Nanotechnology Perceptions
ISSN 1660-6795
www.nano-ntp.com

Assessment of Effect of Modified Pectin on Solubility and Bioavailability Enhancement of Lercanidipine

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Objective: Lercanidipine is calcium channel blockersused to treat high blood pressure. It belongs to a class BCS II drugs known for its low water solubility, which affect its bioavailability and therapeutic efficacy.The objectives of present researchwereto improve the solubility, dissolution and bioavailability of lercanidipine.Method:Natural modified pectin extracted from the mango peels was utilised for the formulation of solid dispersion.The physical mixtures and solid dispersion lercanidipinewas made using extracted native and chemically modified pectin. Solid dispersion of drug with pectin was prepared by kneading method. Prepare solid dispersion was further evaluated for solubility study, drug content, Fourier-transform infrared (FTIR), differential scanning calorimeter (DSC), powder X-ray diffractometry (PXRD), scanning electron microscopy (SEM) and dissolution studies. Result:Solubility study suggested that use of modified pectin markedly increases the drug solubility with increased in concentration. The FTIR and DSC show compatibility between drug and polymer.Broadening of DSC peak suggested the reduction in intensity and amorphous conversion of drug. XRD study also confirmed the crystallinity reduction in complex. The SEM of optimized SD showed homogeneous surface compare to its irregular large size cluster form in native form. Conclusion:Solid dispersionprepared with pectin and modified pectin showed increase in drug solubility and dissolution rate as compare to pure drug. SD with 1:3 ratio of drug to modified pectin showed fastest drug release of 99.74 in 60 min.This research proved the effectiveness of natural carriers, such as modified pectin, in the solubility enhancement of for poorly soluble compounds.

Keywords: Lercnidipine, Modified pectin, DSC, XRD, SEM etc.

1. Introduction

The solubility and bioavailability of poorly water-soluble drugs represent a significant challenge in pharmaceutical sciences, particularly for drugs like lercanidipine, a calcium channel blocker used for hypertension management. Despite its efficacy, the therapeutic application of lercanidipine is often hindered by its low aqueous solubility and subsequent poor bioavailability. Solid dispersion techniques have emerged as an effective strategy to address these limitations by enhancing solubility and dissolution rates. [1] In this context, the use of natural and modified polymers such as pectin has gained considerable attention. Pectin, a biopolymer derived from plant cell walls, is known for its biodegradability, biocompatibility, and versatile functional properties. [2,3] By modifying pectin, its solubility-enhancing and

drug-carrier characteristics can be significantly improved, making it an ideal candidate for the preparation of solid dispersions. This study focuses on the formulation of lercanidipine solid dispersions using modified pectin as a carrier to improve its solubility and bioavailability. Various solid dispersion techniques, including solvent evaporation and spray drying, were explored to optimize the drug-carrier interaction and achieve a homogenous amorphous phase. [4,5] The research also evaluates the physicochemical properties, dissolution profiles, and stability of the prepared formulations. By leveraging the unique properties of modified pectin, this study aims to provide a robust and scalable solution for enhancing the therapeutic efficacy of lercanidipine, thereby addressing a critical unmet need in hypertension treatment.

2. Materials and Methods

Material

Lercanidinewas obtained as a gift sample from Sun Pharma Ltd., Ahmedabad, India. All other chemicals and solvents used were of pharmaceutical and analytical grade.

Saturation Solubility Study of Lercanidipine

Saturation solubility studyof lercanisipinewas tested in different solvent like and distilled water, 0.1 N Hcl and Phosphate buffer pH 6.8 as per method reported by huguchi and Connors. Extra amount of drug was added in to the 10 ml of glass vial, which was shaken mechanically on shaker for 72 hrs. Filter sample was then analysed at 256 nm after suitable dilution. [6]

Extraction of pectin from mango peels

The fresh fruit peels of ripened mango were collected and cut into small pieces and washed with water three times. It was then dried in the oven at 60°C to lower down moisture content to 5–6%. The dried peel was milled to sieve size of 80 meshes and packed in the airtight, moisture-proof bag at room temperature and prepared to the extraction process.

Extraction Procedure

Ground and defatted mango peels were mixed well with water of various pH (1.5, 2.0, 2.5, 3.0, 3.5), keeping substrate to water ratio 1:40 (w/v). The specified pH of the mixture was adjusted with 0.1 N sulphuric acid on pH meter. Thereafter, the mixture was heated at 100°C temperature for an hour with frequent stirring. The contents were filtered through a muslin cloth and the filtrate was precipitated with 95% ethanol. Dried pectin was obtained by drying the precipitates at 40°C in vacuum pump. [7]

Modification of Native Extracted Pectin

Native extracted pectin was initially dissolved in a 1.5% solution in distilled water and pH raised to 10.0 with NaOH and incubated for 1 h at 50–60^{o} C. The sample was then cooled up to room temperature and its pH adjusted to 3.0 with HCl. After being stored overnight, the samples were precipitated the next day with ethanol 95% and incubated at 20^{o} C during 2 h. The material was filtrated, washed with acetone and dried in hot air oven at 25^{o}C. [8]

Preparation of Physical Mixture (PM) and Solid Dispersion of Lercanidipine Using Native and Modified Pectin

The physical mixtures (PM) and solid dispersion of drug lercanidipine using extracted native and chemically modified pectin was prepared in the ratio 1: 1,1:2, 1:3 and 1:4. Physical mixture was prepared by simple mixing of drug and pectin in mortar and mixed for 5 min with the use of a pestle. Solid dispersion of drug with pectin was prepared by kneading method.The drug and carrier were gently mixed to get a uniform mixture. Water: methanol in the ratio of 1: 1 was added in small quantity to make a paste. The paste was allowed to stand for 45 min and dried in a hot air oven at 40 ± 2°C. The product obtained was pulverized and passed through the mesh (#) 85. The solid dispersion containing chemically modified pectin was prepared in the same manner. [9]

Characterization of The Ternary Inclusion Complex

Solubility Study of Physical Mixture and Solid Dispersion

The prepared physical mixture and solid dispersions were subjected to solubility studies, as described by Higuchi and Connors, 1965. The prepared Physical mixtures were added to 25 ml of aqueous solution in screw-capped bottles, Samples were shaken for the 24 hr at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. The filtrate was diluted suitably with 0.1 N HCl and analysed spectrophotometrically. [10]

Fourier Transform Infrared Spectroscopy (FTIR)

The complex formation was assessed by evaluating the change in peak shape, position, and intensity using a spectrophotometer (FTIR Shimadzu 8400S, Lab Wrench). The spectra of pure drug and solid dispersion were compared to interpret the spectra. The analysis was performed between 4000 and 400 cm−1 and the conformational changes were observed.

Differential Scanning Calorimetry (DSC)

The thermal behavior of pure lercanidipineand solid dispersionwere examined using a differential scanning calorimeter (Metler)including withaluminum-sealed pan cell. Samples were placed in hermetically sealed aluminium pans and heated in a temperature range of 30 to 300 °C with 10 °C/min increment rate in a nitrogen atmosphere. [11]

Powder X-Ray Diffraction

X-ray powder diffraction patterns of drug, carrier and solid dispersion was recorded on an X-ray powder diffraction system (Rigaku, Mini Flex 600). The scanning was done over range of 5° to 60°. The position and intensities of diffraction peaks were considered for the comparison of crystallinity [12].

Surface Morphology Study

The surface morphology of the pure druglercanidipine and optimized solid dispersion was investigated using a scanning electron microscope. The study was performed using an electron microscope (JOEL, Tokyo, Japan). The samples were coated with gold and detected under the microscope at high resolution to reveal the change in morphology. [13]

In Vitro Dissolution Study

Dissolution study was conducted on pure drug lercanidipine and prepared solid dispersion formulation. USP dissolution test apparatus (Electrolab, India)type IIwas used for the study.

The study was performed at 37 °C ±0.5 °C temperature with a paddle rotation speed of 50 rpmusing 0.1 N HCl (900 ml) as dissolution medium. Aliquots of 5 ml was withdrawingfrom the dissolution sample at fixed time interval of 10, 20,30,40,50 and 60 min.The equivalent amount of fresh dissolution medium was added in order to maintain sink conditions. These aliquots were diluted suitably and analysed by UV–Visible spectroscopy at 256 nm using blank. All these experiments were carried out in triplicate. [14,15]

In-vivo Pharmacokinetic study

Solid dispersion formulation that showing promising evaluation results in term of its drug solubility and dissolution rate, such optimized SD formulation of lercanidipinewas chosen to conduct the in-vivo study and compare it with pure lercanidipine. In vivo pharmacokinetic study was carried out on wistermale rats according to the guidelines of the CPCSEA, after approval of study.

Study Design

The study was conducted on healthy male Wistar rats weighing between 250 and 300 grams. The rats were randomly separated into two groups, each with six rats (n=6). Before the test, all rats were fasted overnight with free access to water. lercanidipine oral bioavailability was tested at a dose of 10 mg/kg of body weight. The drug sample was made by suspending the drug I 1 % w/v aqueous sodium carboxyl methyl cellulose and diluting it with water to produced 1 mg/ml concentration. Aqueous solution of pure lercanidipine was administered orally to one set of animals, which was treated as a control using an oral feeding sonde, based on their body weight.

The second group of animals was considered as test and given the optimized lercanidipine solid dispersion formulation at the same dose. At specific time intervals of 0.5, 1, 2, 3, 4, 6, 8, 12 hours, 0.5 ml of blood was taken from the postorbital vein sinus into a micro centrifuge tube treated with EDTA. The plasma was separated by centrifugation at 3000 rpm for 10 minutes, then treated with a small amount of acetonitrile before centrifugation at 3000 rpm for another 10 minutes. 50µl of plasma were combined with 0.5 ml of mobile phase. The 20 µl sample was injected into a C 18 column (Cosmosil, 5m, 4.6 x 250 mm) at a flow rate of 0.7 ml/min and examined by HPLC method. [15]

Pharmacokinetic Parameters Estimation and Statistical Analysis

The drug concentration in plasma vs. time was plotted as a result of the HPLC analysis. The PK Solver computer software was used to calculate non-compartmental pharmacokinetic parameters such as T_{max}, C_{max}, and AUC. The AUC values for each curve were determined using the trapezoidal rule and extrapolation to infinity from time zero to the last data point. The relative bioavailability was calculated using the AUCo-∞values obtained from the curve. The results of in vivo investigations are shown as mean standard deviation. Graph Pad Prism 5.0 software was used to perform statistical significance tests. A one-way ANOVA was used to compare the variables. Significant was defined as a P-value of less than 0.05. [16]

3. Results and Discussion

Saturation Solubility Study of Lercanidipine

The solubility profile of lercanidipine was studied in three solvents: water, 0.1 N HCl, and phosphate buffer (pH 6.8). The solubility data reveals that lercanidipine exhibits limited solubility in all tested solvents. Lercanidipine exhibited moderate solubility in water (0.0526 ± 0.014 mg/mL). The limited solubility in water can be attributed to its hydrophobic nature, which reduces its ability to dissolve in polar solvents. The highest solubility was observed in 0.1 N HCl (0.0862 ± 0.023 mg/ml), followed by water (0.0526 ± 0.014 mg/ml). The lowest solubility was found in phosphate buffer pH 6.8 (0.0135 ± 0.008 mg/ml). The higher solubility in 0.1 N HCl compared to water can be attributed to the ionization of lercanidipine in the acidic medium. Lercanidipine, being a weakly basic drug, can form salts in acidic conditions, which generally exhibit higher solubility than the free base form. The significantly lower solubility in phosphate buffer pH 6.8 suggests that lercanidipine's solubility decreases as the pH approaches neutral or slightly alkaline conditions. This is consistent with the behavior of weakly basic drugs, which tend to be less soluble in less acidic or basic environments.

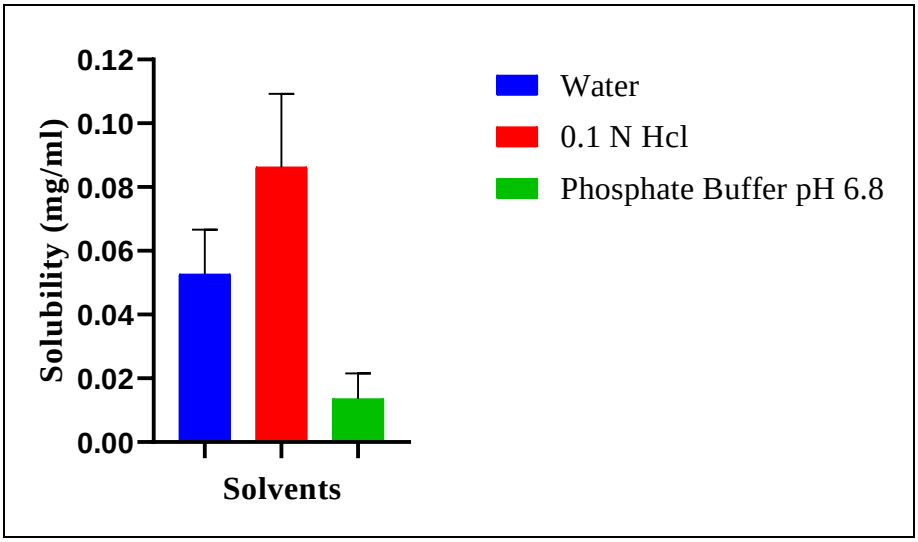

Figure 1: Saturation Solubility of Lercanidipine in different Solvents

Solubility Study of Physical Mixture and Solid Dispersion

The solubility study of pure lercanidipine, its physical mixtures (PM) with native pectin, and solid dispersions (SD) prepared using native and modified pectin was conducted in distilled water. The solubility of pure lercanidipine was found to be 0.0526 ± 1.23 mg/mL, indicating its poor aqueous solubility due to its hydrophobic nature.The solubility drug in Physical Mixtures (PM) with Native Pectin seen to be improved progressively with increasing ratios of pectin.At a 1:1 ratio (LPPM 1), the solubility was 0.432 ± 0.32 mg/mL, increasing to 0.723 ± 0.28 mg/mL at a 1:4 ratios (LPPM 4).The enhancement can be attributed to improved wettability and partial interaction between the drug and pectin.The gradual increase in solubility in physical mixtures suggests improved drug wettability and dispersion in the presence of pectin. However, the solubility enhancement was limited due to the lack of significant molecular interaction or transformation of the drug's crystalline state.

Solid Dispersions (SD) of lercanidipine with Native Pectin showed significant improvement

in solubility was compared to PM.At a 1:1 ratio (LPSD 1), solubility reached 6.61 ± 0.67 mg/mL and further increased to 13.18 ± 0.51 mg/mL at a 1:4 ratios (LPSD 4).This improvement is due to the amorphization of the drug and strong molecular interactions between lercanidipine and pectin.The transition from physical mixtures to solid dispersions markedly enhanced solubility, highlighting the role of solid dispersion techniques. The amorphization of lercanidipine and hydrogen bonding with pectin contributed to the observed increase in solubility.

The highest solubility was achieved SDs with modified pectin.At a 1:1 ratio of drug to modified pectin (LMPSD 1), solubility was 9.37 ± 0.62 mg/mL, increasing to 13.14 ±0.72mg/mL, 15.18 ±1.04mg/mL and 16.24 ± 1.12 mg/mL at a 1:2, 1:3 and 1:4 ratios (LMPSD 2 to LMPSD4) respectively.Solubility of lercanidipine was seen to increases as the modified pectin concentration increases till 1:3 ratio, after that the drug solubility was not seen to be increased marginally. The use of modified pectin further enhanced solubility due to its better hydrophilicity and stronger interaction with the drug.The highest solubility values were observed for solid dispersions using modified pectin. Modification of pectin likely improved its hydrophilicity and drug-carrier compatibility, resulting in better drug dispersion and molecular stabilization in an amorphous form.Modified pectin outperformed native pectin in enhancing solubility at all ratios, with LMPSD 4 (1:4) achieving the highest solubility (16.24 ± 1.12 mg/mL). The structural modification of pectin may have enhanced its binding capacity and ability to prevent drug recrystallization.

The study demonstrated a progressive improvement in the solubility of lercanidipine with the use of pectin as a carrier. Solid dispersions, particularly those prepared with modified pectin, significantly outperformed both pure lercanidipine and physical mixtures. This highlights the potential of using modified pectin as an effective carrier for solubility and bioavailability enhancement of poorly water-soluble drugs.Solubility study data pure lwrcanidipine along with its physical mixture, and solid dispersion was shown in table 1 and figure 2.

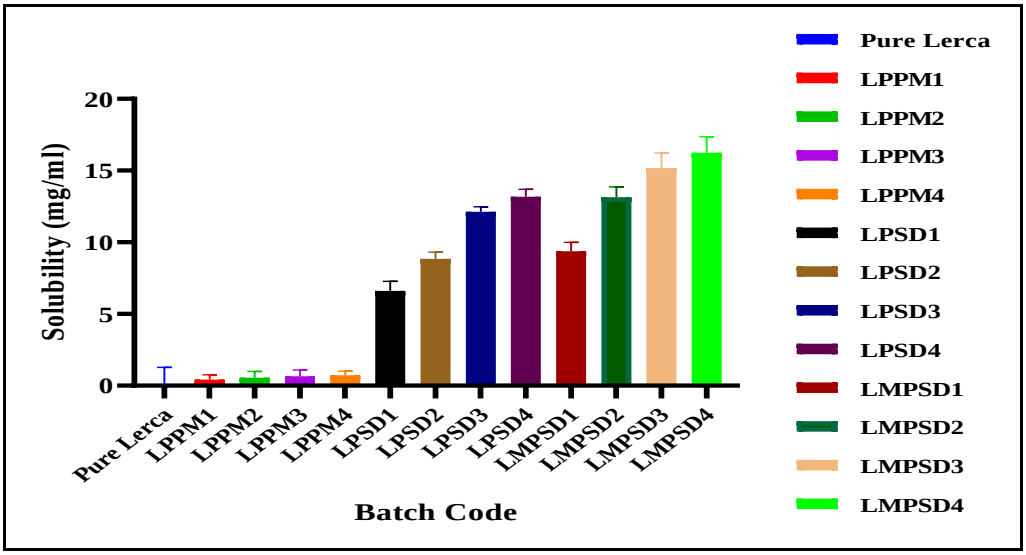

Figure 2: Solubility Profile of Pure Lercanidipine, Physical Mixture and Solid Dispersion

with Native and Modified Pectin in Distilled Water

Table 1: Solubility Study of Pure Lercanidipine, Physical Mixture and Solid Dispersion with Native and Modified Pectin in Distilled Water

Batch Code	Lerca:Pectin (w/w)	Solubility (mg/ml)
Pure Lerca	LERCA	0.0526 ±1.23
LPPM 1	LERCA:Pectin 1:1(PM)	0.432 ± 0.32
LPPM 2	LERCA: Pectin 1:2(PM)	0.566 ± 0.43
LPPM 3	LERCA: Pectin 1:3(PM)	0.654 ±0.44
LPPM 4	LERCA: Pectin 1:4(PM)	0.723 ±0.28
LPSD 1	LERCA: Pectin 1:1(SD)	6.61 ±0.67
LPSD 2	LERCA: Pectin 1:2(SD)	8.84 ±0.46
LPSD 3	LERCA: Pectin 1:3(SD)	12.13 ±0.34
LPSD 4	LERCA: Pectin 1:4(SD)	13.18 ±0.51
LMPSD 1	LERCA: Modified Pectin 1:1 (SD)	9.37 ±0.62
LMPSD 2	LERCA: Modified Pectin 1:2 (SD)	13.14 ±0.72
LMPSD 3	LERCA: Modified Pectin 1:3 (SD)	15.18 ±1.04
LMPSD 4	LERCA: Modified Pectin 1:4 (SD)	16.24 ±1.12

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR analysis has been carried out to study the interaction between lercanidipinewith modified pectin polymers. The pure lercanidipine showed characteristic peaks at 3423 cm^{-1}(O-H stretching), 3060 cm^{-1} (C-H stretching), 2369 cm^{-1}(C≡N or CO_2 stretching), 1691cm^{-1} (C=O stretching), 1675 cm^{-1}(C=C stretching), 1482 cm^{-1} (C-H bending) and 1347cm^{-1} (C-H bending),1222cm^{-1} (C-O stretching), 1091cm^{-1} (C-O or C-N stretching) and 702 cm^{-1}(C-H bending). (Fig.3)Typical principle peaks was detectable and showed minor shift in IR spectra in solid dispersion with modified pectin, confirmed no interaction between drug and modified pectin.

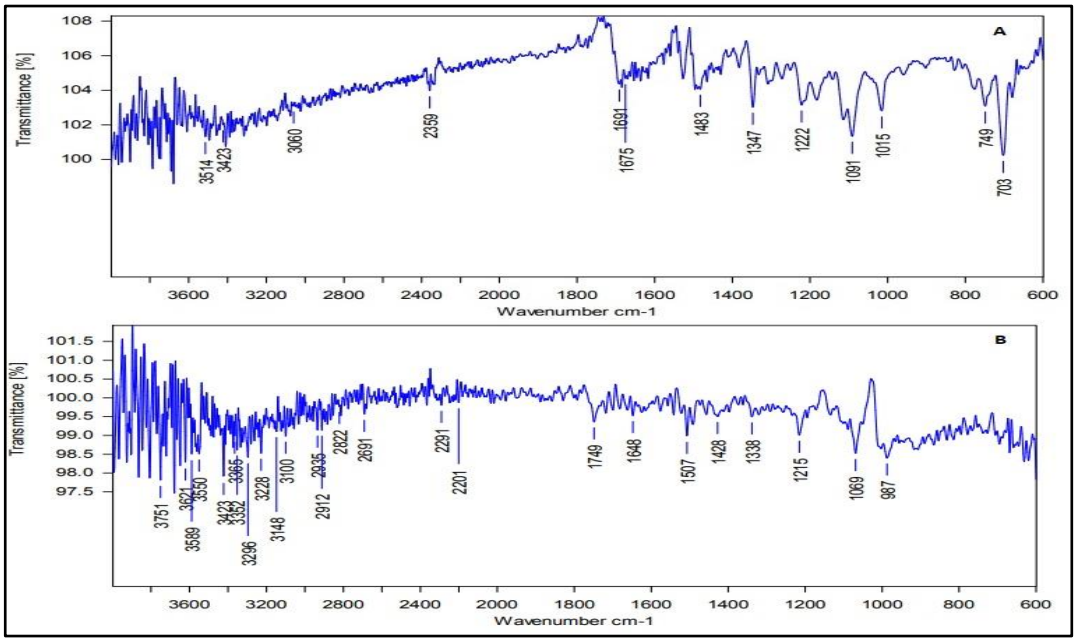

Figure 3: FTIR Spectra of pure Lercanidipine (A) and Solid Dispersion with Modified

Pectin(B)

Differential Scanning Calorimetry (DSC)

The DSC thermogram of pure lercanidipine showed a sharp single endothermic peak at 191.20°C, (fig. 4A) which corresponds to the melting temperature of lercanidipine, the sharpness of the peak indicating and confirmed the crystalline nature of the lercanidipine. Optimized solid dispersion formulation of drug with modified pectin (LMPSD3) drug: modified pectin(1:3%w/w), (fig. 4B)showed broader of endothermic peak of at 98.93°C corresponding to peak of pectin, while the peak of lercanidipine was completely disappeared in the SD formulation, indicating that the crystallinity of the drug was reduced and drug wascompletely converted to amorphous form.

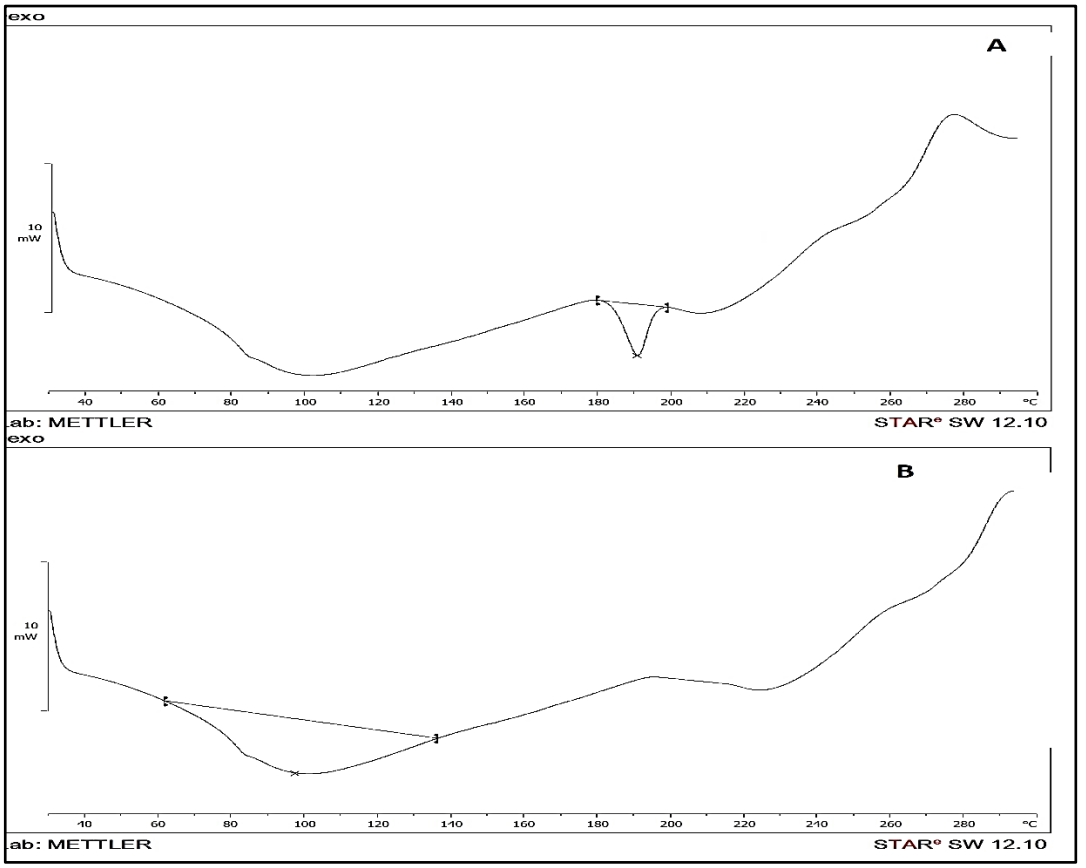

Figure 4: DCS thermogram of pure Lercanidipine (A) and optimized solid dispersion with modified pectin (B) (LMPSD3)

Powder X-Ray Diffraction

XRD spectra of pure lercanidipineand its solid dispersion with modified pectin was shown in figure of lercanidipine(figure 5 A and B). the presence of distinct numerous peaks in the XRD spectrum of lercanidipine (fig5A) indicated that lercanidipine was present in crystalline form. XRD spectra of optimized solid dispersion (LMPSD 3) (figure 5 B) showed specific peaks

corresponding to the modified pectin and diffraction peaks specific to lercanidipine was senn to be absent, indicating amorphous presence of drug in solid dispersion formulation.

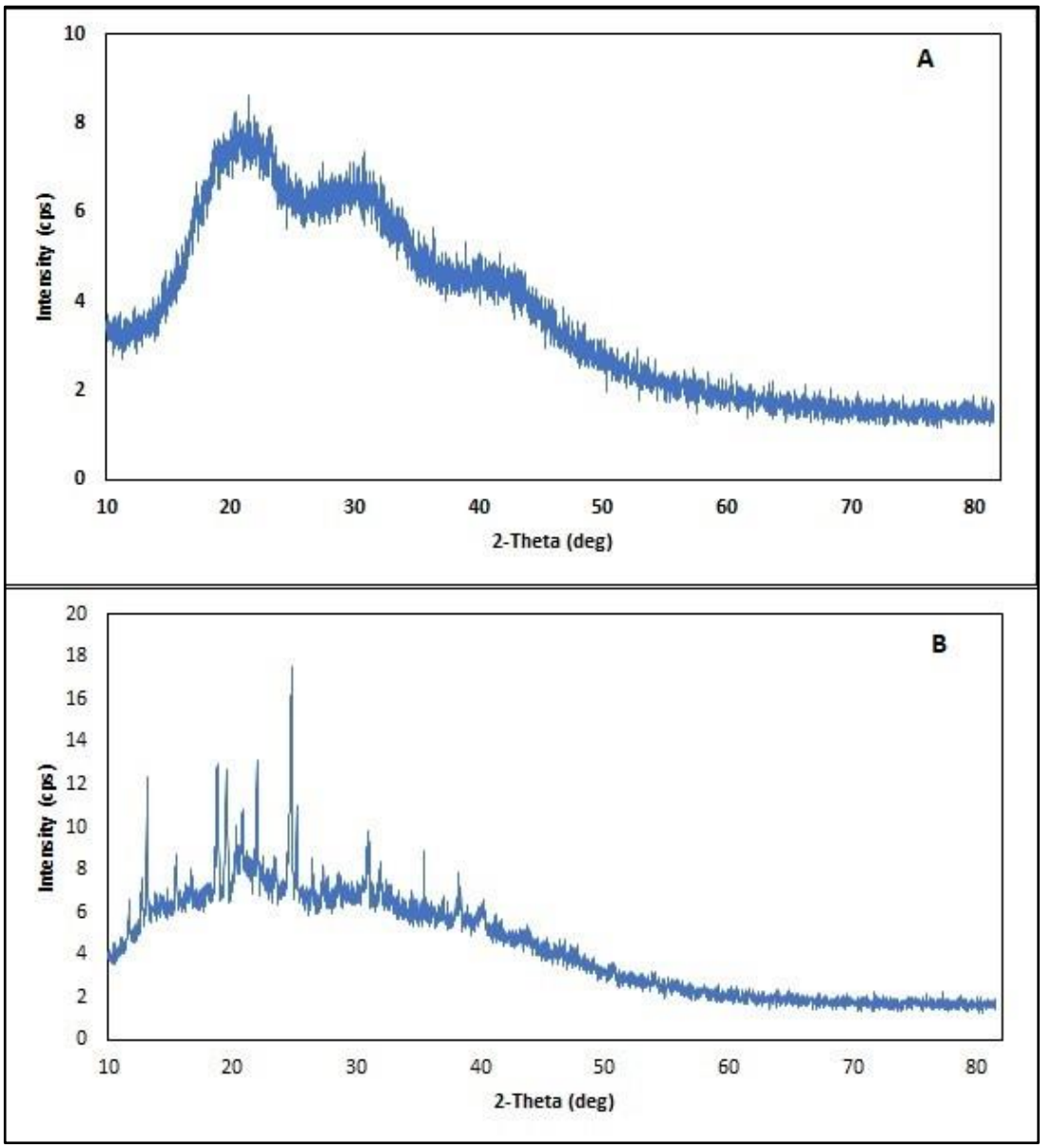

Figure 5: XRD spectra of Pure Lercanidipine (A) and Optimized Solid dispersion (B) (LMPSD3)

Surface Morphology Study (SEM)

The surface morphology study SEM was done to evaluate surface morphology of the pure drug lercanidipineand optimizedsolid dispersion formulation.SEM image of pure drug lercanidipineseen as irregular morphology having clustered and uneven rough surface

crystalline shaped structure. (fig.6A). SEM micrograph of the solid dispersion (fig.6B) appeared as smooth surface showed amorphous surface, indicated that drug crystallinity was reduced to much higher extend.

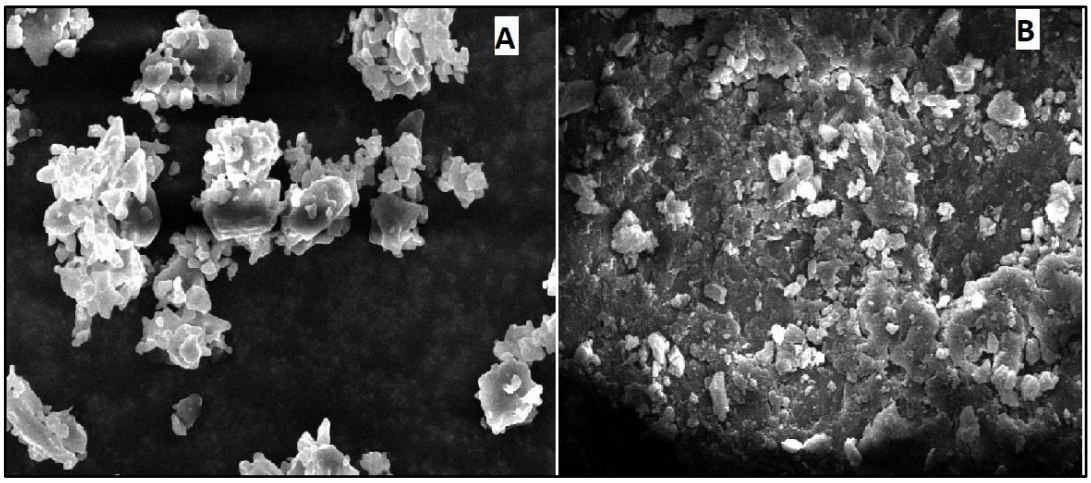

Figure 6: SEM image of Pure Lercanidipineand (A) and Optimized Solid Dispersion (LMPSD3)

In Vitro Dissolution Study

The dissolution profiles of pure lercanidipine, solid dispersions with native pectin (LPSD1 to LPSD4), and solid dispersions with modified pectin (LMPSD1 to LMPSD4) were evaluated over a 60-minute period. Pure form of lercanidipine showed a limited dissolution rate, reaching only 40.18% drug release at 60 minutes.The poor dissolution is attributed to the hydrophobicity and crystalline nature of the drug, which hinder its interaction with the aqueous medium.Solid dispersions prepared with native pectin (LPSD1 to LPSD4) demonstrated improved dissolution rates compared to pure lercanidipine.Drug release increased as the drug-to-pectin ratio increased (higher pectin content).At 60 minutes, dissolution ranged from 64.32% (LPSD1, 1:1) to 78.53% (LPSD4, 1:4).The enhancement is attributed to improved wettability, increased surface area, and partial amorphization of the drug.Solid dispersions markedly enhanced the dissolution rate compared to pure lercanidipine. This highlights the effectiveness of solid dispersion techniques in improving the bioavailability of hydrophobic drugs.

Solid Dispersions formulation with modified pectin (LMPSD1 to LMPSD4)resulted in significantly higher dissolution rates.LMPSD1 (1:1) achieved a dissolution of 81.24%, while LMPSD4 (1:3) reached near-complete drug release of 99.74% within 60 minutes (fig. 7). Modified pectin likely provided better hydrophilicity and stronger molecular interactions, enhancing drug stabilization and preventing recrystallization.Dissolution rates were consistently higher for solid dispersions prepared with modified pectin (LMPSD series) compared to those with native pectin (LPSD series).At 60 minutes, LMPSD3 (99.74%) outperformed compare with other formulations. This demonstrates the superior solubilizing properties of modified pectin.At the 10-minute mark, LMPSD3 exhibited the highest drug release (71.51%), followed by LMPSD4 (66.86%). This indicates that solid dispersions with

modified pectin not only improved the overall dissolution but also significantly accelerated the initial release, which is beneficial for achieving faster therapeutic effects.Modified pectin enhanced dissolution more effectively due to its better hydrophilicity and interaction with the drug, which likely prevented recrystallization and improved the stabilization of the amorphous drug.Increasing the drug-to-pectin ratio resulted in progressively higher dissolution rates for both native and modified pectin systems. The higher pectin content likely provided better dispersion, wettability, and stabilization of the amorphous drug form.The study demonstrated that solid dispersion is a highly effective technique for enhancing the dissolution rate of poorly soluble drugs like lercanidipine. Among the formulations tested, solid dispersions with modified pectin (LMPSD1 to LMPSD4) exhibited superior dissolution performance compared to those with native pectin (LPSD series), highlighting the potential of modified pectin as a carrier for improving the solubility and bioavailability of hydrophobic drugs.

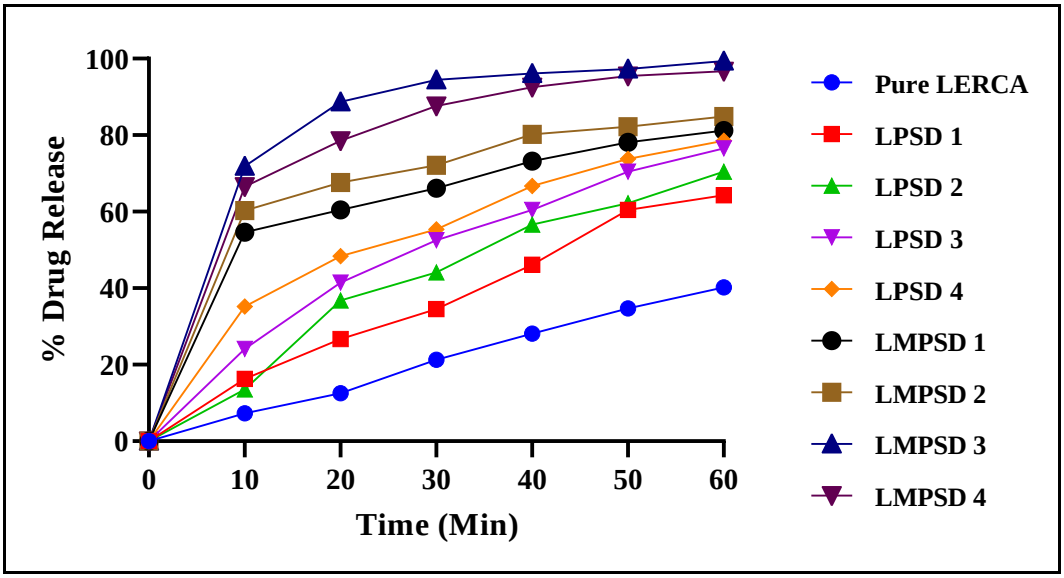

Figure 7: In Vitro Dissolution Profile of Pure Lercanidipine, PMs and SDs with Native and Modified Pectin

In Vivo Study:

The pharmacokinetic parameters of pure lercanidipine and its optimized solid dispersion formulation (LMPSD 3) were evaluated to assess the bioavailability enhancement achieved by the solid dispersion technique. Pure Lercanidipine showed $T_{max}$of 2 ± 0.00 hours, while optimized SD formulation (LMPSD 3) showed T_{max} of 1 ± 0.00 hours. The reduction in T_{max} for LMPSD 3 indicates faster absorption of lercanidipine from the optimized formulation. $C_{max}$for Pure Lercanidipine gives 488.14 ± 20.132 ng/mL and SD formulation (LMPSD 3) gives 1032.36 ± 21.641 ng/mL.The optimized formulation exhibited a 2.11-fold increase in C_{max}, demonstrating enhanced bioavailability. This improvement can be attributed to the increased solubility, faster dissolution, and potentially better absorption facilitated by the amorphous drug state in the solid dispersion.The AUC 0-t and AUC 0-inf. For Pure Lercanidipine was obtained as 2655.59 ± 136.27 ng/mL*h and 2872.77 ± 242.32 ng/mL*h respectively, while for those SD formulation it was obtained as 5214.33 ± 166.43 ng/mL*h

and 5472.87 ± 414.16 ng/mL*h respectively. The AUC 0-t for LMPSD 3 was nearly 1.96 times higher, whileAUC 0-inf. for LMPSD 3 was approximately 1.9-fold higher than pure lercanidipine, which further supports the enhanced bioavailability of the optimized formulation, ensuring better therapeutic efficacy. MRT for Pure Lercanidipine was found to be 5.39 ± 1.219 hours and for SD formulation LMPSD 3 it was found as 4.52 ± 1.243 hours. The reduced MRT for LMPSD 3 reflects faster drug clearance from the body, consistent with the increased absorption and shorter T_{max}. From the study it was observed that, the optimized solid dispersion formulation (LMPSD 3) significantly enhanced the pharmacokinetic performance of lercanidipinein solid dispersion compared to the pure drug. The faster absorption (reduced Tmax) and increased plasma concentration (higher Cmax and AUC values) indicate that LMPSD 3 overcomes the solubility and dissolution limitations of pure lercanidipine. These improvements are a direct result of the amorphous state of the drug and enhanced wettability achieved through the solid dispersion technique.Pharmacokinetic parameters and plasma concentration time profile of Pure Lercanidipine and Optimized Lercanidipine SD Formulation (LMPSD 3) was shown in table 2 and figure 8.

Table 2: Pharmacokinetic parameters of Pure Lercanidipineand Optimized Lercanidipine SD Formulation (LMPSD 3)

Pharmacokinetic Parameter	Pure Lercanidipine	Optimized LERCA SD (LMPSD 3)
T_{max} (h)	2 ± 0.00	1 ± 0.00
C_{max} (ng/ml)	488.14 ± 20.132	1032.36 ± 21.641
$t_{1/2}$ (h)	2.76 ± 0.548	2.41 ± 0.652
AUC $_{0\text{-}t}$ (ng/ml*h)	2655.59 ± 136.27	5214.33 ± 166.43
AUC $_{0\text{-}inf.}$ (ng/ml*h)	2872.77 ± 242.32	5472.87 ± 414.16
MRT (hr)	5.39 ± 1.219	4.52 ± 1.243

Mean ± SD (n=6)

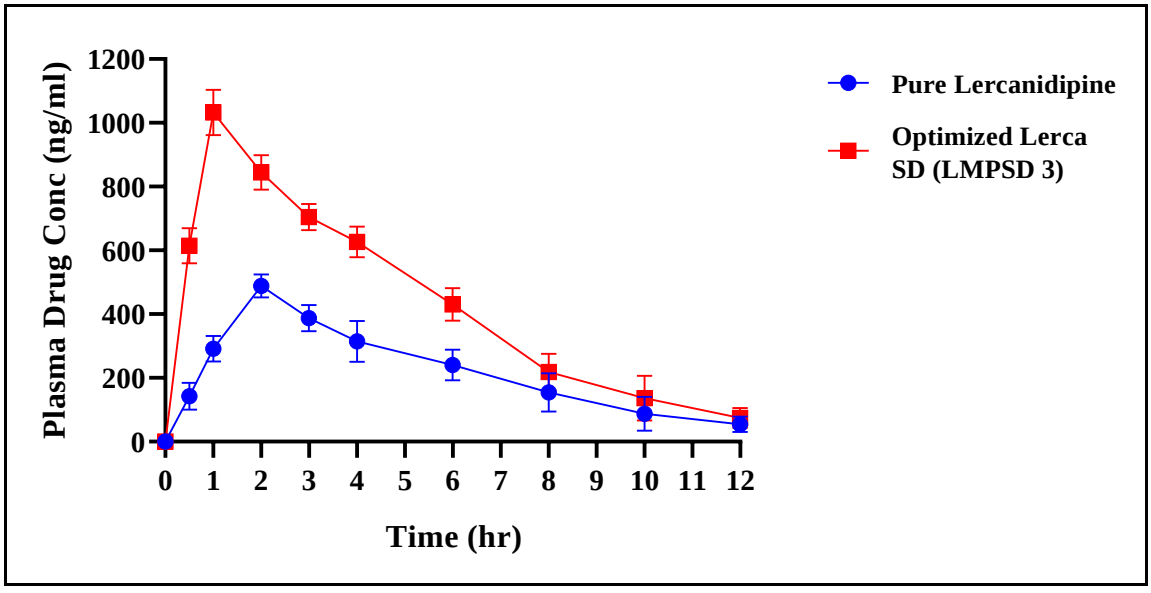

Figure 8: Plasma concentration profile of Pure Lercanidipine and Optimized Lercanidipine SD Formulation (LMPSD 3)

4. Conclusion:

The present researchdemonstrates the successful formulation of solid dispersion of drug using modified pectin.The study successfully demonstrated the potential of solid dispersion techniques, particularly using modified pectin, to enhance the solubility and bioavailability of the poorly water-soluble drug lercanidipine. The solubility assessments revealed a significant improvement in drug solubility when lercanidipine was formulated with both native and modified pectin, with the latter showing superior results. The optimized solid dispersion (LMPSD 3) achieved the highest solubility (16.24 ± 1.12 mg/mL) and exhibited marked improvements in dissolution rates, reaching near-complete drug release (99.74%) within 60 minutes. FTIR, DSC, and XRD confirmed the successful conversion of lercanidipine from a crystalline form to an amorphous state Additionally, pharmacokinetic evaluations indicated a notable enhancement in absorption, as evidenced by a reduced T_max and increased C_max values for the optimized formulation compared to pure lercanidipine. The findings underscore the effectiveness of solid dispersion techniques in overcoming solubility limitations of hydrophobic drugs, thereby offering a promising approach for improving therapeutic efficacy and patient outcomes. This research highlights the importance of selecting appropriate natural carriers, such as modified pectin, to optimize drug delivery systems for poorly soluble compounds.

Acknowledgements: Authors are thankful to the Sun Pharma Ltd., halolVadodara , India for proving gift sample of drug Lercanidipine for this research work.

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