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FORMULATION OPTIMIZATION AND IN-VITRO EVALUATION OF APREMILAST-LOADED GASTRORETENTIVE FLOATING MATRIX TABLETS FOR PROLONGED GASTRIC RETENTION

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Abstract:
The present study aimed to develop and evaluate Apremilast floating tablets as a gastro-retentive drug delivery system for prolonged gastric residence and sustained drug release. Preformulation studies, UV spectrophotometric analysis, and FTIR compatibility studies were performed to characterize the drug and confirm its suitability with the selected excipients. Twelve formulations were prepared using Carbopol 934P, HPMC K4M, and sodium alginate as release-retarding polymers and evaluated for flow properties, physical characteristics, drug content, floating behavior, and in-vitro drug release. All formulations demonstrated satisfactory properties and prolonged floating ability. Based on the overall evaluation, F7 was selected as the optimized formulation. Drug-release kinetics indicated predominantly zero-order release with anomalous/non-Fickian behavior, suggesting drug release through combined diffusion and polymer swelling mechanisms. Overall, the study demonstrated the potential of Apremilast floating tablets as a promising gastro-retentive system for sustained drug delivery.

Keywords: *Apremilast; Floating tablets; Gastro-retentive drug delivery; HPMC K4M; Sustained release; Zero-order kinetics; Non-Fickian release.*

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INTRODUCTION

Gastroretentive drug delivery systems (GRDDS) are specialized oral dosage forms designed to remain in the stomach for an extended period and release the incorporated drug in a controlled manner. Prolonging gastric residence can be advantageous for drugs that are preferentially absorbed from the upper gastrointestinal tract, have greater solubility in acidic conditions, possess a narrow absorption window, or are intended to act locally within the stomach.[1]

Several approaches have been investigated to achieve gastric retention, including floating, bioadhesive or mucoadhesive, swelling or expandable, high-density, raft-forming and magnetic systems. Among these, floating systems are particularly attractive because they can maintain buoyancy in gastric fluid while simultaneously providing sustained drug release.

Approaches for Gastric Retention

Different technological approaches have been developed to prolong the residence of oral dosage forms in the stomach. The major approaches include the following:

Floating Systems

Floating drug delivery systems are designed to have a bulk density lower than that of gastric fluid, allowing the dosage form to remain buoyant on the gastric contents for an extended period. Drug release can occur gradually while the formulation remains in the stomach. Floating systems may be **effervescent** or **non-effervescent**. Effervescent systems commonly contain gas-generating agents such as sodium bicarbonate, which produces carbon dioxide in the presence of gastric fluid and an acid source. The generated gas decreases the effective density of the dosage form and promotes flotation.[2]

Bioadhesive Systems

Bioadhesive or mucoadhesive systems prolong gastric residence by interacting with the mucus layer or mucosal surface of the stomach. The interaction between the polymer and gastric mucosa may involve hydrogen bonding, electrostatic interactions, wetting, diffusion and other mechanisms.

Swelling/Expandable Systems

Swelling or expandable systems are designed to increase their dimensions after exposure to gastric fluid. Hydrophilic polymers capable of absorbing gastric fluid and undergoing substantial swelling are commonly used. The system must maintain sufficient mechanical integrity to prevent premature disintegration or gastric emptying.[3]

High-Density Systems

High-density systems utilize the density of the dosage form as the mechanism of gastric retention. These systems are formulated with a density greater than that of gastric contents and consequently tend to sink toward the lower region of the stomach. Materials such as barium sulfate and other high-density excipients have been investigated for this purpose.

Raft-Forming Systems

Raft-forming systems produce a viscous, cohesive gel layer or **raft** when exposed to gastric fluid. Polymers such as sodium alginate can hydrate and form a gel, while gas-generating agents can produce carbon dioxide that reduces the density of the formed system and promotes flotation. The resulting raft remains on the surface of gastric contents and can provide prolonged local drug release.

Magnetic Systems

Magnetic gastroretentive systems contain a small magnetic component incorporated within or associated with the dosage form. An external magnet positioned near the stomach can theoretically exert an attractive force and help maintain the dosage form at a desired location. Although magnetic systems provide a distinctive mechanism for gastric retention, their practical application requires careful consideration of magnet size, positioning, strength and patient safety.

Floating Drug Delivery Systems

Floating drug delivery systems (FDDS) are a type of gastro-retentive drug delivery system designed to remain buoyant in the gastric fluid for a prolonged period without significantly affecting the normal gastric emptying process. The primary objective of these systems is to increase the gastric residence time of the dosage form and thereby improve the absorption and bioavailability of drugs that have a narrow absorption window in the upper gastrointestinal tract.[4]

The floating behavior is achieved by incorporating materials that reduce the apparent density of the dosage form below that of gastric fluid, generally less than approximately 1 g/cm³. Once administered orally, the dosage form comes into contact with gastric fluid and floats on the gastric contents. While retained in the stomach, the drug is gradually released at a predetermined rate.

Floating drug delivery systems are particularly useful for drugs that are preferentially absorbed from the stomach or upper part of the small intestine, drugs with poor solubility at higher intestinal pH, and drugs that undergo degradation or metabolism in the distal gastrointestinal tract. However, their performance can be influenced by gastric motility, fed or fasted conditions, gastric-fluid composition, and the presence of food.[5]

Aim

To formulate and optimize apremilast-loaded gastroretentive floating matrix tablets using suitable polymers and gas-generating agents, with the aim of achieving prolonged gastric retention and controlled

drug release, and to evaluate the optimized formulation by in-vitro physicochemical and drug-release studies.

Objectives

1. To conduct a preformulation study of apremilast to determine its relevant physicochemical properties and suitability for incorporation into a gastroretentive floating matrix tablet.
2. To study the compatibility of apremilast with selected formulation excipients using appropriate analytical techniques such as Fourier-transform infrared spectroscopy (FTIR) .
3. To select suitable hydrophilic polymers for the preparation of floating matrix tablets.
4. To formulate apremilast-loaded gastroretentive floating matrix tablets using an appropriate tablet manufacturing technique and incorporating suitable gas-generating agents
5. To optimize the formulation variables affecting floating behavior and drug release, including polymer concentration, polymer type, and concentration of gas-generating agent, using an appropriate experimental design or optimization approach.
6. To evaluate the prepared tablets for pre-compression and post-compression parameters, including powder flow properties, weight variation, hardness, friability, thickness, drug content, and other relevant physicochemical characteristics.
7. To evaluate the floating characteristics of the prepared formulations by determining floating lag time and total floating duration.
8. To investigate the in-vitro drug-release behavior of the formulated floating matrix tablets using an appropriate dissolution medium and suitable dissolution apparatus.
9. To analyze the drug-release kinetics and mechanism using mathematical models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas models.
10. To establish the potential of the optimized apremilast floating matrix tablet as a gastroretentive controlled-release dosage form capable of providing prolonged gastric residence and sustained drug delivery.

I. Pre formulation studies:

Solubility.
Determination of λ max.
Preparation of standard graph of Apremilast using Spectrophotometric method.
Drug-excipient compatibility (FTIR) studies.

II. Formulation of Apremilast floating tablet by direct compression technique.

III. Evaluation Parameters:

1. Pre evaluation parameters of tablet

- Angle of Repose
- Bulk Density
- Tapped Density
- Carr's Index
- Hausner's ratio

2. Post Compression parameters of tablet.

- Weight variation
- Hardness
- Friability
- Tablet thickness and
- Drug content
- Disintegrating time(sec)

3. In vitro buoyancy.

4. In vitro drug release studies

5. Release kinetics models

METHODS

Preformulation Studies[6]

Preformulation investigations were undertaken as an initial step in the development of the Apremilast gastro-retentive floating tablet formulation. These studies were conducted to establish the basic physicochemical characteristics of Apremilast and to assess its suitability for incorporation into the proposed dosage form. The investigations included determination of solubility, melting point, ultraviolet absorption maximum (λmax), construction of the calibration curve, and drug–excipient compatibility assessment.

Solubility Studies[7]

The solubility behavior of Apremilast was investigated in selected aqueous and organic media. The solvents and dissolution media included distilled water, 0.1 N hydrochloric acid, phosphate buffer solutions of pH 6.8 and 7.4, methanol, and ethanol.

An excess quantity of Apremilast was added separately to accurately measured quantities of each selected solvent, were agitated periodically and maintained for approximately 24 h to facilitate attainment of equilibrium. Filtered through Whatman filter paper No. 41 to remove undissolved drug and was estimated using a UV-visible spectrophotometer.

Determination of Melting Point[8]

The melting point of Apremilast was determined by the capillary tube method. The capillary containing the drug was attached alongside the bulb of a calibrated thermometer and immersed in a liquid paraffin bath. The bath was heated gradually while the sample was observed continuously. The temperature corresponding to the initial appearance of melting and the temperature at which the sample completely liquefied were noted.

Determination of Absorption Maximum (λmax)[9]

The maximum wavelength of ultraviolet absorption of Apremilast was determined using a UV-visible double-beam spectrophotometer. Apremilast equivalent to 10 mg was transferred into a 10 mL

volumetric flask and initially dissolved in approximately 2–3 mL of methanol. Then diluted to volume with 0.1 N hydrochloric acid to obtain the primary stock solution having a concentration of 1000 µg/mL.

From this solution, 1 mL was transferred into a separate 10 mL volumetric flask and diluted to volume with 0.1 N hydrochloric acid, producing a secondary stock solution containing 100 µg/mL of Apremilast. Subsequently, 1 mL of the secondary stock solution was transferred to another 10 mL volumetric flask and diluted to the mark with 0.1 N hydrochloric acid to obtain a final concentration of 10 µg/mL.

The resulting solution was scanned over the wavelength range of 200–400 nm against an appropriate blank using a UV-visible double-beam spectrophotometer. The wavelength corresponding to the highest absorbance was recorded as the λmax of Apremilast.

Preparation of Calibration Curve of Apremilast

A standard calibration curve was prepared to establish the relationship between Apremilast concentration and absorbance. A 1000 µg/mL stock solution was prepared by dissolving 10 mg of Apremilast in methanol and making the volume up to 10 mL with 0.1 N HCl. This was diluted to obtain a 100 µg/mL working solution. Aliquots of 0.2–1.2 mL were further diluted to obtain concentrations of 2–12 µg/mL. The absorbance of each solution was measured at 232.0 nm using 0.1 N HCl as the blank. The calibration plot showed a linear relationship between concentration and absorbance and was used for quantitative estimation of Apremilast in the formulation studies.

Drug–Excipient Compatibility Study by FTIR[10]

FTIR spectroscopy was performed to assess the compatibility of Apremilast with the selected formulation excipients. The pure drug and drug–excipient physical mixtures were analyzed over the range of 4000–500 cm^{-1}. The characteristic absorption peaks of Apremilast were compared with those observed in the physical mixtures. No significant changes in peak position, shape, or intensity were observed, indicating the absence of major drug–excipient interactions. The results confirmed the compatibility of Apremilast with the selected polymers and excipients and supported their suitability for formulation development.

Pre-compression Evaluation[11]

Prior to compression, the prepared powder blends were evaluated for their flow and packing characteristics. These tests are important for assessing the suitability of the powder blends for uniform die filling and consistent tablet production. The pre-compression characteristics evaluated included angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio.

Formulation of Apremilast Gastro-Retentive Floating Tablets

Apremilast gastro-retentive floating tablets were prepared using Carbopol 934P, HPMC K4M, and sodium alginate as release-retarding polymers. Each polymer was evaluated at four concentrations (30, 45, 60, and 75 mg/tablet). Sodium bicarbonate and citric acid were used as effervescent agents, while PVP K30, talc, magnesium stearate, and MCC PH 102 served as binder, glidant, lubricant, and diluent, respectively.

Apremilast and the required excipients were accurately weighed, passed through a suitable sieve, and blended uniformly by geometric dilution. Sodium bicarbonate, citric acid, and PVP K30 were incorporated during blending. Talc and magnesium stearate were added at the final stage and mixed gently. MCC PH 102 was adjusted to obtain a constant tablet weight of 400 mg.

The final powder blends were evaluated for pre-compression properties and subsequently compressed using a suitable tablet compression machine. Twelve formulations (F1–F12) were prepared by varying the type and concentration of polymer while maintaining the quantities of other ingredients constant.

Table no:1 Composition of Apremilast gastro-retentive floating tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Apremilast	30	30	30	30	30	30	30	30	30	30	30	30
Carbopol 934P	30	45	60	75	-	-	-	-	-	-	-	-
HPMC K4M	-	-	-	-	30	45	60	75	-	-	-	-
Sodium alginate	-	-	-	-	-	-	-	-	30	45	60	75
NAHCO3	60	60	60	60	60	60	60	60	60	60	60	60
Citric Acid	30	30	30	30	30	30	30	30	30	30	30	30
PVP K30	10	10	10	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Mg stearate	5	5	5	5	5	5	5	5	5	5	5	5
MCC PH 102 qs.	230	215	200	185	230	215	200	185	230	215	200	185
Total	400	400	400	400	400	400	400	400	400	400	400	400
FLT(Seconds)	48	56	65	75	35	42	50	58	44	52	61	72

TFT (hrs)	>12	>12	12	>12	>12	>12	>12	>12	12	>12	>12	>12

Post-compression Evaluation of Formulated Tablets[12]

The prepared Apremilast floating tablets were evaluated for their physical characteristics, mechanical strength, drug content, floating behavior, and drug-release performance using the following parameters.

a. Weight Variation

Twenty tablets were randomly selected from each formulation and weighed individually. The mean tablet weight was calculated, and the individual weights were compared with the average weight to determine the percentage weight variation.

b. Hardness

The crushing strength of the tablets was determined using a **Pfizer hardness tester**. Tablets from each formulation were individually tested, and the hardness values were recorded.

c. Friability

Friability was assessed using a **Roche friabilator**. A pre-weighed sample of tablets was placed in the friabilator and rotated at 25 rpm for 100 revolutions. The tablets were removed, carefully dedusted, and weighed again. The percentage friability was calculated as:

$$\text{Friability (\%)} = [(W_0 - W)/W_0] \times 100$$

Where:

- W_0 = initial weight of tablets
- W = final weight of tablets after friability testing

d. Thickness and Diameter

The thickness and diameter of the tablets were measured using a digital Vernier caliper. Five tablets from each formulation were randomly selected, and the measurements were recorded in millimeters.

e. Drug Content

One tablet from each formulation was powdered and the drug was extracted using 0.1 N hydrochloric acid. The resulting solution was suitably filtered and diluted. The absorbance was measured spectrophotometrically at **232.0 nm** against a suitable blank. The Apremilast content was calculated using the appropriate analytical method.

f. In-vitro Buoyancy Study

The floating characteristics of the prepared tablets were evaluated in 100 mL of 0.1 N HCl (pH 1.2) maintained at 37 ± 0.5°C. The tablet was introduced into the medium and the time required to reach the surface was recorded as the floating lag time (FLT). The duration for which the tablet remained continuously floating on the surface was recorded as the total floating time (TFT).

g. In-vitro Dissolution Study

The drug-release behavior of the floating tablets was evaluated using USP Dissolution Apparatus II (paddle type). The dissolution medium consisted of 900 mL of 0.1 N HCl, maintained at 37 ± 0.5°C, with the paddle operated at 50 rpm. Samples were withdrawn at predetermined time intervals and replaced immediately with an equal volume of fresh dissolution medium maintained at the same temperature. The samples were suitably diluted and analyzed spectrophotometrically for Apremilast content.

Kinetic Analysis of In-vitro Drug Release[13-15]

The dissolution data obtained from the formulations were fitted to different mathematical models to determine the kinetics and probable mechanism governing Apremilast release. The following models were evaluated:

1. **Zero-order model:** cumulative percentage drug released versus time.
2. **First-order model:** logarithm of cumulative percentage drug remaining versus time.
3. **Higuchi model:** cumulative percentage drug released versus square root of time.
4. **Korsmeyer–Peppas model:** logarithm of fractional drug release versus logarithm of time.

RESULTS AND DISCUSSION:

Preformulation Studies

Determination of melting point

The melting point of Apremilast was found to be in range of 155°C.

Determination of Solubility

Table No 2: Solubility data of Apremilast

Buffers	Solubility(µg/ml)
0.1N HCL	0.890
6.8pH Phosphate Buffer	0.651
7.4 pH Phosphate Buffer	0.550

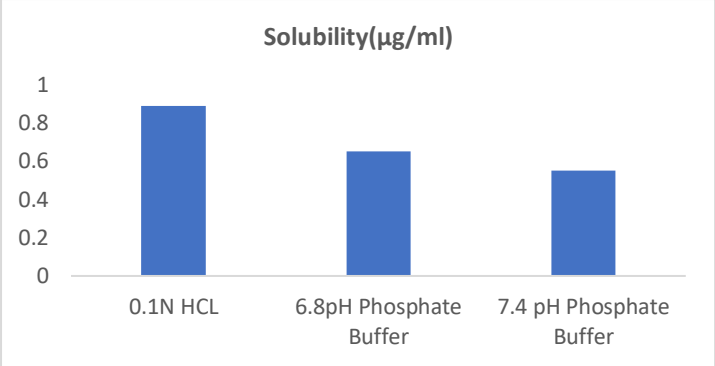

Fig 1: Solubility studies of Apremilast

Discussion: Based on these findings, 0.1 N HCl was selected as the dissolution medium for subsequent in-vitro dissolution studies because it provides an acidic environment representative of the gastric conditions targeted by the gastro-retentive formulation.

Determination of lambda max

UV Spectra of Apremilast at 4 µg/ml concentration the Wavelength of maximum absorption in 0.1N HCL solution was found to be 232.0 nm.

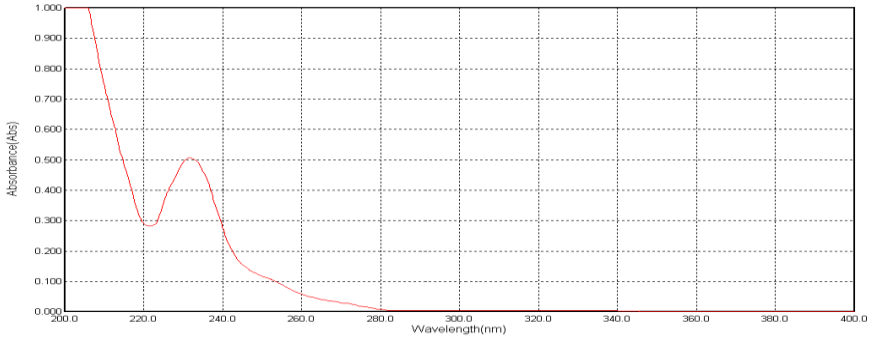

Fig: 2: Uv Spectrum of Apremilast

Discussion: The maximum absorbance of the Apremilast in 0.1N HCl was found to be 232.0 nm and was selected for analysis of drug in dissolution media.

Calibration curve

Table No 3: Absorbance data for the calibration curve of Apremilast in 0.1N HCl

Concentration(µg/ml)	Absorbance
0	0
2	0.129
4	0.246
6	0.361
8	0.482
10	0.615
12	0.734

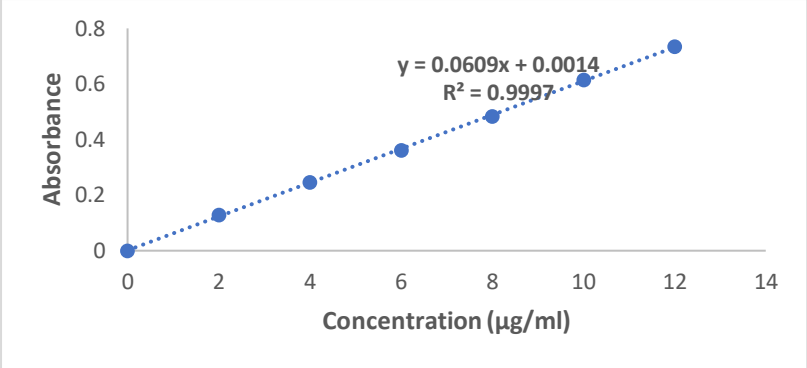

Fig 3: Calibration curve of Apremilast

Discussion: The calibration curve of Apremilast showed good linearity over the concentration range of 2–12 µg/mL at 232 nm, with the correlation coefficient (R^2 = 0.9997). The high R^2 value confirmed the linearity and suitability of the method for quantitative estimation of Apremilast.

Compatibility Studies: FTIR Spectroscopy

Identification of Apremilast: The IR spectrum of pure drug was found to be similar to the standard spectrum of Apremilast.

Pure Drug

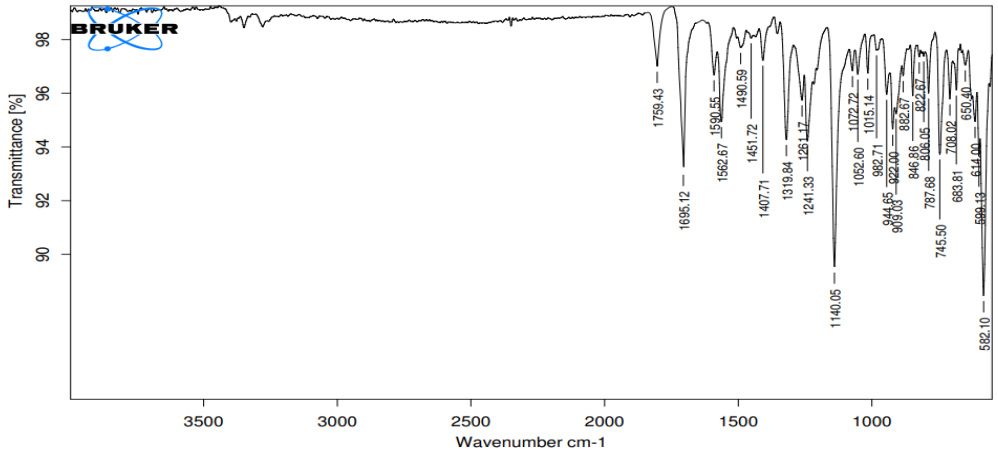

Fig 4: IR spectra of Apremilast.

Optimized Formulation

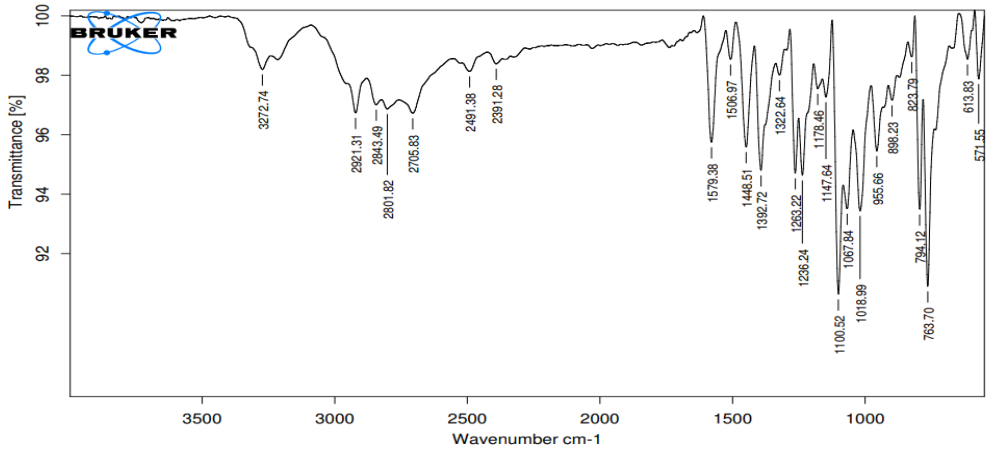

Fig 5: FT-IR Spectra of Apremilast best formulation

Discussion: The compatibility study showed that the characteristic functional groups present in the pure Apremilast were also retained in the optimized formulation, with only minor changes in peak position or intensity. This indicates that there were no significant chemical interactions.

Table No:4: Pre-Compression Evaluation of Apremilast Floating Tablets

Formulation code	Angle of repose (θ) ±SD	Bulk density (gm/cm) ±SD	Tapped density (gm/cm) ±SD	Hausner ratio (HR)±SD	Carr index (CI) ±SD
F1	28.74±0.18	0.311±0.024	0.424±0.021	1.22±0.021	17.45±0.58
F2	27.36±0.75	0.323±0.017	0.458±0.018	1.13±0.015	18.72±0.94
F3	24.42±0.19	0.346±0.026	0.426±0.006	1.15±0.013	16.17±0.25
F4	23.19±0.38	0.368±0.008	0.457±0.005	1.16±0.010	15.24±0.47
F5	27.67±0.45	0.324±0.005	0.438±0.026	1.18±0.008	18.48±0.46
F6	25.46±0.37	0.316±0.024	0.416±0.020	1.16±0.009	18.21±0.14
F7	24.37±0.49	0.369±0.013	0.448±0.017	1.14±0.010	16.36±0.47
F8	23.19±0.85	0.343±0.016	0.458±0.021	1.13±0.012	14.08±0.28
F9	28.47±0.68	0.326±0.009	0.436±0.026	1.17±0.024	15.24±0.48
F10	27.34±0.84	0.315±0.015	0.448±0.034	1.13±0.012	16.04±0.29
F11	24.68±0.45	0.354±0.012	0.454±0.022	1.12±0.016	13.28±0.46
F12	21.28±0.28	0.366±0.014	0.466±0.037	1.13±0.024	12.12±0.18

 # All the values are expressed as mean ± SD. (n=1)

Discussion: The angle of repose of different formulations was ≤ 28.74% which indicates that material had good flow property. So, it was confirmed that the flow property of blends was free flowing. The bulk density of blend was found between 0.311g/cm^3 to 0.369g/cm^3.Tapped density was found between 0.416g/cm^3 to 0.466g/cm^3.These values indicate that the blends had good flow property. Carr's index for all the formulations was found to be between 18.72-12.12±0.18. and Hausner's ratio from 1.22-1.12which reveals that the blends have good flow character.

Table No:5 Post Compression Evaluation of Apremilast Floating Tablets

Formulation code	Weight variation (mg)±SD	Hardness (Kg/cm2)±SD	Diameter in (mm)±SD	Thickness in (mm)±SD	Friability (%) ±SD	Drug content uniformity (%) ±SD
F1	400.37± 0.10	6.37± 0.41	8.27± 0.57	3.57± 0.07	0.85± 0.04	93.42±0.74
F2	403.41± 0.19	6.25± 0.28	8.25± 0.18	3.65± 0.05	0.76± 0.08	95.21±0.28
F3	398.20± 0.27	6.24± 0.41	8.34± 0.24	3.74± 0.03	0.68± 0.06	96.36±0.46
F4	399.37± 0.18	6.14± 0.62	8.25± 0.39	3.84± 0.04	0.34± 0.07	96.46±0.47
F5	300.67±0.37	6.46± 0.84	8.34± 0.27	3.62± 0.08	0.54± 0.09	91.28±0.65
F6	400.46± 0.25	6.78± 0.45	8.26± 0.45	3.71± 0.07	0.35± 0.06	93.51±0.45
F7	397.18± 0.37	6.28± 0.15	8.25± 0.25	3.82± 0.09	0.42± 0.04	98.96±0.28
F8	399.20± 0.61	6.44± 0.68	8.36± 0.28	3.93± 0.05	0.39± 0.06	95.38±0.18
F9	398.37± 0.24	6.58± 0.87	8.35± 0.14	3.63± 0.07	0.55± 0.08	96.61±0.36
F10	401.65± 0.45	6.45± 0.21	8.45± 0.32	3.72± 0.04	0.36± 0.06	97.24±0.21
F11	402.48± 0.58	6.76± 0.28	8.25± 0.27	3.81± 0.08	0.42± 0.06	96.58±0.25
F12	400.37± 0.67	6.88± 0.20	8.56± 0.44	4.06± 0.07	0.49± 0.04	96.37±0.38

 # All the values are expressed as mean ± SD. (n=3)

Discussions:

Weight Variation Test: The percentage weight variations for all formulations were given. All the formulated (F1 to F12) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits. The weights of all the tablets were found to be uniform with low standard deviation values.
Hardness test: The measured hardness of tablets of all the formulations ranged between 6.88-6.14 kg/cm2. This ensures good handling characteristics of all batches.
Thickness and Diameter: The measured Thickness and Diameter of tablets of all the formulations ranged between 4.06-3.57mm.
Friability Test: The % friability was less than 1 % in all the formulations ensuring that the tablets were mechanically stable.
The Drug Content: The Content of drug content for F1 to F12 was found to be between 91.28% - 98.96%. It complies with official specifications.

***In-Vitro* Drug Release Studies**

Table No 6: In-vitro drug release data of Apremilast floating tablets of Batch F1 to F12 Table 7.5:

Time (Hrs)	% Cumulative release											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	10.47	13.12	19.27	17.62	19.58	14.32	12.47	11.12	19.27	17.62	21.58	14.32
2	17.52	25.38	25.45	25.44	29.26	21.33	19.52	25.38	25.45	25.44	29.26	21.33
3	24.21	37.45	34.22	32.75	34.18	37.77	28.21	37.45	34.22	32.75	34.18	27.77
4	44.68	41.46	45.69	35.94	39.48	45.45	34.68	41.46	45.69	45.94	39.48	35.42
5	61.49	54.25	51.56	43.74	47.63	56.71	51.49	54.25	51.56	53.74	47.63	41.71
6	78.51	63.48	59.21	49.83	55.21	68.58	68.51	63.48	59.21	69.83	55.21	51.58
7	98.38	86.21	65.19	57.86	68.28	76.47	77.38	76.21	65.19	77.86	68.28	66.47
8		98.17	71.48	76.48	79.48	83.42	81.54	88.17	71.48	81.48	74.48	70.42
9			97.74	99.38	98.24	89.42	90.47	93.12	89.27	87.62	81.58	78.32
10						97.2	99.92	96.25	94.22	93.21	91.21	89.12

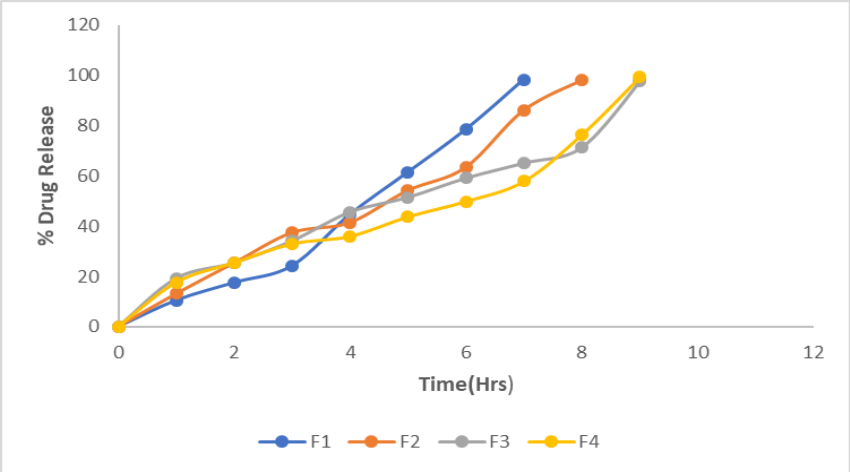

Fig6: Drug release profile(F1-F4)

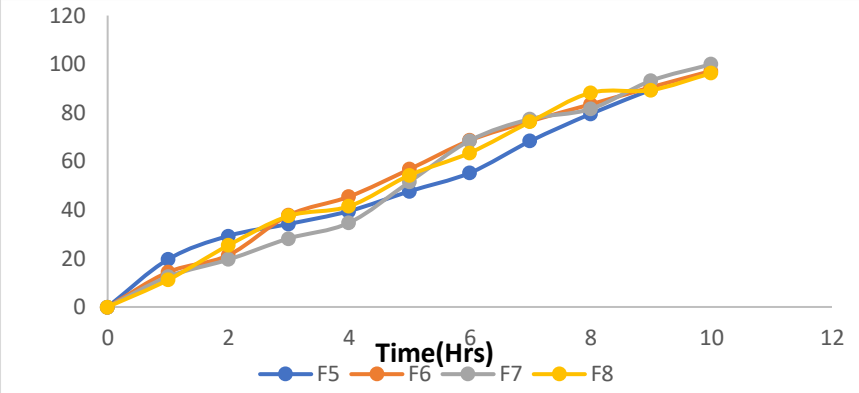

Fig7: Drug release profile(F5-F8)

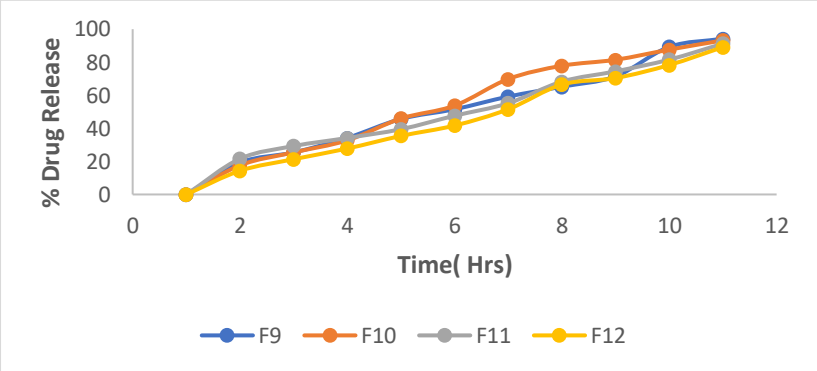

Fig 8: Drug release profile(F9-F12)

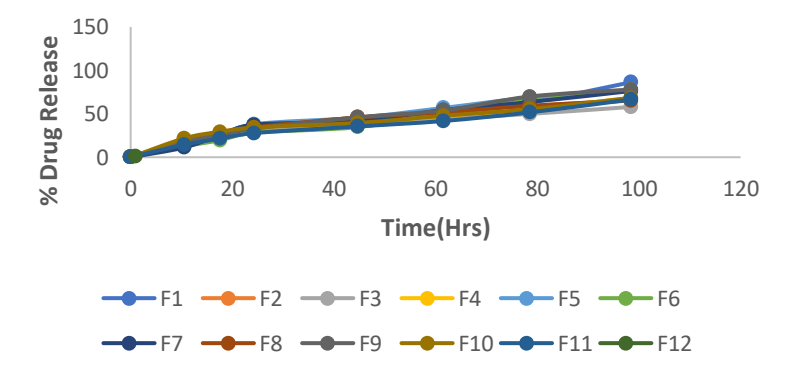

Fig9: Drug release profile(F1-F12)

Discussion

The in-vitro drug release study showed a formulation-dependent and time-dependent increase in Apremilast release. Considerable differences were observed among F1–F12 due to variations in polymer type and concentration. Higher polymer concentrations generally produced slower drug release because of increased swelling and formation of a stronger gel barrier.

Among the HPMC K4M formulations (F5–F8), F7 showed the most desirable release profile, achieving 99.92% drug release at 10 h. F5, F6, and F8 showed comparatively different release rates, confirming the influence of HPMC K4M concentration on drug release. The Carbopol 934P and sodium alginate formulations also exhibited wide variations in release, with release extending from approximately 7 to 10 h. Tthe results indicate that polymer type and concentration significantly influenced Apremilast release. F7 was selected as the optimized formulation based on its prolonged and controlled drug release up to 10 h.

The floating lag time of the prepared Apremilast floating tablets ranged from 42 to 75 seconds. All formulations showed satisfactory total floating time of approximately 12 h or more, indicating their potential to remain buoyant in the gastric environment for prolonged periods.

Drug release kinetics:

Zero Order Release Studies for Optimized Formulation:

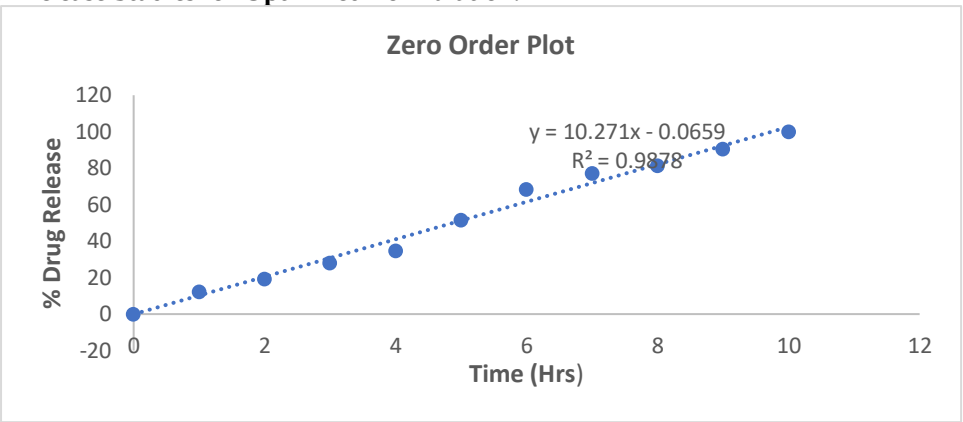

Fig10: Zero order plot of optimized formulation(F7)

First Order Release Studies for Optimized Formulation:

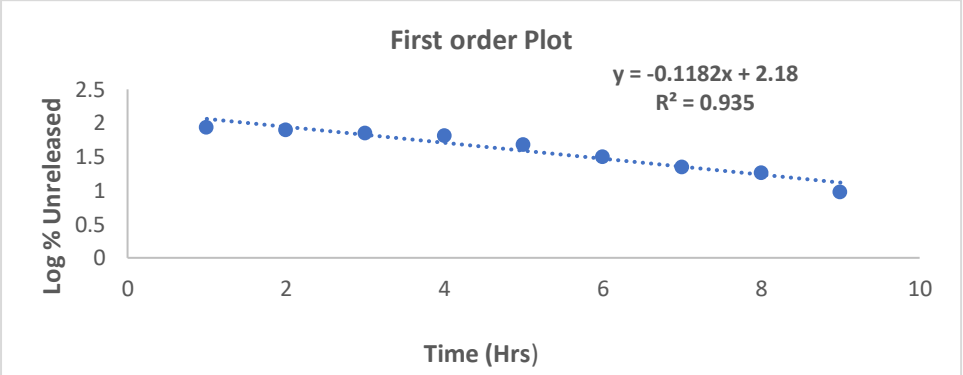

Fig11: First order plot of optimized formulation(F7)

Higuchi Plot Release Studies for Optimized Formulation:

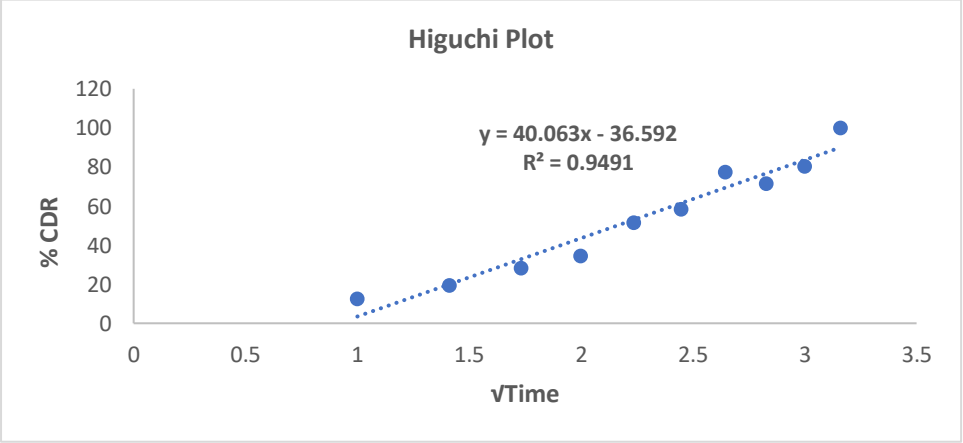

Fig12: Higuchi plot of optimized formulation(F7)

Peppa's Plot Release Studies for Optimized Formulation:

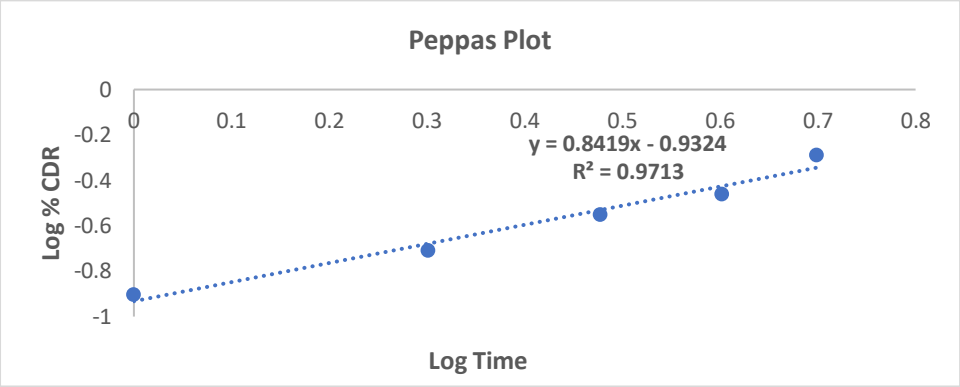

Fig13: Peppas plot of optimized formulation(F7)

Table No 7: Regression values

Formulation Code	Zero order	First order	Higuchi	Peppas	Peppas
	R^2	R^2	R^2	R^2	n
F7	0.9878	0.935	0.949	0.973	0.841

Discussion: The optimized formulation F7 showed the highest correlation coefficient (R^2 = 0.9878) for the zero-order model, indicating that drug release was predominantly concentration-independent and controlled over the study period. The Korsmeyer–Peppas model gave an n value of 0.8417, suggesting anomalous (non-Fickian) drug transport, indicating that both drug diffusion and polymer relaxation/swelling contributed to Apremilast release. The Higuchi model also showed a good correlation (R^2 = 0.949), supporting the contribution of diffusion-controlled release. F7 exhibited a controlled and sustained drug-release pattern suitable for gastro-retentive drug delivery.

SUMMARY AND CONCLUSION:

SUMMARY

The present study was undertaken with the objective of developing and evaluating Apremilast floating tablets as a gastro-retentive drug delivery system capable of providing prolonged gastric residence and sustained drug release. Initially, preformulation studies were carried out to establish the physicochemical characteristics of the drug. The melting point of Apremilast was found to be 155°C, confirming the identity of the drug. Solubility studies showed that Apremilast exhibited the highest solubility in 0.1 N HCl (0.890 µg/mL), was selected as the dissolution medium for further studies.

The drug was further analyzed by UV spectroscopy, where the maximum wavelength of absorption (λmax) was found to be 232 nm in 0.1 N HCl. The calibration curve prepared at this wavelength showed excellent linearity over the concentration range of 2–12 µg/mL, with a correlation coefficient of R^2 = 0.9997, confirming the suitability of the analytical method for estimation of Apremilast. FTIR compatibility studies demonstrated that the characteristic functional groups of Apremilast were retained in the optimized formulation, indicating no significant drug–excipient interaction.

Twelve Apremilast floating tablet formulations (F1–F12) were prepared and evaluated. The powder blends exhibited satisfactory flow properties, with angle of repose of 21.28–28.74°, Carr's index of 12.12–18.72%, and Hausner's ratio of 1.12–1.22. The tablets showed satisfactory physical properties, with hardness of 6.14–6.88 kg/cm², friability <1%, and drug content of 91.28–98.96%, indicating good mechanical strength and drug uniformity.

In-vitro drug release studies of F1–F12 demonstrated sustained and formulation-dependent drug release. Among all formulations, F7 was selected as the optimized formulation, showing 99.92% drug release at 10 h. The floating lag time of the prepared Apremilast floating tablets ranged from 42 to 75 seconds. All formulations showed satisfactory total floating time of approximately 12 h or more, indicating their potential to remain buoyant in the gastric environment for prolonged periods. The optimized formulation showed the highest correlation with the zero-order model (R^2 = 0.9878), while the Korsmeyer–Peppas model

showed an n-value of 0.841, indicating anomalous/non-Fickian drug release

CONCLUSION

The present investigation successfully demonstrated the feasibility of developing Apremilast floating tablets as a gastro-retentive drug delivery system. The preformulation and compatibility studies confirmed the suitability of Apremilast and its compatibility with the selected excipients. The prepared formulations exhibited satisfactory powder-flow characteristics and acceptable post-compression properties, including adequate hardness, low friability, and uniform drug content.

Among the twelve formulations, F7 was identified as the optimized formulation based on its desirable physical properties and sustained drug-release performance. F7 achieved 99.92% drug release at 10 h, indicating effective control and prolongation of Apremilast release. The floating lag time of the prepared Apremilast floating tablets ranged from 42 to 75 seconds. All formulations showed satisfactory total floating time of approximately 12 h or more, indicating their potential to remain buoyant in the gastric environment for prolonged periods. The kinetic analysis showed that the release followed predominantly zero-order kinetics (R^2 = 0.9878), while the Korsmeyer–Peppas n-value of 0.841 indicated anomalous/non-Fickian release behavior. This suggests that drug diffusion along with polymer swelling and relaxation contributed to the overall release mechanism.

The developed F7 Apremilast floating tablet demonstrated satisfactory physicochemical characteristics, drug content uniformity, and prolonged drug release for up to 10 h. Therefore, the optimized formulation may be considered a promising approach for gastro-retentive sustained drug delivery of Apremilast, with potential to improve the control and duration of drug release compared with conventional immediate-release dosage forms. Further studies, including floating behavior, stability studies, and in-vivo gastro-retention and pharmacokinetic evaluation, may be undertaken to establish its performance and suitability for further development.

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