**Original Research Article**

**Design and Evaluation of Soluplus-Based pH-Modulated Solid Dispersion as an Immediate Release Tablet of Lornoxicam**

**ABSTRACT**

Lornoxicam, a potent nonsteroidal anti-inflammatory drug (NSAID), suffers from poor aqueous solubility, leading to limited dissolution and variable bioavailability. This study aimed to enhance its solubility and oral performance by developing pH-modulated solid dispersions with Soluplus® as a carrier and sodium bicarbonate as a pH modifier. Solid dispersions were prepared via solvent evaporation and optimized using a Central Composite Design approach. The optimized batch (F7) was characterized through FTIR, DSC, PXRD, and SEM to confirm drug–excipient compatibility, amorphization, and morphological changes. Three immediate-release tablet formulations (F1–F3) were then developed using PROSOLV® EASYtab SP. The optimized solid dispersion (F7) exhibited significantly improved solubility (1.73 mg/mL). Among the prepared tablets, F1 demonstrated superior properties, including 97.45% drug content, 40-second disintegration time, and 98.54% drug release. Pharmacokinetic evaluation in Wistar rats revealed enhanced bioavailability for F1 (AUC₀–∞ = 18,270 ng·h/mL; Cmax = 3,446 ng/mL) compared to the marketed formulation, Lorsaid SP® (AUC₀–∞ = 17,814.5 ng·h/mL; Cmax = 3,198 ng/mL). Accelerated stability studies (40 °C/75% RH, 30 days) further confirmed the formulation’s stability. The Soluplus®-based pH-modulated solid dispersion strategy effectively improved the solubility, dissolution, and pharmacokinetic performance of Lornoxicam. The optimized F1 tablets demonstrated promising potential for clinical application by offering rapid disintegration, enhanced bioavailability, and good stability.

**PIC 1. Graphical abstract**

**A close-up of a white powder

Description automatically generated**

**Keywords: Lornoxicam, Soluplus®, solid dispersion, immediate release, bioavailability.**

**1.INTRODUCTION**

The design of safe, effective, and patient-friendly oral drug delivery methods remains a significant problem in pharmaceutical research. The low water solubility of many active pharmaceutical ingredients (APIs) is a significant constraint, resulting in sluggish dissolution, inconsistent absorption, and limited bioavailability. It is estimated that approximately 40% of commercialized drugs and over 70% of novel chemical entities suffer from solubility problems 1,2. Therefore, advanced formulation strategies are essential to improve their therapeutic performance.

Several ways to improve drug solubility have been studied, including physicochemical alterations such as particle size reduction3, salt formation, and co-crystallization4,5, as well as formulation-based tactics such as cyclodextrin complexation6 and lipid-based delivery systems. Solid dispersion technique which allows pharmaceuticals to be molecularly dispersed inside a polymeric matrix, enhancing wettability, dissolution rate, and bioavailability 7.

Soluplus®, a polyvinyl caprolactam–polyvinyl acetate–polyethylene glycol (PVCL-PVA-PEG) graft copolymer, has sparked widespread interest as a carrier for solid dispersions. It not only improves solubility by keeping medicines amorphous, but it also produces self-assembling micelles in aqueous settings, which increases wettability and dissolution. These properties make Soluplus® an excellent choice for poorly soluble drugs 8,9.

Lornoxicam, a nonsteroidal anti-inflammatory medication (NSAID), is commonly recommended to treat rheumatoid arthritis, osteoarthritis, and postoperative pain10. Despite its effectiveness, its solubility is highly pH-dependent: it is more soluble in acidic conditions but poorly soluble at neutral to basic pH, lead to inconsistent dissolution and bioavailability11. Addressing this restriction demands solutions that not only improve solubility but also provide consistent performance across physiological pH ranges.

In this regard, the current study looks at Soluplus®-based pH-modulated Lornoxicam solid dispersions. The use of pH modifiers like sodium bicarbonate generates a favorable milieu for drug breakdown over a wide pH range 12. The solvent evaporation approach was used to create the solid dispersions, which improving the wettability and amorphization of poorly soluble medicines 13. The improved dispersion was then manufactured into immediate-release (IR) tablets to provide a rapid action, which is crucial for pain treatment.

Immediate-release tablets were created through direct compression with PROSOLV® EASYtab SP, a multifunction excipient technology. The formulations were tested for *in vitro* and *in vivo* pharmacokinetics in Wistar rats. This work not only solves Lornoxicam's solubility issues, but also demonstrates a scalable, patient-friendly way to improving the clinical performance of poorly soluble drugs.

**2. MATERIALS AND METHODS**

**2.1 Materials**

Lornoxicam was obtained as a gift sample from Microlabs Pvt. Ltd. (Mumbai, India). Soluplus® was kindly provided by BASF Pharma Solutions (Mumbai, India). Analytical grade methanol, acetonitrile, disodium hydrogen phosphate, PEG 4000, and PVP K-90 were procured from Merck Pvt. Ltd. (Mumbai, India). Sodium bicarbonate, potassium carbonate, and calcium carbonate were purchased from Sigma-Aldrich (St. Louis, USA). PROSOLV® EASYtab SP, a multifunctional excipient system for direct compression, was sourced from JRS Pharma (Rosenberg, Germany). All excipients were of analytical or pharmaceutical grade and used without further purification.

Excipient selection was guided by their functional performance: Soluplus® as a solubilizing polymer, sodium bicarbonate as a pH-modifying alkalizer, and PROSOLV® EASYtab SP to ensure flowability, compressibility, and rapid disintegration in direct compression formulations.

**2.2 Formulation of Lornoxicam pH-Modulated Solid Dispersions**

2.2.1 Selection of Alkalizers

To determine the most suitable alkalizer for enhancing solubility, equilibrium solubility studies were performed. Excess Lornoxicam was added to 1% w/v aqueous solutions of sodium bicarbonate, disodium hydrogen phosphate, calcium carbonate, and potassium carbonate. Mixtures were shaken at 37 ± 0.5 °C for 24 h to reach equilibrium, centrifuged at 5,000 rpm for 15 min, filtered (0.45 µm), and analyzed spectrophotometrically at 382 nm. This screening step ensured rational selection of the alkalizer based on its ability to modify the microenvironmental pH and promote dissolution of the weakly acidic drug.

2.2.2 Optimization Using Experimental Design

A Central Composite Design (CCD) was employed with Design-Expert® software (version 13.0) to optimize the solid dispersion formulation. Two formulation variables were studied: Soluplus® concentration (X1: 40–200 mg) and sodium bicarbonate concentration (X2: 15–30 mg). Responses evaluated included saturation solubility (Y1, mg/mL) and drug content (Y2, %). Thirteen experimental runs were generated as per the CCD matrix.

CCD was chosen because it systematically evaluates both linear and interactive effects of formulation variables, offering statistical models that facilitate prediction and optimization with fewer experimental trials compared to traditional one-variable-at-a-time approaches.

2.2.3 Preparation of Solid Dispersions

Solid dispersions were prepared by solvent evaporation. Accurately weighed Lornoxicam and Soluplus® were dissolved separately in methanol (5 mL each), then combined and stirred until homogenous. Sodium bicarbonate was incorporated as per the design matrix. Solvent was removed on a water bath at 50 °C, leaving behind a solid mass, which was dried, pulverized, sieved (#40 mesh), and stored in a desiccator until use.

The solvent evaporation method was selected because it enables molecular-level dispersion of drug in the polymer matrix, reduces crystallinity, and enhances wettability without subjecting the drug to high thermal stress, as occurs in melt-based techniques.

**2.3 Characterization of Solid Dispersions**

2.3.1 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of pure Lornoxicam, Soluplus®, sodium bicarbonate, and solid dispersions were obtained using an FTIR-8400S spectrometer (Shimadzu, Japan) in the range 4000–400 cm⁻¹. This was used to assess compatibility and identify potential interactions such as hydrogen bonding between drug, polymer, and alkalizer.

2.3.2 Differential Scanning Calorimetry (DSC)

DSC thermograms were recorded on a Mettler Toledo instrument. Samples (2–5 mg) were sealed in aluminum pans and heated at 10 °C/min to 300 °C under nitrogen (25 mL/min). DSC was used to study thermal transitions and crystallinity. The disappearance or broadening of Lornoxicam’s endothermic peak would indicate amorphization.

2.3.3 Powder X-ray Diffraction (PXRD)

PXRD patterns were obtained on a Bruker D2 Phaser diffractometer (40 kV, 40 mA, Cu-Kα radiation). Samples were scanned between 5° and 50° 2θ at 2°/min. PXRD provided crystallinity profiles, allowing assessment of amorphous transformation induced by Soluplus®.

2.3.4 Scanning Electron Microscopy (SEM)

Morphology was analyzed using a CamScan Maxim-2000 SEM operated at 20 kV. Samples were mounted on aluminum stubs, coated with gold under vacuum, and imaged. SEM allowed visualization of surface morphology and qualitative changes in particle shape and structure following solid dispersion formation.

**2.4 Tablet Formulation and Evaluation**

2.4.1 Pre-compression Studies

Powder blends of solid dispersions with PROSOLV® EASYtab SP were evaluated for flowability and compressibility. Parameters measured included bulk and tapped density, Carr’s index, Hausner’s ratio, and angle of repose, in line with USP guidelines (2014). These parameters predict flow and packing behavior, critical for uniform die filling and weight consistency in direct compression.

2.4.2 Tablet Compression

Immediate-release tablets were prepared by direct compression. Each tablet contained an amount of solid dispersion equivalent to 8 mg of Lornoxicam, blended with PROSOLV® EASYtab SP at different levels (F1: 140 mg, F2: 100 mg, F3: 180 mg). The final tablet weights were 200, 160, and 240 mg, respectively. Compression was performed on a rotary press using 8-mm concave punches at a hardness of 3 ± 0.5 kg/cm².

Direct compression was chosen because it is a simple, scalable, and cost-effective method suitable for large-scale production. The multifunctional excipient blend PROSOLV® EASYtab SP minimizes formulation variability by combining filler, binder, disintegrant, and lubricant in optimized proportions.

**2.5 Evaluation of Compressed Tablets**

Tablet Thickness

The thickness of three randomly selected tablets from each formulation was measured using a calibrated Vernier caliper (Mitutoyo, Tokyo, Japan). Consistent thickness is essential to ensure uniform die filling and tablet weight, which in turn influences dose accuracy and mechanical strength.

Drug Content / Content Uniformity

To assess uniformity, one tablet from each batch was dissolved in methanol in a 50 mL volumetric flask, sonicated for 30 min, filtered through a 0.45 µm membrane filter, and analyzed spectrophotometrically at 382 nm using a Shimadzu UV-1900I spectrophotometer. Uniformity of content guarantees accurate dosing and reflects the homogeneity of powder blends prior to compression.

Friability Test

Mechanical strength was assessed using a Roche friabilator, in which twenty pre-weighed tablets were rotated at 25 rpm for 4 min. Tablets were reweighed and friability calculated as percentage weight loss. A friability value below 1% is typically considered acceptable for uncoated tablets, as it indicates sufficient resistance to abrasion during handling, transport, and packaging.

Weight Variation

Ten tablets were weighed individually, and the mean weight was calculated. Individual deviations from the mean were compared against pharmacopeial limits. Weight uniformity is a critical indicator of blend flowability and die filling consistency, ensuring dose reproducibility.

In Vitro Disintegration Time

Disintegration time was measured in distilled water at 37 ± 0.5 °C using a USP disintegration tester (TDT-08L, Electrolab). Rapid disintegration is essential for immediate-release tablets, as it directly influences dissolution rate and subsequent drug absorption. Optimizing disintegration is especially important for poorly soluble drugs like Lornoxicam, where faster breakup into fine particles enhances surface area for dissolution.

In Vitro Dissolution Studies

Dissolution testing was performed in 900 mL of phosphate buffer (pH 6.8) at 37 ± 0.5 °C, using a USP type-II (paddle) apparatus at 75 rpm. Aliquots were withdrawn at predetermined intervals (0–60 min), filtered, and analyzed at 382 nm, with equal volume of fresh medium replaced each time. Dissolution serves as the most critical predictor of in vivo performance for Biopharmaceutics Classification System (BCS) Class II drugs, where solubility is the rate-limiting step. For solid dispersion-based formulations, dissolution studies not only confirm enhanced solubility but also validate the stability of the amorphous drug form in physiological conditions.

In Vivo Pharmacokinetic Study

A pharmacokinetic comparison of the optimized Lornoxicam immediate-release formulation (F1) with a marketed tablet (Lorsaid SP®, 8 mg) was performed in compliance with CPCSEA guidelines and approved by the Institutional Animal Ethics Committee of R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, India (Reg. No. 651/PO/ReBi/S/02/CPCSEA; Protocol No. RCPIPER/IAEC/2020-21/18). Ethical measures were strictly followed to minimize animal suffering and use.

Animal Handling and Dosing

Adult Wistar rats (220–250 g, 10–15 weeks old) were maintained under controlled environmental conditions (25 ± 2 °C, 12-h light/dark cycle, 55 ± 5% RH) with free access to food and water. Animals were fasted overnight prior to dosing and randomized into two groups (n = 3 each): Group I received the marketed formulation (8 mg/kg), while Group II received the optimized F1 tablets (8 mg/kg).

Sample Collection and Analysis

Blood samples (0.5 mL) were withdrawn via retro-orbital puncture at 0.5–24 h post-dose and collected in heparinized tubes. Plasma was isolated by centrifugation (4000 rpm, 5 min), deproteinized with acetonitrile (1:3 v/v), and analyzed by a validated RP-HPLC method. Chromatographic separation was achieved on a C18 column (250 × 4.6 mm, 5 µm) using acetonitrile: water (70:30 v/v, pH 2.5 with acetic acid) at 1 mL/min. Detection was performed at 382 nm with a 10-min runtime. Pharmacokinetic parameters (Cmax, Tmax, AUC, t½) were calculated by non-compartmental analysis using PKSolver.

**2.6 Stability Study**

The optimized formulation (F1) was subjected to accelerated stability testing under ICH Q1A (R2) conditions (40 ± 2 °C, 75 ± 5% RH) for one month. Tablets stored in amber glass vials were evaluated at 30 days for assay, disintegration time, and dissolution performance. Such testing is essential to confirm that formulation stability and release characteristics are retained during storage.

**3. RESULTS AND DISCUSSION**

**3.1 Selection of Carriers and Alkalizers**

The solubility screening of Lornoxicam (LORX) with different alkalizers revealed substantial variations in its solubilization profile. Among the tested alkalizers, Sodium Bicarbonate demonstrated the highest solubility of 4.31 mg/ml, significantly outperforming Calcium Carbonate (1.6 mg/ml), Potassium Carbonate (1.56 mg/ml), and Disodium Hydrogen Phosphate (1.34 mg/ml). The superior performance of Sodium Bicarbonate may be attributed to its ability to strongly elevate the local microenvironmental pH, thereby reducing the weakly acidic drug’s ionization barrier and promoting dissolution. This is particularly important for LORX, a Biopharmaceutics Classification System (BCS) Class II drug characterized by poor aqueous solubility and dissolution-limited absorption.

These findings are consistent with prior reports14. demonstrated that bicarbonate salts create a dynamic pH-buffered microenvironment around poorly soluble drugs, enhancing their ionization and solubility. Similarly,15 reported that sodium bicarbonate improved dissolution of poorly soluble NSAIDs by mitigating pH-dependent solubility limitations. In contrast, phosphate salts have been more effective for basic compounds, highlighting the importance of drug–alkalizer specificity. Hence, Sodium Bicarbonate was selected as the preferred alkalizer in this study, offering a strong rationale for its use in pH-modulated amorphous solid dispersion (ASD) systems to improve LORX solubility and oral bioavailability.

**3.2 Optimization through Response Surface Methodology (RSM)**

The development of LORX pH modulated ASDs was optimized using a Central Composite Design (CCD) under Response Surface Methodology (RSM). Experimental results demonstrated variations in saturation solubility (1.12–1.89 mg/ml) and drug content (81.43–93.89%) across the formulations. Among all the prepared batches, formulation F7 exhibited superior performance with the highest saturation solubility (1.73 mg/ml) and maximum drug content (93.89%). These outcomes indicate that the optimal combination of carrier (Soluplus) and alkalizer (Sodium Bicarbonate) concentrations significantly contributes to enhancing solubility and incorporation of LORX into the polymer matrix.

These findings align with 16, who demonstrated that optimizing polymer concentration and alkalizer levels via CCD improved solubility for poorly soluble drugs. The results also suggest that both components act synergistically: Soluplus disperses LORX in an amorphous form while Sodium Bicarbonate stabilizes its dissolution environment. Thus, F7 was selected for further detailed evaluation.

**3.3 Optimization, Data Analysis, and Model Validation**

3.3.1 Fitting of Data to the Model

The experimental data for saturation solubility (Y1) and drug content (Y2) across 13 formulations were analyzed using Design-Expert® 13.0. A linear model initially provided a good fit; however, the quadratic model was ultimately selected as it better explained the interactive effects of independent variables: Soluplus concentration (X1: 40–200 mg) and Sodium Bicarbonate concentration (X2: 15–30 mg).

The regression equations obtained were:

Saturation Solubility (Y1): Y1 = 1.38231 – 0.63500 × X1 – 8.80000 × X2

% Drug Content (Y2): Y2 = 89.39692 – 3.70352 × X1 – 42.67789 × X2

The high coefficient of determination (R² = 0.9873 for Y1 and 0.8083 for Y2) and adjusted R² values (0.9783 for Y1, 0.7445 for Y2) confirmed the models’ predictive reliability. The models were statistically significant with P-values <0.05 (0.0225 for Y1 and 0.0068 for Y2). Furthermore, ANOVA results (F-values of 9.51 for Y1 and 18.10 for Y2) validated the contribution of both independent variables to the responses. Precision indicators such as standard deviation (0.0321 for Y1 and 1.96 for Y2) and coefficient of variance (0.66% for Y1 and 0.58% for Y2) confirmed experimental reproducibility.

These outcomes are consistent with 17, who emphasized the relevance of quadratic models in predicting solubility optimization for ASD systems. Collectively, the results support that both polymer and alkalizer concentrations significantly influence drug solubility and loading.

**3.4 Effect of Soluplus and Sodium Bicarbonate on Solubility and Drug Content**

3.4.1 Response Surface Plots Analysis

The response surface plots (Figure 1) generated in Design Expert® illustrate the combined effects of Soluplus (X1) and Sodium Bicarbonate (X2) on saturation solubility (Y1) and drug content (Y2). The three-dimensional (3D) plots demonstrated a clear trend of increasing solubility and drug content with rising levels of both independent variables.

For solubility (Figure 1A, B), F7 containing 200 mg Soluplus and 30 mg Sodium Bicarbonate demonstrated maximum saturation solubility (1.73 mg/ml). This improvement is attributed to the amphiphilic property of Soluplus, which enhances drug wettability and dispersion, and Sodium Bicarbonate, which creates a favorable pH microenvironment. Similar effects were noted in the work of 18, where Soluplus improved drug amorphization and dissolution.

For % drug content (Figure 1C, D), F7 again showed the best performance with 93.89%. This suggests that higher polymer and alkalizer concentrations facilitate efficient entrapment of the drug in the ASD matrix19, 20 also reported similar improvements in drug content in polymeric ASDs due to stronger drug–polymer interactions.

Together, the response surface analysis confirmed that increasing Soluplus and Sodium Bicarbonate concentrations significantly enhances solubility and drug incorporation, validating the optimization approach and supporting F7 as the most promising batch.

**3.5 FTIR Analysis**

FTIR analysis was used to identify potential drug-excipient interactions (Figure 2). LORX had prominent peaks at 717.54, 2918.40, 1375.29, 1458.23, 1195.91, and 1020.38 cm⁻¹. These peaks were mostly preserved in the improved ASD, showing that the drug had not been chemically degraded. Soluplus revealed peaks at 1734.06 cm⁻¹ (C=O stretching), 3446.91 cm⁻¹ (OH stretching), and 1327 cm⁻¹ (SO₂N stretch), whereas Sodium Bicarbonate showed peaks at 1458.23 cm⁻¹ (carbonate group) and 1020.38 cm⁻¹ (C-O stretching).

In the optimized formulation, some peaks were slightly displaced and widened, indicating intermolecular hydrogen bonding. The C=O peak changed from 1734.06 to 1739.85 cm⁻¹, and OH stretching expanded, suggesting interactions between LORX and Soluplus. The SO₂N peak shifted, indicating polymer-drug compatibility. Such interactions are helpful because they diminish medication crystallinity and increase dispersion. Similar findings were reported by celecoxib ASDs and 21 slightly acidic NSAIDs13.

**3.6 Differential Scanning Calorimetry (DSC) Analysis**

The DSC thermograms (Figure 3A) shed light on the crystalline-amorphous transitions of LORX in the ASD. Pure LORX showed a pronounced endothermic peak at 223.18°C, confirming its crystalline structure. Soluplus exhibited a broad endotherm between 178.99°C and 228.16°C, which is consistent with its semi-amorphous nature.

In the optimized ASD, the LORX melting peak disappeared and was replaced by a broad endotherm at 175.11°C, indicating partial amorphization. The significant decrease in crystallinity (from 100% in LORX to 682.32% relative crystallinity in ASD) promotes good molecular dispersion. 22,18. found similar reductions in crystallinity in Soluplus-based dispersions. These findings indicate that amorphization improves solubility and dissolution.

**3.7 Powder X-ray Diffraction (PXRD) Analysis**

PXRD diffractograms (Figure 3B) confirmed the crystallinity alterations. Pure LORX exhibited distinct peaks at 2θ values of 12.14°, 15.52°, and 24.88°, indicating its crystalline structure. In contrast, the optimized ASD showed a broad halo with no sharp peaks, indicating that it had completely transitioned to the amorphous state. The decrease of crystallinity supports DSC findings and demonstrates the efficacy of the solid dispersion technique23.Amorphization resulted in better dissolving in LORX dispersions with hydrophilic carriers.

**3.8 SEM Analysis**

SEM scans (Figure 4) showed clear morphological changes between pure LORX and the optimized ASD. Pure LORX showed angular crystalline particles, whereas ASD showed uneven, smooth, and amorphous structures with smaller particle sizes. These morphological changes indicate successful molecular dispersion, the elimination of crystalline domains, and increased wettability. Similar changes have been observed by refences10, demonstrating that amorphous shape contributes to increased solubility and dissolution.

**3.9 Pre-compression Parameters of Lubricated Blend**

The pre-compression properties of blends (F1, F2, F3) were evaluated (Table 1). F1 demonstrated the most favorable flow properties with a Carr’s Index of 14.15%, Hausner’s ratio of 1.15, and angle of repose of 23°, all indicative of excellent flow and compressibility. In contrast, F2 and F3 showed poorer flow with Carr’s Index values above 20% and higher angles of repose (>26°), suggesting potential processing challenges.

These findings align with24, who noted that flow indices within these ranges ensure consistent die filling and minimal compression defects. Thus, F1 was identified as the most suitable formulation for compression into tablets.

**3.10 Evaluation of Compressed Tablets**

Post-compression evaluation (Table 2) demonstrated significant differences between F1, F2, and F3. F1 exhibited optimal physicochemical properties, including average weight (200 mg), thickness (2.5 mm), and drug content (97.45±0.5%). The hardness (3.0 kg/cm²) ensured mechanical strength while maintaining friability below acceptable limits (0.61%).

Importantly, F1 had the fastest disintegration time (40 sec) and highest drug release (98.54% in 30 min) compared to F2 and F3. While F3 had higher hardness (3.7 kg/cm²), its disintegration time was prolonged (79 sec), reducing dissolution efficiency. F2 showed mechanical fragility with higher friability (0.86%). The superior performance of F1 is attributed to PROSOLV® EASYtab SP, a multifunctional excipient system designed to improve compressibility, wettability, and disintegration. Comparable excipient-based improvements were reported by 25,26. Collectively, these results validate F1 as the optimized tablet formulation.

**3.11 Pharmacokinetic Study**

The pharmacokinetic performance of F1 was compared with the marketed tablet (Lorsaid SP) (Table 3). F1 showed a higher Cmax and AUC, confirming enhanced systemic exposure. The reduced Tmax indicated faster absorption, while prolonged mean residence time (MRT) suggested extended systemic retention. These enhancements can be attributed to improved solubility, rapid disintegration, and efficient absorption due to PROSOLV® EASYtab SP. Similar pharmacokinetic advantages of ASD-based formulations have been reported by refences 27,28.

**3.12 Stability Study**

The stability of F1 was assessed under accelerated conditions (40°C/75% RH) for 30 days (Table 4). No significant changes were observed in color, appearance, or mechanical properties. Disintegration time remained nearly unchanged (45 sec at day 0 vs. 42 sec at day 30). Drug release was consistent (96.62% to 97.52%), and assay values showed minimal degradation (97.42±0.5% to 96.25±0.3%). These results confirm both physical and chemical stability of the optimized formulation. Comparable stability was reported by29in short-term accelerated tests of NSAID formulations.

**3.13 CONCLUSION**

The current work effectively designed and tested Lornoxicam immediate-release tablets by optimizing carrier-alkalizer combinations to improve solubility, dissolving, and bioavailability. Among the formulations studied, the sodium bicarbonate-based system showed superior solubility and dissolution augmentation, while solid-state characterizations revealed effective drug-excipient interactions without jeopardizing drug stability. The optimized formulation demonstrated considerably improved in vivo pharmacokinetic performance as compared to the marketed reference product, indicating a possibility for faster onset of action and increased therapeutic efficacy. These findings create a strong formulation strategy for medications with low water solubility, such as Lornoxicam, ensuring enhanced oral delivery by logical excipient selection and formulation optimization.

**ABBREVIATION**

NSAID- Nonsteroidal **anti-inflammatory drug**

CCD-Central Composite Design

**FTIR - Fourier Transform Infrared Spectroscopy**

**DSC - Differential Scanning Calorimetry**

**PXRD - Powder X-ray Diffraction**

**SEM - Scanning Electron Microscopy**

DC - Drug Content

DT - Disintegration Time

DR - Dissolution Rate

LORX- Lornoxicam

ASDs-amorphous solid dispersions

APIs - active pharmaceutical ingredients

PVCL-PVA-PEG- polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol

IR -immediate-release

CPCSEA- Committee for the Purpose of Control and Supervision of Experiments on Animals

IAEC-Institutional Animal Ethics Committee

**HPLC – High-Performance Liquid Chromatography**

**ICH – International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use**

**AUC – Area under the Curve**

**Cmax – Maximum Plasma Concentration**

**Tmax – Time to Reach Maximum Plasma Concentration**

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**REFERENCES**

1. Salunke, S. et al. (2022) ‘Oral drug delivery strategies for development of poorly water soluble drugs in paediatric patient population’, Advanced Drug Delivery Reviews, 190, p. 114507. <https://doi.org/10.1016/j.addr.2022.114507>
2. Alqahtani, M.S. et al. (2021) ‘Advances in Oral Drug Delivery’, Frontiers in Pharmacology, 12, p. 618411. <https://doi.org/10.3389/fphar.2021.618411>
3. O’Sullivan, A. et al. (2022) ‘Solid-state and particle size control of pharmaceutical cocrystals using atomization-based techniques’, International Journal of Pharmaceutics, 621, p. 121798. <https://doi.org/10.1016/j.ijpharm.2022.121798>
4. Yadav, A.V. et al. (2009) ‘Co-crystals: a novel approach to modify physicochemical properties of active pharmaceutical ingredients’, Indian Journal of Pharmaceutical Sciences, 71(4), pp. 359–370. <https://doi.org/10.4103/0250-474X.57283>
5. Serajuddin, A.T.M. (2007) ‘Salt formation to improve drug solubility’, Advanced Drug Delivery Reviews, 59(7), pp. 603–616. <https://doi.org/10.1016/j.addr.2007.05.010>
6. Fang, G. et al. (2022) ‘γ-Cyclodextrin-based polypseudorotaxane hydrogels for ophthalmic delivery of flurbiprofen to treat anterior uveitis’, Carbohydrate Polymers, 277, p. 118889. <https://doi.org/10.1016/j.carbpol.2021.118889>
7. Kumari, L. et al. (2023) ‘Advancement in Solubilization Approaches: A Step towards Bioavailability Enhancement of Poorly Soluble Drugs’, Life, 13(5), p. 1099. <https://doi.org/10.3390/life13051099>
8. Guembe-Michel, N., Nguewa, P. and González-Gaitano, G. (2025) ‘Soluplus®-Based Pharmaceutical Formulations: Recent Advances in Drug Delivery and Biomedical Applications’, International Journal of Molecular Sciences, 26(4), p. 1499. <https://doi.org/10.3390/ijms26041499>
9. Mali, K.D., Shinde, D.T. and Patil, K.R. (2025) ‘Review on Soluplus®: Pharmaceuticals Revolutionizing Drug Delivery and Formulation Strategies’, International Journal of Pharmaceutical Investigation, 15(2), pp. 344–360. <https://doi.org/10.5530/ijpi.20250146>
10. Fule, R. et al. (2014) ‘Preparation and characterisation of lornoxicam solid dispersion systems using hot melt extrusion technique’, Journal of Pharmaceutical Investigation, 44(1), pp. 41–50. <https://doi.org/10.1007/s40005-013-0099-7>
11. Dadej, A. et al. (2022) ‘Improved solubility of lornoxicam by inclusion into SBA-15: Comparison of loading methods’, European Journal of Pharmaceutical Sciences, 171, p. 106133. <https://doi.org/10.1016/j.ejps.2022.106133>
12. Tran, P.H.-L. et al. (2010) ‘Dissolution-modulating mechanism of pH modifiers in solid dispersion containing weakly acidic or basic drugs with poor water solubility’, Expert Opinion on Drug Delivery, 7(5), pp. 647–661. <https://doi.org/10.1517/17425241003645910>
13. Marasini, N. et al. (2013) ‘Fabrication and evaluation of pH-modulated solid dispersion for telmisartan by spray-drying technique’, International Journal of Pharmaceutics, 441(1–2), pp. 424–432. <https://doi.org/10.1016/j.ijpharm.2012.11.012>
14. McFall, H. et al. (2019) ‘Formulation of aripiprazole-loaded pH-modulated solid dispersions via hot-melt extrusion technology: In vitro and in vivo studies’, International Journal of Pharmaceutics, 554, pp. 302–311. <https://doi.org/10.1016/j.ijpharm.2018.11.005>
15. Poudel, S. and Kim, D.W. (2021) ‘Developing pH-Modulated Spray Dried Amorphous Solid Dispersion of Candesartan Cilexetil with Enhanced In Vitro and In Vivo Performance’, Pharmaceutics, 13(4), p. 497. <https://doi.org/10.3390/pharmaceutics13040497>
16. Srivastava, A. et al. (2023) ‘Design, Optimization, and Characterization of a Novel Amorphous Solid Dispersion Formulation for Enhancement of Solubility and Dissolution of Ticagrelor’, International Journal of Applied Pharmaceutics, 15(4), pp. 296–305. <https://doi.org/10.22159/ijap.2023v15i4.47618>
17. Chakraborty, P. et al. (2013) ‘Design Expert Supported Mathematical Optimization and Predictability Study of Buccoadhesive Pharmaceutical Wafers of Loratadine’, BioMed Research International, 2013, p. 197398. <https://doi.org/10.1155/2013/197398>
18. Almotairi, N. et al. (2022) ‘Design and Optimization of Lornoxicam Dispersible Tablets Using Quality by Design (QbD) Approach’, Pharmaceuticals, 15(12), p. 1743. <https://doi.org/10.3390/ph15121743>
19. Verma, S. et al. (2011) ‘Formulation, evaluation and optimization of solid dispersion of Glipizide using face centered central composite design’, International Journal of Pharmacy and Pharmaceutical Sciences, 3(Suppl 5), pp. 475–482.
20. Emam, M.F. et al. (2022) ‘Optimization of Meloxicam Solid Dispersion Formulations for Dissolution Enhancement and Storage Stability Using 3³ Full Factorial Design Based on Response Surface Methodology’, AAPS PharmSciTech, 23(7), p. 248. <https://doi.org/10.1208/s12249-022-02394-7>
21. Kesisoglou, F. et al. (2015) ‘Development of In Vitro–In Vivo Correlation for Amorphous Solid Dispersion Immediate-Release Suvorexant Tablets and Application to Clinically Relevant Dissolution Specifications and In-Process Controls’, Journal of Pharmaceutical Sciences, 104(9), pp. 2913–2922. <https://doi.org/10.1002/jps.24362>
22. Ankur, S., Vaishali, K. and Santosh, P. (2016) ‘Lornoxicam Based Solid Dispersion of Spray-Dried Cellulose Nanofibers as Novel Tablet Excipient’, Inventi Rapid: Novel Excipients, 2016(4), pp. 1–11.
23. Panda, R. and Lankalapalli, S. (2023) ‘Design of Experiments and Optimization of Amorphous Solid Dispersion of a BCS Class IV Anti-Platelet Drug Through Factorial Design’, International Journal of Applied Pharmaceutics, 15(6), pp. 353–364. <https://doi.org/10.22159/ijap.2023v15i6.48767>
24. Sakure, K., Kumari, L. and Badwaik, H. (2020) ‘Development and evaluation of solid dispersion based rapid disintegrating tablets of poorly water-soluble anti-diabetic drug’, Journal of Drug Delivery Science and Technology, 60, p. 101942. <https://doi.org/10.1016/j.jddst.2020.101942>
25. Eisa, A.M., El-Megrab, N.A. and El-Nahas, H.M. (2022) ‘Formulation and evaluation of fast dissolving tablets of haloperidol solid dispersion’, Saudi Pharmaceutical Journal, 30(11), pp. 1589–1602. <https://doi.org/10.1016/j.jsps.2022.09.002>
26. Juan, C. et al. (2023) ‘Development of ivermectin orally disintegrating tablets using factorial design: In-vitro evaluation and in vivo absorption pattern in rats’, Journal of Drug Delivery Science and Technology, 87, p. 104757. <https://doi.org/10.1016/j.jddst.2023.104757>
27. Li, F. et al. (2015) ‘Preparation and pharmacokinetics evaluation of oral self-emulsifying system for poorly water-soluble drug Lornoxicam’, Drug Delivery, 22(4), pp. 487–498. <https://doi.org/10.3109/10717544.2014.885615>
28. Salama, A., El-Hashemy, H.A. and Darwish, A.B. (2022) ‘Formulation and optimization of lornoxicam-loaded bilosomes using 2³ full factorial design for the management of osteoarthritis in rats: Modulation of MAPK/Erk1 signaling pathway’, Journal of Drug Delivery Science and Technology, 69, p. 103175. <https://doi.org/10.1016/j.jddst.2022.103175>
29. Furqan Ahsan, S. et al. (2019) ‘Formulation and stability studies of fast disintegrating tablets of amlodipine besylate’, Indian Journal of Pharmaceutical Education and Research, 53(3), pp. 480–493. <https://doi.org/10.5530/ijper.53.3.80>
30. Tekade, A.R. and Yadav, J.N. (2020) ‘A Review on Solid Dispersion and Carriers Used Therein for Solubility Enhancement of Poorly Water-Soluble Drugs’, Advanced Pharmaceutical Bulletin, 10(3), pp. 359–369. <https://doi.org/10.34172/apb.2020.044>
31. Xie, B. et al. (2024) ‘Solubilization techniques used for poorly water-soluble drugs’, Acta Pharmaceutica Sinica B, 14(11), pp. 4683–4716. <https://doi.org/10.1016/j.apsb.2024.08.027>

**Figure**

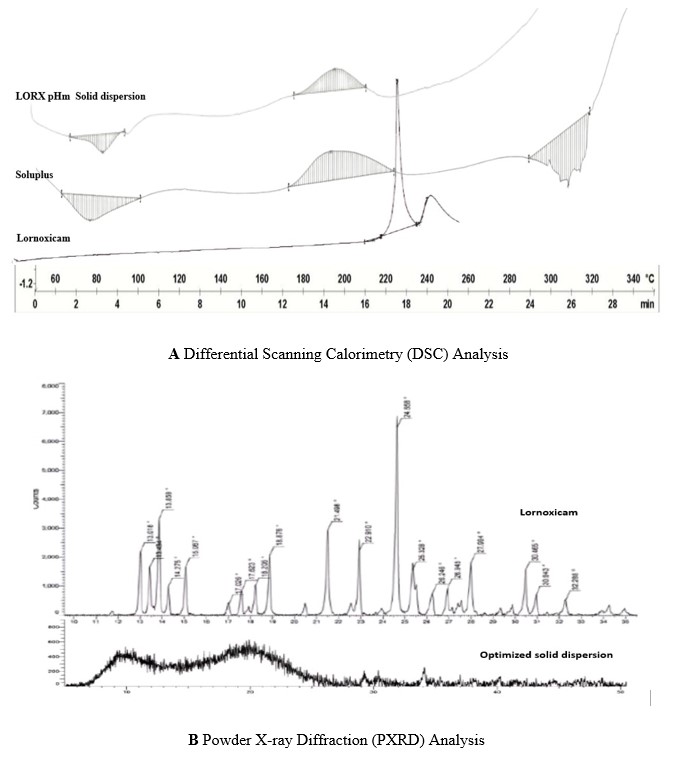
A collage of graphs showing different colors

Description automatically generated **Figure 1** Response Surface Plots Analysis

A graph of a graph showing the number of objects

Description automatically generated with medium confidence

**Figure 2** FTIR analysis



**Figure 3** DSC and PXRD Analysis

A close-up of several images

Description automatically generated

**Figure 4** SEM analysis

**A graph of different colored bars

Description automatically generated**

**Figure 5** *In vitro* dissolution study

**Table**

**Table 1:** Precompression parameter

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **B. No** | **BD (gm/ml)** | **T D (gm/ml)** | **HR** | **CI (%)** | **AR ( O)** |
| F1 | 0.38 ±0.34 | 0.41±0.08 | 1.15±0.22 | 14.15 | 23 |
| F2 | 0.45±0.12 | 0.54±0.16 | 1.26±0.14 | 26.20 | 26 |
| F3 | 0.55±0.18 | 0.61±0.24 | 1.21±0.42 | 21.32 | 28 |

**Table 2:** Post compression parameter

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **F1** | **F2** | **F3** | **Marketed Tablet** |
| **Weight (mg)** | 200 ± 2 | 160 ± 1.5 | 240 ± 2 | 200 ± 2.5 |
| **Thickness (mm)** | 2.5 ± 0.1 | 2.0 ± 0.2 | 2.7 ± 0.2 | 2.2 ± 0.1 |
| **Drug Content (%)** | 97.45 ± 0.5 | 95.45 ± 0.5 | 96.45 ± 0.5 | 97.45 ± 0.5 |
| **Hardness (kg/cm²)** | 3.0 ± 0.3 | 2.5 ± 0.4 | 3.7 ± 0.5 | 3.5 ± 0.5 |
| **Friability (%)** | 0.61 | 0.86 | 0.75 | 0.53 |
| **Disintegration Time (sec)** | 40 sec | 68 sec | 79 sec | 58 sec |
| **% Drug Release (%DR)** | 98.54 ± 4.0 | 95.12 ± 4.5 | 93.37 ± 3.5 | 97.12 ± 5.5 |

**Table 3:** Pharmacokinetic parameters

|  |  |  |
| --- | --- | --- |
| **Pharmacokinetic Parameters** | **Marketed tablet (Lorsaid SP)** | **F1** |
| AUC 0-t (ng/mL\* h) | 17314.5 | 18270 |
| Cmax(ng/mL) | 3198 | 3446 |
| t1/2 (h) | 3.4 | 3.1 |
| Tmax(h) | 2.5 | 2.2 |
| MRT (h) | 6.46±17 | 13.28±2.2 |