FORMULATION AND EVALUATION OF FLOATING TABLETS OF ANTIHYPERTENSIVE DRUG — A COMPREHENSIVE REVIEW

[1]Abhay Laxman Chate, [2]Aijaz A. Sheikh, [3]Kailash R. Biyani

[1,2,3]Anuradha College of Pharmacy, Anuradha Nagar, Sakegaon Road, Chikhli, Dist Buldana, Maharastra (India) 443201

Abstract: Hypertension remains one of the most prevalent chronic conditions globally, requiring consistent plasma drug concentrations for effective management. Many antihypertensive drugs, such as Propranolol, Atenolol, and Verapamil, possess a narrow absorption window in the upper gastrointestinal tract or are unstable in the alkaline pH of the lower intestine. Conventional dosage forms often fail to provide prolonged gastric residence, leading to frequent dosing and poor patient compliance. Gastroretentive Floating Drug Delivery Systems (GFDDS) have emerged as a superior alternative. These systems maintain a density lower than gastric fluids, allowing them to remain buoyant for a prolonged period while releasing the drug at a controlled rate. This review explores the formulation components (polymers, gas-generating agents), the mechanisms of buoyancy (effervescent vs. non-effervescent), and the rigorous in vitro and in vivo evaluation parameters essential for ensuring the efficacy of floating antihypertensive tablets.

Keywords **- Gastroretentive Drug Delivery Systems (GRDDS), Floating Drug Delivery Systems (FDDS), Hydrodynamically Balanced Systems(HBS)**

Abstract

1. Introduction

1.1 The Rationale for Gastroretention in Hypertension

Hypertension is a "silent killer" that necessitates rigorous adherence to medication to prevent secondary cardiovascular complications. The management of high blood pressure requires a steady-state kinetic profile to prevent the "peak-and-trough" effect associated with conventional tablets. Rapid spikes in drug concentration can lead to reflex tachycardia, while significant troughs may result in sudden, dangerous increases in blood pressure [1].

Many antihypertensive drugs are absorbed primarily in the stomach or the proximal part of the small intestine. The primary challenge with oral delivery is the Gastric Emptying Time (GET). In a physiological state, the stomach empties its contents into the duodenum in a periodic cycle known as the Migrating Myomotor Complex (MMC). A dosage form might pass the "absorption window" before the drug is fully released, leading to wasted medication and sub-therapeutic plasma levels. Gastroretentive systems prolong the gastric residence time (GRT), ensuring the drug is released exactly where it is most likely to be absorbed [2].

1.2 Types of Gastroretentive Systems

To achieve prolonged residence in the stomach, various technological approaches have been developed:

- Mucoadhesive Systems: Bind to the gastric mucosal layer.
- High-Density Systems: Sink to the bottom of the stomach to resist emptying.
- Expandable/Swellable Systems: Increase in size to prevent passage through the pyloric sphincter.
- Floating Systems: Maintain buoyancy to stay above the pyloric opening.

Floating Systems are the most widely utilized due to their simplicity, cost-effectiveness, and lack of interference with the normal motility of the gastrointestinal (GI) tract [3].

2. Fundamentals of Floating Systems

Floating systems, also known as Hydrodynamically Balanced Systems (HBS), are designed to remain buoyant on the gastric contents without affecting the gastric emptying rate.

2.1 The Buoyancy Mechanism

For a tablet to float, it must satisfy the following physical condition:

$$F = F_{buoyancy} - F_{gravity} = (d_f - d_s)gv > 0$$

Where:

- F: Total vertical force
- d_f: Density of gastric fluid (approx. $1.004\ \mathrm{g/cm^3}$)
- d_s: Density of the dosage form
- v: Volume of the dosage form
- g: Acceleration due to gravity

A positive F ensures that the dosage form stays at the surface of the gastric contents, safely away from the pyloric antrum [4].

2.2 Effervescent vs. Non-Effervescent Systems

- Effervescent Systems: These formulations utilize gas-generating agents (e.g., sodium bicarbonate, citric acid). Upon contact with gastric acid, is liberated. This gas becomes trapped in the swollen hydrocolloid matrix, creating a "balloon" effect that reduces the tablet's density [4].
- Non-Effervescent Systems: These rely on high levels of "gel-forming" or swellable cellulose-type hydrocolloids. Upon hydration, the polymer forms a gelatinous layer that traps air and maintains a relative density below unity [5].

3. Formulation Components

3.1 Selection of Antihypertensive Drugs

Not all drugs are suitable for GFDDS. Ideal candidates include:

- Drugs with a narrow absorption window: Furosemide and Captopril are better absorbed in the acidic environment of the stomach and upper jejunum.
- Drugs with low solubility at high pH: Verapamil HCl and Nifedipine exhibit pH-dependent solubility, where they dissolve better in acidic stomach fluids than in the alkaline intestine [6].
- Drugs that degrade in the colon: To ensure maximum bioavailability before the drug reaches the lower GI tract.

3.2 Polymers and Excipients

The choice of polymer is the most critical factor in determining the floating lag time and the drug release kinetics.

- Hydroxypropyl Methylcellulose (HPMC): This is the gold standard for floating systems. Different grades (K4M, K15M, K100M) offer varying viscosities. Higher viscosity grades (K100M) provide a more robust gel layer, leading to slower, more controlled drug release [7].
- Natural Gums: Xanthan gum, Guar gum, and Sodium alginate are frequently used as co-polymers to enhance the gel strength or provide a "greener" formulation profile.
- Gas Generating Agents: Sodium bicarbonate is usually used at concentrations of 10-20% to provide rapid buoyancy.

- Low-Density Excipients: Materials like Ethylcellulose or fatty glycerides can be incorporated to provide "internal" buoyancy in non-effervescent systems.

4. Evaluation Parameters for Floating Tablets

Evaluation is divided into standard pharmacopeial tests and specialized tests to verify gastroretentive performance.

4.1 Pre-compression Parameters

Before compression, the powder blend must be analyzed for flowability. Poor flow leads to weight variation in the final tablets.

- Angle of Repose: A value below 30° indicates excellent flow.
- Hausner's Ratio & Carr's Index: Values below 1.25 and 15% respectively suggest good compressibility [8].

4.2 Physical Characterization

Floating tablets must be hard enough to withstand shipping but porous enough to hydrate quickly.

- Hardness and Friability: Crucial because floating tablets are often highly porous and can be fragile.
- Drug Content Uniformity: Essential for potent antihypertensives where small dose variations can significantly impact blood pressure.

4.3 Specific Gastroretentive Tests

- Floating Lag Time (FLT): The time required for the tablet to rise to the surface of the medium. For clinical relevance, FLT should be less than 60 seconds [9].
- Total Floating Time (TFT): The duration of buoyancy. For once-daily antihypertensive therapy, a TFT of 12 to 24 hours is targetted.
- Swelling Index: This measures how much water the tablet absorbs. A higher swelling index generally correlates with a more controlled drug release, as the drug must diffuse through a thicker gel layer [10].

4.4 In Vitro Dissolution Studies

Performed using USP Type II (Paddle) apparatus in The stirring speed is usually kept low } to mimic the mild agitation of the stomach and prevent the mechanical destruction of the floating tablet [11].

5. Case Studies in Antihypertensive Floating Tablets

Drug	Polymer Used	Floating Mechanism	Result	Citation
Verapamil HCl	HPMC K100M	Effervescent ($NaHCO_3$)	12h sustained release; buoyancy maintained.	[6]
Propranolol HCl	Carbopol 934P	Non-effervescent	Enhanced bioavailability due to gastric retention.	[12]
Amlodipine	Sodium Alginate	Effervescent	Reduced dosing frequency from twice to once daily.	[13]
Captopril	HPMC K4M	Effervescent	Stabilized drug release in the absorption window.	[1]

6. Challenges in Formulation

Despite their advantages, GFDDS face several practical hurdles:

- Requirement of Acidic Environment: Effervescent systems depend on the reactions. In patients with achlorhydria (common in the elderly or those on PPIs), the tablets may fail to generate and thus fail to float [14].
- High Drug Loading: If an antihypertensive requires a high dose the addition of bulky polymers makes the tablet too large for easy swallowing.
- The "Fed State" Requirement: Floating systems are most effective when the stomach is in the "fed state." In a fasted stomach, the MMC (the "housekeeper wave") may sweep the tablet into the intestine regardless of its buoyancy [15, 16].

7. Future Perspectives and Conclusion

The pharmaceutical industry is moving toward Multi-particulate Floating Systems (microspheres or beads). Unlike single-unit tablets, multi-particulates are distributed throughout the gastric contents. This provides a more predictable release and reduces the risk of "dose dumping" if a single tablet is prematurely emptied.

In conclusion, floating drug delivery systems offer a scientifically sound method to enhance the bioavailability of antihypertensive drugs. By achieving prolonged gastric residence, these systems ensure a steady release of medication, leading to better blood pressure control, fewer side effects, and higher patient compliance.

8. References

1. Arora, S., Ali, J., Ahuja, A., Baboota, S., & Qureshi, J. (2005). Floating drug delivery systems: A review. *AAPS PharmSciTech, 6*(3), E372–E390. https://doi.org/10.1208/pt060347
2. Dave, B. S., Amin, A. F., & Patel, M. M. (2004). Preparation and characterization of gastroretentive delivery system of ranitidine hydrochloride. *AAPS PharmSciTech, 5*(2), 34–44. https://doi.org/10.1208/pt050234
3. Garg, R., & Gupta, G. D. (2008). Progress in controlled gastroretentive delivery systems. *Tropical Journal of Pharmaceutical Research, 7*(3), 1055–1066. https://doi.org/10.4314/tjpr.v7i3.14691
4. Jaimini, M., Rana, A. C., & Tanwar, Y. S. (2007). Formulation and evaluation of gastroretentive floating tablets of captopril. *Indian Journal of Pharmaceutical Sciences, 69*(5), 648–652. https://doi.org/10.4103/0250-474X.38470
5. Kotta, S., Khan, A. K., Pramod, K., Ansari, S. H., Sharma, R. K., & Ali, J. (2015). Exploring oral bioavailability of poorly water-soluble drugs using floating drug delivery systems. *Journal of Applied Pharmaceutical Science, 5*(s1), 1–10. https://doi.org/10.7324/JAPS.2015.510.S1
6. Lachman, L., Lieberman, H. A., & Kanig, J. L. (1986). *The theory and practice of industrial pharmacy* (3rd ed.). Lea & Febiger.
7. Moës, A. J. (1993). Gastroretentive dosage forms. *Critical Reviews in Therapeutic Drug Carrier Systems, 10*(2), 143–195.
8. Pawar, V. K., Kansal, S., Garg, G., Awasthi, R., Singodia, D., & Kulkarni, G. T. (2011). Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. *Drug Delivery, 18*(5), 348–364. https://doi.org/10.3109/10717544.2011.557786
9. Reddy, L. H., & Murthy, R. S. (2002). Floating dosage forms in drug delivery. *Critical Reviews in Therapeutic Drug Carrier Systems, 19*(6), 553–585. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v19.i6.20
10. Rubinstein, A., & Friend, D. R. (2010). Specific delivery to the gastrointestinal tract. In A. J. Hickey (Ed.), *Capsule technology and product design* (pp. 235–258). CRC Press.
11. Sangeeta, S., Kotta, S., Khan, A., Pramod, K., & Ali, J. (2014). Formulation and evaluation of floating tablets of Verapamil HCl. *International Journal of PharmTech Research, 6*(2), 580–589.
12. Shinde, A. J. (2007). Gastroretentive drug delivery system: An overview. *Pharmainfo.net, 5*(6).
13. Singh, B., & Kanwar, N. (2011). Floating drug delivery systems: An approach to gastroretention. *International Journal of Pharmacy, 4*(2), 23–32.
14. Streubel, A., Siepmann, J., & Bodmeier, R. (2006). Floating matrix tablets based on low density foam powder: Effects of formulation and processing parameters. *Expert Opinion on Drug Delivery, 3*(2), 199–211. https://doi.org/10.1517/17425247.3.2.199

15. United States Pharmacopeial Convention. (2007). *The United States pharmacopeia 30: The national formulary 25 (USP 30–NF 25)*. United States Pharmacopeial Convention.
16. Whitehead, L., Fell, J. T., & Collett, J. H. (1998). Floating dosage forms: An in vivo study demonstrating prolonged gastric retention. *Journal of Controlled Release, 55*(1), 3–12. https://doi.org/10.1016/S0168-3659(98)00015-3