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Formulation and Evaluation of Oral Disintegrating Tablets of Lornoxicam by 3^2 Factorial Design

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ABSTRACT

Oral disintegrating dosage form provides an opportunity to manufacturers to extend product life cycle and to expand market. Oral disintegrating tablets (ODT) have this opportunity over conventional tablets. Lornoxicam is non steroidal anti-inflammatory drug and used in treatment of post traumatic pains, muscular and skeletal pains, joint disorder and rheumatic arthritis. Fast onset of action is required in these indications. Therefore it was thought to prepare ODT of Lornoxicam which would help to avoid first pass metabolism and to improve bioavailability as well. ODT were prepared by direct compression method by using crospovidone as superdisintegrating agent and optimized by 3^2 factorial design. Independent variables were concentration of crospovidone (X_1) and hydroxypropyl cellulose (X_2) while dependent variables were disintegration time and percent drug released. Optimised formulation, F4, showed drug content (97.90±0.37%), disintegration time (20.33±0.317 sec), percent drug released (101.5±0.59%), water absorption ratio (113.5±1.26%). This formulation was stable at 40^0C ±2^0C and RH 75%±5% for three months. Present study demonstrated potential for rapid absorption, improved bioavailability, effective therapy and patient compliance.

INTRODUCTION

Drug delivery system is a strategic tool for growth of product, its life cycles and overall market expansions. Though tablets and capsules are the most popular dosage forms, one important drawback of such dosage forms is difficulty in swallowing. This is observed to afflict around 35% of the general population. Now days improved patient compliance has achieved enormous demand consequently, demand for their technologies is also increasing many folds. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects (Chein, 1992). It has been always the aim of a formulator to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in novel drug delivery systems aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance (Kuchekar *et al.*, 2005). Recently pharmaceutical technologists have put in their best efforts to develop a mouth dissolving drug delivery system, i.e oral disintegrating tablet. Lornoxicam, (2-[2-[2-(2,6 dichlorophenyl)aminophenyl] acetyl] oxyacetic acid), a nonsteroidal anti-inflammatory, analgesic and antipyretic drug used in rheumatoid arthritis, post-traumatic pain, masculo-skeletal and joint disorders, with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment. Lornoxicam is practically insoluble. For poorly soluble and oral administered drugs, the rate of absorption is usually controlled by the rate of dissolution, which is the rate limiting step for absorption (Metker V and Kumar A., 2011). The dissolution of a drug can also be influenced by disintegration time of the tablets (Indurwade NH *et al.*, 2002). Faster disintegration of tablets delivers a fine suspension of drug particles resulting in a higher surface area and faster dissolution. The widely used superdisintegrants are crospovidone, croscarmellose sodium and sodium starch glycolate (Gohel *et al.*, 2007). Rationale behind developing oral disintegrating tablet is the availability of larger surface area in the oral dosage form allows rapid wetting in the moist buccal environment that leads to rapid disintegrating and

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dissolution in the oral cavity (Habib, 2002). Rapid disintegration of tablet results in fast dissolution and rapid absorption, in turn rapid onset of action, hence improved patient compliance and convenience. The oral or buccal mucosa being highly vascularised, drugs can be absorbed directly and can enter the systemic circulation without undergoing first pass hepatic metabolism. Patients can take oral ODT dosage form at any time and any place as per their convenience (Reddy et. al., 2002).

MATERIALS AND METHODS

Materials

Lornoxicam was kind gift from Aarti Drugs, Mumbai, India. Croscarmellose sodium and hydroxyl cellulose were obtained from Colorcorn, Asia Pvt Ltd. (Goa, India) as gift samples. Sodium starch glycolate, and other excipients were of standard pharmaceutical grade or analytical grade.

UV spectrum analysis of Lornoxicam (Shailendra *et al.,* 2009)

Accurately weighed 10 mg of lornoxicam was transferred to 100 ml volumetric flask containing 50 ml of 0.1 N HCl and was sonicated for 30 min, the final volume was made up with 0.1 N HCl. The solution was scanned in the range of 200 to 400 nm to fix the maximum wave length and UV spectrum was obtained.

Standard plot of lornoxicam in 0.1 N HCl (Shailendra *et al.,* 2009)

Various dilutions (4 -20 µg/ml) were prepared from the stock solution. The absorbances of prepared solutions were measured against blank (0.1N HCl) at 371nm using UV visible spectrophotometer (2600, Chemito Instruments Pvt. Ltd, Mumbai, India) and calibration curve graph was plotted for absorbance vs. concentration.

Drug excipients compatibility studies

Interactions in dosage form can give rise to changes in the chemical nature, solubility, absorption and therapeutic response of drugs. Therefore, during the formulation of new drugs or the reformulation of existing products, the study of the interaction between drug and excipients in the solid is an important stage. Drug polymer compatibility study was carried out using FTIR and DSC.

FTIR spectroscopy

The pure drug (approximately 10 mg) Lornoxicam and a mixture of drug with crospovidone (1:1) were triturated separately with infrared grade KBr in the ratio of 1:10 in porcelain mortar pestle and corresponding samples were scanned over a range of 400 cm^{-1} – 4600 $cm^{-1}$with diffraction reflectance scanning technique using Prestige 21 (Shimadzu, Japan) (Seager, 1998).

Differential Scanning Colorimetry

In this study DSC thermograms of pure drug, Lornoxicam and drug in 1:1 combination (physical mixture) with excipients were recorded and compared, using DSC TA60 WS thermal analyser (Shimadzu, Japan). The system was calibrated with a high purity sample of Indium. The sample weighing about 6.5 mg was taken in an aluminium crucible covered with a pierced lid; sample free aluminium crucible with pierced lid was used as a reference material. The sample was heated at the rate of 10°C/min, in an atmosphere of nitrogen gas, with the dry gas flowing at the rate of 80 ml/min. (Gohel, 2004)

Full factorial design (Tejvir et al., 2011)

A 3^2full factorial design was used in the present study. In this design 2 factors were evaluated each at 3 levels, and experimental trials were performed at all 9 possible combinations as reflected from table 1. The amount of superdisintegrant, crospovidone (X_1) and the amount of hydroxy propyl cellulose (X_2) were selected as independent variable and in vitro disintegration time (DT) and percent drug dissolved (DP) were selected as dependent variables. The actual formulation design of oral disintegrating tablets of Lornoxicam according to full factorial design 3^2 layout is shown in table1.

Formulation of oral disintegrating tablets of Lornoxicam

The oral disintegrating tablets of Lornoxicam were prepared using crospovidone as superdisintegrant, hydroxypropyl cellulose (HPC) as a polymer, colloidal silicon dioxide as a glidant, sodium saccharine as sweetening agent, mixed fruit flavour as flavouring agent and magnesium stearate as lubricant. The composition of each batch is shown in table1.

Orally disintegrating tablets can be produced by conventional method like wet granulation, dry granulation and direct compression or by specialized techniques like tablet molding, freeze drying. However, direct compression was preferred for present investigation because of its simplicity and cost effectiveness. Direct compression is regarded as a relatively quick process where the powdered materials are compressed directly without changing the physical and chemical properties of the drug. Lornoxicam, sodium saccharine, directly compressible filler (starch), superdisintegrant (crospovidone), colloidal silicon dioxide, talc and mixed fruit flavour were sifted through the sieve #44 and admixed for about 15 minutes to make a uniform blend. Magnesium stearate was passed through seive #100 and mixed with the above blend for approximately 5-7 minutes. The resulting uniform blends of composition per tablet as mentioned in table 1 were directly compressed using 6mm, round convex faced tooling to make the tablets of said compression specifications using 8 station compression machine. The tablet press setting was kept constant across all formulation (Lawrence, 2009; Bagul et al., 2010; Saroha, 2010; Shishu *et al.,* 2010)

Evaluation of formulated tablets (Bhupendra and Patel, 2010; Kumar *et al.,* 2011)

Dimensions of tablet

Any variation in tablet thickness within the particular lot of tablets or between manufacturer's lots should not be apparent to unaided eyes for consumer acceptance of the product. In addition

thickness and diameter must be controlled to facilitate packaging. Thus thickness and diameter of tablets were important for uniformity of tablet size. Twenty randomly selected tablets were taken and their thickness and diameter were recorded using vernier caliper (Mitutoyo Corporation, Japan). Results are expressed as mean value ±SD.

Average weight and weight variation

Indian Pharmacopoeial procedure was followed for weight variation test. Randomly selected twenty tablets were taken and their weight was determined individually and collectively using single pan electronic balance (Wensar weighing scales Ltd, Mumbai, India). The average weight of the tablets was calculated from collective weight. Results are expressed as mean value ±SD. (Indian Pharmacopoeia, 2007)

Hardness

The force needed to fracture the tablet by diametrical compression is referred as crushing strength of tablet. The hardness of the six tablets from each formulation batch was determined using Monsanto type hardness tester. Results are expressed as mean value ±SD.

Friability

Friability test indicates physical strength of compressed tablets. During handling tablets are subjected to mechanical shocks and abrasion which can result in the removal of small fragments and particles from tablet surface. Tablets from each formulation were tested for friability using Roche friabilator (Rolex Scientific Engineers Limited). Twenty tablets were weighed initially and transferred to the friabilator. The instrument was operated at the speed of 25 rpm for 4 minutes, the tablets were removed dedusted and accurately weighed and percentage weight loss was calculated using following equation (Eq^{n}1):

$$\text{Percentage friability} = \frac{\text{Initial weight-Final weight X 100}}{\text{Initial weight}} \quad \ldots(1)$$

Drug content uniformity

For the content uniformity test, twenty tablets were individually weighed and crushed to a fine powder. A quantity of powder equivalent to 2 mg of Lornoxicam was extracted into distilled water and liquid was filtered through Whatman filter paper Grade1 (11 µm). The drug content was determined by Double beam UV spectrophotometer Pharm Spec 1700 (Shimadzu, Japan), at a wavelength 371 nm after suitable dilution with distilled water.

Wetting time and water absorption ratio

A tissue paper twice folded, was placed in a petridish containing 6 ml of water containing dissolved amaranth dye. A tablet was placed carefully on the surface of tissue paper in the petridish. The time required for red colored solution to reach the upper surface of the tablet and to completely wet it was noted as the wetting time. For measuring water absorption ratio, the weight of the tablet before keeping in the petridish was noted (W_b). The wetted tablet from the petridish was taken and reweighed (W_a) Water absorption ratio (R) was then calculated from equation 2 (Eq^{n}2).

$$R = \frac{Wa - Wb}{Wb} \times 100 \quad \ldots.2$$

In vitro disintegration time

Disintegration of ODT was generally occurring due to water uptake by superdisintegrant via capillary action, which results in swelling of superdisintegrant and tablet get disintegrated. It was also reported that increased compaction force may increase or decrease disintegration time. In the present study disintegration test was carried out on six tablets using the apparatus specified in USP (Electrolab, India). The 0.1 N HCl at 37^0C ± 2^0C was used as a disintegration medium and time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus.

In vitro dissolution study

In vitro dissolution of the tablets (n=6) were carried out using USP Type II dissolution test apparatus Disso 2000 (Labindia, India). The dissolution vessel were filled with 900 ml 0.1N HCl maintained at 37 ± 0.5 ºC and paddle rotation kept at 50 rpm. Aliquots of 5ml were withdrawn at intervals of 5 min for 45 minutes. The amount of lornoxicam in solution was analysed spectrophotometrically at 371 nm, after suitably dilution using Pharm Spec 1700 (Shimadzu, Japan). Sink conditions was maintained throughout the study. Results are summarised in table 2.

Regression analysis and polynomial equation (Shailendra KS *et al.,* 2009)

Statistical optimization was carried out in design expert software (version 8.1.3), which suggested that linear model was followed for release at 45 min with p-value of 0.0094. This indicated the model was highly significant. Therefore, linear model was selected for percent release. In order to find out contribution of each components and their interaction, analysis of

Table. 1: Formulation design of fast disintegrating tablets of lornoxicam: A 3^2 factorial design layout.

Ingredients in (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lornoxicam	4	4	4	4	4	4	4	4	4
HPC	3.125	4.375	5.625	3.125	4.375	5.625	3.125	4.375	5.625
Crospovidone	7.5	7.5	7.5	10	10	10	5	5	5
Starch	101.7	100.5	99.25	99.25	98	97.87	104.25	103	101.75
Sod. Saccharine	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Colloidal silicon dioxide	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Mixed fruit flavor	1.30	1.30	1.30	1.30	1.30	1.30	1.30	1.30	1.30
Mg. stearate	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625
Total Weight	120	120	120	120	120	120	120	120	120

Table. 2: Evaluation parameters of lornoxicam ODT.

Batch	Weight variation€ (mg)	Hardness€ (Kg/cm^2)	Friability† (%)	In-vitro Disintegration Time (Sec)*	Drug Content* (%)	Percent drug dissolved	Thickness (mm)†	Water Absorption Ratio(%)
F1	0.714±2.539	4.35±0.057	0.271±0.007	24.1±0.091	98.07± 0.12	93.3±12	3.23±0.065	98.01±0.256
F2	0.713±2.661	4.32±0.057	0.186±0.005	27.00±0.045	99.01± 0.57	92.6±22	3.45±0.030	92.08±0.098
F3	0.718±2.615	4.02±0.057	0.357±0.003	27.66±0.078	98.00± 0.98	91.5±04	3.63±0.037	99.25±0.073
F4	0.735±2.412	4.13±0.100	0.263±0.037	20.33±0.317	97.90± 0.37	101. 5±57	3.98±0.017	113.5±1.263
F5	0.625±2.856	4.20±0.057	0.351±0.015	22.21±0.240	99.12± 0.22	97.4±46	3.93±0.015	111.5±0.653
F6	0.532±2.149	4.16±0.057	0.054±0.01	23.33±0.168	99.45± 0.14	96.0±10	3.37±0.015	101.59±0.351
F7	0.546±2.433	4.26±0.057	0.340±0.02	32.66±0.155	99.56± 0.28	90.9±68	3.43±0.032	80.78±0.029
F8	0.632±1.954	3.97±0.057	0.381±0.01	33.66±0.130	98.14± 0.91	84.4±81	3.48±0.060	110.29±0.665
F9	0.489±2.536	4.31±0.057	0.321±0.02	35±0.358	99.21± 0.45	86.5±02	3.52±0.036	113.19±0.386

All values are mean ± SD, (n = 3)

Table. 3: ANOVA for statistical model.

Response model	Percent drug dissolved	Disintegration time
Sum of Squares	155.18	169.73
Degree of Freedom	2	2
Mean Square	77.59	84.87
Model F Value	11.22	16.53
P Value	0.0094	0.0036
R Square	0.7890	0.8464

Table. 4: Evaluation Parameters of Stability of tablet.

Evaluation parameters	Initial	After 1month	After 2 month	After 3 month
Disintegration time (sec)	20.33±1.1	20.24±1.5	20.22 ± 0.6	20.21 ± 1.3
Drug content(%)	98±2.0	97.91 ±1.8	97.74 ± 2.0	97.66 ± 2.4
Weight variation(mg)	120±0.7	120±0.8	119± 0.8	119 ±1.2

The data are presented as mean value ± S.D. (n = 3)

Table 5: Dissolution Rate Studies of formulation F4 kept for Stability at 40^0 C±2^0C /75%±5% RH

Time (min)	Cumulative % drug released			
	Initial	1 month	2 month	3 month
1	45. 937	45.762	45.762	45.588
5	59.804	59.803	59.629	59.628
10	64.847	64.672	64.671	64.495
15	82.307	82.305	82.130	82.128
20	89.391	89.389	89.213	89.211
30	97.210	97.033	97.030	96.854
45	101.579	101.576	101.398	101.395

variance (ANOVA) was carried. Table 3 shows the results of ANOVA, which was used to generate mathematical models. F-value (11.22) implied the model was significant. Value of probability $p<0.05$, indicate model terms were significant. In this case, linear mixture components, A and B were significant model terms (where, A = crospovidone and B = HPC). The equation 3 (Eqn3) for percent drug release at the end of 45 min

$$\mathbf{Y_1 = +92.16+4.70*A -1.95*B…(3)}$$

Model adequacy was checked for percent drug release at twenty hour. Model which gave highest order polynomial where the additional terms were significant was selected. The linear model was suggested by the software followed for DT, with *p*-value 0.0036. this indicated the model was significant. In order to find out contribution of each component and their interaction, ANOVA was carried out. *F*-value of 16.53, implied the model was significant. Value of $p<0.05$ indicate model terms were significant. In this case, linear mixture components A and B were significant model terms. The equation 4 is used for disintegration time

$$Y_2 = +27.87-5.11*A -1.48 *B....(4)$$

Where, A = crospovidone, B = HPC

Stability study (Kuchekar BS *et al.*, 2005)

The optimised formulation of Orally Disintegrating Tablets were packed in aluminium foil and stored under the following environmental conditions for a period as prescribed by ICH (ICH Q1A1R2) guidelines for accelerated studies that is 40^0C ± 2^0C and RH 75% ± 5% (Thermolab, India).

The tablets were withdrawn at the end of 1 month, 2 months and 3 months and evaluated for appearance, hardness, disintegration time, wetting time, percent drug release, dissolution study and test for dispensability. This is depicted in table 4 and table 5.

RESULTS AND DISCUSSION

UV spectrum analysis of Lornoxicam

As shown in Figure 1, the absorption maximum of pure lornoxicam was found to be at wavelength 371 nm in 0.1 N HCl. Standard curve of lornoxicam in 0.1 N HCl at 371 nm was plotted between concentrations versus absorbance (Figure 2). It follows Beer-Lambert's law in the range of 2-20 µg/ml and coefficient of correlation was found to be 0.9983.

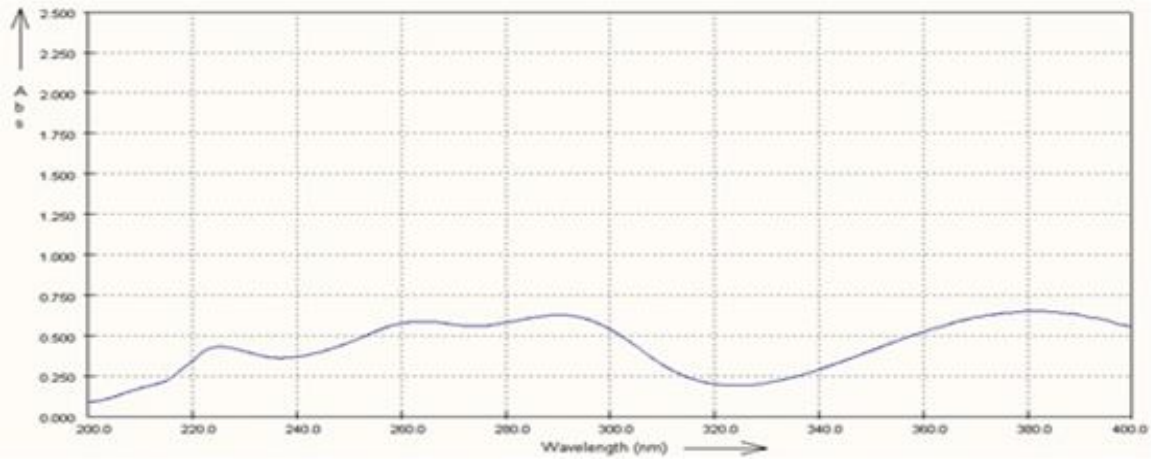

Fig.1: Determination of wavelength for lornoxicam.

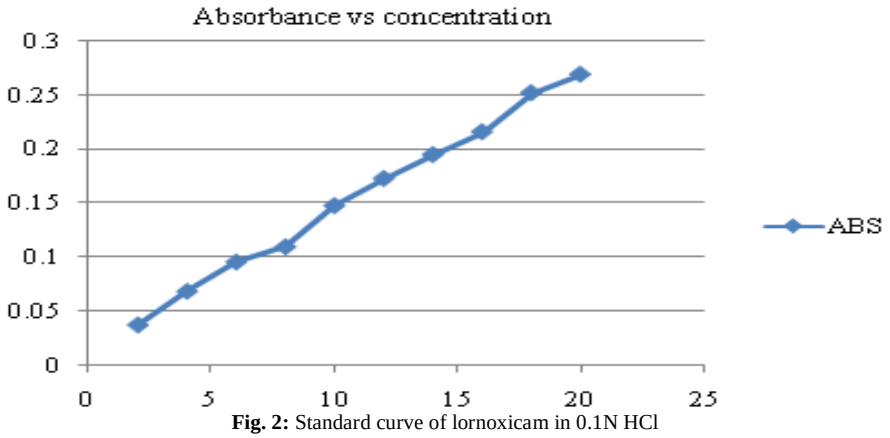

Fig. 2: Standard curve of lornoxicam in 0.1N HCl

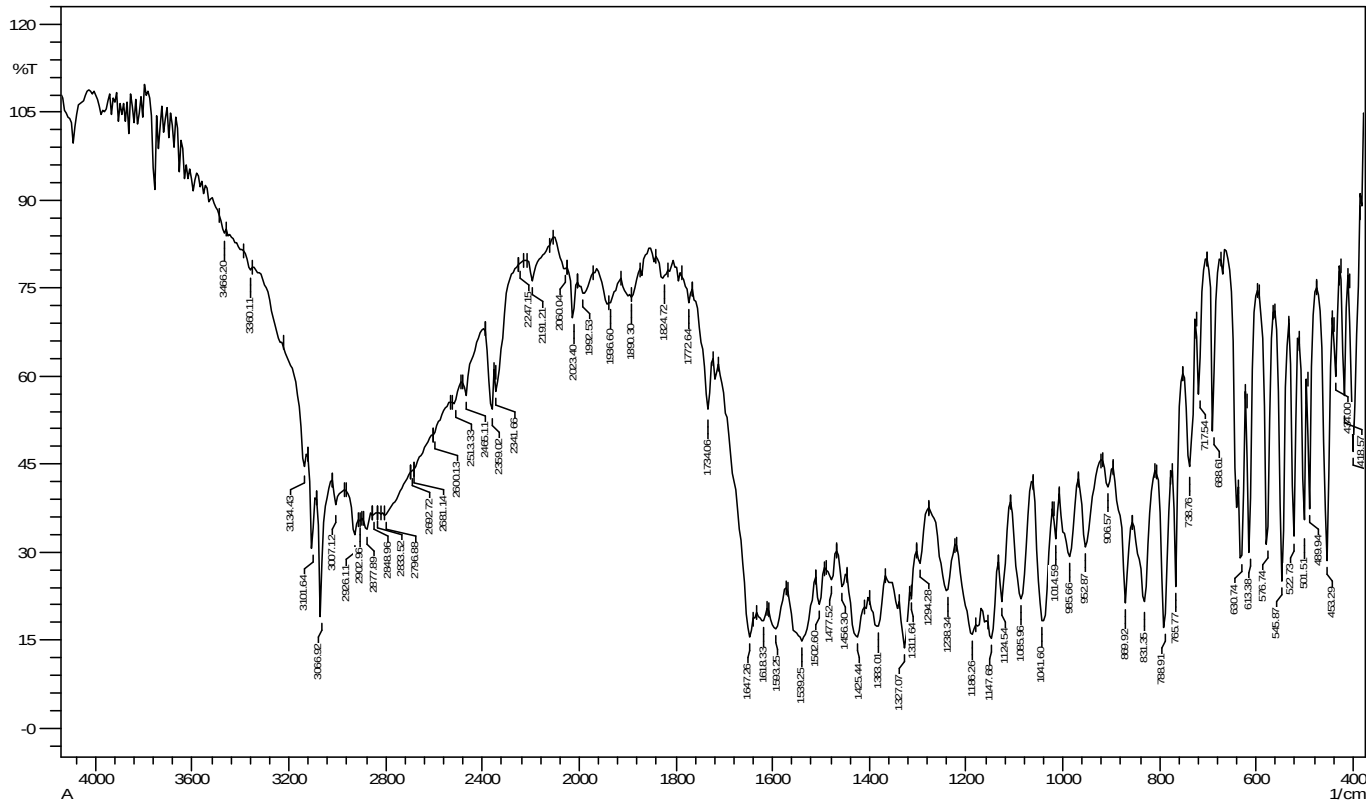

Fig. 3 a: The FTIR spectrum of Lornoxicam.

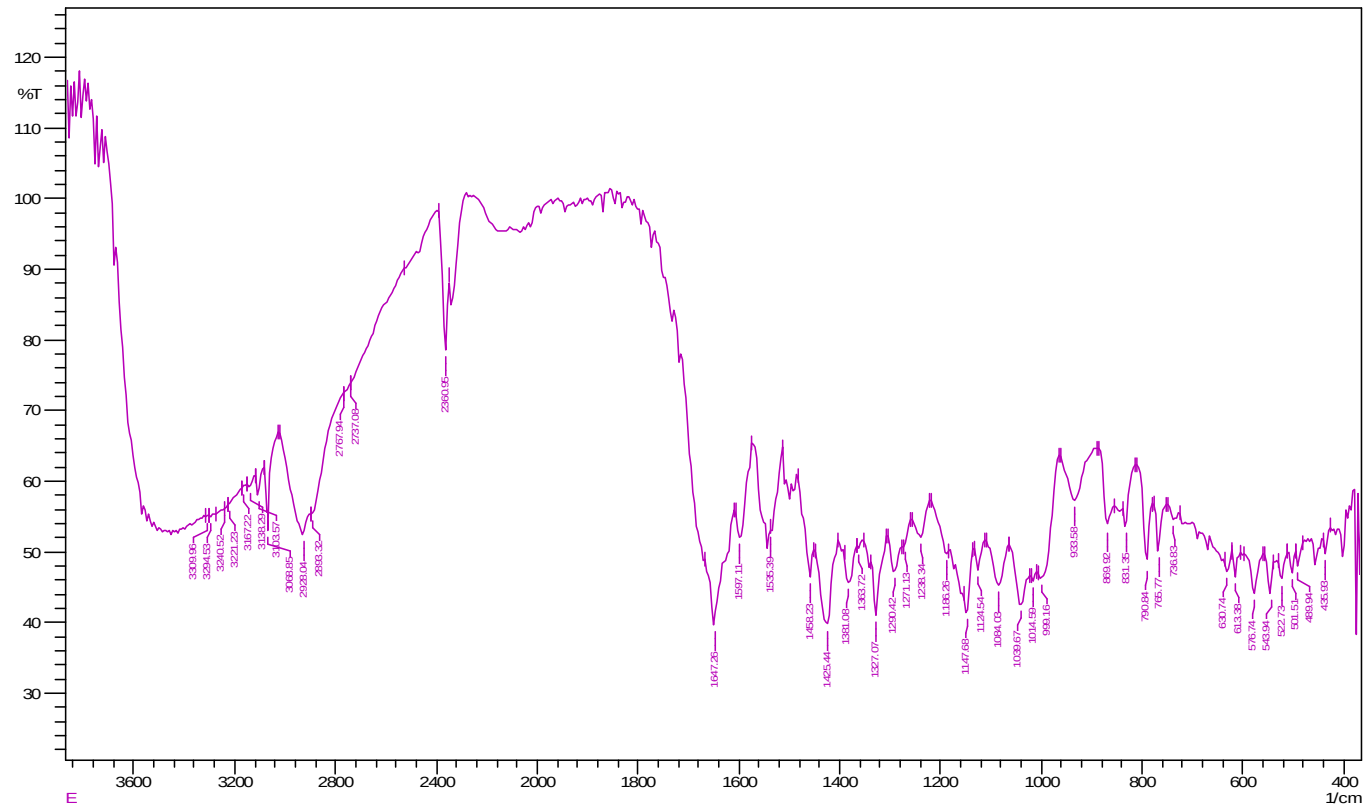

Fig. 3 b: FTIR spectra of drug with Crospovidone.

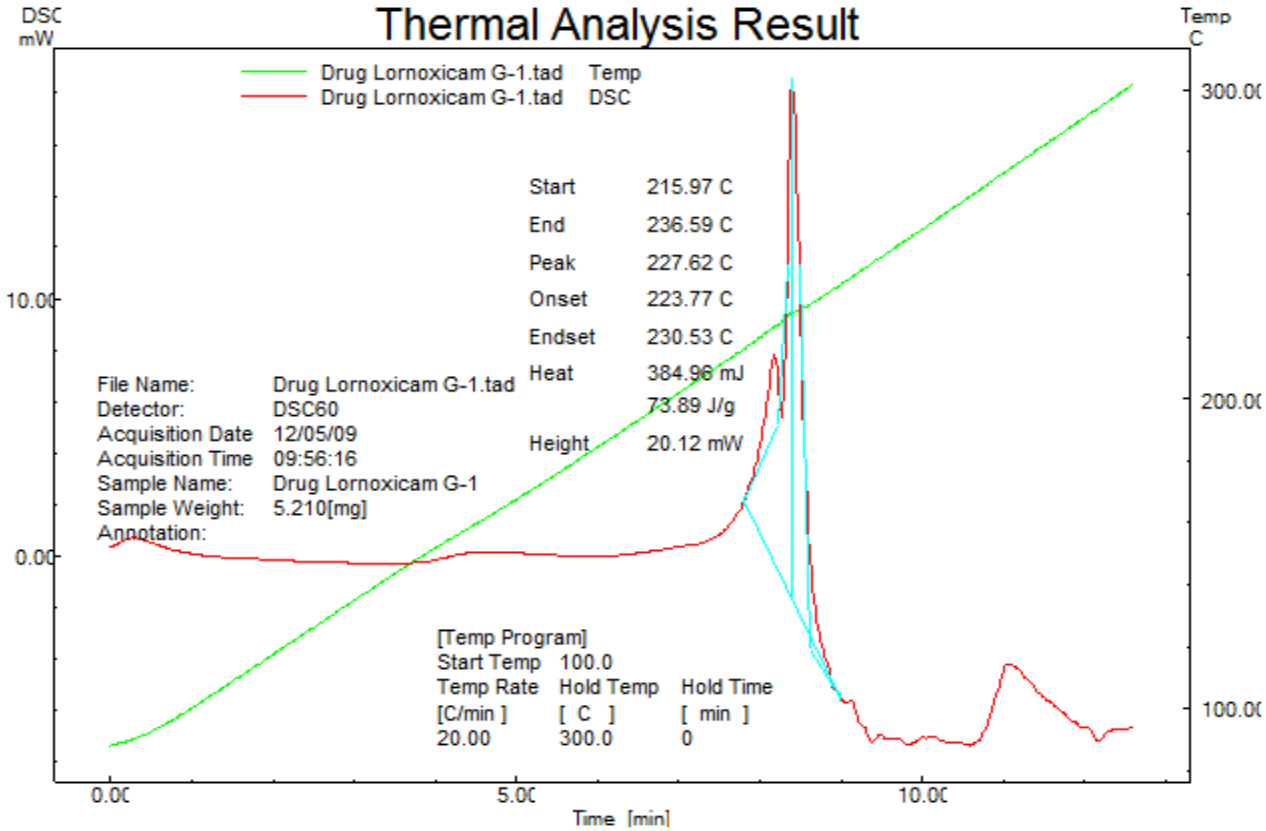

Fig. 4 a: DSC Thermogram of lornoxicam.

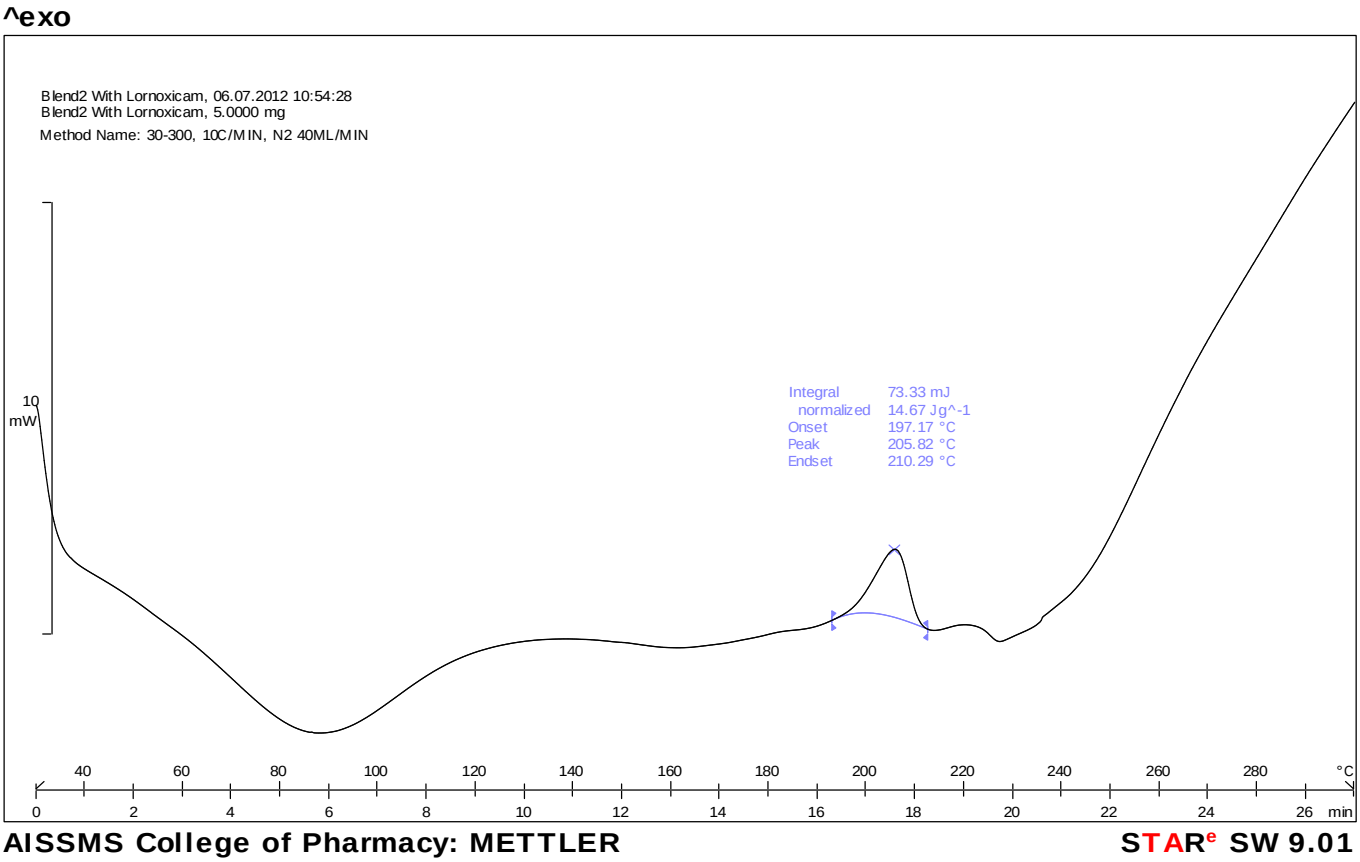

Fig. 4 b:DSC Thermogram of drug with crospovidone.

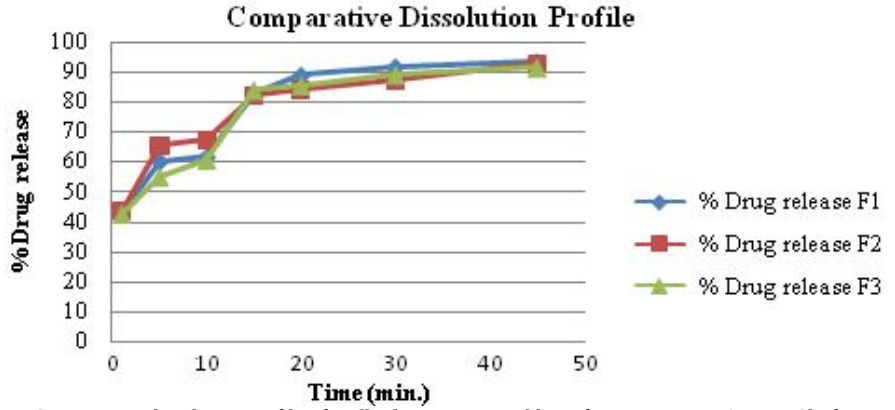

Fig. 5: Comparative dissolution profile of orally disintegrating tablets of Lornoxicam in 0.1 N HCl of F1 to F3.

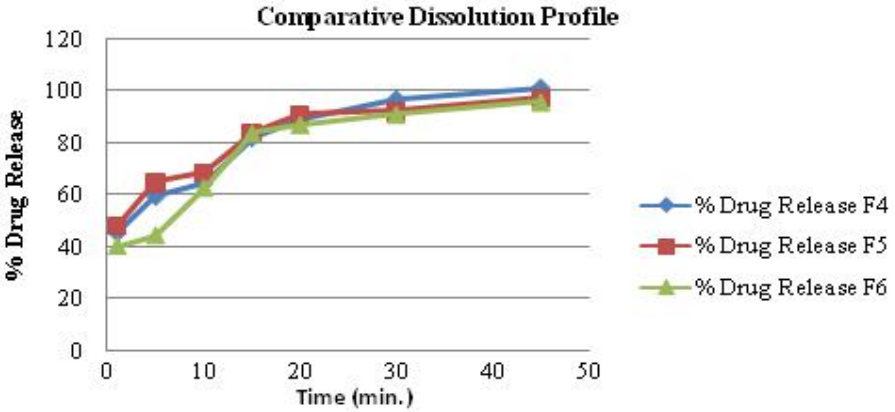

Fig. 6: Comparative dissolution profile of orally disintegrating tablets of lornoxicam in 0.1 N HCl of F4 to F6.

Drug excipients compatibility study

In the formulation development of lornoxicam, drug-excipient interaction was evaluated successfully by FTIR and DSC. In both of these techniques, the peaks in physical mixture were compared with peaks of pure drug. Drug excipient compatibility study permits use of excipients in formulation and also indicates that this will not affect on disintegration and dissolution of drug which rather carries little more importance in case of such oral disintegrating dosage forms.

FTIR spectroscopy

Figure 3a shows FTIR spectra of pure lornoxicam and figure 3b shows FTIR spectra of representative physical mixture of drug in 1:1 ratio with crospovidone. It was found that the spectra of physical mixture contain the same peaks as that found in pure drug. This indicates there was no predominant drug interaction (Seager HJ., 1998).

Differential Scanning Colorimetry

DSC thermograms were obtained for pure drug-lornoxicam (Figure 4a) and for physical mixture of lornoxicam and crospovidone in 1:1 ratio (Figure 4b). The DSC analysis shows no change in endothermic peak of lornoxicam. Hence there was no drug excipient interactions.

Evaluation of oral disintegrating tablets of lornoxicam

Dimensions of tablet

The thickness and diameter of all tablet formulations was found within the range. Drug content of all formulations was observed between 97.90 to 99.56%.

The values for thickness and diameter signify uniformity and it was due to uniformity in die fill, good flow properties, uniform pressure and appropriate punch movement. Drug content for all formulations showed uniformity which indicated that there was an uniform flow and uniform distribution of drug.

Average weight and weight variation

Weight variation tests for all formulations showed weight variation with deviation less than ± 5, which complies with I.P specification and signifies that there was uniformity in flow of powder blend which leads to uniform die fill.

Hardness

Test for all factorial design batches i.e. F1 to F9 showed variation in the range of 3.97 to 4.35 Kg/cm^2. Hardness for all formulations was observed to be proper, which signify that tensile strength of all formulations was maintained after direct compression.

Friability

For all formulations friability was found to be in the range of 0.286 to 0.342 and that for factorial design batches i.e. F1 to F9 showed wide variation in the range of 0.054 to 0.381. Friability test for all formulations indicated that percent friability was less than 1, which compiles the I.P specification and reveals that all formulations have possessed good physical strength and can withstand the mechanical shocks that can be observed during handling, shipping and transportation.

In vitro disintegration

The factorial design batches F1 to F3 comprised of 6% w/w crospovidone as directly superdisintegrant and 2.5% w/w, 3.5%w/w, 4.5%w/w HPC respectively, *in vitro* disintegration time was found to be 24.1 and 27.66 seconds. However, the factorial design batches F4 to F6 comprised of 8% w/w crospovidone as directly superdisintegrant and 2.5% w/w, 3.5% w/w, 4.5% w/w HPC respectively. In vitro disintegration time was found between 20.33 to 23.33 seconds.

Moreover, the factorial design batches F7 to F9 comprised of 4%w/w crospovidone as directly superdisintegrant and 2.5% w/w, 3.5% w/w, 4.5% w/w HPC respectively, *in vitro* disintegration time was found between 32.66 and 35 seconds. Hence it was evident that *in vitro* disintegration time was increased with increase in concentration of HPC, whereas increase in concentration of crospovidone, decrease in disintegration time was observed. In vitro disintegration study showed that, as there was an increase in concentration of cros povidone, time required to disintegrate the tablet was increased.

An objective behind formulation of ODT was to improve disintegration time and to serve that purpose, water absorption by ODT should be appropriate. So for evaluation of water uptake by ODT wetting time and water absorption ratio of lornoxicam ODT was carried out.

In-vitro Dissolution study

Percent drug dissolved for factorial design batches i. e. F1 to F9 showed variation in the range 84.4% to 101.579%. This variation range was observed due to developmental changes in formulation to attain preliminary objectives.

The formulation batches F1 to F3 comprised of crospovidone in 6% and hydroxyl propyl cellulose in ratio 2.5 to 4.5%, DP was found between 43.144 and 93.312% (figure 5). However, formulation batches F4 to F6 comprised of crospovidone in 8% and hydroxyl propyl cellulose in ratio 2.5 to 4.5 %, DP was found between 45.937 to 101.579% (figure 6). Moreover, formulation batches F7 to F9 comprised of crospovidone in 4% and hydroxyl propyl cellulose in ratio 2.5 to 4.5%, DP was found between 37.560 to 90.968% (figure 7).

These Batches showed wide variation in their DP because of change in not only amount of superdisintegrants taken for study but also the amount of hydroxyl propyl cellulose.

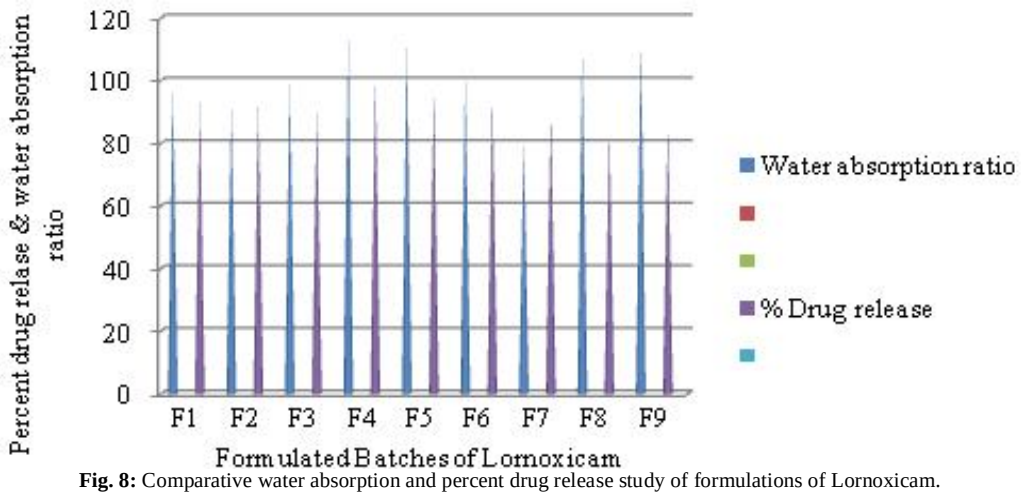

Fig. 8: Comparative water absorption and percent drug release study of formulations of Lornoxicam.

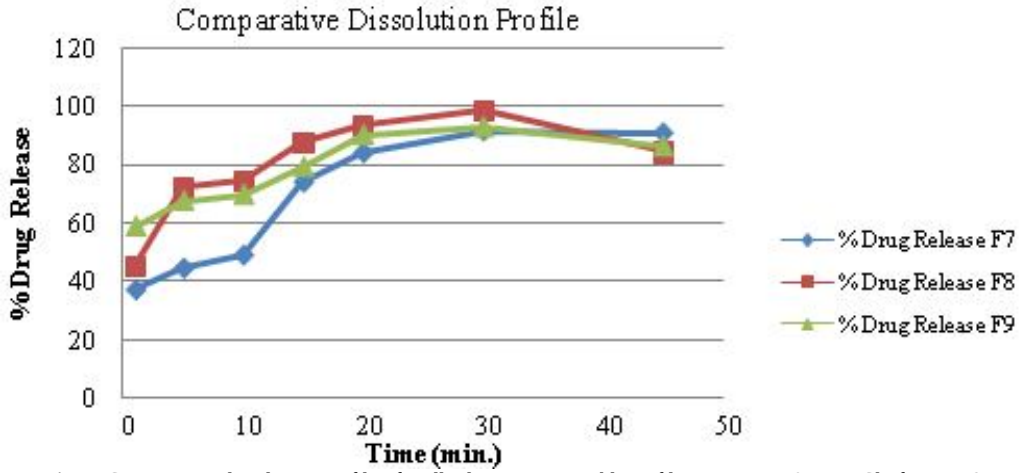

Fig. 7: Comparative dissolution profile of orally disintegrating tablets of lornoxicam in 0.1 N HCl of F7 to F9.

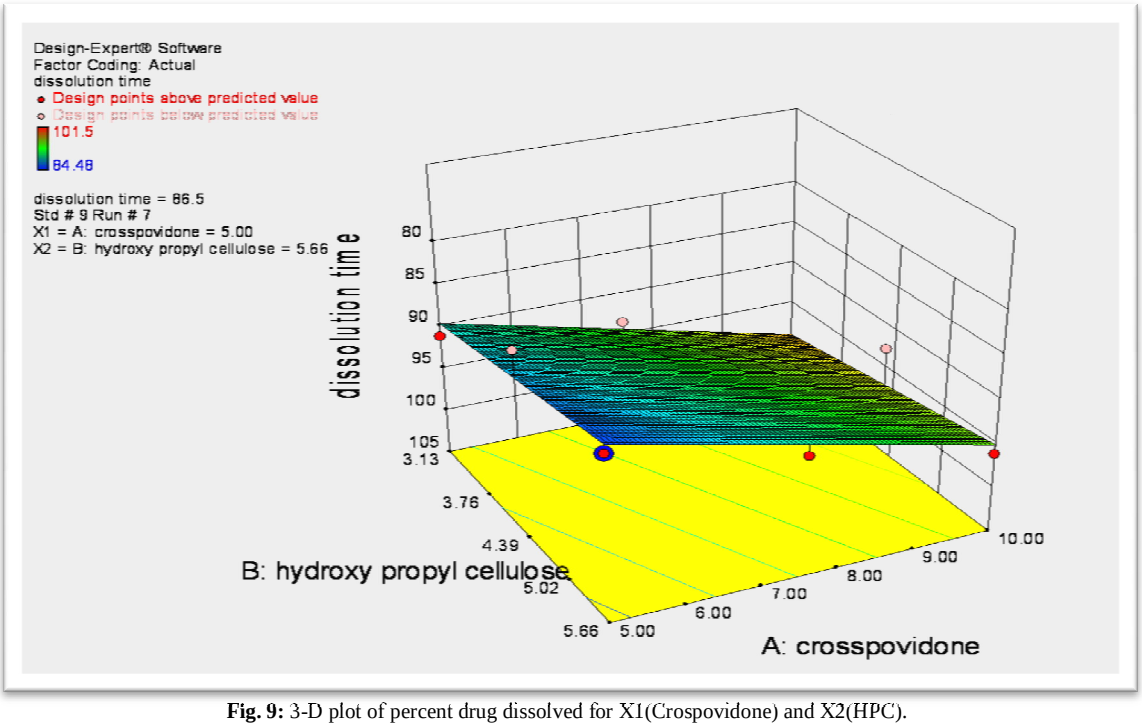

Fig. 9: 3-D plot of percent drug dissolved for X1(Crospovidone) and X2(HPC).

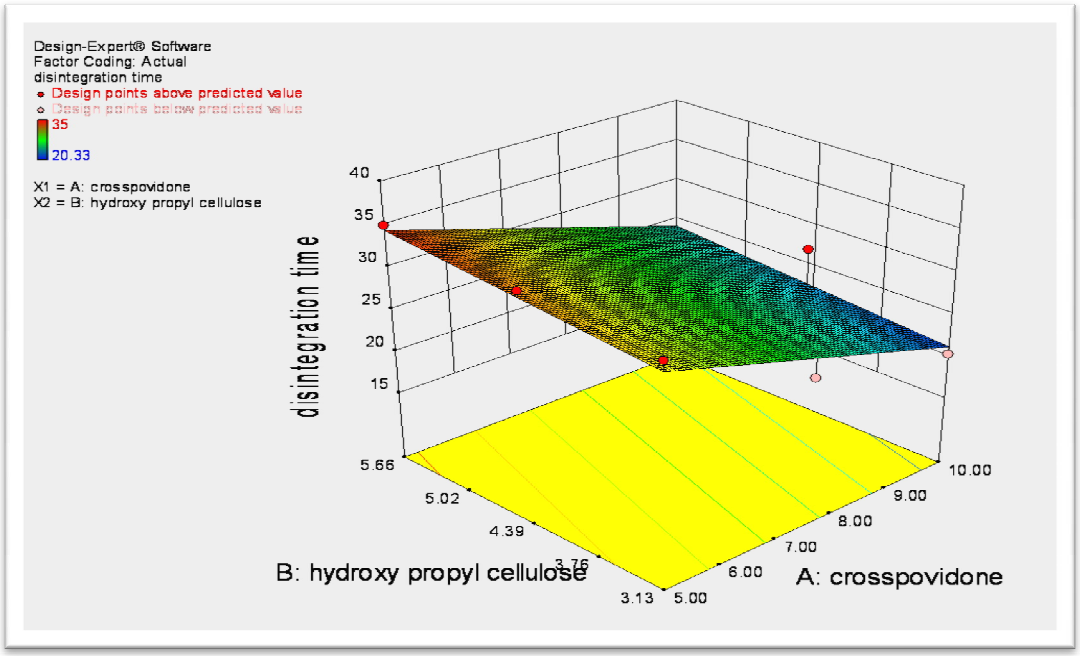

Fig. 10: 3-D plot of disintegration time for X1(Crospovidone) and X2(HPC) combination.

Wetting time and water absorption ratio

Wetting time and water absorption ratio was determined for all formulations. A time at which water soluble, red colored dye solution occupies upper surface of the formulation was designated as wetting time. Wetting time for all formulation batches of factorial design batches i.e. F1 to F9 showed variation in the range of 5.5 to 12 seconds. Each fiber can act as a hydrophilic channel to facilitate water uptake into the tablet matrix and help increase the total water contact area with drug. Water absorption ratios for all formulation batches of factorial design batches i.e. F1 to F9 showed wide range of variation 80.78 to 113.50%. This is represented in figure 8.

The improvement in water absorption ratio, wetting time, in vitro disintegration time, percent drug dissolved was evident in F1 to F3 due to constant tablet press setting across all batches of factorial design irrespective of weight variation which might have led to decreased hardness and increased friability. This has further resulted in increased porosity of tablets and subsequent maximal water uptake volume. If porosity is sufficiently high, water can easily penetrate in the tablet. Accordingly, a suitable hardness depends in part on the tablet composition and the desired level of oral disintegration speed. The comparative profiles of water absorption ratio and percent drug dissolved with their interrelationship of orally disintegrating tablets of lornoxicam for factorial design batches. From the all study of formulated batches of lornoxicam tablets it was found that the F4 formulation shown best results as compare to other eight formulations. The percent drug release was found to be 101.57% more than others. Disintegration time is also preferable as compare to other batches. As compare to other batches F4 formulation has given best results hence it was optimized.

Response surface plots

The 3D graph as shown in figure 9 shows that percent drug release is plotted on Y axis where as the concentration of excipients were plotted on X and Z axis. As the concentration of crospovidone and HPC increased from 5 to 7.5 mg and 3 to 5 mg respectively, the percent drug release decreased signifying that the polymers have definite effect on drug release. The contour plot justifies that optimum formulation complying with the acceptance criteria can be achieved by selecting the formulations near to the centre of the triangle shaped contour plot which is the diagram obtained from the evaluation result of (F1 to F9) formulations. Almost similar results were observed with 3D graph as shown in figure 10 and contour plot for disintegration time. Here major effect on the drug release was due to polymer use.

Stability study

Stability study of formulated tablets was carried out and no any change in formulation was observed indicating prepared tablets were stable at given conditions as per ICH guidelines.

CONCLUSION

From the present study it can be concluded that oral disintegrating tablets of lornoxicam can be prepared successfully by using crospovidone as superdisintegrating agent and direct compression method. Among all the evaluation tests taken, formulation F4 was found the best. A 3^2 factorial design was found suitable to optimize the formulation. The optimized formulation F4 was found stable in stability study. This study demonstrates the potential of formulation for rapid absorption and early onset of action in turn, effective therapy and patient compliance.

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