RESEARCH ARTICLE

Process Validation of Dispersible Tablet Comprising of Tenofovir, Bictegravir and Emtricitabine

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ABSTRACT

In the formulation of Orodispersible tablets, process parameters were checked to ensure consistent tablet quality, including factors like uniformity in size, shape, and coating. Monitoring these parameters helps optimize disintegration**,** dissolution**,** and hardness, ensuring the tablet meets its intended release profile and complies with regulatory standards. In this research, process validation for drying time, prelubrication time, lubrication time, hardness and % weight gain parameters were checked. Drying time was set as 20 min, 25 min and 30 min, Prelubrication time was set as 8 min, 10 min and 12 min and lubrication time was set as 1 min, 3 min and 5 min. Evaluation was done for the optimum selection of these parameters which affects the dissolution, disintegration, assay and LOD. In this research, three validation batches were taken amongst batch F2 showed the results in acceptable range. Disintegration time for the batch F2 was found in acceptable range i.e 1min 23 sec. % weight check was determined during coating of the tablets and it was found is acceptable range. Optimum hardness was selected which was15 to 17 kp, For F2 it was found to be16.56±0.6 The dissolution for the batches observed in the acceptable ranges amongst F2 showed maximum release it may be due to optimum selection of the hardness, % weight gain lubrication time and prelubrication time. F2 batch was found to be stable for 3 months at accelerated condition and long-term conditions.

Keywords: Process validation, process parameters, in process check, dissolution, dispersible tablets

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INTRODUCTION

Dispersible tablets are tablets designed to disintegrate and dissolve quickly in water or saliva, forming a uniform suspension for easy administration, especially for patients with difficulty swallowing. Dispersible tablets are easy to administer, especially for children and elderly patients who struggle with swallowing pills. They offer faster onset of action as they dissolve quickly in water or saliva. These tablets ensure accurate dosing and improve patient compliance with their convenient and often palatable formulation. Formulating dispersible tablets involves challenges such as achieving rapid disintegration while maintaining sufficient mechanical strength to prevent breakage during handling. Taste masking is critical to ensure patient compliance, especially for bitter drugs. Stability is a concern, as these tablets are sensitive to moisture and require careful packaging. Uniform dispersion must be ensured to deliver accurate dosing. Additionally, selecting suitable excipients, such as superdisintegrant and flavouring agents, without compromising drug efficacy or shelf life, is essential.[1, 2] The model features of active pharmaceutical ingredients (APIs) for dispersible tablets include high water solubility to ensure rapid dissolution and bioavailability. The APIs should have good stability to withstand moisture exposure during formulation and storage. A favourable taste profile or the ability to undergo effective taste masking is essential for patient compliance. The particle size of the API should be optimized to aid in uniform dispersion and fast action. Additionally, the API must be compatible with excipients like superdisintegrant and flavouring agents to ensure proper tablet functionality and stability.[3] Pediatric and geriatric populations are particularly sensitive to the unpleasant taste of medications. Additionally, there is a growing trend toward developing drugs as orally disintegrating dosage forms, owing to their ease of ingestion and efficient absorption process. Therefore, in these situations, patient compliance depends critically on flavour. Additionally, a competitive edge is provided by great palatability. Although taste-masking flavours are available in dispersible tablets, many medications have a strong bitter flavour that cannot be covered up by a taste-masking agent. In these situations, a variety of technologies obscure taste.[4-6] Dispersible tablets are formulated using various techniques to ensure rapid disintegration and dissolution in water. Common methods include direct compression, where powders are compressed directly into tablets with disintegrants; wet granulation, which involves binding powders into granules before compression; and effervescent tablets, where acids and bases react in water to aid disintegration. Lyophilization (freeze-drying) creates porous tablets that dissolve quickly, while superdisintegrants like croscarmellose sodium enhance tablet breakdown. Other

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Table 1: Formulation of dispersible tablet.

S. No.	Ingredients	Composition mg/ tablets		
Formulation		F1	F2	F3
Layer - I (Tenofovir and Emtricitabine)				
Dry Mix				
1	MCC PH-112	50.19	50.19	50.19
2	Tenofovir Alafenamide Hemi fumarate	28.32	28.32	28.32
3	Emtricitabine	200.49	200.49	200.49
4	Mannitol SD 200	20	20	20
5	Mannitol Pearlitol 25 C	20	20	20
6	Aspartame IP	25	25	25
7	Croscarmellose sodium	10	10	10
Binding-				
10	Ethyl Cellulose N-7	5	5	5
11	MDC	q.s (225 gm)	q.s (225 gm)	q.s (225 gm)
Extra Granular Ingredients				
12	Croscarmellose sodium	10	10	10
15	Aspartame	20	20	20
16	Ponceu Colour	1	1	1
17	Syloids AL -1-FP	11	11	11
18	Strawberry Flavour	7	7	7
Lubrication				
19	Sodium stearyl fumarate	2	2	2
	Total weight part-1	410 mg	410 mg	410 mg
Layer – II (Bictegravir Sodium)				
Dry Mix				
1	MCC-PH-112	131.28	131.28	131.28
2	PVPK-30	5	5	5
3	Croscarmellose sodium	10	10	10
Binding				
4	Bictegravir Sodium	52.72	52.72	52.72
5	Acetone BP	Q.S (120 gm)	Q.S (120gm)	Q.S (120gm)
Extra granulation				
6	Poloxamer f-127	30	30	30
7	Croscarmellose sodium	10	10	10
8	Syloids AL -1-FP	5	5	5
Lubrication				
9	Sodium stearyl fumarate	2	2	2
	weight part-2	246	246	246
	weight of core tablets	656.0 mg	656.0 mg	656.0 mg
Coating				
1	Lecithin	2	2	2
2	HPMC – E-5	8.5	8.5	8.5
3	Titanium dioxide	0.5	0.5	0.5
4	Vanillin IP	2	2	2
5	Talc IP	0.5	0.5	0.5
6	PEG 6000	2.75	2.75	2.75
7	IPA	Q.S	Q.S	Q.S
8	MDC	Q.S	Q.S	Q.S
	Total weight of tablets	672.25 mg	672.25 mg	672.25 mg

techniques include molded tablets for a highly porous structure and sublimation, where volatile substances are removed to leave a fast-dissolving tablet. Each technique is selected based on the drug's properties and desired release profile.[7] In the formulation of dispersible tablets, several key in-process parameters must be carefully monitored to ensure quality and performance. These include particle size distribution of the active ingredients and excipients, which affects the tablet's disintegration and dissolution. Moisture content should be controlled, especially in granulation or lyophilization processes, to avoid tablet degradation or inconsistent disintegration. Hardness and friability are assessed to ensure the tablets are sufficiently robust yet capable of breaking apart in

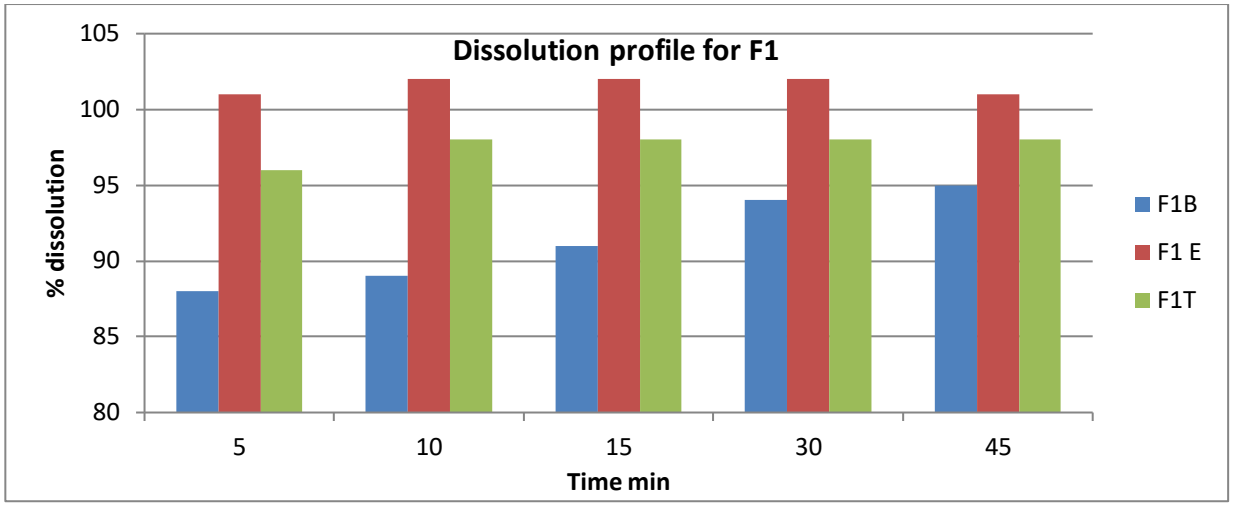

Figure 1: Dissolution profile for F1.

Table 2: Observation of LOD for granules.

Formulation	Drying time	LOD %	Mean
		2.3	
F1	20 min	2.17	2.23±0.1
		2.22	
		1.19	
F2	25 min	1.18	1.21±0.1
		1.26	
		1.11	
F3	30 min	1.26	1.14±0.1
		1.05	

water. Disintegration time is critically monitored, as it ensures rapid breakdown in water. Additionally, uniformity of content is checked to ensure consistent dosing across the batch. In present research, fixed dose combination of Tenofovir, Bictegravir and Emtricitabine were used to formulate the dispersible bilayer tablet.[9,10] Tenofovir belongs to the antiviral drug class, specifically a nucleotide reverse transcriptase inhibitor (NRTI). It is classified in BCS Class III, characterized by high solubility but low permeability[11] while Bictegravir is classified as BCS Class II, indicating low solubility but high permeability. It has moderate solubility in aqueous media and an oral bioavailability of approximately 35%, limited by solubility. Emtricitabine is classified as BCS Class I, indicating high solubility and high permeability. It is highly soluble in water, and its oral bioavailability is approximately 93%, making it efficiently absorbed.

MATERIALS AND METHOD

Material

Emtricitabine, tenofovir alafenamide and bictegravir were received as gift samples from Hetero Drugs Ltd. Microcrystalline cellulose used in the formulation development is Avicel pH112, supplied from DuPont Nutrition Ireland. The grade of Sodium starch glycolate, Ph. Eur. used in the formulation development is Primojel, supplied from DFE Pharma. Syloids AL1 FP was purchased from GRACE suppliers. Mannitol SD 200, Mannitol 25 C supplied from Roquette pharma, Croscarmellose Sodium from JRS pharma, Aspartame, Ethyl Cellulose 7 CPS from Global calcium pvt lmt, Ponceau 4 R supra Colour purchased from Dynemic Product Ltd, Strawberry Flavor purchased from Fab flavours, Sodium Stearyl Fumarate, Povidone k 30, Poloxamer 407 (Plutonic F-127) purchased from PharmaCompass.com, Lecithin, TPGS, HPMC - E-5 LV Purchased from Pioma chemicals, Titanium Dioxide, Vanillin IP Snow orchid, Talc and PEG 6000 these excipients used in the formulation development. Other chemicals used the formulation were of analytical grade.

Methods

Formulation of bilayer dispersible tablet

Accurately weighed and sifted MCC-PH-112, Pearlitol 25C, Mannitol SD 200 Croscarmellose sodium, Tenofovir Alafenamide Hemi fumarate, Emtricitabine and Aspartame IP (as mentioned in table 1) through 40 # mesh. MDC was taken in SS vessel add ethyl Cellulose N-7 to get dissolve and stirrered for 30 minutes. blend was laoded in FBP & granulate it with solution, using Top spray assembly to form a granular mass. LOD should be NMT 2.5 % at 105 °C & sifted the dried granules through 30 # mesh. If any retained granules observed, milled it through

Table 3: Observations of drug content for granules.

Blend Uniformity					
F1 (8 min)		F2 (10 min)		F3 (12 min)	
E	T	E	T	E	T
100.3	101.1	101	101.2	99.7	100.4
100.2	101.1	101.1	101.1	99.2	100.2
100.1	101.4	101.2	101.2	99.6	99.8
100.2±0.1	101.2±0.1	100.1±0.1	101.16±0.1	99.5±0.1	100.13±0.1

Table 4: Observation of drug content for granules for Layer I.

Blend Uniformity (layer I)					
F1 (1 min)		F2 (3 min)		F3 (5 min)	
E	T	E	T	E	T
100	99	102	109	100.4	102.2
100.2	100.1	102.1	107.1	100.2	100.2
100.1	101	100	104.2	100.6	100.8
100.1±0.1	100.03±0.1	101.36±0.1	106.76±0.1	100.06±0.1	101.13±0.1

Table 5: Observation of drug content for granules for layer II.

Blend Uniformity (Layer II)		
F1(1min)	F2 (3 min)	F3 (5 min)
B	B	B
97	97	96.2
97.2	97.1	96.3
97.4	97.03	94.1
97.2±0.1	97.04±0.1	95.53±0.1

Table 6: Flow properties of granules.

Batch No	F1	F2	F3
B.D	0.45± 0.125	0.46± 0.015	0.52± 0.024
T.D	0.52± 0.111	0.51± 0.054	0.54± 0.065
Angle of Repose	31± 0.195	31± 0.111	32± 0.125
C. Index	13± 0.039	11± 0.032	12± 0.024
H.R	1.150.029	1.12± 0.029	1.08± 0.033
Flow	Good	Good	Good

multi mill using suitable screens. Dried granules were stored in double polythene bags sealed with triple laminated Alu pouches containing silica canisters. Formulation component are shown in Table 1.

Sifting of extra granulation

Aspartame, Croscarmellose sodium, Ponceau Color, Syloid AL-1 FP and Strawberry Flavor passed through mesh at # 40 and Sodium Steryl Fumarate pass through at # 60. Both blend mixed for 8/10/12 minutes in octagonal Blender.

Bictegravir sodium(Part-II)

Accurately weighed and sifted MCC-PH-112, Croscarmellose sodium and PVPK-30 through 40 # mesh. Acetone was taken in SS vessel add Bictegravir sodium and stirrer for 30 minutes. Above mixture was blended in FBP & granulate it with solution, using Top spray assembly to form a granular mass.

Sifting of extra granulation

Sifted Syloid AL-1 FP, Poloxamer f 127 and Croscarmellose sodium pass through mesh at # 40 and Sodium Steryl Fumarate passed through at # 60. Blending was done for both 1/3/5 minutes in octagonal Blender. Part I and II were punched using 17.5X8.0 mm, Capsule shaped, Standard Concave, Bilayer, one side break other side is plain dies to formulate the tablets.

Coating of tablets

About 80 % Isopropyl Alcohol was taken in a cleaned S.S. Vessel. Dispersed Hydroxyl Propyl Methyl Cellulose to the Vessel and mixed with Stirrer. Dichloromethane was added to the Vessel and mix well. Remaining 20 % Isopropyl Alcohol was taken in another cleaned S.S. Vessel. Dispersed Lacithin, Vanillin, Polyethylene Glycol 6000, Talc and Titanium Dioxide to the Vessel and mixed with Stirrer. Milled the suspension using Colloidal Mill. Above both solutions were mixed and stir then add remaining qty. of MDC. Tablets transferred into the pan and warm the tablets while jogging the pan until the bed temperature reaches approximately 45°C ± 5°C. Start the coating pan, spray the film coating suspension, and record the mass gain of the tablets. F 1 with 1.0 to 2.0 % (1.5%) F2 with 2.0 to 3 % (2.5%) and F3 with 2.5 to 3.5 % (3.0%) trials were taken till desired weight gain obtained. After completion of film coating continues drying of coated tablets for 10-15 minutes with low pan rpm and cools the coated tablets to reach room temperature.

Process optimisation

Optimisation of drying time

The wet granules obtained after granulation were dried at 60^0C for 20 min, 25 min and 30 min in hot air oven. The samples were taken each time point and LOD of the granules was determined.

Optimization of pre-lubrication blending time

To optimize the pre-lubrication time, pre-lubricated material was blended for 8 min, 10 min and 12 min. The specimens were collected at each time point and assay/drug content was determined.

Optimization of lubrication blending time

To optimize the lubrication time, lubricated material was blended for 1 min, 3 min and 5 min. The specimens were collected at each time point and assay/drug content was determined.[12]

Characterisation of granules[13]

Angle of repose (θ):

It was determined by using funnel. A measured amount of lubricated granules was maintained in the funnel at a specific height so that the powder pile will touch the tip of funnel. After determining the diameter of the heap, it was computed using the formula below.

$$\tan\theta = \frac{h}{r}$$

Where h = Height of the pile and r= radius of the base

Bulk density (BD)

Gradually filling a 50 ml measuring cylinder with precisely weighted lubricated granules, the bed was made evenly and without disturbing. Below mentioned formula applied to determine the BD from the volume, which was expressed in millilitres.

Table 7: Characterization of tablets.

S. No.	Parameter	F1	F2	F3
1	Average Weight (mg)	674±1.0	671±1.0	678±1.0
		674.5±1.1	672.5±1.1	677.5±1.1
		677.5±1.0	670.5±1.0	680.5±1.0
2	Thickness (mm)	5.63±0.3	5.65±0.3	5.55±0.3
		5.50±0.3	5.67±0.3	5.77±0.3
		5.71±0.6	5.72±0.4	5.82±0.4
3	Hardness (Kp)	11.23±0.4	15.7±0.4	15.6±0.4
		13.2±0.3	16.8±0.35	16.33±0.6
		12.32±0.1	17.2±0.4	18.76±0.7
4	Disintegration Time (minutes)	1Min 26 sec	1Min21sec	1Min 27 sec
		1 min 22 sec	1Min21sec	1Min25sec
		1min 26 sec	1Min23sec	1Min24sec

Table 8: Characterization of coated tablet.

S. No.	Parameter	F1	F2	F3
1	Average Weight (mg)	675±1.2	668±1.1	677±1.1
		677±1.2	668±1.1	678±1.1
		678±1.0	677.2±1.0	680±1.2
2	Thickness (mm)	5.56±0.1	5.63±0.1	5.61±0.1
		5.66±0.1	5.60±0.1	5.60±0.1
		5.36±0.1	5.65±0.1	5.62±0.1
3	Hardness (Kp)	16.5±0.4	13.8 ±0.4	12.7 ±0.8
		14.6±0.5	13.5±0.6	12.22±0.2
		15.3±0.1	15.4±0.41	13.55±0.6
4	Disintegration Time (minutes)	1 min 26 seconds	1 min 21 seconds	1 min 27 seconds
		1 min 28 seconds	1 min 25 seconds	1 min 24 seconds
		1 min 25 seconds	1 min 23 seconds	1 min 26 seconds
5.	Assay	95.45±0.1	100.24±0.1	98.87±0.1
		95.25±0.1	100.48±0.1	98.87±0.1
		96.45±0.1	100.74±0.1	98.87±0.1
6.	% weight gain	1.53±0.21	2.1±0.1	3.1±0.3
		1.56±0.1	2.53±0.1	2.9±0.1
		1.33±0.2	2.483±0.1	2.5±0.2

$$\text{BD} = \frac{\text{mass of specimen in gm}}{\text{volume occupied by sample in ml}}$$

Tapped density (TD)

After precisely weighing and filling a measuring cylinder within a bulk density tester, lubricated granules were taken. When the sample was tapped 50, 100, or 250 times before there was not any changes in volume, primary volume occupy by sample was noted TD was calculated using the subsequent formula.

$$\text{TD} = \frac{\text{Mass of specimen in gm}}{\text{tapped volume occupy by sample in ml}}$$

Compressibility Index (CI)

The below mentioned formula was used to compute the CI.

$$\text{CI} = \frac{\text{TD} - \text{BD}}{\text{TD}} \text{X } 100$$

Hausner's Ratio (HR)

HR was computed using the following formula.

$$\text{HR} = \frac{\text{TD}}{\text{BD}}$$

Characterisation of tablets

Average weight

About 20 tablets were chosen at random and their weights were measured accurately in milligrams. The mean, as well as standard deviations, were determined.

Thickness

Thickness was determined using digital vernier caliper. Ten tablets were randomnly selected. The observations were noted in mm and the standard deviation was determined.

Hardness

The hardness of ten tablets that were selected at random was assessed using the Stokes Monsanto hardness tester. The average, as well as the standard deviation, was calculated. F1 with Low hardness (11-13kp), F2 with with Optimum hardness (15-17kp) and F3 with High hardness (18-21kp) trials were taken.

Friability

An automatic friabilator was used for this test. 20 tablets were randomly chosen from different batches for this test, and 100 rotations of the test were performed. The dedusted tablets were weighed, and the average of three evaluations of friability was computed. Typically, tablets were regarded as appropriate when there was a weight loss of less than 1%.

Disintegration test (DT)

Table 9: Dissolution profile for dispersible tablet.

Dissolution profile									
	F1			F2			F3		
Time point	B	E	T	B	E	T	B	E	T
5	88	101	96	85	100	97	84	99	95
10	89	102	98	90	103	101	89	98.44	99
15	91	102	98	91	102	101	90	99	99
30	94	102	98	93	102	101	92	100.1	99
45	95	101	98	95	102	101	94	100.1	99

Table 10: Accelerated stability data for dispersible tablet.

Pack: HDPE Bottle					
Parameter	Specification		Condition F2		
			Initial 3 M	40°C/75%RH 3 M	30°C/75%RH 3 M
Description	Light colour pink on one side and off white to light yellow on other side, Bialyer, Capsule shaped tablets on one side break line		Complies	Complies	Complies
LOD	Not more than 6 %w/w		3.5	3.6	3.58
Assay %	95 to105	Bictegravir	99.4	96.6	98.3
		Emtricitabine	102.4	98.5	100.6
		Tenofovir	99.8	97	97.7
Dissolution %	70 % D	Bictegravir	98	97	100
		Emtricitabine	102	100	100
		Tenofovir	100	97	99

The DT of the compressed tablets was performed on 6 tablets in DT apparatus containing 900 ml of DW maintained at 37 ± 0.50C. The DT in seconds was noted when no visible residue was observed in DW. DT for all the three formulation batches were determined.

Percentage weight gain

In coating of the tablets F 1 with 1.0 to 2.0 % (1.5%) F2 with 2.0 to 3 % (2.5%) and F3 with 2.5 to 3.5 % (3.0%) trials were taken till desired weight gain obtained. The % weight gain of a coated tablet is calculated by comparing the weight of the coated tablet to the weight of the uncoated tablet.

Assay

Tablet powder equivalent to about 50 mg was transferred into a 200 ml volumetric flask. About 140 ml of diluent added and sonicated it for not less than 10 minutes with occasional shaking. Diluted it to volume with diluent and mix. the solution was filtered through 0.45 µm membrane filter and discarded first few ml of the filtrate. Assay was determined by HPLC chromatographic system.

Dissolution

Citrate buffer pH 5.5 selected as dissolution medium, 900 ml volume, Apparatus Paddle and speed 50 RPM,

Dissolution time selected as 15 minutes. Temperature sated as 37±5ºC. Placed one tablet into each of the six dissolution jars. At the end of the specified time withdraw 10 ml of the sample solution from each dissolution vessel and replaced the aliquots with equal volumes of dissolution medium maintained at 37.0±0.5°C. Filtered the solution through 0.45 µm filter and discarded few ml of the filtrate and and sample solution was analysed by HPLC chromatographic system.

Stability study

Based on acceptable physicochemical parameters, the optimised formulation was packed in HDPE bottle. Accelerated stability study was conducted for dispersible film-coated tablets in accelerated stability condition at 40±2°C/75± 5 %RH and 37±2°C/75± 5 %RH for 3 month in HDPE Bottle. The stability results were compared with initial time points and stability was predicted.

RESULT AND DISCUSSION

Process parameters

Optimisation of drying time

Optimization of drying time was determined at 20 min, 25 min, and 30 min, and LOD values were checked and reported in Table 2. At 20 min drying time, % LOD of the granules was found to be 2.23±0.1, for 25 min it was 1.21±0.1 and for 30 min it was 1.14±0.1%. As the temperature, airflow, and drying time increased, the granules moisture content dropped there may be a chance of alteration of LOD due to the size of the granules. Because of their comparatively higher surface area, smaller granules dried more quickly and had a lower moisture content. After a specific amount of drying time, consistent moisture was obtained depending on the airflow and drying air temperature.[14] The required LOD was set as 1.21% hence the drying time was optimized as 25 min. Further at 30 min LOD goes down and obtained too dry granules hence 25 min drying time was selected.

Optimization of pre-lubrication blending time

For determination of pre-lubrication time collected samples were determined for their drug content and observations are summarised in Table 3. It was observed

that even with changes in the prelubrication time from 8 to 12 min there was no significant change in the blend assay. The blend assay was found to be 100.2±0.1 for Emtricitabine and 101.2±0.1 for Tenofovir in 8 min lubrication time. 100.1±0.1 and 101.16±0.1 for Emtricitabine and Tenofovir respectively in 10 min blending time. In 12 min blending time, blend assay was found to be 99.5±0.1 and 100.13±0.1 for Emtricitabine and Tenofovir respectively. Based on this data the pre-lubrication time was selected as 10 min to comply with the blend assay.

Optimization of lubrication blending time

Drug content for the lubricated material at different lubrication times was determined and observations were summarised in Table 4 and Table 5. It was observed that at highest lubrication time (5 min) the drug content was slightly lower (100.06±0.1% and 101.13±0.1) as compared to the 3 min (101.36±0.1% and 106.76±0.1) and 1 min (100.1±0.1% and 100.03±0.1) lubrication time. For Layer II, it was found 97.2±0.1%, 97.04±0.1, and 95.53±0.1 for 1 min, 3 min and 5 min lubrication blending time respectively. However, in all cases, the blend assay was found to be more than 95% which ranged in acceptable limit. The slight decrease in an assay may be due to detachment of the drug particles from the excipients and may be due to the highest density of particles separated or settled on one side. The duration of lubrication also affects the dissolution characteristics of the tablets so optimum lubrication time needs to be decided for every drug product. If the lubrication time is insufficient, it may not allow for adequate mixing, resulting in uneven distribution of the lubricant leading to the sticking and picking problems during compression. Inadequate lubrication can also lead to variations in drug content among different tablets.[15,16] Based on the results obtained, the lubrication time was set as 3 min.

Characterization of granules

Angle of repose, bulk density, tapped density, Carr's Index; Hausner's ratio was determined to check the good flow of granules. Observations for formulations F1, F2 and F3 are shown in Table 6. All the parameters for batches F1, F2 and F3 were found to be satisfactory and can be conclude that flow of the granules was good. Formulation F2 showed angle of repose 31± 0.111and Carr's index was found to be11± 0.032 which indicates the good flow property. The physical parameter such as bulk

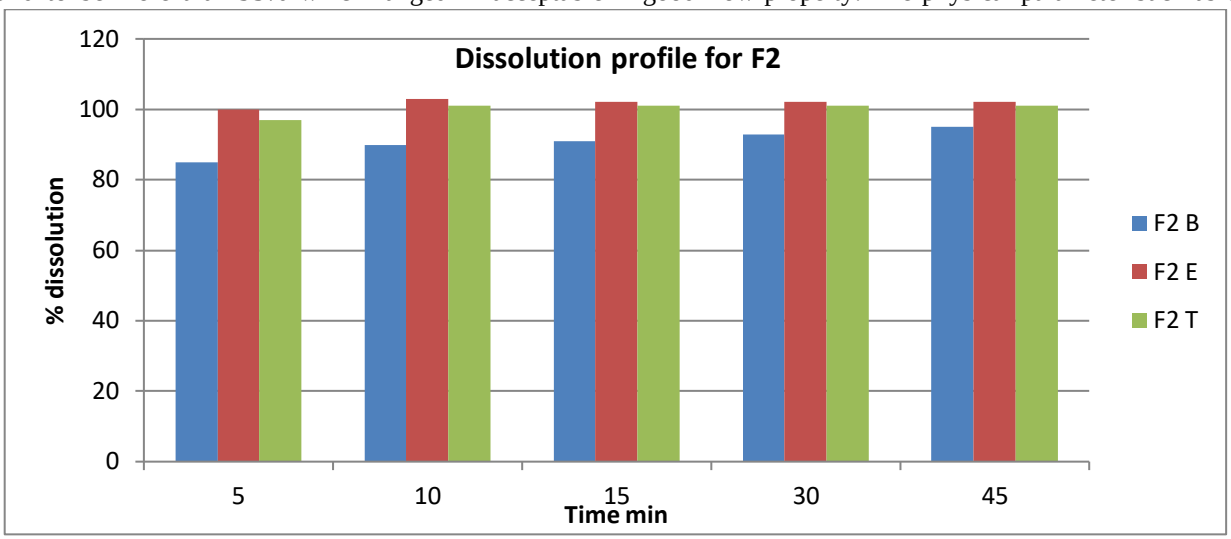

Figure 2: Dissolution profile for F2.

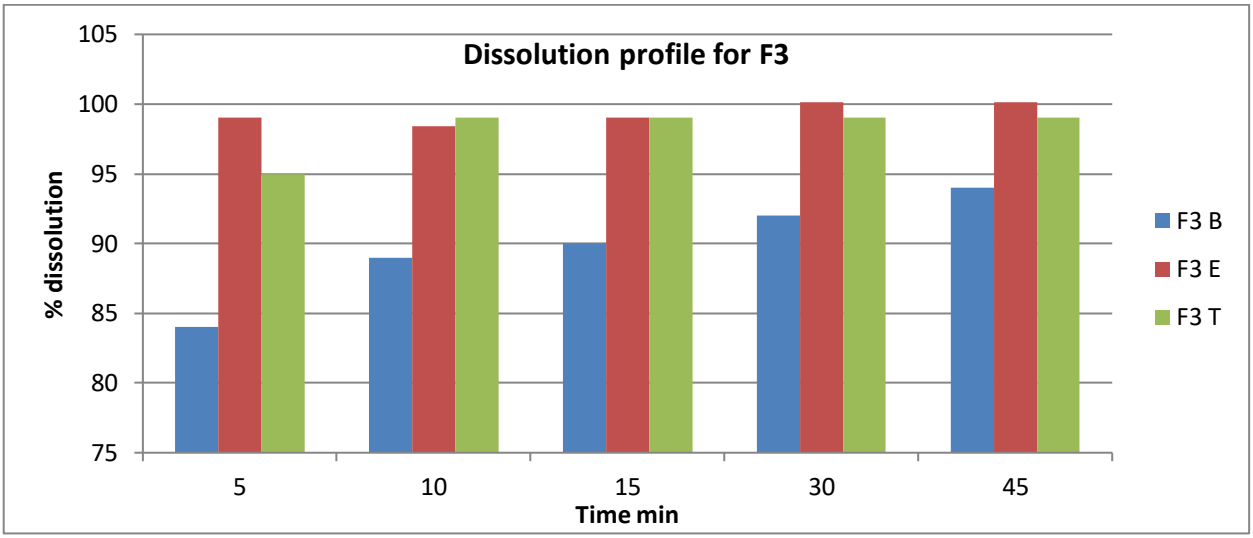

Figure 3: Dissolution profile for F3.

density, tapped density, compressibility index and Hausner's ratio and angle of repose for three validation batches were satisfactory and found consistent. No significant observation related to the flow of the blend was observed throughout the compression activity.

Characterisation of tablets

In characterization, average weight, thickness, hardness, disintegration time and friability was determined. The results for formulation F1, F2 and F3 for uncoated tablets are shown in Table 7 and for coated tablets shown in Table 8. Average weight for F1, F2 and F3 was found to be 675.33±1.0mg, 671.33±1.0mg and 678.66 mg respectively. Thickness was found within range while hardness was found in acceptable range. Thickness for F1 was found 5.61±0.5, for F2, 5.68±0.6, and for F3 it was found to be 5.71±0.4. Hardness for all the batches were found in acceptable range. Optimum hardness was selected which was15 to 17 kp, For F2 it was found to be16.56±0.6. Disintegration time for F2 was found in acceptable range i.e. 1 min 22 sec. Disintegration is also affected by the hardess. Harder tablets typically disintegrate more slowly because they resist breaking apart when exposed to fluids, delaying the release of the active ingredient. Softer tablets disintegrate more quickly, allowing for faster drug release. However, excessive hardness can hinder proper disintegration, affecting the tablet's effectiveness and release profile. The ideal hardness should be optimum. Hence optimum hardness which was selected for F2 formulation was selected.[17] Similarly characterizations for coated tablets were done and the results for the same are tabulated in the table 8**.** Disintegration time for the batch F2 was found in acceptable range i.e 1min 23 sec. % weight check was determined during coating of the tablets and it was found is acceptable range. For F1 it was found to be 1.47±0.1, for F2, 2.37±0.1 and for F3 it was found as 2.83±0.1. % weight gain was selected optimum as 2.5% weight gain which was selected for F2 batch. The percentage weight gain in tablet coating affects several parameters, including tablet hardness, dissolution rate, and disintegration time. A higher coating weight can increase the tablet's hardness, potentially slowing disintegration and drug release. Conversely, a thinner coating may result in faster dissolution and quicker drug release. The coating weight must be carefully controlled to achieve the desired release profile without compromising stability.[18] Hence optimum % weight was selected.

Dissolution

Dissolution for bilayer tablet was performed in Citrate buffer pH 5.5. Observations for dissolution of batch F1, F2 and F3 are shown in Table 9 and their respective graphs are shown in figure 1, 2 3. F2 formulation showed maximum drug release within 10 min other than two formulation. F1 formulation belongs to have the different process parameters like prelubrication time, lubrication time, hardness and % weight gain as 8min, 1 min, 11-13KP and1.5% respectively (Figure 1). For F2 it was 10 min, 3 min, 15-17 kp and 2.5% respectively (Figure 2). And for F3 it was 12 mn, 5 min, 18-21kp and 3% respectively (Figure 3). The dissolution for the batches observed in the acceptable ranges amongst F2 showed maximum release it may be due to optimum selection of the hardness, % weight gain lubrication time and prelubrication time. a tablet with optimal hardness will break apart at the right speed, allowing for efficient drug release and absorption. Lubrication time of granules affects the dissolution of a tablet by influencing the uniformity and rate at which the tablet disintegrates. Over-lubrication can lead to a film-like coating on the granules, reducing their ability to absorb water and causing slower disintegration and dissolution. Insufficient lubrication, on the other hand, can cause excessive friction during compression, leading to poor tablet formation. Proper lubrication ensures smooth compression and optimal disintegration for effective drug release.[19]

Stability

Results for Stability of the batch F2 is represented in Table 10. Description, LOD, assay, dissolution was found satisfactory. Product is found to be stable in HDPE bottle pack for 3 months at accelerated condition and long-term conditions. A film-coated OD tablet with final composition of F2 batch was found to be stable for 3 months at accelerated condition and long-term conditions.

CONCLUSION

In the formulation of Orodispersible tablets, process parameters were checked to ensure consistent tablet quality, including factors like uniformity in size, shape, and coating. Monitoring these parameters helps optimize disintegration**,** dissolution**,** and hardness, ensuring the tablet meets its intended release profile and complies with regulatory standards. In this research, process validation for drying time, prelubrication time, lubrication time, hardness and % weight gain parameters were checked and which are found within acceptable range i.e. 25 min, 10 min, 3 min, 15-17kp and 2.5% respectively and thereby dissolution, assay and disintegration was found within acceptable range. It was established that the production process of Dispersible Tablet of Tenofovir, Bictegravir and Emtricitabine was validated in accordance with guidelines for the pre-set acceptance criteria based on the results of the validation test, reviews, assessment, and evaluation.

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