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Research Article

Formulation and Evaluation of Fast Disintigrating Meloxicam Tablets and Its Comparison with Marketed Product

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ABSTRACT

The present investigation deals with the formulation of fast disintegrating tablets of Meloxicam that disintegrate in the oral cavity upon contact with saliva and there by improve therapeutic efficacy. Meloxicam is a newer selective COX-1 inhibitor. The tablets were prepared by wet granulation procedure. The influence of superdisintegrants, crosspovidone, croscaremellose sodium on disintegration time, wetting time and water absorption ratio were studied. Tablets were evaluated for weight and thickness variation, disintegration time, drug content, *in vitro* dissolution, wetting time and water absorption ratio. The *in vitro* disintegration time of the best fast disintegrating tablets was found to be 18 sec. Tablets containing crospovidone exhibit quick disintegration time than tablets containing croscaremellose sodium. The fast disintegrating tablets of Meloxicam with shorter disintegration time, acceptable taste and sufficient hardness could be prepared using crospovidone and other excipients at optimum concentration.

Keywords: Crosspovidone, Fast disintegrating tablet, Meloxicam, Superdisintigrants, Wetting time.

INTRODUCTION

Orally administered dosages form e.g. tablets, capsules are convenient dosage form for many drugs –but they are challenging to formulate if the active substances has poor dissolution or low bioavailability. Polymer coating enables the formulation of mouth dissolving and taste masking of bitter taste drugs-thereby giving better patient compliance (1). Most pharmaceutical forms for oral administration are formulated for direct ingestion, for chewing, for prior dispersion and /or dissolution in water; some of them are absorbed in mouth (sublingual or buccal tablets). Elderly individuals have difficulty in swallowing when prescribed in conventional tablet and capsule form (2, 3, 4). The problem of swallowing is also evident in pediatrics, psychiatric as well as traveling patients who may not have ready access to water (5).The rapidly disintegrating tablet in mouth or orodispersible tablets overcome all the above problems and thus offer an alternate form of oral medication, which provide patients with a more convenient means of taking their medication (6). Addition of super disintegrating agent in the formulation is one of the approaches to formulate orodispersible tablets. Orally disintegrating tablets contain wide variety of pharmaceutical active ingredients covering many therapeutic categories. The time for disintegration of orally disintegrating tablets are generally considered less than one minute. Orally disintegrating tablets are characterized by high porosity, low density and low hardness. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and is subsequently swallowed (7).

Meloxicam is a nonsteroidal anti-inflammatory drug of the oxicam class, used to relieve the symptoms of arthritis, primary dysmenorrhea, fever and as an analgesic, especially where there is an inflammatory component (8). Meloxicam inhibits cyclooxygenase (COX) synthesis. This enzyme is responsible for converting arachidonic acid into prostaglandin H2. This is the first step in the synthesis of prostaglandins, which are mediators of inflammation. Meloxicam has been shown, especially at its low therapeutic dose, selectively to inhibit COX-2 over COX-1 (9). A primary advantage of the oxicam family of drugs is their long half-life which permits once-day dosing (10). In gastric disease, lower dose of meloxicam is required 7.5 mg/day. Meloxicam is safer then other NSAID's (11). Hence in present study an attempt was made for preparation of fast disintegrating tablets of meloxicam with aim of providing faster onset of action.

MATERIALS AND METHODS

Materials:

Meloxicam was gifted from Dr.Reddy's Laboratories (Hyderabad, India). Crospovidone, Croscarmellose sodium were obtained from SD Fine chem. LTD (Mumbai). Micro crystalline cellulose was purchased from (S.D. Fine Chemicals, Mumbai). Magnesium stearate and talc were obtained from (Loba Chemicals, Mumbai). All other ingredients used were of analytical grade.

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Table 1: Composition of different batches of fast disintegrating Meloxicam tablets.

Ingredients	Formulation code					
	F-1	F-2	F-3	F-4	F-5	F-6
Meloxicam	7.5	7.5	7.5	7.5	7.5	7.5
B-Cyclodextrin	18	18	18	18	18	18
Micro crystalline cellulose	107.5	91.5	76.5	107.5	91.5	76.5
Dextrose	40	50	60	40	50	60
Starch powder	05	05	05	05	05	05
Croscarmellose sodium	14	20	25	-	-	-
Crosspovidone	-	-	-	14	20	25
Sodium saccharin	02	02	02	02	02	02
Vanillin	02	02	02	02	02	02
Magnesium stearate	02	02	02	02	02	02
Talc	02	02	02	02	02	02

Preparation of Meloxicam orally disintegrating tablets:

The prepared β-Cyclodextrin complex and the excipients were granulated using starch mucilage (10% solution), to form cohesive masses, then were passed through sieve # No 22. The formed granules were dried in hot air oven at 60°C for 2-3 hours. The dried granules were passed through sieve # No 22.and again passed through sieve # No 100. The blend was compressed into tablets using 10 station rotary tabletting machine.

Evaluation of granules:

The angle of repose was measured by using funnel method (12), which indicates the flowability of the granules. Loose bulk density (LBD) and tapped bulk density (TBD) (13) were measured using the formula: LBD= weight of the powder / volume of the packing. TBD= weight of the powder / tapped volume of the packing. Compressibility index (14) of the granules was determined by using the formula: CI (%) = [(TBD-LBD/TBD)] ×100.The physical properties of granules were shown in Table 2.

Evaluation of the tablets

All prepared matrix tablets were evaluated for its uniformity of weight, hardness, friability and thickness according to official methods (15) shown in Table 3.

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability (16)

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight Variation

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5% (USP XX).

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20mg of Meloxicam was dissolved in 100ml of pH 7.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 273nm using UV-Visible spectrophotometer (UV 160 Shimadzu, Japan).

Wetting time (17)

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 9ml of buffer solution simulating saliva pH 7.4, which had the following composition, NaCl (0.126g), KCl (0.964g), KSCN (0.189g), KH2PO4 (0.655g) and urea (0.200g) in 1Litre of distilled water. A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted. The results are tabulated in Table 2.

Water absorption ratio (R)

The weight of the tablet prior to placement in the petri dish was noted (*wb*) utilizing a Shimadzu digital balance. The wetted tablet was removed and reweighed (*wa*). Water absorption ratio, *R*, was then determined according to the following equation.

$$R = 100 \times (w_a - w_b) / w_b$$

where *wb* and *wa* were tablet weights before and after water absorption, respectively

Table 2: Data for blend evaluation of formulation (F-1 to F-6)

Parameters	Formulation code						
	F-1	F-2	F-3	F-4	F-5	F-6	
Angle of repose	26.79 ± 0.32	28.34 ± 0.53	24.83 ± 0.24	26.45 ± 0.19	27.82 ± 0.39	26.85 ± 0.48	
Loose bulk density (LBD) (g/ml)	0.487 ± 0.34	0.532 ± 0.385	0.5182 ± 0.17	0.470 ± 0.29	0.514 ± 0.28	0.527 ± 0.49	
Tapped bulk density (TBD) (g/ml)	0.580 ± 0.48	0.675 ± 0.48	0.522 ± 0.27	0.592 ± 0.71	0.583 ± 0.16	0.614 ± 0.29	
Compressibility index (%)	13.92 ± 0.36	15.71 ± 0.83	14.72 ± 0.87	17.68 ± 0.19	16.41 ± 0.18	17.09 ± 0.35	

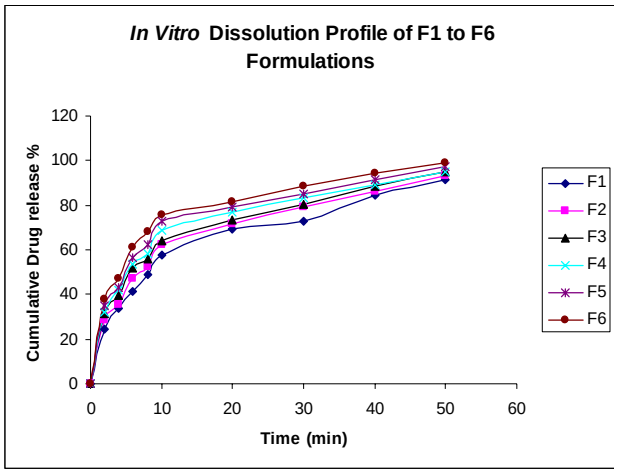

Figure 1. Comparison of *In-vitro* release profile of Meloxicam from formulations F-1 to F-6.

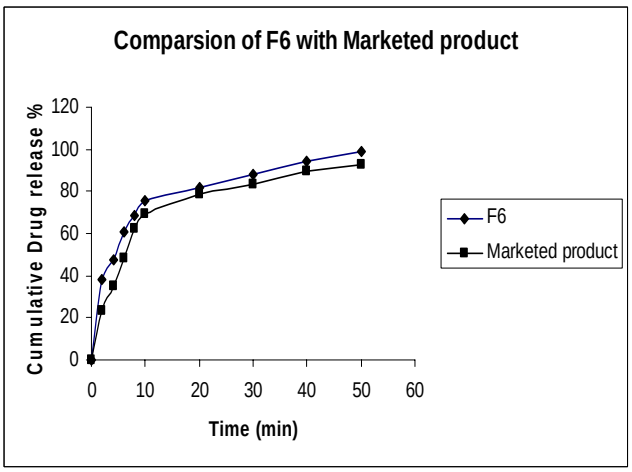

Figure 2. Comparison of *In-vitro* release profile of formulation F6 with marketed sample

In-vitro dispersion time (18)

In-vitro dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing 6ml of buffer solution (pH 7.4).

***In Vitro* disintegration time**

10 ml of water at 25°C was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted.

In-vitro drug release studies

In-vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP XXII type II Electro lab, Mumbai, India) at 50 rpm. Phosphate buffer pH7.4 was used as the dissolution media with temperature maintained at 37±1ºC. Samples were withdrawn at different intervals, diluted suitably and analyzed at 363nm for cumulative drug release using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India). The study was performed in triplicate.

Stability studies

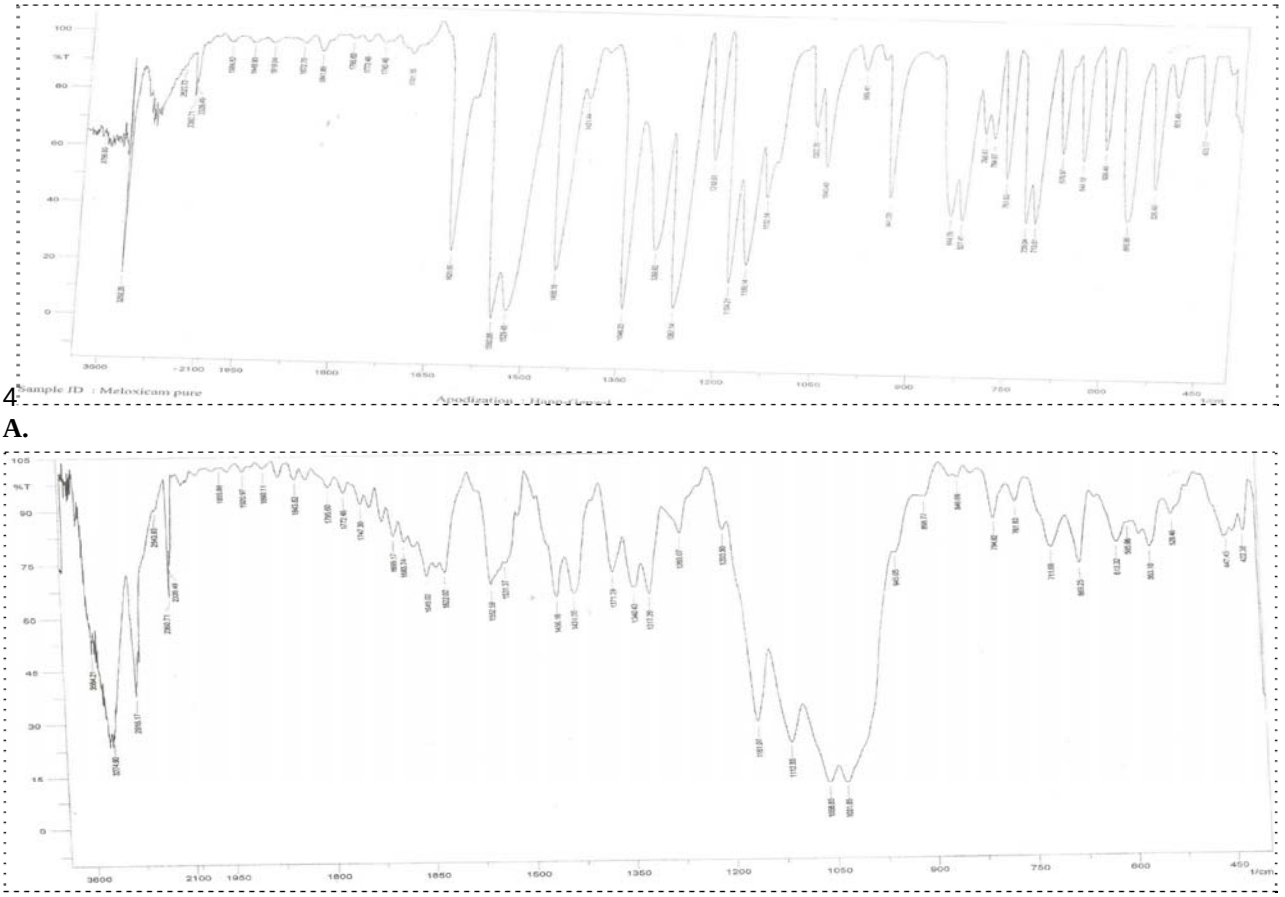

Figure 3. Fourier transform infrared spectra of A: Pure Meloxicam B: Meloxicam tablet (From top to bottom)

Short term stability studies on the optimum formulation (F6) were carried out by storing the tablets (in amber colored rubber stoppered vials) at 40°/75% RH for 3 weeks. At every 1 week intervals, the tablets were examined for physical changes, properties, drug content and in vitro release studies (19).

RESULTS AND DISCUSSION

The supplied drug passed the various tests of identification and analysis. The pure drug Meloxicam and the solid admixture of drug and various excipients used in the preparation of fast dispersible tablet formulations were characterized by FT-IR spectroscopy to know the compatability, figure-3. The FT-IR study did not show any possibility of interaction between Meloxicam and superdisintegrants used in the fast dispersible tablets. Since the flow properties of the powder mixture are important for the uniformity of the mass of the tablets, the flow of the powder mixture was analyzed before compression of the tablets. The results of angle of repose and compressibility index (%) ranged from (24.83 ± 0.24 to 28.34 ± 0.53) and (13.92 ± 0.36 to 17.68 ± 0.19), respectively. The results of loose bulk density and tapped bulk density ranged from (0.470 ± 0.29 to 0.532 ± 0.385) and (0.522 ± 0.27 to 0.675 ± 0.48), respectively. The results of angle of repose (<30) indicate good flow properties of granules. This was further supported by lower compressibility index values. The lowest compressibility index is 5-15 % which indicates excellent flow properties (Table 2). The physical properties of different batches of fast dissolving tablets are given in (Table 3). Tablet mean thickness was almost uniform in all the formulations. The thickness varies between 2.34 ± 0.29 to 2.83 ± 0.15 mm. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.392 ± 1.5 to 3.821 ± 1.4 kg/sq cm. Friability values below 1% were an indication of good mechanical resistance of the tablets. Formulations prepared by sublimation method were found to be more friable. All the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weight variation in all the six formulations was found to be 199.98 to 202.15 mg, which was in pharmacopoeial limits of ±7.5% of the average weight. The percentage drug content of all the tablets was found to be between 91.43 ± 0.54 to 99.18 ± 0.32 % of Meloxicam which was within the acceptable limits. The wetting time for all the six formulations was performed in triplicate. The values lie between 21 to 63 sec. In vitro dispersion is a special parameter in which the time taken by the tablet to produce complete dispersion is measured. The time for all the six formulations varied between 32 to 67 sec. Tablets were prepared with croscarmellose sodium F-1 to F-3 and with crospovidone F-4 to F-6. The wetting time, in vitro dispersion time of the tablets were also considerably reduced in tablets containing crospovidone which may be attributed due to the wicking type of disintegrants (crospovidone) formed thus facilitating the disintegrants to bring about faster disintegration. The results of water absorption ratio (%) and in vitro disintegrating time (sec) ranged from (71 to 132) and (18 to 86), respectively.

The *in vitro* dissolution profile indicated faster and maximum drug release from formulation F6. Stability studies shown that there was no significant change when compared with zero day of formulation (F-6). The disintegration time of crospovidone tablets are comparatively lower than the sodium starch glycolate. The faster disintegration of crospovidone tablets may be attributed to its rapid capillary activity and pronounced hydration with little tendency to gel formation. Thus, these results suggest that the disintegration time can be decreased by using wicking type of disintegrants (crospovidone).

CONCLUSION

The oral disintegrating tablets of Meloxicam with sufficient mechanical strength, acceptable taste and smaller disintegration time were achieved employing suitable superdisintegrants and other excipients at optimum concentration. Stability studies revealed that there was no significant change in drug content and dissolution profile of oral disintegrating tablets. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between Meloxicam and other ingredients used. Among two

Table 3: Thickness, hardness, friability, drug content, weight variation, wetting time, water absorption ratio, *in vitro* dispersion time, in vitro disintegration time of Meloxicam fast disintegrating tablets

Parameters	Formulation code					
	F-1	F-2	F-3	F-4	F-5	F-6
Thickness (mm)	2.45 ± 0.04	2.83 ± 0.15	2.52 ± 0.27	2.79 ± 0.16	2.59 ± 0.12	2.34 ± 0.29
Hardness (kg/cm^2)	3.752 ± 1.2	3.461 ± 1.8	3.392 ± 1.5	3.541 ± 2.6	3.821 ± 1.4	3.674 ± 1.2
Friability (%)	0.341	0.528	0.476	0.421	0.571	0.526
Drug content (%)	99.5 ± 0.12	98.1 ± 0.17	97.9 ± 0.23	98.6 ± 0.53	97.8 ± 0.31	99.1 ± 0.38
Weight variation (mg)	202.15	200.18	201.86	199.98	200.29	200.45
Wetting time (sec)	63	52	35	56	44	21
Water absorption ratio	71	82	94	116	125	132
In vitro dispersion time (sec)*	67	54	41	47	39	32
In Vitro disintegrating time (sec)	86	79	58	41	25	18

superdisintegrants used cross povidone showed better performance in disintegration time when compared to croscaremellose sodium. In the *in vitro* dissolution comparison study between F6 and marketed product (Muvera) the formulation F6 shows 38.123% release of drug with in two minutes and marketed product showed 18% release with in the same time. F6 shows 99.189% with in 50 minutes and marketed product shows only 92.456% in 50 minutes. So the formulation of F6 was found to be best among all other formulations, because it has exhibited faster wetting time, good taste and faster disintegration time when compared to all other formulations.

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REFERENCES

1. Birudaraj R, Berner B, Shen S, Li X, Buccal permeation of buspirone: mechanistic studies on transport pathways. J Pharm Sci Issue 94, 2005, 70-78.
2. Rajitha K, Shravan Y K, Adukondalu D, Ramesh G, Rao Y M, Formulaton and evauation of orally disintegrating tablets of buspirone. Int J Pharmaceutical Sciences and Nanotechnology Volume 4, Issue 1, 2009, 327-334.
3. Chang R K, Guo X, Burnside B A, Couch R.A, Fast dissolving tablets. Pharm. Tech. Volume 6, Issue 24, 2000, 52-58.
4. Yeola B S, Pisal S S, Paradkar A R, Mahadik K R, New drug delivery systems.Indian Drugs Volume 7, Issue 37, 2000, 312-318.
5. Sastr Y S V, Nyshadham J R, Fix J A, Recent technological advances in oral drug delivery –A Review. Pharm. Sci. Tech. Today Volume 4, Issue 3, 2000, 138-145.
6. Ito A, Sugihara M, Development of oral dosage forms for elderly patients: Use of ager as base of rapidly disintegrating oral tablets. Chem. Pharm. Bull. Volume 11, Issue 44, 1996, 2132-36.
7. Dobetti L, Fast-Melting Tablets: Developments and Technologies. Pharm. Tech. 2001; 44-50.
8. Corveleyn S, Remon J P, Formulation and production of rapidly disintegrating tablets by lyophilization using hydrochlorothiazide as a model drug. Int J Pharm, Issue 152, 1997, 215-225.
9. Remon J P, Corveleyn S, Freeze-dried rapidly disintegrating tablets. US patent 6 010 719, 2000.
10. Heinemann H, Rothe W, Preparation of porous tablets. US patent 3 885 026, 1975.
11. Knistch A, Hagen E, Munz H D, Production of porous tablets. US patent 4 134 843, 1979.
12. Cooper. J, Gunn G. 1986. Powder flow and compaction, In; Tutorial pharmacy, CBS Publisers and distributers, New Dehli, 211-233.
13. Shah D, Shah Y, Rampadhan M, Development and evaluation of controlled release diltiazem hydrochloride microparticles using cross-linked polymer (vinayl alcohol). Drug Dev Ind Pharm, Volume 6, Issue 23, 1997, 567-574.
14. Aulton. M.E, Well. T.I. 1998. Pharmaceutics: The Sciences of Dosage form Design, Churchill Livingstone, London, England.
15. Chang. R, Robinson. J.R. 1990. Sustained release from tablets and particles through coatin, In : Libreman HA, Lachman L and Schwartz JB (Eds), Phamaceuticls Dosage form Tablets, Vol. 3, Marceel Dekker, 199-302.
16. Marshall. K, Lachman. N, Liberman. H.A. 1987. The theory and practice of industrial pharmacy, Varghese Publishing House, Mumbai, 66-69.
17. Yunxia B, Yorinobu Y, Kazumi D, Akinobu O, Preparation and evaluation of oral tablet rapidly dissolving in oral cavity. Chem. Pharm. Bull. Volume 11, Issue 44, 1996, 2121-2127.
18. Kimura S, Imai T, Otagiri M, Pharmaceutical evaluation of Ibuprofen syrup containing low molecular weight gelatine. J. Pharm. Sci. Issue 81, 1992, 141-144.
19. Swamy P V, Shahidulla S M, Shirsand S B, Hiremath S N, Ali Y, Orodispersible tablets of carbamazepine prepared by direct compression method using 3^2 full factorial design. Dhaka Univ. J. Pharm. Sci. Volume 1, Issue 7, 2008, 1-5.