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ORIGINAL ARTICLE

Design Development and Evaluation of Solid Dispersion Incorporated into Hard Gelatin Capsule

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ABSTRACT
This study aimed to develop and evaluate solid dispersions of Dolutegravir (DTG) using hydrophilic carriers to enhance its dissolution profile and oral bioavailability, subsequently formulating these dispersions into hard gelatin capsules. Solid dispersions were prepared via solvent evaporation and melt fusion, using Polyethylene glycol 6000 (PEG 6000) and Poloxamer 188 at drug: polymer ratios of 1:1, 1:2, and 1:3. Characterization included preformulation studies, saturation solubility, drug-excipient compatibility (FTIR, DSC), drug content, dissolution studies, and stability analysis. The optimized formulation was incorporated into hard gelatin capsules and evaluated for standard pharmacopeial quality parameters. Solid dispersions exhibited significantly enhanced solubility of DTG. The optimized formulation (F6, DTG: Poloxamer 188 at 1:3) achieved 98.93% cumulative drug release within 60min and demonstrated satisfactory physicochemical and stability parameters. Capsules showed excellent weight uniformity, disintegration (5.35min), and stable drug content post-accelerated storage.
Keywords: *Dolutegravir, Solid dispersion, Poloxamer 188, Hard gelatin capsule, Bioavailability enhancement*

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INTRODUCTION

The oral route remains the most convenient and preferred route for drug administration due to its ease of use, patient compliance, and cost-effectiveness [1]. However, a major limitation in the successful delivery of many therapeutic agents via this route is their poor aqueous solubility, which leads to low oral bioavailability [2]. According to the Biopharmaceutical Classification System (BCS), class II drugs exhibit low solubility and high permeability, where the dissolution rate is the rate-limiting step for absorption. Dolutegravir, an antiretroviral drug belonging to the integrase strand transfer inhibitor (INSTI) class, is widely used in the treatment of HIV-1 infection [2-4]. Despite its potent antiviral activity, Dolutegravir suffers from poor aqueous solubility, which significantly affects its bioavailability and therapeutic efficacy [5]. Enhancing the solubility of such poorly water-soluble drugs is a key challenge in pharmaceutical formulation development. Among the various solubility enhancement strategies, solid dispersion is a well-established technique that involves dispersing the drug in an inert hydrophilic carrier matrix. This approach can improve dissolution rate by enhancing wettability, reducing particle size, and converting the crystalline drug into an amorphous form. Polymers such as polyethylene glycol (PEG 6000) and polyvinylpyrrolidone (PVP K30) have shown significant potential in solid dispersion systems due to their solubilizing and stabilizing properties [6-10]. SD has been manufactured in a variety of techniques, including via fusion and solvent evaporation. Solvent evaporation is one of the most common methods used in the pharmaceutical industry to increase the solubility of weakly water-soluble medications. Because the Drug and Carrier are combined using a solvent rather than heat as in the melting process, this approach was designed primarily for heat-unstable components. The fusion technique uses heat to melt a physical mixture of medicine and polymer, which is then cooled and solidified while vigorously stirring. To attain the desired particle size, the solid form is broken, pulverized, and sieved. Although this

method has several advantages, including low cost and simplicity, it also has significant drawbacks, including heat-labile product degradation, incompatibility with high melting point carriers, and the requirement for drug and carrier Compatibility to prevent phase separation. Solubility, or the process of dissolving a solute with a solvent to get a homogeneous solution, is a critical factor in attaining the drug concentration in systemic circulation required for the desired(anticipated) pharmacological action. Solubility is one of the most important physicochemical qualities of a medicine, and an orally administered drug's bioavailability is mostly influenced by its Solubility in the digestive tract and permeability across cell membranes. Oral ingestion is the most widely used and easy way of drug delivery since it is straightforward to provide medications orally, and drugs designed for oral administration provide advantages such as stability, accurate dosing, and convenience of production. Capsules provide an alternative to tablets for the oral delivery of medicinal substances. Capsules have an advantage over tablets since they can deliver solids, non-watery liquids, semisolids, and hard dosage forms in a single dose. The shell is an essential part of capsule dosage forms. The capsule shells can be hard or soft, and they are made of gelatin or a non-gelatin polymer component like hypromellose or starch, as well as water and a non-volatile plasticizer.

The present study was undertaken with the objective to develop and evaluate Dolutegravir solid dispersions using hydrophilic carriers, and to incorporate the optimized formulation into hard gelatin capsules. The study aimed to improve the drug's solubility, dissolution rate, and overall oral bioavailability through formulation optimization and standard evaluation protocols.

MATERIAL AND METHODS

Material

Dolutegravir was received as a gift sample from Emcure Pharmaceuticals Pvt. Ltd., Pune, India. Polyethylene glycol 6000 (PEG 6000) and polyvinylpyrrolidone K30 (PVP K30) were procured from Loba Chemie Pvt. Ltd., Mumbai. All other chemicals and reagents used were of analytical grade and used as received without further purification. Hard gelatin capsules (size “0”) were obtained from a local supplier.

Dolutegravir sample preparation for UV spectrophotometric method

A stock solution of Dolutegravir was prepared by dissolving 10 mg of pure drug in a small amount of methanol and making up the volume to 100 ml with methanol in a volumetric flask to obtain a concentration of 100 µg/ml. This was further diluted with solvent to prepare working standards in the range of 5–25 µg/ml. The absorbance of each solution was measured at the maximum wavelength (λmax) of 258 nm using a UV-Visible spectrophotometer (Shimadzu UV-1800, Japan) against a blank. A calibration curve was plotted to determine the linearity and correlation coefficient [11].

Preparation of Solid Dispersions

Solid dispersions of dolutegravir were prepared utilizing two main methods: solvent evaporation and melt fusion, employing hydrophilic carriers PEG 6000 and Poloxamer 188 at varying drug-to-polymer ratios (1:1, 1:2, and 1:3).

Solvent Evaporation Method

Accurately weighed quantities of dolutegravir and the selected polymer (PEG 6000 or Poloxamer 188) were dissolved in methanol. The resulting solution was subjected to sonication and subsequent stirring for 1 hour on a magnetic stirrer to ensure homogeneity. Methanol was then evaporated using a water bath maintained at 60°C until complete solvent removal was achieved. The resulting solid mass was dried thoroughly, pulverized, and then sifted through a #100 sieve. The final solid dispersion was stored in a desiccator until further use [12-14].

Melt Fusion Method

Solid dispersions were also prepared using the melt fusion technique. The polymer (PEG 6000 or Poloxamer 188) was weighed accurately and melted in a porcelain dish at 60°C. The calculated quantity of dolutegravir was incorporated into the molten polymer and stirred to achieve uniform mixing. The mixture was quickly cooled in an ice bath to solidify. The solidified mass was then powdered using a mortar and pestle and passed through a suitable sieve. The dispersions were stored in a desiccator for further analysis [12-14].

Characterization of Solid dispersions

Physical Examination

Each batch of prepared solid dispersion (via solvent evaporation and melt fusion methods, using PEG 6000 and Poloxamer 188 at ratios 1:1, 1:2, 1:3) was evaluated visually for colour, odour and appearance and observations were recorded [13-17].

Determination of Percent Practical Yield

Percent practical yield was calculated to assess process efficiency:

$$\% \text{ Practical yield} = \frac{\text{Practical mass (Solid dispersion)}}{\text{Theoretical mass (Drug + Carrier)}} * 100$$

Saturation Solubility Study

The shake flask method was employed to determine the improvement in drug solubility. A measured excess of solid dispersion was agitated in water at 25°C ±2°C for 24h. The mixture was centrifuged and the supernatant analyzed at 258nm via UV spectrophotometry [13-17].

Drug Content Determination

The drug content of each batch was quantified to ensure uniform dispersion. Solid dispersion samples equivalent to 10 mg dolutegravir were dissolved in methanol, filtered, and analyzed at 258nm [13-17].

In Vitro Dissolution Study

Dissolution profiles were evaluated using a USP Type I (Basket) apparatus at 50 RPM in 900 mL water (37±0.5°C). Aliquots withdrawn at regular intervals up to 60 minutes, analyzed spectrophotometrically at 258nm [13-17].

Differential scanning calorimetry (DSC)

The differential scanning calorimetry (DSC) measurement was performed using a Mettler Toledo Differential scanning calorimeter instrument, Mumbai, India. Optimized solid dispersion weighing around 6–7 mg was heated under nitrogen gas in sealed aluminum pans over a temperature range of 25– 375 °C and the thermograms were recorded at a heating rate of 40 °C/min [13-17].

Formulation of capsules

The optimized solid dispersion batch was selected based on solubility and dissolution data. A fixed amount equivalent to 50 mg of Dolutegravir was filled manually into hard gelatin capsules (size 0). Each capsule batch was evaluated for pharmaceutical quality control parameters.

Pre-capsulation study

The solid dispersion powders were evaluated for flow properties prior to encapsulation:

Angle of repose was measured by the fixed funnel method.

Bulk density and **tapped density** were determined using standard procedures.

Carr's Index and **Hausner's ratio** were calculated to assess flow behavior [18].

Post-capsulation evaluation

Physical Appearance

The appearance of the core capsule i.e., colour uniformity, dents or cracks if any were observed [18-21].

Locked Length and Diameter

Using vernier calipers the locked length and diameter of capsules were measured during the filling of capsules [18-21].

Weight variation

Twenty capsules from each batch were individually weighed using an analytical balance. The mean weight and standard deviation were calculated. The test was performed as per the Indian Pharmacopoeia specifications [18-21].

Disintegration time

Disintegration was assessed using a USP disintegration apparatus (Electro lab ED-2L) in 900 ml of distilled water maintained at 37 ± 0.5 °C. The time taken for complete disintegration of six capsules was recorded [18-21]**.**

Drug content uniformity

Ten capsules were randomly selected, and the content from each was dissolved in phosphate buffer pH 6.8. The solutions were filtered, suitably diluted, and analyzed for Dolutegravir content using a UV-visible spectrophotometer at 260 nm [18-21].

In vitro dissolution studies

Dissolution testing was carried out using USP Type II (paddle) apparatus. Capsules were placed in 900 ml phosphate buffer pH 6.8 at 37 ± 0.5 °C and stirred at 50 rpm. Samples were withdrawn at predetermined time intervals (5, 10, 15, 30, 45, and 60 minutes), filtered, and analyzed spectrophotometrically [18-21].

RESULTS

Determination of λmax for Dolutegravir

The UV absorption spectrum of dolutegravir was recorded using a double-beam UV-Visible spectrophotometer. Methanol was employed as solvents to confirm the drug's characteristic wavelength. The λmax was observed at 258 nm [Fig.1]. The calibration curve of dolutegravir was drawn by measuring the absorbance of different concentrations in water at 258 nm [Tab. 1, Fig. 2].

Table 1: Determination of λmax for Dolutegravir

Sr.no.	Concentration (ppm)	Absorbance
1.	5	0.2335
2.	10	0.4658
3.	15	0.7024
4.	20	0.9053
5.	25	1.1005

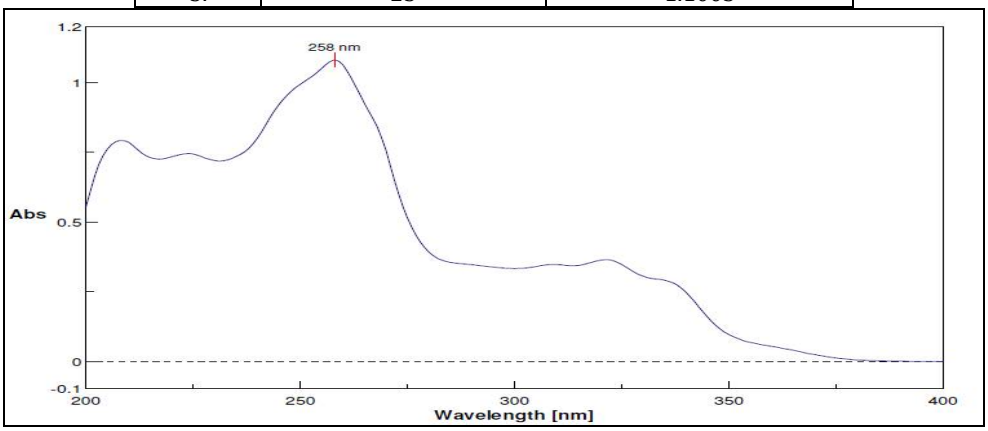

Figure 1: Spectra of Dolutegravir

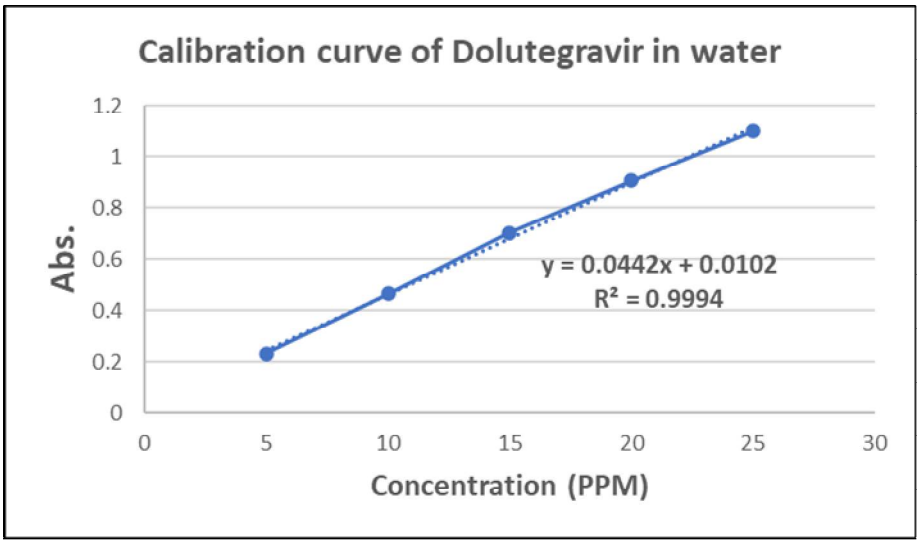

Figure 2: Calibration curve of Dolutegravir

FT-IR of Dolutegravir

The IR spectrum of Dolutegravir was recorded by using FTIR spectrometer. IR spectra were shown in figure 6. Characteristic functional groups were observed in FTIR spectrum as shown in Figure 3.

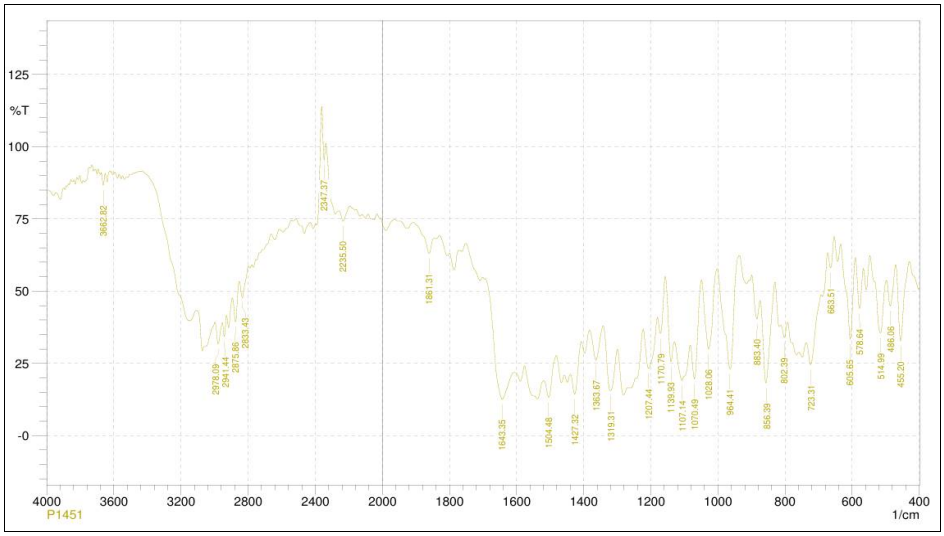

Figure 3: IR of Dolutegravir

Drug excipient compatibility study:

The FTIR Spectra of Dolutegravir in pure form and their physical mixture was observed, the result showed that there is no interaction between drug and polymer. IR spectra for compatibility study were shown in figure 4 and 5.

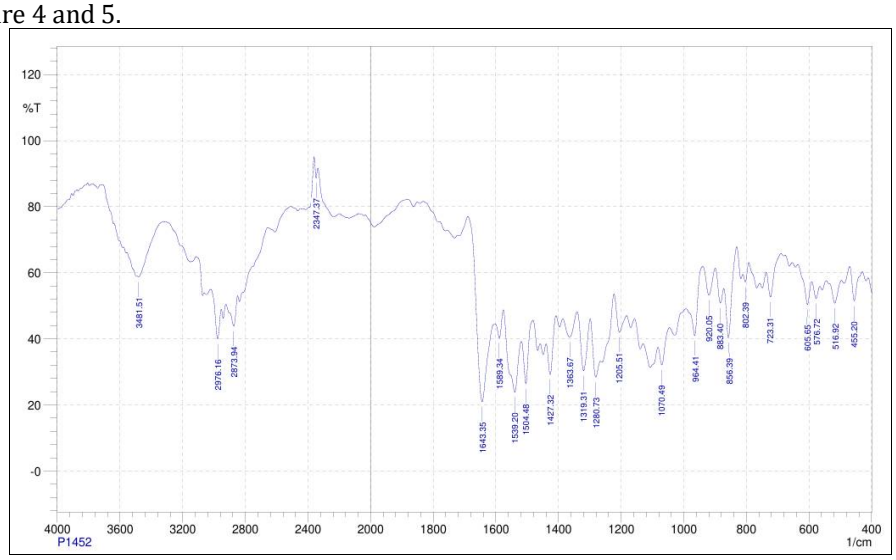

Figure 4: IR of Dolutegravir

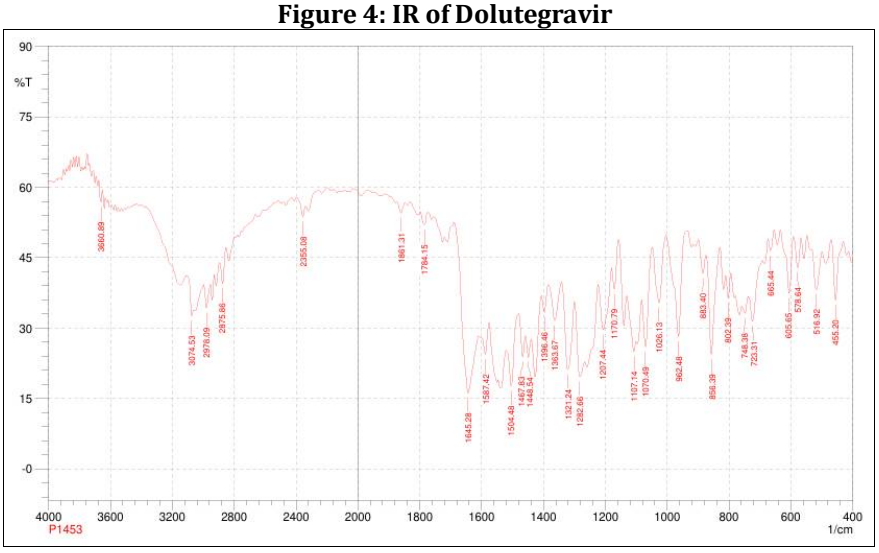

Figure 5: IR of Physical mixture (Dolutegravir: Poloxamer 188)

Phase Solubility Study of Carriers:
Phase solubility study of drug and carriers were performed by using different polymeric solutions of 1% and 2% of PEG 6000 and Poloxamer 188. Concentration of Dolutegravir in individual polymeric solution was calculated by using equation of line obtained from calibration curve in water. On the basis of results obtained from solubility data maximum solubility of Dolutegravir was found in polymeric solution of Poloxamer 188 (2%) that was 0.0145 mg/ml and PEG 6000 (2%) that was 0.0125 mg/ml. On the basis of solubility study Poloxamer 188 and PEG 6000 were selected for the preparation of solid dispersion.

Polymer	Quantity of Drug (mg)	Quantity of Carrier (mg)	Ratio (Drug: Carrier)
PEG 6000	300	300	1:1
	300	600	1:2
	300	900	1:3
Poloxamer 188	300	300	1:1
	300	600	1:2
	300	900	1:3

Table 2: Phase Solubility Study of Carriers

Preparation of Physical mixture:
Physical mixtures were created using mortar and pestle with trituration method. Accurately weighed quantity of drug and polymer were used for preparation of physical mixture.

Polymer	Quantity of Drug (mg)	Quantity of Carrier (mg)	Ratio (Drug: Carrier)
PEG 6000	300	300	1:1
	300	600	1:2
	300	900	1:3
Poloxamer 188	300	300	1:1
	300	600	1:2
	300	900	1:3

Table 3: Physical Mixtures

Formulation of Solid Dispersion:

Batch code	Drug (Dolutegravir) in mg	Polymer in mg	
		PEG 6000	Poloxamer 188
Solvent evaporation method			
F1	300	300	-
F2	300	600	-
F3	300	900	-
F4	300	-	300
F5	300	-	600
F6	300	-	900
Melt fusion method			
F7	300	300	-
F8	300	600	-
F9	300	900	-
F10	300	-	300
F11	300	-	600
F12	300	-	900

Table 4: Formulation of Solid Dispersion

Evaluation of Solid Dispersions:
Prepared solid dispersions by both methods were evaluated for different parameters and results were mentioned as follows:

Physical evaluation
All prepared batches were examined for physical evaluation parameters such as colour, odour and appearance. All batches were having a uniform appearance and there was no odour difference in between any batch as all batches were characteristic in odour. Colour difference was observed among some batches as per polymer and its concentration in formulation. The results for all the batches were mentioned in table 5.

Table 5: Physical evaluation of solid dispersions

Batches	Colour	Odour	Appearance
F1	White	Characteristic	Amorphous powder
F2	Off-white	Characteristic	Amorphous powder
F3	Off-white	Characteristic	Amorphous powder
F4	White	Characteristic	Amorphous powder
F5	White	Characteristic	Amorphous powder
F6	Off-white	Characteristic	Amorphous powder
F7	Off-white	Characteristic	Amorphous powder
F8	Off-white	Characteristic	Amorphous powder
F9	Off-white	Characteristic	Amorphous powder
F10	White	Characteristic	Amorphous powder
F11	White	Characteristic	Amorphous powder
F12	Off-white	Characteristic	Amorphous powder

Determination of Percent Practical Yield:

All the formulated batches were examined for percent practical yield determination and results were found in range of 85 – 95 %. The results were expressed in table 6.

Table 6: Determination of percent practical yield

Batches	Practical mass (Solid dispersion) mg	Theoretical yield (Drug + Carrier) Mg	% Practical yield
F1	529	600	88.11
F2	822	900	91.36
F3	1123	1200	93.62
F4	535	600	89.23
F5	831	900	92.36
F6	1139	1200	94.88
F7	519	600	86.55
F8	802	900	89.12
F9	1113	1200	92.77
F10	525	600	87.45
F11	827	900	91.88
F12	1125	1200	93.71

Saturation solubility study of solid dispersion and physical mixture:

Saturation solubility study of solid dispersion and physical mixture were performed by using water as solvent. Shake flask method was used for determination of solubility for both solid dispersion as well as physical mixture. Concentration of Dolutegravir in solid dispersion and physical mixture was calculated by using equation of line obtained from calibration curve in water.

Physical mixture	Ratio	Absorbance obtained	Concentration obtained (µg/ml)	Dilution factor (*10) (µg/ml)	Concentration obtained (mg/ml)
Dolutegravir: PEG6000	1:1	0.2854	6.23	62.26	0.062
	1:2	0.3458	7.59	75.93	0.076
	1:3	0.3788	8.34	83.39	0.083
Dolutegravir: Poloxamer 188	1:1	0.2811	6.13	61.29	0.061
	1:2	0.3356	7.36	73.62	0.074
	1:3	0.4555	10.07	100.75	0.101

Table 7: Saturation solubility study for Physical mixture

Drug content determination:

The actual drug content of all the 12 formulations is shown in Table 8. The drug content of the prepared solid dispersion formulations was found to be in the range of 94.00 – 101 % indicating the application of the present methods for the preparation of Solid dispersions with high content uniformity. The maximum % drug content was found to be 100.41 % in F6 batch.

Batches	Drug content (%)
F1	94.85
F2	100.32
F3	98.92
F4	96.04
F5	98.69
F6	100.41
F7	97.52
F8	99.62
F9	98.92
F10	100.12
F11	94.97
F12	100.08

Table 8: Drug Content Determination

In vitro dissolution study:

In vitro dissolution study was performed for all the prepared batches as well as with physical mixtures of different polymers in different ratios. The percent cumulative drug release for all the 12 batches were found in the range of 80.33– 98.93 %. As the concentration of polymer in solid dispersion increases percent cumulative drug release also increases with decrease in time. On the basis of in vitro dissolution data, it was found that F6 batch was having highest percent cumulative drug release that is 98.93 % with respective to other batches. The results were expressed in table 9.

In vitro dissolution study was also performed with physical mixtures of dolutegravir: Polymers in different ratios and results were found in range of 28.87 – 36.00 %. The results were expressed in table 9.

Table 9: In vitro dissolution study for Batches

Time (min.) / Batches	% Cumulative Drug Release (%)											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
15	11.45	12.05	18.51	14.15	17.34	24.04	11.47	14.26	18.46	15.13	16.04	20.25
30	37.95	39.23	48.64	41.44	44.77	63.66	35.07	38.82	41.57	44.92	43.77	46.17
45	63.33	67.31	84.83	74.85	80.46	95.77	58.1	62.3	70.55	76.15	78.07	76.00
60	85.76	87.64	94.77	89.14	93.31	98.93	80.33	84.53	89.05	90.42	90.86	94.51

Table 10: In vitro dissolution study for physical mixtures

Time (min.) ↓ / Batches →	% Cumulative Drug Release (%) for Physical mixtures					
	Drug: PEG 6000			Drug: Poloxamer 188		
	1:1	1:2	1:3	1:1	1:2	1:3
15	8.82	10.82	11.38	9.8	11.37	12.27
30	16.2	17.8	19.67	17.8	18.45	20.99
45	19.69	20.81	24.13	21.77	24.85	26.14
60	28.87	31.87	34.7	30.11	32.99	36

Conclusion: On the basis of results obtained from evaluation of all the batches as well as dissolution profile study of solid dispersions F6 was concluded as optimised batch which was having ratio of 1:3 (Dolutegravir: Poloxamer 188) and % cumulative drug release was found as 98.93%.

Characterization of optimized solid dispersion batch (F6):

a. FTIR spectroscopy for optimized batch:

The FTIR spectroscopy for optimized solid dispersion batch was performed and observed frequencies were compared with the standard IR of pure drug sample. The respective IR was represented in figure 12, 13.

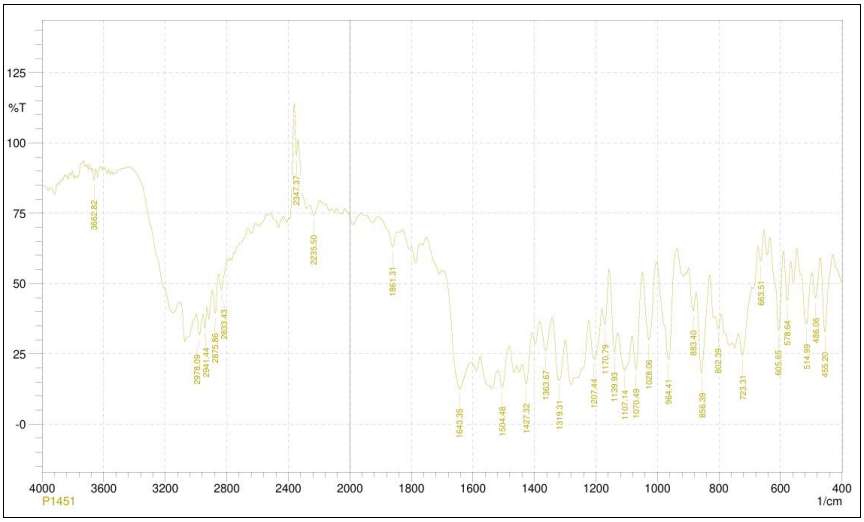

Figure 12: IR of pure Dolutegravir

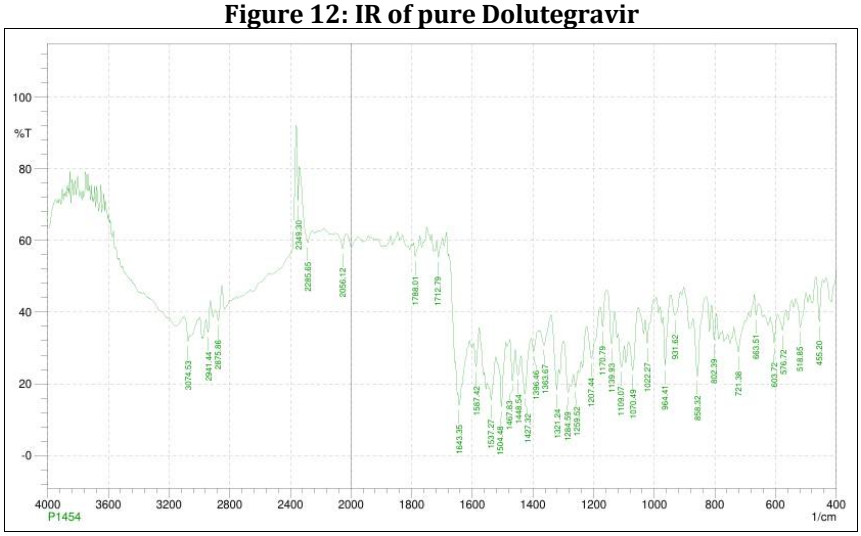

Figure 13: IR of Optimized batch (Solid dispersion of Dolutegravir)

Differential Scanning Calorimetry (DSC) Study:

The DSC thermogram of Dolutegravir and optimized batch of solid dispersion was taken by using DSC-60, Shimadzu. The results were expressed in figure 14 and 15.

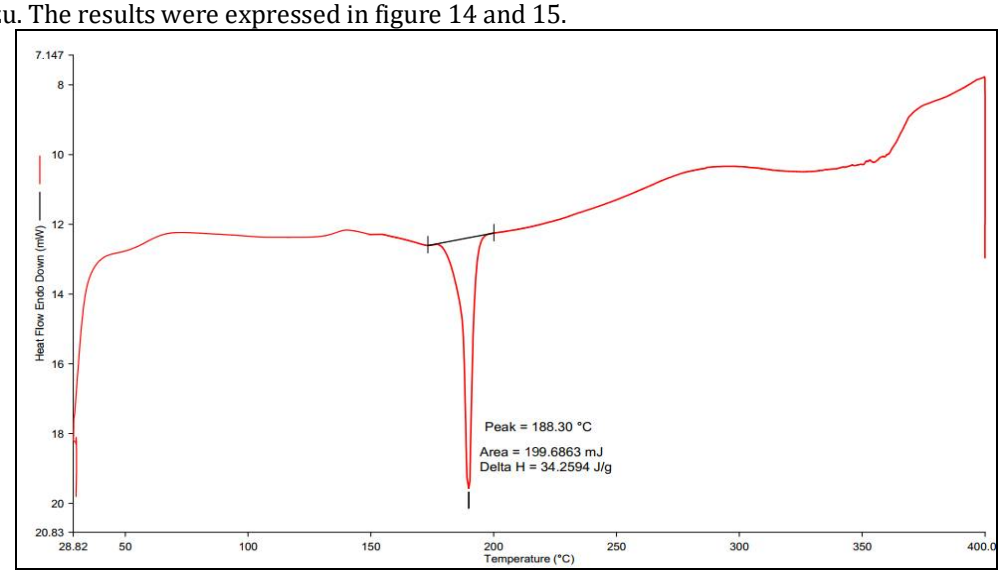

Figure 14: DSC of Pure Dolutegravir

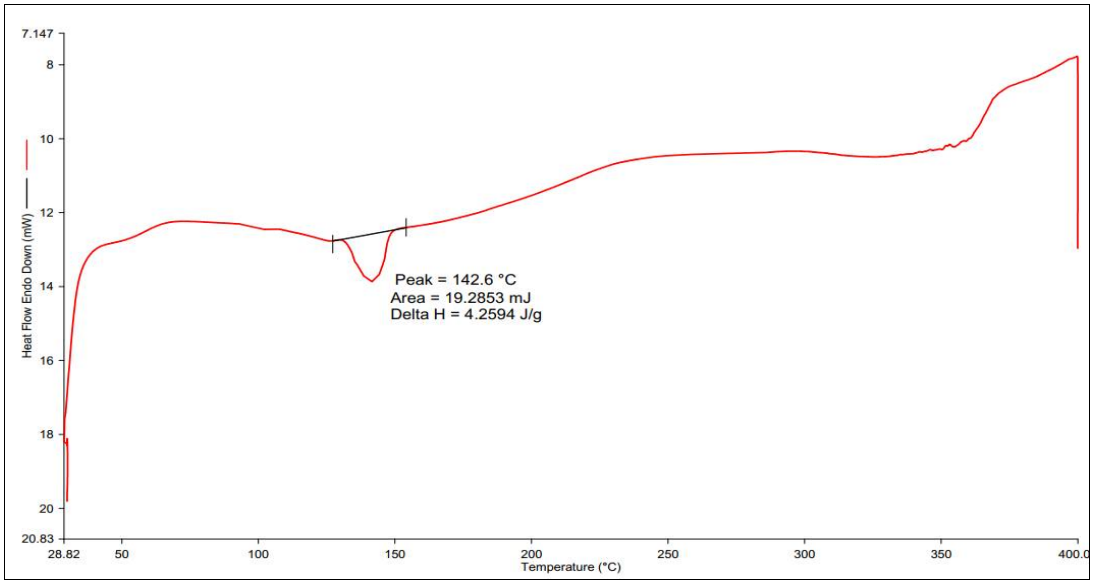

Figure 15: DSC of Optimized batch of solid dispersion

Differential Scanning Calorimetry (DSC) was employed to evaluate the thermal behavior of pure Dolutegravir and its solid dispersion. The DSC thermogram of pure Dolutegravir exhibited a sharp endothermic peak at 188.3°C with an enthalpy of fusion of 34.26 J/g, indicating its highly crystalline nature. In contrast, the DSC curve of the solid dispersion showed a broad endothermic event at approximately 142.6°C, with no detectable melting peak corresponding to crystalline Dolutegravir. This marked disappearance of the drug's characteristic melting endotherm suggests that Dolutegravir has been successfully converted into an amorphous or molecularly dispersed form within the carrier matrix. The absence of crystallinity in the dispersion confirms the effectiveness of the solid dispersion technique in enhancing the solubility profile of Dolutegravir.

Formulation of capsules:

A hard-gelatin capsule formulation was developed to convert the optimized Dolutegravir solid dispersion (SD, 25 % w/w drug) into a patient-friendly oral dosage form that ensures dose accuracy, rapid disintegration, and robust stability. The fill blend comprised Dolutegravir SD as the active carrier, lactose monohydrate (spray-dried) as diluent to achieve the target 300 mg fill weight, sodium starch glycolate (SSG) or croscarmellose sodium (CCS) as super-disintegrants for fast capsule break-up, talc as glidant to improve flow, and magnesium stearate as lubricant to minimize die-wall friction during filling.

Table 14: Formulation Strategy

Sr.no.	Ingredients	Quantity (mg)							
		F1	F2	F3	F4	F5	F6	F7	F8
1.	Dolutegravir SD eq. to 50 mg Dolutegravir	200	200	200	200	200	200	200	200
2.	Sodium starch glycolate	6	9	12	15	-	-	-	-
3.	Croscarmellose sodium	-	-	-	-	6	9	12	15
4.	Lactose monohydrate	88	85	82	79	88	85	82	79
5.	Magnesium stearate	3	3	3	3	3	3	3	3
6.	Talc	3	3	3	3	3	3	3	3
Total weight of blend		300 mg							
Avg. weight of empty capsule		60 mg							
Total weight of capsule		360 mg.							

Pre compression evaluation of powder blend:

The powder blend from all the batches were evaluated for density and flow property parameters which includes Bulk density, Tapped density, Compressibility index, Hausner's ratio and Angle of repose. The results were expressed as follows in table 15.

Table 15: Precompression parameters

Batches	Bulk density	Tapped density	Compressibility index	Hausner's ratio	Angle of repose
F1	0.462	0.531	13	1.15	28.4
F2	0.465	0.531	12.4	1.14	27.6
F3	0.468	0.53	11.7	1.13	26.8
F4	0.472	0.528	10.6	1.12	25.7
F5	0.459	0.531	13.5	1.16	29.1
F6	0.461	0.527	12.5	1.14	27.9
F7	0.465	0.526	11.6	1.13	26.4
F8	0.47	0.525	10.4	1.11	25.2

The precompression evaluation of capsule blend batches (F1–F8) indicated satisfactory flow and compressibility characteristics. Bulk density values ranged between 0.459–0.472 g/cm^3, while tapped density values were between 0.525–0.531 g/cm^3. Hausner's ratio for all batches was below 1.25, indicating good to excellent flow properties. Carr's index values ranged from 10.4% to 13.5%, reflecting excellent compressibility behavior. The angle of repose for all formulations was observed between 25.2° and 29.1°, supporting the good flowability of the blends. Thus, the powder mixtures were found to be suitable for uniform capsule filling without processing issues.

Evaluation of Capsules:

Physical Appearance:

The physical appearance of the prepared capsules (Batches F1–F8) was visually inspected for attributes such as color uniformity, shape, surface texture, and integrity. All capsules were found to be uniform in appearance, exhibiting a smooth, glossy surface without any cracks, dents, or deformities. The capsules maintained their structural integrity without any signs of brittleness or stickiness. No visible color variation or surface imperfections were observed, confirming the proper encapsulation process and compatibility of solid dispersion with excipients. The results indicated that all capsule formulations possessed an elegant and pharmaceutically acceptable appearance, suitable for further evaluation and storage.

Locked length and diameter:

The locked length and diameter of the filled capsules for all eight batches (F1–F8) were measured using a digital vernier caliper to ensure dimensional uniformity and consistency. The locked length of the capsules was found to be in the range of 18.4 mm to 18.6 mm, while the diameter was recorded between 6.6 mm to 6.8 mm across all batches. The minimal variation observed was within acceptable pharmaceutical limits, indicating the precision of the capsule filling process. No significant differences were observed among the batches, suggesting uniform encapsulation and the appropriate selection of capsule size for the given formulation. These results confirmed that all capsules maintained dimensional integrity essential for aesthetic quality, patient compliance, and mechanical stability during handling and storage.

Table 16: Locked length and Diameter

Batches	Locked length (mm)	Diameter (mm)
F1	18.4 ± 0.05	6.6 ± 0.04
F2	18.5 ± 0.04	6.7 ± 0.03
F3	18.6 ± 0.06	6.8 ± 0.05
F4	18.5 ± 0.04	6.7 ± 0.03
F5	18.4 ± 0.05	6.6 ± 0.04
F6	18.6 ± 0.06	6.7 ± 0.04
F7	18.5 ± 0.05	6.8 ± 0.03
F8	18.4 ± 0.04	6.6 ± 0.03

Weight Variation:

The weight variation of the filled capsules for all eight batches (F1–F8) was evaluated by individually weighing capsules from each batch using a digital analytical balance. The average capsule weights ranged between 354 mg and 362 mg, with standard deviations within acceptable limits. All capsules complied with the Indian Pharmacopoeia (IP) specifications, which allow a ±7.5% deviation for capsule weights between 300 mg and 500 mg. The low standard deviation values indicated uniformity in capsule filling and excellent control over the encapsulation process. Thus, the prepared capsules exhibited consistent weight distribution suitable for uniform dosing.

Table 17: Weight variation results

Batches	Weight variation	
	Weight (mg) ± S. D	Weight variation (7.5 %)
F1	354.2 ± 2.3	Passes
F2	356.8 ± 1.9	Passes
F3	359.1 ± 2.1	Passes
F4	360.3 ± 2.5	Passes
F5	355.7 ± 2.0	Passes
F6	358.4 ± 2.2	Passes
F7	361.2 ± 1.8	Passes
F8	361.2 ± 2.4	Passes

Drug content uniformity:

The drug content of Dolutegravir in all eight capsule batches (F1–F8) was determined using a validated UV spectrophotometric method at 258 nm after appropriate dilution. The drug content was found within the range of 96.4% to 99.2%, which lies well within the acceptable IP range of 90% to 110% of the label claim. The results indicated excellent drug-excipient compatibility and uniform distribution of the solid dispersion within the capsule matrix. Minimal batch variation confirmed that the encapsulation process was consistent and did not impact the drug's stability or homogeneity.

Table 18: Drug content

Batches	Drug content
F1	96.4 ± 1.1
F2	97.2 ± 0.9
F3	98.3 ± 0.8
F4	99.2 ± 0.7
F5	97.4 ± 1.2
F6	98.6 ± 1.0
F7	98.1 ± 0.9
F8	97.6 ± 1.0

Disintegration time:

The disintegration test was carried out for all capsule batches using a USP disintegration apparatus in distilled water at 37 ± 0.5 °C. The disintegration time for all batches ranged between 4.50 to 6.30 minutes, indicating rapid breakdown of the capsule shell and internal contents. All batches complied with the pharmacopeial limit of not more than 30 minutes. The variation in disintegration time is attributed to changes in super disintegrant concentration across batches. These results confirmed the effective disintegration capability necessary for prompt drug release.

Table 19: Disintegration time results

Batches	Disintegration time (min.)
F1	6.30
F2	5.45
F3	5.10
F4	4.50
F5	6.10
F6	5.35
F7	5.00
F8	4.55

In vitro Dissolution study:

The in-vitro dissolution study of the formulated capsules was performed using USP Type I (Basket) apparatus at 50 rpm in 900 mL of 0.1 N Hydrochloric acid maintained at 37 ± 0.5 °C. Samples were withdrawn at specified intervals up to 60 minutes and analyzed spectrophotometrically at 258 nm. The cumulative drug release after 60 minutes ranged between 96.17% and 99.12% across the batches. The variation was primarily influenced by the disintegrant concentration, with higher levels facilitating faster drug release. All batches exhibited satisfactory dissolution behavior, suitable for immediate-release profile.

Table 20: In vitro dissolution study

Time (min.) ↓ / Batches →	% Cumulative Drug Release (%)							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5	12.54	13.12	14.05	15.08	12.65	13.75	13.21	14.02
10	25.71	26.85	29.22	31.45	26.11	28.63	27.92	29.31
15	40.15	42.34	45.23	48.02	41.17	44.76	43.63	45.25
20	55.27	58.12	61.54	64.31	57.62	60.83	59.44	61.21
30	71.48	74.66	77.91	80.72	74.03	76.84	75.29	77.11
40	82.15	85.31	88.74	91.24	84.66	87.92	86.73	88.06
50	90.03	92.44	94.25	95.93	91.28	93.72	92.51	93.84
60	96.17	97.83	98.94	99.12	97.02	98.31	97.45	98.02

Stability Study:

The optimized formulation batch of Dolutegravir Solid dispersion loaded capsule wrapped in aluminum foil and subjected to 40 ± 2^0C temperature and 75 ± 5% RH in stability chamber for the period of 3 months. The formulation was analyzed for Physical appearance, Locked length, Diameter, Drug content uniformity and Disintegration time study. Stability studies were carried out as per ICH Q1A(R2) guidelines and the results were mentioned in table.

CONCULSION

The present research successfully demonstrated that formulating dolutegravir as a solid dispersion using hydrophilic carriers, specifically Poloxamer 188, significantly improves its solubility and dissolution rate. The optimized solid dispersion (dolutegravir: Poloxamer 188, 1:3, solvent evaporation method) achieved nearly complete drug release within 60 minutes, far surpassing both physical mixtures and other formulations. Incorporation of the optimized solid dispersion into hard gelatin capsules resulted in a final dosage form exhibiting excellent physicochemical attributes—uniform appearance, ideal mechanical properties, rapid disintegration, uniform drug content, and robust in vitro dissolution. Accelerated stability studies further confirmed the formulation's integrity and consistent performance over three months. These findings establish the suitability of solid dispersion technology, combined with capsule dosage form, as a robust strategy for overcoming the limitations of poor aqueous solubility associated with BCS Class II drugs like dolutegravir. The developed capsule formulation enables enhanced oral bioavailability, dose accuracy, and patient compliance, supporting its potential translation to clinical development and commercialization. This work contributes to the growing body of evidence that rational formulation design using solubility-enhancing carriers and immediate-release technologies can significantly impact antiretroviral therapy outcomes.

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