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Development and Evaluation of Immediate Release Tablets of Dolutegravir Sodium by Solid Dispersion Technique

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ABSTRACT

The Dolutegravir Sodium is an antiretroviral drugs bear some significant drawbacks such as, low solubility, low bioavailability, and undesirable side effects. Efforts have been made to design immediate release drug delivery systems for anti-HIV agents to increase the solubility & bioavailability and decrease the degradation/metabolism in the gastrointestinal tract, and to deliver them to the target cells selectively with minimal side effects. The half-life of Dolutegravir is 15 hours. It gets metabolized mainly in the liver, dolutegravir is a BSC class-II drug, it has low solubility and high permeability, hence need to enhance the solubility of by using different solid dispersion techniques. Solid dispersion of dolutegravir is prepared by rotary solvent evaporation method. The purpose of this study was to develop immediate release tablets of poorly water soluble dolutegravir. In this study dolutegravir immediate release tablet were prepared by direct compression method using superdisintegrants at a concentration range 0.5-5% .The tablet is based on interactive mixture of components, consisting of carrier particles covered by fine particles of dolutegravir. The tablets were evaluated for hardness, friability, DT, swelling index ratio and in-vitro drug release. FT-IR, XRD and physical compatibility study were conducted for drug excipient interactions.

Keywords: *Antiretroviral, bioavailability, immediate release, solubility etc.*

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) is a retrovirus that progressively damages the immune system, making the body vulnerable to opportunistic infections and certain diseases. Over the past decade, while efforts have been made to eliminate HIV, it has become evident that complete eradication is highly improbable. As a result, long-term antiretroviral therapy is essential to suppress the virus and slow the progression of the disease.

Solubility is a critical physicochemical factor influencing drug absorption and therapeutic effectiveness. Recently, researchers have focused on developing oral dosage forms for poorly water-soluble drugs using various solubility-enhancement techniques. Among these, solid dispersion is a widely utilized approach. Solid dispersion refers to a group of solid products composed of at least two components: a hydrophilic matrix and a hydrophobic drug. This study aims to develop immediate release tablets of dolutegravir sodium using the solid dispersion technique to enhance its solubility and dissolution rate. Dolutegravir sodium, an antiretroviral agent, inhibits the enzyme HIV integrase, which is essential for viral replication. As a Biopharmaceutical Classification Scheme (BCS) Class II drug, dolutegravir sodium is water-insoluble, lipophilic, and highly permeable. Therefore, its bioavailability can be improved by increasing its apparent solubility in water using solid dispersion technology. Immediate release tablets are solid dosage forms containing active pharmaceutical ingredients that rapidly disintegrate, typically within min. upon contact with the gastric mucosa. This leads to faster drug release and improved therapeutic outcomes. While many synthetic carriers have been developed, natural carriers are gaining prominence due to their ease of availability

A novel solid dispersion formulation of dolutegravir sodium was developed using the rotary solvent evaporation method with PEG 600 as a carrier. Immediate release tablets were prepared using the direct compression method, incorporating the optimized solid dispersion and crosspovidone sodium starch glycolate crosscarmelose. This innovative approach highlights the superdisintegrant properties of crosspovidone, making it a promising superdisintegrant for this formulation.

Materials

All materials used in present research were commercial samples. Active pharmaceutical ingredient: Dolutegravir Sodium (Chemsar Research Institute) Hydrophilic polymers: Polyethylene glycol 6000, (Fusion scientific laboratories Pvt. Ltd. Mumbai), Excipients: Croscarmellose sodium, Sodium starch glycolate, Crosspovidone, (Rubicon labs mumbai), Microcrystalline cellulose, Magnesium stearate, Aspartame, Talc (Research lab fine chem. Mumbai)

Analysis of Dolutegravir Sodium

The received sample of Dolutegravir Sodium was characterized according to different compendial methods and was found to be a white crystalline powder with characteristic odour. The melting point was determined by using melting point apparatus (PMP-D, Veego) by introducing small amount of substance in the capillary attached to graduated thermometer and constant heat was supplied to the assembly suspended in the paraffin bath. The temperature at which drug melted was recorded it was found to have a melting point in range of 109-103 C, λ_{max} all the findings matched the official reports.

Solubility Study of Dolutegravir

The solubility study of Dolutegravir in distilled water and 0.1 N HCL

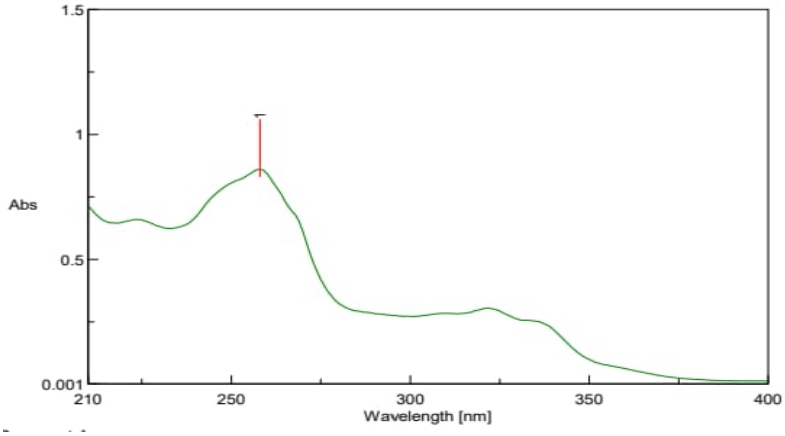
Table 10.3 solubility of Dolutegravir

Sr. No.	Medium	Solubility (mg/ml)
1.	Distilled Water	0.0421±0.05
2	0.1 N HCL	1.015± 0.09

Results are mean of three determinations

10.1.2. Spectrophotometric Analysis of Dolutegravir Sodium

Scanning of Dolutegravir in 0.1N HCL



In UV spectroscopy study, the maximum wavelength (λ-max) of 0.1 N HCL was found to be 260 nm. The reported λ-max value of Dolutegravir in 0.1 N HCL was also 260 nm respectively, so the values similar with the reported values indicates that the given sample of Dolutegravir was in pure form.

10.1 UV spectra of Dolutegravir in 0.1 N HCL at 260 nm

Preparation of Standard Calibration Curve of Dolutegravir in 0.1 N HCL

The Standard curve of was determined by plotting absorbance Vs concentration at 260 nm. It was found that there was linear relationship between concentration and absorbance with R^2 value respectively, which reveals that, the drug Dolutegravir obeys the Beers lamberts law.

Table 10.4 Standard Calibration Curve of Dolutegravir in 0.1 N HCL

Sr. No.	concentration	Absorbance at 260 nm
1	0	0
2	2	0.196
3	4	0.311
4	6	0.495
5	8	0.651
6	10	0.826

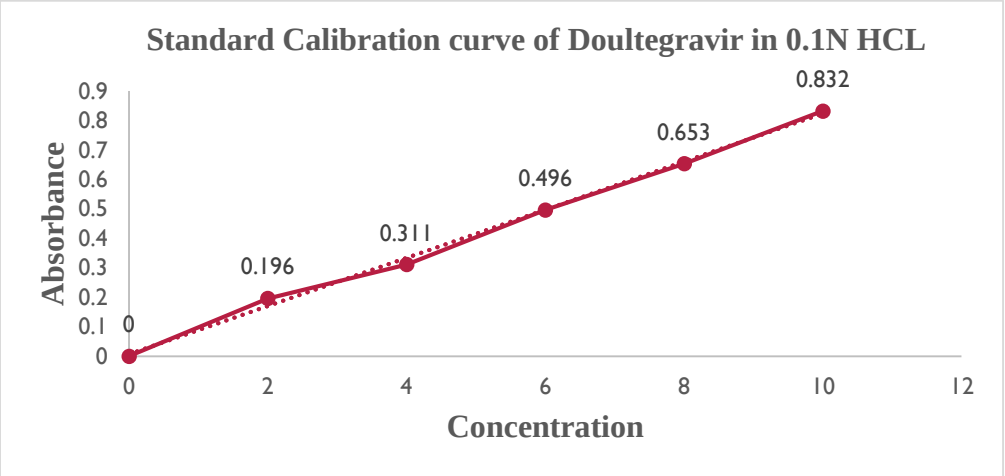


Figure 10.2 Standard Calibration Curve of in Dolutegravir Sodium 0.1 N HCL

Drug Excipient Compatibility Study

Fourier Transform Infra-Red Spectroscopy (FTIR) Interpretation of Dolutegravir Sodium

Major functional groups present in show characteristic peaks in Dolutegravir IR spectrum. Table No. shows peaks observed at different wave numbers and the functional group associated with these peaks. The major peaks are identical to functional group of Dolutegravir. Hence, the sample was confirmed as Dolutegravir.

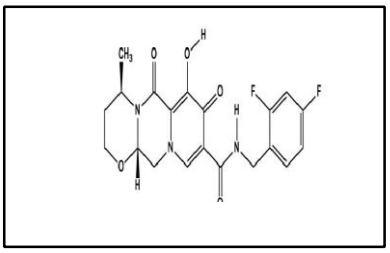
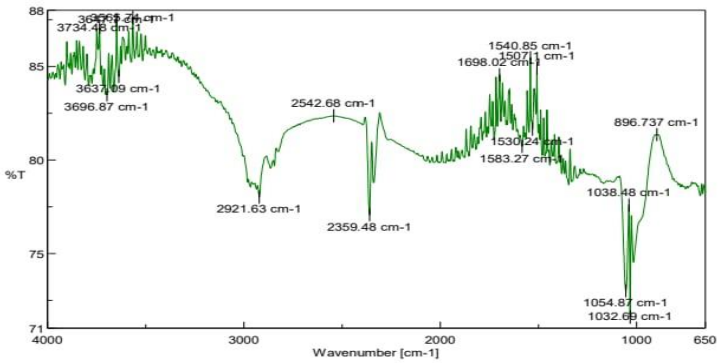


Figure Chemical Structure of Dolutegravir

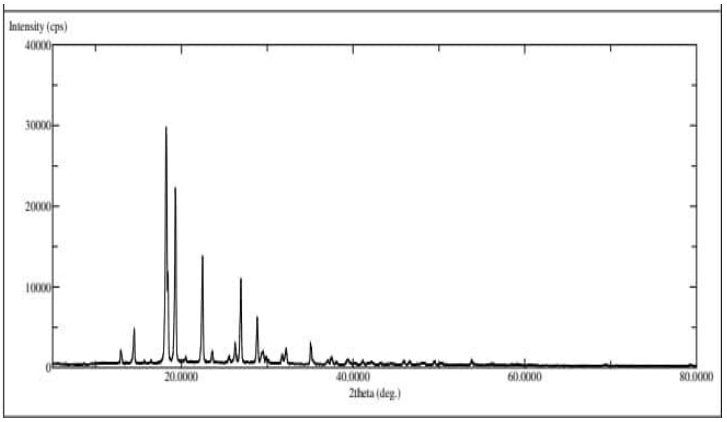
FTIR- Study of Dolutegravir



10.4 FTIR Study of Dolutegravir

Table 10.5 Interpretation of FTIR Spectrum of Dolutegravir

10.1.5. X-Ray Diffraction (XRD) of Dolutegravir Sodium

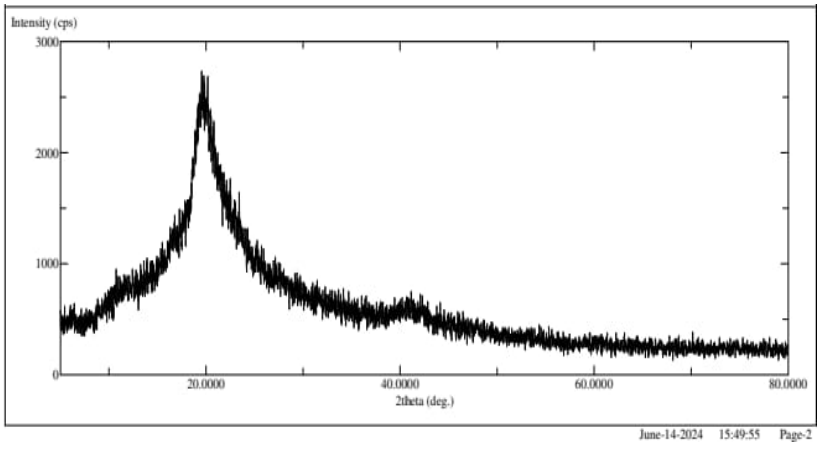


X-ray diffraction patterns were traced employing x-ray diffractometer bruker for all the samples using nickel filter, Cuk (α) radiations a current of 20 mA and receiving silt of 0.2 inches. XRD studies of Dolutegravir Sodium showed so many numbers of peaks, it indicates that the drug substance is crystalline in nature.

Figure. X-Ray Diffraction (XRD) of Dolutegravir

X-Ray Diffraction (XRD) of Solid Dispersion of Dolutegravir Sodium

The X- ray diffractogram of Dolutegravir confirms its crystalline nature, as evidenced by the number of sharp and intense peaks as shown in fig. ().However, the diffraction pattern of selected formula S5 represents disappearance of crystalline peaks of the drug, and these finding suggest the improvement of drug solubility by the formation of an amorphous form of the drug



From the diffractogram of solid dispersion prepared Rotary Solvent Evaporation S5 Batch 1:3 ratio exhibited a single broad, and undefined peak typically associated with amorphous material. Most of the characteristics crystalline peaks of Dolutegravir Sodium it was clearly evident that the intensity (heights) of peaks has been reduced significantly. This indicates that the percentage of crystallinity was reduced by solid dispersion prepared by Rotary Solvent Evaporation Method.

10.1.6. Differential Scanning of Calorimetry

The DSC has performed to determine the thermal stability of drug. DSC thermo gram of Dolutegravir illustrated in (figure) pure Dolutegravir showed a characteristic sharp endothermic peak at (204.03 C) which corresponding to its melting point which is near the reported one (192-196)

10.2 PREPARATION OF SOLID DISPERSIONS OF DOLUTEGRAVIR PREPARED BY ROTATRY SOLVENT EVAPORATION METHOD

The solid dispersions were prepared by Rotary Solvent Evaporation Method with polymer PEG 6000 various ratios of Dolutegravir and PEG 6000 (1:0.5, 1:1.0, 1:1.5, 1:2.0,1:3.0). The solid dispersion prepared by Rotary Solvent Evaporation Method were S1, S2, S3, S4, S5.respectively

10.3 EVALUATION OF SOLID DISPERSION OF DOLUTEGRAVIR PREPARED BY ROTARY SOLVENT EVAPORATION METHOD

The solid dispersion of Dolutegravir and PEG 6000 (S1 to S5) of were evaluated for number of parameters like physical characteristic, solubility study, drug content, % practical yield, in-vitro dissolution study and compatibility study.

Batch	Drug: Carrier (Ratio)	Method	Ratio
S1	Dolutegravir + PEG 6000	Rotary Solvent Evaporation	(1:0.5)
S2	Dolutegravir + PEG 6000	Rotary Solvent Evaporation	(1:1.0)
S3	Dolutegravir + PEG 6000	Rotary Solvent Evaporation	(1:1.5)
S4	Dolutegravir + PEG 6000	Rotary Solvent Evaporation	(1:2.0)
S5	Dolutegravir + PEG 6000	Rotary Solvent Evaporation	(1:3.0)

10.3.1 Physical Characteristics

All batches of solid dispersion (S1 to S5) were evaluated for colour, appearance and odour. The Dolutegravir crystalline is converted into amorphous form indicating enhanced solubility. The physical appearance of each formulation is shown below table

Table 10.6 Physical Characteristics of Solid Dispersion of Dolutegravir

Sr. No.	Formulations	Physical Appearance		
		Colour	Appearance	Odour
1	S1	White	Amorphous Powder	Odourless
2	S2	White	Amorphous Powder	Odourless
3	S3	White	Amorphous Powder	Odourless
4	S4	White	Amorphous Powder	Odourless
5	S5	White	Amorphous Powder	Odourless

10.7 Solubility Study of Prepared Solid Dispersion

The solubility study of various solid dispersion batches (S1 to S5) was performed. Solid dispersion prepared by Rotary Solvent Evaporation Method showed improved solubility of Dolutegravir as compared to pure drug. The ratio 1:3 (S5) was more soluble than pure drug and other solid dispersions. Solubility of solid dispersion is increased by 4.17 fold compare to pure drug.

Table 10.7 Solubility Study of Prepared Solid Dispersion

10.2.3 Drug Content

The drug content was found to be within the range of two indicating uniform distribution of drug in the formulated tablets as per pharmacopeia specification.

Table 10.8 Drug Content

Sr. No.	Medium	Drug: Carrier (Ratio)	Solubility (mg/ml)
1	Distilled Water	Pure drug	0.0420
2	Distilled Water	Dolutegravir + PEG 6000 (1:0.5) S1	0.0576
3	Distilled Water	Dolutegravir + PEG 6000 (1:1.0) S2	0.0802
4	Distilled Water	Dolutegravir + PEG 6000 (1:1.5) S3	0.1032
5	Distilled Water	Dolutegravir + PEG 6000 (1:2.0) S4	0.1178
6	Distilled Water	Dolutegravir + PEG 6000 (1:3.0) S5	0.1753

Formulation	Ratio	% Drug content
S1	1:0.5	90.63±0.99
S2	1:1.0	94.05±0.50
S3	1:1.5	95.65±0.05
S4	1:2.0	97.09±0.64
S5	1:3.0	98.42±0.35

Results are mean of three determinations

10.2.4 Percentage Practical Yield Study of Solid Dispersion

Percentage practical yield was calculated to know about % yield or efficiency of any method which will help in selection of appropriate method. The practical yield for each batch is reported below.

Table 10.9 Percentage Yield Study of Solid Dispersion

Formulation	Ratio	Initial Weight	Final Weight	% Practical Yield
S1	1:0.5	0.150	0.108	72±0.85
S2	1:1.0	0.200	0.167	83.5±0.60
S3	1:1.5	0.250	0.219	87.16±0.75
S4	1:2.0	0.300	0.271	90.33±0.11
S5	1:3.0	0.400	0.384	96±0.34

.

Results are mean of three determinations

Different trial batches of solid dispersion show % practical yield from range 72±0.85 to 96± 0.34 Batch S5 Showed 96± 0.43 practical yield.

Drug Excipient Compatibility Studies of Solid Dispersion of Dolutegravir

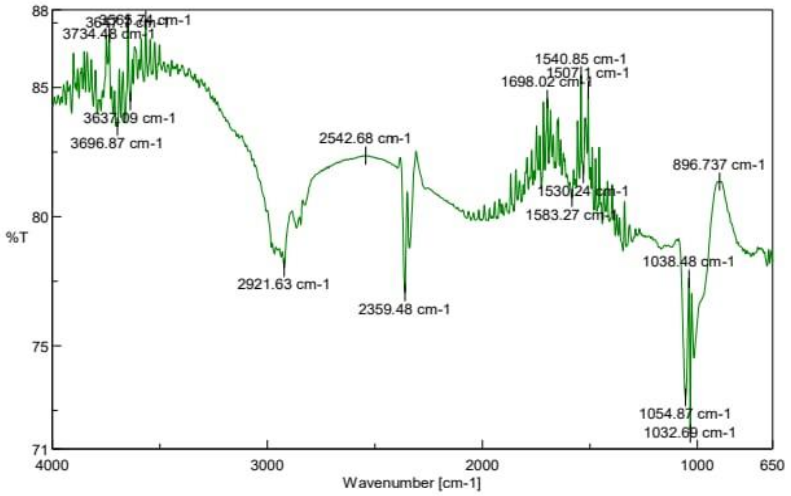


Figure 10.5. Drug Excipient Compatibility Studies of Solid Dispersion of Dolutegravir

Table 10.10. Interpretation of FTIR Spectrum of Dolutegravir

Sr. No.	Functional Group	Reference Peak	Observed Peak Wavenumber (cm^{-}
1	C-N stretching (Aromatic)	1350-1000	1054.87
2	C-O-C stretching	1300-1000	1032.69
3	O-H	3650-3600	3637.69
4	C-F	1400-1000	1038.48
5	C = O	1820-1660	1698.02

10.5 In vitro Dissolution Study and Observation of Pure Drug with Solid Dispersion prepared by Rotary Solvent Evaporation Method

The dissolution study of pure drug and solid dispersion were carried out to calculate the % drug release

Dissolution Study of Pure Drug

Dissolution study of pure drug in 0.1 N HCL was carried out and absorbance was taken in UV spectrophotometer which is reported below Table

Table 10.11 Dissolution Profile of Dolutegravir Pure Drug

Time (min)	Cumulative % drug release
0	0.00
5	4.45±1.11
10	9.53±1.49
15	14.84±1.25
20	22.07±1.32
25	27.96±0.86
30	33.18±1.65

Results are mean of three determinations

The cumulative % drug release of pure drug of Bromocriptine Mesylate after 30 min was found to be 33.18±1.65

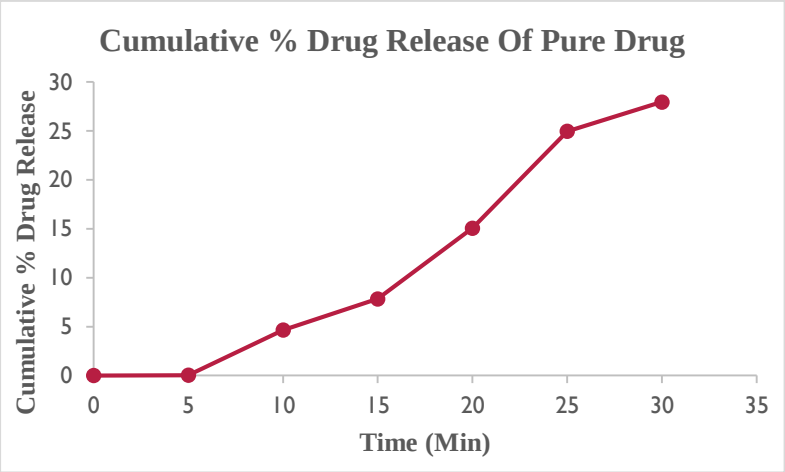


Figure 10.20 Dissolution profile of Dolutegravir Pure Drug

Dissolution Profile of Solid Dispersion Prepared by Rotary Evaporation Method

Dissolution study of solid dispersion prepared by Kneading Method S1, S2, S3, S4 & S5 was carried out in 0.1 N HCL and analyzed spectrophotometrically at 260 nm. Each preparation was tested in triplicate and then mean values were calculated. The table 10.18 indicates the % drug release of each formulation at the end of 30 min. The graph was plotted to show % drug release which was represented in Table below.

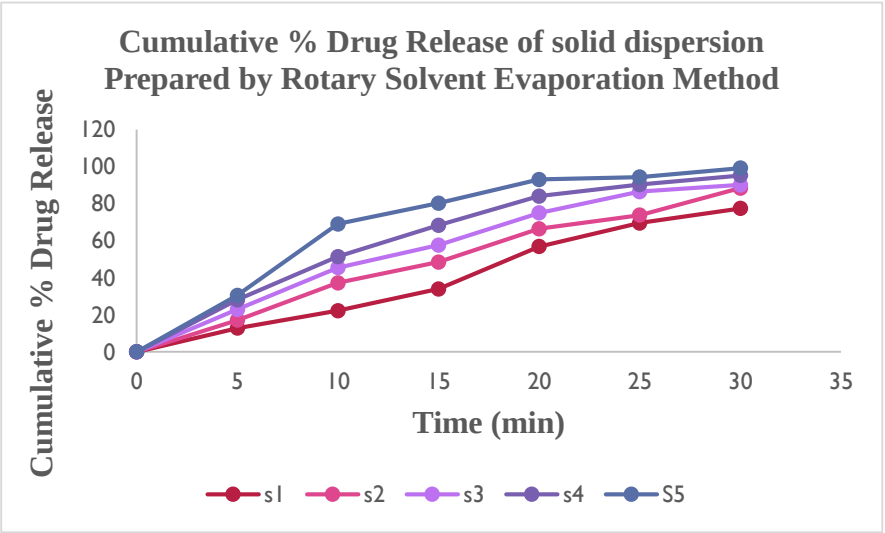


Figure 10.21 Dissolution Profile of Solid Dispersions Prepared by Rotary Solvent Evaporation Method

Out of four formulations S5 shown maximum drug release i.e., 99.12 %. Solid dispersion (S5) of Dolutegravir (1:3) prepared by Rotary Evaporation Method significantly improved its solubility and dissolution rate. Increased wetting and solubilizing effect of PEG 6000 as well as the molecular dispersion of drug in solid dispersion and alteration of surface properties of drug particle may be responsible for the enhanced dissolution rate of Dolutegravir from solid dispersion.

Comparative Dissolution Study

For the selection of best solid dispersion, the dissolution of pure drug was compared with solid dispersion prepared by Rotary Solvent Evaporation Method which is shown in Table 10.18 and 10.19 And graph was plotted to show % drug release which was represented in Figure 10.20

Table 10.13 Comparative Dissolution Study of Pure drug with Solid Dispersion Prepared by Rotary Solvent Evaporation Method

Time (min)	Cumulative % Drug Release	
	Pure Drug	S5
0	00	00
5	4.45±1.11	30.45±1.87
10	9.53±1.49	69.01±2.12
15	14.84±1.25	80.23±1.67
20	22.07±1.32	92.98±1.09
25	27.96±0.86	94.34±1.76
30	33.18±1.65	99.12±1.10

Results are mean of three determination

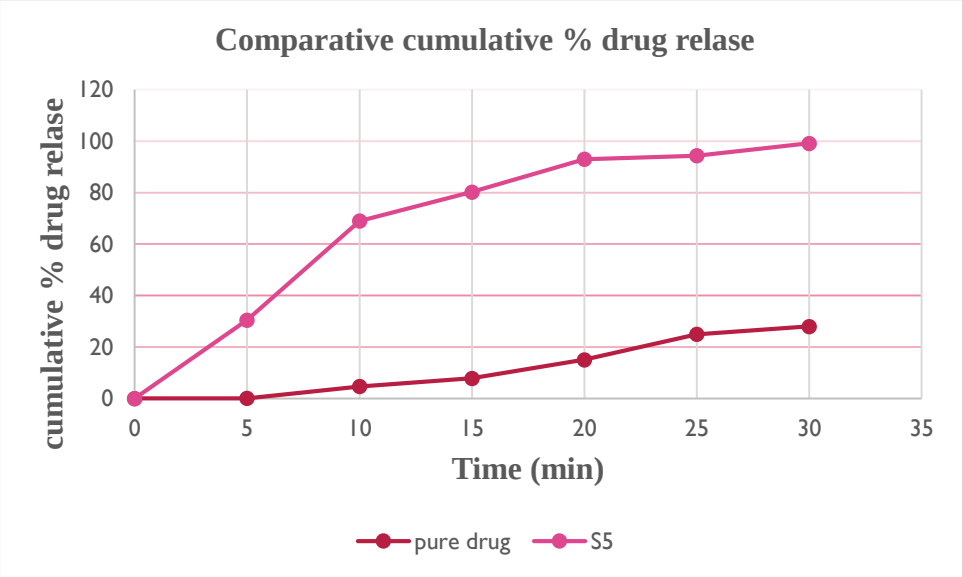


Figure 10.23 Comparative dissolution study of pure drug with Solid Dispersion Prepared by Rotary Solvent Evaporation Method

According to graph 10.23. It was concluded that the S5 formulation give highest drug release i.e 99.12 % in 30 min, in 0.1 N HCL whereas the pure drug was found to be 42.18% drug release in 0.1 N HCL in 30 min. In this comparative study Rotary solvent Evaporation Method of solid dispersion exhibit significant improvement in solubility and dissolution rate compared to that of pure drug Thus, Lyophilization technology offers a promising alternative method of solid dispersion for Dolutegravir with significant enhancement of the in-vitro dissolution rate, hence batch S5 was selected for the further studies.

2. FORMULATION OF IMMEADIATE RELEASE TABLET OF DOLUTEGRAVIR

According to comparative dissolution study showed in graph 10.23. It is concluded that the solid dispersion prepared by Rotary Evaporation Method containing Dolutegravir + PEG 6000 (1:3) i.e. batch S5 had shown maximum percent drug release as compared to other solid dispersion batches and pure drug. Hence the solid dispersion S5 is selected for further tablet formulations. Total six formulations [F1-F9] were developed by using various concentration of superdisintegrants sodium starch gylcolate, and crosspovidone etc.

Formulations	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Ingredients	**Unit Formula (mg per tablet)**								
Dolutegravir SD (equivalent wt. is equal to 125 mg)	125	125	125	125	125	125	125	125	125
Crosspovidone	2.5	5	7.5	-	-	-	-	-	-
Sodium starch glycolate	-	-		2.5	5	7.5	-	-	-
Crosscarmelose	-	-	-	-	-	-	2.5	5	7.5
Spray dried Lactose	80	80	80	80	80	80	80	80	80
Micro crystalline cellulose	85.5	83	80.5	85.5	83	80.5	85.5	83	80.5
Aspartame	3	3	3	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Total	300 mg	300mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg	300 mg

PRE-COMPRESSION EVALUATION OF IMMEADIATE RELEASE TABLET BLEND OF SOLID DISPERSION OF DOLUTEGRAVIR

The characterization of mixed blend was done for determination of mass-volume relationship parameter. The parameter like angle of repose, bulk density, tapped density, Hauser's ratio and compressibility index was evaluated and values are reported in Table below-

Table 10.14 Pre-Compression Evaluation of Tablet Blend for Immediate Release Tablets

Formulation	**Angle of Repose (θ˚)**	**Bulk Density (gm/ml)**	**Tapped Density (gm/ml)**	**Hauser's Ratio (HR)**	**Compressibility Index (%)**
F1	26.10 ± 0.74	0.37±0.70	0.46±0.82	1.10±0.82	5.6±0.26
F2	28.75 ± 0.20	0.40±0.34	0.35±0.39	1.18±0.11	8.69±0.32
F3	29.02 ± 0.84	0.41±0.64	0.42±0.50	1.09±0.18	10.76±0.30
F4	27.74 ± 0.50	0.42±0.32	0.37±0.42	1.12±0.28	9.81±0.34

F5	25.63 ± 0.68	0.35±0.54	0.54±0.27	1.23±0.15	6.9±0.22
F6	30.10 ± 0.64	0.37±0.25	0.49±0.77	1.08±0.19	11.2±0.39
F7	27.33± 0.32	0.43±0.45	0.41±0.99	1.17±0.76	10.54±0.65
F8	25.72±0.21	0.32±0.76	0.53±0.54	1.25±0.32	7.98±0.21
F9	30.88± 0.87	0.45±0.33	0.54±0.41	1.19±0.30	7.34±0.54

Results are mean of three determinations

From the results of precompression studies of the batch F1-F9, it is concluded that powder mixtures has good flow property and compressibility property. Angle of repose of various powder mixed blends (F1-F9), prepared with different superdisintegrant, and was measured by funnel method. Angle of repose was found in the range **-25.63 ± 0.68 to 30.10 ± 0.64.** The excellent flow ability of powder blend was also evidence with angle of repose, all formulations showed the angle of repose within 30 θ˚. It indicates that all formulations showed good flow properties. The bulk density of various powder mixed blends (F1-F9) prepared with different superdisintegrant was measured by graduated cylinder. The bulk density was found in the range **0.35± 0.54– 0.42± 0.32g/ml.** indicating good packaging capacity of tablets. The Tapped density of various powder mixed blends (F1-F6) prepared with different superdisintegrant was measured by using measuring cylinder. The tapped density was found in the range **0.35 ± 0.39- 0.54±0.77 g/ml .**The Hauser's rat.io of various powder mixed blends (F1-F9), prepared with different superdisintegrant, it is calculated by using bulk density and tapped density data. It was found in the range of **1.08±0.19 –1.23±0.15** reveals good flow properties (<1.25)**.**The Compressibility index of various powder mixed blends (F1-F9), prepared with different superdisintegrant, using bulk density and tapped density data, compressibility index was calculated. It was found in the range **5.6±0.30- 11.2±0.39%.** This indicates good flow properties. All formulations are showing good compressibility. The powder blend was compressed using direct compression technique. Tablets prepared by direct compression method have found to be good without any chipping, capping and sticking.

3. POST-COMPRESSION EVALUATION OF SUBLINGUAL TABLETS

The Immediate Release Tablets of solid dispersion of were prepared & subjected to post-compression parameters like weight variation, thickness, hardness, friability, drug content, in vitro disintegration time, wetting time, water absorption ratio, in vitro dissolution studies were carried out. All the formulations were passed the parameter which was reported in Table below.

Formulations	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Thickness (mm)	5.02±0.44	4.86±0.17	4.13±0.48	4.92±0.33	4.22±0.14	4.69±0.57	4.42±0.65	5.69±0.43	5.13±0.57
Hardness (kg/cm ^{2})	4.16±1.06	4.34±0.76	4.63±0.60	4.93±0.75	4.75±0.80	4.22±0.52	4.10±0.65	4.00±0.11	4.79±0.59
Weight Variation (mg)	301±1.62	298±1.14	300±1.00	302±1.08	299±1.50	298±1.02	297±1.10	300 ±0.06	299±0.02
Friability (%)	0.54±0.25	0.53±1.49	0.55±1.83	0.54±1.24	0.57±0.11	0.54±0.32	0.55±0.72	0.50±0.26	0.56±0.87
Disintegration time (min)	2.40±1.37	2.23±1.12	2.15±1.24	3.15±1.20	2.98±1.41	2.92±1.20	2.70±0.20	2.12±0..10	2.22±0.31
Water absorption ratio	93.01±1.31	96.48±1.33	96.74±1.88	89.53±1.37	94.53±1.03	95.55±1.48	94.55±0.63	97.55±0.32	96.95±0.14

(%)									
Wetting time (sec)	12.65± 0.53	10.95±0 .73	10.87 ±0.42	13.05±0.3 9	12.19±0. 61	11.28± 0.04	11.69± 0.78	10.32 ± 0.98	11.96± 0.28
Drug Content	97.36± 0.52	97.52±1 .66	98.21 ±1.43	99.10±1.7 5	98.26±1. 18	97.26±1. 34	98.09±1. 34	99.86±0.3 4	98.26± 0.12

Table 10.15 Post-Compression Evaluation of Immediate Release Tablet of Dolutegravir

Results are mean of three determinations

Various physical parameters like weight variation, thickness, hardness, friability, drug content, *in vitro* disintegration time, wetting time, water absorption ratio, *in vitro* dissolution studies were measured to evaluate tablets. The thickness of the tablets was measured by using Vernier caliper by picking the tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from **4.13-5.69 mm**. Uniform in the values indicates that formulations were compressed without sticking to the dies and punches. Tablets were evaluated by using Monsanto Hardness tester. Hardness of the tablets was in the range **4.00–4.93 kg/cm^2**. Uniform hardness was obtained due to equal compression force. The obtained hardness range showed good mechanical strength with an ability to with stand physical and mechanical stress conditions. Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained in the range with acceptable weight variations as per Pharmacopoeia specifications, limit of ±5%. It was found to be from **298 - 302 mg.** Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in acceptable range. **0.50 -0.57%** (less than 1%) This indicated a good mechanical resistance of the prepared immediate release tablets. Tablets were evaluated by using assay method. The drug content was obtained in the acceptable limit. The drug content was found in the range **97.26 – 99.86 %w/w.** (i.e., 99-101% w/w). The found range was within the specified limit as per Pharmacopoeia. Tablets were subjected for the *in-vitro* disintegration time in the USP Disintegrating test apparatus. The *in-vitro* disintegration time for all six formulations varied from **2.12-3.15 min.** Wetting time of tablet the average time for the wetting with standard deviation was recorded. It was found in the range of **10. 32-13.05 Sec.**

In vitro % Drug Release of Drug from Tablet

All the nine tablet batches of immediate release tablets of solid dispersion of Dolutegravir were subjected for the in vitro dissolution studies using tablet dissolution apparatus (USP Type II). 0.1 N HCL was used as dissolution medium.

Table 10.16. In vitro Cumulative % Drug Release of Drug from Tablet

Time (min)	**Cumulative % Drug Release**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	00	00	00	00	00	00	00	00	00
5	20.96±3.0 3	21.67±3. 45	24.25±2. 30	19.91± 3.05	21.98±1. 76	27.43± 1.39	23.76±1. 56	24.58±1. 98	23.62 ±3.22
10	27.71±2.3 8	32.54±1. 58	36.61±1. 27	34.09± 1.42	35.07±1. 54	38.35± 1.87	39.23±2. 01	43.93±2. 26	42.09 ±1.49
15	44.35±2.5 6	46.84±1. 70	48.00±1. 32	48.72± 1.56	49.23±0. 99	50.99± 2.63	49.56±1. 95	62.70±3. 35	46.13 ±1.56
20	65.34±1.5 4	69.03±1. 82	70.91±2. 50	65.94± 2.32	69.11±1. 82	71.20± 2.20	73.76±2. 54	76.79±1. 55	72.03 ±1.78

25	87.78±1.77	89.52±1.44	91.26±1.65	79.13±1.72	80.54±1.33	83.65±1.20	85.32±2.13	88.18±1.79	82.43±2.19
30	90.35±1.56	94.52±2.92	98.52±1.85	87.94±1.40	90.43±176	97.34±2.41	96.12±1.53	99.41±2.92	97.79±1.86

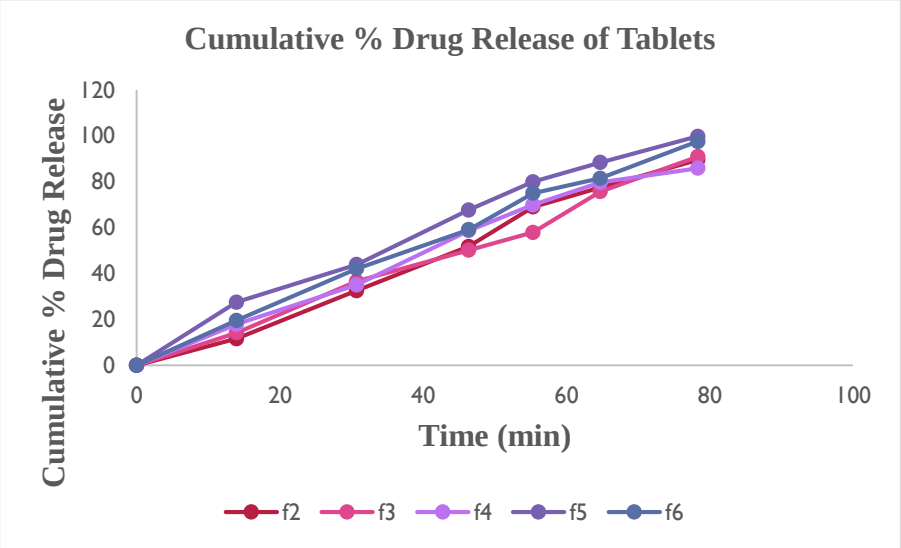


Figure In vitro Cumulative % Drug Release of Drug from Tablet

The rapid dissolution was observed in formulation F8 releases 99.41% at the end of 30 minutes. Formulations F1-F9 released 87.94 to 99.41 at the end of 30 min. Rapid dissolution might be due to fast breakdown of particles and rapid absorption of drugs. The drug release was completely achieved in shorter duration of time. In all the formulations the drug release was within 30 minutes. High dissolution may occur due to faster breakdown in comparative study F8 formulation gives higher percent drug release compared to with other remaining five formulations at the end of 30 minutes and graphical representation is shown in Figure 10.15. Therefore, it was concluded that the best optimized batch was found to be F8 because of lesser disintegration time and highest percentage drug release at the end of 30 min amongst all the formulations.

Stability Study

The formulations F8 was selected for stability studies on the basis of their high cumulative % drug release and also result of *in vitro* disintegration time studies. Stability study was conducted by storing tablet at 40ºC±2ºC/75±5% relative humidity for three months. The content and dissolution behaviors from immediate release tablets were tested monthly for three months, which is shown in below Table. Each tablet was individually weighed and wrapped in a aluminum foil and packed in black PVC bottle and put at above specified conditions in a heating humidity chamber for three months. After each month tablet sample was analyzed for hardness, disintegration time, dissolution and drug content.

Table 10.17. Stability Study

Formulation		**Initial**	**After 1 Months**	**After 3 Months**
F8	**Appearance**	white amorphous powder	white amorphous powder	white amorphous powder
	Drug content (%)	99.47±1.11	99.30±1.16	99.12±1.09

	In vitro drug release	99.41±2.92	98.60±1.26	97.45±1.47
	Disintegration Time(min)	2.12±1.05	2.13±1.65	2.54±1.21

4. RESULT AND DISCUSSIONS

The study aimed to enhance the dissolution of Dolutegravir Sodium, a BCS class II drug, by utilizing hydrophilic polymers such as polyethylene glycol (PEG) 6000 using a Rotary Solvent Evaporation Method solid dispersion, were explored to achieve this goal. The Drug-polymer complexes were prepared using a batch method. The study observed that the combination of Dolutegravir Sodium with PEG 6000 (1:3 ratio) achieved the maximum dissolution rate when tested in a distilled water.

The solid dispersions were analyzed for physical appearance, percentage practical yield, solubility, in vitro dissolution, and compatibility. The dispersions (S1-S5) were white, amorphous powders. Dissolution Study of Pure Dolutegravir Sodium exhibited a cumulative drug release of 13.45% after 30 minutes.

Dissolution profiles for solid dispersions prepared using the Rotary Solvent Evaporation method (S1-S5) were 56.31%, 64.40%, 70.27%, and 81.42%, respectively, with S5 showing the highest release (81.42%).

Solid dispersion S5 was selected for tablet formulation due to its superior dissolution rate. Nine tablet batches (F1-F9) were developed using different concentrations (2.5%, 5%, and 7.5%) of superdisintegrants like crosscarmellose sodium, sodium starch glycolate, and crosspovidone.

Batch F8, containing 5% crosspovidone, was found to be the most effective, with a disintegration time of 2.12 min and a dissolution rate of 99.89 ± 1.06% F8 demonstrated superior drug release. Batch F8 was subjected to stability studies at 40°C/75% RH for three months. Monthly evaluations confirmed consistent disintegration time, drug content, and dissolution behavior.

5. CONCLUSION

The study successfully prepared Dolutegravir Sodium solid dispersions using the Rotary Solvent Evaporation methods with carriers such as PEG 6000, among these, formulation prepared via the Rotary Solvent Evaporation methods exhibited significantly improved solubility and dissolution due to the solubilizing and wetting effects of PEG 6000 along with the molecular dispersion of the drug.

Tablet formulation F8, which utilized crosspovidone as a superdisintegrant (5%), achieved the highest drug release due to its superior swelling properties. Increased superdisintegrant concentration correlated with enhanced drug release. This novel, cost-effective, immediate-release tablet formulation demonstrates potential for improved bioavailability and effective drug delivery.

Conflict of Interest:

The authors declare no conflicts of interest.

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