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Fabrication and evaluation of Lercanidipine hydrochloride solid dispersions to improve its solubility and stability

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Abstract

Most commonly, hypertension and angina pectoris are treated with lercanidipine, a vasoselective dihydropyridine calcium antagonist. Nevertheless, lercanidipine main drawbacks include its food-dependent absorption, its low solubility, and its oral bioavailability of only around 10% as a result of its significant first-pass metabolism. In order to manage the early morning increase in blood pressure and improve bioavailability, this study set out to produce a solid dispersion of lercanidipine HCl for oral administration. Solvent evaporation powder comprising Lercanidipine a solid dispersion for oral administration was developed and evaluated in this work to overcome the aforementioned limitations. The solvent evaporation method was used to generate a solid dispersion of lercanidipine with β-cyclodextrin (β-CD) and PVP in a drug polymer ratio of 1:3:2. The resulting product was then analyzed. This research looked into how PVP affected the solubilization of lercanidipine in β-CD. Additional powders containing lercanidipine were subjected to physicochemical analyses, solid-state characterization, and *in vitro* dissolving tests. The X-ray diffraction, differential scanning calorimetry, and Fourier transform infrared spectroscopy were used to qualify the formulation. The use of PVP significantly improved the solubility of Lercanidipine, as demonstrated by the release rate. The chosen formulation for the oral release mechanism, LH5, demonstrated a 98.37% ± 0.95% efficacy in 30 minutes. With its potential to enhance Lercanidipine's solubility and bioavailability, the technology shows promise as a method for managing the morning spike in blood pressure.

Keywords: Solvent evaporation method, β-cyclodextrin, Lercanidipine, Hypertension, Angina pectoris.

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1. Introduction

Efforts to improve the solubility of pharmaceuticals have recently expanded to include the modification of already-existing medications. Since many medications have low solubility in water, it is crucial to develop drug solubilization technology [1]. Oral bioavailability may also be poor due to poor solubility [2]. Solid dispersions (SDs), particulate systems, and small-sized drug crystalsare only a few of the drug solubilization strategies that have been explored [3-14]. The chemical formula for lercanidipine hydrochloride (LH) is 2-[(3,3-diphenylpropyl) methylamine]. The compound is 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl) and 1,1-dimethyl ethyl methyl Hydrochloride of a 3,5-pyridine carboxylic ester. Because of its selectivity and specificity on the smooth vascular cells, LH is utilized in the treatment of hypertension [15-16]. Oral administration of the hydrochloride version of the medication, at a dosage of 10–20 mg daily, considerably lowers diastolic blood pressure [17]. The gastrointestinal tract absorbs LH entirely and irregularly upon oral delivery [18].The significant conversion to inactive metabolites during the first pass of metabolism, however, reduces absolute bioavailability to around 10% [19].

According to the literature, a single dose of 10 mg of LH has an average half-life of 2.8 hours, while a dose of 20 mg of LH has an average half-life of 4.4 hours [20]. Since LH has these desirable pharmacokinetic properties, it could be administered trans-dermally. Many other formulations have been created to increase LH's solubility; these include SD's, nano-emulsions, co-crystals, and complexes [21-24]. Due to its facile powder manufacture and high yield, the SD system was the most investigated formulation for increasing LH solubility among the ones mentioned above [25]. Solubilizing LH with alkalizers such MgO, sodium carbonate, meglumine, NaOH, and KOH has been the norm in most prior research on SD formulation [26]. A number of alkalizers, including MgO, $NaHCO_3$, $NaCO_3$, bentonite, Na_2HPO_4, NaOH, and KOH, were tested in representative tests to determine how well the SD MgO:TEL:PEG 6000 (1:8:24, weight ratios) dissolved in each [27-28]. In pH 1.2, distilled water (DW), and pH 6.8 buffer, these SD formulations dissolved more than 90% of the time. Additionally, in pH 1.2 medium at 25°C for three months, the stability of the dissolving percentage was successfully preserved. Some examples of such formulations are chitosan co-crystals and SD containing either chitosan or hydrochloric acid [29]. There were no stability data for any of the LH-chitosan formulations, however the LH dissolution percentages were around 60% (co-crystals) and 30% (SD). A one-month solubility and drug content evaluation were conducted on LH-HCl formulations;however, a dissolution test was not. We acknowledged that there was a lack of substantial research on LH-SD formulations in acidic pH. The present investigation used LH as a model drug and utilized β-cyclodextrin (β-CD) and PVP as carriers to create solid dispersions that improved LH's solubility. An optimization strategy was used to carefully study the solid dispersions of LH that were generated using the solvent evaporation method. The generated solid dispersions were characterized using a variety of imaging and analytical techniques, including differential scanning calorimetry (DSC), FTIR, XRD, SEM, and dissolution tests.

2. Materials & Methods

Our source for LCP was hetero pharm. Pvt. ltd. of Hyderabad, India. In Mumbai, India, Himedia Laboratories Pvt Ltd was where the β-Cyclodextrin was bought. We acquired Eudragit® L100-55 from Evonik Industries in Germany. Loba Chemie Pvt. Ltd. of Mumbai, India, supplied the polyethylene glycol (PEG) 400, triethyl citrate, hydroxy propyl methyl cellulose (HPMC) 5LV, and ethyl cellulose. The following analytical grade excipients were acquired from Merck Ltd., Mumbai, India: microcrystalline cellulose (MCC), lactose, polyvinyl alcohol (PVP), magnesium stearate, talc, acetone, ethanol, acetonitrile, methanol, isopropyl alcohol (IPA), phosphoric acid, potassium dihydrogen orthophosphate, dipotassium hydrogen orthophosphate, hydrochloric acid, in addition to water.

2.1. Characterization of Drug

The obtained LH sample was evaluated for its physical characteristics, organoleptic traits, melting point, and solvent solubility.

2.2. Melting Point Determination

Using the melting point device, a little amount of LH was placed in a capillary tube with one end capped. In order to compare the melting point with the LH value found in literature, it was recorded.

2.3. Preparation of Solid Dispersions

The LH-SD solid dispersions were made via solvent evaporation (Table 1). A clear solution was prepared by dissolving β-cyclodextrin (β-CD) and PVP in 80% ethanol while stirring until the mixture was homogeneous. Then, LH-SD was added while stirring for 45 minutes. The solvent was extracted by vaporization in a vacuum at temperatures ranging from 60 to 70 degrees Celsius (Rotavapor, Heidolph, Germany), and it was subsequently utilized to prepare the subsequent SD batch. For the subsequent batch, the solvent that was recovered was utilized [29]. After a day of room temperature storage in a desiccator, the solid dispersions were ground and sieved. The equation described below was used to compute the yield of solid dispersion:

$$\% \text{ Yield} = \frac{A}{B+C} X100$$

Here, A is the mass of the solid dispersion after passing it through a #120 sieve, B is the mass of LH used to make the solid dispersion, and c is the mass of the polymers used to make the solid dispersion.

2.4. Characterizations of solid dispersion

2.4.1. Solubility study

Saturated solutions were prepared by dissolving an excess of the pure medication and its crystalline dispersions in 50ml of a buffered phosphate solution, pH 6.8. For twenty-four hours at a temperature of 35 °C, the materials were aggressively mixed using a magnetic stirrer. The liquids were subsequently passed through a 0.45µm transmembrane filter made of Whattman filter paper. A UV spectrophotometer (V-560, UV-visible Spectrophotometer, JASCO, Japan) was used for analysis at 210 nm after diluting the filtrate with an appropriate blank solution. A total of three analyses were performed on each sample[30].

2.4.2. Drug content of solid dispersions

All of the formulations had their drug content in SD's checked three times. One hundred milliliters of a buffer with phosphate (pH 6.8) were mixed with a standard dose (10 mg) of medication. The samples underwent filtration using 0.45µm Whatman filter paper. After making the necessary dilutions, the filtrate was examined with a UV spectrophotometer (Model UV-1700, UV visible spectrophotometer, Shimadzu) set at 243nm against a blank. The drug extraction and identification at the prescribed wavelength were unaffected by the polymers [31].

2.5. Solid state characterizations

2.5.1. Drug excipients compatibility studies

Experimental methods such as X-ray diffraction (XRD), Differential scanning calorimetry (DSC), and Fourier transform infrared spectrophotometer analysis (FTIR) were used to determine whether the drug and excipients were chemically compatible [32].

2.5.2. Fourier Transform Infrared Spectroscopy

For the purpose of FTIR analysis, a spectrometer manufactured by Thermo Fisher Scientific, Inc. of Waltham,

MA, USA, called a Nicolet Nexus FTIR 670 was employed. A transparent infrared matrix called KBr was used to grind the samples and combine them thoroughly. In order to make the sample disks, the mixtures were compressed. The scanning was carried out between 450 and 4,400 cm^{-1} [33].

2.5.3. Differential Scanning Calorimetry

The Perkin-Elmer DSC7 differential scan calorimeter, manufactured by Perkin-Elmer and installed in a Pyris Series Workstation, was used to conduct the DSC experiments. We utilized an empty aluminum pan as a reference and put the precisely weighed sample in an aluminum pan. Between 40 and 280 degrees Celsius, the DSC run was heated at a rate of 10 degrees Celsius per minute. Twenty milliliters per minute of liquid nitrogen was circulated through the system to serve as a coolant [34].

2.5.4. X-Ray Diffraction Studies

The sample was attached to a glass slide using vacuum grease. It was covered with a layer that was approximately 0.5 mm thick after 100 mg of the sample was sprinkled on top. A sensitivity of 0.1 mg was maintained throughout all studies using an X-ray diffraction (X'Pert PRO, PANalytical, The Netherlands). The samples were subjected to CuKα radiation at 40 kV and 40 mA across the 2θ range of 0° to 40° at 0.5°/min intervals every 0.033° [35].

2.5.5. Scanning Electron Microscopy Analysis

The exterior appearance of TH and its solid dispersion with β-cyclodextrin (β-CD) and PVP were examined using SEM. We used adhesive carbon tape to attach the samples on a brass stage, and then we put them in a low-humidity room before we analyzed them. After applying a gold-palladium coating to the samples, they were examined under a 20 kV excitation beam by means of a PHILIPS electromagnetic scanning electron microscope (XL 30 ESEM, PHILIPS Inc.) [36].

2.6. In Vitro Dissolution Studies

A dissolve apparatus (RCZ-8A, Precise Instrument of Tianjin University Co., Ltd., China) was used to conduct tests for solubility, following the guidelines laid out in US Pharmacopeia XXIX (25). To meet the sink condition, 900 mL of deionized water containing 0.5% Tween-80 was mixed with 10 mg of LH from each of the solid dispersion formulations including original TH. A temperature of $37 \pm 0.5°C$ was maintained while the paddle rotational speed was set at 100 rpm. A 5-milliliter sample was taken from each container and passed through a 0.45-micrometer membrane filter at pre-arranged intervals (0, 5, 10, 15, 20, 30 and 45 minutes). Spectrophotometric analysis was performed on all samples using a UV visible spectrophotometer (Model UV-1700, Shimadzu) set at 243 nm. Following the sampling, the equal amount of new medium was added. With the help of a regression equation derived from the standard curve, the percentage of dissolved LH was determined ($r^2 = 0.9999$). Previous experiments have shown that the maximum release rate (λ_{max}) of LH was unaffected by the presence of β-cyclodextrin (β-CD), PVP, and β-cyclodextrin (β-CD) surplus in the solution. Triplicates of each test were run [37].

2.7. Stability test

After 6 months of storage, the amount of medication and pre-dissolution (%) of LH-SD were measured to determine the stability of the optimized SD formulations. The glass vials with the caps on were kept at the ambient temperature (20 °C ± 5.0 °C) and a relative humidity of 50-60% to preserve the samples. In addition, we tested how well the SD formulations dissolved. In short, three separate experiments were conducted using 10 mg of LH in SD formulations, 4 mL of DW in 20 mL vials, and stirring at 200 rpm for 24 hours. Centrifugation at 10,000 × g for 10 minutes removed the insoluble LH, and a UV-VIS spectrophotometer was used to examine the supernatants (n = 3)[38].

3. Results & Discussion

3.1. Pre-formulation studies

It was necessary to conduct the pre-formulation study before the dosage forms were developed. Hence, we recorded the infrared spectra of the drug/polymer physical combination. Additionally, the medication and polymer infrared spectra were recorded. For the most part, infra-red spectroscopy is useful for establishing structures and for qualitatively identifying chemicals, whether they are in a pure or mixed state. The spectra can reveal intricate details about the chemical compound's structure due to the fact that I.R. is associated with covalent bonds. This can be proven by comparing the substance's spectrum to that of the drug.

3.2. Characterization of Drugs

There was an analysis of LH's organoleptic qualities, melting point, pH, solution color and clarity, loss upon drying, bulk density, and tapped density. The findings are presented in Table 2.

3.3. Melting Point

Through the use of the capillary fusion method, the drug's melting point was determined. It was determined that the drug's melting point fell within the reference value range. The Table 3 displays the values. The glass capillaries method and the boiling point apparatus were used to determine that the melting temperature of LH was 196.13 °C. This value was then compared to the standard boiling point of LH, which is described in literature to be 195–1980 °C.

3.4. Solubility

This study examined the impact of β-CD, PVP, and soluplus on the water solubility of LH, both individually and in combination. Together, β-CD and PVP (LH1-LH3) enhanced the solubility of LH from 0.32 ± 0.0026 mg/ml to 2.68 ±0.24 mg/ml, with a p-value of less than 0.05. The solubility value increased (6.35 ± 0.21 mg/ml) as the level of β-CD (LH2) increased. The soluble concentration of LH remained relatively unchanged (6.41 ± 0.16 mg/ml) as the amount of β-CD increased even more (LH 3), with a p-value greater than 0.05. Because of this, LH2 was chosen as the optimal formulation to test how PVP affects LH solubility.

The combination of PVP with β-CD (LH4) significantly increased the solubility of LH, as found at 7.95 ± 0.16 mg/ml. This is due to the fact that a water-soluble hydrogel with β-CD is formed when a number of cyclodextrin units graft onto a PVP chain using a copolymerization process. Adding a higher amount of PVP (LH5) resulted in a higher solubility

of LH (8.69 ± 0.11 mg/ml). A small decrease in LH solubility (8.42 ± 0.21 mg/ml) was observed when the concentration of PVP was further raised (LH6) (P > 0.05). Therefore, for subsequent assessment investigations, the optimal formulation was chosen as the solid dispersion LH5, which contains Drug, β-CD, and PVP in a ratio of 1:3:2 w/w/w.The combination of soluplus with β-CD (LH7) significantly increased the solubility of LH, as seen at 6.21 ± 0.16 mg/ml. The reason behind this is that a water-soluble hydrogel with β-CD is formed when several kinds of cyclodextrin units graft onto a soluplus chain using a copolymerization process. Adding a higher amount of soluplus (LH8) resulted in greater solubility of LH (6.23 ± 0.08 mg/ml). The solubility of LH was somewhat reduced (6.02 ± 0.21 mg/ml) (P > 0.05) as the amount of soluplus was further increased (LH9). Therefore, the optimal formulation for future assessment studies was the solid dispersion LH5, which contains Drug: γ-CD: PVP; 1:3:2 w/w/w, based on the comparison with the soluplus and PVP polymer.

3.5. Formulation of solid dispersions

An insoluble medicine showed great promise as a candidate for improved solubility through solid dispersion. The medication can be distributed throughout the polymer as crystals, amorphous particles, or molecules by using the β-CD and PVP as carriers. When it comes to improving solubility, solid solutions work best when particle size is reduced. Following the formation of LH-SDs, the combination polymers exhibited superior dissolving profiles, releasing over 80% of the medication relative to the pure drug solution and the commercial formulation. Also, if LH could change its physical state from crystalline to amorphous, or if the drug were in a highly dispersible state in the carrier, it would greatly improve drug release. Therefore, we proceeded with additional research and development based on the drug polymer ratios that provided sufficient dissolution and physicochemical characteristics.

3.6. Drug Content and % Yield

The Table 4 displayed the greatest yield or drug content of the LH-SDs. We found out how much medicine was in the SD formulation. There was consistency in the drug content, as measured within the specified limits, with concentrations ranging from 84.26±1.32 to 96.84±0.85. The medication's content was determined using triple analysis. Formulation LH5, made with the following ingredients: β-CD, PVP (1:3:2 w/w/w), and formulation LH9, made with the following ingredients: β-CD, soluplus, had the lowest percentage yield, whereas the other two formulations ranged from 85.36±0.05 to 98.61±0.37%. Table 4 displays the percentage yield data for each formulation.

3.7. Solid state Characterizations

3.7.1. FT-IR studies

The FTIR spectrum of lercanidipine HCl showed distinct absorption peaks at 3186 cm^{-1} (NH stretching), 3078.8 cm^{-1} (CH aromatic stretching), 3100-2800 cm^{-1} (alkyl and phenyl stretching), 2565 cm^{-1} ($^{+}$H stretching), 1672.95 cm^{-1} (>C=0 stretching vibrations), 1347.03 cm^{-1} (-NO_2), and 785-685 cm^{-1} (out-of-plane bending of 5 and 3 adjacent hydrogens on aromatic rings). The bandwidth at around 3475 cm^{-1} in pure PVP is attributed to the stretching vibration of the hydroxyl group (OH) of PVP [12-13]. The band corresponding to the asymmetric stretching vibration of CH_2 is visible at around 2933 cm^{-1}. The stretching modes of the Cdouble bondO and Cdouble bondC have been attributed, respectively, to the peaks at 1713 and 1658 cm^{-1} [13-14]. Symmetric bending of CH_2 is the reason behind the absorption peak at 1432 cm^{-1}. The carbonyl groups included in the PVP backbone are stretched at around 1096 cm^{-1}, as indicated by the band at that frequency. The stretching vibrations of the Csingle bondC in the intermediate absorption planar zigzag carbon backbone are detected at 844 cm^{-1}. The wagging mode of (OH) groups is ascribed to the peak at 651 cm^{-1}, CH_2 rocking to the peak at 921 cm^{-1}, and ($CH^{+}OH$) bending to the peak at 1332 cm^{-1} [13]. The hallmark peak at 3,300-3,400 cm^{-1} in the FTIR spectrum of BCD was caused by the stretching of the O-H group. C-H assymetric/symmetric stretching also caused an intense peak at 2,854cm^{-1}. Furthermore, the H-O-H deformation bands of water in BCD were shown by a peak at 1,650 cm^{-1}. C-H overtone stretching was suggested by peaks at 1,153 and 1,029 cm^{-1}, whereas C-H and C-O stretching was indicated by the peak at 1,029 cm^{-1}. At 1,153 cm^{-1}, the C-O-C vibration was observed to be absorbed. The inclusion complexes' FTIR spectra were in perfect agreement with the β-CD spectrum, as anticipated. Every one of the distinct peaks associated with β-CD was noticed. The peaks that are indicative of LH vanished. It is clear that no interaction has evolved between the drug and excipients, as indicated by the distinctive drug peaks in the IR spectra (Figure 1). This observation is further supported by the fact that no contact has occurred during the dispersion process. Drug and excipient physical and chemical qualities are key considerations in dosage form design and manufacture. Within the infrared spectra of PVP, β-cyclodextrin, and drug, there was a small reduction in the intensity of the aromatic nitro group, while the carboxyl group showed an increase in intensity and a slightly wider peak. The lack of noticeable alterations as compared to the pure medicine suggests that there is no interaction. The drug's authenticity and purity are validated by the peaks in the infrared spectra that were collected before. When compared to the pure medication, the improved formulation showed no discernible alterations in the infrared spectra. Because of this, we may say that the medication and the excipients are chemically compatible.

3.7.2. Differential scanning calorimetry (DSC)

Differential scanning calorimetry was used to assess the samples' thermal characteristics. One distinct peak at 196.13ºC in the differential scanning calorimetry (DSC) thermogram of pure LH demonstrated the drug's crystalline nature. A pronounced endothermic peak at various melting points was seen in the physical combination of the medication and carrier. It was clear that thermal changes had taken place when the LH of SD peak vanished. In earlier research, a melting peak of β-cyclodextrin was observed in SD and optimized formulations with β-cyclodextrin and PVP, while the boiling peak of β-cyclodextrin was observed in SD and optimized formulations with PVP [4,30]. When the endothermic peak in the improved formulation of LH solid dispersion disappeared, it meant that the medication was in an amorphous state (Figure 2). Research on the compatibility of drugs with excipients was conducted both for the medicine alone and for combinations of the two. No shift in the peak when compared to the pure drug, indicates that the drug and the excipients are compatible.

Table 1: Formulations of solid dispersions.

F.Code	Composition	Ratios	Method
LH-1	Drug: β-CD	1:1	Solvent evaporation method
LH-2		1:3	
LH-3		1:6	
LH-4	Drug: β-CD: PVP	1:3:1	Solvent evaporation method
LH-5		1:3:2	
LH-6		1:3:3	
LH-7	Drug: β-CD:soluplus	1:3:1	Solvent evaporation method
LH-8		1:3:2	
LH-9		1:3:3	

Table 2: Pre-formulation Characterization of Pure LH.

S. No	Characteristics	Lercanidipine	
		Specifications	Test Results
1	Nature	Crystalline	Crystalline
2	Color	Pale yellow	Pale yellow
3	Taste	Bitter	Bitter
4	Melting point	195-198^{0}C	----
5	pH of 5% solution	4-5	4.8
6	Clarity and color of solution	Clear and light pale-yellow color	Clear and light pale-yellow color
7	Loss on drying	Max 0.5%	0.325±0.024
8	Bulk density	---	0.62±0.21
9	Tapped density	---	0.84±0.13

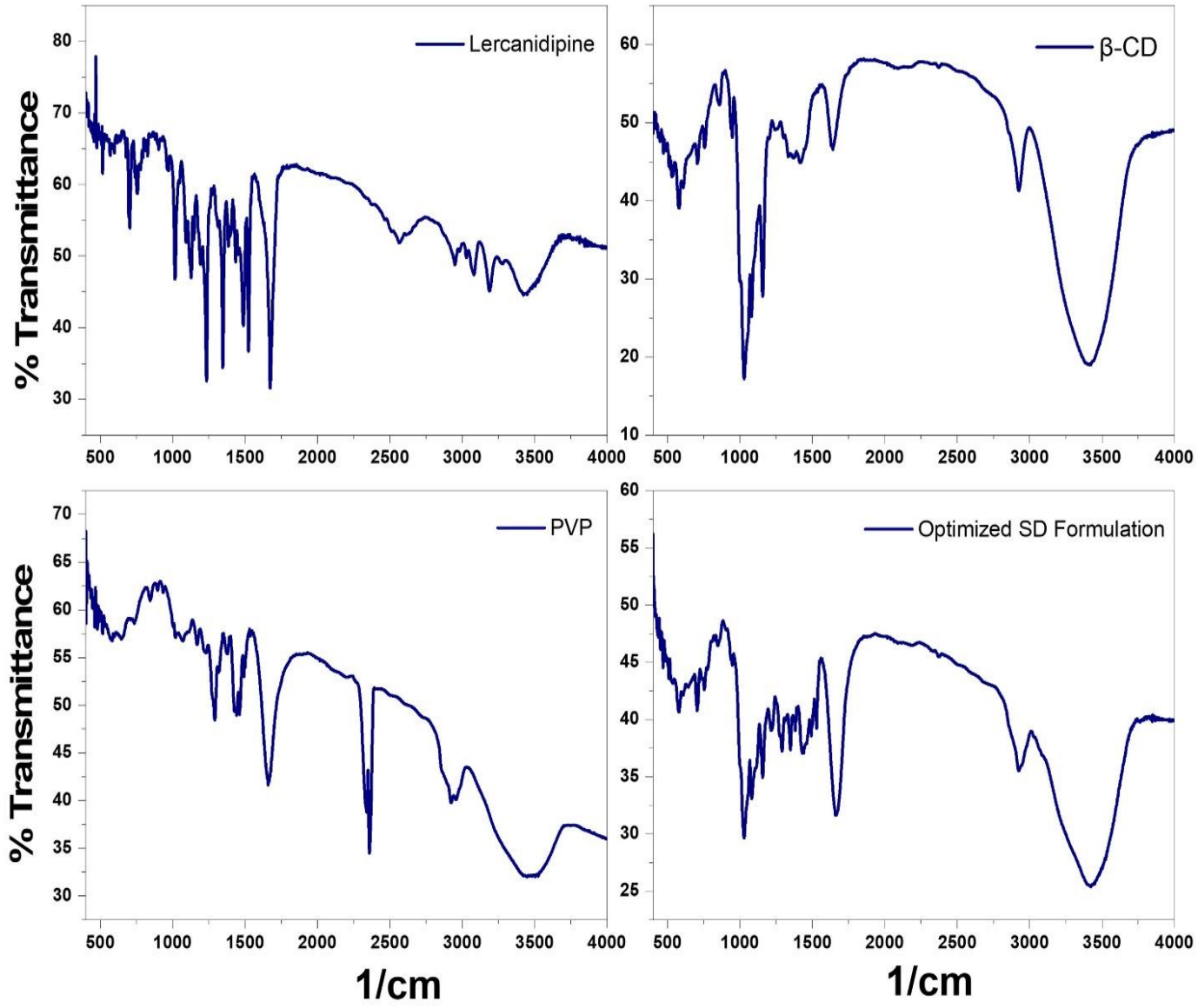

Figure 1: FTIR structural studies of Pure drug, β-cyclodextrin, PVP and Optimized solid dispersion.

Table 3: Melting Point of Lercanidipine.

Apparatus	Observed value	Reference Value
Melting point apparatus	196.13±0.38^{0}C	195-198^{0}C

Table 4: Characterization of LH solid dispersions.

F. code	% Yield	% Drug content
LH-1	84.82±0.05	85.36±0.05
LH-2	86.31±0.06	86.85±0.08
LH-3	85.03±0.03	87.03±0.06
LH-4	95.89±0.14	95.84±0.01
LH-5	96.84±0.85	98.61±0.37
LH-6	94.23±0.39	94.28±0.24
LH-7	90.21±0.86	93.68±0.35
LH-8	86.32±0.42	94.26±0.12
LH-9	84.26±1.32	92.56±0.21

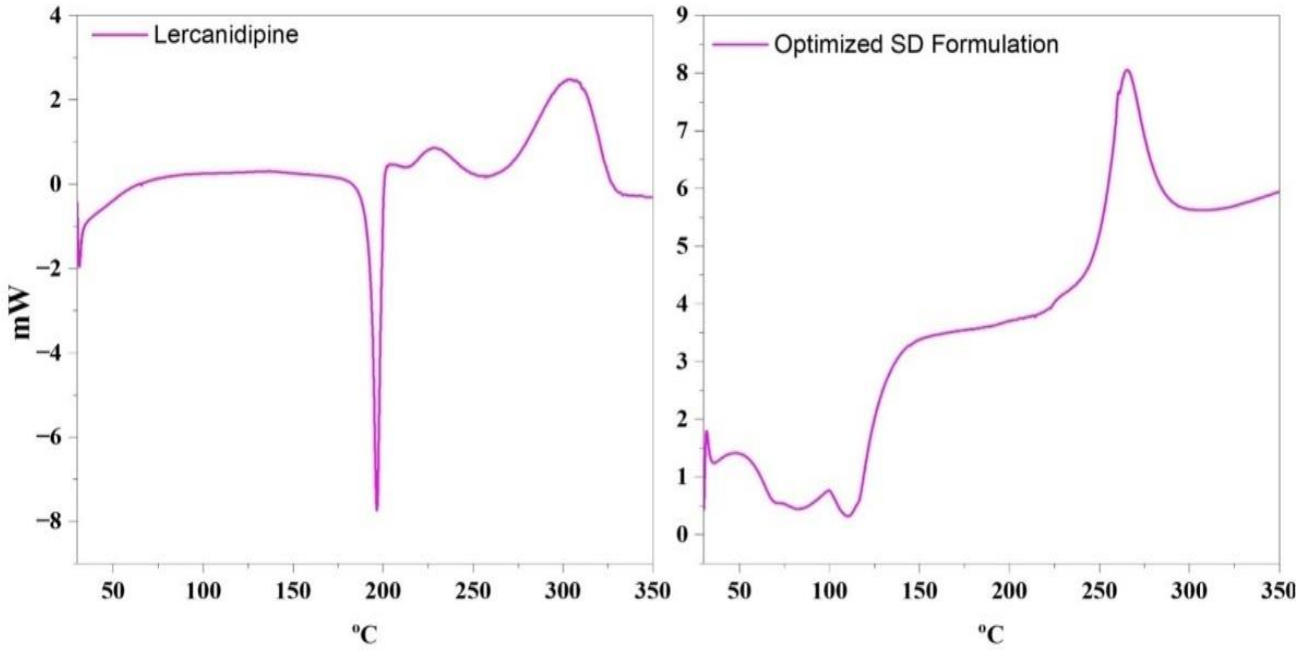

Figure 2: DSC thermogram of Pure drug and optimized solid dispersion.

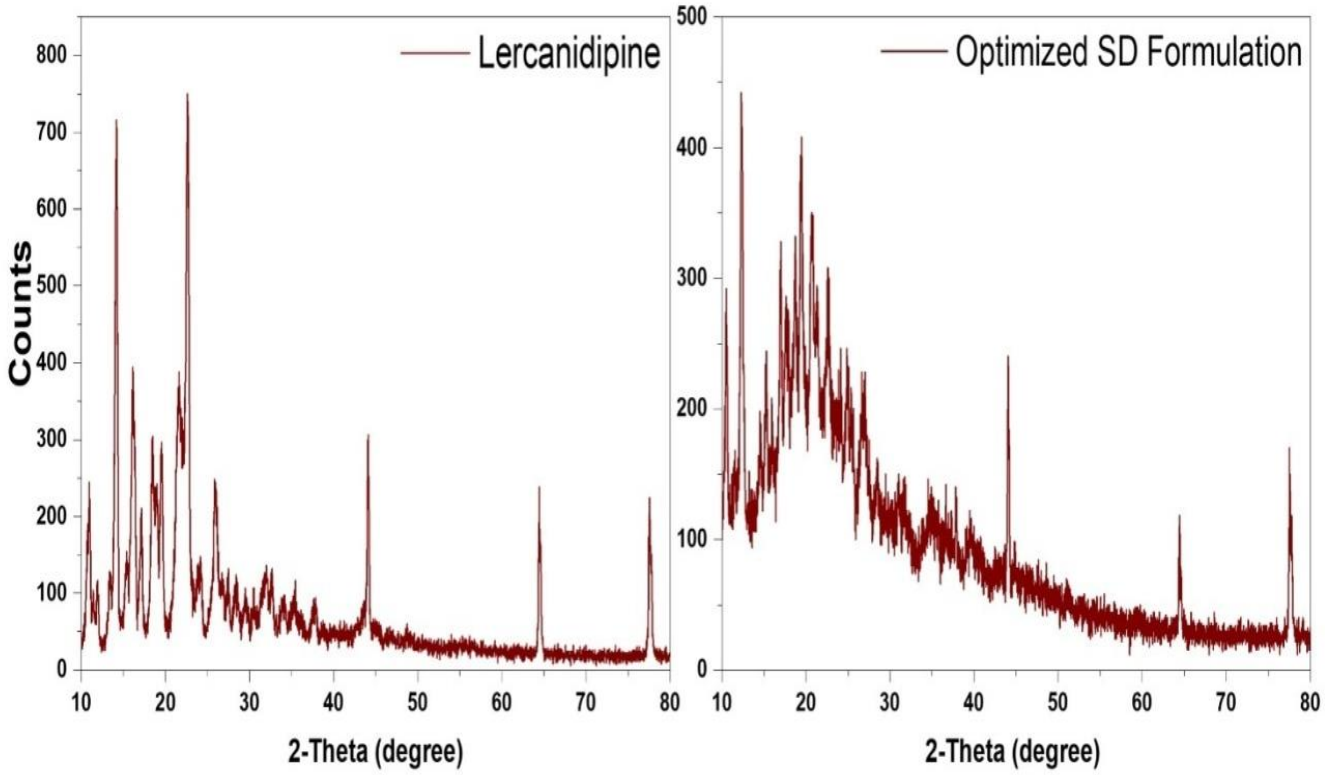

Figure 3: Powdered X- ray diffractogram of Pure drug and optimized solid dispersion.

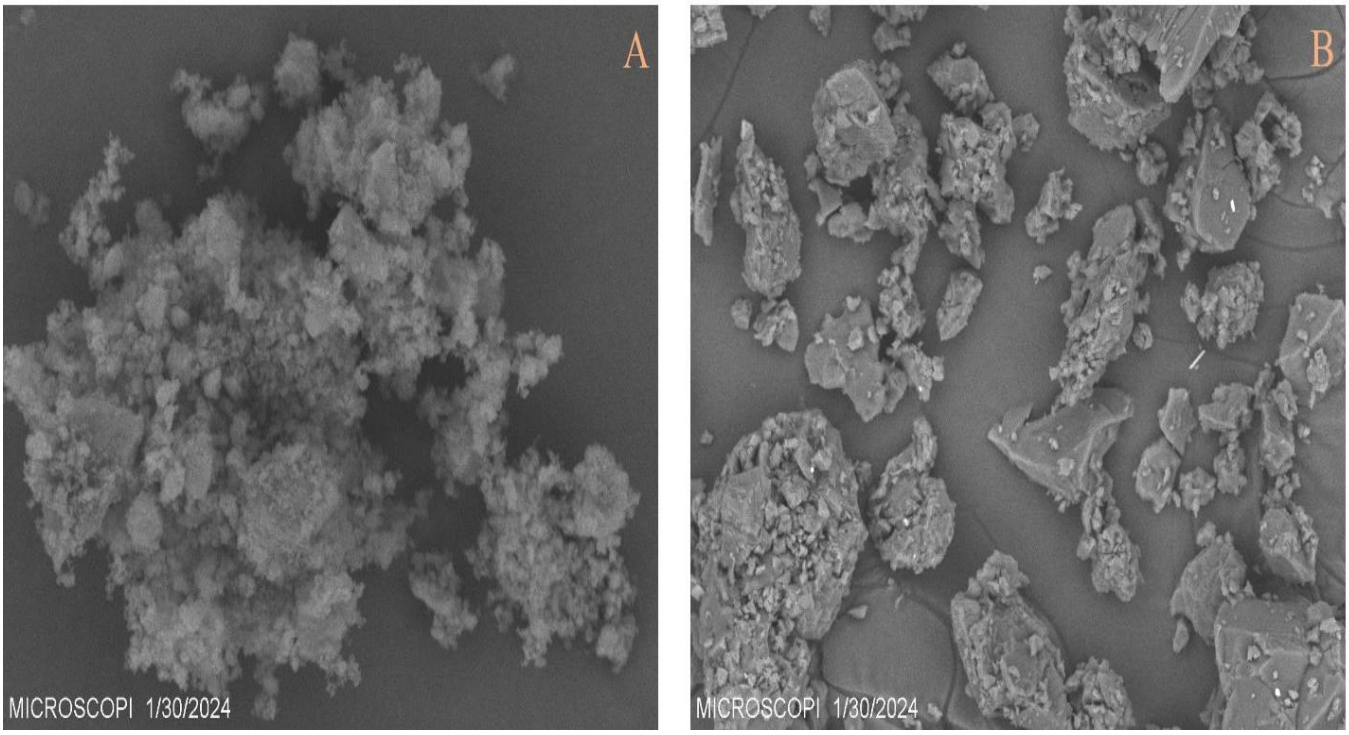

Figure 4: SEM images of Pure drug and optimized formulation of LH5.

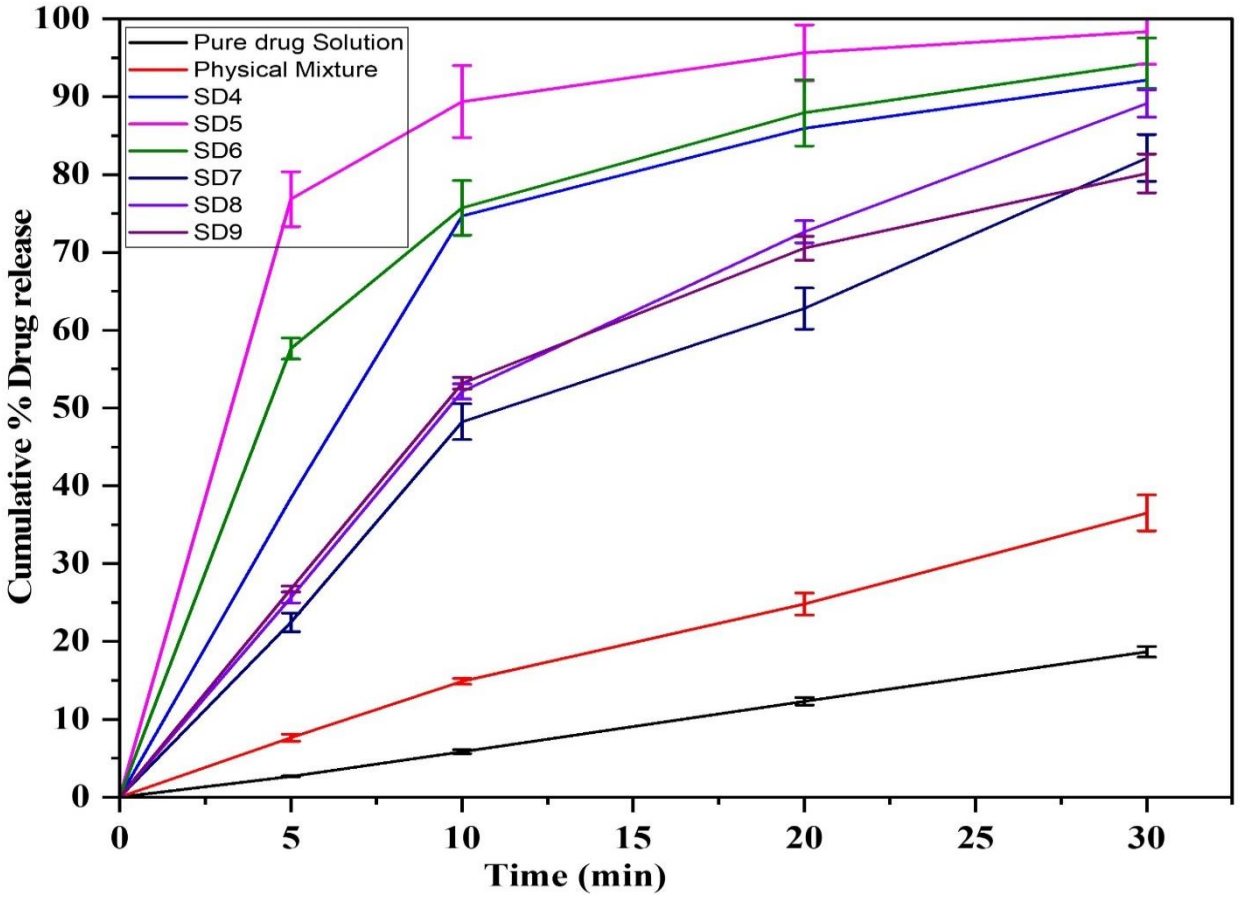

Figure 5: In vitro drug release profile of LH solution, LH loaded β-cyclodextrin, PVP and physical mixture.

3.7.3. Powder X-ray diffraction

We used powder X-ray diffraction to check how crystallin the LH was in the samples. Optimal standard deviation (6.7, 14.1, 20.7, 22.2, 25.0, 29.7, 31.9, and 35.7), as well as linear hydrodynamics (LH) (6.81, 14.2, 20.6, 25.0, 29.7, 31.9, 35.8, and 36.7), were the two primary peaks of the samples. The improved formulation showed two primary peaks that were in agreement with β-cyclodextrin and PVP, while LH did not show any peaks. The β-cyclodextrin and PVP peaks were similarly believed to have originated from the PVP peaks. Because of this, LH in the SD formulations became amorphous rather than crystallized[33]. Additionally, as depicted in figure 3 the peaks of the improved SD formulation were assessed following storage for 6 months. Twenty-5.6, 29.7, and 35.8 were the primary 2θ peaks of the optimized standard deviation (Figure 3). Consequently, following 6 months of storage, neither formulation exhibited any alteration in crystallinity (amorphous form). These results indicated that the amorphous state lasted for 6 months.

3.7.4. Scanning Electron Microscopy

A smooth irregular-shaped mixed mass was observed in the scanning electron micrographs of the optimal SDs formulation, spherical particles with a smooth surface in the β-cyclodextrin and PVP samples (Figure 4b), and an unformed sheet with particles smaller than 5µm in the LH sample (Figure 4a). Despite being comparable in size to β-cyclodextrin and PVP, SD's have a significantly larger particle size than LH. Additionally, SD's have a little rougher surface compared to β-cyclodextrin and PVP, indicating that their surface morphology is rather similar to that of β-cyclodextrin and PVP.

3.7.5. Dissolution studies

Figure 5 depicts the results of *in-vitro* dissolving tests conducted on pure LH, a physical mixture, and a solid dispersion made with β-CD and PVA. The rate of LH release was higher in all of the solid dispersions compared to the pure medication. Maximum drug release of 98.37 ± 0.95% in 30 minutes was demonstrated by the *in vitro* optimized formulation (LH5).

3.7.6. Stability study

By analyzing the drug content and pre-dissolution percentage of LH after 6 months of storage, we were able to assess the stability of SD formulations (LH5) with a high pre-dissolution percentage (Table2). Optimal LH-5 SD formulations preserved their medicinal substance for six months without degradation. Optimal LH 5-SD formulation (a) pre-dissolutions in DW were 98.37 ± 0.36 on the first day

and 92.56 ± 1.27% on the sixth month, as shown in the figures.

4. Conclusions

Lercanidipine hydrochloride solid dispersion formulation and evaluation are the subjects of the current investigation. To formulate solid dispersions, it was ideal to employ the solvent evaporation process, which yielded perfect results every time. The use of PVA and β-CD as hydrophilic carriers in the solid dispersions enhanced the solubility and rate of dissolution of Lercanidipine. The solubility and dissolution rate of all the solid dispersions were higher than those of the bulk medication. The optimized formulation (LH5) outperformed the others in terms of LH solubility and dissolving rate. Analysis using FTIR, DSC, and XRD was used to characterize the solid dispersions that were generated. Research into the properties of LH-SD solid dispersion indicated that it improved LH solubility, likely as a result of LH's transformation into a less crystalline and/or amorphous state. Ultimately, the solvent evaporation approach was used to prepare solid dispersions of LH in β-cyclodextrin and PVP, which improved its solubility.

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