ORIGINAL ARTICLE

Design and Optimizing Lansoprazole Solubility through Nanocrystallization: A Dual Polymer Approach

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Abstract

Aims: The objective of the present study is to increase the aqueous solubility and acid stability of lansoprazole, one of the most common proton pump inhibitors because of poor bioavailability due to poor aqueous solubility and acid sensitivity by formulation as nanocrystals through the antisolvent precipitation method. **Materials and Methods:** The preparation of lansoprazole nanocrystals was performed by means of an antisolvent precipitation method. The drug was dissolved in ethanol, followed by its immediate injection into an aqueous phase with a stabilizer under high-speed homogenization. Two hydrophilic polymers including polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA) were evaluated as stabilizers at different drug-to-polymer ratios (1:1, 1:2, and 1:3). The compositions of the produced nanocrystals were analyzed in terms of particle sizes, dissolving properties, as well as the physicochemical properties utilizing various tests like Fourier-transform infrared spectroscopy (FTIR) and also using the process of the differential scanning calorimeter. **Results:** Of the formulations, the nanocrystals at the ratio 1:3 drug and polymer in the PVP format performed the better. It showed superior physical stability, mastery of agglomeration of particles, and fast drug release within 1 h. FTIR analysis was used to indicate that there were no chemical interactions between the drug and the polymer. Differential scanning calorimetry analysis showed evidence of partial amorphization in favor of successful nanocrystal formation. The formulations using PVP have performed better in uniformity of particle size and the ability to dissolve more easily as compared to PVA-based ones. **Conclusion:** The research findings conclude that PVP is a better stabilizer than PVA in the preparation of lansoprazole nanocrystals by a process of antisolvent precipitation. Having the best ratio of drug to polymer equal to 1:3 with PVP gives the best outcomes in accordance with stability and enhancement of dissolution that may enhance the oral bioavailability of the drug.

Key words: Antisolvent precipitation, lansoprazole, nanocrystals, polyvinyl alcohol, polyvinylpyrrolidone

INTRODUCTION

Oral drug administration can be considered the most popular and frequently chosen type of drug delivery due to the convenience of its practical use, low cost, and acceptability by the patient. In spite of these benefits, poor aqueous solubility of a large number of pharmacologically active compounds is one of the most significant drawbacks of oral drug delivery since it results in inefficient absorption and low bioavailability.[1] It has been reported that almost 40% of the drugs proceeding through discovery pipelines have low solubility in water, which is a therapeutic challenge.[2]

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Lansoprazole is a proton pump inhibitor (PPI) similar to omeprazole, a derivative of benzimidazole, often used in the treatment of conditions such as gastroesophageal reflux disease (GERD), duodenal ulcer, and Zollinger-Ellison syndrome.[3] It works by specifically suppressing the gastric H+/K+ATPase enzyme and inhibiting gastric acid secretion in the stomach.[4] The great permeability characteristic of lansoprazole, which categorizes it as a BCS Class II drug, limits its solubility in water and acidic stability, limiting its oral availability and clinical consistency.[5,6] Therefore, measures to enhance its aqueous solubility and acidic stability remain key to clinical success.

Some formulation techniques have been established to improve and augment the disorders of poorly water-soluble medications such as solid dispersions, induction with cyclodextrins, lipid-based vehicles, and nanosized drug delivery systems.[7,8] Nanocrystal technology is of prominent consideration because it may boost dissolution velocity, saturation solubility, and bioavailability of the inefficiently solvable medications.[9] Nanocrystals constitute pure drug particles that are reduced to the nanometer level through a stabilizing medium like a hydrophilic polymer or surfactant to ensure stability and prevent any aggregation.[10,11]

The antisolvent precipitation method is a bottom-up process that is based on the simplicity, low costs, and scalability of this method as a method of producing drug nanocrystals.[12] In this method, the drug is dissolved in a solvent that is microsed with water and is rapidly added to an aqueous phase (antisolvent) containing a stabilizer under high-shear mixing. This causes high rates of supersaturation and nucleation of the drug into nanocrystals.[13] The success of this process is immensely related to the stabilizer type and its concentration used which prevents the agglomeration of particles and the final particle size as well.[14]

Most researched stabilizers include water-soluble polymers such as polyvinylpyrrolidone (PVP) and polyvinyl alcohol (PVA) which are mostly used because of their biocompatibility, nontoxic nature, and their ability to stabilize drug particles in protective layers. The main advantage of PVP is steric stabilization which is the fixation by the adsorption of PVP on the surface of the particle and the formation of the repulsive barrier to aggregations. It has been effectively employed in the efforts to construct nanocrystals of drugs such as carbamazepine, itraconazole, and fenofibrate. Conversely, PVA offers steric and electrostatic stabilization and it is biodegradable and non-toxic in nature, providing it with the appropriate profile to be employed in the pharmaceutical realm. Its utility has been proven to enable the formulation of nanocrystals of compounds such as naproxen and curcumin.

Researchers have also found that the ratio of drug to polymer is a decisive factor, which can influence physical properties, as well as the performance of nanocrystal formulations. An appropriate ratio may guarantee full coverage of the surface of particles, enhance stability, and promote better dissolution, but too much polymer can make the process too viscous and difficult.

In the work under consideration, nanocrystals of lansoprazole were obtained through the antisolvent precipitation technique with the help of PVP and PVA as separate stabilizers. The drug-to-polymer ratio (1:1, 1:2, and 1:3) was used to formulate formulations, determining the influence of polymer type and concentration on particle size, stability, drug release, and solid-state features. The reason that ethanol was selected as the organic solvent is that it is an outstanding solubilizer of lansoprazole and is easy when it comes to remove in the course of processing.[15]

The produced nanocrystals were characterized in terms of the physicochemical and functional properties by means of particle size analysis, *in vitro* dissolution testing, Fourier-transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC). Of all the tested ratios, 1:3 was the most desirable in terms of such parameters as the decreased particle size, enhanced dissolution rate, and better stability. The findings of FTIR and DSC indicated that there was no chemical interaction between the drug and polymeric substance and directed toward some conversion to an amorphous state, which helped to increase solubility.

This introduction brings into the limelight the importance of enhancing oral drug delivery to highly insoluble compounds with special emphasis being lansoprazole, a lowly soluble PPI. Considering that almost 40% of drugs encounter the same kind of solubility problems, this study is expected to manage these problems through nanocrystal technology. This study will help in early investigations by increasing solubility and stability by use of the antisolvent method to precipitate the drug and enable more efficient drug formulations with enhanced oral bioavailability and clinical consistency of conventional drugs such as lansoprazole.

MATERIALS AND METHODS

Lansoprazole was purchased in Vasudha Pharma Private Limited, Visakhapatnam, whereas PVP and PVA were acquired in Natco Pharma Limited, Hyderabad.

Saturated solubility studies of lansoprazole

Saturated solubility of lansoprazole in different media was performed to ascertain the solubility profile of lansoprazole in different physiological pH. This experiment was completed with the assistance of distilled water, 0.1 N hydrochloric acid, phosphate buffer, pH 6.8, and phosphate buffer, pH 7.4. Here, add an excess amount of lansoprazole (approximately 50 mg) accurately hence in 5 different glass vials containing

10 mL of standard solvent medium. The vials were securely capped and incubated on a revolving shaker at a consistent temperature of 25 ± 2°C over a length of 24 h to enable the achievement of the equilibrium solubility. Within 15 min, all the vials that had non-dissolved particles of the drug were centrifuged at a rate of 5000 rpm. The supernatant was then collected very carefully and centrifuged through using 0.45 membrane filter. The filtrates were adequately diluted, and lansoprazole concentration was calculated by a ultraviolet (UV)-visible approach by assembly response spectrophotometer and against the respective media as a blank using a wavelength of 285 nm.[16] All the measurements were performed in triplicate, and mean solubility was determined and reported as mean + standard deviation (SD). The results are shown in Table 1.

Method of preparation of lansoprazole nanocrystals

The antisolvent precipitation method was used to prepare lansoprazole nanocrystals in the bottom-up processing approach, which involved the reduction of particle size and improvement of dissolution rate. In our procedure, lansoprazole was dissolved in ethanol to obtain the organic phase first. The aqueous medium pre-mixed with either PVP or PVA as stabilizers and distilled water was then rapidly injected with this drug solution. The ratios of drug to polymer used were 1:1, 1:2, and 1:3. A high-shear homogenizer was used to homogenize the mixture at 10,000 rpm over 15 min during the addition of the organic phase to the aqueous phase.[17] This made the nucleation and formation of nanocrystals rapid under supersaturation on mixing. The resultant nanosuspensions were subsequently sonicated by a probe sonicator (5 min) to minimize particle size and avert aggregation. These nanosuspensions were also incubated at room temperature for 30 min before stabilization.[18] The composition is shown in Table 2.

Table 1: Solubility of lansoprazole in various media at 25±2°C

S. No.	Solvent medium	Solubility (µg/mL)
1	Distilled water	7.9±0.4
2	0.1 N Hydrochloric acid (pH~1.2)	2.1±0.2
3	Phosphate buffer pH 6.8	38.2±1.1
4	Phosphate buffer pH 7.4	61.7±1.5

Evaluation of lansoprazole nanocrystals

The physical properties of the lansoprazole nanocrystals such as angle of repose, Carr's index, particle size, and the drug content were determined according to the regular pharmacopeia methods. The measurement of these parameters was done to identify the flow behavior, compressibility, and consistency of the formulation. Table 3 gives the results that were obtained.

Estimation of lansoprazole nanocrystals

Weigh 10 mg of the active drug in an amount of lansoprazole nanocrystals. Pour it over into a beaker and add some methanol to dissolve the sample in a small amount. The mixture should

Table 2: Formulation composition of lansoprazole nanocrystals

Code	Drug (mg)	Polymer (mg)	Polymer amount (mg)	Drug: Polymer ratio	Ethanol volume (mL)	Aqueous phase volume (mL)
F1	100	PVA	100	1:1	5	50
F2	100	PVA	200	1:2	5	50
F3	100	PVA	300	1:3	5	50
F4	100	PVP	100	1:1	5	50
F5	100	PVP	200	1:2	5	50
F6	100	PVP	300	1:3	5	50

PVA: Polyvinyl alcohol, PVP: Polyvinylpyrrolidone

Table 3: Physical parameters of lansoprazole nanocrystals

Code	Drug: Polymer ratio	Angle of Repose (°)	Carr's index (%)	Average particle size (nm)	Drug content (%)
F1	1:1 (PVA)	29.6±0.5	17.4±0.8	312±6	92.3±1.2
F2	1:2 (PVA)	28.3±0.4	15.8±0.9	275±5	94.7±1.1
F3	1:3 (PVA)	27.1±0.3	13.9±1.0	248±4	96.2±1.0
F4	1:1(PVP)	28.9±0.4	16.5±0.7	298±5	93.6±1.3
F5	1:2 (PVP)	27.5±0.5	14.7±0.6	261±4	95.8±1.0
F6	1:3 (PVP)	26.2±0.4	12.5±0.9	225±3	98.1±0.8

PVA: Polyvinyl alcohol, PVP: Polyvinylpyrrolidone

be sonicated between 5 and 10 min to allow full dispersion. Pour out the filtrate into a 100 mL volumetric flask. Pipette a convenient aliquot of this solution into a clean tube and then dilute with pH 7.4 phosphate buffer, as needed. Record an absorbance at 285 nm on a UV-visible spectrophotometer. By comparing to the already constructed standard calibration curve, the drug content is calculated.

In vitro drug release of lansoprazole nanocrystals

In vitro release of the lansoprazole as a nanocrystal was assessed in a United States Pharmacopeia dissolution apparatus Type II (paddle method). A weighed amount of nanocrystals amounting to 10 mg in the form of lansoprazole was added into the dialysis bag or directly added to the dissolution medium, depending on the nature of the formulation. A phosphate buffer pH 7.4 (900 L) was employed in the study and stirred at 100 rpm at a temperature of 37 ± 0.5°C. Samples (5 mL) of the dissolution vessel were taken at preset time points (e.g., 5, 10, 15, 30, 45, and 60 min) and immediately replaced with fresh dissolution medium to ensure sink conditions. The samples collected were filtered, and the absorbance was measured at 285 nm by UV-visible spectrophotometer. A standard calibration curve was constructed to determine the concentration of the drug discharged at every time point, and the cumulative percent drug release was taken. The *in vitro* data and release profiles are shown in Tables 4,5 and Figure 1.

Characterization of lansoprazole nanocrystals

The FTIR and DSC methods were used to characterize pure lansoprazole and the F6 optimized formulation. Any potential chemical interaction between the drug and excipients was determined via FTIR. DSC experiments were conducted to determine the thermal conductivity of the samples and the phase state. These analyses authenticated the compatibility and effective development of the nanocrystals.

FTIR

A Bruker FTIR spectrophotometer was used to perform FTIR analysis of the formulated mixture and pure lansoprazole. 2 mg of the substance was weighed and combined with 200 mg of potassium bromide and pressed into discs. The spectra were measured at 400–4000 cm^{-1} with 1 cm^{-1} resolution. The FTIR spectra interpretation tables are shown in Figures 2 and 3, Table 6.

DSC

The DSC analysis of pure lansoprazole and optimized formulation (F6) was carried out using a SHIMADZU DSC-60 system. About 10 mg of each sample was plated inside a covered pan made of aluminum. The temperatures started at 25°C and increased to 250°C at the rate of 20°C/min.The resultant DSC table and thermograms are shown in Table 7 and Figures 4 and 5.

Table 4: *In vitro* dissolution data of lansoprazole nanocrystals

Time (min)	F1	F2	F3	F4	F5	F6
5	18.5	22.3	27.9	21.6	26.8	34.5
10	28.1	34.6	42.2	33.5	40.3	50.7
15	36.7	45.2	54.8	45.9	52.7	63.1
30	51.9	60.8	70.5	63.4	70.2	82.8
45	63.6	72.3	81.7	74.8	82.4	91.3
60	72.1	80.4	88.9	83.5	90.8	97.5

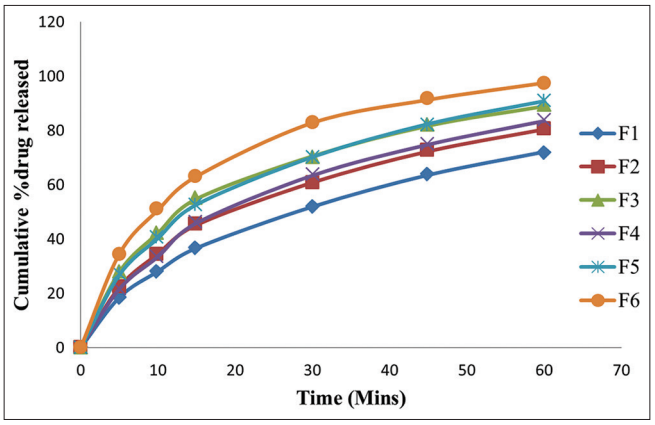

Figure 1: Drug release profiles of lansoprazole nanocrystals

RESULTS AND DISCUSSION

Evaluation of lansoprazole solubility in different physiological media

The solubility profile of lansoprazole in 4 solvent media (similar to physiological conditions) was studied to determine its dissolution profile. The solubility study showed that lansoprazole had the best solubility in the phosphate buffer pH 7.4 (61.7 ± 1.5 µg/mL), buffer pH 6.8 (38.2 ± 1.1 µg/mL), distilled water (7.9 ± 0.4 µg/mL), and lowest solubility in 0.1 N HCl (2.1 ± 0.2 µg/mL). These data show that lansoprazole is more soluble at higher pHs; thus, it is more soluble in slightly alkaline solutions. Low solubility in acidic conditions implies that the drug would have a poor gut bioavailability or be prone to degradation, indicating a rationale for pH-sensitive formulations. Means and SD of triplicate experiments were used to record all values and ensure validity and repeatability.

Formulation of lansoprazole nanocrystals through antisolvent precipitation: Optimization using PVP and PVA stabilizers

The antisolvent precipitation technique is a basically accepted bottom-up technology in size reduction;

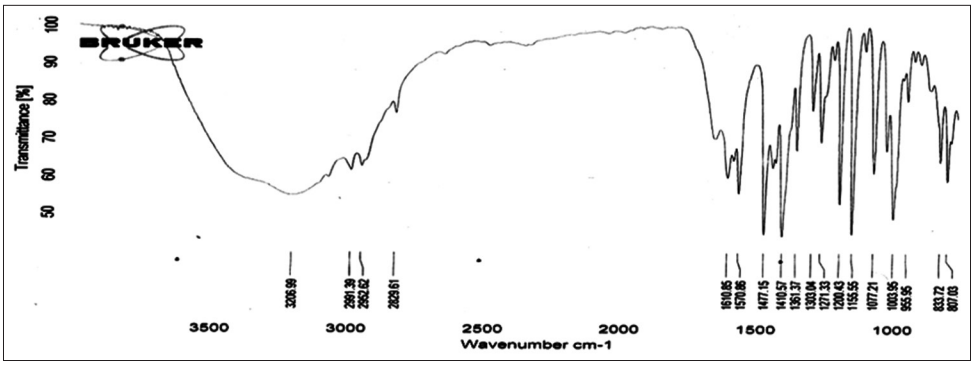

Figure 2: Fourier-transform infrared spectroscopy spectra of the lansoprazole pure drug

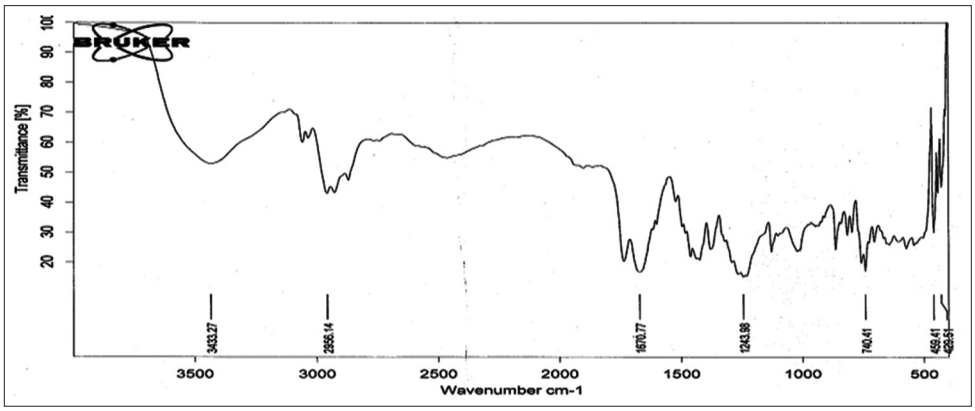

Figure 3: Fourier-transform infrared spectroscopy spectrum of optimized formulation (F6)

Table 5: *In vitro* dissolution parameters of lansoprazole nanocrystals

Formulation	T_{50} (min)	T_{90} (min)	K (min^{-1})	R^2
F1	27.91	92.73	0.0248	0.9277
F2	20.83	69.21	0.0333	0.9235
F3	14.77	49.07	0.0469	0.9356
F4	19.71	49.07	0.0352	0.9614
F5	15.17	50.41	0.0457	0.9634
F6	10.25	34.05	0.0676	0.9774

Table 6: FTIR interpretation of lansoprazole

Functional group	Wave number cm^{-1}	
	Lansoprazole	Optimized formulation F6
N-H Stretching	3222 cm^{-1}	3301 cm^{-1}
C=C Stretching	2625 cm^{-1}	2658 cm^{-1}
C-N Stretching	2248 cm^{-1}	2114 cm^{-1}

FTIR: Fourier-transform infrared spectroscopy

lansoprazole nanocrystals were therefore achieved. The organic solvent used in the drug was ethanol and was added to the aqueous solution of stabilizer (PVP or PVA) under high-shear homogenization. The effect of differences in the drug-to-polymer ratio (1:1, 1:2, and 1:3) was tested in six formulations (F1-F6). The mixing of the solvents resulted

Table 7: DSC thermogram of lansoprazole

Lansoprazole	Optimized formulation F6
189.41°C and 184.01°C	170.86°C
Sharp	Broad
Endothermic peak	Endothermic peak

DSC: Differential scanning calorimetry

in immediate supersaturation that drove the formation of nanocrystals and also the probe sonication also facilitated the production of smaller sizes and prevented aggregation. Table 2 gives the compositions of all formulations. Preliminary findings showed that the stabilization of nanocrystals could be enhanced by an increase in polymer concentration, whereby formulations involving PVP (F4-F6) were particularly good in subsequent studies, with a lower stabilization agent concentration, F6, proving to be the most promising.

Physicochemical characterization of lansoprazole nanocrystals formulated with PVA and PVP

The lansoprazole nanocrystals prepared were characterized in the major physical parameters such as angle of repose, Carr's index, mean particle size, drug content to identify the flowability, compressibility, and formulation efficiency. Table 3 shows the data that the concentration of polymer,

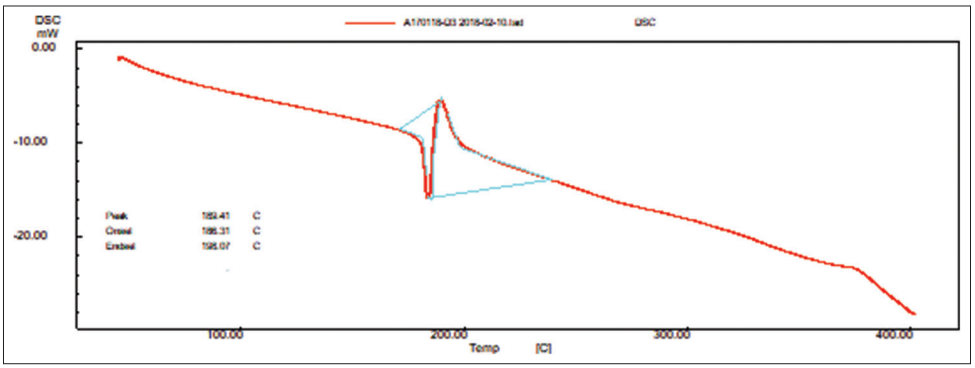

Figure 4: Differential scanning calorimeter thermogram of the lansoprazole pure drug

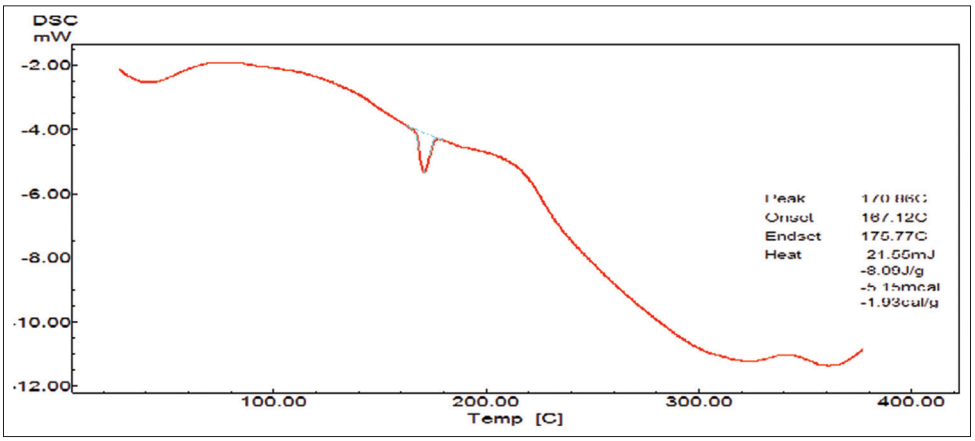

Figure 5: Differential scanning calorimeter thermogram of optimized formulation (F6)

either PVA or PVP, increased, resulting in improved flow of powder and subsequently making the particle size smaller. F6 (drug-to-PVP ratio of 1:3) formulation had the least particle size (2252 ± 3 nm), good flowability (angle of repose 26.2), and had the highest drug content (98.12.08). Another trend of a lower value of Carr's index as the concentration of polymer increases further indicates an increase in compressibility. Based on these results, it can be seen that the type of polymer has a huge effect on the physical properties of nanocrystals and can provide better results whilst some are not able to bind the nanocrystals due to their concentration, and thus, the systems based on PVP are more suited for stabilizing nanocrystals.

In vitro drug release profile of lansoprazole nanocrystals prepared using PVA and PVP

The dissolution behavior of different lansoprazole nanocrystal formulations (F1 to F6) was characterized at a time range of 60 min in comparison of the effect of type and quantity of polymer on dissolution rate. The release data clearly indicated a pattern because an increase in the concentration of the polymer led to increased release of the drug. Formulation F6 with a drug-to-PVP ratio of 1:3 released the highest (97.5%) after 60 min, and hence, it has the best dissolution characteristics, probably because of the small particle size and improved stabilization. On the contrary, F1 (1:1 with PVA) had the least release (72.1%), implying that the type of polymer and concentration both affect the efficiency of release. The enhanced release in the presence of PVP-based formulations can be explained by enhanced solubilization and decreased crystallinity. In general, a higher ratio of PVP showed that it was more effective compared to PVA in increasing the solubility of lansoprazole nanocrystals.

Kinetic evaluation of lansoprazole nanocrystals: t_{50}, t_{90}, release rate constant (k), and correlation coefficient (R^2)

The release kinetics of different lansoprazole nanocrystal formulations (F1-F6) were evaluated by determining the time taken to release 50% (t_{50}) and 90% (t_{90}) of the drugs and rate constant (k), and the correlation coefficient (R 2). In the batches tested, formulation F6 showed the fastest release and had the best t_{50} (10.25 min) and t_{90} (34.05 min) as well as the highest rate constant (0.0676 min^{-1}) and very good linearity ($R^2 = 0.9774$). It means that the release profile is quite effective, which is probably connected to the smaller particle size and enhanced stabilization of PVP. On the other hand, F1 had the slowest-releasing behavior, with an increased t_{50} (27.91 min) and a reduced K-value (0.0248 min^{-1}), which means that the dissolution rate was lower. The total data indicate that enhancement of polymer concentration, especially PVP, will increase drug release kinetics, and therefore, the F6 will be

the highly optimized formulation when compared to all and it has a consistent drug release with the rapidity in drug release.

FTIR spectral evaluation of lansoprazole and optimized nanocrystal formulation

The FTIR spectroscopy was used to analyze potential drug interactions between the lansoprazole and the excipient in the recommended formulation of nanocrystal (F6). The pure drug and formulation were recorded as spectra with the KBr disc method and the spectra were scanned in the region of 400–4000 cm^{-1}. The FTIR spectrum of the pure lansoprazole had characteristic peaks which were indicative of various functional groups including N-H stretch (3222 cm^{-1}), C=C stretch (2625 cm^{-1}), and C-N stretch (2248 cm^{-1}). In the optimized formulation (F6), these were found at slightly different positions, 3301 cm^{-1}, 2658 cm^{-1}, 2114 cm^{-1}, respectively. These are due to physical interactions presumably caused by hydrogen bonding or polymer entrapment but not due to chemical modification. The survival of most of the vital functional group peaks in the formulation indicates that the molecular structure of the drug has not altered, which proves the excellent compatibility of the drug and the stabilizing agents.

Thermal behavior assessment of lansoprazole and nanocrystal formulation through DSC

DSC analysis has been done to estimate the thermal behavior and crystalline nature of lansoprazole and optimized formulation (F6). The thermograms were taken by heating about 10 mg of each sample into 25, 250°C at 20°C/min in a SHIMADZU DSC-60 apparatus. The DSC thermogram of the pure lansoprazole presented a sharp endothermic peak at 189.4°C and 184.0°C, which represents the melting point of the drug in crystalline form, hence describing its very high crystalline nature. On the contrary, the optimal nanocrystal composition (F6) exhibited a wide endothermic peak detected at 170.8°C and it was associated with the lower crystallinity. The broad distribution and shift of the endothermic peak of the formulation could be explained because of the partial amorphization or smaller size of crystal because of nanonization. This change indicated that the formation of nanocrystals had occurred successfully which is likely to increase the dissolution of drugs and bioavailability.

CONCLUSION

This study proved successful in proving the propensity of nanocrystal technology in modifying the solubility and speed of dissolution of lansoprazole, a poorly soluble drug. Nanosized particles were effectively prepared through the process of antisolvent precipitation in the presence of these hydrophilic stabilizers, PVP and PVA. The formulations at the drug-to-polymer ratio of 1:3 with PVP as the most effective stabilizer yielded the best result with excellent reduction in particle size, stability, and highly increased drug release. Confirmation that chemical interactions were not present and the degree of amorphous transformation, to some extent, was achieved with FTIR and DSC analysis, adding to the improved solubility. High dispersibility of PVP-based nanocrystals owes to the effective steric hindrance which caused a decrease in particle association and enhanced dispersion. In general, the findings point out that nanocrystallization of the lansoprazole with PVP as stabilizer is a potential method to overcome the issue of solubility and bioavailability of lansoprazole, and this will provide a useful option in developing oral dosage form in future and also highlights the prospects of nanocrystal technology in improving the solubility and dissolution profile of lansoprazole and thus offers hope upon seeking a way to solve bioavailability problems. Such formulations can be further optimized to make them applicable in other more applications when dealing with oral drug delivery of other poorly soluble compounds in future research.

REFERENCES

1. Lipinski CA. Drug-like properties and the causes of poor solubility and poor permeability. J Pharmacol Toxicol Methods 2000;44:235-49.
2. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: Importance and enhancement techniques. ISRN Pharm 2012;2012:195727.
3. Freston JW. Review article: The clinical pharmacology and mechanism of action of lansoprazole. Aliment Pharmacol Ther 1994;8 Suppl 1:9-15.
4. Hatlebakk JG, Berstad A. Pharmacokinetic and pharmacodynamic properties of lansoprazole. Clin Pharmacokinet 1996;31:410-24.
5. Patel RP, Patel MM. Studies on dissolution enhancement of lansoprazole using various solid dispersions. Indian J Pharm Sci 2007;69:248-51.
6. Bhise SB, Rajkumar M. Formulation and evaluation of enteric-coated lansoprazole tablets. Indian Drugs 2006;43:117-21.
7. Craig DQ. The mechanisms of drug release from solid dispersions in water-soluble polymers. Int J Pharm 2002;231:131-44.
8. Douroumis D, Fahr A. Nanoparticulate systems for delivering poorly soluble drugs. Curr Drug Deliv 2006;3:267-85.
9. Muller RH, Keck CM. Challenges and solutions for the delivery of biotech drugs–a review of drug nanocrystal technology and lipid nanoparticles. J Biotechnol 2004;113:151-70.
10. Kesisoglou F, Panmai S, Wu Y. Nanosizing-oral formulation development and biopharmaceutical evaluation. Adv Drug Deliv Rev 2007;59:631-44.
11. Junghanns JU, Muller RH. Nanocrystal technology, drug delivery and clinical applications. Int J Nanomedicine 2008;3:295-309.

12. Merisko-Liversidge E, Liversidge GG. Nanosizing for oral and parenteral drug delivery: A perspective on formulating poorly water-soluble compounds using wet media milling technology. Adv Drug Deliv Rev 2011;63:427-40.
13. Kumar S, Sinha S, Singh A. Antisolvent precipitation for nanocrystal preparation: A review. Int J Pharm Sci Res 2018;9:2220-30.
14. Shah B, Khunt D, Misra M. Influence of stabilizers on particle size, *in vitro* dissolution and stability of albendazole nanocrystals prepared by antisolvent precipitation. Asian J Pharm Sci 2016;11:385-95.
15. Tran P, Lee BJ. Enhancing solubility and oral bioavailability of poorly water-soluble drugs using nanocrystals technology. Pharmaceutics 2018;10:118.
16. Paradkar AR, Pawar AP, Chordiya JK, Patil VB, Ketkar AR. Dissolution rate enhancement of fenofibrate using liquisolid tablet technique. Asian J Pharm 2007;1:60-4.
17. Duret C, Wauthoz N, Sebti T, Vanderbist F, Amighi K. Solid lipid microparticles as a sustained release system for pulmonary drug delivery. Asian J Pharm 2012;6:238-44.
18. Jain S, Jain P, Umamaheshwari RB, Jain NK. Development and characterization of mucoadhesive microspheres bearing salbutamol for nasal delivery. Asian J Pharm 2007;1:42-8.

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