

## CURRENT PERSPECTIVES ON USING NANOPARTICLES FOR DIABETES MANAGEMENT

NITESH KUMAR YADAV<sup>1</sup>, RUPA MAZUMDER<sup>1\*</sup>, ANJNA RANI<sup>1</sup>, ARVIND KUMAR<sup>1</sup>

Noida Institute of Engineering and Technology (Pharmacy Institute), Greater Noida, Uttar Pradesh-201306, India

\*Corresponding author: Rupa Mazumder; Email: rupa\_mazumder@rediffmail.com

Received: 08 Apr 2024, Revised and Accepted: 02 Jul 2024

### ABSTRACT

If ignored, Diabetes Mellitus (DM), a chronic metabolic disease marked by high levels of blood glucose, can have serious negative effects on one's health. The efficacy, safety, and patient compliance of traditional treatment approaches, like insulin injections and oral medications, are frequently hampered. Nanoparticle-based methods have shown promise in recent years as improved diabetes management techniques. Enhanced bioavailability, prolonged therapeutic effects, and targeted drug delivery are just a few of the special benefits that come with using nanoparticles. An overview of current perspectives on using nanoparticles for diabetes control is given in this review. The properties, production processes, and potential uses of several types of nanoparticles, such as polymeric, lipid-based, and inorganic nanoparticles, in the management of diabetes are covered. These nanoparticles allow for the precise delivery of therapeutic agents, such as insulin or anti-diabetic medications, to specific target tissues, like the liver or pancreas. It discusses how inorganic nanoparticles, Polymeric Nanoparticles (PNPs), and Lipid-Based Nanoparticles (LNPs) contribute to improved drug solubility, targeted delivery, and controlled release. Several methods for synthesizing polymeric nanoparticles are described. It also discusses the potential anti-inflammatory and antioxidant properties of some nanoparticles and how crucial they are to lowering diabetes-related issues. By incorporating the most recent research, this review offers a comprehensive summary of the current developments in the use of nanoparticles for diabetes control, paving the way for enhanced therapeutic outcomes and tailored interventions.

**Keywords:** Diabetes mellitus, Polymeric nanoparticles, Lipid-based nanoparticles, Inorganic nanoparticles

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DOI: <https://dx.doi.org/10.22159/ijap.2024v16i5.51084> Journal homepage: <https://innovareacademics.in/journals/index.php/ijap>

### INTRODUCTION

Diabetes Mellitus (DM) is a complex metabolic disorder marked by persistent high blood glucose levels (hyperglycemia) caused by anomalies in the secretion or action of insulin. It involves chronic and diverse dysfunctions in carbohydrate, fat, and protein metabolism, following a progressive and heterogeneous pattern [1, 2]. There are mainly two types of DM. Although there is a strong hereditary component to type 1 DM (T1DM), environmental factors are also believed to be involved in the etiology of the disease. The autoimmune destruction of  $\beta$  cells may be triggered by these factors, or they may quicken a continuing process. Though conclusive causality is yet unknown, viral illnesses such as enteroviruses, Cytomegalovirus, coxsackie virus B, mumps, and rubella have been linked to T1DM [3]. Type 2 Diabetes (T2D), is characterized by a progressive dysfunction in insulin secretion coupled with insulin resistance [4]. It constitutes about 90% of all cases of diabetes [5]. Aging, obesity, a family history of diabetes, physical inactivity, and embracing contemporary lifestyles have all been linked more frequently to T2D [2]. The United States, India, Brazil, China, the United Kingdom, Russia, Algeria, Saudi Arabia, Nigeria, and Germany have the highest rates of new T1DM diagnoses among children under the age of fifteen (around 96,000 cases yearly), based on information made public by the International Diabetes Federation (IDF) in 2017. This represented about 60% of all new cases [6]. By 2030, the number of individuals with T2D globally is estimated to make it to 7079 per 100,000, highlighting persistent growth in all parts of the world. Concerning indications indicate that prevalence is on the rise in lower-income nations [7]. Diabetes is more than just a condition marked by elevated blood sugar. It usually has a great deal of problems. Hyperosmolar nonketotic coma and hyperglycemic acidosis are two acute effects of uncontrolled diabetes. Many tissue injuries that result in cardiovascular disorders, renal failure, eye damage, seizures, podiatric ulcers, compromised immunity, and reduced eyesight are among the long-term effects. Several other dysfunctions have been recognized, such as imbalances in electrolytes, high weight, organ inflammation, stroke, lipid abnormalities, and peripheral coronary diseases [8, 9]. DM affects millions of people, and its effects go beyond personal health to put a burden on economics and healthcare systems around the world. There is a need for immediate clinical preventative and public health actions [10].

Even with the extensive use of several antidiabetic medications for diabetes control, a full and effective recovery is still unattainable. Problems include the danger of hypoglycemia, difficulty in intelligently altering dose forms depending on glucose fluctuations, and insufficient drug concentrations in target locations owing to chemical instability and vulnerability to degradation. In addition, there are obstacles such as limited bioavailability, short plasma half-life, restricted therapeutic window, short absorption efficiency, and inadequate patient compliance [11]. It is well recognized that taking insulin orally causes limited bioavailability and inadequate therapeutic impact because of the polypeptide's physiological instability, which is caused by the Gastrointestinal Tract's (GIT) enzymatic and chemical breakdown coupled with its rapid systemic clearance [12]. Improving diabetes treatment requires addressing these problems. Herein lies the pivotal role of nanoparticles in revolutionizing diabetes treatment. Because of their distinctive biological, physical, optical, chemical, and magnetic characteristics, nanoparticles are useful for diagnostic applications, especially in glucose biosensors that detect diabetes early. One common enzyme in biosensors, Glucose Oxidase (GO), has difficulties because of its low electron transfer efficiency. To improve the efficacy of enzyme-based biosensors, nanomaterials with greater conductivity, such as graphene and Gold Nanoparticles (AuNPs), are being investigated. Nanoparticles such as graphene, AuNPs, Cadmium Telluride (CdTe) quantum dots, and carbon nanotubes have been used in several studies, showing enhanced sensitivity and better electron transport characteristics in glucose biosensors. Notably, protein nanoparticles exhibit attomolar sensitivity and function as ultrasensitive probes for the detection of disease indicators, including autoantibodies linked to T1DM. The use of nanoparticles in biosensors can progress in the area of diagnosis allowing early management of diabetes [13]. Drug delivery methods using nanoparticles are essential for increasing the bioavailability and bioactivity of pharmaceuticals. These multipurpose nano-formulations can be used to treat illnesses ranging from minor ailments to life-threatening conditions, as well as in nanoscale Drug Delivery Systems (DDS), nanomachines, and nanorobots. By addressing drug absorption, distribution, metabolism, and excretion, nanoparticles dramatically improve pharmacokinetic parameters and improve therapeutic results. Enhanced bioavailability and solubility, prolonged drug release, targeted distribution, lower dose needs, and fewer adverse effects

are just a few of the notable benefits of nanoparticles [14]. Because of their specific reaction to certain stimuli and ability to release their payloads solely at the region of interest, stimuli-responsive nanoparticles formulations have demonstrated great promise in addressing issues related to premature or off-target drug release [15]. Enhancing the transport of nanoparticles across the layer of epithelium can be achieved by receptor-mediated endocytosis, specifically through transcytosis. Ligand functionalization promotes particular receptor recognition, which increases cellular absorption. Examples of ligands that do this include vitamin B12, Apical Sodium-Dependent Bile Acid Transporter (ASBT), Neonatal Fc Receptor (FcRn), CSKSSDYQC (CSK) peptide, folic acid, transferrin, butyrate, and zwitterions [16] (fig. 1). Combination therapy can be made possible by the ability of nanoparticles to co-deliver multiple medications simultaneously, addressing various areas of diabetic pathology at once [17]. Personalized medicine in the treatment of diabetes is made possible by nanoparticles, which allow for the

customization of DDS to best suit the needs of each patient [18]. Nanoparticles may reduce the need for invasive procedures by offering alternative techniques for administering drugs, including buccal or transdermal delivery [19, 20]. Inhaled insulin is administered directly into the bloodstream by inhalers. It is encapsulated in nanoparticles inside dry powder formulations. Insulin breakdown is avoided using this technique. It does, however, require patients to undergo frequent, somewhat expensive pulmonary function testing [21]. Nanoparticles are a promising new tool in regenerative medicine that can help deliver therapeutic molecules for tissue regeneration and repair in issues associated with diabetes [22]. We thoroughly searched the databases in MEDLINE, Scopus, Science Direct, PubMed, and Google Scholar. Diabetes mellitus, polymeric nanoparticles, lipid-based nanoparticles, and inorganic nanoparticles were among the search phrases used. We went through more than 90 published papers from 2001 to 2024.

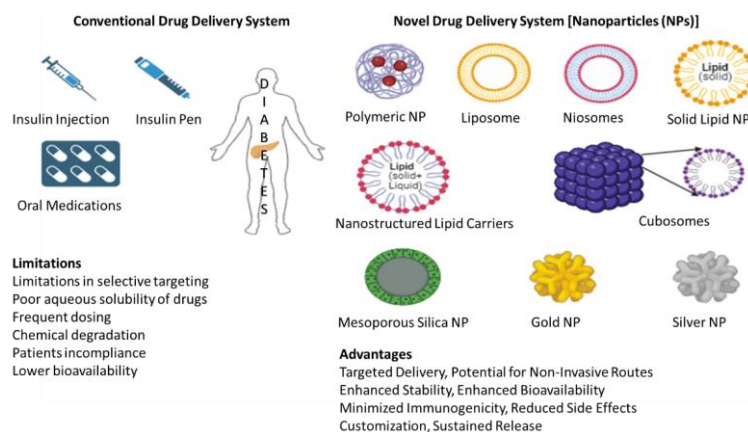


Fig. 1: Benefits of nanoparticles over conventional drug delivery system [23]

### Polymeric nanoparticles

The term "Polymeric Nanoparticles (PNPs)" describes particles made of polymers at the nanoscale. Large molecules known as polymers are composed of monomers, which are repeating components. These polymers can produce nanoparticles with special characteristics and are used when they are organized at the nanoscale [24]. The main ingredient in PNPs is polymer, which is combined with other elements to create the particles. Natural and synthetic polymers are the two main kinds of polymers used in the formation of PNPs. Natural polymers, including gelatin, chitosan, albumin, sodium alginate, and synthetic polymers like polycaprolactone, Poly(Lactide Co-Glycolides) (PLGA), polyglycolides, Poly malic acid, Poly(methyl methacrylate) and polyactides are commonly used [25, 26]. Achieving adaptation goals such as biocompatibility, biodegradability, and guaranteeing non-antigenicity and non-toxicity depend heavily on the choice of polymers [27]. Researchers may modify the stability, targeting capabilities, and drug-release kinetics of PNPs by choosing certain polymers [28]. In the GIT, chitosan nanoparticles have mucoadhesive qualities and the ability to affect molecular processes such as lysosome degradation, claudin-4 redistribution, tight junction weakening, and enhanced paracellular permeability [29, 30]. Alginate is a pH-responsive and mucoadhesive polymer. The polymer's guluronic acid acts like a magnet for divalent ions, forming a gel-like net that captures and stores insulin within the nanoparticles through an ion exchange process [31]. PNPs exist in various forms such as Polymeric Nanospheres, Polymeric Nanocapsules, Polymeric Micelles, Polymeric Nanogels, Polymeric Dendrimers, Polymeric Nanorods, Polymeric Nanofibers [32, 33]. The target location, the kind of medication contained, and the intended drug release profile all influence the choice of PNPs. Researchers consistently investigate novel polymeric substances and compositions to enhance the effectiveness and stability of pharmaceutical delivery mechanisms [34, 35]. Some of the recent

work on PNPs in the field of diabetes management is mentioned in table 1.

### Synthesis methods for polymeric nanoparticles

#### Single emulsification method

It is the oldest technique for creating nanoparticles from preformed polymers and is particularly used for encapsulating hydrophobic compounds and drugs that are primarily insoluble in water. During emulsification and subsequent evaporation, the drug and polymer are dissolved together in an organic phase in this process, which helps to produce the interfaces that are essential for drug entrapment. But when it comes to hydrophilic drugs like peptides, proteins, and vaccinations, their effectiveness diminishes. The use of the emulsification technique for hydrophilic drugs is limited because it leads to quick diffusion of these compounds into the outer aqueous phase, which causes poor loading and low encapsulation efficiencies [36].

#### Double emulsion-solvent evaporation method (W1/O/W2)

With the addition of a crucial third emulsion phase for increased encapsulation efficiency and quick solidification, it is an improved method for the encapsulation of hydrophilic drugs. The process requires the evaporation of the organic solvent to transform the emulsion into a nanoparticle suspension. Because W/O/W emulsion is thermodynamically unstable, a rapid procedure is essential. Double-emulsion droplet rapid solidification greatly increases encapsulation efficiency. During the first water-in-oil emulsion, it is critical to quickly deposit a polymer barrier to maximize efficiency and inhibit drug penetration into the organic phase. This is accomplished by either raising the concentration of the stabilizer in the inner aqueous phase to enhance viscosity or employing a high concentration of a high molecular weight polymer in the oil phase. Recovering, cleaning, and lyophilizing the nanoparticles are steps in the finalization processes shown in fig. 2 [36].

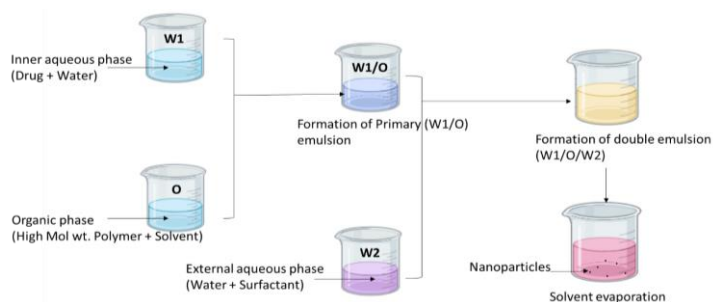


Fig. 2: Preparation of polymeric nanoparticles by double solvent evaporation method [37]

**Nanoprecipitation**

A nanoprecipitation technique entails dissolving the drug and the polymer in a water-miscible organic solvent. Next, while stirring continuously, this solution is gradually added drop by drop to an aqueous phase. When there is water present, the solvent diffuses quickly, causing nanoparticles to develop on their own as shown in fig. 3 the benefit of this technique is its simplicity, which makes it a

rather simple and scalable procedure. Precise control over the mixing process is a difficulty in traditional nanoprecipitation procedures, making it difficult to precisely regulate interactions during nanoparticles production. When compared to more sophisticated technologies like flash nanoprecipitation and microfluidic-based approaches, these techniques could produce bigger particle sizes with wider size distributions [38].

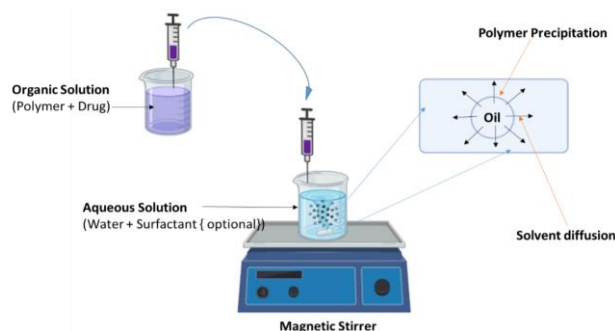


Fig. 3: Preparation of polymeric nanoparticles by nanoprecipitation technique [39]

Table 1: Recent advancements in PNPs in the management of DM

| Polymers used   | Drug encapsulated           | Synthesis method  | Size (nm)      | Encapsulation efficiency % | Effect in <i>in vivo</i> and <i>in vitro</i>  | Reference (s) |
|---|-----------------------------|---|----------------|----------------------------|---|---------------|
| Polyethylene glycol (PEG)   | Insulin                     | Self-assembly method of nanoprecipitation                       | 91.06±2.01     | 53.94±0.05                 | Enhanced the stronger hypoglycemic response in diabetic rats, Achieved a remarkable 9.28% relative bioavailability                                  | [40]          |
| Eudragit RSPO   | Alogliptin                  | Nanoprecipitation   | 290.34±3.24    | 95.45±2.65                 | Enhanced oral bioavailability and anti-diabetic effect  | [41]          |
| Eudragit  | Empagliflozin               | Emulsification solvent evaporation                              | 270.03         | 95.82                      | Showed significant antidiabetic action in <i>in vivo</i> and <i>in vitro</i> studies.   | [42]          |
| Chitosan and gum arabic   | Glycyrrhizin                | Ionotropic gelation   | 181.4 nm       | 99.8                       | Significant anti-diabetic effect  | [43]          |
| Eudragit, tween 80 and Polyvinyl Alcohol (PVA)  | Sitagliptin                 | Combined technique of solvent evaporation and nanoprecipitation | 135.29±5.12 nm | 82.34±3.27                 | Produce sustained and prolonged action, enhance the permeation across the intestinal mucosa, and successfully reduce the elevated blood sugar level | [44]          |
| Poly (ε-caprolactone), PVA  | Nateglinide                 | Emulsion solvent evaporation                                    | 310.40±11.42   | 64.09± 4.27%               |   | [45]          |
| Chitosan  | Polydatin                   | Modified ionic gelation method                                  | 144.25±3.37    | 96.74±0.39%                | Prolonged release pattern, much greater antidiabetic effectiveness in diabetic rats compared to free Polydatin                                      | [46]          |
| PLGA  | Diospyros melanoxylon Roxb. | Emulsion solvent evaporation                                    | 365.7 nm       | 60.67%.                    |   | [47]          |
| Chitosan, Polyethylene Glycol (PEG), PLGA   | Pioglitazone                | Single emulsion solvent evaporation                             | 813.25         | 48.93                      | Prolonged potency of nanoparticles <i>in vivo</i> than pure drug  | [48]          |
| Conjugated Linoleic Acid (CLA) linked to Carboxymethyl Chitosan (CMCS forming CLA-CMCS (CC), Grafting Arginine to CC via amide bonding resulting in a novel CLA-CMCS-Arg (CCA) polymer. | Insulin                     | A combination of several techniques                             | 203.4±3.42     | 83.78±3.73                 | Enhanced transdermal delivery, controlled release   | [49]          |
| Acryloyl crosslinked dextran dialdehyde   | Human insulin               |   | 75 nm          | 48.68                      | Glucose-sensitive insulin release   | [50]          |
| Waxy maize starch (>98% amylopectin)  | Insulin                     | Combination of gelatinization and coacervation                  | 100-300        | 69.73                      | Glucose-sensitive insulin release   | [51]          |

### Lipid-based nanoparticles (LNPs)

Lipids and surfactants are the main constituents of LNPs, while occasionally other functional molecules are also present. The structural framework of the nanoparticles is formed by lipids, which act as the building blocks. Surfactants help to stabilize the nanoparticles, keep them from aggregating, and make sure they are distributed uniformly. To impart certain qualities, such as ligand targeting for targeted distribution, additional functional molecules may be added [52]. Active Pharmaceutical Ingredients (API) loading in a lipid system can improve solubility in water, leading to high bioavailability. Additionally, lipid-based systems prevent API oxidation, breakdown, and decomposition while improving delivery and storage [53]. LNPs provide easy surface modification and tailored distribution via many pathways. Pharmaceutical research is becoming more interested in them because they offer stability, less toxicity, and controlled release. The *in vivo* destiny of LNPs is determined by their size, composition, and surface features [54]. There are various types of lipid-based DDS namely liposomes, niosomes, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs), cubosomes, exosomes, etc. each of them having specific advantages over others [52, 55-57].

#### Liposomes

Hydrophilic as well as hydrophobic drugs can be encapsulated in liposomes, which are spherical structures with an aqueous space within and hydrophobic lipid bilayers outside that protect the drugs from enzyme destruction. Similar to cell membranes, their bilayer shape improves absorption by intestinal cells. There are three varieties of liposomes: cationic, anionic, and neutral. Because of their hydrophilic and electroneutral surface, neutral liposomes are better at penetrating mucus [16].

#### Solid lipid nanoparticles

SLNs are 50–1000 nm-sized colloidal DDS. They consist of a solid biodegradable lipid core made up of fatty acids, complicated glyceride mixes, and mono-, di-, or triglycerides. An exterior aqueous surfactant dispersion of Tween 80, poloxamers, soy lecithin, or sodium dodecyl sulfate stabilizes the lipid core [57, 58]. The use of physiological lipids, the avoidance of organic solvents, a potentially broad application range (intravenous, pulmonary, cutaneous), sustained drug release, better stability, better % entrapment efficiency and Drug Loading percentage (%DL), compatibility with hydrophilic and lipophilic drugs, biocompatibility and biodegradability, cost-effectiveness, and high-pressure

homogenization as a tried-and-true manufacturing process are all benefits of SLN [59-61].

#### Nanostructured lipid carriers

With a distinct lipid matrix nanostructure, a new class of NLCs has surfaced that improves drug loading and maintains stability throughout storage. This technique, which produces lipid particle dispersions with solid concentrations ranging from 30% to 80%, involves high-pressure homogenization. By combining liquid and solid lipids, the novel method produces a matrix that has a lower melting point yet is still solid at body temperature [59]. Three types of NLCs exist Type I has an imperfect crystal core that hinders drug expulsion; Type II has an amorphous, structureless core because the solid lipid is polymorphic; and type III is an oil-in-solid fat-in-water (O/F/W) system that works well for drugs that are more soluble in liquid lipid/oil than in solid lipid. Because of their unique structures and compositions, NLCs minimize problems that are related to SLNs and provide better stability, reduced drug ejection, and greater drug loading [62, 63].

#### Cubosomes

Cubosomes are nanocarriers with bicontinuous cubic phases formed by dispersing cubic liquid crystalline aggregates in an aqueous medium. Using amphiphilic lipids like glycerol monooleate and phytantriol, cubosomes self-assemble in an aqueous medium to form structures that resemble honeycombs and range in size from 100 to 500 nm. Cubosomes are noteworthy for having a large surface area and a microstructure that is identical to parent cubic aggregates. This makes them promising for several uses, such as drug delivery and nanotechnology [64].

#### Niosomes

Niosomes are nonionic surfactant-based vesicles. The structure and physical characteristics of niosomes are comparable to those of liposomes. Additionally, they are prepared as single- or multilamellar vesicles using the same techniques and conditions [65]. Despite having similarities niosomes are an alternative to liposomes because of their advantages over the latter. Given that the phospholipids that make up liposomes are chemically fragile, niosomes have superior chemical stability. Niosomes are less expensive than liposomes and don't require the same handling, storage, or purification procedures for phospholipids as liposomes do [66]. Table 2 presents recent advancements in LNPs within the realm of diabetes management, including the type of drug encapsulated, other components utilized, preparation methods, and key advantages.

**Table 2: Recent advancements: characteristics and advantages of lipid-based nanoparticles**

| Lipid-based NP type                            | Drug encapsulated                                       | Other component used  | Preparation method                         | Key advantages   | Reference (s) |
|--|---|---|--|--|---------------|
| Thiamine/nonmodified liposome<br>Nano liposome | Recombinant human insulin                               | Soybean phosphatidylcholine, cholesterol, thiamine, niacin  | Reversed-phase evaporation                 | 72-81% glucose level reduction   | [67]          |
|  | Recombinant Cas9-RNP complex                            | Lecithin, cholesterol, 1,2-dioleoyl-sn-glycerol-3-[(N-(5-Amino-1-Carboxypentyl) Iminodiacetic Acid) Succinyl] (Nickel salt) DOGS-NTA-Ni | Lipid film formation, fluorescent labeling | Successful gene editing with low cytotoxicity, stable <i>in vivo</i> delivery  | [68]          |
| Solid lipid nanoparticles                      | Gliclazide  | Glyceryl behenate, poloxamer 188  | Ultra-sonication technique                 | Biphasic <i>in vitro</i> release consisting of a prolonged release phase after an initial burst effect, a 5-fold increase in GLZ oral BA loaded in slns, better anti-diabetic action | [69]          |
| Pegylated slns                                 | Metformin hydrochloride                                 | Phospholipon®, sorbitol, polyethylene glycol 4000, beeswax, Tween® 80   | Fusion method                              | Pegylated slns showed greater diabetic control than the commercial formulation (Glucophage®) after 24 h.   | [70]          |
| SLN suspensions                                | Extracts of <i>P. Acaciae</i> and <i>P. Curviflorus</i> | Sodium Dodecyl Sulfate (SDS)  | Emulsion solvent evaporation               | Better antihyperglycemic and antioxidant activities.   | [71]          |
| SLNs   | <i>Murraya koenigii</i> leaves extract (murrayanol)     |   | Solvent diffusion method                   | Prolonged release, superior to commercially available synthetic anti-diabetic medications.   | [72]          |
| SLNs   | Tetrahydrocurcumin                                      | Glyceryl monostearate, soy lecithin, tween 80   | Emulsification followed by sonication      | Rapid burst at first followed by control release, greater bioavailability, and antidiabetic action than ordinary drug dispersion   | [73]          |
| Cumbersome                                     | Gliclazide  | Glyceryl monooleate, poloxamer 407  | Emulsification method                      | A doubled up on the bioavailability relative to plain gliclazide suspension  | [56]          |
| Niosomes                                       | Metformin hcl and glipizide                             | Tween 80, phosphate buffer saline, cholesterol, chloroform, methanol  | Thin film hydration                        | Sustained release of the drugs   | [55]          |

## Inorganic nanoparticles

Inorganic nanoparticles are nanoscale particles composed of non-carbon-based elements, including metals, metal oxides, and other inorganic materials [74]. Because of their inherent qualities, which are unavailable and unpossessed in their conventional polymer-based or organic counterparts, such as tunable morphology, desirable physiological stability, simple functionalization, and unique physiochemical properties like optical, acoustic, electrical, and magnetic natures, inorganic nanoparticles among these designs hold great promise [75]. Within the realm of medicine, inorganic nanoparticles are being investigated for targeted drug delivery. This approach involves encasing or attaching drugs to the surface of the nanoparticles, so enabling controlled release and improved therapeutic effectiveness [76]. Several inorganic elements have demonstrated antidiabetic properties *in vitro* and/or *in vivo*. These

elements include silver, iron, magnesium, zinc, copper, chromium, selenium, vanadium, palladium, platinum, nickel, titanium, gold, molybdenum, cerium, manganese, and tungsten. They do this through a variety of mechanisms, such as increasing levels of antioxidant enzymes, glucose utilization, and insulin sensitivity [77]. Inorganic nanoparticles, including zinc oxide and silver nanoparticles, display antibacterial characteristics that can help in wound healing, particularly significant for diabetes patients prone to delayed wound healing [78]. Some inorganic nanoparticles such as AUNP have antiangiogenic properties, which might affect the development of new blood vessels while plant-mediated synthesis of silver nanoparticles possesses potential antimicrobial applications and helps control diabetic retinopathy [79, 80]. Table 3 provides an overview of Inorganic nanoparticles, detailing their synthesizing method, size in nanometers (nm), surface functionalization, and antidiabetic mechanism.

**Table 3: Characteristics of inorganic nanoparticles and their role in antidiabetic mechanisms**

| Inorganic nanoparticles         | Synthesizing method   | Size (nm) | Surface functionalization   | Antidiabetic mechanism   | Reference (s) |
|---------------------------------|---|-----------|---|--|---------------|
| AuNPs                           | Bioreduction of auric chloride using phytoconstituents present in <i>Eclipta alba</i> (green synthesis) | 26.6      | <i>Eclipta alba</i>   | Prevent $\beta$ -cell damage induced by streptozotocin in <i>rin-5f</i> cells.   | [81]          |
| Silver nanoparticles            | Green synthesis   | 250–800   | <i>Galaxaura elongata</i> {GE}, <i>Turbinaria ornata</i> {TO} and <i>Enteromorpha flexuosa</i> {EF} |  | [82]          |
| Mesoporous silica nanoparticles | The Stober method with silane polymerization  | 50–130    | Morin   | Compared to traditional inhibitors, Morin interacts with $\alpha$ -amylase and $\alpha$ -glucosidase more well at the molecular level. | [83]          |
| Selenium nanoparticles          | Chemical synthesis  | 50        | <i>Catathelasma ventricosum</i>   | Improve cholesterol levels, blood sugar, antioxidant enzyme activity, and body weight.   | [84]          |
| Zinc oxide nanoparticles        | Solution combustion synthesis   | 29        | <i>Areca catechu</i> leaves extract   | Inhibit carbohydrate digestive enzymes   | [85]          |
| Silver nanoparticles            | Green synthesis   | 34        | Seed extract of <i>N. Sativa</i>  | Increased inhibition of Dipeptidyl peptidase-IV, $\alpha$ -glucosidase, and $\alpha$ -amylase  | [86]          |
| Silver nanoparticles            | Green synthesis   | >100      | <i>Cucumis melo</i> L. Leaf   | Inhibition of $\alpha$ -amylase and $\alpha$ -glucosidase  | [87]          |
| Mesoporous silica nanoparticles | Chemical synthesis  | 120       | Insulin, camp   | Glucose triggered the release of insulin and camp  | [88]          |

## CONCLUSION

The fascinating potential of nanotechnology to transform the treatment of diabetes has been examined in this paper. Conventional treatments frequently include drawbacks such as limited absorption, dosing difficulties, and the possibility of hypoglycemia. Targeted distribution, controlled release, and improved drug solubility are among the special qualities that nanoparticles provide, overcoming these drawbacks and opening the door to more efficient and individualized treatment modalities.

The review demonstrated the noteworthy contributions of polymeric, lipid-based, and inorganic nanoparticles, offering encouraging directions for better therapeutic interventions. Liposomes, SLNs, and NLCs are useful tools in the lipid-based approach, and methods like double emulsion-solvent evaporation and single emulsification show promise for the controlled synthesis of PNPs. Interestingly, in addition to helping transport drugs, inorganic nanoparticles may also have anti-inflammatory and antioxidant qualities that may reduce the complications associated with diabetes.

Even though there has been a lot of development, further study is necessary to improve nanoparticles systems, handle any safety issues, and convert preclinical results into clinical uses. Scalability, long-term safety profiles, and regulatory obstacles must all be addressed if this technology is to reach its full potential. However, the current developments show promise for the use of nanotechnology to provide effective and individualized diabetes management in the future. This could lead to better treatment outcomes, fewer complications from diabetes, and eventually, a higher standard of living for the millions of people who suffer from this chronic illness.

## ACKNOWLEDGEMENT

The authors express their gratitude to the faculty members of the Noida Institute of Engineering and Technology (Pharmacy Institute)

and other supporting staff members for their invaluable contributions to the preparation of the review article.

## FUNDING

Nil

## AUTHORS CONTRIBUTIONS

Nitesh Kumar Yadav conceptualized and initially wrote the paper. Rupa Mazumder, the corresponding author, was responsible for the design and final revision. Anjna Rani handled data collection and interpretation, while Arvind Kumar performed the quality check on the manuscript.

## CONFLICT OF INTERESTS

There is no conflict of interest among the authors of the review article.

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