Role of Nanotechnology in Diabetes Control and Management

Mudassir Alam*¹, Kashif Abbas¹, Mohd Tanjeem Raza¹, Sana Asif¹, Aharas Siddiqui², Zulnurain Khan³
¹Department of Zoology, Aligarh Muslim University, Aligarh (202002) India
²Interdisciplinary Nanotechnology Centre, Aligarh Muslim University, Aligarh (202002) India
³Department of Chemistry, Aligarh Muslim University, Aligarh (202002) India

Corresponding Author:- Mudassir Alam* Department of Zoology Aligarh Muslim University, Aligarh (202002) India Orcid ID: 0000-0001-8255-0273

Abstract:- Diabetes mellitus, a pervasive global health concern characterized by elevated blood glucose levels, necessitates innovative therapeutic approaches for enhanced efficacy and improved patient compliance. Nanotechnology, operating at the nanoscale (1-100 nanometers), presents a transformative paradigm in medicine-nanomedicine-that holds promise for revolutionizing drug delivery systems. This review explores nanotechnology's potential in reshaping diabetes management, with a focus on optimizing drug delivery for diabetes control. Nanoparticles, including liposomes, polymeric nanoparticles, and dendrimers, offer controlled release kinetics, improved bioavailability, and targeted delivery. Exploiting enhanced permeability and retention, these formulations selectively accumulate therapeutic agents in diabetic tissues. Smart nanoparticles, equipped with sensors and feedback mechanisms, respond to fluctuating glucose levels, providing real-time personalized therapy. Beyond drug delivery, nanosensors detecting diabetes-associated biomarkers offer insights into disease progression. This integrated approach aligns with personalized medicine, tailoring treatments to individual profiles. This review critically analyzes existing knowledge, spanning materials science. pharmacology, and bioengineering, contributing to discussions on nanotechnology's transformative role in diabetes care. The goal is to usher in innovative therapeutic strategies, advancing diabetes management into a new era of precision medicine for improved patient outcomes and reduced treatment-related burdens.

Keywords:- Nanotechnology, Diabetes, Drug-Delivery, Liposomes, Nano-Particles.

I. INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, has emerged as a global epidemic, affecting millions of individuals worldwide [1]. Among its various forms, Type 2 Diabetes (T2D) stands out as the most prevalent, accounting for approximately 90% of all diabetes cases. The multifaceted nature of T2D demands innovative therapeutic approaches to enhance treatment efficacy, minimize side effects, and improve patient compliance [2]. In recent years, nanotechnology has emerged as a revolutionary paradigm in medical science, offering unprecedented opportunities to revolutionize drug delivery systems and significantly impact the management of chronic diseases. Nanotechnology involves the manipulation of materials at the nanoscale, typically ranging from 1 to 100 At this scale, materials exhibit unique nanometers. physicochemical properties that differ from their bulk counterparts, presenting a wide array of possibilities for targeted drug delivery and improved therapeutic outcomes [3]. The application of nanotechnology in medicine, known as nanomedicine, has gained significant traction, particularly in the field of diabetes treatment, where precision and efficiency are paramount [4]. This review seeks to explore the potential of nanotechnology in transforming the landscape of diabetes management, with a specific focus on optimizing drug delivery systems for controlling diabetes. The integration of nanotechnology into diabetes treatment holds promise for addressing several challenges associated with conventional therapeutic approaches, including poor bioavailability, systemic side effects, and the need for frequent dosing [5]. One of the key challenges in diabetes management is achieving sustained and controlled release of anti-diabetic drugs to maintain optimal blood glucose levels while minimizing adverse effects [6]. Nanoparticles, such as liposomes, polymeric nanoparticles, and dendrimers, offer a versatile platform for drug delivery by providing controlled release kinetics, improved bioavailability, and targeted delivery to specific tissues [7]. Furthermore, the nanoscale formulations can exploit the enhanced permeability

and retention effect commonly associated with pathological tissues, allowing for the selective accumulation of therapeutic agents in diabetic tissues [8]. In addition to drug delivery, nanotechnology enables the development of smart and responsive systems that can adapt to the dynamic nature of diabetes. Smart nanoparticles equipped with sensors and feedback mechanisms hold the potential to release drugs in response to fluctuating glucose levels, offering a personalized and real-time therapeutic approach [9]. This level of precision is crucial in mitigating the risk of hypoglycemia and enhancing overall treatment efficacy. Use of nanotechnology extends beyond drug delivery to diagnostic and monitoring applications. Nanosensors capable of detecting biomarkers associated with diabetes can provide valuable insights into disease progression and aid in the early detection of complications. This integrated approach aligns with the concept of personalized medicine, tailoring treatment strategies to individual patient profiles for optimal outcomes [10]. This review aims to critically analyze the existing body of knowledge on nanotechnology applications in diabetes treatment, emphasizing the potential for optimizing drug delivery systems to enhanced diabetes control. By synthesizing information from diverse scientific disciplines, including materials science, pharmacology, and bioengineering, this study seeks to contribute to the ongoing discourse on the transformative role of nanotechnology in diabetes care and its implications for the future of personalized medicine. The ultimate goal is to pave the way for innovative therapeutic strategies that improve patient outcomes, reduce treatmentrelated burdens, and advance the field of diabetes management into a new era of precision medicine.

II. TYPES OF NANOPARTICLES

Nanoparticles come in various types (Figure 1), each with specific properties and applications. Gold nanoparticles, often in the range of 1 to 100 nanometers, exhibit unique optical properties, making them valuable in medical applications. Due to their biocompatibility, they are extensively used in diagnostics, imaging, and drug delivery systems [11]. Their surface plasmon resonance properties enable efficient interaction with light, leading to applications in cancer imaging and therapy [12]. Quantum dots are semiconductor nanoparticles with exceptional optical properties. Their sizedependent electronic structure allows for precise tuning of the emitted light, making them ideal for fluorescence imaging and sensing [13]. Quantum dots find applications in biological imaging, with potential uses in tracking cellular processes and detecting diseases at the molecular level [14]. Iron oxide nanoparticles, commonly in the form of magnetite (Fe3O4) or maghemite (γ -Fe2O3), are notable for their magnetic properties. These nanoparticles are extensively utilized in medical imaging, especially magnetic resonance imaging (MRI) [15]. Their ability to respond to external magnetic fields also makes them valuable for targeted drug delivery systems [16]. Silica nanoparticles, with their high surface area and biocompatibility, have found applications in drug delivery and imaging. Mesoporous silica nanoparticles, in particular, possess ordered porous structures, making them suitable for loading and controlled release of therapeutic agents. Their versatility allows for functionalization to enhance targeting and imaging capabilities [17]. Polymeric nanoparticles, such as those made from poly(lactic-co-glycolic acid) (PLGA), are widely used in drug delivery due to their biodegradability and tunable properties [18]. PLGA nanoparticles can encapsulate a variety of drugs, providing sustained release and targeted delivery. Their applications extend to cancer therapy, vaccine delivery, and treatment of inflammatory diseases [19]. Liposomes are phospholipid vesicles with a lipid bilayer structure, resembling cell membranes. These nanoparticles are versatile drug carriers, encapsulating hydrophilic and hydrophobic drugs alike. Liposomes enhance drug solubility, bioavailability, and allow for targeted drug delivery. They have been extensively explored in cancer therapy and infectious disease treatment [20]. Carbon nanotubes, cylindrical structures composed of carbon atoms, exhibit remarkable electrical, thermal, and mechanical properties. They find applications in drug delivery, sensors, and nanoelectronics [21]. Graphene nanoparticles, single-layer sheets of carbon atoms arranged in a hexagonal lattice, are known for their exceptional conductivity and have potential uses in various fields, including electronic devices and biomedical applications [22]. Upconversion nanoparticles, typically composed of rare-earth elements, have the unique ability to convert lower-energy photons into higher-energy ones. This property makes them valuable for bioimaging, as they can emit visible light in response to near-infrared (NIR) Upconversion nanoparticles have potential excitation. applications in targeted drug delivery and photothermal therapy [23]. Dendrimers are highly branched macromolecules with well-defined structures. They have been extensively explored for drug delivery due to their ability to encapsulate drugs within their interior voids. Dendrimers can also be functionalized with various groups for targeted delivery and imaging applications [24]. Lipid nanocarriers, including liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), are widely employed in drug delivery. These lipid-based systems offer biocompatibility and the ability to encapsulate both hydrophilic and hydrophobic drugs, ensuring controlled release and enhanced therapeutic efficacy [25]. Hybrid nanoparticles combine two or more types of materials, such as metals, polymers, or ceramics, to create multifunctional structures. These hybrids can synergize the unique properties of each component, leading to enhanced performance. Hybrid nanoparticles have applications in imaging, sensing, and drug delivery [26]. Mesoporous ceramic nanoparticles, characterized by their ordered porous structures, have applications in drug delivery and catalysis. Their high surface area and pore volume allow for efficient loading and release of therapeutic agents, making them promising candidates for controlled drug delivery systems [27]. Protein nanoparticles are composed of proteins or peptides and are utilized in drug delivery and medical imaging. These nanoparticles can be engineered for targeted drug delivery and may have improved biocompatibility compared to some synthetic counterparts [28]. Polymer-drug conjugates involve attaching drugs to polymers, often for controlled release and targeted therapy. These conjugates can improve the pharmacokinetics of drugs, enhance their solubility, and reduce side effects. Superparamagnetic nanoparticles, often composed of iron oxide, find applications in magnetic resonance imaging (MRI) and hyperthermia therapy [29]. These nanoparticles

respond to external magnetic fields, allowing for imaging contrast enhancement and localized heating for therapeutic purposes. Table 1 shows various types of nanomaterial with their clinical aspect.

Table 1: The table summarizes different types of nanoparticles used in the context of diabetes, focusing on their composition,
applications in imaging, sensing, and treatment

Nanoparticle Type	Composition	Imaging Modality	Sensing	Treatment	Examples
Gold Nanoparticles	Gold	MRI, CT, Photoacoustic Imaging	Glucose Detection	Drug Delivery	AuNPs coated with glucose-binding molecules for imaging and insulin delivery.
Quantum Dots	Semiconductor Nanocrystals	Fluorescence Imaging	Glucose Sensing	Insulin Delivery	CdSe/ZnS Quantum Dots for real- time glucose monitoring and targeted drug release.
Iron Oxide Nanoparticles	Iron Oxide	MRI	Glucose Monitoring	Hyperglycemia Treatment	Superparamagnetic Fe3O4 NPs for non-invasive glucose monitoring and targeted drug delivery.
Silica Nanoparticles	Silica	Optical Imaging	Glucose Sensing	Drug Encapsulation	Mesoporous silica NPs loaded with anti-diabetic drugs for controlled release.
Liposomes	Lipid Bilayers	Fluorescence Imaging	Glucose Detection	Insulin Delivery	Liposomal formulations for glucose- responsive insulin release.
Polymeric Nanoparticles	Various Polymers	PET, NIR Imaging	Glucose Sensing	Controlled Drug Release	PLGA-based NPs for glucose- triggered drug delivery and imaging.
Carbon Nanotubes	Carbon	Photoacoustic Imaging	Glucose Detection	Drug Delivery	Functionalized carbon nanotubes for glucose sensing and targeted drug delivery.
Magnetic Nanoparticles	Magnetite	MRI	Glucose Monitoring	Hyperglycemia Treatment	Magnetic NPs for glucose-sensitive MRI and magnetic hyperthermia.
Upconversion Nanoparticles	Rare Earth Elements	Upconversion Luminescence	Glucose Sensing	Photothermal Therapy	NaYF4:Yb/Er UCNPs for glucose sensing and light-triggered insulin release.
Dendrimers	Repeated Branched Units	Fluorescence Imaging	Glucose Detection	Drug Delivery	PAMAM dendrimers for glucose- sensitive drug delivery and imaging.



Fig 1: Illustration of commonly used nanoparticles for various clinical applications

III. NANOTECHNOLOGY AS THERAPEUTIC APPROACH

Nanotechnology, a field focused on manipulating and engineering materials at the nanoscale level, has revolutionized the landscape of medical interventions. Its transformative potential lies in its ability to manipulate matter at dimensions that approach the size of biological molecules and cellular structures. In the domain of diabetes therapy, nanotechnology introduces innovative solutions to longstanding challenges in drug delivery, offering a customizable and precise approach to enhance treatment efficacy. Nanotechnology's foundational principles stem from the unique properties exhibited by materials at the nanoscale. At this size range, materials often exhibit distinctive physical, chemical, and biological properties that differ from their macroscopic counterparts. These properties have paved the way for the design and engineering of nanomaterials that can be tailored to specific medical applications, such as drug delivery for diabetes treatment [30]. Diabetes, particularly Type 2 diabetes mellitus (T2DM), is characterized by altered glucose metabolism and chronic hyperglycemia. Successful diabetes management necessitates precise regulation of blood glucose levels to prevent associated complications [31]. Traditional drug delivery methods often fall short due to limitations in drug stability, bioavailability, and targeted delivery. Through the manipulation of nanocarriers, nanoparticles, and nanostructured materials, nanotechnology offers unparalleled capabilities in diabetes drug delivery. Nanocarriers, such as liposomes, micelles, and polymer-based nanoparticles, can encapsulate drugs, protecting them from enzymatic degradation and facilitating their transport to target sites [32]. This encapsulation prolongs drug circulation, minimizing premature drug degradation and clearance from the body. As a result, therapeutic agents maintain their potency and remain available for an extended duration, leading to improved treatment outcomes [33]. Moreover, the precise engineering of nanoparticles enables the creation of drug formulations with controlled release profiles. Nanoparticles can be designed to release therapeutic agents in a sustained, controlled manner over time. This is particularly advantageous for diabetes therapy, as it mimics the physiological release of insulin and allows for prolonged maintenance of therapeutic drug levels [34]. By modulating nanoparticle characteristics such as size, surface charge, and composition, researchers can tailor drug release kinetics to suit the specific needs of patients, optimizing treatment effectiveness [35]. Nanotechnology's impact on diabetes therapy is further magnified by its capacity for targeted drug delivery. Ligand-functionalized nanoparticles can be engineered to recognize and bind to specific cellular receptors or disease-specific markers. This targeting ability enables the precise delivery of therapeutic agents to diabetic cells or tissues, minimizing exposure to healthy tissues and reducing potential side effects. This level of specificity enhances treatment efficacy while mitigating unintended consequences of off-target drug distribution [36]. The incorporation of nanotechnology into medicine, particularly in diabetes therapy, signifies a paradigm shift in drug delivery strategies. By harnessing the unique properties of nanoscale materials, researchers and clinicians can design drug formulations that achieve controlled release, targeted delivery, and enhanced cellular uptake [37]. This approach maximizes the therapeutic impact of drugs while minimizing off-target effects, offering a new era of precision and effectiveness in treating Type 2 diabetes mellitus. As nanotechnology continues to evolve, its potential to reshape diabetes management holds promise for revolutionizing the field of medical interventions as a whole (Figure 2).



Fig 2 : Role of nanotechnology in diabetes management: Antidiabetic drugs when encapsulated with nanoparticles may help in increasing the bioavailability and efficacy of the medication while also minimizing its side effects

IV. DIAGNOSIS AND DISEASE MONITORING

Diabetes manifests as a complex physiological condition, marked by intricate cellular, molecular, and immunological events that collectively influence its progression. At the cellular level, resistance of hepatocytes and myocytes to insulin disrupts pivotal signaling pathways essential for the maintenance of glucose homeostasis [38]. Concurrently, pancreatic beta cells within the Islets of Langerhans contend with oxidative stress and diminished insulin secretion due to prolonged exposure to heightened levels of glucose and free fatty acids [39]. This dysfunction extends to adipose tissue, where the release of adipokines, such as leptin and adiponectin, contributes to inflammation and exacerbates insulin resistance [40]. The integration of nanotechnology provides a promising avenue for intervention at the cellular level. Specifically engineered nanoparticles, exemplified by liposomes, can selectively target hepatocytes and myocytes, delivering compounds designed to enhance insulin sensitivity. Moreover, these nanoparticles serve a protective role for pancreatic beta cells by facilitating the transport of antioxidants, such as catalase, to mitigate oxidative stress [41]. The elevated blood glucose levels characteristic of diabetes instigate the formation of advanced glycation endproducts (AGEs), causing structural disruptions to molecular entities like proteins and lipids. Concurrently, a chronic lowgrade inflammatory milieu ensues, propelled by cytokines such as TNF-alpha and IL-6, with immune cells, notably macrophages, assuming pivotal roles. Dysregulation of lipid metabolism, evidenced by the accumulation of lipid intermediates like ceramides, further contributes to the escalation of insulin resistance and inflammation [43]. Nanotechnology assumes a critical role in addressing molecular intricacies. Dendrimers, for instance, can be intricately engineered to scavenge and neutralize AGEs, presenting a potential countermeasure to their deleterious effects. Additionally, nanoparticles designed for lipid targeting offer a prospective approach to rectify dysregulated lipid metabolism, thereby contributing to the restoration of insulin sensitivity [44]. The innate immune system orchestrates the activation of macrophages in adipose tissue and the liver, culminating in the release of pro-inflammatory cytokines in response to tissue damage and insulin resistance [45]. An adaptive immune response further complicates the scenario, featuring T lymphocytes, particularly CD8+ cytotoxic T cells, which may contribute to an autoimmune component by targeting pancreatic beta cells [46]. Immunomodulation, notably the dysfunction of regulatory T cells (Tregs), becomes intricately associated with chronic inflammation in Type 2 diabetes [47]. Nanotechnology, however, rises to the immunological challenge. Nanoparticles, including innovative exosome-based delivery systems, demonstrate the capacity to modulate macrophage activity, fostering an anti-inflammatory phenotype. Moreover, targeted nanoparticles exhibit promise in carrying immunomodulatory agents, facilitating the expansion of regulatory T cells to restore immune equilibrium [48]. For instance, liposomes, through their multifaceted design, can transport insulin-sensitizing compounds alongside imaging agents, providing а

comprehensive solution. Smart nanocarriers, responsive to glucose levels, exhibit the capability to release insulin or antiinflammatory agents in a controlled manner [49]. Meanwhile, nanoscale imaging techniques, leveraging quantum dots and superparamagnetic iron oxide nanoparticles, afford highresolution insights into the intricate cellular and molecular changes associated with diabetes.

V. NANOTECHNOLOGY-AIDED DRUG DELIVERY IN DIABETES

At the forefront of nanomedicine for diabetes management, intricate molecular designs underpin nano drug formulations with heightened precision. Poly(lactic-co-glycolic acid) (PLGA) nanoparticles, a fusion of poly(lactic acid) and poly(glycolic acid), intricately encapsulate insulin, leveraging tunable molecular weights and copolymer ratios to orchestrate controlled release kinetics through nuanced polymer degradation [50]. Crosslinked nanogels, crafted from poly(Nisopropylacrylamide-co-acrylic acid) copolymers, intricately respond to temperature variations, enabling thermosensitive insulin encapsulation and release mediated by dynamic changes in polymer conformation [51]. Liposomal formulations, featuring the complexity of phospholipids such as 1,2-dioleoylsn-glycero-3-phosphocholine (DOPC), establish a molecularly intricate bilayer structure, offering a precise amphiphilic milieu for shielding insulin and ensuring meticulous sustained release [52]. Polyamidoamine (PAMAM) dendrimers, characterized by a precisely defined branching architecture with aminoterminated surfaces, provide a molecularly programmable scaffold for insulin encapsulation, orchestrating controlled release through an intricate interplay of dendrimer surface and encapsulated insulin [53]. Gold nanoparticles, meticulously coated with thiolated polyethylene glycol (PEG), introduce a multifaceted molecular assembly with plasmonic resonance properties, creating an intricate nanoenvironment for insulin encapsulation and targeted release dynamics [54]. Multi-walled carbon nanotubes (MWCNTs) and electrospun poly(lactic acid) (PLA) nanofibers, marked by concentric graphene layers and aligned polymer chains, respectively, weave a molecularly intricate matrix serving as an advanced reservoir for insulin encapsulation, utilizing nanoscale structures for controlled release [55]. Medium-chain triglyceride-based nanoemulsions, intricately formulated with a complex arrangement of surfactants, including nonionic and ionic amphiphiles, enhance oral bioavailability through the molecular orchestration of insulin encapsulation within nanodroplets [56]. Chitosan nanoparticles, derived from chitin deacetylation, present a molecularly complex system with variable degrees of quaternization, particularly in trimethyl chitosan derivatives, enhancing mucoadhesive properties for intricate oral insulin delivery and nuanced bioavailability pathways [57]. Engaging with cutting-edge scientific literature and ongoing clinical investigations becomes imperative for staying abreast of the latest advancements in this dynamically evolving field.

VI. INSULIN DELIVERY

Nanotechnology is revolutionizing the landscape of diabetes management by addressing multiple dimensions with precision. Liposomes and nanoparticles, functioning as carriers, encapsulate insulin molecules to facilitate controlled release. For instance, lipid-based nanocarriers loaded with insulin analogs, such as insulin lispro or insulin glargine, ensure sustained release, significantly enhancing glycemic control [58]. Furthermore, glucose-responsive nanoparticles, illustrated by glucose-responsive hydrogels, exhibit the capability to adapt to glucose fluctuations, presenting a tailored and automated insulin delivery system aligned with individual needs [59]. Nanoemulsions, composed of nanoscale oil droplets, interact with digestive enzymes, thereby amplifying insulin bioavailability. Notably, oral insulin nano emulsions showcase the potential to revolutionize diabetes management [60]. Functionalized nanoparticles, like insulin-loaded magnetic nanoparticles, enable targeted delivery to specific cells, addressing insulin resistance effectively [61]. Remarkably, surface modifications on nanoparticles, utilizing ligands that bind to insulin receptors, elevate cellular interactions. Gold nanoparticles engineered with specific surface modifications exemplify this capability by targeting pancreatic beta cells to facilitate efficient insulin release [62]. Nanoparticles also play a pivotal role in facilitating gene delivery for insulin production. Viral vectors encapsulated in nanoparticles, as demonstrated in lipid nanoparticles carrying CRISPR components, offer a means for precise genetic modifications, potentially enhancing insulin sensitivity in target cells [63]. Biocompatible nanoparticles, including those made from chitosan or PLGA, ensure compatibility at the biological level. A noteworthy example is chitosan-coated insulin nanoparticles, showcasing improved bioavailability and reduced immunogenicity [64]. Coatings on insulin delivery devices, utilizing biological polymers such as alginate, serve to protect insulin [65]. Alginate-coated microneedle patches, for instance, enhance the stability and bioavailability of insulin, potentially providing a more patient-friendly delivery method [66]. Polymeric nanoparticles like PLGA microspheres offer controlled release, reducing the frequency of insulin injections. Smart insulin patches, responsive to elevated glucose levels, exemplify strategies for precise insulin dosing tailored to individual glycemic variations [67]. Immunomodulatory nanoparticles, employing exosome-based delivery systems, play a pivotal role modulating macrophage activity and in addressing inflammation associated with insulin resistance [68]. In a targeted immunomodulation approach, nanoparticles carrying cytokines that promote regulatory T cells present a promising avenue for managing chronic inflammation in diabetes [69]. Nanoparticles seamlessly integrate into gene editing technologies, as evidenced by lipid nanoparticles carrying CRISPR components for precise genetic modifications. Nanoscale imaging agents like quantum dots provide highresolution insights into cellular and molecular changes associated with diabetes, thereby contributing significantly to diagnostics and research [70].

VII. FUTURE AVENUES IN NANOTECHNOLOGY-AIDED DIABETES MANAGEMENT

The future outlook for diabetes management is significantly shaped by the promising applications of nanotechnology and nanoparticles. To encourage early detection and diagnosis, engineered nanoparticles, such as quantum dots and gold nanoparticles, exhibit the potential to precisely target diabetes-associated biomarkers, facilitating rapid and accurate detection through various imaging techniques [71]. Smart insulin delivery systems, utilizing nanoparticles like liposomes or polymer-based carriers, hold the promise of responsive insulin release, dynamically responding to glucose levels. This approach ensures a more controlled insulin administration, reducing the risk of hypoglycemia and optimizing glycemic control [72]. Nanotechnology's impact on drug formulations is noteworthy, with nano-sized drug formulations incorporating molecules like lipids or polymers showing promise in enhancing drug bioavailability and stability [73]. This innovation can lead to more effective and personalized treatment regimens with reduced side effects. The development of artificial pancreas systems, combining continuous glucose monitoring with automated insulin delivery, is another frontier where nanoparticles, including nanosensors and nanocarriers, play a pivotal role. These technologies contribute to the creation of biocompatible sensors and efficient insulin delivery devices, ultimately improving the quality of life for individuals with diabetes [74]. Nanoparticles designed for gene delivery or tissue engineering are being explored to repair and regenerate pancreatic beta cells, addressing the root causes of diabetes. This regenerative therapy holds the potential to restore insulin production and enhance long-term outcomes for patients [75]. The era of personalized medicine is also evolving with nanotechnology, enabling the creation of tailored interventions based on an individual's genetic and molecular profile. This approach, incorporating specific molecules and cells, has the potential to revolutionize diabetes treatment, offering more precise and effective strategies [76]. Wearable devices integrated with nanoparticles for continuous glucose monitoring represent a significant advancement in monitoring and feedback systems. These devices provide real-time feedback to individuals with diabetes and their healthcare providers, enabling proactive and personalized adjustments to treatment plans [77]. Furthermore, by optimizing drug delivery and minimizing off-target effects, nanotechnology has the potential to reduce the side effects associated with diabetes medications [78]. As research progresses, addressing safety concerns, regulatory considerations, and ethical implications is crucial to ensure the successful translation of these innovations from the laboratory to clinical practice. The integration of nanotechnology into diabetes care stands poised to revolutionize treatment strategies, enhance patient outcomes, and contribute to the overall advancement of precision medicine.

VIII. DISCUSSION

The integration of nanotechnology into diabetes management holds substantial promise for addressing the complexities associated with Type 2 Diabetes (T2D). The exploration of various nanoparticles, such as liposomes, polymeric nanoparticles, and dendrimers, demonstrates their potential in revolutionizing drug delivery systems for enhanced efficacy and improved patient compliance. The controlled release kinetics, improved bioavailability, and targeted delivery afforded by these nanocarriers present a paradigm shift in the approach to T2D control. One of the key advantages lies in the exploitation of enhanced permeability and retention, allowing nanoparticles to selectively accumulate therapeutic agents in diabetic tissues. This targeted delivery mechanism not only improves the efficiency of treatment but also minimizes offtarget effects. Moreover, the development of smart nanoparticles with sensors and feedback mechanisms adds a layer of sophistication to diabetes therapeutics. These innovative systems can respond dynamically to fluctuating glucose levels, providing real-time personalized therapy that adapts to the unique needs of each patient. Beyond drug delivery, the incorporation of nanosensors capable of detecting diabetes-associated biomarkers offers a holistic approach to disease management. By providing insights into disease progression, these nanosensors contribute to a more comprehensive understanding of T2D, paving the way for tailored interventions aligned with the principles of personalized medicine. This review critically examines the interdisciplinary nature of nanotechnology in diabetes care, encompassing materials science, pharmacology, and bioengineering. The synthesized knowledge contributes to the ongoing discourse on the transformative role of nanotechnology in reshaping diabetes management. As we move forward, the goal is to usher in innovative therapeutic strategies, advancing diabetes care into a new era of precision medicine. This approach not only promises improved patient outcomes but also aims to alleviate treatment-related burdens, marking a significant step towards a more effective and patient-centric diabetes management paradigm.

ACKNOWLEDGEMENT

Authors would like to acknowledge Department of Zoology and Interdisciplinary Nanotechnology Centre, Aligarh Muslim University, India.

Conflict of Interest: Authors declare no conflict of interest.

REFERENCES

- Kharroubi, A. T., & Darwish, H. M. (2015). Diabetes mellitus: The epidemic of the century. World journal of diabetes, 6(6), 850–867. https://doi.org/10.4239/wjd.v6.i6.850
- [2]. Goyal R, Singhal M, Jialal I. Type 2 Diabetes. [Updated 2023 Jun 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513253/
- [3]. Bayda, S., Adeel, M., Tuccinardi, T., Cordani, M., & Rizzolio, F. (2019). The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nanomedicine. Molecules (Basel, Switzerland), 25(1), 112. https://doi.org/10.3390/molecules25010112
- [4]. Zhao, Q., Cheng, N., Sun, X., Yan, L., & Li, W. (2023). The application of nanomedicine in clinical settings. Frontiers in bioengineering and biotechnology, 11, 1219054. https://doi.org/10.3389/fbioe.2023.1219054
- [5]. Veiseh O, Tang BC, Whitehead KA, Anderson DG, Langer R. Managing diabetes with nanomedicine: challenges and opportunities. Nat Rev Drug Discov. 2015;14(1):45-57. doi:10.1038/nrd4477
- [6]. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug based therapeutics. Biomed Pharmacother. 2020;131:110708. doi:10.1016/j.biopha.2020.110708
- [7]. Yetisgin, A. A., Cetinel, S., Zuvin, M., Kosar, A., & Kutlu, O. (2020). Therapeutic Nanoparticles and Their Targeted Delivery Applications. Molecules (Basel, Switzerland), 25(9), 2193. https://doi.org/10.3390/molecules25092193
- [8]. Nakamura, Y., Mochida, A., Choyke, P. L., & Kobayashi, H. (2016). Nanodrug Delivery: Is the Enhanced Permeability and Retention Effect Sufficient for Curing Cancer?. Bioconjugate chemistry, 27(10), 2225–2238. https://doi.org/10.1021/acs.bioconjchem.6b00437
- [9]. DiSanto RM, Subramanian V, Gu Z. Recent advances in nanotechnology for diabetes treatment. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2015;7(4):548-564. doi:10.1002/wnan.1329
- [10]. Shoaib, A., Darraj, A., Khan, M. E., Azmi, L., Alalwan, A., Alamri, O., Tabish, M., & Khan, A. U. (2023). A Nanotechnology-Based Approach to Biosensor Application in Current Diabetes Management Practices. Nanomaterials (Basel, Switzerland), 13(5), 867. https://doi.org/10.3390/nano13050867
- [11]. Dykman, L. A., & Khlebtsov, N. G. (2011). Gold nanoparticles in biology and medicine: recent advances and prospects. Acta naturae, 3(2), 34–55.
- [12]. Das, S., Devireddy, R., & Gartia, M. R. (2023). Surface Plasmon Resonance (SPR) Sensor for Cancer Biomarker Detection. Biosensors, 13(3), 396. https://doi.org/10.3390/bios13030396

- [13]. Wagner, A. M., Knipe, J. M., Orive, G., & Peppas, N. A. (2019). Quantum dots in biomedical applications. Acta biomaterialia, 94, 44–63. https://doi.org/10.1016/j.actbio.2019.05.022
- [14]. Barroso M. M. (2011). Quantum dots in cell biology. The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society, 59(3), 237–251. https://doi.org/10.1369/0022155411398487
- [15]. Ali, A., Zafar, H., Zia, M., Ul Haq, I., Phull, A. R., Ali, J. S., & Hussain, A. (2016). Synthesis, characterization, applications, and challenges of iron oxide nanoparticles. Nanotechnology, science and applications, 9, 49–67. https://doi.org/10.2147/NSA.S99986
- [16]. Liu YL, Chen D, Shang P, Yin DC. A review of magnet systems for targeted drug delivery. J Control Release. 2019;302:90-104. doi:10.1016/j.jconrel.2019.03.031
- [17]. Bharti, C., Nagaich, U., Pal, A. K., & Gulati, N. (2015). Mesoporous silica nanoparticles in target drug delivery system: A review. International journal of pharmaceutical investigation, 5(3), 124–133. https://doi.org/10.4103/2230-973X.160844
- [18]. Lu, Y., Cheng, D., Niu, B., Wang, X., Wu, X., & Wang, A. (2023). Properties of Poly (Lactic-co-Glycolic Acid) and Progress of Poly (Lactic-co-Glycolic Acid)-Based Biodegradable Materials in Biomedical Research. Pharmaceuticals (Basel, Switzerland), 16(3), 454. https://doi.org/10.3390/ph16030454
- [19]. Lü, J. M., Wang, X., Marin-Muller, C., Wang, H., Lin, P. H., Yao, Q., & Chen, C. (2009). Current advances in research and clinical applications of PLGA-based nanotechnology. Expert review of molecular diagnostics, 9(4), 325–341. https://doi.org/10.1586/erm.09.15
- [20]. Nakhaei, P., Margiana, R., Bokov, D. O., Abdelbasset, W. K., Jadidi Kouhbanani, M. A., Varma, R. S., Marofi, F., Jarahian, M., & Beheshtkhoo, N. (2021). Liposomes: Structure, Biomedical Applications, and Stability Parameters With Emphasis on Cholesterol. Frontiers in bioengineering and biotechnology, 9. 705886. https://doi.org/10.3389/fbioe.2021.705886 (Retraction published Front Bioeng Biotechnol. 2023 Sep 04;11:1285118)
- [21]. Anzar, N., Hasan, R., Tyagi, M., Yadav, N., & Narang, J. (2020). Carbon nanotube-A review on Synthesis, Properties and plethora of applications in the field of biomedical science. Sensors International, 1, 100003.
- [22]. Li J, Zeng H, Zeng Z, Zeng Y, Xie T. Promising Graphene-Based Nanomaterials and Their Biomedical Applications and Potential Risks: A Comprehensive Review. ACS Biomater Sci Eng. 2021;7(12):5363-5396. doi:10.1021/acsbiomaterials.1c00875
- [23]. Chen, J., & Zhao, J. X. (2012). Upconversion nanomaterials: synthesis, mechanism, and applications in sensing. Sensors (Basel, Switzerland), 12(3), 2414–2435. https://doi.org/10.3390/s120302414

- [24]. Mittal, P., Saharan, A., Verma, R., Altalbawy, F. M. A., Alfaidi, M. A., Batiha, G. E., Akter, W., Gautam, R. K., Uddin, M. S., & Rahman, M. S. (2021). Dendrimers: A New Race of Pharmaceutical Nanocarriers. BioMed research international, 2021, 8844030. https://doi.org/10.1155/2021/8844030
- [25]. Lu, H., Zhang, S., Wang, J., & Chen, Q. (2021). A Review on Polymer and Lipid-Based Nanocarriers and Its Application to Nano-Pharmaceutical and Food-Based Systems. Frontiers in nutrition, 8, 783831. https://doi.org/10.3389/fnut.2021.783831
- [26]. Macchione MA, Biglione C, Strumia M. Design, Synthesis and Architectures of Hybrid Nanomaterials for Therapy and Diagnosis Applications. Polymers (Basel). 2018;10(5):527. Published 2018 May 14. doi:10.3390/polym10050527
- [27]. Tella, J. O., Adekoya, J. A., & Ajanaku, K. O. (2022). Mesoporous silica nanocarriers as drug delivery systems for anti-tubercular agents: a review. Royal Society open science, 9(6), 220013. https://doi.org/10.1098/rsos.220013
- [28]. Hong, S., Choi, D. W., Kim, H. N., Park, C. G., Lee, W., & Park, H. H. (2020). Protein-Based Nanoparticles as Drug Delivery Systems. Pharmaceutics, 12(7), 604. https://doi.org/10.3390/pharmaceutics12070604
- [29]. Junyaprasert VB, Thummarati P. Innovative Design of Targeted Nanoparticles: Polymer-Drug Conjugates for Enhanced Cancer Therapy. Pharmaceutics. 2023;15(9):2216. Published 2023 Aug 27. doi:10.3390/pharmaceutics15092216
- [30]. Joudeh N, Linke D. Nanoparticle classification, physicochemical properties, characterization, and applications: a comprehensive review for biologists. J Nanobiotechnology. 2022;20(1):262. Published 2022 Jun 7. doi:10.1186/s12951-022-01477-8
- [31]. Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. International journal of molecular sciences, 21(17), 6275. https://doi.org/10.3390/ijms21176275
- [32]. Lombardo, D., Kiselev, M. A., & Caccamo, M. T. (2019). Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine. Journal of nanomaterials, 2019.
- [33]. Kumari, A., Singla, R., Guliani, A., & Yadav, S. K. (2014). Nanoencapsulation for drug delivery. EXCLI journal, 13, 265–286.
- [34]. Mitchell, M. J., Billingsley, M. M., Haley, R. M., Wechsler, M. E., Peppas, N. A., & Langer, R. (2021). Engineering precision nanoparticles for drug delivery. Nature reviews. Drug discovery, 20(2), 101–124. https://doi.org/10.1038/s41573-020-0090-8

- [35]. Sethi M, Sukumar R, Karve S, et al. Effect of drug release kinetics on nanoparticle therapeutic efficacy and toxicity. Nanoscale. 2014;6(4):2321-2327. doi:10.1039/c3nr05961h
- [36]. Nigam, S., Bishop, J. O., Hayat, H., Quadri, T., Hayat, H., & Wang, P. (2022). Nanotechnology in Immunotherapy for Type 1 Diabetes: Promising Innovations and Future Advances. Pharmaceutics, 14(3), 644. https://doi.org/10.3390/pharmaceutics14030644
- [37]. Afzal, O., Altamimi, A. S. A., Nadeem, M. S., Alzarea, S. I., Almalki, W. H., Tariq, A., Mubeen, B., Murtaza, B. N., Iftikhar, S., Riaz, N., & Kazmi, I. (2022). Nanoparticles in Drug Delivery: From History to Therapeutic Applications. Nanomaterials (Basel, Switzerland), 12(24), 4494. https://doi.org/10.3390/nano12244494
- [38]. Röder, P. V., Wu, B., Liu, Y., & Han, W. (2016). Pancreatic regulation of glucose homeostasis. Experimental & molecular medicine, 48(3), e219. https://doi.org/10.1038/emm.2016.6
- [39]. Cerf M. E. (2013). Beta cell dysfunction and insulin resistance. Frontiers in endocrinology, 4, 37. https://doi.org/10.3389/fendo.2013.00037
- [40]. Ouchi, N., Parker, J. L., Lugus, J. J., & Walsh, K. (2011). Adipokines in inflammation and metabolic disease. Nature reviews. Immunology, 11(2), 85–97. https://doi.org/10.1038/nri2921
- [41]. Yücel Ç, Karatoprak GŞ, Aktaş Y. Nanoliposomal Resveratrol as a Novel Approach to Treatment of Diabetes Mellitus. J Nanosci Nanotechnol. 2018;18(6):3856-3864. doi:10.1166/jnn.2018.15247
- [42]. Singh, V. P., Bali, A., Singh, N., & Jaggi, A. S. (2014). Advanced glycation end products and diabetic complications. The Korean journal of physiology & pharmacology : official journal of the Korean Physiological Society and the Korean Society of Pharmacology, 18(1), 1–14. https://doi.org/10.4196/kjpp.2014.18.1.1
- [43]. Popko, K., Gorska, E., Stelmaszczyk-Emmel, A., Plywaczewski, R., Stoklosa, A., Gorecka, D., Pyrzak, B., & Demkow, U. (2010). Proinflammatory cytokines II-6 and TNF-α and the development of inflammation in obese subjects. European journal of medical research, 15 Suppl 2(Suppl 2), 120–122. https://doi.org/10.1186/2047-783x-15-s2-120
- [44]. Padmanaban S, Pully D, Samrot AV, et al. Rising Influence of Nanotechnology in Addressing Oxidative Stress-Related Liver Disorders. Antioxidants (Basel). 2023;12(7):1405. Published 2023 Jul 9. doi:10.3390/antiox12071405
- [45]. Odegaard, J. I., & Chawla, A. (2012). Connecting type 1 and type 2 diabetes through innate immunity. Cold Spring Harbor perspectives in medicine, 2(3), a007724. https://doi.org/10.1101/cshperspect.a007724

- [46]. Scherm, M. G., Wyatt, R. C., Serr, I., Anz, D., Richardson, S. J., & Daniel, C. (2022). Beta cell and immune cell interactions in autoimmune type 1 diabetes: How they meet and talk to each other. Molecular metabolism, 64, 101565. https://doi.org/10.1016/j.molmet.2022.101565
- [47]. de Candia, P., Prattichizzo, F., Garavelli, S., De Rosa, V., Galgani, M., Di Rella, F., Spagnuolo, M. I., Colamatteo, A., Fusco, C., Micillo, T., Bruzzaniti, S., Ceriello, A., Puca, A. A., & Matarese, G. (2019). Type 2 Diabetes: How Much of an Autoimmune Disease?. Frontiers in endocrinology, 10, 451. https://doi.org/10.3389/fendo.2019.00451
- [48]. Yi Q, Xu Z, Thakur A, et al. Current understanding of plant-derived exosome-like nanoparticles in regulating the inflammatory response and immune system microenvironment. Pharmacol Res. 2023;190:106733. doi:10.1016/j.phrs.2023.106733
- [49]. Su, S., & M Kang, P. (2020). Recent Advances in Nanocarrier-Assisted Therapeutics Delivery Systems. Pharmaceutics, 12(9), 837. https://doi.org/10.3390/pharmaceutics12090837
- [50]. Makadia HK, Siegel SJ. Poly Lactic-co-Glycolic Acid (PLGA) as Biodegradable Controlled Drug Delivery Carrier. Polymers (Basel). 2011;3(3):1377-1397. doi:10.3390/polym3031377
- [51]. Kim, Y. K., Kim, E. J., Lim, J. H., Cho, H. K., Hong, W. J., Jeon, H. H., & Chung, B. G. (2019). Dual Stimuli-Triggered Nanogels in Response to Temperature and pH Changes for Controlled Drug Release. Nanoscale research letters, 14(1), 77. https://doi.org/10.1186/s11671-019-2909-y
- [52]. Nsairat, H., Khater, D., Sayed, U., Odeh, F., Al Bawab, A., & Alshaer, W. (2022). Liposomes: structure, composition, types, and clinical applications. Heliyon, 8(5), e09394. https://doi.org/10.1016/j.heliyon.2022.e09394
- [53]. Kolhatkar RB, Kitchens KM, Swaan PW, Ghandehari H. Surface acetylation of polyamidoamine (PAMAM) dendrimers decreases cytotoxicity while maintaining membrane permeability. Bioconjug Chem. 2007;18(6):2054-2060. doi:10.1021/bc0603889
- [54]. Park, J. M., Choi, H. E., Kudaibergen, D., Kim, J. H., & Kim, K. S. (2021). Recent Advances in Hollow Gold Nanostructures for Biomedical Applications. Frontiers in chemistry, 9, 699284. https://doi.org/10.3389/fchem.2021.699284
- [55]. Wang SF, Wu YC, Cheng YC, Hu WW. The Development of Polylactic Acid/Multi-Wall Carbon Nanotubes/Polyethylene Glycol Scaffolds for Bone Tissue Regeneration Application. Polymers (Basel). 2021;13(11):1740. Published 2021 May 26. doi:10.3390/polym13111740

- [56]. Azeem, A., Rizwan, M., Ahmad, F. J., Iqbal, Z., Khar, R. K., Aqil, M., & Talegaonkar, S. (2009). Nanoemulsion components screening and selection: a technical note. AAPS PharmSciTech, 10(1), 69–76. https://doi.org/10.1208/s12249-008-9178-x
- [57]. Mourya, V. K., & Inamdar, N. N. (2009). Trimethyl chitosan and its applications in drug delivery. Journal of materials science. Materials in medicine, 20(5), 1057– 1079. https://doi.org/10.1007/s10856-008-3659-z
- [58]. Souto, E. B., Souto, S. B., Campos, J. R., Severino, P., Pashirova, T. N., Zakharova, L. Y., Silva, A. M., Durazzo, A., Lucarini, M., Izzo, A. A., & Santini, A. (2019). Nanoparticle Delivery Systems in the Treatment of Diabetes Complications. Molecules (Basel, Switzerland), 24(23), 4209. https://doi.org/10.3390/molecules24234209
- [59]. Volpatti, L. R., Facklam, A. L., Cortinas, A. B., Lu, Y. C., Matranga, M. A., MacIsaac, C., Hill, M. C., Langer, R., & Anderson, D. G. (2021). Microgel encapsulated nanoparticles for glucose-responsive insulin delivery. Biomaterials, 267, 120458. https://doi.org/10.1016/j.biomaterials.2020.120458
- [60]. Li, X., Qi, J., Xie, Y., Zhang, X., Hu, S., Xu, Y., Lu, Y., & Wu, W. (2013). Nanoemulsions coated with alginate/chitosan as oral insulin delivery systems: preparation, characterization, and hypoglycemic effect in rats. International journal of nanomedicine, 8, 23–32. https://doi.org/10.2147/IJN.S38507
- [61]. Lemmerman, L. R., Das, D., Higuita-Castro, N., Mirmira, R. G., & Gallego-Perez, D. (2020). Nanomedicine-Based Strategies for Diabetes: Diagnostics, Monitoring, and Treatment. Trends in endocrinology and metabolism: TEM, 31(6), 448–458. https://doi.org/10.1016/j.tem.2020.02.001
- [62]. Liu, L., Kshirsagar, P. G., Gautam, S. K., Gulati, M., Wafa, E. I., Christiansen, J. C., White, B. M., Mallapragada, S. K., Wannemuehler, M. J., Kumar, S., Solheim, J. C., Batra, S. K., Salem, A. K., Narasimhan, B., & Jain, M. (2022). Nanocarriers for pancreatic cancer imaging, treatments, and immunotherapies. Theranostics, 12(3), 1030–1060. https://doi.org/10.7150/thno.64805
- [63]. Dubey, A. K., & Mostafavi, E. (2023). Biomaterialsmediated CRISPR/Cas9 delivery: recent challenges and opportunities in gene therapy. Frontiers in chemistry, 11, 1259435. https://doi.org/10.3389/fchem.2023.1259435
- [64]. Mikušová, V., & Mikuš, P. (2021). Advances in Chitosan-Based Nanoparticles for Drug Delivery. International journal of molecular sciences, 22(17), 9652. https://doi.org/10.3390/ijms22179652
- [65]. Mansoor, S., Kondiah, P. P. D., Choonara, Y. E., & Pillay, V. (2019). Polymer-Based Nanoparticle Strategies for Insulin Delivery. Polymers, 11(9), 1380. https://doi.org/10.3390/polym11091380

- [66]. Chen, C. H., Shyu, V. B., & Chen, C. T. (2018). Dissolving Microneedle Patches for Transdermal Insulin Delivery in Diabetic Mice: Potential for Clinical Applications. Materials (Basel, Switzerland), 11(9), 1625. https://doi.org/10.3390/ma11091625
- [67]. Wu, J. Z., Williams, G. R., Li, H. Y., Wang, D. X., Li, S. D., & Zhu, L. M. (2017). Insulin-loaded PLGA microspheres for glucose-responsive release. Drug delivery, 24(1), 1513–1525. https://doi.org/10.1080/10717544.2017.1381200
- [68]. Wang, C., Xu, M., Fan, Q., Li, C., & Zhou, X. (2023). Therapeutic potential of exosome-based personalized delivery platform in chronic inflammatory diseases. Asian journal of pharmaceutical sciences, 18(1), 100772. https://doi.org/10.1016/j.ajps.2022.100772
- [69]. Benne, N., Ter Braake, D., Stoppelenburg, A. J., & Broere, F. (2022). Nanoparticles for Inducing Antigen-Specific T Cell Tolerance in Autoimmune Diseases. Frontiers in immunology, 13, 864403. https://doi.org/10.3389/fimmu.2022.864403
- [70]. Sim, S., & Wong, N. K. (2021). Nanotechnology and its use in imaging and drug delivery (Review). Biomedical reports, 14(5), 42. https://doi.org/10.3892/br.2021.1418
- [71]. Tillman, L., Tabish, T. A., Kamaly, N., Moss, P., El-Briri, A., Thiemermann, C., Pranjol, M. Z. I., & Yaqoob, M. M. (2022). Advancements in nanomedicines for the detection and treatment of diabetic kidney disease. Biomaterials and biosystems, 6, 100047. https://doi.org/10.1016/j.bbiosy.2022.100047
- [72]. Webber, M. J., & Anderson, D. G. (2015). Smart approaches to glucose-responsive drug delivery. Journal of drug targeting, 23(7-8), 651–655. https://doi.org/10.3109/1061186X.2015.1055749
- [73]. Rizvi, S. A. A., & Saleh, A. M. (2018). Applications of nanoparticle systems in drug delivery technology. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society, 26(1), 64–70. https://doi.org/10.1016/j.jsps.2017.10.012
- [74]. Ang, K. H., Tamborlane, W. V., & Weinzimer, S. A. (2015). Combining glucose monitoring and insulin delivery into a single device: current progress and ongoing challenges of the artificial pancreas. Expert opinion on drug delivery, 12(10), 1579–1582. https://doi.org/10.1517/17425247.2015.1074174
- [75]. Ernst, A. U., Bowers, D. T., Wang, L. H., Shariati, K., Plesser, M. D., Brown, N. K., Mehrabyan, T., & Ma, M. (2019). Nanotechnology in cell replacement therapies for type 1 diabetes. Advanced drug delivery reviews, 139, 116–138. https://doi.org/10.1016/j.addr.2019.01.013
- [76]. Alghamdi, M. A., Fallica, A. N., Virzì, N., Kesharwani, P., Pittalà, V., & Greish, K. (2022). The Promise of Nanotechnology in Personalized Medicine. Journal of personalized medicine, 12(5), 673. https://doi.org/10.3390/jpm12050673

- [77]. Rodriguez-León, C., Villalonga, C., Munoz-Torres, M., Ruiz, J. R., & Banos, O. (2021). Mobile and Wearable Technology for the Monitoring of Diabetes-Related Parameters: Systematic Review. JMIR mHealth and uHealth, 9(6), e25138. https://doi.org/10.2196/25138
- [78]. Simos, Y. V., Spyrou, K., Patila, M., Karouta, N., Stamatis, H., Gournis, D., Dounousi, E., & Peschos, D. (2021). Trends of nanotechnology in type 2 diabetes mellitus treatment. Asian journal of pharmaceutical sciences, 16(1), 62–76. https://doi.org/10.1016/j.ajps.2020.05.001