RESEARCH PAPER

Microballoons in Peptic Ulcer Therapy: A Gastroretentive Novel Approach

[1,2] R. Uma Prabha, [2] Dr. Akilandeswari, [1] Sahala K, [1] Sai sravan P, [1] Sakshi Korgaonkar, [1] Sangeetha R, [1] Tejashwini N, [1] Varshitha A

[1]The Oxford College of Pharmacy, #6l9, 1st cross, Begur road, Hongasandra, Bengaluru – 560068. Contact Number: +918889219391. Email ID: christyprabha4jesus@gmail.com

[2]Dhanalakshmi Srinivasan University, Tiruchirappalli, Tamil Nadu 621112

ABSTRACT

Peptic ulcer is a common gastrointestinal disorder characterized by lesions, inflammation, or irritation in the stomach or duodenal mucosa. The conventional therapy of peptic ulcers has many limitations including frequent dosing, decreased bioavailability, and multiple drug treatments that lead to patient non-compliance. Gastroretentive Drug Delivery Systems (GRDDS) represent an innovative approach to overcome these challenges by enhancing drug bioavailability and improving therapeutic outcomes. In particular, microballoons have demonstrated great potential in prolonging gastric retention, lowering the frequency of doses, and enhancing drug absorption. This review provides an overview of current peptic ulcer treatments, and the novel drug delivery methods, focusing on microballoons in treating peptic ulcers. It highlights properties of microballoons, its preparation, evaluation, advantages, and various antiulcer drug loading microballoons formulated in research.

KEYWORDS: Microballoons, Peptic ulcer, Gastro retentive drug delivery system, Floating drug delivery system, Extended drug release.

How to cite this article: Prabha RU, Akilandeswari, Sahala K, Sai sravan P, Korgaonkar S, Sangeetha R, Tejashwini N, Varshitha A. Microballoons in Peptic Ulcer Therapy: A Gastroretentive Novel Approach. Int J Drug Deliv Technol. 2026;16(10s): 323-332; DOI: 10.25258/ijddt.16.10s.44

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Peptic ulcer, a major concern, is an erosion on the duodenal or stomach mucosa, which is caused by the corrosive and irritant action of pepsin and gastric acid in the lumen of GI.[1],[2] The size of lesion usually ranges greater than 3-5 mm in stomach and duodenum.[3],[4] The management of peptic ulcer includes acid neutralization by antacids like Aluminium hydroxide, sodium bicarbonate, magnesium hydroxide or acid suppression by H2 antagonists including proton pump inhibitor (PPI), ranitidine, cimetidine, nizatidine, famotidine and roxatidine such as lansoprazole, omeprazole, pantoprazole, rabeprazole.[5],[6] The current therapy for *H.pylori* infection and stomach ulcer include combination of antimicrobial drugs, proton pump inhibitors (PPIs), H2 antagonists, double therapy, triple therapy, quadruple therapy and successive therapy to boost the treatment effectiveness, and to promote the mucosal healing to achieve the required patient outcomes. However, this multiple drug therapy results in decreased patient adherence due to complex drug regimen and increased frequency of dosing that can lead to treatment failure. Hence, advanced formulation approaches like prolonged-release GRDDS have the capability to overcome the existing problems related to bioavailability of the drug and simplifies the treatment regimens.[7]

Gastro-retentive drug delivery system (GRDDS) integrates the stomach retention with timed drug release to ensure prolonged drug efficacy. GRDDS is effective both locally and systemically, locally by acting on gastric mucosa or eradicating *H. pylori*, thereby it relieves peptic ulcer, esophagitis, and healing *Helicobacter pylori* infection in the stomach. Systemically, it maintains steady drug levels in plasma for absorption in the upper GIT.[8] This approach is used for drugs having shorter half-life and are easily excreted when administered through the GIT, requiring repeated doses. GRDDS prolongs gastric retention, releasing drug slowly and maintains therapeutic levels over a longer period, reducing reliance on repeated dosing.[9] Conventional oral medications do not show site-specific drug delivery also they exhibit poor bioavailability attributed to fluctuating plasma drug concentration.[10] Hence, in such cases the frequency of dosing increases and thereby they show poor patient adherence. Therefore, GRDDS offers an innovative strategy to overcome these challenges and improve patient compliance.[9]

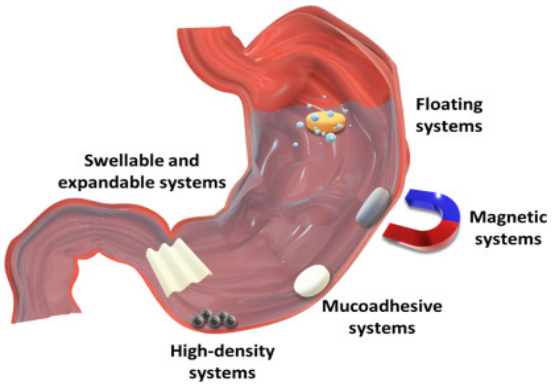


Figure. 1 Different approach of GRDDS [11]

Floating drug delivery system:

The Floating Drug Delivery System (FDDS) is a gastroretentive approach wherein low-density formulation (<1.004 g/cm^3, density lower than gastric fluid) remains buoyant on gastric contents, enabling prolonged stomach residence and sustained drug release as the drug diffuses slowly from the polymeric shell.[12]

Types of FDDS:

FDDS are grouped into categories based upon the mechanism it follows and depending upon the technique applied for the formulation as shown below in Figure 2. It includes effervescent systems, which release CO_2 for buoyancy, non-effervescent systems which utilizes swellable polymers without generating gas to achieve floatability, and raft forming systems, which form a gel-like raft on exposure with gastric contents.[12]

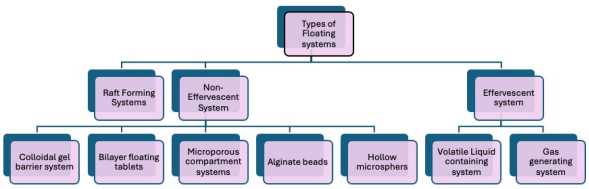
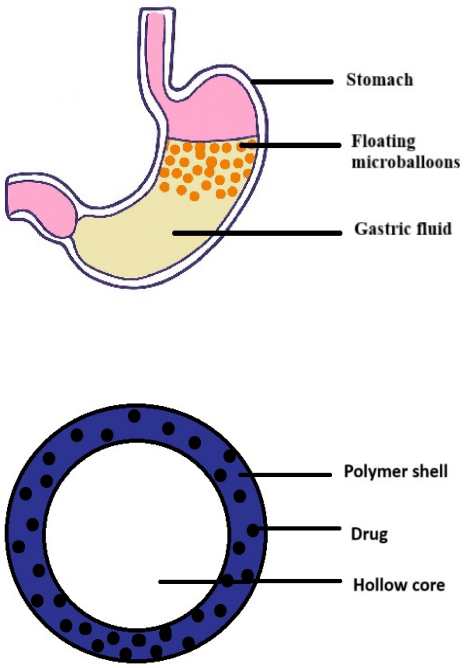


Figure. 2.Types of FDDS

Microballoons:

Microballoons or hollow microspheres are the most efficient buoyant system which is a type of non-effervescent gastroretentive floating drug delivery system. Microballoons are hallow, spherical particles devoid of an internal core. Typically formulated as free-flowing powders, they consist of synthetic polymers such as Cellulose acetate, Carbopol, Eudragit, HPMC, EC, Polyvinyl acetate, Polyacrylate, Methocel, Acrylate or proteins, and they measure less than 200 micrometers in diameter. This approach exhibits gastro retentive and controlled drug delivery, which significantly enhances bioavailability, and hence, this system promises to be an innovative and effective gastric retention method of drug delivery.[13],[14] Microballoons are typically low-density system that float on the gastric content, providing prolonged retention without causing irritation or discomfort to GIT. They have the merit of remaining active and dispersing the drug uniformly in the gastric juice thus stabilizing the gastric emptying rates and releasimg drug for a longer period. This drug delivery can be a promising strategy for the treatment of ulcer, for instance, A novel sustained-release microballoon formulation combining rabeprazole (RBZ) and amoxicillin (AMX) in a single dose showed lower ulcer indices and higher ulcer prevention compared to free RBZ and AMX, enhancing therapeutic efficacy and gastroprotection (Choudhary S *et al.,* 2016). The aforementioned approach is illustrated in Figure 3, which depicts the diagrammatic representation of microballoons.[15],[16]



(a)

(b)

Figure. 4 (a) diagrammatic representation of floating microballoons on the gastric fluid (b) diagrammatic illustration of a microballoon

Floating Mechanism of Microballoons:

As microballoons encounter gastric fluids, the incorporated gel-forming polymers and polysaccharides imbibe water, instigating the formation of colloidal gel barrier, which regulates the fluid ingress and, thereby, governs the drug release kinetics. Hydration from the contiguous hydrocolloid layer preserves the gel barrier even if the outer surface is dissolved. The entrapped air within the polymer decreases the bulk density of the microballoons and offers sufficient buoyancy to float on the gastric fluid. Effective buoyancy is achieved with limited stomach content.[17] By adjusting the ratio of polymer to drug, the drug release rate can be controlled. Microballoons in *in-vitro* float for 12 hours in aqueous medium, against peristaltic movements and they remain in the upper region of stomach for 3 hours.[18] The gel formation, floating and controlled release behavior is achieved by the use of polymers like Cellulose acetate, Carbopol, Eudragit, HPMC, EC, Polyvinyl acetate, Polyacrylate, Methocel, Acrylate or proteins.[13]

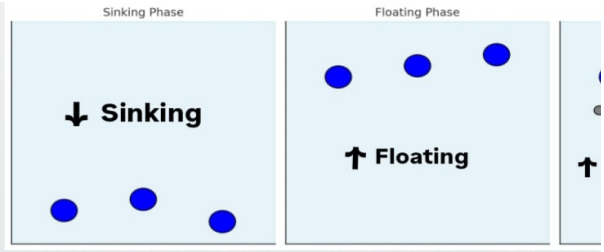


Figure. 5. Mechanism of floating system.

Factors contributing to gastric retention:

Various aspects influence the gastric residence time of the oral formulation.

Density: The density has a great impact on gastric retention time. The dosage forms that are buoyant and have less density can float easily and hence remain in stomach for long duration.

Shape: Devices shaped like tetrahedrons, or ring tend to linger in the stomach for a prolonged period compared to those with other geometries, because of their increased surface area and their ability to resist gastric emptying.

Size: Most reports suggest dosage units with a diameter exceeding 7.5 mm demonstrate longer gastric residence time compared to smaller units, likely by their optimized geometry and interaction with gastric motility.

Single or multiple unit formulation: Multiple-unit forms offer more consistent GI transit pattern in contrast to single-unit systems.[19]

Nature of meal: High protein, fat or carbohydrates do not make a difference provided that the content of calories is the same. Although a boost in the calorie value and acidity can retard the gastric emptying time.[19],[20]

Fed and unfed state: Gastric retention time in fed is considerably longer due to delay in the strong motor activity called migrating myoelectric complex (MMC).

Frequency of feed: With consecutive meals, MMC occurs infrequently resulting in prolonged gastric retention time exceeding 400 minutes.

Age: Elderly individuals, particularly those over 70 years of age, show longer gastric retention time.

Gender: In ambulant subjects, mean gastric retention time is shorter in men (3.4±0.6 h) than in matched women (4.6±1.2 h), independent of body size.

Posture: Posture affects gastric emptying rates, with supine position that significantly delays gastric emptying compared to upright position.[20]

Excipients commonly used in microballoons:

Category	Examples	Role in microballoons
Natural polymers	Chitosan, guar gum, xanthan gum, sodium alginate, gellan gum, agar	Gel formation, floating and controlled release behavior
Synthetic polymers	Eudragit, Carbopol, ethyl acetate, hydroxypropyl methylcellulose (HPMC), Polyacrylate, polyvinyl acetate.	Controls drug release and support formation of microballoons
Solvents	Dichloromethane (DCM), ethanol, isopropyl alcohol (IPA), dimethyl formamide (DMF), acetone, and acetonitrile	Dissolve the polymer and the drug and form low density, hollow microspheres
Processing medium	Water, polyvinyl alcohol, and liquid paraffin	Provides medium for emulsification, hardens the polymer as

		solvent evaporates
Stabilizing and emulsifying agents	Tween 80, SLS, and span 80	Solidify and stabilize the microballoons
Cross-linking agents	Glutaraldehyde, formaldehyde, or diacid chlorides	Enhance mechanical strength by cross-linking the polymer chains

TABLE No. 1 Common excipients utilized in microballoons formulations [13][21]

Preparation methods of microballoons:

The formulation of microballoons includes several techniques influenced by the route of administration, desired release kinetics, and particle size criteria. The common methods include emulsion solvent evaporation, emulsion solvent diffusion, coacervation phase separation, ion gelation, spray drying and spray congealing.[21],[22]

1. Emulsion solvent evaporation technique:

The drug is dissolved in chloroform and then introduced into an aqueous phase composed of 0.2% sodium PVP that acts as an emulsifier. The mixture of drug together with polymer such as Eudragit is rotated at 500 rpm which gets broken down to form fine droplets that solidify to form rigid microballoons by solvent evaporation, filter and the following is washed with distilled water and desiccated for 24 hours at room temperature to remove the moisture. The two primary systems employed in this technique are o/w and w/o emulsion systems.[23]

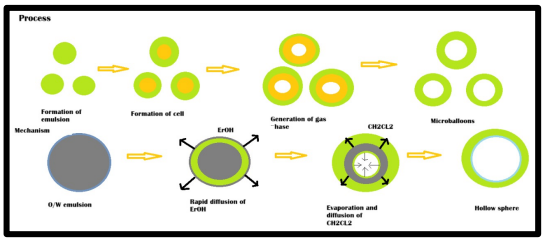


Figure. 6 Emulsion solvent evaporation method

2. Emulsion solvent diffusion method:

According to this process, the drug loaded polymer mixture is solubilized in an organic phase. This mixture is then gradually introduced into polyvinyl alcohol solution and is agitated at 1500rpm for about an hour at different temperature intervals.[21]

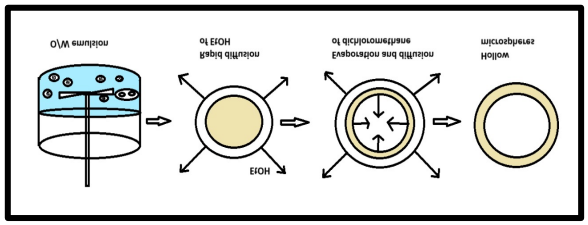


Figure. 7 Emulsion solvent diffusion method

3. Single emulsion technique:

This method involves dispersing suspension or aqueous polymer solution in an organic solvent that may be chloroform or oil with continuous agitation (sonication). Subsequently, the microspheres can be formed in two ways that can be by heat denaturation and chemical cross-linking, then centrifugation is carried out followed by washing and separating the microballoons.[24]

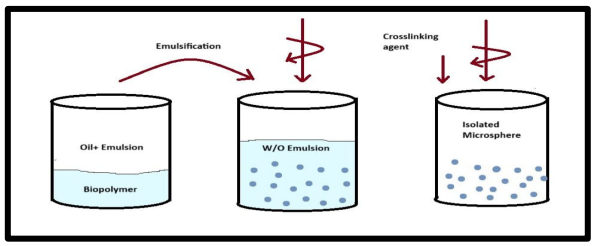


Figure. 8 Single emulsion technique

4. Double emulsion technique:

An aqueous polymer solution and drug is emulsified in organic solvent to produce first emulsion (w/o type). This first emulsion is introduced to an aqueous polyvinyl alcohol (PVA) solution to form multiple emulsions. The multiple emulsion is introduced to a large aqueous phase, and the polymer is denatured to form hollow microspheres in the solution. The hollow microspheres thus formed are separated, washed and dried.[24], [25]

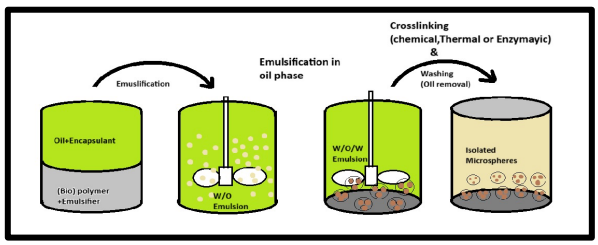


Figure. 9 Double emulsion method

5. Coacervation phase separation technique:

The concept of coacervation relies on reducing the solubility of a polymer in the aqueous organic solvent phase inducing phase separation into polymer enriched phase known as coacervates. Here the drug dispersion is formed in the polymeric solution, and an incompatible polymer is being introduced into the

mixture, leading to the phase separation of the initial polymer, and the active ingredients are encapsulated.[26]

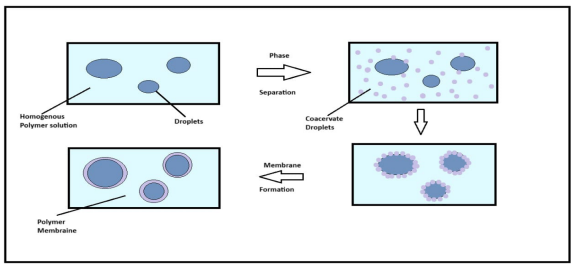


Figure. 10 Coacervation/ Phase separation technique

6. Ion gelatine technique:

In the ionic gelation method, purified water, polymer, copolymer, and cross-linking agent are combined and mixed to form a homogenous solution. The medication is then introduced to the above prepared polymer solution and stirred vigorously in magnetic stirrer to achieve uniform dispersion. For creating gelatin medium, calcium chloride is dissolved in 2% glacial acetic acid. The alginate solution is then added into the gelatin medium using a syringe needle. The microspheres are collected, rinsed twice with distilled water and dried for 24 hours at ambient temperature.[27] The diclofenac sodium release can be prepared by alginate/chitosan particulate method system as follows: the drug is incorporated into 1.2% (v/w) sodium alginate aqueous solution and are constantly stirred without any interruption; this can confirm the complete stability of drug. The resultant mixture is then slowly added to a solution containing Ca2+ and Al3+ ions, along with acetic acid-based chitosan solution, triggering gelation by cross-linking polymers, boosting gel strength and stability. This cross-linking solidifies the microballoons, helping them retain their shape. The microballoons remain sustained in the initial mixture for 24 hours to facilitate the internal gelation. The solution is then filtered to isolate the microballoons. Importantly, the alginate/chitosan particle system exhibits maximum drug release within a pH range of 6.4-7.2.[21]

7. Polymerization technique:

The polymerization techniques are classified as follows:

a. Natural polymerization: Several techniques can be used, like bulk suspension, emulsion, precipitation, and micellar processes.
   Examples: Alginate microballoons cross-linked with Ca^{2+} ions
b. Interfacial polymerization: This method includes monomer reaction at the liquid-liquid interface, resulting in the polymer film formation that surrounds the dispersed components.[21]
   Example: Polyurethane microballoons

8. Spray drying and spray congealing:

Spray drying: The solid drug is dispersed in the polymeric solution using high shear homogenization, and this is sprayed in a hot gas stream to yield fine droplets; the solvent evaporates instantly thus creating microballoons of different sizes.

Spray congealing: The solidification of the coatings can be achieved by thermally congealing the molten materials. A molten mixture of drug and carrier is broken into droplets and cooled to form solid particles, like microballoons. Solvent removal can be done by various methods like extraction, sorption, evaporation.[25]

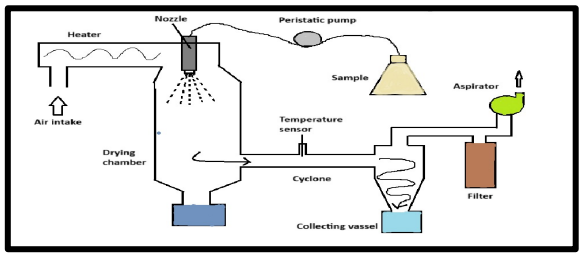


Figure. 11 Spray drying and spray congealing

EVALUATION AND CHARACTERIZATION OF MICROBALLONS:

Microballoons Morphology:

The surface morphology and overall shape of microballoons are typically assessed by scanning electron microscopy (SEM), which provides detailed visualization of their structural features. Upon examination of stavudine-loaded floating microballoons, Vidyadhara *et al.*, observed particles with spherical shape with smooth surface characteristics under SEM examination.[28] In contrast, studies on pentoxifylline-based microballoons revealed porous surface architectures, reflecting the presence of internal cavities that contribute to buoyancy. Collectively, these SEM findings emphasize the impact of polymer selection, solvent evaporation rate, and stirring speed play a decisive role in shaping the surface texture and hollow structure of microballoons, which in turn directly influence their drug release characteristics and floating performance.[29]

Particle size:

Particle size determination of microballoons is typically analyzed with optical microscopy, where the particles are dispersed in a medium such as glycerin to minimize aggregation and ensure uniform distribution. Under the microscope, measurements are commonly

taken for at least 100 individual microballoons using calibrated eyepiece and stage micrometers to obtain reliable data.[30] This method has been generally applied across different formulations, including pentoxifylline-loaded microballoons, to evaluate how factors such as polymer concentration, stirring speed, and the choice of solvent system influence the average particle diameter using the formula:[29]

Average diameter = Total diameter of microballoons / Number of microballoons × Calibration factor.

Micromeritic properties:

Micromeritic parameters such as bulk density, tapped density, Hausner's ratio, Carr's compressibility index, and angle of repose are commonly evaluated to determine the flow properties of microballoons.

Bulk density:

Bulk density represents the ratio of mass of microballoons to the initial volume they occupy in a container without shaking or compression. It indicates the natural packing ability of the hollow particles (Kumar et al., 2021).[31] Okunlala A et al., 2022 in their research reported lower densities of Metoprolol succinate microballoons, which enhanced floating in the gastric fluid, enabling sustained release of the drug.[32] Bulk density is a key micromeritic parameter used to evaluate flow and packaging characteristics during capsule filling and other production steps.[33]

Formula:

ρ_B = *Weight of sample (W) ÷ Bulk volume (BV)*

Tapped density:

Tapped density is the ratio of mass of microballons to the volume after mechanical tapping, causing particles to settle, reducing its voids. It is obtained by the formula given below:

Formula:

Tapped density = Mass of microballoons (grams) / Volume of microballoons after tapping (cm^3).

Tapped density less than the gastric fluid density (1.004 g/cm^3) indicates good buoyancy property in the stomach as per the research of Biswas *et al.,* 2025.[34] Tapped density tend to be higher for particles with regular shape (e.g., Spheres) compared to irregular shapes like needles, which have more void space and pack less compactly.[35]

Hausner's ratio: It reflects the compressibility and flow characteristics of a powder. In the study conducted by Ammar et al, in 2016 reported that Hausner's Ratio, indicates flowability, where values less than 1.25 suggest good flow and greater than 1.5 indicate poor flow.[36] This ratio helps understand the packing behavior of microballoons and is derived from bulk density and tapped density values by using the formula:

Hausner ratio = Tapped density / Bulk density.

Compressibility Index:

The percentage compressibility of the powder will serve as the direct measure of its potential for formation of stable arches or bridges, also known as Carr's index. In a study conducted by Gupta et al.,2014 they have shown that assessing compressibility, with values less than 10% indicating excellent flow, 11-15% good, and greater than 23% poor.[37] It is computed as follows:

% Compressibility index = (Tapped density - Fluff density) / Tapped density × 100.

Angle of repose:

The angle of repose serves as a straightforward yet informative parameter for evaluating flowability of powders, defined as the angle formed between the surface of a particle heap and the horizontal plane. A commonly employed approach in the literature is the fixed-funnel method, where powder is allowed to flow through a funnel until a conical pile is formed, after which the height (h) and base radius (r) of the heap are measured to determine the angle using the relation $\theta = \tan^{-1}(h/r)$.[38] Concerning microballoons, this measurement provides insight into their ease of handling during manufacturing processes such as capsule filling. In 2022, Agarwal *et al.* reported that angle of repose reflects flow properties, where angles less than 30° indicate excellent flow, 30-40° good, and greater than 40° poor flow. Reported variations in the angle of repose across different formulations highlight how factors like polymer composition, solvent system, and processing conditions influence inter-particle interactions and, consequently, the overall flow behavior of the microballoons.[39]

Angle of repose = $\tan^{-1}$ (Height of the pile (h) / Radius of the base of the pile (r))

Percentage yield:

The percentage yield is evaluated by dividing the mass of dried microballoons by the total mass of the non-volatile ingredients and the drug. The equation used is,

% yield= Actual weight of product /Total weight of drug and excipients×100 [38]

Thus, the higher percentage yield indicates greater process efficiency and effective use of materials during the formulation and serves as a primary evaluation parameter. In the study by Manivasakam Prakash *et al.,*2025 the yields ranged from 49% to 82.5% and the statistical findings showed that the solvent composition and polymer concentration were the key factors that had significant impact on the yield of microballoons.[40] Similarly, in another study by Krishna *et al.,*2020 the solvent evaporation technique produced yields higher than 76.4%, confirming the method's efficiency and the

experimental conditions. Both these outcomes collectively indicate that the yield is often influenced by variables like the type of solvents, concentration of polymers and the preparation techniques used.[41]

Entrapment efficiency:

Entrapment efficiency (EE) is typically determined by disrupting the microballoons commonly through solvent dissolution or vortexing to release the encapsulated drug. The liberated drug is then quantified, often using analytical techniques such as UV spectrophotometry, and the measured concentration is compared against the theoretical drug load. The EE is calculated using the formula:

$\%\ Entrapment\ efficiency = (Drug\ content\ calculated / Theoretical\ drug\ content)\ X\ 100$.[38]

Entrapment efficiency is a key parameter used to evaluate how effectively a drug has been incorporated into microballoons. In a study performed by Krishna *et al.,*2020 dipyridamole was formulated as floating microballoons using ethyl cellulose, polymer and span 80 as the surfactant. The formulated microballoons exhibited 73.8% entrapment efficiency, with EE being higher than 92.8% in optimized formulations, significantly influenced by factors such as polymer concentration, solvent composition, stirring speed and surfactant levels.[41]

***In-vitro* Drug release:**

In-vitro drug release studies are vital for accessing the release kinetics of microballoons, which can be studied by USP XXIII basket type apparatus in simulated gastric fluid at 37 ± 1°C at 100 rpm.[42] Studies by Sowjanya M *et al., 2017* have shown that polymer type, formulation composition, particle characteristics, and type of incorporation significantly influence the drug release profile, governing release kinetics through diffusion, erosion, or swelling mechanisms.[43] Research suggest that increasing rotation speed from 300-500 rpm enhances drug release from microballoons, which is possibly due to reduced particle size and increased surface area, facilitating faster dissolution.[44] Decrease in the drug-to-polymer ratio slows the drug release from microballons, as increased polymer amount thickens the microsphere matrix, hindering drug diffusion due to increased diffusional path length and shows reduced initial burst release. Studies also indicate that polymer concentration influences particle size and surface characteristics which impact drug release kinetics (Jagtap YM et al., 2012).[45]

Buoyancy study:

Higher polymer concentrations enhance buoyancy, aligning with Gupta *et al*. (2014), enabling prolonged gastric residence (Ammar *et al*., 2016). Larger particles show improved floating ability (Agarwal *et al*., 2022; Pingale & Amrutkar, 2021). For instance, Eudragit S100 microballoons achieved 92.56% buoyancy (Asthana GS *et al*., 2025), comparable to Gupta *et al.'s* (2014) findings (>90%). This highlights potential for sustained drug release and improved therapeutic outcomes, informing development of efficient gastroretentive drug delivery systems.[44]

%Buoyancy= Weight of floating microballoons/ (Weight of floating + settled microballoons) ×100

Advantages of microballoons:

- The constant release of medication over an extended period reduces dosing frequency and therefore enhances patient compliance.
- Enhanced absorption of those drug that are specifically soluble in the stomach.
- Improved drug utilization can significantly enhance the therapeutic efficacy and lessen the frequency or severity of side effects by maintaining consistent plasma concentration through continuous release of drug, also this approach mitigates first-pass metabolism and thereby improves the therapeutic outcomes.
- Because of its sustained release effect, gastric irritation can be minimized and can also enhance the therapeutic efficacy of those drugs that have short half-life.
- Due to buoyancy, gastric retention time is prolonged, and the material density is decreased.
- Minimizes colon-related harmful effects.
- Microballoons offer site specific delivery of drug to the stomach. They ensure to release the drug uniformly and thus eliminate the risk of dose dumping.[46],[47]

Disadvantages of microballoons:

- Drugs with gastric instability or solubility challenges aren't suitable for microballoons formulations.
- This drug delivery system requires high fluid levels to maintain buoyancy and work efficiently.
- Crushing and chewing are not possible in this type of dosage form.
- This type of drug delivery system usually has a high drug load, so comprising release mechanisms can lead to potential toxicity.
- Drugs that degrade in stomach acid are unfit for this type of novel drug delivery system.
- Intake of food and gut transmit time influences the release rate of controlled release medications.[47],[48],[49]

Drugs formulated in research:

Several drugs formulated in research include microballoon-based formulations for the peptic ulcer treatment, some of which are mentioned in the table.1[10],[25]

DRUG	Brand name
Famotidine	Pepcid AC
Nizatidine	Tazac
Pantoprazole sodium	Protonix

TABLE No. 2 Drugs formulated in research

CONCLUSION

A potentially effective approach to treating peptic ulcers is the use of microballoons. Conventional treatments such as PPIs and H2 blockers have drawbacks of multiple dosing, poor bioavailability, and inconsistent release, leading to decreased effectiveness and increased side effects. Microballoons provide sustained release of medication, improve patient adherence by minimizing the dosing frequency, and also increase therapeutic efficacy. By precisely targeting specific areas of stomach, increasing the drug concentration in the gastric mucosa and eradicating *Helicobacter pylori* it provides relief from peptic ulcer, gastritis, esophagitis. Future research is essential to commercialize microballoons-based formulation for the treatment of peptic ulcers. The favorable outcomes in maximizing patient adherence and lowering healthcare expenses, making them a promising subject for research. The use of microballoons may revolutionize peptic ulcer treatment by providing more efficient and effective solutions.

REFERENCES

1. Bindumol KC, Mathew F, Sunil S, Jose A. Formulation and evaluation of floating controlled drug delivery of anti-ulcer drug loaded microballoons. Journal of Innovations in Applied Pharmaceutical Science (JIAPS). 2023 Nov 30:95-100.

2. Laucirica I, Iglesias PG, Calvet X. Peptic ulcer. Medicina Clínica (English Edition). 2023 Sep 29;161(6):260-6.

3. Kavitt RT, Lipowska AM, Anyane-Yeboa A, Gralnek IM. Diagnosis and treatment of peptic ulcer disease. The American journal of medicine. 2019 Apr 1;132(4):447-56.

4. Jaiswal F, Rai AK, Wal P, Wal A, Singh SP. Peptic ulcer: a review on etiology, pathogenesis and treatment. Asian Journal of Pharmaceutical Education and Research. 2021;10(4):1.

5. Malik TF, Gnanapandithan K, Singh K. Peptic Ulcer Disease. StatPearls StatPearls Publishing.

6. RaviKKumar VR, Rathi S, Singh S, Patel B, Singh S, Chaturvedi K, Sharma B. A comprehensive review on ulcer and their treatment. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2023 Dec 21;39: e20230006.

7. Gupta A, Shetty S, Mutalik S, Mathew EM, Jha A, Mishra B, Rajpurohit S, Ravi G, Saha M, Moorkoth S. Treatment of H. pylori infection and gastric ulcer: Need for novel pharmaceutical formulation. Heliyon. 2023 Oct 1;9(10).

8. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: A recent update. Asian journal of pharmaceutical sciences. 2016 Oct 1;11(5):575-84.

9. Sharma G, Nautiyal U, Ahmad S. An overview on gastroretentive drug delivery system (GRDDS). International Journal of Health and Biological Sciences. 2019;2(2):1–8.

10. Nithyashree RS, Kumar DS, Gosh T, Ranjitha M, Priya SS, Saravanan KS, Azamthulla M. Floating microballoon-a novel formulation for gastrointestinal diseases. Journal of Pharmaceutical Sciences and Research. 2020;12(1):74-8.

11. Lodh H, Sheeba FR, Chourasia PK, Pardhe HA, Pallavi N. Floating drug delivery system: A brief review. Asian Journal of Pharmacy and Technology. 2020;10(4):255-64.

12. Rajendra BA, SJ V, CR S. A comprehensive review on floating drug delivery system (FDDS). Res J Pharm Biol Chem Sci. 2020;10(6):174-82.

13. Kothawade, S.; Pande, V.; Bole, S.; Autade, K.; Sumbe, R.; Albhar, S.; Raut, K. A Floating System for Drug Delivery using Microballoons. Preprints 2022, 2022120112. https://doi.org/10.20944/preprints202212.0112.v1

14. Hajare PP, Rachh PR. Gastroretentive microballoons: a novel approach for drug delivery. International Journal of Pharmaceutical Sciences and Research. 2020;11(3):1075-83.

15. Supriya S, Swetha M. A review on microballoons. World journal of pharmaceutical science and research. 2023;2(4). 21-24

16. Choudhary S, Jain A, Amin MC, Mishra V, Agrawal GP, Kesharwani P. Stomach specific polymeric low density microballoons as a vector for extended delivery of rabeprazole and amoxicillin for treatment of peptic ulcer. Colloids and Surfaces B: Biointerfaces. 2016 May 1; 141:268-77.

17. Chaudhari SK, Pimpalshende PM, Kosalge SB. Microballoons: A novel approach to mitigate diabetes. Asian Journal of Pharmaceutical Education and Research [Internet]. 2024;13(1):27–38.

18. Naveena C, Hadi MA. Preparation And Evaluation of Floating Microsphere J Clinical Case Studies and Review Reports. 1 (1): 1. DOI: CCSRR-RA-02. 2024.
19. Shinde S, Tadwee I, Shahi S. Gastro retentive drug delivery system: A review. Int. J. Pharm. Res. & All. Sci. 2012;1(1):01-13.
20. Gorde NK, Kale M. Microballoons as a Gastro-retentive Floating Drug Delivery System: An Overview. International journal of pharmaceutical and phytopharmacological research. 2013 Jan 1;2(4):230-9.
21. Chavan PB, Malpure PS, Talele GS, Kadam AR. The Latest Advancements: A Comprehensive Review of Microballoons for Enhanced Gastroretention. Asian Journal of Pharmaceutical Research and Development. 2024 Jun 15;12(3):222-9.
22. Ayalasomayajula LU, Navya K, Earle RR, Pravallika AA. Review on non-effervescent gastro retentive drug delivery systems-microballons. Asian Journal of Pharmaceutical Research. 2020;10(4):312-8.
23. Kajal T, Dilip G, Sunil K. Hollow microsphere as a drug carrier: -A review of classification and preparation technique with their application system (FDDS). 2020 Dec 24; 8:10.
24. Verma R, Verma S, Kumar S. Microsphere-a novel drug delivery system. Research Chronicle in Health Sciences. 2019 Jul 30;5(1):5-14.
25. Srivastava A, Shukla R, Sharma K, Jain H, Meshram DB. Microballoons: A Gastro Retentive Drug Delivery System. Journal of Drug Delivery & Therapeutics. 2019 Jul 2;9(4):625-630.
26. Janjale VR, Patil SR, Fegade TD. A Review on: Floating Microsphere. American Journal of Pharmaceutical Research. 2020;10(02):232-59.
27. Soni A, Patil S. A Review on Microparticles Drug Delivery System. International Journal of Pharmaceutical Research and Applications [Internet]. 2023; 8:1355.
28. Vidyadhara S, Sasidhar RL, Balakrishna T, Balaji B, Amrutha R. Formulation and Evaluation of Controlled Release Floating Microballoons of Stavudine. Sci Pharm. 2015 Jun 9;83(4):671-82. doi: 10.3797/scipharm.1501-07. PMID: 26839847; PMCID: PMC4727757.
29. Malik P, Nagaich U, Malik RK, Gulati N. Pentoxifylline Loaded Floating Microballoons: Design, Development and Characterization. J Pharm (Cairo). 2013; 2013:107291. doi: 10.1155/2013/107291. Epub 2013 May 9. PMID: 26555964; PMCID: PMC4590787.
30. Srikar, Grandhi. "Floating microspheres: A prevailing trend in the development of gastroretentive drug delivery system." *Asian Journal of Pharmaceutics (AJP)* 12.04 (2018).
31. Kumar S, Tiwari A, Goyal N. Floating microspheres of lafutidine: Formulation, optimization, characterization, in-vitro and in-vivo floatability studies using eudragit grades. Indian J Pharm EducRes. 2022 Jul 1;56(3):681-8.
32. Okunlola A, Okafor CC. Formulation of gastroretentive microballoons of metoprolol succinate using acetylated cocoyam (Xanthosoma sagittifolium) starch as a sustained release polymer. East and Central African Journal of Pharmaceutical Sciences. 2022;25(1):17-30.
33. Bhise m, Shukla k, jain s, Bhajipale n, Sudke s, Burakle p. Development and Evaluation of Floating Microspheres of Anticonvulsant Drug by 32 Full Factorial Design. Turk J Pharm Sci. 2022 Oct 31;19(5):595-602. doi: 10.4274/tjps.galenos.2021.53050.
34.Biswas S, Sengupta S, Pegu P, Dey N, Sen A, Debnath B, Nag M, Amin N, Das A, Datta S, Bishal A. Design and Characterization of Aceclofenac-Loaded Microballoons using Eudragit with Hydroxypropyl Methylcellulose. Journal of Drug Delivery and Therapeutics. 2025 Jan 1;15(1):130-41.
35. Ulusoy U. A review of particle shape effects on material properties for various engineering applications: from macro to nanoscale. Minerals. 2023 Jan 6;13(1):91.
36. Ammar, H.O., Ghorab, M., Kamel, R. *et al.* Design and optimization of gastro-retentive microballoons for enhanced bioavailability of cinnarizine. *Drug Deliv. and Transl. Res.* **6**, 210–224 (2016).
37. Gupta R, Prajapati SK, Pattnaik S, Bhardwaj P. Formulation and evaluation of novel stomach specific floating microspheres bearing famotidine for treatment of gastric ulcer and their radiographic study. Asian Pacific Journal of Tropical Biomedicine. 2014 Sep 1;4(9):729-35.
38. Archana ray, Dr. NS Lodhi, Prabhat Bais. Formulation and evaluation of griseofulvin loaded microballoons for sustained drug release; International Journal of Pharmacognosy and Pharmaceutical Sciences. January 20246(2):01-06
39. Agarwal S, Thakur A, Sharma A. Development and evaluation of ketoprofen loaded floating microspheres for sustained delivery. Materials Today: Proceedings. 2022 Jan 1; 68:647-52.
40. Prakash M, Nallasamy V, Venkatachalam S. Fabrication of levofloxacin-loaded ph-sensitive

eudragit polymeric floating microballoon biomaterial for gastroretentive drug delivery. Journal of Applied Pharmaceutical Research. 2025 Feb 28;13(1):170-8.
41. Krishna SR, Ramu A, Vidyadhara S. Study of influence of formulation and process variables on entrapment efficiency and particle size of floating micro balloons of dipyridamole by doe. Int J Pharm Pharm Sci [Internet]. 2020:85-91.
42. Prakash M, Nallasamy V, Venkatachalam S. Fabrication of levofloxacin-loaded ph-sensitive eudragit polymeric floating microballoon biomaterial for gastroretentive drug delivery. Journal of Applied Pharmaceutical Research. 2025 Feb 28;13(1):170-8.
43. Sowjanya M, Debnath S, Lavanya P, Thejovathi R, Babu MN. Polymers used in the designing of controlled drug delivery system. Research Journal of Pharmacy and Technology. 2017;10(3):903-12.
44. Asthana GS, Tkts K, Asthana A, Satti SR, Poldasari S. Eudragit S100-based Floating Micro ballons of Antitubercular Drug: Design, Preparation, and in Vitro Characterization. Fabad Eczacılık Bilimler Dergisi. 2025;50(3):635-54.
45. Jagtap YM, Bhujbal RK, Ranade AN, Ranpise NS. Effect of various polymers concentrations on physicochemical properties of floating microspheres. Indian journal of pharmaceutical sciences. 2012 Nov;74(6):512.
46. Kumar R, Kamboj S, Chandra A, Gautam PK, Sharma VK. Microballoons: An advance avenue for gastroretentive drug delivery system-A review. Pharmaceutical and Biosciences Journal. 2016 Jul 18:29-40.
47. Prathibha C, V D, Sheeba F, R V. A Review on Multiple Unit Hallow Microspheres (Microballoons); International Journal of Pharmaceutical Research and Applications. JUNE 2021; 6(3); 950-964.
48. Suhas Patil*, Dr. A. W. Ambekar, Formulation, Development and Characterization of Floating Microballoons, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 12, 2477-2492.
49. Negia R, Goswamia L, Kothiyal P. Microballoons: A better approach for gastro retention. Indian Journal of Pharmaceutical and Biological Research. 2014 Jun 30;2(02):100–7.