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Formulation and Evaluation of Mouth Dissolving Tablets of Meloxicam Using Co-processed Superdisintegrants

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ABSTRACT

In the present study, novel co-processed superdisintegrants were developed by solvent evaporation method using crospovidone and croscarmellose sodium in the different ratios (1:1, 1:2 & 1:3) to formulate mouth dissolving tablet formulations of Meloxicam. The poor aqueous solubility of Meloxicam makes its absorption as dissolution rate-limited and thus delay onset of action. Mouth dissolving tablets of Meloxicam were prepared using the above co-processed superdisintegrants and evaluated for different parameters. Effect of co-processed superdisintegrants (such as crospovidone and sodium starch glycolate) on wetting time, disintegrating time, drug content and *in-vitro* release parameters have been studied. Based on *in vitro* dispersion time (approximately 19 sec), promising formulation CP1 was tested for *in-vitro* drug release pattern. Among the designed formulations, the formulation (CP1) containing 4% w/w of co-processed superdisintegrant (1:1 mixture of crospovidone and sodium starch glycolate) found as the best formulation based on drug release characteristics. From this study, it can be concluded that dissolution rate of Meloxicam could be enhanced by tablets containing co-processed superdisintegrant.

Keywords: Meloxicam, mouth dissolving tablets, direct compression, co-processed superdisintegrants, croscarmellose sodium, crospovidone.

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INTRODUCTION

Meloxicam is a NSAID belonging to the class of Oxicams. Meloxicam is a COX-2 inhibitor preferred in the treatment of osteoarthritis and rheumatoid arthritis. Meloxicam has shown COX-2 inhibition especially at its low therapeutic dose[1-2]. The advantage of the drugs from oxicam family is their long half-life which permits once a day dosing[3]. Meloxicam is safer than other NSAIDs[4].

The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, versatility and most importantly patient compliance. The most popular dosage forms are tablets and capsules. Geriatric patients may have difficulty in swallowing and chewing the tablets resulting in patient non compliance and ineffective therapy. To overcome these problems mouth dissolving tablets are good option. Since, they disintegrate and dissolve rapidly in saliva without need for drinking water[5].

Difficulty in the swallowing of conventional tablets by geriatric and pediatric patients may lead to poor patient compliance and ineffective therapy. To overcome such problems, a new dosage form has been introduced, known as fast-dissolving tablets or mouth dissolving tablets. Mouth dissolving tablets, are relatively novel dosage form that involves the rapid disintegration or dissolution of the dosage form into a solution or suspension in the mouth without the need for the water[6-8].

Mouth dissolving tablets are gaining more demand and popularity from last few years because pharmaceutical industry has become increasingly aware of the need that 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 development of drug delivery system[9].

Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual[10]. Co-processing excipients lead to the formulation of excipients granules with superior properties, compared with physical mixtures of components or individual components, like improved flow properties, improved compressibility, better dilution potential, fill weight uniformity, and reduced lubricant sensitivity[11]. Several co-processed superdisintegrants are commercially available. Widely used superdisintegrants are crospovidone, croscarmellose sodium and sodium starch glycolate.

In the present investigation, the preparation and evaluation of mouth dissolving tablets of

Meloxicam by using co-processed superdisintegrants containing crospovidone and sodium starch glycolate was studied. The reasons for selection of crospovidone are high capillary activity, pronounced hydration capacity and little tendency to form gels[12]. Sodium starch glycolate was chosen because of its high swelling capacity[13].

In the present study, an attempt was made to develop mouth-dissolving tablets of Meloxicam.

MATERIALS AND METHODS

Meloxicam was kindly provided by Hetero drugs Ltd. (Hyderabad, India). Superdisintegrants crospovidone and Sodium Starch Glycolate were gifted from Red son Pharmaceuticals (Ahmedabad, India), Aspartame, Directly compressible mannitol and sodium stearyl fumerate were received from Aan Pharma Pvt Ltd. (Rakanpur-Gujarat) as gift samples. Microcrystalline cellulose and talc were obtained from S.D. Fine Chemicals Mumbai. All other materials were used of AR grade.

Preparation of Co-processed Superdisintegrants[14]:

The co-processed superdisintegrants were prepared by solvent evaporation method. A blend of crospovidone and sodium starch glycolate (in the ratio of 1:1, 1:2 and 1:3) was added to 10 ml of ethanol. The contents of the beaker (250 ml capacity) were mixed thoroughly and stirred till most of ethanol got evaporated. The wet coherent mass was granulated through # 44 mesh sieve. The wet granules were dried in a hot air oven at 60º C for 20 minutes. The dried granules were sifted through # 44 mesh sieve and stored in airtight container till further use.

Table 1: Composition of Meloxicam MDTs Prepared by Direct Compression Method

Ingredients (mg)	CP0	PM1	PM2	PM3	CP1	CP2	CP3
Meloxicam	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Superdisintegrants (Cp+SSG)	--	6	6	6	6	6	6
Sodium stearyl fumarate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mannitol	103.5	97.5	97.5	97.5	97.5	97.5	97.5
Aspartame	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3
Strawberry Flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline cellulose (Avicel PH-102)	30	30	30	30	30	30	30
Total Weight (mg)	150	150	150	150	150	150	150

CP0 -Control formulation (without superdisintegrants)

PM- Physical Mixture of crospovidone and sodium starch glycolate in ratios (1:1, 1:2, 1:3),

CP- Co-processed Superdisintegrants of Crospovidone and Sodium Starch Glycolate in ratios (1:1, 1:2, 1:3),

Cp – Crospovidone, **SSG** – Sodium Starch Glycolate.

Preparation of mouth dissolving tablets by direct compression method[15]:

Mouth dissolving tablets of Meloxicam were prepared by direct compression. All the ingredients (except granular directly compressible excipients) were passed through # 60-mesh separately. The ingredients were weighed and mixed in geometrical order and compressed into tablets of 150 mg by direct compression method using 8 mm round flat punches on a 'Rimek mini press machine. The weight of individual tablet was maintained 150 mg.

Identification of Drug by IR

The IR spectrum of the pure Meloxicam sample recorded by FTIR spectrum using FTIR 1615, Perkin Elmer, USA with KBr pellets is shown in **Figure. 1**.

Evaluation of mouth dissolving Meloxicam tablet[16]

[A] Organoleptic Properties:

Tablets from each formulation were randomly selected and organoleptic properties such as color; odor, taste and shape were evaluated.

[B] Tablet Dimensions:

Thickness and diameter were measured using a Vernier Calliper.

[C] Hardness:

The resistance of tablets to shipping or breakage, under the conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet was measured by Pfizer hardness tester. The hardness was measured in terms of kg/cm^2.

[D] Friability Test:

The friability of tablets was determined using Roche friabilator. 20 tablets were initially weighed and transferred into friabilator, operated at 25 rpm for 4 minutes. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

[E] Weight Variation Test:

Twenty tablets were selected at random and the average weight was determined. Not more than two of the individual weights deviate from the average weight by more than the percentage deviation shown in table and none deviates by more than twice the percentage.

[F] Disintegration time:

Disintegration time for MDTs was determined using USP disintegration apparatus with simulating salivary fluid *(*SSF) (pH 6.2, 900 ml at 37± 2°C*)* as the disintegrating medium. To comply the test all tablets should disintegrate within 3 minutes.

[G] Content uniformity:

One tablet was crushed and 30ml of distilled water was mixed and shaken for 15 minutes. Five

milliliters of the filtrate was diluted to 100 ml with distilled water, and assayed for drug content at 364 nm, using double beam UV/Vis spectrophotometer (Shimadzu, model-1601). The average drug content of the tablets was found to be 98.5%.

[H] *In-vitro* dissolution profile:

Dissolution studies were carried out by USP Type II (Paddle) apparatus at 37 ± 0.5°C, taking 900 ml of simulating salivary fluid *(*SSF) as dissolution medium. Speed of rotation of the paddle was set at 50 rpm. Samples were withdrawn at various time intervals, filtered through a 0.45 micron membrane filter, diluted and the absorbance was measured at 364 nm using Shimadzu UV-Spectrophotometer[17]**.** All the results were performed in triplicate.

[I]Wetting time:

It was measured by taking 5 circular tissue papers (10 cm diameter) to simulate the tongue conditions and were placed in a Petri dish with a 10 cm diameter. 10 ml of water containing amaranth was added to the Petri dish. The tablet was carefully placed on the surface of the tissue paper. The time required for water to reach the upper surface of the tablets was noted as wetting time.

RESULTS AND DISCUSSION:

The present investigation was undertaken to fabricate and evaluate mouth dissolving tablets of Meloxicam using co-processed Superdisintegrants. **Figure 1** shows the IR spectrum of the pure drug. Co-processed superdisintegrants were prepared by solvent evaporation method using crospovidone and sodium starch glycolate in different ratios (1:1, 1:2 and 1:3).

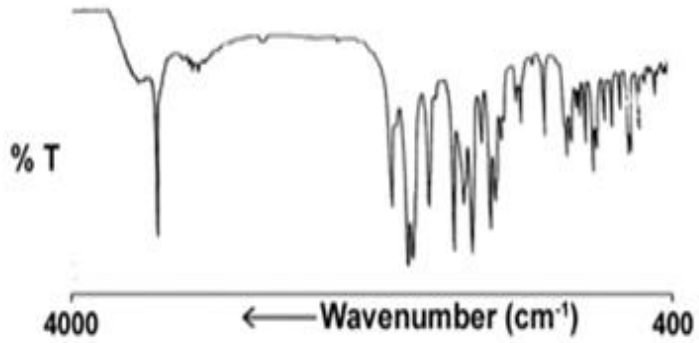

Figure 1 IR Spectra of pure Meloxicam

Mouth dissolving tablets of Meloxicam were prepared using above co-processed superdisintegrants and physical mixtures of superdisintegrants. Directly compressible mannitol was used as a diluent to enhance mouth feel. A total of six formulations and control formulation CP0 (without superdisintegrant) were designed.

The post compressional parameters such as hardness, friability, thickness, drug content, weight variation, wetting time, and *in-vitro* disintegration time were studied shown in Table 2.

Table 2: Evaluation of Meloxicam MDT Tablets

Formulation	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	drug Content (%)	Weight variation	Wetting Time (sec)	Disintegration time (sec)
CPO	3.65	0.48	2.32	99.43	Pass	114	98
PM 1	3.53	0.58	2.28	98.03	Pass	48	38
PM 2	3.44	0.64	2.27	98.08	Pass	67	54
PM 3	3.50	0.52	2.26	99.03	Pass	74	62
CP 1	3.30	0.58	2.22	99.34	Pass	31	19
CP 2	3.10	0.50	2.15	99.46	Pass	44	38
CP 3	3.12	0.48	2.12	99.80	Pass	58	48

In all the formulations, the hardness test indicates good mechanical strength. The results were in the range 3.12 to 3.65 kg/cm^2. Friability was observed in the range 0.48 to 0.64 i. e. less than 1% which indicates that the tablets had a good mechanical resistance. Thickness of all formulations was observed in the range from 2.12 to 2.28 mm. Drug content was found to be in the range of 98.03 to 99.80 %, which is within acceptable limits. Weight variation was found within the specifications of I.P'96.

The wetting time experiment mimics the action of saliva in contact with the tablet to illustrate the water uptake and subsequent wetting of tablet. Wetting time is closely related to the inner structure of the tablet which showed that wetting process was very rapid in almost all formulations The wetting time is an important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water were found to be in the range of 31 to 114 sec.

Among all the designed formulations, formulation CP1 was found to be promising and was displayed an *in-vitro* dispersion time of 19 sec, which facilitates its faster dispersion in the mouth.

Among all the formulations CP1 containing 4% w/w of co-processed superdisintegrant (1:1 mixture of crospovidone and sodium starch glycolate) was found to be promising and has shown an *in-vitro* dispersion time of 19 sec, wetting time of 31sec when compared to the formulation PM1 containing 4% w/w of physical mixture of superdisintegrants (1:1 mixture of crospovidone and sodium starch glycolate) which shows *in-vitro* dispersion time of 38 sec, wetting time of 48 sec and control formulation (CPO) which shows 98 sec, 114 sec. values respectively for the above parameters. The percentage cumulative release is shown in **Table 3**. The dissolution profile of Meloxicam from the tablets is shown in **Figure 2**. This data reveals that among all the formulation CP1 shows faster drug release.

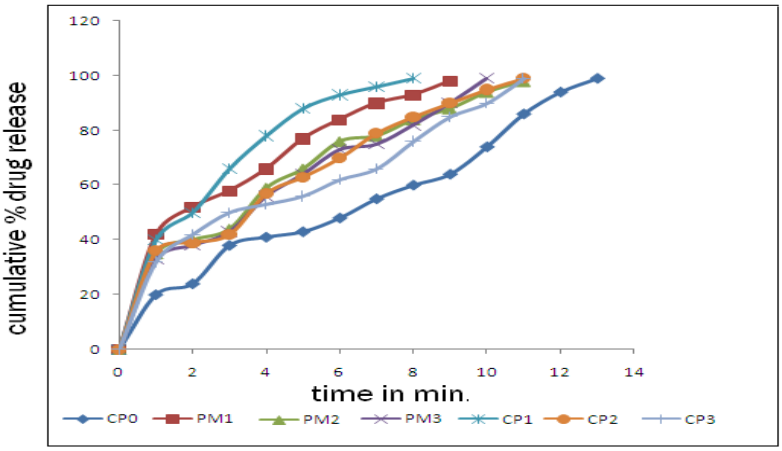

Figure 2: Dissolution profile of prepared tablets CPO to CP3

Table 3: Cumulative % drug Release of Meloxicam from Formulation CPO to CP3

Time (Min)	CP0	PM1	PM2	PM3	CP1	CP2	CP3
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	20	42	35	33	40	36	32
2	24	52	40	38	50	39	42
3	38	58	44	43	66	42	50
4	41	66	59	56	78	57	53
5	43	77	66	64	88	63	56
6	48	84	76	73	93	70	62
7	55	90	78	75	96	79	66
8	60	93	84	82	99	85	76
9	64	98	88	90	--	90	85
10	74	--	94	99	--	95	90
11	86	--	98	--	--	99	99
12	94	--	--	--	--	--	--
13	99	--	--	--	--	--	--

CONCLUSION:

Co-processed superdisitegrants consisting of crospovidone and croscarmellose sodium exhibited good flow and compression characteristics. Mouth dissolving Meloxicam tablets containing co-processed superdisintegrants exhibited quick disintegration and improved drug dissolution. It can be concluded from the present work that co-processed superdisintegrants of crospovidone and croscarmellose are superior to physical mixture of crospovidone and croscarmellose used in preparing tablets.

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