

Emerging Therapies in Diabetes: New Drugs and Innovative Remedies

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 Open Access

Review Article

DOI: 10.68163/ptr.2026.61

How to Cite:

Patel PB, Raval AM, Patel HB, Patel KH, Patel P, Prajapati T. Emerging therapies in diabetes: New drugs and innovative remedies, *Pharmacol Toxicol Res.* 2026;2:65-70.

Keywords:

Advanced drug delivery, complications, diabetes mellitus, emerging therapies, gestational diabetes, global burden, immunotherapy, insulin therapy, limitations of current treatments, oral hypoglycaemic agents, type 1 diabetes, type 2 diabetes

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder with a rapidly increasing global prevalence, posing significant health and economic challenges. More than 500 million adults are currently affected worldwide, with projections indicating further increases, particularly in low- and middle-income countries. The disease manifests primarily as Type 1 diabetes, characterized by autoimmune destruction of pancreatic beta cells; Type 2 diabetes, driven by insulin resistance and beta-cell dysfunction; and gestational diabetes, which increases long-term metabolic risks for both mother and child. Despite advances in insulin formulations, oral hypoglycaemic agents and structured lifestyle interventions, current therapies remain limited and often fail to prevent long-term complications such as cardiovascular disease, nephropathy and neuropathy. These limitations underscore the urgent need for emerging therapies. Novel approaches, including stem cell transplantation, immunotherapy, gene editing and advanced drug delivery systems, are being actively explored, highlighting their potential to restore pancreatic function and reduce diabetes-related complications. Collectively, these innovations represent a paradigm shift toward more effective and potentially curative strategies in diabetes care.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder that has become a major global health challenge. The global burden of diabetes continues to rise, with data indicating that more than 500 million adults are currently affected worldwide, a figure projected to increase substantially in the coming decades. This burden is particularly pronounced in low- and middle-income countries, where access to structured care remains limited.

Clinically, diabetes manifests in several forms: Type 1 diabetes, characterized by autoimmune destruction of pancreatic beta cells, Type 2 diabetes, characterized by insulin resistance and progressive beta-cell dysfunction and gestational diabetes, which arises during pregnancy and predisposes both mother and child to long-term metabolic risks¹. Despite advances in insulin formulations, oral hypoglycemic agents and lifestyle interventions, current treatments remain limited. As highlighted in recent literature, challenges include poor patient adherence, the risk of hypoglycemia and insufficient prevention of long-term complications such as cardiovascular disease, nephropathy and neuropathy². These limitations underscore the urgent need for emerging therapies. Novel approaches, such as stem cell transplantation, immunotherapy, gene editing and advanced drug delivery systems, are being actively explored, emphasizing their potential to restore pancreatic function and reduce diabetes-related complications³.

LITERATURE SEARCH STRATEGY

A comprehensive literature review was conducted using peer-reviewed publications retrieved from PubMed/MEDLINE, Scopus, Web of Science, Google Scholar and ClinicalTrials.gov.

Search terms: The search strategy included combinations of keywords such as:

- "Diabetes Mellitus", "Emerging therapies", "GLP-1 receptor agonists", "Dual incretin agonists", "Stem cell therapy", "Gene therapy", "Nanotechnology", "Artificial pancreas", "Precision medicine", "Digital therapeutics", "Continuous glucose monitoring", "Herbal medicine" and "Novel antidiabetic drugs"
- Boolean operators (AND/OR) were used to combine search terms.

Literature search period: January 2020 to July 2026.

Inclusion criteria: English-language publications, peer-reviewed journal articles, randomized controlled trials, systematic reviews, meta-analyses, international clinical guidelines, landmark clinical trials and recent high-quality review articles were included in the study.

Exclusion criteria: Non-English publications, conference abstracts without full text, duplicate publications, articles lacking sufficient scientific evidence and studies unrelated to emerging therapeutic approaches in diabetes were excluded from the study. Relevant studies were screened by title, abstract and full-text assessment before inclusion in the review.

Pathophysiology of diabetes:

- **Insulin resistance:** Insulin resistance is considered the initiating defect in Type 2 diabetes. Skeletal muscle, liver and adipose tissue fail to respond adequately to insulin, resulting in reduced glucose uptake and increased hepatic glucose output. Ectopic lipid accumulation, mitochondrial dysfunction and altered adipokine signaling are key drivers of insulin resistance. Chronic exposure to elevated free fatty acids and glucose further amplifies this defect, creating a vicious cycle of metabolic dysregulation⁴
- **β-cell dysfunction:** Initially, pancreatic β-cells compensate for insulin resistance by increasing insulin secretion. Over time, however, β-cell function declines due to glucotoxicity, lipotoxicity, endoplasmic reticulum stress and amyloid deposition. Inter-organ

crosstalk, particularly between adipose tissue, liver and pancreas, contributes significantly to β-cell exhaustion. This progressive decline is a hallmark of Type 2 diabetes, explaining why many patients eventually require exogenous insulin despite initial responsiveness to oral agents⁵

- **Incretin effect:** The incretin hormones GLP-1 and GIP normally enhance insulin secretion in response to oral glucose. In Type 2 diabetes, this incretin effect is blunted, leading to impaired postprandial insulin release and hyperglycemia⁶. Reduced GLP-1 secretion, diminished GIP activity and receptor desensitization contribute to this defect. Therapeutically, GLP-1 receptor agonists and DPP-4 inhibitors have been developed to restore incretin signaling, representing a major translational advance in diabetes care⁷
- **Inflammation and oxidative stress:** Chronic low-grade inflammation and oxidative stress are central to the pathophysiology of diabetes. Pro-inflammatory cytokines such as TNF-α and IL-6 interfere with insulin signaling pathways, while reactive oxygen species (ROS) damage β-cells and vascular endothelium. Oxidative stress links metabolic dysfunction directly to diabetic complications, including nephropathy, neuropathy and cardiovascular disease⁸

Current standard treatment: Table 1 shows the standard Treatments in Type 2 diabetes. The management of Type 2 diabetes relies on a combination of lifestyle modification and pharmacological therapies tailored to individual patient needs. Lifestyle modifications, including dietary changes, exercise and behavioral support, remain the foundation of care, while metformin continues to be the first-line pharmacological treatment due to its efficacy and safety⁹. Traditional agents, such as sulfonylureas and insulin therapy, are effective but are limited by the risks of hypoglycemia and weight gain. Newer drug classes, including DPP-4 inhibitors, SGLT2 inhibitors and GLP-1 receptor agonists, have expanded treatment options, offering improved tolerability, weight-related benefits and cardiovascular or renal protection¹⁰.

Emerging drug therapies¹⁶⁻²⁰

Dual GIP/GLP-1 receptor agonists (e.g., tirzepatide): Tirzepatide represents a major therapeutic advance by combining glucose-dependent insulinotropic polypeptide

Table 1: Standard treatments in type 2 diabetes¹¹⁻¹⁵

Therapy	Efficacy	Side effects	Cost/accessibility
Lifestyle modification	Moderate to high (early disease)	Minimal; adherence challenges	Low cost, universally recommended
Insulin therapy	Very high; essential in advanced disease	Hypoglycemia, weight gain	Higher cost, requires injections
Metformin	High efficacy, durable	GI upset, rare lactic acidosis	Very low cost, widely available
Sulfonylureas	Moderate to high	Hypoglycemia, weight gain	Low cost, but declining use
DPP-4 inhibitors	Moderate	Rare side effects, weight neutral	Moderate cost
SGLT2 inhibitors	Moderate to high; strong CV/renal benefits	Genital infections, dehydration	Higher cost, increasing use
GLP-1 receptor agonists	High efficacy; weight loss, CV benefits	GI side effects, injectable	High cost, rapidly expanding role

(GIP) and GLP-1 receptor agonism. Clinical trials have demonstrated superior glycemic control, significant weight reduction and cardiovascular benefits compared with GLP-1 receptor agonist monotherapy.

Triple agonists (GLP-1/GIP/glucagon): Triple agonists simultaneously target incretin and glucagon pathways, enhancing glucose regulation, lipid metabolism and energy expenditure. Early-phase studies have demonstrated their potential to achieve greater weight loss and metabolic improvements than dual agonists.

Oral GLP-1 receptor agonists: Oral semaglutide expands treatment accessibility by eliminating barriers associated with injections, while demonstrating efficacy comparable to that of injectable formulations and potentially improving patient adherence.

GPR119 agonists: These agents stimulate incretin release and insulin secretion, although further clinical trials are required to establish their efficacy and therapeutic potential.

Glucagon receptor modulators: Aiming to balance glucose metabolism and weight control, these therapies have shown encouraging preclinical outcomes, with human clinical trials currently in the early stages of development.

Amylin analogues (e.g., cagrilintide): These agents complement GLP-1 receptor agonists by enhancing satiety and reducing food intake. The combination of cagrilintide and semaglutide produces synergistic effects, resulting in substantial weight loss.

Glucokinase activators: These agents stimulate pancreatic glucose sensing to enhance insulin secretion, although careful dose optimization is required to minimize the risk of hypoglycemia.

Novel SGLT inhibitors (SGLT1/2 dual inhibitors): Sotagliflozin and similar dual inhibitors improve fasting and postprandial glucose control while providing substantial cardiovascular and renal benefits.

Stem cell-derived β -cell replacement therapies: Regenerative approaches aim to restore endogenous insulin production, offering the potential for long-term remission despite ongoing challenges related to immune rejection, engraftment and scalability.

Innovative non-drug therapies²¹⁻²⁵:

- **Artificial pancreas systems:** Integrate Continuous Glucose Monitoring (CGM) with automated insulin delivery to improve time in range and reduce the risk of hypoglycemia

- **Closed-loop insulin delivery:** Utilizes real-time adaptive algorithms and dual-hormone delivery (insulin plus glucagon) to minimize glucose variability
- **Smart insulin:** Formulations designed to release insulin in response to real-time blood glucose concentrations through glucose-responsive nanoparticles
- **Continuous glucose monitoring (CGM):** Provides continuous glucose data that can improve HbA1c control and support predictive analytics
- **Digital therapeutics and AI-based management:** Machine learning models analyze lifestyle and biomarker data streams to personalize daily interventions
- **Telemedicine and wearable biosensors:** Expand access to remote care and enable multi-analyte physiological monitoring through the analysis of interstitial fluid and sweat.

Regenerative and advanced therapies²⁶⁻²⁸:

- **Stem cell therapy and gene therapy:** Utilize pluripotent stem cell differentiation and targeted viral or non-viral vectors, such as transcription factors PDX1 and MAFA, to reprogram cells into insulin-secreting phenotypes
- **Islet and pancreatic transplantation:** Advanced immunosuppression protocols and cell encapsulation technologies aim to minimize immune-mediated attack, although donor scarcity remains a major challenge
- **CRISPR-based approaches:** Enable precise genome editing to correct mutations affecting insulin gene regulation, engineer immune-tolerant cells and enhance cellular resilience.

Nanotechnology in diabetes^{29,30}:

- **Nanoparticle-based drug delivery:** Enhances bioavailability and facilitates targeted delivery to specific tissues, such as the liver or pancreatic β -cells
- **Nano-insulin and glucose-responsive nanocarriers:** Encapsulate insulin within smart polymers that function as self-regulating feedback systems, releasing insulin in proportion to increases in ambient glucose concentrations
- **Microneedle patches:** Provide painless, minimally invasive intradermal delivery systems that can simultaneously sample interstitial fluid and administer precise doses

Table 2 summarizes the herbal and natural remedies used for the management of diabetes, as reported in previous studies³¹⁻³⁵.

Personalized and precision medicine:

- **Pharmacogenomics:** Analyzes genetic variations in drug transporters, such as SLC22A1 for metformin and metabolic enzymes, such as CYP2C9 for sulfonylureas, to facilitate the customization of medication regimens³⁶

Table 2: Herbal and natural remedies for diabetes

Herbal/natural remedy	Source/key compound	Mechanism of action	Therapeutic benefits
Berberine	Alkaloid from <i>Berberis vulgaris</i>	Activates AMPK pathway, improves insulin sensitivity, reduces hepatic glucose output	Lowers blood glucose and lipids
Curcumin	Polyphenol from turmeric	Antioxidant and anti-inflammatory, protects -cells	Reduces oxidative stress, improves HbA1c
Cinnamon	Cinnamaldehyde and polyphenols	Mimics insulin activity, increases glucose uptake, delays gastric emptying	Lowers fasting glucose and lipids
Fenugreek	Seeds rich in fiber and 4-hydroxyisoleucine	Stimulates insulin secretion, reduces intestinal absorption	Improves glycemic control, lowers cholesterol
Gymnema sylvestre	Gymnemic acids from leaves	Inhibits glucose absorption, regenerates-cells	Reduces sugar cravings, stabilizes glucose
Bitter melon	Charantin and polypeptide-p	Insulin-like activity, enhances utilization, reduces gluconeogenesis	Improves sensitivity, lowers fasting glucose
Probiotics	<i>Lactobacillus</i> , <i>Bifidobacterium</i> species	Restores gut flora, reduces inflammation, improves insulin sensitivity	Enhances metabolism and gut health

Table 3: Advantages and limitations of emerging therapies

Parameters	Advantages	Limitations
Efficacy	Superior glycemic control, weight loss, CV protection	Variable inter-patient genetic response
Safety	Improved tolerability, reduced hypoglycemia risk	Potential off-target gene effects, immune rejection
Cost-effectiveness	Long-term reduction in complication expenses	High upfront manufacturing costs
Accessibility	Global research collaborations and telemedicine expansion	Infrastructure barriers in low-resource settings
Long-term outcomes	Potential for durable remission and enhanced quality of life	Insufficient longitudinal real-world data

Table 4: Comparative matrix: current therapies vs. Future perspectives⁴⁵⁻⁴⁷

Aspect	Current therapies	Future perspectives
Approach	Symptom management via standard drugs and lifestyle	Integrated, predictive, preventive care (AI and precision medicine)
Technology	Manual glucose checks; limited digital links	AI analytics, smart continuous sensors, closed loops
Therapeutic goal	Glycemic control and complication prevention	Disease modification, -cell regeneration, cure
Personalization	Standardized dosing algorithms	Multi-omic, genetic and lifestyle customization
Innovation focus	Incremental drug class improvements	Regenerative medicine, CRISPR editing, nanotechnology
Outcome expectation	Lifelong management with residual risk	Long-term remission and restoration of function

- **Biomarkers:** Integrates multi-omic profiles, including HbA1c, C-peptide, microRNAs and inflammatory cytokines, for the early detection of complications and precise patient stratification³⁷

Clinical trials and future pipeline

- **Phase II/III pipeline:** Focuses heavily on dual and triple incretin agonists, oral biologics and advanced SGLT inhibitors, which demonstrate favorable metabolic and cardiovascular safety profiles³⁸
- **disease-modifying and curative horizons:** Aim to transition from conventional approaches focused primarily on blood glucose control toward the long-term restoration of endocrine function through gene editing and stem cell bioengineering³⁹

The advantages and limitations of the emerging therapies identified in previous studies⁴⁰⁻⁴³ are summarized in Table 3.

Challenges and future perspectives: While technological and pharmacological horizons are expanding rapidly, significant challenges remain, including high treatment costs, stringent regulatory requirements for gene-editing platforms, long-term patient adherence to complex smart devices and bioethical concerns surrounding genetic modifications. Looking forward, the integration of AI-driven

predictive analytics with disease-modifying regenerative interventions may help redefine modern diabetology⁴⁴. Table 4 shows a comparative matrix of current therapies and future perspectives in diabetes management.

CONCLUSION

The field of emerging diabetes therapies represents a transformative evolution beyond conventional glucose-lowering drugs. By integrating advances across pharmacology, bioengineering, artificial intelligence and herbal medicine, future care models offer a clear pathway toward sustainable, potentially curative and individualized treatment strategies. Addressing current economic, regulatory and ethical challenges will be essential to ensure that these groundbreaking innovations become globally accessible.

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