FORMULATION, OPTIMIZATION AND EVALUATION OF BILAYER TABLET OF LORNOXICAM

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Abstract:

The goal of the current study was to create, enhance, and evaluate a bilayer tablet containing the powerful NSAID Lornoxicam. The tablet meets the parameters for sustained-release product release, has a brief half-life, and is distinguished by an initial burst of drug release in the GIT. The two proposed bi-layer tablets consist of an immediate-release layer and a sustained-release layer. The quick release layer was prepared by the dry granulation technique using different amounts of sodium starch glycolate and other superdisintegrating agents. The wet granulation method with varying polymer concentrations, such HPMC E50, is used to form the sustained release layer. Each layer was modified and created separately.Weight variation, hardness, friability, disintegration time, wetting time, in vitro dissolving tests, and medication content were all evaluated for the tablets. The optimised batch of bilayer tablet formulation was determined to be batch F4, which contained sodium starch glycolate and demonstrated the highest drug release of 23.92% for one hour in the immediate release layer and 97.5% for twenty-four hours in the sustained release layer using HPMC E50.

Key words: Sustained release, Bilayer Tablet, delayed release tablet, Lornoxicam

1. INTRODUCTION

Two or three layers of granulation are compacted together to form layer tablets. Because the borders of each layer are visible, they resemble a sandwich. The benefit of this dose form is that it creates an inert barrier that separates two incompatible chemicals. With the slow-release component in the second layer and the immediate-release quantity in the first, it enables sustained-release preparations. 1–5 It is possible to introduce a third layer with an interim release.[1] It is possible to carefully control each layer's weight. Compared to compression-coated tablets, two-layer tablets use less material. Multilayer tablets can have monograms and other identifying symbols carved on their surfaces. There are several ways to create a unique tablet character by colouring the separate layers.Analytical work can be made simpler by layer separation prior to test.[6] Formulations for prolonged release have long been developed using the multilayered tablet principle. In order to maintain the medication release, such a tablet may include two or three layers in addition to its fast-releasing layer.[8] Oral sustained release gastroretentive dose forms increase the bioavailability of pharmaceuticals with a narrow absorption window and provide several benefits for drugs that are absorbed from the upper gastrointestinal tract. Creating a novel gastroretentive floating sustained release delivery method for bilayer medication tablets with a small absorption window was the aim of the project.[11]

A drug layer in a bi-layer tablet delivers the medication instantly, while a second layer distributes the drug subsequently, either in a sustained release way or as a second dosage.Two incompatible chemicals can be separated, two drugs can be released consecutively, or a sustained release tablet with an immediate release dose in the first layer and a maintenance dosage in the second layer can be made using a bi-layer tablet.

2. MATERIALS AND METHODS

All the reagents, chemicals and drug were used of analytical grade

and procured from local vendor

3. EXPERIMENTAL WORK

3.1 Preformulation Study

The physicochemical characteristics of the medication that may influence the creation of an effective dosage form were characterised through preformulation experiments prior to the manufacture and characterisation of pharmaceutical dosage forms containing therapeutic moiety.[13]Preformulation investigations were conducted using tests for drug identification (physical appearance, melting point, and infrared spectra), solubility profile, partition coefficient calculation, and quantitative estimation.[14]

3.2 Identification test

(a) Physical Observation

The sample of Lornoxicam was identified and characterized by visual observation.

(b) Melting Point

Melting point equipment was used in the capillary method to determine the melting point. A pre-sealed capillary tube with the pure medication was inserted into the slot behind the eyepiece of the melting point device. Before turning it on, make sure the device was plugged in and set to zero. The temperature at which the medication melted or broke down was noted.[15]

3.3 Solubility

A variety of common solvents will be used to assess the drug's solubility. At room temperature, a certain amount of medication was dissolved in each of the solvents under investigation. The UV technique was used to observe the solubility. The excess medication was dissolved in 10 millilitres of solvent and left on an orbital shaker for 48 hours. The quantity of LX was ascertained by measuring the absorbance using a UV spectrophotometer after the shaken solution had been filtered and appropriately diluted.

3.4 Partition Coefficient

The ratio of un-ionized medication dispersed between the organic and aqueous phases at equilibrium is known as the partition coefficient. Thus, the quotient of two concentrations is the partition coefficient (P), which is typically expressed as Log P. Since octanol shares characteristics with biological membranes, it is used as the solvent for the oil phase.[16]

$$P_{\frac{o}{w}} = \left(\frac{C_{Oil}}{C_{water}}\right) equilibrium$$

$$LogP = LogP_{o/w}$$

Drug lipophilicity and its capacity to pass across biological membranes are gauged by the partition coefficient. The n-octanol:water system's LX s partition coefficient was found. After precisely weighing 10 mg of LX, it was added to 10 mL of n-octanol and aqueous phase, respectively. A mechanical shaker was used to shake the mixture for 24 hours in order to achieve equilibrium.

3.5 Determine absorption maxima and preparation of standard curves

3.5.1 Determination of absorption maxima

Using a solution of LX in various solvents, such as distilled water and 0.1 N HCl (pH 1.2), the absorption maximum was ascertained. These solutions were scanned using the Shimadzu-1700 UV/Visible Spectrophotometer in the 200–400 nm range.

3.5.2 Preparation of 0.1 N HCL ph 1.2

8.64 millilitres of strong hydrochloric acid were collected, and distilled water was added to bring the amount up to one litre. Before quantitative measurement, water was used to bring the pH down to 1.2.

3.5.3 Preparation of standard curve in 0.1 N HCL

100 mL of 0.1N HCL was used to dissolve 10 mg of LX. A 10 mL volumetric flask was used to create several dilutions of this stock solution in the concentration range of 2.0, 4.0, 6.0, 8.0, and 10 μg/mL. The absorbance was measured at 293 nm.

2.3 Drug Excipient Interaction Studies

3.6 FTIR Studies

Using spectrophotometry of infrared absorption, the spectrum of LX hemiydrate was identified. The drug was placed directly on the stub, and the FT-IR spectra demonstrate the distinctive absorption of the drug's several functional groups. FTIR analysis was performed on both the physical mixes and the pure medication. Drug-polymer interactions were examined in the spectra.

3.7 Precompression studies

Physical characteristics were measured, including the final blend's bulk density, tapped density,

compressibility index, Hausner ratio, and angle of repose.[16]

3.7.1 Loose Bulk density

It is the proportion of the powder's bulk volume to total mass. 24 The weighted powder was poured into a measuring cylinder, and the volume was recorded. It is provided by and stated in gm/ml.

$$LBD = \frac{M}{V_o}$$

Where, M is the mass of powder and Vo is the bulk volume of powder.

3.7.2 Tapped Bulk Density

It is the proportion of the powder's total mass to its tapped volume. A 10 ml measuring cylinder was filled with 2 g of powder from each recipe, which had been gently shaken to break up any agglomerates that had formed. The cylinder permitted falling on its own weight onto a hard surface from a height of 2.5 cm at 2-second intervals after the starting volume was noted. 24 The tapping was kept up until there was no more audible variation. The following formula was used to compute TBD:

$$TBD = \frac{M}{V_t}$$

where Vt is the powder's tapped volume and M is its mass.

3.7.3 Angel of repose

The angle of repose may be used to calculate the frictional force in a loose powder. This greatest angle between a powder pile's surface and the horizontal plane is what determines the granules' flow characteristics. 25 The funnel technique was used to calculate the angle of repose. A funnel was used to collect the precisely weighted granule. The funnel's height was changed such that its tip just brushed the top of the granule pile. The granules were free to pour onto the surface through the funnel. The following formula was used to determine the powder cone's diameter and angle of repose.

$$\mathrm{Tan}\,\theta = \frac{h}{r}$$

$$\theta = tan - 1\left(\frac{h}{r}\right)$$

In this case, H represents the powder pile's height and Ris its radius.

3.7.4 Carr's Index

Carr's compressibility index26 was used to calculate the granules' compressibility index.

3.7.5 Hausner's Ratio

Using LBD and TBD26, this value was computed.

$$Hausner's\ ratio\ = \frac{TBD}{LBD}$$

3.8 Formulation of bilayer tablet

Wet granulation (sustained release layer) and direct compression (immediate release layer) were used to create the LX bilayer tablets. After each component was inspected, it was thoroughly combined for fifteen minutes. Isopropyl alcohol was used to granulate the powder mixture. After the wet mixture was run through sieve #16, the granules were dried in a hot air oven for five minutes at 50 degrees Celsius. After passing through sieve #22, the dry granules were further blended for three minutes to lubricate them with talc and magnesium stearate. A 16-station tablet compression machine fitted with 12.7 mm round flat and plain punches was used to softly compress the amount of granules for the sustained release layer.

Table 1: Formulation of Immediate release layer

Ingredients	**F1**	**F2**	**F3**	**F4**
LX	100	100	100	100
Sodium starch glycolate	6.5	9.3	5.5	9.3
Microcrystalline cellulose	2.5	9.7	3.5	9.7
Magnesium stearate	4	4	4	4
Talc	2	2	2	2
Total	**155**	**155**	**155**	**155**

*All the amounts are shown as milligrams (mg).

Table 2: Formulation of sustained release layer

Ingredients	**F1**	**F2**	**F3**	**F4**
LX	150	150	150	150
HPMCK100M	88.5	78.3	69.5	59.3
Xanthan gum	12	15	13	15
Magnesium stearate	46	46	47.5	68

Talc	5.5	5.5	1.5	2.5
Total	**155**	**155**	**155**	**155**

*All the amounts are shown as milligrams (mg).

4. RESULTS AND DISCUSSION

4.1.1 Hardness

4.1 Evaluation of Formulated Bi layered Tablet

4.1.1 Hardness

Tablets should be able to tolerate moderate abuse when in the hands of consumers. Hardness is the strength of the tablet to survive mechanical shocks of handling during manufacturing, packing, and delivery. A Pfizer or Monsanto hardness tester assessed the tablet's hardness. The floating tablet has a hardness of more than 4-6 kg/cm2, which was measured in kg/cm2.

3.1.2 Friability

This test is designed to ascertain the physical strength of tablets and may be used with compressed tablets. Using six tablets, it was tested using a Roche Friabilator that rotated 100 revolutions per minute for four minutes. The USP states that a tablet's acceptability limit should be less than 1%.

4.1.3 Weight variation

Weight variation was computed using the USP technique. Twenty pills were weighed one at a time, and the average was determined. If no two tablets' weights differ by more than the percentage shown on the tablet and no two tablets' weights differ by more than twice that percentage, the conditions are satisfied.

4.1.4 Active Ingredients

The prepared tablets were precisely weighed and ground into a fine powder using a pestle and mortar. The medication was dissolved in the solvent after a weighed piece of each powder, equal to the dosage (250 mg) of the produced tablet, was placed into a volumetric flask. After 10 minutes of sonication, the flask's contents were diluted using 0.1 N HCl as the solvent. At 293 nm, the samples were subjected to spectrophotometric analysis.

4.1.5 In-vitro Dissolution studies of tablet formulation

The United States of Pharmacopoeia Dissolution Testing Apparatus-II (VEEGO, VDA-6DR) was used to

conduct in vitro release investigations. 900 mL of 0.1N HCl (pH 1.2) was used for the dissolving test, which was conducted at 37±0.5oC and 75 rpm. One millilitre of the sample was taken out at prearranged intervals for 12 hours, and the same volume of new medium was added. At a wavelength of around 293 nm, the absorbance of the extracted sample was measured spectrophotometrically. The cumulative percentage drug release was then computed using an equation derived from a standard curve.

4.2 Kinetic analysis of dissolution data

To clarify the water and drug transport mechanisms and forecast the ensuing drug release kinetics, a number of mathematical models have been proposed. The application of each model is limited to certain drug-polymer systems because of the assumptions that each model makes. Several kinetic models were employed to characterise the release kinetics in order to analyse the in-vitro release data. The dissolving data was fitted into a number of models in order to analyse the rate and mechanism of LX release from the produced bilayer tablets.

S. No	Parameters	Sample
1	Colour	Pale yellow colour powder
2	Odour	Odourles

4.3 Result Discussion

Prefomulation Studies

4.3.1 Identification of drugs

4.3.2 Physical Appearance

Table 3: Physical appearance of LX

4.3.3 Melting Point

It was discovered that LX has a melting point between 225 and 227 degrees Celsius.

4.3.4 Solubility of drug

Table 4: Solubility profile of LX in aqueous and nonaqueous solvents

S. No	Solvent	Solubility
1	0.1 N HCL	Soluble
2	Distill water	Soluble
3	Methanol	Soluble

4.3.5 Drug Excipient Interaction

The purpose of the study was to ascertain whether the medicine was compatible with various excipients. Glass vial stoppers with low density polyethylene plugs were used for these investigations. For one, two, and three weeks, API was combined with various excipients and maintained at

various temperatures, such as 40°C, 40°C, and 40°C with 75% relative humidity.

4.3.6 Precompression studies

Table 5: Precompression studies of Sustained layer granules

Formulation Codes	Parameters				
	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's Ratio	Compressibility Index (%)	Angle of Repose (^{o})
F1	0.341±0.025	0.375±0.006	1.12±0.003	10.81±0.761	26.12±0.657
F2	0.378±0.015	0.436±0.012	1.16±0.024	13.45±0.423	29.30±1.041
F3	0.259±0.012	0.304±0.013	1.20±0.012	16.07±1.330	29.04±0.653
F4	0.378±0.004	0.451±0.002	1.05±0.015	17.76±1.221	26.5±0.973

Table 6: Precompression studies of immediate layer granules

Formulation Codes	Parameters				
	Bulk Density (g/cc)	Tapped Density (g/cc)	Hausner's Ratio	Compressibility Index (%)	Angle of Repose (^{o})
F1	0.400±0.062	0.434±0.056	1.11±0.003	10.01±0.631	25.05±0.457
F2	0.480±0.031	0.515±0.012	1.13±0.024	11.92±1.012	29.74±0.752
F3	0.440±0.042	0.492±0.023	1.15±0.012	12.07±0.630	27.75±1.024
F4	0.432±0.004	0.490±0.002	1.13±0.045	11.83±0.841	29.78±1.126

4.4 Evaluation of Formulated Bilayer Tablet

4.4.1 Physical Tests of Bilayer Tablet

Table 7: Physical Tests of Bilayer Tablet

Code	Thickness (mm)^n	Hardness (kg/cm^2)^n	Weight Variation*	Friability (%)	Disintegration time in sec ^{n}	Disintegration time ^{n}
F1	6.76±0.06	5.8	455±2.1	0.51		
F2	6.86±0.03	4.4	452±1.1	0.16		
F3	6..76±0.04	4.9	455±1.7	0.27		
F4	6.63±0.06	4.8	451±1.4	0.34		

n=mean of 3±s.d,*=mean of 20±s.d

To prevent processing variations, all batches of bilayer tablets were made under identical circumstances. The bilayer pills weighed between 451 and 455 mg on average. The thickness ranged from 6.50 to 6.86 mm, while the hardness ranged from 4.4 to 5.8 kg/cm2. All of the formulations had friability percentages between 0.18 and 0.51%. The hardness test results and percentage of friability show that the bilayer tablet has good wear and tear characteristics.

4.5 Drug Content of Active Ingredients

Table 8: Percentage Drug Content of Active Ingredients

Code	Drug content(%)^n
F6	**97.91±1.5**

Values are expressed in Mean±SD, n=3

The UV spectrophotometric approach was used to determine the drug concentration of the active components. Table No. 8.0 shows that the optimised F6 bilayer tablets had a drug content of 97.9%.

4.6 Drug Release profile of Bilayer Tablet

Table 9: Drug Release profile of Bilayer Tablet

Time(mnt)	F1	F2	F3	F4
0	0	0	0	0
10	**7.**9	15.1	12.8	20.5
20	10.1	19.4	14.5	25.8
30	11.4	22.8	17.8	27.2
40	15.6	25.2	19.9	28.4
50	18.4	27.2	22.1	30.9
60	21.7	28.5	23.5	32.1
120	24.8	30.2	25.8	33.9
180	27.4	32.9	29.4	38.3
240	30.2	35.6	32.6	41.4
300	32.7	38.3	37.5	43.2
360	33.9	40.5	42.7	45.7
420	35.8	43.8	46.9	49.3
480	35.9	46.4	49.2	53.6
540	36.6	49.3	53.4	58.1
600	37.3	52.4	55.2	63.2
660	38.2	56.7	57.2	67.2
720	41.7	60.3	62.1	75.5

Time in (minutes).Values are expressed in Mean±SD, n=3

All formulations underwent in-vitro drug release in 0.1 N HCL, and cumulative drug release was computed at predetermined intervals. Table 9 displays the outcomes of LX's in vitro drug release for various formulations. Plotting the cumulative percent drug release against time allowed for the analysis of the release of LX from the produced formulations. Within the first hour of the dissolving investigation, the optimised formulation F6, which contained 42% LX, was discharged. The formulation's quick release layer is responsible for the initial high level of LX. LX's subsequent release was examined for 12 hours.

5. CONCLUSION

Based on the results of the aforementioned experiment, it can be said that the Immediate and Sustain Layer contains a bilayer tablet of LX that lowers pain. Because of the immediate layer, it will act quickly, and because of the sustain layer, it will act for a longer period of time. Therefore, the bilayer tablet can be utilised to control pain instead of using a traditional dose form.

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