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Review Article

Formulation Strategies and Recent Advances in Floating Drug Delivery System (FDDS): A Comprehensive Review

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ABSTRACT

Floating Drug Delivery Systems (FDDS) represent a state-of-the-art oral drug delivery strategy, designed particularly to enhance gastric retention of dosage forms. The floating systems float for long durations in the stomach, allowing for extended drug release and increasing the bioavailability of drugs absorbed predominantly in the upper gastrointestinal tract. FDDS are collectively categorized into effervescent and non-effervescent systems, both having different mechanisms of floating. Different formulation methods—ionotropic gelation, spray drying, melt granulation, hot-melt extrusion, solvent evaporation—have been used to produce various floating systems such as tablets, capsules, beads, and microspheres. This review presents a comprehensive analysis of FDDS, such as types, polymers employed, formulation approaches, evaluation techniques, and conditions affecting gastric retention. It also points towards recent developments, including 3D printed systems, nano-FDDS, and magnetically controlled drug delivery platforms, providing indications of the future potential of floating systems in controlled and targeted drug release.

KEYWORDS: Floating Drug Delivery System, Gastroretentive Drug Delivery System (GRDDS), Gastric Retentive Time, Recent Advances

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INTRODUCTION:

Oral drug delivery is the most employed and sought-after route of medication delivery due to its convenience, non-invasiveness, and affordability. Oral drug delivery provides numerous advantages, including ease of administration, flexible dosing, and improved patient compliance. But the main drawback of conventional oral dosage forms is their reduced and variable residence time in the stomach, which may cause incomplete drug release and decreased absorption for drugs that are mainly absorbed from the upper gastrointestinal (GI) tract.

The problem has been addressed by the development of gastroretentive drug delivery systems (GRDDS). These devices have been engineered to extend the residence time of the dosage form in the stomach, thus enhancing drug absorption and therapeutic response. Amongst the numerous categories of GRDDS, Floating Drug Delivery Systems (FDDS) have emerged with particular interest. Floating Drug

Delivery Systems are able to float on the gastric fluid because of their lesser density and can stay within the stomach for long durations without affecting gastric emptying.

FDDS have a variety of advantages, including increased bioavailability of drugs with restricted windows of absorption, increased drug solubility in acidic media, decreased frequency of dosing, and increased regulation of drug release. These advantages are most useful for drugs that are less stable or poorly absorbed in the gut environment.

This paper concerns the idea and design of FDDS, including their types, floating mechanisms, formulation methods, and assessment techniques. It also speaks of the contemporary trends and future directions of floating drug delivery in enhancing oral drug treatment.

History and Background of Floating Drug Delivery Systems (FDDS): Floating Drug Delivery Systems (FDDS) were developed to overcome the limitations of conventional

oral drug delivery, especially the short gastric residence time of dosage forms. The concept dates back to the 1960s, when researchers began exploring ways to keep drugs in the stomach for longer periods to enhance absorption.

One of the first floating systems was introduced by Davis in 1968, and the field expanded significantly in the 1980s and 1990s with the introduction of gastroretentive technologies. A major milestone was the classification of FDDS by Singh and nKim (2000) into effervescent and non-effervescent systems, based on their floating mechanisms.

FDDS work by maintaining a lower density than gastric fluids, allowing them to float and remain in the stomach for extended periods. This is especially beneficial for drugs that are:

Absorbed in the upper gastrointestinal tract, Poorly soluble or unstable in intestinal fluids, Intended for local action in the stomach.

Over the years, FDDS have been formulated in various forms like tablets, capsules, microspheres, and raft-forming systems. They are widely used for drugs like metformin, domperidone, ciprofloxacin, and amoxicillin, and continue to be a focus of research in oral controlled-release drug

CLASSIFICATION OF FDDS:

1. Effervescent System of Floating Drug Delivery Systems (FDDS): Floating Drug Delivery Systems (FDDS) are new oral drug delivery systems aimed at prolonging gastric residence time and enhancing the bioavailability of drugs absorbed primarily in the stomach or the upper region of the small intestine. Among several FDDS methods, the effervescent system is most commonly employed because of its efficient floating mechanism.

2. Gas generative system: A gas generating system is an effervescent floating drug delivery system (FDDS) that utilizes a chemical reaction of acidic and alkaline materials (like citric acid and sodium bicarbonate) when combined with gastric fluid to generate carbon dioxide (CO_2).

The gas becomes entrapped in the polymer matrix of the dosage form, reducing the density of the dosage form and enabling it to float on gastric fluids, hence increasing gastric residence time and enhancing drug absorption.

3. Mechanism of action: In a gas-producing floating drug delivery system (FDDS), an acid-base reaction happens in the acidic stomach environment to generate carbon dioxide (CO_2). The produced gas gets trapped in a swellable polymer matrix (such as HPMC or carbopol), leading to expansion of the dosage form and the formation of a density less than gastric fluid, allowing the dosage form to float.

This floating action extends gastric residence time, enabling constant release of drugs, improved bioavailability, and dosing frequency reduction.

4. Volatile liquid containing system: A volatile liquid holding system in Floating Drug Delivery Systems (FDDS) is a dosage form employing a volatile liquid

(e.g., ether, cyclopentane) sealed within a polymer shell or microsphere.

Upon exposure to gastric temperature, the volatile liquid evaporates and produces internal gas, resulting in floating (buoyancy) of the system on gastric fluids. This facilitates extended gastric retention and sustained drug release.

5. Mechanism of action: In a volatile liquid-carrying floating drug delivery system, a minute quantity of volatile liquid (such as diethyl ether or cyclopentane) is trapped inside a sealed polymeric capsule consisting of materials such as ethyl cellulose or polyvinyl alcohol. During oral intake, the system ends up in the stomach, and the temperature ($37\text{--}40^\circ\text{C}$) causes the volatile liquid to evaporate because of its low boiling point. This vaporization creates gas within the microsphere, decreasing its density to below gastric fluid density. Consequently, the system floats on stomach contents, extending gastric residence time. During this time, the drug is released slowly, improving bioavailability—particularly for drugs that are absorbed in the stomach or upper intestine.

6. Non-effervescent system of floating drug delivery system (FDDS): Non-Effervescent Floating Drug Delivery System (FDDS) is associated with gastric retention in the absence of gas generation. Such systems incorporate low-density swelling polymers that, when they come in contact with gastric fluid, decrease the overall density and make the dosage form float. Examples include hydrodynamically balanced systems (employing HPMC or carbopol), hollow microspheres, alginate beads, and bio/mucoadhesive systems. Floating is ensured by gelation, trapped air, or adhesive bonding to the lining of the stomach. Non-effervescent systems are particularly beneficial for drugs which are absorbed from the upper parts of the gastrointestinal tract or get degraded in the intestine. They are used to release drug slowly and offer improved bioavailability without depending on effervescence or chemical reaction.

7. Colloidal gel formation system: A colloidal gelation system is a drug delivery system that is based on the gelation of colloidal particles to provide controlled release of the drug. Such systems are especially beneficial in oral, ophthalmic, and parenteral products, particularly in floating and mucoadhesive drug delivery, since they provide improved residence time and drug release. They are composed of colloidal particles—e.g., polymers or nano/microparticles—that create a three-dimensional gel matrix upon exposure to physiologic conditions (e.g., pH, temperature, or ionic strength). The drug is entrapped in this gel matrix, controlling its release over time.

8. Mechanism of action: A colloidal gelation system functions by converting from a liquid or sol form into a gel when it comes into contact with physiological conditions (e.g., pH, temperature, or ionic strength). The systems usually consist of colloidal particles (e.g., polymers or nanoparticles) that gelate in the stomach or site of action, creating a three-dimensional matrix. This gel thickens and traps the drug, enabling sustained and controlled release of the drug.

In gastric applications, stimuli (such as acidic pH or temperature) induce sol–gel transition. The resultant gel is mucoadhesive (if mucoadhesive polymers are employed) to the mucosal lining, extending gastric residence time and improving bioavailability.

9. Microporous compartment system: Microporous Compartment System is an example of non-effervescent floating drug delivery system (FDDS) that floats in the stomach by entrapping air and resisting fluid penetration into the core.

10. Mechanism of action: It includes a core that has a drug load encapsulated within a microporous polymeric membrane (such as cellulose acetate). The outer membrane is porous to gastric fluid so that it can penetrate only the surrounding compartment but not the drug core. The inner core is dry and has entrapped air that keeps the system low in density and buoyant in gastric fluids. This floating action prolongs gastric retention time and ensures controlled drug release. It includes a core that has a drug load encapsulated within a microporous polymeric membrane (such as cellulose acetate). The outer membrane is porous to gastric fluid so that it can penetrate only the surrounding compartment but not the drug core. The inner core is dry and has entrapped air that keeps the system low in density and buoyant in gastric fluids. This floating action prolongs gastric retention time and ensures controlled drug release.

11. Alginate Beads in Floating Drug Delivery Systems (FDDS): Alginate beads are an effervescent-free floating drug delivery system consisting of sodium alginate, a seaweed-derived natural polysaccharide. They are extensively employed for controlled release of drugs as well as gastric retention.

12. Mechanism of action: Sodium alginate is cross-linked ionically with divalent cations such as calcium ions (Ca^{2+}) to produce calcium alginate beads. During preparation, a drug–polymer solution is added into a calcium chloride solution to create beads through gelation. These beads trap air or oils, which decrease their weight and enable them to float on gastric fluids. The drug release is regulated by the gel matrix.

13. Hollow Microspheres (Microballoons) in Floating Drug Delivery Systems: Hollow microspheres or microballoons are a category of non-effervescent floating drug delivery systems (FDDS). Hollow microspheres are spherical, low-density particles with an empty core such that they float on gastric fluids, thus prolonging the gastric residence time and facilitating controlled release

Mechanism of action: Hollow microspheres are generally produced through methods such as solvent evaporation or spray drying.

They consist of floatable polymers like Eudragit, ethylcellulose, or acrylic resins. The air pocket inside the microsphere holds the air, decreasing the overall density of the particle. When given orally, they float in the stomach, releasing the drug slowly over a period of time.

Polymers Employed in Floating Drug Delivery Systems (FDDS)

Polymers serve a pivotal function in the development of FDDS through providing buoyancy, drug release control, swelling, and gelation. Polymers are either natural, semi-synthetic, or synthetic and are chosen depending on the desired drug release trend and floatation mechanism

1. Natural Polymers: Sodium Alginate: Gels in the presence of Ca^{2+} ; applied in alginate beads.

Guar Gum: Swells in gastric juice, applied in sustained release.

Pectin: Biodegradable and gel-forming.

Xanthan Gum: High viscosity; favors sustained release and floatation.

2. Semi-Synthetic Polymers: Hydroxypropyl Methylcellulose (HPMC): Widely applied for swelling and gel-forming floating tablets.

Methylcellulose (MC): Gives buoyancy and regulates drug release.

Ethyl cellulose (EC): Water-insoluble, applied in microspheres and coatings.

Carboxy methyl cellulose (CMC): Viscous gel forming; promotes adhesion and swelling.

3. Synthetic Polymers: Eudragit (RL, RS, NE): Employed for sustained release and buoyancy in microballoons.

Polyvinyl Alcohol (PVA): Employed in microsphere production.

Polyacrylic Acid (e.g., Carbopol): Superior mucoadhesive and swelling capacity.

Polystyrene and Polylactic Acid (PLA): Employed in floating advanced microspheres.

FORMULATION

1. Solvent Evaporation Technique in Floating Drug Delivery Systems (FDDS):

The solvent evaporation technique is a common method in non-effervescent FDDS formulation, especially for the preparation of hollow microspheres (microballoons) which float as a result of their low density and hollow nature.

Principle: The process entails dissolving polymer and drug in a volatile organic solvent (or mixture of solvents). The solution is then emulsified in a distinct phase (usually aqueous), and solvent is progressively removed through evaporation, resulting in the development of hollow microspheres.

Process Involved:

1. Internal Phase Preparation: Drug and polymer (e.g., ethylcellulose, Eudragit) are dissolved in a volatile solvent such as dichloromethane, ethanol, or acetone.

2. Emulsification:

3. The organic solution is dropwise added into an aqueous phase with surfactant or stabilizer (e.g., PVA) under stirring to create an oil-in-water emulsion.
4. **Solvent Evaporation:** Stirring is continued at room or slightly higher temperature to remove the solvent by evaporation, causing the microspheres to solidify.
5. **Collection and Drying:** Solidified hollow microspheres are filtered, washed, and dried for subsequent use.

2. IONOTROPIC GELATION:

Ionotropic gelation is a general method employed in the preparation of floating drug delivery systems, particularly for the generation of beads or microspheres from natural polymers such as alginate, pectin, or gellan gum. It encompasses cross-linking of polyelectrolyte polymers by multivalent counterions in a water-based solution

Principle: The process is dependent on the property of ionic polymers such as sodium alginate to gel when they come in contact with multivalent cations (e.g., Ca^{2+} , Ba^{2+}). The drug-polymer solution is allowed to drop into a cationic solution, and beads or microspheres are obtained by ionic cross-linking.

Steps Involved:

1. **Preparation of Polymer-Drug Solution:** Drug is dissolved or dispersed in sodium alginate solution (or some other ionic polymer).
2. **Bead Formation:** This is dropped (through syringe or nozzle) into a calcium chloride (CaCl_2) solution.
3. **Cross-Linking:** Ca^{2+} ions bond with carboxylate groups in alginate to create a bead structure of gel.
4. **Washing and Drying:** Beads are washed to remove extra ions, and then they are dried.

3. Spray Drying in Floating Drug Delivery Systems (FDDS):

Spray drying is one of the most used formulation methods in the formulation of floating drug delivery systems, particularly for the preparation of hollow microspheres or microballoons, which can float on gastric fluids because of their low density.

Principle of Spray Drying: Spray drying is done by atomizing a drug-polymer solution into a hot drying chamber, resulting in the quick evaporation of the solvent. This causes the development of dry, spherical particles—usually hollow—suitable for buoyancy.

Spray Drying Steps in FDDS:

1. **Solution/Dispersion Preparation:** Drug is dissolved or dispersed in a polymer(s) containing solution (e.g., ethyl cellulose, HPMC, Eudragit).
2. Solvents employed are typically volatile (e.g., ethanol, acetone, dichloromethane).
3. **Atomization:** The solution is atomized by a nozzle into a stream of hot air by a spray dryer.

4. **Drying and Particle Formation:** Evaporation of the solvent quickly produces porous or hollow microspheres of low density.

5. Microspheres are recovered by a cyclone separator.

4. Melt granulation in floating drug delivery system:

Melt granulation is a technique that is solvent-free and applied to the preparation of floating drug delivery systems for the generation of low-density granules that assist in maintaining stomach buoyancy.

Principle: The melt granulation principle is based on the dissolution of a gel-forming lipid or polymer in a melted state, which would encapsulate the drug on solidification and form a gelled matrix or granule. The matrix can be made to be:

Steps in Melt Granulation:

1. **Blending:** Combine drug and excipients (polymers, fillers, etc.)
2. **Heating:** Incorporate and melt the binder at regulated temperature.
3. **Granulation:** Blend to create wet masses, which are formed into granules.
4. **Cooling and Solidifying:** Granules solidify and cool down.
5. **Sizing:** Sieve through for uniform size

5. Hot Melt Extrusion (HME) in Floating Drug Delivery Systems (FDDS):

Hot melt extrusion (HME) is a solventless, continuous processing method employed in FDDS to formulate floating tablets, pellets, or films with controlled drug release and gas-trapping or low-density characteristics to provide buoyancy in gastric fluids.

Principle of Hot Melt Extrusion:

Hot melt extrusion encompasses:

1. Melting a mixture of drug, polymer(s), and functional excipients under regulated heat and shear.
2. Extruding the molten mass through a die to mold it into rods, films, or pellets.
3. Cooling and cutting the extrudates to create the final dosage form

6. Hot Melt Extrusion Steps:

1. Weighing and dry blending of drug and excipients.
2. Charging into extruder barrel.
3. Melting the polymers by heating and creating homogenous mass.
4. Extruding through a die (e.g., rod, sheet).
5. Cooling and cutting to get final form (tablet cores, pellets, films).

1. Direct Compression in Floating Drug Delivery Systems (FDDS):

Direct compression is a cheap, easy, and extensively used method of formulation for floating tablets, particularly in effervescent and non-effervescent floating drug delivery system

Principle of Direct Compression in FDDS: Direct compression is the process of mixing drug with compatible excipients (such as gas-generating agents or swelling polymers) and compressing them into tablets without any preliminary granulation or solvent

Steps in Direct Compression FDDS:

1. Blending of drug, polymers, buoyancy agents, and excipients.
2. Compression of the powder blend into tablets using a tablet press.
3. Optional coating for modified release or protection.
 - a) Melting a mixture of drug, polymer(s), and functional excipients under regulated heat and shear.
 - b) Extruding molten mass through a die to form rods, films, or pellets.
 - c) Cutting and cooling extrudates to produce the final dosage forms.

EVALUATION:

In-Vivo Evaluation

- **Total floating duration:** The period from the start of the dosage form into the medium to its rise up to the top one third of the vessel of dissolution is referred to as floating lag time and the duration for which the dosage form floats is referred to as the floating time. These tests are typically conducted in simulated gastric fluid or 0.1 mole/liter HCl at 37°C in USP dissolution apparatus with 900 ml of 0.1 molar HCl as the medium for dissolution
- **Swelling index:** Upon exposure to water or body fluids, the hydrophilic polymer matrix began hydrating from the outer boundary towards the centre to create a gel layer around the drug. The gel-like swollen region of the matrix significantly controls the drug molecule dissolution and diffusion within the polymer material into the aqueous medium and also offers mechanism of Controlled drug release

In-Vitro Evaluation

- **X-Ray/ Gamma Scintigraphy:** For in vivo studies, X-Ray/Gamma Scintigraphy is the primary evaluation criterion for floating dosage form. During every experiment, the animals were kept on overnight fasting with free access to water, and radiograph was taken before the administration of the floating tablet to confirm the absence of radio-opaque material. Dosage form visualization by X-ray is a result of the presence of a radio-opaque material. The formulation was given by natural swallowing and then 50 ml of water. Radiographic image was taken from each animal

standing, and the distance between the X-ray source and the animal must be kept the same in all imaging so that the movement of the tablet would be easily observable. Gastric radiography was performed at 30-min intervals for 5 h with the aid of an X-ray machine.

- **Gastric Retention Time:** Gastric Retention Time (GRT) is the time a dosage form spends in the stomach prior to its transit to the small intestine. In Floating Drug Delivery Systems (FDDS), increased GRT is of paramount importance to enhance the bioavailability of drugs absorbed mostly in the upper gastrointestinal (GI) tract or are locally active in the stomach.

FACTORS AFFECTING FDDS

1. **Density of dosage form:** Floating is a function of dosage form buoyancy and is density dependent. Density of the dosage form must be less than gastric contents (1.004gm/ml). Less than 1.0gm/cm³ is the required density to possess floating property.[16] Therefore dosage forms with density lower than gastric contents can float to the top whereas high density systems bottom out in stomach.

2. **Dosage form shape and size:** Shape and size of dosage form are some of the factors that affect gastric retention.

Dosage form unit with a diameter of over 7.5 mm are said to prolong GRT compared to those whose diameter is 9.9 mm. The dosage form whose tetrahedron and ring shape designs having a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to show improved GIT for 90 to 100% retention at 24 hours than other.

3. **Food intake and nature:** Food intake, food viscosity and volume of food, caloric content and frequency of feeding exert an important effect on the gastric retention of dosage forms. Whether food is present or not in the gastrointestinal tract (GIT) impacts the gastric retention time (GRT) of the dosage form. Feeding of indigestible polymer or fatty acid salt may modify the pattern of motility of stomach to a fed condition thus results in reduced gastric emptying rate and extending drug release Caloric content.

4. **Caloric content:** Gastric retention time (GRT) can be extended by 4 to 10 hours by a high protein and fat meal.

[18] Floating may rise by more than 400 minutes when consecutive meals are administered compared to a single meal owing to the low frequency of migrating myoelectric complexes (MMC).

5. **Influence of gender, posture and age:** Female shows slower gastric emptying rates compared to male. Posture does not have much more variation in the mean gastric retention time (GRT). Lower GRT is observed in case of elderly people, particularly persons older than 70 years. Gastric emptying is retarded down shifted. Disease state like diabetes and crohn's disease etc. influence drug delivery too.

6. **Fed or Unfed State:** In fasting states the gastric motility is defined by cycles of intense motor activity or the migrating myoelectric complexes (MMC) which happen

every 1.5 to 2 hours. The MMC pushes undigested content out of the stomach and if administration of the formulation is synchronized with that of the MMC, one would expect the GRT of the unit to be highly short. But during the fed state, MMC is retarded and GRT is significantly longer.

7. **Simultaneous drug administration:** Anticholinergics such as atropine and propantheline, opiates such as codeine and prokinetic drugs such as metoclopramide and cisapride may alter floating time.

Benefits of FDDS

Floating dosage systems offer a number of benefits in drug delivery are:

1. Enhanced bioavailability and curative efficiency of drugs and economic utilization of dosage.
2. Drug absorption from floating dosage forms like tablets or capsules will be enhanced due to increased gastric residence time and will stay in the solution for longer duration at its absorption site, even in the alkaline pH of the intestine.
3. Enhanced patient compliance by reducing dosing frequency and ease of dosing.
4. FDDS are beneficial for drugs which are absorbed from the stomach e.g. ferrous salts, antacids.
5. Controlled delivery of drugs. It reduces the gastric or mucosal irritation by releasing drug slowly at controlled rate.
6. Acidic substance like aspirin produce irritation on the stomach wall when come in contact with it thus FDDS formulation can be useful for the dosing of aspirin and other.
7. FDDS are applicable in the therapy of gastrointestinal disease like gastroesophageal reflux.
8. Offer Site-specific drug delivery system.
9. Floating dosage forms are effective in the event of active intestinal movement and in diarrhoea by maintaining the drug in floating state in stomach in order to receive a relatively better response.
10. Easy and conventional equipment needed for production.
11. Gradual release of drug from FDDS dosage form into the system reduces the counter activity resulting in greater efficiency of the drug.
12. FDDS increases the pharmacological action and enhances the clinical results by minimizing the fluctuations in drug concentration over a critical concentration.
13. By the use of FDDS greater therapeutic effect of drugs of short half-lives can be obtained.

Recent Advances in Floating Drug Deliverysystem (FDDS)

Floating Drug Delivery Systems (FDDS) have undergone significant advancements in recent years to enhance gastric retention, improve drug bioavailability, and address the limitations of conventional oral drug delivery. Recent

innovations focus on improving system stability, responsiveness, and precision in drug release.

1. **Multi-Unit Floating Systems:** Recent advances prioritize the application of multi-unit dosage systems like floating microspheres, beads, and nanoparticles. These have improved reproducibility, low risk of dose dumping, and more consistent drug distribution within the stomach. Spray drying, solvent evaporation, and ionotropic gelation are common methods for their preparation.
2. **D Printed Floating Systems:** The use of 3D printing technology has opened up the potential for customization of FDDS according to patient-specific requirements. This allows for better control of system geometry, drug loading, and floating properties, enhancing therapeutic performance and compliance of patients.
3. **Dual-Mechanism Systems:** Recent FDDS formulations are being designed by integrating floating behavior with mucoadhesive, expandable, or swelling characteristics, thus providing enhanced gastric retention even in conditions of motility disturbances or fluctuating gastric emptying states.
4. **Magnetically Controlled FDDS:** The use of magnetic materials in dosage forms enables the spatial control of the drug delivery system by an external magnet. It is particularly beneficial in localized treatment within the stomach and enhancing retention time.
5. **Nano-FDDS:** Nano-technology has made it possible to design floating nanocarriers, including nanoparticles and nanoemulsions, which are known to provide advantages such as improved solubility, permeability, and site-specific delivery of water-insoluble drugs.
6. **Intelligent and Natural Polymers:** There is increased concern for the application of natural polymers such as chitosan and alginate, as well as responsive polymers to pH, temperature, or enzymatic variations. These polymers provide controlled and site-specific delivery of drugs with improved biocompatibility.
7. **Improved Evaluation Techniques:** Recent advances in imaging techniques, such as gamma scintigraphy, MRI, and X-ray radiography, are now used to investigate in vivo gastric retention behavior of FDDS more precisely. These technologies provide real-time monitoring and enhance the in vitro–in vivo correlation predictability.

CONCLUSION

Floating Drug Delivery Systems (FDDS) are a major breakthrough in oral controlled drug delivery by facilitating extended gastric residence and enhanced bioavailability for drugs possessing narrow absorption windows or local gastric activity. Having overcome the drawbacks of traditional dosage forms, FDDS have achieved a lot in maximizing therapeutic efficacy as well as patient compliance. The ongoing creation of new polymers, smart drug release systems, and novel formulation technologies—e.g., 3D printing and nanotechnology—also enhances the promise of FDDS for personalized medicine. Future work will likely be aimed at the development of further improvement in

responsiveness, stability, and targeting properties of FDDS, as well as better in vivo evaluation techniques, to tailor therapeutic results to specific clinical conditions.

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