

Influence of Polymer Composition on Entrapment Efficiency, Buoyancy, and Drug Release Behavior of Pioglitazone Floating Microspheres

Neha Khare^{1}, Sushil Bhargav²*

¹Research Scholar, Faculty of Pharmaceutical Sciences, Madhav University, Pindwara Sirohi, Rajasthan-307032 (Corresponding Author)

Email: nehakhare567@gmail.com

Contact No: +91-8717846468

²Pro-Vice Chancellor, Madhav University, Pindwara, Sirohi, Rajasthan-307032

Received: 28th Jul, 2026 | Revised: 01st Aug, 2026 | Accepted: 05th Aug, 2026 |
Available Online: 17th Aug, 2026

ABSTRACT

Background: Polymer composition plays a crucial role in determining the physicochemical properties and performance of floating microspheres intended for gastro-retentive sustained drug delivery.

Objective: This study evaluated the influence of ethyl cellulose and hydroxypropyl methylcellulose (HPMC) composition on the entrapment efficiency, buoyancy, and drug release behavior of pioglitazone floating microspheres.

Methods: Floating microspheres were prepared by the emulsion solvent diffusion–evaporation technique and evaluated for percentage yield, particle size, drug entrapment efficiency, buoyancy, surface morphology, and in vitro drug release.

Results: Increasing polymer concentration enhanced percentage yield (78.54–92.37%), particle size (220–395 μm), entrapment efficiency (67.48–89.62%), and buoyancy (72.16–95.48%). Formulation F5 exhibited the highest entrapment efficiency (89.62%) and buoyancy (95.48%) and sustained drug release for up to 12 h. SEM analysis confirmed spherical hollow microspheres with a smooth surface.

Conclusion: Optimized polymer composition significantly improved encapsulation efficiency, floating behavior, and sustained release, indicating that formulation F5 is a promising gastro-retentive sustained-release delivery system for pioglitazone hydrochloride.

Keywords: Pioglitazone hydrochloride; Floating microspheres; Ethyl cellulose; HPMC; Gastro-retentive drug delivery.

How to cite this article: Khare N, Bhargav S. Influence of Polymer Composition on Entrapment Efficiency, Buoyancy, and Drug Release Behavior of Pioglitazone Floating Microspheres. *Int J Drug Deliv Technol.* 2026;16(75s): 1121. DOI: 10.25258/ijddt.16.75s.118

1.0 Introduction

Pioglitazone hydrochloride is a thiazolidinedione derivative widely prescribed for the management of type 2 diabetes mellitus. The drug acts as a peroxisome proliferator-activated

receptor gamma (PPAR- γ) agonist and improves insulin sensitivity in peripheral tissues, thereby enhancing glycemic control in diabetic patients (1). However, pioglitazone exhibits variable oral bioavailability and

requires prolonged maintenance of therapeutic plasma concentrations, making it an appropriate candidate for sustained and gastro-retentive drug delivery systems.

Gastro-retentive drug delivery systems have gained considerable attention because they prolong the residence time of dosage forms in the stomach, improve drug absorption in the upper gastrointestinal tract, reduce dosing frequency, and enhance patient compliance (2). Among the various gastro-retentive approaches, floating microspheres are particularly advantageous due to their low density and ability to remain buoyant on gastric fluids for extended periods. The hollow internal cavity formed during microsphere preparation enables prolonged gastric retention while simultaneously providing sustained drug release (3). In the present work, floating microspheres were prepared by the emulsion solvent diffusion–evaporation technique using ethyl cellulose and hydroxypropyl methylcellulose (HPMC), a method widely employed for producing hollow polymeric microspheres with excellent floating characteristics. The polymeric matrix composition plays a crucial role in determining microsphere formation, internal cavity development, and overall performance characteristics.

Polymeric composition is one of the most critical formulation variables affecting the physicochemical and functional properties of floating microspheres. Hydrophobic polymers such as ethyl cellulose provide structural integrity and retard drug diffusion, whereas hydrophilic polymers such as HPMC hydrate

rapidly, swell in gastric fluid, and modulate both buoyancy and drug release behavior (1,4). The proportion and interaction of these polymers influence microsphere morphology, particle size, density, drug encapsulation, and release kinetics. Alterations in polymer concentration can substantially modify the viscosity of the dispersed phase during emulsification, resulting in differences in droplet formation and microsphere characteristics (3).

Entrapment efficiency is a key quality attribute of microspheres because it determines the amount of drug successfully incorporated within the polymeric matrix and directly influences therapeutic performance. Higher polymer concentrations generally increase solution viscosity, reduce drug diffusion into the external aqueous phase during emulsification, and improve drug retention within the microspheres (4). Similarly, buoyancy is strongly dependent on the formation of hollow internal cavities and the density of the polymeric matrix. Microspheres with optimized polymer composition exhibit prolonged floating behavior in simulated gastric fluid, thereby enhancing gastric residence time and improving the potential for sustained drug delivery.

Drug release from floating microspheres is governed by polymer swelling, matrix diffusion, erosion, and the permeability characteristics of the polymer network. Increasing polymer concentration generally results in a denser matrix and longer diffusion pathways, producing a more sustained release profile (3,4). In our formulation studies, increasing the proportion of

ethyl cellulose and HPMC progressively increased particle size, enhanced entrapment efficiency, improved buoyancy, and slowed the release of pioglitazone, with the optimized formulation exhibiting prolonged drug release over 12 h. The observed release behavior was consistent with diffusion-controlled release from the polymeric matrix and was strongly influenced by polymer composition.

Although several studies have reported floating microspheres for gastro-retentive drug delivery, comprehensive evaluation of the influence of polymer composition on entrapment efficiency, buoyancy, particle size, and sustained release behavior of pioglitazone floating microspheres remains limited. Therefore, the present study was undertaken to investigate the effect of varying the ethyl cellulose and HPMC ratio on the physicochemical properties and in vitro performance of pioglitazone-loaded floating microspheres prepared by the emulsion solvent diffusion–evaporation technique. Understanding these polymer-dependent relationships is essential for optimizing gastro-retentive microsphere formulations and developing efficient sustained-release delivery systems for pioglitazone.

2.0 Materials and Methods

2.1 Materials

Pioglitazone hydrochloride was obtained as a gift sample from a pharmaceutical manufacturing company. Ethyl cellulose and hydroxypropyl methylcellulose (HPMC) were selected as the matrix-forming polymers for the preparation of floating microspheres. Polyvinyl

alcohol (PVA) was used as a stabilizing and emulsifying agent, while dichloromethane and ethanol served as the organic solvents for dissolving the drug and polymeric components. All chemicals and reagents employed in the study were of analytical grade and were used without further purification.

2.2 Preparation of Floating Microspheres

Floating microspheres containing pioglitazone hydrochloride were prepared using the emulsion solvent diffusion–evaporation technique (5). Ethyl cellulose and HPMC were dissolved in a solvent mixture consisting of ethanol and dichloromethane to obtain a clear polymeric solution. Pioglitazone hydrochloride was dispersed uniformly in this solution with continuous stirring. The resulting drug–polymer solution was introduced dropwise into an aqueous phase containing 0.5–1.0% w/v PVA under constant mechanical stirring to form an oil-in-water emulsion. Continuous stirring facilitated diffusion of the organic solvents into the external aqueous phase followed by gradual solvent evaporation, resulting in the formation of hollow polymeric microspheres. The hollow internal structure generated during solvent evaporation reduced the density of the particles and imparted buoyancy in gastric fluid. The microspheres were collected by filtration, washed thoroughly with distilled water to remove residual PVA, and dried at room temperature for 24 h before further characterization.

2.3 Evaluation of Floating Microspheres

2.3.1 Percentage Yield

The percentage yield of each formulation was calculated to determine the efficiency of the preparation process by comparing the practical weight of the recovered microspheres with the theoretical weight of the drug and polymers used during formulation (6).

Percentage yield (%) = (Practical weight of microspheres / Theoretical weight of drug and polymers) $\times$ 100

2.3.2 Particle Size Analysis

The mean particle size of the microspheres was determined using an optical microscopy method (7). A small quantity of microspheres was dispersed in distilled water, placed on a glass slide, and approximately 100 particles were measured using a calibrated ocular micrometer. The average particle size was calculated from these measurements.

2.3.3 Drug Entrapment Efficiency

Entrapment efficiency was determined by dissolving a known quantity of microspheres in a suitable solvent to extract the entrapped drug (8). The solution was filtered and analyzed spectrophotometrically at the maximum absorption wavelength of pioglitazone hydrochloride.

Entrapment efficiency (%) = (Actual drug content / Theoretical drug content) $\times$ 100

2.3.4 In Vitro Buoyancy Study

The floating behavior of the microspheres was evaluated in simulated gastric fluid (0.1 N HCl, pH 1.2) using a USP dissolution apparatus (9). A known quantity of microspheres was dispersed in the dissolution medium and agitated for a predetermined period. The floating and

settled microspheres were separated, dried, and weighed.

Buoyancy (%) = (Weight of floating microspheres / Total weight of microspheres) $\times$ 100

2.3.5 Surface Morphology

Surface morphology and structural characteristics of the optimized microsphere formulation were examined using scanning electron microscopy (SEM) (10). Dried microspheres were mounted on aluminum stubs with double-sided adhesive tape and coated with a thin layer of gold before imaging.

2.3.6 In Vitro Drug Release Study

Drug release studies were performed using a USP dissolution apparatus containing 900 mL of simulated gastric fluid (0.1 N HCl, pH 1.2) maintained at $37 \pm 0.5^\circ\text{C}$ (11). Microspheres equivalent to the required dose of pioglitazone hydrochloride were placed in the dissolution medium and agitated at a constant speed. At predetermined time intervals, aliquots of dissolution medium were withdrawn and replaced with an equal volume of fresh medium maintained at the same temperature. The samples were filtered and analyzed spectrophotometrically, and cumulative percentage drug release was calculated for all formulations.

2.3.7 Drug Release Kinetic Analysis

The dissolution data of the optimized formulation were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models to determine the mechanism of drug release from the polymeric microspheres (12). The model exhibiting the highest correlation coefficient (R^2) was

considered the most appropriate release model.

2.3.8 Statistical Analysis

All experiments were performed in triplicate, and the results were expressed as mean $\pm$ standard deviation (SD). The influence of polymer composition on percentage yield, particle size, entrapment efficiency, buoyancy, and drug release behavior was evaluated by comparing the results obtained from different formulations.

3. Results

3.1 Percentage Yield

The prepared pioglitazone floating microspheres exhibited satisfactory production yields, indicating the efficiency and reproducibility of the emulsion solvent diffusion–evaporation technique. The percentage yield of different formulations ranged from 78.54% to 92.37%. As the polymer concentration increased, the percentage yield also increased, suggesting improved recovery of microspheres due to higher viscosity of the polymeric phase and reduced drug diffusion into the external aqueous medium during preparation. Formulation F5 showed the highest percentage yield (92.37%), whereas formulation F1 exhibited the lowest yield (78.54%) (Table 1).

Table 1. Percentage yield of pioglitazone floating microspheres

Formulation	Percentage yield (%)
F1	78.54
F2	82.16
F3	85.32
F4	88.45
F5	92.37

F6	89.28
----	-------

3.2 Particle Size Analysis

The mean particle size of the floating microspheres varied from $220 \pm 6.2 \mu\text{m}$ to $395 \pm 9.4 \mu\text{m}$ depending on the polymer composition. An increase in polymer concentration resulted in a progressive increase in particle size, which can be attributed to increased viscosity of the dispersed phase during emulsification, leading to the formation of larger droplets and subsequently larger microspheres. Formulation F6 exhibited the largest particle size ($395 \pm 9.4 \mu\text{m}$), while F1 showed the smallest particle size ($220 \pm 6.2 \mu\text{m}$) (Table 2).

Table 2. Particle size of pioglitazone floating microspheres

Formulation	Particle size (μm)
F1	220 ± 6.2
F2	248 ± 7.1
F3	280 ± 6.9
F4	315 ± 8.5
F5	350 ± 9.1
F6	395 ± 9.4

3.3 Drug Entrapment Efficiency

Entrapment efficiency of the prepared microspheres ranged from 67.48% to 89.62%, demonstrating the ability of the polymer matrix to effectively encapsulate pioglitazone hydrochloride. Increasing polymer concentration enhanced drug entrapment, likely due to increased viscosity of the polymer solution, which reduced drug migration into the surrounding aqueous phase during microsphere formation. The optimized formulation F5 exhibited the highest entrapment efficiency

(89.62%), whereas F1 showed the lowest value (67.48%) (Table 3).

Table 3. Drug entrapment efficiency of pioglitazone floating microspheres

Formulation	Entrapment efficiency (%)
F1	67.48
F2	72.16
F3	78.35
F4	82.41
F5	89.62
F6	85.74

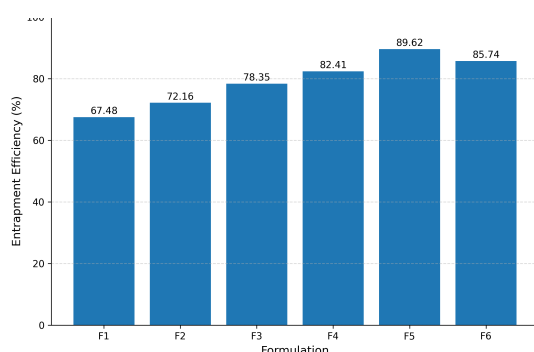


Figure 1. Entrapment efficiency (%) of pioglitazone floating microsphere formulations (F1–F6).

3.4 In Vitro Buoyancy

All formulations demonstrated excellent floating behavior in simulated gastric fluid (0.1 N HCl, pH 1.2), confirming their suitability for gastro-retentive drug delivery. The buoyancy values ranged from 72.16% to 95.48%. Polymer concentration markedly influenced floating ability, with formulations containing higher polymer content exhibiting improved buoyancy due to enhanced formation of hollow internal cavities and reduced particle density. Formulation F5 showed the highest buoyancy (95.48%), followed by F6 (91.36%), while F1

exhibited the lowest buoyancy (72.16%) (Table 4).

Table 4. In vitro buoyancy of pioglitazone floating microspheres

Formulation	Buoyancy (%)
F1	72.16
F2	78.45
F3	84.32
F4	88.57
F5	95.48
F6	91.36

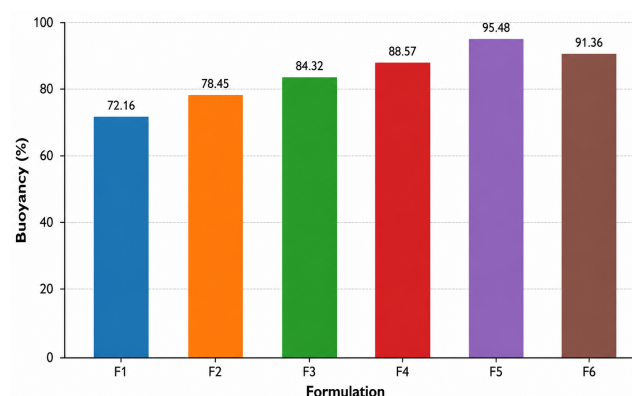


Figure 2. In vitro buoyancy (%) of pioglitazone floating microsphere formulations (F1–F6).

3.5 Influence of Polymer Composition on Microsphere Characteristics

A clear relationship was observed between polymer composition and microsphere performance. Increasing the concentration of ethyl cellulose and HPMC resulted in improved percentage yield, increased particle size, enhanced entrapment efficiency, and superior buoyancy. These findings indicate that polymer concentration plays a decisive role in controlling the physicochemical properties of pioglitazone floating microspheres. Formulation F5 exhibited the most

favorable balance of production yield, particle size, drug entrapment, and floating behavior, suggesting an optimized polymer ratio for gastro-retentive delivery.

3.6 In Vitro Drug Release Behaviour

The cumulative drug release profile demonstrated that polymer composition significantly influenced the release of pioglitazone from floating microspheres. Formulations containing lower polymer concentrations released the drug more rapidly, whereas increasing the proportion of ethyl cellulose and HPMC produced a slower and more sustained release pattern. The denser polymeric matrix formed at higher polymer concentrations increased the diffusional path length and effectively retarded drug release. Among all formulations, F5 exhibited the most controlled release profile and sustained the release of pioglitazone for up to 12 h, whereas formulations with lower polymer content released a greater proportion of the drug during the initial hours of dissolution. The optimized formulation therefore demonstrated prolonged drug release suitable for sustained gastro-retentive delivery.

3.7 Surface Morphology

Scanning electron microscopy of the optimized formulation revealed that the floating microspheres were spherical in shape with a smooth external surface and a hollow internal structure. The presence of internal cavities confirmed successful formation of low-density microspheres during solvent evaporation, which contributed to the excellent buoyancy observed during in vitro floating studies. The microspheres were

discrete, non-aggregated, and uniformly distributed, indicating effective emulsification and polymer solidification during preparation.

4. Discussion

The present investigation was undertaken to evaluate the influence of polymer composition on the physicochemical characteristics and drug release behavior of pioglitazone-loaded floating microspheres prepared by the emulsion solvent diffusion–evaporation technique. The findings clearly demonstrated that variations in the concentration of ethyl cellulose and hydroxypropyl methylcellulose (HPMC) significantly affected percentage yield, particle size, drug entrapment efficiency, buoyancy, and sustained drug release characteristics. Among the prepared formulations, formulation F5 exhibited the most favorable combination of production yield, encapsulation efficiency, floating ability, and prolonged drug release, indicating that optimization of polymer composition is a critical determinant of microsphere performance.

The percentage yield of the prepared microspheres increased progressively with increasing polymer concentration, with F5 showing the highest yield. This improvement can be attributed to the increased viscosity of the polymeric solution, which reduced diffusion of pioglitazone into the external aqueous phase during emulsification and minimized material loss during solvent evaporation. Higher polymer content also promoted better droplet stabilization and efficient solidification of the microspheres, resulting in improved recovery of the

final product. Similar observations have been reported in polymer-based sustained-release formulations, where increased polymer concentration enhanced process efficiency and formulation recovery by reducing drug loss during preparation (13,14).

Particle size analysis revealed a direct relationship between polymer concentration and microsphere size. Formulations containing higher amounts of ethyl cellulose and HPMC produced significantly larger microspheres. The increase in viscosity of the dispersed organic phase with higher polymer loading generates larger emulsion droplets during stirring, which subsequently solidify into larger microspheres after solvent evaporation. Larger microspheres generally possess thicker polymeric walls and greater internal void volume, factors that contribute to improved buoyancy and sustained drug release. Similar findings have been reported in sustained-release microsphere systems, where polymer concentration was identified as one of the most influential factors controlling particle size and structural integrity (15,16).

Entrapment efficiency was significantly affected by polymer composition and increased steadily with increasing polymer concentration. The optimized formulation F5 showed the highest entrapment efficiency, indicating effective incorporation of pioglitazone within the polymeric matrix. The enhanced encapsulation may be explained by the increased viscosity of the polymer solution, which restricted outward diffusion of the drug into the aqueous phase during microsphere formation. Moreover, the

denser polymeric network formed at higher polymer concentrations provided greater matrix volume for drug retention. Previous investigations have similarly demonstrated that increased polymer loading improves encapsulation efficiency by reducing drug leakage during emulsification and enhancing the stability of the developing microspheres (14,17).

The buoyancy study demonstrated excellent floating behavior for all formulations, with F5 exhibiting the highest buoyancy percentage. The superior floating ability observed with increased polymer concentration is attributed to the formation of hollow internal cavities during solvent diffusion and evaporation, which reduced the density of the microspheres below that of gastric fluid. Ethyl cellulose contributed to the formation of a rigid hydrophobic matrix, whereas HPMC rapidly hydrated and formed a swollen gel layer that retained entrapped air within the microspheres. The combined effect of these polymers resulted in prolonged buoyancy and improved gastric retention potential. Similar polymer-dependent improvements in floating efficiency have been reported for gastro-retentive floating microspheres and hollow microsphere systems designed for sustained oral drug delivery (15,18).

The *in vitro* drug release studies clearly demonstrated that polymer composition strongly influenced the release profile of pioglitazone. Formulations with lower polymer concentrations released the drug more rapidly, whereas increasing the proportion of ethyl cellulose and

HPMC produced a slower and more sustained release pattern extending up to 12 h in formulation F5. Ethyl cellulose acts as a hydrophobic diffusion barrier that limits penetration of dissolution medium into the matrix, while HPMC hydrates and swells to form a gel layer that further retards diffusion of the drug through the polymer network. The combined effect of these polymers increased the diffusional path length and effectively controlled drug release from the microspheres. Similar sustained-release behavior has been reported in polymeric matrix systems in which increasing polymer concentration reduced drug diffusion rates and prolonged therapeutic release (16,17,19).

The morphological characteristics observed by scanning electron microscopy further supported the physicochemical findings. The optimized microspheres were spherical, discrete, and possessed a hollow internal structure with a relatively smooth external surface. The hollow architecture is responsible for the excellent buoyancy observed during floating studies, while the intact polymeric shell contributes to sustained diffusion-controlled drug release. Uniform morphology and absence of significant aggregation indicate efficient emulsification and polymer solidification during the preparation process. Similar morphological features have been reported in floating microsphere systems prepared by the solvent diffusion–evaporation technique, where spherical hollow particles were associated with improved floating

behavior and controlled drug release (18,19).

The release profile of the optimized formulation suggested diffusion-controlled drug release from the polymeric matrix. Increasing polymer concentration produced a denser matrix that prolonged the diffusional pathway of pioglitazone and reduced the rate of drug release. Such controlled release behaviour is particularly advantageous for gastro-retentive drug delivery systems intended for chronic diseases such as type 2 diabetes mellitus, where prolonged maintenance of therapeutic drug levels is desirable. Controlled-release formulations based on optimized polymer composition have been reported to improve patient compliance, reduce dosing frequency, and enhance therapeutic efficacy by maintaining sustained plasma drug concentrations over extended periods (15,16,20).

Overall, the present study confirms that polymer composition plays a decisive role in determining the functional performance of pioglitazone floating microspheres. Increasing the concentration of ethyl cellulose and HPMC enhanced percentage yield, particle size, entrapment efficiency, and buoyancy while simultaneously prolonging drug release. Formulation F5 provided the most balanced combination of these characteristics and therefore represents an optimized gastro-retentive sustained-release system for pioglitazone hydrochloride. The findings suggest that appropriate manipulation of polymer composition can be effectively employed to develop floating microsphere formulations with

improved gastric retention, reduced dosing frequency, and enhanced therapeutic efficacy in the management of type 2 diabetes mellitus.

5. Conclusion

The present study successfully demonstrated the preparation of pioglitazone-loaded floating microspheres using the emulsion solvent diffusion–evaporation technique and established the significant influence of polymer composition on the physicochemical and functional characteristics of the formulation. Variations in the concentration of ethyl cellulose and HPMC markedly affected percentage yield, particle size, drug entrapment efficiency, buoyancy, and in vitro drug release behaviour. An increase in polymer concentration resulted in improved microsphere recovery, enhanced drug encapsulation, superior floating ability, and prolonged drug release. Among all the formulations, F5 exhibited the most favourable overall performance, with high percentage yield, excellent entrapment efficiency, prolonged buoyancy, appropriate particle size, and sustained release of pioglitazone for up to 12 hours. The optimized polymer ratio provided a balanced combination of hydrophobic matrix integrity and hydrophilic swelling behaviour, which effectively controlled drug diffusion and enhanced gastro-retentive performance. These findings indicate that careful optimization of polymer composition is a crucial strategy for developing efficient floating microsphere systems for pioglitazone hydrochloride. The optimized formulation has the potential to

improve gastric residence time, reduce dosing frequency, and enhance therapeutic efficacy, making it a promising sustained-release gastro-retentive drug delivery system for the long-term management of type 2 diabetes mellitus.

6. References

1. Aulton ME, Taylor KMG. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*. 6th ed. Elsevier; 2022.
2. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. *Expert Opin Drug Deliv*. 2006;3(2):217–233.
3. Jain NK. *Progress in Controlled and Novel Drug Delivery Systems*. CBS Publishers & Distributors; 2005.
4. Vyas SP, Khar RK. *Controlled Drug Delivery: Concepts and Advances*. Vallabh Prakashan; 2012.
5. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. *J Pharm Sci*. 1992;81(2):135–140.
6. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia*. Ghaziabad: IPC; 2022.
7. Banker GS, Rhodes CT. *Modern Pharmaceutics*. 4th ed. New York: Marcel Dekker; 2002.
8. United States Pharmacopeial Convention. *United States Pharmacopeia and National*

- Formulary (USP-NF). Rockville (MD): USP; 2023.
9. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. *Expert Opin Drug Deliv.* 2006;3(2):217–233.
 10. Goldstein J, Newbury D, Joy D, Lyman C, Echlin P, Lifshin E, et al. *Scanning Electron Microscopy and X-Ray Microanalysis*. 3rd ed. New York: Springer; 2003.
 11. Higuchi T. Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J Pharm Sci.* 1963;52(12):1145–1149.
 12. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. *Int J Pharm.* 1983;15(1):25–35.
 13. Rao T, Anand A. A detailed review on polyherbal chewable tablets. *Braz J Pharm Sci.* 2024.
 14. Kamaljeet, Das R, Kriplani P, Kaur P. Formulation, optimization, and characterization of hepatoprotective polyherbal tablet. *J Pharm Technol Res Manag.* 2025;13(1).
 15. Aulton ME, Taylor KMG. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*. 6th ed. Elsevier; 2022.
 16. Kumar R, Singh P, Verma N, Tiwari A. Quality by Design approaches in herbal and phytopharmaceutical product development: Recent advances and future perspectives. *J Drug Deliv Sci Technol.* 2024;91:105263.
 17. Patel VR, Saini S, Dwivedi J, et al. Exploring the concept and scope of polyherbal formulations: A comprehensive review. *Int J Herb Med.* 2025;13(2):9–16.
 18. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. *Expert Opin Drug Deliv.* 2006;3(2):217–233.
 19. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. *J Pharm Sci.* 1992;81(2):135–140.
 20. Higuchi T. Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J Pharm Sci.* 1963;52(12):1145–1149.