

# Preparation and Characterization of Lornoxicam- $\beta$ -Cyclodextrin Inclusion Complex for Solubility Enhancement & Taste Masking

Saurabh Sharma<sup>1\*</sup> and Anurag Bhargav<sup>2</sup>

1. Research Scholar, CMJ University, Shillong, Meghalaya, India -793 003
2. Chaudhari Devlal College of Pharmacy, Yamunanagar, Haryana, India

## Abstract

Lornoxicam (LXM) is a practically insoluble BCS Class II drug. Attempt is made to convert an insoluble drug into a water soluble complex by solubility enhancement techniques like by kneading method, spray drying method and complexation method using  $\beta$ -Cyclodextrin. The Complex was characterized by Differential Scanning Calorimetry (DSC), Powder X-ray Diffraction (XRD), Fourier-transform infrared spectroscopy (FT-IR), Solubility and Dissolution studies. According to the DSC data, lornoxicam in complex form was converted from crystalline to amorphous state resulting in better dissolution rate. FTIR study reveals that there is no interaction between drug and polymer. The PXRD study revealed that the crystallinity of lornoxicam is reduced to amorphous. The dissolution study was conducted in dissolution medium having pH 6.8.. The solid dispersion of lornoxicam- $\beta$ -CD inclusion complex showed maximum  $99.67 \pm 0.75\%$  drug release in 90 min than physical mixture  $41.10 \pm 0.50\%$  drug release in 120 min and Pure drug lornoxicam only  $37.50 \pm 0.82\%$  release in 120 min., resulting in enhanced dissolution rate and bioavailability. It can be concluded that inclusion complex of lornoxicam with  $\beta$ -CD was prepared by kneading method used for taste masking of bitter drug (lornoxicam) and solubility enhancement were found to be effective for solubility and dissolution rate leads to enhanced bioavailability of lornoxicam.

**Key Words:** Lornoxicam;  $\beta$ -Cyclodextrin; kneading method; spray drying method; complexation method; Solubility; Dissolution rate.

## Introduction

Poorly water-soluble drugs often show low bioavailability when administered orally, because the absorption of the drugs in the gastro-intestinal tract can usually be a rate-limiting step. Therefore, it is important for such kind of drugs to enhance their dissolution rate. To enhance the dissolution rate, increasing the drug solubility is necessary according to the Noyes-Whitney equation<sup>1</sup>. Various studies have been done in attempt to improve solubilities of poorly water-soluble drugs; they include micronization<sup>2</sup>, solid dispersion<sup>3</sup>, solvent deposition<sup>4</sup>, ordered mixture<sup>5</sup>, roll-mixing<sup>6</sup>, complexation<sup>7</sup>, co-grinding method<sup>8</sup>, microparticles<sup>9-10</sup>, nanoparticles<sup>10-11</sup>,

liquisolid compacts<sup>12</sup>, ball milled<sup>13</sup>, dry mixing<sup>14</sup>, grinding<sup>15</sup>, cosolvent<sup>16</sup>. Lornoxicam is a non-steroidal anti-inflammatory drug with extremely potent anti-inflammatory and analgesic activity. It is widely used for the symptomatic treatment of pain and inflammation in patients with rheumatoid arthritis and osteoarthritis. Moreover it showed great efficacy in various clinical trials in the management of preoperative and postoperative pain associated with gynecological, orthopedic, abdominal and dental surgeries. Lornoxicam shows bitter taste and distinct pH-dependent solubility characterized by very poor solubility in acidic condition present in the stomach<sup>17</sup>.

Cyclodextrins (CDs) are known for their ability to molecularly encapsulate a wide variety of drugs into their hydrophobic cavity<sup>18</sup>. The interaction of CDs with labile compounds can retard drug degradation, accelerate degradation, or have no effect on drug molecules reactivity<sup>19-20</sup>. The main purpose of this study is to enhance the solubility, increase the dissolution rate and bioavailability of Lornoxicam which is well demonstrated by Differential scanning calorimetry (DSC), X-ray powder diffractometry (XRD), Fourier transform infrared spectroscopy (FTIR), solubility study and dissolution study. The aim of present work is to uplift the solubility and dissolution rate leads to enhance the bioavailability of lornoxicam.

## MATERIAL AND METHOD

Lornoxicam was gratis sample from Piramal Healthcare Pvt. Ltd., Mumbai, India.  $\beta$ -Cyclodextrin was purchased from HI-MEDIA. All other materials and reagents were of analytical grade of purity.

### Preparation of Solid Dispersion

#### Ratio optimization of drug and $\beta$ -Cyclodextrin

Apparent solubility method has been used for ratio optimization. Physical mixtures of drug-  $\beta$ -Cyclodextrin ( $\beta$ -CD) in different ratios were prepared<sup>21</sup>. Then Physical mixtures equivalent to (10 mg of drug was added to 10 mL of 0.1N HCl having pH 6.8) i.e. 1:1 similarly 1:2, 1:3 & 1:4 were taken in glass vials with rubber closures. Then the vials were kept on a shaker incubator maintained at  $37 \pm 0.5^\circ\text{C}$  for 24 h. After shaking, the vials were kept in an incubator at  $37 \pm 0.5^\circ\text{C}$  for equilibrium for 12 h. The solution was then filtered through 0.45  $\mu\text{m}$  millipore filter and the filtrate was assayed spectrophotometrically at  $\lambda_{\text{max}}$  377.5 nm. From the results shown in (Table 1 and Fig.1) the drug-  $\beta$ -CD ratio was optimized and used for solid dispersions formulation.

\* Corresponding Author

E.mail: saurabhapex1975@gmail.com



### Preparation of drug-β-CD inclusion complex by kneading method

Solid dispersion with a optimized ratio of Lornoxicam with β-CD were prepared with Kneading method. In this a mixture of Lornoxicam-β-CD Complex (1:2) were mixed in mortar with a pestle and the required amount of solvent (methanol-water 1:1 mixture) just to make a smooth paste was added. The paste was then further kneaded for about 1 h in a glass mortar. A similar method was reported by Fernandes et al<sup>22</sup>. The paste formed was dried under vacuum for 24 hours. Dried powder was passed through sieve no. 100 and stored in a desiccator until further evaluation See (Table 2 & Fig.2)

### Preparation of drug-β-CD inclusion complex by Spray drying method

Approximately 10 L of an aqueous solution containing lornoxicam/β-cyclodextrin complex were prepared following the above-described phase-solubility study procedure, at a molar ratio of 1:2 (6 mM of lornoxicam and 12 mM of β-cyclodextrin). The solution was spray-dried using a Niro Production spray dryer, under the following operating conditions: inlet air temperature, 175°C; outlet air temperature, 99°C; atomizer rotation rate, 10,900 rpm; and feed solution flow, 143 mL min<sup>-1</sup>. The yield of the spray-drying process was measured as the powder weight percentage obtained at the end of the operation compared with the amount of solid materials (lornoxicam/β-cyclodextrin) present in the sprayed solution.<sup>23</sup> Dried powder was passed through sieve no. 100 and stored in a desiccator until further evaluation See (Table 2 & Fig.2)

### Preparation of drug-β-CD inclusion complex by complexation method

In this method complex was prepared in ratio of 1:2 w/w completely dissolving lornoxicam in organic solvent (methanol) and finally β-CD was added with continuous stirring until homogenous mixture is formed. The mixture was then dried in an oven for 6 hrs at 45 °C.<sup>21</sup> Dried powder was passed through sieve no. 100 and stored in a desiccator until further evaluation See (Table 2 & Fig.2)

### Evaluation of Solid dispersions

#### Saturation solubility studies

Saturation solubility studies were performed according to the method reported by Higuchi and Connors<sup>24,25</sup> to analyze the improvement in solubility in 0.1N HCl having pH 1.2 in triplicate. Excess of pure drug, physical mixture, and inclusion complex were added to 20ml of distilled water in glass vials which were subsequently tightly closed and shaken for 24 h on a mechanical shaker at room temperature to achieve the equilibrium. In preliminary studies, it was found that equilibrium solubility was achieved in 24 h and therefore, samples were shaken for 24 h. The samples were withdrawn and filtered through a 0.22 μm membrane filter (Millipore, India) followed by dilution and analyzed

lornoxicam content was determined in triplicate by (UV/Vis Spectrophotometer, Shimadzu-1800) spectrophotometrically at at λ<sub>max</sub> 377.5 nm. The results were shown in (Table 2 & Fig.1)

### Production Yield

The yields of production of solid dispersions of various batches were calculated using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of solid dispersions and percent production yields were calculated as per the formula mentioned below,<sup>26</sup> and are reported in (Table 3 & Fig.2)

$$\% \text{ yield} = \frac{\text{Practical mass (solid dispersions)}}{\text{Theoretical mass (polymer + drug)}} \times 100$$

### Drug Content

Solid dispersions equivalent to 10 mg of drug according to theoretical mass was dissolved in the sufficient amount of methanol into 100 mL volumetric flask and volume was made up to the mark by methanol.<sup>26</sup> Then the concentration of drug present in the solution was determined using UV spectroscopy by taking absorbance at λ<sub>max</sub> 377.5 nm. Results are reported in (Table 3 & Fig.3)

### Taste Evaluation of Lornoxicam with β-CD inclusion complex

Taste evaluation of lornoxicam with β-CD inclusion complex with ratio 1:2 prepared by kneading method was done to compare bitterness of the optimized solid dispersion inclusion complex with pure drugs. Time sensitivity method was used for bitterness evaluation, in which 10 healthy human volunteers were selected and a sample of solid dispersion inclusion complex equivalents to 10mg (oral dose) were kept on tongue in mouth cavity without swallowing for 10-15sec and all the volunteers were asked for verbal judgment followed by scoring in a taste scale of 0-3, finally all the volunteers were asked to gargle their mouth by distilled water after competition of taste evaluation. Bitterness levels were noted by verbal judgments at different time intervals.<sup>27</sup> Results were shown in (Table 4)

Taste scale was calibrated as follows:

- 0 Being = Tasteless
- X Being = Thresholds bitter
- 1 Being = Slight bitter
- 2 Being = Moderate bitter
- 3 Being = Strong bitter

### Characterization of Solid Dispersions

#### Fourier Transform Infra red Spectroscopy (FTIR)

The optimized lornoxicam with β-CD inclusion complex with ratio 1:2 prepared by kneading method were subjected to fourier transform infra red spectroscopy (FTIR) studies to check drug interaction and complex

formation using FTIR (IR IFFINITY-1 CE, Shimadzu corps, Japan). The sample of pure drug,  $\beta$ -CD, physical mixture and solid dispersion inclusion complex were previously grounded and thoroughly mixed with KBr and formed an infrared transparent solid disk. The KBr disks were prepared by compressing the powder blend. Three scans were executed at a resolution of  $1\text{ cm}^{-1}$  (from  $4000\text{-}400\text{ cm}^{-1}$ ). Results are reported in (Fig.4)

#### Differential Scanning Calorimetry (DSC)

DSC curves of lornoxicam,  $\beta$ -CD, physical mixtures solid dispersions inclusion complex were obtained by a differential scanning calorimeter (DSC 60 Shimadzu) at a heating rate of  $10\text{ }^{\circ}\text{C}/\text{min}$  from  $30\text{ to }300\text{ }^{\circ}\text{C}$  in nitrogen atmosphere, which are shown in (Fig.5)

#### X-Ray Powder Diffraction Studies (XRPD)

Powder XRD patterns of lornoxicam,  $\beta$ -CD physical mixtures solid dispersions inclusion complex were recorded using Philips diffractometer (PW 1140) and  $\text{Cu-}\alpha$  radiation, diffractograms were run at a scanning speed of  $2^{\circ}/\text{mm}$  and a chart speed of  $2^{\circ}/2\text{ cm per }2\theta$ , which are shown in (Fig.6)

#### Scanning Electron Microscopy (SEM)

The surface morphology of pure drug, physical mixture and solid dispersion inclusion complexes with  $\beta$ -CD prepared by various methods was examined by Scanning Electron Microscope (JEOL 5400, Tokyo, Japan). In this study the samples were fixed on a brass stub using double-sided tape and then gold coated in vacuum by a sputter coater. The pictures were then taken at an excitation voltage of  $15\text{ kV}$ . Results are reported in (Fig.7 & 8)

#### In-vitro Dissolution Study

The in-vitro dissolution of lornoxicam, physical mixture and prepared solid inclusion complexes with  $\beta$ -CD and was carried out using powder dispersion method by using Dissolution test apparatus-TDT-06T (Electrolab, Mumbai, India) at the USP type II apparatus at  $100\text{ rpm}$ . The dissolution study was conducted in dissolution medium of having pH 6.8 as a dissolution media at  $37^{\circ}\text{C} \pm 0.5\text{ }^{\circ}\text{C}$ . Optimized batches of ratio 1 : 2 lornoxicam- $\beta$ -CD inclusion complex containing equivalent of  $10\text{ mg}$  of lornoxicam were suspended in  $900\text{ ml}$  of pH 6.8 and A  $5\text{ ml}$  aliquot of dissolution medium was withdrawn at 5, 10, 15, 30, 45, 60, 90, 105, 120 min with a pipette and filter through  $0.45\text{ }\mu\text{m}$  Whatman filter and then analyzed lornoxicam content was determined in triplicate by (UV/Vis Spectrophotometer, Shimadzu-1800) spectrophotometrically at  $\lambda_{\text{max}}\ 377.5\text{ nm}$ . Fresh medium ( $5\text{ ml}$ ), which was prewarmed at  $37^{\circ}\text{C}$ , was replaced immediately into the dissolution medium after each sampling maintain its constant volume throughout the test. Previous tests determined that there was no change in the  $\lambda_{\text{max}}$  of lornoxicam due to the presence of carrier dissolved in the dissolution medium.<sup>22</sup> The dissolution studies were carried out in triplicate and

the mean  $\pm$  SD values were calculated. The solid dispersion of lornoxicam- $\beta$ -CD inclusion complex showed maximum  $99.67 \pm 0.75\%$  drug release in 90 min than physical mixture  $41.10 \pm 0.50\%$  drug release in 120 min and Pure drug lornoxicam only  $37.50 \pm 0.82\%$  release in 120 min. (Table 5 & Fig. 9)

## Result and Conclusion

### Evaluation of Solid dispersions

Evaluation of Lornoxicam with  $\beta$ -CD inclusion complex prepared by kneading method selected on the basis of maximum solubility observed as compared to other method and was evaluated by different evaluation parameters like production yield, drug content, solubility determination Taste evaluation, Differential scanning calorimetry, X-ray diffraction study, FTIR study, Micromeritic properties, SEM and In vitro drug release study.

### Saturation solubility studies

Saturation solubility studies were performed according to the method reported by Higuchi and Connors. Lornoxicam with  $\beta$ -CD inclusion complex with ratio 1:2 prepared by kneading method, spray drying method and complexation method. The samples were withdrawn and filtered through a  $0.22\text{ }\mu\text{m}$  membrane filter (Millipore, India) followed by dilution and analyzed lornoxicam content was determined in triplicate by (UV/Vis Spectrophotometer, Shimadzu-1800) spectrophotometrically at  $\lambda_{\text{max}}\ 377.5\text{ nm}$ . Lornoxicam with  $\beta$ -CD inclusion complex with ratio (ratio 1:2) shows maximum solubility in  $35.34 \pm 1.0\text{ mg/ml}$ ,  $26.24 \pm 1.2\text{ mg/ml}$  and  $20.19 \pm 1.1\text{ mg/ml}$  was found and optimized the kneading method on the basis of maximum solubility and further study was carried out. The results were shown in (Table 2 & Fig.1)

### Production Yield

The production yields of Lornoxicam with  $\beta$ -CD inclusion complex with ratio 1:2 prepared by kneading method, spray drying method and complexation method were calculated using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of solid dispersions and percent production yields were calculated as per the formula. The results are reported in (Table 3 & Fig.2)

### Drug content:

Drug content of Lornoxicam with  $\beta$ -CD inclusion complex with ratio 1:2 prepared by kneading method, spray drying method and complexation method, solid dispersion complex weigh equivalent to  $10\text{ mg}$  of drug according to theoretical mass was dissolved in the sufficient amount of methanol into  $100\text{ mL}$  volumetric flask and volume was made up to the mark by methanol. The samples were withdrawn and filtered through a  $0.22\text{ }\mu\text{m}$  membrane filter (Millipore, India)



followed by dilution and analyzed lornoxicam content was determined in triplicate by (UV/Vis Spectrophotometer, Shimadzu-1800) spectrophotometrically at  $\lambda_{\text{max}}$  377.5 nm. Results are reported in (Table 3 & Fig.3)

#### **Taste Evaluation of Lornoxicam with $\beta$ -CD inclusion complex**

Taste evaluation of lornoxicam with  $\beta$ -CD inclusion complex with ratio 1:2 prepared by kneading method was done to compare bitterness of the optimized solid dispersion inclusion complex with pure drugs. Evaluation of taste of drug- $\beta$ -CD inclusion complex was carried out using time sensitivity method and by using panel of human volunteers. From the observation most of the volunteers passes the taste of lornoxicam with  $\beta$ -CD inclusion complex with ratio 1:2 which was prepared by kneading method. The results are revealed in (Table 4)

Taste scale was calibrated as follows:

- 0 Being = Tasteless
- X Being= Thresholds bitter
- 1 Being= Slight bitter
- 2 Being= Moderate bitter
- 3 Being= Strong bitter

#### **Characterization of Solid dispersions**

##### **Fourier Transform Infrared Spectroscopy**

The IR spectra of the LXM,  $\beta$ -CD, physical mixtures and lornoxicam- $\beta$ -CD inclusion complex are shown in (Fig.4). The IR spectroscopy has also been used to assess the interaction between cyclodextrin and guest molecules in the solid state, since upon the complexation, shifts or changes in the absorption spectrum occur. The IR spectrum of the LXM showed an absorption band at 3,400  $\text{cm}^{-1}$  due to an O-H stretching vibration; the broadness of this band is indicative of hydrogen bonding. The absorption band at 3,090  $\text{cm}^{-1}$  due to N-H stretching; aromatic C-H stretching at 2,927  $\text{cm}^{-1}$  and an absorption band located at 766  $\text{cm}^{-1}$  is due to the stretching vibration of C-Cl38. The IR spectra of the  $\beta$ -CD had an intense bands at 3,300-3,500  $\text{cm}^{-1}$  due to O-H stretching vibrations and vibration band located at 2,800-3,000  $\text{cm}^{-1}$  due to the -CH and CH<sub>2</sub> groups. The IR spectra of lornoxicam- $\beta$ -CD inclusion complex was compared with physical mixtures and LXM, there was no significant change in the characteristics stretching band of LXM were observed in physical mixtures, the above bands are unchanged for position and intensity with respect to the IR spectra of LXM alone in physical mixture. The O-H band of LXM and LXM-  $\beta$ -CD which confirmed the existence of interaction of the drug,  $\beta$ -CD and these spectral changes due to dissociation of intermolecular hydrogen bonds of pure drug through inclusion complexation, similarly the C- O stretching band was highly diminished and interact with  $\beta$ -CD and shifted to lower frequencies in all spectral patterns of solid complexes prepared by kneading method. It was clearly

verified that the magnitude of alteration of the original C-O stretching band was clearly influenced by the method of preparation. This result confirmed the existence of strong interactions between LXM,  $\beta$ -CD. In IR spectra of lornoxicam- $\beta$ -CD inclusion complex, absorption band at 1078  $\text{cm}^{-1}$  could not be detected which might be due to co- occurrence of C-O band with other band and this existence indicated a strong interaction and complete formation of the solid complex with  $\beta$ -CD. Inclusion complexes showed absence of the above-mentioned peaks, which indicates entrapment of LXM into the cavity and confirmed the complex formation.

##### **Differential Scanning Calorimetry**

The thermal behavior of LXM,  $\beta$ -CD, physical mixtures and lornoxicam- $\beta$ -CD inclusion complex is shown in (Fig.5). The DSC thermograms of LXM showed a typical behavior of an anhydrous crystalline drug with a well defined endothermic peak at 230°C corresponding to its melting point in optimized solid complex. The DSC thermogram of  $\beta$ -CD showed an endothermic peak at about 135°C due to the liberation of water of crystalline. Both the characteristic peak of LXM and  $\beta$ -CD was clearly distinguishable in the physical mixture.. The DSC curves of lornoxicam- $\beta$ -CD inclusion complex exhibited a complete disappearance of the endothermic melting peak of LXM and this may be attributed to amorphization of LXM and due to formation of inclusion complex. Disappearance of endothermic melting peak of LXM showed that only lornoxicam- $\beta$ -CD inclusion complex formed a true inclusion complex which was differing from physical mixture.

##### **X-Ray Powder Diffractometry**

The XRPD patterns of pure LXM,  $\beta$ -CD, physical mixture and lornoxicam- $\beta$ -CD inclusion complex is shown in (Fig.6). It is a useful method for the detection of complexation in powder of microcrystalline states. The diffractogram of LXM showed sharp and intense peaks which indicating its crystalline nature. The XRPD pattern of pure  $\beta$ -CD showed crystallinity but in the comparison with the diffractogram of the correspondent to the physical mixture, it was possible to observe disappearance of some diffraction peaks of  $\beta$ -CD and LXM. Furthermore, for lornoxicam- $\beta$ -CD inclusion complex obtained XRPD patterns were indicating the amorphous state reached by kneading method. SEM and DSC studies also supported the same hypothesis, which was confirmed by X-ray diffractometry.

##### **Scanning Electron Microscopy**

Scanning electron microscopy photographs of Lornoxicam and optimized batches of ratio 1 : 2 lornoxicam- $\beta$ -CD inclusion complex are given in (Fig.7 & 8). SEM study indicated that pure drug Lornoxicam in particles were irregular in shape and crystalline in nature, while inclusion complex of drug and carrier shows that drug particle remains

dispersed and physically adsorbed on the surface of the carrier particles. The solid dispersion of lornoxicam- $\beta$ -CD inclusion complex showed a homogeneous dispersions indicating that the Lornoxicam molecules were dispersed uniformly in carriers matrices of solid dispersions prepared kneading method. It can be seen in (Fig.5 & 6) which shows crystalline nature of drug convert into amorphous state, which is further confirmed by DSC and XRD study.

#### In-vitro dissolution study:

The in-vitro dissolution of lornoxicam, physical mixture and prepared solid inclusion complexes with  $\beta$ -CD and was carried out using powder dispersion method by using Dissolution test apparatus-TDT-06T (Electrolab, Mumbai, India) at the USP type II apparatus at 100 rpm. The dissolution study was conducted in dissolution media at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ . Optimized batches of ratio 1 : 2 lornoxicam- $\beta$ -CD inclusion complex containing equivalent of 10mg of lornoxicam were suspended in 900 ml of pH 6.8 and a 5 ml aliquot of dissolution medium was withdrawn at 5, 10, 15, 30, 45, 60, 90, 105, 120 min with a pipette and filter through 0.45  $\mu\text{m}$  Whatman filter and then analyzed lornoxicam content was determined in triplicate by (UV/Vis Spectrophotometer, Shimadzu-1800) spectrophotometrically at  $\lambda_{\text{max}}$  377.5 nm. The statistical analysis of the data is done using Microsoft Excel<sup>®</sup> and the data are presented in (Table 17 & Fig. 33). The solid dispersion of lornoxicam- $\beta$ -CD inclusion complex showed maximum  $99.67 \pm 0.75\%$  drug release in 90 min than physical mixture  $41.10 \pm 0.50\%$  drug release in 120 min and Pure drug lornoxicam only  $37.50 \pm 0.82\%$  release in 120 min.

#### Conclusion:

Lornoxicam is a non-steroidal anti-inflammatory drug with extremely potent anti-inflammatory and analgesic activity. But it shows bitter taste and distinct pH-dependent solubility characterized by very poor solubility in acidic condition present in the stomach. The research work was start with aim of preparation and evaluation of lornoxicam- $\beta$ -CD inclusion complex of solid dispersion were prepared by kneading method, spray drying method and complexation method in different ratio like 1:1, 1:2, 1:3 & 1:4 and optimized the ratio on the basis of maximum solubility of drug in prepared complex at pH 1.2. The ratio (ratio 1:2) shows maximum solubility in  $35.34 \pm 1.0$  mg/ml which was selected for further study. like production yield 95.12%, drug content  $99.84 \pm 1.6\%$ , solubility  $35.34 \pm 1.0$  mg/ml, pass taste with scale i.e. 0 Being = Tasteless of lornoxicam with  $\beta$ -CD inclusion complex, Solid dispersions of lornoxicam with  $\beta$ -CD inclusion complex was characterized and confirmed by X-ray diffractometry, SEM and DSC, FTIR studies also supported the same hypothesis. The dissolution study was conducted in dissolution media having pH 6.8 as a dissolution media at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ . The solid dispersion

of lornoxicam- $\beta$ -CD inclusion complex showed maximum  $99.67 \pm 0.75\%$  drug release in 90 min than physical mixture  $41.10 \pm 0.50\%$  drug release in 120 min and Pure drug lornoxicam only  $37.50 \pm 0.82\%$  release in 120 min. It can be concluded that inclusion complex of lornoxicam with  $\beta$ -CD was prepared by kneading method used for taste masking of bitter drug (lornoxicam) and solubility enhancement were found to be effective for solubility and dissolution rate, which leads to enhanced bioavailability of lornoxicam.

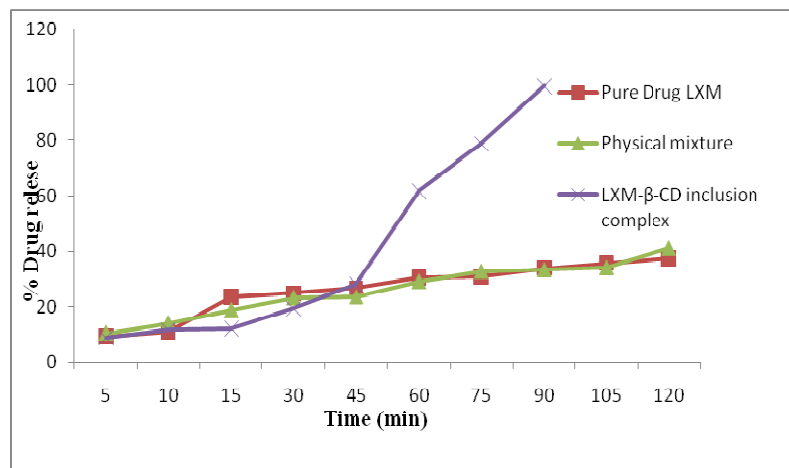
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**Table 1: Ratio optimization of drug and  $\beta$ -Cyclodextrin**

Ratio	Drug Concentration (Solubility in mg/ml)
1:1	1.6 $\pm$ 0.7
<b>1:2</b>	<b>2.6 <math>\pm</math> 0.8</b>
1:3	1.9 $\pm$ 0.4
1:4	2.2 $\pm$ 0.7



**Fig. 9: In-vitro dissolution profile of LXM, Physical mixture and LXM- $\beta$ -CD inclusion complex**

**Table 2: Solubility study of solid dispersion inclusion complexes at pH 1.2**

Methods	Solubility $\pm$ SD (mg/ml)
Pure LXM	0.034 $\pm$ 1.0
Kneading Method	35.34 $\pm$ 1.0
Spray drying method	26.24 $\pm$ 1.2
Complexation method	20.19 $\pm$ 1.1

**Table 3: Evaluation of Lornoxicam with  $\beta$ -CD inclusion complex**

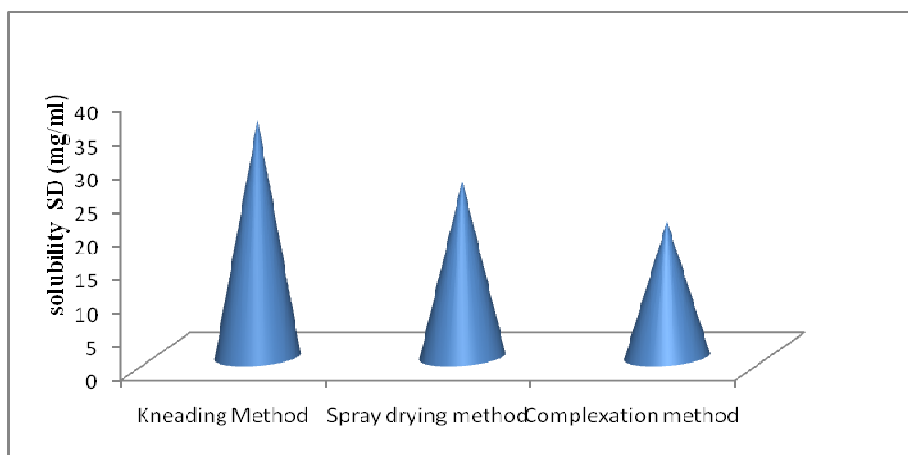
Lornoxicam with $\beta$ -CD inclusion complex (1:2 ration)	% Yield	% Drug content	Solubility mg/ml (Mean $\pm$ SD)
Kneading Method	95.12	99.84 $\pm$ 1.6	35.34 $\pm$ 1.0
Spray drying method	85.67	88.45 $\pm$ 0.64	26.24 $\pm$ 1.2
Complexation method	93.95	90.02 $\pm$ 0.74	20.19 $\pm$ 1.1

**Table 4: Taste Evaluation of Lornoxicam with  $\beta$ -CD inclusion complex**

Volunteers	Bitterness level after					
	10 sec.	1 min.	2 min.	5 min.	10 min.	15min.
1	X	0	0	0	0	0
2	X	X	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	X	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0

**Table 5: In-vitro dissolution study of LXM, Physical mixture and LXM-β-CD inclusion complex**

Time	Pure Drug LXM	Physical mixture	LXM-β-CD inclusion complex
5	9.21 ± 0.67	10.47 ± 0.62	8.64 ± 0.35
10	10.94 ± 1.28	14.17 ± 0.93	11.44 ± 0.64
15	23.48 ± 1.07	18.73 ± 0.77	11.97 ± 0.94
30	24.87 ± 0.89	23.18 ± 0.33	19.24 ± 0.77
45	26.69 ± 0.68	23.59 ± 0.60	27.94 ± 0.68
60	30.48 ± 1.13	29.05 ± 0.67	61.71 ± 0.92
75	30.92 ± 1.09	32.71 ± 0.67	78.80 ± 0.99
90	33.90 ± 0.86	33.31 ± 0.76	99.67 ± 0.75
105	35.76 ± 0.83	34.05 ± 0.71	----
120	37.50 ± 0.82	41.10 ± 0.50	----



**Fig.1: Solubility studies LXM-β-CD inclusion complex prepared by method**

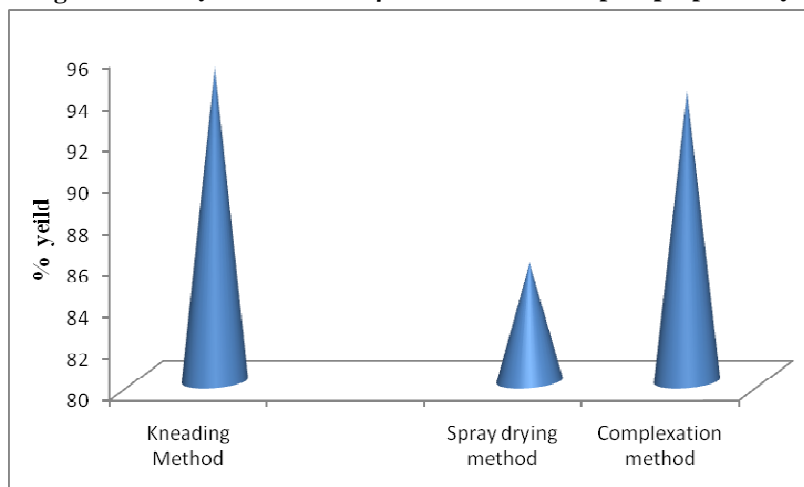




Fig.2: Production Yield of Lornoxicam with  $\beta$ -CD inclusion complex prepared by method

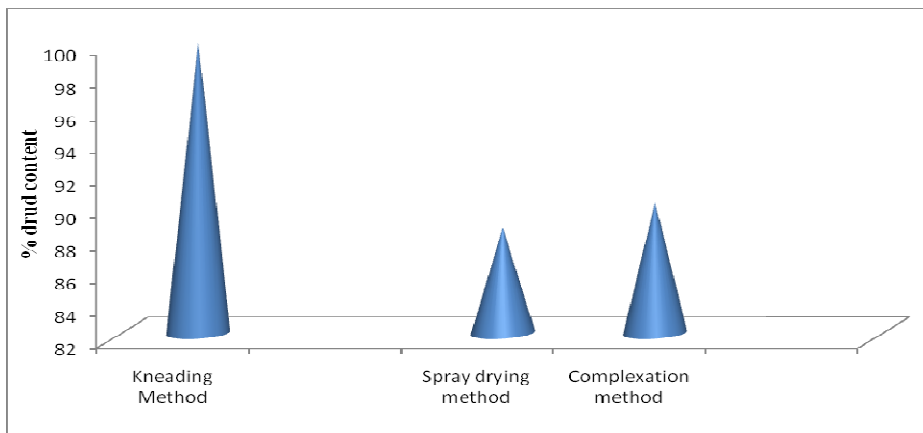


Fig.3: Drug Content of Lornoxicam with  $\beta$ -CD inclusion complex prepared by method

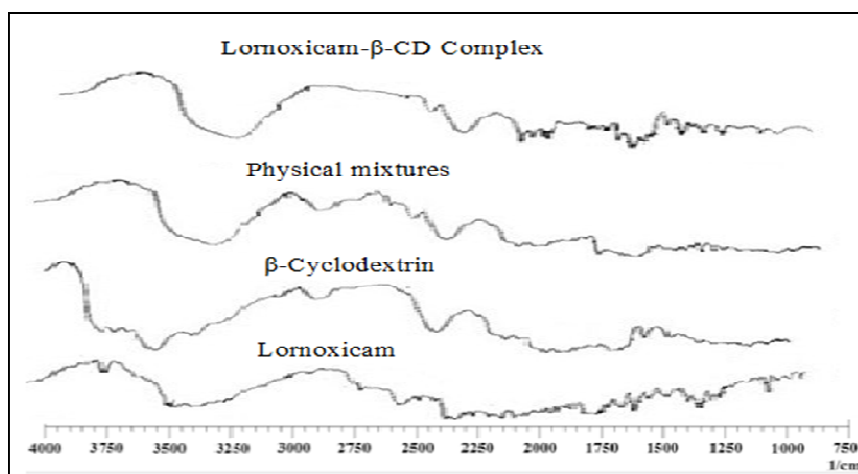


Fig. 4: FTIR spectra of Lornoxicam,  $\beta$ -Cyclodextrin, Physical mixture and Lornoxicam- $\beta$ -CD inclusion complex

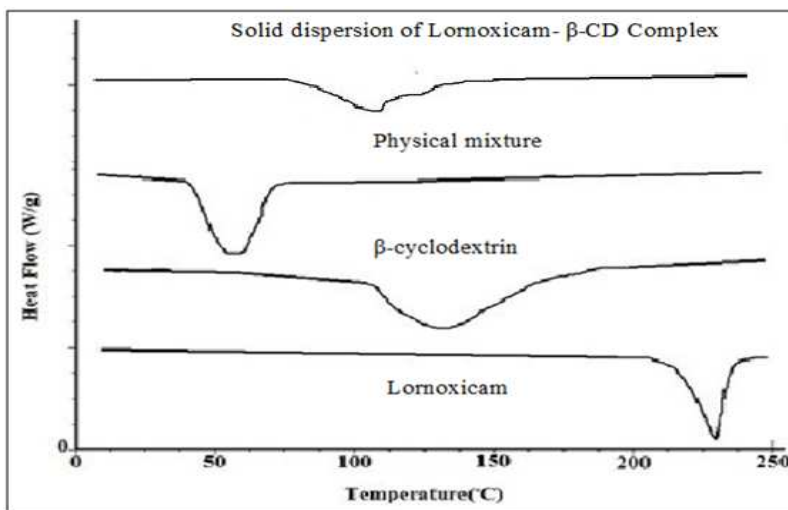


Fig.5: DSC thermograms of LXM,  $\beta$ -CD, physical mixtures and lornoxicam- $\beta$ -CD inclusion complex

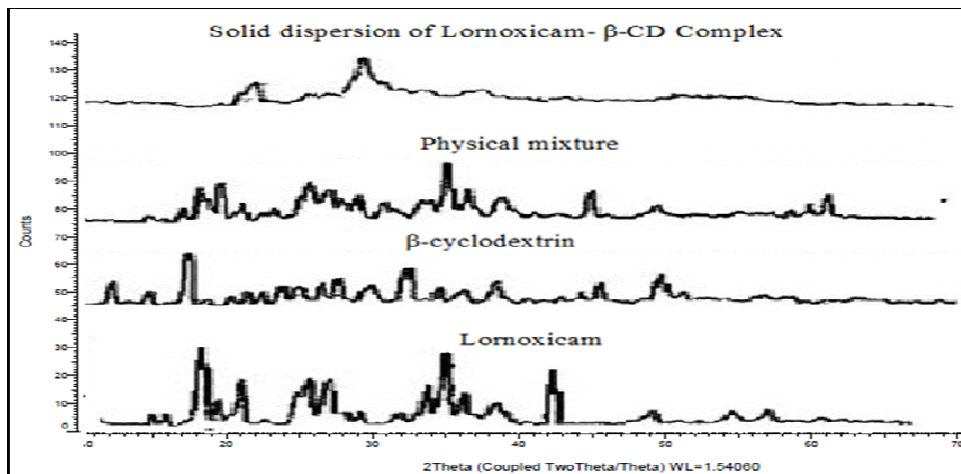


Fig. 6: Diffractogram of LXM,  $\beta$ -CD, physical mixtures and lornoxicam- $\beta$ -CD inclusion complex

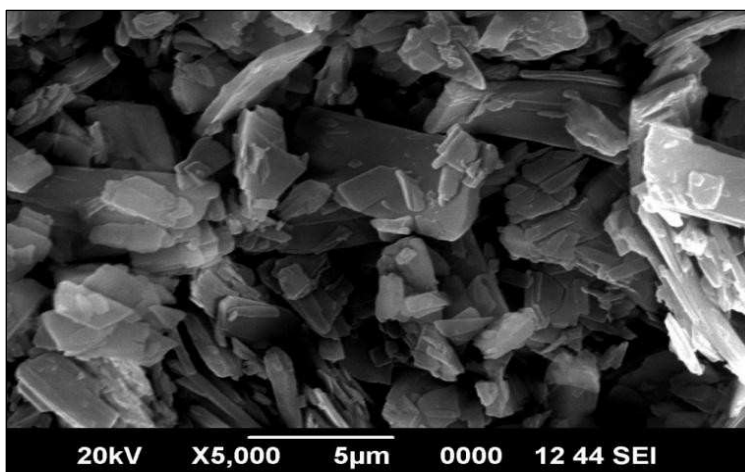


Fig. 7: SEM of Lornoxicam

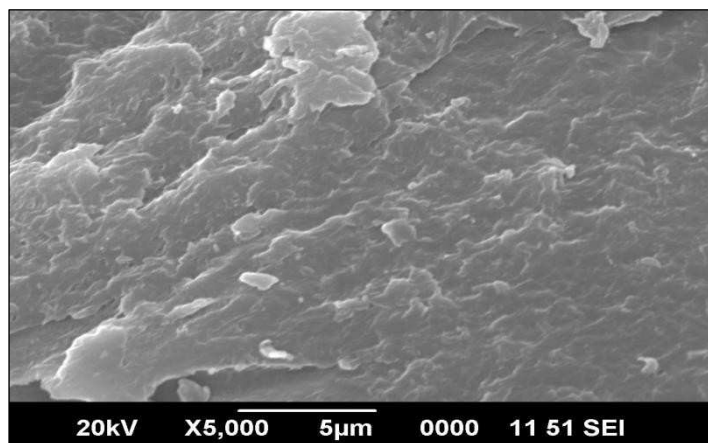


Fig. 8: SEM of solid dispersion of lornoxicam- $\beta$ -CD inclusion complex