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Formulation Development and Assessment of Lornoxicam Colon Targeted Drug Delivery System

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ABSTRACT

The current study set out to create Lornoxicam colon targeted tablets by employing different quantities of polymers HPMC and ethyl cellulose as carriers. The direct compression method was used to prepare the tablets for sustained release. A number of pharmacopoeial tests, including hardness, friability, thickness, percentage drug content, weight variation, and in-vitro drug release research, were performed on the prepared formulations, and the findings indicated that all of them were within in pharmacopoeial limits. The formulation of tablets with a high concentration of HPMC (300 mg) and a low content of ethyl cellulose (100 mg) demonstrated the intended release of medication in the intestinal environment, according to in vitro investigations. Greater medication release retardation is shown when retardants are combined. FTIR spectroscopy was used to assess the medication and polymer's compatibility. The medication was shown to be compatible with all polymers.

Keywords: *Lornoxicam, HPMC, Ethyl cellulose, Colon Targeting, Sustained Release, and FTIR.*

INTRODUCTION

Oral drug administration is the most practical and significant way to administer medications for a systemic effect. Patients and doctors alike favor tablets, which are the most widely used oral solid formulations on the market. This is due to a variety of factors, not the least of which are patient acceptance and simplicity of administration[1-2].

Conventional formulations have various drawbacks because they must be taken in multiple doses for treating chronic disease conditions. However, many medicinal agents undergo significant presystemic elimination during oral administration due to gastrointestinal breakdown and/or first-pass hepatic metabolism. This results in low systemic bioavailability, a shorter duration of therapeutic activity, and the formation of toxic or inactive metabolites.

When a disease or ailment arises that requires a higher drug concentration at a particular site, the standard dosage form presents a challenge because it releases the drug instantly and exhibits a vast distribution over all organs with the least concentration reaching the desired spot. Thus, the medication must be directed toward a certain location. In the past ten years, there has been a growing interest in creating medication formulations that are unique to specific sites in the colon [3-4].

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Belonging to the Oxicams class, lornoxicam is a non-steroidal anti-inflammatory medication with analgesic properties. Lornoxicam inhibits the cyclo-oxygenase enzyme, which prevents prostaglandin synthesis from occurring. It is used to treat colonic abnormalities as well as inflammatory bowel diseases. After oral treatment, lornoxicam experiences a prolonged and extremely variable hepatic first-pass metabolism, with a reported 15% to 23% systemic bioavailability. The half-life of lornoxicam is 3 to 5 hours. As a result, patients are frequently instructed to take Lornoxicam multiple times daily. Such frequent medication delivery may decrease therapeutic efficacy and patient compliance [6-8].

For Lornoxicam to effectively address the aforementioned issues and reduce gastrointestinal disturbances, such as peptic ulcers with or without bleeding, if they occur in greater concentrations in the GI tract, colon-targeted formulation is required. The current study's objective was to create Lornoxicam matrix tablets specifically intended for the colon.

MATERIALS AND METHODS

Materials used in this study were obtained from the different sources. Doxofylline was a gift sample from Chandra Labs, Hyderabad, India. HPMC, Ethyl cellulose was procured from Essel Fine Chemicals Ltd, Mumbai. Micro crystalline cellulose, Crospovidone, Croscaramellose, Sodium starch glycollate were procured from Loba Chemie Pvt.Ltd, Mumbai. Other excipients such as magnesium stearate, Talc were procured from S.D. Fine Chem. Ltd., Mumbai.

Formulation Development of LornoxicamColon Targeted Tablets:

Formulation involves Enteric Press coated Lornoxicam Tablets. The rapid release core tablet was formulated using using various superdisintegrants such as Crospovidone, Crosscaramellose sodium, Sodium starch glycolate at 3 levels. Totally nine formulations were developed using three superdisintegrants with 3,6,9 mg respectively. Among all nine formulations F_6 is considered as best formulation (from the dissolution parameters). It was subjected to enteric press coating with 400 mg of Polymer blend (Barrier Layer) with variable concentrations of HPMC, Ethyl Cellulose alone and in Combination. The prepared formulations were evaluated to find out the significance of combined effects of polymersto select the best combination and the concentration required to achieve the desired colon targeted release of drug from the dosage form.

Formulation of core tablets by direct compression:

The inner core tablets were prepared by using direct compression method. powder mixtures of Lornoxicam, microcrystalline cellulose, cross-carmellose sodium Sodiumstarch glycollate, crospovidone, ingredients were dry blended for 20 min. followed by addition of Magnesium Stearate. The mixtures were then further blended for 10 min., Blend was subjected to compression by using 8 station rotary tablet punching machine (Minipress, RIMEK), Ahmedabad) using 8 mm circular punches and same hardness used for required number of tablets. (Core Tablet)

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From the in-vitro dissolution studies of rapid release core it was concluded that the formulation F6 i.e, the formulation containing croscarmellose sodium is the best formulation.

Formulation of Mixed Blend for Barrier Layer

The various formulations containing Ethylcellulose and HPMC in different compositions were weighed dry blended at about 10 min and used as press-coating material to prepare press-coated tablets respectively by direct compression method.

Preparation of Press-coated Tablets

The core tablets were press-coated with 400mg of mixed blend/granules. 200mg of barrier layer material was weighed and transferred into a 12mm die then the core tablet was placed manually at the centre. The remaining 200mg of the barrier layer materiel was added into the die and compressed.

Preparation of Enteric Coating Solution

Polymer solution was prepared with HPMC phthalate, myvacet and colour in ethanol as solvent. Formulation can be coated with sensitive polymer which dissolves at the p of the colon. most of the enteric polymer's dissolve in the terminal ileum. To target the drug specifically to colon, it is to be coated with either hydrophilic or hydrophobic polymer along with enteric polymers. For that reason, press coated tablets coated with enteric solution.

Table 1: Formulae for Rapid Release Core Tablets

Name of Ingredients	Quantity of Ingredients per each Tablet (mg)								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Lornoxicam	8	8	8	8	8	8	8	8	8
Microcrystalline Cellulose	137	134	131	137	134	131	137	134	131
Crospovidone	3	6	9	-	-	-	-	-	-
Croscaramellose sodium	-	-	-	3	6	9	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	3	6	9
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total Weight	150	150	150	150	150	150	150	150	150

Table 2: Formulae for Press Coat

Press Coat	Quantity of Ingredients per each Tablet (mg)				
	P_1F_6	P_2F_6	P_3F_6	P_4F_6	P_5F_6
HPMC	400	100	300	200	0
Ethyl Cellulose	0	300	100	200	400
Total Weight	400	400	400	400	400

Table 3: Composition for Enteric Coating Solution

Name of the Ingredient	Quantity (mg)
HPMC Phthalate 55	17.17
Myvacet	1.72
Ferric oxide (red)	2.58
Ethanol	q.s

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Evaluation of rapid release core (RRCT) and Enteric press-coated tablets of Lornoxicam [9-10]

Hardness

The hardness of the tablets was tested by diametric compression using a Monsanto Hardness Tester. A tablet hardness of about 2-4 kg/cm^2 is considered adequate for mechanical stability.

Friability

The friability of the tablets was measured in a rochefriabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W_0) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. [9-10]

Friability (%) = [(Initial weight- Final weight) / (Initial weight)] x 100

Content Uniformity

In this test, 20 tablets were randomly selected and the percent drug content was determined, the tablets contained not less than 85% or more than 115% of the labelled drug content can be considered as the test was passed.

Assay

The drug content in each formulation was determined by triturating 20 tablets and powder equivalent to 100 mg was dissolved in 100ml of phosphate buffer pH 6.8, followed by stirring. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically at 378 nm using phosphate buffer pH 6.8 as blank [6-8].

Thickness

Thickness of the all-tablet formulations were measured using vernier calipers by placing tablet between two arms of the vernier calipers. [9-10]

***In-vitro* Dissolution Study**

The *In-vitro* dissolution study for the Doxofylline sustained release tablets were carried out in USP XXIII type-II dissolution test apparatus (Paddle type) using 900 ml of 0.1 N HCl as dissolution medium for first two hours followed by phosphate buffer pH 6.8 at 50 rpm and temperature 37±0.5°C. At predetermined time intervals, 5 ml of the samples were withdrawn by means of a syringe fitted with a pre-filter, the volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium. The resultant samples were analyzed for the presence of the drug release by measuring the absorbance at 378 nm using UV -Visible spectrophotometer after suitable dilutions. The determinations were performed in triplicate (n=3) [9-10].

Kinetic modeling of drug release:

The dissolution profile of all the formulations was fitted in to zero-order, first-order, Higuchi and Korsmeyer-peppas models to ascertain the kinetic modeling of drug release [11].

RESULTS AND DISCUSSION

All the prepared tablets (rapid release core tablets) were evaluated for different post compression parameters, drug content, mean hardness, friability, mean thickness as per

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official methods The hardness of tablets was in the range of **5.1-5.8 Kg/cm^2.** Weight loss in the friability test was less than **0.54%**. Drug content of prepared tablets was within **acceptance range only**.

Results for all post-compression parameters were tabulated. *In-vitro* Dissolution studies were performed for rapid release core tablets using phosphate buffer pH 6.8 as a dissolution media at 50 rpm and temperature 37±0.5°C. Results revealed that F_6 showed better results. Hence is further processed with barrier layer and finally prepared enteric press coated tablets.

In-vitro Dissolution studies were performed for prepared press coated tablets using 0.1 N HCl for first two hours followed by phosphate buffer pH 6.8 as a dissolution media at 50 rpm and temperature 37±0.5°C.

The *In-vitro* dissolution profiles of tablets were shown in Fig.1-2. Cumulative % drug release of factorial design formulations F_1-F_9 at 12Hr were found to be in the range of **75-98.4%**. From the result it reveals that the release rate was higher for formulations containing Low level of HPMC compared with other Formulations containing Higher level, due to High concentration of polymer drug may have entrapped within a polymer matrix causing a decrease in rate of drug release. variable concentrations of Ethyl cellulose produce modified release properties but high retardation of drug release also not advisable. Therefore, required release of drug can be obtained by manipulating the composition of HPMC and ethyl cellulose.

CONCLUSION

The present research work envisages the applicability of Polymers such as HPMC and Ethyl cellulose in the design and development of colon targeted tablet formulations of Lornoxicam. From the results of *In vitro* dissolution studies, it was clearly understood that as the retardant (HPMC) concentration increases the release rate of drug was retarded and both of these polymers can be used in combination since do not interact with the drug which may be more helpful in achieving the desired targeted release of the drug for longer periods.

On the basis of evaluation parameters, the optimized formulation **P_3F_6** may be used once a day administration in the management of IBW and other colonic disorders and to reduce the risk of Problems associated with them. This may improve the patient compliance by reducing the dosing frequency. which will ultimately improve the therapeutic outcome. We could be able to minimize the per oral cost of the Formulation.

Table 4: Post-Compression Parameters for Rapid Release Core Tablets

S. No	Physical parameter	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
1	**Avg Weight (mg)**	151	150	148	149	152	150	150	149	148
2	**Hardness (Kg/cm^2)**	5.1	5.3	5.6	5.1	5.2	5.3	5.4	5.7	5.8
3	**Thickness (mm)**	3.51	3.48	3.51	3.5	3.5	3.47	3.49	3.52	3.61
4	**Friability %**	0.33	0.46	0.41	0.50	0.54	0.45	0.35	0.39	0.37
5	**Disintegration time**	2min 42 sec	2min 52 sec	2min 4 sec	2min 21 sec	1min 16 sec	1min 08 sec	2min 34 sec	1min 48 sec	2min 26 sec

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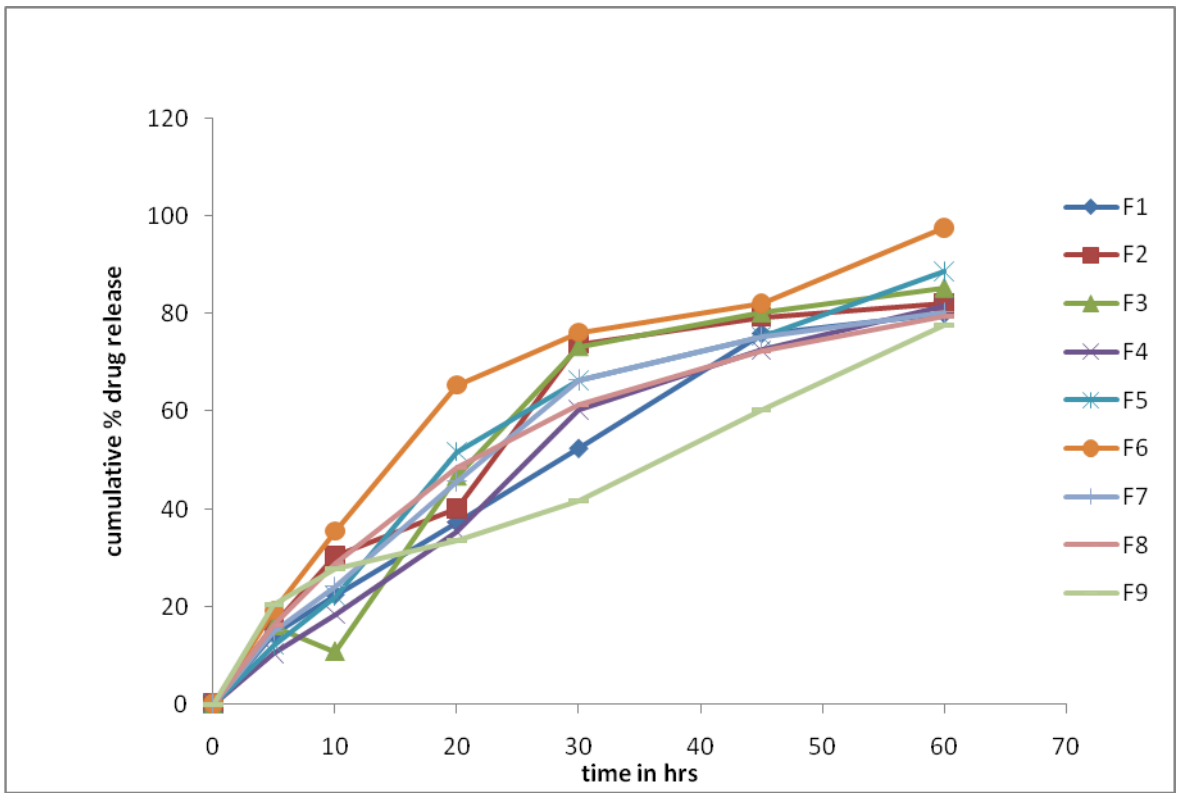

Fig.1 ComparativeIn-vitro dissolution Plots for F_1-F_9

Table 5: Post-Compression Parameters For Enteric Press Coated Tablets

S. No	Physical Parameter	P1F6	P2F6	P3F6	P4F6	P5F6
1	**Avg Weight (mg)**	551	550	549	549	550
2	**Hardness (Kg/cm^2)**	7.4	7.0	7.7	7.4	7.5
3	**Thickness (mm)**	2.45	2.49	2.5	2.51	2.5
4	**Friability %**	0.5	0.45	0.46	0.36	0.24

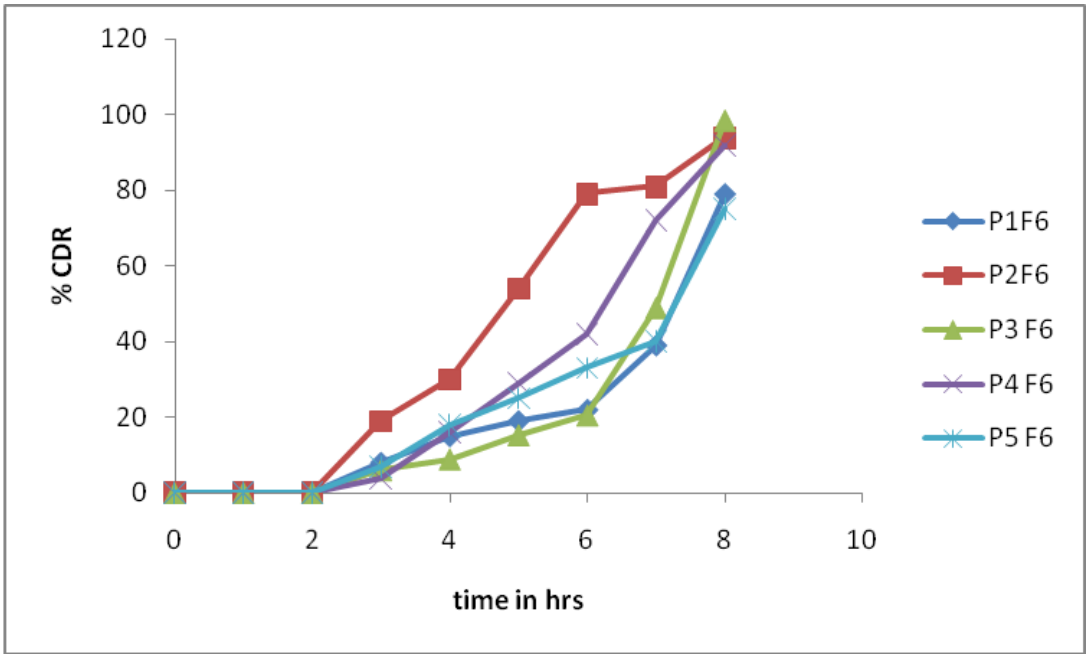

Fig.2 Comparative In-vitro dissolution Plots for P_1F_6-P_6F_6

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