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Comparative Study on Effect of Natural and Synthetic Superdisintegrants in Formulation of Lornoxicam Orodispersible Tablet

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ABSTRACT

The purpose of this research was to introduce and evaluate natural excipients (soy polysaccharides, CP) that have versatile property in the orally disintegrating tablets. The main objective of this work was to assess the excipient for its activity as a disintegrant and compare its properties with other synthetic superdisintegrants. Orodispersible tablets containing a model drug, Lornoxicam was prepared using different ratios of banana powder, soy polysaccharides, crosspovidone, croscarmellose sodium (CCS) and sodium starch glycollate (SSG) as disintegrants. The prepared tablets were evaluated for their physiochemical properties like wetting time, water absorption ratio, dispersion time, disintegration time and drug release studies. It was observed that the results obtained from formulations containing the soy polysaccharides and CP as superdisintegrant showed a better profile in comparison to banana powder, CCS and SSG. Disintegration time of the formulations varied from 15 to 36s for all the formulations. Dissolution studies suggested that the drug dissolution from formulations containing soy polysaccharides was more than 90% within 15min in comparison to 82% and 85% for CCS and SSG respectively. Stability studies of the prepared tablets showed non-significant drug loss and drug release. Hence, it was concluded that banana powder can be used as a natural disintegrant in orodispersible tablets. The excipient being available naturally and having nutritional benefits adds value to the formulation and can be utilized as an effective excipient in preparing tablets with less cost.

Keywords: Orodispersible tablet, soy polysaccharides, banana powder, dispersion time, dissolution studies.

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INTRODUCTION

Recent advances in novel drug delivery aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for ease of administration and to achieve better patient compliance. Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the food stuffs that are ingested daily. Fast dissolving tablets are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in oral cavity within a minute without the need of water or chewing. It has been reported that Dysphagia[1] (difficulty in swallowing) is common among all age groups and more specific in paediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting and motion sickness complications[2]. Orally disintegrating tablets (ODTs) with good taste and flavour increase the acceptability of bitter drugs by various groups of population. Often people experience inconvenience in swallowing conventional tablets and capsules when water is not available, in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic conditions and bronchitis. For these reasons, tablets which 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 are ideal for active people.

The main objective of this study was to compare natural superdisintegrants such as soy polysaccharides and banana powder (Musa accuminata) as a pharmaceutical excipient and evaluate its disintegration properties in comparison with the other synthetic superdisintegrants.

MATERIALS AND METHODS

Lornaxicam was obtained as a gift sample from Glenmark Pvt. Ltd, Pune, Soy polysaccharides was gifted by JRS Pharma, Germany, Banana powder was purchased from Safety food (P) ltd, Kerala. SSG and CCS were obtained as gift sample from Apex laboratories, Chennai, CP was gifted by ISP Pharma, Mumbai. All other chemicals and reagents used are of analytical grade.

Preparation of orodispersible tablets by direct compression method:

Orodispersible tablets of Lornoxicam were prepared by direct compression method as per the formula given in Table 1 and Table 2.

Table 1: Formulation compositions of ODT

Ingredients	F1	F2	F3	F4	F5	F6
Lornaxicam (mg)	8	8	8	8	8	8
Mannitol (mg)	110	106	102	110	106	102
MCC (mg)	64	60	60	64	60	60
Banana powder (mg)	4	12	16	-	-	-
Soy polysaccharides (mg)	-	-	-	4	12	16
Aspartame (mg)	8	8	8	8	8	8
Magnesium stearate (mg)	4	4	4	4	4	4
Aerosil (mg)	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200

Table 2: Formulation compositions of ODT

Ingredients	F7	F8	F9	F10	F11	F12	F13	F14	F15
Lornaxicam (mg)	8	8	8	8	8	8	8	8	8
Mannitol (mg)	110	106	102	110	106	102	110	106	102
MCC (mg)	64	60	60	64	60	60	64	60	60
CCS (mg)	4	12	16	-	-	-	-	-	-
CP (mg)	-	-	-	4	12	16	-	-	-
SSG (mg)	-	-	-	-	-	-	4	12	16
Aspartame (mg)	8	8	8	8	8	8	8	8	8
Magnesium stearate (mg)	4	4	4	4	4	4	4	4	4
Aerosil (mg)	2	2	2	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200	200	200	200

The superdisintegrants (CCS, CP, SSG, Soy polysaccharides and Banana powder) in varying concentrations (2% to 8%) based on tablet weight were used to develop the tablets. The drug was mixed properly with the superdisintegrants and other additives in geometrical mixing to ensure thorough mixing of the ingredients. Lornoxicam and MCC were passed through sieve no. 60 mesh simultaneously. Co-shift above material and mannitol through sieve no. 60 mesh. Co-shift prepared material and superdisintegrants and aspartame (4%) through sieve no. 60 mesh. Reshift above material through sieve no. 60 mesh. Blend above step material in 1 lit. blender for 10 min. at 12 rpm. Blend above material and aerosil (1%) shifted through sieve no 40 mesh for 10 min. at 12 rpm. Finally, lubricate above step material with magnesium stearate (2%) shifted through sieve no. 60 mesh for 5 min. at 10 rpm and subjected to compression.

Pre-compression Parameters:

The quality of a tablet is generally dictated by the quality of physiochemical properties of then granule blend prepared. There are many process variables which may affect the characteristics of the finished tablet. Hence the prepared granules were evaluated for the mass-volume relationship parameters like bulk density, tapped density, Hausner's ratio, Compressibility index and flow properties (Angle of Repose)[3].

Post-compression parameters:

The prepared tablets were evaluated for hardness (Pfizer hardness tester), friability (Roche friabiliator), weight variation, disintegration time[4], wetting time[5], drug content, In vitro dispersion time, in vitro release studies. In weight variation test, twenty tablets were selected at random from each formulation and average weight was determined using an electronic balance. Tablets were weighed individually and compared with average weight. Thickness of the tablet was determined by using a dial caliper. Wetting time was measured by placing a tablet on a piece of tissue paper folded twice in a small petri-dish containing 6ml of water and measuring the time required for complete wetting of the tablet. The wetted tablet was then weighed and the water absorption ratio was calculated by using the following equation:

$$R = (Wb-Wa)/Wa$$

Where, Wa and Wb are the weights before and after water absorption respectively.

Water Absorption Ratio:

A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio(R) was determined using equation.

$$R = 100 \times (Wa-Wb) / Wb$$

Where, Wa = weight of the tablet before water absorption, Wb = weight of the tablet after water absorption Three tablets from each formulation were analyzed and SD was determined.

In-vitro dispersion time:

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6ml of pH 6.8 (simulated saliva fluid). Three tablets from each formulation were randomly selected and in vitro dispersion time was noted and expressed in seconds.

Disintegration test:

The test was performed using Disintegration apparatus with water which was heated to 25^0C. A tablet was added to each of 6 tubes of apparatus and the time in seconds for complete disintegration of the tablets was found out. The test performed three times and average values were found out.

Drug content:

Six tablets were weighed and powdered. An amount of powder equivalent to 8mg of Lornoxicam was dissolved in 6.8 phosphate buffer, filtered, diluted the sample suitably and analyzed for drug content at 371 nm using UV-Visible Spectrophotometer.

In-vitro dissolution studies:

Dissolution studies were performed using USP Type II standard paddle apparatus at 37±0.5°c. The dissolution rate was studied in 900 ml of dissolution medium (pH 6.8 phosphate buffer) with a paddle speed of 75 rpm. Aliquots were withdrawn at specified time intervals and were replenished immediately with the same volume of fresh medium. The withdrawn aliquots were diluted suitably and assayed spectrophotometrically at 371nm.

Comparative study of optimized formulation with marketed formulation:

In vitro dissolution studies for optimized formulation and Lorsumo (Hetero health care Ltd. Hyderabad) dose 8 mg were carried out using USP apparatus type II at 75 rpm.

RESULTS AND DISCUSSIONS

Oral drug delivery system represents one of the frontier areas of drug delivery system. Such dosage forms are having a major advantage in patient compliance. Orodispersible tablets belong to oral drug delivery systems that are capable of disintegrating in the oral cavity and thus rapidly releasing the drug. All the formulations were prepared under similar conditions to avoid process variables.

Flow Properties:

The tablets prepared by direct compression method showed an angle of repose of less than 30, which reveals good flow property. The loose bulk density and tapped bulk density for all formulation granules varied from 0.40 gm/cm^3 to 0.44 gm/cm^3 and 0.50 gm/cm^3 to 0.53 gm/cm^3 respectively (Table 3).

Table 3: Physical properties of tablet blend

Batches	Evaluation Parameters					
	Angle of Repose(ø)	**Bulk Density(g/cm^3)**	**Tapped Density (g/cm^3)**	**CI (%)**	**Hausner's Ratio**	**Flowability**
F1	28^0.32±1.45	0.40±0.34	0.51±0.22	21.56±1.11	1.27±0.25	GOOD
F2	30^0.24±1.24	0.42±0.24	0.50±0.26	16.00±1.27	1.19±0.57	GOOD
F3	27^0.23±1.9	0.40±0.26	0.52±0.52	23.07±1.23	1.3±0.54	GOOD
F4	28^0.17±1.54	0.41±0.30	0.53±0.33	22.64±1.34	1.29±0.56	GOOD
F5	23^0.15±1.65	0.42±0.33	0.52±0.43	19.23±1.42	1.23±0.45	GOOD
F6	24^0.13±1.34	0.43±0.43	0.51±0.29	15.68±1.54	1.18±0.65	GOOD
F7	27^0.35±1.45	0.43±0.38	0.53±0.28	18.86±1.12	1.23±0.29	GOOD
F8	26^0.24±1.24	0.40±0.26	0.51±0.22	21.56±1.34	1.27±0.55	GOOD
F9	29^0.33±1.9	0.41±0.36	0.50±0.55	18.00±1.43	1.21±0.59	GOOD
F10	26^0.17±1.54	0.40±0.38	0.52±0.37	23.07±1.42	1.30±0.66	GOOD
F11	27^0.25±1.65	0.42±0.33	0.53±0.49	20.75±1.47	1.26±0.53	GOOD
F12	24^0.43±1.34	0.44±0.47	0.50±0.62	12.00±1.44	1.13±0.66	GOOD
F13	23^0.16±1.22	0.41±0.39	0.51±0.57	19.60±1.52	1.24±0.67	GOOD
F14	22^0.88±1.35	0.42±0.38	0.52±0.39	19.23±1.46	1.23±0.46	GOOD
F15	24^0.28±1.28	0.41±0.29	0.53±0.56	22.64±1.59	1.29±0.48	GOOD

The results of Carr's consolidation index or (%) compressibility index for the entire formulation blend ranged from 12.0 to 23.07 indicating excellent compressibility index.

Physical Properties of Tablet:

The physical properties of tablets prepared with soy polysaccharides and CP showed better results than that of the tablets prepared with CCS, and SSG. This clearly demonstrated the efficiency of soy polysaccharides and CP as a pharmaceutical excipient. The hardness values ranged from 4.1 to 4.8 kg/cm^2 for all formulations (Table 4). The entire tablets passes weight variation test as the average % weight variation was within the pharmacopoeial limit of 10%. It was found to be 200.1 ± 1.11 mg to 202.5 ± 1.52 mg. The weight of all the tablets was found to be uniform with low standard deviation (Table 4). The friability values were found to be within the limit (0.32-0.58%).

Table 4: Physical properties of Tablet.

Batch No.	Thickness (mm)	Hardness (Kg/cm^3)	Friability (%)	%Weight variation
F1	3.63±0.12	4.3±0.11	0.57±0.15	202.3±1.21
F2	3.66±0.11	4.5±0.13	0.58±0.18	201.4±1.32
F3	3.53±0.17	4.8±0.14	0.55±0.22	200.4±1.22
F4	3.62±0.10	4.5±0.12	0.32±0.09	200.7±1.16
F5	3.61±0.08	4.7±0.15	0.33±0.08	200.1±1.11
F6	3.71±0.09	4.2±0.11	0.37±0.10	201.4±1.35
F7	3.60±0.14	4.6±0.15	0.47±0.17	201.3±1.31
F8	3.58±0.13	4.8±0.11	0.48±0.18	201.7±1.42
F9	3.54±0.15	4.7±0.12	0.45±0.23	202.5±1.52
F10	3.70±0.11	4.4±0.17	0.38±0.11	200.8±1.46
F11	3.58±0.12	4.8±0.18	0.36±0.15	200.4±1.31
F12	3.63±0.10	4.6±0.14	0.37±0.15	202.4±1.25
F13	3.50±0.14	4.3±0.16	0.54±0.14	200.7±1.34
F14	3.53±0.16	4.2±0.11	0.57±0.13	200.8±1.22
F15	3.57±0.19	4.1±0.16	0.55±0.18	200.2±1.30

***In-vitro* Study:**

The drug content of Lornoxicam determined at 371nm ranges from 81.7% to 99.8% and complies with IP standard.

Wetting time is closely related to the inner structure of tablet. This experiment mimics the action of saliva in contact with the tablet to illustrate the water uptake and subsequent wetting of tablet. This shows the wetting process was very rapid in almost all formulations. This may be due to the ability of swelling followed by breaking and also capacity of water absorption and cause swelling. It was found to be in the range of 17.42s to 32.36s.

Water absorption ratio which is important criteria for understanding the capacity of disintegrants to swell in the presence of little amount of water, was calculated. The water absorption showed values in the range of 77.61% to 98.01% (Table 5). This shows all the formulations have good water absorption capacity.

Table 5: Evaluation of compressed tablet

Batch No.	Disintegration time(Sec)	Dispersion time (Sec)	Wetting time (Sec)	Water absorption ratio (%)	Uniformity of Content (%)
F1	18.23±2.10	30.22±0.45	26.12±0.52	81.59±1.11	83.9
F2	22.34±2.11	36.17±0.37	30.17±0.45	77.61±0.88	83.9
F3	21.24±2.32	30.31±0.43	29.23±0.44	80.01±1.10	81.7
F4	17.23±1.11	28.22±0.54	25.27±0.33	79.00±0.56	93.5
F5	15.22±1.24	26.34±0.33	19.53±0.23	82.09±0.49	91.7
F6	12.33±1.25	24.22±0.45	18.22±0.37	97.00±0.39	99.8
F7	14.43±1.10	24.32±0.35	19.43±0.58	84.00±1.17	81.7
F8	13.34±2.11	25.18±0.47	20.22±0.46	88.06±0.76	84.8
F9	18.24±1.32	30.41±0.53	26.43±0.48	89.95±1.54	83.00
F10	16.23±1.27	30.32±0.44	24.47±0.38	83.5±0.67	89.2
F11	10.22±1.34	24.22±0.38	19.43±0.29	86.00±0.49	95.2
F12	09.33±1.28	20.24±0.46	17.42±0.39	98.01±0.44	98.5
F13	36.31±1.44	45.36±0.39	32.36±0.48	79.79±0.54	92.1
F14	30.12±1.17	34.33±0.46	28.42±0.53	88.44±0.63	93.8
F15	32.23±1.19	29.37±0.41	27.41±0.45	82.9±0.47	90.7

The use of superdisintegrants for preparing ODTs is highly effective and commercially feasible. These superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. In this study, soy polysaccharides and banana powder was employed as superdisintegrant and its effect was compared with CCS, CP and SSG which are the three commonly employed superdisintegrants. Formulations containing soy polysaccharides as superdisintegrant showed better results in comparison with banana powder, CCS, CP and SSG. In the wetting studies, the formulation F6 containing 8% soy polysaccharides showed the faster time of about 18.22s than the banana powder, CCS and SSG whereas F3, F9, F12 and F5 containing 8% of banana powder, CCS, CP and SSG gave a value of 29.23, 26.43, 17.42 and 22.64s respectively. Similarly in the water absorption studies formulations containing 8% superdisintegrants gave values of 97.0, 80.01, 89.95, 98.01 and 82.9 for soy polysaccharides, banana powder, CCS, CP and SSG respectively. From the observed values it was concluded that the formulations containing soy polysaccharides gave superior results than banana powder, CCS

and SSG and closed results with the CP. The most important parameter that needs to be optimized in the development of ODTs is the disintegration time of tablets. In the present study all the tablets disintegrated within 55s fulfilling the official requirements (>3min) for dispersible. Table 5 gives the disintegration time achieved by all the formulations.

Disintegration time for tablets prepared with soy polysaccharides (F6) was faster than banana powder (F3), CCS (F9) and SSG (F15) formulations and slower than CP (F12). The dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet. The influence of superdisintegrants on the dissolution of Lornoxicam from the tablets is given in Table 6, Table 7.

Table 6: Dissolution studies of Lornaxicam ODT

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
0	0	0	0	0	0	0
5	83	75	76	82	84	90
10	88	81	81	86	87	92
15	93	83	84	92	91	94
20	97	86	85	95	94	97
25	101	90	88	100	98	100
30	103	92	90	103	101	102

Table 7: Dissolution studies of Lornaxicam ODT

Time (min)	F7 (%)	F8 (%)	F9 (%)	F10 (%)	F11 (%)	F12 (%)	F13 (%)	F14 (%)	F15 (%)
0	0	0	0	0	0	0	0	0	0
5	73	76	79	73	84	91	74	75	76
10	79	80	82	79	87	94	74	77	79
15	82	83	86	84	89	95	75	80	81
20	87	8	88	87	91	97	78	86	84
25	80	94	100	91	101	96	96	90	90
30	79	98	102	98	102	98	101	95	93

It was observed that the tablets containing soy polysaccharides and CP as superdisintegrants exhibited a higher percentage release in comparison with tablets containing banana powder, CCS and SSG. The rapid increase in dissolution of Lornoxicam may be attributed to rapid swelling and disintegration of tablet into apparently primary particles, while tablets prepared with SSG disintegrate by rapid uptake of water followed by rapid and enormous swelling into primary particle but more slowly due to the formation of a highly viscous gel layer. Soy polysaccharides and CP exhibits higher capillary activity and pronounced hydration with a little tendency to form a viscous gel layer. Comparative studies of optimized formulation with the marketed formulation shown in Table 8.

Table 8: Comparative studies of optimized formulation with marketed formulation.

Time (min)	F6(%)	F12(%)	MF(Lorsumo)(%)
0	0	0	0
5	90	91	81
10	92	94	85
15	94	95	89
20	97	97	92
25	100	96	98
30	102	98	100

CONCLUSION

From the all batch results we have concluded that the batch F6 containing soy polysaccharides and batch F12 containing CP shows the better and comparative results with the marketed formulation as compare to other batches, as it shows better flow properties of granules as well as better results for the tablet.

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