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Design Development and Evaluation of Gastroretentive Floating Extended-Release Tablets of Dolutegravir for Enhanced Bioavailability

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Abstract:
The objective of this study was to formulate and evaluate a gastroretentive floating drug delivery system (GFDDS) for Dolutegravir, a potent integrase strand transfer inhibitor used in HIV therapy. Due to Dolutegravir's narrow absorption window and enhanced solubility in acidic conditions, a floating system was designed to prolong gastric residence and improve oral bioavailability. Various polymeric formulations (F1–F21) were developed using hydroxypropyl methylcellulose (HPMC) and glyceryl behenate in different drug-to-polymer ratios. The formulations were evaluated for pre-compression and post-compression characteristics including flow properties, hardness, friability, drug content, in vitro buoyancy, and dissolution profiles. The optimized formulation F7, demonstrated satisfactory physicochemical properties, floating lag time of less than one minute, and sustained buoyancy for over 12 hours. It showed a cumulative drug release of 94.32% over 12 hours, following Higuchi kinetics and non-Fickian diffusion, suggesting controlled release through a combination of diffusion and erosion. Comparative studies with marketed formulation (Tivicay) and pure drug indicated enhanced release kinetics and retention within the stomach. Differential scanning calorimetry (DSC) and scanning electron microscopy (SEM) confirmed drug-excipient compatibility and uniform surface morphology. The developed system showed significant promise as a gastroretentive platform for improving the therapeutic performance of Dolutegravir. The findings validate the potential of floating tablets as a strategy for antiretroviral drugs with limited absorption windows, thus enhancing patient compliance and therapeutic outcomes.

Key Words: *Dolutegravir, Gastroretentive Floating Drug Delivery System, Sustained Release, HPMC, Bioavailability*

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I. Introduction:

Oral administration remains the most widely adopted route for drug delivery due to its ease of use, non-invasive nature, and cost-effectiveness. Despite these advantages, challenges persist in achieving consistent therapeutic efficacy through this route, particularly when dealing with drugs that are unstable in the gastrointestinal (GI) environment or require site-specific absorption**.[1,2]** Many oral drugs suffer from limited bioavailability due to rapid gastric emptying, poor solubility at intestinal pH, enzymatic degradation, or extensive first-pass metabolism in the liver. These limitations become more pronounced in drugs with narrow absorption windows, where the therapeutic efficacy is closely tied to the site and duration of exposure within the upper gastrointestinal tract.**[3,4]**

To address these challenges, controlled and targeted drug delivery systems have been extensively explored. Among these, gastroretentive drug delivery systems (GRDDS) have gained significant attention. These systems are specifically engineered to remain buoyant or anchored in the stomach for extended periods, enabling localized and sustained release of the drug at its optimal site of absorption. Floating drug delivery systems (FDDS), a subclass of GRDDS, utilize polymers and gas-generating agents to reduce tablet density, allowing the formulation to float on gastric fluids. This approach enhances gastric retention time, reduces drug wastage in the lower intestines, and improves overall bioavailability.**[5-8]**

Dolutegravir, a potent HIV-1 integrase strand transfer inhibitor, is widely used in antiretroviral therapy. Its oral absorption is most efficient in the acidic environment of the stomach and proximal small intestine. However, conventional formulations may transit rapidly through the gastrointestinal tract, limiting the drug's absorption. Therefore, the development of a GRDDS for Dolutegravir offers a promising strategy to prolong

gastric residence, provide controlled release, and enhance therapeutic efficacy. The present research focuses on the design and evaluation of a floating matrix tablet of Dolutegravir using hydrophilic and lipophilic polymers, aimed at achieving prolonged drug release and improved bioavailability.**[9-15]**

II. Materials and Methods:

Dolutegravir was obtained as a gift sample from Lantec pharmaceuticals, Hyderabad for research purposes. Hydroxypropyl methylcellulose (HPMC) of varying viscosity grades, including HPMC K4M and K15M, was procured from Colorcon Asia Pvt. Ltd. Glyceryl behenate (Compritol® 888 ATO), a hydrophobic matrix-forming lipid, was sourced from Gattefossé India Pvt. Ltd. Citric acid anhydrous and sodium bicarbonate, used as gas-generating agents to facilitate buoyancy, were purchased from S.D. Fine-Chem Ltd., Mumbai. Microcrystalline cellulose (MCC) PH 102, serving as a diluent and flow aid, was obtained from FMC Biopolymer. All chemicals and reagents used were of analytical grade and were used as received without further purification.**[16,17]**

Dolutegravir multi-unit floating tablets were formulated using various primary polymers at a 1:1 drug-to-polymer ratio to assess their influence on drug release and gastric retention. Formulations F1 and F2 incorporated hydrophilic polymers HPMC K4M and HPMC K100, respectively, whereas formulations F3 to F7 employed different lipid-based polymers: glyceryl behenate (F3), glyceryl palmitostearate (F4), hydrogenated vegetable oil (F5), ethoxylated castor oil (F6), and Hard Fat (F7), with F7 ultimately selected for optimization based on superior dissolution and floatation performance. Each formulation contained 150 mg of Dolutegravir and 150 mg of the respective polymer. Common excipients across all formulations included citric acid anhydrous (40 mg) to support buoyancy through gas generation, microcrystalline cellulose PH 102 (80 mg) as a compressible filler, magnesium stearate (4 mg) as a lubricant, and talc (6 mg) to improve flow properties. The total tablet weight was maintained at 430 mg. This design approach aimed to ensure prolonged gastric residence, controlled drug release, and consistent therapeutic levels with reduced inter-subject variability.**[18,19]**

The Dolutegravir multi-unit granules were prepared via melt granulation technique, with Hard Fat serving as the lipid-based matrix-forming agent. The required quantity of Hard Fat was weighed and melted at a temperature approximately 5°C above its melting point. Dolutegravir, pre-sifted through a 40# mesh, was gradually added to the molten Hard Fat under continuous stirring to ensure uniform dispersion of the drug within the polymer matrix. The hot melt dispersion was subsequently allowed to cool and solidify at 4°C. The hardened mass was passed through a 16# sieve to obtain granules of uniform size. These granules were then blended with the remaining excipients citric acid anhydrous, microcrystalline cellulose, talc, and magnesium stearate in geometric dilution. The final blends were compressed into tablets using a rotary compression machine, targeting a total tablet weight of 430 mg for each unit.Tablet weight and hardness were maintained consistently across batches to ensure uniformity.The powder blends were subjected to flow property assessment, including measurements of bulk density, tapped density, Carr's compressibility index, Hausner's ratio, and angle of repose. These parameters were evaluated to predict flowability and compressibility of the formulation before compression.**[20-25]**

Ingredients	F1	F2	F3	F4	F5	F6	F7
Dolutegravir	150	150	150	150	150	150	150
HPMC K4M	150	--	--	--	--	--	--
HPMC K100	--	150	--	--	--	--	--
Glyceryl behenate	--	--	150	--	--	--	--
Glycerylpalmitostearate	--	--	--	150	--	--	--
Vegetable Oil, Hydrogenated	--	--	--	--	150	--	--
Ethoxylated castor oil	--	--	--	--	--	150	--
Hard Fat	--	--	--	--	--	--	150
Citric Acid Anhydrous	40	40	40	40	40	40	40

Microcrystalline Cellulose PH 102	80	80	80	80	80	80	80
Magnesium Stearate	4	4	4	4	4	4	4
Talc	6	6	6	6	6	6	6
Total Weight	**430**	**430**	**430**	**430**	**430**	**430**	**430**

Table- 1: Composition for the Extended-release floating tablets of Dolutegravir

After formulation, the prepared multi-unit granules were subjected to a series of post-compression evaluations to ensure their functional and pharmaceutical performance. Buoyancy characteristics were investigated using 0.1 N hydrochloric acid (pH 1.2) maintained at 37 ± 0.5°C to simulate gastric conditions. Each formulation was tested for floating lag time, defined as the time taken for the dosage unit to rise to the surface, and total floating duration, which indicates how long the formulation remained buoyant on the medium.**[26-29]**

Weight Variation: Weight variation twenty tablets were selected at random, weighed, and the average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more than 7.5%

Friability: For each formulation, pre-weighed tablet sample (20 tablets) was placed in the Roche Friability test apparatus (USP) EF02 (Electrolab, Mumbai, India), which was then operated for 100 revolutions. The tablets were deducted and reweighed. Conventional compressed tablets that lose <0.5–1% of their weight were considered acceptable.

Hardness: Hardness of tablet was determined before and after sintering using Monsanto Hardness Tester.

Content Uniformity: The drug content in each formulation was determined by triturating ten tablets and a quantity of powder equivalent to the mass of one tablet was extracted with pH 1.2 buffer and the solution was filtered through 0.45 µm membranes. The absorbance was measured at 266 nm after suitable dilution using UV-visible spectrophotometer at lmax of 266 nm and the amount of dolutegravir was found using the calibration curve method.

Buoyancy Studies: Floating lag time and total floating duration were evaluated in 0.1 N HCl (pH 1.2) at 37 ± 0.5 °C. The lag time was recorded as the time required for the tablet to rise to the surface, and the total floating time was noted.

In-Vitro Dissolution studies: The in vitro drug release studies were carried out using a USP Type II paddle apparatus (Model: Disso 2000, LabIndia). A volume of 900 mL of 0.1 N HCl served as the dissolution medium, agitated at a speed of 50 rpm and maintained at physiological temperature (37 ± 0.5°C). At pre-set time intervals, 5 mL samples were withdrawn using a pre-filtered syringe and immediately replaced with an equal volume of fresh medium to maintain sink conditions. The withdrawn samples were diluted appropriately and analyzed spectrophotometrically at 266 nm using a Cyberlab UV-visible spectrophotometer to determine the amount of drug released.**[30,31]**

The drug release data were fitted to various kinetic models including zero-order, first-order, Higuchi, and Korsmeyer-Peppas models to interpret the mechanism of release. Drug-excipient compatibility was evaluated by Differential Scanning Calorimetry (DSC). **[32]**Surface morphology and structural features of optimized formulations were examined using Scanning Electron Microscopy (SEM) to confirm the integrity and porosity of the matrix system.**[33]**

III. Results and Discussion:

The present study aimed to formulate a gastroretentive floating drug delivery system (GFDDS) of Dolutegravir using various lipid-based polymers through different granulation techniques and evaluate their suitability based on physicochemical, in vitro buoyancy, and drug release characteristics. A total of 21 formulations (F1–F21) were prepared using three drug-to-polymer ratios (1:1, 1:1.5, and 1:2), and the optimized formulation was identified as F7.**[34-37]**

In the present study, the calibration curve of Dolutegravir was established at a wavelength of 266 nm using UV-Visible spectrophotometry in 0.1 N HCl as the medium. A series of standard solutions with concentrations ranging from 5 to 25 µg/mL were prepared and analyzed. The absorbance values were recorded and plotted against the respective concentrations, resulting in a linear regression curve with a high correlation coefficient ($R^2 = 0.999$), indicating excellent linearity. This calibration curve was used for the quantification of drug content and in vitro dissolution samples throughout the study. **(Fig-1) [38]**

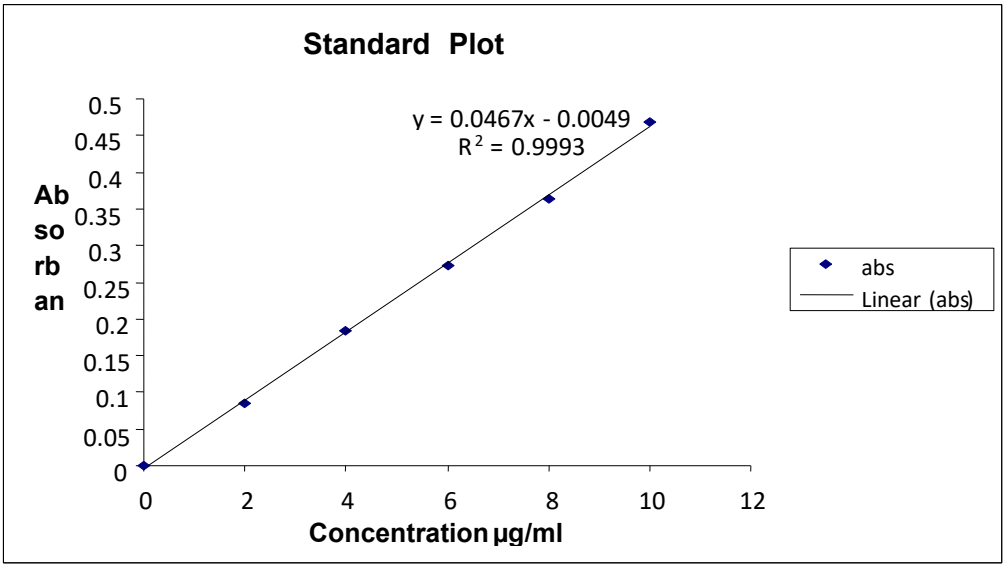

Figure-1: Calibration Curve of Dolutegravir at 266 nm.

Pre-Compression Flow Properties: All formulations (F1–F7) were assessed for flow properties to determine their suitability for compression. Flow behavior was evaluated using Carr's compressibility index, Hausner ratio, and angle of repose. Formulations F1 and F2, containing cellulose polymers, exhibited superior flowability with Carr's index values of 12.3% and 15.9%, and Hausner ratios of 1.14 and 1.18, respectively. Their angles of repose were below 25°, indicating excellent flow. Lipid-based formulations (F3–F7) showed slightly higher values, yet remained within acceptable limits. Specifically, F7 demonstrated a Carr's index of 18.6%, Hausner ratio of 1.32, and angle of repose of 32.8°, confirming acceptable flow characteristics for further processing.**[39]**

Formulation	Compressibility Index	Angle of Repose	Hausner Ratio
F1	12.3	20.6°	1.14
F2	15.9	23.5°	1.18
F3	18.8	31.2°	1.23
F4	17.7	30.7°	1.38
F5	19.4	26.8°	1.24
F6	18.2	33.1°	1.23
F7	18.6	32.8°	1.32

Table-2: Pre-Compression Flow Properties

Post-Compression Evaluation: All formulations (F1–F7) underwent post-compression evaluation to assess physical and pharmaceutical properties. Tablet weights ranged from 429.41 ± 3.87 mg to 431.12 ± 3.98 mg, remaining within pharmacopoeial limits. Hardness values varied between 3.12 and 3.94 kg/cm², ensuring sufficient mechanical strength. Thickness values were consistent, ranging from 2.55 to 2.69 mm. Drug content across all formulations was within ±5% of the labeled amount, with F7 showing the highest content uniformity at 100.76 ± 0.66%. Friability values were below 1% for all batches, indicating good tablet integrity during handling and transport.

Code	Weight Variation(mg)	Hardness (kg/cm²)	Thickness (mm)	% Drug Content	Friability (%)
F1	429.85 ± 4.35	3.62 ± 0.14	2.58 ± 0.026	100.18 ± 0.61	0.149
F2	431.12 ± 3.98	3.25 ± 0.22	2.61 ± 0.030	98.97 ± 1.01	0.021
F3	430.34 ± 4.11	3.77 ± 0.19	2.67 ± 0.030	96.88 ± 1.26	0.290
F4	430.76 ± 3.74	3.12 ± 0.21	2.65 ± 0.069	98.63 ± 0.92	0.902
F5	430.59 ± 4.22	3.94 ± 0.25	2.55 ± 0.044	99.46 ± 0.65	0.568
F6	429.41 ± 3.87	3.58 ± 0.20	2.63 ± 0.037	100.14 ± 0.74	0.575
F7	429.89 ± 3.93	3.33 ± 0.24	2.69 ± 0.061	100.76 ± 0.66	0.429

Table-2: Physicochemical Evaluation of Formulated Tablets Including Weight Variation, Hardness, Thickness, Drug Content and Friability

In Vitro Buoyancy Behaviour: All formulations (F1–F7) were evaluated for buoyancy characteristics in 0.1 N HCl (pH 1.2). Floating lag times ranged from 22 to 90 seconds. F7 exhibited the shortest lag time (22–33 sec), indicating rapid buoyancy initiation. Most formulations (F1–F3, F5–F7) maintained floating for over 12 hours, with F3 showing a slight reduction in duration (10–20%). F4 displayed the weakest buoyancy performance, with a shorter floating duration of approximately 2 hours (60% reduction), suggesting limited gastric retention. Overall, F7 demonstrated superior buoyancy with rapid floatation and prolonged gastric residence.**[40]**

Formulation	Buoyancy Lag time (Min)	Duration of Floating (Hrs)
F1	30-55 sec	>12
F2	60-65 sec	>12
F3	55 - 68 sec	>12 (10-20%) ↓
F4	63 - 68 sec	2 (60%) ↓
F5	84 - 88 sec	>12
F6	77 - 90 sec	>12
F7	22 - 33 sec	>12

Table-4: *In-Vitro* Buoyancy study results for prepared formulations

In Vitro Drug Release Studies: The release profile of Dolutegravir from all formulations was determined using USP Type II apparatus in 0.1 N HCl. Among the 1:1 ratio formulation, F7 exhibited the most controlled release profile, with 98.96% cumulative drug release over 12 hours. Formulations F1 and F2 released over 94% within 5–6 hours, while F3–F6 showed varied release durations between 4 and 10 hours. (Fig-2) The extended release from F7 was attributed to the hydrophobic matrix formed by Gelucire 43/01, which slowed down the drug diffusion and maintained buoyancy.**[41]**

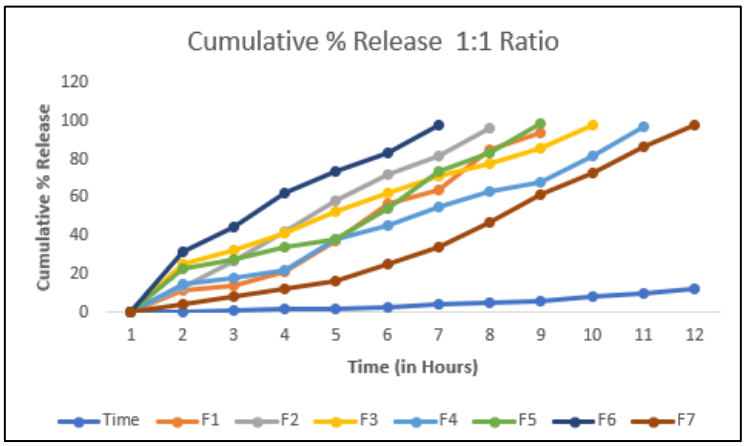

Figure-2: Comparative Dissolution profiles of Formulations F1-F7

The dissolution profile of F7 was compared against a single-unit GFDDS (drug: polymer 1:3), pure Dolutegravir, and the marketed formulation TIVICAY. The single-unit formulation released ~81% drug in 12 hours, whereas the pure drug and TIVICAY released over 93% and 97% within 30 minutes and 1 hour, respectively. F7 demonstrated a more gradual and controlled release, making it preferable for sustained plasma levels.**(Fig-3) [42]**

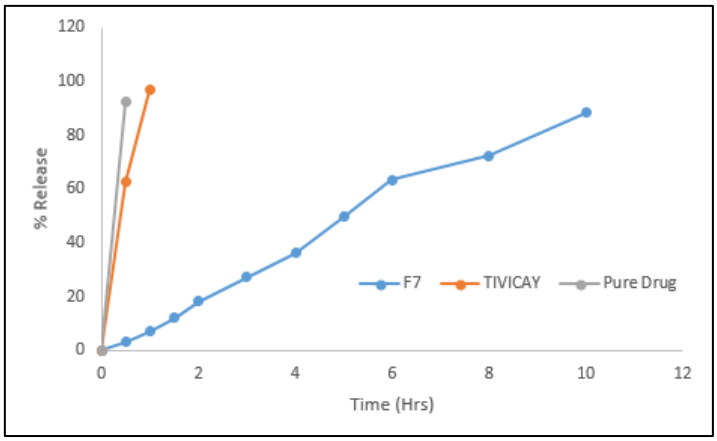

Figure-3: Comparative Dissolution Profiles of Formulations F7, TIVICAY and Pure Drug

Drug Release Kinetics: To elucidate the release mechanism, dissolution data were fitted into zero-order, first-order, Higuchi, erosion, and Korsmeyer-Peppas models. F7 exhibited a higher correlation coefficient (R^2 = 0.995) with the zero-order model, suggesting constant drug release over time. Additionally, the Peppas exponent (n > 1) indicated super case-II transport, pointing toward polymer swelling and erosion contributing to the controlled release mechanism. **[43]**

Drug-Polymer Compatibility (DSC & SEM Studies): Differential Scanning Calorimetry (DSC) and Fourier-transform infrared (FTIR) spectroscopy were employed to assess compatibility between Dolutegravir and Gelucire 43/01. The DSC thermograms of the physical mixture and optimized formulation exhibited no significant shift in endothermic peaks compared to the pure drug, indicating no interaction. SEM images of the optimized formulation revealed uniform dispersion of lipid material and consistent surface morphology. Ageing studies confirmed the physical and thermal stability of the optimized system over time.**[44-46]**

IV. Conclusion:

A gastroretentive floating tablet of Dolutegravir was successfully formulated using Hard Fat (Gelucire 43/01) as the matrix-forming agent through melt granulation. The optimized formulation (F7) demonstrated immediate buoyancy, prolonged floating duration exceeding 12 hours, and a controlled drug release profile sustained over the same period. This system offers significant potential to enhance the oral bioavailability of Dolutegravir by retaining the drug in the upper gastrointestinal tract, where its absorption is most efficient. Compared to conventional formulations, this gastroretentive approach minimizes fluctuations in plasma drug levels and may contribute to improved therapeutic outcomes in antiretroviral therapy. The study confirms the suitability of lipid-based floating systems for drugs with limited solubility in intestinal pH and narrow absorption windows. Future research should include in vivo pharmacokinetic studies, long-term stability evaluation, and clinical validation. Additionally, this formulation concept may be extended to other antiretrovirals or similar drugs, offering a platform for targeted delivery and enhanced patient adherence.

References:

[1]. Hoffman AS. The Origins and Evolution of "Controlled" Drug Delivery Systems. J Control Release. 2008;132:153–63.
[2]. Garg R, Gupta GD. Progress in Controlled Gastroretentive Delivery Systems. Trop J Pharm Res. 2008;7(3):1055–66.
[3]. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating Drug Delivery Systems: A Review. AAPS PharmSciTech. 2005;6(3):E372–E386.
[4]. Kim S, Kim JH, Jeon O, Kwon IC, Park K. Engineered Polymers for Advanced Drug Delivery. Eur J Pharm Biopharm. 2009;71:420–2.
[5]. Dhumal RS, Rajmane SKT, Dhumal ST, Pawar AP. Design and Evaluation of Bilayer Floating Tablets of Cefuroxime Axetil. J Sci Ind Res. 2006;65:812–6.
[6]. Davis SS. Formulation Strategies for Absorption Windows. Drug Discov Today. 2005;10(4):249–57.
[7]. Hwang SJ, Park H, Park K. Gastric Retentive Drug Delivery Systems. Crit Rev Ther Drug Carrier Syst. 1998;15:243–84.
[8]. Chavanpatil MD, Jain P, Chaudhari S, Shear R, Vavia PR. Novel Sustained Release, Swellable and Bioadhesive Gastroretentive System for Ofloxacin. Int J Pharm. 2006;316:86–92.
[9]. Krogel I, Bodmeier R. Floating or Pulsatile Drug Delivery Systems Based on Coated Effervescent Cores. Int J Pharm. 1999;187:175–84.
[10]. Streubel A, Siepmann J, Bodmeier R. Floating Matrix Tablets Based on Low Density Foam Powder. Eur J Pharm Sci. 2003;18(1):37–45.
[11]. GUDE S, GUDE YS. The synergy of artificial intelligence and machine learning in revolutionizing pharmaceutical regulatory affairs. Translational and Regulatory Sciences. 2024;6(2):37-45.
[12]. GUDE S, ABBURI SK, GALI PK, GORLAGUNTA S. Advancing single-shot vaccine design through AI and computational models. Translational and Regulatory Sciences. 2025;7(1):8-14.

[13]. GUDE S. Exploring innovative drug delivery systems for the targeted treatment and rehabilitation of individuals affected by narcotics and psychotropic substances: a multidisciplinary approach in pharmaceutics. Translational and Regulatory Sciences. 2024;6(3):72-83.
[14]. KagitaT, Gude S, Abburi Sk, Devarakonda a, Maddineni S. Advancing 3D printing for personalized pediatric medicines: quality, safety, and Good Manufacturing Practice compliance. Translational and Regulatory Sciences. 2025.
[15]. Gude S, Abburi Sk, Devarakonda a, Gali pk, Gorlagunta S. Surface bio-engineering of polymeric nanoparticles: advancing precision in biomedical applications. Translational and Regulatory Sciences. 2025;7(1):30-6.
[16]. Kattamuri SB, Potti L, Vinukonda A, Bandi V, Changantipati S, Mogili RK. Nanofibers in pharmaceuticals—a review. Am. J. Pharmtech. Res. 2012;2(6):188-212.
[17]. Panditi VR, Vinukonda A. Development of second order spectroscopic method for the determination of Stavudine in bulk and pharmaceutical Dosage forms. Journal of Pharmacy Research. 2011 Feb;4(2):492-3.
[18]. Putikam JK, Rao YN, Anjaneyulu V, Undralla VK. Formulation and evaluation of metoprolol succinate extended release tablet. Research Journal of Pharmacy and Technology. 2012;5(1):75-8.
[19]. Saisri B, Anjaneyulu V, KUMAR GV. Design and charaterization of pramipexole dihydrochloride nanoparticles. Journal For Innovative Development in Pharmaceutical and Technical Science (JIDPTS). 2021 Nov;4(11).
[20]. RANI R, Anjaneyulu V, KUMAR GV. Forulation And Evaluation of Colon Specific Drug Delivery System of Celecoxib. International Journal of Pharmacy Research & Technology (IJPRT). 2023 Mar 21;13(2):65-76.
[21]. Khan SL, Gandla K, Kakaravada I, Rao PB, Vinukonda A, Hasan HG, Hussain Z, Sheikh AA. Silica-Polymer Composites for Biomedical Applications. InFiber and Ceramic Filler-Based Polymer Composites for Biomedical Engineering 2024 Aug 11 (pp. 109-142). Singapore: Springer Nature Singapore.
[22]. Caldwell LJ, Gardner CR, Cargill RC, Higuchi T. Drug Delivery Device for Retention in Stomach. US Patent 4758436. 1988 Jul 19.
[23]. Klausner EA, Lavy E, Barta M, Cserepes E, Friedman M, Hoffman A. Novel Gastroretentive Dosage Forms. J Control Release. 2003;90:143–62.
[24]. Basak SC, Reddy MB, Mani KK. Floating Gastroretentive Tablet of Metformin Hydrochloride. Indian J Pharm Educ Res. 2007;41(4):302–5.
[25]. Jaimini M, Rana AC, Tanwar YS. Formulation and Evaluation of Famotidine Floating Tablets. Curr Drug Deliv. 2007;4(1):51–5.
[26]. Badve SV, Sher P, Korde A, Pawar AP. Development of Hollow Calcium Pectinate Beads for Floating-Pulsatile Drug Delivery. Eur J Pharm Biopharm. 2007;65:85–93.
[27]. Srivastava A, Ridhurkar D, Wadhwa S. Floating Microspheres of Cimetidine. Indian J Pharm Sci. 2005;67(6):751–6.
[28]. Choi BY, Park HJ, Hwang TS, Park JB. Preparation of Alginate Beads for Floating Drug Delivery System: Effects of CO_2 Gas-Forming Agents. Int J Pharm. 2002;239:81–91.
[29]. Jain SK, Awasthi AM, Jain NK, Agrawal GP. Calcium Silicate Based Microspheres for Gastroretentive Floating Drug Delivery. Int J Pharm. 2005;285:35–49.
[30]. Muthusamy K, Govindarajan G, Ravi TK. Floating Micropellets of Lansoprazole. Drug Dev Ind Pharm. 2005;31(4-5):437–44.
[31]. Desai S, Bolton S. Floating Controlled Release Drug Delivery Systems. Pharm Res. 1993;10:1321–5.
[32]. Bolton S, Desai S. Floating Sustained Release Compositions. US Patent 4814179. 1989 Mar 21.
[33]. Singh BN, Kim KH. Floating Drug Delivery Systems: An Approach to Oral Controlled Drug Delivery via Gastric Retention. J Control Release. 2000;63:235–59.
[34]. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled Release Drug Delivery Systems for Prolonged Gastric Residence. Drug Dev Ind Pharm. 1996;22(6):531–9.
[35]. Moses AJ. Gastroretentive Dosage Forms. Crit Rev Ther Drug Carrier Syst. 1993;10:143–95.
[36]. Mojaverian P, Vlasses PH, Kellner PE, Rocci ML Jr. Effects of Gender, Posture, and Age on Gastric Residence Time of an Indigestible Solid. Pharm Res. 1988;10:639–44.
[37]. Grubel P, et al. Gastric Emptying of Non-digestible Solids in Fasted Dogs. J Pharm Sci. 1987;76:117–22.
[38]. Jannin V, Musakhanian J, Marchaud D. Approaches for the Development of Solid and Semi-Solid Lipid-Based Formulations. Adv Drug Deliv Rev. 2008;60:734–46.
[39]. Breitenbach J. Melt Extrusion: From Process to Drug Delivery Technology. Eur J Pharm Biopharm. 2002;54(2):107–17.
[40]. Griffin BT, O'Driscoll CM. Intestinal Lymphatic Transport of Saquinavir from Lipid Formulations. J Pharm Pharmacol. 2006;58(7):917–25.
[41]. Zhou F, Zhang ZR, et al. Preparation and Evaluation of Ibuprofen Pellets Using Wax Matrix. Eur J Pharm Biopharm. 1999;48:191–6.
[42]. El-Gibaly I. Development of Melatonin Floating Microcapsules. Eur J Pharm Biopharm. 2002;52:81–8.
[43]. Umamaheshwari RB, Jain S, Tripathi P, Agrawal GP. Floating Microspheres Containing Acetohydroxamic Acid. AAPS PharmSciTech. 2003;4(2):E32.
[44]. Joseph NJ, Laxmi S, Jayakrishnan A. Floating Microspheres of Piroxicam. Drug Dev Ind Pharm. 2002;28:815–25.
[45]. Yu Y, Wang Y, Wang X, Li X. Long-Term Drug Release from Melt Granulation. Int J Pharm. 1994;109(2):127–34.
[46]. Ito Y, et al. Oral Solid Gentamicin Using Emulsifier and Adsorbent. J Control Release. 2005;105:23–31.