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Pharmaceutical Approaches for Sustained Release Drug Deliver in Diabetes Management

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ABSTRACT

Diabetes is one of the most common chronic diseases in the world, with 537 million adults worldwide living with it in 2021 and predictions estimating that the number may rise to over 783 million by 2045. Current immediate-release antidiabetic treatment options have limitations, such as short half-lives, large peak-trough fluctuations in plasma concentrations, and low patient compliance, leading to a strong interest in Sustained-Release (SR) drug delivery systems. In an effort to review advances in SR drug delivery systems, a wide variety of new technologies and methods have been established. The first section of this review will provide a detailed overview of advanced polymeric matrix systems and nano-carrier systems that help deliver SR drugs, including poly (Lactic-Co-Glycolic Acid) (PLGA), chitosan nanoparticles, Solid Lipid Nanoparticles (SLN), Nanostructured Lipid Carriers (NLC), liposomes, and dendrimers. The second section of this report will review new ways to deliver drugs, including experimental pH, glucose, and temperature-responsive hydrogels; gastroretentive formulations; transdermal systems using microneedles; and implantable systems.

The third section of this review will also discuss new technologies that may be used as SR delivery systems, including 3D-printed dosage forms, exosome-based delivery, oral insulin delivery systems using an excipient SNAC, and glucose-responsive "smart" systems. Pharmacokinetic advantages of these technologies, drug release mechanisms, currently available SR products on the market, regulatory issues, and future directions to connect research with diabetes care will also be discussed.

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Introduction

Diabetes Mellitus is a progressive chronic metabolic disorder of worldwide importance that is characterized by continuous high levels of glucose (sugar) in your bloodstream due to a failure in producing and/or using the hormone insulin. There were an estimated 537 million adults in the world with diabetes in 2021, and this number is expected to increase above 783 million by 2045 according to the International Diabetes Federation (IDF) [1]. There are two main types of diabetes: Type 1, which results from an auto-immune attack on the cells that produce insulin, and Type 2, which results from increasing resistance to the effects of insulin. Together, these represent over 95% of all people living with diabetes [2]. As of 2021, the total annual global expenditure on diabetes reached $966 billion USD [3]. Currently, pharmaceutical agents used for managing diabetes include, but are not limited to, insulin analogue formulations, biguanides, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors, and GLP1R agonists, however, despite the diversity of these classes of agents, the majority of people who require pharmacological management of their diabetes do not achieve optimal control of their blood glucose levels due to complex dosing regimens, inconsistent gastrointestinal absorption, metabolism of the medication by the liver prior to it entering the bloodstream, short half-life of the medications and fluctuations in drug plasma concentrations causing both side effects and treatment failures, thereby perpetuating the unmet need for other means of achieving satisfactory blood glucose control [4,5].

Sustained Release (SR) delivery systems overcome these limitations by maintaining plasma levels within the therapeutic range for a longer duration, reducing the frequency of dosing, minimizing the peak-to-trough variation of drug levels, and enhancing patient compliance [6]. The variety of SR drug delivery platforms (classical matrix tablets, stimuli-responsive hydrogels and smart microneedle arrays) indicates there have been many pharmaceutical innovations created for the benefit of managing diabetes. This review provides a critical and systematic review of all of the above types of platforms.

Antidiabetic Drug Classes and Rationale for Sustained Release

There are multiple types of antidiabetic medication, which can be classified into groups according to their mechanism of action: biguanides (i.e., metformin), sulfonylureas, meglitinides, thiazolidinediones or glitazones, DPP-4 inhibitors (gliptins) and SGLT2 inhibitors (i.e., gliflozins). Each group of drugs acts by a different mechanism to control blood glucose levels in individuals with Diabetes Mellitus (DM) although effective, when most of these drugs are administered as immediate release formulations, they do have limitations. Controlled Release (CR) Drug Delivery Systems are now available for many antidiabetic drugs to help

resolve problems associated with immediate release formulations. CR Drug Delivery Systems facilitate a controlled, continuous release of medication into the body over an extended period of time and allow for longer periods of time between dosing of the medication; thereby increasing patient compliance. In addition, many antidiabetic agents have dose-related adverse effects (primarily GI related) that occur secondary to rapid increases in plasma concentration after doses of the medication. CR Drug Delivery Systems provide for steady plasma concentrations of the medication and, thus, reduce the occurrence of dose-dependent adverse effects such as nausea or diarrhea. CR Drug Delivery Systems improve the ability of the formulation to mimic physiological conditions and function to provide the longest duration of therapeutic activity with the medication [7].

Table 1: Antidiabetic Drug Classes Mechanism of Action and Suitability for Sustained Release Formulation

S. No.	Drug Class	Representative Agents	Mechanism of Action	Suitability for SR
1.	Biguanides	Metformin	Inhibits hepatic gluconeogenesis; activates AMPK pathway	High – Short t½ 4–8h; reduces GI intolerance via SR
2.	Sulfonylureas	Glipizide, Glibenclamide	Stimulates β-cell insulin secretion via K^+-ATP channels	High – Reduces peak-related hypoglycemia risk
3.	DPP-4 Inhibitors	Sitagliptin, Vildagliptin	Inhibits DPP-4; prolongs incretin (GLP-1/GIP) action	Moderate – ER combination tablets available
4.	GLP-1 Agonists	Exenatide, Semaglutide	GLP-1R agonism; stimulates insulin, suppresses glucagon	High – Weekly PLGA microsphere SC injections
5.	SGLT-2 Inhibitors	Empagliflozin, Dapagliflozin	Blocks SGLT-2; reduces renal glucose reabsorption	Moderate – Once-daily adequate; SR under study
6.	Thiazolidinediones	Pioglitazone	PPAR-γ agonist; improves peripheral insulin sensitivity	Low-Moderate – Long t½ limits SR advantage
7.	Insulin Analogs	Glargine, Detemir, Degludec	Exogenous insulin; SC depot long-acting formulations	High – Ultra-long-acting engineered analogs

Abbreviations: t½= Elimination half-life; GI= Gastrointestinal; PPAR-γ= Peroxisome proliferator-activated receptor gamma; SC= Subcutaneous; IR= Immediate Release

Polymer Based Sustained Release Systems

Polymers are the structural foundation of the majority of SR drug delivery systems in medicine. There are three ways in which polymers can be involved in this process: they can serve as rate-limiting matrices, they can act as a barrier to diffusion of drug molecules, and they can encapsulate drugs for sustained release. In Figure 1, the four primary polymer-based SR drug delivery systems are depicted: HPMC hydrophilic matrix SR (A), OROS® osmotic pump SR (B), membrane-coated reservoir system SR (C), and PLGA biodegradable microsphere SR (D). The table below (Table 2) lists all the key polymers presently utilized in SR formulations with respect to their respective antidiabetic applications [8].

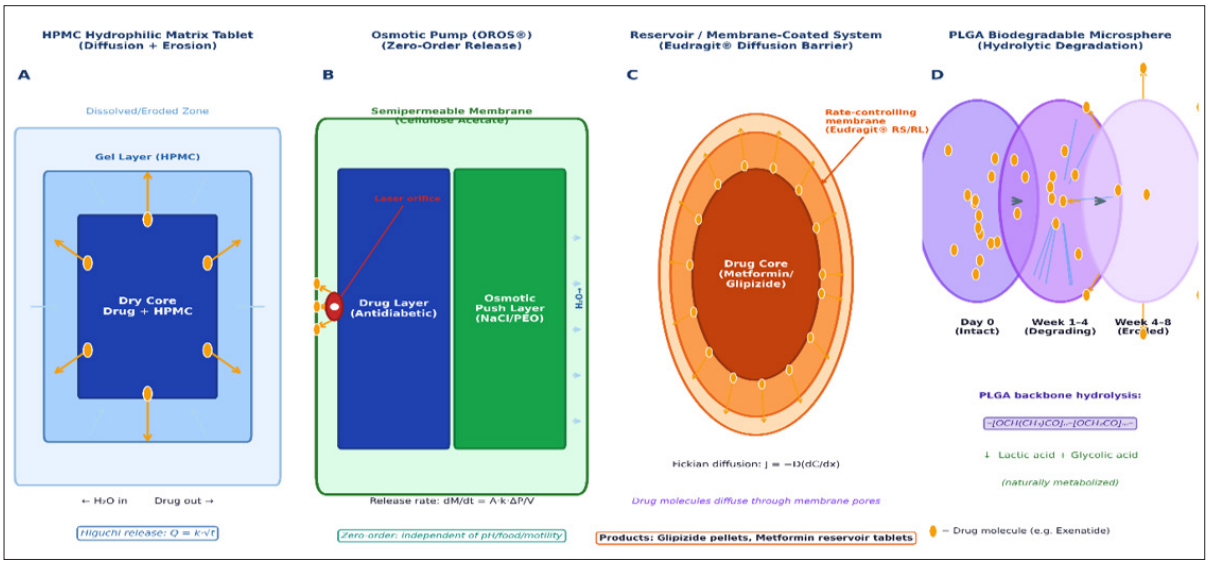

Figure 1: Mechanism of four key polymer-based Sustained release drug delivery systems for antidiabetic therapy

Hydrophilic Matrix Systems

HPMC-based hydrophilic matrix tablets are the most commonly used oral sustained release (SR) dosage forms in the world. When HPMC comes into contact with gastrointestinal (GI) fluids, it hydrates the polymer chains to form a viscous gel layer on the surface. Drugs diffuse through this complex mass of polymer by diffusing through the polymer to varying degrees depending on the concentration of polymer, polymer viscosity and solubility of drug [9]. In a study comparing SR metformin and IR metformin, the two formulations had similar effects on decreasing HbA1c levels while the SR formulation produced significantly fewer GI related events [10].

Osmotic Pump OROS® Systems

Osmotic Drug Delivery Systems (ODDS) provide controlled drug delivery at a constant rate of release, which is not significantly affected by factors such as food consumption, motility, or the acidity of the gastrointestinal tract. ODDS are designed to be near zero-order discharge systems through the use of a Push–Pull Osmotic Pump (PPOP) with an osmotic core that consists of a drug-containing layer and an osmotic push layer. The outer surface of the ODDS is a semi-permeable membrane (usually cellulose acetate) with one or more precisely drilled delivery orifices [11]. As the ODDS interacts with the fluids of the gastrointestinal tract, water is absorbed through the semi-permeable membrane and penetrates into the osmotic push layer, causing it to swell, thus exerting a pressure on the drug-containing layer and forcing it from the delivery orifice at a constant rate [12].

Table 2: Pharmaceutical Polymer used in Sustained Release Antidiabetic Formulations

S. No.	Polymer	Type	Key Properties	SR Application	Example Drug
1.	HPMC (K4M, K100M)	Hydrophilic	Gel-forming; viscosity-dependent release rate	Matrix tablets	Metformin ER (Glucophage XR®)
2.	Eudragit® RS/RL	Polyacrylate	pH-independent; tunable membrane permeability	Reservoir-coated pellets	Glipizide GITS
3.	Ethyl Cellulose	Hydrophobic	Insoluble; diffusion barrier via aqueous pores	Matrix / reservoir coating	Repaglinide SR
4.	PLGA	Biodegradable	Hydrolytic ester degradation (weeks–months)	Injectable microspheres	Exenatide (Bydureon®)
5.	Cellulose Acetate	Semipermeable	Osmotic pressure-driven zero-order release	Osmotic pump membrane	Glipizide GITS, Glumetza®
6.	Chitosan	Natural, cationic	Mucoadhesive; opens tight junctions	Nanoparticles, oral films	Oral insulin NPs
7.	Sodium Alginate	Natural, anionic	Ionotropic gelation with Ca^{2+}; biodegradable	Microspheres, in situ gel	Metformin, Insulin
8.	Carbopol (PAA)	Synthetic	High mucoadhesion; pH-responsive swelling	Gastroretentive; buccal	Glibenclamide
9.	Poloxamer 407	Thermosensitive	Sol at room temperature; gel at 37°C	Injectable SC depot gel	Insulin (subcutaneous)

Abbreviations: HPMC = Hydroxypropyl Methylcellulose; PLGA = Poly (Lactic-co-Glycolic acid); PCL = Polycaprolactone; TPP = Tripolyphosphate; PAA = Polyacrylic Acid; SC = Subcutaneous; NP = Nanoparticle.

4. Nanoparticulate Drug Delivery System

Nanoparticle-based systems for delivering drugs are now recognized as an effective alternative to overcome the problems associated with traditional oral dosing, particularly for compounds such as antidiabetic agents or peptides such as insulin. By providing a means to improve the bioavailability of poorly soluble drugs through the promotion of solubilization, the enhancement of intestinal permeation, and the facilitation of transport across biological membranes, those delivery systems will protect enzymatically labile molecules against harsh environments in the human gastrointestinal tract while demonstrating drug structural stability and drug therapeutic effect.

Different types of nanocarriers (eg. polymeric nanoparticles, lipid-based carriers, vesicular carriers) may be created/engineered to permit prolonged, site-specific, or stimulus-responsive release of drugs. Through surface modification and functionalization, these carriers enable localized drug delivery and increased interaction with intestinal epithelial cells [13].

PLGA and Polymeric Nanoparticles

Due to having good biocompatibility, controlled degradation, and approved by regulatory agencies, PLGA (poly lactic-co-glycolic acid) nanocarriers are considered the standard biodegradable nanocarrier for delivering insulin and other antidiabetic peptides. PLGA nanoparticles are capable of protecting peptides from being hydrolyzed by enzymes and providing a longer duration of release compared to peptide drugs delivered without a nanocarrier. In preclinical studies with diabetic rats, insulin-loaded PLGA nanoparticles have resulted in a longer duration of hypoglycemic activity and a maintenance of therapeutic effect for 10–14 days after subcutaneous administration, leading to a reduced frequency of dosing [14].

Surface modification techniques such as PEGylation (the addition of polyethylene glycol chains) will enhance the pharmacokinetic properties of PLGA nanoparticles. By providing a "stealth" feature to the nanocarrier, PEGylation decreases protein adsorption (opsonization), and thus decreases the likelihood that the nanocarrier will be identified and removed from the bloodstream by the mononuclear phagocyte system. Therefore, PEGylation will reduce the rate at which macrophages will clear PLGA nanoparticles resulting in a longer period of circulation time in the body and ultimately resulting in improved bioavailability and therapeutic effect [15].

Chitosan Nanoparticle for Oral Peptide Delivery

Due to their ability to withstand severe conditions (i.e., protect the biological activity of the drug), Chitosan (CS) and Tripolyphosphate (TPP)-based nanoparticles have raised great interest in the delivery of peptide drugs, such as insulin, perorally (orally). Chitosan nanoparticles carry out two distinct activities: they strongly adhere to the mucosal surfaces of the GI tract (due to their cationic nature) and temporarily alter tight junction integrity (which leads to increased permeability). The orally absorbed relative bioavailability of insulin loaded into chitosan nanoparticles was significantly increased compared with plain insulin solutions in diabetic animal models. Increased retention on the mucosal surface, protection from enzymatic degradation, and enhancement of epithelial uptake are the major contributing factors

to the improved relative bioavailability of insulin loaded chitosan nanoparticles [16]. Surface modifications of chitosan nanoparticles have been evaluated to improve their effect as a drug delivery system. PEGylation of the nanoparticles extends the circulation time and decreases the rate of elimination, while targeting ligands provide for selective interactions at specific tissues/receptors. Together, these modifications produce extended systemic exposure and/or improved targeting of the drug, resulting in improved therapeutic outcomes from the delivery of antidiabetic agents [17].

Table 3: Comparative Characteristics of Nanoparticulate System for Antidiabetic Drug Delivery

S. No.	Nanocarrier	Size Range	Core Material	Drug Loading	BA Enhancement	Main Limitation
1.	PLGA NPs	100–500 nm	Poly (lactic-co-glycolic acid)	20–50%	2–5× oral BA	Burst release; scale-up cost
2.	Chitosan NPs	100–400 nm	Chitosan + TPP (ionic gel)	Moderate	High (oral peptides)	pH sensitivity; aggregation
3.	Solid Lipid NPs	50–400 nm	Glyceryl monostearate, stearic acid	Low–Moderate	High (BCS II lipophilic)	Drug expulsion on storage
4.	NLC	100–500 nm	Solid + liquid lipid blend	High (>70%)	High; improved stability	Complex preparation
5.	Liposomes	50–1000 nm	Phospholipid bilayer (DPPC/DSPE)	Variable	Moderate–High	Sterilization; cost
6.	Dendrimers	1–10 nm	PAMAM, polypropyleneimine	High (surface)	High (surface-active)	Toxicity at high generation
7.	Nano-emulsions	100–500 nm	Oil–water–surfactant system	Moderate	High (BCS II drugs)	Physical instability
8.	Exosomes	40–160 nm	Endogenous phospholipid vesicle	Low	Very high (immune evasion)	Production scale; heterogeneity

Abbreviations: NPs = Nanoparticles; SLN = Solid Lipid Nanoparticle; NLC = Nanostructured Lipid Carrier; PAMAM = Polyamidoamine; BA = Bioavailability; BCS = Biopharmaceutics Classification System.

Hydrogel-Based Drug Delivery Systems

Three-dimensional, cross-linked polymer networks that can absorb large quantities of water form hydrogels and are highly useful for Sustained Release (SR) drug delivery via an antidiabetic medicine. The structure of a hydrogel provides researchers with excellent control over both the rate of drug diffusion and the rate of drug release through varying the composition of the polymer and the density of cross-linking. In particular, glucose-responsive hydrogels based on phenylboronic acid (PBA) provide important mechanisms by which drugs can be released based on the concentration of glucose in the bloodstream. The PBA group reversibly associates with glucose molecules resulting in alterations to the structure of the hydrogel (i.e., swelling) that regulate the release of insulin from the hydrogel matrix. Therefore, the release of insulin from the hydrogel will increase during times of hyperglycemia and decrease during times of normal glucose concentration through a closed-loop feedback control system [18].

pH Responsive Hydrogels

Hydrogels made of anionic polyacrylic acid (such as Carbopol or Eudragit S100) will remain collapsed at the acidic pH found in the stomach and will swell at the pH found in the small intestine (6.8-7.4), thereby delivering the encapsulated drug at the appropriate site for absorption. Insulin-loaded hydrogel microspheres with enteric coating protect the insulin from the hydrochloric acid of the stomach, while also allowing for the release of intact insulin into the intestinal tract [19].

Glucose-Responsive Smart Hydrogels

Systems that respond to glucose form the cutting edge of developing bio-engineered systems for autonomous, glucose-controlled release of insulin proportional to the amount of glucose in the bloodstream. There are 3 main methods of sensing glucose that have been developed, including:

- Reversible covalent binding of boronic acid to glucose that leads to hydrogel swelling;
- Use of glucose oxidase (GOx) to catalyze the oxidation of glucose, creating gluconic acid and H2O2 that will expand a pH-sensitive hydrogel; and
- Competitive displacement of concanavalin A (Con A)-glygoplymers.
- Recently injectable self-repairing hydrogels that respond to glucose have been developed that can provide long-term closed-loop glycemic control in diabetic animal models [20, 21].

Thermosensitive in Situ Hydrogels

Hydrogels created from Poloxamer 407 are in a liquid state at room temperature until they reach 37°C, whereupon they form a gel-like consistency and act as a slow-release SC depot after injection. Insulin-containing Pluronic F127 hydrogels have been shown to produce significant hypoglycemia for 3-5 days in diabetic rats with a single injection [22].

Gastroretentive, Transdermal, and Impalantable Systems

Gastroretentive Drug Delivery

Gastroretentive Drug Delivery Systems (GRDDS) extend the time they spend in the stomach from less than 4 to greater than 12 hours for drugs with limited absorption through the gastrointestinal tract. In studies evaluating gamma scintigraphy of floating metformin tablets, the tablet had more than 8 hours of retention in the stomach using a combination of HPMC and sodium bicarbonate [23]. The use of mucoadhesive drug delivery systems consisting of carbopol or chitosan bind to the gastric mucosa, increasing the time of contact between the drug and the epithelial cells, therefore improving the absorption of the drug once it is absorbed into the system [24]. The use of bilayer floating tablets to co-deliver metformin with glipizide offers synergistic means to control blood sugar from one once daily prescribed dosage [25].

Transdermal and Microneedle System

Continuous delivery of antidiabetic medications through the skin avoids the first pass metabolism - the degradation of medication by metabolism of these medications that occurs when taking them orally. Repaglinide is an example of an antidiabetic medication that maintained 24-hour steady state plasma drug concentrations when delivered through the skin using oleic acid microneedles [26]. Glucose sensitive microneedles for transdermal delivery of insulin are made using dissolving hyaluronic acid (a naturally occurring polymer), and integrated Glucose Oxidase (GOx) for sensing glucose and releasing appropriate amounts of insulin when needed, will allow the possibility of developing a transdermal closed loop system [27].

Implantable Systems and Closed Loop Technology

The ITCA 650 system (subcutaneous osmotic mini-pump, exenatide) allows patients to receive a continuous infusion of medication rather than having to administer their weekly injections of medication every 3-12 months. The Medtronic MiniMed 780G integrates continuous glucose monitor (CGM) with adaptive insulin delivery to provide a closed-loop delivery system and achieve a mean reduction in hemoglobin A1c between 0.7%-1.5% and a significant reduction in rates of hypoglycemia per pivotal trial [28].

Marketed Sr Antidiabetic Formulations

The characteristics of currently available Sustained Release (SR) anti-diabetes products including their delivery systems, dosing regimens and important clinical benefits are provided in Table 3. The manufacturing and commercialisation of these products provide evidence of the validity of a clinical translation for Sustained Release (SR) pharmaceutical innovation, as highlighted by examples such as Hydroxypropyl Methylcellulose (HPMC)-based metformin Extended Release (ER), polylactic-co-glycolic acid (PLGA)-based weekly exenatide ER, and the oral formulation of semaglutide [29].

Table 4: Marketed Sustained Release Drug Delivery Products for Antidiabetic Therapy

S. No.	Brand Name	Drug	SR Technology	Dosing	Key Clinical Advantage
1.	Glucophage XR®	Metformin HCl	HPMC matrix (Diffucaps)	Once daily	Reduced GI side effects vs IR
2.	Glumetza®	Metformin HCl	OROS® osmotic pump	Once daily	Zero-order, food-independent
3.	Glipizide GITS	Glipizide	GI osmotic therapeutic system	Once daily	Low hypoglycemia, constant release
4.	Bydureon®	Exenatide	PLGA microspheres (SC)	Once weekly	Prolonged GLP-1R agonism
5.	Ozempic®	Semaglutide	Albumin-binding fatty acid chain	Once weekly	CV risk reduction (SUSTAIN-6)
6.	Rybelsus®	Semaglutide	SNAC oral absorption enhancer	Once daily (oral)	First oral GLP-1 agonist
7.	Toujeo®	Insulin glargine U-300	Concentrated SC microprecipitate	Once daily	Flatter PD profile; ↓ nocturnal hypoglycemia
8.	Tresiba®	Insulin degludec	Multi-hexameric SC depot	Once daily	~42h action; flexible dosing
9.	ITCA 650	Exenatide	Osmotic SC mini-pump (implant)	Every 3–12 months	Eliminates weekly injections
10.	Janumet® XR	Sitagliptin + Metformin	ER combination tablet	Once daily	Simplified dual-mechanism therapy

Abbreviations: SC = Subcutaneous; SNAC = Sodium N-[8-(2-hydroxybenzoyl) amino] Caprylate; OROS = Oral Osmotic System; PLGA = Poly (lactic-co-Glycolic acid); CV = Cardiovascular; PD = Pharmacodynamic.

Drug Release Mechanisms and Mathematical Models

Table 5 provides a systematic outline of the primary release mechanisms available in different types of SR systems, the associated mathematical model representation, and several examples of antidiabetic formulations for each type of SR system. Each of the models identified must be understood to optimize formulation performance, establish in vitro/in vivo correlation, and support regulatory submission of a formulation [30].

Table

S. No.	Release Mechanism	System Type	Kinetics	Mathematical Model	Antidiabetic Example
1.	Matrix Diffusion	Hydrophilic/hydrophobic matrix	Non-zero order (Fickian)	Higuchi: Q = k·t^0.5	Metformin HPMC matrix tablet
2.	Membrane Diffusion	Reservoir coated system	Zero-order (membrane-controlled)	Fick's 1st law: J = −D(dC/dx)	Glipizide Eudragit® pellets
3.	Osmotic Pressure	Osmotic pump (OROS®)	Zero-order (pH/food-independent)	dM/dt = (A·π·k)/V	Metformin Glumetza® (OROS®)
4.	Swelling-Erosion	Swellable polymer matrix	Anomalous / Non-Fickian	Power law: Mt/M∞ = k·t^n	HPMC metformin SR tablet
5.	Biodegradation	PLGA microspheres/ implants	Biphasic (burst + sustained)	Peppas–Sahlin model	Exenatide Bydureon®
6.	pH-Responsive Swelling	Polyelectrolyte hydrogel/enteric	Site-specific, pulsatile	Donnan equilibrium	Insulin enteric NPs (colon)
7.	Thermal Gelation	Thermosensitive hydrogel	Sustained diffusion from depot	Modified Arrhenius diffusion	Insulin Pluronic® F127 gel (SC)
8.	Glucose-Responsive	PBA/GOx smart hydrogel/MN	Autonomous, proportional	Feedback kinetics model	Glucose-responsive MN insulin patch

Abbreviations: PBA = Phenylboronic Acid; GOx = Glucose Oxidase; OROS = Oral Osmotic System; MN = Microneedle; Q = Cumulative Drug Released; k = Release Rate Constant; t = Time; n = Diffusion Exponent.

Challenges, Regulatory Considerations and Future Directions

The manufacturing of nanoparticulate sustained release systems for potential clinical application is primarily impeded by the technical difficulties associated with demonstrating Critical Quality Attributes for clinical translation, such as uniformity of particle size distribution, encapsulation efficiency, repeatability of production batches, and long-term physical and chemical stability [31]. Despite recent advances in nanotechnology, the oral availability of insulin is still very low due to Gastrointestinal (GI) barriers; acid denaturation, protease degradation, mucus entrapment, and tight junctions restrict the oral availability of insulin to less than 1% for most formulations of oral insulin [32]. Regulatory pathways leading to the commercialization of novel sustained release systems require extensive in-vitro to in-vivo comparison data (associated with FDA Guidance 1997), gastric retention studies using pharmacoscintigraphy for Gastroretentive Drug Delivery Systems (GRDDS), and clinical studies establishing bioequivalence and clinical efficacy of novel delivery technologies.

The use of Artificial Intelligence (AI) for formulating patient-centered sustained-release formulations through the application of machine-learning techniques for predicting optimal polymer composition and release kinetics presents a significant opportunity for accelerating the sustained release drug-development process [33]. Glucose-responsive microneedle patches that utilize Continuous Glucose Monitoring (CGM) and transdermal insulin delivery will, in the near term, provide a transformative clinical approach to replacing multiple daily blood glucose checks by patients and injecting insulin with a single weekly patch system for millions of patients.

Conclusion

The use of sustained release drug delivery technologies has started to revolutionise the management of diabetes mellitus, providing the opportunity for patients to receive treatment by way of once-daily or once-weekly dosing, producing an improvement in glycemic stability, a decrease in side effects, and ultimately leading to enhancements in the quality of life for patients living with diabetes. There has been a number of sustained release drug delivery systems developed within the diabetes market, including HPMC matrix tablets and OROS osmotic pumps, which currently hold a dominant position as the oral sustained release drug delivery systems in this market. Additionally, there are weekly GLP-1 injectable drugs based on PLGA microsphere formulations, ultra-long-acting insulin depot analogues, and developing technologies for glucose-responsive hydrogel and microneedle platforms.

As the field progresses toward its next frontier, which involves the development of autonomous closed-loop drug delivery systems that detect physiological glucose signals and respond via the real-time delivery of insulins that have been precisely calibrated, these technologies are advancing from proof-of-concept stages in the laboratory towards validation in clinical settings. Achieving the full potential of sustained release drug delivery systems for enhancing therapeutic effectiveness and improving outcomes in the more than 537 million patients worldwide with relentless chronic diseases requires ongoing interdisciplinary collaboration and innovative approaches by the regulatory body and the pharmaceutical industry.

References

1. International Diabetes Federation (2021) IDF diabetes atlas. International Diabetes Federation https://idf.org/about-diabetes/resources/idf-diabetes-atlas-2021/.
2. American Diabetes Association (2023) Standards of medical care in diabetes-2023. Diabetes Care 46: 1-290.
3. Bommer C, Heesemann E, Sagalova V, Jennifer Manne-Goehler, Rifat Atun, et al. (2017) The global economic burden of diabetes in adults aged 20-79 years: a cost-of-illness study. Lancet Diabetes Endocrino l5: 423-430.
4. Kalra S, Gupta Y (2015) The insulin of today and tomorrow. Diabetes Ther 6: 219-226.
5. Cramer JA (2004) A systematic review of adherence with medications for diabetes. Diabetes Care 27: 1218-1224.
6. Peppas NA, Bures P, Leobandung W, Ichikawa H (2000) Hydrogels in pharmaceutical formulations. Eur J Pharm Biopharm 50: 27-46.
7. Vyas SP, Khar RK (2002) Controlled drug delivery: concepts and advances. Vallabh Prakashan pp: 38-50.
8. Rowe RC, Sheskey PJ, Quinn ME (2009) Handbook of

pharmaceutical excipients Pharmaceutical Press pp: 506-509.
9. Colombo P, Bettini R, Santi P, Peppas NA (2000) Swellable matrices for controlled drug delivery. Pharm Sci Technol Today 3: 198-204.
10. Blonde L, Dailey GE, Jovanovič L (2004) Gastrointestinal tolerability of extended-release metformin tablets. Diabetes Obes Metab 6: 467-474.
11. Verma RK, Krishna DM, Garg S (2002) Formulation aspects in the development of osmotically controlled oral drug delivery systems. J Control Release 79: 7-27.
12. Fujioka K, Brazg RL, Raz I (2005) Efficacy and safety of once-daily extended-release metformin (Glucophage XR). Diabetes Obes Metab 7: 539-547.
13. Couvreur P (2013) Nanoparticles in drug delivery: past, present and future. Adv Drug Deliv Rev 65: 21-23.
14. Danhier F, Ansorena E, Silva JM, Régis Coco, Aude Le Breton, et al. (2012) PLGA-based nanoparticles: an overview of biomedical applications. J Control Release 161: 505-522.
15. Damgé C, Michel C, Aprahamian M, Couvreur P (1988) New approach for oral administration of insulin with polyalkylcyanoacrylate nanocapsules. Diabetes 37: 246-251.
16. Sarmento B, Ribeiro A, Veiga F, P Sampaio, R Neufeld, et al. (2007) Alginate/chitosan nanoparticles for oral insulin delivery. Pharm Res 24: 2198-2206.
17. Fonte P, Araújo F, Silva C, Carla Pereira, Salette Reis, et al. (2015) Polymer-based nanoparticles for oral insulin delivery: revisited approaches. Biotechnol Adv 33: 1342-1354.
18. Hoffman AS (2012) Hydrogels for biomedical applications. Adv Drug Deliv Rev 64: 18-23.
19. Gupta P, Vermani K, Garg S (2002) Hydrogels: from controlled release to pH-responsive drug delivery. Drug Discov Today 7: 569-579.
20. Gu Z, Aimetti AA, Wang Q, Tram T. Dang, Yunlong Zhang, et al. (2013) Injectable nano-network for glucose-mediated insulin delivery. ACS Nano 7: 4194-4201.
21. Mo R, Jiang T, DiSanto R, Wanyi Tai, Zhen Gu, et al. (2014) ATP-triggered anticancer drug delivery. Nat Commun 5: 33-64.
22. Schmaljohann D (2006) Thermo-and pH-responsive polymers in drug delivery. Adv Drug Deliv Rev 58: 1655-1670.
23. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P (2016) Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int J Pharm 510: 144-158.
24. Arora S, Ali J, Ahuja A, Khar RK, Baboota S (2005) Floating drug delivery systems: a review. AAPS PharmSciTech 6: 372-390.
25. Andrews GP, Laverty TP, Jones DS (2009) Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm 71: 505-518.
26. Prausnitz MR, Langer R (2008) Transdermal drug delivery. Nat Biotechnol 26: 1261-1268.
27. Chen MC, Ling MH, Lai KY, Pramuditya E (2012) Dissolving microneedles for transdermal delivery of insulin. Biomacromolecules13: 4022-4031.
28. Tooker AC, Shah KN, Bhagra PL (2012) Subcutaneous implantable insulin delivery systems. J Biomed Mater Res A100: 985-994.
29. Bailey CJ, Turner RC (1996) Metformin. N Engl J Med 334: 574-579.
30. (1997) US Food and Drug Administration. Guidance for industry: extended-release oral dosage forms: development, evaluation, and application of in vitro/in vivo correlations. Rockville (MD): FDA https://www.fda.gov/regulatory-information/search-fda-guidance-documents/extended-release-oral-dosage-forms-development-evaluation-and-application-vitroin-in-vivo-correlations.
31. Ventola CL (2012) The nanomedicine revolution: current and future clinical applications. PT 37: 582-591.
32. Khafagy ES, Morishita M, Onuki Y, Takayama K (2007) Current challenges in non-invasive insulin delivery systems: a comparative review. Adv Drug Deliv Rev 59: 1521-1546.
33. Reker D, Blum SM, Steiger C (2019) Computationally guided high-throughput design of self-assembling drug formulations. Nat Commun 10: 1-12.