Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 2, 2015

Original Article

EFFECT OF ADDITIVES ON *IN-VITRO* RELEASE OF ORODISPERSIBLE DOSAGE FORM

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Received: 22 Nov 2014 Revised and Accepted: 15 Dec 2014

ABSTRACT

Objective: The aim of this investigation was to prepare orodispersible tablets of meloxicam using various concentrations of superdisintegrants like Ac-DI-Sol, crospovidone, sodium starch glycolate by the direct compression method.

Methods: Nine formulae of Meloxicam orodispersible tablets were prepared. These tablets were evaluated for their drug content, weight variation, friability, hardness, wetting time, *In-vitro* disintegration time and drug release.

Results: All the formulation exhibited hardness between 4.21–4.55 kg/cm^2. The tablets were disintegrating within 8.3 to 21.9 sec. Dissolution studies revealed that formula containing 7.5 % sodium starch glycolate showed 100% of drug release, at the end of six minutes. Among the formulated tablets, formula F9 containing 7.5 % sodium starch glycolate showed superior organoleptic properties along with excellent *In-vitro* disintegration time and drug release as compared to other formulae. The concentration of superdisintegrants had an effect on disintegration time and *In-vitro* drug dissolution whereas hardness and friability of resulting tablets were found to be independent of disintegrant concentration. It was concluded that the superdisintegrants addition technique is a useful method for preparing orodispersible tablets by the direct compression method.

Keywords: Meloxicam, Orodispersible tablets, Ac-Di-Sol, Crospovidone, Sodium starch glycolate, Superdisintegrant, Direct Compression, *In-vitro*.

INTRODUCTION

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance [1]. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage form for some patients, is the difficulty to swallow [2].

A constant focus on Novel Drug Delivery systems that offer greater patient compliance, effective dosages and minimal chances of side effects has led to the development of orodispersible tablets [3]. Mouth dissolving tablets are gaining more demand and popularity from the last few years because Pharmaceutical industry has become increasingly aware of the need that the elderly be considered as a separate and unique Medicare population. Though geriatric patients constitute a minor proportion of the population, its growth rate is high and hence will have significant impact on the development of drug delivery system [4]. Orodispersible tablets (ODTs) are not only indicated for people who have swallowing difficulties, but also are ideal for active people [5].

Orodispersible tablets are also called as mouth dissolving tablets, melt-in the mouth tablets, fast dissolving tablets, rapimelts, porous tablets, quick dissolving etc. Orodispersible tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva [6]. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach [7].

The advantage of mouth dissolving dosage forms is increasingly being recognized in both, industry and academics [8]. Their growing importance was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet, " as a tablet that to be placed in the mouth where it disperses rapidly before swallowing [9].

According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in the development of MDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrollidone (polyplasdone) etc., which provide instantaneous disintegration of the tablet after putting on the tongue, their by release the drug in saliva [10]. 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 subject to first pass metabolism is reduced as compared to standard tablet [11].

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 [12]. Meloxicam inhibits cyclooxygenase (COX) synthesis. This enzyme is responsible for converting arachidonic acid into prostaglandin H_2. 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 [13]. A primary advantage of the oxicam family of drugs is their long half-life which permits once-day dosing [14]. In gastric disease, lower dose of meloxicam is required 7.5 mg/day. Meloxicam is safer than other NSAID's [15]. Hence, in the present study an attempt was made for preparation of fast disintegrating tablets of meloxicam with the aim of providing faster onset of action.

MATERIALS AND METHODS

Meloxicam was received as a gift sample from Medical Union Pharmaceuticals (MUP). Ac-Di-Sol, Crospovidone and Sodium starch glycolate were obtained as gift samples from Egyptian International Pharmaceutical Industries Company (EIPICO). Aspartame and Microcrystalline cellulose kindly donated by Amoun pharmaceutical Company. Mannitol, Magnesium stearate and Talc were of analytical grade and were used as received. Methanol, PureLab, Madison, (USA). Sodium hydroxide, OxfordLab, Mumbai, (India). Sodium dihydrogen phosphate, PureLab, Madison, (USA).

Methodology

Selection of tableting method

For selecting the tableting method, compressible characteristics of the drug are to be considered. For drugs, which are poorly compressible and have moderate to high dose the most obvious and

direct attack would be to follow wet granulation method. For drugs with low to moderate doses, direct compression technique offers various advantages to the pharmaceutical formulation in terms of: - Economy, because the less number of processing steps, persons and time is required; - Stability, because a product is not required to expose to a moisture and heat; - Performance, since tablets will directly disintegrate gives higher dissolution. In the present work, the direct compression technique was used to prepare Orodispersible Meloxicam tablets.

Choice of tablet excipients

Excipients are critical to the design of any drug delivery system and play a major role in determining its quality and performance. The following excipients were selected for the formulation of Orodispersible meloxicam tablets. Diluents: a combination of Mannitol and microcrystalline cellulose (Avicel PH102); Disintegrants: Ac-Di-Sol (croscarmellose sodium), polyplasdone-XL (crospovidone), Primogel (sodium starch glycolate); Binders: microcrystalline cellulose (Avicel PH 102); Sweetener: Aspartame; Lubricants/Glidants: magnesium stearate and talc.

Micromeritic properties of mixed blend of meloxicam and excipients

All the elements were passed through sieve number 60. Required quantity of each ingredient was taken for each specified formulation and all the ingredients were co-ground in a mortar and pestle. The powder blend was evaluated for the following flow tests:

Angle of repose

Angle of repose was determined using the funnel method. The blend was poured through a funnel that can be raised vertically at a fixed height (h) in all experiments. The radius of the heap (r) was measured and the angle of repose (θ) was calculated using the following equation**:**

Angle of repose, Tan (θ) = h / r; Where θ = Angle of repose, h = Height of the heap, are = Radius of pile [16].

Bulk and tapped densities

Apparent bulk density (D_b) was determined by pouring the blend into a graduated cylinder. The bulk volume (V_b) and weight of the powder (M) was determined [17].

$D_b = M / V_b$; where M = Weight of powder, V_b = Bulk volume

The measuring cylinder containing a known mass of the blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured to calculate the apparent tapped density [17].

$D_t = M / V_t$; where M = Weight of powder, V_t = Volume after tapping (tapped volume)

Carr's index (compressibility %)

The simplest way of measurement of free flow of powder is compressibility. This percent is indirectly related to the relative flow rate, cohesiveness, and particle size of a powder. The compressibility percent of a material can be estimated as [18].

$$\text{Compressibility \%} = [(D_t - D_b) / D_t] \times 100$$

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow [19]. It is the ratio between bulk density and tapped density

Hausner ratio = D_t / D_b; where D_t = Tapped density, D_b= Bulk density

Preparation of orodispersible tablets

Meloxicam orodispersible tablets were prepared by direct compression method according to the formulae given in the table (1). A total number of nine formulations were prepared. All the ingredients were passed through 60-mesh sieve separately and collected. The drug and microcrystalline cellulose were mixed in a small portion of both at each time and blended to get a uniform mixture and kept aside. Then the remaining ingredients were weighed and mixed in geometrical order and the tablets were compressed using flat face 8 mm size punch to get a tablet of 200 mg weight using 10 stations rotary tabletting compression machine.

Evaluation of the formulated meloxicam ODTs

Weight variation

Twenty tablets from each formulation were selected randomly and average weight was determined. Then individual tablets were weighed and was compared with average weight [20].

Thickness and diameter

The thickness and diameter of the tablets were measured using vernier caliber. It is expressed in mm [20].

Hardness

Hardness or tablet crushing strength (Fc), the force required to break a tablet in a diametric compression, was measured using Campbell tablet hardness tester[21]. It is expressed in kg/cm^2.

Friability test

Friability of tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches at each revolution. Preweighed sample of tablets was placed in a friabilator and the tablets were subjected to 100 revolutions. Tablets were then dusted using a soft muslin cloth and reweighed[22].

The friability (F) is given by the following formula:

F = Winitial - Wfinal / Winitial x 100

***In vitro* disintegration time**

Tablets were added to 10 ml of phosphate buffer solution of pH 7.4 at 37 ± 0.5˚C. The time required for the disintegration of the tablets was noted[23].

Wetting time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers were placed in a Petri dish which covered the entire surface area of the Petri dish. Phosphate buffer solution pH 7.4 (10 ml) at 37 ± 0.5˚C was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time[24].

Water absorption ratio

The weight of the tablet prior to placement in the Petri dish was noted (wb). The wetted tablet was removed and reweighed (wa). The water absorption ratio was then determined according to the following equation [25].

$R = 100 \times (w_a - w_b) / w_b$, Where w_b and w_a were tablet weights before and after water absorption, respectively.

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 30 mg of Meloxicam was transferred to a clean, dry, calibrated 100 ml volumetric flask, dissolved in 10 ml of 1M NaOH and 40 ml methanol and mix well for 5 minutes. Further 40 ml methanol was added and mixed for 3 hours using a magnetic stirrer. The flask was cooled and sufficient methanol was added to produce 100 ml and filter to produce stock solution (300 mcg/ml). Five mls of the stock solution was transferred to clean, dry, calibrated 100 ml volumetric flask and the volume was made up with methanol. The concentration of this solution was (15 mcg/ml). This solution was analyzed for drug content at 364 nm using UV-Visible spectrophotometer[26].

***In-vitro* dissolution study**

In-vitro drug release studies of all the formulations were carried out using USP dissolution test apparatus Type 2 (paddle) at 50 rpm.

Phosphate buffer pH 7.4 was used as the dissolution medium with temperature maintained at 37±0.5ºC. Five ml aliquot was withdrawn at the specified time interval, filtered through whatmann filter paper, and assayed spectrophotometrically at 362 NM using UV-Visible spectrophotometer. An equal volume of fresh medium, which was pre warmed at 37°C was replaced in the dissolution medium after each sampling to maintain the constant volume throughout the test. The study was performed in triplicate[27].

RESULTS AND DISCUSSION

Selection of tableting method

In the present study, the direct compression technique was employed to prepare Orodispersible tablets of Meloxicam. Direct compression technique offers various advantages to the pharmaceutical formulation in terms of the economy, because the less number of processing steps, persons and time are required; stability, because a product is not required to expose to a moisture and heat; performance, since tablets will directly disintegrate gives higher dissolution.

Selection of tablet excipients

Excipients are critical to the design of any drug delivery system and play a major role in determining its quality and performance. The following excipients were selected for the formulation of Orodispersible tablets of Meloxicam.

Diluents

Tablet prepared using the insoluble nature of crystalline cellulose were found to have a gritty mouth feel. To overcome this problem we attempted the use of water-soluble diluents Mannitol. But the tablet prepared with Mannitol took long time to disintegrate probably for the fact that tablets prepared with Mannitol often tends to dissolve rather than disintegrate[28]. Thus, novel diluents, a combination of Mannitol and microcrystalline cellulose (Avicel PH 102) were employed in this study.

Disintegrants

Short disintegration time with good dispersibility is the most important characteristics of an orally disintegrating or mouth dissolving tablets. The necessity of an orally disintegrating tablet is to disintegrate within seconds, in a limited amount of the water available in the form of saliva. This demands the use of special type of disintegrants called as “Superdisintegrants” [29]. In the present study, Ac-Di-Sol (croscarmellose sodium), polyplasdone-XL (crospovidone), Primogel (sodium starch glycolate) were used as superdisintegrants.

Binders

In the present study the microcrystalline cellulose (Avicel PH 102) is as effective as a binder in direct compression.

Sweetener

Aspartame is used as an intense sweetening agent in pharmaceutical preparation, including tablets, powder mixers and vitamin preparation. Its appropriate sweetening power is 180-200 times that of sucrose. It does not posses bitter after taste.

Lubricants/Glidants

Lubricants are intended to reduce the friction during compression, and ejection of tablets. In the present study, magnesium stearate and talc were used.

Micromeritic properties of mixed blend of Meloxicam and excipients

Direct method for calculating the flowability

Angle of repose (θ)

The angle of repose has been used in several branches of sciences to characterize the flow properties of solids. Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles. Angle of repose results is reported to be very dependent upon the method used. Experimental difficulties arise as a result of segregation of material and consolidation or aeration of a powder as the cone is formed. Despite its difficulties, the method continues to be used in the pharmaceutical industry, and a number of examples demonstrating its value in predicting manufacture problems appear in the literature.

The angle of repose is the constant, three dimensional angle (relative to the horizontal base) assumed by a cone-like pile of material formed by any of several different methods [30].

The two most important attributes for the direct compression formula are good flow and good compressibility. The values obtained for bulk density and tapped density does not affect the compression of tablets. The angle of repose gives important information about the flow characteristics of the powder mixture. The powder flow depends on three general areas: the physical properties of the particle (e. g., shape, size, compressibility), the bulk powder properties (e. g., size distribution, compaction); and the processing environment (e. g., storage, humidity) [31].

The angle of repose was found to affect the flowability of the particles or granules. The values less than 20° exhibit excellent flowability; the values between 20 and 30° show good flowability; the values between 30 and 34° exhibit passable flowability; while the values above 34° show very poor flowability [32]. USP specificationsfor the values of the angle of repose were different from the previous publication and these values are: 25-30°indicates excellent flow, 31-35° indicates a good flow, 36-40° the flowability of a powder is fair, 41-45° passable flowability, 46-55° poor, and > 55° indicates very poor flow properties for a powder.

The values obtained for the angle of repose of the Meloxicam powder blend ranged from 31.96° to 38.75°, as shown in table (2). These values indicate that all formulae have good to fair flowability. Good flowability was shown in four formulae, while five formulae had a fair flowability. Thus, it is concluded that the blend of powder was free flowing and can be used for direct compression.

The rank order for the calculated values of the Angel of repose was arranged in descending order as follows: F9 (7.5 % sodium starch glycolate), F8 (5 % sodium starch glycolate), F4 (2.5 % crospovidone), F1 (2.5 % croscarmellose sodium), F2 (5 % croscarmellose sodium), F7 (2.5 % sodium starch glycolate), F5 (5 % crospovidone), F6 (7.5 % crospovidone, F3 (7.5 % croscarmellose sodium).

Indirect methods for calculating the flowability

a- The bulk and tapped densities

The flow properties of the prepared Meloxicam powder blend were investigated by measuring both the bulk density and the tapped density. From theses values both the Hausner ratio and the Carr’s index can be derived [33]. Both the bulk and tapped densities were determined by equations described before, as illustrated in table (2). These two parameters are related to the flow properties of the prepared powder blend formulae. The values obtained for the bulk densities of the prepared Meloxicam powder blend ranged from 0.417 (F4 and F7) to 0.500 (F3). While the values obtained for the tapped densities of the prepared Meloxicam powder blend ranged from 0.556 (F9) to 0.625 (F3).

b- The Hausner ratio

The Hausner ratio is a value that is correlated to the flowability of a powder or granular material. The Hausner ratio is measured from the bulk and tapped densities. The accepted scale of flowability of a powder was described in USP 30 (2007). The value of the Hausner ratio was found to give an indication about the flow properties of solid dispersion. The values less than 1.25 indicate better flowability than values more than 1.25[32].

The values obtained for the Hauser ratio of the prepared Meloxicam powder blend ranged from 1.178 (F9) to 1.364 (F4), as shown in table (3). So, the obtained results showed that five formulae have good flowability while the other four formulae showed passable flowability.

The rank order for the calculated values of Hausner ratio was arranged in descending order as follows: F9 (7.5 % sodium starch glycolate), F2 (5 % croscarmellose sodium), F1 (2.5 % croscarmellose sodium), F8 (5 % sodium starch glycolate), F3 (7.5 % croscarmellose sodium), F5 (5 % crospovidone), F6 (7.5 % crospovidone), F7 (2.5 % sodium starch glycolate), F4 (2.5 % crospovidone).

c- Compressibility % (Carr's index)

Compressibility percent is indirectly related to the relative flow rate, a compressible material will be less flowable. The value of the compressibility percent was found to affect the flow properties of solid materials. The values between 5 and 12 show excellent flowability; the values between 12 and 16 exhibit good flowability; the values between 18 and 21 show fair passable flowability; the values between 23 and 35 exhibit poor flowability; while the values between 33 and 38 exhibit very poor flowability [32].

The values obtained for compressibility percent of the prepared Meloxicam powder blend ranged from 15.094 (F9) to 26.667 (F4), as shown in table (3).

The rank order for the calculated values of compressibility percent was arranged in descending order as follows: F9 (7.5 % sodium starch glycolate), F2 (5 % croscarmellose sodium), F1 (2.5 % croscarmellose sodium), F8 (5 % sodium starch glycolate), F3 (7.5 % croscarmellose sodium), F5 (5 % crospovidone), F6 (7.5 % crospovidone), F7 (2.5 % sodium starch glycolate), F4 (2.5 % crospovidone). It was concluded that the good flowability was seen in formulae containing sodium starch glycolate followed by croscarmellose sodium and crospovidone. It was also noticed that as the concentration of sodium starch glycolate increased from 2.5% to 7.5%, the flow properties of the powder blend increased. So, the formula (F9) containing 7.5% sodium starch glycolate showed superior flow properties as compared to other formulae.

Table 1: The suggested formulae of Meloxicam Orodispersible Tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Meloxicam	15	15	15	15	15	15	15	15	15
Croscarmellose sodium	5	10	15	-	-	-	-	-	-
Crospovidone	-	-	-	5	10	15	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	5	10	15
Avicel ph 102	25	25	25	25	25	25	25	25	25
Aspartame	2	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4	4
Magnesium stearate	2	2	2	2	2	2	2	2	2
Mannitol	147	142	137	147	142	137	147	142	137
Total	200	200	200	200	200	200	200	200	200

Table 2: The data collected for the angle of repose, the bulk densities and the tapped densities of the Meloxicam powder blend

Formulation Code	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)
F1	35.18˚±0.25	0.476±0.005	0.581±0.002
F2	36.52˚±0.37	0.472±0.004	0.575±0.008
F3	38.75˚±0.59	0.500±0.005	0.625±0.004
F4	34.51˚±0.28	0.417±0.008	0.568±0.002
F5	37.42˚±0.61	0.435±0.007	0.562±0.005
F6	38.21˚±0.84	0.455±0.009	0.602±0.011
F7	37.19˚±0.33	0.417±0.003	0.562±0.007
F8	34.12˚±0.27	0.463±0.004	0.575±0.005
F9	31.96˚±0.19	0.472±0.003	0.556±0.002

Table 3: Hausner ratio and Carr's index of Meloxicam powder blend

Formulation Code	Hausner ratio	Carr's index
F1	1.221	18.095
F2	1.218	17.925
F3	1.250	20.000
F4	1.364	26.667
F5	1.292	22.609
F6	1.325	24.545
F7	1.348	25.833
F8	1.241	19.444
F9	1.178	15.094

Evaluation of meloxicam orodispersible tablets

In the present investigation, Meloxicam orodispersible tablets were prepared in nine formulations with varying concentration of three superdisintegrants: Croscarmellose Sodium (Ac-Di-Sol), Crospovidone (Polyplasdone XL),) and Sodium starch glycolate (Primojel). Each was used in three different concentrations (2.5%, 5% and 7.5%). All batches of the tablets were evaluated for various post compression parameters such as weight variation, thickness, diameter, hardness, friability, *In-vitro* disintegration time, amount of drug content, wetting time, and water absorption ratio. Post compression parameters of all formulations are reported in table (4-6).

The weights of the tablets were between 199.6 to 202.1 mg. The calculated weight variation was found to be in acceptable weight variation range stated in the pharmacopeias (±7.5%). The USP pharmacopeia specified that the tablets < 80 mg, the deviation will be ± 10%; tablets between 80 – 250 mg, the deviation will be ± 7.5%; while tablets > 250 mg, the deviation will be ± 5%. All Meloxicam ODTs formulations passed the weight variation test. Thickness of all the formulations was between 3.808 to 3.877 mm showings a fairly uniform tableting. The diameter of all formulations was between 8.071 to 8.08 mm.

The hardness of all formulations was measured in kg/cm^2. Hardness of all formulations was in the range of 4.21 to 4.55 kg/cm^2. The loss

in total weight of the tablets due to friability was in the range of 0.3718 to 0.7894%. As shown in table (4-6), the friability values of none of the formulations exceeded 0.88%. The results of friability indicate that Meloxicam tablets were mechanically stable and could handle the rigors of transportation and handling.

The results of *In vitro* disintegration were within the prescribed limit and comply with the criteria for orally disintegrating tablets. The values were in the range of 8.3 - 21.9 sec. The rapid disintegration was seen in the formulation containing sodium starch glycolate followed by crospovidone and then Crosscarmellose sodium. It was also noticed that as the disintegrant concentration increased from 2.5 to 7.5%, the time taken for disintegration was reduced. Formulations containing crospovidone as superdisintegrant in which the disintegration time was reduced upon increasing the concentration up to 5% only and further increase in crospovidone concentration will increase the disintegration time was exception from the above rule. Effect of superdisintegrant concentration at a disintegration time is shown in fig. (1).

Wetting time is used as an indicator of the ease of tablet disintegration and corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue. The values lie between 27 to 58.6 sec. Water absorption ratio ranged from 55.16 to 153.46%.

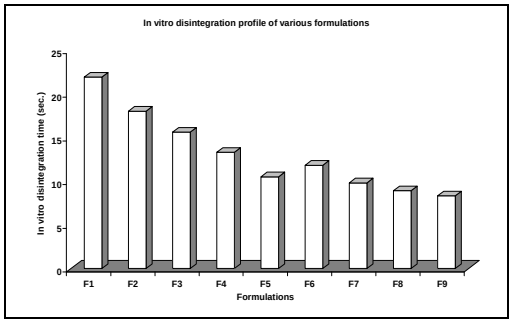

Fig. 1: Effect of superdisintegrants on disintegration time of Meloxicam orodispersible tablets

Percentage drug content of all Meloxicam formulations was found to be between 98.04 to 99.59%. These values were within the acceptable limits stated in the pharmacopeias.

Table 4: Quality control tests of formulae containing Crosscarmellose sodium as superdisintegrant

	F1	F2	F3
1-Weight Variation (mg)	199.565±2.161	200.92±1.866	201.09±1.660
2-Thickness (mm)	3.838±0.0123	3.816±0.0107	3.83±0.0125
3-Diameter (mm)	8.073±0.0067	8.079±0.0057	8.079±0.0057
4-Hardness (kg/cm2)	4.25±0.19	4.51±0.20	4.40±0.19
5-Friability (%)	0.7894	0.4113	0.5071
6-Disintegration Time (sec.)	21.90±0.88	18.00±0.94	15.60±0.70
7-Wetting Time (sec.)	36.40±0.8944	32.80±0.8367	27.00±0.7071
8-Water Absorption Ratio (%)	60.80±0.53	78.12±3.12	90.03±1.16
9-Drug Content (%)	98.04±0.8864	99.02±0.5781	99.42±0.6650

Table 5: Quality control tests of formulae containing Crospovidone as superdisintegrant

	F4	F5	F6
1-Weight Variation (mg)	200.765±1.763	200.115±1.854	200.375±1.759
2-Thickness (mm)	3.877±0.0067	3.85±0.0094	3.85±0.0094
3-Diameter (mm)	8.08±0.0047	8.075±0.0053	8.076±0.005
4-Hardness (kg/cm2)	4.37±0.18	4.21±0.10	4.55±0.24
5-Friability (%)	0.5258	0.4087	0.3737
6-Disintegration Time (sec.)	13.30±0.82	10.50±0.71	11.80±0.79
7-Wetting Time (sec.)	45.40±0.5477	34.60±0.5477	43.00±2.00
8-Water Absorption Ratio (%)	55.16±2.74	64.82±0.91	78.30±3.14
9-Drug Content (%)	98.87±0.4884	99.59±0.4669	98.72±1.0706

Table 6: Quality control tests of formulae containing sodium starch glycolate as superdisintegrant

	F7	F8	F9
1-Weight Variation (mg)	202.065±1.969	200.88±1.607	201.815±2.488
2-Thickness (mm)	3.842±0.0114	3.808±0.0063	3.815±0.0135
3-Diameter (mm)	8.071±0.0074	8.071±0.0074	8.076±0.0097
4-Hardness (kg/cm2)	4.55±0.21	4.48±0.22	4.34±0.24
5-Friability (%)	0.6768	0.4132	0.3718
6-Disintegration Time (sec.)	9.80±0.63	8.90±0.74	8.30±0.82
7-Wetting Time (sec.)	34.00±0.7071	42.60±1.8166	58.60±1.1402
8-Water Absorption Ratio (%)	88.80±3.23	130.98±7.39	153.46±2.42
9-Drug Content (%)	99.10±0.2335	98.99±0.8866	98.88±0.9430

In-vitro dissolution studies

All the nine formulations of Meloxicam ODTs were subjected to *In-vitro* dissolution studies by using phosphate buffer pH 7.4 as dissolution medium. *In-vitro* release studies of all nine formulations were plotted and shown in the fig. (2).

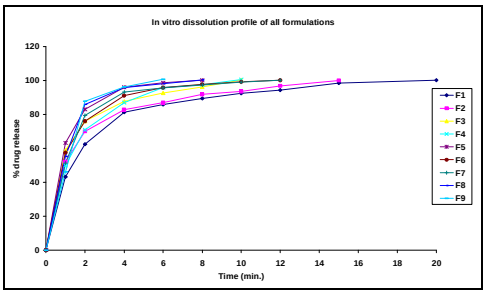

Fig. 2: *In vitro* dissolution profile of the prepared Meloxicam formulations

Meloxicam formulae (F1, F4 and F7) which contain 2.5% superdisintegrant concentration release 85.75%, 95.88% and 95.57%, respectively, at the end of six minutes. An increase in drug release was observed when 5% superdisintegrant concentration was used in Meloxicam formulae (F2, F5 and F8). The drug release was found to be 86.99 %, 98.66% and 98.18%, respectively, at the end of six minutes. Upon further increasing the superdisintegrants concentration up to 7.5% in Meloxicam formulae (F3, F6 and F9), it was found that the drug release becomes 92.65%, 95.75% and 100%, respectively, at the end of six minutes.

It was noticed that as the disintegrant concentration increased from 2.5 to 7.5%, the drug is released rapidly from the formulae. Formulations containing crospovidone as superdisintegrant in which the drug release was increased upon increasing the concentration up to 5% only and further increase in crospovidone concentration will decrease the release was exception from the above rule.

The rapid drug release was observed in the formulation containing sodium starch glycolate followed by crospovidone and then croscarmellose sodium. Among all the formulated tablets, F9 which contains 7.5% sodium starch glycolate as superdisintegrant gave the highest dissolution (100%) at the end of six minutes. The rapid drug dissolution might be due to easy breakdown of particles and rapid absorption of drug into the dissolution medium. In all nine formulations the dug release was almost up to 90 – 100 %, after ten minutes.

From the total rank order shown in table (7), formula F9 which contain 7.5 % sodium starch glycolate was found to be the best formula from the tested Meloxicam ODTs. This formula acquires the best Micromeritic properties, the higher values for Meloxicam quality control tests and the best *In-vitro* drug release.

Table 7: Rank order of different formulae depending on Micromeritic properties, quality control tests and *In vitro* release study

Formula Number	F1	F2	F3	F4	F5	F6	F7	F8	F9
Micromeritic properties	3	2	5	7	5	8	8	3	1
Quality control tests	9	6	2	8	2	7	5	4	1
In vitro drug release	9	8	7	6	2	5	4	2	1
Total	21	16	14	21	9	20	17	9	3
Final Rank Order	8	5	4	8	2	7	6	2	1

CONCLUSION

Orodispersible tablets of Meloxicam were prepared by direct compression method using Croscarmellose Sodium (Ac-Di-Sol), Crospovidone (Polyplasdone XL),) and Sodium starch glycolate (Primojel) as superdisintegrant. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. *In vitro* drug release from the tablets shows significantly improved drug dissolution. Hence it could be concluded that the superdisintegrant based orodispersible tablets of Meloxicam would be quite effective, providing quick onset of action without need for water for swallowing or administration.

ACKNOWLEDGEMENT

The authors are very much thankful to MUP, EIPICO and Amoun pharmaceutical companies for providing gift samples of Meloxicam and other excipients that facilitate to carry out this work.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Chein yw. Oral drug delivery and delivery system, 2nd, New York: Marcel Dekker; 1992:587-682.
2. Indurwade NH, Rajyaguru TH, Nakhat PD. Novel approach–fast dissolving tablets. Indian Drugs 2002;39(8):405-9.
3. Radke RS, Jadhav JK, Chajeed MR. Formulation and evaluation of orodispersible tablets of baclofen. Int J Chem Tech Res 2009;1(3):517-21.
4. Deshpande Kiran Bhaskar, More MR, GN Sockan, Kunchu K, Tamiz Mani. Formulation and evaluation of orodispersible tablets of propranolol hydrochloride. Int J Pharm Res Dev 2011;2(12):214-9.
5. Shastry CS, Srinath MS. pharmaceutical approaches of taste masking oral dosage forms. Ind Drug 2004;41(5):253-7.
6. Bhushan SY, Sambhaji SP, Anant RP, Mahadik KR. New drug delivery system for elderly. Indian Drugs 2003;37(7):312-8.
7. Seager H. Drug delivery product and zydis fast dissolving dosage form. J Pharm Pharmcol 1998;50:375-82.
8. Mishra B, Panigrahi D. Mouth dissolving tablets: an overview of preparation techniques, evaluation and patented technologies. J Pham Res 2005;4(3):33-6.
9. Dandagi PM, Sreenivas SA, Mastiholimath VS. Orodispersible tablets: new-fangled drug delivery system-a review. Ind J Pharm Edu Res 2005;39(4):177-81.
10. Allen LV, Wang B. Method of making a rapidly dissolving tablet US Patent; 1997.
11. Kaushik D, Dureja H, Saini TR. Review article: mouth dissolving tablets. Ind Drugs 2004;41(4):187-93.
12. Corveleyn S, Remon JP. Formulation and production of rapidly disintegrating tablets by lyophilization using hydrochlorothiazide as a model drug. Int J Pharm 1997;152:215-25.
13. Remon JP, Corveleyn S. Freeze-dried rapidly disintegrating tablets US patent 6 010 719
14. Heinemann H, Rothe W. Preparation of porous tablets. 1975 US patent 3 885 026.
15. Knistch A, Hagen E, Munz H D. Production of porous tablets. 1979 US patent 4 134 843.
16. Shariff A, Monna PK, Paranjothy KLK, Manjula M. Entrapment of andrographolide in cross linked alginate pellets. Pak J Pharm Sci 2007;20:1-9.
17. Tayade PT, Kale RD. Encapsulation of water-insoluble drugs by a cross-linking technique: effect of process and formulation variables on encapsulation efficiency, particle size, and *In vitro* dissolution rate. Pharm Sci 2004;6:12-9.
18. Staniforth J. in "Powder Flow In Pharmaceutics", Aulton M. E., (ed.). 2nd ED., Churchill Livingstone, London; 2002. p. 207.
19. Kumar V, Medina MLR, Yang D. Preparation, Characterization, and tableting properties of a new cellulose-based pharmaceutical aid. Int J Pharm 2002;235(1-2):129-40.

20. Chaudhari PD, Chaudhari SP, Lanke SD. Formulation and *In vitro* evaluation of taste masked orodispersible dosage form of levocetirizine dihydrochloride. Indian J Pharm Educ Res 2007;41(4):319-28.
21. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: a novel drug delivery system. Indian Drugs 2004;41(10):592-8.
22. Marshall K, Lachman N, Liberman HA. The theory and practice of industrial pharmacy, 3rd Ed, Varghese Publishing House, Mumbai; 1987. p. 66-9.
23. Khan S, Kataria P, Nakhat P, Yeole P. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS Pharm Sci Tech 2007;8(2):1-7.
24. M Gohel, M Patel, A Amin, R Agrawal, R Dave, N Bariya. Formulation, Design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS Pharm Sci Tech 2004;5(3):10–5.
25. Singh J, Philip AK, Pathak K. Optimization studies on design and evaluation of orodispersible pediatric formulation of indomethacin. AAPS Pharm Sci Tech 2008;9(1):60-6.
26. British pharmacopoeia, BP. The British Pharmacopoeia, The Pharmaceutical Press, London, UK; 2009.
27. Jashanjit Singh, Rajmeet Singh. Optimization and formulation of orodispersible tablets of meloxicam. Trop J Pharm Res 2009;8(2):153-9.
28. Shah UA, Augsburger LG. Evaluation of the functional equivance of crospovidone NF from different sources: standard performance test. Pharm Dev Technol 2001;6:419-30.
29. Weller P. In; Handbook of Pharmaceutical Excipients; 4th Edn. Pharmaceutical Press. London; 2003.
30. The United States Pharmacopeia: USP 30/NF 25, the USP Convention, Rockville; 2007. p. 2960.
31. Bi X, Sunada H, Yonezawa Y, Danjo K. Evaluation of rapidly disintegrating tablets prepared by a direct compression method. Drug Dev Ind Pharm 1999;25(5):571-81.
32. Bhowmik D, Chiranjib B, Krishnakanth Pankaj R, Chandira M. Fast dissolving tablet. J Chem Pharm Res 2009;1(1):163-77.
33. Sahoo SK, Mallick AA, Barik BB, Senapati PC. Preparation and *In vitro* evaluation of ethylcellulose microspheres containing stavudine by the double emulsion method. Pharm 2007;62:117-21.