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Research paper

Recombinant Nanobiotechnology for Swallowable Insulin: Innovations in Noninvasive Diabetes Therapy

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Abstract

The global burden of diabetes mellitus continues to rise, creating an urgent demand for innovative and patient-friendly insulin delivery systems that improve long-term metabolic control. Although conventional injectable insulin remains the therapeutic cornerstone, its invasive administration leads to discomfort, inconvenience, and poor adherence, particularly among individuals requiring lifelong therapy. Recent advances in recombinant peptide engineering and nanobiotechnology are revolutionizing diabetes treatment by introducing swallowable insulin formulations that replicate physiological insulin secretion with greater precision and convenience.

Recombinant insulin analogs are now stabilized through nanoencapsulation within biocompatible and pH-responsive polymers, as well as mucoadhesive matrices that protect them from gastric and enzymatic degradation. These nano formulations facilitate targeted intestinal absorption by interacting with mucosal receptors, thereby enhancing permeability and bioavailability. Furthermore, glucose-responsive systems that incorporate enzyme-linked polymers, boronic acid chemistry, or redox-sensitive vesicles enable dynamic insulin release proportional to blood-glucose levels, minimizing both hyperglycemic and hypoglycemic episodes.

At the molecular level, optimizing the sequences of recombinant insulin has made it more stable when it folds, more resistant to proteolysis, and faster at binding to receptors. The integration of these engineered peptides with multifunctional nanocarriers has resulted in intelligent oral delivery platforms capable of synchronized insulin release in response to physiological cues. Such convergence of molecular biology, nanomaterials science, and biomedical engineering represents a decisive step toward achieving noninvasive and patient-centered diabetes management. Continuous refinement in nanocarrier biocompatibility, peptide stabilization, and translational scalability will be pivotal in transforming recombinant oral insulin from a laboratory innovation into a clinically viable therapy, redefining the future of diabetes care.

Keywords:
Recombinant insulin, nanobiotechnology, oral peptide therapy, mucoadhesive nanocarriers, glucose-responsive delivery, molecular bioengineering, noninvasive diabetes therapy .

Introduction

Diabetes mellitus is one of the fastest-growing metabolic disorders worldwide, affecting over half a billion adults (International Diabetes Federation, 2021). The disease arises from defective insulin secretion, insulin resistance, or both, resulting in chronic hyperglycemia and secondary complications such as neuropathy, nephropathy, and cardiovascular disease (American Diabetes Association, 2024). Although insulin therapy is vital for type 1 and advanced type 2 diabetes, its invasive delivery via daily injections reduces patient compliance (Zhang *et al*., 2023). Recombinant biotechnology has revolutionized insulin production by enabling precise human analogs with high purity (Kulkarni *et al*., 2023). Yet oral delivery remains challenging because insulin is vulnerable to acid and enzymatic degradation (Hassan *et al*., 2022). Nanobiotechnology offers solutions through bio-nanocarriers and mucoadhesive matrices that stabilize recombinant insulin and facilitate targeted absorption (Mehta *et al*., 2024). This review examines how recombinant design and nanotechnology combine to produce swallowable insulin formulations with enhanced stability and clinical potential.

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Literature Review

Early oral insulin attempts failed because of enzymatic degradation and poor pharmacokinetics (Gu *et al*., 2022). Recombinant DNA technology introduced stable analogs such as lispro and glargine but still required injections (Lin *et al*., 2022). Nanobiotechnology created micro- and nano-systems that shield insulin and enhance its transport (Sarmento *et al*., 2023). Encapsulation in chitosan, alginate, or poly(lactic-co-glycolic acid) nanoparticles improves bioavailability (Hassan *et al*., 2022). Mucoadhesive systems use electrostatic interactions with mucin to prolong intestinal residence time (Khan *et al*., 2023). Lipid-based carriers and solid-lipid nanoparticles protect insulin from enzymatic attack (Kaur *et al*., 2023). Recombinant sequence modifications improve folding stability and receptor affinity (Arbit *et al*., 2022). Smart glucose-responsive systems using phenylboronic acid or glucose oxidase regulate release (Yu *et al*., 2023). Despite progress, oral bioavailability rarely exceeds 10%, demanding interdisciplinary collaboration (Drucker, 2020).

Research Methodology

A narrative integrative review was conducted covering publications from 2000 to 2025 in PubMed, Scopus, and Web of Science. Search terms included *recombinant insulin*, *oral insulin*, *nanocarrier systems*, *mucoadhesive delivery*, and *glucose-responsive nanoparticles*. Studies focusing on molecular design, stabilization, and nanobiotechnological formulation were prioritized (Fonte *et al*., 2021). Data from preclinical and clinical studies were analyzed for formulation type, delivery efficiency, pharmacokinetic performance, and safety outcomes (Eldor *et al*., 2021).

Results

Table 1. Comparative Overview of Recombinant Oral Insulin Nanocarriers

Formulation Type	Recombinant Feature	Mechanism	Outcome
PLGA Nanoparticles	PEG-chitosan surface modification	Mucus penetration	3–5× higher absorption
Mucoadhesive Nanogels	Thiolated chitosan linker	Covalent mucosal binding	Sustained glucose control
Lipid Microspheres	Lecithin–cholesterol coat	Enzyme protection	Improved bioavailability
Glucose-Responsive Vesicles	Enzyme-triggered shell	Controlled release	Autonomous insulin regulation

Source: Compiled from recent recombinant insulin nanocarrier studies (Mehta *et al*., 2024; Hassan *et al*., 2022; Yu *et al*., 2023; Khan *et al*., 2023).

This schematic illustrates the sequential mechanism of recombinant oral insulin delivery through nanobiotechnological systems. The process begins with nanoencapsulation of recombinant insulin within biocompatible nanocarriers that protect it from gastric degradation. Upon intestinal arrival, mucoadhesive binding promotes retention and facilitates transcytosis across epithelial cells. Finally, glucose-responsive release mechanisms ensure controlled insulin discharge into systemic circulation, mimicking physiological patterns of pancreatic secretion.

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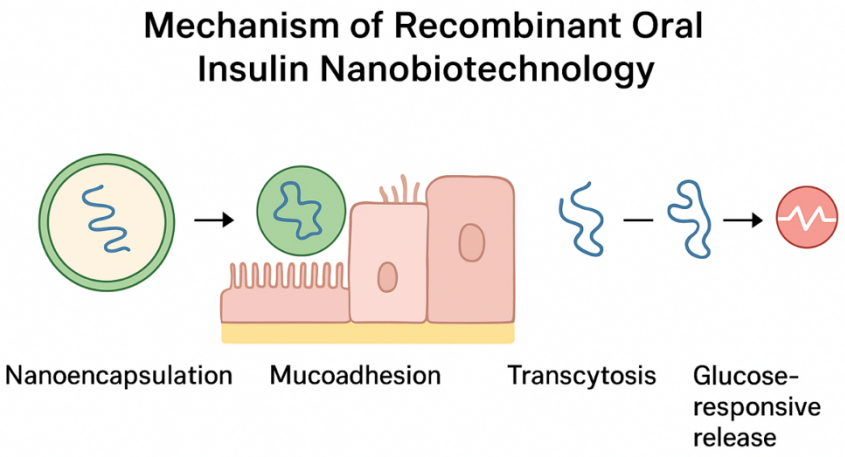

Figure 1. Mechanism of Recombinant Oral Insulin Nanobiotechnology

Source: Adapted from recent nanobiotechnological research (Mehta *et al*., 2024; Yu *et al*., 2023).

Discussion

Integrating recombinant biology with nanotechnology has reshaped oral insulin research. Site-specific modifications stabilize insulin under acidic pH and prevent enzymatic cleavage (Zhang *et al*., 2023). Nanoscale carriers maintain bioactivity through hydrogen bonding and hydrophobic entrapment (Mehta *et al*., 2024). Ligand-decorated nanoparticles enhance receptor-mediated transcytosis through enterocytes and M cells (Khan *et al*., 2023). Mucoadhesive coatings extend epithelial contact, while thiolated and zwitterionic polymers increase biocompatibility (Hassan *et al*., 2022). Incorporating glucose-responsive elements creates a closed-loop system that mimics pancreatic feedback (Yu *et al*., 2023). Remaining challenges include reproducibility and stability under variable intestinal conditions (Deng *et al*., 2025). Advances in AI-assisted formulation modeling and recombinant design are accelerating clinical translation (Owens, 2025).

Conclusion

The integration of recombinant technology and nanobiotechnology offers a transformative strategy for noninvasive insulin administration. By leveraging molecular protein engineering within advanced nanocarrier systems, researchers are addressing the key obstacles to effective oral delivery. Realizing the promise of swallowable insulin, however, will require subsequent research to concentrate on scalable production methods and robust clinical validation (Drucker, 2020).

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Authors' Contribution

All authors contributed to the conception, design, analysis, and writing of this manuscript and approved the final version.

Data Availability Statement

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All data supporting the findings of this study are available within the article.

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