Recent Advances in Gastroretentive Drug Delivery Systems for Enhancing Oral Bioavailability of Antidiabetic Agents

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***Abstract*—**Diabetes mellitus is a chronic metabolic disorder requiring consistent pharmacotherapy. Many antidiabetic agents, including metformin, glipizide, and glimepiride, exhibit limited oral bioavailability due to narrow absorption windows and rapid gastrointestinal transit. Gastroretentive drug delivery systems (GRDDS) prolong gastric residence time, enabling controlled release and enhanced absorption of these agents. Recent advances in GRDDS include floating, mucoadhesive, swellable/expandable systems, and nanotechnology-based carriers. This review summarizes contemporary strategies for enhancing the oral bioavailability of antidiabetic drugs, highlighting polymer selection, design innovations, challenges, and future perspectives in personalized and stimuli-responsive GRDDS.

***Index Terms*—**Gastroretentive drug delivery, Antidiabetic agents, Metformin, Floating systems, Mucoadhesive, Oral bioavailability, Controlled release.

I. INTRODUCTION

Oral drug delivery is preferred for chronic diseases like diabetes mellitus due to ease of administration and patient compliance. However, several antidiabetic drugs are absorbed primarily in the stomach or upper small intestine and exhibit poor solubility or short half-lives. Conventional oral dosage forms often result in fluctuating plasma levels and suboptimal therapeutic efficacy. Gastroretentive drug delivery systems (GRDDS) are designed to prolong gastric residence, ensuring sustained drug release in the stomach or proximal intestine. By maintaining therapeutic concentrations over extended periods, GRDDS can reduce dosing frequency and improve glycemic control.

II. RATIONALE FOR GRDDS IN ANTIDIABETIC THERAPY

- **Absorption window limitation:** Many drugs, such as metformin, are primarily absorbed in the upper gastrointestinal tract.
- **Short half-life:** Frequent dosing is required to maintain plasma levels.
- **Variable gastric emptying:** Physiological factors, food intake, and disease state affect drug residence and absorption.

Advantages of GRDDS:

- Prolonged gastric retention
- Controlled drug release
- Improved oral bioavailability
- Reduced dosing frequency
- Enhanced patient compliance

III. FORMULATION STRATEGIES & MATERIALS

Polymers and Excipients

- Important choice of polymers: viscosity, molecular weight, pH response.
- Gas formers: sodium bicarbonate, citric acid, etc., used for floating systems.
- Mucoadhesive polymers: chitosan, thiolated polymers, polyacrylates.

Controlled Release Techniques

- Combining GRDDS with controlled-release technologies can optimize both retention and drug release.
- Layered systems, matrix systems, multi-particulate systems.

Microparticulate Systems

- Microparticles (microspheres, microcapsules) to deliver antidiabetics like metformin.
- Advantages: uniform distribution, avoid dose dumping, possible reduced GI irritation.

Novel Fabrication Techniques

- Use of 3D printing / additive manufacturing for custom geometry.
- Nanoparticles embedded in GRDDS for dual control (retention + release).

IV. RECENT ADVANCES (2023–2025)

- **Osmotically Controlled Expandable Systems:** Long gastric retention for metformin (up to 24 h).
- **Dual-Drug Nanocarriers:** Co-delivery of metformin and glipizide for combination therapy with controlled release.
- **Floating-Mucoadhesive Hybrids:** Combine buoyancy and adhesion to maximize gastric retention.

- **Stimuli-Responsive GRDDS:** Systems that adapt to gastric pH or motility for on-demand release.
- **3D-Printed Personalized GRDDS:** Tailored geometry and dose for patient-specific therapy.

V. CHALLENGES IN GRDDS DEVELOPMENT

- Inter- and intra-individual variability in gastric motility
- Altered gastric emptying in diabetic patients
- Risk of obstruction or discomfort from expandable systems
- Scale-up and manufacturing challenges
- Regulatory concerns and in vivo variability
- Patient acceptability of larger or complex dosage forms

VI. FUTURE PERSPECTIVES

- **Personalized GRDDS:** Tailored to patient-specific gastric physiology
- **Integration with Controlled Release Technologies:** Multi-layer tablets, osmotic pumps
- **Stimuli-Responsive Polymers:** Smart systems releasing drugs in response to pH or gastric motility
- **Combination Therapy:** GRDDS for dual or multiple antidiabetic agents
- **Improved In Vitro/In Vivo Correlation:** Predictable performance for regulatory approval

VII. CONCLUSION

GRDDS provide a promising platform for enhancing the oral bioavailability of antidiabetic agents. Recent innovations in floating, mucoadhesive, swellable, and nanotechnology-based systems have demonstrated enhanced gastric retention, controlled release, and improved therapeutic outcomes. Future research focusing on personalized, stimuli-responsive, and combination GRDDS could further revolutionize oral antidiabetic therapy.

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