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Preparation and Evaluation of Lercanidipine HCl Nanosuspension to Improve the Dissolution Rate

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Abstract

Lercanidipine HCl, a third-generation calcium channel blocker, blocks calcium entry into smooth muscle L-type calcium channels. This action leads to a decrease in blood pressure and induces peripheral vasodilation. Lercanidipine HCl belongs to the Biopharmaceutical classification system, which is a class II category of drugs. It is practically insoluble in water and has high solubility in methanol. The oral bioavailability of lercanidipine HCl is 10%; in addition to that, it has irregular absorption due to its poor solubility and significant first-pass metabolism. This study aimed to produce and evaluate the preparation of nanosuspension of lercanidipine HCl with improved solubility and dissolution rates. The research used the solvent/antisolvent precipitation technique to generate the nanosuspension, using different stabilizers with various concentrations. The study examined the impact of several procedure factors on the particle size and polydispersity index of chosen lercanidipine HCl nanosuspension formulations. The evaluation parameters include particle size, polydispersity index, drug content, entrapment efficiency, and in-vitro dissolution rates. Together, these characteristics assisted in determining the optimum formula for lercanidipine HCl nanosuspension. The optimal formula (F2) has a particle size of 92.94 nm and a polydispersity index of 0.2515. It consisted of soluplus as a stabilizer in a ratio of 1:2 and a solvent: antisolvent ratio of 3:10 with a stirring speed of 1500 rpm, while the EE% was 97.76%. The prepared formulation significantly improved the dissolution rate of lercanidipine HCl compared to the pure drug. The release profiles of formula (F2) reached 100% within 20 minutes. The selected formula was examined for surface morphology using a field emission scanning electron microscope, and the optimized nanoparticles generated by the lyophilization process were assessed for compatibility using Fourier Transform Infrared Spectroscopy while the determination of crystalline state using X-ray powder diffraction. Research results indicate that using the solvent anti-solvent technique for producing lercanidipine HCl nanosuspension showed an effective enhancement of the dissolution rate of lercanidipine HCl.

Keywords: Lercanidipine HCl, Preparation, Nanosuspension, Particle Size, Soluplus.

Introduction

Hypertension is the most prevalent chronic illness observed in primary care and one of the significant risk factors for cardiovascular death and morbidity. Lowering high blood pressure is beneficial in preventing target organ damage and death in older people, as evidenced by major randomized clinical studies and meta-analyses [(1)]. Third-generation calcium channel blocker lercanidipine HCl (LER) is a member of the 1,4-dihydropyridine class. It prevents calcium from entering smooth muscle L-type calcium channels, which lowers blood pressure and causes peripheral vasodilatation [(2)]. LER is a BCS class II drug. It is practically insoluble in water and freely soluble in methanol. It is available commercially in dosage forms as tablets with 10 and 20 mg strengths [(3)]. It has an octanol/water partition coefficient value of 6.4 at 20–25 °C, making it a highly lipophilic drug. Due to its low solubility and significant first - pass metabolism, LER has a 10% oral bioavailability and irregular absorption [(4)]. In drug research and development, the low solubility of drug candidates leads to many issues. Therefore, a drug's low solubility results in a limited dissolution rate, lowering the drug's oral bioavailability [(5)]. Various approaches may achieve solubility increase, including solid dispersion, complexation, hydrotrophy, co-solvents, surfactant use, particle size reduction, and others [(6)]. Reducing the size of drug particles is the most effective way to increase drug solubility and bioavailability, opening up novel opportunities for the use of nanotechnology [(7)].

Colloidal dispersions of nanosized drug particles that are stabilized by polymer and/or surfactant are known as nanosuspensions (NS). They may also be described as a biphasic system of pure drug particles dispersed in an aqueous medium with

suspended particles with diameters less than 1 µm [8]. Noyes-Whitney and Ostwald-Freundlich's principles state that particles with sizes in the nanometer range could enhance NS's saturation solubility and dissolution velocity, often followed by improved bioavailability. Top-down or bottom-up approaches may generally be used to prepare NS [9]. Large solid particles are broken down into nanosized particles in top-down procedures, while dissolved drug molecules precipitate into nanoparticles in bottom-up techniques [10]. This research aims to produce and evaluate LER nanosuspension using the solvent antisolvent precipitation method to enhance LER's solubility and dissolution rate.

Materials and Experimental Procedures

Materials

Lercanidipine HCl (LER) was purchased from Hyper chem company(china), soluplus (SLU) and tocopheryl polyethylene glycol succinate (TPGS) were purchased from Kathy (China), poloxamer 407 (PXM407) was supplied by Eastman chemical company (USA), methanol was obtained from Panreac applichem (Spain), and Sodium lauryl sulfate (SLS) was provided by Alpha chemika (India).

Methods

Preparation of lercanidipine HCl nanosuspension

The solvent/anti-solvent precipitation technique, or solvent evaporation, generated lercanidipine HCl nanosuspensions. LER powder 10 mg (equivalent to 9.4 mg lercanidipine) dissolved in (3 ml) of methanol at ambient temperature and added to (10 ml) of deionized water with different stabilizers (soluplus, TPGS and poloxamer 407) kept at 37° C. The drug-to-stabilizer ratios used for producing the nanosuspension were 1:1, 1:2, and 1:3 [11]. The mixture was then stirred on a magnetic stirrer, moving at a rate of 1500 revolutions per minute (rpm) for 60 minutes to enable the volatile solvent to evaporate. A plastic syringe with the needle inserted straight into the aqueous solution (water-containing stabilizer) added drops of the drug's resulting organic solution (organic phase) at a speed of 1 mL/min [12]. Investigating the impact of formulation and process parameters on the particle size and polydispersity index of LER nanosuspension contributed to identifying the best formula. Table (1) illustrates Information on the formula's composition and different preparation conditions.

Table1. The formula's composition and various conditions of preparation

F. code	Drug (mg)	Stabilizer type	Stabilizer amount (mg)	Drug: stabilizer ratio	Stirring speed rpm	Inj. speed ml/min	Organic to aqueous ratio
F1	10	Soluplus	10	1:1	1500	1	3:10
F2	10	Soluplus	20	1:2	1500	1	3:10
F3	10	Soluplus	30	1:3	1500	1	3:10
F4	10	PXM 407	10	1:1	1500	1	3:10
F5	10	PXM 407	20	1:2	1500	1	3:10
F6	10	PXM 407	30	1:3	1500	1	3:10
F7	10	TPGS	10	1:1	1500	1	3:10
F8	10	TPGS	20	1:2	1500	1	3:10
F9	10	TPGS	30	1:3	1500	1	3:10
F10	10	Soluplus	20	1:2	2000	1	3:10
F11	10	PXM 407	30	1:3	2000	1	3:10
F12	10	Soluplus	20	1:2	1500	1	3:8
F13	10	PXM 407	30	1:3	1500	1	3:8
F14	10	Soluplus	20	1:2	1500	0.5	3:10
F15	10	PXM 407	30	1:3	1500	0.5	3:10

Characterization of lercanidipine HCl nanosuspension

Determination of the particle size and polydispersity index of lercanidipine HCl nanosuspension

The particle size analyzer nano Laser (Malvern zeta sizer, Ultra rate Company, USA) was used to measure the size and distribution of lercanidipine HCl nanosuspension in all formulations using the dynamic light scattering (DLS) approach at room temperature. Both the polydispersity index (PDI) and particle size (PS) are measured [13].

Factors impacting the PDI and particle size of the produced lercanidipine HCl nanosuspension

The following is a list of factors that may affect the PDI and particle size of lercanidipine HCl nanosuspension:

Effect of concentration and type of stabilizer

Different stabilizer kinds, such as Soluplus, PXM 407, and TPGS, were used in the various ratios shown in Table (1) Measurements and

records were made of the polydispersity index and particle size.

Effect of stirring rate

This study examined the effects of varying the stirring rate from 1500 rpm to 2000 rpm on the properties of lercanidipine HCl nanosuspensions.

Effect of solvent/antisolvent ratio

The effect of two alternative solvent/antisolvent ratios (3:10–3:8) on particle size and polydispersity index was studied.

Effect of Injection speed

The effect of changing injection speed on the particle size of lercanidipine HCl nanosuspensions was examined using two different injection speeds: 0.5 ml/min and 1 ml/min.

Determination of lercanidipine HCl drug content in specific nanosuspension formulas

In a 10 mL volumetric flask, methanol and a measured volume of nanosuspension (1 mL) were combined. After being sonicated for one hour in (Fuyang, China), the material was filtered using a 0.45μm filter syringe. The obtained samples were examined using a UV-visible spectrophotometer, which used the wavelength (λ max) 236 nm at which the drug contained in methanol had its highest absorbance [14]. Next, the drug content was computed using the following equation:

$$\boldsymbol{Drug\ content} = \frac{(\boldsymbol{Practical\ conc})}{\boldsymbol{Theaortical\ conc}}\ \boldsymbol{x}\ \mathbf{100\%} \ldots \boldsymbol{Eq.1}$$

Entrapment efficiency measurement

A precise 4ml sample of the selected lercanidipine HCl nanosuspension was put inside an Amicon ultra-4 centrifugal filter with a M WT of 10 KD. The sample was then centrifuged for 30 minutes at 4000 rpm to assess the entrapment efficiency and determine the quantity of drug incorporated into the nanoparticles. Then, using UV spectrophotometry at λmax 236 nm, the quantity of free LER was calculated [15]. The following equation was used to determine the entrapment efficiency:

$$\%\boldsymbol{EE} = \frac{\boldsymbol{Actual\ amount\ of\ drug - Amount\ of\ Free\ drug}}{\boldsymbol{Actual\ amount\ of\ drug}} \times \mathbf{100\%}\quad \boldsymbol{Eq.2}$$

The in-vitro dissolution profile of lercanidipine HCl nanosuspension formula

Using USP apparatus type II (paddle type), the dissolution test for certain lercanidipine HCl nanosuspension formulae was carried out. LER nanosuspension (10 mg) was evaluated in a 200 ml solution of pH 6.8 phosphate buffer containing 1% SLS, which was added to maintain the sink condition. The paddle was moved at 50 rpm, and the temperature was maintained at 37±0.5 °C. At predetermined intervals (5, 10, 15, 20,25, 30, and 45 minutes), a 5 ml sample was withdrawn and replaced with a fresh dissolution medium. At the specified λ max of 239 nm for this medium, the quantity of LER was measured using spectrophotometry. Every measurement was carried out three times [16].

Compatibility study

Field emission scanning electron microscope (FESEM)

There were carbon tapes on both sides attached to an aluminum stub. After dropping the nanosuspensions onto the tape, they were set aside to dry in a desiccator. They were each given ten minutes of gold spray. After being inserted into the vacuum chamber of an electron microscope, the samples are scanned (FEI Company, Inspect F50). The surface morphology of the particles was observed [17].

Fourier Transform Infrared Spectroscopy (FTIR)

The drug-excipient interactions were identified by analyzing the infrared spectra of pure lercanidipine HCl powder and lyophilized lercanidipine HCl nanoparticles, recorded between 400 and 4000 cm−1. The spectra of FTIR for the test components were obtained using an FTIR spectrometer and the KBr disk technique. The resulting spectra were compared to check for any possible variations in the spectrum's peaks [18].

X-ray powder diffraction analysis (XRPD)

X-ray diffraction was employed to validate the crystallinity of pure lercanidipine HCl and produced LER nanoparticles. The powder X-ray diffractometer confirmed the investigation; the operating voltage and current were 40 (kV) and 30 (mA), respectively. For qualitative evaluations, samples were scanned at 2θ from 0-80° at a scanning rate of 4°/min [19].

Results and Discussion

The particle size and polydispersity index of lercanidipine HCl nanosuspension

The particle size and PDI outcomes of the obtained lercanidipine HCl nanosuspension are shown in Table (2). A particle size analyzer (Malvern Zeta Sizer, Spectris Company, United Kingdom) operating based on dynamic light scattering principles was used to analyze the average particle size and PDI for each generated formula. Every produced formulation was nanoscale in size. The mean particle size ranged from 64.26 nm to 272.9 nm. The estimated PDI for each formula ranges from 0.1678-0.7658. Monodisperse samples have lower PDI values, whereas polydisperse samples have greater PDI values, which indicates more particle size distribution. PDI values vary from 0 to 0.05 for monodisperse systems, 0.05 to 0.08 for nearly monodisperse systems, 0.08 to 0.7 for midrange polydisperse systems, and >0.7 for very polydisperse samples [20]. Except for F13, which showed highly polydisperse features, most formulations showed midrange polydispersity (PDI).

Table 2. Particle size and PDI data of prepared lercanidipine HCl nanosuspension

F. code	P.S (nm)	PDI	F. code	P.S (nm)	PDI	F. code	P.S (nm)	PDI
F1	121.5	0.3219	F6	64.26	0.2364	F11	69.13	0.4707
F2	92.94	0.2515	F7	272.9	0.4062	F12	93.3	0.2772
F3	96.9	0.2497	F8	198.7	0.3957	F13	118.5	0.7658
F4	140.2	0.2522	F9	189.8	0.4644	F14	96.67	0.1678
F5	91.9	0.3647	F10	122.4	0.2223	F15	68.34	0.1447

Effect of concentration and type of stabilizer

Three different stabilizers (Soluplus, PXM 407, and TPGS) were utilized to produce the formulae at three different drug-stabilizer ratios: 1:1, 1:2, and 1:3. The influence of stabilizer type and concentration on the formulations of lercanidipine HCl nanosuspensions could be seen in formulae (F1-F9). A significant difference in particle size ($P<0.05$) was detected through the three types of stabilizers. The formulae stabilized by Soluplus and PXM 407 have the smallest particle size, followed by nanosuspensions produced with TPGS, as shown in Figure 1. The explanation for this may be related to the inherent chemical composition with exceptional surface activity and wettability of Soluplus. Soluplus is an amphipathic graft copolymer comprising a hydrophilic component (polyethylene glycol backbone) and a lipophilic component (vinyl caprolactam/vinyl acetate side chain). Soluplus adsorbs onto drug particles, reducing the interfacial tension of the surface particles. This creates steric hindrance, which prevents the aggregation of the recently generated nanoparticles [21].

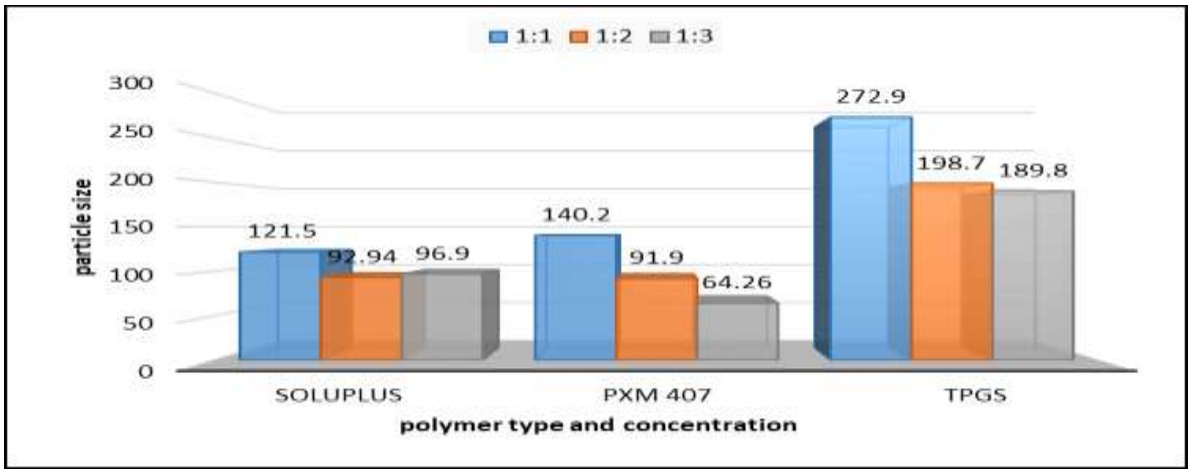

Figure 1. Effect of concentration and type of stabilizer on the particle size of lercanidipine HCl nanosuspensions.

PXM 407 is a linear tri-block copolymer that is amphiphilic, meaning it has both hydrophobic and hydrophilic properties. It consists of a central segment made of polypropylene oxide (PPO), which is hydrophobic, and two side segments made of polyethylene oxide (PEO), which is hydrophilic. The hydrophobic PPO segment induces the polymer to adsorb onto the surface of the drug particles. Additionally, the hydrophilic PEO chains surround the particles, forming a steric hindrance and preventing the particles from aggregating and growing [22]. The TPGS demonstrates a fair decrease in particle size, ranging from 189.8 to 272.9 nm. TPGS is a vitamin E derivative that is soluble in water. It could stabilize the NS by forming hydrophobic interactions between the particles [23]. It was noticed that when the concentration of stabilizers increased. There was a significant decrease in particle size ($p<0.05$). The concentration of a stabilizer is crucial for maintaining the particle size. The optimum concentration of the stabilizer will improve its ability to bind to the drug's surface. At a low concentration, the stabilizer amount was insufficient to completely surround the newly produced nanoparticles, resulting in their aggregation. Increasing the concentration of stabilizer leads to a reduction in the particle size of LER nanoparticles. This is due to the complete wrapping or enveloping of the drug particles, resulting in their stabilization at a smaller size [24]. The investigation demonstrated that increasing the polymer ratio of Soluplus in F3 increases the particle size. The rise in the particle size may be attributed to the elevated viscosity, restricting the mobility of particles in the solution and hindering adequate coverage of the newly formed nanoparticles. In addition, a higher concentration of stabilizer might increase the thickness of the coating around the nanoparticles. This thicker

coating acts as a barrier, preventing the diffusion of the solvent and antisolvent phases during the precipitation of the nanoparticles [25].

Effect of stirring rate

A study investigated the influence of stirring speed on the particle size of lercanidipine HCl nanoparticles. Four alternative formulas (F2, F6, F10, and F11) were created using two differing speeds, 1500 and 2000 rpm, as illustrated in Figure 2. The particle sizes obtained from these formulations were (92.94 and 64.26) at 1500 rpm and (122.4 and 69.13) at 2000 rpm for the soluplus 1:2 formulae and PXM 407 1:3 formulae, respectively. The results showed a significant difference in particle size ($P<0.05$) when the stirring speed was altered during the nanosuspension formation. Using a high stirring speed (2000 rpm) is not always ideal due to excessive agitation leading to foams forming. These foams can cause the drug particles to separate from the vehicle medium, hindering the preparation process. Therefore, an optimal speed of 1500 rpm is necessary to ensure that the drug particles remain within the acceptable range [26].

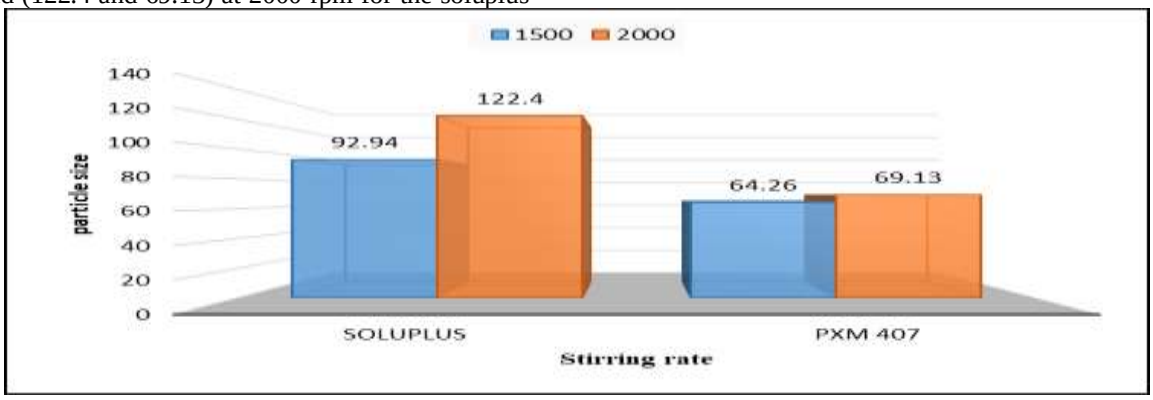

Figure 2. Effect of stirring rate on the particle size of lercanidipine HCl nanosuspensions

Effect of solvent/antisolvent ratio

The influence of varying antisolvent-to-solvent ratios on forming lercanidipine HCl nanoparticles was investigated by producing formulae F2, F6, F12, and F13. Two distinct solvent-to-antisolvent ratios, including 3:10 and 3:8, were used. Figure 3 demonstrates a significant difference in particle size ($P<0.05$) when the antisolvent-to-solvent ratio is altered in F13. The higher ratio of solvent to antisolvent has resulted in an increased supersaturation ratio, leading to an elevated rate of nucleation and a reduction in particle size [27]. The soluplus formula F12 did not exhibit a significantly different change in particle size ($P > 0.05$).

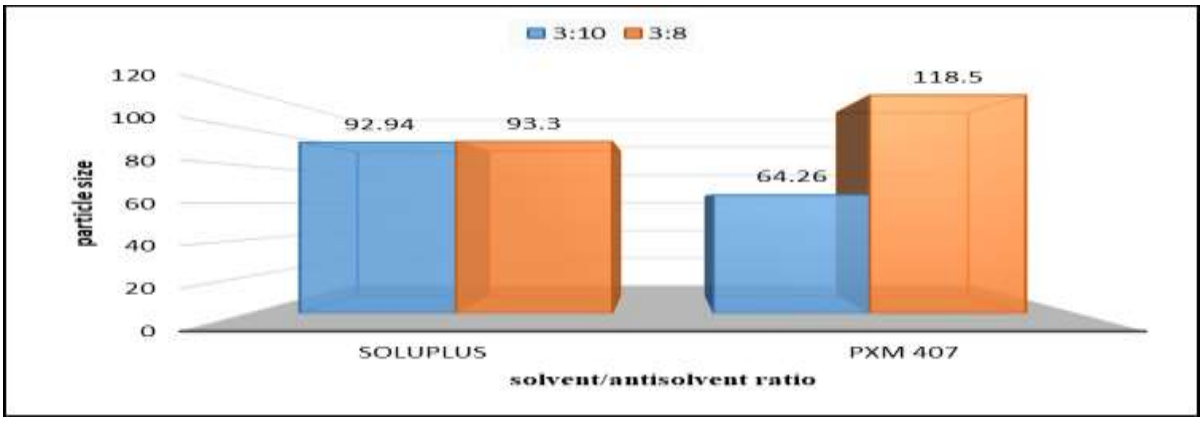

Figure 3. Effect of solvent/antisolvent ratio on the particle size of lercanidipine HCl nanosuspensions

Effect of Injection speed

Formulations (F14-F15) were produced to demonstrate the impact of the injection speed of the solvent phase into the anti-solvent phase, as seen in Figure 4. The size of the generated nanoparticles (NPs) significantly increases ($P < 0.05$) as the injection speed is reduced due to a decrease in mixing effectiveness between the solvent and the anti-solvent at a lower rate (0.5 mL/min). This reduction in mixing efficiency encourages crystal development, leading to the generation of larger particles [28].

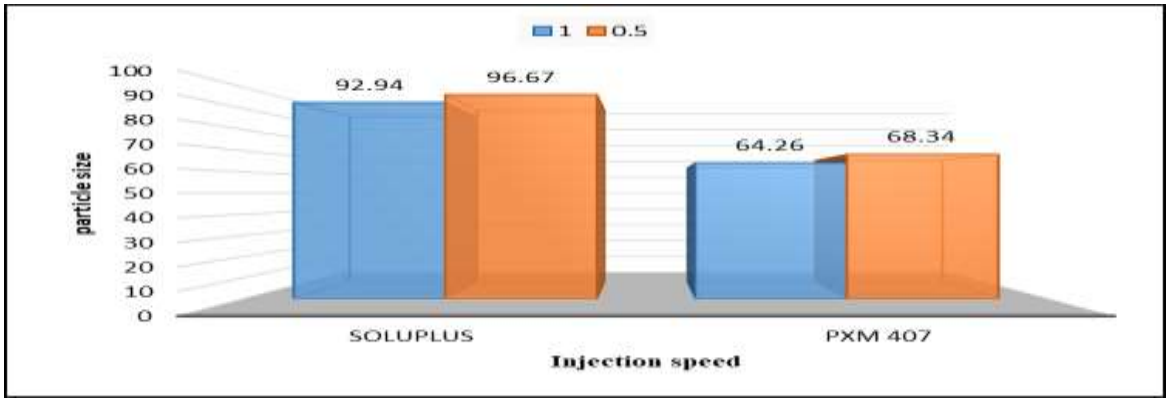

Figure 4. Effect of Injection speed on the particle size of lercanidipine HCl nanosuspensions

Determination of lercanidipine HCl drug content in specific nanosuspension formulas

The drug content percentage of the selected lercanidipine HCl nanosuspension formulae was examined and found to be 99.2% ± 0.2516 for F2 and 96.5% ± 0.0763 for F6. They complied with the British Pharmacopoeia (BP) standards and came within the allowed range of 95% to 110% [29], meaning there was neither any precipitation nor any loss of drugs.

Entrapment efficiency measurement

The nanoparticle entrapment efficiency of lercanidipine HCl was found to be 97.76% ± 1.0598 for F2 and 94.46% ± 1.5631 for F6. The high encapsulation efficacy has been attributed to the drug's low solubility in the external phase and its high solubility in the organic solvent. Consequently, a smaller amount of the drug is directed into the exterior aqueous phase [30].

The in-vitro dissolution profile of lercanidipine HCl nanosuspension formula

The USP dissolution apparatus type II was used to evaluate the release of lercanidipine HCl nanosuspension formulations and lercanidipine HCl's pure powder. The dissolution medium included 200 ml of phosphate buffer with a pH of 6.8 and 1% SLS. A dissolution test was conducted on pure LER powder and selected formulations, including F2 and F6, which exhibited sizes less than 100 nm. Figure 5 shows that the pure LER had a release rate of 33.6% after 20 minutes. Furthermore, the nanosuspension formulations of LER (F2 and F6) displayed significantly improved release profiles, with F2 exhibiting exceptional performance by reaching complete release of LER within just 20 minutes. The release profiles of F2 and F6 reached 100% and 92.53%, respectively, within this short time interval.

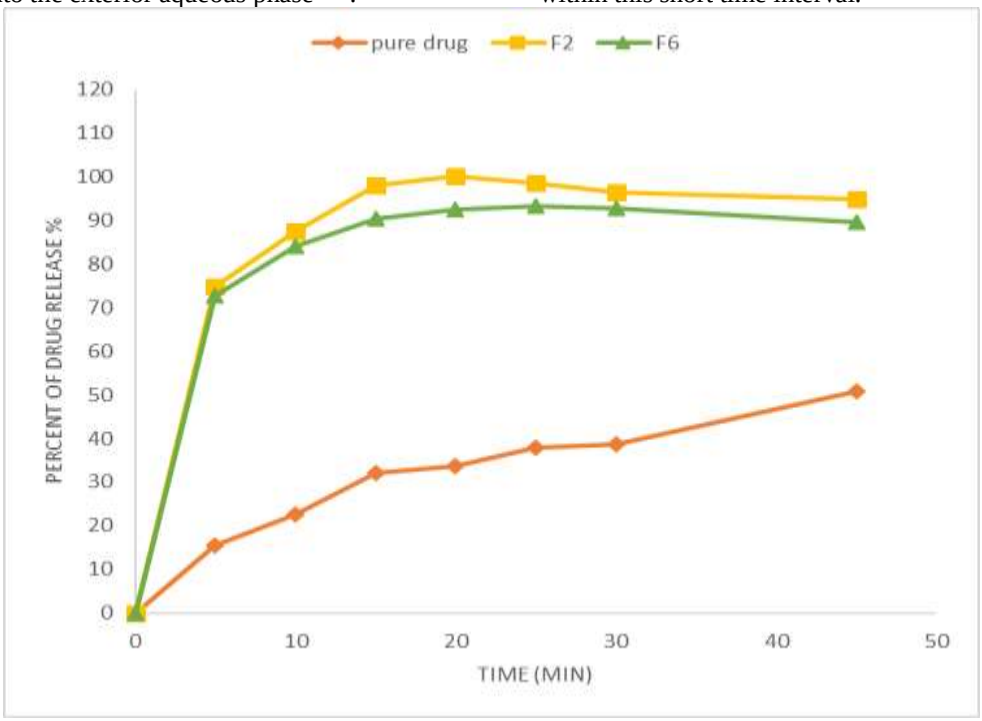

Figure 5. In-vitro dissolution of the pure lercanidipine HCl, F2, and F6

The similarity factor f2 determines the degree of similarity in the dissolution percentage between two curves. According to the current FDA guidelines, the dissolution profiles are regarded as similar if the f2 value is more than 50 (ranging from 50 to 100). A comparative study was performed to assess the release profiles of LER nanosuspension formulations (F2, F6) with the pure powder of LER, utilized as a reference. The similarity factor f2 was used for this purpose. The obtained similarity factor value is below 50, as Table (3) illustrates. This indicates that the produced LER nanosuspension and the pure Lercanidipine HCl powder have an apparent difference in dissolution behaviors [31].

Table 3. Comparison of the similarity factor test of F2 and F6 with pure lercanidipine HCl

F. code	f2 value
F2	12.43
F6	14.31

Selection of the optimal formula

According to the results of the tests performed to assess particle size, PDI, drug content, entrapment efficiency, and in-vitro drug release, it can be determined that the F2 nanosuspension formula is the optimal formula. Further examination, such as FTIR, FESEM, and XRPD, will be conducted on this formula.

Compatibility study

Field emission scanning electron microscope (FESEM)

The surface morphology and size of lercanidipine HCl nanoparticles were investigated using a field emission scanning electron microscope. The selected formula F2 was examined, as shown in Figure 6. The results showed that the formula had uniform and small particle sizes with a homogenous surface.

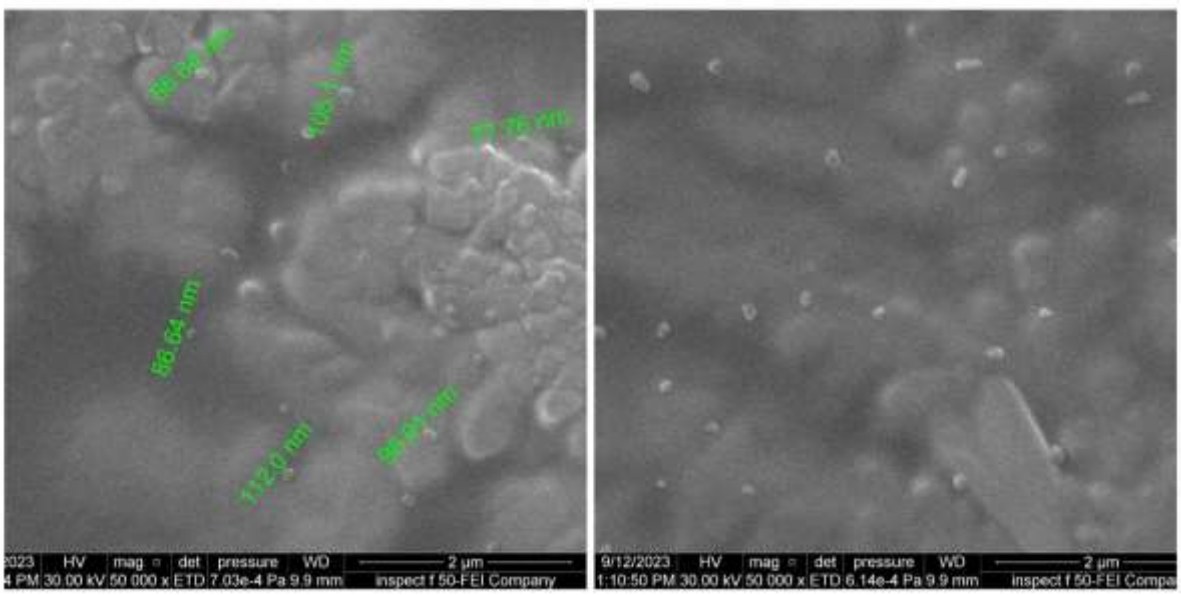

Figure 6. FESEM of selected lercanidipine HCl nanosuspension (F2)

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectra of pure lercanidipine HCl, a physical mixture of pure LER: soluplus (1:2), and lyophilized LER nanoparticles (F2) are shown in Figures 7, 8, and 9, respectively. The pure LER powder's infrared spectra were compared to a reference spectrum and determined to be similar [32]. The lyophilized LER nanoparticles exhibited the same characteristic peaks but with reduced intensity and no appearance of more peaks. This suggests that there is no interaction between the drug and polymers, as Table (4) illustrates. The existence of a broad peak could be ascribed to the formation of hydrogen bonds between the drug and polymer.

Table 4. FTIR peaks of pure lercanidipine HCl, lercanidipine HCl nanoparticles and physical mixture of pure LER: soluplus (1:2) .

Functional group	Pure drug (cm^{-1})	Lercanidipine HCl NPs (cm^{-1})	physical mixture of pure LER: soluplus (1:2)	Reference (cm^{-1})
N-H stretching	3184.86	3387.35	3184.86	3184
C-H stretching of aromatic ring	3076.87	2930.31	3076.87	3080
c=o stretching	1671.02	1632.45	1671.02	1672
CH-NO2 stretching	1523.49	1555.31	1523.49	1525
bending of geminal methyl groups	1402.96 , 1384.64	1412.60 , 1365.60	1404.89 , 1346.07	1406 , 1386
out of place bending of 5 and 3 adjacent hydrogens on aromatic rings	812.85 – 643.14	812.68 – 620	812.85 – 643.14	813 – 640

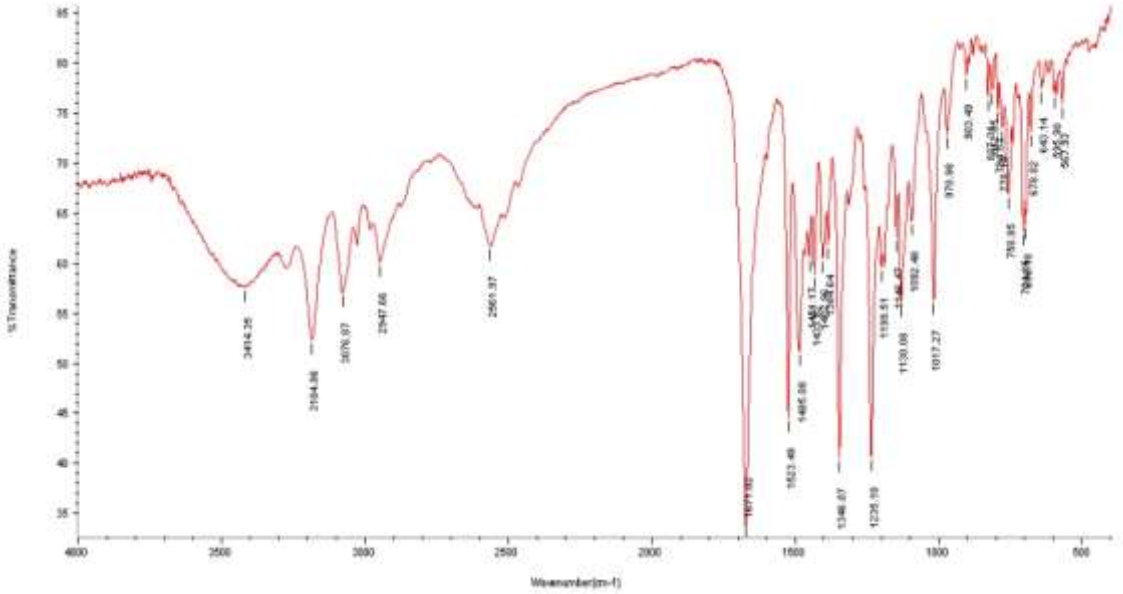

Figure 7. FTIR spectrum of pure lercanidipine HCl

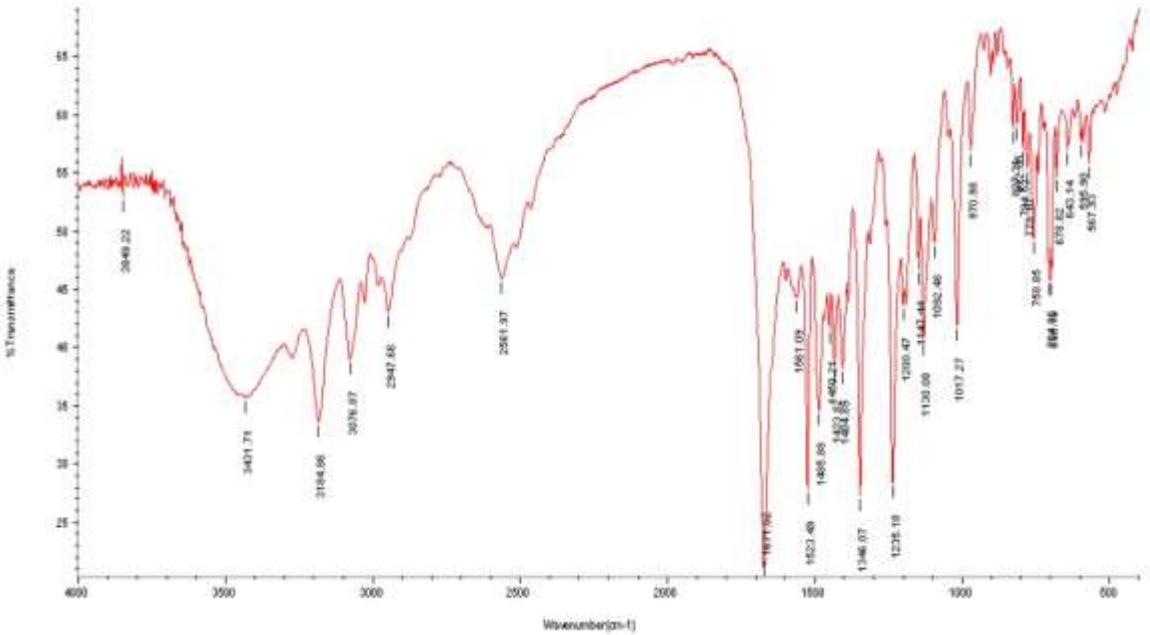

Figure 8. FTIR spectrum of physical mixture of pure LER: soluplus (1:2)

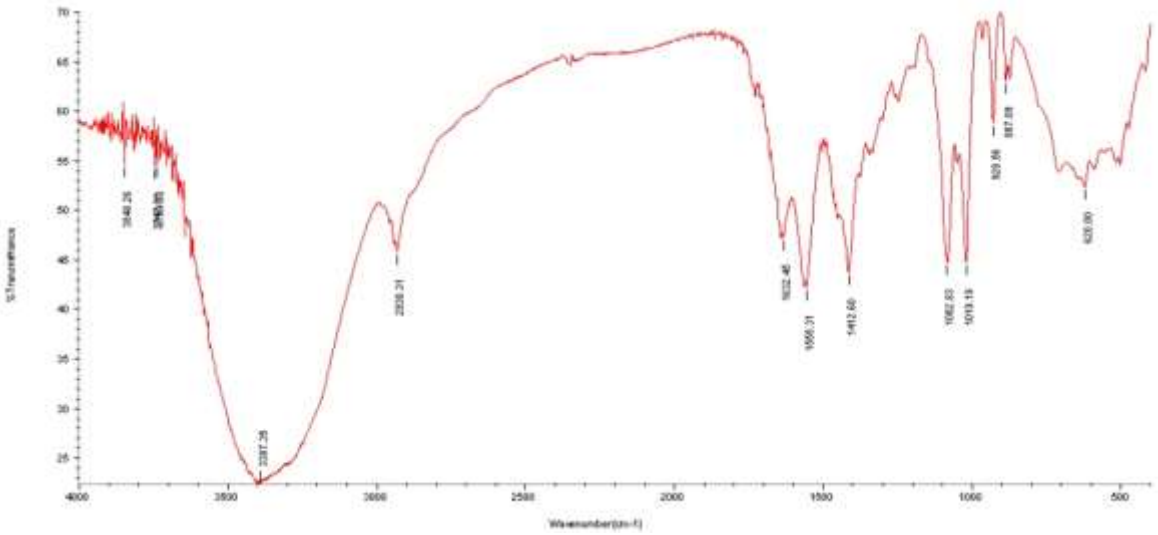

Figure 9. FTIR spectrum of lercanidipine HCl nanoparticles (F2)

X-ray powder diffraction analysis (XRPD) X-ray diffraction (XRD) study was performed on pure lercanidipine HCl powder, lyophilized LER nanoparticles (F2), and a physical combination of pure LER to soluplus in a ratio of 1:2. To determine possible changes in the crystalline arrangement of LER as shown in Figure 10. The peaks' intensity was decreased in the nanoformulation. This indicates that the crystalline nature of the drug has mostly reduced during nanonization. A significant variance in the crystallinity of the nanoparticles compared to pure LER was observed. A possible reason may be attributed to the differences in particle size and crystal arrangement during the procedure of precipitation [33].

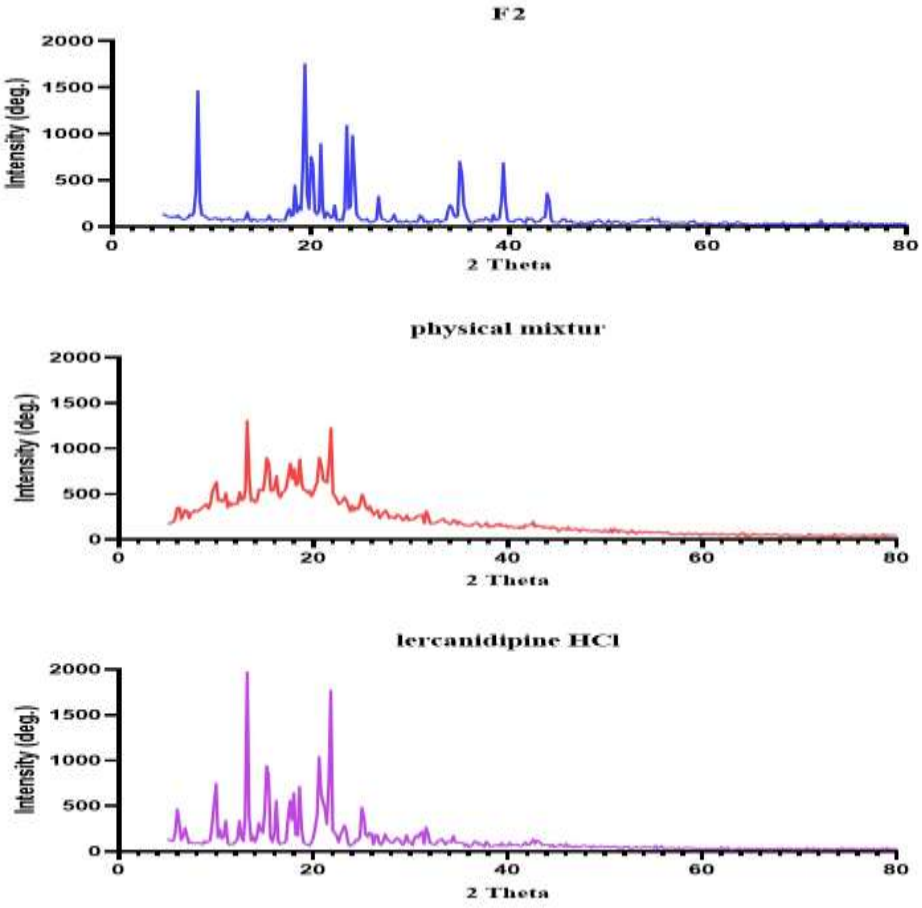

Figure 10. XRPD spectrum of pure lercanidipine HCl, lercanidipine HCl nanoparticles (F2) and physical mixture of pure LER: soluplus (1:2)

Conclusion

Based on the results of this research, the use of soluplus as a stabilizer at various concentrations successfully produced a nanosuspension of lercanidipine HCl. The best formula, consisting of lercanidipine HCl and soluplus in a ratio of 1:2 and the solvent to the antisolvent ratio of 3:10, generated nanoparticles measured 92.94 nm in size, with a polydispersity index of 0.2515. The optimal formula significantly improved the dissolution rate of lercanidipine HCl in comparison with the pure drug. Hence, using the solvent anti-solvent technique to produce lercanidipine HCl nanoparticles successfully improved the dissolution rate of lercanidipine HCl.

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Conflicts of Interest

No conflicts.

Funding

No funding.

Ethics Statements

This experiment did not need ethical approval since it did not include animals or humans.

Author Contribution

Zahraa A. Alsafar contributed to the work by collecting data, analyzing and interpreting outcomes, and preparing the initial manuscript. Zahraa A. Alsafar and Fatima J. Jawad contributed to the text's final version. Fatima J. Jawad supervised the project.

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تحضير وتقييم معلق هيدروكلوريد ليركانيديبين النانوي لتحسين معدل الانحلال

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الخلاصة

ليركانيديبين هيدروكلوريد، وهو حاصر لقنوات الكالسيوم من الجيل الثالث، يمنع دخول الكالسيوم إلى قنوات الكالسيوم من النوع ل في العضلات الملساء. يؤدي هذا الإجراء إلى انخفاض في ضغط الدم ويؤدي إلى توسع الأوعية الدموية الطرفية. ينتمي ليركانيديبين هيدروكلوريد إلى صنف الأدوية من الفئة الثانية في نظام تصنيف الأدوية الحيوية. وهو غير قابل للذوبان عمليا في الماء ولديه قابلية عالية للذوبان في الميثانول. يبلغ التوافر البيولوجي لليركانيديبين هيدروكلوريد عن طريق الفم ١٠٪، وامتصاصه غير منتظم بسبب ضعف قابليته للذوبان واستقلابه الأول بشكل كبير. تهدف هذه الدراسة إلى إنتاج وتقييم المعلق النانوي ليركانيديبين هيدروكلوريد مع تحسين معدلات الذوبان والانحلال. استخدم البحث تقنية الترسيب بالمذيب / المذيب المضاد لتوليد معلق نانوي، باستخدام مثبتات مختلفة بتركيزات مختلفة. تناولت الدراسة تأثير العديد من عوامل العملية على حجم الجسيمات ومؤشر التوزيع لتركيبات المعلق النانوي هيدروكلوريد ليركانيديبين المختارة. تتألف عوامل التقييم من حجم الجسيمات، ومؤشر التوزيع، ومحتوى الدواء ،وكفاءة الانحباس، ومعدلات التحرر في المختبر. ساعدت هذه الخصائص معًا في تحديد الصيغة المثالية للتعليق النانوي ليركانيديبين هيدروكلوريد. تحتوي الصيغة المثالية على حجم جسيم يبلغ ٩٢,٩٤ نانومتر ومؤشر التوزيع يبلغ ٠,٢٥١٥. يتكون من السولوبلس كمثبت بنسبة ١:٢ ونسبة مذيب: مضاد الإذابة ٣:١٠ مع سرعة تقليب ١٥٠٠ دورة في الدقيقة، وكفاءة الانحباس ٩٧,٧٦٪. أدت التركيبة المحضرة إلى تحسين معدل ذوبان هيدروكلوريد ليركانيديبين بشكل ملحوظ مقارنة بالدواء النقي. وصل معدل التحرر للصيغة المثلى إلى ١٠٠٪ خلال ٢٠ دقيقة. تم فحص هذه الصيغة لمعرفة شكل السطح باستخدام المجهر الماسح الثانوي الانبعاث، وتم تقييم الجسيمات النانوية المحسنة الناتجة عن إجراء التجفيد من أجل التوافق باستخدام الفحص بالأشعة تحت الحمراء وحالتها البلورية باستخدام تفريق الأشعة السينية

تشير نتائج البحث إلى أن استخدام تقنية المذيب /المذيب المضاد لإنتاج معلق هيدروكلوريد ليركانيديبين النانوي يُظهر فعاليته في تعزيز معدل انحلال الهيدروكلوريد ليركانيديبين.

الكلمات المفتاحية: هيدروكلوريد ليركانيديبين، ترسيب الميذيب ،مضاد المذيب، معلق نانوي، حجم الجسيمات، سولوبلس.