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ENHANCING THE SOLUBILITY OF BCS CLASS II DRUG RALOXIFENE THROUGH SOLID DISPERSION TECHNIQUES

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ABSTRACT

Improving the solubility and rate of dissolution of Raloxifene Hydrochloride (RLX), a selective estrogen receptor modulator used to prevent and cure postmenopausal osteoporosis, was the aim of the current study. The poor water solubility of RLX, a medication that falls under BCS Class II medicines, restricts its oral bioavailability. In order to tackle this problem, solid RLX dispersions were made in a 1:1 ratio utilizing a variety of hydrophilic carriers, including β-cyclodextrin, Poloxamer 407, PVA, and others, using the solvent evaporation approach.

FTIR spectroscopy and other preformulation studies verified that RLX and the chosen carriers were compatible. Excellent flow characteristics were demonstrated by the generated solid dispersions, which were then directly crushed into tablets.

Weight variation, hardness, friability, disintegration time, and drug content were all evaluated physicochemically and found to be within acceptable pharmacopeial parameters. When compared to the pure medication, dissolution experiments showed a noticeably improved release profile for RLX from solid dispersions and tablet forms. PVA, β-cyclodextrin, and Poloxamer 407 were the carriers that showed the best dissolution enhancement.

The results show that solid dispersion is a viable method for enhancing the bioavailability and solubility of medications that are not very soluble in water, such as RLX. The development of effective, immediate-release oral dosage forms that satisfy quality criteria and have the potential to be scaled for commercial manufacturing is made possible by this formulation technique.

KEYWORDS - FTIR, Raloxifene, Osteoporosis, Solid Dispersions, Solubility.

INTRODUCTION

The oral route is among the most commonly accepted and favored methods for administering drugs because of its convenience, safety, and adherence by patients. Nonetheless, the efficacy of oral medication administration primarily relies on the solubility and dissolution characteristics of the drug in gastrointestinal fluids. Medications with limited water solubility frequently show inconsistent absorption and reduced bioavailability, presenting a major obstacle in drug development.

Raloxifene Hydrochloride (RLX) is a synthetic derivative of benzothiophene that functions as a Selective Estrogen Receptor Modulator (SERM) and is commonly used for preventing and treating osteoporosis in women after menopause. Although RLX has therapeutic potential, it is characterized by very low water solubility, categorizing it as a Biopharmaceutics Classification System (BCS) Class II drug—having high permeability but low solubility. This low solubility results in restricted dissolution within the gastrointestinal tract and, consequently, inadequate oral bioavailability.[1,3]

To address these solubility-related challenges, numerous methods have been investigated in pharmaceutical sciences, such as solid dispersion, nano-sizing, and micronization. Among these, solid dispersion has been shown to be one of the most efficient and straightforward techniques to improve solubility. This method entails the distribution of the medication within an inert carrier matrix, usually utilizing hydrophilic polymers or surfactants, leading to enhanced surface area, better wettability, and smaller particle size, which promotes quicker dissolution.[4,5]

In the present research, solid dispersions of RLX were created through the solvent evaporation technique utilizing various pharmaceutical carriers including β-cyclodextrin, Poloxamer 407, PVA, PVP K17, PEG 6000, and Polyplasdone XL10 at a 1:1 ratio of drug to carrier.[7,8] These carriers were chosen for their capacity to improve solubility via methods such as inclusion complex development, surfactant behavior, and polymeric distribution. The resulting solid dispersions were assessed for compatibility in preformulation, flow characteristics, and then compressed into tablets through direct compression, removing the necessity for wet granulation.

FTIR spectroscopy was used to evaluate the compatibility of the drug and carriers, verifying that there was no interaction between RLX and the carriers. In addition, the solid dispersions displayed outstanding flow properties and compressibility, confirming their appropriateness for tableting. The created tablets were evaluated for weight consistency, hardness, friability, disintegration time, and drug content, and were determined to comply with pharmacopoeial standards.[9,11]

The research also incorporated in vitro dissolution testing utilizing USP dissolution apparatus II. The findings indicated improved dissolution rates from solid dispersions and tablet formulations relative to the pure drug, with Poloxamer 407, β-cyclodextrin, and PVA demonstrating the most notable enhancements.[12]

This study seeks to confirm solid dispersion as an economical and scalable approach to increase the solubility and bioavailability of poorly water-soluble medications such as RLX, which could result in better therapeutic effectiveness and patient results.[13]

MATERIALS AND METHOD

API was acquired from Orchid HealthCare Pharmaceuticals. A precise weighing was conducted using an electronic balance (Mettler Toledo and Sartorius). A mechanical sifter (Sams Techno, Mumbai) was utilized to sift powders. KAY Enterprises supplied the equipment utilized for optical microscopy. A double cone blender (Sams Techno, Mumbai) was employed to uniformly mix particles. Tablet compression was performed using a compression machine (Cadmach, 16 stations, Ahmedabad). Tap density was evaluated using a tap density tester (Electrolab, Mumbai). Tests were conducted using a disintegration tester (Electrolab, Mumbai).

Hardness and thickness were evaluated using Erweka and Varian testers (Mumbai). A Friabilator (Electrolab, Mumbai) was utilized to assess tablet friability. A mechanical stirrer (Remi Motors) was employed for stirring and mixing. Tablets were coated with a standard coating pan (Sams Techno, Mumbai). The dissolution test was performed using a USP XXIV dissolution apparatus. A Shimadzu high-efficiency liquid chromatography (HPLC) system was utilized. A UV spectrophotometer from Shimadzu was utilized to conduct ultraviolet (UV) spectroscopy.[14,15]

Preparation of RLX Solid Dispersions

Technique of Solvent Evaporation

RLX solid dispersions were created through the solvent evaporation method. In this procedure, 2 g of RLX were dissolved in 5 mL of methanol in a porcelain dish. To the solution, 2 g of the chosen carrier was incorporated, and the blend was left at room temperature for 24 hours to aid in solvent evaporation. The resultant solid was gathered, enclosed in airtight containers, and preserved at room temperature in amber glass vials to shield from light and humidity. Table 1. displays the formulations of different RLX solid dispersions.[16]

Table 1: Formulation Details of RLX Solid Dispersions.

S.No	Composition	Ratio
1	RLX + PEG 6000	1:1
2	RLX + PVA 4-88	1:1
3	RLX + β-Cyclodextrin	1:1
4	RLX + PVP K17	1:1
5	RLX + PVP K30	1:1
6	RLX + Polyplasdone XL10	1:1
7	RLX + Poloxamer 407	1:1
8	RLX + HPC-L.S	1:1
9	RLX + HPMC K4MCR	1:1
10	RLX + Pharmatose 200M	1:1
11	RLX + Supertab 11SD	1:1
12	RLX + Supertab 21AN	1:1
13	RLX + Mannitol	1:1

Angle of Repose

The angle of repose (θ) is a crucial factor for assessing the flow characteristics and frictional properties of powdered substances. It denotes the steepest inclination between a powder pile's surface and the horizontal plane, after which the material starts to move. This angle represents the balance between gravitational forces and interparticle friction.[17]

Measurement Method

The fixed funnel technique was used to evaluate the angle of repose. A funnel was firmly attached at a designated height (h) above a level plane lined with graph paper. The powder mixture was permitted to flow unhindered through the funnel, creating a conical pile whose tip barely touched the outlet of the funnel.[18,19] The radius (r) at the base of the cone was determined, and the angle of repose was obtained using the subsequent formula:

$\tan\theta = h / r$

Where:

θ = Angle of repose

h = Height of the powder cone

r = Radius of the cone base

Compressibility Index

The compressibility index is frequently utilized as an indirect measure to evaluate the flow characteristics of powders. It showcases the impacts of different physical traits of a substance, such as bulk density, particle dimension and form, surface area, moisture level, and cohesiveness.[20]

Measurement Method

The compressibility index was determined by assessing the bulk volume (V_0) and the tapped volume (Vf) of the powder. The bulk volume was recorded by pouring the loose powder into a graduated cylinder. The cylinder was subsequently tapped until a steady volume was obtained, which was noted as the tapped volume.[21] The compressibility index (CI) was determined using the equation:

$\text{Compressibility index} = 100 \times \text{tappeddensity/bulkdensity}$

In certain situations, the consolidation rate (i.e., the volume change when tapped) might also be taken into account for assessing powder flow.[22] The relationship among flow characteristics, angle of repose, and compressibility index is presented in Table 2.

Table 2: Flow characteristics determined by angle of repose and compressibility factor.

S. No	Flow Properties	Angle of Repose (°)	Compressibility Index (%)
I	Excellent	25–30	<10
II	Good	31–35	11–15
III	Fair	36–40	16–20
IV	Passable	41–45	21–25
V	Poor	46–55	26–31
VI	Very Poor	56–65	32–37
VII	Very Very Poor	>66	>38

Identification of Drug Content of Solid Dispersions

Preparation of Mobile Phase for HPLC

The mobile phase was created by combining acetonitrile and a pH 2.5 buffer in a 67:33 (v/v) proportion. The solution was passed through a 0.45 µm membrane filter and then degassed.[23,24]

Preparation of Diluents

A solution of pH 2.5 buffer and acetonitrile in a 40:60 (v/v) ratio served as the diluent for the preparation of samples and standards.[25]

Sample Preparation

A precise amount of 360 mg of the solid dispersion was weighed and placed into a 250 mL volumetric flask. A suitable amount of diluent was incorporated, and the blend was sonicated for 30 minutes with periodic shaking to guarantee full dissolution. The final solution was centrifuged at 2500 rpm for 10 minutes in capped centrifuge tubes.[26,27]

A 5 mL aliquot from the clear supernatant was transferred into a 50 mL volumetric flask and brought to volume with the identical diluent. The final solution was completely blended and passed through a 0.45 µm PTFE membrane filter.[28]

Chromatographic Conditions

- **Detector**: UV detector set at 280 nm
- **Column**: C8 column (150 mm × 4.6 mm) filled with 5 µm porous silica bonded with octylsilane
- **Column Temperature**: 35 °C
- **Flow Rate**: 1.5 mL/min
- **Injection Volume**: 10 µL
- **Run Time**: 8 minutes

Parameters for System Suitability

System suitability was assessed by injecting 10 µL of blank (diluent) and standard solution in quintuplicate.[29,30] The criteria listed below were utilized to evaluate system performance:

• The USP tailing factor for the RLX peak must not be greater than 2.0.

• The USP plate count for the RLX peak must be at least 2000.

• The % relative standard deviation (%RSD) of the peak area from five repeated injections of the standard solution must not be greater than 2.0%.

Studies on Dissolution

The dissolution characteristics of RLX solid dispersions were assessed using a calibrated USP dissolution apparatus II (paddle type) with eight stations. Every test was conducted in 1000 mL of purified water held at 37 ±

0.5 °C. The paddle rotation speed was adjusted to 50 rpm.

Aliquots of 5 mL were taken at set time points of 10, 20, 30, and 45 minutes, in accordance with the FDA dissolution database. After each sampling, an equal volume of fresh dissolution medium was added to sustain sink conditions. The collected samples were suitably diluted and examined with a UV spectrophotometer at 285 nm to measure the amount of dissolved drug.[31]

Tablet Preparation

Seven optimized RLX solid dispersions were chosen for tablet formulation based on their dissolution performance. The tablets were made using the direct compression technique. Although the proportion of drug to disintegrant stayed the same, the amount of diluent was modified according to assay outcomes to ensure consistency in drug content.

Every ingredient was precisely measured and sifted through sieve #40 to guarantee consistent particle size. The sieved substances were mixed in a double-cone blender for 15 minutes. Then, magnesium stearate was incorporated and blended for another 5 minutes to guarantee consistent lubrication.

The resulting powder mixture was compressed into tablets with a Cadmach 16-station micro tablet press, applying a consistent compression force to reduce process variability. The formulated powder mixtures were assessed for pre-compression characteristics like angle of repose and compressibility index.[32]

The tablets that were compressed were evaluated for quality parameters after compression, such as weight variation, hardness, friability, disintegration time, and drug content. The formulation of different RLX solid dispersion tablets is described in **Table 3**, while physical evaluation data are presented in Table 4.

Table 3: RLX Solid Dispersion Tablets Composition (mg/tablet)

Ingredient	RLX1	RLX2	RLX3	RLX4	RLX5	RLX6	RLX7
Solid dispersions*	120.4	113.6	121.5	129.1	127.7	123.4	120.9
Supertab DCL 21 AN*	83.0	80.0	82.0	74.0	76.0	80.0	83.0
Supertab DCL 11 SD	20.88	20.88	20.88	20.88	20.88	20.88	20.88
Polyplasdone XL	14.4	14.4	14.4	14.4	14.4	14.4	14.4
Magnesium stearate	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Opadry white	7.2	7.2	7.2	7.2	7.2	7.2	7.2
Total weight (mg)	247.2	247.2	247.2	247.2	247.2	247.2	247.2

Assessment of Tablets

The RLX solid dispersion tablets were assessed for different quality control metrics, such as weight consistency, hardness, friability, disintegration duration, and active ingredient content.[33,34]

Weight Consistency

To evaluate weight consistency, twenty tablets were randomly chosen from each group. Every tablet was weighed separately, and the average weight of the tablets was determined. The individual weights were subsequently evaluated against the mean to ascertain whether they remained within acceptable limits, in accordance with Indian Pharmacopoeia (I.P.) standards. A batch is deemed compliant if no more than two tablets exceed the allowable limits and none exceed the specified percentage by more than double. **Table 5** provides the I.P. guidelines for acceptable weight variation:

Table 5: Limits for Average Weight of Tablets (as per I.P.)

Average Tablet Weight	Permissible Percentage Deviation
80 mg or less	±10%
More than 80 mg but <250 mg	±7.5%
250 mg or more	±5%

Test of Hardness

The hardness of the tablets was assessed with an Erweka hardness tester. Every tablet was positioned on the testing platform, and the pressure (in kilopascals, kP) needed to fracture the tablet was noted. Tablet hardness is affected by formulation elements like compression force, punch separation, and the makeup of materials.

Friability

Friability was assessed utilizing a Roche friabilator. A constant weight of tablets (~6.5 grams) from every batch was put into the friabilator and rotated for 100 revolutions. With each rotation, the tablets underwent a drop of around 6 inches, replicating mechanical strain during transportation and handling. The tablets were weighed again following the test, and the percentage weight reduction was determined. A friability value that does not go beyond 1% is deemed acceptable.

Disintegration Duration

Disintegration testing was performed with 800 mL of water kept at 37 ± 2 °C. Six tablets were individually inserted into six tubes of a USP disintegration apparatus

basket. The duration required for each tablet to fully dissolve was noted.

Evaluation of Medication Concentration

For the measurement of drug content, 20 tablets, amounting to 180 mg of RLX, were ground and placed into a 250 mL volumetric flask. An appropriate diluent (according to HPLC mobile phase) was incorporated, and the solution was sonicated for 30 minutes with periodic shaking. The yielded mixture was centrifuged at 2500 rpm for a duration of 10 minutes. A portion (5 mL) of the clear supernatant was diluted to 50 mL with the same diluent. A 2 mL aliquot was filtered using a 0.45 µm PTFE membrane filter and analyzed by HPLC to assess the RLX content.

RESULT

The FTIR spectra of various Raloxifene formulations are illustrated in Fig. 1 to 8

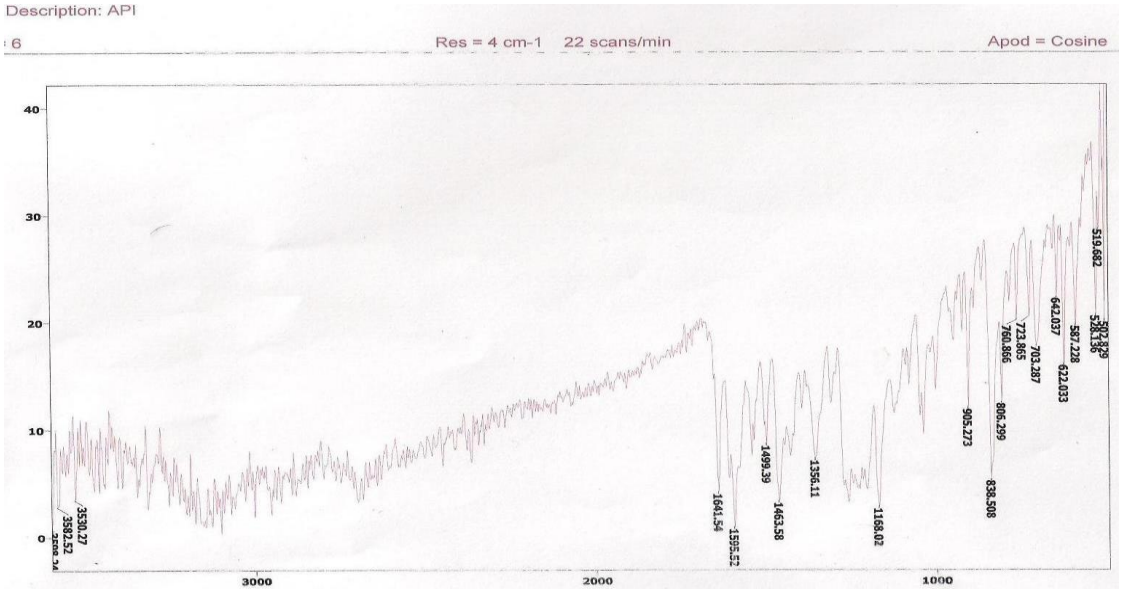

Fig.1: FTIR Spectrao frlx.

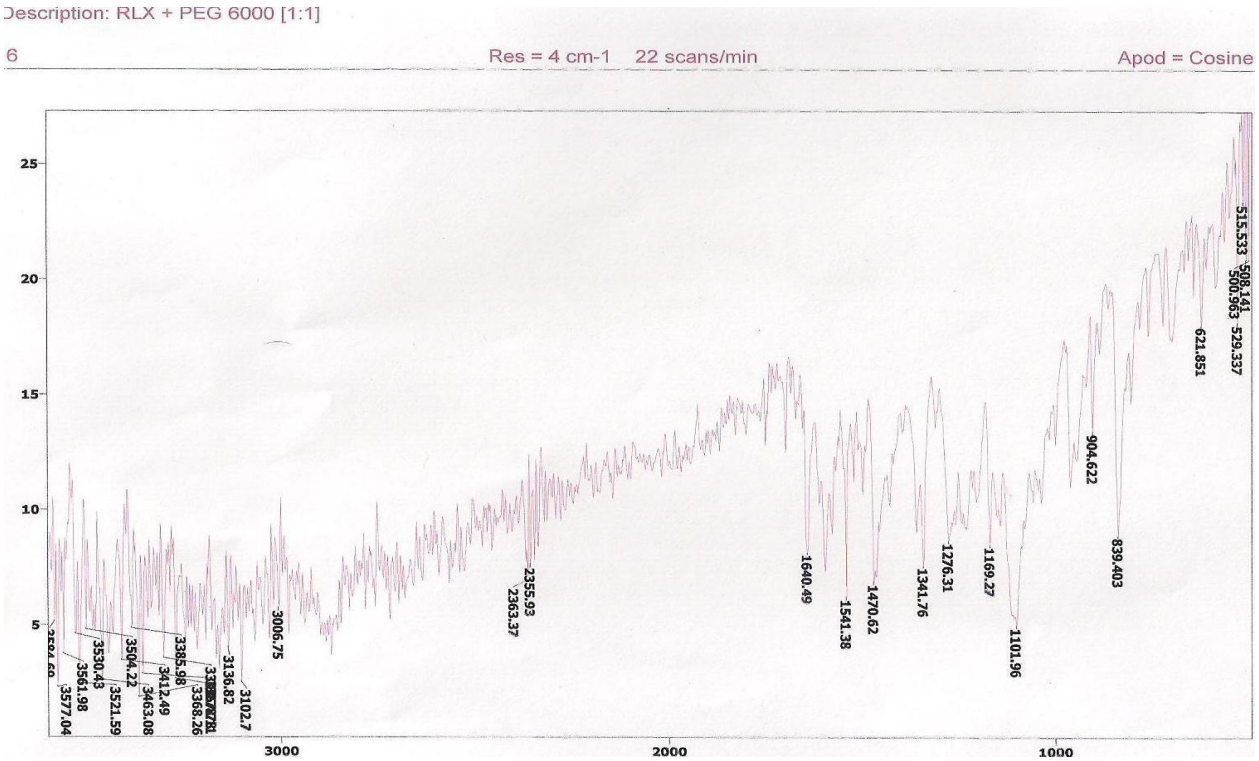

Fig. 2: FTIRspectraofRLX-PEG6000.

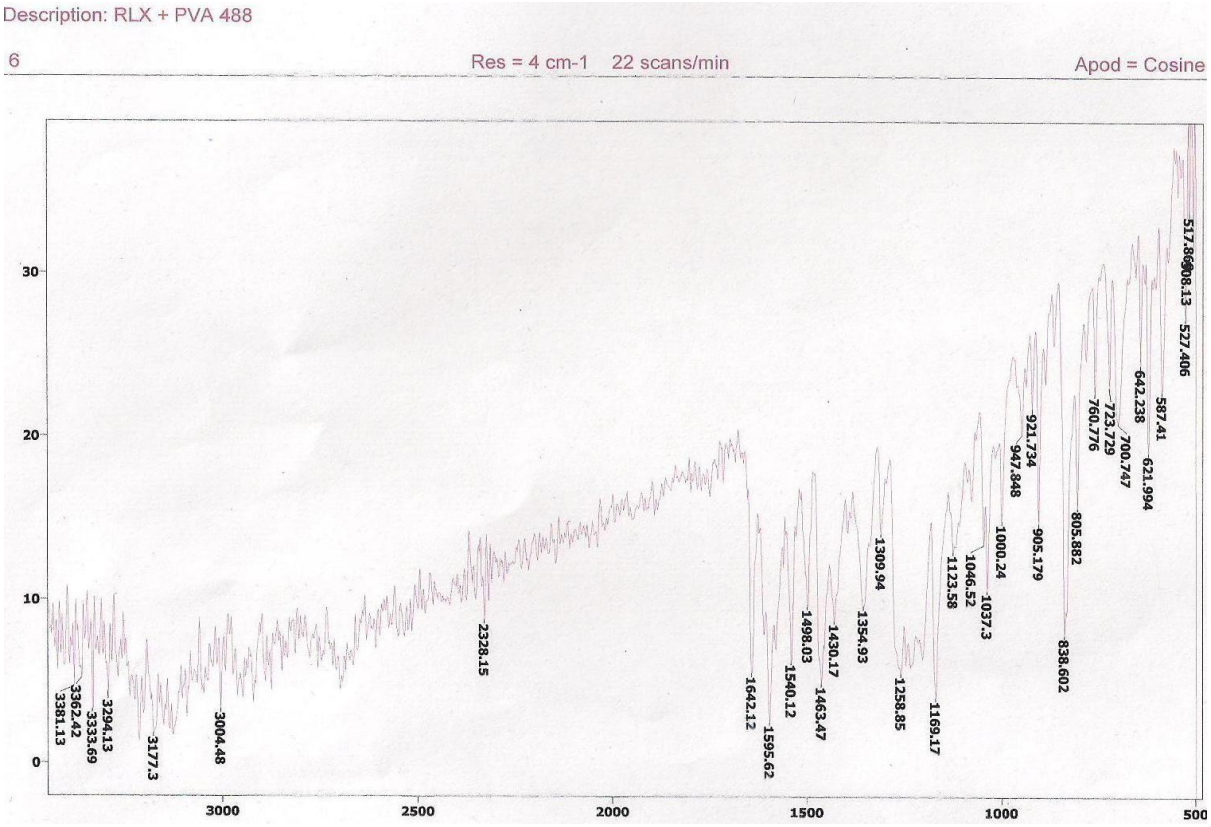

Fig.3: FTIRspectraofRLX-PVA4-88.

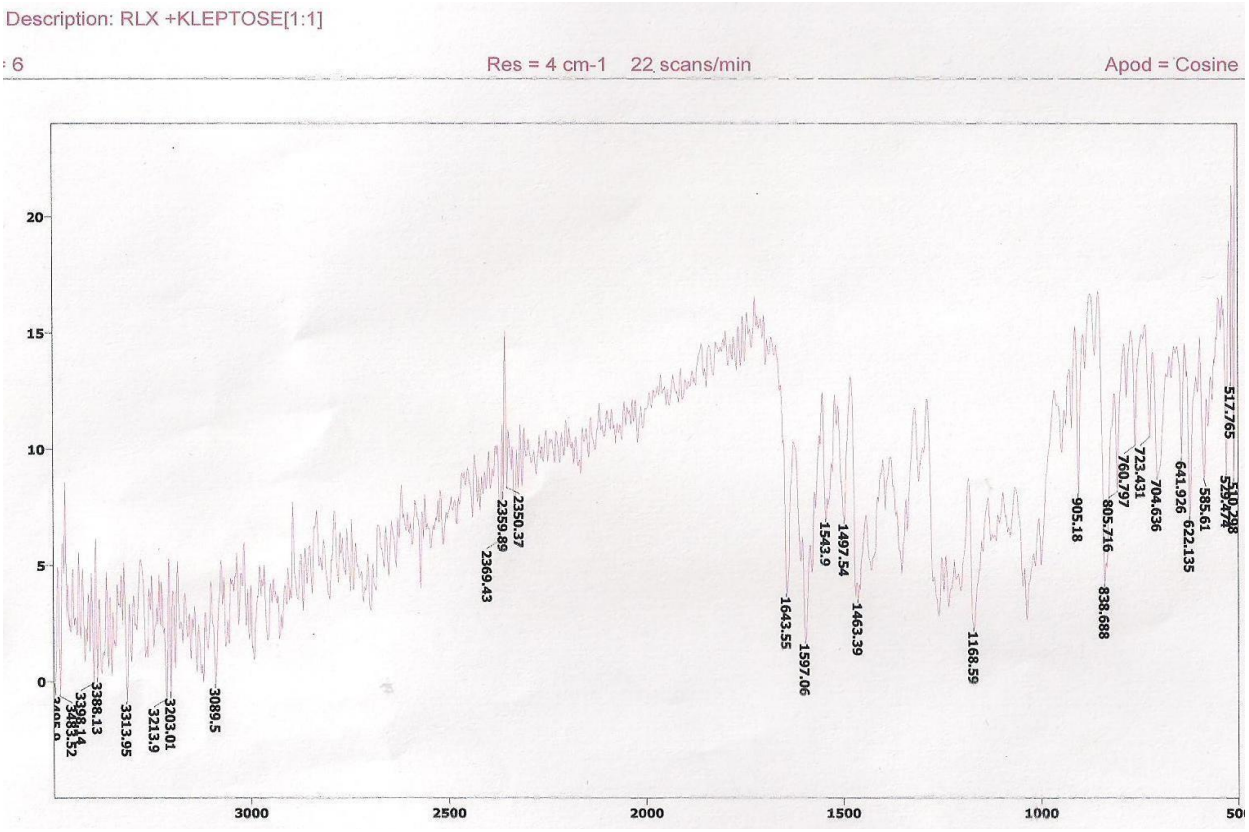

Fig.4: FTIRspectraofRLX-ß CD.

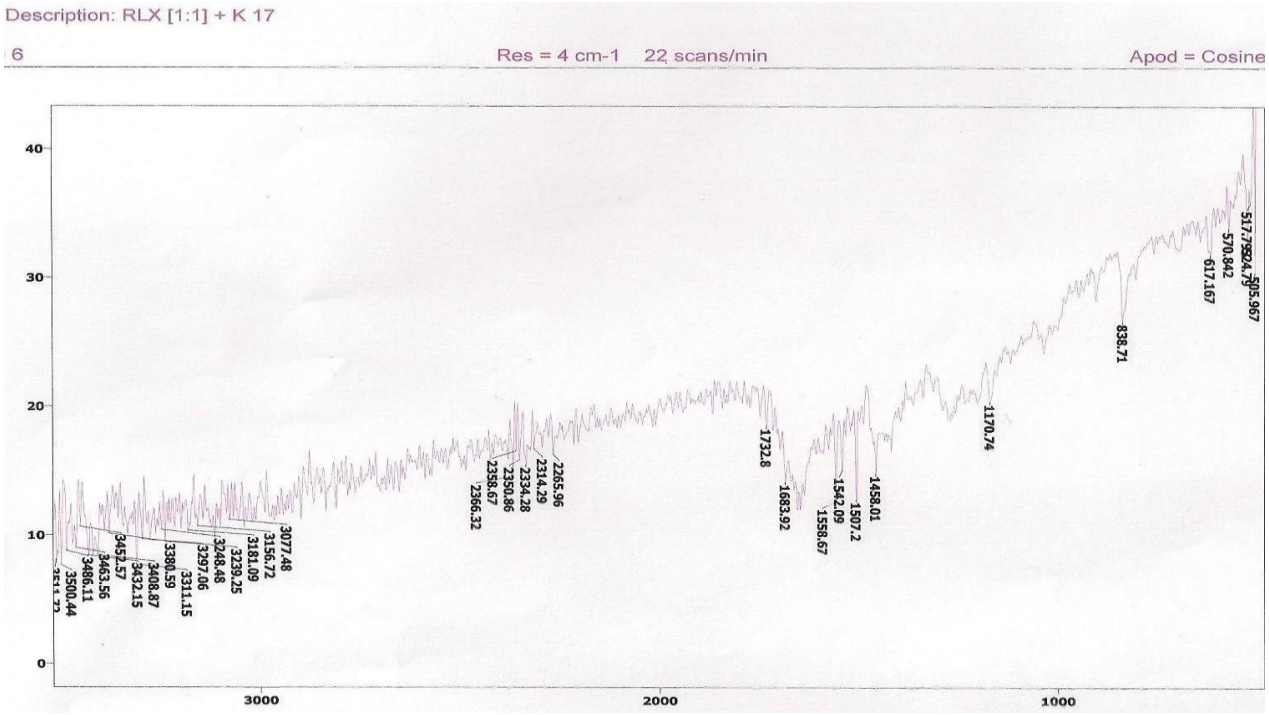

Fig.5: FTIRspectraofRLX-K17.

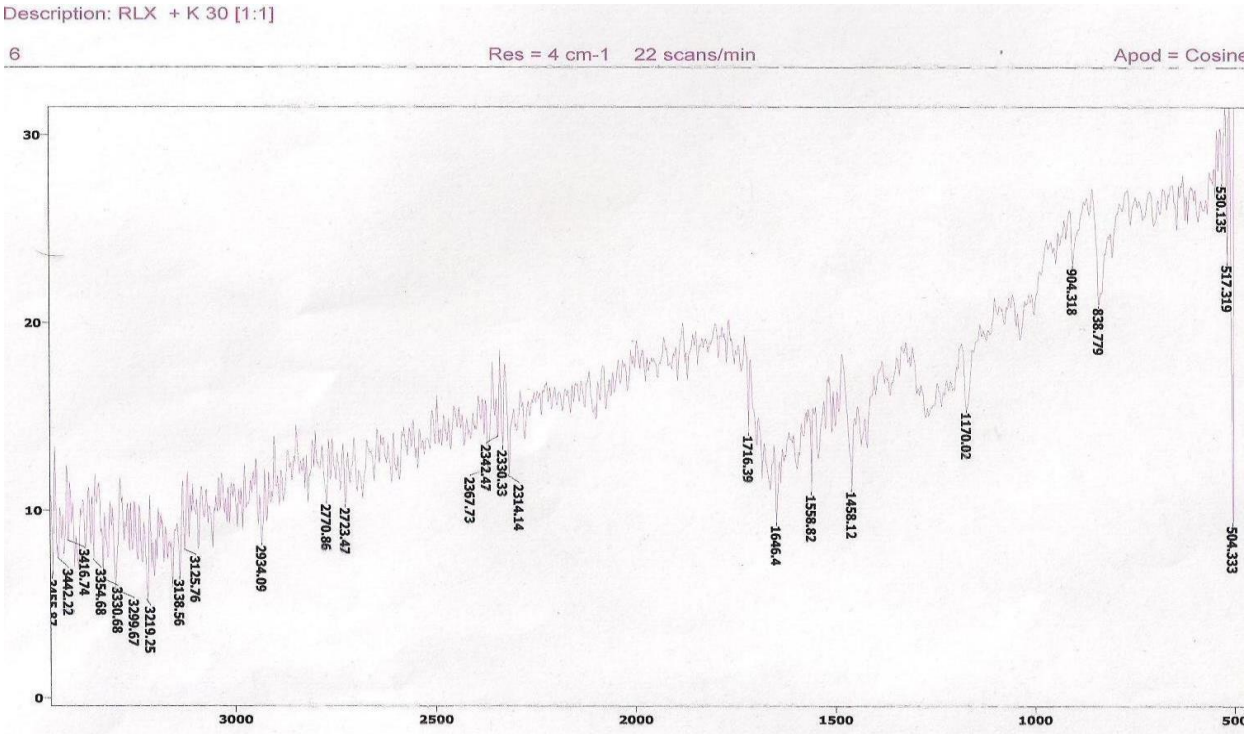

Fig.6: FTIRspectraofRLX-K30.

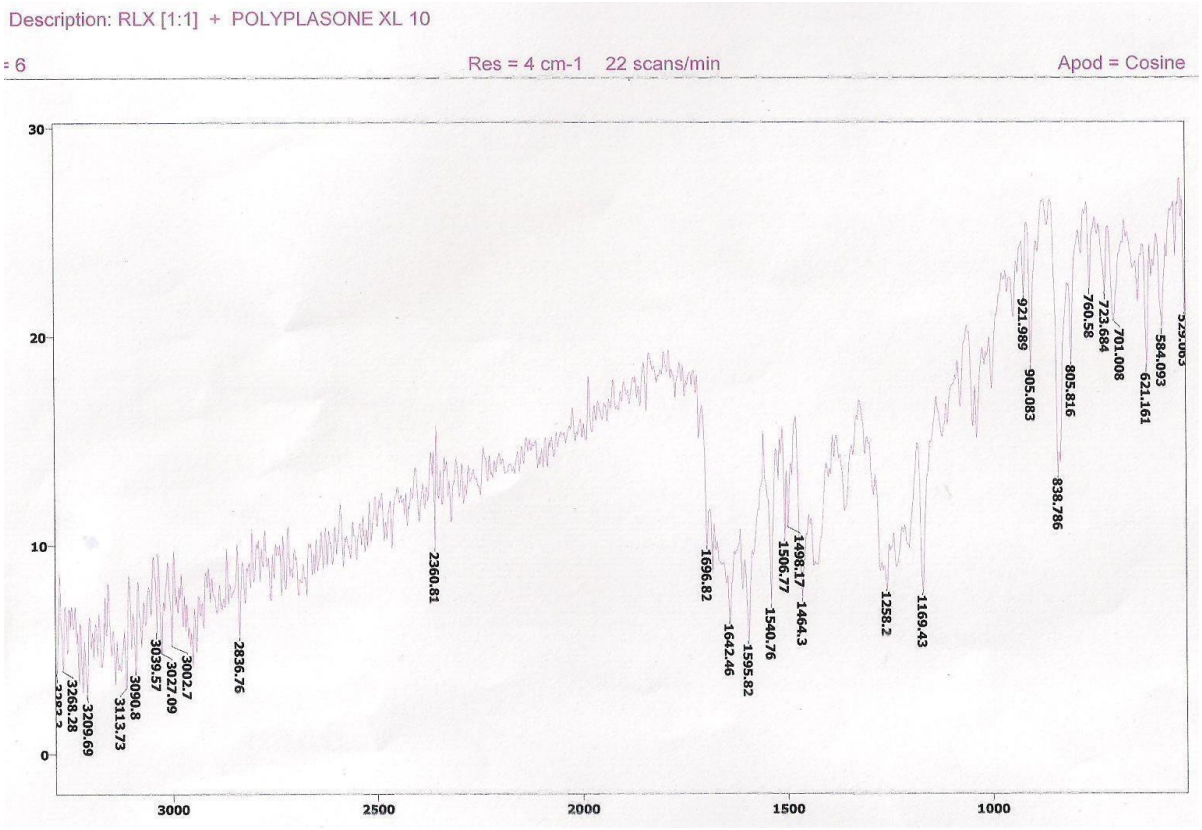

Fig.7: FTIRspectraof RLX-POLYXL10.

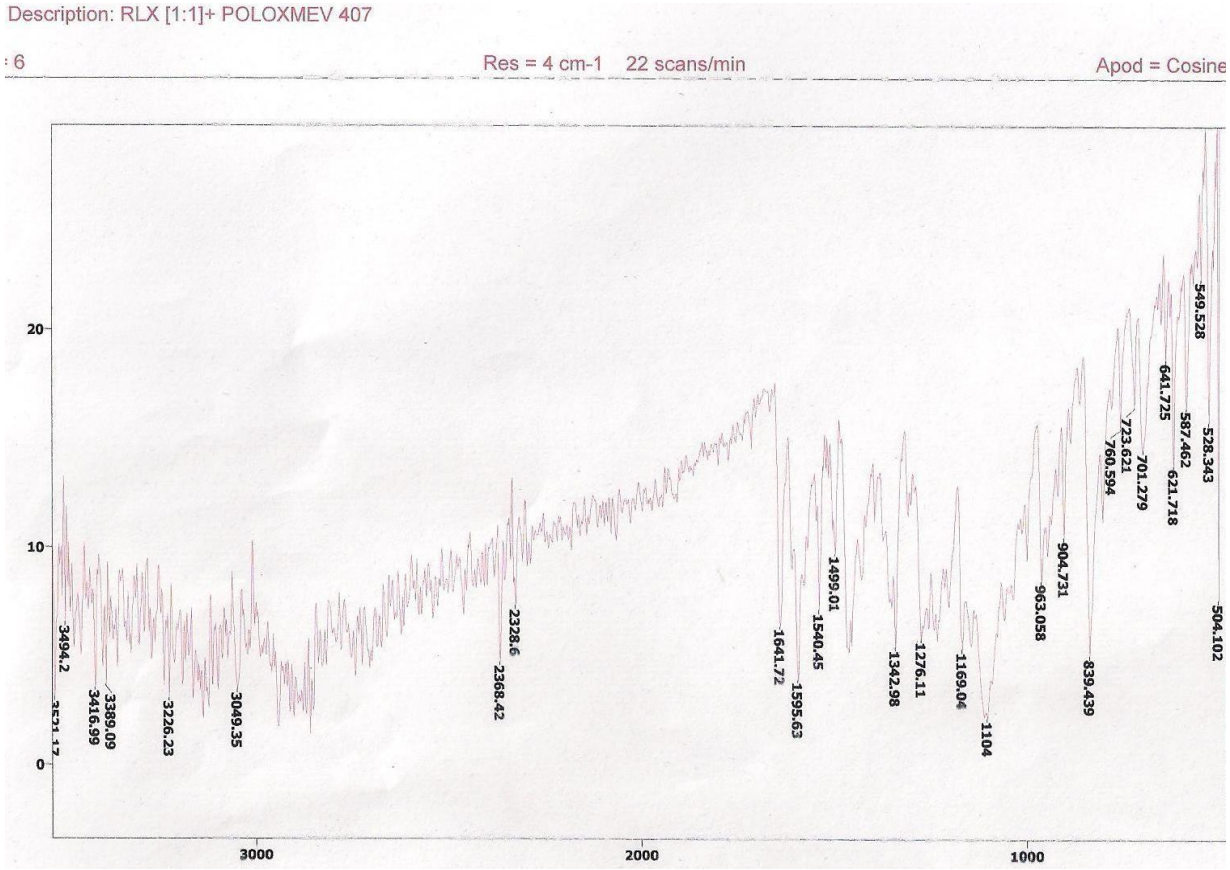

Fig. 8: FTIRspectraofRLX-POLAXOMER 407.

Table 6. Solid Dispersions of RLX Composition & Corresponding Solubility.

S. No.	Composition	Code	Ratio (RLX : Carrier)	Solubility (mg/mL)
1	RLX + PEG-6000	RLX1	1 : 1	0.64
2	RLX + PVA4-88	RLX2	1 : 1	0.90
3	RLX + β-Cyclodextrin	RLX3	1 : 1	2.18
4	RLX + PVP K17	RLX4	1 : 1	1.97
5	RLX + PVP K30	RLX5	1 : 1	1.48
6	RLX + Polyplasdone XL10	RLX6	1 : 1	1.19
7	RLX + Poloxamer 407	RLX7	1 : 1	1.07
8	RLX + HPC-L.S	RLX8	1 : 1	0.41
9	RLX + HPMC K4M CR	RLX9	1 : 1	0.46
10	RLX + Pharmatose 200M	RLX10	1 : 1	0.48
11	RLX + Supertab 11SD	RLX11	1 : 1	0.48
12	RLX + Supertab 21AN	RLX12	1 : 1	0.49
13	RLX + Mannitol	RLX13	1 : 1	0.47

Table 7. In-vitro Drug Release Profile of RLX Solid Dispersions

Time (min)	RLX	RLX1	RLX2	RLX3	RLX4	RLX5	RLX6	RLX7
10	2 ± 1.8	8 ± 4.1	18 ± 1.5	5 ± 2.2	9 ± 2.8	6 ± 2.1	6 ± 2.4	20 ± 4.1
20	7 ± 2.1	20 ± 1.7	76 ± 0.9	16 ± 1.6	25 ± 1.7	20 ± 2.2	28 ± 1.8	52 ± 4.1
30	12 ± 1.7	22 ± 1.8	87 ± 0.8	29 ± 1.7	41 ± 2.6	25 ± 2.4	41 ± 2.1	54 ± 4.1
45	19 ± 0.6	29 ± 2.1	95 ± 4.1	70 ± 1.6	43 ± 1.4	32 ± 1.3	53 ± 2.5	62 ± 4.1
∞ (Final)	32 ± 1.9	40 ± 1.1	96 ± 1.7	100 ± 2.4	65 ± 0.8	36 ± 2.1	55 ± 1.6	78 ± 4.1

Note: All values are expressed as mean ± SD (n = 3).

The cumulative percentage drug release for each formulation was calculated and is presented in **Table 8**. All values are expressed as mean ± standard deviation (SD), n = 3.

Table 8. Cumulative % Drug Release of RLX Solid Dispersions (Mean ± SD, n = 3)

Time (min)	RLX	RLX1	RLX2	RLX3	RLX4	RLX5	RLX6	RLX7
10	2 ± 1.8	8 ± 4.1	18 ± 1.5	5 ± 2.2	9 ± 2.8	6 ± 2.1	6 ± 2.4	20 ± 4.1
20	7 ± 2.1	20 ± 1.7	76 ± 0.9	16 ± 1.6	25 ± 1.7	20 ± 2.2	28 ± 1.8	52 ± 4.1
30	12 ± 1.7	22 ± 1.8	87 ± 0.8	29 ± 1.7	41 ± 2.6	25 ± 2.4	41 ± 2.1	54 ± 4.1
45	19 ± 0.6	29 ± 2.1	95 ± 4.1	70 ± 1.6	43 ± 1.4	32 ± 1.3	53 ± 2.5	62 ± 4.1
∞ (Infinity)	32 ± 1.9	40 ± 1.1	96 ± 1.7	100 ± 2.4	65 ± 0.8	36 ± 2.1	55 ± 1.6	78 ± 4.1

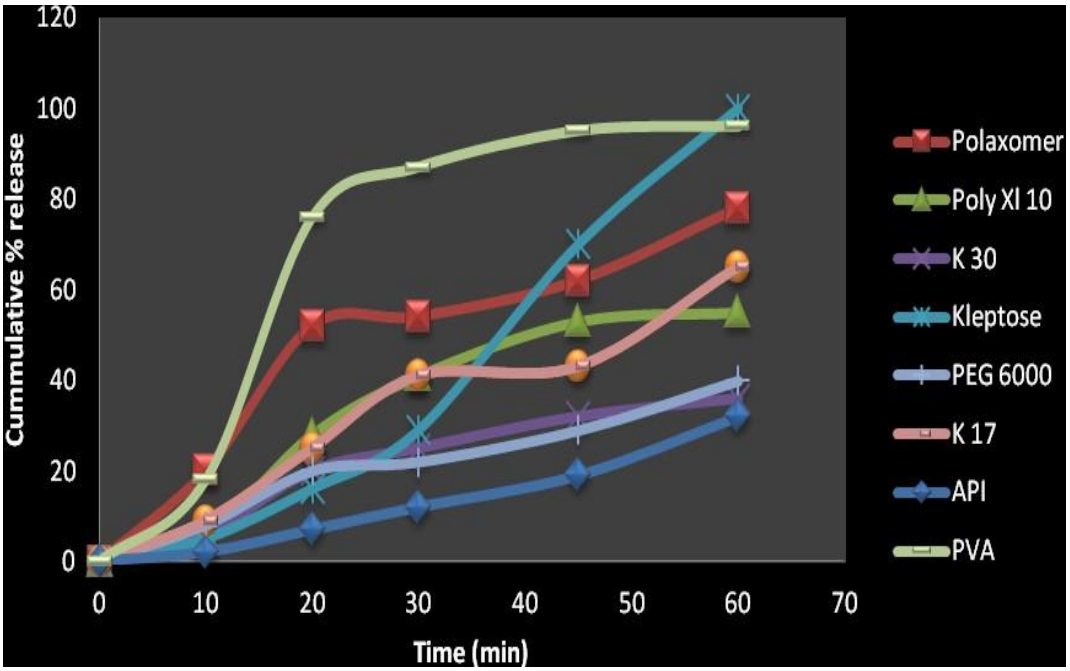

Figure 9: Drug Release Profiles of RLX Solid Dispersion-Based Tablet Formulations.

Table 4. Evaluation of RLX Tablet Formulations Prepared Using Solid Dispersions.

Tablet	Weight Uniformity (mg/tablet)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Disintegration Time (min)	Drug Content (%)
RLX1	241 ± 0.62	4.2 ± 0.21	6.0 ± 0.46	0.21	5–6	101.1
RLX2	240 ± 0.92	4.2 ± 0.16	5.0 ± 0.39	0.23	2–3	99.4
RLX3	241 ± 0.61	4.2 ± 0.11	9.0 ± 0.53	0.46	2–3	98.6
RLX4	240 ± 0.51	4.6 ± 0.12	6.0 ± 0.85	0.15	3–4	102.3
RLX5	240 ± 0.71	3.0 ± 0.12	5.0 ± 0.86	0.20	8–9	101.4
RLX6	240 ± 0.62	4.4 ± 0.11	10.0 ± 0.24	0.79	1–2	102.1
RLX7	238 ± 0.91	4.5 ± 0.12	3.0 ± 0.43	0.17	9–10	103.4

Note: All values are expressed as mean ± SD, $n = 10$.

Table 9. Drug Release Profiles of RLX Tablet Formulations Prepared by Solid Dispersion Technique.

Time (min)	RLX1	RLX2	RLX3	RLX4	RLX5	RLX6	RLX7
10	3 ± 2.2	10 ± 1.7	14 ± 0.5	5 ± 0.3	9 ± 1.5	12 ± 2.3	12 ± 1.6
20	18 ± 2.4	25 ± 0.5	35 ± 0.9	27 ± 1.6	17 ± 2.5	25 ± 1.6	44 ± 1.8
30	23 ± 2.6	34 ± 1.6	63 ± 2.3	36 ± 0.6	28 ± 2.0	32 ± 1.5	64 ± 0.7
45	35 ± 0.6	46 ± 1.1	74 ± 1.2	47 ± 1.8	40 ± 2.5	46 ± 1.5	89 ± 0.7

Note: All values are expressed as mean ± SD, $n = 3$.

DISCUSSION

Solubility Investigations

The solubility of Raloxifene (RLX) was assessed over a wide pH spectrum. The results showed that RLX has very low water solubility, which could impede its bioavailability. As a result, improving its solubility was recognized as an essential phase in formulation development.

Preformulation Research

Initial experiments were carried out by mixing RLX with different carriers in a 1:1 ratio. The physical stability of these blends was observed over a duration of one month. There were no alterations in physical appearance, like discoloration or phase separation, noted. Furthermore, the assay results stayed within permissible ranges, demonstrating the stability of the drug-carrier mixtures.

FTIR Examination

Fourier-transform infrared spectroscopy (FTIR) was utilized to assess the compatibility of RLX with chosen carriers. The distinctive peaks of RLX were detected at 3530 cm^{-1} (phenolic –OH stretching), 1641 cm^{-1} (C=O stretching), 1595 cm^{-1} (C=C stretching), 806 cm^{-1} (thiophene C–H), and 1158 cm^{-1} (C–O stretching). The FTIR spectra of RLX with different carriers exhibited no notable shifts or disappearance of these peaks. This indicates that there was no interaction between the drug and excipients, implying compatibility between RLX and the chosen carriers.

Saturated Solubility of Solid Mixtures

Different carriers were used to prepare solid dispersions of RLX, which were then assessed for saturated solubility in purified water. Of all the compounds, β-cyclodextrin and Poloxamer 407 demonstrated the greatest enhancement in solubility. Seven carriers were identified as effectively enhancing the solubility of RLX, qualifying them for additional formulation development.

β-Cyclodextrin can create inclusion complexes with poorly soluble drugs because of its hydrophilic exterior and hydrophobic interior. The hydrophobic segments of drug molecules may be inserted into the β-cyclodextrin cavity, leading to enhanced apparent solubility. This incorporation is motivated by the relocation of high-energy water molecules from the cavity and is supported by van der Waals forces.

Poloxamer 407, an innovative surfactant, improves solubility via an alternative method. When in contact with water, the polymer matrix quickly absorbs moisture, creating a gel-like consistency that aids in dissolving nearby drug particles. This system greatly enhances the enhanced drug release rate seen in formulations with Poloxamer.

Flow Characteristics and Particle Dimensions

Every solid dispersion that was prepared was assessed for micromeritic characteristics, such as angle of repose, Carr's compressibility index, particle size, and drug content. The findings showed outstanding flow properties and reasonable compressibility in all samples. The mean particle size varied from 72 ± 5 µm to 102 ± 4 µm. The drug content in all dispersions ranged from 93% to 105%, demonstrating a consistent distribution of RLX within the carrier matrices. These findings indicate that the solid dispersions are effectively optimized for direct compression into immediate-release tablet formulations.

In Vitro Dissolution Investigations of Solid Dispersions

Dissolution testing was conducted utilizing USP Apparatus II (paddle method) to assess the release characteristics of RLX from different solid dispersion systems. Every formulation showed a marked improvement in drug release compared to the pure drug, with the release hierarchy noted as follows: PVA > Poloxamer > Polyplasdone XL10 > PVP K17 > β-cyclodextrin > PVP K30 > PEG 6000. This improvement

can be linked to the better wettability, smaller particle size, and amorphous characteristics of the drug within the dispersion.

Tablet Formulation Assessment

The solid dispersions were pressed into tablets and then assessed for important quality characteristics such as hardness, friability, assay, and disintegration time. All formulations satisfied the acceptable pharmacopoeial criteria, validating their appropriateness for oral use.

Dissolution Research of Tablet Formulations

Studies on drug release were also performed on the tablet formulations. A significant enhancement in the dissolution rate was noted when compared to the pure RLX. Among the different carrier-based tablets, those made with Poloxamer showed the greatest drug release, followed by β-cyclodextrin, PVP K17, PVA, Polyplasdone XL10, PVP K30, and PEG 6000. This trend closely aligned with the solubility enhancement data and highlights the significance of carrier selection in enhancing the dissolution properties of poorly soluble drugs such as RLX.

CONCLUSION

The main aim of this research was to develop and assess solid dispersions of Raloxifene hydrochloride (RLX) employing various pharmaceutical carriers, with the primary intention of improving its water solubility and dissolution rate. RLX, a selective estrogen receptor modulator (SERM), is commonly employed in the prevention and management of osteoporosis in postmenopausal females. Nonetheless, its therapeutic effectiveness is constrained by its extremely low water solubility, categorizing it as a Class II drug under the Biopharmaceutics Classification System (BCS)—showing high permeability but low solubility. This restricted solubility results in low oral bioavailability, requiring the creation of novel formulation techniques to address this challenge.

In this study, solid dispersions of RLX were created through the solvent evaporation method, utilizing different hydrophilic carriers in a 1:1 ratio of drug to carrier. The chosen carriers comprised β-cyclodextrin, Poloxamer 407, Polyplasdone XL10, PVP K17, PVP K30, PEG 6000, and PVA, among others. These carriers were selected due to their established abilities to increase drug solubility via mechanisms like inclusion complexation, enhanced wettability, micellar solubilization, and molecular dispersion.

Preformulation studies were carried out to assess the physicochemical compatibility of RLX with the chosen carriers. The findings, especially from FTIR spectroscopic analysis, validated that no substantial chemical interactions occurred between the drug and the carriers. The distinct functional group peaks of RLX stayed unchanged in the physical mixtures and solid dispersions, showing no incompatibility or degradation occurred during the formulation process. This created a strong basis for advancing the development of solid dispersion systems.

Saturated solubility investigations revealed a significant enhancement in the solubility of RLX when accompanied by specific carriers, particularly β-cyclodextrin and Poloxamer 407. β-Cyclodextrin enhanced solubility through the formation of inclusion complexes, in which the hydrophobic part of RLX is trapped within the hydrophobic cavity of the cyclodextrin, thus improving its solubility in water. Poloxamer 407, functioning as a non-ionic surfactant, improved solubility via its micellar characteristics and increased wettability. Polyplasdone XL10, a super-disintegrant, demonstrated promise by aiding in the swift dispersion and dissolution of the medication.

Besides improving solubility, the flow characteristics of the resulting solid dispersions were assessed through metrics like angle of repose, Carr's index, and particle size distribution. The findings showed that the dispersions demonstrated outstanding flow properties and acceptable compressibility, which allows them to be directly compressed into tablet forms without requiring extra granulation processes. This discovery is especially beneficial for manufacturing, as it streamlines the tablet formulation method and decreases costs and time in production.

The prepared solid dispersions were subsequently compressed into tablets and analyzed for physicochemical properties such as weight variation, hardness, thickness, friability, disintegration time, and uniformity of drug content. All tablet formulations adhered to the acceptable pharmacopoeial standards, showing reliable quality and mechanical integrity appropriate for oral use.

Dissolution studies in vitro were performed to assess the rate and level of drug release from solid dispersions as well as their corresponding tablet formulations. The findings showed that the release of the drug from solid dispersions was considerably quicker and more thorough in comparison to the pure RLX. Among the different carriers, the sequence of improved drug release from solid dispersions was noted as PVA > Poloxamer 407 > Polyplasdone XL10 > PVP K17 > β-cyclodextrin > PVP K30 > PEG 6000. Likewise, the tablet formulations exhibited a somewhat modified release profile, with Poloxamer 407 > β-cyclodextrin > PVP K17 > PVA > Polyplasdone XL10 > PVP K30 > PEG 6000.

The overall findings indicate that the solid dispersion method, especially with β-cyclodextrin (acting as an inclusion complex creator), PVA (a water-soluble polymer), and Poloxamer 407 (a surfactant), is an extremely effective tactic for enhancing the solubility and dissolution characteristics of Raloxifene hydrochloride. These results emphasize the capability of

these carriers to address solubility-related challenges linked to BCS Class II medications, facilitating increased oral bioavailability and better therapeutic results.

In conclusion, the research effectively shows that formulating RLX as solid dispersions with suitable carriers improves its solubility and dissolution rate while also yielding tablets that satisfy quality requirements. These refined formulations can act as a promising foundation for additional development and potential expansion for commercial manufacturing.

CONFLICT OF INTEREST

The author declares no conflict of interest in writing this article.

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