RESEARCH ARTICLE

Liquisolid Technique: A Strategy for Enhancing Poorly Water-Soluble Drugs and Evaluating their Physicochemical Properties

Tomer K*, Jain D

Research Scholar, Faculty of Pharmacy, Mandsaur University, Mandsaur-458001, MP, India

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ABSTRACT

The present study was carried out to enhance the solubility and dissolution rate of Eluxadoline, a poorly water-soluble drug, based on the liquisolid concept. Eluxadoline was identified as a white, amorphous, odorless powder with a melting point of 188–189°C, consistent with the standard range of 187–189°C. Solubility studies revealed that it is practically insoluble in water (0.0023 mg/mL) and methanol (0.00866 mg/mL), but slightly soluble in an acetonitrile water mixture (50:50, 1.47 mg/mL). FTIR spectral analysis of the pure drug and its physical mixture showed no significant changes in characteristic peaks, indicating compatibility between the drug and excipients. In accordance with the liquisolid concept, the drug was dissolved in a suitable non-volatile solvent and converted into a dry, free-flowing, and compressible powder using appropriate carrier and coating materials. Three liquisolid formulations (LS-01, LS-02, and LS-03) were prepared and evaluated for *in vitro* dissolution. Among them, LS-01 exhibited the fastest and most complete drug release, achieving 99.77% within 45 minutes, whereas LS-02 and LS-03 showed 92.96% and 82.26% release, respectively. The improved dissolution of LS-01 may be attributed to enhanced surface wetting, increased surface area exposure, and improved drug dispersion within the carrier matrix. Comparative dissolution studies with the pure drug demonstrated that the liquisolid formulation released 95.42% of the drug within 30 minutes, compared to only 55.06% release from the pure drug after 60 minutes. These results confirm that the liquisolid concept is an effective approach for improving solubility, dissolution rate, and potentially the oral bioavailability of poorly water-soluble drugs like Eluxadoline.

Keywords: Liquisolid technique, Eluxadoline, Solubility enhancement, Dissolution rate, Oral bioavailability

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INTRODUCTION

Oral drug delivery is the most preferred and convenient route of administration due to its ease of use, patient compliance, and cost-effectiveness. However, the formulation of poorly water-soluble drugs remains a major challenge in achieving satisfactory bioavailability. More than 40% of newly developed drugs exhibit low aqueous solubility, which leads to erratic absorption and variable therapeutic outcomes[1]. Eluxadoline, a mixed μ-opioid receptor agonist and δ-opioid receptor antagonist used in the treatment of irritable bowel syndrome with diarrhea (IBS-D), is one such drug with limited aqueous solubility, resulting in poor dissolution and reduced oral bioavailability[2].

Several formulation techniques such as micronization, solid dispersions, inclusion complexation, and surfactant solubilization have been explored to overcome this limitation; however, these methods often suffer from drawbacks like poor stability, complex processing, and scalability issues. The liquisolid technique offers a simple and effective approach to enhance the solubility and dissolution rate of poorly soluble drugs. This technique involves converting liquid medications or drug solutions into dry, free-flowing, and compressible powders by adsorbing them onto suitable carrier and coating materials[3,4].

The resulting powders can be easily processed into tablets or capsules while maintaining improved dissolution characteristics. Hence, the present study focuses on developing an oral liquisolid system of Eluxadoline to enhance its solubility, dissolution rate, and overall oral bioavailability[5,6].

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

Physical Identification and Melting Point

Physical identification of drug was visually recognized and the melting point of Eluxadoline was determined by using the capillary method and compared with reference data that is show in Table 1[7].

Determination of Solubility of Eluxadoline

**Author for Correspondence: kirtitomarmip@gmail.com*

Table 1: Physical Appearance and Melting Point of Eluxadoline

S. No.	Properties	Standard	Drug
1.	Color	White Amorphous powder	White Amorphous powder
2.	Odour	Odourless	Odourless
3.	Melting point	187-189 ºC	188-189ºC

Table 2: Solubility of Eluxadoline

Solvent	Solubility (mg/ml)	Description
Water	0.00230	Practically insoluble
Methanol	0.00866	Practically insoluble
Acetonitrile: water (50:50)	1.47	Slightly soluble

Solubility study of Eluxadoline was carried in demineralized water, methanol and water: acetonitrile (50:50). Drug added in the excess amount and slowly to 5 ml of each solvent. Then, solutions shaken on the mechanical shaker on room temperature for 12 hours.

Solutions were allowed for 24 hours for obtained equilibrate. Then, the solutions were transferred into the centrifuge tubes and centrifuged on about 1000 rpm for 5 min and filtered by using filter paper and obtained filtrates were correctly diluted. The prepared diluted solutions analyzed at 243 nm by using the suitable blank solution[8].

Preparation of Liquisolid Compacts

A non-volatile, water-miscible solvent system of propylene glycol and PEG 400 (1:1) was selected for the fast-release liquisolid formulation of Eluxadoline. Solid solubilizers were added using the liquisolid concept to form Blends A, B, and C, which showed maximum solubility and were chosen for further study[9]. Microcrystalline cellulose (Avicel PH 200) was selected as the carrier due to its high adsorptive capacity, while Aerosil (5%) served as the coating material to ensure free flow and compressibility. The carrier-to-coating ratio was optimized between 50:1 and 5:1. Eluxadoline (500 mg) was dissolved in 3.8 mL (Blend A), 3.3 mL (Blend B), and 3.6 mL (Blend C) to form clear solutions, which were mixed with the carrier and coated to obtain dry, free-flowing powders. Three liquisolid formulations—LS-01, LS-02, and LS-03—were prepared, each equivalent to 25 mg of the drug per dose[10].

FT-IR Study of Pure Drug and Physical Mixture

For physical mixture and Eluxadoline the pellets have been prepared using potassium bromide (KBr) for FT-IR study. The samples were analyzed in 'Agilent FTIR spectrometer. IR spectra analyzed which are illustrated in figures 4 and 5[11,12].

Table 3: Comparative Dissolution Profile of Liquisolid Formulations (LS-01, LS-02, and LS-03)

Time (min)	Cumulative Drug Release		
	LS-01	LS-02	LS-03
1	1.49	0.80	0.67
2	3.80	4.81	2.79
5	56.69	64.52	48.04
10	86.26	75.12	74.60
15	94.95	78.36	75.04
30	98.07	88.46	79.76
45	99.77	90.31	82.24
60	99.72	92.96	82.26

Table 4: 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

***In-vitro* Release Studies**

Accurately weighed 50 mg of sample was used for the dissolution study. Sample has been withdrawn by predetermined time intervals and analyzed intended for *in-vitro* drug release by measuring the absorbance at 243nm using 0.1 N HCl as medium. The volume was withdrawn at each one-time intervals and replaced by using same amount of fresh medium[13].

RESULTS AND DISCUSSION

Physical Identification and Melting Point

Physical Identification of a drug was visually identified and melting point of Eluxadoline was determined by capillary method[14].

The results of solubility studies of Eluxadoline are summarized in table 2.

IR Spectrum of Eluxadoline and physical mixture shown in Fig. 1 and 2 there was no important change in the peak value

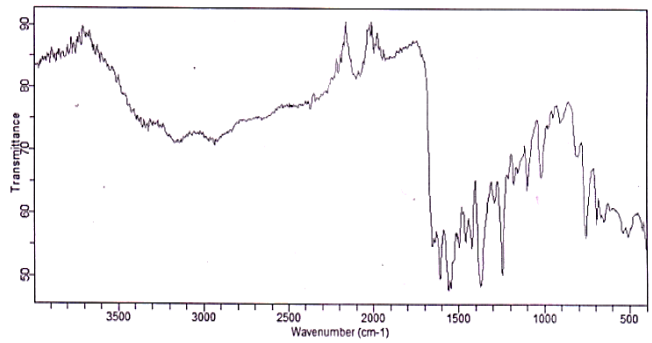

Figure 1: IR Spectrum of Eluxadoline

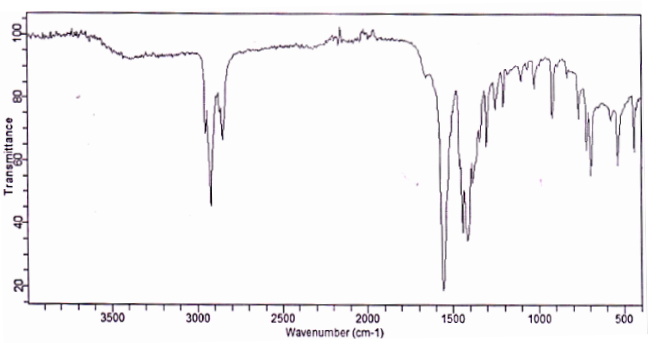

Figure 2: IR Spectrum of Physical Mixture

with solubiliser. Thus, it can be concluded that the solubiliser interfere in IR is compactable with Eluxadoline[15].

The dissolution profile of the three liquisolid formulations (LS-01, LS-02, and LS-03) demonstrated significant improvement in the drug release rate, with LS-01 showing the fastest and most complete release[16]. LS-01 achieved nearly complete drug release (99.77%) within 45 minutes, while LS-02 and LS-03 reached 92.96% and 82.26%, respectively, at 60 minutes. The enhanced dissolution observed in LS-01 may be attributed to better solubilization and efficient adsorption of the drug onto the carrier system, resulting in improved wettability and surface area exposure[17].

Overall, the results indicate that the liquisolid technique effectively enhanced the dissolution of Eluxadoline, with LS-01 exhibiting the most desirable release characteristics[18].

Comparative Dissolution Profile

Dissolution 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 tested in 900 ml of 0.1 N HCl using a USP Basket Apparatus at 100 rpm and 37 ± 0.5°C. Samples (20 ml) were withdrawn at 1, 2, and subsequent time intervals, replaced with equal volumes of fresh medium, filtered, and analyzed spectrophotometrically at 243 nm to determine cumulative drug release. From the dissolution profile of the final batch, it was observed that the capsule containing liquisolid formulation released 95.42 % of drug within 10 minutes, and only 56.25% drug was released[19].

CONCLUSION

The study successfully demonstrated that the liquisolid concept is an effective and simple technique for enhancing the solubility and dissolution rate of poorly water-soluble drugs like Eluxadoline. Among the formulations developed, LS-01 showed the most rapid and complete drug release, achieving nearly 99.00 % dissolution within 45 minutes. The improved performance was attributed to better wetting, increased surface area, and uniform drug distribution within the carrier matrix. Overall, the liquisolid technique offers a promising approach to improve the oral bioavailability of drugs with poor aqueous solubility.

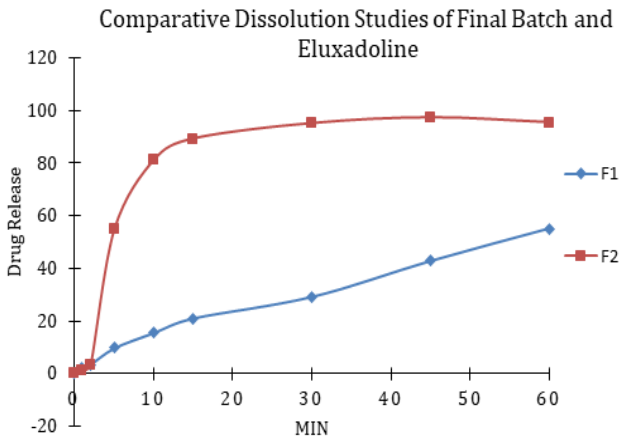

Figure 3: Comparative Dissolution Profile of Final Batch and Eluxadoline

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