ORIGINAL ARTICLE

Improvement of Dissolution Characteristics of Edoxaban through Solid Dispersion Technique

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Abstract

Aim: This study aimed to identify the most effective carrier system for enhancing the solubility of Edoxaban (EDO) through the preparation of solid dispersions (SDs) using a novel microwave-induced fusion technique. **Materials and Methods:** Various carriers including PEGs (3350–20000), PVPs (K-12–K-90), Poloxamers (108–407), and urea were employed to prepare SDs of EDO. Drug–carrier compatibility was assessed, followed by evaluation of SD flow properties. SDs were compressed into tablets and analyzed for physicochemical parameters such as thickness, hardness, friability, drug content, solubility, and in vitro dissolution. A high-performance liquid chromatography method was developed to quantify drug release. **Results:** Among all carriers, a blend of PEG-8000, PVP-K-30, and Poloxamer 188 showed the best enhancement in EDO solubility and dissolution rate. The optimized formulation exhibited superior physical tablet properties and content uniformity. Accelerated stability studies confirmed formulation robustness. In vivo release studies and pharmacokinetic comparisons with a marketed product confirmed enhanced bioavailability. **Conclusion:** The combination of PEG-8000, PVP-K-30, and Poloxamer 188 in microwave-induced SDs significantly improved the solubility and performance of EDO, demonstrating a promising strategy for enhancing poorly soluble drugs.

Key words: Dissolution characteristics, Edoxaban, improvement, solid dispersion technique

INTRODUCTION

Oral administration refers to the process of delivering a medicine through the mouth. Because many drugs have a systemic effect, which means they travel through the bloodstream to other parts of the body, they are frequently administered orally. A tablet is a solid dosage form that has been compressed and includes medication, with or without excipients. Pharmaceutical tablets are defined as solid, flat, or biconvex dishes formed by compressing a pharmaceutical or drug mixture, with or without diluents. This is from the Indian Pharmacopoeia. Their size, weight, and shape vary substantially depending on the amount of drug and the method of delivery.[1,2] Tablets are the most popular dose form, accounting for 70% of all drugs administered. Solid drugs may be administered orally in the form of capsules, tablets, powders, cachets, or pills. Even prolonged action preparations, which potentially contain the equivalent of multiple conventional doses of medicine, are referred to as solid unit dosage forms since they contain a single unit of drug. A tablet that quickly dissolves or disintegrates in the patient's mouth is convenient for small children, the elderly, mentally retarded, and bedridden patients who previously likely suffered from hand and dysphasia problems.[3,4] When a fast-dissolving sublingual tablet is placed in the mouth, it dissolves quickly and becomes liquid after swallowing. Sublingual tablets operate by allowing the medication to be absorbed quickly or directly through the mucosal lining of the mouth beneath the tongue, resulting in an immediate systemic action. Following

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stomach absorption, the drug reaches the mesenteric circulation through the portal vein. Absorption through the oral mucosa eliminates the need for first-pass metabolism. Sublingual tablets are typically flat, small, and very slightly crushed to keep them soft. To allow the drug to be absorbed, the tablets must dissolve quickly. Because it dissolves in a small amount of saliva, the patient must refrain from eating, drinking, smoking, and possibly talking for as long as the tablet is in the mouth beneath the tongue.[5] The goal of achieving a rapid onset of pharmacological activity led to systemic drug delivery through the sublingual route. Sublingual drugs have been produced for a wide range of illnesses, including mental illness (where patient compliance is critical for treating chronic indications such as depression and schizophrenia) and migraines, which require a rapid onset of action. When it comes to medicine absorption, the sublingual strategy outperforms the oral route; only the hypodermic injection method comes close. Short-acting drugs are best suited to the sublingual approach. The sublingual approach is the most effective in terms of medication absorption compared to the oral route; only the hypodermic injection method comes close. When it comes to medicine absorption, the sublingual strategy outperforms the oral route; only the hypodermic injection method comes close. Short-acting drugs are best suited to the sublingual approach. Not all compounds are permeable and accessible to the oral mucosa, but the majority of medications supplied sublingually are absorbed by simple diffusion; in this case, the sublingual area behaves like a litmus paper, rapidly soaking up the contents.[6] The majority of sublingual drugs are antinational. The goal of achieving a rapid onset of pharmacological effect led to systemic drug delivery through the sublingual route. Pills often act faster when taken sublingually than orally. Furthermore, the amount absorbed by sublingual blood vessels bypasses the liver's first-pass metabolic processes. Underdeveloped children typically have problems with their muscles and nerve systems when swallowing, which can be treated with swiftly dissolved sublingual tablets to aid in recovery. The oral route of drug administration has long been regarded as the most preferable way due to its several advantages over other routes, including being the most natural, simple, safe, and convenient, providing greater design freedom for dose forms, being simple to manufacture, and being economical. Effective preparation of the sublingual tablets might be achieved by using the right pharmaceutical excipients in the right amounts together with the best manufacturing practices.[7,8]

MATERIAL S AND METHODS

Preformulation studies

Preformulation investigations were carried out before beginning the formulation of solid dispersion fast-dissolving tablets (FDTs). This section contains the preparation of standard graphs, analytical method development, and solubility studies of the drug.[9]

Drug-carrier interaction studies

FTIR analysis was performed on Edoxaban (EDO) pure drug, carriers, and EDO solid dispersions to examine potential drug-excipient interactions. The samples were investigated using differential scanning calorimetry (DSC) and X-ray diffraction (XRD) to see how the medication changed from crystalline to amorphous form.[10]

Fourier transform infrared (FTIR) spectroscopy studies

FTIR studies offer information on the physicochemical features of compounds that affect compatibility (164). The spectra of EDO pure drug, carriers, and optimal formulation were recorded on an FTIR (Shimadzu, Japan) with a KBr pellet in the 4000–400 cm^{-1} region. The pellets were made by combining 5 mg of the sample with 100 mg of potassium bromide and compacting them under vacuum for 3 min at about 12,000 psi. The resulting spectra were compared to detect any changes in the spectra's peaks.[11]

DSC studies

A DSC investigation was performed on EDO pure drug, carriers, and improved formulations, and thermograms were generated using DSC. Samples (5–10 mg) were accurately weighed and deposited in closed, perforated, flat-bottomed aluminum pans. Nitrogen gas was pumped at a flow rate of 50 mL/min and heated at a continuous rate of 15°C/min in a temperature range of 50°C–350°C. The melting point, peak maxima, appearance of any additional peaks, and change in peak morphology were all recorded.[12,13]

Preparation of EDO solid dispersions by solvent evaporation method

Solid dispersion of EDO with different carriers (PEG 4000, PEG 6000, PEG 20000, Gelucire 44/14, and Gelucire 50/13) in different weight ratios was prepared by the solvent evaporation method.[14] Accurately weighed volumes of medication and carriers in varied ratios were dissolved in ethanol in a round bottom flask, which was then evaporated at 45°C. The solid dispersions were then kept in a vacuum oven at room temperature for 48 h to remove the remaining solvent. The dried solid dispersions were pulverized in a mortar and pestle, passed through sieve #60, and stored in a desiccator. Table 1 shows the compositions of various solid dispersions.

Formulation of EDO FDTs

The FDTs were created for specific solid dispersion preparations, and their composition is shown in Table 2. The FDTs were created using a direct compression method. The solid dispersion powder containing 50 mg of EDO and other excipients was passed through mesh number 60#.

Table 1: Preparation of EDO solid dispersions using various carriers by the solvent evaporation method

Solid dispersion code	Ingredients quantity in mg						Ratio
	EDO	PEG 4000	PEG 6000	PEG 20000	Gelucire 44/14	Gelucire 50/13	
EDO1	50	25	-	-	-	-	1:0.5
EDO2	50	50	-	-	-	-	1:1
EDO3	50	100	-	-	-	-	1:2
EDO4	50	200	-	-	-	-	1:4
EDO5	50	250	-	-	-	-	1:5
EDO6	50	300	-	-	-	-	1:6
EDO7	50	-	25	-	-	-	1:0.5
EDO8	50	-	50	-	-	-	1:1
EDO9	50	-	100	-	-	-	1:2
EDO10	50	-	200	-	-	-	1:4
EDO11	50	-	250	-	-	-	1:5
EDO12	50	-	300	-	-	-	1:6
EDO13	50	-	-	25	-	-	1:0.5
EDO14	50	-	-	50	-	-	1:1
EDO15	50	-	-	100	-	-	1:2
EDO16	50	-	-	200	-	-	1:4
EDO17	50	-	-	250	-	-	1:5
EDO18	50	-	-	300	-	-	1:6
EDO19	50	-	-	-	25	-	1:0.5
EDO20	50	-	-	-	50	-	1:1
EDO21	50	-	-	-	100	-	1:2
EDO22	50	-	-	-	150	-	1:3
EDO23	50	-	-	-	200	-	1:4
EDO24	50	-	-	-	250	-	1:5
EDO25	50	-	-	-	-	25	1:0.5
EDO26	50	-	-	-	-	50	1:1
EDO27	50	-	-	-	-	100	1:2
EDO28	50	-	-	-	-	150	1:3
EDO29	50	-	-	-	-	200	1:4
EDO30	50	-	-	-	-	250	1:5

EDO: Edoxaban

Crospovidone was added to the powdered solid dispersion in a proportional amount. Then, excipients other than glidant and lubricant were added and combined in a plastic bag for 5–10 min. The obtained blend was lubricated with talc and magnesium stearate for another 5 min and the resultant mixture was directly compressed into tablets by 8 mm round, flat punches using a rotary tablet machine.[15]

Evaluation of physical parameters of EDO FDTs[16-18]

The prepared FDTs were assessed for different physical parameters to check their quality.

Determination of weight variances

In this test, twenty tablets were randomly selected and weighed separately on a digital scale (AW 120, Shimadzu Corporation, Japan) to calculate the average weight. The % variation of weight was calculated using the supplied formula. % Deviation = (Individual weight - Average weight/Average weight) × 100.

Determining tablet hardness

Tablet hardness exhibits the tablet's resistance to chipping and abrasion, indicating its mechanical integrity. For each formulation, six tablets were chosen to be measured for hardness using a Monsanto hardness tester, and the average was calculated and reported with standard deviation.

Table 2: Formulation of EDO fast dissolving tablets using solid dispersions

Formulation code	Ingredientsin mg						
	EDO solid dispersion equivalent to 50 mg EDO	Pure EDO	Crospovidone (5%)	Spray-dried lactose	Magnesium stearate (1%)	Talc (2%)	Total tablet weight
EDO1	75	-	15	201	3	6	300
EDO2	100	-	15	176	3	6	300
EDO3	150	-	15	126	3	6	300
EDO4	250	-	15	26	3	6	300
EDO7	75	-	15	201	3	6	300
EDO8	100	-	15	176	3	6	300
EDO9	150	-	15	126	3	6	300
EDO10	250	-	15	26	3	6	300
EDO13	75	-	15	201	3	6	300
EDO14	100	-	15	176	3	6	300
EDO15	150	-	15	126	3	6	300
EDO16	250	-	15	26	3	6	300
EDO19	75	-	15	201	3	6	300
EDO20	100	-	15	176	3	6	300
EDO21	150	-	15	126	3	6	300
EDO22	200	-	15	76	3	6	300
EDO25	75	-	15	201	3	6	300
EDO26	100	-	15	176	3	6	300
EDO27	150	-	15	126	3	6	300
EDO28	200	-	15	76	3	6	300
EDO31	75	-	15	201	3	6	300
EDO32	100	-	15	176	3	6	300
EDO33	150	-	15	126	3	6	300
EDO34	250	-	15	26	3	6	300
EDO37	75	-	15	201	3	6	300
EDO38	100	-	15	176	3	6	300
EDO39	150	-	15	126	3	6	300
EDO40	250	-	15	26	3	6	300
EDO43	75	-	15	201	3	6	300
EDO44	100	-	15	176	3	6	300
EDO45	150	-	15	126	3	6	300
EDO46	250	-	15	26	3	6	300
EDO49	75	-	15	201	3	6	300
EDO50	100	-	15	176	3	6	300
EDO51	150	-	15	126	3	6	300
EDO52	200	-	15	76	3	6	300
EDO55	75	-	15	201	3	6	300
EDO56	100	-	15	176	3	6	300
EDO57	150	-	15	126	3	6	300
EDO58	200	-	15	76	3	6	300
Control	-	50	7.5	88	1.5	3	150

EDO: Edoxaban

Determining friability

It is another indicator of the tablet's mechanical durability and robustness. For tablets weighing <650 mg, a sample of the entire tablets measuring approximately 6.5 g was obtained. The tablets were dedusted and weighed (W1). The tablets were placed in the friabilator (Electrolab, Mumbai, India) and rotated 100 times (25 rpm for 4 min). The tablets were extracted, any loose dust was removed, and they were reweighed (W2).

% Friability = ([W1–W2]/W1) × 100

Determining the disintegration time

The *in vitro* disintegration time of FDTs was evaluated using the method published by Gohel *et al*.[13] A petridish of 10 cm in diameter was filled with 10 mL of water. The tablet was then carefully placed in the center of the petridish, and the time it took for the tablet to totally disintegrate into small particles was recorded. The measurements were taken in triplicate.

Determining wetting time

A tiny petri plate was used, with a piece of tissue paper folded twice and saturated with 6 mL of 0.5% v/v amaranth solution. A tablet is gently placed on tissue paper, and the time required for complete wetness is measured.

Determination of drug content

To estimate the assay, 100 mg of powder was carefully weighed by breaking ten randomly selected tablets and transferred to a 100 mL volumetric flask. The solution was produced to a volume of 100 mL using 7.2 pH phosphate buffer. The samples (triplicates) were filtered and analyzed for EDO content.

Stability tests of optimized EDO FDTs

Stability studies were done to assess EDO stability in optimized tablets in accordance with the International Council for Harmonisation (ICH) recommendations. The sample pills were packaged in aluminum packaging covered with polyethylene, and three sets were stored in a stability chamber (40 ± 2°C and 75 ± 5% RH) for 6 months (ICH Q1A). Samples were collected after 6 months of storage and tested for assay and EDO release. The results were statistically analyzed using a paired t-test at the $P < 0.05$ level of statistically significance.[19]

RESULT AND DISCUSSION

Preformulation studies

Determination of λ_{max} of EDO

The absorption maximum (λmax) of EDO was obtained by scanning 10 µg/mL stock solution in different media (0.1N HCl, distilled water and 7.2 pH phosphate buffer). The solutions were scanned in the 200–400 nm range with a ultraviolet (UV) spectrophotometer (Systronics 2202, Ahmedabad, India), and the results are given in Figure 1.

Standard curve for EDO

The UV spectrophotometric investigation revealed that EDO has a λmax of 247 nm. Linearity was found in the concentration range of 2–12 µg/mL. The standard graphs exhibited r^2 values of 0.9995 in 0.1 N HCl, 0.9992 in distilled water, and 0.9999 in 7.2 pH phosphate buffers, indicating that it follows the Beer–Lambert rule [Table 3 and Figures 2-4].

EDO solubility investigations

According to the solubility investigations, EDO is more soluble in 7.2 pH phosphate buffer than in pure water or 0.1 N HCl [Figure 5].

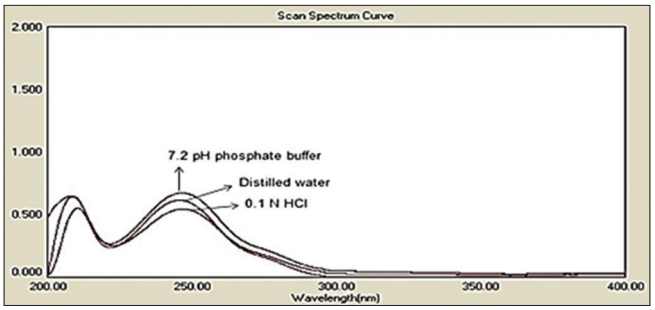

Figure 1: Ultraviolet scan of Edoxaban in 0.1N HCl, distilled water and 7.2 pH phosphate buffer

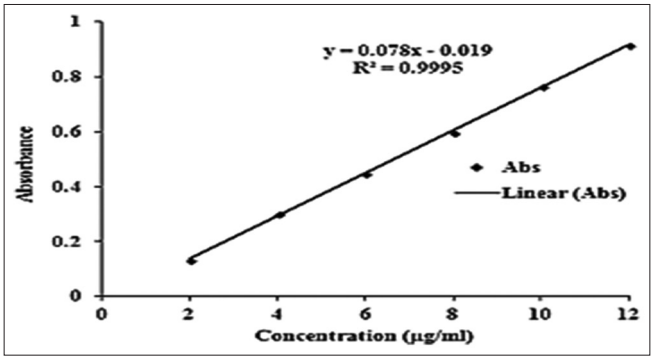

Figure 2: Edoxaban calibration curve in 0.1N HCl

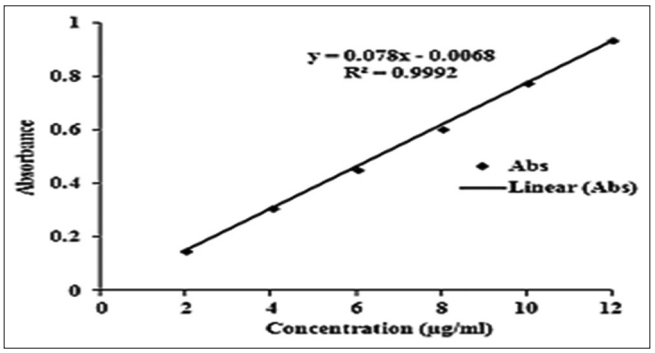

Figure 3: Edoxaban calibration curve in distilled water

Drug-carrier interaction studies

FTIR spectroscopy studies

Figure 6 shows the FTIR spectra of EDO and carriers. Figure 6 shows the FTIR spectra of solid dispersions. The FTIR spectra of Edo show characteristic peaks at 2998.43 cm^{-1} (C-H stretching vibration), 1463.51 cm^{-1} (C-H bending vibration), 1721.38 cm^{-1} (C=O carbonyl stretch of acid), 1576.24 cm^{-1} (C=C stretch of aromatic ring), and 1236.63 cm^{-1} (C-F stretching). The presence of peaks corresponding to C-H stretching vibration at 3015.27 cm^{-1}, carbonyl (C=O) stretch of acid at 1713.27 cm^{-1}, C=C aromatic group peak at 1598.76 cm^{-1}, and C-F stretching at 1242.20 cm^{-1} in the optimized solid dispersion EDO-glacier 44/14, as well as the absence of additional peaks, indicate that there was no interaction between drug and excipients. Similar results were obtained using EDO-PEG 4000, EDO-PEG 6000, EDO-PEG 20000, and EDO-glacier 50/13 dispersions.

Table 3: EDO standard curve in various media

Concentration (µg/mL)	Absorbance		
	0.1 N HCl	Distilled water	7.2 Phosphate buffer
2	0.132	0.153	0.163
4	0.302	0.312	0.324
6	0.448	0.454	0.476
8	0.598	0.605	0.639
10	0.767	0.776	0.791
12	0.915	0.937	0.954

EDO: Edoxaban

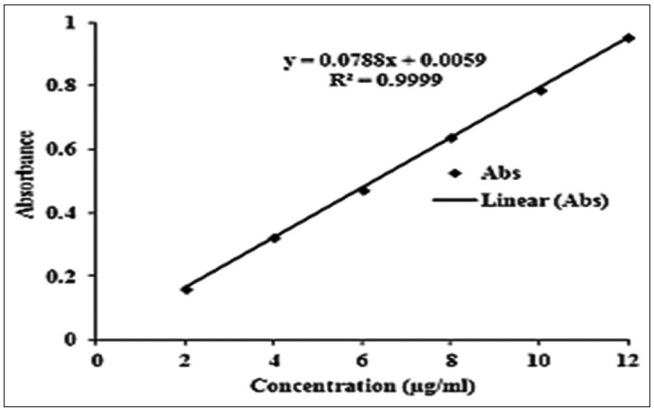

Figure 4: Edoxaban calibration curve in7.2 pH phosphate buffer

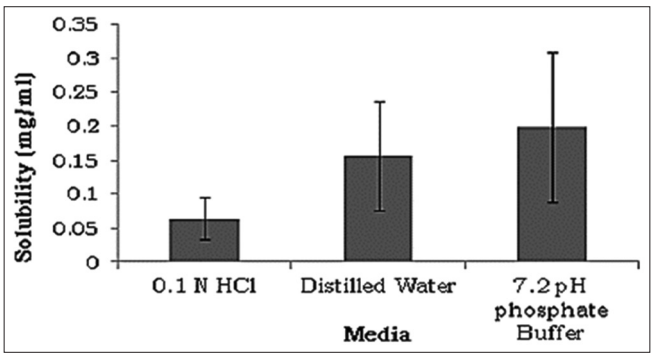

Figure 5: Solubility profile of edoxaban in different media

DSC studies

Figure 7 shows the DSC thermograms for EDO, PEG 4000, PEG 6000, PEG 20000, Gelucire 44/14, and Gelucire 50/13. EDO's DSC thermogram shows a sharp endothermic peak at 113.4°C with normalized energy of 57.8 mJ/mg, PEG 4000 shows a sharp peak at 60.2°C with normalized energy of 42.5 mJ/mg, PEG 6000 shows a sharp peak at 64.2°C with normalized energy of 58.3 mJ/mg, PEG 20000 shows a sharp peak at 69.3°C with normalized energy of 65.8 m J/mg, and Gelucire 44/14 shows a sharp peak at 45.2.2°C with normalized energy of 69.3 m. The thermogram of the optimized EDO-Gelucire 44/14 solid dispersion revealed two broad endotherms at 47.3°C and 114.6°C, with energies of 47.2 mJ/mg and 35.7 mJ/mg, respectively. These may be due to the melting of Gelucire 44/14 and EDO, respectively. The addition of Gelucire 44/14 to the solid dispersion reduced the EDO melting onset temperature. Similar results were obtained with EDO-PEG solid dispersions and EDO-Gelucire 50/13 solid dispersions.

Powder characterization of EDO solid dispersions

Table 4 shows the characteristics of the EDO solid dispersion powder. The angle of repose ranged between 27.13 ± 1.52

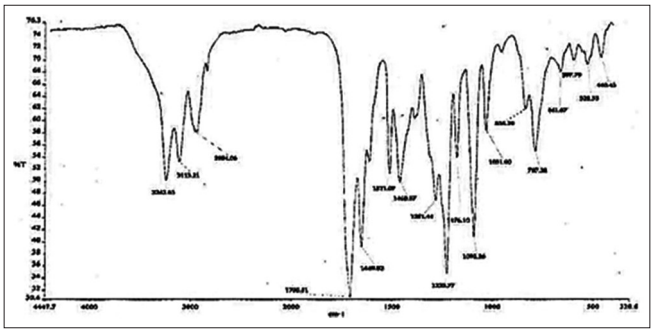

Figure 6: Fourier transform infrared spectra of edoxaban-poly ethylene glycols 6000 solid dispersion

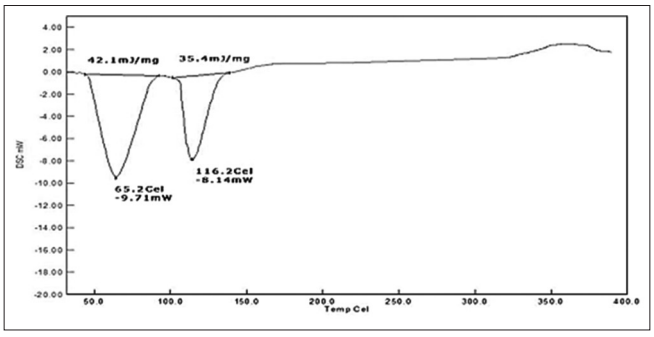

Figure 7: Differential scanning calorimetry thermogram of edoxaban-poly ethylene glycols 6000 solid dispersion

Table 4: Characterization of EDO solid dispersion powder blend

Formulation	Angle of repose (0)	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)
EDO1	28.24±0.57	0.321	0.378	15.08
EDO2	30.06±0.79	0.326	0.385	15.32
EDO3	27.87±1.56	0.324	0.382	15.18
EDO4	29.83±0.51	0.336	0.398	15.57
EDO7	30.46±0.83	0.334	0.385	13.24
EDO8	29.49±0.72	0.327	0.383	14.62
EDO9	29.64±0.86	0.332	0.384	13.54
EDO10	30.06±0.79	0.326	0.385	15.32
EDO13	28.64±0.93	0.328	0.389	15.63
EDO14	30.75±1.76	0.325	0.385	15.58
EDO15	28.59±0.95	0.328	0.378	13.22
EDO16	27.88±1.56	0.324	0.382	15.18
EDO19	30.28±1.02	0.327	0.379	13.72
EDO20	29.65±0.68	0.336	0.386	12.95
EDO21	29.34±0.37	0.329	0.387	14.98
EDO22	27.13±1.52	0.321	0.342	6.14
EDO25	28.94±0.35	0.332	0.382	13.08
EDO26	29.63±0.94	0.331	0.385	14.02
EDO27	30.24±0.62	0.326	0.383	14.88
EDO28	30.64±1.31	0.324	0.345	6.08
EDO31	30.29±1.02	0.327	0.379	13.72
EDO32	29.63±0.94	0.331	0.385	14.03
EDO33	30.12±0.41	0.332	0.397	16.37
EDO34	29.68±0.64	0.324	0.379	14.51
EDO37	28.73±0.82	0.329	0.381	13.65
EDO38	28.37±0.12	0.330	0.385	14.28
EDO39	29.37±1.28	0.327	0.356	8.15
EDO40	30.06±0.79	0.326	0.385	15.32
EDO43	29.49±0.72	0.327	0.383	14.62
EDO44	27.87±1.56	0.324	0.382	15.18
EDO45	29.83±0.51	0.336	0.359	6.40
EDO46	30.06±0.79	0.326	0.385	15.32
EDO49	30.24±0.62	0.326	0.383	14.88
EDO50	28.64±0.93	0.328	0.389	15.68
EDO51	30.28±0.32	0.336	0.376	10.64
EDO52	27.17±1.52	0.323	0.383	15.67
EDO55	28.97±0.35	0.333	0.381	12.60
EDO56	30.65±0.73	0.325	0.385	15.58
EDO57	29.47±0.62	0.331	0.388	14.69
EDO58	29.65±0.68	0.336	0.386	12.95
Control	23.31±1.60	0.320	0.354	9.60

*All values represent mean±standard deviation, n=3. EDO: Edoxaban

and 30.75 ± 1.76°. The bulk and tapped density values were found to be 0.321–0.336 and 0.342–0.398%. Carr's index was determined to be 6.08–15.68.

Evaluation of EDO FDTs

Based on the solubility investigations, the best solid dispersions were converted into FDTs. Table 5 displays all of the evaluation parameters determined for EDO tablets. In the weight variation test, the pharmacopoeial limits for tablets of no more than 5% of the average weight were found to be 300.12 ± 1.72–301.95 ± 1.35 mg.

Tablet hardness and friability ranged from 3.0 ± 0.19 to 3.1 ± 0.53 kg/cm^2 and 0.31–0.39%, respectively, indicating their integrity and strength. The disintegration test revealed that

Table 5: Evaluation of EDO fast dissolving tablets

Formulation batch	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration time (sec)	Wetting time (sec)	Drug content (%)
EDO1	300.51±1.05	3.0±0.24	0.36	122±4	28±6	98.98±1.35
EDO2	301.12±1.25	3.0±0.27	0.31	119±3	26±3	99.04±1.24
EDO3	301.22±1.36	3.0±0.28	0.39	120±4	40±2	98.94±1.28
EDO4	301.51±1.18	3.0±0.27	0.38	120±4	34±4	98.92±1.53
EDO7	300.62±1.29	3.0±0.19	0.32	119±3	49±5	98.04±1.32
EDO8	301.28±1.68	3.0±0.29	0.35	121±4	30±3	98.46±1.28
EDO9	300.28±1.93	3.0±0.23	0.38	121±3	31±4	99.75±1.64
EDO10	300.12±1.72	3.1±0.43	0.33	121±3	34±3	99.34±1.26
EDO13	300.32±1.68	3.1±0.25	0.37	120±3	30±4	99.13±1.52
EDO14	301.23±1.68	3.1±0.24	0.34	121±2	30±6	99.38±1.27
EDO15	301.23±1.45	3.0±0.24	0.38	120±4	31±7	98.09±1.58
EDO16	301.72±1.26	3.0±0.21	0.38	121±4	28±2	99.14±1.32
EDO19	300.25±1.94	3.0±0.26	0.32	120±3	30±9	99.48±1.63
EDO20	301.69±1.67	3.1±0.19	0.35	121±4	41±5	98.67±1.59
EDO21	300.68±1.84	3.1±0.24	0.33	120±3	42±3	99.52±1.83
EDO22	301.42±1.46	3.0±0.45	0.38	119±5	29±6	99.12±1.16
EDO25	301.95±1.35	3.1±0.53	0.34	120±4	31±4	98.67±1.53
EDO26	300.58±1.34	3.1±0.34	0.33	119±3	34±2	98.95±1.43
EDO27	301.83±1.57	3.0±0.42	0.34	120±3	45±7	99.38±1.72
EDO28	300.23±3.68	3.1±0.29	0.33	122±5	47±9	99.03±1.82
EDO31	301.52±1.16	3.0±0.25	0.38	120±4	34±2	98.93±1.54
EDO32	300.62±1.26	3.0±0.27	0.35	119±3	49±5	99.08±1.35
EDO33	300.22±1.63	3.0±0.23	0.37	120±4	32±2	98.46±1.22
EDO34	300.26±1.96	3.0±0.24	0.34	121±3	31±4	99.73±1.62
EDO37	300.14±1.75	3.1±0.42	0.33	121±3	34±3	99.14±1.26
EDO38	301.32±1.68	3.1±0.23	0.33	120±3	30±4	99.15±1.54
EDO39	301.23±1.68	3.1±0.24	0.34	121±2	30±6	99.38±1.27
EDO40	301.23±1.45	3.0±0.27	0.38	120±4	31±7	98.09±1.58
EDO43	300.64±1.27	3.1±0.24	0.34	121±2	31±6	99.38±1.27
EDO44	300.26±1.62	3.0±0.28	0.35	120±4	27±5	98.94±1.28
EDO45	301.53±1.12	3.0±0.24	0.32	120±3	34±3	98.93±1.52
EDO46	300.61±1.23	3.0±0.27	0.32	119±3	49±5	99.04±1.32
EDO49	301.24±1.65	3.0±0.24	0.34	121±2	30±4	98.44±1.25
EDO50	300.25±1.93	3.0±0.42	0.34	120±3	45±7	99.35±1.72
EDO51	301.65±1.62	3.1±0.24	0.33	120±3	32±2	99.52±1.83
EDO52	300.64±1.34	3.0±0.23	0.33	119±5	36±3	99.14±1.17
EDO55	301.20±1.34	3.1±0.34	0.33	119±3	40±3	98.95±1.43
EDO56	300.51±1.14	3.0±0.23	0.38	121±3	29±3	99.63±1.47
EDO57	300.52±1.23	3.0±0.64	0.33	121±4	41±6	99.12±1.34
EDO58	301.23±1.68	3.0±0.26	0.32	120±3	38±4	99.48±1.63
Control	151.12±1.13	3.1±0.10	0.45	112±4	34±3	99.98±1.54

All values represent mean±standard deviation, *n=20;n=10;n=6. EDO: Edoxaban

Table 6: Stability studies of EDO 22 fast dissolving tablets

Time (min)	Cumulative percentage of EDO released (Mean±SD)		t-test at 0.05 LS	Similarity factor (F2)
	Before storage	After 6 months of storage		
0	0.00±0.00	0.00±0.00	Not significant	86.92
5	56.72±1.24	54.85±1.81		
10	88.64±1.93	86.92±0.67		
15	99.82±1.07	98.12±0.93		
% Assay	99.12±1.16	98.23±1.07	Not significant	--

EDO: Edoxaban, SD: Standard deviation

the produced pills decomposed quickly, within 119 ± 3–122 ± 5 s. The wetting time was determined to be 26 ± 3–49 ± 5 s. The tablet assay yielded 98.04 ± 1.32–99.75 ± 1.64%.

Stability studies of optimized EDO FDTs

In the stability investigations, assay values and drug release were calculated after 6 months of storage, as shown in Table 6. The data discovered were subjected to statistical analysis, which revealed that they were not statistically different from one another ($P > 0.05$). The similarity factor value was determined to be 86.92, which was >50, showing similarity between the dissolution profile before and after storage.

SUMMARY AND CONCLUSION

The current study aims to improve the solubility, dissolution rate, and bioavailability of a weakly water-soluble EDO using the solid dispersion approach. In this study, EDO solid dispersions were synthesized using both solvent evaporation and fusion processes, with PEG 4000, PEG 6000, PEG 20000, Gelucire 44/14, and Gelucire 50/13 as carriers in varying ratios. The preparations were then analyzed for various physical parameters, solubility studies, FTIR, DSC, XRD, and drug release experiments to identify the optimal formulation with a high dissolving rate. The final EDO 22 batch found more prominent results than other batches. Following the manufacture of solid dispersions, the determination of water solubility is one of the important parameters that regulate the dissolution rate and is the rate-limiting step in the absorption of poorly soluble medicines.[18-20] The solubility of EDO 22 batch solid dispersion formulations was tested in three distinct media: 0.1 N HCl, distilled water, and 7.2 pH phosphate buffer. The solubility investigations revealed that increasing the pH of the fluid enhanced its solubility. In comparison to other media, all of the formulations showed a considerable improvement in solubility in phosphate buffer pH 7.2. The drug's pKa of 4.16 reduced solubility in all mediums from high to low pH. As a weak acid, EDO is more soluble in a basic aqueous environment.

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