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Formulation And Evaluation Of Levodopa Floating Tablet For Prolonged Gastric Retention And Sustained Release For The Management Of Parkinson's Disease

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This study focused on the formulation, evaluation, and comparison of levodopa floating tablets designed for controlled release, with immediate-release tablets serving as a reference. Levodopa floating tablets were developed to enhance gastric retention and provide sustained drug release, aiming to improve therapeutic outcomes for conditions such as Parkinson's disease. Pharmacokinetic analysis showed that immediate-release tablets achieved a higher maximum plasma concentration (Cmax) of 233.83 ng/mL, while the floating tablets reached 156.85 ng/mL. Despite similar time to peak concentration (Tmax) between both formulations, the floating tablets demonstrated a prolonged gastric

retention time of 12 hours compared to less than 1 hour for immediate-release tablets. Drug release studies revealed that formulation FF2 provided controlled drug release, reaching over 100% within 8 hours, while FF5 showed the most prolonged release. Kinetic modelling indicated that FF2 offered an ideal balance between sustained drug release and gastric retention. In contrast, immediate-release tablets offered rapid, intense drug release but with shorter retention. FF2 emerged as the most effective floating tablet formulation, providing both sustained drug release and extended gastric retention, making it suitable for long-term therapeutic management.

Keywords: Floating drug delivery, Levodopa, Parkinson's Disease,Gastric retention

INTRODUCTION

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder primarily affecting the motor system, with symptoms including tremors, rigidity, bradykinesia (slowness of movement), and postural instability(Dauer & Przedborski, 2003). These symptoms arise due to the depletion of dopamine, a neurotransmitter that plays a crucial role in regulating movement, as a result of the degeneration of dopaminergic neurons in the substantia nigra. As the disease progresses, the loss of dopamine causes significant motor and non-motor symptoms, leading to disability and impaired quality of life for patients(Dauer & Przedborski, 2003; Davie, 2008).Levodopa, a precursor to dopamine, has long been considered the gold standard treatment for managing the motor symptoms of Parkinson's disease. Unlike dopamine, which cannot cross the blood-brain barrier, levodopa can enter the brain and be converted into dopamine, helping to alleviate the symptoms. However, despite its effectiveness, the use of levodopa presents several challenges, particularly with regard to its pharmacokinetic profile. Levodopa has a short half-life of 1-2 hours, and its absorption primarily occurs in the upper part of the small intestine. This leads to fluctuating plasma concentrations, causing periods of high symptom relief ("on" times) followed by periods of reduced symptom control ("off" times)(Mohammed, Alqahtani, & Ahmed, 2024; Munusamy & Shanmugasundharam, 2024b; Rajora & Nagpal, 2022; Saady et al., 2024). Additionally, the rapid gastrointestinal transit of immediate-release levodopa formulations can result in erratic absorption, contributing to unpredictable therapeutic effects(Dauer & Przedborski, 2003; Pezzoli & Zini, 2010).

One approach to overcoming these challenges is the development of a floating drug delivery system for levodopa. Floating tablets are designed to remain buoyant on gastric fluid, thus extending the drug's residence time in the stomach. This system offers several advantages, particularly for drugs like levodopa, which are absorbed primarily in the upper gastrointestinal tract(Adepu & Ramakrishna, 2021; Park, 2014). By staying in the stomach for an extended period, floating tablets ensure a more consistent and controlled release of the drug, leading to more stable plasma concentrations and improved symptom management. Moreover, this approach can reduce the frequency of dosing, as the sustained release of levodopa provides longer therapeutic effects, reducing the peaks and troughs associated with immediate-release formulations(Bruck, 1983; Dsouza, Dinesh, & Sharma, 2024; Kállai-Szabó et al., 2024; Mohammed et al., 2024; Munusamy & Shanmugasundharam, 2024b; Park, 2014; Rajora & Nagpal, 2022; Saady et al., 2024; Zheng et al., 2023). The rationale for fabricating levodopa

floating tablets is based on the need to provide a more stable and controlled release of the drug, minimizing the fluctuations in plasma levels that contribute to the motor complications seen in Parkinson's patients. This system can improve the bioavailability of levodopa by allowing it to be absorbed in the most effective part of the gastrointestinal tract, enhancing its therapeutic efficacy while reducing the risk of side effects caused by high plasma peaks. Furthermore, the prolonged gastric retention provided by floating tablets may improve patient compliance by reducing the frequency of medication administration, making the treatment regimen more manageable for patients who require long-term therapy(Budriesi et al., 2007; Elliott & Ram, 2011; Essali, Deirawan, Soares-Weiser, & Adams, 2011; Triggle, 2006).

The primary aim of this study is to design, formulate, and evaluate levodopa floating tablets to enhance gastric retention and provide controlled, sustained drug release. This approach seeks to optimize the therapeutic outcomes of levodopa by ensuring stable plasma concentrations over an extended period, thereby improving symptom control in Parkinson's disease patients(Albetawi, Abdalhafez, & Abu-Zaid, 2021; Kumari, Khansili, Phougat, & Kumar, 2019; Pezzoli & Zini, 2010; Rajora & Nagpal, 2022; Rathor, Aamir, Bhatt, Kumar, & Kumar, 2021; Sheraz, Ahsan, Khan, Ahmed, & Ahmad, 2016). The study also aims to compare the performance of these floating tablets with immediate-release formulations in terms of pharmacokinetics, drug release kinetics, and overall therapeutic efficacy. Through this research, the goal is to demonstrate that floating levodopa tablets offer a superior delivery system for managing Parkinson's disease, with potential benefits in terms of both efficacy and patient adherence to treatment.

MATERIAL AND METHODS

Chemicals and Drugs

Various chemicals and drugs were used to prepare and evaluate floating tablets for controlled drug release. Levodopa, the active ingredient, was provided by Arizon Lifesciences, Himachal Pradesh, India, and selected for its role in treating Parkinson's disease through a sustained-release formulation aimed at improving patient compliance.Excipients included Hydroxypropyl methylcellulose (HPMC) K100M for controlled release, Carbopol 934P for mucoadhesion, and citric acid with sodium bicarbonate as gas-generating agents for tablet buoyancy. Polyvinylpyrrolidone (PVP) K-30 served as a binder, while magnesium stearate and talc acted as lubricants. These were sourced from Sigma Aldrich, Mumbai, India, chosen for their proven compatibility in controlled-release formulations.Distilled water was used for solution preparation, and 0.1 N HCl (pH 1.2) simulated gastric conditions during in vitro dissolution studies to evaluate levodopa release. All chemicals were of analytical grade, ensuring precision in procedures like UV spectroscopy, which measured drug content and release rates, ensuring the formulation met the desired performance criteria.

Preparation Method for Levodopa Floating Tablets

Levodopa floating tablets were made via wet granulation (Munusamy & Shanmugasundharam, 2024a; Putta et al., 2024).The preparation of levodopa floating tablets followed a systematic process using the composition outlined in Table 1. Initially, all ingredients, including 200 mg of levodopa and varying quantities of HPMC K100M, Carbopol

934P, citric acid, sodium bicarbonate, PVP K-30, magnesium stearate, and talc, were accurately weighed according to the specific formulation (FF1-FF5). The dry ingredients, such as levodopa, HPMC K100M (where applicable), Carbopol 934P (if included), citric acid, and sodium bicarbonate, were thoroughly mixed in a blender for 10-15 minutes to ensure even distribution. Care was taken during this step to avoid premature gas formation from sodium bicarbonate and citric acid.Following dry mixing, wet granulation was performed by adding a PVP K-30 solution in isopropyl alcohol as a binder. The binder solution was added gradually while stirring continuously to form granules. It was important to avoid over-wetting the mixture during this step. The wet granules were then dried in a hot air oven at a controlled temperature of 40-45°C until the desired moisture content was achieved. After drying, the granules were passed through a 20-mesh sieve to ensure uniform size and better flowability.The next step involved lubrication, where the sieved granules were blended with magnesium stearate and talc. These lubricants were mixed gently to ensure that they coated the granules uniformly, preventing sticking during the compression process. Finally, the lubricated granules were compressed into tablets using a rotary tablet press, with the compression force optimized to produce tablets with sufficient hardness and integrity.The prepared floating tablets were then evaluated for various parameters, including hardness, friability, floating lag time, total floating duration, and in vitro drug release. The dissolution studies were conducted using 0.1 N HCl (pH 1.2) to simulate gastric conditions, ensuring that the floating and sustained release properties of the tablets met the intended design for prolonged levodopa delivery.

Table 1. Levodopa floating tablet composition. Ingredients are listed as milligrams per tablet.

Formulation	Drug	HPMC K 100M	Carbopol 934P	Citric acid	Sodium bicarbonate	PVP k-30	Magnesium Stearate	Talc
FF1	200	100	-	15	50	80	5	5
FF2	200	150	-	15	50	80	5	5
FF3	200	-	100	15	50	80	5	5
FF4	200	-	150	15	50	80	5	5
FF5	200	80	80	15	50	80	5	5

Evaluation of the Floating tablets

Weight Variation

A sample of tablets from each batch was weighed individually, and the average weight was calculated to check for consistency. The weight variation should fall within the pharmacopeial limits(Shaikh, Payghan, & Desouza, 2011).

Hardness and Friability

The hardness of the tablets was measured using a hardness tester to determine their ability to withstand mechanical stress during handling and transport. This was crucial to ensure the

tablets maintained their integrity.Friability testing was performed using a friabilator, where the tablets were subjected to rolling and dropping within a rotating drum to evaluate the loss of mass due to friction. Tablets with friability below 1% were considered acceptable(Shaikh et al., 2011).

Drug Content Assay

Twenty tablets were weighed and pulverised into a powder for each composition. It was put into a 100 ml volumetric flask along with 70 ml of distilled water and 100 mg of the drug's powder (Shaikh et al., 2011). The volume was adjusted to 100 millilitres using water. The solution was filtered, suitable dilutions were made, and absorbance at 624 nm was measured using an Elico UV spectrophotometer. This experiment was repeated three times.

Swelling Index

The Swelling Index of the floating tablets was assessed to determine their capacity to absorb fluids and swell, a crucial factor in enhancing gastric retention and regulating drug release. The swelling behavior is vital for maintaining tablet buoyancy and controlling the drug release profile. As the tablets swell, their volume increases, while their density decreases, allowing them to float in the gastric fluid for an extended period. To measure the swelling index, pre-weighed tablets were immersed in 0.1 N HCl (pH 1.2) at 37°C, which simulates gastric conditions. At 60 minutes time point, the swollen tablets were carefully removed, blotted dry to remove excess surface moisture, and weighed immediately(Saxena, Gaur, Singh, Singh, & Dashora, 2014; Younis, Tareq, & Kamal). The swelling index was calculated using the formula: Swelling index (%) = Wet Weight – Dry Weight / Dry Weigh X 100, The swelling index provided a measure of the tablet's ability to absorb fluid, and a higher index indicated greater fluid uptake, contributing to prolonged buoyancy and controlled drug release.This evaluation was significant as it confirmed the effectiveness of the hydrophilic polymers, such as Hydroxypropyl methylcellulose (HPMC) and Carbopol, used in the formulation. These polymers form a gel layer upon hydration, which governs the rate of drug release by diffusion. Additionally, the swelling index played a crucial role in ensuring the tablet remained afloat in gastric fluid for an extended duration, thereby enhancing gastric retention and allowing sustained release of the drug. By optimizing the swelling index, the formulation's structural integrity and drug release efficiency were maintained, ensuring improved therapeutic outcomes.

Floating or Buoyancy Test

The floating or buoyancy test was performed to evaluate the ability of the tablets to remain afloat in a simulated gastric environment. This test was carried out using a USP type II dissolution apparatus containing 900 millilitres of simulated gastric fluid (pH 1.2) maintained at a temperature of 37±0.5°C to mimic stomach conditions. The floating behavior of the tablets was closely monitored throughout the process.Two key parameters were measured during this test: the floating lag time (FLT), also referred to as the buoyancy lag time (BLT), and the total floating time (TFT). The FLT represented the time it took for the tablet to rise to the surface of the dissolution medium after being introduced, indicating how quickly the tablet became buoyant. A shorter lag time was desirable as it demonstrated the tablet's prompt ability to

float.The TFT, on the other hand, measured the total duration for which the tablet remained floating on the surface of the medium. Ideally, the tablet should stay buoyant for an extended period to ensure prolonged gastric retention, which is essential for sustained drug release. This floating ability is critical for the effectiveness of gastro-retentive drug delivery systems, as it allows the drug to be released gradually in the stomach, improving its absorption and therapeutic efficacy(Younis et al.).

In Vitro Drug Release Study

The in vitro drug release study was conducted using a USP-approved paddle dissolution test apparatus to assess the release profile of the floating tablets. The dissolution medium consisted of 900 milliliters of 0.1 N HCl with a pH of 1.2, which was continuously stirred at a speed of 100 revolutions per minute (rpm). The medium's temperature was maintained at 37±0.5°C to simulate gastric conditions. The release study spanned over 12 hours, during which samples were withdrawn at predetermined time intervals, and the same volume of fresh dissolution medium was replaced to maintain sink conditions.The collected samples were analyzed using a Shimadzu UV spectrophotometer at a wavelength of 624 nm to determine the concentration of levodopa released from the tablets. The dissolution data were then processed and plotted to study different release kinetics models. For first-order kinetics, the data were plotted as the log of cumulative percentage drug retention versus time. To analyze the release behavior using the Higuchi equation, the cumulative percentage drug release was plotted against the square root of time, which is useful for studying diffusion-controlled release systems. Additionally, the log of the fraction of drug released was plotted against the log of time for the Korsmeyer-Peppas model, which helps understand the release mechanism, particularly in systems exhibiting anomalous or non-Fickian diffusion. Lastly, cumulative percentage drug release was plotted against time to examine the release pattern under zero-order kinetics, which would indicate a constant release rate over time.These plots enabled the identification of the drug release mechanism, helping to confirm whether the floating tablets provided sustained and controlled drug delivery as intended.

In vivo Pharmacokinetic study

The in vivo pharmacokinetic study was conducted to evaluate the pharmacokinetic behaviour and gastric retention of levodopa from floating tablets in a rat model. Male Wistar rats, weighing between 200-250 g, were selected for this randomized, crossover study. The experiment was carried out over a 12-hour period with multiple dosing and sampling intervals. Before the start of the study, the rats were fasted overnight but were allowed free access to water. Each rat was administered a single oral dose of either the levodopa floating tablet or an immediate-release levodopa tablet.Blood samples were collected at predetermined time points (such as 0.5, 1, 2, 4, 6, 8, and 12 hours) post-dosing via tail vein puncture. These samples were then analysed for plasma concentrations of levodopa using a validated method. To assess the gastric retention of the floating tablets, the rats were sacrificed at the end of the study, and their stomach contents were visually examined.Pharmacokinetic parameters including the maximum plasma concentration (Cmax), the time to reach this concentration (Tmax), and the area under the plasma concentration-time curve (AUC) were calculated for both formulations.

The results were compared between the floating and immediate-release formulations. Statistical analyses, such as t-tests or ANOVA, were employed to determine any significant differences in the pharmacokinetic parameters between the two formulations, providing insights into the absorption and retention of levodopa from the floating tablets(Bębenek et al., 2024; Souza et al., 2024; Vaidya et al., 2024; Xiao et al., 2024).

Statistical analysis

In this study, statistical analysis was performed using GraphPad Prism software, Version 8. A One-Way ANOVA was applied to assess variability among groups, followed by Dunnett'spost hoc test for multiple comparisons. Data were presented as mean ± standard deviation (SD), with each variable averaged three times to improve accuracy. A p-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

Physicochemical Characteristics

The physical and chemical properties of the floating tablets, as presented in Table 2, reveal key differences among the batches. The hardness values ranged from 5.3 to 6.1 Kg/cm², with FF2 and FF5 showing slightly higher hardness (6.1 Kg/cm²), indicating greater mechanical strength, which could enhance their durability during handling. All batches exhibited friability values below 1%, demonstrating good mechanical integrity, with FF3 having the lowest friability (0.55%), indicating superior resistance to breakage, while FF5 had the highest friability (0.68%).Drug content was consistent across all batches, with values ranging from 97.2% to 98.9%, ensuring uniformity in the amount of levodopa present. FF5 showed the highest drug content at 98.9%, reflecting excellent uniformity. The buoyancy lag time, which measures how quickly the tablets become buoyant, varied between 2 minutes 16 seconds and 3 minutes 24 seconds. FF2 exhibited the shortest lag time (2 minutes 16 seconds), meaning it floated the fastest, whereas FF3 took the longest (3 minutes 24 seconds).The total floating time, a key factor for gastric retention and prolonged drug release, ranged from over 7 hours to over 13 hours. FF4 and FF5 displayed the longest floating durations (>13 hours and >12 hours, respectively), making them ideal for sustained drug release. FF2, despite its quick buoyancy, had the shortest floating duration at over 7 hours. Overall, FF4 and FF5 demonstrated the best combination of mechanical strength, drug content uniformity, and extended floating time, making them strong candidates for effective and prolonged drug delivery systems.

Table 2. Physical and Chemical Properties of the Floating Tablets (All values are mean ± standard deviation; n = 3)

Batch	Hardness (Kg/cm²)	Friability (%)	Drug Content (%)	Buoyancy Lag Time	Total Floating Time (hrs)
FF1	5.4±0.2	0.62±0.04	98.6±0.54	3min 11 sec	>8
FF2	6.1±0.1	0.57±0.05	97.2±0.63	2min 16sec	>7
FF3	5.4±0.1	0.55±0.03	97.5±0.52	3min 24 sec	>10
FF4	5.3±0.2	0.65±0.04	98.6±0.54	2min 57 sec	>13

FF5	6.1±0.3	0.68±0.05	98.9±0.81	3 min 05 sec	>12

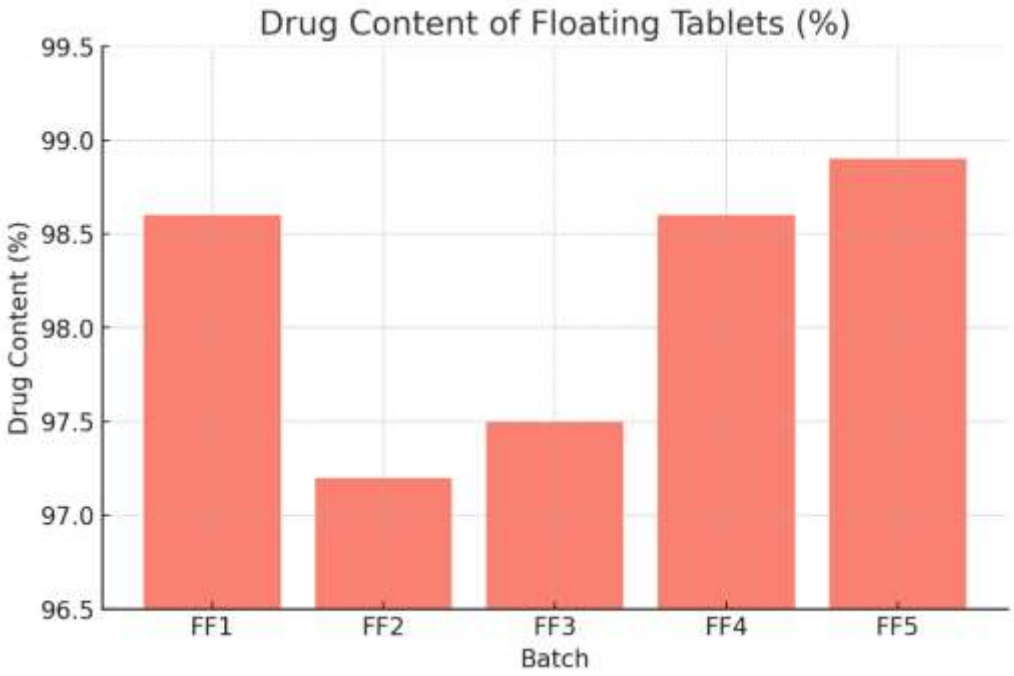

Figure 1. Depicting drugs content graphically.

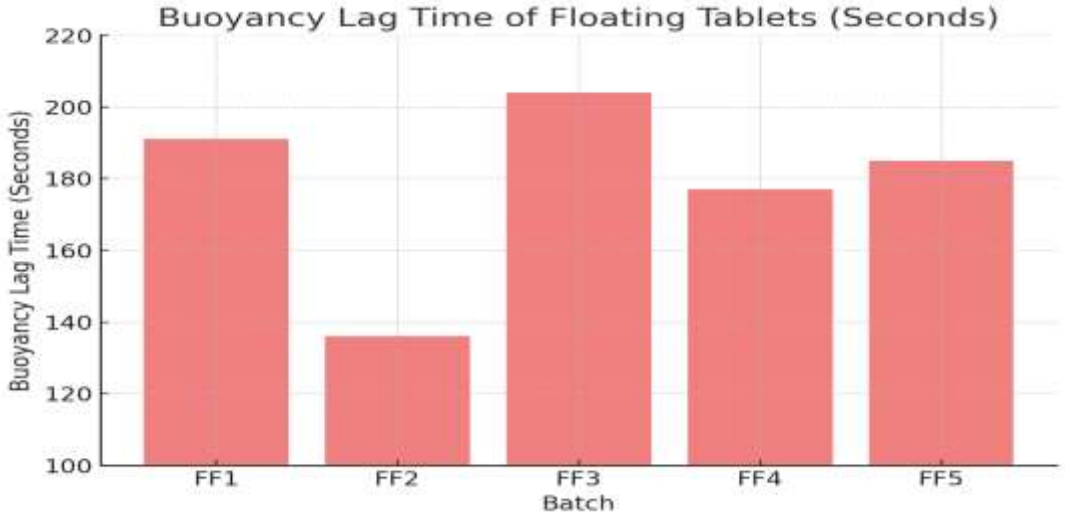

Figure 2. Depicting the buoyancy lag time graphically.

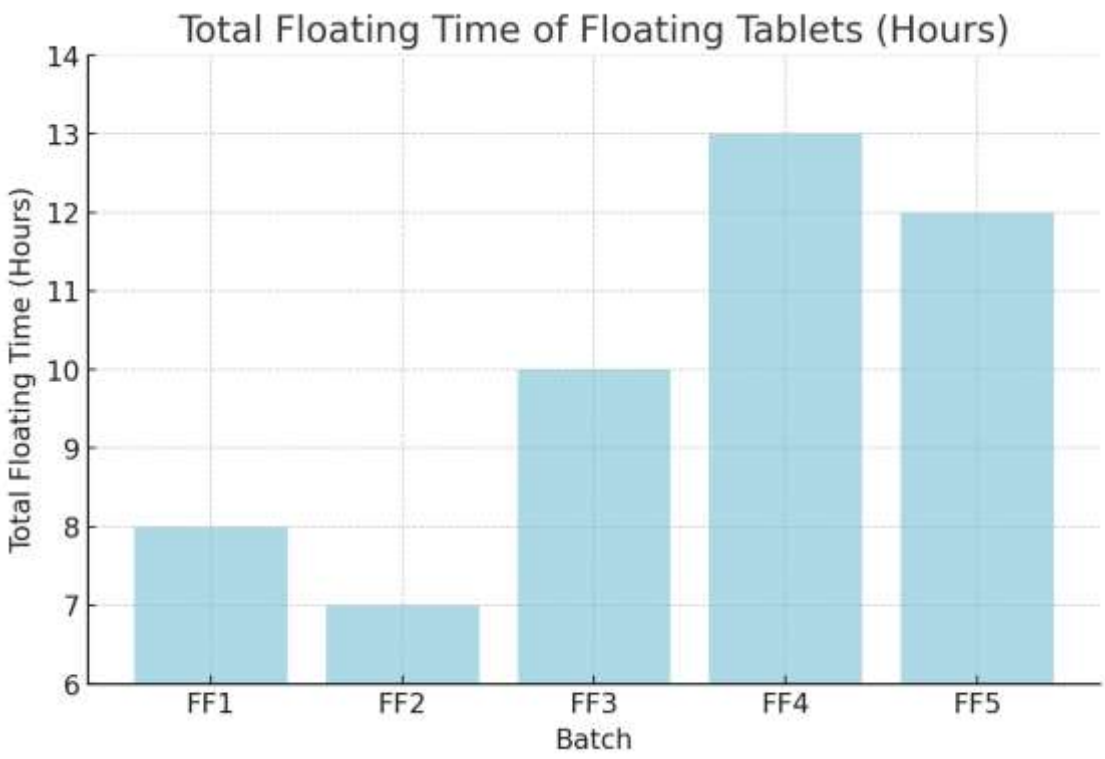

Figure 3. Depicting the total floating timegraphically.

Invitro drug release: Cumulative percentage release

The cumulative drug release data presented in Table 3 reveals distinct differences in release patterns across the various formulations. In the initial phase (1-2 hours), FF1 and the marketed formulation exhibited the fastest drug release, with 30.12% and 29.24%, respectively, at the 1-hour mark. FF5, on the other hand, had the slowest release, showing only 22.33% drug release at 1 hour. By the 2-hour point, FF1 maintained the highest release at 53.66%, while FF5 remained the slowest at 34.44%.At the midpoint (4-6 hours), FF1 continued to lead with a release of 72.28% at 4 hours and 85.98% at 6 hours, followed closely by the marketed formulation, which reached 64.18% and 79.48% at the same intervals. FF5 continued its slow, sustained release with 39.28% at 4 hours and 47.28% at 6 hours, indicating a more prolonged drug release profile compared to the other formulations.In the later phase (8-12 hours), FF1 and FF2 reached nearly complete drug release by 8 hours, with over 100% release, while FF3 and FF4 exhibited more controlled release, achieving 94.64% and 98.55% at 12 hours, respectively. FF5, which demonstrated the slowest release across all time points, reached only 82.44% drug release by 12 hours, suggesting a highly extended-release profile. The marketed formulation showed a moderately fast release, achieving 97.76% release by the 12-hour mark.Overall, FF1 and FF2 were characterized by fast drug release, while FF3, FF4, and especially FF5 exhibited more sustained release, with FF5 being the slowest. The marketed formulation served as a reference, showing a balanced release rate between the fast and

sustained-release formulations. This data highlights that FF5 may be the most suitable for extended-release purposes, while FF1 and FF2 could be used when faster drug release is desired.

Table 3. Drug release cumulative percentage (mean± S.D.; n = 3) across different formulations Time in hours

	Time (Hour)						
Formulation	**1**	**2**	**4**	**6**	**8**	**10**	**12**
FF1	30.12±0.641	53.66±0.941	72.28±0.511	85.98±0.481	101.84±0.581	102.78±1.011	-
FF2	26.34±0.411	45.77±0.771	67.28±0.651	81.58±0.691	100.72±0.751	102.74±0.951	-
FF3	27.11±0.711	34.47±0.281	47.98±0.671	59.48±0.901	77.69±0.711	86.65±0.881	94.64±0.911
FF4	24.49±0.801	28.14±0.701	53.68±0.781	69.18±1.011	81.26±0.681	87.21±0.830	98.55±0.921
FF5	22.33±0.681	34.44±0.671	39.28±0.911	47.28±0.911	70.55±0.771	74.10±0.681	82.44±0.621
Marketed	29.24±0.801	39.34±0.581	64.18±0.811	79.48±0.941	86.56±0.529	95.24±1.011	97.76±1.011

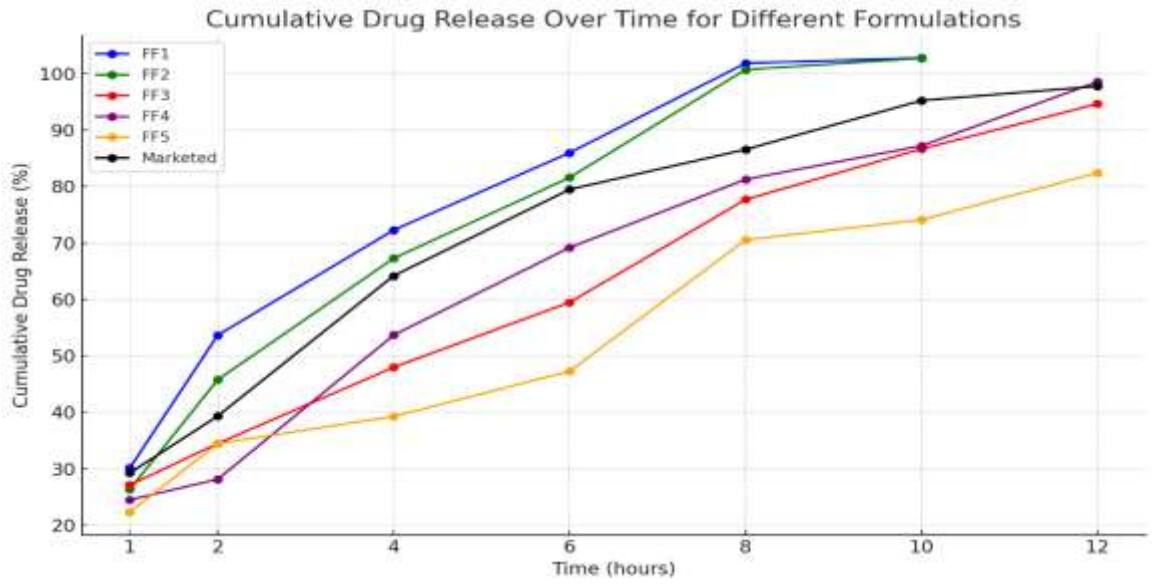

Figure 4. The graph above illustrates the cumulative drug release percentages over time for different formulations, including FF1 to FF5 and the marketed formulation

Mathematical Modelling: Pharmacokinetic

The disintegration kinetics and dissolving characteristics of the levodopa floating tablets, as shown in Table 4, provide insights into the behavior of the different formulations. The correlation coefficients (r) for the first-order kinetics are very close to 1 for all formulations, indicating that the drug release follows first-order kinetics, where the release rate is proportional to the drug concentration. FF2 (r = 0.9957) and FF1 (r = 0.994) show the strongest fit, with FF5 having the highest first-order rate constant (k = 0.1968), indicating a faster release.Similarly, the zero-order kinetics also shows strong correlation across all formulations, with FF2 exhibiting the highest correlation (r = 1.003), implying that it provides a constant drug release over time. FF5 again has the highest zero-order rate constant (k = 6.9398), suggesting the fastest release rate under this model as well.The Higuchi model, which describes diffusion-controlled release, also fits well for most formulations, with FF1 having the highest correlation (r = 1.006), indicating a strong diffusion-based release pattern. The rate constants (k) in the Higuchi model are similar across formulations, with FF5 showing a slightly faster diffusion-based release.In terms of the Peppas model, the exponent (n) values between 0.57 and 0.68 suggest that most formulations exhibit non-Fickian (anomalous) diffusion, where the drug release is governed by both diffusion and polymer relaxation. FF4 has the highest n value (0.6848), indicating a more complex release mechanism involving both diffusion and erosion, whereas FF5 has the lowest (0.5741), indicating a more diffusion-dominated release.Overall, FF5 demonstrates the fastest drug release across all kinetic models, while FF2 and FF1 provide more controlled and consistent release profiles. The Peppas model indicates that most formulations exhibit a combination of diffusion and erosion, with FF4 showing the most balanced mechanism. These insights help in understanding the varying release behaviours of the different levodopa floating tablet formulations.

Table 4. Levodopa floating tablet disintegration kinetics and dissolving characteristics

Formulation	First order eqn. (r)	First order eqn. (k)	Zero order eqn. (r)	Zero order eqn. (k)	Higuchi eqn. (r)	Higuchi eqn. (k)	Peppas eqn. (n)
FF1	0.994	0.1618	0.998	5.3548	1.006	1.0119	0.6738
FF2	0.9957	0.1708	1.003	6.745	1.001	1.0086	0.6738
FF3	0.9828	0.1788	0.9933	6.1691	0.9952	1.0109	0.6708
FF4	0.985	0.1898	0.9905	6.1048	1.0036	1.0102	0.6848
FF5	0.9907	0.1968	1.002	6.9398	0.9962	1.0081	0.5741

In vivo Pharmacokinetic study

The results showed that the immediate-release Levodopa tablets reached a higher maximum plasma concentration (Cmax) than the floating tablets, indicating a faster release of the drug into the bloodstream. Both formulations achieved their Cmax at the same time (Tmax), suggesting similar absorption rates once released. However, the floating tablets had a longer gastric retention time, as designed, to remain in the stomach for an extended period, allowing for more controlled and sustained drug release. The area under the curve (AUC), representing overall drug exposure, was lower for the floating tablets compared to the immediate-release tablets, likely due to their slower release profile. While the immediate-release tablets provided

higher Cmax and AUC values, the floating tablets offered prolonged gastric retention and a more controlled release, which may be beneficial for sustained release and reduced dosing frequency.

The comparison of pharmacokinetic parameters between the floating tablets (FF2) and immediate-release tablets reveals several important differences. The immediate-release tablets achieved a higher maximum plasma concentration (Cmax) of 233.83 ng/mL, indicating a faster and more intense drug release into the bloodstream compared to the floating tablets, which had a Cmax of 156.85 ng/mL. Despite this difference, both formulations reached their peak concentrations at nearly the same time, with Tmax values of 6.5 hours for the floating tablets and 6.6 hours for the immediate-release tablets, suggesting similar absorption rates once the drug is released.In terms of overall drug exposure, the area under the curve (AUC) was higher for the immediate-release tablets at 1198.90 ng·h/mL, compared to 944.67 ng·h/mL for the floating tablets. This reflects the rapid and higher drug absorption seen with immediate-release formulations. However, a key advantage of the floating tablets is their significantly longer gastric retention time, which extends up to 12 hours, compared to less than 1 hour for the immediate-release tablets. This prolonged retention allows for a more controlled and sustained release of the drug over time, contributing to a more gradual drug absorption profile.In summary, while the immediate-release tablets provide quicker and more concentrated drug delivery, the floating tablets offer a sustained release with longer gastric retention, making them suitable for therapies that require prolonged drug action and reduced dosing frequency.

Table 5.A comparative pharmacokinetic parameter for immediate-release tablets and floating tablets (FF2).

Parameter	**Floating Tablets (FF2)**	**Immediate-Release Tablets**
Cmax (ng/mL)	156.85	233.83
Tmax (hours)	6.5	6.6
AUC (ng·h/mL)	944.67	1198.90
Gastric Retention Time	12 hours	<1 hour

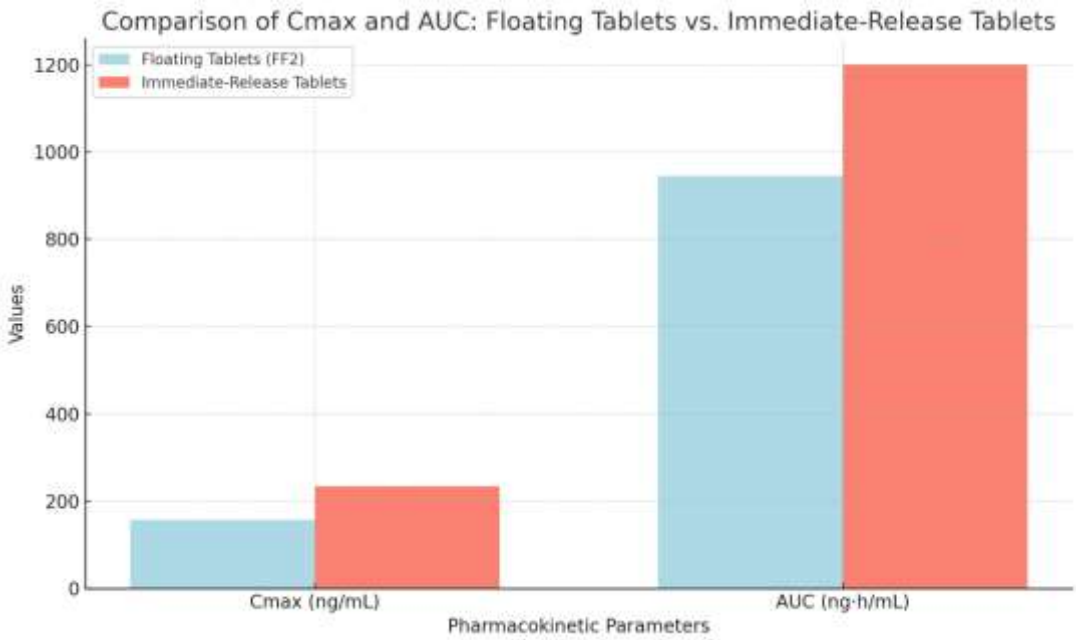

Figure 5. Cmax and AUCfor floating tablets (FF2) and immediate-release tablets.

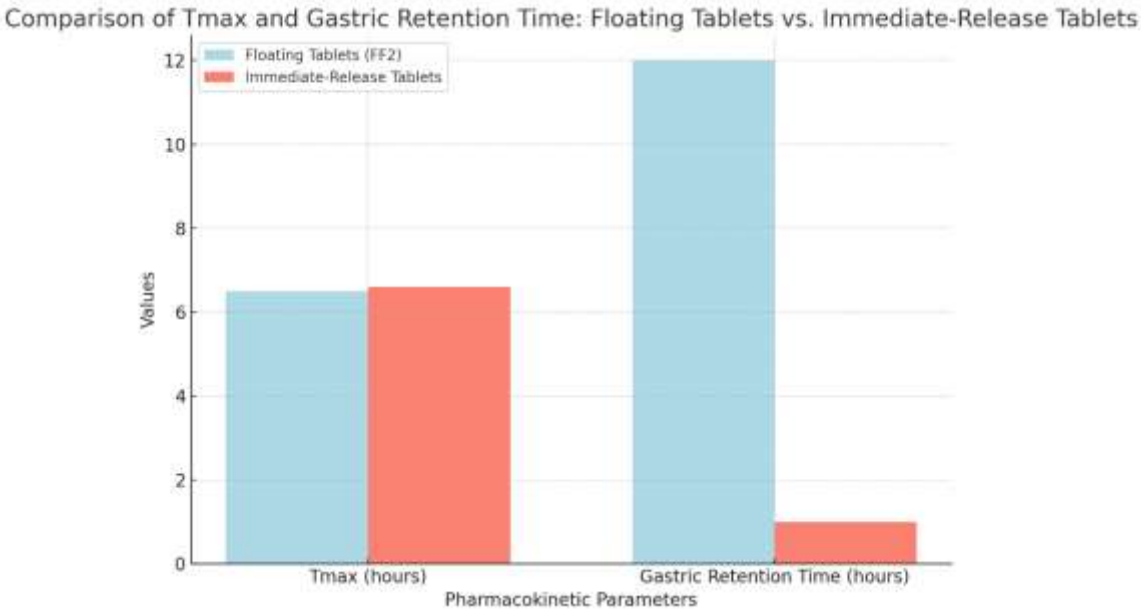

Figure 6. Tmax and gastric retention time for floating tablets (FF2) and immediate-release tablets.

CONCLUSIONS

The comprehensive evaluation of levodopa floating and immediate-release tablets demonstrated distinct benefits and trade-offs between rapid and sustained drug delivery. Immediate-release tablets provided a high Cmax and rapid drug absorption, which is beneficial for immediate therapeutic needs but exhibited a short gastric retention time. Floating tablets, particularly formulation FF2 (Best), showcased superior performance with prolonged gastric retention (12 hours) and controlled drug release, making them ideal for sustained therapeutic action. FF2 achieved over 100% drug release by the 8-hour mark, demonstrating its ability to maintain consistent drug levels for extended periods. Kinetic analysis confirmed that FF2 followed a balanced release pattern, driven by first-order, zero-order, and Higuchi models, ensuring predictable and controlled drug release. This formulation represents a promising solution for chronic conditions like Parkinson's disease, where sustained drug delivery is crucial for maintaining therapeutic efficacy. Ultimately, while immediate-release formulations are useful for rapid symptom control, floating tablets like FF2 offer a more controlled, prolonged release, reducing the need for frequent dosing and enhancing patient compliance. This makes them a preferable choice for long-term treatment strategies.

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