

VARIOUS APPROACHES TO ENHANCE THE DISSOLUTION OF LORNOXICAM FAST DISSOLVING TABLETS PREPARED BY USING DIFFERENT CATEGORIES OF SUPERDISINTEGRANTS: A COMPARATIVE STUDY

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ABSTRACT

Background: Recent developments in fast dissolving tablets have brought convenience in dosing to pediatric and elderly patients who have trouble in swallowing tablets. The main objective of the present study is to formulate fast dissolving tablet of Lornoxicam by direct compression method.

Methods: Guar gum and crospovidone were used as natural and synthetic superdisintegrants respectively. Fast dissolving tablet of Lornoxicam were prepared by direct compression technique using three different approaches; superdisintegrant addition, sublimation, and solid dispersion.

Results: IR and DSC studies showed no interaction between the drug and the excipients. All formulation showed disintegration time ranging from 16.09-42.54 second. Wetting time and disintegration time decreased by increasing the super disintegrant concentration from 2.5% to 5% w/w. Formulae L16 gave the best *in-vitro* disintegration and dissolution results, which would be due to swelling effect of Guar gum and amorphization of the drug during the solid dispersion preparation. The best formulation L16 was subjected to stability testing for 3 month and results showed no significant change in appearance, hardness, drug content and dissolution profile of the tablets, hence tablet is stable throughout its stability studies.

Conclusion: It was concluded that fast dissolving tablets of Lornoxicam were formulated successfully with desired characteristics which disintegrated rapidly; provided rapid onset of action; and enhanced the patient convenience and compliance.

Keywords: *Disintegration time, Fast dissolving tablet, Lornoxicam, PEG 6000, Sublimation, Solid dispersion.*

INTRODUCTION

Drug delivery system is an efficient tool for extending the product life cycles, creating wonderful opportunities to the pharmacist and also it makes a significant contribution to global pharmaceutical sales through market segmentation¹.

Despite of tremendous innovations in drug delivery, oral route of drug administration have wide acceptance up to 50-60% of total available dosage forms². Among all dosage forms solid oral dosage forms (tablets and capsules) are more popular because of ease of administration, accuracy in dose, self-medication, pain less, and most important is good patient compliance³. Problem related to dysphagia i.e. difficulty in swallowing, is common among all age groups. According to a survey, dysphagia is common in about 35% of the general population as well as an additional 30–40% of elderly institutionalized patients. Geriatric, paediatric and traveling patients who may not have ready access to water are most in need of easy swallowing dosage forms³. In order to avoid above problem approaches have been taken for the development of a new dosage form that can improve patient compliance⁴. Solid oral dosage forms that can be dissolved or suspended with water in the mouth for easy swallowing are highly desirable for the paediatric and geriatric population, as well as traveling patients who prefer the convenience of readily administered dosage forms. Fast disintegrating tablet (FDTs) technologies has been developed during last decades that make tablets which disintegrate in the mouth without chewing and additional water intake and/or with a very small amount (e.g., 1–2 mL) of water but disintegration fluid is provided by the saliva of the patient⁵. FDTs have all the advantages of solid dosage forms such as good stability, accurate dosing, easy manufacturing, small packaging size, and easy handling by patients⁶. Fast dissolving tablet is also known as fast melting, fast dispersing, rapid dissolve, rapid melts, fast dissolving tablets and/or quick disintegrating tablet. Fast dissolving tablet is approved by various regulatory agencies like Food and Drug Administration (FDA) and European Pharmacopeia, where FDA defines FDTs as “A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”⁷. The disintegration time for good FDTs varies from few seconds to about a minute. Decrease in disintegration time assists easy swallowing and also plays a role in drug absorption in buccal cavity, thus increases bioavailability by bypassing hepatic metabolism of drugs and moreover, the amount of drug is reduced as compared to conventional tablets^{3,7}.

Sugar-based excipients i.e. Mannitol shows a negative heat of dissolution, dissolve quickly in saliva, and provide a pleasing mouth feel and sweetness to the final product⁷. To improve porosity of prepared tablets, volatile substances such camphor can be used in tableting process which gets sublimated from the formed tablets^{8,9}.

An attempt has been made to formulate fast dissolving tablet of Lornoxicam using synthetic and natural super disintegrants. Gaur gum was used as natural super disintegrant as it is non-toxic, non-irritating, abundantly available and cheaper. Since Gaur gum gives promising results on disintegration time and dissolution rate, it is helpful for Pharma industry as well as patients from economic point view^{10,11}. In this present study Lornoxicam was selected for the formulation of fast dissolving tablet. Two combined approaches; solid dispersion and sublimation technique along with superdisintegrant addition was used to prepare FDTs, which shall not only increases solubility and bioavailability but also improve patient compliances and patient convenience^{3,4,11}.

Lornoxicam is one of the oxamic acid derivative belongs to non-steroidal anti-inflammatory drugs (NSAIDs) which possess analgesic, anti-inflammatory and anti-pyretic properties. It is also prescribed for osteoarthritis, rheumatoid arthritis, acute lumbar-sciatica conditions and for post-operative pain management. It has half-life of 3 to 5 hrs and peak plasma concentration is attained within 2.5hrs. Lornoxicam is ten times more potent than other oxamic acid derivatives. Its daily dose is 8-16 mg taken before meal but dose above 8 mg should be divided into two

or more doses. Like all NSAIDs it acts by inhibiting the metabolites of COX branch of arachidonic acid pathway. It inhibits both isoforms in the same concentration range i.e. COX-1/COX-2=1. Thus, a perfectly balanced inhibition of COX-1 and COX-2 is achieved. Lornoxicam is slightly soluble in simulated gastric fluid^{12, 13, 14, 15}.

In the present study Lornoxicam fast dissolving tablet was prepared by direct compression technique using three different approaches namely; superdisintegrant addition, sublimation and solid dispersion using novel superdisintegrants in order to improve its dissolution rate and hence its bioavailability.

MATERIALS AND METHODS

Drugs and chemicals

Lornoxicam was obtained as gift sample from Naprod Life Sciences P.LTD (India), Crospovidone, Gaur gum, PEG 6000 were procured from S.D fine chem limited, Mumbai (India), Camphor, Magnesium stearate, Aspartame and Mannitol were analytical grade.

Methods

Differential scanning calorimetric studies (DSC)

Thermal properties of the pure Lornoxicam and the physical mixture of drug and excipients were analysed by Shimadzu DSC-60, Shimadzu Limited Japan. The samples were heated in a thermally sealed aluminium pans. Heat runs for each sample were set from 25 to 350°C at a heating rate of 10°C/min using nitrogen as blanket gas to eliminate the oxidative and pyrolytic effects. Samples of weight 3-5mg were used for the analysis and finally the DSC thermograms were recorded.

Fourier transform infrared spectroscopy (FTIR)

IR spectra of the pure drug and the physical mixture of drug and excipients were conducted using a Thermo Nicolet FTIR and the spectrum was recorded in the region of 4000 to 400 cm⁻¹. All spectra were collected as an average of three scans at a resolution of 2 cm⁻¹.

Preparation of Lornoxicam fast dissolving tablet by superdisintegrant addition method

FDTs of Lornoxicam were prepared by direct compression technique using three different approaches; superdisintegrant addition, sublimation and solid dispersion⁴. Table 1 shows the composition of Lornoxicam FDTs, each containing 8 mg of pure drug. In all formulations Mannitol was used as diluent. Aspartame was used as sweetening agent. The calculated quantity of drug and excipients were weighed accurately and passed through sieve 100 # separately. Sieved powder materials were transferred to mortar in geometrical dilution method and mixed well for about 10 min and at the end of mixing lubricants were added (Talc, Mg stearate) and further mixed for 5 min. Finally physical mixtures were compressed into tablets using single punch tablet machine (Lab Press, India) using 8mm flat surface punches under 2-4kg/cm³ compression force.

Preparation of Lornoxicam fast dissolving tablets by sublimation method

The steps involved in the preparation of FDTs by sublimation technique were same as superdisintegrant addition technique except that this technique possesses sublimating agents like Camphor. After compression tablets were heated in a hot air oven at 60°C until constant weight was obtained which indicated complete removal of volatilizable component¹⁶. Formulations bearing code L5 to L12 were prepared by sublimation technique (table 2).

Table 1:Composition of Lornoxicam fast dissolving tablets prepared by superdisintegrant addition method

Ingredients (mg)	Formulation code			
	L1	L2	L3	L4
Lornoxicam	8	8	8	8
Crospovidone	2.5	5	-	-
Gaur gum	-	-	2.5	5
Aspartame	1.5	1.5	1.5	1.5
Menthol	1	1	1	1
Magnesium stearate	2	2	2	2
Talc	1	1	1	1
Mannitol up to	100	100	100	100

Table 2: Composition of Lornoxicam fast dissolving tablets prepared by sublimation method.

Ingredients (mg)	Formulation code							
	L5	L6	L7	L8	L9	L10	L11	L12
Lornoxicam	8	8	8	8	8	8	8	8
Camphor	5	5	10	10	5	5	10	10
Crospovidone	2.5	5	2.5	5	-	-	-	-
Gaur gum	-	-	-	-	2.5	5	2.5	5
Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Menthol	1	1	1	1	1	1	1	1
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1

Mannitol up to	100	100	100	100	100	100	100	100
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Preparation of Lornoxicam fast disintegrating tablets by solid dispersion method

Lornoxicam solid dispersions were prepared by solvent evaporation method using PEG 6000 as polymeric carrier in drug to carrier ratios of 1:4. Drug was weighed accurately and transferred into a china dish, drug was dissolved in methanol and then polymeric carrier was added. The china dish was kept in water bath at 45⁰ C and mixture was triturated until complete evaporation of added solvent. Finally dried mass formed on china dish was scrapped, crushed with spatula and then passed through sieve # 100. The powdered solid products were kept in a desiccator to dry for 24 hrs over anhydrous calcium chloride¹¹. An amount equivalent to 8mg of drug was formulated as fast dissolving tablets where, formulation L13-L14 and L15-L16 contains Crospovidone and Gaur gum superdisintegrants, respectively.

Determination of solubility of solid dispersion

Solid dispersion equivalent to 8mg of Lornoxicam was added to 10 ml each of distilled water and phosphate buffer (pH 6.8). The dispersions were shaken well and kept aside for 24 hrs. The solution was filtered and analysed spectrophotometrically at 371nm (UV-1800 spectrophotometer, shimadzu, Japan) after appropriate dilutions¹¹.

Solubility studies

According to results obtained from solubility studies, there were significant changes in solubility of drug and physical mixtures compared to that of pure drug in distilled water as well as phosphate buffer (pH 6.8). Solubility of physical mixtures in distilled water and phosphate buffer (pH 6.8) found to be increased with increase in carrier ratio up to 1:4. Solubility was slightly decreased at drug to carrier ratio of 1:5. The obtained results showed that with increase in concentration of carriers, solubility of Lornoxicam increases up to certain level (1:4), further increase in concentration slightly lowers its solubility. Enhanced solubility of Lornoxicam from the physical mixtures could be related to surface activity which may reduce agglomeration and hence increased surface area, and solubilizing effect of PEG 6000. Hence, based on solubility results solid dispersion containing drug to carrier ratios of 1:4 was selected for preparation of tablets.

Table 3: Solid dispersion of Lornoxicam in different drug and carrier ratios.

Ratio	Physical mixtures code	Solubility in water (mg/ml)	Solubility in 6.8 pH Phosphate buffer (mg/ml)
Lornoxicam:PEG6000			
Lornoxicam pure drug	AA-1	0.038	0.143
1:1	AA-2	0.052	0.171
1:2	AA-3	0.068	0.194
1:3	AA-4	0.073	0.199

1:4	AA-5	0.089	0.238
1:5	AA-6	0.086	0.215

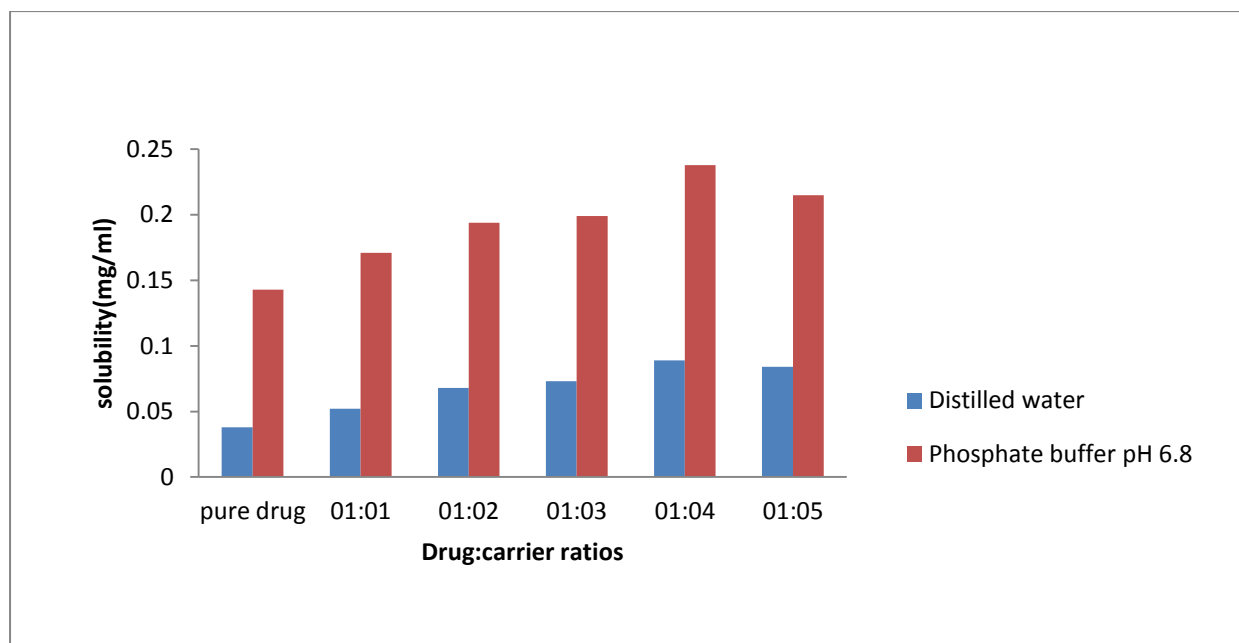


Fig 1: Solubility profile of Lornoxicam in solid dispersion prepared by different drug and carrier ratios.

Table 4: Composition of Lornoxicam fast dissolving tablets prepared by solid dispersion method.

Ingredients(mg)	Formulation code			
	L13	L14	L15	L16
AA-5 (SD) # 8	40	40	40	40
Crospovidone	2.5	5	-	-
Gaur gum	-	-	2.5	5
Aspartame	1.5	1.5	1.5	1.5
Menthol	1	1	1	1
Magnesium stearate	2	2	2	2
Talc	1	1	1	1

Mannitol up to	100	100	100	100
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Pre-compression evaluations

Before compression, powder mixtures were evaluated for their pre-compression parameters such as angle of repose (Θ), bulk density (D_v), true density (D_t), compressibility index (CI), Hausner ratio (H). From these parameters flow properties and compressibility properties of powder mixtures were determined^{1, 17, 18}.

Post compression parameters of prepared tablets

After compression, prepared tablets were evaluated for various parameters such weight variation, hardness, friability, wetting time, water absorption ratio, drug content, disintegrating time^{10, 16, 17, 18, 19, 20}.

In- vitro dissolution studies

In- vitro dissolution studies were carried out using USP type II paddle type dissolution apparatus (Lab India). The dissolution medium used was pH 6.8 phosphate buffer (900ml) maintained $37 \pm 5^\circ\text{C}$ with a paddle rotation speed at 50 rpm. 10ml sample was withdrawn at predetermined time interval 1, 5, 10, 15, 30 min and replaced with same volume of fresh dissolution medium. Absorbance of this solution was measured at 371nm. Drug concentration was calculated and expressed as cumulative percentage of the drug released. The dissolution tests were carried out three times²⁰.

Kinetic data analysis

The *in-vitro* release data were analysed by various kinetic model, such as Zero order kinetic model, First order kinetic model, Higuchi model, and Korsmeyer/Peppas model²¹.

Stability testing

Short-term stability studies of an optimized formulation were carried out at $25^\circ\text{C}/60\% \text{RH}$ and $40^\circ\text{C}/75\%$ for 3 months (as per ICH guidelines) in stability chamber (LAB TOP, Mumbai). First tablets were sealed in aluminium packing and then packed in the amber coloured rubber stoppered vial. Tablets were withdrawn periodically at 1, 2 and 3 month respectively and evaluated for hardness, friability, drug content, and *in-vitro* dissolution studies as per ICH-Guidelines²⁰.

RESULTS AND DISCUSSION

Three different approaches i.e. superdisintegrant addition, sublimation, solid dispersion methods were used. In this present work, two different categories of super disintegrants were used; Crospovidone as synthetic superdisintegrant and Gaur gum as natural superdisintegrant in two different concentrations like 2.5% and 5%. Mannitol was used to impart multifunctional benefits like good aqueous solubility and good wetting properties which facilitated tablet breakdown as well as negative heats of solution giving cooling effect in the mouth. PEG 6000 was used as carrier for preparation of solid dispersion with Lornoxicam due to its solubility in water, physiologically inert, thermally stable at melting temperature, lack of absorption, and improved compound wettability.

Compatibility study

Fourier transform infrared spectroscopy (FTIR)

Compatibility between the pure drug (Lornoxicam) and its physical mixtures with various excipients used in preparation of fast dissolving tablet formulations were characterized by FT-IR spectroscopy to test. FT-IR spectra of Lornoxicam and its physical mixture with excipients showed the same characteristic bands of the drug in the same region and same ranges, indicating no interaction between the drugs and excipients. Lornoxicam showed significant bands at 3065.53 cm^{-1} for NH stretch, 1594.04 cm^{-1} for C=O and 1083.51 cm^{-1} for S=O stretch and 788.41 cm^{-1} for -Cl stretch. This indicated further identity and purity of LXM. The chemical integrity of the drug was not changed when drug was mixed with the physical mixture, indicating drug was compatible with the excipients used.

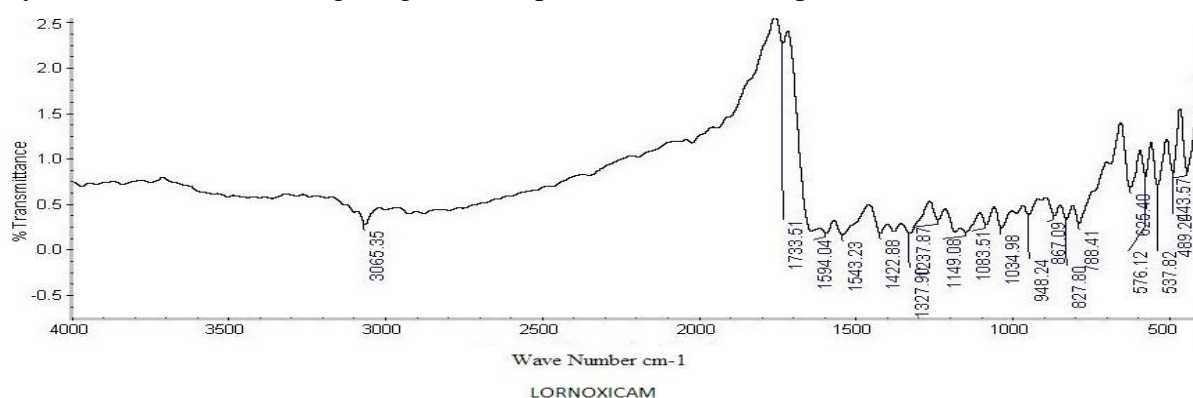


Fig 2: FT-IR Spectrum of Lornoxicam

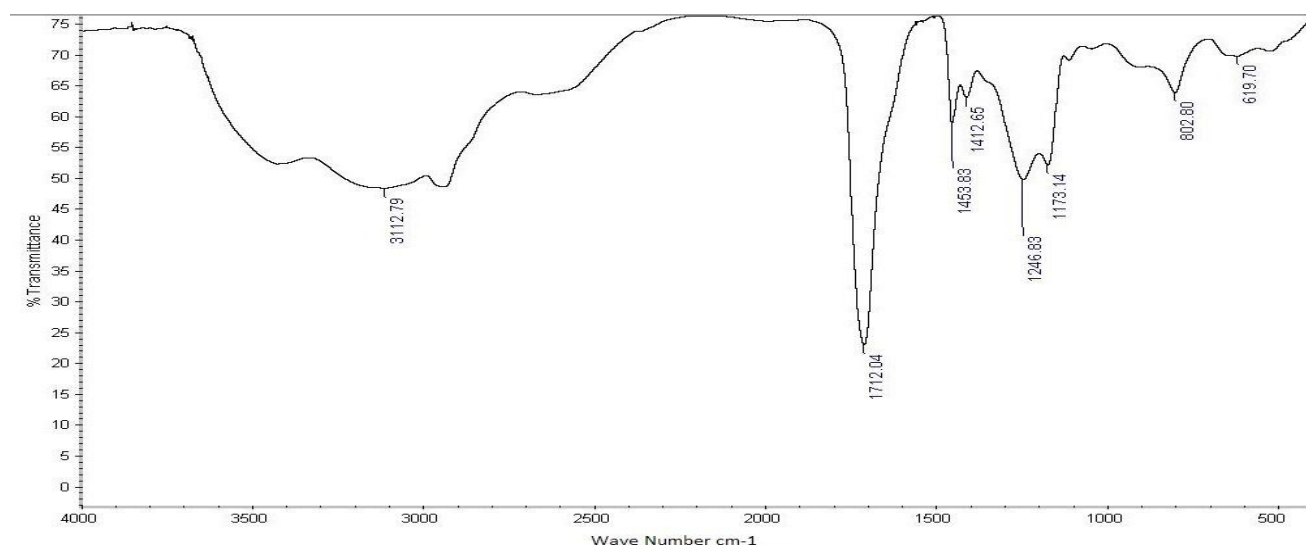


Fig 3: IR Spectrum of Lornoxicam + excipients

Differential scanning calorimetric (DSC) studies

The DSC thermogram of Lornoxicam was typical, exhibiting a sharp exothermic peak at 239.07°C corresponding to its melting and decomposition. These findings were similar to the Mohanty S et al study.²² The thermogram of the physical mixtures of Lornoxicam with excipient showed the existence of the drug exothermic peak at 223.66°C . This showed no significant change in melting point of Lornoxicam in presence of excipients, which indicates absence of interactions between Lornoxicam and other excipients.

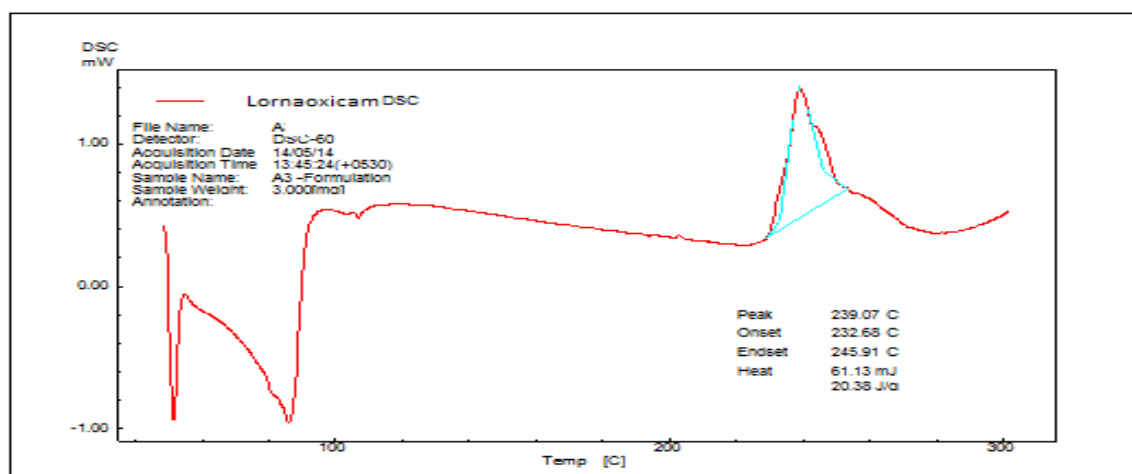


Fig 4: DSC thermogram of Lornoxicam pure drug

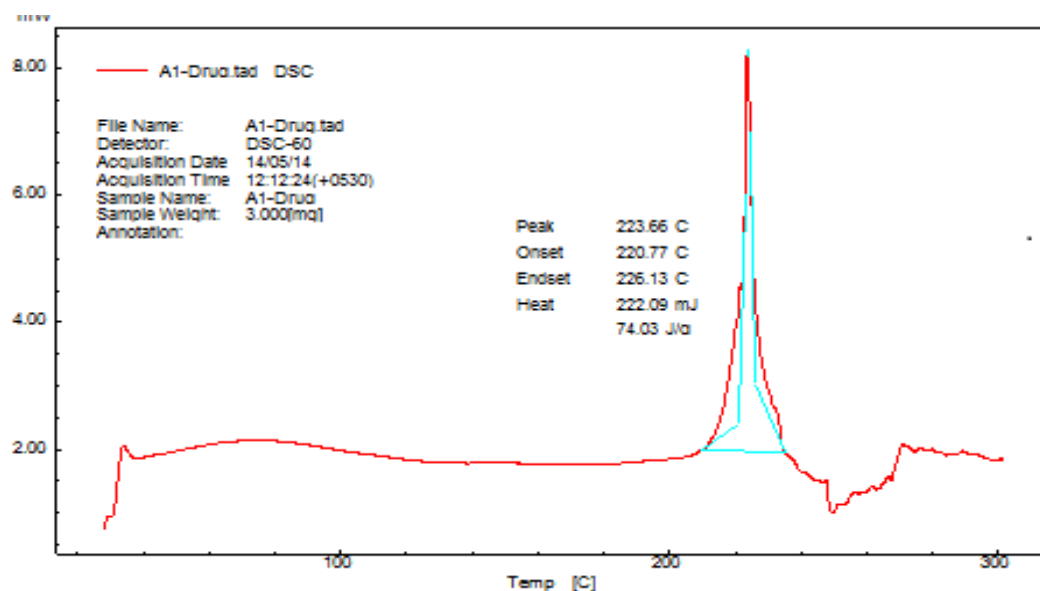


Fig 5: DSC thermogram of Lornoxicam + excipients

Pre compression evaluation

Powder is cohesive when value of angle of repose is high and non-cohesive if its value is low. The value of angle of repose ($21.44^{\circ} - 32.33^{\circ}$) represented that all formulations showed good to acceptable flow properties. Carr's index showed values up to 19.22, indicating all formulations were of acceptable to good flowability. Hausner ratio values up to 1.233 showed that powders with low inter particle friction. All formulations had Hausner ratio values within the prescribed limits and indicated a good free flowing property.

Table 5: Results of pre-compression evaluation of 16 different formulations

Formulation code	Angle of repose(Θ)	Bulk density(g/ml)	Tapped density(g/ml)	Carr's Index	Hausner ratio
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L1	32.20 ± 0.032	0.367 ± 0.032	0.439 ± 0.042	15.61 ± 0.14	1.185
L2	30.56 ± 0.022	0.337 ± 0.087	0.434 ± 0.018	23.29 ± 0.35	1.203
L3	32.33 ± 0.014	0.397 ± 0.032	0.440 ± 0.0091	15.48 ± 0.21	1.183
L4	30.94 ± 0.19	0.367 ± 0.061	0.470 ± 0.021	17.60 ± 0.09	1.210
L5	24.18 ± 0.087	0.483 ± 0.043	0.441 ± 0.032	19.11 ± 0.14	1.230
L6	28.27 ± 0.26	0.338 ± 0.073	0.541 ± 0.230	18.38 ± 0.04	1.220
L7	22.99 ± 0.08	0.341 ± 0.007	0.415 ± 0.051	18.02 ± 0.08	1.219
L8	27.45 ± 0.041	0.420 ± 0.028	0.416 ± 0.081	16.83 ± 0.05	1.202
L9	27.22 ± 0.056	0.382 ± 0.061	0.505 ± 0.095	16.21 ± 0.23	1.191
L10	25.47 ± 0.021	0.430 ± 0.090	0.456 ± 0.023	13.81 ± 0.76	1.160
L11	22.62 ± 0.052	0.466 ± 0.031	0.499 ± 0.064	19.22 ± 0.09	1.237
L12	24.70 ± 0.052	0.367 ± 0.103	0.577 ± 0.052	17.98 ± 0.41	1.219
L13	21.44 ± 0.047	0.388 ± 0.045	0.447 ± 0.006	18.91 ± 0.05	1.233
L14	24.11 ± 0.012	0.431 ± 0.039	0.478 ± 0.034	17.51 ± 0.12	1.212
L15	21.89 ± 0.073	0.395 ± 0.21	0.481 ± 0.038	17.77 ± 0.16	1.216
L16	27.49 ± 0.042	0.357 ± 0.027	0.405 ± 0.012	12.02 ± 0.47	1.136

Post-compression evaluation

As the powder mixture exhibited free flowing property, tablet produced were of uniform weight with acceptable weight variation in the range from 96.21 mg to 101.41 mg with the standard deviation less than 1.5% due to uniform die fill. Hardness (2.60-3.43 kg/cm²) and friability loss (0.30-0.862 %) indicated that tablets had a good mechanical resistance to withstand abrasion in handling, packaging and at the time of application. Drug content was found to be 95.26% to 101.54% which was within pharmacopoeial limits. Water absorption ratio and wetting time, which are important criteria for understanding dissolution profile of tablet, indicating capacity of disintegrants to swell in pressure of little amount of water. Water absorption ratio and wetting time were found to be in the range of 63.39-91.35% and 58.23-9.67 sec respectively. These results correlate with disintegration time results. The result *in-vitro* disintegration were within the prescribe limit and comply with the criteria for orally disintegrating tablets, the value were with 18±2.14 to 42±3.41. Each category of superdisintegrants (natural and synthetic) was used in two concentrations 2.5% and 5% to study their effects on disintegrating time.

Formulae L1-L4 was prepared by superdisintegrant addition method. Wetting time decrease with increase in the concentration (from 2.5% to 5%) of both superdisintegrants. Formulation

containing Gaur gum showed less wetting time (from 32.41 to 22.33 sec) compared to Crospovidone (from 42.54 to 37.29 sec) this may be due to increased ability of Gaur gum to absorb water and it swells which intern causes rupture of tablets.

Formulae L5-L12 was prepared by sublimation method. Camphor as subliming agent was used in two concentrations 5% and 10%. The values of tablet hardness and friability were in the range of 2.75-3.44 kg/cm² and 0.33-0.92 respectively. Present study showed addition of subliming agents had no pronounced effect on hardness and friability of prepared tablets. The concentration of subliming agents could be arranged in a descending order of decreased wetting and disintegrating time as follows: 10% camphor > 5% camphor.

Formulae L12 containing 10% w/w camphor and 5% Gaur gum exhibited shortest disintegration time about 18±2.14 sec which may be due to formation of tiny pores on tablets after evaporation of volatilizable component (camphor). The porous structure is responsible for faster water uptake, so it facilitates the swelling action of Gaur gum causing rupture of the tablets. The rapid disintegration of tablet assists easy swallowing and also plays important role in drug absorption in buccal cavity, thus promoting its bioavailability.

Formulae L13 to L16 were prepared by solid dispersion technique using PEG 6000 as polymeric carrier. Solubility of physical mixtures in distilled water and phosphate buffer (pH 6.8) found to be increased with increase in carrier ratio up to 1:4. This might be due to complete dispersion of drug with carrier (PEG 6000) at 1:4 ratio. Solubility was slightly decreased at 1:5 ratio. This might be due to formation of viscous boundary layer around the drug particle. So, solid dispersions containing the drug and carrier ratio of 1:4 was selected and tablets were formulated. The values of tablet hardness, friability and wetting time was found to be 3.33-3.78 kg/cm² 0.3-0.69 and 21.23-27.45 sec respectively.

Formulae L16 prepared by solid dispersion approach containing 5% Gaur gum showed a decrease wetting time (21.23 sec) compared to other formulations i.e. L13, L14, and L15. The addition of PEG 6000 as carrier promoted the wettability of the tablets thus accelerating Gaur gum swelling, leading to rapid breakdown of the tablet.

Table 6: Post compression evaluation of Lornoxicam fast dissolving tablet

Formulation code	Weight variation	Hardness kg/cm ²	% Friability	Wetting time (sec)	Water absorption ratio	Disintegration time (sec)	% drug content	% weight increased (after 1 month)
L1	100.51	3.21	0.67	58.23	80.21	42.54	99.78	0.92
L2	101.41	2.98	0.69	47.05	82.56	37.29	98.58	1.12
L3	99.87	3.54	0.53	42.72	72.45	32.41	101.6	1.67
L4	100.23	3.22	0.43	41.68	63.39	22.33	96.56	1.93
L5	98.64	2.98	0.72	32.11	75.12	30.20	97.99	1.23
L6	97.09	3.32	0.63	29.23	79.88	27.00	98.78	2.72

L7	96.12	2.89	0.62	26.41	82.59	25.43	101.10	2.28
L8	96.76	2.67	0.51	22.19	83.73	19.51	101.56	3.30
L9	96.98	2.44	0.75	28.76	77.98	25.10	100.06	2.41
L10	98.45	3.74	0.77	24.55	81.51	23.41	96.68	2.45
L11	97.68	3.18	0.82	19.29	85.66	17.79	98.10	2.62
L12	98.54	2.90	0.83	17.33	89.92	16.09	97.45	2.85
L13	99.72	3.44	0.89	28.71	83.71	25.45	98.08	1.19
L14	99.59	3.47	0.83	21.93	88.27	22.09	97.51	0.78
L15	98.80	3.42	0.75	24.24	84.62	24.11	101.40	1.71
L16	97.54	3.52	0.62	9.67	91.28	21.16	99.72	0.523

***In-vitro* dissolution study**

In this present study newer concept was applied to know effects of various categories of superdisintegrants on Lornoxicam fast dissolving tablets prepared by three approaches namely; superdisintegrant addition, sublimation, and solid dispersion techniques. The results obtained from the dissolution study are included in table 7. All sixteen formulae showed acceptable dissolution rate, where more than 85% to 90% of the labelled dose was dissolved at 30 minutes. The order of increased drug dissolution using three different techniques are as follows; solid dispersion>sublimation>superdisintegrant addition. In case of superdisintegrant addition technique; formulae L3 and L4 containing 2.5% and 5% Gaur gum as super disintegrating agent showed increased dissolution rate after 15 min from 69.87 to 70.95% compared to formulae containing Crospovidone as super disintegrating agent, 58.23% and 61.11% for L1 and L2 respectively.

Combined approaches namely superdisintegrant addition with sublimation or solid dispersion resulted in an increased dissolution rate of the drug. The incorporation of 5% Gaur gum in the formulae L12 prepared by sublimation method showed increased dissolution rate compared to tablet formulation prepared by superdisintegrant addition i.e. formulae L1 to L4. Formulae L12 containing camphor 10% showed the highest dissolution rate where 91.98% of labelled dose released at 10 min; this might be due to increased surface porosity of tablets produced by sublimation of camphor which increased the penetration of dissolution medium into tablets thus accelerating the swelling of the Gaur gum and facilitating rapid tablet breakdown. Both formulation L4 and L12 contains same concentration and category of superdisintegrant but formulae L12 showed highest dissolution rate which might be due to presence of camphor. Formulae L13-L16 were prepared by another combined approach; superdisintegrant addition with Lornoxicam solid dispersions using PEG 6000 as polymeric carrier. Formulae L16 containing the drug and carrier ratio of 1:4 solid dispersion as well as Gaur gum 5% showed increased dissolution rate of drug to 98.43% compared to that drug released from remaining formulations, this might be due to formulation containing solid dispersion exhibited higher degree of drug amorphization.

Table 7: Dissolution parameters of Lornoxicam fast dissolving tablets prepared by three different methods.

Formulation Code	Dissolution parameters				
	D _{1min}	D _{5min}	D _{10min}	D _{15min}	D _{30min}
L1	8.450	25.430	27.300	58.230	72.200
L2	9.700	28.450	50.450	61.110	74.110
L3	9.450	31.040	44.340	69.870	77.940
L4	13.290	37.120	58.240	70.950	80.090
L5	14.200	36.520	52.120	65.420	74.280
L6	17.010	38.400	58.540	72.200	85.900
L7	15.730	38.120	59.590	72.550	88.570
L8	22.260	43.220	48.210	81.650	94.740
L9	15.230	41.010	47.230	65.220	70.420
L10	18.500	46.120	52.030	69.410	81.100
L11	19.240	47.210	59.120	71.620	78.620
L12	25.440	49.030	61.240	75.330	93.450
L13	20.450	44.120	57.430	72.470	89.600
L14	24.090	51.060	62.790	86.430	96.210
L15	27.520	48.270	55.690	82.180	94.190
L16	22.3630	52.9330	65.810	89.330	98.430

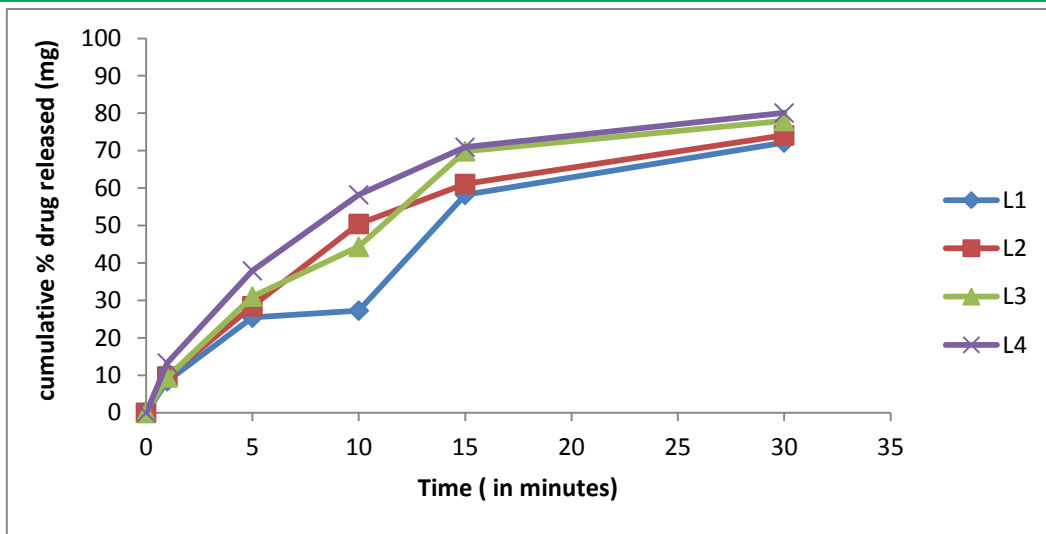


Fig 6: Dissolution profiles of Lornoxicam fast dissolvingtablets prepared by superdisintegrants addition method

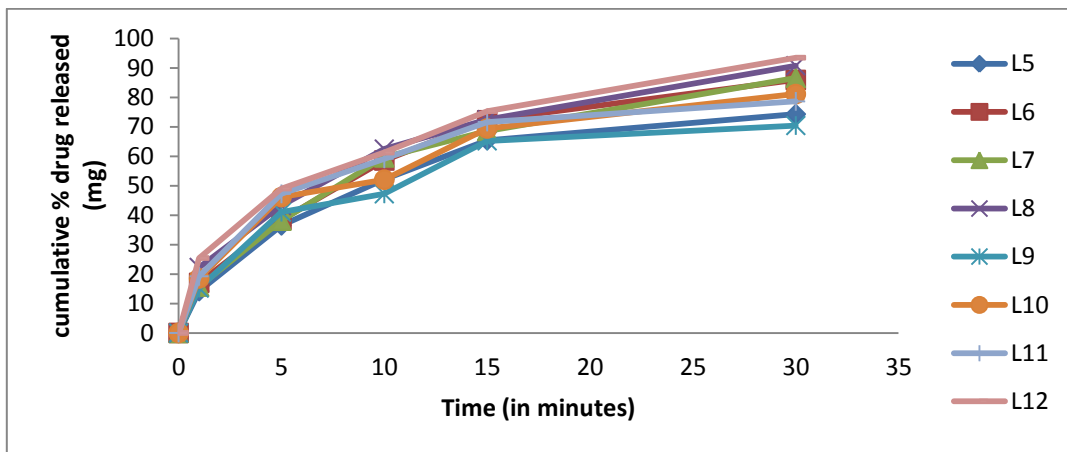


Fig 7: Dissolution profile of Lornoxicam fast dissolving by first combined approaches; sublimation + superdisintegrants addition method

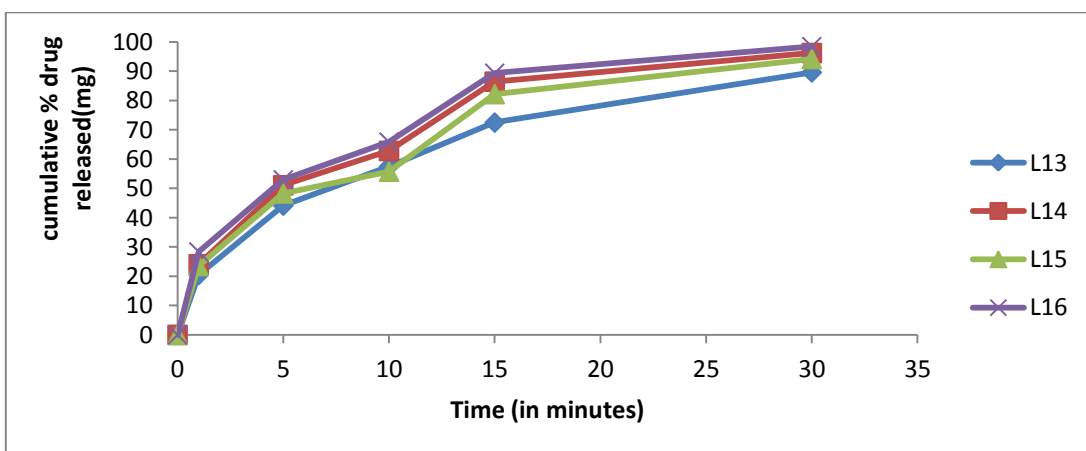


Fig 8: Dissolution rate profiles of Lornoxicam fast dissolving tablets prepared by second combined approaches; solid dispersion + superdisintegrants addition method

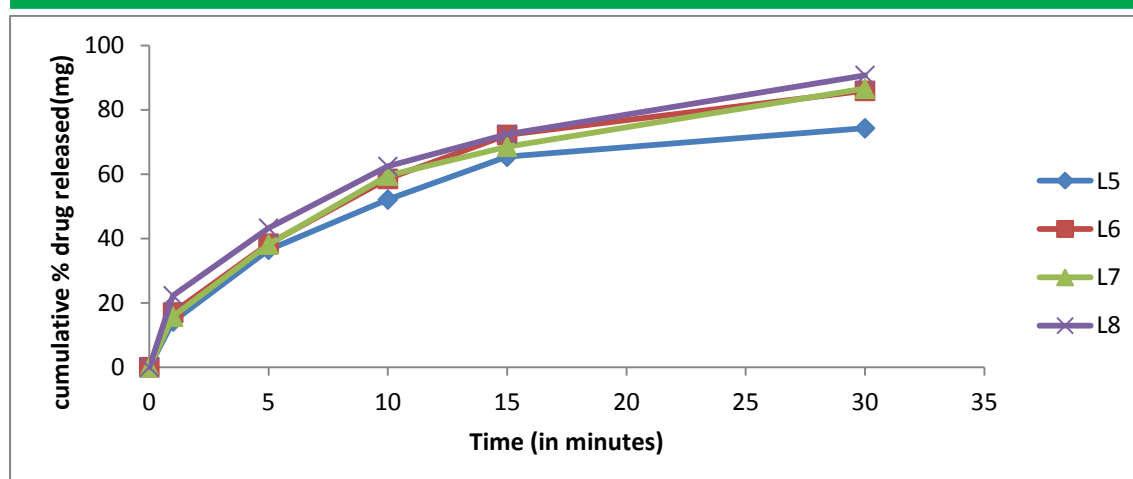


Fig 9: Effect of different concentrations of superdisintegrants [2.5% (L5), and 5% (L7)] and subliming agents (camphor) [5% (L5), and 10% (L8)] on dissolution rate profiles of Lornoxicam fast dissolving tablets

Release kinetics studies

Kinetic release studies were performed for formulae L16. Based on the “n” value of 0.458 obtained for formulae L16, the drug release was found to follow Fickian (case I) release. Also, the drug release mechanism was best explained by first order release kinetics. It was found that the value of ‘r’ is 0.9885, which is near to 1 when compared to Higuchi square root (0.960) and Zero order kinetic (0.782) model. The drug release kinetics of formulae L16 best fitted to first order release kinetics model. Results of release kinetics studies are shown in table 8.

Table 8: *In-vitro* kinetic release studies of formulation L16

<i>In-vitro</i> release kinetic models					
Formulae	Zero order	First order	Higuchi	Korsmeyer-Peppas	
L16	R ²	R ²	R ²	R ²	N
	0.789	0.9885	0.960	0.936	0.458

Stability Testing

Based on the results obtained from disintegration time and dissolution of Lornoxicam from its fast dissolving tablets, formulae L16 was considered as best. So, formulae L16 was chosen for stability testing. Results obtained from stability testing showed no any changes in colour or appearance of prepared fast dissolving tablets throughout the storage period. There is no significant change in the dissolution rate profile of Lornoxicam from its fast dissolving tablets stored at 25°C/60% and 45°C/75 % relative humidity but 1.23% of weight was increased after 3 month, which was under limits (as per ICH-Guidelines).

Table IX: Results of stability studies

Stability period	Stability conditions							
	25°C/60% RH				45°C/75 % RH			
	Hardness	% Friability	Drug content	Dissolution Profile	Hardness	% friability	Drug content	Dissolution profile
Initial	3.52	0.62	99.72	98.43	3.52	0.62	99.72	98.43
After 1 month	3.50	0.65	99.70	98.22	3.42	0.67	99.64	98.19
After 2 month	3.38	0.72	99.68	98.04	3.21	0.77	99.39	97.54
After 3 month	3.18	0.75	99.54	97.56	2.98	0.83	99.12	97.21

CONCLUSION

Fast dissolving tablets of Lornoxicam could be considered as useful solid oral dosage form as it increases drug dissolution rate which is directly related to its bioavailability. Among three approaches, combined approaches of solid dispersion and super disintegrant addition technique could be applied more effectively in formulating fast dissolving tablets with better disintegration as well as drug release properties. Therefore solid dispersion of Lornoxicam: PEG 6000 in the ratio of 1:4 along with addition of Gaur gum as natural superdisintegrant was found to improve the dissolution properties of the tablets prepared by the combined approach.

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