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DESIGN AND EVALUATION OF FAST DISSOLVING TABLETS OF ROFLUMILAST SOLID DISPERSIONS

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ABSTRACT: The main objective of the present investigation was to formulate and evaluate fast dissolving tablets of Roflumilast solid dispersions using a direct compression method. Roflumilast solid dispersions were prepared by solvent evaporation as well as melting method. Roflumilast is a selective, long-acting inhibitor of the enzyme PDE-4 and has anti-inflammatory effects. It is used orally in the treatment of chronic obstructive pulmonary disease (COPD). The roflumilast drug belongs to BCS class II drugs that have low solubility and high permeability. The current research work was focused on improving the aqueous solubility of Roflumilast using solid dispersion technique and enhancing the dissolution rate. Based on the results of solubility analysis, phosphate buffer pH 6.8 was chosen as the dissolution medium. The powder blend of Roflumilast solid dispersions was evaluated for flow characteristics. The fast dissolving tablets of Roflumilast solid dispersions were subjected to post-compression parameters such as weight variation, hardness, thickness, friability, drug content, wetting time, water absorption ratio, *in-vitro* dispersion time and *in-vitro* disintegration time and the results were found to be within the acceptable limits. Based on FT-IR spectra obtained, it was evident that there was no significant interaction of Roflumilast with carriers and other excipients. From the results of dissolution study, SD1 and SD18 formulations were considered as best formulations.

INTRODUCTION: Drug administration by the oral route is a widely accepted route of drug administration which is occupying up to 50-60% of total dosage forms available. Solid dosage forms have been popular due to the accuracy of dosage, ease of administration, pain avoidance, self-medication as well as patient compliance. Tablets and capsules are being the most commonly used solid dosage forms. The main drawback of such dosage forms in case of few patients is the difficulty in swallowing.

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Drinking water is important in the swallowing of oral solid dosage forms. People experience inconvenience in swallowing tablets when water is unavailable as in case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, bronchitis and other allergic conditions [1]. Therefore, nowadays, there have been growing interests in the development of tablets that can rapidly disintegrate or dissolve in the oral cavity. Orodispersible tablets are not only advantageous for people who have difficulty in swallowing but at the same time, they are also suitable for active people. Fast dissolving tablets are also known as orodispersible tablets, mouth-dissolving tablets, porous tablets, melt-in-mouth tablets and quick dissolving tablets [2]. Roflumilast is a drug that acts as a selective, long-acting inhibitor of the enzyme PDE-4.

It has anti-inflammatory effects and is used as an orally administered drug for the treatment of inflammatory conditions of the lungs such as chronic obstructive pulmonary disease (COPD) [3]. Roflumilast is a lipophilic, highly permeable molecule that exhibits rapid and nearly complete absorption after oral administration. The absolute bioavailability of Roflumilast after a 500 µg oral dose is approximately 80%, and it appears to be affected primarily by gut and hepatic first-pass metabolism [4]. Roflumilast undergoes extensive hepatic metabolism by both phase 1 (cytochrome P450 [CYP]) and phase 2 (conjugation) reaction. Protein binding is approximately 99%.

Roflumilast belongs to BCS class II drugs which have low solubility and high permeability. For BCS class II drugs, dissolution is the rate-limiting step. The drugs that have poor aqueous solubility often show poor oral bioavailability due to the low levels of absorption. In case of drugs that undergo dissolution rate limited absorption, the dissolution rate of such drugs can be increased by size reduction, but this leads to aggregation of particles and poor wettability. The bioavailability of poorly aqueous soluble drugs can be increased using various other approaches such as the use of solubility enhancers, salt formation, micronization and complexation with cyclodextrin; but such approaches have several drawbacks.

Development of solid dispersions of poorly water-soluble drugs overcame the limitations of the previous approaches. When the solid dispersion comes in contact with the aqueous medium, the inert carrier dissolves, and the drug is released, the increased surface area produces a higher dissolution rate thus increasing the bioavailability of the poorly soluble drug. The present study was aimed to design and evaluate the fast dissolving tablets of Roflumilast solid dispersions by direct compression method. The objective of the present research was to develop an oral patient-friendly fast dissolving tablet formulation of Roflumilast with rapid dissolution and improved bioavailability.

MATERIALS AND METHODS: Roflumilast was obtained as a gift sample from Hetero Drugs Pvt. Ltd., Hyderabad, India. Polyethylene glycol (PEG) 4000, PEG 6000, hydroxypropyl methylcellulose (HPMC K15M), microcrystalline cellulose were purchased from Rolex Chemical., Mumbai. PVP K30 and Magnesium stearate were obtained from Loba Chemie, Tarapur. Croscarmellose sodium (CCS) and crospovidone (CP) were received as gift samples from Ciron Drugs and Pharmaceuticals, Palghar. Talc was purchased from Oxford Laboratory, Mumbai. Sodium hydroxide and potassium dihydrogen phosphate were purchased from Loba Chemie.

Drug-Carrier-Excipients Compatibility Testing: The drug and the excipients interaction studies were done out by checking the physical appearance and using FT-IR analytical technique. The interaction studies were carried out to ascertain any interaction of the drug with the excipients used in the preparation of fast dissolving tablets of Roflumilast solid dispersions.

Fourier Transform Infra Red (FTIR) Analysis: [5]An FT-IR spectrophotometer was used for infrared analysis of samples. About 4-5 mg of sample was mixed with dry potassium bromide (KBr), and the sample was examined at transmission mode over the wave number range of 4000 - 400 cm^{-1}.

Formulation Development:

Calibration of Standard Curve of Roflumilast:

Determination of Wavelength: 10 mg of Roflumilast pure drug was dissolved in 10 ml of ethanol (Primary stock). From this primary stock solution, 1 ml was taken in a 10 ml volumetric flask, and the volume was made up to 10 ml with pH 6.8 phosphate buffer (Secondary stock-100µg/ml). From secondary stock solution, 1 ml was taken, and volume made up to 10 ml with pH 6.8 phosphate buffer (Working stock - 10 µg/ml). The final concentration prepared was scanned between 200 nm to 400 nm on spectrum mode using UV-visible spectrophotometer to determine the λ_{max} of Roflumilast.

Preparation of Standard Graph of Roflumilast in pH 6.8 Phosphate Buffer: From the secondary stock solution, 0.5 ml, 1 ml, 1.5 ml, 2.0 ml, 2.5 ml and 3.0 ml were taken and volume made up to 10ml with pH 6.8 phosphate buffer to get concentrations of 5 µg/ml, 10 µg/ml, 15 µg/ml, 20µg/ml, 25 µg/ml and 30 µg/ml concentrations respectively. The prepared solutions were subjected to UV - visible spectrophotometric study at the

obtained λ_{max} for roflumilast using phosphate buffer, pH 6.8 as blank.

Solubility Analysis of Roflumilast: An excess quantity of Roflumilast pure drug was added to 10 ml of water, propylene glycol, polyethylene glycol 400, 0.1 N HCl and pH 6.8 phosphate buffer in screw-capped bottles. The samples were shaken in an orbital shaker for 48 h at room temperature. Subsequently, the obtained suspensions were filtered through Whatman filter paper no. 0.22 µ. The filtered solutions were suitably diluted using respective solvents and further analyzed by UV – visible spectrophotometer at the maximum wavelength of Roflumilast.

Preparation of Roflumilast Solid Dispersions

Solvent Evaporation Method: Twelve formulations of Roflumilast solid dispersions were prepared using different carriers in various proportions, *i.e.*, 1:1, 1:2, 1:3 (Drug: Carrier) as shown in **Table 1**. The drug and carrier were dissolved in ethanol followed by trituration in a dry mortar till the solvent was completely evaporated, and a clear dry mixture of drug and carrier was obtained. Roflumilast SD thus obtained was scraped off using a spatula. Solid dispersions were pulverized in a mortar with pestle and sieved through # 60 sieve and packed in an airtight container.

TABLE1: FORMULATION OF ROFLUMILAST SOLID DISPERSIONS BY SOLVENT EVAPORATION

Formulation code	Drug	PVP K30	PEG 4000	PEG 6000	HPMC K15M	Ethanol
SE1	50	50	-	-	-	q.s.
SE2	50	100	-	-	-	q.s.
SE3	50	150	-	-	-	q.s.
SE4	50	-	50	-	-	q.s.
SE5	50	-	100	-	-	q.s.
SE6	50	-	150	-	-	q.s.
SE7	50	-	-	50	-	q.s.
SE8	50	-	-	100	-	q.s.
SE9	50	-	-	150	-	q.s.
SE10	50	-	-	-	50	q.s.
SE11	50	-	-	-	100	q.s.
SE12	50	-	-	-	150	q.s.

Melting Method: Roflumilast solid dispersions of 12 formulations were prepared by melting method using different carriers in 1:1, 1:2, 1:3 (Drug: Carrier) proportions as mentioned in **Table 2**. Carrier was melted at 40 ºC. The drug was dispersed in the molten carrier and then kept aside for cooling. After solidification, the obtained SD was scraped off using a spatula. SDs were further subjected to milling in a mortar with pestle and passed through a 45 µm sieve before packing in an airtight container.

TABLE 2: FORMULATION OF ROFLUMILAST SOLID DISPERSIONS BY MELTING METHOD

Formulation code	Drug	PVP K30	PEG 4000	PEG 6000	HPMC K15M	Ethanol
M1	50	50	-	-	-	q.s.
M2	50	100	-	-	-	q.s.
M3	50	150	-	-	-	q.s.
M4	50	-	50	-	-	q.s.
M5	50	-	100	-	-	q.s.
M6	50	-	150	-	-	q.s.
M7	50	-	-	50	-	q.s.
M8	50	-	-	100	-	q.s.
M9	50	-	-	150	-	q.s.
M10	50	-	-	-	50	q.s.
M11	50	-	-	-	100	q.s.
M12	50	-	-	-	150	q.s.

Selection of Super-disintegrants: Placebo tablets were prepared using different super-disintegrants with 5% for a total weight of the tablets and a different ratio of excipients as mentioned in **Table 3**. Croscarmellose sodium and crospovidone were chosen as superdisintegrants.

The compressed placebo tablets were placed in 10 ml of water to assess the superdisintegrant which would be disintegrated within a short time. The selected superdisintegrant was used in the formulation of fast dissolving tablets of Roflumilast solid dispersion.

TABLE 3: FORMULATION OF PLACEBO TABLETS FOR SELECTION OF SUPERDISINTEGRANT

Formulation code	CCS (mg)	CP (mg)	Magnesium stearate (mg)	Talc (mg)	Mannitol (mg)	Total weight (mg)
PT1	4	-	1	1	q.s.	80
PT2	-	4	1	1	q.s.	80

Evaluation of Roflumilast Powder Blends:

Pre-compression Parameters for Solid Dispersions:

Bulk Density (D_b): [6] It is the ratio of the total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder, and initial weight was noted. This initial volume is called the bulk volume. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_b$$

Where M is the mass of powder, V_b is the bulk volume of the powder.

Tapped Density (D_t): [7] It is the ratio of the total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder 750 times, and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times, and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where M is the mass of powder, V_t is the tapped volume of the powder.

Carr's Index or % Compressibility: [8, 9] It indicates powder flow properties. It is expressed in percentage and is given as,

$$I = (D_t - D_b) / D_t \times 100$$

D_t has tapped density of the powder, Db is the bulk density of the powder.

Hausner's Ratio: [10] Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\text{Hausner's ratio} = D_t / D_b$$

Where D_t is tapped density, D_b is bulk density. Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (> 1.25).

The angle of Repose (Ɵ): [11] The friction forces in a loose powder can be measured by the angle of repose (Ɵ). It is indicative of the flow properties of the powder. It is defined as the maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$Ɵ = \tan^{-1} (h / r)$$

Where "Ɵ" is the angle of repose, "h" is height in cm, "r" is radius in cm.

The powder mixture was allowed to flow through funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of the powder formed.

% Practical Yield for Solid Dispersion: Percentage of practical yield was calculated to know about percent yield or efficiency of any method; thus it helps in the selection of the appropriate method of production. Solid dispersions were collected and weighed to determine practical yield using the following equation,

% Practical Yield = Practical mass (Solid dispersion) / Theoretical mass (Drug + Carrier) × 100

Compression of Solid Dispersion Tablets: The prepared solid dispersions were compressed into tablets taking different ratios by direct compression method using rotary tablet compression machine (Karnavathi) with 6 mm of punch. The solid dispersion along with required excipients was blended properly using polybag and then compressed into tablets. Each tablet weight was taken as 80 mg.

TABLE 4: COMPOSITION OF SOLID DISPERSION TABLETS BY SOLVENT EVAPORATION METHOD

Formulation code	Roflumilast SD (Equivalent to 500 µg)	CP (mg)	Magnesium stearate (mg)	Talc (mg)	Mannitol (mg)	Total weight (mg)
SD1	SE1 1.0 mg	4	1	1	q.s.	80
SD2	SE2 1.5 mg	4	1	1	q.s.	80
SD3	SE3 2.0 mg	4	1	1	q.s.	80
SD4	SE4 1.0 mg	4	1	1	q.s.	80
SD5	SE5 1.5 mg	4	1	1	q.s.	80
SD6	SE6 2.0 mg	4	1	1	q.s.	80
SD7	SE7 1.0 mg	4	1	1	q.s.	80
SD8	SE8 1.5 mg	4	1	1	q.s.	80
SD9	SE9 2.0 mg	4	1	1	q.s.	80
SD10	SE10 1.0 mg	4	1	1	q.s.	80
SD11	SE11 1.5 mg	4	1	1	q.s.	80
SD12	SE12 2.0 mg	4	1	1	q.s.	80

TABLE 5: COMPOSITION OF SOLID DISPERSION TABLETS BY MELTING METHOD

Formulation code	Roflumilast SD (Equivalent to 500 µg)	CP (mg)	Magnesium stearate (mg)	Talc (mg)	Mannitol (mg)	Total weight (mg)
SD13	M1 1.0 mg	4	1	1	q.s.	80
SD14	M2 1.5 mg	4	1	1	q.s.	80
SD15	M3 2.0 mg	4	1	1	q.s.	80
SD16	M4 1.0 mg	4	1	1	q.s.	80
SD17	M5 1.5 mg	4	1	1	q.s.	80
SD18	M6 2.0 mg	4	1	1	q.s.	80
SD19	M7 1.0 mg	4	1	1	q.s.	80
SD20	M8 1.5 mg	4	1	1	q.s.	80
D21	M9 2.0 mg	4	1	1	q.s.	80
SD22	M10 1.0 mg	4	1	1	q.s.	80
SD23	M11 1.5 mg	4	1	1	q.s.	80
SD24	M12 2.0 mg	4	1	1	q.s.	80

Evaluation of Fast Dissolving Tablets:

Weight Variation: [12] 10 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification was considered as per I.P.

Hardness: [13] Tablet crushing strength or hardness is the force required to break a tablet in a diametric compression. Monsanto tablet hardness tester was used to measure the hardness of tablets, and the values were expressed in kg/cm ^{2}.

Thickness: 3 tablets were selected randomly from each formulation, and the thickness of tablets was measured using a Vernier caliper.

Friability: [14] Friability of the tablet was determined using Roche friabilator. In Roche friabilator, the tablets were subjected to the combined effect of both abrasions as well as shock in a plastic chamber which was revolved at 25 rpm and the tablets were dropped at the height of 6 inches in each revolution. Pre-weighed a sample of Roflumilast tablets from each formulation was placed in the friabilator and then subjected to the hundred revolutions. The tablets after friability test were dusted by using a soft muslin cloth and then reweighed. The formula gave the friability,

$$\% F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Drug Content: Three tablets were selected randomly, weighed and then finely powdered. A quantity of the powder equivalent to 1 tablet was added to 100 ml of phosphate buffer, pH 6.8 in a conical flask. The conical flask was then kept on a rotary shaker. An aliquot of the solution was subjected to centrifugation, and the supernatant was filtered through a 0.22 µ filter. The absorbance of the resultant solution was measured using UV - visible spectrophotometer at the λ_{max} of Roflumilast against phosphate buffer, pH 6.8 as blank. Concentrations, as well as the amount of Roflumilast contained in one tablet, were determined using the calibration curve.

Wetting Time and Water Absorption Ratio: [15] A piece of tissue paper folded twice was kept in a small Petri plate (i.d. = 6.5 cm) consisting 6 ml of

phosphate buffer, pH 6.8. A tablet was kept on the wet tissue paper and the time taken for complete wetting was determined with the help of a stopwatch. Then, the wetted tablet was re-weighed. Water absorption ratio (R) was calculated using the below-mentioned equation,

$$R = 100 \times (W_a - W_b / W_b)$$

W_a = Weight of the tablet after water absorption, W_b = Weight of the tablet before water absorption.

***In-vitro* Dispersion Time:** For the determination of *in-vitro* dispersion time of prepared tablets, 10 ml measuring cylinder was taken in which 6 ml of phosphate buffer, pH 6.8 was added, and the tablet was dropped in the measuring cylinder. The time taken for the complete dispersion was determined.

***In-vitro* Disintegration Time:** *In-vitro* disintegration time was determined by using disintegration test apparatus (Lab India). Three tablets were selected randomly from each formulation for determining the time of disintegration.

***In-vitro* Dissolution Time:** *In-vitro* dissolution test was performed by using USP dissolution test apparatus (type II). Phosphate buffer, pH 6.8 was used as the dissolution medium (900 ml), the agitation speed of the paddle was 50 rpm and the temperature was maintained at 37 ºC ± 1 ºC. 5 ml samples were withdrawn at pre-determined intervals, *i.e.*, 5, 10, 15, 20, 30, 45 and 60 min, filtered and then replaced with 5 ml of the fresh dissolution medium to maintain the sink conditions. The samples collected were diluted suitably with phosphate buffer, pH 6.8, where ever necessary. Finally, the samples were analyzed for Roflumilast at the λ_{max} using UV-visible spectrophotometer. Each dissolution study was carried out in triplicate, and the mean values were calculated.

Stability Studies: The stability studies were carried out on the optimized formulation as per the International Conference on Harmonization (ICH) guidelines. The optimized formulation packed in aluminum foil was subjected to accelerated stability testing for 3 months according to ICH norms at a temperature of 40 ºC ± 2 ºC and relative humidity of 75% RH ± 5%. The samples were taken at regular time intervals of one month throughout three months and analyzed for any change in the physical appearance and drug content (assay) as per the procedure stated earlier. Any changes in evaluation parameters, if observed were noted down. The tests were performed three times and the mean value of the observed values was noted along with the standard deviation.

RESULTS AND DISCUSSION:

Drug-polymer-excipients Compatibility Testing: The compatibility studies were performed to ascertain interaction if any drug with the excipients and polymers used in the preparation of tablets.

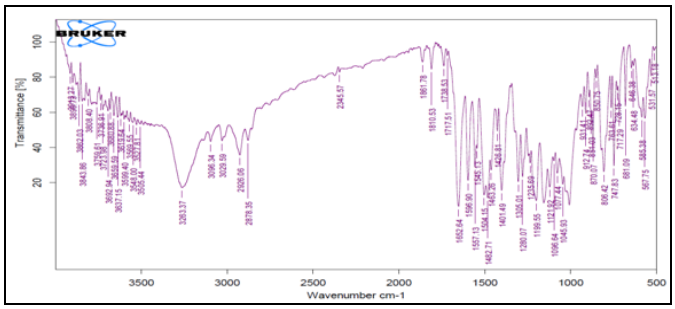

FIG. 1: FT-IR SPECTRA FOR ROFLUMILAST

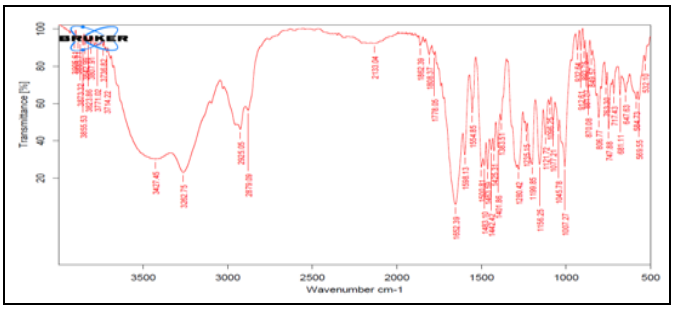

FIG. 2: FT-IR SPECTRA FOR ROFLUMILAST + PVP K30

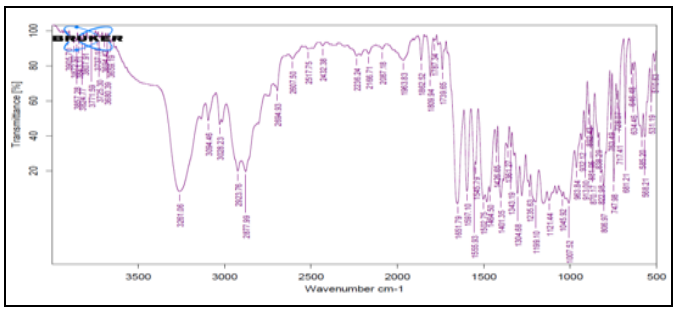

FIG. 3: FT-IR SPECTRA FOR ROFLUMILAST + PEG 4000

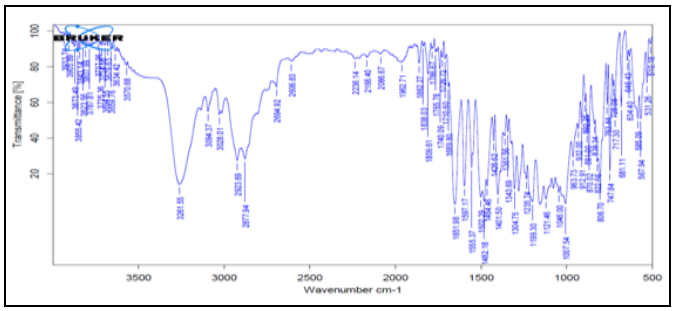

FIG. 4: FT-IR SPECTRA FOR ROFLUMILAST + PEG 6000

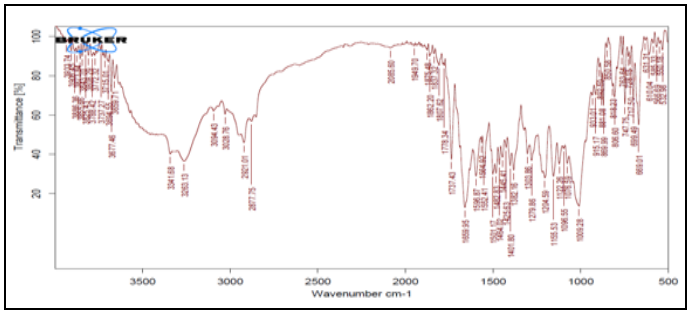

FIG. 5: FT-IR SPECTRA FOR OPTIMIZED FORMULATION SD1

FT-IR studies were conducted to know the possible interactions between selected drug Roflumilast; carriers (PVP K30, PEG 4000, PEG 6000 and HPMC K15M) and other excipients. FT-IR of Roflumilast+PVP K30, Roflumilast+PEG 4000, Roflumilast+PEG 6000 and Formulation SD1 showed similar peaks as that of Roflumilast pure drug. Based on FT-IR spectra obtained, it was evident that there was no significant interaction of Roflumilast with carriers and other excipients.

Formulation Development:

Roflumilast Spectrophotometric Determination: Estimation of Roflumilast was done using a UV - visible spectrophotometric method in phosphate buffer, pH 6.8. The standard concentration was scanned over a range of 400 nm - 200 nm and resulted in a peak at the wavelength of 250 nm, and it was considered as absorption maxima (λ_{max}) for Roflumilast.

Calibration Graph for Roflumilast: The calibration curve of Roflumilast in phosphate buffer, pH 6.8 was constructed by making the solutions of 5 µg/ml, 10 µg/ml, 15 µg/ml, 20µg/ml, 25 µg/ml and 30 µg/ml concentrations.

TABLE 6: CALIBRATION GRAPH OF ROFLUMILAST

Concentration (µg/ml)	Absorbance at 250.0 nm (in phosphate buffer, pH 6.8)
0	0
5	0.148
10	0.301
15	0.455
20	0.616
25	0.779
30	0.935

The absorbance of the solutions was measured using UV-visible spectrophotometer at the λ_{max} of 250 nm. The calibration graph was plotted by taking the concentrations on X-axis and absorbance on Y-axis. Roflumilast concentration and absorbance followed a linear relationship and the correlation coefficient (R^2) value in phosphate buffer; pH 6.8 was observed to be 0.999.

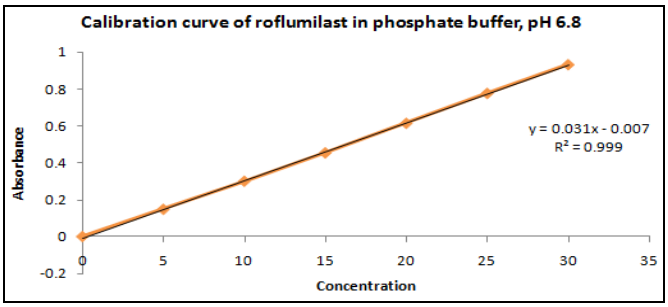

FIG. 6: CALIBRATION CURVE OF ROFLUMILAST IN PHOSPHATE BUFFER, pH 6.8

Solubility Studies: The solubility of Roflumilast was determined in different solvents separately and was mentioned in **Table 7**. The solubility of Roflumilast contributes to the molecular dispersion which will further improve the dissolution rate. Based on the solubility data obtained, phosphate buffer pH 6.8 was chosen as the dissolution medium. As per USFDA also, phosphate buffer pH 6.8 was used as the dissolution medium for Roflumilast.

TABLE 7: SOLUBILITY STUDY OF ROFLUMILAST IN DIFFERENT MEDIA

Solvent	Solubility (mg/ml)
0.1N HCl	0.006
Phosphate buffer pH 6.8	0.012
Water	0.007

Solubility Studies of Roflumilast Solid Dispersion in Phosphate Buffer pH 6.8: Solubility studies were done for the 24 formulations of Roflumilast solid dispersions prepared by solvent evaporation as well as melting or fusion techniques along with their respective carriers. Based on the results obtained, it was observed that the formulation with PVP K30 as a carrier in 1:1 (drug to the carrier) ratio had increased the solubility of Roflumilast in comparison with that of the pure Roflumilast drug.

The results were shown in **Table 8** and **Table 9**. The solubility of Roflumilast pure drug - 0.012 mg/ml. Solubility of formulation SD1 (Roflumilast with PVP K30 in 1:1 ratio) - 0.119 mg/ml (for solvent evaporation method). Solubility of formulation SD18 (Roflumilast with PEG 4000 in 1:3 ratio) - 0.115mg/ml (for fusion method). The results revealed that in case of Roflumilast solid dispersions prepared by a solvent evaporation method, the solubility of Roflumilast was found to decrease with the increasing concentrations of PVP K30, *i.e*., the maximum solubility of the drug was achieved with 1:1 drug: carrier ratio.

TABLE 8: SOLUBILITY STUDIES OF SOLID DISPERSION BY SOLVENT EVAPORATION METHOD

Formulation	Solubility (mg/ml)
SD1	0.119 ± 0.04
SD2	0.110 ± 0.01
SD3	0.104 ± 0.02
SD4	0.094 ± 0.02
SD5	0.174 ± 0.07
SD6	0.082 ± 0.06
SD7	0.099 ± 0.05
SD8	0.186 ± 0.01
SD9	0.076 ± 0.08
SD10	0.202 ± 0.01
SD11	0.215 ± 0.03
SD12	0.224 ± 0.06

TABLE 9: SOLUBILITY STUDIES OF SOLID DISPERSION BY MELTING (FUSION) METHOD

Formulation	Solubility (mg/ml)
SD13	0.082 ± 0.01
SD14	0.098 ± 0.05
SD15	0.110 ± 0.02
SD16	0.084 ± 0.06
SD17	0.092 ± 0.02
SD18	0.115 ± 0.03
SD19	0.086 ± 0.03
SD20	0.113 ± 0.04
SD21	0.097 ± 0.04
SD22	0.242 ± 0.02
SD23	0.280 ± 0.09
SD24	0.231 ± 0.02

Further, the results obtained for solubility studies of Roflumilast solid dispersions prepared by melting method suggested that the solubility of the drug was observed to increase with the increasing concentrations of both PVP K30 and PEG 4000. In all 24 formulations, there was a significant increase in solubility of Roflumilast SDs compared to that of its pure drug.

% Practical Yield: The % practical yield for all the 12 formulations developed by solvent evaporation technique was observed to be 90.14% to 95.23% as mentioned in **Table 10**. The 12 formulations prepared by melting method were found to be 85.92% to 94.87% as depicted in **Table 11**.

TABLE 10: % PRACTICAL YIELD FOR ROFLUMILAST SOLID DISPERSIONS BY SOLVENT EVAPORATION METHOD

Formulation	Percentage yield (%)
SD1	95.23
SD2	92.15
SD3	93.22
SD4	90.14
SD5	91.07
SD6	91.47
SD7	90.19
SD8	91.32
SD9	92.05
SD10	91.08
SD11	93.12
SD12	91.42

TABLE 11: % PRACTICAL YIELD FOR ROFLUMILAST SOLID DISPERSIONS BY MELTING METHOD

Formulation	Percentage yield (%)
SD13	91.48
SD14	92.81
SD15	91.13
SD16	87.48
SD17	86.05
SD18	94.87
SD19	88.12
SD20	87.49
SD21	85.92
SD22	92.26
SD23	90.14
SD24	92.32

Evaluation of Pre-compression Parameters of Powder Blend:

Pre-Compression Parameters for Solid Dispersion Blend Prepared by Solvent Evaporation Technique: The powder blends of various formulations were evaluated for bulk density, tapped density, Carr's index, the angle of repose and Hausner's ratio and values obtained were represented in **Table 12**.

The bulk density values were observed to be 0.27 ± 0.08 to 0.58 ± 0.04. The tapped density values were in between 0.32 g/cc ± 0.06 and 0.64 g/cc ± 0.07. The Carr's index values were found to be 09.37 ± 0.06 to 16.98 ± 0.03. The angle of repose values was observed to be below $30^{o,}$ and Hausner's ratios were found to be <1.2, which suggests that formulations of blend powder had good flow characteristics.

TABLE 12: PRE-COMPRESSION PARAMETERS FOR SOLID DISPERSION BLEND PREPARED BY SOLVENT EVAPORATION METHOD

Formulation	Bulk Density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Angle of repose (^{o})	Hausner's ratio
SD1	0.58 ± 0.04	0.64 ± 0.07	09.37 ± 0.06	25.01 ± 0.07	1.10 ± 0.07
SD2	0.53 ± 0.07	0.60 ± 0.06	11.66 ± 0.02	26.49 ± 0.05	1.13 ± 0.05
SD3	0.51 ± 0.05	0.58 ± 0.04	12.06 ± 0.02	28.10 ± 0.03	1.13 ± 0.03
SD4	0.50 ± 0.06	0.58 ± 0.05	13.79 ± 0.08	27.32 ± 0.03	1.16 ± 0.09
SD5	0.51 ± 0.07	0.61 ± 0.04	16.39 ± 0.04	25.42 ± 0.06	1.19 ± 0.04
SD6	0.44 ± 0.04	0.53 ± 0.08	16.98 ± 0.03	26.82 ± 0.09	1.14 ± 0.06
SD7	0.48 ± 0.05	0.56 ± 0.02	14.28 ± 0.05	28.64 ± 0.05	1.17 ± 0.05
SD8	0.54 ± 0.07	0.62 ± 0.04	12.90 ± 0.03	25.10 ± 0.08	1.15 ± 0.03
SD9	0.52 ± 0.05	0.60 ± 0.08	13.33 ± 0.07	26.84 ± 0.03	1.15 ± 0.02
SD10	0.27 ± 0.08	0.32 ± 0.06	15.62 ± 0.06	26.38 ± 0.08	1.18 ± 0.07
SD11	0.36 ± 0.03	0.43 ± 0.07	16.27 ± 0.02	27.29 ± 0.05	1.19 ± 0.04
SD12	0.56 ± 0.06	0.64 ± 0.05	12.50 ± 0.04	29.05 ± 0.06	1.14 ± 0.08

Pre-compression Parameters for Solid Dispersion Blend by Melting Method: The powder mixtures of different Roflumilast solid dispersion formulations were evaluated for the flow properties, and the results were mentioned in **Table 13**. The bulk densities and tapped densities of all the 12 powder solid dispersion formulations of Roflumilast prepared by melting method were found to be in the range of 0.23 ± 0.04 to 0.60 ± 0.07 and 0.28 ± 0.02 to 0.67 ± 0.03, respectively. The Carr's index values of all formulation blends were in the range of 09.25 ± 0.07 to 17.85 ± 0.01. The Hausner's ratios were found to be below 1.22, and angle of repose values was observed to be < 30^o which indicated that the powder blends had good flow properties.

TABLE 13: EVALUATION OF PRE-COMPRESSION PARAMETERS OF POWDER BLEND FOR ROFLUMILAST SOLID DISPERSION BY MELTING TECHNIQUE

Formulation	Bulk Density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Angle of repose (^{o})	Hausner's ratio
SD13	0.27 ± 0.04	0.32 ± 0.05	15.62 ± 0.03	29.13 ± 0.02	1.19 ± 0.07
SD14	0.60 ± 0.07	0.67 ± 0.03	10.44 ± 0.03	26.98 ± 0.16	1.12 ± 0.03
SD15	0.52 ± 0.04	0.59 ± 0.06	11.86 ± 0.04	27.62 ± 0.12	1.13 ± 0.02
SD16	0.35 ± 0.06	0.42 ± 0.02	16.66 ± 0.02	28.03 ± 0.08	1.21 ± 0.08
SD17	0.34 ± 0.07	0.40 ± 0.06	15.00 ± 0.08	26.47 ± 0.04	1.18 ± 0.06
SD18	0.49 ± 0.05	0.54 ± 0.04	09.25 ± 0.07	26.34 ± 0.05	1.10 ± 0.05
SD19	0.26 ± 0.05	0.31 ± 0.09	16.12 ± 0.04	27.08 ± 0.06	1.19 ± 0.08
SD20	0.28 ± 0.07	0.33 ± 0.03	15.15 ± 0.06	28.26 ± 0.04	1.18 ± 0.06
SD21	0.50 ± 0.03	0.58 ± 0.06	13.79 ± 0.02	26.42 ± 0.06	1.16 ± 0.05
SD22	0.47 ± 0.07	055 ± 0.04	14.54 ± 0.05	27.94 ± 0.08	1.17 ± 0.06
SD23	0.23 ± 0.04	0.28 ± 0.02	17.85 ± 0.01	26.82 ± 0.15	1.22 ± 0.09
SD24	0.32 ± 0.06	0.38 ±0.07	15.78 ± 0.03	28.54 ± 0.06	1.19 ± 0.07

Evaluation of Post-compression Parameters: All the developed formulations of fast dissolving tablets from Roflumilast solid dispersions by both solvent evaporation as well as melting method were subjected to post-compression analysis and values were observed to be within limits.

Friability and Drug Content: Friability for all the developed formulations by solvent evaporation and melting methods was observed to be in the range of 0.15% ± 0.03 - 0.30% ± 0.01 and 0.16% ± 0.08 - 0.30% ± 0.16 respectively. The drug content values for the formulations SD1 to SD12 and SD13 to SD24 were in the range of 99.46% ± 0.51 - 100.29% ± 0.48 and 98.36% ± 0.53 - 99.79% ± 0.62 respectively, indicating that the values obtained complied with the Pharmacopoeial limits [16].

Wetting Time and Water Absorption Ratio: The wetting time of tablet formulations prepared by a solvent evaporation method and melting methods was observed to be in the range of 33 sec ± 1.19 to 94 sec ± 1.20 and 34 sec ± 1.12 to 92 sec ± 0.92 respectively. Water absorption ratios of formulations SD1 to SD12 and SD13 to SD24 were found to be in the range of 138 ± 1.29 to 200 ± 1.35 to 136 ± 1.75 to 205 ± 1.15, respectively. The results were shown in **Table 16** and **17** respectively.

TABLE 14: POST-COMPRESSION PARAMETERS FOR FAST DISSOLVING TABLETS OF ROFLUMILAST SOLID DISPERSIONS PREPARED BY SOLVENT EVAPORATION TECHNIQUE

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)
SD1	79.28 ± 0.15	3.1 ± 0.2	2.1 ± 0.54	0.20 ± 0.03	100.29 ± 0.48
SD2	81.43 ± 0.05	3.0 ± 0.1	2.4 ± 0.45	0.19 ± 0.06	99.14 ± 0.28
SD3	78.17 ± 0.15	3.2 ± 0.2	2.3 ± 0.14	0.23 ± 0.09	99.02 ± 0.44
SD4	77.32 ± 0.21	3.5 ± 0.1	2.7 ± 0.21	0.16 ± 0.08	98.93 ± 0.70
SD5	80.28 ± 0.58	3.3 ± 0.3	2.5 ± 0.15	0.22 ± 0.06	98.77 ± 0.55
SD6	75.92 ± 0.39	3.1 ± 0.4	2.2 ± 0.33	0.27 ± 0.04	99.46 ± 0.51
SD7	79.92 ± 0.14	3.0 ± 0.1	2.8 ± 0.84	0.21 ± 0.02	99.21 ± 0.53
SD8	82.43 ± 0.21	3.2 ± 0.2	2.1 ± 0.54	0.19 ± 0.03	99.35 ± 0.51
SD9	81.65 ± 0.33	3.4 ± 0.2	2.3 ± 0.14	0.25 ± 0.08	99.29 ± 0.53
SD10	84.71 ± 0.18	3.2 ± 0.1	2.4 ± 0.45	0.30 ± 0.01	98.86 ± 0.60
SD11	79.13 ± 0.12	3.4 ± 0.2	2.7 ± 0.41	0.29 ± 0.02	98.64 ± 0.88
SD12	75.63 ± 0.43	3.1 ± 0.2	2.6 ± 0.58	0.20 ± 0.04	98.20 ± 0.55

TABLE 15: POST-COMPRESSION PARAMETERS FOR FAST DISSOLVING TABLETS OF ROFLUMILAST SOLID DISPERSIONS PREPARED BY MELTING METHOD

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)
SD13	76.13 ± 0.37	3.0 ± 0.1	2.2 ± 0.33	0.16 ± 0.08	99.27 ± 0.88
SD14	79.82 ± 0.57	3.2 ± 0.1	2.4 ± 0.45	0.17 ± 0.05	99.52 ± 0.49
SD15	82.13 ± 0.44	3.4 ± 0.2	2.6 ± 0.54	0.23 ± 0.07	99.79 ± 0.62
SD16	84.71 ± 0.83	3.3 ± 0.1	2.8 ± 0.81	0.20 ± 0.08	98.36 ± 0.53
SD17	79.43 ± 0.50	3.5 ± 0.2	2.1 ± 0.17	0.24 ± 0.12	98.64 ± 0.71
SD18	76.12 ± 0.59	3.1 ± 0.4	2.5 ± 0.43	0.23 ± 0.09	99.71 ± 0.64
SD19	80.73 ± 0.68	3.3 ± 0.3	2.7 ± 0.44	0.21 ± 0.05	99.29 ± 0.62
SD20	83.42 ± 0.43	3.2 ± 0.1	2.8 ± 0.82	0.28 ± 0.10	99.18 ± 0.66
SD21	78.29 ± 0.50	3.4 ± 0.2	2.3 ± 0.14	0.30 ± 0.16	99.41 ± 0.65
SD22	84.26 ± 0.57	3.2 ± 0.1	2.6 ± 0.45	0.27 ± 0.14	99.25 ± 0.57
SD23	77.43 ± 0.43	3.3 ± 0.3	2.5 ± 0.21	0.17 ± 0.05	99.06 ± 0.60
SD24	81.92 ± 0.45	3.5 ± 0.2	2.7 ± 0.18	0.23 ± 0.07	99.16 ± 0.52

TABLE 16: WETTING TIME AND WATER ABSORPTION RATIOS OF ROFLUMILAST FDTS PREPARED BY SOLVENT EVAPORATION METHOD

Formulation	Wetting time (sec)	Water absorption ratio	*In-vitro* dispersion time (sec)	*In-vitro* disintegration time (sec)
SD1	33 ± 1.19	138 ± 1.29	24 ± 1.89	90 ± 1.60
SD2	36 ± 1.18	156 ± 1.75	29 ± 1.63	96 ± 1.53
SD3	89 ± 1.24	166 ± 1.23	27 ± 1.14	111 ± 1.10
SD4	92 ± 1.96	179 ± 1.57	33 ± 1.52	124 ± 1.78
SD5	78 ± 1.03	147 ± 1.22	47 ± 1.15	119 ± 2.78
SD6	52 ± 1.29	156 ± 1.77	30 ± 1.74	124 ± 1.78
SD7	94 ± 1.20	166 ± 1.48	44 ± 1.57	133 ± 1.32
SD8	34 ± 1.12	176 ± 1.45	29 ± 1.63	111 ± 1.10
SD9	59 ± 1.77	198 ± 1.02	36 ± 1.18	115 ± 1.24
SD10	94 ± 2.01	158 ± 1.87	52 ± 1.29	117 ± 1.00
SD11	62 ± 1.98	169 ± 1.92	34 ± 1.12	120 ± 2.20
SD12	80 ± 0.92	200 ± 1.35	48 ± 1.89	136 ± 1.36

TABLE 17: WETTING TIME AND WATER ABSORPTION RATIOS OF ROFLUMILAST FDTS PREPARED BY MELTING METHOD

Formulation	Wetting time (sec)	Water absorption ratio	*In-vitro* dispersion time (sec)	*In-vitro* disintegration time (sec)
SD13	34 ± 1.12	154 ± 1.57	32 ± 1.69	132 ± 1.30
SD14	36 ± 1.18	136 ± 1.75	47 ± 1.46	115 ± 1.83
SD15	52 ± 1.29	205 ± 1.15	44 ± 1.54	119 ± 1.12
SD16	89 ± 1.24	116 ± 0.25	28 ± 1.62	126 ± 1.48
SD17	58 ± 1.13	147 ± 1.22	39 ± 1.14	115 ± 1.38

SD18	76 ± 1.49	178 ± 1.75	40 ± 1.84	90 ± 1.68
SD19	33 ± 1.20	164 ± 1.24	48 ± 1.87	96 ± 1.34
SD20	59 ± 1.19	186 ± 1.45	39 ± 1.26	117 ± 1.40
SD21	64 ± 1.37	152 ± 1.02	42 ± 1.16	125 ± 1.64
SD22	86 ± 1.48	172 ± 1.92	27 ± 1.26	132 ± 1.40
SD23	58 ± 1.12	179 ± 1.65	46 ± 1.08	127 ± 1.20
SD24	92 ± 0.92	192± 1.87	42 ± 1.89	132 ± 1.16

***In-vitro* Dispersion Time and *in-vitro* Disintegration Time:** The *in-vitro* dispersion time and *in-vitro* disintegration time in all 12 formulations (SD1 to SD12) were found to be in the range of 24 sec ± 1.89 to 52 sec ± 1.29 and 90sec ± 1.60 to 136 sec ± 1.36, respectively. The results obtained were represented in **Table 16**. The *in-vitro* dispersion time and *in-vitro* disintegration time in all formulations (SD13 to SD24) were found to be in the range of 27 sec ± 1.26 to 48 sec ± 1.87 and 115 sec ± 1.38 to 132 sec ± 1.30 respectively as shown in **Table 17**.

***In-vitro* Drug Release Studies:** The dissolution test conditions employed in order to study the drug release from the prepared fast dissolving tablet formulations of Roflumilast solid dispersions were: Dissolution medium used: phosphate buffer, pH 6.8, volume of dissolution medium: 900 ml, dissolution apparatus type: type II (Paddle type), paddle stirring speed: 50 rpm, temperature: 37 ºC ± 1 ºC, sampling intervals: 5, 10, 20, 30, 45 and 60min, sample volume withdrawn: 5 ml.

The *in-vitro* dissolution studies of all formulations (SD1 to SD12) were conducted, and the results were represented in **Table 18** and **Fig. 7**. The amount of drug release from different formulations SD1, SD2, SD3, SD4, SD5, SD6, SD7, SD8, SD9, SD10, SD11 and SD12 at end of 60 min were 98.69%, 98.45%, 98.25%, 96.54%, 97.84%, 98.16%, 97.89%, 94.56%, 96.86%, 92.48%, 94.84% and 95.32% respectively. In the case of formulation SD1, in which the carrier used was PVP K30 (drug: carrier 1: 1 ratio), the maximum percentage of drug release was observed within 10 min.

TABLE 18: *IN-VITRO* DRUG RELEASE STUDIES FOR ROFLUMILAST SOLID DISPERSION BY SOLVENT EVAPORATION METHOD

Time (min)	SD1	SD2	SD3	SD4	SD5	SD6	SD7	SD8	SD9	SD10	SD11	SD12
0	0	0	0	0	0	0	0	0	0	0	0	0
5	65.33 ± 0.50	64.84 ± 0.56	62.92 ± 0.34	58.62 ± 0.51	64.75 ± 0.61	68.15 ± 0.50	56.16 ± 0.58	68.54 ± 0.12	58.92 ± 0.45	54.23 ± 0.82	52.16 ± 0.61	52.52 ± 0.47
10	98.69 ± 0.44	82.95 ± 0.40	76.49 ± 0.61	66.94 ± 0.72	76.98 ± 0.42	79.84 ± 0.26	63.48 ± 0.71	76.95 ± 0.54	69.16 ± 0.36	68.47 ± 0.52	66.23 ± 0.23	61.45 ± 0.58
15	-	98.45 ± 0.55	84.75 ± 0.50	73.12 ± 0.49	85.92 ± 0.32	88.23 ± 0.15	78.56 ± 0.64	84.28 ± 0.36	78.28 ± 0.64	72.98 ± 0.35	73.28 ± 0.52	68.98 ± 0.61
20	-	-	98.25 ± 0.48	86.43 ± 0.25	97.84 ± 0.45	92.46 ± 0.45	85.15 ± 0.51	94.56 ± 0.58	86.92 ± 0.52	79.13 ± 0.26	84.36± 0.64	77.69 ± 0.25
30	-	-	-	96.54 ± 0.43	-	98.16 ± 0.34	97.89 ± 0.34	-	96.86 ± 0.21	84.26 ± 0.52	94.84± 0.47	89.98 ± 0.35
45	-	-	-	-	-	-	-	-	-	92.48 ± 0.56	-	95.32 ± 0.46
60	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 19: *IN-VITRO* DRUG RELEASE STUDIES FOR ROFLUMILAST SOLID DISPERSION BY MELTING METHOD

Time (min)	SD13	SD14	SD15	SD16	SD17	SD18	SD19	SD20	SD21	SD22	SD23	SD24
0	0	0	0	0	0	0	0	0	0	0	0	0
5	69.58 ±0.6	56.98 ±0.25	68.92 ±0.52	68.95 ±0.36	69.12 ±0.65	79.58 ±0.65	54.58 ±0.32	56.12 ±0.62	69.92 ±0.58	61.38 ±0.24	43.11 ±0.24	59.47 ±0.35
10	82.13 ±0.42	67.29 ±0.45	78.82 ±0.26	84.26 ±0.35	86.45 ±0.52	99.02 ±0.46	68.49 ±0.24	63.58 ±0.48	78.46 ±0.43	74.46 ±0.39	68.78 ±0.45	72.84 ±0.54
15	94.58 ±0.75	86.43 ±0.36	83.13 ±0.12	96.82 ±0.62	96.13 ±0.34	-	74.13 ±0.38	73.59 ±0.59	86.13 ±0.38	89.42 ±0.62	83.04 ±0.64	84.95 ±0.62
20	-	96.58 ±0.40	90.15 ±0.72	-	-	-	86.15 ±0.16	89.32 ±0.38	94.59 ±0.61	96.16 ±0.78	89.39 ±0.79	93.84 ±0.75
30	-	-	96.98 ±0.79	-	-	-	95.23 ±0.68	92.13 ±0.28	-	-	96.72 ±0.84	95.92 ±0.84
45	-	-	-	-	-	-	-	96.48 ±0.62	-	-	-	-
60	-	-	-	-	-	-	-		-	-	-	-

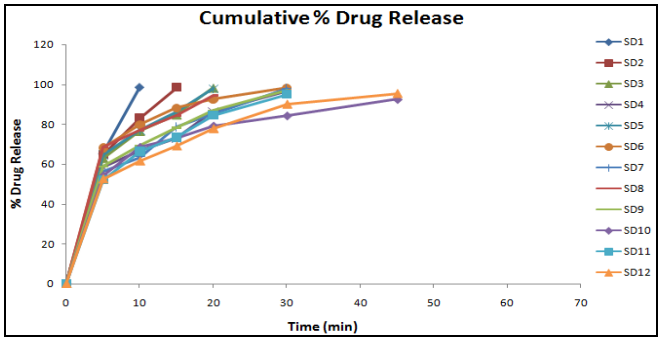

FIG. 7: DRUG RELEASE PROFILES FOR FAST DISSOLVING TABLETS OF ROFLUMILAST SOLID DISPERSION PREPARED BY SOLVENT EVAPORATION METHOD

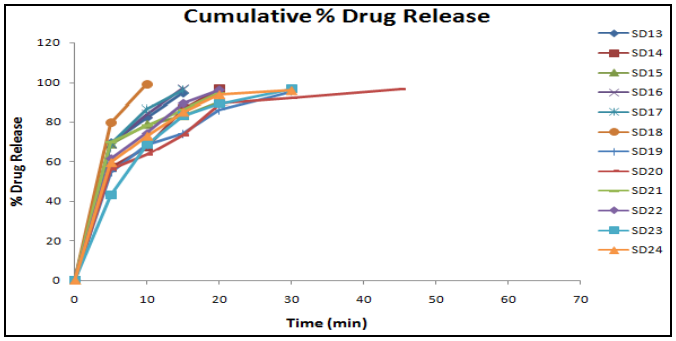

FIG. 8: DRUG RELEASE PROFILES FOR FAST DISSOLVING TABLETS OF ROFLUMILAST SOLID DISPERSION PREPARED BY MELTING METHOD

All Roflumilast solid dispersions prepared using PVP K30 showed ≥ 85% of drug release within 15min. Formulations SD4 to SD12 showed maximum % of drug release within 45 min. Hence, in the case of Roflumilast solid dispersions prepared by the solvent evaporation method, SD1 was considered as the optimized formulation. The *in-vitro* dissolution studies of formulations SD13 to SD24 were carried out, and the results were depicted in **Table 19** and **Fig. 8**. In case of formulation SD18, in which the carrier used was PEG 4000 (drug: carrier 1: 3 ratio), the maximum percentage of drug release was observed within 10 min, *i.e.*, 99.02%. All Roflumilast solid dispersions developed using PEG 4000 showed ≥ 85% of drug release within 15 min. All the formulations showed a maximum % of drug release within 45 min. Hence, in the case of Roflumilast solid dispersions prepared by melting method, SD18 was considered as the optimized formulation.

Accelerated Stability Studies: The optimized formulations were subjected for the accelerated stability studies. The optimized formulations SD1 and SD18 were analyzed for drug content for every month up to 3 months. Results of the accelerated stability studies revealed that there was no significant change in the physical appearance and drug content values of the optimized formulations as shown in **Table 20** and **Table 21** respectively, which mean that optimized formulations had good stability for a period of up to 3 months.

TABLE 20: ACCELERATED STABILITY STUDIES OF OPTIMIZED FORMULATION SD1

Test parameter	Initial	After 1 month	After 2 months	After 3 months
Physical appearance	No change	No change	No change	No change
Drug content (%)	99.98 ± 0.33	99.42 ± 0.54	99.38 ± 0.67	99.27 ± 0.42

TABLE 21: ACCELERATED STABILITY STUDIES OF OPTIMIZED FORMULATION SD18

Test parameter	Initial	After 1 month	After 2 months	After 3 months
Physical appearance	No change	No change	No change	No change
Drug content (%)	99.84 ± 0.25	99.68 ± 0.63	99.59 ± 0.72	99.41 ± 0.91

CONCLUSION: Fast dissolving tablets of Roflumilast solid dispersions were successfully prepared using different carriers (PVP K30, PEG 4000, PEG 6000 and HPMC K15M) by a solvent evaporation method and melting method. The maximum percentage of drug release was observed within 10 min in case of formulation SD1, in which the carrier used was PVP K30 (drug: carrier 1: 1 ratio). All Roflumilast solid dispersions prepared using PVP K30 showed ≥ 85% of drug release within 15 min. Formulations SD4 to SD12 showed maximum % of drug release within 45 min. Hence, in the case of Roflumilast solid dispersions prepared by the solvent evaporation method, SD1 was considered as the optimized formulation. The maximum percentage of drug release was observed within 10min, *i.e.*, 99.02% in case of formulation SD18, in which the carrier used was PEG 4000 (drug: carrier 1: 3 ratio). All Roflumilast solid dispersions developed using PEG 4000 also showed ≥ 85% of drug release within 15 min. All the formulations showed a maximum % of drug release within 45 min. Therefore, SD18 was considered as the optimized formulation among

Roflumilast solid dispersions prepared by melting method.

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REFERENCES:

1. Debjit B, Chiranjib B, and Augsburger L: Fast dissolving tablets: an overview. Journal of Chemical and Pharmaceutical Research 2009; 1(1): 163-177.
2. Hirani JJ, Rathod DA and Vadalia KR: Orally disintegrating tablets: a review. Tropical Journal of Pharmaceutical Research 2009; 8(2): 161-172.
3. Daliresp (roflumilast) tablets, prescribing information. New York: Forest; 2011. Available at: www.frx.com/pi/ Daliresp_pi.pdf
4. Bethke TD and Lahu G: High absolute bioavailability of the new oral phosphodiesterase-4 inhibitor Roflumilast. International Journal of Pharmacology and Therapeutics 2011; 49(1): 51-57.
5. Torrado JJ and Augsberger LL: Tableting of multi-particulate modified release systems. In: pharmaceutical dosage forms-tablets. Rational design and formulation. Informa Healthcare, London, Edition 3rd, Vol. 2, 2008: 509-533.
6. Sharma D, Kumar D, Singh M, Singh G and Rathore MS: Fast disintegrating tablets: a new era in novel drug delivery system and new market opportunities. Journal of Drug Delivery and Therapeutics 2012; 2(3): 74-86.
7. Deshmukh VN: Mouth is dissolving drug delivery system: A review. International Journal of Pharm Tech Research 2012; 4(1): 412-421.
8. Patel ST and Sengupta M: Fast dissolving tablet technology - a review. World Journal of Pharmacy and Pharmaceutical Sciences 2013; 2(2): 485-508.
9. Bi Y: Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chemical and Pharmaceutical Bulletin 1996; 44: 2121-2127.
10. Jeong SH, Takaishi Y and Park K: Material properties for making fast dissolving tablets by a compression method. Journal of Material Chemistry 2008; 18: 3527-3535.
11. Patel MS and Patel NM: Flowability testing of directly compressible excipients according to British Pharmacopeia. Jou of Pharm Res 2009; 8: 66-69.
12. Kumar S, Gupta S and Sharma P: A review of recent trends in oral drug delivery-fast dissolving formulation. Advances in Biological Research 2012; 6(1): 6-13.
13. Hindustan AA, Suresh KC, Kishore KR, Anil KB, Chandra SA, Sushma K, Sairam T and Sivaji S: A novel technique in formulation and evaluation of mouth dissolving nimesulide tablets. Journal of Advances in Pharmaceutical Research 2010; 1(2): 101-107.
14. Bhupendra GP and Nayan R: A review on recent patents on fast-dissolving drug delivery system. International Journal of Pharm Tech Research 2009; 1(3): 790-798.
15. Gohel MC, Bansal G and Bhatt N: Formulation and evaluation of orodispersible taste masked tablets of famotidine. Pharma-Bio World 2005, 3: 75-80.
16. Indian Pharmacopoeia, Vo. 3, 2018: 3137-3138.

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