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Research Article

**FORMULATION OF CONTROLLED RELEASE DRUG  
DELIVERY OF LORNOXICAM****Qaiser Rasheed<sup>1\*</sup>, Ghulam Razaque<sup>2</sup>, Ghulam Musatafa Shahwani<sup>2</sup>, Noman ul Haq<sup>2</sup>, Nisar  
Ahmed Shahwani<sup>2</sup>, Shafi Muhammad<sup>3</sup>**<sup>1</sup> M. Phil Scholar, Faculty of Pharmacy, University of Balochistan Pakistan<sup>2</sup> Assistant Professor, Faculty of Pharmacy, University of Balochistan Pakistan<sup>3</sup> Associate Professor, Faculty of Pharmacy, University of Balochistan Pakistan**Abstract:**

*The aim of the present work was to develop controlled release matrix tablets of Lornoxicam using polymers such as carbopol, Eudragit RS100 and ethyl cellulose as carriers in various concentrations. Matrix tablets were prepared by direct compression method. Prepared formulations were subjected to various evaluation parameters like hardness, friability, thickness, % drug content, weight variation etc. In-vitro dissolution studies were carried out for 12 hrs. The tablets were subjected to in-vitro drug release in 1.2 pH for first 2 hrs then followed by 6.8 pH phosphate buffer for next 10 hrs and the results showed that among the ten formulations F1 and F6 showed good dissolution profile to control the drug release respectively. Combination of polymers shows greater retarding of drug release. The compatibility of the drug and polymer were determined by UV- spectroscopy. Results showed that the drug was compatible with all polymers. The drug release follows mixed order kinetics and mechanism was found to be non-fickian diffusion. The stability studies were carried out which indicated the selected formulation (F1 & F6) was stable. In conclusion, the results suggest that the developed matrix tablets of Lornoxicam shows to improved efficacy and better patient compliance.*

**Keywords:** Lornoxicam, NSAID's, Controlled release, In-Vitro.**Corresponding Author:****Qaiser Rasheed,***M.Phil Scholar,**Department of Pharmaceutics,**Faculty of Pharmacy, University of Balochistan.*[qaiserrasheedgsk@yahoo.com](mailto:qaiserrasheedgsk@yahoo.com)

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## INTRODUCTION:

The drug delivery is the which is designed for different treatments in different rots but as compare to all of these drug deliveries the oral is the safer one and ease to the patients for drug delivery. The oral drug delivery has, any advantages as it formulation cast is less, patient compliance; therefore it is widely used drug delivery in the world [1]. As the pharmaceutical industries are growing day by day and introducing the drugs having less side effects, safety and the effectiveness is highly improved, they redesigning the drugs applying latest techniques, one of which is Controlled drug delivery. This is the drug latest drug delivery technique which is widely used to change the traditional drug deliver to CR drug delivery Controlled release drug delivery has a major proceed by which lots of organ related issue have been solved with tissue targeting these drugs liberate the active ingredient to the target, that may be tissue or organ [2]. The oral CRS formulation was a big confront for the scientists related to pharmaceutical sciences to formulae the control release due to their failure to detain and limit the system of GIT at targeted areas with causing multiple sides effect which cannot be tolerated. Matrix system of drug delivery and microencapsulation formulation is the vital parts of drug delivery system and proficient option when we develop an oral CRS [3]. The capabilities of an ideal CRDS is that which delivers the active ingredient of a drug at a determined rate both Vivo and Vitro for a specified time period in evaluation with conventional drug delivery system, generally plasma and its secretion effects the efficacy as well as bioavailability at desired site for controlled release oral preparations [2]. Formulation of drug implanted matrix is one of the slightest difficult and most commonly used approaches [4].

Lornoxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxamic class with analgesic (pain relieving), anti-inflammatory and antipyretic (fever tumbling) properties [5]. It is available in oral and parenteral formulations. Lornoxicam is used for the treatment of various types of pain, especially resulting from inflammatory diseases of the joints, osteoarthritis, surgery, sciatica, and other inflammations [6]. Lornoxicam having half life of 3-4 hours is usually administered twice a day for the relief of above mentioned conditions [7]. Polymers are playing major and important role in the formulation of CR formulations and its innovation technology which is widely used in the Sustain and CR drug delivery system [8]. Eudragit is a synthetic derivative of acrylic polymers which is frequently used to slow down the drug release, the advantages included as it is insoluble in water and also in

digestive juices. Guar gum is a natural polymer widely used in Pharma industries to enhance the viscosity properties, by nature it is chemically galactomannan [9]. The ability of the Guar gum is to swell up rapidly in water to form gel and viscous medium is being used for CR formulation which increases the remedial effect as well patient conformity. Guar gum also have the affinity to combine with lots of active ingredients with causing and change [10]. Carbopol 974 polymer is also used to augment the concentration of drug delivery resulting in providing the benefits to the community as well cost efficiency to the patient and Pharmaceutical industries [11].

The aim of this work was to prepare uncoated controlled release tablet of lornoxicam for once a day administration. Another objective of this work was to evaluate drug release data using various kinetic models in order to determine the mechanism of drug release.

## METERIAL AND METHOD:

**Chemicals.** Different chemicals were used in this research work without any further purifications the chemicals were Lornoxicam ( $C_{13}H_{10}ClN_3O_4S_2$ ,  $M_r = 371.82$  g/mol), Carbopol (934 P), Xanthan Gum, Guar Gum, Eudragit RS 100, HPMC (Hydroxy Propyl Methyl Cellulose), Sodium hydroxide, Mg-Stearate 0.5%, Lactose and Starch.

**Instruments.** Following are the different instruments used in this research work and all the instruments were well calibrated. These instruments were PH-Meter Denver, USA), Pharma test dissolution apparatus (Germany), Beakers, Test tubes and volumetric flask (Pyrex, Japan), Friabilator (Erweka, Germany) Vernier Caliper (Germany), UV-Visible spectrophotometer model no. 1610 (Shimadzu, Japan), Syringes (Otsuka, Pakistan), Electronic Balance (Shimadzu, Japan). Hardness Tester (Erweka, Germany) and Single Punch Tableting machine (Erweka GMBH, Germany).

### Standard Curve of Lornoxicam.

To construct standard curve, phosphate buffer and stock solution was prepared. Different dilutions were prepared from stock solution and absorbances were checked spectrophotometrically.

### Phosphate buffer solution

A pH 7.2 Phosphate cradle (200 ml) was readied (0.2 M) dissolving 27.218 g of potassium phosphate in 1L Distilled Water that delivered 0.2 M of potassium phosphate arrangement. After that 0.2 M turf. Hydroxide was preparing by dissolving the crystalline NaOH (8g) in one L Distilled Water. Making weakening of 200 ml with Distilled Water blended 50 ml of 0.2M potassium phosphate and 34.7 ml of NaOH arrangement (0.2 M).

**Preparation of stock solution.**

Making the stock arrangement 100 ml Lornoxicam by dissolving 20 mg Lornoxicam in a 7.2 pH phosphate cushion in volumetric carafe (100 ml) than the volume was made to 100 ml with 7.2 pH phosphate cradle, coming about of this stock arrangement which contained 0.2 mg/ml of lornoxicam.

**Preparation of dilutions.**

The first stock arrangement was used to get ready 5 weakening. A 50 ml of stock arrangement was taken in a 100-ml volumetric jar and was additionally weakened to 100 ml by the option of cradle arrangement produced using phosphate cushion (pH 7.2). Every ml of the subsequent arrangement now constituted 0.1 mg of lornoxicam. This arrangement was additionally used (50 ml) as portrayed above to make advance weakening of lornoxicam with phosphate cradle (pH 7.2). Presently the subsequent arrangement contained 0.05 mg of lornoxicam. In the comparative way encourage weakening having quality 0.025mg/ml, 0.0125mg/ml and 0.00625mg/ml were gotten.

**Spectrophotometric analysis.**

The readied stock arrangement and the weakening of lornoxicam were additionally subjected to UV-

Visible spectroscopy (Shamadzu, Japan). The absorbance was noted at 294.5 nm and the readings were classified as under.

**Solubility studies.**

Solvency ponders were directed in phosphate pH (6.8 and 7.2) and refined water at different temperatures (25°C, 37°C and 40°C) for 24 hours. 100mg of medication was included 100ml of every dissolvable in volumetric carafes and set in shaker whose temperature was kept up thermostatically for every temperature condition. 5ml examples were taken and dissected utilizing twofold pillar UV-Visible spectrophotometer demonstrate No. 1610 (Shimadzu, Japan) at measuring wavelength of 295nm.

**Formulation of Lornoxicam Matrix Tablets.**

CR tablets of 4mg of lornoxicam in which tranquilize was 4mg and two sorts of polymers blend were utilized i.e. Eudragit RS 100+ Carbopol 934P+ Xanthan gum, and Eudragit RS 100+ Carbopol 934P+ Guar gum. Splash dried lactose was fused as filler and Magnesium Stearate 0.5% was utilized as ointment. Diverse medication to-polymers proportions of 10:1, 10:2 and 10:3 were utilized as a part of various definitions as given in table no. 1 and 2.

**Table 1: Composition of 4 mg lornoxicam CR Matrix Tablets using Carbopol 934 P +Eudragit RS 100 + Xanthan Gum**

Drug to Polymer ratio	Drug (lornoxicam)	Polymer	Lubricant (Magnesium Stearate 0.5%)	Filler (Spray dried Lactose)
		Carbopol 934 P + Eudragit RS 100 + Xanthan Gum		
10:1	60 mg	6mg	0.5mg	33.5mg
10:2	60 mg	12mg	0.5mg	27.5mg
10:3	60 mg	18mg	0.5mg	21.5mg

**Table 2: Composition of 4 mg lornoxicam CR Matrix Tablets using Carbopol 934 P +Eudragit RS 100 + Guar Gum**

Drug to Polymer Ratio	Drug (lornoxicam)	Polymer	Lubricant (Magnesium Stearate 0.5%)	Filler (Spray dried Lactose)
		Carbopol 934 P + Eudragit RS 100 + Guar Gum		
10:1	60 mg	6mg	0.5mg	33.5mg
10:2	60 mg	12mg	0.5mg	27.5mg
10:3	60 mg	18mg	0.5mg	21.5mg

**Table 3: Micromeritic properties of controlled release granules**

Formulation code	Angle of repose(°) ± SD	Bulkdensity(gm/ml) ± SD	Tappeddensity(gm/ml) ± SD	Carr'sindex(%) ± SD	Hausner's ratio ± SD
F-1	24.75 ± 0.16	0.39 ± 0.01	0.45 ± 0.03	15.31 ± 1.14	1.15 ± 0.02
F-2	26.82 ± 1.15	0.49 ± 0.03	0.55 ± 0.05	10.62 ± 0.89	1.11 ± 0.30
F-3	21.30 ± 0.51	0.42 ± 0.03	0.44 ± 0.02	14.86 ± 1.35	1.05 ± 0.03
F-4	27.10 ± 0.44	0.39 ± 0.09	0.43 ± 0.04	18.61 ± 1.78	1.14 ± 0.01
F-5	30.27 ± 0.50	0.41 ± 0.10	0.43 ± 0.12	15.28 ± 1.39	1.06 ± 0.02
F-6	26.25 ± 0.62	0.44 ± 0.02	0.46 ± 0.18	15.03 ± 2.75	1.05 ± 0.03

### Preparation of lornoxicam Matrix Tablets.

Later to plan every one of the fixings required to get ready CR network tablet were weighed using electronic adjust by Shamadzu, japan. At that point the medication and polymers were blended in three pre-essential proportions i.e. 10:1, 10:2 and 10:3. At that point fillers were included and if required co-excipients were likewise included and blended. At first blending was done geometrically by mortar and pestle then the entire powdered blend, having D: P (three proportions separately) was gone through #30 Mesh sifter for uniform blending. Oil (0.5% W/W Mg-Stearate) was added to the arranged powdered blends and again sieving was done twice to accomplish appropriate blending. Coordinate pressure was finished utilizing single punch machine (by Erweka, Germany), get ready tablets.

### Physical characterization of lornoxicam Matrices.

#### Hardness Test.

An example part of ten tablets were haphazardly chosen from each sort of details and were subjected to hardness investigation by utilizing hardness analyzer (Erweka, Germany). All readings were noted and normal tablet hardness was figured and classified. Worthy scope of hardness is 5-10 kg/cm<sup>2</sup> [12].

#### Friability test.

Pre-measured 20 tablets were chosen haphazardly and were put in friabilator by Erweka Germany. The mechanical assembly was made to make 100 rounds for 4 minutes. At that point the example tablets were again weighed and %age friability was figured. The adequate scope of friability is <0.8% [11].

#### Dimensional test.

Pre-aligned Vernier caliper was utilized to take dimensional examination of ten tablets of each sort of details. Worthy points of confinement for thickness is 2-4mm while breadth is 4-13mm [11].

#### Weight variation test.

Weights of 20 tablets were resolved separately and mean weight of each kind of plans were resolved per standard strategy [13]

### In-Vitro Dissolution Studies of CR Tablets.

As indicated by USP technique 1 (turning wicker bin strategy) was utilized for in-vitro disintegration considers. Trials were performed in 8 station pharma test mechanical assembly (Hunburg, Germany). Each station vessel was filled 900ml with Phosphate cushion (pH 7.2) as disintegration medium to watch arrival of the medication from tablets at 100 rpm and 37±1 °C, at characterized time interims. 5ml of tests were brought with syringe, went through film channel (0.45µ) and were broke down on UV obvious spectrophotometer (UV 1601, Shimadzu, Japan), location was noted at 294.5nm. After every perception volume was made up to the stamp with

disintegration medium and examinations were performed in triplicate. From standard bend for lornoxicam and UV ingestion esteems the percent sedate discharge was registered.

### Investigation of drug release kinetics of lornoxicam from matrix tablets.

Power law was applied to determine drug release mechanism from different formulations.

Power Law Equation (diffusion/relaxation model)

$$M_t / M_\infty = kt^n \text{----- (3.1)}$$

Where,

W = percent drug release at time t

k = release rate constants

$M_t / M_\infty$  = fraction drug release into dissolution medium.

Exponent 'n' = characterizes the drug release transport mechanism by diffusion.

When n = 0.5 the drug diffuses through and is released from the polymeric matrix with a Quasi-Fickian diffusion mechanism.

When n > 0.5, anomalous, non-Fickian, Case II or zero order release kinetics occurs.

When n = 1, non-Fickian, Case II or zero order release kinetics occurs[13].

### Applying difference and similarity factor for dissolution profiles comparisons.

Comparison of dissolution profiles of CR tablets and reference standard (Zafon fast<sup>®</sup> tablets) by applying difference factor (f<sub>1</sub>) and similarity factor (f<sub>2</sub>). The acceptable limits of f<sub>1</sub> and f<sub>2</sub> are 1-15 and 50-100 respectively.

$$f_1 = \left\{ \frac{\sum_{t=1}^n (R_t - R_t)}{\sum_{t=1}^n R_t} \right\} \times 100 \text{ Equation 3.2}$$

$$f_2 = 50 \times \log \left\{ \left[ 1 + \frac{1}{n} \sum_{t=1}^n (R_t - R_t)^2 \right]^{0.5} \times 100 \right\} \text{ Equation 3.3}$$

R<sub>t</sub> is the reference dissolution profile

T<sub>t</sub> is test formulation dissolution profile after time t. while n shows null points

W<sub>t</sub> is optional weight fraction (Costa and Jose, 2001; Yuksel et al., 2000).

### Expected Results

Expected results are concern directly with reduction in dosage frequencies, patient compliance and have a low formulation cost which ultimately benefits all the community using this NSAID.

## RESULTS AND DISCUSSION:

### Drug polymer compatibility study

The drug polymer compatibility studs and analytical investigation of drug showed that there is no interaction between drug and polymer. So, the drug and polymer are compatible.

### Pre-formulation studies

Estimation of lornoxicam was carried out by UV-Visible spectrophotometer model no. 1610 (Shimadzu, Japan) at  $\lambda_{max}$  376 nm 0.1N NaOH

solution. The linear coefficients of each were found closer to 1. By using the regression coefficient equation the assay and % CDR were calculated.

#### UV spectrum analysis of lornoxicam

At the outset, method for the estimation for the drug was developed. Lornoxicam showed maximum absorption at wavelength 376 nm in 0.1N NaOH solution. Standard calibration curve obeyed Beer's law at given concentration range of 2 µg/ml to 12 µg/ml and when subjected to regression analysis, the value of regression coefficient was found to be 0.999, which showed linear relationship between concentration and absorbance.

#### Micrometric properties of granules

##### Angle of repose

The results of angle of repose were ranged between  $21.30^\circ \pm 0.51$  to  $30.27^\circ \pm 0.50$  which indicates good flow properties of powder.

##### Compressibility index

The results of angle of repose were ranged between  $21.30^\circ \pm 0.51$  to  $30.27^\circ \pm 0.50$  which indicates good flow properties of powder.

#### Evaluation of physicochemical parameters

##### Tablet Hardness

Hardness of the developed formulations F1 to F6 varied from  $4.56 \pm 0.04$  to  $7.6 \pm 0.34$  kg/cm<sup>2</sup> in all the formulation indicating good mechanical strength with an ability to withstand physical and mechanical stress condition while handling.

##### Tablet Thickness

Thickness of the developed formulations F1 to F6 varied from  $3.72 \pm 0.05$  mm to  $4.56 \pm 0.11$  mm in all the formulation and the average thickness is within the range of  $\pm 5\%$ . Each sample was analyzed in triplicate.

##### Friability

The loss in total weight of the tablets due to friability was in the range of  $0.21 \pm 0.13\%$  to  $0.49 \pm 0.08\%$  in all the formulation and the friability value is less than 1% which ensures that formulated tablets were mechanically stable.

##### Weight variation

The maximum % deviation was found to be  $\pm 2.19\%$  from all the formulations. As none of the formulation showed a deviation of more than  $\pm 5\%$  (I.P. limit) for any of the tablets tested, the prepared formulations comply with the weight variation test, thus it fulfills the I.P. requirements.

##### Uniformity of drug content

The drug content in different tablet formulations was highly uniform and in the range of  $97.56 \pm 1.86\%$  to  $103.57 \pm 2.19\%$ . The maximum % drug content for all the formulation was found to be  $103.57 \pm 2.19\%$ . The minimum % drug content for all the formulation

was found to be  $97.56 \pm 1.86\%$ . It is in the limits specified by IP (i.e.  $\pm 10\%$ ).

#### CONCLUSION:

Various formulations were developed by using release rate controlling and gel forming polymers by wet granulation method. Different proportion of HPMC was associated with decrease in the overall cumulative drug release rate. The higher viscosity polymer had been seen to inhibit the initial burst release of lornoxicam. Thus, we conclude that from among all the developed formulations, F2 formulation controlled the drug release for longer period of time over 12 h when compare to other formulations. So, F2 was selected as the best formulation which has HPMC K4M as a polymer.

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