



Research article

Preparation and evaluation of mouth dissolving tablets of meloxicam

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Abstract:

The aim of the present study was to develop evaluate mouth dissolving tablet of meloxicam. Drug delivery systems became sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance. Over the past three decades, mouth dissolving or orally disintegrating tablets have gained considerable attention as a preferred alternative to conventional tablets due to better patient compliance. The most preferable route of drug administration (e.g. oral) is limited to drug candidate that show poor permeability across the gastric mucosa and those, which are sparingly soluble. A large majority of the new chemical entities and many new existing drug molecules are poorly soluble, thereby limiting their potential uses and increasing the difficulty of formulating bioavailable drug products,so lastlly the purpose of this study was to grow mouth dissolve tablets of Meloxicam. Meloxicam is a newer selective COX-1 inhibitor. These tablets were prepared by wet granulation procedure. The tablets were evaluated for % friability, wetting time and disintegration time. Sublimation of camphor from tablets resulted in better tablets as compared to the tablets prepared from granules that were exposing to vacuum. The systematic formulation approach helped in understanding the effect of formulation processing variables.

Keywords: Mouth dissolving tablet; Maloxicam; Bioavailability; NSAID

Introduction

Orally administered dosages form e.g. tablets, capsules are convenient dosage form for many drugs –but they are challenging to the 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-therby giving better patient compliance [1]. Tablets that are fast

disintegrate or dissolve rapidly in the patient's mouth, are convenient for young children, aged and patients with swallowing difficulties [2]. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity [3]. The medication then be absorbed partially or entirely into the systemic circulation from blood

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vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract (GIT) [4].

The bioavailability of some drugs may be enhanced due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. The amount of drug that is subject to first pass metabolism is reduced as compared to mouth dissolving tablets [5]. 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 [6]. Recently, the Nomenclature and Labeling committee at USP has approved the Orally Disintegrating Tablets terminology.

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 [7]. 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 [8].

A primary advantage of the oxicam family of drugs is their long half-life which permits once-day dosing [9]. In gastric disease, lower dose of meloxicam is required 7.5 mg/day. Meloxicam is safer than other NSAID's [10]. The fundamental approach used in the progress of the fast-dissolving or mouth dissolving tablet is the use of a super disintegrants. Sodium starch glycolate, and crospovidone were screened in the present study. A different approach used in developing Mouth dissolving tablets is maximizing the pore arrangement of the tablets [11]. I Freeze-drying and II vacuum-drying techniques have been tried by researchers to maximize the pore structure of tablet matrix. Freeze drying is burdensome and it yields brittle and hygroscopic products. Consequently, it was determined to accept the vacuum-drying technique in the present study [12-14]. Vacuum drying was adopted after

adding of a subliming agent to augment porosity of the tablets. It is possible that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly. NSAIDs are the most recurrently prescribed by physicians for inflammatory disorders. NSAIDs exert their effect through inhibition of cyclooxygenase-II, the main form of isozyme associated with inflammation but the simultaneous inhibition of cyclooxygenase-I and the resulting gastric and renal dysfunction limit their frequent use [15-17].

Materials

Meloxicam was gifted from Zydus Hetero drugs Ltd. (Hyderabad, India). Crospovidone was gifted from Red son Pharmaceuticals (Ahmedabad, India). Sodium starch glycolate and lactose-IP were gifted samples from Mundipharma Pvt. Ltd. (Delhi, India). Polyvinylpyrrolidone (PVP-K40) and colloidal silicon dioxide were obtained from Gaurav pharma (Ahmedabad, India), Magnesium stearate was gifted from Kotharipharma Pvt. Ltd. (Sagar, India).

Method Preparation of granules

All ingredients were weighted as per required quantity and store separately. To maintain uniformity the particle size, each material was passed through # 100 mesh-sized screen before mixing.

Table 1. List of ingredients used in formulation of fast dissolving tablets of Meloxicam

Ingredients	Batch No.				
	AI	AII	AIII	AIV	AV
Meloxicam. (mg)	7.5	7.5	7.5	7.5	7.5
Crospovidone. (mg)	10	10	10	10	10
Colloidal Silica dioxide. (mg)	-	1	2	1	2
Camphor. (mg)	10	10	20	20	-
Lactose .(mg)	150	150	150	150	150
Talc	1%	1%	1%	1%	1%
Magnesium Stearate	0.8 %	0.8%	0.8 %	0.8%	0.8 %
PVP solution in ethyl alcohol	10%	10%	10%	10%	10%

Camphor, crospovidone, and lactose were mixed using a glass pestle & mortar, and then added Meloxicam. Prepare a alcoholic solution of Polyvinylpyrrolidone (PVP) 15% w/v, it was added in the mixture in such quantity that sufficient to bind the mass. Then that

mass was passed through 100 mesh sized screen and granules was collected. These granules were dried (Vacuum dried) at about 60°C for 24 hrs that facilitate sublimation of camphor. Prepared granules were mixed with the crospovidone. These granules were lubricated with 1% w/w of talc and 0.8 % w/w of magnesium stearate.

Tablets formation by single punch machine

Dried granules were compressed by using single-punch tablet machine (Cadmach, Bhopal India) and converted into tablets. Sublimation was performed from tablets instead of granules at 60°C in selected batches.

Table 2. Various evaluation parameters of prepared tablets batches of Meloxicam

Batch No.	Hardness (kg/cm ²)	Friability (%)	Weight variation	Thickness (mm) ±S.D	Waiting Time (sec)	Disintegration Time (sec)
AI	3.56 ± 0.01	0.19	Passes	2.91 ± 0.2	101.21	1 min. 12 sec.
AII	4.25 ± 0.01	0.23	Passes	2.69 ± 0.1	100.07	1 min. 10 sec.
AIII	3.04 ± 0.02	0.21	Passes	2.66 ± 0.1	99.90	59 sec.
AIV	3.14 ± 0.04	0.26	Passes	2.48 ± 0.1	98.12	52 sec.
AV	3.99 ± 0.03	0.22	Passes	2.74 ± 0.1	100.95	1 min 02 sec.

Evaluation of tablet properties

I. Hardness

The crushing strength or hardness of the tablets was measured with help of a Monsanto hardness tester and expressed in kg/cm².

II. Uniformity of Weight

Weight variation test is done with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets.

III. Friability

The friability of tablets using 10 tablets as a sample was measured using a Roche Friabilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

IV. Disintegration Time

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

V. Dissolution Time

Dissolution Study of Tablets On the basis of disintegration data, formulation I, II and III was chosen for dissolution study, as it was showing least disintegration time i.e. 52 seconds. In vitro dissolution study on prepared tablets was performed in SSF (pH

6.2) using USP type II (paddle) apparatus operated at 50 rpm (900 ml) for 60 minutes (37 ± 0.5°C).

VI. Wetting Time

The wetting time of the tablets was measured using a very simple process. Five circular tissue papers of 10-cm diameter were placed in a Petri dish with a 10-cm diameter. Ten milliliters of water containing a water-soluble dye (eosin) 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 tablet was noted as the wetting time. All tests are summarized in Table 2.

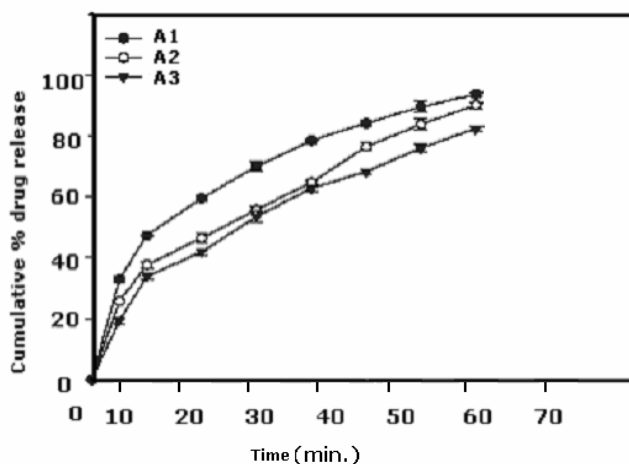


Figure 1. Dissolution profile of batch AI, AII, AIII

Results and Discussion

Water insoluble diluents such as microcrystalline cellulose and dicalcium phosphate were not used in this study because they can be expected to cause an unacceptable feeling of grittiness in the patient mouth. Along with the soluble diluents, lactose was selected as a soluble diluents considering its advantages in terms of availability, low cost and relative moisture insensitivity. Polyvinylpyrrolidone was used as a binder at a concentration of 15% wt/vol, in ethyl alcohol considering its well-known applicability in the pharma industry. The crushing strength of the tablets was adjusted 3.14 to 4.25 kg/cm². Sublimation agents such as menthol, camphor and thymol were used to increase porosity of the tablets. Camphor-containing tablets show faster disintegration or shorter disintegration time as compared with tablets containing menthol and thymol. The batches AI, AIII and AV were prepared using camphor at different concentrations to study its effect on disintegration time. The sublimation time (5-10 hrs) depending upon the quantity of camphor present initially (10%, 20% and 0%).

The results shown in Table 1 indicate that concentration-dependent disintegration was observed in batches prepared using camphor as a sublimation agent. The porous structure is responsible for faster water uptake, hence it facilitates wicking action of crospovidone in bringing about faster disintegration. In the first few attempts (AI, AIII and AV), sublimation of camphor was performed from granules prior to compression into tablets. Batches AI, AII and AV showed good mechanical integrity, but the disintegration time was a little longer than the arbitrarily chosen value of less than 60 seconds. In Batch AIV, sublimation was performed after compression. The results showed in Table 1 reveal that sublimation of camphor from tablets resulted in faster disintegration. The compaction process might have caused breakage of porous granules and subsequent reduction in porosity. The low value of wetting time and disintegration time indicate that the porosity of tablets of batch AIV would be greater than batches AI, AII and AV. The granules required 2 hours of vacuum drying, whereas the tablets required 10 hours of vacuum drying. The longer drying time was required in the case of tablets probably because of the decreased surface area and porosity. In order to investigate the

factors systematically, a factorial design was employed in the present investigation.

On the basis of above results it can be concluded that an oral disintegrating tablet of Lornoxicam can be prepared.

Conclusion

In this research work it was found that the amount of camphor and crospovidone considerably affect the various parameters such as waiting time, disintegration time, and percentage friability. It is thus concluded that by adopting a systematic formulation approach, an optimum point can be reached in the shortest time with minimum efforts. Vacuum-drying technique would be an effective alternative approach compared with the use of more expensive adjuvant in the formulation of Mouth Dissolving tablets.

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