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Development Of Oral Liquisolid Systems For The Poorly Water-Soluble Drug Eluxadoline Using The Mixed Solvency Concept

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ABSTRACT

The present study aimed to enhance the solubility and dissolution rate of the poorly water-soluble drug Eluxadoline through the development of an oral liquisolid system using the mixed solvency concept. Calibration curves of Eluxadoline in distilled water and 0.1 N HCl showed linearity at 241 nm over the concentration range of 20–100 µg/ml. Solubility enhancement was achieved using a mixed solvent system of propylene glycol (PG) and polyethylene glycol 400 (PEG 400) (1:1) incorporating solid solubilizers such as sodium caprylate, sodium benzoate, and PVP K25. Among various blends, Blend A (5% SC + 2.5% SB + 2% PVP K25 + 0.5 ml PG + 0.5 ml PEG 400) exhibited the highest equilibrium solubility of 142.012 mg/ml. Compatibility and interference studies confirmed no interaction between the drug and excipients. Microcrystalline cellulose (Avicel PH 200) was used as the carrier and Aerosil (5%) as the coating material. Three liquisolid formulations (LS-01, LS-02, LS-03) were prepared and evaluated. All showed uniform drug content (97.77–99.52%) and improved dissolution compared to pure drug. LS-01 exhibited the best performance, achieving 99.77% release within 45 minutes. The optimized formulation was successfully scaled up using 9.5 mL of Blend A, 1250 mg of Eluxadoline, and 19,375 mg of Avicel PH 200. The final batch demonstrated a drug content of 98.92%, with a disintegration time ranging from 57 seconds to 3 minutes 10 seconds. In comparison studies, LS-01 exhibited 95.42% drug release within 10 minutes, whereas the pure drug showed only 55.06% release after 60 minutes. These outcomes confirm a significant improvement in dissolution rate and suggest enhanced bioavailability of the optimized formulation.

KEYWORDS: Liquisolid system, Eluxadoline, Solubility enhancement, Dissolution rate, Mixed solvency.

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INTRODUCTION

Oral administration remains the most widely accepted and convenient route for drug delivery; however, formulating drugs with poor water solubility continues to be a major challenge in achieving satisfactory bioavailability.[1] More than 40% of newly discovered drug molecules exhibit limited aqueous solubility, resulting in inconsistent absorption and variable therapeutic outcomes. Eluxadoline, a mixed µ-opioid receptor agonist and δ-opioid receptor antagonist, is prescribed for the treatment of irritable bowel syndrome with diarrhea (IBS-D). Despite its clinical efficacy, Eluxadoline's poor solubility in water restricts its dissolution rate and, consequently, its oral bioavailability. Various formulation strategies, including micronization, solid dispersion, complexation, and surfactant-based solubilization, have been explored to enhance solubility, but these approaches often face challenges related to stability and large-scale production. The liquisolid technique provides a promising alternative by transforming liquid drugs or solutions into dry, free-flowing, and compressible powders through adsorption onto carrier and coating materials. Furthermore, applying the mixed solvency concept—which combines different hydrotropic agents and co-solvents—can synergistically enhance solubility without depending on a single solubilizer. Therefore, the present research aims to develop an oral liquisolid formulation of Eluxadoline utilizing the mixed solvency approach to improve its solubility, dissolution behavior, and overall oral bioavailability.[2-3]

MATERIALS AND METHODS

MATERIALS

Eluxadoline was provided by Torrent Pharmaceuticals Limited, Ahmadabad, India, Sodium benzoate, Distilled water, Hydrochloric acid (0.1 N HCl), Sodium caprylate, Polyvinylpyrrolidone K25 (PVP K25), Propylene glycol, Polyethylene glycol 400 (PEG 400), Microcrystalline cellulose (Avicel PH 200), Aerosil were purchased from S.K. Traders, M. P. India., All other chemicals used were of analytical grade.

METHODS

Preparation of Calibration Curves: An accurately weighed quantity of 100 mg of Eluxadoline was placed in a 100 mL volumetric flask, dissolved in 20 mL of a 30% sodium benzoate solution, and then the volume was adjusted to 100 mL with distilled water to obtain a stock solution with a concentration of 1000 µg/mL. From this stock, aliquots were further diluted to

prepare working solutions in the concentration range of 20–100 µg/mL. The absorbance of these solutions was recorded at 241 nm using a Shimadzu UV-1700 spectrophotometer. The same experimental procedure was repeated using 0.1 N hydrochloric acid as the solvent medium.[5]

Development of Solvent System: To improve the solubility of Eluxadoline, different solid solubilizing agents—sodium caprylate (SC), sodium benzoate (SB), and PVP K25—were dissolved separately and in combination in propylene glycol (PG) and polyethylene glycol 400 (PEG 400) to form mixed solvent systems. The solubility of Eluxadoline in each prepared blend was evaluated using the shake-flask technique, with equilibrium solubility determined after 24 hours of shaking followed by 12 hours of equilibration.[6]

Drug–Excipient Compatibility Studies: Physical mixtures of Eluxadoline and excipients (1:1 ratio) were stored under room and maintained conditions for four weeks and examined weekly for any change in color, odor, or texture.[7]

Formulation of Liquisolid System: Eluxadoline (500 mg) was dissolved in 3.8 ml, 3.3 ml, and 3.6 ml of Blends A, B, and C, respectively, to form clear solutions. The solutions were incorporated into microcrystalline cellulose (Avicel PH 200) and mixed with Aerosil (5%) to obtain free-flowing powders. Three formulations (LS-01, LS-02, LS-03) were prepared, each equivalent to 25 mg of drug.[8]

Evaluation: Formulations were evaluated for drug content, dissolution rate (in 0.1 N HCl using USP Basket Apparatus at 100 rpm, 37 ± 0.5°C), and disintegration time. The optimized batch (LS-01) was scaled up and re-evaluated for uniformity and performance.[9]

RESULT DISCUSSION

Preformulation Studies

Preparation Of Calibration Curves

Preparation Of Calibration Curve of Eluxadoline in Water

Approximately 100 mg of Eluxadoline was accurately weighed and transferred into a 100 mL volumetric flask. The drug was dissolved by adding 20 mL of a 30% sodium benzoate solution, and the volume was adjusted to 100 mL with distilled water to obtain a stock solution with a concentration of 1000 µg/mL. From this solution, 2 mL was withdrawn and diluted to 100 mL with distilled water to achieve a 20 µg/mL solution. Similarly, 4.0 mL, 6.0 mL, 8.0 mL, and 10.0 mL of the stock solution were each diluted to 100 mL to prepare solutions of 40, 60, 80, and 100 µg/mL concentrations, respectively. The absorbance of these solutions (20–100 µg/mL) was measured at 241 nm using a Shimadzu UV-1700 spectrophotometer against respective reagent blanks. The absorbance data obtained for the calibration curve of Eluxadoline in distilled water (in the presence of sodium benzoate) are presented in the accompanying table, and the corresponding calibration plot is illustrated in Figure 1.[11]

Table 1: Absorbance data for calibration curve of eluxadoline in distilled water (in presence of sodium benzoate) at 241 nm

S. No.	Concentration (µg/ml)	Absorbance (Mean±SD) (n=3)
1	0	0.0 ± 0.0
2	20	0.303±0.005
3	40	0.599±0.001
4	60	0.887±0.001
5	80	1.001±0.005
6	100	1.321±0.005

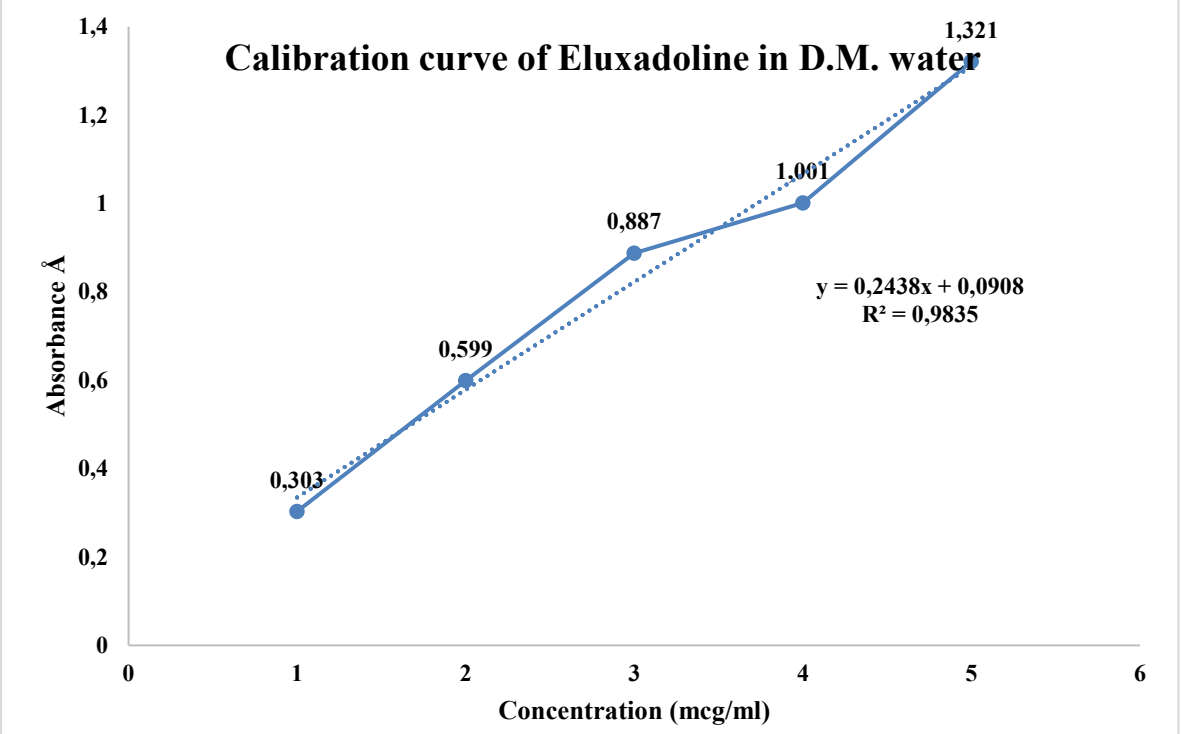

Figure 1: Calibration curve of eluxadoline at 241 nm in distilled water

Preparation of Calibration Curve of Eluxadoline In 0.1 N HCl

Approximately 100 mg of the drug was accurately weighed and transferred into a 100 mL volumetric flask. The drug was dissolved by adding 20 mL of a 30% sodium benzoate solution, and the volume was adjusted to 100 mL with 0.1 N hydrochloric acid to prepare a stock solution of 1000 µg/mL concentration. From this stock, 2 mL was pipetted out and diluted to 100 mL with 0.1 N HCl to obtain a 20 µg/mL solution. Similarly, 4.0 mL, 6.0 mL, 8.0 mL, and 10.0 mL aliquots were each diluted to 100 mL with 0.1 N HCl to prepare solutions of 40, 60, 80, and 100 µg/mL concentrations, respectively. The absorbance of these solutions (20–100 µg/mL) was recorded at 241 nm using a Shimadzu UV-1700 spectrophotometer with 0.1 N HCl as the blank.[12]

The absorbance data for the calibration curve of eluxadoline in 0.1 N HCl (in the presence of sodium benzoate) at 241 nm is shown in Table 2 and Figure 2 shows the Eluxadoline calibration curve in 0.1 N HCl (in presence of sodium benzoate).

Table 2: Absorbance data for calibration curve of Eluxadoline in 0.1 N HCl (in presence of sodium benzoate) at 241 nm

S. No.	Concentration (µg/ml)	Absorbance (Mean±SD) (n=3)
1	0	0.0±0.0
2	20	0.308±0.001
3	40	0.516±0.001
4	60	0.918±0.001
5	80	1.205±0.002
6	100	1.502±0.004

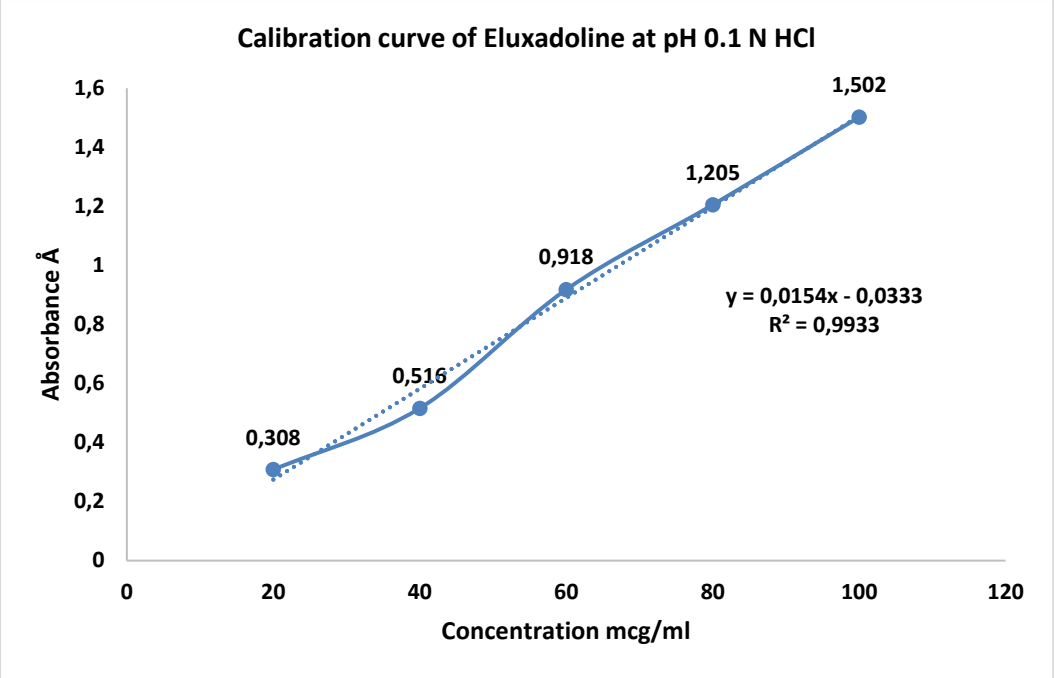

Figure 2: Calibration curve of eluxadoline at 241 nm in 0.1 N HCl

Development of Solvent System

As the solubility of Eluxadoline in propylene glycol alone was found to be lower than the desired level, the mixed solvency approach was adopted to develop an enhanced solvent system. In this method, different solid solubilizers were incorporated within their respective safe concentration limits into propylene glycol and PEG 400 to produce a more potent solvent suitable for dosage form development. These solid solubilizers were utilized both individually and in combination to prepare various solvent blends, and solubility studies of the drug were subsequently carried out using these prepared systems.[13]

Approximate solubility of various solublizers in propylene glycol Procedure:

1 milliliter of propylene glycol was transferred into a 10 mL volumetric flask, and 10 mg of sodium caprylate (SC) was added. The mixture was vortexed for approximately 20 minutes to facilitate dissolution. Once the solubilizer completely dissolved, an additional 10 mg of SC was added, and the vortexing process was repeated for another 20 minutes. This procedure was continued incrementally until a suspension was observed, indicating the solubility limit. It was determined that up to 300 mg of sodium caprylate could dissolve completely in 1 mL of propylene glycol to form a clear solution, while the addition of an extra 10 mg resulted in the formation of a suspension. Following the same method, the solubility of sodium benzoate and PVP K25 in propylene glycol was also evaluated.[14]

Table 3: Solubility of various solublizers in propylene glycol

Solublizers (abbreviation)	%w/v Solubility in propylene glycol
Sodium caprylate (SC)	30
PVP K25	5
Sodium benzoate (SB)	5

Approximate solubility of various solublizers in PEG 400 Procedure

1 ml of PEG 400 was transferred into a 10 mL volumetric flask, and 10 mg of sodium caprylate (SC) was added. The mixture was vortexed for approximately 20 minutes to ensure complete dissolution. Once the solubilizer was fully dissolved, an additional 10 mg of SC was introduced, and the process was repeated with continuous vortexing for another 20 minutes. This stepwise addition was continued until a suspension appeared, indicating the solubility limit of the solubilizer. It was observed that up to 100 mg of sodium caprylate dissolved completely in 1 mL of PEG 400 to form a clear solution, while the addition of a further 10 mg (total 110 mg) resulted in the formation of a suspension. Using the same procedure, the solubility of sodium benzoate and PVP K25 in PEG 400 was also determined.

Table 4: Solubility of various solublizers in PEG 400

Solublizers (abbreviation)	% w/v Solubility in PEG 400
Sodium caprylate (SC)	10
Sodium benzoate (SB)	5

PVP K25	5

Determination of approximate solubility of Eluxadoline in Propylene glycol and PEG 400
Procedure-
The solubility of Eluxadoline was evaluated in propylene glycol, PEG 400, and their 1:1 mixture. For propylene glycol, 1 mL was taken in a 10 mL volumetric flask, and 2.5 mg of the drug was added, followed by vigorous vortexing for 20 minutes. Additional 2.5 mg portions were added sequentially with intermittent vortexing until a suspension formed, and the solubility was recorded. The same procedure was applied using 1 mL of PEG 400, and similarly, a mixture containing 0.5 mL of propylene glycol and 0.5 mL of PEG 400 was tested. The study indicated that both propylene glycol and PEG 400 alone were weak solvents for Eluxadoline. To enhance solubility in the 1:1 solvent mixture, solid solubilizers were incorporated at safe concentrations, increasing drug loading in the system. The results of this investigation are summarized in Table 5.

Table 5: Results of approximate solubility studies of Eluxadoline in propylene glycol and PEG 400

S. No.	Solvent system	Approximate solubility
1	Propylene Glycol	12.0 mg/ml
2	PEG 400	29.5 mg/ml
3	50% PG + 50% PEG 400	32.6 mg/ml

Results of approximate solubility studies of Eluxadoline in various blends
Different solvent blends containing varying concentrations of solubilizers were prepared, and 2.5 mg of the drug was added to 1 mL of each blend. The vials were vortexed for approximately 20 minutes to achieve complete dissolution. Additional 2.5 mg portions of the drug were added incrementally, with vortexing after each addition, until a suspension was observed. The same procedure was applied to all prepared blends, and the solubility of the drug in each system was determined. The results of these studies are presented in Table 6.

Table 6: Results of approximate solubility studies of Eluxadoline in various blends

Blend No.	Composition	Approximate Solubility
1.	25% SC + 5% PVP K25 + 1 ml PG	29 mg/ml
2.	25% SC + 1 ml PG	32.5 mg/ml
3.	15% SC + 5% PVP K25 + 5% SB + 1ml PG	31.5 mg/ml
4.	20% SC + 5 % PVP K25+ 5% SB+ 5% B-cyclodextrin + 0.5ml PEG 400 + 0.5 ml PG	25.5 mg/ml
5.	20% SC + 0.5ml PEG 400 + 0.5 ml PG	65 mg/ml
6. (Blend A)	**5% SC+ 2.5% SB +2% PVP K25 + 0.5ml PG + 0.5ml PEG 400**	**115 mg/ml**
7.	5% SC + 5% SB + 5% PVP K25+ 0.8 ml PG + 0.2 ml PEG 400	55 mg/ml
8. (Blend B)	**10% SC + 2.5% SB + 2% PVP K25 + 0.5 ml PEG 400 + 0.5 ml PG**	**125.5 mg/ml**
10.	5% SC + 2% PVP K25 +2.5%SB+ 1ml PG	70.5 mg/ml
11.	5% PVP K25 + 2 drops benzyl alcohol + 1 ml PG	35mg/ml
12.	15% SC +5% SB + 5% PVP K25 + 10% B cyclodextrin + 1 ml PG	25mg/ml

13.	5%SC + 5% SB+ 0.5 ml PEG 400 + 0.5ml PG	40 mg/ml
14.	10% SC+ 2.5%SB+ 2% PVP K25+ 1ml PG	55 mg/ml
15.(Blend C)	**% SB + 2% PVP K25 + 0.5ml PEG400 + 0.5 ml PG**	**120 mg/ml**
16.	8% SC+ 3.5% SB + 2% PVP K25 + 1ml PG	70 mg/ml

Determination of equilibrium solubility of Eluxadoline in selected blends:
4 ml of the selected solvent blends, based on preliminary solubility studies, were transferred into clean glass vials, and an excess amount of the drug was added. The vials were sealed and placed on a mechanical shaker for 24 hours to reach equilibrium. Following this, the vials were left undisturbed for 12 hours to prevent supersaturation. The solutions were then filtered using Whatman grade 41 filter paper, appropriately diluted with water, and analyzed using UV spectroscopy to determine the equilibrium solubility of the drug.[16]

Table 7: Results of equilibrium solubility study of Eluxadoline in selected blends

Blend	Composition	Equilibrium Solubility
A	5% SC+ 2.5% SB +2% PVP K25 +0.5ml PG + 0.5ml PEG 400	142.012 mg/ml
B	10% SC + 2.5% SB + 2% PVP K25 + 0.5ml PEG 400 + 0.5ml PG	158.220 mg/ml
C	8% SC + 3.5% SB + 2% PVP K25 + 0.5ml PEG400 + 0.5 ml PG	146.113 mg/ml

Equilibrium Solubility of Eluxadoline in Different Mediums
Solubility studies in different aqueous mediums were carried out by adding an excess amount of drug (Eluxadoline) in the 5 ml of respective mediums in clean glass vials and sealed and kept on mechanical shaker at room temperature for 24 hours, and then kept undisturbed for 12 hrs. Then, the solutions were filtered through Whatman filter. The absorbances of the solutions were measured at 241 nm on UV/Visible spectrophotometer after appropriate dilution with respective medium. The results are reported in Table 8.

Table 8: Equilibrium Solubility of Eluxadoline in different mediums

S. No.	Solvent	Solubility (mg/ml)	Description
1	stilled water	0.324	Very slightly soluble
2	0.1 N HCl	0.295	Very slightly soluble

Drug Solublizers Interference Studies in UV Spectrophotometric Analysis
It was important to study that the solublizers to be used must not interfere with absorbance of drug at 241 nm to make accurate estimations. For this, 100 mg of drug was taken in 100 ml volumetric flask and dissolved in 30 ml ethanol by shaking on vortex for about 5-10 mins to get drug dissolved, then the volume was made up to 100 ml with Distilled water. So, 1000 mcg/ml stock solution was prepared.

100 mg sodium caprylate or other excipient was taken in another 100 ml volumetric flask, and dissolved using 50 ml of Distilled water and then the volume was made up to 100 ml with Distilled water to get 1000 mcg/ml stock solution.

2 ml of drug solution and 10 ml of sodium caprylate solution was then taken in another 100 ml volumetric flask and volume was made up to 100 ml using Distilled water. So here, 20 mcg/ml drug solution was prepared and the solution of sodium caprylate was of 100 mcg/ml and absorbance of drug was noted against reagent blank at 241 nm.

Similar experiment was performed for all the other excipients such as PVP K25, sodium benzoate, propylene glycol, PEG 400 and ethanol. Here it is important to know that the absorbance of drug solution of concentration 20 mcg/ml which was reported to be 0.217 against Distilled water.

Table 9: Absorbance data for interference study

Drug	Excipients	Drug conc. (µg/ml)	Additives conc.(µg/ml)	λ-max (nm)	Absorbance
Eluxadoline (ELUX)	--	20	-	241	0.217
ELUX	Sod benzoate	20	100	241	0.219
ELUX	PVPK25	20	100	241	0.217
ELUX	Sod caprylate	20	100	241	0.219
ELUX	Ethanol	20	100	241	0.218
ELUX	PEG 400	20	100	241	0.218
ELUX	opylene glycol	20	100	241	0.218

The values of absorbances in presence of solubilizers and the absorbance of drug solution were approximately same. Therefore, it was concluded that the solublizers were not interfering in the UV spectrophotometric analysis of drug at 241 nm.

DRUG - EXCIPIENT INTERACTION STUDIES

Interaction studies of drug-excipients assessed the physical compatibility of the drug with the excipients. The drugs and excipients were mixed in separate clean glass vials in a 1:1 ratio, which were then properly sealed and kept undisturbed under different temperature conditions; that is to say, for a duration of one month at room temperature and in the refrigerator. After each week, vials were examined and material was noticed for any change in their physical appearance. The findings thus observed have been listed in table 10.

Table10: Observations of physical interaction between the drug and excipients

S. No.	Drug-excipients mixture	Initial appearance	Storage conditions							
			Refrigerator (2-8ºC)				Room temperature			
			Weeks				Weeks			
			1	2	3	4	1	2	3	4
1	ELUX	White powder	N	N	N	N	N	N	N	N
2	ELUX + SB	White powder	N	N	N	N	N	N	N	N

3	ELUX +PVP K25	White powder	N	N	N	N	N	N	N	N
4	ELUX + SC	White powder	N	N	N	N	N	N	N	N
5	ELUX + ET	Whitish suspension	N	N	N	N	N	N	N	N
6	ELUX + PEG 400	Whitish suspension	N	N	N	N	N	N	N	N
7	ELUX + BA	Whitish suspension	N	N	N	N	N	N	N	N
8	ELUX + PG	Whitish suspension	N	N	N	N	N	N	N	N

ELUX = Eluxadoline, N = No Change, SB = Sodium benzoate, PVPK25 = Poly vinyl pyrrolidone K25, SC = Sodium caprylate, ET = Ethanol, PEG 400 = Poly ethylene glycol 400, BA = Benzyl alcohol, PG = Propylene glycol

Formulation Development of Liquisolid System of Eluxadoline

Selection of Solvent System

A non-volatile, water-miscible solvent system consisting of propylene glycol and PEG 400 (1:1) was selected for the formulation of a fast-release liquisolid system. To enhance the solubility of Eluxadoline in this base system, solid solubilizers were incorporated using the mixed solvency concept, forming Blends A, B, and C. These blends exhibited maximum drug solubility and were selected for further studies.

Selection of Carrier and Coating Material

A porous and highly adsorptive carrier, microcrystalline cellulose (MCC, Avicel PH 200, 180 µm), was selected due to its excellent flowable liquid retention capacity. Aerosil (5%) was chosen as the coating material to obtain a free-flowing, non-adherent, and compressible powder. The carrier-to-coating ratio was optimized within the 50:1 to 5:1 range to achieve ideal flow and compressibility characteristics.

Procedure and Preparation of Liquisolid System

To determine the optimal carrier, 1 mL of Blend A was mixed with various carriers in small increments until a free-flowing powder was obtained. The required carrier quantity was determined by difference in pre- and post-weighed amounts. As shown in Table 11, microcrystalline cellulose (Avicel PH 200) required the least quantity (3345 mg) to achieve flowability and was therefore selected. Magnesium carbonate was excluded due to its drug re-adsorption tendency.

Table 11. Selection of Carrier Material

S. No.	Carrier Material	Volume of Blend A (mL)	Approx. Carrier Required (mg)
1	Avicel PH 200 (MCC)	1	3345
2	Lactose	1	12541
3	$MgCO_3$	1	2527
4	Talc	1	3981

Preparation Method

Accurately weighed 500 mg of Eluxadoline was dissolved in 3.8 mL (Blend A), 3.3 mL (Blend B), and 3.6 mL (Blend C) separately using trituration to form clear drug solutions. Each solution was gradually incorporated into pre-weighed MCC (carrier) until completely adsorbed, followed by addition of Aerosil (coating material, 5%) to yield a dry, free-flowing, and compressible powder.

Three liquisolid formulations (LS-01, LS-02, LS-03) were prepared, each equivalent to 25 mg drug per dose, as summarized in Table 12.

Table 12: Composition of Liquisolid Formulations

Batch	Carrier (MCC, mg)	Coating (Aerosil, mg)	Blend Used	Volume (mL)	Net Weight (g)
LS-01	**7750**	**600**	**A**	**3.8**	**12.805**
LS-02	**6720**	**600**	**B**	**3.3**	**11.124**
LS-03	**7205**	**600**	**C**	**3.6**	**12.282**

Evaluation of Liquisolid System

Drug Content

Drug content uniformity was determined by dissolving a quantity of liquisolid powder equivalent to 12.5 mg Eluxadoline in 500 mL of 0.1 N HCl. After continuous shaking for 30 minutes, the absorbance was measured at 241 nm using UV spectrophotometry. All formulations showed satisfactory drug content ranging from 97.77% to 99.52%, indicating uniform drug distribution (Table 13).

Table 13: Drug Content of Liquisolid Formulations

Batch	Amount Analyzed (mg/500 mL)	Drug Content (%)
LS-01	12.44	99.52
LS-02	12.22	97.77
LS-03	12.33	98.64

Dissolution Studies

Dissolution profiles were determined to identify the optimized formulation. The study was conducted using USP Basket Apparatus in 0.1 N HCl (900 mL) at 100 rpm and 37 ± 0.5°C. Samples (20 mL) were withdrawn at predetermined intervals and replaced with fresh medium. Each capsule contained liquisolid powder equivalent to 25 mg Eluxadoline (Table 14).

Table 14: Powder Quantity in Capsules for Dissolution Study

Batch	Powder per Capsule (mg)	Drug Dose (mg)
LS-01	643.33	25
LS-02	568.94	25
LS-03	622.56	25

Dissolution Profiles

All formulations demonstrated rapid drug release compared to the pure drug. Among the three, LS-01 exhibited the highest release rate, achieving 99.77% release within 45 minutes (Tables 15-17).

Table 15. Dissolution Profile of LS-01 (Blend A)

Time (min)	Cumulative Drug Release (%)
1	1.49
2	3.80
5	56.69
10	86.26
15	94.95
30	98.07
45	99.77
60	99.72

Table 16. Dissolution Profile of LS-02 (Blend B)

Time (min)	Cumulative Drug Release (%)
1	0.80
2	4.81
5	64.52
10	75.12
15	78.36
30	88.46
45	90.31
60	92.96

Table 17. Dissolution Profile of LS-03 (Blend C)

Time (min)	Cumulative Drug Release (%)
1	0.67
2	2.79
5	48.04
10	74.60
15	75.04

30	79.76
45	82.24
60	82.26

Dissolution Profile of Pure Drug (Eluxadoline)

To compare the enhancement in dissolution rate, the dissolution behavior of pure Eluxadoline was evaluated under identical conditions (0.1 N HCl, 900 mL, 100 rpm, 37 ± 0.5°C). The cumulative percentage of drug released at various time intervals is presented in Table 18.

Table 18. Dissolution Profile of Pure Eluxadoline

Time (min)	Cumulative Drug Release (%)
1	2.04
2	3.45
5	9.67
10	15.49
15	20.98
30	29.14
45	42.76
60	55.06

A marked improvement in dissolution rate was observed in all liquisolid formulations compared to the pure drug. While the pure drug exhibited only 9.67% release within 5 minutes, all liquisolid formulations achieved over 50% release in the same duration, confirming a significant enhancement in dissolution efficiency due to the liquisolid technique

Final Batch Preparation

Based on the dissolution study results, batch LS-01 was identified as the optimized formulation and was therefore selected for scale-up to assess the effects of key formulation parameters such as carrier concentration, dissolution characteristics, and disintegration time. For the preparation of the final batch, 9.5 mL of Blend A was transferred into a clean, dry mortar, and 1250 mg of Eluxadoline was accurately weighed and incorporated into it with continuous trituration until a clear solution was obtained. The calculated quantity of carrier, 19,375 mg of Avicel PH 200, was then added to the mixture to allow complete adsorption of the drug. The remaining steps were carried out following the same procedure used for the liquisolid preparation in the trial formulations.Considering the 25 mg dose of Eluxadoline, a total of 50 doses of the liquisolid system were prepared using 9.5 ml of Blend A and 1250 mg of drug.

Drug Content

To evaluate the drug content, a quantity of the liquisolid formulation equivalent to 12.50 mg of Eluxadoline was accurately weighed and transferred into a 500 mL volumetric flask. About 300 mL of 0.1 N HCl was added, and the mixture was continuously shaken for 30 minutes to achieve complete dissolution of the drug. The volume was then adjusted to 500 mL with 0.1 N HCl, and the resulting solution was filtered. The absorbance of the filtrate was recorded at 241 nm using a UV spectrophotometer. The analyzed drug content was determined to be 12.36 mg, which corresponds to 98.92% of the labeled amount in the scale-up formulation.

Disintegration Time Studies

Six capsules were individually placed into the tubes of the disintegration testing apparatus. The disintegration medium consisted of 900 mL of 0.1 N HCl, maintained at a temperature of 37 ± 2°C and operated at a frequency of 28–32 cycles per minute. The capsules containing the LS-01 liquisolid formulation exhibited disintegration times ranging from 57 seconds to 3 minutes and 10 seconds.

Comparative Dissolution Profile

The dissolution behavior of the prepared liquisolid batch was compared with that of the pure drug. A formulation equivalent to 25 mg of Eluxadoline was filled into a size “00” capsule and evaluated using a USP Basket Apparatus in 900 mL of 0.1 N HCl at 37 ± 0.5°C and a rotation speed of 100 rpm. Samples of 20 mL were withdrawn at 1, 2, and subsequent time intervals, with an equal volume of fresh dissolution medium replaced each time. The collected samples were filtered and analyzed spectrophotometrically at 241 nm to determine the cumulative percentage of drug release. The dissolution profile of the optimized batch revealed that the capsule containing the liquisolid formulation released 95.42% of the drug within 10 minutes, whereas the pure drug exhibited only 56.25% release in the same duration.

Table 19: Comparative dissolution profiles of final batch preparation and pure drug

Time (min)	(%) Cumulative drug release	
	Pure Drug	Final batch
01	2.04	1.27
02	3.45	3.42
05	9.67	54.74
10	15.49	81.09
15	20.98	89.24

30	29.14	95.07
45	42.76	97.24
60	55.06	95.42

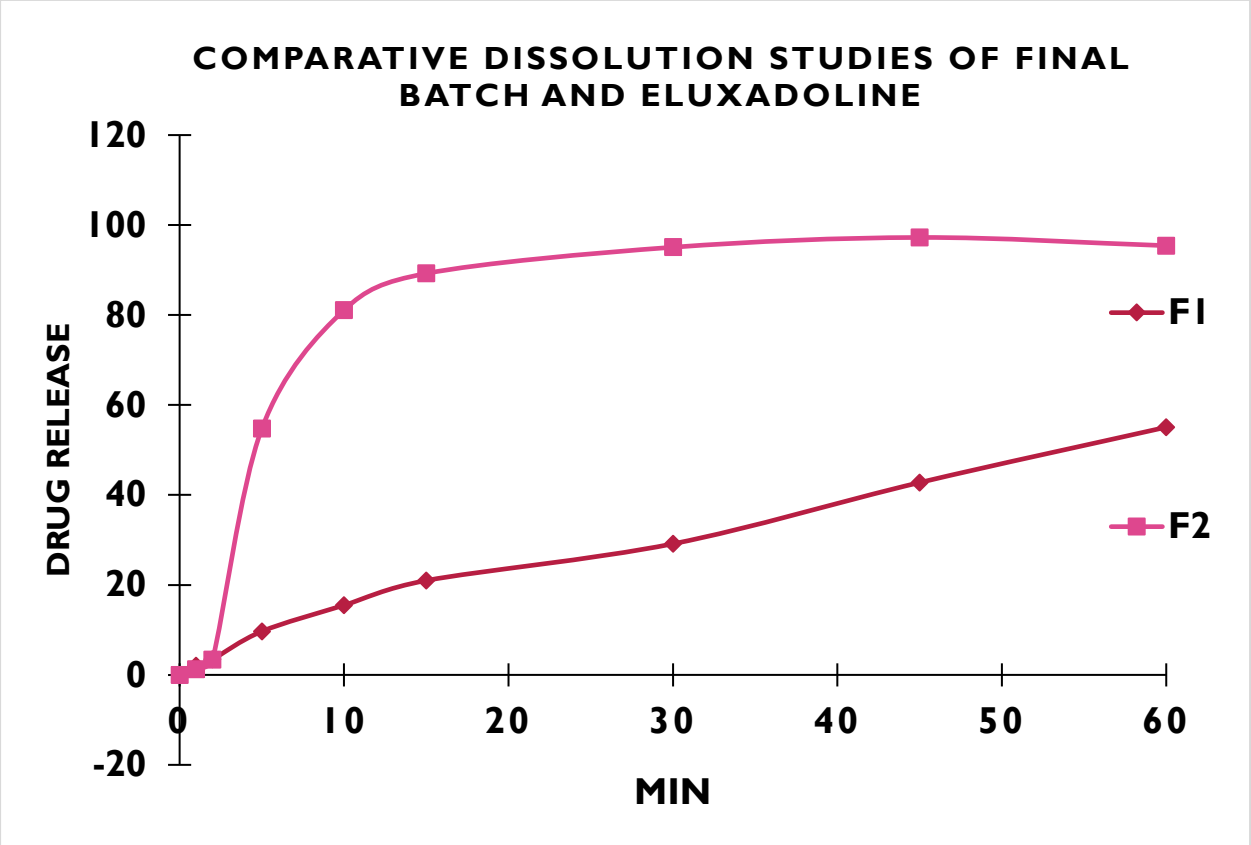

Figure 3: Comparative Dissolution Profile of Final Batch and Eluxadoline

DISCUSSION

The study successfully improved the solubility and dissolution rate of the poorly water-soluble drug Eluxadoline using a mixed solvency-based liquisolid system. A blend of propylene glycol and PEG 400 (1:1) with solid solubilizers (sodium caprylate, sodium benzoate, and PVP K25) significantly enhanced solubility, with Blend A showing the highest value of 142.012 mg/mL. Compatibility studies confirmed no drug–excipient interactions. Avicel PH 200 and Aerosil were used as carrier and coating materials to convert the liquid medication into a compressible powder. Among the formulations, LS-01 was optimized, showing 99.77% drug release within 45 minutes and maintaining 98.92% drug content after scale-up. The optimized batch achieved 95.42% drug release in 10 minutes, while the pure drug released only **55.06% in 60 minutes,** confirming that the **mixed solvency-based liquisolid approach** effectively enhanced Eluxadoline's solubility and dissolution rate.

CONCLUSION

This study demonstrated that employing a **mixed solvency-based liquisolid system** is an effective approach to enhance the solubility and dissolution rate of the poorly water-soluble drug **Eluxadoline.** The optimized formulation prepared using **Blend A** with suitable carrier and coating materials, exhibited good flow characteristics, uniform drug distribution, fast disintegration, and a significantly improved dissolution profile compared to the pure drug. The enhanced drug release—from **55.06% in 60 minutes** for the pure drug to **95.42% within 10 minutes** for the liquisolid formulation—clearly indicates the success of this strategy. Overall, the developed **liquisolid system based on the mixed solvency concept** provides a simple, economical, and scalable method to improve the dissolution efficiency and oral bioavailability of poorly soluble drugs like Eluxadoline.

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