Formulation And Evaluation of Torsemide Floating Tablet

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Abstract- *To prolong the retention of dosage forms in the stomach, several techniques have been developed, including systems that swell or expand, adhere to the gastric lining, have modified shapes, These systems are especially useful for drugs that are poorly soluble at higher pH levels, require absorption in the upper gastrointestinal tract, are unstable in the intestinal environment, or act locally in the stomach. This review discusses key formulation and physiological factors affecting gastric retention and provides an overview of different types of floating systems, their design principles, and evaluation parameters. FDDS offer a promising approach to enhance drug bioavailability and improve patient compliance.*

Keywords- Floating Drug Delivery, Sustained Release, Gastric Retention, Bioavailability, Patient Compliance

I. INTRODUCTION

Floating Drug Delivery Systems (FDDS) are innovative oral drug delivery methods that aim to enhance the residence time of a dosage form in the stomach. These systems remain buoyant in the gastric fluids for extended periods, allowing for prolonged and controlled drug release. This approach is especially beneficial for medications absorbed primarily in the upper part of the gastrointestinal tract or those requiring a local action in the stomach.

II MECHANISM OF FLOATING SYSTEM

FDDS function based on buoyancy principles, where the dosage form floats on the gastric contents and releases the drug slowly over time. Once the drug is completely released, the remaining system is cleared from the stomach. A critical factor for this system's effectiveness is the floating force (F), which keeps the dosage form afloat. Studies have introduced techniques to evaluate this force over time, determining the system's floating capability. A higher positive force indicates improved floatation and stability on the gastric fluid surface.

III. GASTROINTESTINAL RETENTION STRATEGY

This is particularly useful for drugs with a narrow absorption window, drugs that degrade in the intestinal environment, or those intended for targeted action in the stomach.

IV. ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEMS

1. Improved Absorption: FDDS can enhance the bioavailability of certain drugs like riboflavin and levodopa, which are better absorbed in the stomach.
2. Reduced Dosing Frequency: Sustained drug release from FDDS may reduce the need for frequent dosing, benefiting drugs with short half-lives and increasing patient compliance.
3. Targeted Gastric Action: For conditions requiring localized treatment in the stomach, FDDS can offer prolonged therapeutic effects.
4. Enhanced Effectiveness: Slow and steady drug absorption minimizes rapid concentration changes, leading to more consistent therapeutic outcomes.
5. Reduced First-Pass Effect: Continuous drug exposure to metabolic enzymes (e.g., CYP3A4) in the stomach may reduce the extent of pre-systemic metabolism.

V. LIMITATIONS OF FLOATING DRUG DELIVERY SYSTEMS

1. Need for Gastric Fluid: The effectiveness of FDDS depends on the presence of sufficient gastric fluid for the system to float and release the drug.
2. Unsuitability for Certain Drugs: Drugs that are unstable or poorly soluble in the acidic stomach environment are not ideal candidates for FDDS.
3. Limited Use with Systemically Absorbed Drugs: Medications like nifedipine, which are absorbed throughout the gastrointestinal tract, may not benefit from FDDS.
4. Potential for Irritation: FDDS may not be appropriate for drugs that can irritate the stomach lining, potentially leading to discomfort or ulcers.

VI. MATERIAL AND METHOD

Table 3 List of material

Sr. no.	Material	Company Name
1	Torsemide	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 TORSEMIDE FLOATING TABLETS

Torsemide 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.

Table 5 Composition of Torsemide floating tablets

Ingredients	F1	F2	F3	F4	F5
Torsemide (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 Torsemide:

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

Melting Point of Torsemide:

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

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

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

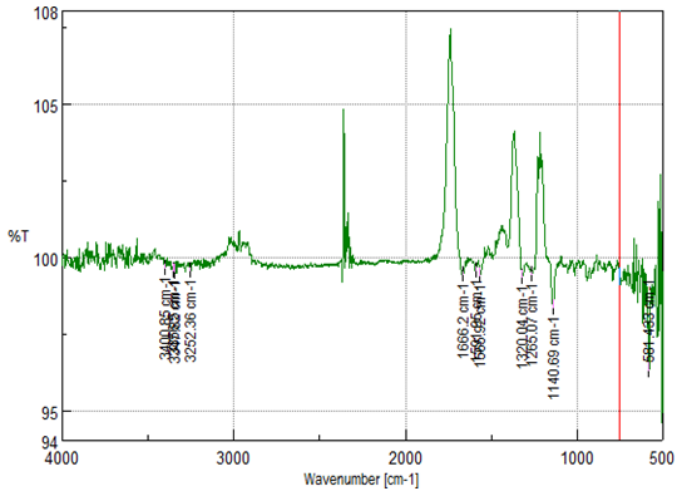

Figure FT-IR spectrum of pure drug Torsemide

U.V SPECTROPHOTOMETRIC ANALYSIS:

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

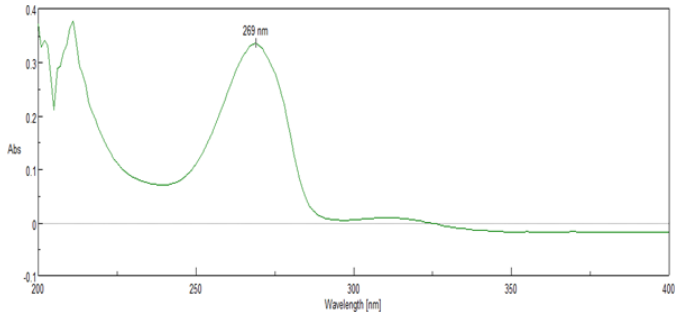

Fig. λmax of Torsemide in 0.1N HCL

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

Construction of calibration curve of Torsemide in 0.1N HCL:

Table 11 Conc. and absorbance of Torsemide 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

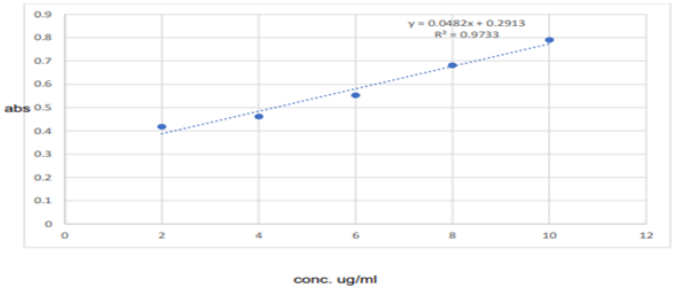

Fig. Calibration curve of Torsemide in 0.1N HCL

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 TORSEMIDE

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

The tablets floated and stayed buoyant after being submerged in 0.1 N HCl at 37°C.

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.

SWELLING STUDY

The swelling ratio, which depends on the network structure, hydrophilicity, and ionization of the functional groups, defines the water volume in the hydrogel at equilibrium. For eight hours, a swelling investigation was conducted on each batch. According to the study, tablet swelling increased for all formulations for up to 4-5 hours before it started to decline. The swelling index data are shown in Table 21 whereas the swelling index against the time plot shows an increase over time as a result of the polymer's hydrophilicity gradually absorbing water. A gel barrier is created at the outside surface of the polymer's top layer as it hydrates, expands, and swells. The hydration swelling release process is repeated towards new tissues as the gelatinous layer gradually dissolves and/or is disseminated.

Table 21 Swelling index

Time (Hrs.)	Swelling index %				
	F1	F2	F3	F4	F5
1	34.68	30.14	45.36	44.25	49.50
2	51.21	47.33	55.69	58.65	62.65
3	61.45	54.83	68.25	69.25	80.65
4	71.56	65.44	76.24	75.45	88.95
5	87.45	78.33	85.69	82.36	86.26
6	75.65	55.42	59.78	55.98	63.11
7	52.25	39.22	36.20	35.45	33.15
8	28.36	27.93	30.45	29.21	17.20

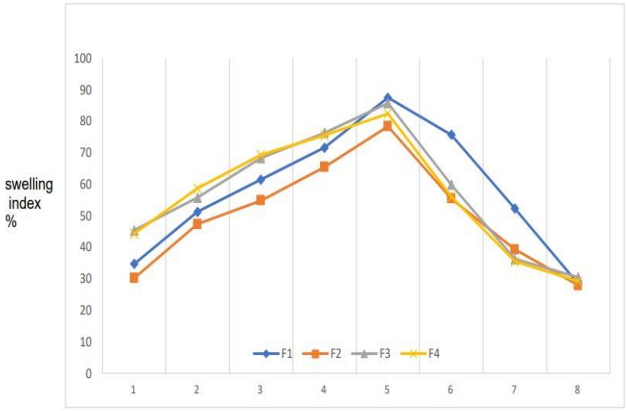

Fig. Swelling index of F1 to F4

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

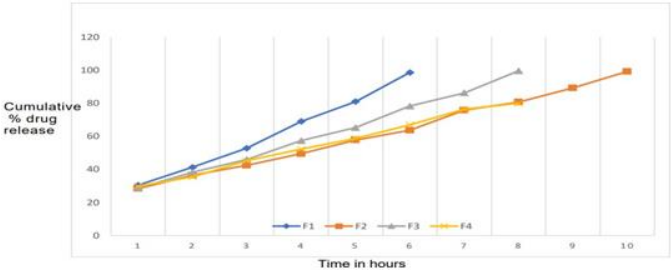

Fig. Cumulative % drug release of F1 to F4

VII. CONCLUSION

The development of floating tablets of Torsemide using a hydrodynamically balanced approach proved to be a viable strategy for enhancing gastric retention and improving oral bioavailability. The formulations were prepared through direct compression, incorporating sodium bicarbonate as the effervescent agent and HPMC as the swelling polymer.

All developed tablets were evaluated and found to meet acceptable criteria in terms of size, floating duration, density, and uniformity of drug content. Among the batches tested, formulations F8 and F9 showed favorable drug release characteristics, with formulation F2 demonstrating the highest and most efficient drug release performance.

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