Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v29i03.6556

PREPARATION AND IN VITRO EVALUATION OF IMMEDIATE-RELEASE TABLETS OF EMTRICITABINE

Shaik Neha Samreen[1*], B Sandhya Rani[2], K. Lakshmikanth[3], M. Priyanka[4], MD Iftekhar Ahmed Khan[5], MISBA[6], Dr. Md Sultan Ali Basha[7]

[1*,3,4]Research scholar Department of Pharmaceutics, Safa College of Pharmacy, Kurnool
[5]Associate Professor, Department of Pharmaceutics, Safa College of Pharmacy, Kurnool
[2,6] Assistant Professor, Safa College of Pharmacy, Kurnool
[7]Professor and Principal, Safa College of Pharmacy, Kurnool

***Corresponding Author**: Shaik Neha Samreen
*Email id: 16samreenneha@gmail.com

Abstract
Immediate-release tablets disintegrate rapidly in the gastrointestinal tract, ensuring swift drug release and absorption. Recently, these tablets have gained popularity and acceptance as a drug delivery system due to their ease of administration and enhanced patient compliance. This study aims to formulate and evaluate various direct compression immediate-release tablets of Emtricitabine using different superdisintegrants (Sodium starch glycolate, Polyplasdone XL10, and Ac-Di-Sol). Fourier-transform infrared spectroscopy (FTIR) was employed to investigate the interactions between the drug and excipients. Emtricitabine granules and tablets were subjected to various pre- and post-compression assessments, including angle of repose, compressibility index, Hausner's ratio, tablet hardness, friability, and in vitro disintegration and dissolution tests. The results were satisfactory across all parameters. Among the formulations, the F3 procedure demonstrated the highest in vitro dissolution profile, suggesting that it is the most effective formulation for immediate drug release.

Keywords: Emtricitabine, Sodium starch glycolate, Polyplasdone XL10, Ac-Di-Sol, Immediate-release tablets.

Introduction
Immediate release tablets (IRTs) are a widely utilized dosage form within the pharmaceutical industry, favored for their simplicity, convenience, and capability to ensure rapid drug release and absorption in the gastrointestinal tract. This dosage form is particularly advantageous for medications requiring quick onset of therapeutic action. Emtricitabine, a nucleoside reverse transcriptase inhibitor, plays a vital role in antiretroviral therapy, often in combination with other antiretroviral agents for the effective management of HIV-1 infection. Enhancing the bioavailability and therapeutic efficacy of emtricitabine through an optimized immediate release formulation can significantly improve patient outcomes.

The formulation of immediate release tablets necessitates the careful selection of excipients, with superdisintegrants being critical components. Superdisintegrants facilitate rapid tablet disintegration upon contact with gastrointestinal fluids, promoting swift drug dissolution and absorption. Extensive research has demonstrated the effectiveness of various superdisintegrants in enhancing the

disintegration and dissolution profiles of IRTs. For instance, Tanoy Saha et al. (2021) and Dr. Y. Krishna Reddy et al. (2020) highlighted the utility of croscarmellose sodium (CCS) and sodium starch glycolate (SSG) in achieving optimal disintegration times and dissolution rates. These studies underscore the importance of optimizing both the concentration and combination of superdisintegrants to achieve the desired drug release characteristics.

Furthermore, different formulation techniques such as wet granulation and direct compression have been explored to develop immediate release tablets. S. Murugesan et al. (2019) and Rajesh Bhatt et al. (2019) emphasized the significance of both pre-formulation and post-compression parameters—including hardness, friability, and in vitro dissolution—in ensuring the quality and performance of the final tablet product. These parameters are critical in maintaining the integrity and efficacy of the tablet during manufacturing, storage, and administration.

Compatibility studies between the drug and excipients are crucial to ensure the stability and efficacy of the final formulation. Techniques such as Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) are commonly employed to identify potential interactions between the drug and excipients. Research by Kanhu Charan Panda et al. (2019) and Snehal B. Kulkarni et al. (2019) demonstrated the absence of significant interactions between the active pharmaceutical ingredient and the excipients, confirming the stability of the formulations.

Given the extensive research and advancements in the field of immediate release tablet formulations, this study aims to develop and evaluate immediate release tablets of emtricitabine using direct compression techniques. By leveraging the insights from previous studies and employing a comprehensive formulation approach, this research seeks to enhance the therapeutic efficacy and patient compliance of emtricitabine through an optimized immediate release tablet formulation. The use of different superdisintegrants, including sodium starch glycolate, Polyplasdone XL10, and Ac-Di-Sol, will be explored to identify the most effective formulation for rapid drug release and absorption.

Materials & Methods

Buffer Preparation

Preparation of 0.2M Potassium Dihydrogen Orthophosphate Solution:

27.218 g of monobasic potassium dihydrogen orthophosphate was accurately weighed and dissolved in 1000 mL of distilled water. The solution was thoroughly mixed.

Preparation of 0.2M Sodium Hydroxide Solution:

8 g of sodium hydroxide pellets were accurately weighed and dissolved in 1000 mL of distilled water, followed by thorough mixing.

Preparation of pH 6.8 Phosphate Buffer:

250 mL of 0.2M potassium dihydrogen orthophosphate and 112.5 mL of 0.2M sodium hydroxide were accurately measured and transferred into a 1000 mL volumetric flask. The volume was adjusted to 1000 mL with distilled water, and the solution was mixed thoroughly.

Preformulation Studies

Preformulation involves applying biopharmaceutical principles to characterize the physicochemical parameters of the drug substance, aiming to design an optimal drug delivery system.

Analytical Method Development for Emtricitabine

Determination of Absorption Maxima:

A spectrum of the working standard solution was obtained by scanning from 200-400 nm against a reagent blank to determine the absorption maxima (λ_max). The λ_max was found to be 280 nm, and all subsequent investigations were conducted at this wavelength.

Preparation of Standard Graph in pH 6.8 Phosphate Buffer:

100 mg of Emtricitabine was dissolved in 100 mL of pH 6.8 phosphate buffer to obtain a 1 mg/mL

(1000 µg/mL) solution. A 1 mL aliquot of this stock solution was further diluted to 100 mL with pH 6.8 phosphate buffer to achieve a 0.01 mg/mL (10 µg/mL) concentration. Aliquots of 0.5 mL, 1 mL, 1.5 mL, 2 mL, and 2.5 mL were taken from this stock solution and diluted to 10 mL with pH 6.8 phosphate buffer to produce concentrations of 5, 10, 15, 20, and 25 µg/mL, respectively. The absorbance of each concentration was measured at 280 nm.

Formulation Development

The drug and various concentrations of superdisintegrants along with other required ingredients were accurately weighed and passed through a 40-mesh screen to obtain uniform particle sizes. The mixture was blended in a glass mortar for 15 minutes. The blend was then lubricated with magnesium stearate, and talc was added as a glidant, followed by further mixing for 5 minutes. The final blend was directly compressed into tablets using a rotary tablet compression machine, maintaining a constant compression force for all formulations.

INGREDIENTS (MG)	FORMULATIONS								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Emtricitabine	200	200	200	200	200	200	200	200	200
Sodium starch glycolate	50	100	150	-	-	-	-	-	-
Polyplasdone XL10	-	-	-	50	100	150	-	-	-
Ac- Di- Sol	-	-	-	-	-	-	50	100	150
Talc	5	5	5	5	5	5	5	5	5
Mg.stearate	4	4	4	4	4	4	4	4	4
Mannitol	15	15	15	15	15	15	15	15	15
Lactose	226	176	126	226	176	126	226	176	126
Total weight (mg)	500	500	500	500	500	500	500	500	500

Total weight of tablets = 500mg

Evaluation Parameters

Pre-Compression Parameters:

Angle of Repose:

The angle of repose of the API powder was determined using the funnel method. The accurately weighed powder blend was allowed to flow through a funnel until the tip of the funnel just touched the apex of the powder cone. The diameter of the powder cone was measured, and the angle of repose was calculated using the equation:

$$\tan \theta = h/r \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where h is the height and r is the radius of the powder cone.

Bulk Density:

25 g of the powder sample, screened through sieve No. 18, was filled in a 100 mL graduated cylinder. The bulk density was calculated using the formula:

Bulk density = M/V_0 ..... (2)

M= Powder mass

V_0= apparent unstirred volume

Tapped Density:
25 g of the powder sample, screened through sieve No. 18, was filled in a 100 mL graduated cylinder. The mechanical tapping of the cylinder was carried out at a nominal rate for 500 taps initially, and the tapped volume \(V_0 \) was noted. Further tapping was done for an additional 750 taps, and the final tapped volume \(V_f \) was noted. If the difference between two tapping volumes was less than 2%, \(V_f \) was considered the final tapped volume. The tapped density was calculated using the formula:

Tapped density=M/V_f .....(3)

M= weight of sample power taken

V_f= Tapped volume

Compressibility Index:
The Compressibility Index of the powder blend was determined using Carr's Compressibility Index:

Carr's Index (%)=[(TD-BD)/TD]x100 .....(4)

where TD is the tapped density and BD is the bulk density.
Hausner's Ratio:
Hausner's Ratio was calculated using the equation:

$H=\rho T / \rho B$ .....(5)

Where ρT= tapped density, ρB = bulk density

Post-Compression Parameters
Thickness:
The thickness of tablets was determined using a digital micrometer. Ten individual tablets from each batch were measured, and the results were averaged.

Weight Variation:
Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation for three batches were calculated. More than the allowed percentage deviation and none deviated by more than twice the allowed percentage passed the test if no more than two tablets deviated from the average weight.

Friability:
Friability was determined using a Roche-type friabilator. Six tablets were accurately weighed and placed in the friabilator, which was rotated at 25 rpm for 4 minutes. Friability was calculated using the equation:

$$\text{Friability} = ([\, w_0 - w] / w_0) \times 100$$

where W_0 is the initial weight and W is the final weight of the tablets.

Assay:
The content of the drug was determined using five randomly selected tablets from each formulation. The tablets were powdered, dissolved in pH 6.8 phosphate buffer by sonication for 30 minutes, and filtered. The drug content was analyzed spectrophotometrically at 280 nm. Each measurement was carried out in triplicate, and the average drug content was calculated.

Disintegration Test:
Six tablets were randomly selected from each batch and placed in the USP disintegration apparatus. The apparatus was operated for 10 minutes, and the tablets were observed to ensure complete disintegration.

Dissolution Test of Emtricitabine Tablets:
Drug release from Emtricitabine tablets was determined using the USP type II (paddle) dissolution apparatus. The dissolution medium was 500 mL of pH 6.8 phosphate buffer, maintained at 37°C, with a paddle speed of 50 rpm. 5 mL aliquots of the dissolution medium were withdrawn at suitable time intervals (5, 10, 15, 20, 25, and 30 minutes) and replaced with fresh medium. The samples were filtered, appropriately diluted, and analyzed using a UV spectrophotometer at 280 nm. The concentration was calculated using the standard calibration curve.

Drug-Excipients Compatibility Studies
Drug-excipients compatibility studies were conducted by mixing the drug with various excipients in different proportions (1:1 ratio). The mixtures were placed in vials, sealed with rubber stoppers, and stored properly to observe any potential interactions (Bokshi & Malakar, 2012; Patel, Naruka, Chauhan, & Modi, 2013; Panda, Reddy, Reddy, & Panda, 2015; Satyavathi, Annapurna, Gayathri, Bhojaraju, Kanthal, & Veerraju, 2014a, 2014b; Remya, Saraswathi, Sangeetha, Damodharan, & Kavitha, 2016; Karim, Bhuiyan, & Rana, 2015; Parikh, Patel, Patel, Dave, Gothi, & Patel, 2010)..

RESULTS

Determination of λ_max
The absorption maxima (λ_max) of the prepared Emtricitabine stock solution were determined by scanning the solution between 200-400 nm. The λ_max was found to be 280 nm.

Calibration Curve of Emtricitabine
A standard curve for Emtricitabine was generated using pH 6.8 phosphate buffer as the medium. The calibration curve demonstrated excellent linearity with an R^2 value of 0.999, indicating a strong correlation between concentration and absorbance at 280 nm.

Table 1: Standard Graph Values of Emtricitabine at 280 nm in pH 6.8 Phosphate Buffer

Concentration (µg/ml)	Absorbance
0	0
5	0.101
10	0.193
15	0.281
20	0.369
25	0.455

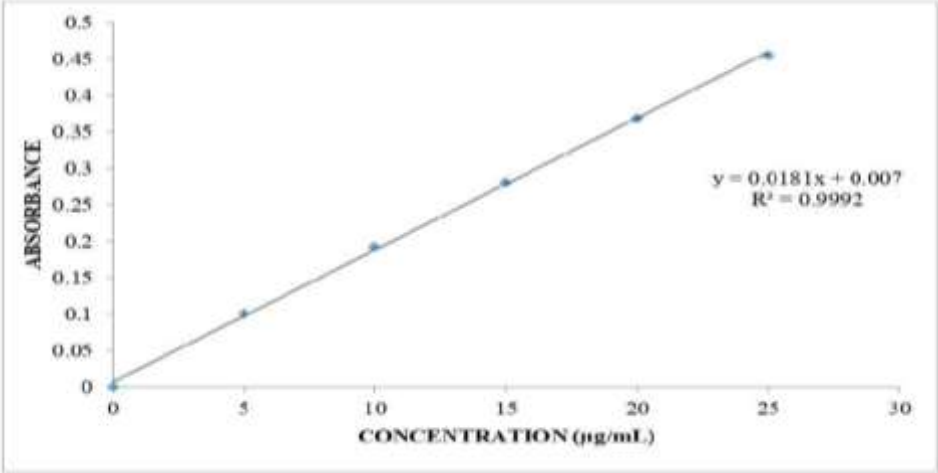

Fig 1: Standard curve of Emtricitabine

Characterization of Precompression Blend

The precompression blend of Emtricitabine was evaluated for various physical properties, including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. The angle of repose was less than 29.9°, and Carr's index values were below 27.75 for all batches, indicating good to fair flowability and compressibility. Hausner's ratio was less than 1.43 for all batches, suggesting good flow properties.

Table 2: Physical Properties of Precompression Blend

Formulation code	Angle of repose (Θ)	Bulk density (gm/cm^3)	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	25.8^0	0.532	0.657	19.45	1.17
F2	27.5^0	0.476	0.594	25.22	1.24
F3	29.5^0	0.456	0.633	27.51	1.38
F4	29.7^0	0.488	0.685	24.84	1.40
F5	29.9^0	0.461	0.661	27.75	1.43
F6	26.8^0	0.588	0.720	22.24	1.22
F7	27.3^0	0.567	0.705	18.33	1.24
F8	28.4^0	0.543	0.711	17.13	1.30
F9	29.6^0	0.477	0.660	23.52	1.38

All the values represent n=3

Evaluation of Tablets

Physical Evaluation of Emtricitabine Immediate Release Tablets

The physical attributes of Emtricitabine immediate release tablets, including weight variation, hardness, thickness, friability, and drug content, were assessed. All tablet batches complied with official weight variation requirements. Tablet hardness ranged from 3.15 to 3.95 kg/cm², and friability values were less than 0.69%, indicating the tablets were compact and durable. The thickness of the tablets varied from 5.11 to 5.98 mm. Drug content was uniformly distributed, with values ranging from 96.12% to 99.35% of Emtricitabine, demonstrating consistent quality across all batches.

Table .3: Evaluation of Emtricitabine Immediate Release Tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)	*In Vitro* Disintegration time (seconds)
F1	499.92	6.96	3.68	0.23	96.34	61
F2	500.01	6.62	3.95	0.41	98.15	53
F3	499.34	6.85	3.27	0.40	99.56	35
F4	500.12	6.71	3.15	0.51	99.34	69
F5	498.67	6.11	3.78	0.49	98.25	57
F6	497.32	6.98	3.89	0.32	97.69	50
F7	500.01	6.76	3.52	0.29	99.41	53
F8	500.25	6.69	3.17	0.56	98.30	49
F9	496.81	6.57	3.28	0.43	97.62	41

In Vitro Disintegration

The in vitro disintegration times of the tablets were recorded, and the results are presented in Figure All formulations demonstrated satisfactory disintegration times.

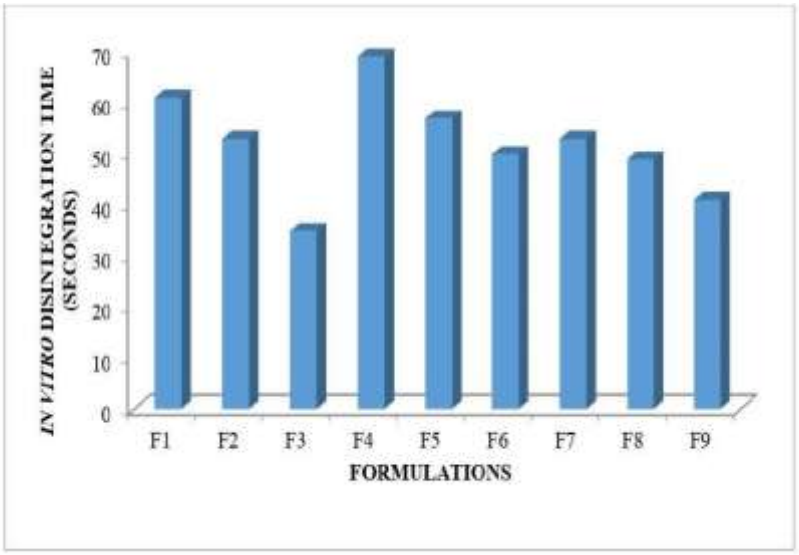

Figure 2: In Vitro Disintegration Time Graph

In Vitro Dissolution

The drug release rate from the tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 500 mL of pH 6.8 phosphate buffer, maintained at 37 ± 0.5 °C with a paddle speed of 50 rpm. Samples of 5 mL were collected at various time intervals up to 30 minutes and analyzed using a UV spectrophotometer at 280 nm.

Time (Minutes)	*IN VITRO DRUG RELEASE*								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	55.75	60.20	63.96	52.42	58.71	61.58	57.99	64.14	67.73
10	62.18	73.71	77.14	60.95	62.96	65.74	60.57	72.61	79.92
15	70.62	76.62	80.27	67.15	70.35	74.93	65.52	76.39	82.70
20	86.10	89.92	90.58	76.50	78.82	86.46	71.78	82.27	87.21
25	87.73	90.80	92.16	81.89	85.96	90.33	76.44	87.98	91.64
30	93.14	95.42	99.10	86.32	91.28	94.92	89.12	92.71	95.83

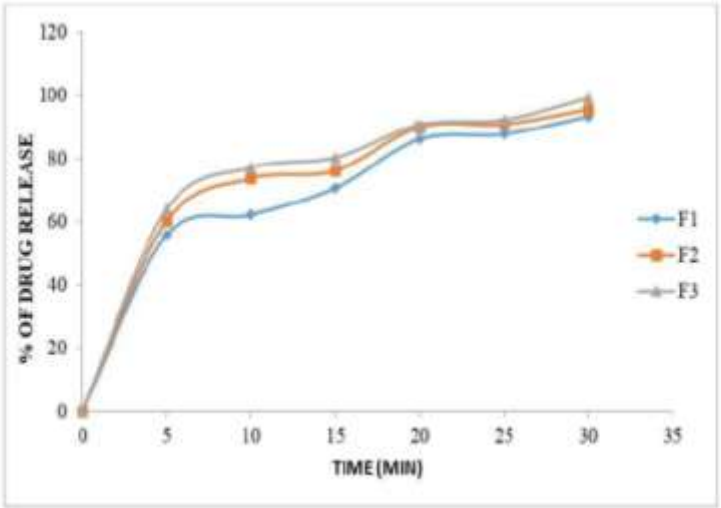

Fig 3: In vitro data for formulation F1- F3

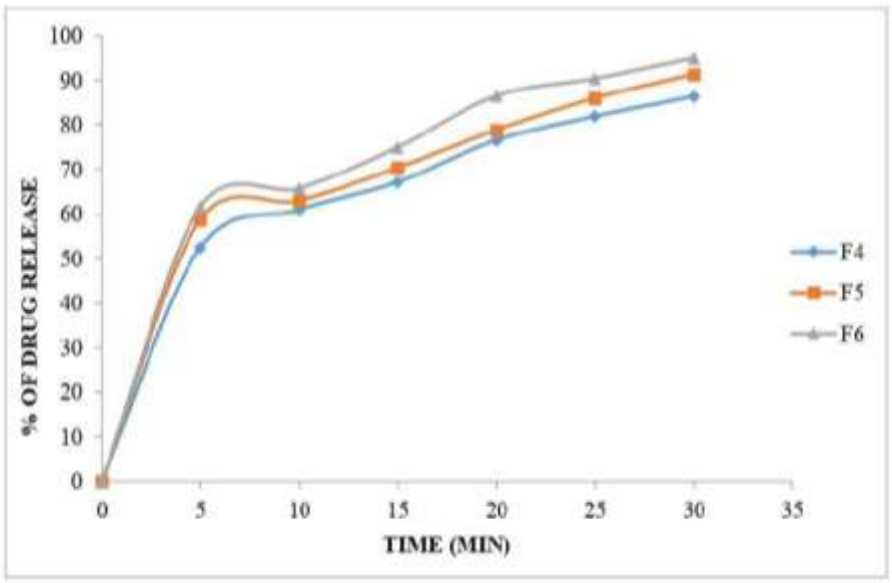

Fig 4: In vitro data for formulation F4- F6

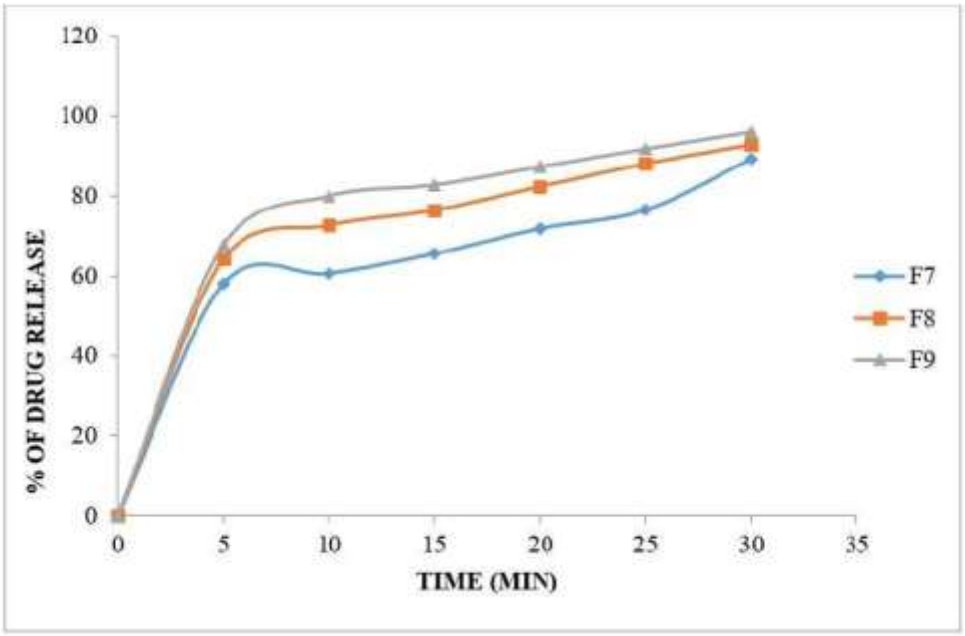

Fig.5: In vitro dissolution data for formulations F7-F9

Drug-Excipient compatibility studies by FTIR studies:

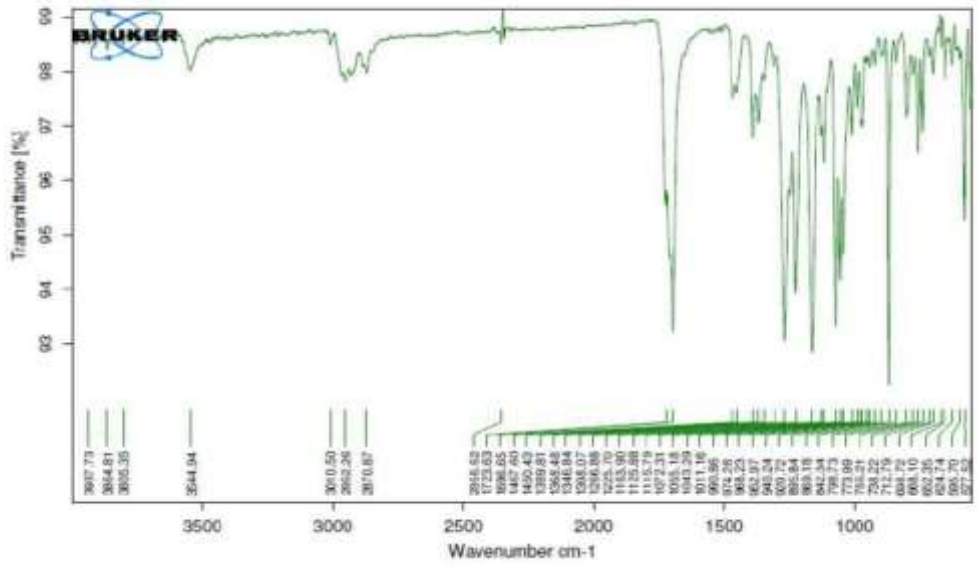

Fig 6: FTIR spectra of pure drug

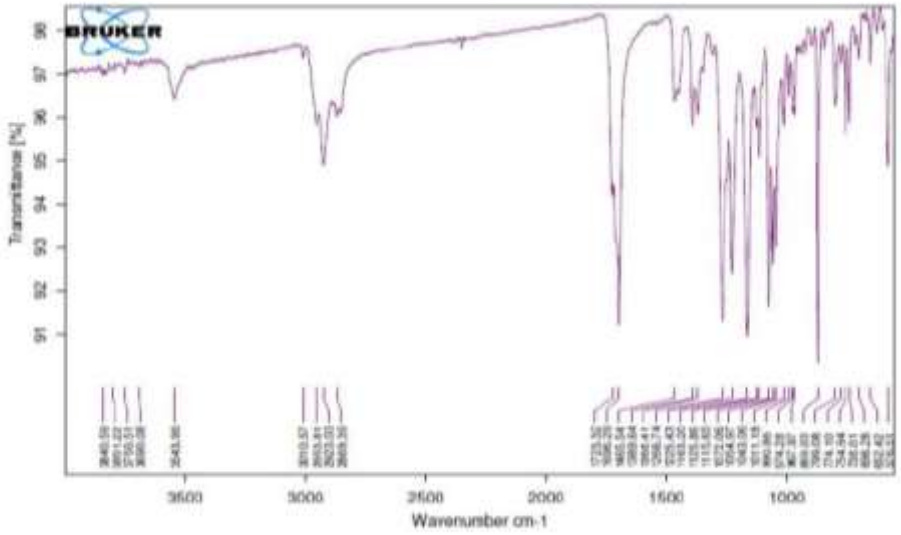

Fig 7: FTIR spectra of optimized drug formulation

The results showed that the formulation prepared with Sodium Starch Glycolate (F3) exhibited the highest drug release, achieving 99.10% release within 30 minutes at a concentration of 150 mg. Formulations with Polyplasdone XL10 demonstrated a good release rate, with F6 showing 94.92% release at 150 mg concentration. However, an increase in the concentration of Polyplasdone XL10 led to a retardation of drug release. Formulations containing Ac-Di-Sol showed a maximum release of 95.83% (F9) at 30 minutes with a blend concentration of 150 mg. Among all formulations, F3 was identified as the optimized formulation due to its maximum drug release rate of 99.10% within 30 minutes. Emtricitabine mixed with various excipients in different proportions showed no color change at the end of two months, indicating no drug-excipient interactions.

The determination of the absorption maxima (λ_max) for Emtricitabine at 280 nm is a fundamental step for its spectrophotometric analysis, ensuring accurate identification and quantification of the drug. By scanning the solution between 200-400 nm, the precise λ_max was established, aligning with known values for Emtricitabine and thereby validating the method for subsequent analytical procedures.

Discussion

The calibration curve generated using pH 6.8 phosphate buffer demonstrated excellent linearity, with an R^2 value of 0.999. This strong correlation between concentration and absorbance indicates that the UV spectrophotometric method employed is highly reliable for quantifying Emtricitabine. The high linearity assures precision and accuracy in measurements, which is crucial for consistent drug formulation and quality control.

Characterizing the precompression blend of Emtricitabine involved assessing its physical properties such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. The angle of repose, with values less than 29.9°, suggested good flowability of the powder blend, which is essential for uniform die filling during tablet compression. Carr's index values below 27.75 and Hausner's ratio less than 1.43 indicated good to fair flow properties and compressibility. These findings suggest that the precompression blend is suitable for direct compression, a method known for its efficiency and simplicity in tablet manufacturing.

The physical evaluation of the Emtricitabine immediate release tablets included tests for weight variation, hardness, thickness, friability, and drug content. All tablet batches complied with official weight variation requirements, ensuring dose uniformity and consistent therapeutic effects. The hardness of the tablets ranged from 3.15 to 3.95 kg/cm², and friability values were less than 0.69%, indicating that the tablets were robust and capable of withstanding mechanical stress during handling and transportation. The thickness of the tablets varied from 5.11 to 5.98 mm, maintaining uniformity in tablet size across different batches. Drug content uniformity, with values ranging from 96.12% to 99.35%, confirmed even distribution of Emtricitabine within the tablets, essential for predictable and effective treatment outcomes.

In vitro disintegration tests revealed that all formulations had satisfactory disintegration times, crucial for immediate release tablets. Rapid disintegration is necessary for quick drug release and absorption, ensuring prompt therapeutic action. The dissolution profiles of the tablets were studied using the USP type II dissolution test apparatus, with a dissolution medium of 500 mL of pH 6.8 phosphate buffer maintained at 37 ± 0.5 °C and a paddle speed of 50 rpm. Samples were collected at various time intervals up to 30 minutes and analyzed using a UV spectrophotometer at 280 nm.

The dissolution results showed that formulation F3, containing Sodium Starch Glycolate, exhibited the highest drug release rate, achieving 99.10% release within 30 minutes at a 150 mg concentration. This indicates that Sodium Starch Glycolate is an effective superdisintegrant for Emtricitabine tablets, promoting rapid disintegration and drug release. Formulations with Polyplasdone XL10 demonstrated a good release rate, with F6 showing 94.92% release at 150 mg concentration. However, higher concentrations of Polyplasdone XL10 led to a retardation of drug release, likely due to the formation of a gel-like barrier that hinders dissolution. Formulations containing Ac-Di-Sol achieved a maximum release of 95.83% (F9) within 30 minutes, indicating its efficacy as a superdisintegrant, although not as effective as Sodium Starch Glycolate in this formulation. Stability studies indicated no significant color changes in Emtricitabine mixed with various excipients over two months, suggesting the absence of drug-excipient interactions. This is crucial for maintaining the stability and efficacy of the drug during storage and shelf life, ensuring that the tablets remain effective until their expiration date.

Conclusion

In conclusion, the study successfully optimized the formulation of Emtricitabine immediate release tablets. The precompression blend demonstrated excellent flowability and compressibility, and the tablets met all physical and chemical evaluation criteria. Formulation F3, containing Sodium Starch Glycolate, was identified as the optimal formulation, achieving the highest drug release rate of 99.10% within 30 minutes. No significant drug-excipient interactions were observed, ensuring the stability of the formulation. These findings provide a robust basis for the development of effective Emtricitabine immediate release tablets, ensuring rapid therapeutic action and consistent quality. The optimized formulation and method can be used as a reference for future development and production of Emtricitabine tablets, contributing to the effective treatment of HIV infection.

Conflict of interest

All authors declare no conflicts of interest.

References

1. Saha, T., Alam, M. M., Lira, D. N., & Rouf, A. S. S. Formulation and Evaluation of Effects of Superdisintegrants on Immediate Release Tablet of Linagliptin, a DPP-4 Inhibitor.
2. Reddy, Y. K., & Kalpana, D. (2020). Formulation Development and Evaluation of Immediate Release Tablet Dosage form of Sorafenib Tosylate. *Asian Journal of Pharmacy and Technology*, *10*(1), 38-42.
3. Murugesan, S., Rasmi, P. S., & Ramasubramaniyan, P. (2014). Formulation development and evaluation of metoprolol succinate sustained release and hydrochlorothiazide immediate release bilayer tablet. *Journal of Chemical and Pharmaceutical Research*, *6*(12), 213-221.
4. Bhatt, R., Sharma, A., Kumar, P., Upadhyay, S., & Upadhyay, P. (2019). Formulation and evaluation of immediate release tablet of zopiclone using wet granulation method. *Journal of Drug Delivery and Therapeutics*, *9*(2-s), 132-137.
5. Panda, K. C., Panda, N., Sahoo, C. K., Bhaskar, J., & Ramana, D. V. (2019). Formulation and Evaluation of Immediate release tablets of Topiramate using Sodium starch glycolate. *Research Journal of Pharmacy and Technology*, *12*(6), 3024-3028.
6. Kulkarni, S. B., Bari, M. M., Barhate, S. D., & Tripathi, A. (2019). Formulation and Evaluation of Immediate Release Tablet of Efavirenz by Micellar Solubilization Technique. *Asian Journal of Pharmaceutical Research*, *9*(1), 12-18.
7. Bokshi, B., & Malakar, A. (2012). Formulation and evaluation of allylestrenol immediate release tablets. *International journal of pharmaceutical sciences and research*, *3*(6), 1679.
8. Patel, N., Naruka, P. S., Chauhan, C. S., & Modi, J. (2013). Formulation development and evaluation of immediate release tablet of topiramateanti epileptic drug. *J Pharm Sci Bio-sci Res*, *3*, 58-65.
9. Panda, N., Reddy, A. V., Reddy, G. S., & Panda, K. C. (2015). Formulation design and in vitro evaluation of zolmitriptan immediate release tablets using primojel and AC-Di-Sol. *Journal of Pharmaceutical Sciences and Research*, *7*(8), 545.
10. Satyavathi, K., Annapurna, K. V. S. S., Gayathri, P., Bhojaraju, P., Kanthal, L. K., & Veerraju, T. (2014). Formulation and evaluation of immediate release tablets of eprosartan mesylate. *Int. J. Pharm. Sci. Rev. Res*, *25*(1), 36-40.
11. Satyavathi, K., Annapurna, K. V. S. S., Gayathri, P., Bhojaraju, P., Kanthal, L. K., & Veerraju, T. (2014). Formulation and evaluation of immediate release tablets of eprosartan mesylate. *Int. J. Pharm. Sci. Rev. Res*, *25*(1), 36-40.
12. Remya, P. N., Saraswathi, T. S., Sangeetha, S., Damodharan, N., & Kavitha, R. (2016). Formulation and evaluation of immediate release tablets of acyclovir. *Journal of Pharmaceutical Sciences and Research*, *8*(11), 1258.00000000000000000
13. Karim, S., Bhuiyan, M. A., & Rana, M. S. (2015). Formulation and In vitro Evaluation of Glimepiride Sustained Release Tablets: Comparison with Immediate Release Tablets. *Bangladesh Pharmaceutical Journal*, *18*(2), 157-162.
14. Parikh, B. N., D. M. Patel, C. N. Patel, J. B. Dave, G. D. Gothi, and T. D. Patel. "Formulation optimization and evaluation of immediate release tablet of telmisartan." *J. Glob. Pharma Technol* 2 (2010): 79-84.