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Effect of Binding Agents and Disintegrants on the Dissolution Rate of Lornoxicam from Compressed Tablets

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Research Article

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Abstract

In the present study, Lornoxicam immediate-release tablets were formulated using different types of selected binders and disintegrants and their effect on the dissolution rate was evaluated. The binding agents used were sucrose, acacia, gelatin, polyvinyl pyrrolidone (PVP), methylcellulose (MC), and hydroxypropyl methylcellulose (HPMC). Dry potato starch, starch paste (SP), and microcrystalline cellulose (MCC) were used as disintegrants, and sodium starch glycolate (SSG) was used as super-disintegrant. The wet granulation technique was used in the preparation of Lornoxicam tablets and was then evaluated for different parameters of pre-compression such as bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio, and post-compression parameters such as weight variation, hardness, friability, time of disintegration, drug content, and in vitro dissolution studies. Based on Dissolution efficiency (DE)(30%)min values, the order of performance of binders was found to be HPMC-SSG (LX1) >PVP-SSG (LX3)>SP-SSG (LX4). Among the tablet formulations (LX1-LX7), formulations LX3 and LX4 exhibited promising t50% and t70% of 10.5 min and 21 min respectively. DE(30%)min was higher in LX4 formulation, which showed a DE of 50.13 min. The regression coefficient 'r' values were observed, and it was found in the range of 0.9484 to 0.9964, indicating first-order drug release kinetics from all the formulations.

Key words: Binders, Disintegrants, Dissolution efficiency, Lornoxicam, Super disintegrants

Introduction

The most common type of medication is tablets, accounting for 70% of all medicines prescribed. Since there is a great demand for faster disintegrating formulations, the pharmacist must formulate disintegrants, or super-disintegrants, that are effective at low concentrations and have higher disintegrating efficiency. When in contact with water, super-disintegrants swell up to ten-fold in 30 seconds, but its hygroscopic nature restricts its use in drugs sensitive to moisture. Super-disintegrants operate by swelling, causing the tablet to burst or accelerate water absorption, leading to a huge increase in the volume of granules to facilitate disintegration.[1-8]

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Materials

Lornoxicam was a gift sample from Micro-Lab Limited, Bengaluru. Lactose, sucrose, acacia, gelatin, hydroxypropyl methylcellulose, polyvinyl pyrrolidone, starch paste, dry potato starch, methylcellulose, and talc was gifted from SD Fine-Chem Limited, Mumbai. Microcrystalline cellulose was obtained as a gift sample from Loba Chemie Pvt Ltd, Mumbai. Sodium starch glycolate and magnesium stearate was obtained as a gift sample from Himedia Laboratories Pvt Ltd, Mumbai.

Methods

Preparation of Lornoxicam tablets

The compressed tablets of Lornoxicam, each containing 8mg, were prepared by conventional wet granulation method as per the formula given in Table 1. One series of tablets (LX1-LX7)

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was formulated with sucrose, acacia, gelatin, methylcellulose, hydroxypropyl methylcellulose, polyvinyl pyrrolidone, starch paste (4%) as binders, dry potato starch (10%) and microcrystalline cellulose as disintegrant and sodium starch glycolate as super disintegrant. Magnesium stearate and talc were used as lubricant and glidant respectively in the formulations.

Table 1: Formulation of Lornoxicam tablets prepared with different binders, disintegrants, and super-disintegrants

Ingredient (mg/tablet)	LX_1	LX_2	LX_3	LX_4	LX_5	LX_6	LX_7
Lornoxicam	8	8	8	8	8	8	8
Lactose	80	80	80	80	80	80	80
Sucrose	-	-	-	-	-	-	4
Acacia	-	4	-	-	-	-	-
Gelatin	-	-	-	-	-	4	-
Methyl cellulose	-	-	-	-	4	-	-
HPMC*	4	-	-	-	-	-	-
PVP*	-	-	4	-	-	-	-
Starch paste	-	-	-	10	-	-	-
Dry Potato Starch	-	10	1 0	-	-	-	10
MCC*	-	-	-	-	5	5	-
SSG*	5	-	-	5	-	-	-
Magnesium stearate	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2
Total	101	106	106	107	101	101	106

*HPMC- hydroxy propyl methyl cellulose;

*PVP- polyvinylpyrolidone;

*MCC- microcrystalline cellulose;*SSG -sodium starch glycolate

All the ingredients were precisely weighed and passed through sieve no. 60. Except for magnesium stearate and talc, the drug, lactose, and half the quantity of disintegrant were transferred to a clean porcelain mortar. The binding solution was added to the powder mixture in geometric proportion and mixed thoroughly until a cohesive mass was formed and passed through sieve no. 12. The wet granules were scattered on paper and dried in 30-40°C hot air oven for 30 minutes. Finally, the remaining amounts of disintegrant, magnesium stearate, and talc were added and mixed. On a rotary punching machine (clit pilot press), tablets were compressed using a flat surface and round-shaped punches.

Evaluation of Lornoxicam tablets

Precompression evaluation parameters[9-10]

Angle of Repose (θ): The angle of repose of the prepared granules was determined by the fixed funnel method. A funnel was lined up by the powder mix, and the powder mix was allowed to pass through the opening smoothly under gravity. The flowability of the granules was calculated by measuring the area and height of the pile. The results of the angle of repose are shown in Table 2.

Bulk density: In a 25ml measuring cylinder, a quantity of precisely weighed powder (bulk) was allowed to fall from a height of 2.5 cm at 2-second intervals, after observing the initial volume in the cylinder. The measuring cylinder was tapped until no further change in volume was noticed. Table 2 illustrates the results of bulk density.

Tapped density: For a fixed time, the measuring cylinder containing a known amount of the powder blend was tapped. The minimum volume occupied and the weight of the blend was determined in the cylinder. Table 2 shows the results of the tapped density.

Hausner's ratio: Hausner's ratio is an indirect index of ease of powder flow. The values <1.25 indicate better flow properties. Table 2 illustrates the results of Hausner's ratio.

Percentage compressibility: Carr's compressibility index was determined by the percent compressibility of the powder mix. Table 2 provides the results of percentage compressibility.

Post compression evaluation parameters[11-12]

Weight variation test: 20 tablets were taken and weighed individually. The average weight was calculated and the weight of each tablet was compared to the average weight. The results are given in Table 3.

Hardness: To test the hardness of the Lornoxicam tablet formulation, Monsanto's hardness tester was used. The tablet was put between two anvils.

Strength is added to the anvils and the crushing force that causes the tablet to break was recorded. The results are given in Table 3.

Friability: The Roche friabilator was used to assess the friability of a tablet, dropping the tablets in the friabilator over a distance of 6 inches, and operating at 100 revolutions. The tablets were reweighed after dusting and the percent friability was measured. The results of the friability test are given in Table 3.

Content uniformity test: Five tablets were powdered in a glass mortar and 100 mg of the powder was put in a 100 ml stoppered conical flask. The test substance was extracted with methanol and filtered through cotton wool into a 50 ml volumetric flask, and the filtrate was suitably diluted up to the mark with methanol. Absorption against blank was measured at 373 nm. The results of the content uniformity test are given in Table 3.

Disintegration test: The tablet was placed in a tube and the basket rack was positioned in a 1L beaker of water, with simulated gastric fluid, or simulated intestinal fluid at 37±2.. The basket containing the tablets was moved mechanically at a frequency of 28-32 cycles per minute, and the time taken for tablet disintegration was noted. Table 3 illustrates the results of the disintegration test.

Dissolution test: A single tablet was mounted in a small wire mesh basket attached to a variable speed motor connected to the bottom of the shaft. The basket was immersed in a 0.1 N HCl 900ml dissolution medium stored in a cylindrical flask of 1000 ml with a hemispherical rim. The flask was held at 37±1°C in a constant temperature bath. The motor has been calibrated to turn at the specified speed and the fluid sample was withdrawn at regular intervals to determine the quantity of the drug in the solution. The results are given in Tables 4 and 5

Table 2: Pre-compression parameters of LX1 - LX7 formulation

Sl. No.	Formulation Code	Bulk density (g/cc)	Tapped Density (g/cc)	Angle of Repose (degree)	Carr's Index (%)	Hausner's ratio
1	LX_1	0.43	0.52	29.35	17.40	1.21
2	LX_2	0.49	0.59	26.68	17.90	1.21
3	LX_3	0.45	0.55	28.39	18.91	1.22
4	LX_4	0.45	0.55	27.75	18.21	1.22
5	LX_5	0.45	0.53	28.65	18.72	1.23
6	LX_6	0.49	0.60	28.13	19.95	1.24
7	LX_7	0.49	0.59	29.80	16.92	1.20

Table 3: Post compression parameters of LX1- LX7 formulation

Sl. No.	Formulation code	Weight variation**	Percent deviation*	Hardness (kg/cm^2) ± SD*	Friability* (%)	Disintegration Time (min) ± SD*	% Drug content ± SD*
1	LX_1	101	4.75	4.03±1.34	0.228	4.98±1.66	97.37±2.60
2	LX_2	106	4.03	4.06±1.35	0.356	5.33±1.77	93.75±2.50
3	LX_3	106	1.65	4.13±1.37	0.291	4.99±1.66	97.37±2.60
4	LX_4	107	6.02	4.00±1.33	0.340	6.28±2.09	97.37±2.60
5	LX_5	101	7.08	4.13±1.37	0.398	9.9±3.31	93.75±2.50
6	LX_6	101	3.77	3.86±1.28	0.296	9.8±3.26	93.75±2.50
7	LX_7	106	2.95	4.33±1.44	0.322	5.00±1.66	93.75±2.50

**Average of twenty determinations

*Average of three determinations

Table 4: Comparative in vitro drug release data of formulations LX1-LX4

Sl. No.	Time(min)	Cumulative percent drug release			
		LX_1±SD*	LX_2±SD*	LX_3±SD*	LX_4±SD*
1	0	0	0	0	0
2	5	18.0±0.012	20.1±0.114	23.1±0.124	30.2±0.089
3	10	23.0±0.129	29.4±0.131	42.1±0.129	43.2±0.091
4	15	38.9±0.139	41.2±0.136	56.2±0.012	59.1±0.129
5	30	64.2±0.012	68.5±0.019	74.3±0.129	72.8±0.012
6	45	79.6±0.019	79.6±0.012	89.6±0.131	83.9±0.128
7	60	88.4±0.019	89.4±0.139	97.5±0.189	95.4±0.134
8	75	94.3±0.164	96.0±0.012	97.7± 0.189	97.1±0.142
9	90	99.1±0.189	96.8±0.013	98.1±0.124	99.2±0.014
10	105	99.1±0.018	96.1±0.013	98.1±0.124	99.2±0.014
11	120	99.1±0.018	96.1±0.013	98.1±0.124	99.2±0.014

*Average of three determinations

Table 5: Comparative in vitro drug release data of formulations LX5-LX7

Sl. No.	Time (min)	Cumulative percent drug release		
		LX_5 ± SD*	LX_6± SD*	LX_7± SD*
1	0	0	0	0
2	5	18.0 ± 0.179	20.9 ± 0.129	21.0 ± 0.141
3	10	26.7 ± 0.094	37.2 ± 0.014	39.0 ± 0.129
4	15	36.8 ± 0.082	49.5 ± 0.129	48.2 ± 0.040
5	30	45.9 ± 0.014	56.4 ± 0.164	59.3 ± 0.012
6	45	58.6 ± 0.019	68.9 ± 0.131	68.7 ± 0.019
7	60	69.7 ± 0.124	74.3 ± 0.089	73.9 ± 0.151
8	75	79.8 ± 0.131	83.2 ± 0.149	79.9 ± 0.172
9	90	81.2 ± 0.129	89.9 ± 0.129	88.6 ± 0.141
10	105	84.3 ± 0.131	92.4 ± 0.131	94.2 ± 0.131
11	120	85.9 ± 0.129	94.5 ± 0.121	96.3 ± 0.089

*Average of three determinations

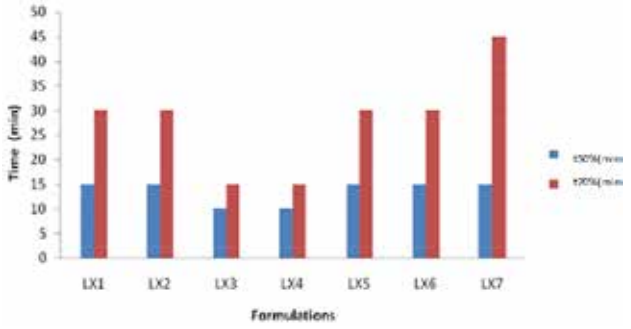

Fig 3: Comparative representation of t50% and t70% data of the formulations LX1-LX7

Table 6: Percent drug dissolved at 10 min, 30 min, and 60 min of the formulation LX1-LX7

Sl. No.	Formulation Code	Percent drug dissolved		
		10 min	30 min	60 min
1	LX_1	23.0	64.2	88.4
2	LX_2	29.4	68.5	89.4
3	LX_3	42.1	74.3	97.5
4	LX_4	43.2	72.8	95.4
5	LX_5	26.7	45.9	69.7
6	LX_6	37.2	56.4	74.3
7	LX_7	39.0	59.3	73.9

Table 7: Kinetic data of the formulations LX1-LX7

Sl. No.	Formulation Code	A	B	R	K	$DE_{30\%}$	$DE_{60\%}$
1	LX_1	2.0524	0.0183	0.9835	0.0422	31.19	56.9
2	LX_2	1.9256	0.0135	0.9645	0.0312	39.10	59.19
3	LX_3	1.8465	0.0162	0.9484	0.0373	48.17	67.96
4	LX_4	1.9067	0.0174	0.9809	0.0402	50.13	67.06
5	LX_5	1.9391	0.0071	0.9893	0.0165	35.85	44.69
6	LX_6	1.9373	0.0099	0.9943	0.0228	40.28	53.70
7	LX_7	1.9588	0.0010	0.9843	0.0246	40.89	54.27

Table 8: t50% and t70% data of the formulations LX1-LX7

Sl. No.	Formulation code	$t_{50\%}$ (min)	$t_{70\%}$ (min)
1	LX_1	15	30
2	LX_2	15	30
3	LX_3	10	15
4	LX_4	10	15
5	LX_5	15	30
6	LX_6	15	30
7	LX_7	15	45

Results and discussion

In the present study, Lornoxicam immediate-release tablets were formulated using different types of selected binders, disintegrants, and super-disintegrants and their effect on the dissolution rate from these tablets was evaluated. The binders used in this study were gelatin, acacia, sucrose, polyvinylpyrrolidone, methylcellulose, and hydroxylpropyl methylcellulose. The disintegrating agents used were starch paste, dry potato starch, and microcrystalline cellulose. The super-disintegrants used were sodium starch glycolate. All the binders were used at a concentration of 4% of the formula, except starch paste which was used at a concentration of 10% w/v in the form of a paste. One series of tablets (LX1-LX7) was formulated with selected binding agents and dry potato starch (10%), MCC (5%), and SSG (5%) as the disintegrants. Table 2 illustrates the results of pre-compression parameters like bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio. The results of post-compression parameters like weight variation, hardness, friability, disintegration time, and drug content have been given in Table 3. Drug content uniformity was performed and low standard deviation values indicated the uniformity of drug content within the tablets. The percent drug content uniformity of the tablet formulations (LX1- LX7) was in the range of 93.75% to 97.37% within the limits of ±0.5%. In vitro release studies were performed in USP XXIII tablet dissolution apparatus-I employing basket at 100 rpm at a temperature of 37±0.5°C. Table 4 and 5 illustrates the in vitro dissolution data of the tablet formulations. Figure 2 and 1 depicts the dissolution profiles of the tablet formulations. From the dissolution data of tablet formulations (LX1- LX7), it is evident that

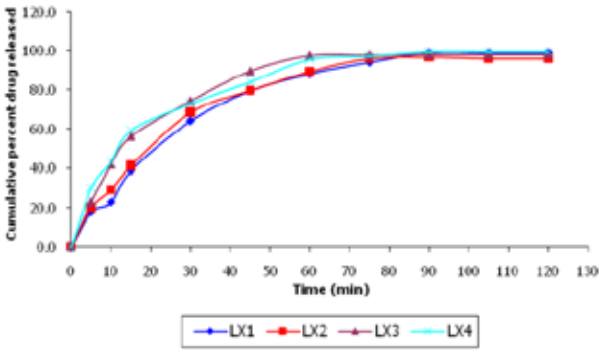

Fig 1: Comparative in vitro drug releases time plots (zero order) of formulationsLX1-LX4

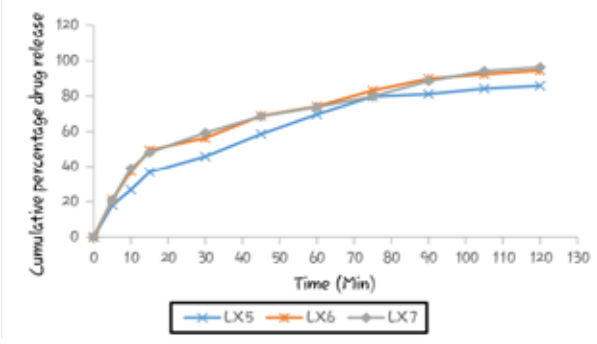

Fig 2: Comparative in vitro drug releases time plots (zero order) of formulations LX5-LX7

formulation LX1 containing HPMC, formulation LX2 containing acacia, formulation LX3 containing PVP, formulation LX4 containing starch paste, and formulation LX7 containing sucrose exhibited good dissolution characteristics and rapid dissolution of Lornoxicam. Table 6 illustrates the results of the percent of drug dissolved in 10 min of the tablet formulations (LX1- LX7) and it is found to be in the range of 23.0-43.2% and in 30 min it is found to be 45.9-74.3%. Table 7 demonstrates the results of the dissolution efficiency (DE30% min) of the formulations (LX1-LX7) was found to be in the range of 31.19-50.13 min and dissolution efficiency (DE60% min) was in the range of 44.69-67.96 min. The regression coefficient 'r' value of first-order plots was in the range of 0.9484 to 0.9964 indicating the drug release to follow the first-order kinetics. Table 8 shows the results of the t50% value of the formulations (LX1- LX7) and it was found to be in the range of 10-15 min.

Conclusion

LX1 formulation was found to be promising with a disintegration time of 4.99 min amongst all the tablet formulations (LX1-LX7). Variation was observed in the dissolution characteristics of the tablet formulations (LX1-LX7). Tablets prepared with HPMC, starch paste, PVP, acacia, and sucrose exhibited good dissolution characteristics and rapid dissolution of Lornoxicam was observed from these tablets. Based on DE(30%)min values the order of performance of tablet formulations (LX1-LX7) was found to be HPMC>acacia>MC>gelatin>sucrose> PVP>starch. Tablets formulated with HPMC and SSG, starch paste and SSG, PVP, and SSG exhibited significantly higher dissolution rates and efficiency values. Among all the tablet formulations, LX1-LX7 formulation LX3 and LX4 exhibited promising t50% and t70% of 10.0 min and 15.0 min respectively. Tablets prepared using SSG as super-disintegrants showed better dissolution and efficiency values compared to other disintegrants. The order of performance of the tablet formulations was found to be HPMC-SSG (LX1)>PVP-SSG (LX3)>SP-SSG (LX4). Among all the binders used, HPMC, SP, and PVP exhibited promising dissolution profiles. Among all disintegrants used, SSG was found to be a promising disintegrant. The prepared formulation exhibited better dissolution profiles compared to the commercial formulations.

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Conflict of interest

None

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