L. Moving beyond nanotechnology to uncover a glimmer of hope in diabetes medicine: effective nanoparticle-based therapeutic strategies for the management and treatment of diabetic foot ulcers. *Cell Biochem Funct*. 2023 Jul;41(5):517-41. doi: [10.1002/cbf.3816](https://doi.org/10.1002/cbf.3816), PMID 37282756.
  24. DiSanto RM, Subramanian V, Gu Z. Recent advances in nanotechnology for diabetes treatment. *Wiley Interdiscip Rev Nanomed Nanobiotechnol*. 2015 Jul;7(4):548-64. doi: [10.1002/wnan.1329](https://doi.org/10.1002/wnan.1329), PMID 25641955.
  25. El Baz YG, Moustafa A, Ali MA, El Desoky GE, Wabaidur SM, Iqbal A. Green synthesized silver nanoparticles for the treatment of diabetes and the related complications of hyperlipidemia and oxidative stress in diabetic rats. *Exp Biol Med (Maywood)*. 2023 Dec;248(23):2237-48. doi: [10.1177/15353702231214258](https://doi.org/10.1177/15353702231214258), PMID 38205769.
  26. Mitra RN, Nichols CA, Guo J, Makkia R, Cooper MJ, Naash MI. Nanoparticle-mediated miR200-b delivery for the treatment of diabetic retinopathy. *J Control Release*. 2016 Aug 28;236:31-7. doi: [10.1016/j.jconrel.2016.06.020](https://doi.org/10.1016/j.jconrel.2016.06.020), PMID 27297781.
  27. Anand K, Tiloke C, Naidoo P, Chuturgoon AA. Phytonanotherapy for management of diabetes using green synthesis nanoparticles. *J Photochem Photobiol B*. 2017 Aug 1;173:626-39. doi: [10.1016/j.jphotobiol.2017.06.028](https://doi.org/10.1016/j.jphotobiol.2017.06.028), PMID 28709077.
  28. Pan W, Zheng X, Chen G, Su L, Luo S, Wang W. Nanotechnologies application in type 1 diabetes. *Wiley Interdiscip Rev Nanomed Nanobiotechnol*. 2020 Nov;12(6):e1645. doi: [10.1002/wnan.1645](https://doi.org/10.1002/wnan.1645), PMID 32558337.
  29. Ribeiro MC, Correa VL, Da Silva FK, Casas AA, Das Chagas AL, De Oliveira LP. Wound healing treatment using insulin within polymeric nanoparticles in the diabetes animal model. *Eur J Pharm Sci*. 2020 Jul 1;150:105330. doi: [10.1016/j.ejps.2020.105330](https://doi.org/10.1016/j.ejps.2020.105330), PMID 32268198.
  30. Om H, El Naggar ME, El Banna M, Fouda MM, Othman SI, Allam AA. Combating atherosclerosis with targeted diosmin nanoparticles-treated experimental diabetes. *Investig New Drugs*. 2020 Oct;38(5):1303-15. doi: [10.1007/s10637-020-00905-6](https://doi.org/10.1007/s10637-020-00905-6), PMID 32048108.
  31. Shaheen TI, El Naggar ME, Hussein JS, El Bana M, Emara E, El Khayat Z. Antidiabetic assessment; *in vivo* study of gold and core-shell silver-gold nanoparticles on streptozotocin-induced diabetic rats. *Biomed Pharmacother*. 2016 Oct 1;83:865-75. doi: [10.1016/j.biopha.2016.07.052](https://doi.org/10.1016/j.biopha.2016.07.052), PMID 27505844.
  32. Tang KS. The current and future perspectives of zinc oxide nanoparticles in the treatment of diabetes mellitus. *Life Sci*. 2019 Dec 15;239:117011. doi: [10.1016/j.lfs.2019.117011](https://doi.org/10.1016/j.lfs.2019.117011), PMID 31669241.
  33. Sheir MM, Nasra MM, Abdallah OY. Chitosan alginate nanoparticles as a platform for the treatment of diabetic and non-diabetic pressure ulcers: formulation and *in vitro/in vivo* evaluation. *Int J Pharm*. 2021 Sep 25;607:120963. doi: [10.1016/j.ijpharm.2021.120963](https://doi.org/10.1016/j.ijpharm.2021.120963), PMID 34363919.
  34. Alomari G, Hamdan S, Al Trad B. Gold nanoparticles as a promising treatment for diabetes and its complications: current and future potentials. *Braz J Pharm Sci*. 2021 Nov 26;57:e19040. doi: [10.1590/s2175-97902020000419040](https://doi.org/10.1590/s2175-97902020000419040).
  35. Samavati SS, Kashanian S, Derakhshankhah H, Rabiei M. Nanoparticle application in diabetes drug delivery. *J Nanopart Res*. 2022 Sep;24(9):178. doi: [10.1007/s11051-022-05547-8](https://doi.org/10.1007/s11051-022-05547-8).
  36. Subramani K, Pathak S, Hosseinkhani H. Recent trends in diabetes treatment using nanotechnology. *Dig J Nanomater Biostructures (DJNB)*. 2012 Jan 1;7(1):85-95.
  37. Natesan V, Kim SJ. The trend of organic based nanoparticles in the treatment of diabetes and its perspectives. *Biomol Ther (Seoul)*. 2022 Sep 20;31(1):16-26. doi: [10.4062/biomolther.2022.080](https://doi.org/10.4062/biomolther.2022.080), PMID 36122910.
  38. Nazief AM, Hassaan PS, Khalifa HM, Sokar MS, El Kamel AH. Lipid-based gliclazide nanoparticles for treatment of diabetes: formulation pharmacokinetics, pharmacodynamics and subacute toxicity study. *Int J Nanomedicine*. 2020 Feb 18;15:1129-48. doi: [10.2147/IJN.S235290](https://doi.org/10.2147/IJN.S235290), PMID 32110012.

39. El Salamouni NS, Gowayed MA, Seiffen NL, Abdel Moneim RA, Kamel MA, Labib GS. Valsartan solid lipid nanoparticles integrated hydrogel: a challenging repurposed use in the treatment of diabetic foot ulcer *in-vitro/in-vivo* experimental study. *Int J Pharm.* 2021 Jan 5;592:120091. doi: [10.1016/j.ijpharm.2020.120091](https://doi.org/10.1016/j.ijpharm.2020.120091), PMID 33197564.
40. Souto EB, Souto SB, Campos JR, Severino P, Pashirova TN, Zakharova LY. Nanoparticle delivery systems in the treatment of diabetes complications. *Molecules.* 2019 Nov 20;24(23):4209. doi: [10.3390/molecules24234209](https://doi.org/10.3390/molecules24234209), PMID 31756981.
41. Veisheh O, Tang BC, Whitehead KA, Anderson DG, Langer R. Managing diabetes with nanomedicine: challenges and opportunities. *Nat Rev Drug Discov.* 2015 Jan;14(1):45-57. doi: [10.1038/nrd4477](https://doi.org/10.1038/nrd4477), PMID 25430866.
42. Debele TA, Park Y. Application of nanoparticles: diagnosis therapeutics and delivery of insulin/anti-diabetic drugs to enhance the therapeutic efficacy of diabetes mellitus. *Life (Basel).* 2022 Dec 11;12(12):2078. doi: [10.3390/life12122078](https://doi.org/10.3390/life12122078), PMID 36556443.
43. Torabian F, Akhavan Rezayat A, Ghasemi Nour M, Ghorbanzadeh A, Najafi S, Sahebkar A. Administration of silver nanoparticles in diabetes mellitus: a systematic review and meta-analysis on animal studies. *Biol Trace Elem Res.* 2022 Apr;200(4):1699-709. doi: [10.1007/s12011-021-02776-1](https://doi.org/10.1007/s12011-021-02776-1), PMID 34114175.
44. Woldu MA, Lenjisa JL. Nanoparticles and the new era in diabetes management. *Int J Basic Clin Pharmacol.* 2014 Mar;3(2):277-84. doi: [10.5455/2319-2003.ijbcp20140405](https://doi.org/10.5455/2319-2003.ijbcp20140405).
45. Choudhury H, Pandey M, Lim YQ, Low CY, Lee CT, Marilyn TC. Silver nanoparticles: advanced and promising technology in diabetic wound therapy. *Mater Sci Eng C Mater Biol Appl.* 2020 Jul 1;112:110925. doi: [10.1016/j.msec.2020.110925](https://doi.org/10.1016/j.msec.2020.110925), PMID 32409075.
46. El Gharbawy RM, Emara AM, Abu Risha SE. Zinc oxide nanoparticles and a standard antidiabetic drug restore the function and structure of beta cells in type-2 diabetes. *Biomed Pharmacother.* 2016 Dec 1;84:810-20. doi: [10.1016/j.biopha.2016.09.068](https://doi.org/10.1016/j.biopha.2016.09.068), PMID 27723572.
47. Loera Valencia R, Neira RE, Urbina BP, Camacho A, Galindo RB. Evaluation of the therapeutic efficacy of dressings with ZnO nanoparticles in the treatment of diabetic foot ulcers. *Biomed Pharmacother.* 2022 Nov 1;155:113708. doi: [10.1016/j.biopha.2022.113708](https://doi.org/10.1016/j.biopha.2022.113708), PMID 36162373.