A COMPREHENSIVE REVIEW OF FLOATING MICROBALLOONS AS A GASTRORETENTIVE DRUG DELIVERY SYSTEM

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Abstract

Hollow microspheres, often referred to as microballoons, have emerged as a promising gastroretentive drug delivery approach designed to enhance absorption and improve therapeutic outcomes. Due to their low density, these carriers are capable of floating on gastric fluids, thereby extending gastric retention and enabling a controlled release of the drug. A variety of fabrication methods, including solvent evaporation–diffusion, spray drying, and emulsion techniques, have been utilised for their development, with polymers such as ethyl cellulose, hydroxypropyl methylcellulose, and Eudragit commonly employed. Evaluation of microballoons typically involves analysing particle size, surface characteristics, entrapment efficiency, floating capacity, drug release behaviour, and stability. Recent studies indicate that these systems can help overcome challenges such as rapid elimination, poor solubility, and inconsistent oral bioavailability. This review summarises current progress in formulation design, process optimisation, and characterisation, while also addressing therapeutic applications, existing limitations, and future perspectives. Overall, microballoons provide a flexible and effective platform for sustained and site-specific drug delivery.

Keywords:
Microballoons, Gastroretentive drug delivery, Floating drug delivery system, Controlled release, Ethyl cellulose, Solvent evaporation method, Buoyancy, Drug entrapment efficiency, In vitro drug release.

INTRODUCTION:

Gastroretentive drug delivery systems (GRDDS)

These are dosage forms designed to stay in the stomach for a longer duration than conventional formulations. These systems provide several therapeutic benefits, including prolonged gastric retention time (GRT), enhanced bioavailability, and improved drug effectiveness[(1,2)].

Gastroretentive drug delivery systems (GRDDS) prolong gastric residence, reducing dose, drug loss, and dosing frequency. Drugs with short half-life and rapid GIT absorption require frequent dosing. GRDDS are useful for drugs with poor solubility at higher pH, as they enhance solubility and absorption in acidic conditions, improving bioavailability through controlled release. Oral controlled-release (CR) systems sustain drug levels by gradually releasing the drug. Prolonged and predictable GRT is essential for effective CR systems[2,3]

Microballoons[4,5,6]

These, also known as hollow microspheres, have become an effective carrier system among other FDDS methods. These are spherical, low-density particles that float on gastrointestinal juices and provide prolonged, controlled medication release. These low-density spheres float on gastric fluids, enabling prolonged, controlled drug release. They are typically under 200 µm. Drug-loaded microballoons, prepared by solvent evaporation or diffusion, enhance gastric residence time and float on acidic media with surfactant for over 12 hours.

Advantages [7,8,9]

1. Microballoons can sustain the release of a drug over an extended period, reducing the frequency of administration and improving patient compliance.
2. Floating microballoons remain buoyant in the gastric fluid for longer durations, enhancing drug absorption in the upper gastrointestinal tract where most drugs have their primary absorption site.
3. The controlled release property minimises the risk of sudden drug release (dose dumping), which can lead to adverse effects.
4. By maintaining the dosage form in the stomach, microballoons help in the localised treatment of gastric disorders and optimise drug concentration at the absorption site.
5. Encapsulation of drugs within polymeric shells protects them from degradation due to environmental conditions such as light, moisture, or gastric pH variations.
6. The floating nature and sustained action reduce the need for multiple daily doses, offering greater convenience to patients, especially in chronic therapies.

Disadvantages[10,11,12]

1. The preparation of microballoons often involves multiple steps such as solvent evaporation, emulsification, or drying, which requires precise control and can increase production time and cost.
2. In some cases, achieving high drug loading within the microballoon structure is challenging, which may limit their use for drugs requiring higher doses.
3. Microballoons are most effective for drugs absorbed in the stomach or upper small intestine. They are unsuitable for drugs that are absorbed in the lower gastrointestinal tract.
4. The buoyancy and performance of microballoons can be affected by variations in gastric emptying time, fed or fasted state, and motility, leading to inconsistent drug release.
5. Many preparation techniques require organic solvents like ethanol, chloroform, or dichloromethane, which can pose toxicity and environmental hazards if not completely removed.

METHOD OF PREPARATION

Solvent evaporation method [13,14]

Polymers like Eudragit, HPMC K4M, and ethyl cellulose were used to prepare floating microballoons. The drug and polymer are dissolved in ethanol, acetone, or dichloromethane to form a uniform solution, which was added to 100 mL of liquid paraffin (external phase) under stirring (1500 rpm) at 35 °C for 3 hours. After solvent evaporation, solid hollow microspheres are formed, collected by filtration, and exhibit buoyancy with sustained release for gastroretentive delivery.

EMULSION SOLVENT DIFFUSION TECHNIQUE: (O/W)[15,16]

The drug was dissolved along with the polymer (such as ethyl cellulose) in a suitable mixture of volatile organic solvents like dichloromethane and ethanol. This solution acts as the internal phase. Liquid paraffin was placed in a beaker, then added a small quantity of a surfactant, such as Span 80, was added, and continuous stirring was performed at a controlled speed. The prepared internal phase was gradually poured into the external phase while stirring. Continued stirring was done for a specific period for the solvents to diffuse and evaporate. This leads to the precipitation of polymer around the core, creating hollow microballoons. Dry the microballoons under vacuum or in a hot air oven at a controlled temperature and store them in airtight containers.

Solvent Diffusion–Evaporation Technique[16]

This approach is a modified form of the conventional emulsion solvent evaporation and emulsion solvent diffusion methods. In this process, the drug and polymer were dissolved together in a mixed solvent system of ethanol and dichloromethane in a 1:1 ratio, along with 0.1% surfactant, such as polyethene glycol (PEG), at room temperature.

The prepared organic phase was then gradually added to 80 mL of an aqueous solution containing 0.46% w/w polyvinyl alcohol, which acts as an emulsifying agent. The mixture was stirred using a propeller-type agitator for about one hour to facilitate solvent diffusion and evaporation of the organic phase. After complete evaporation, the formed particles are collected by filtration. The final formulation was chosen based on optimisation of critical process parameters, including the polymer-to-drug ratio, the drug-to-polymer proportion, stirring speed, and emulsifier concentration, to achieve desired characteristics.

Spray Drying[15,16]

Spray drying is one of the most widely employed industrial techniques for drying materials and producing particulate systems. It is considered highly efficient when desired characteristics such as particle size distribution, bulk density, and particle morphology can be achieved in a single processing step.The polymer was first dissolved in a volatile organic solvent such as acetone or dichloromethane, resulting in a uniform slurry. The mixture was then sprayed into a drying chamber, where it breaks down into fine droplets. As the solvent evaporates faster than the solute can diffuse, a rigid outer layer forms around each droplet, leading to the development of microspheres. Finally, the dried particles are collected using a cyclone separator and further vacuum-dried to eliminate any remaining solvent traces.

Mechanism of Microballoons[17,18]

Microballoons are low-density systems that float on gastric fluids, allowing controlled drug release and prolonged gastric retention. On contact with gastric fluid, the polymer layer hydrates to form a gel barrier, regulating fluid penetration and drug diffusion. Air entrapment lowers density, ensuring buoyancy, while some gastric fluid is required to initiate floating.

Evaluation Methods

i . Percentage Yield[18,19,20]

The yield of the formulated microballoons was calculated by relating the weight of the recovered product to the combined weight of the drug and polymer initially used in the preparation process.

Percentage Yield (%) = (Actual Yield / Theoretical Yield) × 100%

ii. Micromeritic Properties[21,22]

To assess the physical properties of the microballoons, parameters such as particle size, bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose were evaluated.

- **Particle Size**: Measured using an optical microscope fitted with a calibrated ocular micrometre. The mean diameter was calculated from observations of 200–300 particles.
- **Angle of Repose**: Evaluated using the fixed funnel method to determine flow behaviour.
- **Surface Morphology**: Scanning Electron Microscopy (SEM) was used to confirm the hollow nature and surface structure of the microballoons.

iii. In Vitro Buoyancy Test[23,24]

An accurately weighed sample of microballoons were added to 900 mL of 0.1 N HCl solution (pH 1.2) and kept at 37 ± 1 °C in a USP dissolution apparatus, with the medium agitated at a speed of 100 rpm. The buoyancy percentage was determined using the formula:

Buoyancy (%) = {Wf / (Wf + Ws)} × 100

Where, Wf = weights of the floating microsphere, Ws=weights of the settled microspheres

iv. Scanning Electron Microscopy (SEM)[25,26]

For surface analysis, the dried microballoons were subjected to gold coating using an ion sputtering technique to create a thin conductive layer. The samples were then mounted on a metal stub and observed under a scanning electron microscope at an accelerating voltage of 20 kV to capture detailed images of morphology and surface texture.

v. In Vitro Drug Release Study[27,28]

The drug release profiles were evaluated using a USP XXIII basket-type dissolution apparatus. A sample of microballoons equivalent to the required dose was filled in a hard gelatin capsule and placed in the dissolution basket containing 900 mL of 0.1 N HCl (pH 1.2), maintained at 37 ± 1°C and rotated at a pre-set

rpm. Samples of 5 mL were taken at specific time intervals and promptly replenished with an equal amount of fresh dissolution medium to ensure a constant volume and maintain sink conditions. The collected samples were filtered and analysed for drug content using a suitable analytical method, such as UV spectrophotometry or HPLC.

Applications[29,30]

1. Microballoons provide controlled and prolonged drug release, reducing the need for frequent administration and improving patient compliance.
2. Due to their low density and floating ability, microballoons remain in the stomach for an extended time, making them ideal for drugs absorbed primarily in the upper gastrointestinal tract.
3. These systems can target drugs to the stomach or duodenum, which is beneficial for conditions like peptic ulcers or gastritis where local drug action is required.
4. Drugs with poor solubility or stability in the intestinal environment show enhanced bioavailability when formulated as microballoons, as they remain longer at the absorption site.
5. Microballoons allow gradual drug release, minimising the direct exposure of high drug concentration to the gastric mucosa, which reduces irritation and adverse effects.
6. They can be designed for time-controlled release.
7. Microballoons are suitable for low-dose drugs that require sustained levels for therapeutic activity, ensuring a steady pharmacological effect without fluctuations.
8. Drugs that are absorbed only in the upper part of the gastrointestinal tract can benefit from microballoon formulations because of their prolonged gastric retention.

LIST OF PATENTS FOR MICROBALLOONS

PATENT NO.	YEAR	PATENT TITLE
US0062071971B1	2001	Gastroretentive controlled release microspheres for improved drug delivery
US2006/0013876	2006	Novel floating dosage form
US2010/0015224A1	2010	Programmable buoyant delivery technology
EP2329810 A1	2011	Gastric retention drug delivery system, preparation method
US2012/0201892A1	2012	Porous wall hollow glass microspheres as carriers for biomolecules

Conclusion

Floating microballoons have emerged as an effective gastroretentive drug delivery approach for improving the bioavailability of drugs with a narrow absorption window.Various studies reviewed in this article highlights the significance of formulation parameters, polymer selection,and preparation methods in achieving desirable properties like low density, extended floating time, and controlled drug release. The use of polymers such as ethyl cellulose and HPMC, along with techniques like solvent evaporation and diffusion, has been extensively explored to enhance gastric retention. Overall, microballoon-based systems offer promising benefits, including prolonged gastric residence, reduced dosing frequency, and better therapeutic outcomes for hypertensive patients. However, Further advancements in polymer science and in vivo evaluation are essential to optimise these systems for clinical application.

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