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Formulation and Evaluation of Bumetanide Floating Tablet

Jori Vaibhav L., Prof Lohakane P. D., Dr. Megha T. Salve

Shivajirao Pawar College of Pharmacy, Pachegaon Tal. Newasa Dist. Ahilyanagar
Email- vaibhavjori148@gmail.com

ABSTRACT

The present study aims to formulate and evaluate floating tablets of Bumetanide, a potent loop diuretic used in the treatment of edema associated with congestive heart failure, liver cirrhosis, and renal disease. Due to its short biological half-life and poor bioavailability from the lower gastrointestinal tract, a gastroretentive drug delivery system was designed to enhance its therapeutic efficacy and patient compliance.

Floating tablets were prepared using the direct compression method employing various polymers such as Hydroxypropyl methylcellulose (HPMC), Carbopol, and sodium bicarbonate as a gas-generating agent to achieve buoyancy. The formulations were evaluated for physicochemical parameters including tablet hardness, friability, weight variation, drug content, in vitro buoyancy, and in vitro drug release profile.

Results indicated that the optimized formulation exhibited a desirable floating lag time of less than 1 minute and sustained drug release for up to 12 hours. The drug release kinetics followed the Higuchi model, indicating a diffusion-controlled mechanism. Stability studies conducted over three months revealed no significant changes in tablet properties.

In conclusion, the floating tablet formulation of Bumetanide developed in this study provides a promising approach to improve the drug's bioavailability by prolonging its gastric residence time.

Keywords: Floating Tablets, Controlled Drug Release, Patient Compliance, Improved Bioavailability.

INTRODUCTION

Drug delivery systems are used to deliver pure, unprocessed drugs in solid, liquid, or semisolid form to specific body sites. These systems must be therapeutically effective, safe, and stable enough to deliver the required dosage of the drug, achieve the desired concentration, and then maintain the adjusted concentration. Oral medication delivery systems make up a large portion of commercialized drug delivery systems.

Oral drug delivery is typically favored due to reduced treatment costs, higher patient compliance, and ease of administration. Despite several advantages, a medication's frequency of administration should be increased because it is quickly eliminated from the stomach.

The distribution of medications must offer a longer duration of stomach residence in order to get beyond these obstacles. The time of medication release is improved, drug waste is reduced, and drug solubility is improved for drugs that are less soluble in high ambient pH levels, thanks to gastroretention. Since their release is continuously delayed and regulated, many medications that are released in the stomach offer the strongest therapeutic effects. The need for repeated dosages would be unnecessary, and this form of drug delivery technology would have significantly fewer negative effects.

GASTROINTESTINAL INTENSION

Advantages of Floating Drug Delivery

1. Prolonged Gastric Retention Time:

FDDS remain buoyant in the stomach for an extended period, enhancing drug absorption in the upper gastrointestinal tract.

2. Improved Bioavailability:

By increasing gastric residence time, drugs with a narrow absorption window or those poorly absorbed in the lower GI tract can show better bioavailability.

3. Reduced Fluctuations in Drug Levels:

Sustained drug release leads to more consistent plasma concentration levels, reducing side effects and improving therapeutic efficacy.

4. Better Control Over Drug Release:

Floating tablets can be engineered to release drugs at a controlled rate, minimizing dosing frequency.

5. Minimized Drug Wastage:

Enhanced absorption efficiency means more of the active drug is utilized, reducing wastage.

6. Reduced Risk of Dose Dumping:

Controlled release minimizes the sudden release of a large drug dose, improving safety.

7. Patient Compliance:

Less frequent dosing and better therapeutic outcomes can improve patient adherence to treatment

regimens.

8. Useful for Local Action in the Stomach:

Ideal for drugs that act locally in the stomach (e.g., antacids, antibiotics for H. pylori).

1.2.6 Disadvantages of Floating Drug Delivery

1. Not Suitable for All Drugs:

Drugs that are not well absorbed from the stomach or upper GI tract are not ideal candidates.

2. Requirement for Sufficient Gastric Fluid:

FDDS need gastric fluid to activate buoyancy mechanisms; in patients with dry stomachs or fasting conditions, effectiveness may be reduced.

3. Delayed Gastric Emptying Variability:

The gastric retention time can be unpredictable due to factors like food intake, posture, or individual physiology.

4. Risk of Dose Dumping:

Improper formulation may lead to rapid drug release, especially if the tablet fails to float or disintegrates prematurely.

5. Complex Manufacturing Process:

Requires careful selection and optimization of excipients and formulation techniques, increasing development cost and time.

MATERIAL AND METHOD

Table 3 List of material

Sr.no.	Material	Company Name
1	Bumetanide	Balaji chemical pvt. Ltd, Gandhinagar Gujrat
2	HPMC K4M	Swapnavat Chemical Agency, Aurangabad
3	Sodium Bicarbonate	Swapnavat Chemical Agency, Aurangabad
4	PVP K30	Adora Product Pvt. Ltd. Aurangabad
5	Magnesium stearate	Adora Product Pvt. Ltd. Aurangabad
6	Talc	Swapnavat Chemical Agency Aurangabad
7	Avicel Ph 101	Adora Product Pvt. Ltd. Aurangabad

Table 4 List of equipment used

Sr.no	Equipment	Manufacture	Model no.
1	UV-VIS Spectrophotometer	Jasco	V-630
2	Electronic Balance	Shimadzu, Japan.	BL-220H
3	Rotary Tableting Machine	Karnavati	Rimek Minipress-1

4	FTIR Spectrophotometer	Jasco	FT/IR-4600
5	Friability Test Apparatus	Electrolab, India	ELECTROLAB
6	Vernier Calipers	Indolabs, Chennai	-
7	Dissolution Test Apparatus	Shimadzu, Japan.	60-PLUS
8	Hardness Test Apparatus	Sohamm calibration service	-
9	Differential scanning calorimetry	Shimadzu, Japan.	TA60WS

FORMULATION OF BUMETANIDE FLOATING TABLETS Bumetanide tablets were prepared by direct compression method. All the ingredients weigh accurately and pass through sieve no. 44 The drug with other powders was mixed for 10 min in a polythene bag followed by the addition of magnesium stearate and further mixed for 5 min. 200 mg of the mixture was weighed and fed manually in the die of a tablet punch machine and directly compressed. In this way nine formulations were designed, containing the different ratios of three polymers, and tablets were evaluated for various parameters and find out the best formulation. The composition of floating tablets of Bumetanide was shown in the table below Table 6.

Table 5 Composition of Bumetanide floating tablets

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**
Bumetanide (mg)	40	40	40	40	40
HPMC K4M (mg)	55	70	70	70	70
Sodium Bicarbonate (mg)	50	25	50	50	25
PVP K30 (mg)	4	4	4	10	10
Magnesium Stearate (mg)	4	4	4	4	4
Talc (mg)	6	6	6	6	6
Avicel PH 101 (mg)	Q.S	Q.S	Q.S	Q.S	Q.S
Total mg)	200	200	200	200	200

PRE-FORMULATION STUDY

Physical characteristics of Bumetanide:

The physical characteristics of Bumetanide were found to be colour was white and the odour was odourless.

Melting Point of Bumetanide:

The melting point of Bumetanide was found to be 205°c

IDENTIFICATION AND CHARACTERIZATION OF DRUGS AND EXCIPIENTS BY FT-IR.

FT-IR spectra of pure drug Bumetanide and Bumetanide with HPMC:

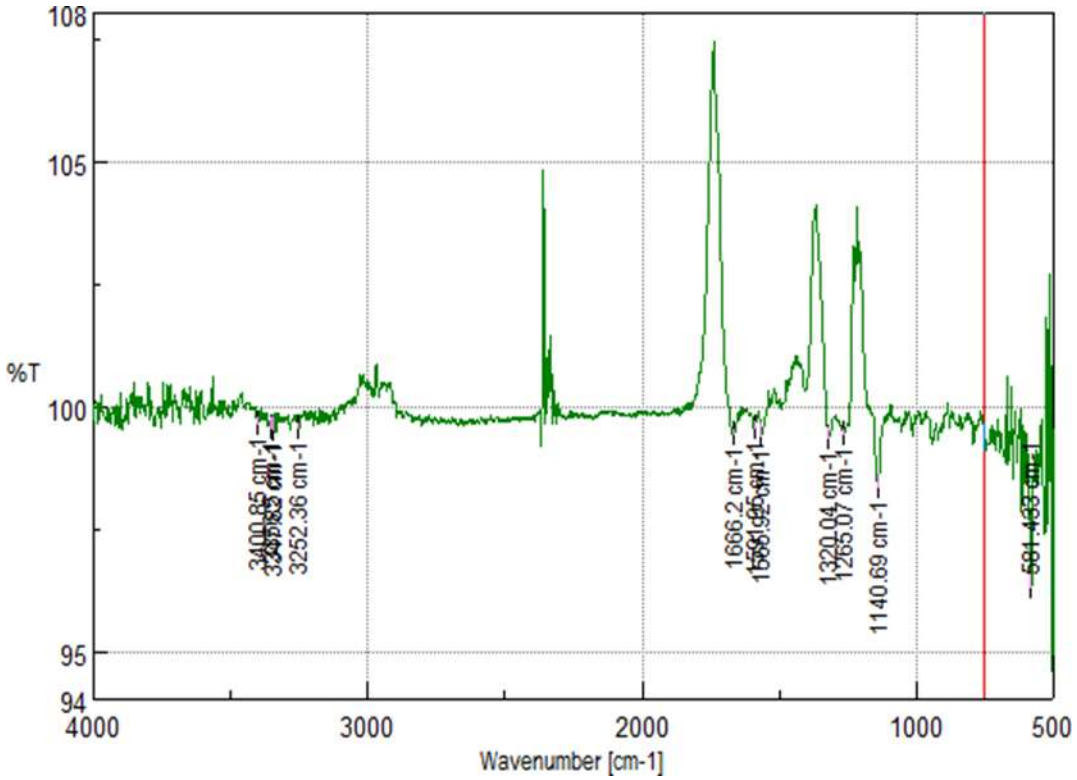

Figure FT-IR spectrum of pure drug Bumetanide

U.V SPECTROPHOTOMETRIC ANALYSIS:

Determination of λmax and Calibration curve of Bumetanide in 0.1 N HCL:

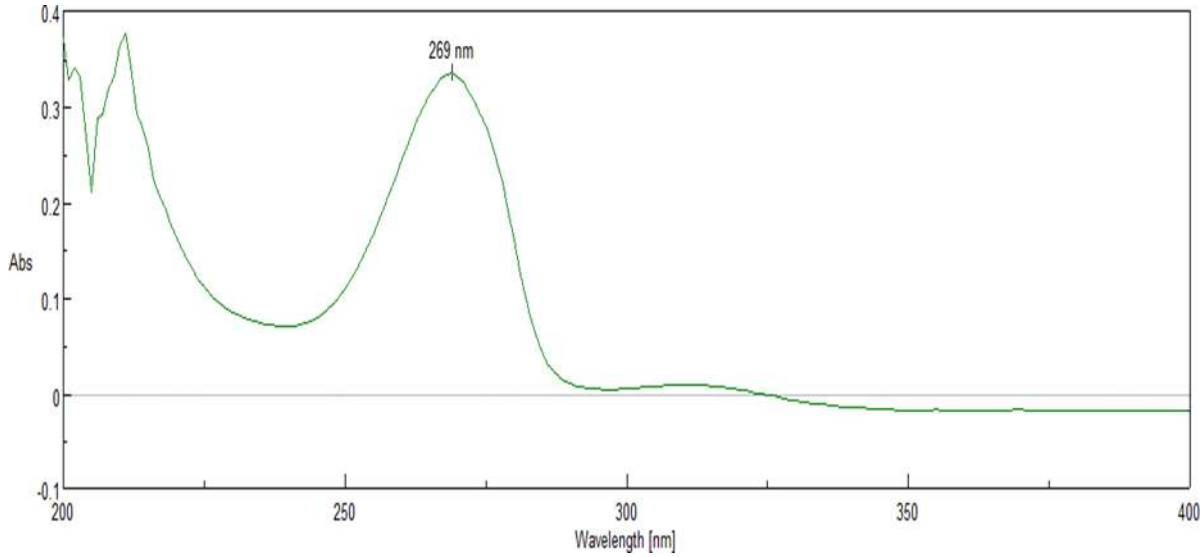

Fig. λmax of Bumetanide in 0.1N HCL

The absorption spectra in the range (200-400nm) were obtained for Bumetanide in 0.1N HCL. The drug exhibited an absorption maximum of 269 nm.

Construction of calibration curve of Bumetanide in 0.1N HCL:

Table 11 Conc. and absorbance of Bumetanide in 0.1N HCL

Sr. No.	Conc. µg/ mL	Absorbance at 269 (nm)

1.	2	0.418
2.	4	0.4613
3.	6	0.552
4.	8	0.6813
5.	10	0.7901

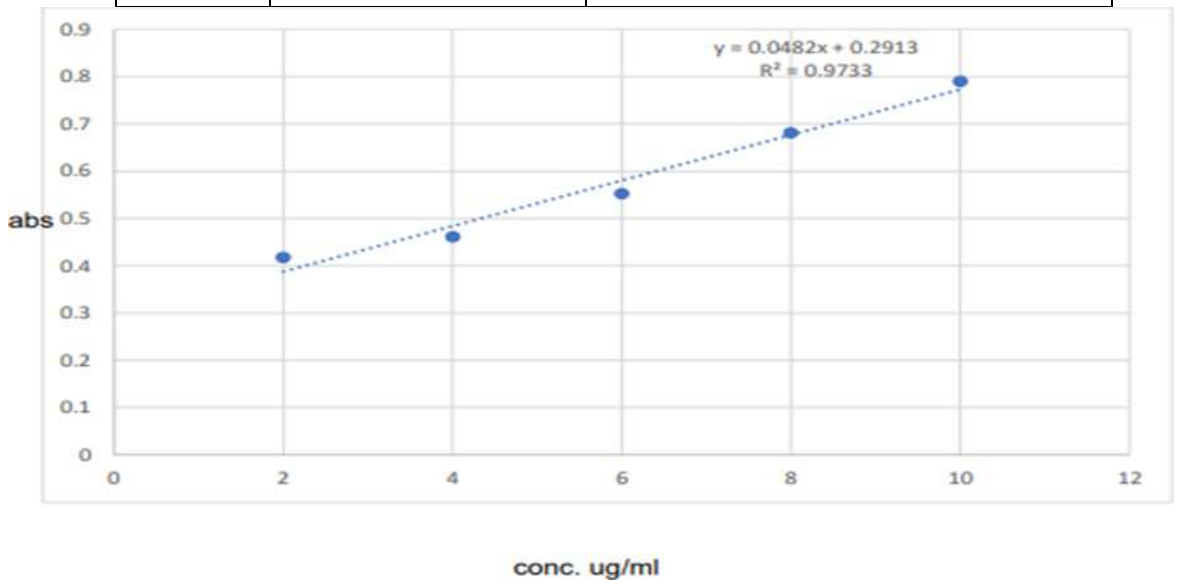

Fig. Calibration curve of Bumetanide in 0.1N HCL

Table 15 Solubility Determination

Sr.no.	Ingredient	Solubility mg/ml
1	Distilled Water	0.1
2	Methanol	50
3	Ether	8
4	Chloroform	0.98

EVALUATION OF FLOATING TABLETS OF BUMETANIDE

Pre-Compression Parameters:

The powder value's bulk density is used to determine the compressibility index and Hausner ratio. The compressibility index of all formulations indicates a good flow property in Table 18.

Table 18 Pre-Compression parameters

Formulation	Parameter				
	LBD (gm/ml)	TBD (gm/ml)	Compressibility Index (%)	Angle of Repose	Hausner Ratio (%)
F1	0.55	0.66	16.06%	26.57	1.2
F2	0.54	0.62	12.9%	27.30	1.14
F3	0.53	0.63	15.8%	25.40	1.16
F4	0.55	0.64	14.06%	28.2	1.16
F5	0.51	0.60	15.%	26.3	1.17

Post-Compression Parameters:

Formulation	Parameter				
	Weight Variation (%)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	1.01	6.01	5.20	0.58	97.30
F2	1.41	6.24	5.69	0.79	97.20
F3	1.21	6.69	5.79	0.45	96.10
F4	1.65	6.54	5.21	0.55	95.30
F5	1.21	6.22	5.21	0.65	98.40

FLOATING TEST

When the tablet containing the effervescent ingredient comes into touch with the acidic medium (0.1 N HCl), carbon dioxide is produced inside the tablet. The tablets floated and stayed buoyant after being submerged in 0.1 N HCl at 37°C. The floating lag time results for all nine formulas in one minute. The F2 and F9 formulas have more than 13 hours of combined floating time.

Table 20 Floating parameter

Formulation	Parameter	
	Floating lag time (sec)	Total floating time (Hrs.)
F1	70	10 Hrs.
F2	65	13 Hrs. 15 min.
F3	80	9 Hrs. 55 min
F4	60	11 Hrs. 30 min.
F5	58	12 Hrs.

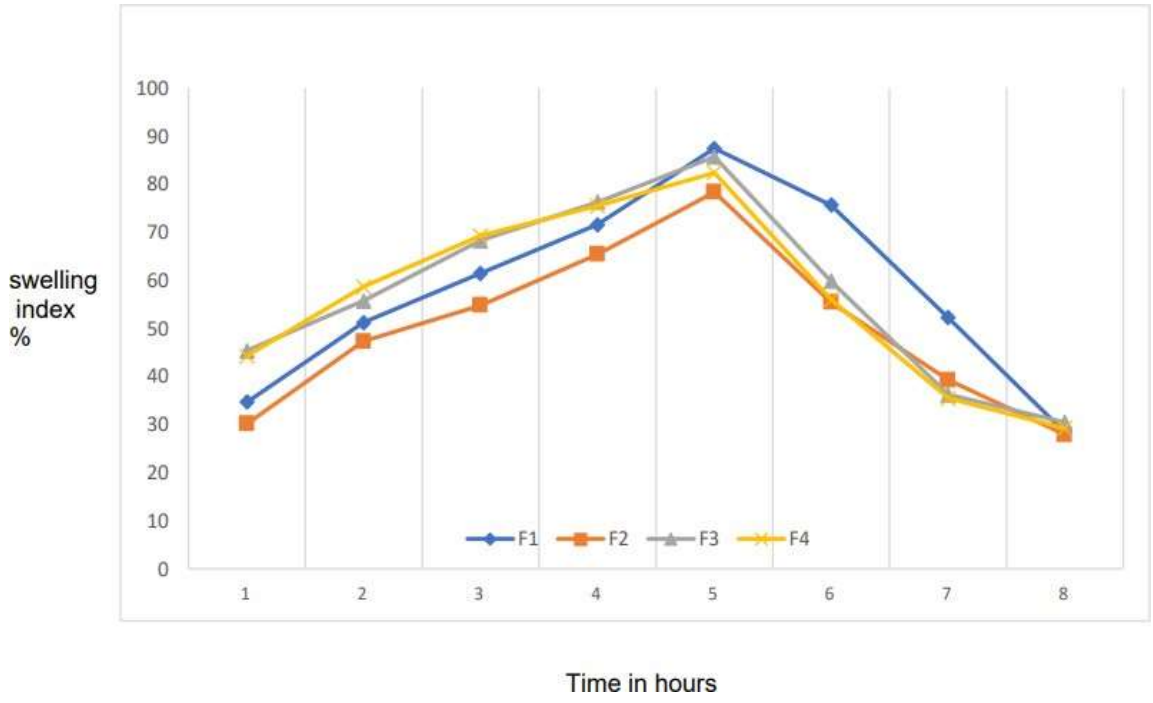

Fig. Swelling index of F1 to F4

IN-VITRO DISSOLUTION STUDIES

Time (hrs.)	**Cumulative % drug release**				
	F1	**F2**	**F3**	**F4**	**F5**
1	30.41	28.29	28.65	29.83	29.40
2	41.25	36.45	38.20	35.45	38.71
3	52.79	42.42	45.90	45.21	55.26
4	68.98	49.42	57.36	52.23	69.30
5	80.95	57.69	65.28	58.65	79.35

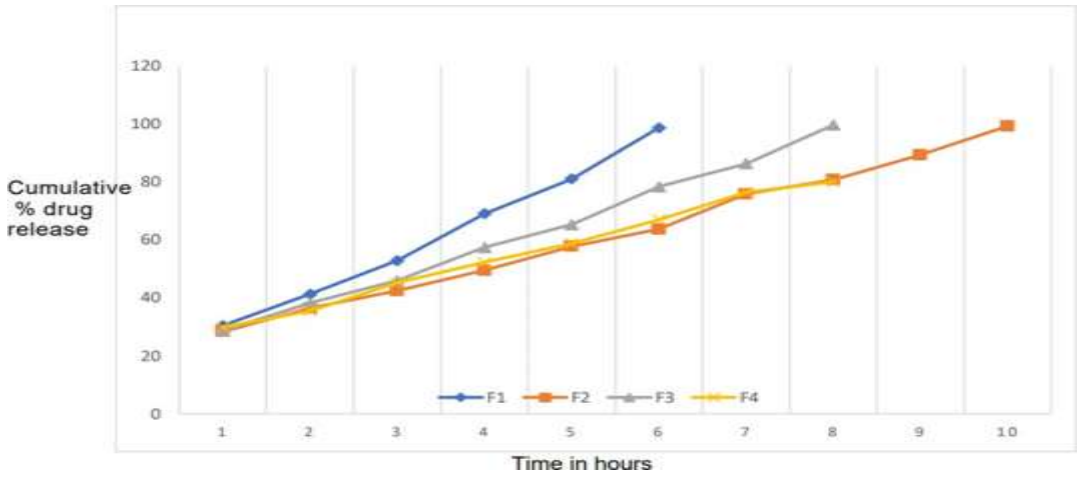

Fig. Cumulative % drug release of F1 to F4

8. CONCLUSION

- Hydrodynamically balanced tablets of Bumetanide can be formulated with an approach to increase gastric residence and thereby improve drug bioavailability.
- An attempt to develop floating tablets of Bumetanide by using sodium bicarbonate as a gas- generating agent and HPMC as a hydrophilic polymer by direct compression the technique was achieved.
- The formulated tablets showed compliance for various physiochemical parameters viz. tablet dimensions, total floating time, tablet density, and drug content.
- The dissolution studies formulations of F8 and F9 were good release and the F2 formulation was excellent.

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