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Nanotechnology-Enabled Drug Delivery Systems for Enhanced Antidiabetic Therapy: A Comprehensive Review

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Abstract

Context: Diabetes mellitus remains one of the most prevalent and challenging metabolic disorders worldwide. Despite the availability of numerous pharmacological agents, conventional antidiabetic therapies often face limitations such as poor bioavailability, low stability, and undesirable side effects. Recent advances in nanotechnology have provided innovative strategies for improving drug delivery, enabling controlled release, enhanced solubility, and targeted transport of therapeutic agents.

Evidence Acquisition: This review systematically compiles and analyzes recent publications from 2015 to 2025 focusing on nanotechnology-based drug delivery systems for diabetes management. Relevant literature was retrieved from scientific databases including Scopus, PubMed, and ScienceDirect using keywords such as “nanocarriers,” “antidiabetic therapy,” “controlled release,” and “targeted drug delivery.” Studies were selected for inclusion based on their contribution to advances in nanocarrier design, drug encapsulation efficiency, pharmacokinetic improvement, and therapeutic outcomes.

Results: A range of nanocarrier systems, including polymeric nanoparticles, liposomes, micelles, dendrimers, and metallic nanoparticles, have demonstrated superior delivery performance compared to traditional formulations. These platforms enhance glucose control, improve insulin bioavailability, and reduce systemic toxicity. Furthermore, functionalization and surface modification techniques have enabled site-specific delivery and stimuli-responsive drug release. Experimental and preclinical findings indicate that nanocarriers can significantly enhance therapeutic efficacy while minimizing side effects.

Conclusions: Nanotechnology-enabled drug delivery represents a transformative approach to diabetes management by addressing the shortcomings of conventional therapies. Continued progress in nanoparticle design, biocompatibility, and

large-scale production will be essential for clinical translation. This review highlights the critical role of nanocarrier-based strategies in developing next-generation antidiabetic therapeutics. From a patient-centered clinical perspective, nanotechnology-enabled drug delivery systems improve the bioavailability, efficacy, and consistency of antidiabetic therapies through controlled and targeted drug release. These advantages can reduce dosing frequency and side effects, thereby enhancing patient adherence and enabling safer, more effective diabetes management in real-world clinical practice.

Keywords: Nanocarrier; Chitosan-Calcium Alginate; Empagliflozin; Drug Delivery Systems; Dapagliflozin Delivery Eudragit; Vitamin E; Nanoliposome Nanocarrier

Introduction

Diabetes is a chronic disease in which the body cannot properly use or store glucose. Glucose is a type of sugar that raises blood sugar levels if it accumulates in the blood. Diabetes occurs when the pancreas is no longer able to produce insulin, or the body is unable to use the insulin produced properly. Insulin is a hormone secreted by the pancreas that acts like a switch, allowing glucose to enter the body's cells from the bloodstream for energy. All carbohydrate foods are broken down into glucose in the body. The hormone insulin helps glucose enter the cells. Inability to produce insulin or to use it effectively leads to an increase in the level of glucose in the blood, which is called hyperglycemia. In the long term, high blood glucose levels are associated with damage to the body and failure of various organs and tissues [1, 2].

According to the latest reports from the International Diabetes Federation (IDF) and the World Health Organization (WHO), the prevalence of diabetes worldwide is increasing alarmingly. In 2021, about 537 million people between the ages of 20 and 79 were diagnosed with diabetes. This year, diabetes caused 6.7 million deaths worldwide. It is predicted that this number will reach 643 million by 2030 and 783 million by 2045. More than 75% of these people live in low- and middle-income countries [3].

Several review articles have addressed the application of nanotechnology-based drug delivery systems in diabetes management, often focusing on specific nanocarrier classes or selected therapeutic agents. This review aims to complement the existing literature by compiling and organizing recent studies published between 2015 and 2025, with a focus on controlled and targeted drug delivery, pharmacokinetic considerations, and therapeutic outcomes. By presenting a structured overview of polymeric, lipid-based, vesicular, and hybrid nanocarrier systems, including examples relevant to SGLT2 inhibitors, this review aims to provide a clear and balanced reference for researchers and clinicians interested in antidiabetic drug delivery strategies.

Diabetes Types

Type 1 diabetes is treated with insulin injections. In type 2 diabetes, in addition to insulin, there are also different categories of oral or injectable drugs used to treat type 2 diabetes [4]. Each of these categories lowers blood sugar through a different mechanism.

Drug Treatment of Diabetes

Oral or injectable antidiabetic drugs lower blood sugar by different mechanisms. The mechanisms include:

- Stimulating the pancreas to produce insulin
- Inhibiting the production and release of glucose by the liver
- Inhibition of digestive enzymes that are responsible for breaking down carbohydrates in the stomach
- Improving the sensitivity of cells to insulin

- Inhibition of glucose reabsorption in the kidneys
- Regulating the passage of food through the stomach more quickly

Drug Delivery Systems

There are many different types of drug delivery systems, some of which have been well known for years (such as oral, mucosal, nasal, ocular, dermal, and vaginal drug delivery systems). There are also new techniques to deliver drugs to specific organs or tissues to treat various diseases. All drug delivery systems have advantages and disadvantages due to their specific characteristics [5].

Oral Drug Delivery Systems

Oral drug delivery is the most common and widely used method of drug administration. This type of drug delivery is easy, and there is a traditional belief that when administered orally, the drug is absorbed like food.

There are different forms of medication that are administered orally, including solid, semi-solid, or liquid, all of which can have different dosages. Most of them are of the immediate-release type, which are designed to release the drug immediately for rapid absorption.

Physiological features of the gastrointestinal tract must be considered for the manufacture of all drug products formulated for oral delivery, regardless of delivery mode (immediate, sustained, or controlled release) and drug form (solid, semi-solid, or liquid).

Although the use of this type of drug delivery is easy and often preferred for systemic administration, there are limitations such as elimination by gastrointestinal degradation and hepatic metabolism, low systemic bioavailability, short duration of therapeutic activity, and the formation of inactive or toxic metabolites [6].

Nanotechnology in Drug Delivery during the Transport Process Systems

Nanotechnology includes the production of nanoparticles with a diameter of 1 to 100 nm. There are different types of nanoparticles, such as micelles, liposomes, and hydrogels. This technology has made great progress in drug delivery systems by improving the solubility of hydrophobic drugs, increasing drug stability, reducing cytotoxic side effects, and reducing harmful effects on natural tissues.Nanotechnology has been widely used and studied to treat various types of cancers, arteriosclerosis, and other cardiovascular diseases.

Lipid-Based Drug Delivery Systems

Lipid-based drug delivery systems are used in anti-aging therapy to increase the solubility of hydrophobic drugs with a higher degree of biocompatibility and adaptability. By changing the composition, lipids improve the absorption of drugs from the intestinal environment, and they can also influence drug absorption, the rate of absorption, and the formation of metabolites **during the transport process**. Microemulsions, nanoemulsions, self-emulsifiers, solid lipid nanoparticles, and lipid nanostructure carriers are among these systems [7].

Vesicular Systems

Vesicular systems are colloidal in nature and consist of bilayers of concentric amphiphilic molecules surrounding an aqueous core. There are different vesicular systems such as niosomes, liposomes, micelles, niosomes, and transferosomes.The simplest use of liposomes is as a carrier for drugs and for the targeted delivery of antibodies. The medicinal properties of liposomes de-

pend on the composition of the lipid bilayer and its permeability and fluidity. The increasing use of liposomes in research, as well as cost-effective drug delivery, is often due to their biodegradability, biocompatibility, and low toxicity. They can entrap both lipophilic and hydrophilic drugs and facilitate targeted delivery [7].

Micelles

Micelles are a collection of amphiphilic molecules that are able to dissolve hydrophobic drugs. They form clusters after reaching a concentration equivalent to the critical micelle concentration. Their molecular structure and combinatorial behavior allow easy preparation of drug solutions stabilized by micelles. However, low stability in the body and limited drug loading capacity are weaknesses of this system and limit the use of micelles [7].

Polymer Nanoparticles

Nanoparticles are colloidal drug delivery systems that include particles in the size range of 10 to 1000 nm in diameter. The main advantage of encapsulating drugs in a nanoparticle-based delivery system is their high bioavailability, elimination of primary metabolism, and thus dose reduction and reduced drug toxicity to non-target cells. Drug delivery using nanoparticles reduces side effects, increases the local concentration of the drug, and also facilitates the rapid onset of action [7].

Table 1: Formulated Anti-Diabetic Drug Nanocarriers

No.	Drug Delivery System	Drug	Components Size (nm)	Drug Loading (%)	Drug Release (%)	Ref No.
1	Nanoliposomes (NLs)	Dapagliflozin	DGF@EDPEGVE (99.9 nm)	99.8	94.9	[8]
2		Sorafenib	NL-PEG-SOR FUM (80 nm)	99.08	52.4	[9]
3		Sorafenib	NL-PEG-SOR TOS (90 nm)	99	53.4	[9]
4	Nanoparticles (NPs)	Pioglitazone	Poloxamer 188 and Eudragit L100 NPs (138.8 nm; 160.5 ± 11.24–245.4 ± 15.96 nm)	97.38	98.22	[10]
5		Empagliflozin	EMP@CACSNC	81.65	77	[11]
6		Empagliflozin	EMP@CANC	58.4	94	[11]
7		Glipizide	PLGA NPs and Eudragit RS100 NPs (200 nm)	70	80	[12]
8		Metformin	Alginate NPs (60–150 nm)	78	100	[13]
9		Glibenclamide	HPMC K15M and lactose NPs (168.6 nm)	—	94.2	[14]
10		Repaglinide	PLGA and methoxypolyethylene glycol biodegradable NPs (310.2 ± 12.4 nm)	27.4	47.8	[15]
11	Micro-/Nano-emulsion	Repaglinide	Sefsol-218, Tween 80, and Transcutol nanoemulsion (76.23 nm)	—	98.22	[16]
12		Repaglinide	Span 80, Tween 80, olive oil, and acetone nanoemulsion (121.5 nm)	—	89.8	[17]

13	Self-emulsifying drug delivery systems (SEDDS)	Glipizide	Phosphatidylcholine (Phosal 53 MCT), Tween 80, and Transcutol P SEDDS (55.94 nm) / S-SEDDS (78.03 nm)	—	85	[18]
14		Pioglitazone	Tween 80, Polyethylene glycol 400, cottonseed oil SMEDDS (10.75 nm)	—	79	[19]
15	Solid Lipid Nanoparticles (SLNs) / Nanostructured Lipid Carriers (NLCs)	Exenatide	NLC of Precirol ATO 5, Miglyol, Tween 80, and Poloxamer 188 (161 ± 4 nm)	87.5	—	[20]
16	Vesicular systems	Metformin	Phosphatidylcholine and cholesterol multilamellar liposomes	—	83	[21]
17	Micelles	Repaglinide	Repaglinide–phospholipid complex enriched micelles with poloxamer 188 (525.79 ± 23.62 nm)	99.38	99.05	[22]
18	Nanoformulations in Transdermal Patches (TDP)	Glibenclamide	Chitosan and poloxamer 188 nanocrystals in TDP (429 nm)	92	85	[23]

A comparative characterization of drug delivery systems recently performed by our research group is based on empagliflozin and dapagliflozin nanocarriers, as shown in Table 2.

Table 2: Comparative Characteristics of Nanocarrier-Based Drug Delivery Systems for Empagliflozin and Dapagliflozin

No.	Drug Delivery System	Drug	Nanocarrier Composition Mean Size (nm)	Encapsulation / Drug Loading (%)	Cumulative Drug Release (%)	Release Medium / pH	Key Observations	Reference
1	Alginate–Chitosan Nanocarrier System	Empagliflozin (EMP@CACSNC)	Alginate–chitosan polyelectrolyte nanoparticles; ionic gelation; size ≈ not explicitly stated (typical range 60–150 nm)	81.65	77	Simulated intestinal fluid (pH 6.8)	Sustained release up to 24 h; reduced burst in acidic medium; suitable for oral controlled delivery	[11]
2	Alginate–Chitosan Nanocarrier System	Empagliflozin (EMP@CANC)	Alginate–chitosan nanoparticles (CANC); size ≈ 58.4 nm	58.4	94	Simulated intestinal fluid (pH 6.8)	High cumulative release at intestinal pH; gradual diffusion–erosion mechanism; high mucoadhesive stability	[11]
3	PEGylated Eudragit–Vitamin E Liposomal System (DGF@EDPEGVE)	Dapagliflozin	PEGylated Eudragit L30D-55 and Vitamin E liposomes; reverse-phase evaporation; size ≈ 99.9 nm	99.8	94.9	Intestinal buffer (pH 6.8–7.4)	Minimal release in gastric medium (~10–13% at pH 1.1); nearly complete release at intestinal pH within 12–24 h	[8]

* Typical nanoparticle size range based on reported alginate–chitosan formulations (60–150 nm) when not explicitly specified.

Both nanocarrier systems provide controlled and pH-responsive release suited to oral delivery of SGLT2 inhibitors. The alginate–chitosan systems (EMP@CACSNC, EMP@CANC) enable sustained release with improved bioavailability, while the PEGylated Eudragit–Vitamin E liposomal formulation (DGF@EDPEGVE) achieves almost complete encapsulation efficiency and targeted intestinal release. The combination of polymeric and lipidic nanostructures demonstrates strong potential for enhancing therapeutic efficacy and patient adherence in antidiabetic therapy.

Outlook

While nanotechnology-enabled drug delivery systems have demonstrated promising results in preclinical and experimental studies, several challenges remain before widespread clinical adoption can be achieved. Future research should focus on:

Clinical Translation: Large-scale, multicenter clinical trials are needed to validate the safety, efficacy, and reproducibility of nanocarrier-based antidiabetic therapies.

Scalability and Manufacturing: Developing cost-effective and standardized production methods will be essential to ensure consistent quality and regulatory approval.

Biocompatibility and Long-Term Safety: Comprehensive studies on the long-term biodistribution, metabolism, and potential toxicity of nanocarriers are required to ensure patient safety.

Personalized Medicine: Integration of nanocarrier systems with patient-specific factors, such as genetic background and disease progression, could enable precision dosing and individualized therapy.

Smart and Responsive Systems: Advances in stimuli-responsive nanocarriers (pH, glucose, enzyme, or temperature-sensitive) may further enhance controlled release and therapeutic outcomes.

Combination Therapies: Exploring nanocarrier platforms for co-delivery of multiple antidiabetic agents or synergistic compounds could improve glycemic control and reduce drug resistance.

By addressing these translational and practical considerations, nanotechnology-enabled drug delivery systems can move beyond experimental promise toward becoming a cornerstone of next-generation diabetes management.

Conclusion

Releasing drugs directly in the acidic environment of the stomach, in addition to causing rapid elimination of the drug in the biological environment due to the low half-life of the drug, may cause unwanted side effects for the patient due to the occurrence of unwanted reactions in this environment. Therefore, in more advanced and optimal applications, by encapsulating drugs, their release can be controlled from the point of view of time and place of release, so that they are released gradually and with appropriate dosage at the target location or at specific times.In the review of the above findings, by using different formulations and various pharmaceutical systems that are appropriate to the nature of the drug, in addition to the optimal use of the active pharmaceutical ingredient, the half-life of the drug in the body can be increased, and with its targeted release in the tissues, the therapeutic process can be more effective.Nanotechnology-enabled drug delivery represents a transformative approach to diabetes management by addressing the shortcomings of conventional therapies. Continued progress in nanoparticle design, biocompatibility, and large-scale production will be essential for clinical translation. This review highlights the critical role of nanocarrier-based strategies in developing next-generation antidiabetic therapeutics.

References

1. Alam U, Asghar O, Azmi S, Malik RA (2014) General Aspects of Diabetes Mellitus. Handbook of Clinical Neurology, 126: 211-22.

2. Poretsky L (2009) Principles of Diabetes Mellitus. Principles of Diabetes Mellitus, 2nd ed. Springer.

3. Whiting D, Guariguata L, Weil C, Shaw J (2011) IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Research and Clinical Practice, 94: 311-21.

4. Vigneri P, Frasca F, Sciacca L, Pandini G, Vigneri R (2009) Diabetes and Cancer. Endocrine-Related Cancer, 16: 1103-23.

5. Chien YW (1987) Nano-liposome Mediated Delivery of the Anti-diabetic Protein. Drug Development and industrial Pharmacy, 13: 589-651.

6. Chien Y (1991) Novel Drug Delivery Systems. CRC Press.

7. Uppal S, Italiya K S, Chitkara D, Mittal A (2018) Nanoparticulate-based Drug Delivery Systems for Small Molecule Anti-diabetic Drugs: An Emerging Paradigm for Effective Therapy. Acta Biomaterialia, 81: 20-42.

8. Pourhosein Parizad M, Khalili B, Mahmoodi NO (2025) Improving the Synthesis of Dapagliflozin and its New Homologs: An Investigation into the Release of a Liposomal Nano Drug Delivery System (DGF@EDPEGVE). Journal of Molecular Structure, 1346: 143-57.

9. Mahmoodi NO, Alavi SM, Yahyazadeh A (2022) Formulation and Therapeutic Efficacy of PEG-liposomes of Sorafenib for the Production of NL-PEG-SOR FUM and NL-PEG-SOR TOS. Research on Chemical Intermediates, 48: 3915-35.

10. Appana Chowdary K, Suravarapu NLR, Meddala S (2015) Formulation and Characterization of Pioglitazone Hydrochloride Nanoparticles. World Journal of Pharmacy and Pharmaceutical Sciences, 4: 1638-48.

11. Mahmoodi NA, Ramazanzadeh N (2022) Synthesis and Characterization of Alginate-Chitosan Nanocarrier System for Empagliflozin Delivery. Iranian Journal of Chemistry and Chemical Engineering, 41: 1107-18.

12. Naha PC, Byrne HJ, Panda AK (2013) Role of Polymeric Excipients on Controlled Release Profile of Glipizide from PLGA and Eudragit RS 100 Nanoparticles. Journal of Nanopharmaceutics and Drug Delivery, 1: 74-81.

13. Kumar S, Bhanjana G, Verma RK, Dhingra D, Dilbaghi N (2017) Metformin-loaded Alginate Nanoparticles as an Effective Antidiabetic Agent for Controlled Drug Release. Journal of Pharmacy and Pharmacology, 69: 143-50.

14. Deshpande RD, Gowda DV, Vegesna NSKV, Vaghela R, kulkami PK (2015) The Effect of Nanonization on Poorly Water Soluble Glibenclamide Using a Liquid Anti-solvent Precipitation Technique: Aqueous Solubility, In vitro and In vivo study. Royal Society of Chemistry, 99: 81728-38.

15. Jain S, Saraf S (2009) Repaglinide-loaded Long-circulating Biodegradable Nanoparticles: Rational Approach for the Management of Type 2 Diabetes Mellitus. Journal of Diabetes, 1: 29-35.

16. Akhtar J, Siddiqui HH, Fareed S, Badruddeen M, Aqil Khalid M (2016) Nanoemulsion: for Improved Oral Delivery of Repaglinide. Drug Delivery, 23: 2026-34.

17. Nanjwade BK, Varia PJ, Kadam VT, Srichana T, Kamble MS (2013) Development and Evaluation of Nanoemulsion of Repaglinide. JSM Nanotechnology and Nanomedicine, 1: 1016.

18. Agrawal AG, Kumar A, Gide PS (2015) Self Emulsifying Drug Delivery System for Enhanced Solubility and Dissolution of Glipizide. Colloids and Surfaces B: Biointerfaces, 126: 553-60.

19. Hyma P, Abbulu K (2013) Formulation and Characterisation of Self-microemulsifying Drug Delivery System of Pioglitazone. Biomedicine & Preventive Nutrition, 3: 345-50.

20. Shrestha N, Bouttefeux O, Vanvarenberg K, Lundquist P, Cunarro J, et al. (2018) The Stimulation of GLP-1 Secretion and Delivery of GLP-1 Agonists via Nanostructured Lipid Carriers. Nanoscale, 10: 603-13.

21. Divakar P, Kumar D, Praveen C, Sowmya C, Reddy CS (2013) Formulation and In vitro Evaluation of Liposomes Containing Metformin Hydrochloride. International Journal of Research in Pharmaceutical and Biomedical Sciences, 4: 479-85.

22. Kassem AA, El-Alim SHA, Basha M, Salama A (2017) Phospholipid Complex Enriched Micelles: A Novel Drug Delivery Approach for Promoting the Antidiabetic Effect of Repaglinide. European Journal of Pharmaceutical Sciences, 99: 75-84.

23. Ali H SM, Hanafy AF (2017) Glibenclamide Nanocrystals in a Biodegradable Chitosan Patch for Transdermal Delivery: Engineering, Formulation, and Evaluation. Journal of Pharmaceutical Sciences, 106: 402-10.