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Review Article

Floating Multi-particulate Drug Delivery Systems: A Comprehensive Review

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Oral drug delivery remains the most preferred route of administration due to its convenience, cost-effectiveness, and patient compliance. However, conventional oral dosage forms often suffer from limitations such as short gastric residence time, fluctuating plasma drug concentrations, and incomplete drug absorption. Gastro-retentive drug delivery systems (GRDDS) have emerged as a promising strategy to overcome these drawbacks. Among them, floating multiparticulate drug delivery systems (FM-DDS) represent an advanced approach that enhances gastric retention by maintaining buoyancy in gastric fluids. These systems provide controlled and sustained drug release, improve bioavailability of drugs with narrow absorption windows, and minimize side effects. This review comprehensively discusses the physiological basis of gastric retention, factors affecting gastric emptying, suitable drug candidates, classification of floating systems, formulation approaches, preparation techniques, characterization methods, advantages, limitations, applications, and future perspectives of floating multiparticulate drug delivery systems.

Keywords: Multi-particulate Drug Delivery Systems, Oral drug delivery, Gastro-retentive drug delivery systems (GRDDS)

INTRODUCTION

Oral controlled drug delivery systems have gained significant attention due to their ability to maintain therapeutic drug concentrations for extended periods. Despite numerous advancements, conventional oral dosage forms such as tablets and capsules are often associated with rapid gastric emptying, resulting in incomplete drug absorption and reduced therapeutic efficacy**. [1]**

The stomach presents a favorable absorption site for certain drugs, particularly those**: [2]**

- Primarily absorbed in the upper gastrointestinal tract
- Having a narrow absorption window
- Unstable in the alkaline environment of the intestine
- Intended for local gastric action

Gastro-retentive drug delivery systems (GRDDS) are designed to prolong gastric residence time (GRT). These systems include:

- Floating systems
- Swelling and expandable systems
- Bioadhesive systems
- High-density systems

Among these, floating multiparticulate systems have emerged as a superior alternative to single-unit floating systems due to reduced risk of dose dumping, uniform distribution in the gastrointestinal tract, and improved reproducibility of drug absorption**. [3]**

Fig: Gastro-retentive drug delivery systems

2. Physiology of the Stomach and Basis of Gastric Retention [4,5]

The stomach is anatomically divided into:

- Fundus
- Body
- Antrum
- Pylorus

Gastric motility follows a cyclic pattern known as the Migrating Myoelectric Complex (MMC), which consists of four phases:

1. Basal phase (minimal contractions)
2. Pre-burst phase
3. Burst phase (intense contractions)
4. Transition phase

During the fasted state, the burst phase can rapidly empty indigestible materials from the stomach. Therefore, designing dosage forms that resist this process is critical for effective gastric retention. Floating systems achieve retention by maintaining a bulk density lower than gastric fluid (~1.004 g/cm³), enabling buoyancy over gastric contents.

3. Factors Affecting Gastric Emptying [6,7]

Gastric retention is influenced by multiple physiological and formulation-related factors:

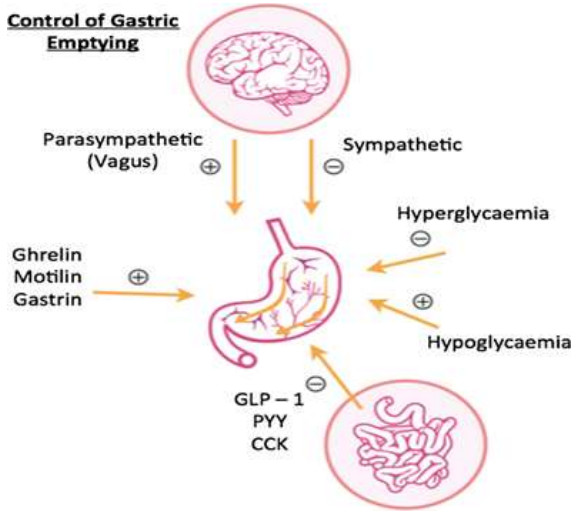

Fig: Factors Affecting Gastric Emptying

3.1 Dosage Form Factors

- Density
- Size (larger units >7.5 mm show better retention)
- Shape
- Swelling ability

3.2 Physiological Factors

- Fed or fasted state
- Caloric content of food
- Frequency of feeding
- Gender and age
- Posture
- Disease conditions (e.g., diabetes)

3.3 Pharmacological Factors

- Anticholinergics delay gastric emptying
- Prokinetic agents accelerate emptying
- Opioids reduce motility

Understanding these factors is essential for designing effective floating multiparticulate systems.

4. Suitable Drug Candidates [8,9]

Floating multiparticulate systems are ideal for:

4.1 Drugs with Narrow Absorption Window

- Levodopa
- Riboflavin

4.2 Drugs Absorbed Mainly in Stomach/Upper GIT

- Calcium salts
- Chlordiazepoxide

4.3 Drugs Acting Locally in the Stomach

- Antacids
- Misoprostol

4.4 Drugs Unstable in Intestinal pH

- Ranitidine
- Metronidazole

4.5 Drugs That Disturb Colonic Flora

- Amoxicillin

5. Floating Multiparticulate Drug Delivery Systems [10,11]

Multiparticulate systems consist of small discrete units such as:

- Microspheres
- Microballoons
- Pellets
- Microbeads

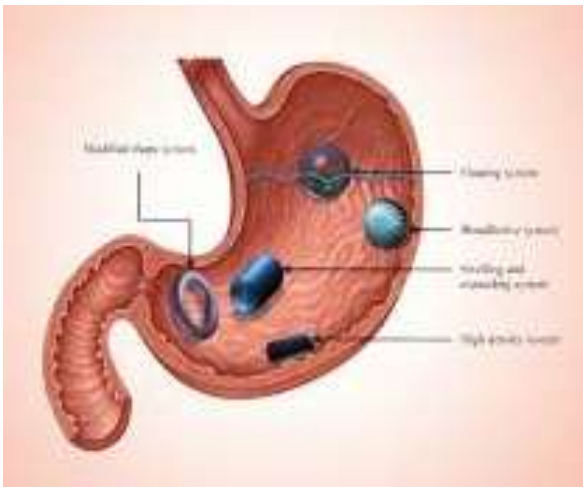

Fig: Floating Multiparticulate Drug Delivery Systems

These systems distribute uniformly in the stomach and reduce the risk of localized irritation. Floating multiparticulates remain buoyant due to entrapped air, hollow core formation, or gas generation.

Advantages over single-unit systems include:

- Reduced dose dumping
- Improved gastric distribution

- Predictable drug release
- Reduced inter-patient variability

6. Classification of Floating Drug Delivery Systems [12]

Floating systems are broadly classified into:

6.1 Effervescent Systems

These systems contain gas-generating agents such as:

- Sodium bicarbonate
- Citric acid
- Tartaric acid

Upon contact with gastric fluid, carbon dioxide is released and trapped within the polymer matrix, enabling buoyancy.

Mechanism:

CO_2 generation → Entrapment in gel matrix → Reduced density → Floating

6.2 Non-Effervescent Systems

These systems rely on swellable polymers such as:

- Hydroxypropyl methylcellulose (HPMC)
- Chitosan
- Carbopol
- Polyacrylates

Upon hydration, polymers swell and entrap air, lowering system density.

7. Methods of Preparation of Floating Multiparticulates [13]

7.1 Solvent Evaporation Method

- Drug and polymer dissolved in organic solvent
- Emulsified in aqueous phase containing stabilizer
- Organic solvent evaporates
- Hollow cavity formation occurs

Advantages:

- High encapsulation efficiency
- Suitable for heat-sensitive drugs

7.2 Ionotropic Gelation Method [14]

Based on cross-linking of polyelectrolytes with counter ions.

Common polymers:

- Sodium alginate
- Gellan gum
- Chitosan

Mechanism:
Polymer solution dropped into calcium chloride solution → Ionic cross-linking → Bead formation

Advantages:

- Mild processing conditions
- Suitable for proteins and peptides

7.3 Emulsion Solvent Diffusion Method [15]

- Polymer + drug dissolved in ethanol/methylene chloride
- Emulsified into aqueous PVA solution
- Ethanol diffuses outward
- Polymer precipitates
- Internal cavity formed

Produces hollow microspheres (microballoons).

7.4 Spray Drying Method [16]

- Drug-polymer solution atomized
- Rapid solvent evaporation
- Porous microparticles formed

Suitable for large-scale production.

8. Characterization of Floating Multiparticulate Systems [17]

8.1 Micromeritic Properties

- Bulk density
- Tapped density
- Angle of repose
- Hausner’s ratio
- Compressibility index

8.2 Particle Size and Morphology

- Scanning Electron Microscopy (SEM)
- Optical microscopy

- Laser diffraction

8.3 Encapsulation Efficiency [18]

%Entrapment=Actual Drug Content
Theoretical Drug Content×100\% Entrapment = \frac{Actual\ Drug\ Content}{Theoretical\ Drug\ Content} \times 100%Entrapment=Theoretical Drug Content
Actual Drug Content×100

8.4 Buoyancy Studies [19]

Floating percentage calculated as:

Buoyancy (%) =WfWf+Ws×100Buoyancy (\%) = \frac{W_f}{W_f + W_s} \times 100Buoyancy(%)=Wf+WsWf×100

Where:

- Wf = weight of floating particles
- Ws = weight of settled particles

8.5 In-Vitro Drug Release Studies [20]

- USP dissolution apparatus
- Simulated gastric fluid (pH 1.2)
- Temperature: 37 ± 0.5°C

Drug release kinetics analyzed using:

- Zero-order
- First-order
- Higuchi model
- Korsmeyer–Peppas model

8.6 In-Vivo Studies [21]

- X-ray imaging (with barium sulfate)
- Gamma scintigraphy
- Pharmacokinetic studies

9. Advantages of Floating Multiparticulate Systems [22]

1. Improved bioavailability
2. Reduced dosing frequency
3. Controlled and sustained release
4. Enhanced patient compliance
5. Site-specific gastric delivery
6. Reduced plasma fluctuation
7. Avoidance of dose dumping
8. Reduced gastric irritation

10. Limitations [23]

- Not suitable for drugs unstable in acidic pH
- Unsuitable for drugs irritating to gastric mucosa
- Requires sufficient gastric fluid for floating
- Variability due to patient physiology

11. Applications [24]

11.1 Sustained Drug Delivery

Floating microspheres of NSAIDs reduce gastric irritation while maintaining therapeutic levels.

11.2 Site-Specific Delivery

Effective for drugs targeting:

- Gastric ulcers
- Helicobacter pylori infection

11.3 Absorption Enhancement

Improves bioavailability of drugs with upper GIT absorption.

11.4 Treatment of Gastric Disorders [25]

- Ulcers
- Gastritis
- Gastric cancer

FUTURE SCOPE

Future research focuses on:

- Floating systems for peptide and protein delivery
- Nanotechnology-integrated floating systems
- Targeted therapy for gastric carcinoma
- Combination of bioadhesion and floating mechanisms
- Development of smart pH-responsive floating systems

Emerging technologies such as 3D printing may enable personalized gastro-retentive dosage forms.

CONCLUSION

Floating multiparticulate drug delivery systems represent a significant advancement in gastro-retentive drug delivery. By prolonging gastric residence time and enabling controlled drug release, these systems enhance bioavailability and therapeutic efficacy while minimizing side effects. Multiparticulate approaches provide superior performance compared to single-unit systems due to uniform distribution and reduced dose dumping risk. With continued advancements in polymer science and pharmaceutical engineering, floating multiparticulate systems are expected to play pivotal role in future oral drug delivery technologies.

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