www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2016; 5(7): 01-07

www.thepharmajournal.com
Received: 01-05-2016
Accepted: 02-06-2016

Jitender Mor
Doon Valley Institute of Pharmacy and Medicine, Karnal, Haryana

Parveen Chauhan
Doon Valley Institute of Pharmacy and Medicine, Karnal, Haryana

Pawan Jalwal
Department of Pharmaceutical sciences, Baba Mastnath University, Rohtak, Haryana

Correspondence
Jitender Mor
Doon Valley Institute of Pharmacy and Medicine, Karnal, Haryana

Development and Evaluation of Oral Fast Dissolving Tablets of Lornoxicam using Superdisintegrants - A Comparative Study

Jitender Mor, Parveen Chauhan, Pawan Jalwal

Abstract
The concept of fast dissolving drug delivery system emerged from the desire to provide patient with more convenient means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. The main objective of the study is to develop reproducible formulation of fast dissolving tablets of Lornoxicam already used therapeutic molecule to enhance effectiveness, and to avoid side effects (gastric irritation) of the drug. Different batches of tablets were prepared by direct compression method using different concentration of superdisintegrants like *Plantago ovata,* Cross povidone, Cross carmellose sodium, Sodium starch glycollate. Before compression preformulation studies were done which includes characterization of blend and physical compatibility studies with excipients. Effect of change in superdisintegrant and there concentration on the formulation was studied. Final batches were compared for superiority of superdisintegrants in the formulation of FDT of Lornoxicam.

Keywords: FDT, *Plantago ovata,* Cross povidone, Cross carmellose sodium, Sodium starch glycollate, Lornoxicam.

Introduction
Many patient groups such as pediatric, geriatric, young individuals due to underdeveloped muscular and nervous system, and patients who are mentally retarded, uncooperative, nauseated have difficulties in swallowing tablets and capsules [1]. Difficulties in swallowing of solid dosage forms are also occur when water is not available, coughing during the common cold, allergic condition and bronchial infection [2].
This results in poor compliance with oral tablet drug therapy which leads to reduced overall therapeutic effectiveness [3]. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also for ideal for active people [4] To overcome this weakness, scientists have developed innovative drug delivery system to achieve better patient compliance. One such approach is "Fast Dissolving Tablet". Their growing importance was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet''. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes [5]. FDT is solid oral preparations that disintegrate rapidly in the oral cavity with an *in vivo* disintegration time of approximately 30 seconds or less [6]. Patient compliance is gaining significant importance in design of various type of dosage form. Fast Dissolving Tablet instead of dissolving or disintegrating in water is expected to dissolve or disintegrate in oral cavity without drinking water [7]. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach & it may produce rapid onset of action [8].
FDT dosage form disintegrates instantaneously releasing the drug which dissolves or disperses in the saliva [9]. Faster the drug into solution, quicker the absorption and onset of clinical effect. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. More ever, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet [10].
Disintegrants are substances or mixture of substances added the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1 – 10 % by weight relative to the total weight of the dosage unit. Examples of superdisintegrants are crosscarmelose, crosspovidone,

sodium starch glycollate which represent example of crosslinked cellulose, crosslinked polymer and a crosslinked starch respectively.

Materials and Methods

Preparation of Powder Blend

The drug and excipients were passed through sieve (#80) to ensure better mixing. MCC was used as a direct compressible vehicle. Super disintegrants like SSG, Crosspovidone, Ac-di-sol and husk of *Plantago ovata,* were used in different proportions. All the ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. The prepared powder blend was evaluated for various parameters like Bulk density, Tapped density, Angle of repose, Carr's index and Hausner's ratio.

Preparation of Fast Dissolving Tablets

Fast dissolving tablets containing 8 mg of Lornoxicam were prepared by direct compression method and the various formulae used in the study. After evaluation of powder blend the tablets were compressed with a Mini Rotary tablet punching machine (Fluid Pack) using 3.5 mm round punches set.

Formulations of Lornoxicam Tablets containing different concentrations of superdisintegrants

Formulations of Lornoxicam were prepared containing different concentrations of *Plantago ovata,* Cross povidone, Cross carmellose sodium of Sodium starch glycollate. Composition of formulation is given in Table 1, 2, 3 and 4.

Table 1: Formulations of Lornoxicam containing different concentrations of superdisintegrant *Plantago ovata.*

Ingredients (mg)	Formulation 1	Formulation 2	Formulation 3	Formulation 4
Lornoxicam	8	8	8	8
Plantago ovate	--	9	12	15
Micro crystalline Cellulose	100	100	100	100
Mannitol	24	15	12	9
Sodium saccharin	8	8	8	8
Talc	3	3	3	3
Magnesium stearate	2	2	2	2
Orange flavor	5	5	5	5
Avg. weight	**150 mg**	**150 mg**	**150 mg**	**150 mg**

Table 2: Formulations of Lornoxicam containing different concentrations of superdisintegrant Cross Carmellose Sodium.

Ingredients (mg)	Formulation 5	Formulation 6	Formulation 7
Lornoxicam	8	8	8
Ac-Di-Sol	9	12	15
Micro crystalline Cellulose	100	100	100
Mannitol	15	12	9
Sodium saccharin	8	8	8
Talc	3	3	3
Magnesium stearate	2	2	2
Orange flavor	5	5	5
Avg. weight	**150 mg**	**150 mg**	**150 mg**

Table-3: Formulations of Lornoxicam containing different concentrations of superdisintegrant Cross Povidone (CP).

Ingredients (mg)	Formulation 8	Formulation 9	Formulation 10
Lornoxicam	8	8	8
Cross Povidone	9	12	15
Micro crystalline Cellulose	100	100	100
Mannitol	15	12	9
Sodium saccharin	8	8	8
Talc	3	3	3
Magnesium stearate	2	2	2
Orange flavor	5	5	5
Avg. weight	**150 mg**	**150 mg**	**150 mg**

Table 4: Formulations of Lornoxicam containing different concentrations of superdisintegrant Sodium Starch Glycollate (S.S.G)

Ingredients (mg)	Formulation 11	Formulation 12	Formulation 13
Lornoxicam	8	8	8
Sodium Starch Glycollate	9	12	15
Micro crystalline cellulose	100	100	100
Mannitol	15	12	9
Sodium saccharin	8	8	8
Talc	3	3	3
Magnesium stearate	2	2	2
Orange flavor	5	5	5
Avg. weight	150 mg	150 mg	150 mg

Results and Discussion

Preformulation Studies

Drug Identification tests

- UV scan of Lornoxicam was done in Phosphate buffer pH 7.2 and λ max 380 nm was observed.
- Drug Lornoxicam was found to be yellow crystalline powder with no odour.
- Melting Point of Lornoxicam was determined by Capillary fusion method and found to be 217°C.
- The solubility of Lornoxicam in different solvents showed that drug is soluble slightly soluble in water, soluble in HCl, sparingly soluble in Methanol.

Identification of drug by FT-IR

The infrared spectrum of Lornoxicam confirms the presence of the relevant functional groups (as the important peaks are listed in Table-5 and is compared with the literature. FT-IR spectrum of Lornoxicam (in KBr) displays a characteristic –NH_2 absorption peak at 1621 cm^{-1}, which is a normal range of absorption of primary amines. It exhibits a strong band for C=O stretching of the non conjugated carboxylic acid at 1646 cm^{-1}whereas the second band which is expected to shift to lower frequency (owing to conjugation) appears as a overlapping band. The O=S=O as well as acyclic amide appears at 1387 cm^{-1}. The corresponding C-H stretching appears in the region 1547–1501 cm^{-1}.

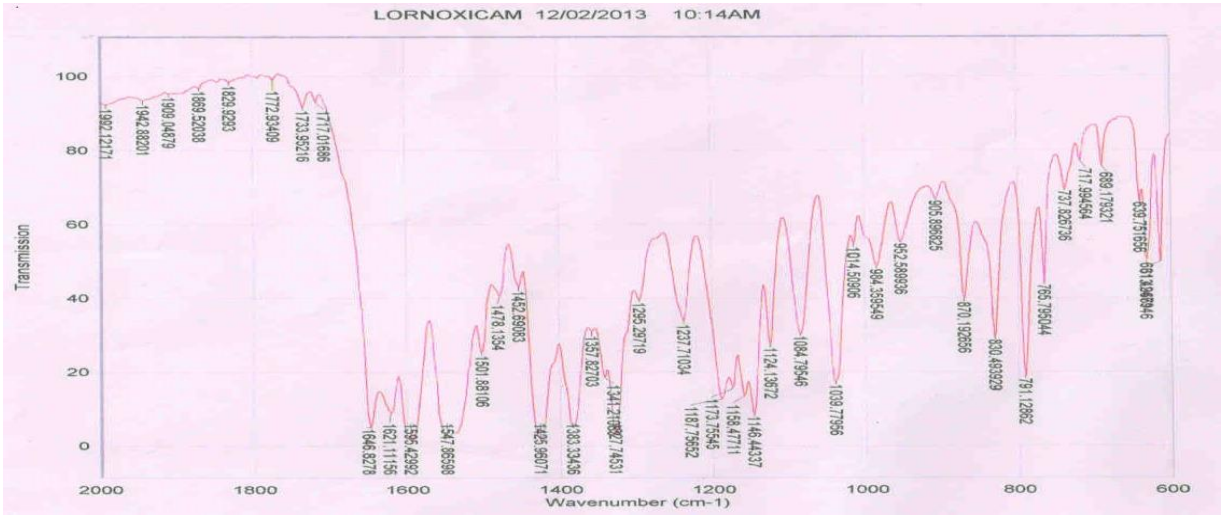

Fig 1: FTIR spectrum of Lornoxicam

Table 5: Interpretation of FT-IR spectrum of Lornoxicam

IR Absorption Band(cm^{-1}) (Experimental)	Functional Groups
1621 cm^{-1}	N-H stretching(NH_2)
1646 cm^{-1}	C=O stretching
1387cm^{-1}	S=O stretching(O=S=O)
1547 cm^{-1}	C-H stretching
1200 cm^{-1}	C–O–C stretching

Results of Drug Excipients compatibility studies

FT-IR Studies

IR spectra of Lornoxicam and combination of Lornoxicam with *Plantago ovata*, Cross carmellose sodium, and Crosspovidone, Sodium starch glycollate are given in the Figure-2 to 5. FT-IR spectrum showed that the peaks and the pattern of the spectra were similar in all cases, although they does not show any appreciable change in the position of assigned bands which indicated that there was no chemical interaction or decomposition of Lornoxicam during the preparation of the tablets.

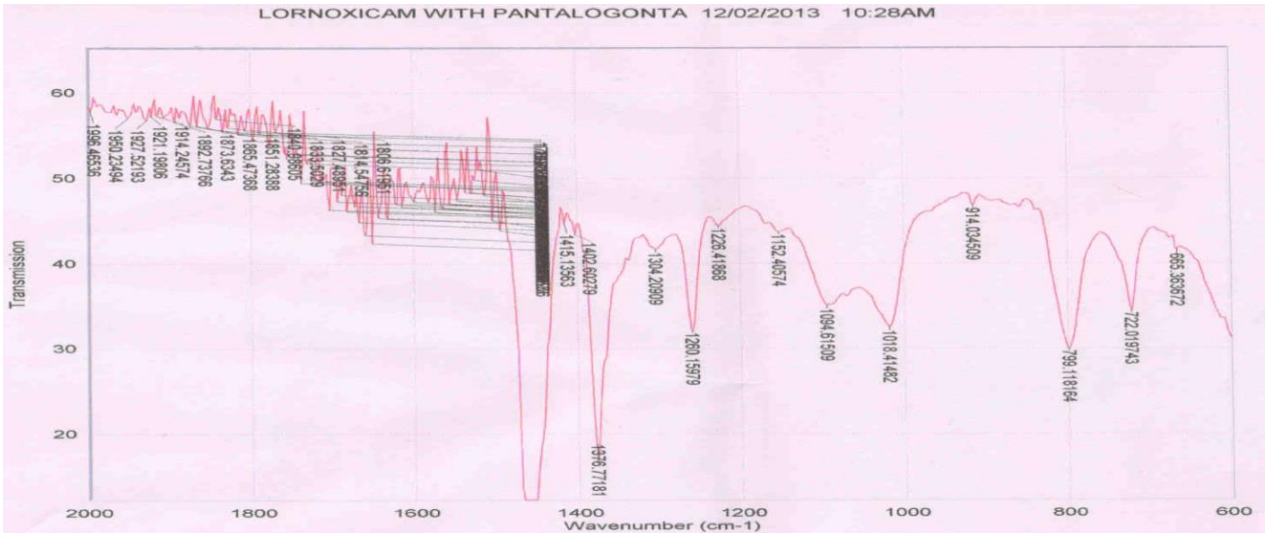

Fig 2: FT-IR spectrum of Lornoxicam with *Plantago ovate*

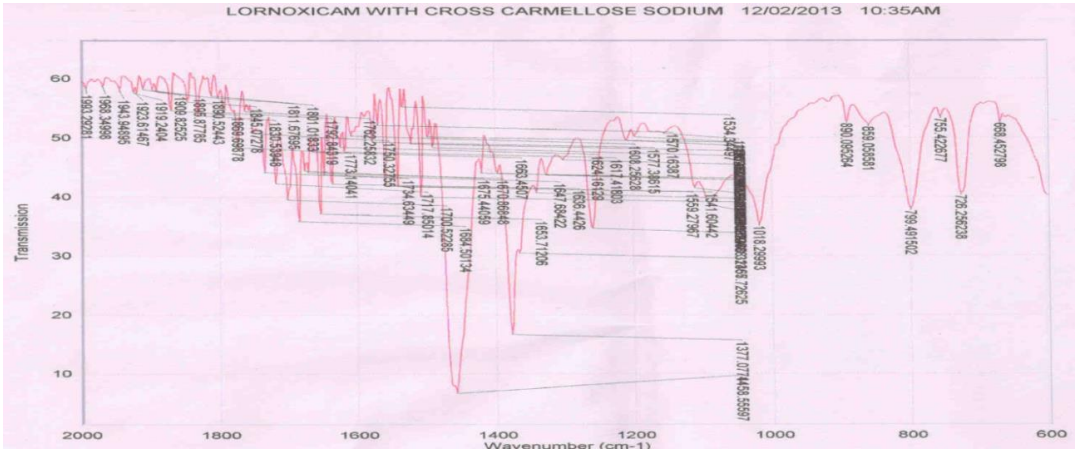

Fig 3: FT-IR spectrum of Lornoxicam with Cross carmellose sodium

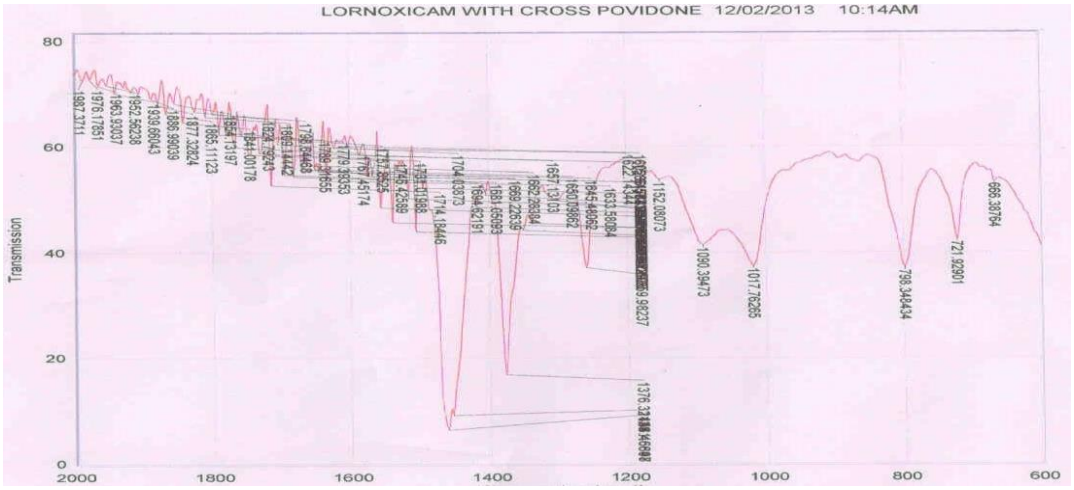

Fig 4: FT-IR spectrum of Lornoxicam with Cross povidone

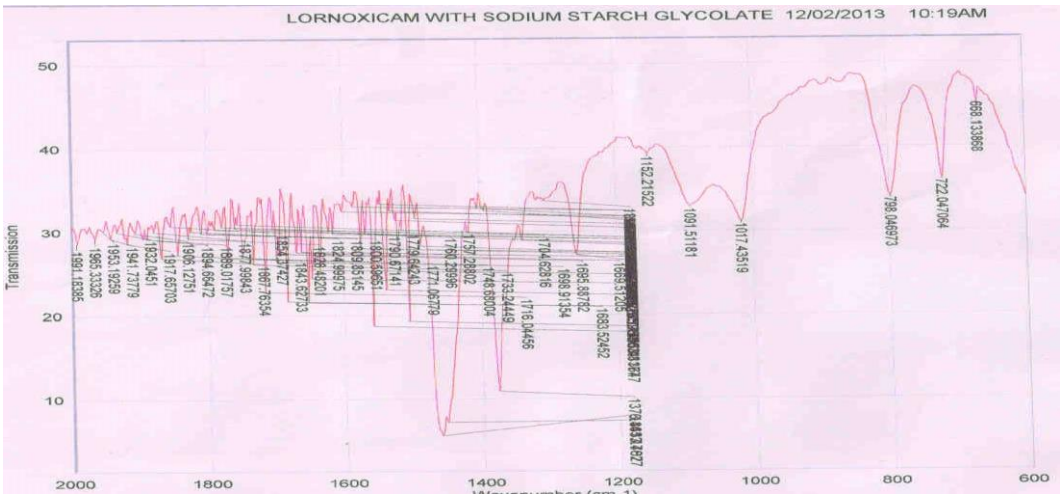

Fig 5: FT-IR spectrum of Lornoxicam with Sodium starch Glycollate

Swelling Index

Swelling Index of different superdisintegrants was obtained as shown below:

Table 6: Swelling index of different superdisintegrants

Name of superdisintegrants	Swelling Index (%v/v)
Plantago ovata	92±2.0
Cross Carmellose sodium	68±1.8
Crosspovidone	56±1.5
Sodium starch glycollate	48±1.2

Results of pre-compression parameter for tablets prepared by direct compression method

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study the flow properties of granules, to achieve uniformity of tablet weight. The results of all the preformulation parameters are given in Table-7.

Results of Post- Compression Parameters of fast dissolving tablets of Lornoxicam

QC tests for FDT of all formulations were performed, and the average values were calculated. All the tablets were evaluated

for different parameters as appearance, weight variation, hardness, Thickness, friability, wetting time, water absorption ratio, Disintegration time, *In vitro* dispersion time, and *In vitro* dissolution study. The weight variation was found in all designed formulations in the range 148 to 152 mg. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the official limits. The hardness of the tablets was maintained within the range of 3.2 to 3.6 kg/cm^2. The mean thickness was almost uniform in all the formulations and values ranged from 2 ±0.079 to 2.1±0.167 mm The standard deviation values indicated that formulations were within the range. The friability was found in all designed formulations 0.37 to 0.55% to be well within the approved range (<1%).

Table 7: Preformulation Evaluations of powder Blend

Formulation	Bulk Density (gm/cm^3) ±SD	Tapped Density (gm/cm^3) ±SD	Angle of Repose (θ) ±SD	Carr's Index (%) ±SD	Hausner's Ratio ±SD
1	0.530±0.02	0.68±0.01	28.43± 1.23	23.27±1	1.28±0.03
2	0.577±0.04	0.70±0.02	28.78±1.32	17.57±1.51	1.21±0.03
3	0.588±0.05	0.72±0.01	22.59±1.22	18.33±1.21	1.22±0.01
4	0.597±0.04	0.76±0.03	24.50±1.44	15.34±1.86	1.27±0.03
5	0.610±0.05	0.82±0.02	27.24±1.33	22.60±1.47	1.34±0.02
6	0.647±0.04	0.80±0.03	28.45±1.51	23.25±1.57	1.23±0.02
7	0.629±0.03	0.83±0.01	27.65±1.46	21.21±1.39	1.31±0.03
8	0.538±0.03	0.67±0.02	27.77±1.37	23.12±1.62	1.24±0.02
9	0.548±0.02	0.69±0.01	28.93±1.45	20.37±1.45	1.25±0.03
10	0.544±0.04	0.70±0.02	24.81±1.49	22.28±2.02	1.28±0.01
11	0.610±0.05	0.80±0.02	23.40±1.55	23.27±2.09	1.31±0.03
12	0.638±0.04	0.81±0.03	22.29±1.56	23.04±1.78	1.26±0.03
13	0.625±0.02	0.83±0.02	25.60±1.19	21.69±1.39	1.30±0.02

Wetting time

Wetting time is closely related to inner structure of the tablet. The wetting time of Lornoxicam dispersible tablets prepared by direct compression method were found to be in the range of 51 to 145 seconds. Promising formulations no.2, 3, 4 containing 6%, 8%, 10% conc. of *Plantago ovata* showed a wetting time of 52, 48, 52 sec. respectively, which facilitate the faster dispersion in the mouth.

Water absorption ratio

The formulations prepared by adding different conc. of superdisintegrants shows water absorption ratio in the range 35 to 71%. It was observed that formulation 2 to 4 which containing *Plantago ovata* as superdisintegrants shows lower water absorption ratio.

***In-vitro* Disintegration time and *In vitro* Dispersion time**

Table 8: *In vitro* disintegration and dispersion time of Fast Dissolving Tablets of Lornoxicam

Formulation	Disintegration time (seconds)±SD	*In vitro* Dispersion Time (seconds)±SD
1	160±1.0	67.15±1.0
2	25±1.5	24.18±1.03
3	22±1.33	21.52±1.34
4	20±1.6	21.24±1.12
5	28±1.64	22.17±1.23
6	27±1.98	22.25±1.67
7	25±1.1	21.39±1.0
8	70±1.17	26.09±1.05
9	65±2.23	28.47±1.56
10	67±2.01	30.59±1.98
11	75±1.35	37.09±1.08
12	70±1.57	33.47±1.99
13	67±1.3	33.59±2.09

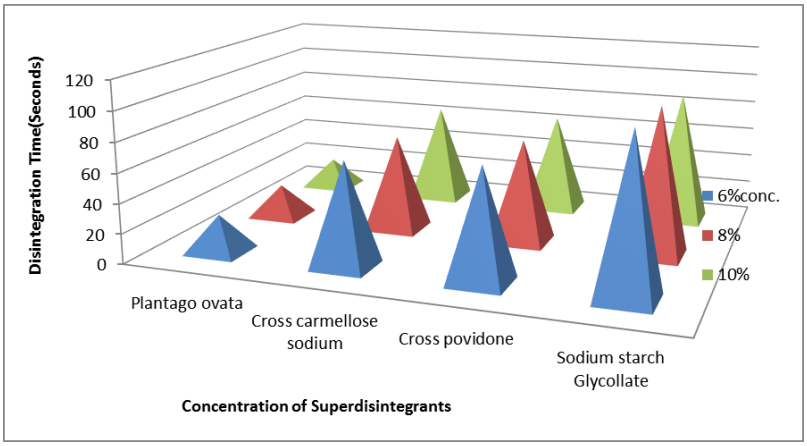

Fig 6: Disintegration time of various superdisintegrants formulated with Lornoxicam.

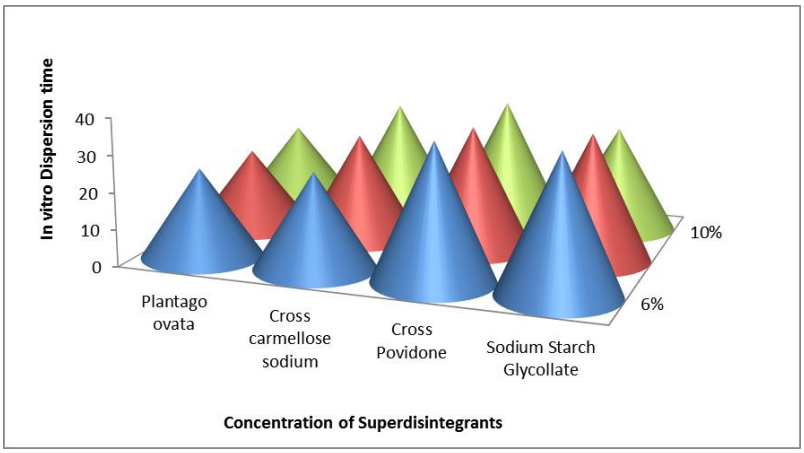

Fig 7: *In vitro* dispersion time of various superdisintegrants formulated with Lornoxicam.

Drug content

The drug content uniformity was performed for all the 16 formulations. The average value and standard deviations of all the formulations were calculated.

The percentage drug content of Lornoxicam in all the formulated tablets was found to be within limit. Percentage drug content values of Lornoxicam are within 98.12 to 102.78% for all the 13 formulations. The results indicate that uniformity of mixing. Table-9 shows all values of drug content uniformity.

Table 9: Drug content analysed from different formulations of Lornoxicam

Formulation Code	Percentage Content of Drug (±SD)
1	100.12±0.86
2	100.56±0.75
3	99.21±1.98
4	98.19±1.44
5	99.20±1.23
6	98.98±1.05
7	98.76±1.89
8	101.12±1.45
9	102.41±1.12
10	99.45±1.12
11	98.12±1.57
12	100.98±1.04
13	102.78±0.76

In vitro dissolution Test (Drug release)

Dissolution rate was studied by using USP type-1 apparatus at 100 rpm using 900 ml of 0.05 M potassium phosphate buffer pH (7.2) as dissolution medium.

Table 10: *In vitro* drug release of different formulation at 6% concentration of different superdisintegrants.

Time (minutes)	*In vitro* Percentage (%) drug release			
	Plantago ovata	Crosscarmellose sodium	Cross povidone	Sodium starch glycollate
5	80.18	70.44	68.22	71.98
10	82.67	72.90	70.14	72.63
15	84.14	74.87	72.45	74.19
20	85.65	75.12	74	75
25	86.64	77.09	75.34	78.18
30	88	78	78	80.66
35	90.10	80	80.10	83.15
40	92.98	82.40	82.68	85.76
45	94.45	84.13	84.48	86.05

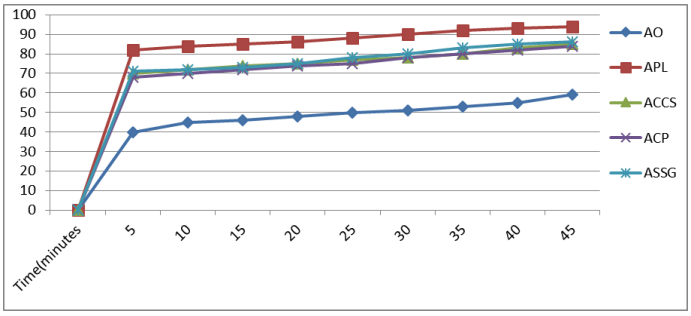

Fig 8: *In vitro* drug release of different formulation at 6% concentration of different superdisintegrants. A0: Control formulation without the superdisintegrants, APL: *Plantago ovata* mucilage formulation, ACCS: Ac-di-Sol Formulation, ACP: Crosspovidone, ASSG: Sodium starch glycollate.

Table 11: *In vitro* drug release of different formulation at 8 % concentration of different superdisintegrants.

Time (minutes)	*In vitro* Percentage (%) drug release			
	Plantago ovata	Crosscarmellose sodium	Cross Povidone	Sodium starch glycollate
5	83.12	70.44	68.72	71.28
10	84.08	72.10	71	72. 71
15	85.00	74.57	72.55	73
20	86.08	76.02	74.33	75.56
25	87.12	77.29	75. 89	79.68
30	90	78.44	77.76	80.36
35	93.10	80.65	80.50	83.95
40	94.38	83.44	82.88	86
45	95.08	88.23	87	88.05

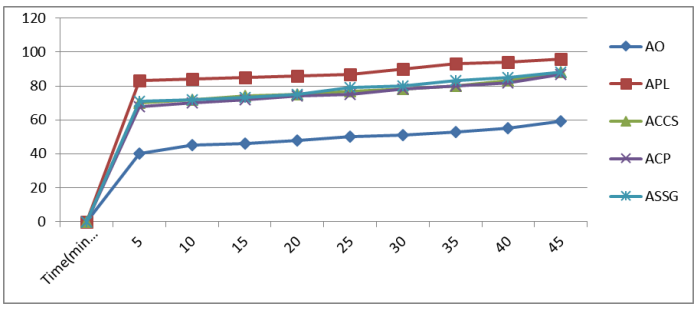

Fig 9: *In vitro* drug release of different formulation at 8% concentration of different superdisintegrants. A0: Control formulation without the superdisintegrants, APL: *Plantago ovata* mucilage formulation, ACCS: Ac-di-Sol Formulation, ACP: Crosspovidone, ASSG: Sodium starch glycollate.

Conclusion

All the formulations disintegrated within 20-160 seconds. Disintegration time for tablets prepared with *Plantago ovata* was nearer to that prepared with Ac-di-sol. Disintegration time of SSG and CP were comparatively greater. This indicates that the *Plantago ovata* had good disintegrating property. The mucilage of *Plantago ovata* showed very high percentage of swelling index as compared to the other superdisintegrating agents. *Plantago ovata* was most effective at 10 % concentration.

Based on the disintegration time formulation containing natural superdisintegrants like *Plantago ovate* (Formulation no. 2-4) were found to be promising and showed a disintegration time of less than 25 seconds, wetting time less than 52 seconds respectively, which facilitate the faster dispersion. The formulation have displayed good water absorption ratio of which indicate better and faster swelling ability of the disintegrants in presence of little amount of water. The drug content of tablets was uniform in all the batches and was between 98.12-102.78%. *In vitro* dissolution study on an optimized formulation revealed that more than 90% drug was released within 15 minutes. The FTIR spectra of formulation shows that there was no interaction between drug and excipients. It reflects drug and superdisintegrants used are compatible with each other.

Comparative evaluation studies proved that natural superdisintegrant like *Plantago ovate* is superior to synthetic superdisintegrants like Sodium starch glycollate (SSG), Cross carmellose sodium (Ac-Di-Sol) and Cross Povidone (CP) in the formulations of FDT of Lornoxicam.

References

1. Gupta A, Mishra AK, Gupta V, Bansal P, Singh R, Singh AK. Recent Trend of Fast Dissolving Tablet – An Overview of Formulation Technology. International Journal of Pharmaceutical & Biological Archives. 2010; 1(1):1-10.
2. Chang R, Guo X, Burnside B. A review of fast dissolving tablets. Pharmaceutical Technology. 2000; 24(6):52-4.
3. Yonezawa BY, Sunanda H. Rapidly disintegrating tablets prepared by the wet compression method. Mechanism and optimization. International Journal of Pharmaceutical & Biological Archives. 1999; 88(1):1004-10.
4. Lea and Febiger. Diffusion and Dissolution. In: Martin A Editor. Physical Pharnacy, 3rd edition, Philadelphia, 1983, 399-344.
5. European Pharmacopoeia. Supplement 4.2.France: Directorate for quality of medicines of the council of Europe, 2002, 4.
6. European Pharmacopoeia. Supplement 2. France: Directorate for quality of medicines of the council of Europe, 2006, 5.
7. Behnke K, Sogaard J, Martin S, Bauml J, Ravindran AV, Agren H. Mirtazapine orally disintegrating tablet versus sertraline: A prospective onset of action study. Journal Clinical Psychopharmacol. 2003; 23:358-364.
8. Susijit Sahoo, Mishra B, Biswal PK, Omprakash Panda, Santosh Kumar Mahapatra, Goutam Kumar Jana. Fast Dissolving Tablet: As a potential Drug Delivery System. Drug Invention Today. 2010; 2(2):130-133.
9. Sreenivas SA, Dandagi PM, Gadad AP, Godbpersible AM, Hiremath SP, Bhagawati ST, Orodispersible tablets: New-fangled drug delivery system-A review. Ind J Pharm Educ Res. 2005; 39(4):177-181.
10. Jaysukh J, Dhaval A, Kantilal R. Orally Disintegrating Tablets: A Review. Trop. Journal of Pharmaceutical Research. 2009; 8(2):161-172.