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Solubility enhancement of lornoxicam with poloxamer 188 by solvent evaporation method

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Abstract---This investigation aimed to enhance the solubility and bioavailability of the BCS class II poorly water-soluble drug Lornoxicam by solid dispersion (SD) techniques using Polaxomer 188 as a hydrophilic carrier. Solid dispersion of Lornoxicam was made through physical mixing (kneading method) and solvent Evaporation technique via different drug: carrier ratios. Prepared solid dispersion was characterized for solubility, drug content, percentage yield, and in vitro dissolution study. Solid-state characterization was performed by differential scanning calorimetry and Fourier-transform infrared spectroscopy. Lornoxicam's apparent solubility increased with an increasing level of carrier. A solid dispersion study revealed a better dissolution of lornoxicam than physical blends. In the phase solubility study, the drug demonstrated a higher solubility over phosphate buffer pH range 6.8 compared to distilled water. Solid Dispersion of Lornoxicam: Polaxomer188 solvent evaporation (1:3) showed maximum dissolving effectiveness between all solid dispersion and physical mixture. IR spectra showed no clear interaction between the drug and the polymer. Solubility increases with Solvent Evaporation than with physical mixing and alongside use of water-soluble polymer Polaxomer 188.

Keywords---BCS class II, Lornoxicam, Poloxamer 188, Solubility, Solvent Evaporation.

Introduction

Poorly water-soluble BCS class II molecules, having high permeability, are affiliated with slow drug absorption, leading to low and varying bioavailability. It assumes that mainly absorption rate based on the drug solubility and dissolution, successive transport on intestinal membrane and liver. Attempt trials to enhance the dissolution rate of these drug candidates performed by different approaches (Kumar et al., 2011; Vasconcelos et al., 2007; Mahesh et al., 2012). The solid dispersion (SD) approach has captivated great attentiveness as a promising way of enhancing the dissolution rate of drugs, that improves the bioavailability of a range of low aqueous soluble drugs (Verma et al., 2005; Patidar et al., 2011; Lubna & Rajasekaran, 2022). Apparently, drug dissolution via solid dispersions (SD) is exemplified because of increased wettability, better dispersibility of drug molecules, and the presence of the drug in amorphous form with enhanced solubility and absence of accumulation of drug particles using various hydrophilic carriers (Kulkarni et al., 2012; Dua et al., 2010). Lornoxicam is an Oxycam and non-steroidal anti-inflammatory drug (NSAID), with analgesic, anti-pyretic, anti-thrombotic, and anti-inflammatory activities (Olkola et al., 1994). It comes under Biopharmaceutical Classification System (BCS) - class II drugs having poor solubility and very high permeability. It has been reported that low aqueous solubility (0.0385 ± 0.01 mg/ml) at ambient temperature impairs its dissolution in the upper gastric fluid, which alters bioavailability and hinders its therapeutic application (Amidon et al., 1995; Hance & Beril, 2005; Lobenberg & Amidon, 2000; Cook et al., 2008). The present investigation focused to improve the water solubility and therapeutic effectiveness of the drug by formulating solid dispersions (SD) of LOR with a hydrophilic carrier Poloxamer 188(PXM) by the solvent evaporation method

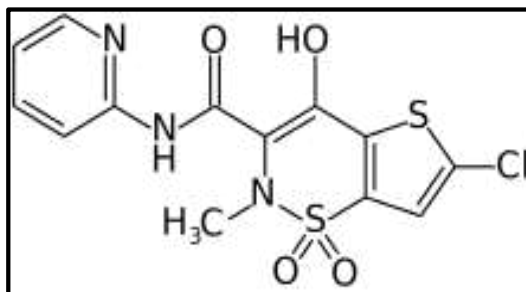


Fig. I: Structure of Lornoxicam

Material and Methods

Materials

Lornoxicam was gifted by Shri Sai Krishna Enterprises, Kaplana Society, Chintal, Hyderabad, poloxamer 188 purchased from S.D. Fine Chemicals Limited. All additional chemicals utilized were of analytical grade and procured from commercial sources.

Preparation of Physical Mixtures

Physical mixtures were prepared by mixing Lornoxicam and poloxamer 188 in mortar and pestle according to 1:1, 1:2, and 1:3 ratios by geometrical dilution method. The geometric mix blends passed through sieve no#60 and were kept in the desiccator ([Gupta & Ranawat, 2012](#)).

Preparation of SD by Solvent Evaporation Technique

Lornoxicam and poloxamer 188 Were weighed according to 1:1, 1:2, and 1:3 ratios. Approximately 20 ml of methanol was taken as a common solvent to solubilize drug and polymer in different ratios, forming a clear solution. Then the solution was poured into Petri d, kept overnight for evaporation of solvent at room temperature. Then the resultant product was scrapped away, kept in the desiccator for 24hrs to complete the removal of moisture and passed through sieve no#60, and kept in the desiccator ([Payal et al., 2021](#); [Kauslya et al., 2021](#)).

Phase Solubility Analysis

Solubility of the selected drug Lornoxicam was determined in water and pH 6.8 phosphate buffer medium. The outcome of concentrations of Poloxamer 188 on the balancing solubility of Lornoxicam in aqua and pH 6.8 phosphate buffer medium at particular room temperature was accomplished by the addition of an excess quantity of drug about 20 mg within a screw-capped glass vial containing 20 ml of solvent with various concentrations of the carrier. The suspension was shaken for 24hrs. On a rotary bath shaker & filtered through Whatman no.1 filter paper. The filtrate so obtained was diluted & analyzed spectrophotometrically ([Chetan et al., 2020](#); [Lubna & Rajasekaran, 2019](#)).

Analysis of Drug Content in Solid Dispersions

The drug content of Lornoxicam in each physical mixture and solid-dispersions were observed utilizing UV-spectroscopy. Accurately weighed quantity of solid dispersion or physical mixture equivalent to 10 mg of Lornoxicam was sent to 100 ml of volumetric flask and volume makeup up to 100 ml along with methanol, and 1 ml from this solution mixture was taken. It was diluted to 10 ml along with methanol, and absorbance was noted at 378 nm. The concentration of Lornoxicam was determined using a calibration curve of Lornoxicam in methanol.

Percentage Yield Value

The following formula measured the Percentage yield value of solid dispersions and physical mixtures ([Lakshmi et al., 2012](#)).

$$\text{Percent Yield Value} = \text{Practical yield value} / \text{Theoretical yield value} \times 100$$

Characterization of Solid Dispersion Fourier transform infrared spectroscopy (FT-IR)

The FT-IR spectra were obtained using an FT-IR spectrometer (Shimadzu). The samples were ground and triturated properly with KBr, an infrared transparent matrix in a ratio of the 1:5 (sample: KBr). The KBr discs were prepared by blending the powders at the pressure range of 5 tons for 5 minutes in hydraulic pressure. Forty-five scans were found at a resolution of 4 cm^{-1} from 4500 to 400 cm^{-1} (Aungst et al., 1997).

Differential Scanning Calorimetry

The DSC observation were carried out on a Pyris Diamond TG/DTA differential scanning calorimetry along with the thermal analyzer. All perfectly weighed 5 mg. samples were kept in fully sealed aluminum pans. The aluminum pan which is empty was used as a reference (Subrahmanyawari et al., 2019).

In-vitro Dissolution Rate Studies

In vitro dissolution observation of physical mixtures and SD of Lornoxicam were carried out on USP type II dissolution apparatus after that, and the outcomes were compared with those for pure Lornoxicam. The dissolution vessels contained 900 mL of phosphate buffer ranging pH 6.8 maintained at $37\text{ }^{\circ}\text{C} \pm 0.5\text{ }^{\circ}\text{C}$ and the paddle speed fixed at 50 rpm. Solid dispersions equivalent to 20 mg. of Lornoxicam powder were mixed into the dissolution medium. Then, 5 mL. Samples were withdrawn from dissolution medium at time intervals of 5, 10, 20, 30, 45, and 60 minutes. The withdrawn sample was replenished with 5 milliliters of media. The withdrawn samples were analyzed for Lornoxicam content by estimating the absorbance at 378 nm using a UV (Shimadzu). Dissolution studies for each formulation were performed in triplicates (Modi & Tayade, 2006; Iyan et al., 2020).

Result and Discussion Phase Solubility Study

The phase solubility curves of pure Lornoxicam in the existence of poloxamer 188 at $25\text{ }^{\circ}\text{C}$ are shown in Figure 2. The apparent solubility of Lornoxicam was found at 0.071 mg/mL in pH 6.8 phosphate buffer. Solubility of Lornoxicam increased with increasing carrier concentrations. Using the highest carrier concentration, the solubility increased approximately 8.26 fold in distilled water and 8.14 fold in pH 6.8 phosphate buffer as standardized with pure drug. The solubility found in this study for Lornoxicam at 25°C was 0.562 mg/mL in distilled water and 0.578 mg/mL pH 6.8 buffer.

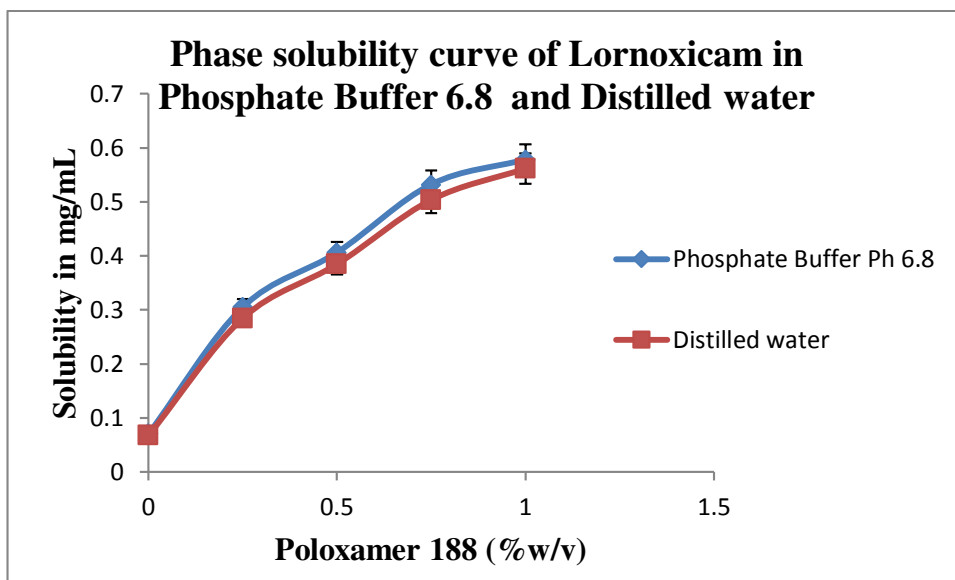


Fig. II: Phase solubility diagram of Lornoxicam/poloxamer 188 system in pH 6.8 buffer

Percent Yield and Drug Content

The physical mixtures and solid dispersions percent yield of various Lornoxicam was within the range of $90.09 \pm 0.13\%$ to $99.05 \pm 0.21\%$. The percentage drug content in physical mixtures and solid dispersions was within the range of $93.08 \pm 0.11\%$ to $98.24 \pm 0.59\%$ and $91.75 \pm 0.21\%$ to $93.90 \pm 0.15\%$ respectively. This showed that the drug was uniformly distributed in all of these prepared solid dispersions and physical mixtures.

Characterization of Solid Dispersion In-vitro Dissolution Rate Studies

In vitro dissolution data of the selected drug, various solid dispersions using poloxamer 188, and their respective physical mixtures using phosphate buffer (pH = 6.8) are shown in Figures 3 and 4. All of the solid dispersion and the physical mixture samples showed improved dissolution of Lornoxicam. The dissolution enhancement is mainly aimed at the increased surface area of drug-exposed to big carrier molecules and increased wettability. Again, all of the solid dispersion samples showed more improved Lornoxicam dissolution than their respective physical mixture samples. The formulation LOR-PXM 188 Se 1:3 showed the highest percentage of drug discernment of 87.24% at 45 min. This observation showed that the improved dissolution of Lornoxicam from solid dispersion is because of the presence of the drug in the amorphous state when standardized with the physical mixture and pure drug, where the drug is present in the crystalline state.

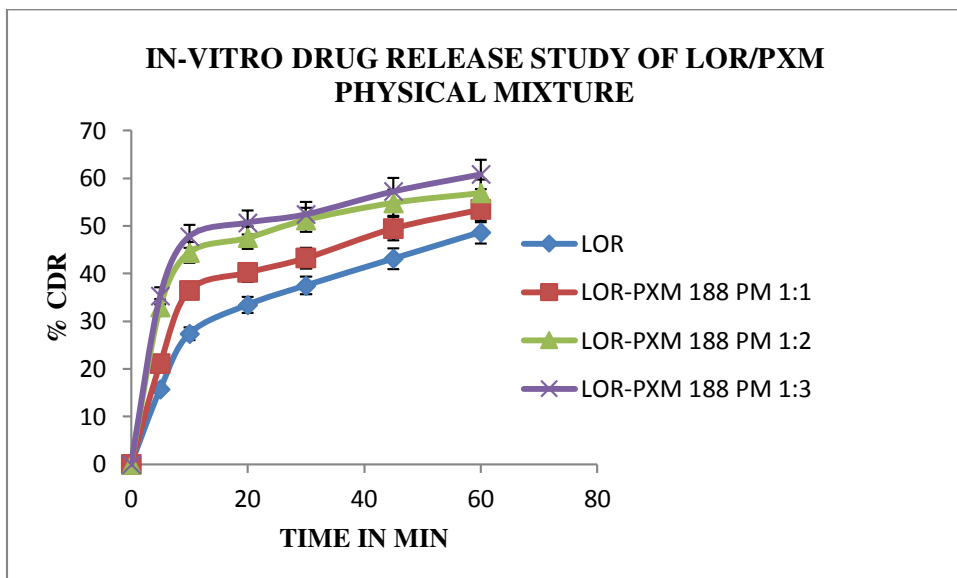


Fig.III: In-vitro drug release observation of Lornoxicam and poloxamer 188 physical mixtures

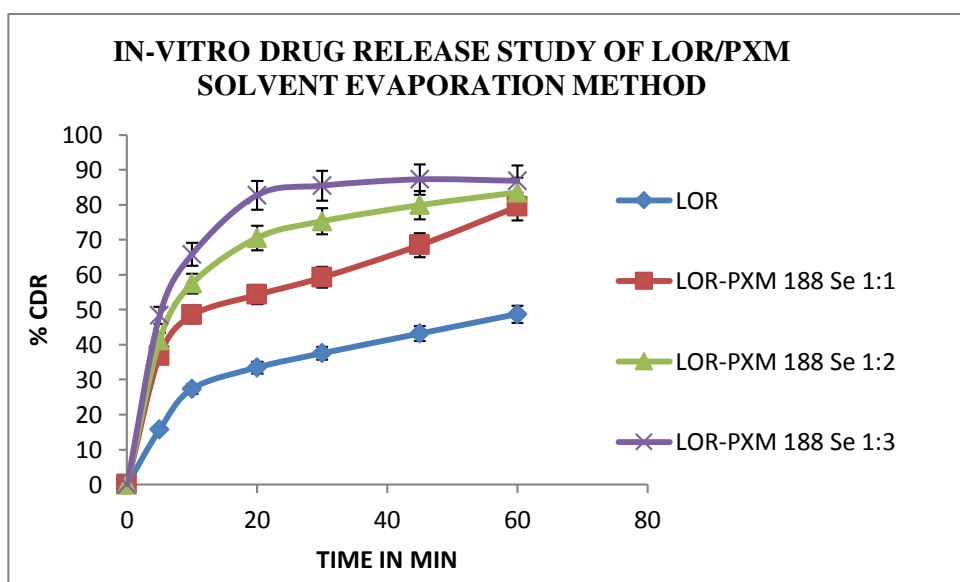


Fig. IV: In-vitro drug release study of Lornoxicam and poloxamer 188 Solid dispersions by solvent evaporation technique

FTIR Spectroscopy Analysis Fourier Transform infrared Spectroscopy

(FTIR) spectroscopy analysis was done to analyze physicochemical interactions between Lornoxicam and poloxamer 188. FTIR data of pure Lornoxicam, poloxamer 188, and physical mixture are shown in Figure 4. The characteristic peaks of pure Lornoxicam were initiated to be present in the spectra of the

physical mixture. Most important peaks seen were at Aromatic-CH: 3100 cm^{-1} , -NH: 3066 cm^{-1} , -C=O: 1647 cm^{-1} , -CONH-: 1594 cm^{-1} , -SO₂: 1327 cm^{-1} , C-Cl: 790 cm^{-1} . FTIR spectrum of poloxamer 188 showed important peaks at 1107 cm^{-1} (C-O stretch), 1448 cm^{-1} (C-H bending), and 2884 cm^{-1} (aliphatic C-H stretch). This finding reveals the lack of interaction between drug and the carrier in the sample.

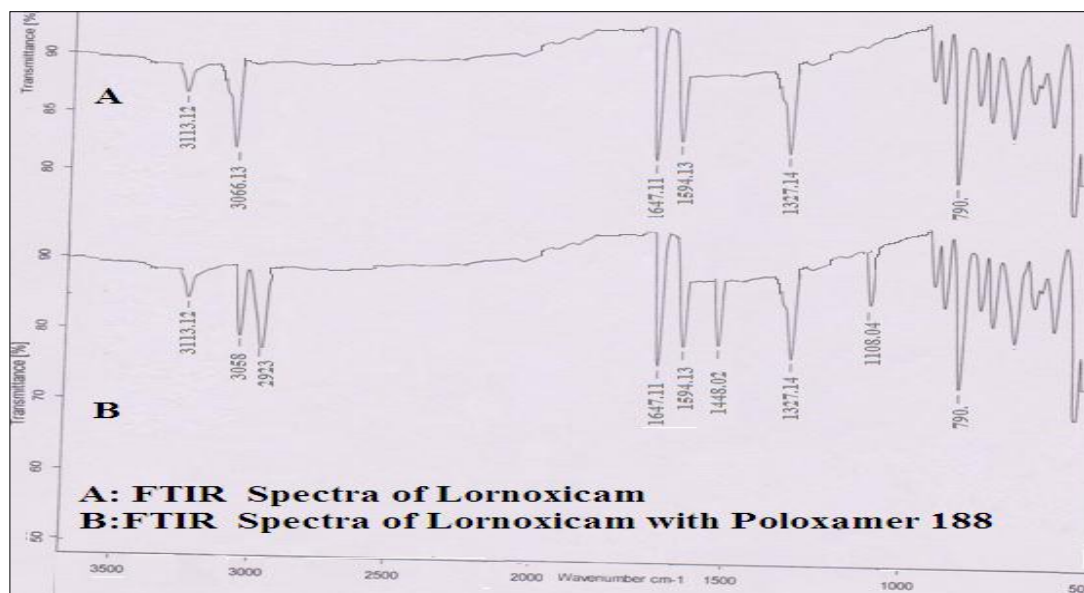


Fig. V: FTIR Spectra of pure lornoxicam and its physical mixtures with poloxamer 188

DSC Analysis

DSC analysis was done for pure Lornoxicam, and solid dispersions using poloxamer 188 have shown in Figure 5. The DSC thermogram data of pure Lornoxicam showed a very sharp endothermic peak observation at 221.46°C, corresponding its melting point. The DSC curve of poloxamer 188 showed an endothermic peak(sharp) at 65.2°C. The DSC data of the physical mixture from Lornoxicam with poloxamer 188 showed an endothermic peak at 65.2°C and 220.56 °C, which were the peaks of poloxamer 188 and Lornoxicam, respectively. Solid dispersion showed a melting point reduction to 201.45 deg Centigrade ranges with the widening of a peak. This reduction in melting point and broadening of the peak indicated conversion of crystalline fraction into amorphous one. We can assume a positive conversion here.

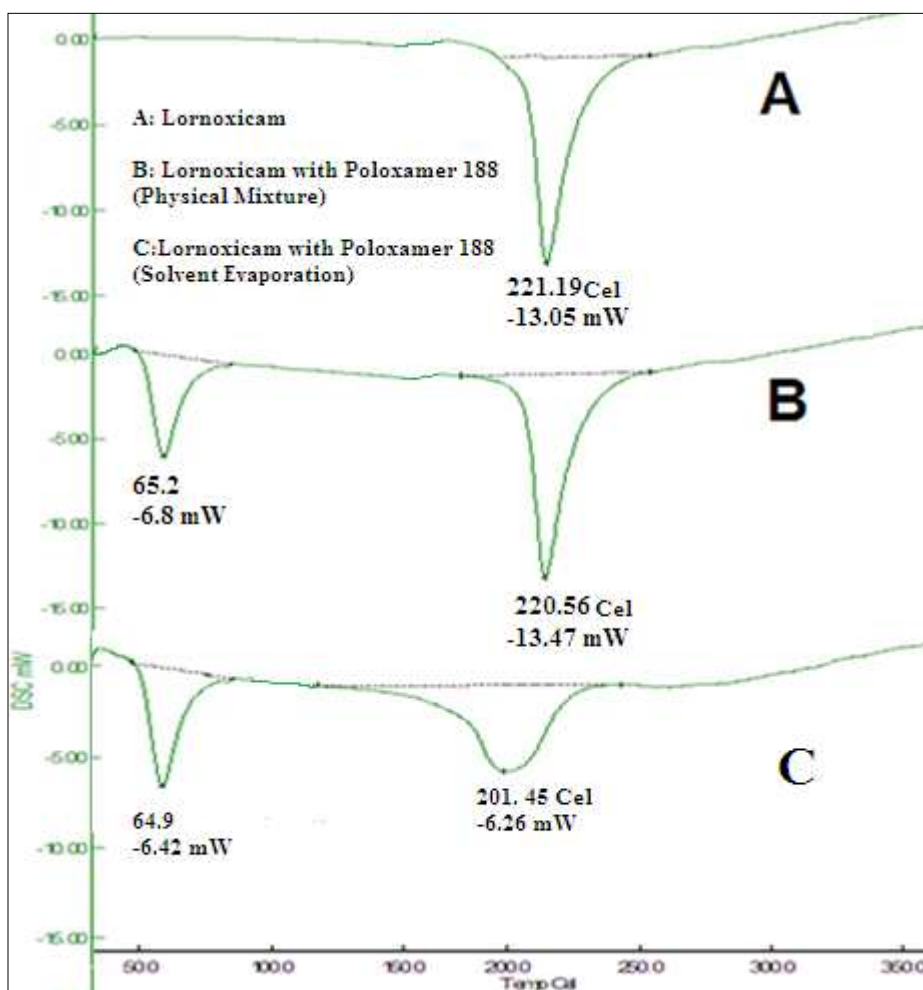


Fig.VI: DSC thermogram of Lornoxicam and its physical mixture; solid dispersion with poloxamer 188 made through solvent evaporation technique

Conclusion

This work prepared solid dispersions with Lornoxicam and poloxamer 188 using a solvent evaporation technique. In the phase solubility study, the drug showed better solubility using phosphate buffer pH 6.8 than distilled water. The distinct solubility of Lornoxicam increased with increasing carrier concentrations. Solid dispersions showed better dissolution of Lornoxicam than physical mixtures. Solid dispersion of LOR: PXM 188 Se (1:3) showed the maximum dissolution efficiency among all solid dispersions and physical mixtures. IR spectra indicated no well-defined interaction among the drug and polymer. DSC thermograms of solid dispersion indicated the complete miscibility of the drug in a carrier. The amorphous form of the Lornoxicam in SD was verified by a reduction in enthalpy of the drug melting in SD when compared to the pure drug. In conclusion, these results could indicate that SD made by the solvent evaporation techniques could help develop pharmaceutical products containing Lornoxicam.

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References

- Amidon, GL., Lennernas, H., & Shah, VP. (1995). A theoretical basis for a biopharmaceutics drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. *Pharmaceutical Research*, 12(3), 413–420
- Aungst, BJ., Nguyen, NH., Rogers, NJ., (1997). Rowe SM, Hussain MA, White SJ, Shum L. Amphiphilic vehicles improve the oral bioavailability of a poorly soluble HIV protease inhibitor at high doses. *Int J Pharm*, 156, 79–88.
- Chetan, VP., Swati, SM., Sagar, VB., (2020). Formulation and evaluation of mouth dissolving tablet of meloxicam using natural super disintegrants. *Asian J Pharm Clin Res*, 13(2), 197-203.
- Cook, J., Addicks, W., & Wu, YH. (2008). Application of the biopharmaceutical classification system in clinical drug development—An Industrial View. *The AAPS Journal*, (2), 306–310.
- Dua, K., Pabreja, K., & Ramana, MV. (2010). Preparation, Characterization, and In Vitro Evaluation of Aceclofenac Solid Dispersions. *ARS Pharm*. 51(1), 57-76.
- Gupta, S., & Ranawat, MS. (2012). Effect of Hydrophilic Polymers on Solubility Enhancement of Oral Antidiabetic Agent by Solid Dispersion Technique. *Asian Journal of Biochemical and Pharmaceutical Research*, 2(2), 299-306.
- Hance, L., & Beril, A. (2005). The regulatory in drug discovery and development: current status and future extension. *J Pharm Pharmacol*, 57(3), 273-85.
- Iyan, S., Insan, SKS., Desi, N., Arif, B. (2020). Improvement of simvastatin dissolution rate using the derivative non-covalent approach by solvent drop grinding method. *Int J App Pharm*, 12(1), 21-24.
- Kauslya, A., Payal, D., & Borawake, Jitendra, VS. (2021). Formulation and evaluation of floating microspheres of ciprofloxacin by a solvent evaporation method using different polymers. *Int J Pharm Sci*, 13(7), 101-108.
- Kulkarni, PK., Dixit, M., & Panner, S. (2012). Preparation and Evaluation of Naproxen solid Dispersion Technique. *International Research Journal of Pharmacy*, 3(9), 174-177.
- Kumar, B.P., Rao, S., & Murthy, K.V.R. (2011). Solid dispersion technique: A tool for enhancing the bioavailability of poorly soluble drugs. *Journal of Chemical and Pharmaceutical Sciences*, 4(4), 170-179.
- Lakshmi, K., Pranav, KRM., & Kaza, R. (2012). Dissolution enhancement of Telmisartan by surface solid dispersion technology. *International Journal of Innovative Pharmaceutical Research*, 3(4), 247-251.
- Lobenber, R., & Amidon, GL. (2000). Modern bioavailability, bioequivalence, and biopharmaceutics classification system. New scientific approaches to international regulatory standers. *European Journal of Pharmaceutics and Biopharmaceutics*, 50, 3-12.
- Lubna, Nousheen., & Rajasekaran, S. (2019). Preformulation Study on Enhancing the Solubility of Lornoxicam with Hydrophilic Carriers. *Indo Am. J. P. Sci*, 06(07). 14019-14026.

- Lubna, Nousheen., & Rajasekaran, S. (2022). Enhancement of Solubility And Dissolution Rate of Blonanserine By Lyophilization Technique. *High Technology Letters*, 28(4). 253-265.
- Mahesh, Limbachiya, N.T. (2012). Technique's solubility enhancement poorly soluble drugs: a review. *IJPRD*, 4(04), 71-86.
- Modi, A., & Tayade. (2006). Enhancement of dissolution profile by solid dispersion (kneading) technique. *PAAPS PharmSciTech*. 7(3), 68.
- Olkola, KT., Brunetto, AV., & Mattila, MJ. (1994). Pharmacokinetics of oxicam nonsteroidal anti-inflammatory agents. *Clin Pharmacokinet*, 26(2), 107-20.
- Patidar, K., Kshirsagar, MD., & Saini, V. (2011). Solid Dispersion Technology: A Boon for Poor Water-Soluble Drugs. *Indian Journal of Novel Drug delivery*, 3(2), 83-90.
- Payal, D., Borawake, KA., & Jitendra, VS. (2021). Formulation of solid dispersions for enhancement of solubility and dissolution rate of simvastatin. *Int J Pharm Pharm Sci*, 13(7), 94-100.
- Subrahmanyeswari, D., Prasanth, Y., & Sameeda, R. (2019). Formulation and development of efavirenz tablets by a paper technique using co-solvency method. *Int J Curr Pharm Res*, 11(6), 87-92
- Vasconcelos, T., Sarmiento, B., & Costa, P. (2007). Dispersions as a strategy to improve oral bioavailability of poor water-soluble drugs. *Drug Discovery Today*, 12(23/24), 1069-1075.
- Verma, S., Rawat, A., Kaul, M., & Saini, S. (2011). Solid dispersion: A strategy for solubility enhancement. *International Journal of Pharmacy and Technology*, 3(2), 1062-1099.