

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.

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 (Sarmiento *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

Formulation Type	Recombinant Feature	Mechanism	Outcome
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.

Mechanism of Recombinant Oral Insulin Nanobiotechnology

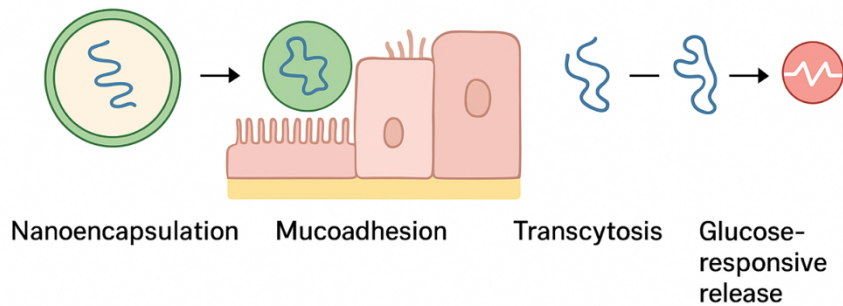


Figure 1. Mechanism of Recombinant Oral Insulin Nanobiotechnology

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