

A Biphasic Release System of Lornoxicam Based on “Tablets in Capsule” Device

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ABSTRACT

The aim of the present investigation is to obtain a programmed drug delivery from a novel system containing a fast release and prolonged release tablet (PRT) placed into a capsule to achieve the biphasic release pattern of lornoxicam. Fast release tablets (FRT) with 3.25 mg were prepared with different diluents and varying concentrations of disintegrant and binders. Hydrogenated castor oil and hydrogenated vegetable oil are used to modulate drug release for the development of PRT with a 12.25 mg dose calculated as a zero-order principle. The compressed tablets were evaluated for various physicochemical parameters like hardness, friability, drug content uniformity, weight variation and *in-vitro* drug release studies. The optimized FRT and PRT tablets were placed in the size 2 capsule to attain biphasic release in which the immediate rapid release was obtained by the FRT followed by slow release from the PRT for 24 hours. The optimized ‘tablet in capsule’ (TCHV) (containing 3%w/w of HVO) followed first-order release with a Non-Fickian diffusion mechanism. FT-IR studies revealed no interaction between the drug and polymers. There were no marketed dosage forms of lornoxicam with biphasic release; hence, the present study indicated the applicability of the ‘tablets in capsule’ technique in the design of biphasic release systems of lornoxicam.

Keywords: Lornoxicam, biphasic release, fast release component, prolonged release component, tablet in capsule, release kinetics.

INTRODUCTION

Assuming that physiological processes and biological functions display constancy over time, much effort has been devoted in the past to developing the drug delivery systems that maintain a flatter plasma level for an extended period of time. Along with many applications in the local and systemic delivery of drugs, the biphasic release system would also be advantageous when an immediate or fast release along with prolonged or sustained release of drugs is desired from a therapeutic point of view for the treatment of chronic diseases such as asthma, angina and rheumatoid

arthritis. Biphasic delivery systems are designed to release a drug at two different rates or in two different periods of time, either fast/prolonged or prolonged/fast. A fast/prolonged release system provides an initial burst of drug release followed by a constant or prolonged rate of release over a defined period of time and in prolonged/fast release system, the release is vice versa. The biphasic release system is used primarily when maximum relief needs to be achieved fast, and it is followed by a sustained/prolonged release phase to avoid repeated administration of the dosage form. Generally, immediate release tablets give fast release to provide a rapid onset of action but fail to provide a longer duration of action whereas conventional sustained dosage forms delay the time to attain maximum therapeutic systemic levels and do not provide a rapid onset of action. Therefore, by developing the biphasic device, plasma peak is

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obtained at an optimal time with a single dose and maintained over a period of time. Suitable candidate drugs for this type of administration include non-steroidal anti-inflammatory drugs, antihypertensive, antihistaminic, and anti-allergic agents.¹

Oral drug administration represents by far the most common and convenient way of drug delivery. The gastrointestinal tract is still the route of choice for drug administration and absorption.² An important goal of drug delivery systems is to achieve well controlled drug release rates, while offering versatility that can be used in various drug release strategies.³ The problems, like the repeated administration of immediate release conventional dosage forms, lead to fluctuations in the drug plasma concentrations, which may cause either toxic effects or end up having no therapeutic effect at all or the typical "peak and valley" fluctuations caused by the administration of frequent dosage forms with minimal intervals. This can be overcome by designing a modified release dosage form capable of providing the desired concentration of drug at the absorption site, which allows the maintenance of drug plasma levels within the therapeutic range over an extended period of time associated with the conventional immediate or sustained/controlled release dosage forms.

This modified release can be achieved by using novel drug delivery systems like the 'tablet in capsule' device. This device consists of tablets packed into a suitable capsule. This reduces the number of doses per day, extensive first pass metabolism and tolerance developed by the body. The pharmacokinetic advantage relies on the fact that the drug release from a fast releasing component leads to a sudden rise in blood concentration and the steady state is maintained by the prolonged release of the component.⁴ Combination of this immediate and prolonged release (biphasic or multi-unit) has various advantages over single unit systems, which include a lower risk of dose dumping, flexibility of blending units with different release patterns, taste masking, excipient tolerability, child acceptability, less inter- and intra-subject variability and a higher degree of dispersion in the digestive tract, thus minimizing the risks of high local drug concentrations.^{5,6} Mini tablets offer an alternative for micro-

particles and beads because of their relative ease of manufacturing and because dosage forms of equal dimensions and weight with smooth regular surfaces are produced in a reproducible and continuous way. Micro-particles and beads are very suitable for coating in order to sustain the drug release, but the coating process may be expensive, time consuming and sometimes associated with poor reproducibility of drug release.⁷ Mini tablet systems offer a sustained release, site specific delivery and potential zero-order drug release without the coating process.^{7,8} The in-vitro and in-vivo performance of such systems has been studied and described by Munday et al.⁹

In the present study, the biphasic release of lornoxicam, a non-steroidal anti-inflammatory drug was studied by the formulation of tablets in capsules which consists of a fast release component and a prolonged release component. The prolonged release component was formulated using hydrogenated vegetable oil (HVO) and hydrogenated castor oil (HCO). HVO is made from fully hydrogenated refined vegetable oil that is sprayed into a dry, fine powder. It is used as a lubricant, binder and also as a controlled release polymer for pharmaceutical applications.¹⁰ HCO is a white to slightly yellow fine powder obtained by hydrogenating castor oil using a catalyst. It has been used in pharmaceutical formulations or technology as a sustained release coating material and binding agent.^{11,12}

Material and Methods

Materials

Lornoxicam was a generous gift sample from Macleods Pharmaceuticals Ltd. Hydrogenated castor oil was purchased from Dabur India Ltd (Mumbai), India, and hydrogenated vegetable oil (Lubritab) was obtained from S. Zhaveri Pharmakem PVT Ltd. India. All other chemicals used were of analytical grade.

Methods

Preparation of the Biphasic 'Tablet in Capsule' System

Calculation of Dose¹³

As per the zero-order release principle, the rate of delivery must be independent of the amount of drug remaining in the dosage form and constant over time. The

release from the dosage form should follow zero-order kinetics, as shown by the following equation:

$$K_0 = \text{Rate in} = \text{Rate out} = K_e \cdot C_p \cdot V_d \quad (1)$$

where K_0 is the zero-order rate constant for drug release (amount/time), K_e is the first-order rate constant of overall drug elimination (h^{-1}), C_p is the desired plasma drug level (amount/volume), and V_d is the volume of drug distribution.¹⁴ If the elimination half life of lornoxicam is 3-5 hours ($k_e = 0.693/4.0$), C_p is 0.28 mg/L¹⁵ and V_d is 10.5 L, then K_0 is 0.5093 mg/h. For a system in which the maintenance dose releases the drug by a zero-order process for a specified period of time, the total dose is as given in the below equation:

$$D_{\text{Total}} = (D_1 - K_0 t_p) + K_0 t_d \quad (2)$$

where D_1 is the initial dose, K_0 is the zero-order rate constant, t_p is the time of the peak drug level (1.5 hours) and t_d is the total time desired for controlled release from a single dose (i.e. 24 hours). If the maintenance dose begins to release the drug at the time of dosing ($t = 0$), it will add to that which is provided by the initial dose, thus increasing the initial drug level. In this case, a correction factor is needed ($K_0 t_p$) to account for the added drug from

the maintenance dose. This correction factor is the amount of drug provided during the period from $t = 0$ to the time of the peak drug level, t_p . If D_1 is 4.0 mg, K_0 is 0.5093 mg/hr, t_p is 1.5 hours, and t_d is 24 hours, then as per Eq. 2, the total dose would be 15.46 mg of lornoxicam. From the above calculations, the total dose obtained for the controlled release of lornoxicam for 24 hours is 15.46 mg. The total dose was rounded to 15.5 mg for convenience. The dose in the formulation of the fast release tablet was 3.25 mg and the PRT was 12.25 mg of lornoxicam.

Fast Release Component

An optimized fast release tablet was developed by using different diluents (AVICEL PH 101, pregelatinised starch and DCL 21) and varying concentrations of binder (PVP K 30) and disintegrant (croscarmellose sodium). The drug, diluents, disintegrant and binder were weighed for a batch of 100 tablets as per formulae given in Table 1. These were then sifted through a #40 (420 μm) sieve, transferred to a poly bag and blended for 5 min. To the homogeneous blend, magnesium stearate sifted through a #60 (250 μm) sieve was added and blended for 2 min. The resulting blend was compressed with a Cadmach 16 station compression machine under a common compression force of 1-2 Kg/ cm^2 , using a flat punch 4 mm in diameter.

Table 1: Formula of the fast release tablet

Ingredient	LF1 (mg/Tab)	LF2 (mg/Tab)	LF3 (mg/Tab)	LF4 (mg/Tab)	LF5 (mg/Tab)	LF6 (mg/Tab)
Lornoxicam	3.25	3.25	3.25	3.25	3.25	3.25
Avicel PH102	34.35	-	-	-	-	-
Pregelatinised starch	-	34.35	-	-	-	-
DCL 21	-	-	34.35	35.15	33.55	33.15
PVP K 30	1.2	1.2	1.2	0.4	2	1.2
Croscarmellose sodium	0.8	0.8	0.8	0.8	0.8	2
Magnesium stearate	0.4	0.4	0.4	0.4	0.4	0.4
Total weight	40	40	40	40	40	40

Prolonged Release Component

The prolonged release component was formulated

using HVO or HCO in different concentrations.

Accurately weighed drug, polymer (HVO or HCO) and

diluent were weighed for a batch of 100 tablets as per formulae given in Table 2, transferred to a china dish and melted to form a molten mass. To this molten HVO or HCO mass, lornoxicam and DCL 21 presifted through a #40 (420 µm) sieve was added and thoroughly mixed, the

obtained damp mass was passed through a #40 (420 µm) sieve. The blend was then compressed into tablets using a Cadmach 16 station compression machine under a common compression force of 2-3 Kg/cm², using 5 mm diameter punches.

Table 2: Formulae of prolonged release tablet prepared using hydrogenated vegetable oil

Ingredient	LHV 1 (Mg/Tab)	LHV 2 (Mg/Tab)	LHV 3 (Mg/Tab)	LHV 4 (Mg/Tab)
Lornoxicam	12.25	12.25	12.25	12.25
Hydrogenated vegetable oil	0.6	1.2	1.8	2.4
DCL 21	47.15	46.55	45.95	45.35
Total weight (mg)	60	60	60	60

Table 3: Formulae of prolonged release tablet prepared using hydrogenated vegetable oil

Ingredient	LHC 1 (Mg/Tab)	LHC 2 (Mg/Tab)	LHC 3 (Mg/Tab)	LHC 4 (Mg/Tab)	LHC 5 (Mg/Tab)	LHC 6 (Mg/Tab)
Lornoxicam	12.25	12.25	12.25	12.25	12.25	12.25
Hydrogenated castor oil	0.6	1.2	1.8	2.4	3	3.6
DCL 21	47.15	46.55	45.95	45.35	44.75	44.15
Total weight (mg)	60	60	60	60	60	60

Evaluation of Tablets

The prepared tablets were subjected to quality control tests such as uniformity of weight, friability test, hardness, drug content and *in vitro* dissolution studies.

Uniformity of Weight

According to Indian Pharmacopoeia (I.P.)¹⁶, twenty tablets were selected at random, weighed together and then individually. The mean and the standard deviation were determined. Prepared tablets complied with the test if not more than two of the individual weights deviated from the average weight (>250 mg) by more than the percentage (5%) and none deviated more than twice that percentage.

Disintegration

The disintegration test¹⁷ was performed at 37±2° C in deionized water for six tablets from each formulation using a tablet disintegration unit (Electrolab, India). The tablets passed the test if all of them disintegrated. If 1 or 2 tablets failed to disintegrate, then the test was repeated on

12 additional tablets, but not less than 16 of the total 18 tablets tested should disintegrate.

Friability

The friability test¹⁸ was carried out in a dual chamber friabilator (Electrolab, India). Tablets equivalent to 6.5 gm were weighed (W_2) initially and put in a rotating drum. Then, they were subjected to 100 falls of 6 inch height (25 rpm for four min). After the completion of rotations, the tablets were dedusted by using a camel hair brush and weighed (W_1). The percent loss in weight or friability was calculated by the formula given in the below equation:

$$\text{Friability} = \frac{W_2 - W_1}{W_2} \times 100 \quad (3)$$

Hardness¹⁹

Tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing. Ten tablets were

randomly selected and the hardness of each tablet was measured using a Monsanto hardness tester. The mean hardness was determined and expressed in Kg/cm².

Determination of Drug Content

From each batch of prepared tablets, 10 tablets were randomly collected and powdered.²⁰ Powder equivalent to 3.25 mg of fast release and 12.25 mg of PRT of lornoxicam was weighed accurately from each batch and transferred separately to a 100 mL volumetric flask. A pH 6.8 phosphate buffer was added to make up a volume of 100 mL and subjected to vortex mixing and sonication for dissolving the drug. Appropriate dilutions were made with pH 6.8 phosphate buffer and the amount of lornoxicam was analyzed at 378 nm using a double beam UV/visible spectrophotometer (Elico Ind Ltd, India). The drug content was calculated using the following equation:

$$\text{Drug content} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100 \quad (4)$$

In Vitro Dissolution Study

The *in vitro* release tests were performed, according to the US Pharmacopoeia 27, and the compressed fast release, PRT and 'tablets in capsule' were introduced into a dissolution medium. The dissolution medium used was phosphate buffer pH 6.8, and rotational speed of the paddle was set at 100 rpm at 37 ± 0.5°C. Aliquots (5 mL each) were withdrawn at predetermined time intervals by means of a syringe fitted with a 0.45 µm pre-filter and immediately replaced with 5 mL of fresh medium maintained at 37 ± 0.5°C. The samples were analyzed for lornoxicam at 378 nm using a double beam UV/visible spectrophotometer (Elico Ind Ltd, India). All the dissolution experiments were carried out in triplicate.

Release Kinetics

The analysis of a drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of matrix systems. As a model-dependent approach, the dissolution data was fitted to five popular release models such as zero-order, first-order, Higuchi, Hixon-Crowel and Korsmeyer-Peppas equations. The order of drug release

from the matrix systems was described by using zero-order kinetics or first-order kinetics and the mechanism of drug release by using Higuchi and Hixon-Crowel equation. Zero-order release kinetics²¹ is defined as a linear relationship between the fractions of drug released versus time. A plot of the fraction of drug released against time will be linear if the release obeys zero-order release kinetics. It is given by the following equation:

$$Q = K_0 t \quad (5)$$

where Q is the fraction of drug released at time t and K_0 is the zero-order release rate constant.

In first-order release kinetics,²² Wagner assumed that the exposed surface area of a tablet decreased exponentially with time during dissolution process. This suggests that drug release from most of the slow release tablets could be described adequately by the apparent first-order kinetics. First-order kinetics is defined by the below equation:

$$\ln(1-Q) = -K_1 t \quad (6)$$

where Q is the fraction of drug released at time t and K_1 is the first-order release rate constant. Thus, a plot of the logarithm of the fraction of drug remaining against time will be linear if the release obeys first-order release kinetics. The Higuchi equation²³ defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time calculated by the below equation:

$$Q = K_2 t^{1/2} \quad (7)$$

where K_2 is the release rate constant. Hence, a plot of the fraction of drug released against the square root of time will be linear if the release obeys the Higuchi equation. This equation describes drug release as a diffusion process based on Fick's law, square root time dependent. The erosion equation²⁴ defines the drug release based on tablet erosion alone as given in the below equation:

$$Q = 1 - (1 - K_3 t)^2 \quad (8)$$

where Q is the fraction of drug released at time t , and K_3 is the release rate constant. Thus, a plot between $[1 - (1 - Q)^{1/2}]$ against time will be linear if the release obeys the erosion equation. In order to find out the mechanism of drug release, first 60% of the drug release data was fitted in a Korsmeyer-Peppas model as given below:

$$\frac{M_t}{M_\infty} = K_4 t^n \quad (9)$$

where M_t/M_∞ is a fraction of drug released at time, t , K_4 is the release rate constant and n is the release exponent. The n value is used to characterize different releases for cylindrical shaped matrices. For the case of cylindrical tablets, $n=0.45$ corresponds to a Fickian diffusion mechanism, $0.45 < n < 0.89$ a non-Fickian transport, $n = 0.89$ Case II (relaxation) transport, and $n > 0.89$ to super case II transport.²⁵

Fourier Transform Infrared Spectroscopy

Infrared spectroscopy was conducted using a Shimadzu FTIR 8300 Spectrophotometer and the spectrum was recorded in the region of 4,000 to 400 cm^{-1} . The procedure consisted of dispersing a sample (drug and drug resin mixture, 1:1 ratio) in KBr (200-400 mg) and compressing into discs by applying a pressure of 5 tons

Table 4: Physical parameters of the fast release tablets

Formulations	Uniformity of weight (mg)	Hardness (kg/cm ²) [*]	Friability (%)	Disintegration (sec) ^{***}	Drug Content (%) [*]
LF1	40.12± 1.22	2.3± 0.15	0.69± 0.02	25	100.10± 1.98
LF2	40.03± 2.12	2.6± 0.15	0.42± 0.05	30	99.60± 1.31
LF3	40.08± 1.70	2.2± 0.21	0.54± 0.06	22	100.5± 2.92
LF4	40.13± 1.34	1.2± 0.25	1.23± 0.03	31	99.93± 2.35
LF5	40.22± 1.45	2.1± 0.25	0.24± 0.05	26	99.87± 1.34
LF6	40.31± 2.32	2.5± 0.20	0.37± 0.04	33	100.03± 2.83

* All values are expressed as mean ± s.d., n = 10

** All values are expressed as mean ± s.d., n = 20

*** All values are expressed as mean ± s.d., n = 6

for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained. Spectra were recorded in duplicate for each sample.

Results and Discussion

Evaluation of Tablets

The physical attributes of the fast and PRT were found to be satisfactory. Typical tablet defects, such as capping, chipping, and picking were not observed. Tablet properties like uniformity of weight, hardness, friability and drug content of each batch are represented in Tables 4, 5 and 6. All batches passed the weight variation test and were found to be within range ($\pm 7.5\%$). Disintegration was found to be < 15 min for all the fast release tablets, thereby compelling as per the official limit of disintegration for tablets. Friability of all batches were found to be less than 1% which indicates that tablet surfaces are strong enough to withstand mechanical shock or attrition during storage and transportation until they are consumed. Hardness of the tablet was found to be 1-2 kgcm^{-2} for the fast release and 2-3 kgcm^{-2} for PRT. The drug content of all batches was found within the limit (90–110%). Low s.d. values in drug content indicated uniformity of drug distribution in all the prepared tablets. Thus, the prepared fast and PRT of lornoxicam were found to be of good quality fulfilling all the official compendia for tablets.

Table 5: Physical parameters of the prolonged release tablet prepared with HVO

Formulations	Uniformity of weight ** (mg)	Hardness ₂ (kg/cm ²)	Friability (%)	Drug Content (%) *
LHV 1	61.09± 1.89	3.5± 0.23	0.23± 0.12	99.97± 2.67
LHV 2	60.12± 2.56	3.3± 0.18	0.12± 0.76	100.09± 1.89
LHV 3	60.56± 1.12	3.4± 0.54	0.34± 0.18	99.93± 2.43
LHV 4	60.87± 2.87	3.2± 0.44	0.25± 0.56	99.89± 1.87

* All values are expressed as mean ±s.d., n = 10

** All values are expressed as mean ± s.d., n = 20

Table6:Physical parameters of the prolonged release tablet prepared with HCO

Formulations	Uniformity of weight ** (mg)	Hardness ₂ (kg/cm ²)	Friability (%)	Drug Content (%) *
LHC 1	60.91± 2.34	3.2± 0.15	0.19± 0.02	99.23± 2.76
LHC 2	61.02± 1.87	3.4± 0.15	0.32± 0.05	100.04± 1.78
LHC 3	60.21± 1.98	3.5± 0.21	0.24± 0.06	100.12± 2.56
LHC 4	61.12± 3.32	3.6± 0.25	0.15± 0.03	99.92± 2.29
LHC 5	60.67± 2.56	3.6± 0.25	0.19± 0.05	99.78± 1.87
LHC 6	60.54± 1.87	3.6± 0.20	0.27± 0.04	100.03± 2.66

* All values are expressed as mean ±s.d., n = 10

** All values are expressed as mean ± s.d., n = 20

In Vitro Dissolution Study

Fast Release Tablet

The prepared fast release tablets were subjected to *in vitro* drug release studies in a suitable dissolution media for 60 min to assess their drug release. Tablets were developed using different diluents (pregelatinised starch, DCL 21 and Avicel pH 102). Formulation LF 3 prepared with DCL 21 gave a better release than the other formulations with pregelatinised starch and Avicel PH 102 due to its hydrophilic nature. Formulations LF 4 failed in friability due to low hardness, hence it was not subjected to dissolution. When formulation LF 5 was

taken with a higher concentration (5% w/w) of binder, the release from these tablets was less when compared to that of LF 3 with a lower concentration (3%) of binder. The release profile of formulation LF 6 with a higher concentration (5%w/w) of disintegrant was similar to that of LF 3. As, LF 3 with optimum concentration of disintegrant and binder gave better release, it was considered as the final optimized formulation to be packed into a capsule along with the PRT to attain biphasic release. The release profiles of formulations LF 1- 6 are shown in Figure 1.

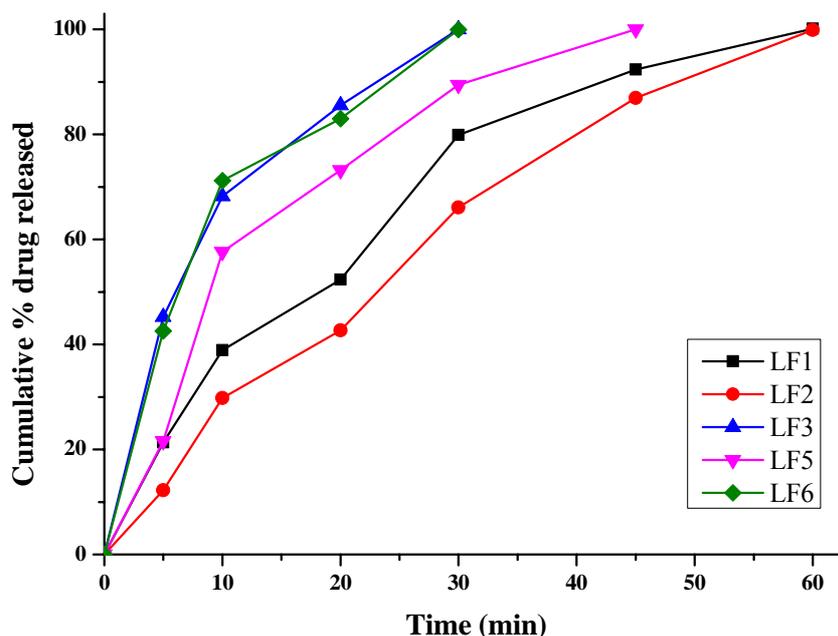


Figure1: In vitro release profile of fast release tablets

Prolonged Release Tablet

In vitro drug release studies of the PRT prepared using HVO and HCO were done in pH 6.8 phosphate buffer, and 900 ml set at 100 rpm. Formulation LHV 1-4 were prepared with 1%, 2%, 3% and 4% w/w HVO, respectively. Drug release from these tablets was prolonged as the concentration of the polymer increased. LHV 3 and LHV 4 formulated with 3% and 4% w/w of HVO gave a prolonged release for 24 hours and more, but LHV 3 was considered as the final formulation as the drug release targeted was for 24 hours and it was obtained by LHV 3. Respective release profiles of LHV

1- 4 are shown in Figure 2. Formulations LHC 1- 6 were formulated using 1%,2%, 3%, 4%, 5% and 6% w/w of HCO. Formulations LHC 5 and LHC 6 prepared with 5% and 6% w/w of HCO gave release profile for 24 hours and more, but LHC 5 was considered as the final formulation due to its 24 hour release profile which is shown in Figure 3. Formulations TCHV (LHV 3 & LF3) and TCHC (LHC5 & LF3) were reformulated with optimized fast release and respective optimized PRT by packing them into size 2 capsules to achieve the biphasic release and their release profiles were given along with their respective PRT profiles.

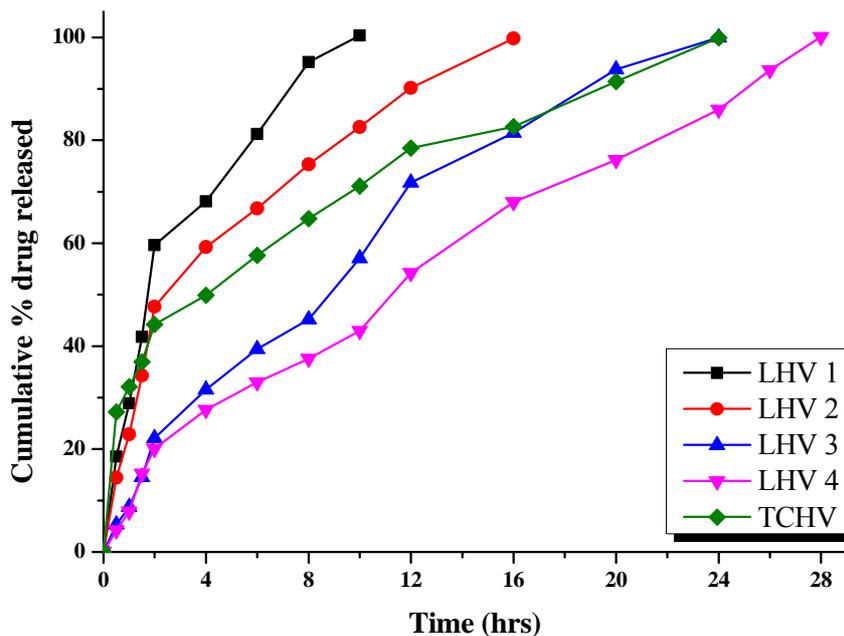


Figure2: In vitro release profile of prolonged release tablets formulated with HVO

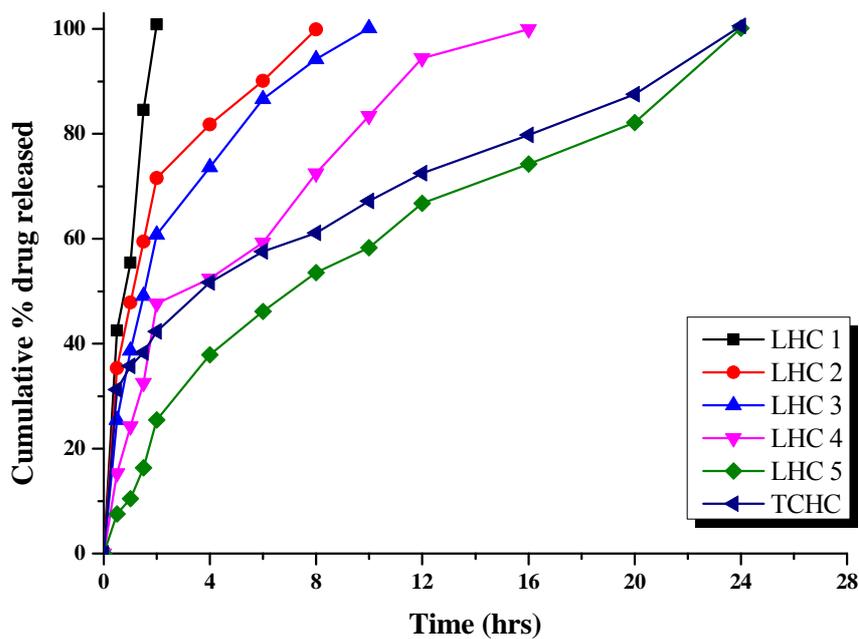


Figure3: In vitro release profile of prolonged release tablets formulated with HCO

Release Kinetics

The drug release of lornoxicam from the formulations TCHV and TCHC followed first-order kinetics which was indicated by higher 'r' values of a first-order release model. The relative contributions of drug diffusion and erosion to drug release were further confirmed by

subjecting the dissolution data to a Higuchi model and a Hixon-Crowell model. It was found that TCHV and TCHC followed first-order kinetics with a Non-Fickian diffusion mechanism as the 'n' value is <0.45. The respective values are given in Table 7.

Table 7: Release order kinetics of 'tablet in capsule'

Model	Zero-order		First-order		Hixon-Crowell	Higuchi	Pepas	
Batch	r	K ₀	r	K	r	R	r	n
TCHV	0.925	3.33	0.987	0.04	0.966	0.986	0.993	0.343
TCHC	0.924	3.13	0.982	0.03	0.967	0.983	0.991	0.325

Fourier Transform Infrared Spectroscopy

Pure lornoxicam spectra showed characteristic peaks at 3,422 cm⁻¹ (OH stretching), 3,091.07 cm⁻¹, 3,066.77 cm⁻¹ (aromatic C-H stretching), 2,923.62 cm⁻¹, 2,823.62 cm⁻¹ (aliphatic C-H stretching vibrations), 1,642.85 cm⁻¹ (C=O stretching vibrations), 1,595.75 cm⁻¹ (C=C stretching), and 1,540.0 cm⁻¹ (C=C stretching). Pure HCO showed the following peaks 3,345.83 cm⁻¹ (OH stretching), 2,955.92 cm⁻¹, 2,921.50 cm⁻¹, 2,850.04 cm⁻¹ (aliphatic C-H stretching vibrations), 1,738.54 cm⁻¹ (C=O stretching vibrations) and pure HVO showed the following peaks 2,955.75 cm⁻¹, 2,917.01 cm⁻¹, 2,849.92 cm⁻¹ (aliphatic C-H stretching vibrations), and 1,737.29 cm⁻¹ (C=O stretching

vibrations).

Optimized formulations (TCHV and TCHC) also exhibited the characteristic peaks of lornoxicam with no additional peaks observed in the spectra, indicating the retention of the chemical identity of lornoxicam as shown in Fig. 4. However, the intensity of peaks corresponding to the drug and polymers was reduced or broadened in the optimized formulations possibly due to the mixing with the polymer and addition of other excipients. The FTIR spectra data confirmed that HCO and HVO did not alter the performance characteristics indicating their compatibility with the drug.

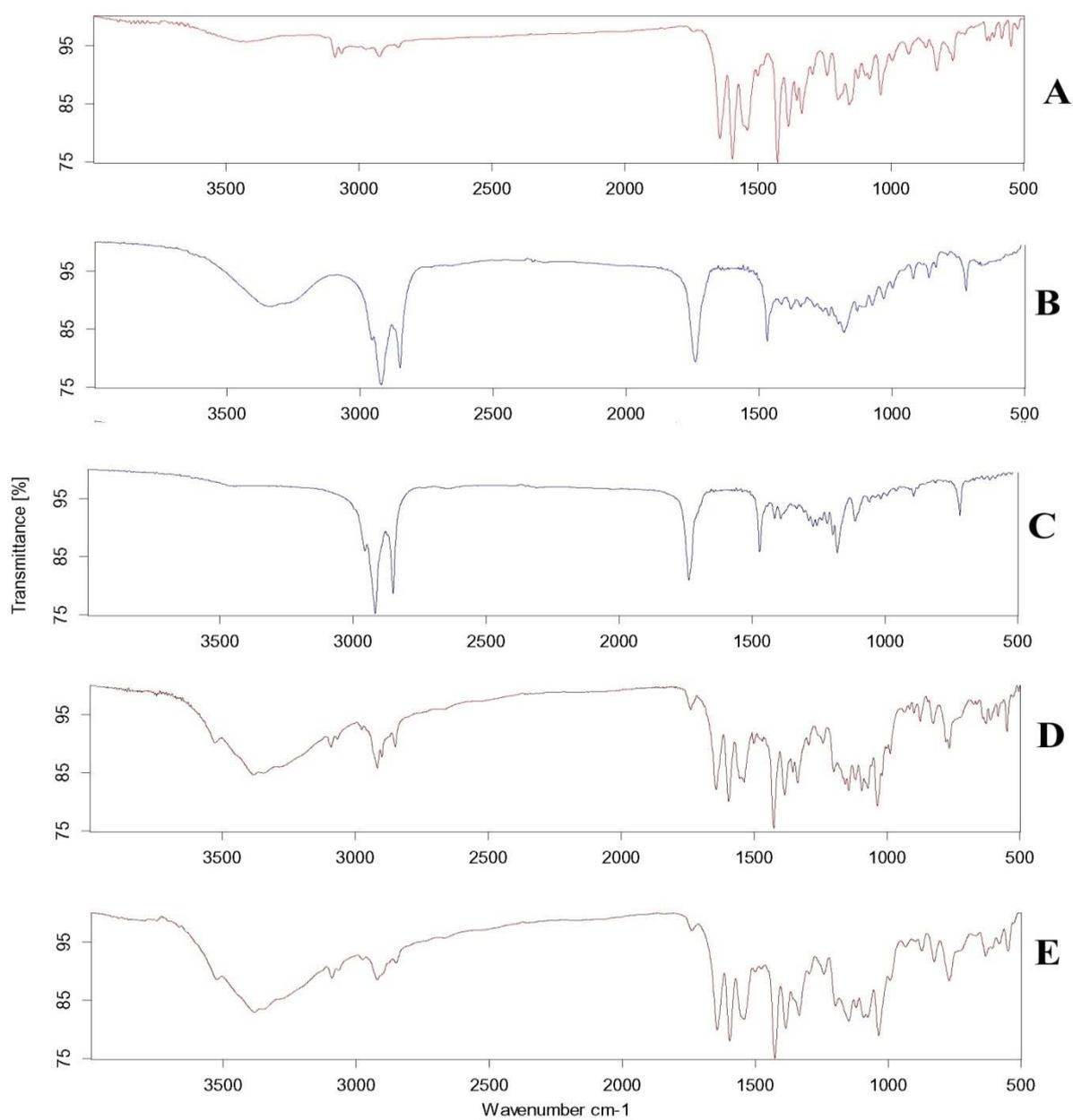


Figure 4: FTIR Spectra of A) lornoxicam B) hydrogenated castor oil C) hydrogenated vegetable oil D) TCHC formulation and E) TCHV formulation

Conclusion

A biphasic oral delivery system was achieved by a 'tablet in capsule' device using fast release and PRT packed into a capsule. This is characterized by an initial rapid release, corresponding to the fast release tablet, followed by a period of slow release, corresponding to the PRT. The two different release phases can be easily adjusted in a wide range of the values of both delivery rate and ratio of the dose fractions, on the basis of the pharmacokinetics and therapeutic needs, to perform the desired *in vivo* profile. The results show that the release profile is strongly dependent on the composition of

subunits. Tablets in capsule (TCHV) formulated with 3% w/w of HVO as a polymer in PRT followed first-order release with a Non-Fickian diffusion mechanism, and it can be used for the development of tablets to be packed in a capsule for biphasic release.

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