IJPSR (2020), Volume 11, Issue 5 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 06 March 2019; received in revised form, 05 April 2020; accepted, 15 April 2020; published 01 May 2020

DEVELOPMENT AND *IN-VITRO* EVALUATION OF LIQUISOLID COMPACTS OF LORNOXICAM

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Keywords:

Lornoxicam, Liquisolid compacts, Liquid load factor, Carrier, Coating material, *In-vitro* characterization

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ABSTRACT: The present study is undertaken with an aim to improve the dissolution profile and availability of a poorly soluble drug, Lornoxicam, through the development of liquisolid tablets. Liquisolid compacts were prepared by employing PEG 400, Avicel PH 112, and Aerosil 200 as solvent, carrier and coating materials, respectively. The flow properties of the drug improved significantly after formulating it into the liquisolid compacts. The post-compressional parameters of prepared tablets revealed the uniformity and maintenance of standards within the different batches. *In-vitro* drug release studies showed significant improvement in the dissolution of lornoxicam in its liquisolid form compared to a commercial product. The effect of formulation parameters, such as drug concentration and carrier to coat ratio, on enhancing drug dissolution, was also explored. FT-IR, DSC and XRD techniques were employed for the physical characterization of the drug in the liquisolid systems. The drug release from the optimized liquisolid compacts (F8) followed first-order release kinetics.

INTRODUCTION: Solubility is one of the important parameters to achieve the desired concentration of drug in systemic circulation for achieving required pharmacological response. Poorly water-soluble drugs often require high doses in order to reach the therapeutic plasma concentrations after oral administration. Most of the drugs are either weakly acidic or weakly basic, having poor aqueous solubility, thus producing major problems with formulation development of new chemical entities. Hence, a significant number of new and possibly beneficial chemical entities do not have suitable pharmaceutical dosage form because of their poor solubility and poor dissolution rate [1, 2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(5).2135-46

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(5).2135-46

To overcome these problems, 'liquisolid compacts', a new and promising technique towards the dissolution enhancement has been recently developed [3]. Liquisolid compacts are acceptably flowing and compressible powdered forms of liquid medications and have industrial application [4, 35]. They are prepared by simple blending with selected powder excipients referred to as the carriers and the coating materials. Many grades of cellulose, starch, lactose can be used as carriers, whereas silica's of very fine particle size can be used as coating materials. In such systems, the drug exists in a molecular state of subdivision and systems were free flowing, non-adherent, dry looking powders [3, 5, 6, 39].

Lornoxicam is an extremely potent member of the oxicam group of NSAIDs that is widely used in the management of peri/postoperative pain associated with different surgeries [7, 8]. It is a congener of tenoxicam and chemically it is 6-chloro-4-hydroxy-2-methyl-N-2-pyridyl- 2H-thieno [2, 3-e]-1, 2-thiazine-3-carboxamide-1,1-dioxide with marked

analgesic properties. Lornoxicam is a highly selective COX-2 inhibitor used for a variety of acute and chronic inflammatory diseases [8]. Studies have shown that it is more effective than 10 mg morphine when used at doses > or = 8 mg to control pain after oral surgery. The drug has a relatively short plasma half-life (3 to 5 h) and is eliminated following biotransformation to 5'-hydroxy-lornoxicam [9]. However, lornoxicam exhibits very poor solubility in low pH conditions present in the stomach which might consequently lead to a delay in its analgesic effect associated with local irritation and ulceration due to the long contact time of the insoluble drug crystals with the stomach wall [10, 36].

Various research works on solubility enhancement of lornoxicam by different techniques like self-emulsifying drug delivery systems [11], solid dispersions [12], complexation with cyclodextrins [13], micronization [14] are reported. Surprisingly, no reports on the development of lornoxicam liquisolid compacts are available till date. Hence, in light of the above, the present study has been undertaken on the development and evaluation of liquisolid compacts of lornoxicam with an aim to improve its solubility and dissolution, thereby increasing the therapeutic efficacy [37, 40].

MATERIALS AND METHODS:

Materials: Lornoxicam was obtained as gift sample from Micro labs, Goa and Avicel PH 112 from Libraw Pharma, New Delhi. Aerosil 200 was obtained from HiMedia Laboratories Pvt., Ltd., Nasik. Sodium Starch Glycolate, Magnesium Stearate, Purified Talc, Propylene Glycol, Polyethylene Glycol 400, Polyethylene Glycol 600, Sodium hydroxide and Hydrochloric Acid were from S. D. Fine-Chem Ltd, Mumbai; Tween 20, Tween 80 and Potassium Dihydrogen Ortho-phosphate were obtained from RFCL Ltd., New Delhi.

Solubility Studies: [15] Solubility studies of Lornoxicam were carried out in water, phosphate buffer of pH 7.4, PEG 400, PEG 600, PG, Tween 80 and Tween 20. Saturated solutions were prepared by adding excess drug to the vehicles and shaking on the water bath shaker for 12 h at 37 ± 0.5 °C under constant shaking. After 12 h solutions were kept for sonication for 20 min. Filtered samples (1 ml) were diluted appropriately with phosphate buffer of pH 7.4 and lornoxicam was determined spectrophotometrically at 377 nm. Average of triplicate was taken.

Holding Capacity of the Excipients: The capacity of each excipient to hold liquid and behave like dry powder (holding capacity) was determined using the following simple technique [16]. Accurately weighed quantity of PEG400 (1g) was transferred to a mortar. Carrier and coating materials were individually and gradually added in small propositions and the mixture was triturated after each addition to help distributing the liquid throughout the powder particles. The addition of each powder and the trituration was continued until mortar contents start to look like dry and free flowing powder which was further confirmed by the determination of angle of slide. The required amount of carrier material was weighed and placed on a slide (glass or metal) and gradually raised till the slide is angular to the horizontal. Angle at which the carrier slides from the slide was measured and is known as angle of slide. The angle of slide value of 33° is optimum for flow of powders [10, 17, 36].

Determination of Liquid load factor (Lf): Liquid load factor (Lf) is defined as the weight ratio of the liquid medication (w) and carrier powder (Q) in the system (*i.e.,* Lf = W/Q), which must be possessed by an acceptably flowing and compressible preparation. Constant weight of PEG 400 was placed indifferent mortars containing different weights of Avicel PH 112, the selected carrier according to the previous results and triturate well. The final mass was checked for their consistency, flowability, and compressibility properties and then compressed into tablets and their texture, hardness were detected. This procedure was repeated by varying the coating: carrier material ratio to improve the flowability and the compressibility properties of the prepared mixtures [18].

Preparation of Liquisolid Compacts: [1] Various liquisolid compacts were prepared by initially dissolving the known quantity of lornoxicam in the nonvolatile vehicle PEG 400. To this, a binary mixture of carrier (Avicel PH 112) and coating material (Aerosil-200) prepared at a ratio of 10:1, 20:1, 30:1 and 40:1 was added. From the calculated

Φ-value, the liquid load factor (Lf) was calculated [19]. Depending upon the drug concentration in liquid medication, different liquid load factors were employed in liquisolid preparations. Different concentrations of Avicel and silica were used to prepare different liquisolid formulations. Finally, sodium starch glycolate as a super-disintegrant and magnesium stearate and talc were added to the above powder blend and mixed. The final powder blend was subjected to compression by using 10 station rotary compression machine (Rimek mini press, Karnavathi Engineering Ltd, Gujarat).The composition of the liquisolid compacts are shown in **Table 1**.

Pre-compressional Evaluation of Liquisolid Systems:

Drug Content: Excess amount of each liquisolid formulation was placed in 100ml volumetric flask and were then dissolved in phosphate buffer of pH 7.4. The content was kept on water bath shaker for 24h and then sonicated for 20 min. Further after suitable dilutions lornoxicam solubility was determined spectrophotometrically at 377 nm using UV spectrophotometer. Results are shown in **Table 4**.

Flow Properties: The flow properties of the liquisolid systems were estimated by determining the angle of repose, angle of slide, Carr's index and Hausner's ratio.

Angle of Repose: [20] Angle of repose was determined using fixed funnel method. A glass funnel is held in place with a clamp on a ring support over a glass plate. Approximately 1 gm of powder is transferred into funnel keeping the orifice of the funnel blocked by the thumb. When the powder is emptied from funnel, the angle of the heap to the horizontal plane is measured. The angle of repose was determined by using the following formula:

$$\text{Angle of repose } (\Theta) = \tan^{-1}(h/r)$$

Apparent Bulk Density: [21] Apparent bulk density was determined by placing pre-sieved drug excipient blend in to a graduated cylinder and measuring the volume and its weight. The density was determined by using the following formula:

$$\text{Density} = \text{Mass} / \text{Volume}$$

Tapped Density: [21] Weighed sample of powder mixture was transferred to a graduated cylinder and was tapped for a fixed time or for a fixed number of taps (100). The tapped density was determined by using the following formula:

$$\text{Tapped density} = \text{Weight of powder taken} / \text{Tapped volume}$$

Carr's Index: [22] Based on the apparent bulk density and the tapped density, the percentage compressibility of the powder mixture was determined by the following formula-

$$\text{Carr's index (\%)} = \text{Tapped density} - \text{Bulk density} \times 100 / \text{Tapped Density}$$

Hausner's Ratio: [22] Hausner's ratio is an indirect index of ease of measuring the powder flow. It is calculated by the following formula.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density}$$

Post-compressional Evaluation of Liquisolid Compacts: Pfizer hardness tester was used for the determination of the hardness. The readings were noted in kg/cm^3 to break tablets. The crown-to-crown thicknesses of 10 tablets from each batch were determined using Vernier calipers. Weight variation was determined by randomly picking twenty tablets from each batch and weighed individually. The average weight and standard deviation was calculated and reported. Friability of the tablets was determined using Roche friabilator. Tablets were re-dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula:

$$F = 1\text{-}W0 \times 100 / W$$

Where, W0 is the weight of the tablets before the test and W is the weight of the tablet after the test.

Infra-Red Spectra Analysis: IR spectrum of optimized formulation was recorded by KBr method using Shimadzu (8400) spectrophotometer. A baseline correction was made by using dried potassium bromide and then the spectrum of powder with potassium bromide was recorded. Sample was scanned from 4000 to 400 cm^{-1}. The compatibility of drug and other excipients in formulation was confirmed by comparing drug and formulation spectra.

Differential Scanning Calorimetry: Thermograms of the Lornoxicam and its liquisolid formulations were recorded. The analysis was carried out by heating 2 to 3 mg of sample on an aluminum crimp pan at rate of 10 °C/min in nitrogen atmosphere.

X-ray Diffraction: Crystallinity study was carried out by comparing XRD spectrum of drug with formulation to check peak of drug in individual state and in formulation. Study was carried out on XRD Instrument. The data was recorded at 2θ range of 10 to 60 °C at time of 0.5 sec. The relative intensity I/I0 and inter- planar distance (d) corresponding to 2θ value were reported and compared.

Drug Content: [23] Ten tablets from each batch were taken randomly to examine its content uniformity. Each tablet was weighed and crushed individually. The crushed tablet powders were dissolved in phosphate buffer of pH 7.4. The solutions were kept on water bath shaker for 24 h. It was then sonicated for 20 min. The solutions were filtered using Whatman filter paper. The drug content was then measured using UV spectrophotometer at 377nm. Results are shown in **Table 4**.

Disintegration Time: [24] The disintegration time of the tablet was measured in phosphate buffer of pH 7.4 (37 ± 2 °C) according to disintegration test apparatus with disk. The time in minutes taken for the complete disintegration of the tablet with no palpable mass in the apparatus was measured in minutes. Three tablets from each batch (formulation) were tested for the disintegration time calculations.

***In-vitro* Dissolution Studies:** The *in-vitro* release profiles of lornoxicam from liquisolid compacts and marketed tablet (Flexilor) were obtained using an 8 station USP (Type-II) dissolution test apparatus (Electro Lab, TDT-08L, Mumbai). The dissolution study was carried out in 900 ml of phosphate buffer of pH 7.4 as the dissolution medium at 37 °C ± 2 °C and 100 rpm. Then 5 ml samples were collected at every 5 min intervals. The dissolution medium was replaced with 5 ml fresh dissolution fluid. The withdrawn samples were filtered and analyzed spectrophotometrically at 377 nm. The mean of three determinations was used to calculate the drug release from each of the formulations [18].

Kinetic Study: [25, 26, 38] The release mechanism was analyzed by fitting the dissolution data into various kinetic models like zero order, first order, Higuchi and KoresmayerPeppas equations.

Stability Studies: [26, 38] The stability study of the selected formulations was carried out according to ICH guidelines at 40±2 °C/75±5% RH for three months by storing the samples in stability chamber.

RESULTS AND DISCUSSION:

Solubility Study: For the preparation of liquisolid compacts, the drug has to be initially dissolved in the non-volatile solvent. The solubility study was carried out in PEG 600, PEG 400, PG, Tween 80, Tween 20, Phosphate buffer of pH 7.4 and distilled water. Lornoxicam showed higher solubility in PEG 400 than PEG 600, PG, Tween 80, Tween 20, Phosphate buffer of pH 7.4 and distilled water. The order of drug solubility in different media was PEG 400 > Tween 20 > PEG 600 > phosphate buffer of pH 7.4 > Tween 80 > distilled water > PG. Hence, PEG 400 was selected as the non-volatile solvent to dissolve the drug in the preparation of liquisolid compacts. The results of solubility study of Lornoxicam in various media are shown in **Table 2**.

FT-IR Studies: In the present work, the physico-chemical parameters of drug and its formulations is established by analytical techniques and spectroscopic methods. The analytical techniques such as differential scanning colorimeter, X-ray diffraction method and spectroscopic technique like infra-red spectroscopy are employed to ascertain the physico-chemical properties of drug and its formulations.

The IR spectrum of the formulation containing the pure drug lornoxicam, polymer Avicel PH-112 and other excipients showed its characteristic absorption bands almost in the same pattern as that of pure drug. By the observation of the spectrum, it is evident that the optimized formulation (F8) had moisture content at the time of taking the spectrum using IR spectrophotometer. If moisture is present in the compound while taking the spectrum generally the peaks will not be resolved properly. Hence, several peaks either disappear or all together appear as a weak broad peak. It is clear from the spectrum of the formulation that all the

important peaks mentioned above in the prescription of the pure drug exist and they appear as very rare peaks without any shift in their positions. The carbonyl groups which will never miss in the spectrum exist in the same position but it's not numbered. The additional peaks present in the spectrum are that of Avicel PH-112 and other excipients. Hence, it can be concluded that the IR spectrum of the formulation has poor resolution but the spectrum gives enough evidence for the characterization of peaks of functional groups and different bands present in the drug molecule without any change in the positions of the band. The spectrum gives information that in addition to the peaks of polymers and excipients, all the peaks of drug do exists with varying intensity suggesting that there is no interaction of the drug with the polymer and other excipients. Thus, there is compatibility of the drug with the polymer and excipients used in the present study as shown in **Fig. 1**.

DSC Studies: The DSC thermograms for the pure drug and its optimized formulation are taken for establishing physico-chemical parameters of the drug. These thermograms explain effect of temperature on the thermal behavior of the drug. The thermogram of pure drug showed sharp, significant, exothermic peaks at 227.55 °C. This temperature correspondence to the melting point reported for the drug. It is evident from the literature survey that the pure drug has the melting range of 225 -230 °C.

The thermogram of optimized formulation (F8) exhibited two broad endothermic peaks around 90 °C and around 340 °C and one sharp intense significant exothermic peak corresponding to the temperature 227 °C as depicted in **Fig. 2**. The two broad endothermic peaks may be that of the polymer Avicel PH-112. The values of these endothermic peaks are close to that of pure polymer Avicel PH-112 in the literature. The peak at highest value of 340 °C might correspond to volatilization of water. The distinct exothermic peak at 227 °C is not changed and is same as the melting point of pure drug. Since, no change in the nature of the peak and melting point, it may be concluded that the drug has not shown any type of interaction and its compatibility with the excipient can be established.

XRD Studies: The X-ray diffraction analysis for the drug and its optimized formulation (F8) are taken for comparative study and establishing physico-chemical properties of the drug. The X-ray diffraction pattern of compound showed neat, sharp and intense peaks (in **Fig. 3**), indicating its crystalline nature. Crystallinity was determined by comparing some representative peak with those of the drug. The relationship used for the calculation of crystallinity was relative degree of crystallinity (RDC).

$$RDC = Isam / Iref$$

Where, Isam is the peak height of the sample under investigation and Iref is the peak height at the same angle of for the reference with the highest intensity.

The X-ray diffraction pattern for the formulation revealed that the peak heights are reduced and different diffraction patterns is observed. The result suggests that the crystallinity of drug has changed to amorphous which is clear in the reduction of peak heights. Since peak position i.e. angle of diffraction, is an indication of crystal structure and peak heights in diffractogram are images of sample crystallinity. It can be concluded that there is change in the crystalline nature to the amorphous without the interaction of the drug with the polymer.

Micromeritic Properties: The method employed for tableting in this study was direct compression for which the drug should possess good flow properties in order to get a uniform feed as well as reproducible filling of tablet dies, the failing of which may lead to high dose variations. In order to ensure the flow properties of the liquisolid systems for direct compression into tablets, angle of repose measurements, Carr's index and Hausner's ratios were adopted for further evaluation [27-30]. Pure drug lornoxicam exhibited high angle of repose value (45.07 ± 0.73) indicating extremely poor flow property. Poor flow property was further supported by high Carr's index value (39.05 ± 0.78%) and Hausner's ratio (1.65 ± 0.56). Hence, lornoxicam liquisolid compacts were prepared which not only increases the solubility but also the flow properties. The prepared liquisolid compacts indicated improved flow properties as witnessed by the values of angle of repose (22.24 ± 0.98° - 30.52 ± 0.98°), Carr's index (7.43 ± 0.98 % - 15.70 ±

0.42%) and Hausner's ratio (1.08 ± 0.43 - 1.18 ± 0.48) compared to pure drug. The flowability improvement can be attributed to the high porosity and high specific surface area of polymers used, which allows penetration of liquid into the particle pores resulting in a weight gain of individual particle accompanied by better flow properties [31]. It was also observed that as the concentration of drug in the liquisolid compacts increased, the flow parameters were reduced proportionately. This could be due to reduced quantity of coating material (Aerosil 200) utilized in the preparation of liquisolid compacts prepared as per the reported mathematical model [1].

Post-compressional Studies:

Hardness: Different batches of lornoxicam liquisolid tablets exhibited hardness within the range of 2.1 - 4.4 Kg/cm^2 as determined by Pfizer hardness tester. The hardness of the liquisolid compacts were within the Pharmacopoeial range[32] and were found to be ideal for easy disintegration of the tablets. Our results of tablet harness are in accordance with El-say KM *et al*.

Friability: Friability test indicates physical strength of compressed tablets. Tablets from each formulation were tested for friability using Roche friabilator. The friability values of different batches of tablets were found to be within 0.41 ± 0.01 - 0.60 ± 0.03, which showed that tablets with higher hardness has lesser friability values as shown in **Table 4**.

Average Weight: Randomly twenty tablets were selected and their weights were determined individually and collectively using single pan electronic balance. The average weight of the tablets was found to be in the range of 107.68 ± 0.30 - 430.21 ± 0.43 and presented in **Table 4**.

Disintegration Time: The disintegration time for the prepared lornoxicam liquisolid tablets are shown in **Table 4**. All investigated tablets met the Pharmacopoeial requirements for disintegration[32]. The disintegration time ranged from 1.54 to 4.52 min for different batches of tablets. It was found that, when the Lf value was increased the disintegration time of the tablets proportionately decreased. This could be due to the fact that, increasing the Lf value in the formulation necessitates a decrease in the amount of powder excipient and this subsequently decreases the disintegration time of the tablets. Similar results of disintegration were also observed by El-Say KM *et al.,* in their work on formulation and evaluation of rofecoxib liquisolid tablets.

Drug Content: Drug content was determined for all the batches of the liquisolid compacts as explained in the methodology. The drug content ranged from 98.58 - 99.92% for the different batches of liquisolid compacts. The drug content in all the batches remained high and reproducible as indicated in **Table 4**. Since, all the formulations contains, not less than 95% and not more than 105% of the labeled potency, thus meeting the IP specifications. The studies were carried out in triplicate and the average values were considered as drug content in the liquisolid tablets.

***In-vitro* Release Study:** Liquisolid formulations not only increases the flowability but also increases the solubility and dissolution of drugs contained in them. Hence, *in-vitro* release profiles of lornoxicam from its pure form, liquisolid compacts and marketed tablets were studied using 8 basket USP-type II dissolution test apparatus. The results of the dissolution studies are depicted in **Fig. 4** & **5**, and further discussed under the following headings:

Pure Drug: Various reports indicate the negligible solubility and dissolution of lornoxicam in lower pH ranges but the solubility increases as the pH of the medium is elevated from acidic to neutral or alkaline. Hence, phosphate buffer of pH 7.4 was used for the dissolution of pure drug lornoxicam. However, even with the medium of higher pH, the dissolution of pure drug was found to be 98.55% at the end of 120 min. This reveals that the pure drug lornoxicam possess poor dissolution rate and thus makes it an ideal candidate for preparing liquisolid compacts in order to improve its solubility, dissolution and bioavailability.

Effect of Carrier:

Coat Ratio: Different batches of lornoxicam liquisolid compacts were prepared by varying the drug concentrations and R values (ratio of carrier: coat material) and subjected for dissolution studies. When the ratio of Avicel: Aerosil was changed from 10:1 to 40:1, the dissolution rate of lornoxicam increased proportionately irrespective of the concentration of drug used in the

formulations. This could be probably due to the fact that, liquisolid compacts with lower R-values contain relatively smaller amounts of carrier powder and larger quantities of fine drug loaded silica particles. Also, the ratios of the amounts of their liquid medication per powder substrate are relatively higher leading to poor dissolution. On the other hand, liquisolid compacts with higher R-values contain low liquid/powder ratios, high presence of cellulose and low presence of silica. This could be directly associated with enhanced wicking, disintegration and deaggregation properties. Therefore, the liquisolid tablets with high R-values showed relatively more dissolution compared to those prepared with low R-values.

Effect of Drug Concentration: The effect of drug concentration on the release of lornoxicam was studied by preparing the liquisolid compacts with drug concentrations (10-40% w/v) and subjected for dissolution studies. It was observed that, as the concentration of drug in the liquisolid compacts increased there was a proportionate decrease in the drug release. The lesser drug concentration in the vehicle means more fraction of the drug is liable to be in the liquid solution form (*i.e.,* molecularly dispersed), which is a prerequisite for fast drug dissolution. Moreover, the more vehicle available means an even distribution of the vehicle over the remaining undissolved drug particles that will help in good wetting of the drug during the dissolution step [33]. This finding can be confirmed by comparing F5 with F9 that depicts 85.29% and 64.07% of drug release after 30 min F5 has % drug value of 20 while F9 has 30 with R being constant 10. Various other researchers also showed the increased dissolution of the drugs from the liquisolid compacts prepared with lower drug concentrations.

Comparison with the Marketed Product: To assess the efficacy of the prepared liquisolid compacts, optimized formulation (F8) was compared with the marketed product (Flexilor 8 mg conventional tablet).

From the dissolution profiles, it can be seen that the optimized liquisolid formulation (F8) significantly improved drug dissolution as compared to marketed tablet. Complete dissolution of drug within 15 min from F8 formulation (99.06%) was observed compared to that Flexilor which extended to 90 min to give complete drug release (98.60%). Due to significantly increased wetting properties and surface area of the drug particles available for dissolution, liquisolid tablets showed enhanced drug release characteristics and thereby improving oral bioavailability.

Release Kinetics: *In-vitro* release data obtained for the optimized formulation F8 and marketed product were fitted to zero order, first order, Higuchi's and Korsemeyer-Peppas equations to understand the mechanism of drug release from the liquisolid compacts. High regression values were observed with first order followed by Peppas, Higuchi's and zero order equations for both optimized formulation as well as marketed product. The R values were found to be 0.956 and 0.973 for F8 and marketed product respectively. Thus, the kinetic analysis of dissolution data indicated the first order release mechanism for both optimized formulation as well as marketed product.

Stability Studies: The stability studies were carried out for the selected formulation (F8) at 40±2 °C/ 75±%5 RH as per ICH guidelines for a period of three months. The results indicated that, the tablets did not show any physical changes (thickness, hardness and friability) during the study period. The drug content was found to be 99.90 ± 0.31% for F8 at the end of three month. The *in-vitro* dissolution study showed 98.64% drug release for F8 indicating that tablets remained fairly stable during storage conditions.

TABLE 1: COMPOSITION OF LORNOXICAM LIQUISOLID COMPACTS

Code	% of drug in PEG 400	R value	Lf Value	Carrier material Q (mg)	Coating material q (mg)	Total Quantity (mg)	Unit dose (mg) for 8mg
F1	10	10	0.417	2634.74	263.47	4201.34	336.10
F2	10	20	0.325	3377.34	168.87	4882.22	390.57
F3	10	30	0.295	3726.28	124.21	5201.99	416.16
F4	10	40	0.279	3931.38	98.28	5390.27	431.22
F5	20	10	0.417	2874.25	287.42	4583.29	183.33
F6	20	20	0.325	3684.37	184.22	5326.05	213.04

F7	20	30	0.295	4065.04	135.50	5674.93	227.00
F8	20	40	0.279	4288.78	107.22	5880.30	235.21
F9	30	10	0.417	3113.77	311.38	4965.25	132.41
F10	30	20	0.325	3991.40	199.57	5770.00	153.87
F11	30	30	0.295	4403.79	146.79	6147.76	163.94
F12	30	40	0.279	4646.17	116.15	6370.40	169.87
F13	40	10	0.417	3353.29	335.33	5347.20	106.94
F14	40	20	0.325	4298.34	214.92	6213.63	124.27
F15	40	30	0.2952	4742.55	158.08	6620.72	132.41
F16	40	40	0.2798	5003.57	125.08	6860.32	137.21

All formulations contain PEG 400 (1000 mg), 2% Sodium starch glycolate as super disintegrate, and 1% talc and magnesium stearate as a lubricant.

TABLE 2: PREFORMULATION STUDIES OF PURE DRUG LORNOXICAM

Studies	Melting Point (°C)	Identification (UV)*	Solubility (mg/ml)*						
			Phosphate buffer of pH 7.4	PEG 600	PEG 400	PG	Tween 80	Tween 20	Distilled water
Result	222 - 226	377 nm	10.34 ±0.23	10.54 ±0.55	15.65 ±0.42	5.54 ±0.42	6.61 ±0.19	10.77 ±0.55	6.19 ±0.38
Reported [46]	225 - 230	371 nm	10.15 ±0.11	9.97 ±0.32	16.12 ±0.35	5.59 ±0.12	8.02 ±0.36	11.32 ±0.52	7.72 ±0.37

*Average of 3 determinations ± SD

TABLE 3: SOLUBILITY STUDIES OF LORNOXICAM COMPACTS IN PHOSPHATE BUFFER OF pH 7.4

Code	F1	F2	F3	F4	F5	F6	F7	F8
Solubility* (mg/ml)	15.81 ±0.37	16.09 ±0.15	15.63 ±0.53	16.55 ±0.35	15.55 ±0.36	16.07 ±0.19	15.66 ±0.41	16.39 ±0.21
Code	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**
Solubility* (mg/ml)	15.35 ±0.05	15.93 ±0.12	16.03 ±0.22	16.13 ±0.62	15.05 ±0.26	15.79 ±0.43	16.21 ±0.33	15.90 ±0.39

*Average of 3 determinations ± SD

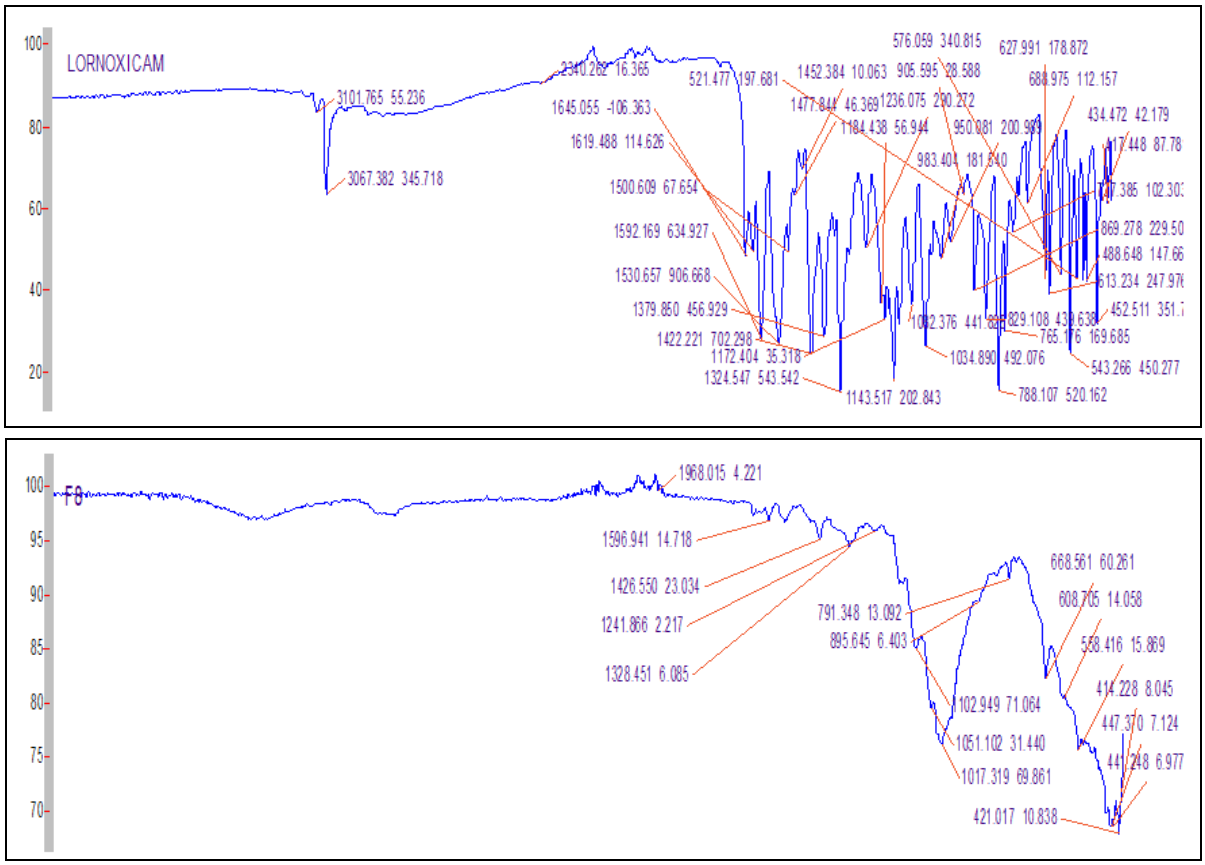

FIG. 1: FTIR OF PURE DRUG LORNOXICAM AND OPTIMIZED LIQUISOLID TABLET (F8)

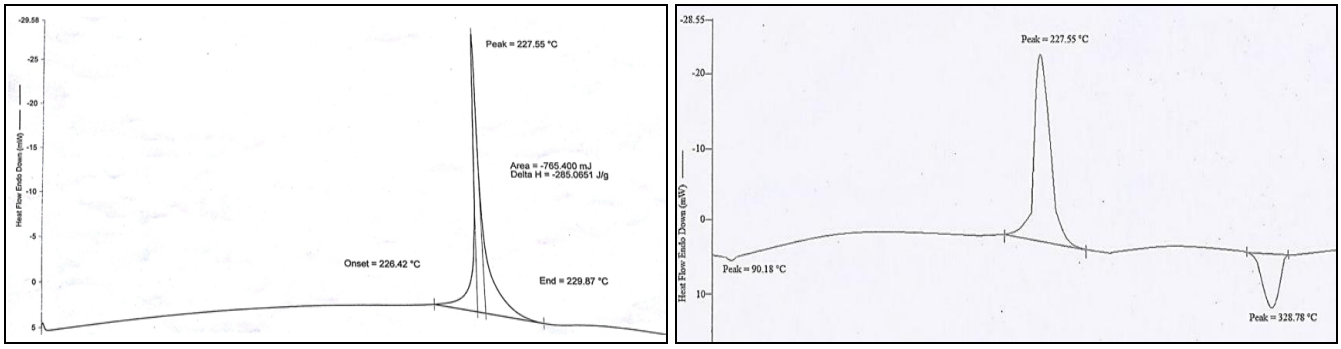

FIG. 2: DSC OF PURE DRUG LORNOXICAM AND OPTIMIZED LIQUISOLID TABLET (F8)

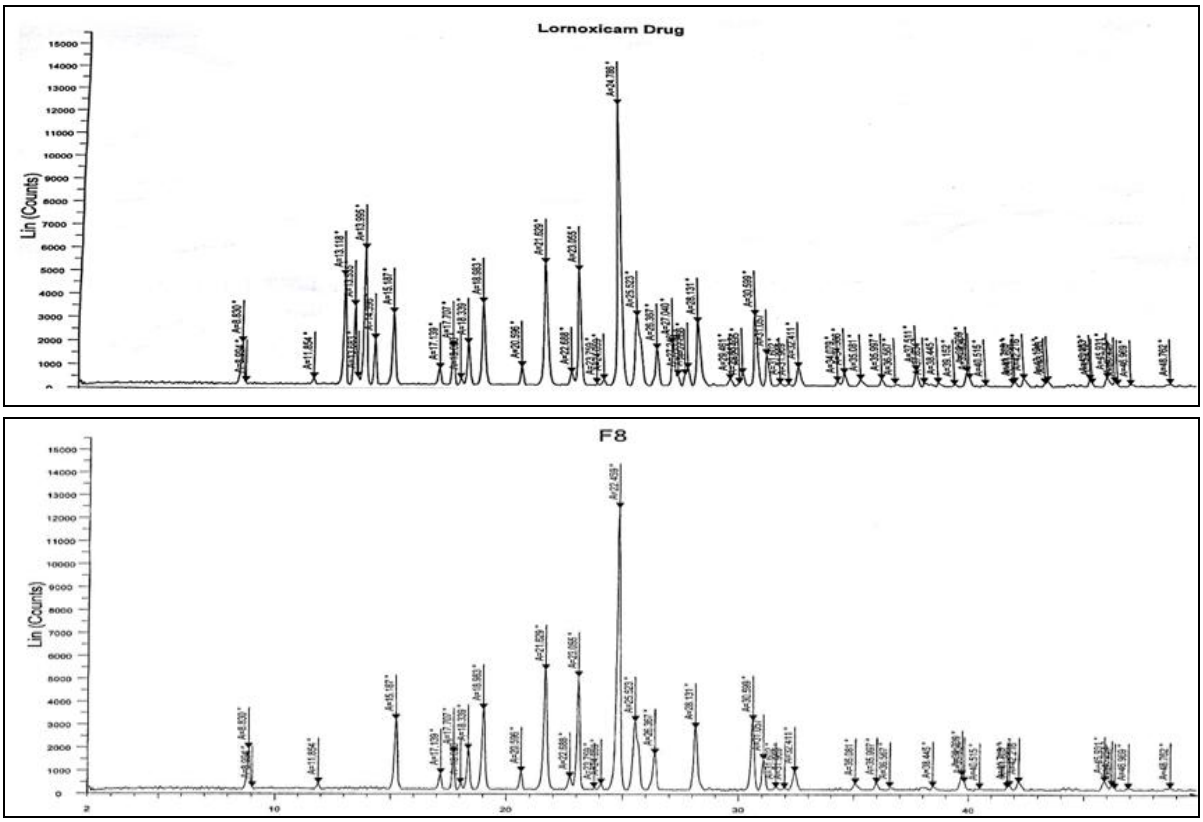

FIG. 3: XRD OF PURE DRUG LORNOXICAM AND OPTIMIZED LIQUISOLID TABLET (F8)

TABLE 4: PHYSICOCHEMICAL EVALUATION OF LIQUISOLID TABLETS

Code	Hardness ^ (Kg/cm^2)	Thickness# (mm)	Friability# (%)	Average weight* (mg)	Drug content* (%)	Disintegration time** (min)
F1	2.2±0.11	0.35±0.15	0.58±0.01	336.17±0.41	98.58±0.03	2.21
F2	2.4±0.12	1.04±0.34	0.55±0.03	390.79±0.25	98.58±0.03	2.32
F3	2.9±0.11	1.04±0.19	0.48±0.02	416.08±0.21	98.68±0.08	2.53
F4	2.8±0.13	1.04±0.37	0.50±0.02	430.21±0.43	98.68±0.06	2.62
F5	2.5±0.16	0.38±0.48	0.52±0.02	183.87±0.39	99.54±0.17	2.39
F6	2.9±0.11	0.29±0.65	0.47±0.04	213.04±0.27	98.77±0.03	3.06
F7	3.4±0.14	0.31±0.75	0.45±0.01	227.10±0.36	98.68±0.10	3.54
F8	2.1±0.12	0.53±0.16	0.60±0.03	235.23±0.08	99.92±0.05	1.54
F9	3.0±0.13	0.29±0.35	0.48±0.06	132.18±0.58	99.64±0.42	2.48
F10	3.5±0.11	0.34±0.29	0.44±0.01	153.85±0.18	99.35±0.16	3.21
F11	3.8±0.12	0.33±0.34	0.41±0.01	163.73±0.26	98.68±0.27	3.23
F12	4.4±0.11	0.34±0.19	0.32±0.03	169.54±0.40	99.16±0.18	3.31
F13	3.0±0.16	0.24±0.37	0.46±0.01	107.68±0.30	98.58±0.27	3.47
F14	4.0±0.14	0.29±0.48	0.38±0.01	124.48±0.38	98.78±0.17	3.51
F15	3.7±0.11	0.38±0.65	0.43±0.06	132.48±0.29	99.44±0.03	4.45
F16	3.2±0.14	0.38±0.16	0.46±0.04	137.52±0.28	98.49±0.05	4.52
MP	2.6±0.07	0.32±0.11	0.41±0.08	143.70±0.48	100.11±0.023	2.11

All values are expressed as mean ± SD; ^n=6, #n=10, *n=20, **n=3.

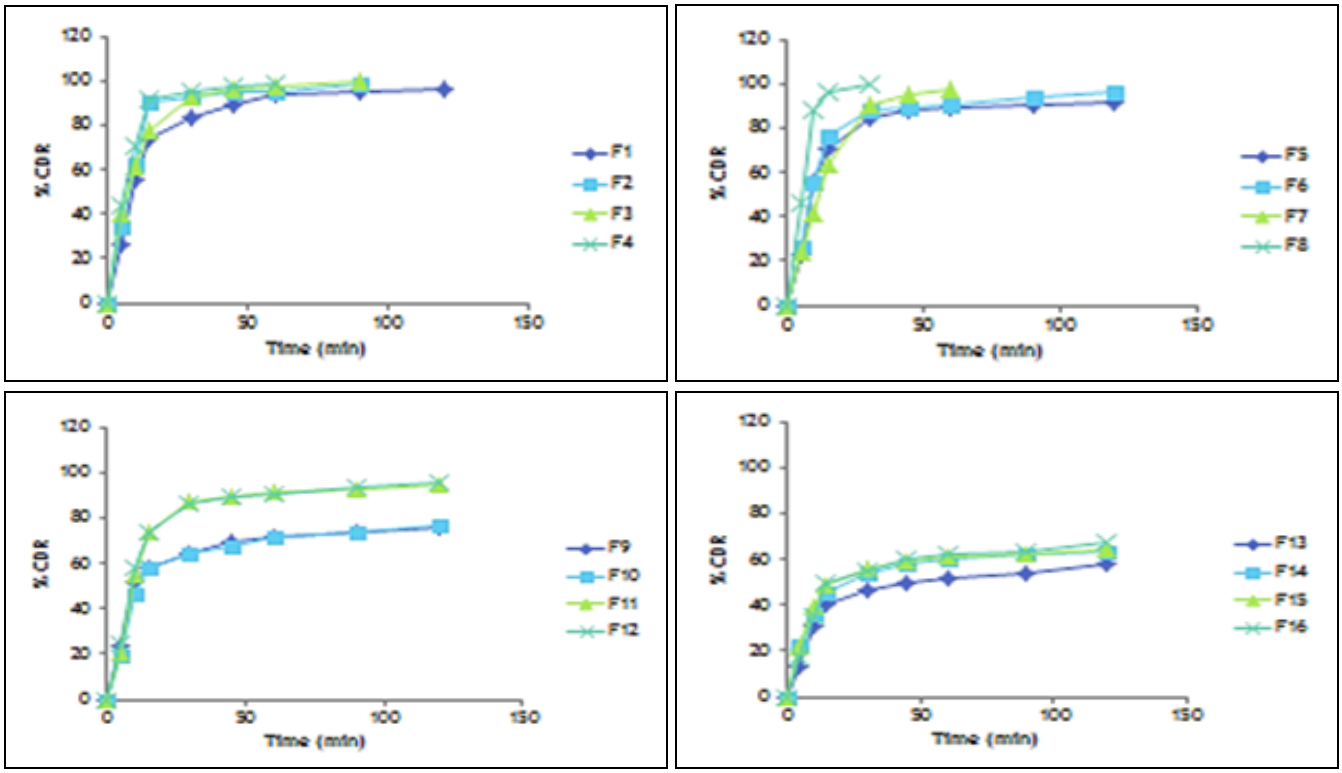

FIG. 4: *IN-VITRO* RELEASE OF LORNOXICAM FROM LIQUISOLID TABLETS

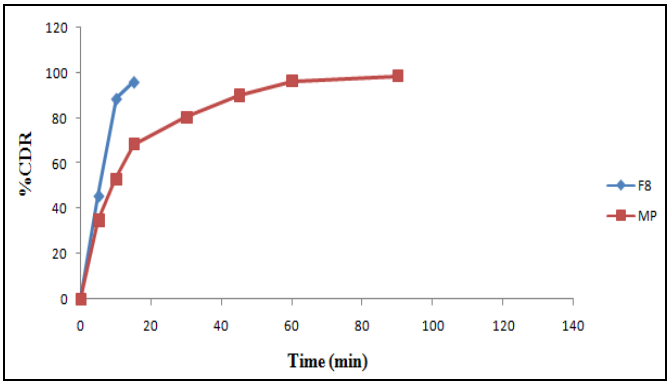

FIG. 5: *IN-VITRO* RELEASE OF LORNOXICAM FROM LIQUISOLID TABLET (F8) AND MARKETED PRODUCT (MP) IN PHOSPHATE BUFFER OF pH 7.42

CONCLUSION: From the results obtained, it can be concluded that the adopted mathematical model for the preparation of liquisolid systems resulted in improved flow properties and the dissolution rate of lornoxicam. Pure drug lornoxicam exhibited poor flow properties, however, the flow properties of the drug improved significantly after formulating it into the liquisolid compact as revealed by the angle of repose, Carr's index, and Hausner's ratio values.

The tablet thickness, friability, average weight variation, drug content, and disintegration time remained within the acceptable range. The Lf value of the formulations has a profound impact on hardness, disintegration, and dissolution of the liquisolid tablets and was found to be inversely proportional to the hardness, disintegration time and dissolution rate of the liquisolid tablets. *In-vitro* drug release studies showed significant improvement in the dissolution of lornoxicam in its liquisolid form compared to the pure form.

The dissolution studies revealed that as the carrier: coat ratio (R-value) increased from 10-40, a proportionate increase in the drug release was observed. However, increasing the drug concentrations from 10-40% in the liquisolid systems resulted in reduced drug release.DSC and XRD suggested the conversion of crystalline form drug into amorphous form, supporting the enhanced solubility and dissolution of lornoxicam from the liquisolid systems.

FT-IR study confirmed the integrity of drugs in the formulation, thereby ruling out any chemical interaction between the drug and excipients used. Liquisolid tablet formulation F3, F4, and F8 showed higher dissolution rates than the marketed product. The drug release from the optimized liquisolid compacts (F8) followed first-order release kinetics. The stability studies showed that aging has not significantly affected the

physicochemical properties and efficacy of the liquisolid tablets.

Overall, the developed liquisolid tablets showed promising *in-vitro* results, thereby suggesting further studies using suitable *in-vivo* models.

ACKNOWLEDGEMENT: The author wishes to thank N.E.T. Pharmacy College, Karnataka, India, for providing facilities and support for this study.

CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest regarding the publication of this paper.

REFERENCES:

1. Neuman RE and Logan MA: The determination of collagen and elastin in tissue. Journal of Biochemistry 1950; 38(11): 549-51.
2. Kamble PR, Shaikh KS and Chaudhari PD: Application of liquisolid technology for enhancing solubility and dissolution of rosuvastatin. Advanced Pharmaceutical Bulletin 2014; 4(2): 197-04.
3. Vemula VR, Lagishetty V and Lingala S: Solubility enhancement techniques. International Journal of Pharmaceutical Sciences Review and Research 2010; 5(1): 41-51
4. Jamakandi VG, Kerur SS and Patil US: Formulation and Evaluation of Immediate Release Tablet of Carvedilol using Liquisolid Compacts Technique for Solubility Enhancement. Asian Journal of Pharmaceutics 2016; 10(3): S324-S332.
5. Khan A and Agrawal S: Formulation and evaluation of lumefantrine capsule prepared by using liquisolid technique. International Journal of Current Pharmaceutical Research 2018; 10: 43-50.
6. Brenda DE, Diva S, Hellen KS, Marcos ASS, Humberto GF and Bianca RP: Liquisolid pellets: A pharmaceutical technology strategy to improve the dissolution rate of ritonavir. Saudi Pharmaceutical Journal 2019; 27(5): 701-12.
7. Sanjayamitra PVSS and Ganesh GNK: Dissolution and solubility enhancement strategies: current and novel prospective. Journal of critical reviews 2018; 5: 1-10.
8. Staunstrup H, Ovesen J, Larsen UT, Elbaek K, Larsen U and Kroner K: Efficacy and tolerability of lornoxicam versus tramadol in postoperative pain. The Journal of Clinical Pharmacology 1999; 39(8): 834-41.
9. Homdrum EM, Likar R and Nell G: Xefo® rapid: A novel effective tool for pain treatment. European Surgical Research Journal 2006; 38(5): 342-52.
10. Pandey A: Formulation Development and Evaluation of sustained release tablets of Lornoxicam. International Journal of Pharmaceutics 2015. DOI:10.20959/wjpr20174-8094
11. Patil DM, Pawar PA, Pagar RY, Ghule RS and Bairagi VA: Formulation and Development of sustained release matrix tablets of Lornoxicam. Journal of Drug Delivery & Therapeutics 2018; 8(2): 102-6.
12. Sireesha K and Kumar AR: Simultaneous estimation of Lornoxicam and Tolperisone by RP – HPLC. International Journal of Research in Ayurveda and Pharmacy 2012; 3(7): 981-87.
13. Usmanova LS, Ziganshin MA, Rakipov IT, Lyadov NM, Klimovitskii AE, Mukhametzyanov TA and Gerasimov AV: Microspherical particles of solid dispersion of polyvinylpyrrolidone K29-32 for inhalation administration. BioMed Research International 2018; 1-12.
14. Sreenivasa RK and Iqbal MM: Preparation and evaluation of cyclodextrin inclusion complexes of water insoluble drug- glimipiride. International Journal of Research in Pharmaceutical and Biomedical sciences 2012; 3(1): 428-34.
15. Babu PRS, Achyuta G, Kharwade M and Subrahmanyam CVS: Solubility behaviour of Lornoxicam in Binary solvents of Pharmaceutical interest. Journal of Solution Chemistry 2012; 41(8): 1364-74.
16. Sagar TM, Smita SA and Saudagar RB: A review on fast dissolving tablet. International Journal of Current Pharmaceutical Review and Research 2017; 8(3): 284-92.
17. Anil A, Thomas L and Sudheer P: Liquisolid compacts: an innovative approach for dissolution enhancement. International Journal of Pharmacy and Pharmaceutical Sciences 2018; 10: 1-7.
18. Jassim ZE: Formulation and evaluation of furosemide liquisolid compact. International Journal of Applied Pharmaceutics 2017; 9: 39-48.
19. El-Say KM, Samy AM and Fetouh MI: Formulation and evaluation of rofecoxib liquisolid tablets. International Journal of Pharmaceutical Sciences Review and Research 2010; 3(1): 135-42.
20. Fujicalin. Unique Spray Dried Carrier for Liquisolid Systems. (www.fujichemical.co.jp) (Accessed Jan 20 2015).
21. Lieberman HA, Lachmann L, Schwartz JB and Marcel Dekker: Pharmaceutical dosage forms: Tablets. Banker GS and Anderson NR, New York 1990.
22. Priya VB, Arati NR and Chandrakant A: Formulation and evaluation of extended release tablet of ranolazine. Inventi Rapid: Pharm Tech 2015; 3: 1-7.
23. Aulton ME and Alderbon G: Pharmaceutics- The science of dosage form design. Churchill Livingstone, London 2002.
24. Yadav AV, Shete AV and Dabke AB: Formulation and Evaluation of Orodispersible Liquisolid Compacts of Aceclofenac. Indian Journal of Pharmaceutical Education and Research 2010; 44(3): 227-35.
25. Hamza YE and Aburahma MH: Design and *in-vitro* evaluation of novel sustained-release matrix tablets for lornoxicam based on the combination of hydrophilic matrix formers and basic pH modifiers. Pharmaceutical Development and Technology 2010; 15(2): 139-53.
26. Imamul IM, Hossain KM, Taksim A, Bhusal P, Rana MS and Tanveer AK: The effect of hydrophilic and hydrophobic polymers on release profiles of diclofenac sodium from matrix tablets. Archives of Pharmacy Practice 2013; 4(3): 120-28.
27. Uddin MS, Mamun AA, Tasnu T and Asaduzzaman M: In-process and finished products quality control tests for pharmaceutical tablets according to pharmacopoeias. Journal of Chemical and Pharmaceutical Research 2015; 7: 180-5.
28. Vaskula S, Vemula SK, Bontha VK and Garrepally P: Liquisolid Compacts: An Approach to Enhance the Dissolution Rate of Nimesulide. Journal of Applied Pharmaceutical Science 2012; 2(5): 115-21.
29. Lohithasu D, Ramana JV, Girish P, Madhu G, Swathi DS, Lavanya K and Harsha INS: A latest review on liquisolid technique as a novel approach. World Journal of Pharmaceutical Research 2014; 4(3): 479-93.

30. Burra S, Yamsani MR and Vobalaboina V: The Liquisolid technique: an overview. Brazilian Journal of Pharmaceutical Sciences 2011; 47(3): 475-82.
31. Gavali SM, Pacharane SS, Sankpal SV, Jadhav KR and Kadam VJ: Liquisolid compact: A new technique for enhancement of drug dissolution. International Journal on Res Methodologies in Phys and Chem 2011; 1(3): 705-13.
32. Prajapati ST, Bulchandani HH, Patel DM, Dumaniya SK and Patel CN: Formulation and evaluation of liquisolid compacts for Olmesartan Medoxomil. Journal of Drug Delivery 2013; 2(3): 111-24.
33. Government of India, Indian Pharmacopoeia, Ministry of health and family welfare, The Controller of Publication, New Delhi (2013).
34. El-Say KM, Samy AM and Fetouh MI: Formulation and evaluation of rofecoxib liquisolid tablets. International Journal of Pharmaceutical Sciences Review and Research 2010; 3(1): 135-42.
35. Yadav VB and Yadav AV: Enhancement of solubility and dissolution rate of BCS class II pharmaceuticals by non-aqueous granulation technique, International Journal of Pharmaceutical Res and Development 2010; 12(1): 1-12.
36. Hamza YE and Aburahma MH: Innovation of novel sustained release compression-coated tablets for lornoxicam: Formulation and *in-vitro* investigations. Drug Development and Industrial Pharm 2010; 36(3): 337-49.
37. Hamza YE and Aburahma MH: Design and *in-vitro* evaluation of novel sustained-release matrix tablets for lornoxicam based on the combination of hydrophilic matrix formers and basic pH modifiers. Pharmaceutical Development and Technology 2010; 15(2): 139-53.
38. Reza MS, Quadir MA and Haider SS: Comparative evaluation of plastic, hydrophobic and hydrophilic polymers as matrices for controlled-release drug delivery, Journal of Pharmaceutical Sciences 2003; 6(2): 282-91.
39. Kulkarni AS,Aloorkar NH, Mane MS and Gaja JB: Liquisolid Systems: a review. International Journal of. Pharmaceutical Sciences and Nanotechnology 2010; 1(3): 795-02.
40. Sisinthy SP, Sarah CYL and Nalamolu KR: Optimization of coconut oil based self-micro emulsifying drug delivery systems of olmesartanmedoxomil by simplex centroid design. International Journal of Applied Pharmaceutics 2016; 8: 47-52.

How to cite this article:
Patil SS, Verma AS, Doddayya H and Udupi RH: Development and *in-vitro* evaluation of liquisolid compacts of lornoxicam. Int J Pharm Sci & Res 2020; 11(5): 2135-46. doi: 10.13040/IJPSR.0975-8232.11(5).2135-46.