CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.23858317

Available online at: http://www.iajps.com Research Article

DEVELOPMENT AND CHARACTERIZATION OF BELZUTIFAN FLOATING DRUG DELIVERY SYSTEM FOR IMPROVED GASTRIC RETENTION

Prathyusha Madireddy[1*], Chilakuri Shreya[2], A. Saritha[3]

[1*]Associate Professor, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District

[2]Student, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District

[3]Professor and HOD, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District

Abstract:

The present study aimed to develop and characterize a floating drug delivery system (FDDS) of Belzutifan to improve gastric retention, provide sustained drug release, and enhance oral bioavailability. Belzutifan floating tablets were prepared by the direct compression method using sodium alginate (F1–F4) and Tragacanth (F5–F8) as matrix-forming polymers, while sodium bicarbonate and citric acid were incorporated as gas-generating agents to impart buoyancy. All formulations exhibited acceptable physical characteristics with weight variation between 399–401 mg, hardness ranging from 5.2–6.9 kg/cm², and friability below 1%, indicating adequate mechanical strength. Floating lag time ranged from 40 to 57 seconds, confirming rapid buoyancy. In vitro dissolution studies showed sustained drug release over 8 hours, with cumulative drug release ranging from 93.25% to 98.58%. Among all formulations, F7 demonstrated the highest drug release (98.58%), shortest floating lag time (40 seconds), and superior overall performance. Accelerated stability studies conducted according to ICH guidelines demonstrated that the optimized formulation remained stable over three months without significant changes in drug release characteristics. The optimized formulation (F7) showed promising physicochemical properties, buoyancy, controlled-release behaviour, and stability, indicating its potential as an effective gastro-retentive oral delivery system for Belzutifan.

Keywords: *Belzutifan, Floating Drug Delivery System, Gastro-retentive Drug Delivery System, Floating Tablets, Sodium Alginate, Tragacanth, Sustained Release, Direct Compression, Drug Release Kinetics.*

Corresponding author:

Prathyusha Madireddy,
Associate Professor, *Department of Pharmaceutics,*
Sri Sai Jyothi College of
Pharmacy, Vattinagulapally, Hyderabad, Telangana 500075.
Mobile: +91 9793101177
Email Id: *prathyusha.madireddy13@gmail.com*

QR CODE

Please cite this article in press ***Prathyusha Madireddy*** *et al.,* ***Development And Characterization Of Belzutifan Floating Drug Delivery System For Improved Gastric Retention.,****. Indo Am. J. P. Sci, 2026; 13(10).*

INTRODUCTION:

Oral drug delivery remains the most preferred and widely utilized route of administration due to its convenience, patient compliance, cost-effectiveness, and ease of manufacturing.[1] The gastrointestinal tract (GIT) exhibits complex physiological variations such as pH changes, motility patterns, enzymatic activity, and gastric emptying rates, all of which significantly influence drug absorption.[2] Floating systems are designed with polymers and gas-generating agents that reduce the density of the dosage form below that of gastric fluids, allowing the formulation to float on the stomach contents.[3] This prolonged gastric retention facilitates sustained drug release, improves drug absorption, minimizes fluctuations in plasma drug concentration, and reduces dosing frequency, thereby enhancing therapeutic efficacy and patient compliance.[4] Belzutifan is a novel orally active hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor approved for the treatment of von Hippel–Lindau (VHL) disease-associated renal cell carcinoma, central nervous system hemangioblastomas, and pancreatic neuroendocrine tumors. It selectively inhibits HIF-2α-mediated transcription, thereby suppressing tumor growth and angiogenesis.[5] The present study aims to develop and characterize a Belzutifan floating drug delivery system for improved gastric retention. The developed floating drug delivery system is expected to prolong gastric residence time, provide sustained drug release, enhance therapeutic efficacy, improve patient compliance, and serve as a promising gastroretentive dosage form for Belzutifan therapy.[6]

MATERIALS:

Belzutifan was procured from Hetero Labs, HYD, Sodium alginate and Tragacanth were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Formulation development

Table-1: Composition of Belzutifan floating tablets

Ingredient	Formulations							
	F1	F2	F3	F4	F5	F6	F7	F8
Belzutifan	120	120	120	120	120	120	120	120
Sodium alginate	50	100	150	200	-	-	-	-
Tragacanth	-	-	-	-	50	100	150	200
Lactose	210	160	110	60	210	160	110	60
Citric acid	5	5	5	5	5	5	5	5
Sodium bi carbonate	10	10	10	10	10	10	10	10
Magnesium stearate	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2
Total wt	400	400	400	400	400	400	400	400

Preparation of Formulation:

Belzutifan floating tablets were prepared by the direct compression method. Sodium alginate (F1–F4) and tragacanth (F5–F8) were used as release-retarding and matrix-forming polymers in varying concentrations. All the ingredients were accurately weighed according to the required formulation. Belzutifan, polymer (sodium alginate or tragacanth), lactose, sodium bicarbonate, and citric acid were passed individually through sieve No. 40 to obtain a uniform particle size. The sieved ingredients were transferred into a clean, dry mortar or blender and mixed thoroughly for 10–15 minutes to achieve a homogeneous powder blend. After uniform mixing, talc and magnesium stearate, previously passed through sieve No. 60, were added to the blend and mixed gently for 2–3 minutes to avoid over-lubrication. The prepared powder blend was evaluated for pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio to assess its flow properties. The final blend was compressed into tablets using a rotary tablet compression machine fitted with 10 mm flat-faced punches. The compression force was adjusted to obtain tablets with adequate hardness (approximately 5–7 kg/cm²) while maintaining a total tablet weight of 400 mg.[7]

Evaluation of tablets[8,9,10,11,12]

Physical Appearance:

The prepared Belzutifan floating tablets were visually inspected for their colour, shape, surface texture, and overall appearance. Tablets were examined under normal daylight for the presence of any visible defects such as cracks, chipping, mottling, capping, lamination, or sticking. The appearance of all tablets was recorded to ensure uniformity in colour, size, and shape.

Hardness
Tablet hardness was determined using a Monsanto Hardness Tester. Ten tablets were selected randomly from each formulation batch. Each tablet was placed between the anvils of the hardness tester, and force was applied gradually until the tablet fractured. The force required to break the tablet was recorded in kilograms per square centimeter (kg/cm^2) or Newton (N). The hardness of each tablet was measured individually, and the average value along with the standard deviation was calculated.

Thickness
The thickness of the tablets was measured using a Digital Vernier Caliper or Digital Micrometer. Ten tablets were selected randomly from each formulation batch. Each tablet was placed between the measuring jaws of the caliper, and the thickness was recorded in millimeters (mm). Measurements were taken individually for all tablets, and the average thickness with standard deviation was calculated.

Weight variation test:

The weight variation test was performed according to the Indian Pharmacopoeia (IP)/United States Pharmacopeia (USP) guidelines. Twenty tablets were selected randomly from each formulation batch and individually weighed using a calibrated digital analytical balance. The average tablet weight was calculated, and the individual weights were compared with the average weight. The percentage deviation of each tablet from the average weight was calculated using the following formula:

% Weight Variation = [(Individual tablet weight − Average tablet weight) / Average tablet weight] × 100

The tablets were considered to comply with the pharmacopeial specifications if the percentage weight variation was within the prescribed limits.

Content Uniformity:
Twenty tablets were randomly selected, and one tablet was finely powdered. A quantity of powder equivalent to 120 mg of Belzutifan was accurately weighed and transferred into a 100 mL volumetric flask containing a suitable solvent (e.g., methanol or the solvent used for analytical method development). The solution was sonicated for 15–20 minutes to ensure complete dissolution of the drug and then made up to volume with the same solvent. The resulting solution was filtered through Whatman No. 1 filter paper or a 0.45 µm membrane filter. An appropriate aliquot was further diluted with the selected dissolution medium or solvent and analyzed using a UV–Visible spectrophotometer at the predetermined λmax of Belzutifan. The drug content was calculated from the calibration curve and expressed as the percentage of the labeled amount. The tablets were considered to pass the test if the drug content was within the pharmacopeial acceptance limits (generally 95–105% of the labeled claim).

Friability:
The friability of the floating tablets was determined using a Roche friabilator. Ten tablets were accurately weighed (initial weight, W_1) and placed in the friabilator. The apparatus was operated at 25 rpm for 4 minutes (100 revolutions). After completion of the test, the tablets were removed, dedusted carefully, and reweighed (final weight, W_2). The percentage friability was calculated using the following equation:
The percentage friability was determined by the formula:

$$\% \text{ friability} = (W_1 - W_2) / W_1 \times 100$$

W_1 = Weight of tablets before test
W_2 = Weight of tablets after test

Floating lag time:

The floating lag time of the prepared Belzutifan floating tablets was determined using the USP Dissolution Apparatus II (Paddle Method). One tablet was placed in 900 mL of 0.1 N hydrochloric acid (pH 1.2) maintained at 37 ± 0.5°C, and the paddle speed was set at 50 rpm. The time taken by the tablet to rise to the surface of the dissolution medium and remain floating was recorded as the Floating Lag Time (FLT). The duration for which the tablet continuously floated on the surface of the medium without sinking was recorded as the Total Floating Time (TFT). The experiment was carried out in triplicate, and the average values were reported.

Drug release studies:
The in-vitro drug release study of Belzutifan floating tablets was performed using the USP Dissolution Apparatus II (Paddle Method). The dissolution medium consisted of 900 mL of 0.1 N hydrochloric acid (pH 1.2) maintained at 37 ± 0.5°C, and the paddle speed was adjusted to 50 rpm.One tablet from each formulation was placed in the dissolution vessel. At predetermined time intervals. 5 mL of the dissolution medium was withdrawn and immediately replaced with an equal volume of fresh medium maintained at the same temperature to maintain sink conditions. The withdrawn samples were filtered through Whatman No. 1 filter paper or a 0.45 µm membrane filter, suitably diluted if necessary, and analyzed using a UV–Visible spectrophotometer at the predetermined λmax of Belzutifan. The cumulative percentage of drug released was calculated using the calibration curve, and the drug release profile of each formulation was plotted as cumulative percentage drug release versus time.

Drug release kinetics:
The dissolution data obtained from the in-vitro drug release study were fitted into various mathematical kinetic models to determine the mechanism of drug release from the floating tablets. The cumulative drug release data were analyzed using the following kinetic models:

- **Zero-order model:** Cumulative percentage drug released versus time.
- **First-order model:** Log cumulative percentage drug remaining versus time.
- **Higuchi model:** Cumulative percentage drug released versus square root of time.
- **Korsmeyer–Peppas model:** Log cumulative percentage drug released versus log time.

Stability studies:
The optimized formulation of Belzutifan floating tablets was subjected to accelerated stability studies according to the International Council for Harmonisation (ICH) Guideline Q1A(R2). The tablets were packed in aluminum foil or high-density polyethylene (HDPE) containers and stored in a stability chamber at 40 ± 2°C and 75 ± 5% relative humidity (RH) for a period of 3 months.

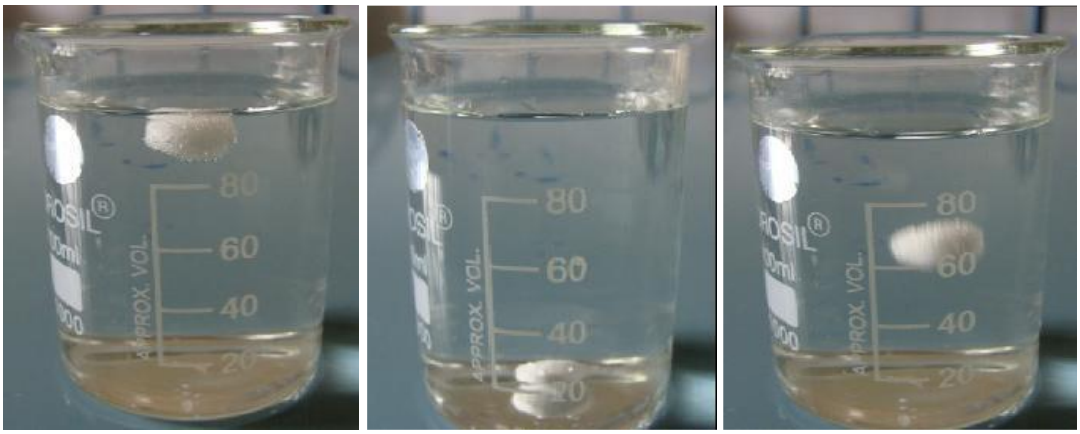
RESULTS AND DISCUSSION:

Evaluation of the Prepared Tablets for Physical Parameters

Table-2: Evaluation parameters of Belzutifan floating tablets

Parameter	F1	F2	F3	F4	F5	F6	F7	F8
Weight variation	400	399	401	400	399	400	400	401
Thickness (mm)	3.5	2.9	3.1	3.6	3.7	3.9	3.5	3.1
Hardness (kg/cm^2)	5.6	5.8	5.7	5.2	5.5	6.1	6.0	6.9
Friability	0.65	0.72	0.63	0.75	0.68	0.73	0.75	0.69
Content uniformity	86.91	83.25	81.93	90.17	85.47	87.63	91.25	90.25
Floating lag time (Sec)	52	57	50	49	43	55	40	53

Floating lag time



DISCUSSION:

The weight variation of all formulations ranged from 399 to 401 mg, which was very close to the theoretical tablet weight of 400 mg. The minimal variation in tablet weight indicated uniform die filling and good flow properties of the powder blends during compression. All formulations complied with the acceptable pharmacopeial limits for weight variation.

The tablet thickness varied between 2.9 and 3.9 mm. The slight differences in thickness among the formulations may be attributed to variations in polymer concentration and compressibility of the powder blend. However, all tablets exhibited uniform dimensions without any visible defects, indicating consistent compression during tablet manufacture.

The hardness of the tablets ranged from 5.2 to 6.9 kg/cm², demonstrating adequate mechanical strength to withstand handling, packaging, and transportation. Formulation F8 exhibited the highest hardness (6.9 kg/cm²), which may be attributed to the higher concentration of tragacanth producing a stronger matrix structure, whereas F4 showed the lowest hardness (5.2 kg/cm²). Nevertheless, all formulations were within the desirable hardness range for floating tablets.

The friability values ranged from 0.63 to 0.75%, which were well below the pharmacopeial limit of 1%. These findings indicate that all formulations possessed sufficient mechanical integrity and resistance to abrasion during handling. Formulation F3 exhibited the lowest friability (0.63%), indicating excellent tablet strength.

The content uniformity values ranged from 81.93 to 91.25%. Formulation F7 showed the highest drug content (91.25%), followed by F4 (90.17%) and F8 (90.25%), whereas F3 exhibited the lowest value (81.93%). These results suggest variability in drug distribution or assay recovery among the formulations. However, these values are below the pharmacopeial acceptance limits for content uniformity (typically 95–105% of the labeled claim). If these are actual experimental results, the formulation or analytical method should be optimized to achieve acceptable drug content before drawing conclusions about product quality.

The floating lag time ranged from 40 to 57 seconds, indicating rapid buoyancy of all formulations in the acidic dissolution medium. Formulation F7 exhibited the shortest floating lag time (40 seconds), suggesting efficient carbon dioxide generation and rapid formation of the hydrated polymer matrix. In contrast, F2 showed the longest floating lag time (57 seconds), although this value is still considered acceptable for gastroretentive floating tablets. The short floating lag times observed for all formulations indicate that the combination of sodium bicarbonate and citric acid effectively generated carbon dioxide, allowing the tablets to float quickly.

In vitro Dissolution studies

Table-3: In vitro drug release of Belzutifan floating tablets

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	19.68	18.52	17.58	18.46	17.83	16.39	18.97	17.46
2	35.72	34.96	33.69	36.98	35.59	34.71	39.66	38.42
3	41.58	42.55	43.81	44.47	45.18	46.38	47.84	45.37
4	53.69	55.78	51.48	55.69	56.37	52.56	53.67	55.13
5	64.58	65.37	66.98	67.48	68.48	67.48	68.78	65.43
6	72.28	73.59	74.51	75.84	74.95	75.35	76.91	77.84
7	81.53	82.58	83.56	85.58	84.49	83.58	86.59	83.16
8	93.25	95.46	96.89	97.55	93.56	95.33	98.58	94.87

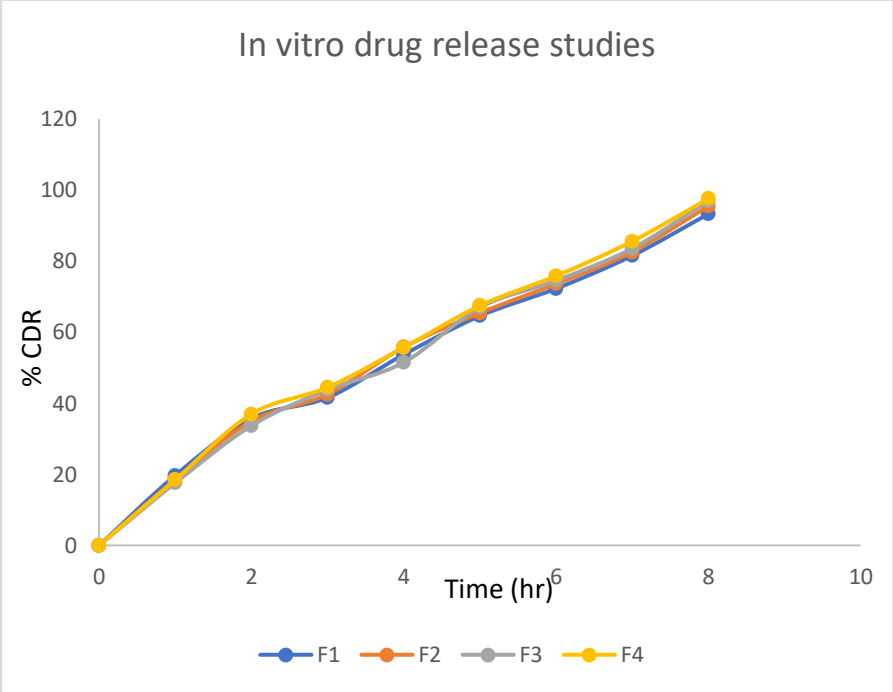


Fig-1: In vitro drug release for (F1-F4) formulations

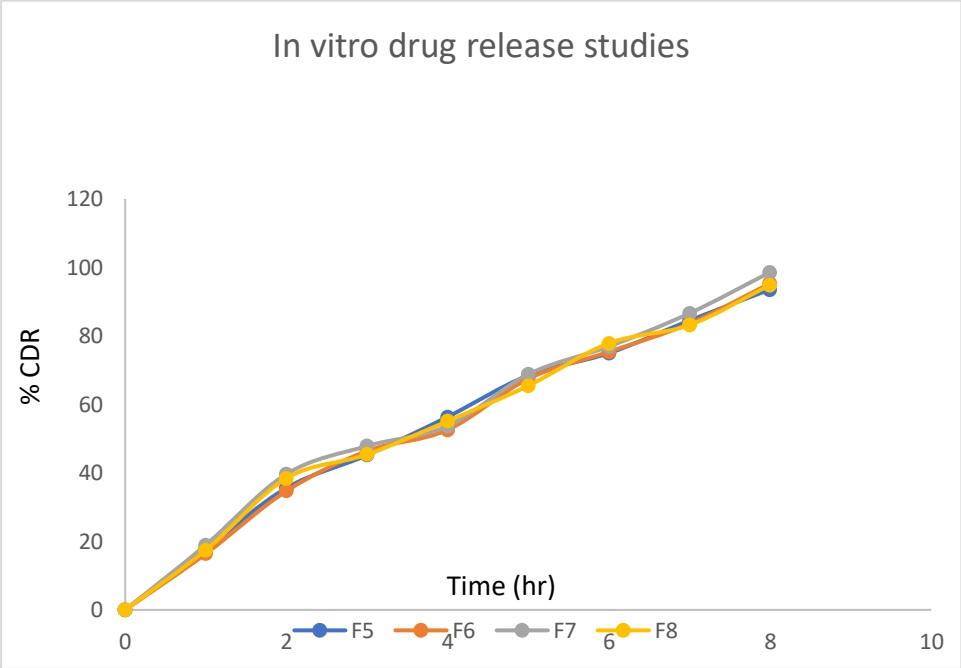


Fig-2: In vitro drug release for (F5-F8) formulations

Discussion

After 8 hours, the cumulative drug release ranged from 93.25% to 98.58%. Among all formulations, F7 exhibited the highest cumulative drug release (98.58%), followed by F4 (97.55%) and F3 (96.89%), while F1 showed the lowest release (93.25%). The superior release profile of F7 may be attributed to the optimized concentration of tragacanth, which provided an appropriate balance between matrix integrity and controlled diffusion of the drug. These findings indicate that formulation F7 produced the most desirable sustained-release profile among all the developed formulations.

Drug release kinetic profile
Zero order kinetics

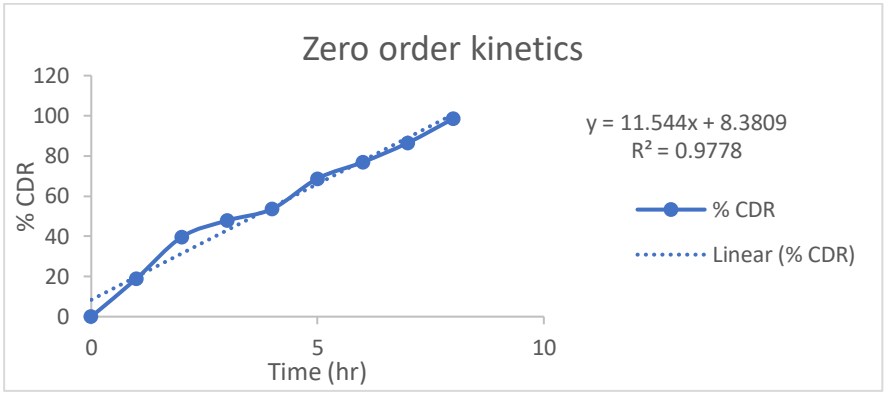


Fig-3: Drug release kinetics of zero order kinetics

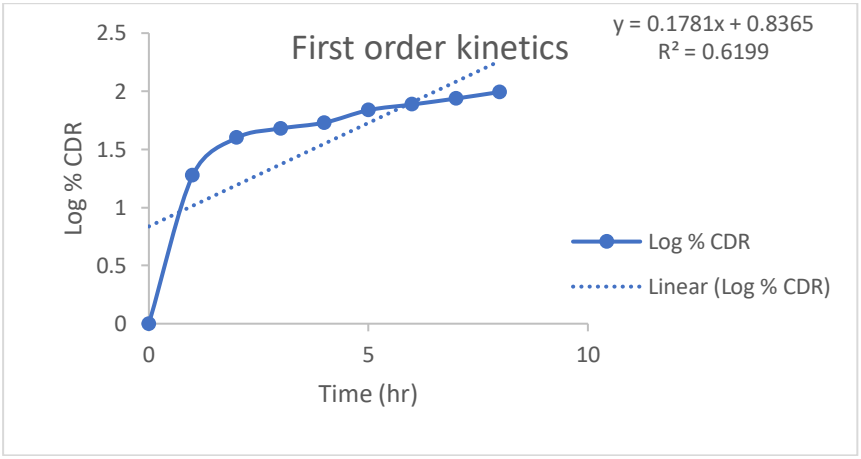


Fig-4: Drug release kinetics of First order kinetics

Higuchi model

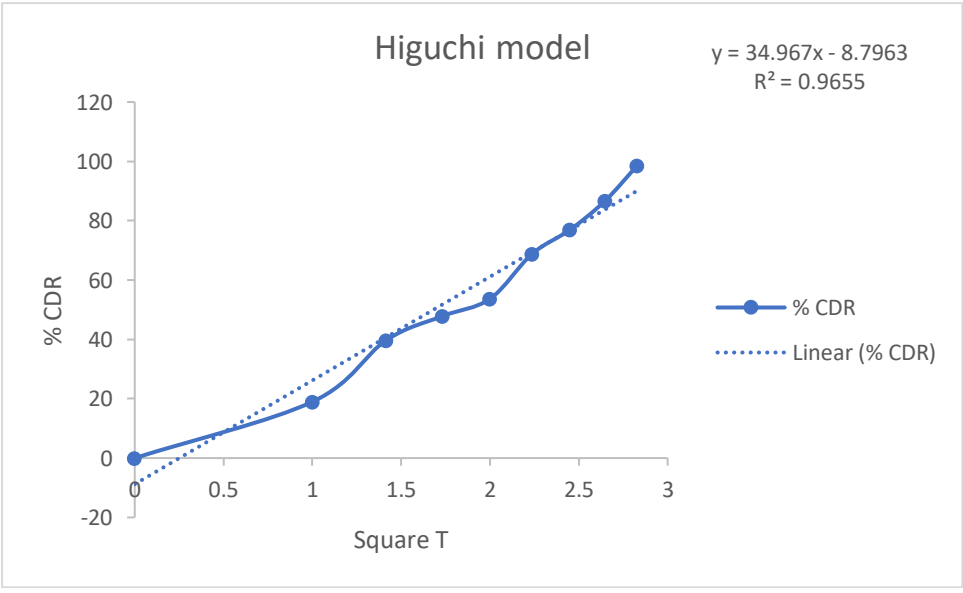


Fig-5: Drug release kinetics of Higuchi plot

Korsmeyer peppas

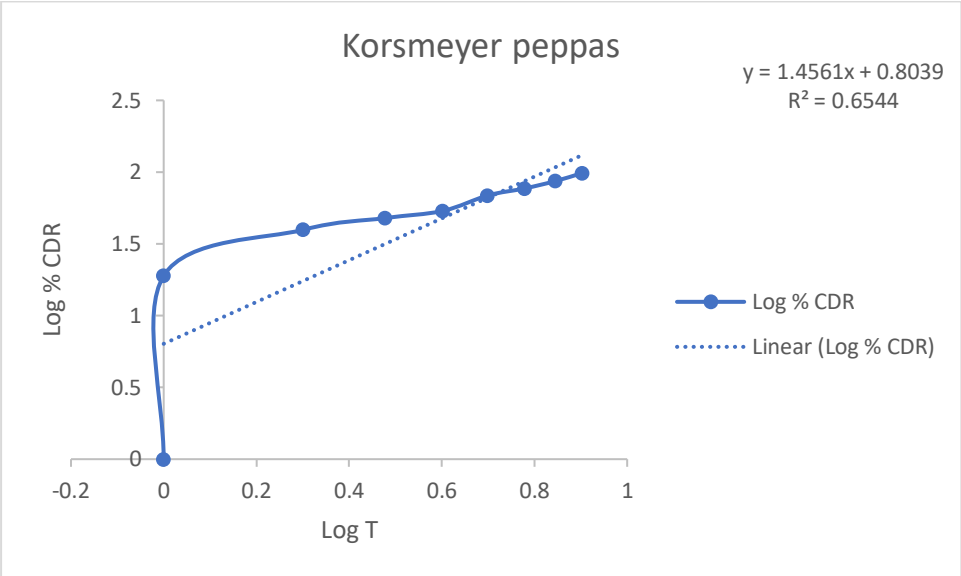


Fig-6: Drug release kinetics of Korsmeyer peppas

Discussion

Based on the dissolution profile and kinetic analysis, formulation F7 was identified as the optimized formulation, as it exhibited the highest cumulative drug release (98.58% in 8 hours), excellent floating characteristics, and a release profile that closely followed Zero-order kinetics with diffusion playing a major role in the drug release mechanism.

Stability Results

Table-4: Stability study for optimized formulation

F. Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-7	**25^{0}C/60%RH % Release**	98.58	97.81	96.28	95.15	**Not less than 85 %**
F-7	**30^{0}C/75% RH % Release**	98.58	97.53	96.12	95.10	**Not less than 85 %**
F-7	**40^{0}C/75% RH % Release**	98.58	97.52	96.18	95.02	**Not less than 85 %**

CONCLUSION:

Among the developed formulations, F7 was identified as the optimized formulation because it exhibited the shortest floating lag time (40 seconds), the highest cumulative drug release (98.58%), satisfactory mechanical strength, and a drug release profile that closely followed Zero-order kinetics with diffusion-controlled release characteristics. Overall, the study indicates that the developed Belzutifan floating tablet formulation has the potential to prolong gastric residence time and provide sustained drug release, which may improve oral drug delivery.

REFERENCES:

1. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. Journal of Controlled Release. 2003;90(2):143–162.
2. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. Expert Opinion on Drug Delivery. 2006;3(2):217–233.
3. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. Journal of Controlled Release. 2006;111(1–2):1–18.
4. Sauzet C, Bruno CM, Nicolas M, Kister J, Piccerdle P, Prinderre P. An innovative floating gastro retentive dosage system. Formulation and *in-vitro* evaluation. Int J Pharm 2009;378:23-29.
5. Abrahamsson, B., Alpsten, M., Hugosson, M., Jonsson, U.E., Sundgren, M., Svenheden, A., Tölli, J., 1993. Absorption, Gastrointestinal

Transit, and Tablet Erosion of Felodipine Extended-Release (ER) Tablets. Pharm. Res. 10, 709-714.
6. Agrawal, A.M., Manek, R.V., Kolling, W.M., Neau, S.H., 2003. Studies on the interaction of water with ethylcellulose: effect of polymer particle size. AAPS Pharm. Sci. Tech. 4, E60.
7. Alvisi, V., Gasparetto, A., Dentale, A., Heras, H., Felletti-Spadazzi, A., D'Ambrosi, A., 1996. Bioavailability of a controlled release formulation of ursodeoxycholic acid in man. Drugs Exp. Clin. Res. 22, 29-33.
8. Amaral, M.H., Lobo, J.M., Ferreira, D.C., 2001. Effect of hydroxypropyl methylcellulose and hydrogenated castor oil on naproxen release from sustained-release tablets. AAPS Pharm. Sci. Tech. 2, E6.
9. Andrews, G.P., Laverty, T.P., Jones, D.S., 2009. Mucoadhesive polymeric platforms for controlled drug delivery. Eur. J. Pharm. Biopharm. 71, 505-518.
10. Atyabi, F., Sharma, H.L., Mohammad, H.A.H., Fell, J.T., 1996b. In vivo evaluation of a novel gastric retentive formulation based on ion exchange resins. J. Control. Rel. 42, 105-113.
11. Babu, V.B., Khar, R.K., 1990. In vitro and in vivo studies of sustained-release floating dosage forms containing salbutamol sulfate. Pharmazie 45, 268-270.
12. Badve, S.S., Sher, P., Korde, A., Pawar, A.P., 2007. Development of hollow/porous calcium pectinate beads for floating-pulsatile drug delivery. Eur. J. Pharm. Biopharm. 65, 85-93.