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Formulation and Evaluation of Molexicam Orally Disintegrating Tablet (ODT)

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ABSTRACT

The aim of the present study was to develop and evaluate an oral disintegrant tablet of meloxicam. Drug delivery systems became sophisticated and 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.

Orally is the most preferable route of drug administration which has some 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 lastly the purpose of this study was to grow mouth dissolve tablets of Meloxicam.

Meloxicam is a non steroidal anti-inflammatory drug (NSAID) which a newer selective COX-1 inhibitor. Different five formulations were prepared in his study and evaluated. These tablets were prepared by direct compress procedure.

Results: The results indicate that formulation number five is the best formula were friability is 0.65% < 1%, wetting time is 5.5 sec. and disintegration time is 18 sec.

Dissolution test indicate that more than 75% of drug dissolve in the first 5min. and assay test is 99.1% which is within the pharmacopeia limit (90-110%). The systematic formulation approach helped in understanding the effect of formulation processing variables.

Keywords: Oral disintegrant tablet; Meloxicam; NSAID, Formulation.

INTRODUCTION

Tablets that are fast disintegrate or dissolve rapidly in the patient's mouth, are convenient for young children, aged and patients with swallowing

difficulties [1]. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity [2]. The medication then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract (GIT) [3].

The bioavailability of some drugs may be enhancing 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 [4]. 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 [5]. Recently, the Nomenclature and Labeling committee at USP has approved the Orally Disintegrating Tablets terminology.

Meloxicam (Figure 1) is a nonsteroidal anti-inflammatory drug, used to relieve the symptoms of arthritis, primary dysmenorrhea, fever and as an analgesic, especially where there is an inflammatory component [6].

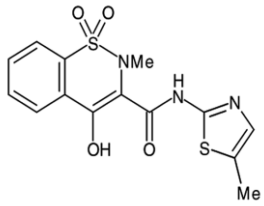


Figure (1): Chemical structure of Meloxicam

Meloxicam inhibits cyclooxygenase (COX) synthesis. responsible for converting arachidonic acid into prostaglandin H2. the first step in the synthesis of prostaglandins, which are mediators of inflammation. [7].

A primary advantage of the meloxicam family of drugs is their long half-life which permits once-day dosing [8]. In gastric disease, lower dose of meloxicam is required 7.5 mg/day. Meloxicam is safer than other NSAID's [9]. 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, pregtnalized starch and croscarmellose were screened in the present study. A different approach used in developing mouth dissolving tablets is maximizing the pore arrangement of the tablets [10]. 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 [11-12].

In this study, an attempt has been made to formulate and evaluate Meloxicam as Orally Disintegrating Tablet.

MATERIALS AND METHOD

Materials:

Meloxicam (Active Ingredient), Croscarmellose (Disintegrant), Sodium starch glycolate (Disintegrant), Lactose-DCL, Mannitol (Diluents), Citric acid (Taste masking), Povidone (Binder) sucrose, Sodium Saccharine (Sweetening agent) and Magnesium stearate , Talc (Lubricant).

All these ingredients and chemicals which used in this study are from Biopharm Co. Ltd.

Method

All ingredients were weighed as per required quantity and store separately. To maintain uniformity the particle size, each material was passed through # 100 mesh-sized screen before mixing [13].

Table (1):Composition of different batches of Meloxicam oral disintegranting tablets

MATERIALS	F1	FII	FIII	FIV	FV
Meloxicam	7.5mg	7.5mg	7.5mg	7.5mg	7.5mg
Lactose DCL	100mg	78.5mg	57mg	82.5mg	100mg
Magnesium stereate	1mg	1.5mg	4mg	4mg	1mg
Sucrose	4mg	-	57mg	50mg	-
Mannitol	77.5mg	70mg	57mg	10mg	70mg
Citric acid	-	7.5mg	7.5mg	7.5mg	7.5mg
Povidone	-	3mg	-	0.5mg	4mg
Croscarmellose	10mg	20mg	10mg	16mg	20mg
Sod. Saccharine	-	-	-	2mg	-
Sod. Starch glyconate	-	-	-	20mg	-
Camphor	-	10mg	-	-	-
TALC	-	2mg	-	-	-

Tablet formulation

Direct compression method was done by using single-punch tablet machine (Cadmach, Bhopal India) and the granules were converted into tablets.

Evaluation tests

All the physico-chemical tests were performed according to the British Pharmacopoeia (BP.) and United State Pharmacopoeia (USP). [17 and 18]

First calibration curve of meloxicam was done using HPLC (Shimadzu) and Figure (2) illustrates the relation between concentration of meloxicam and area under the curve.

I. Hardness test

The crushing strength or hardness of the tablets was measured with help of a Monsanto hardness tester and expressed in kg/cm2 [18].

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 [17].

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 [17].

IV. Disintegration Time

Disintegration time for MDTs was determined using USP disintegration apparatus with (pH 6.2, 900 ml at 37°C) as the disintegrating medium. To comply the test all tablets should disintegrate within 3 minutes [18].

V. Dissolution Time

Dissolution Study of tablets on the basis of disintegration data, formulation I, II and III, IV, V, were 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 (pH 6.2) using USP type II (paddle) apparatus operated at 50 rpm (900 ml) for 30 minutes (37 ± 0.5°C) and Figure 3.Illustrate the results of dissolution profile test for formulations (F1,FII,FIII,FIV,FV) [14].

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.

RESULT

Table (2): Evaluation of Meloxicam Orally Disintegrating

Parameter	FI	FII	FIII	FIV	FV
Weight variation (mg)	203.7	198.4	206.3	204.9	200
Friability (%)	0.55	0.75	0.63	0.84	0.65
Disintegration time (sec)	14	16	50	140	18
Hardness (kg/cm^2)	4.33	3.866	3.533	3.866	3.4
Drug content (Assay)%	97.5	97.9	97.5	97.9	99.1
Wetting time (sec)	4.5	5.2	6.3	6.8	5.5
Water absorption ratio	48%	45%	41%	40%	44%

The above figure 2 of calibration indicate that the linearity of meloxicam at different concentration and the regression equation (r^2) = 0.99

DISCUSSION

Mona Nagar et al [15]. Are doing formulation and evaluation of fast-dissolving tablet by direct compression method using crospovidone as superdisintegrant and also Prasanthi et al [16] doing formulation and characterization of fast-dissolving tablets of raloxifene hydrochloride prepared by direct-compression method by incorporating super disintegrants like crosscarmellose sodium and sodium starch glycolate.

Water insoluble diluents such as microcrystalline cellulose and dicalcium phosphate were not used in this study because they expected to cause an unacceptable feeling of grittiness in the patient mouth. Along with the soluble diluents, lactose-DCL and mannitol were selected as soluble diluents considering its advantages in terms of availability, low cost and relative moisture insensitivity. Povidone and sodium starch glycolate were used as a binder at a concentration of 3-5%. The crushing strength of the tablets was adjusted from 3. 4 to 5.7 kg/cm^2. Sublimation agents such camphor was used in formulation III to increase porosity of the tablets.

Figure (2): Calibration curve of meloxicam

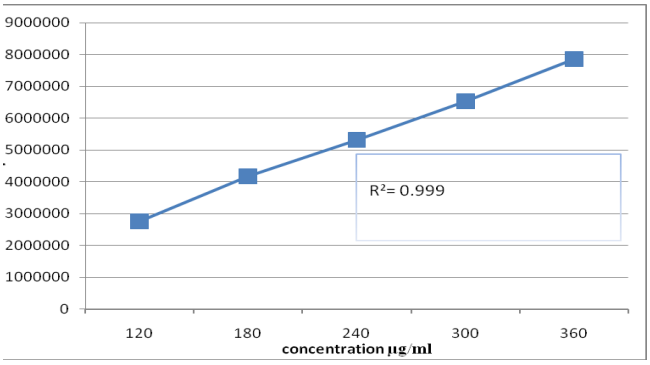
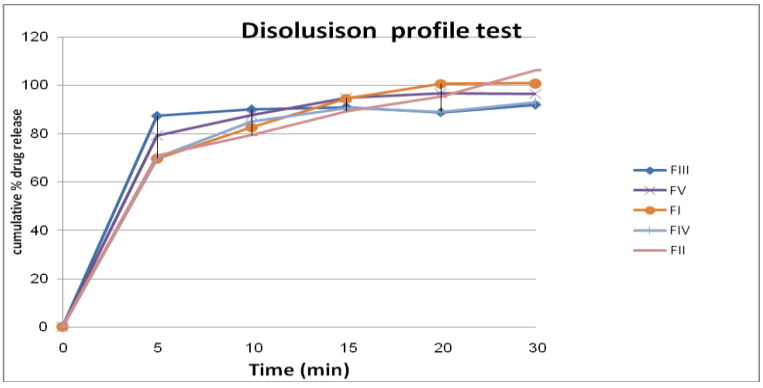


Figure (3): Dissolution profile of meloxicam orally disintegrating tablet formulations as cumulative % release Vs. time



Camphor-containing tablets show faster disintegration or shorter disintegration time but more hygroscopic and as result of tablet compress the porosity was reduced.

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 croscarmellose in bringing about faster disintegration. In the first few attempts FII, sublimation of camphor

was performed from granules prior to compression into tablets. FI, FI1I, FIV and FV were changed in the concentration of the croscarmellose as disintegrant and povidone as binder to prepare good mechanical integrity, and short disintegration time was less than 60 seconds in all formulation except FIV more than 60 seconds as result of used sodium starch glycolate as binder. The results showed in Table 2 reveal that croscarmellose resulted in faster disintegration.

Citric acid was added to the other formulation to improve the bad taste except FI show very bad taste.

Mannitol was used as filler because it has a negative heat of solution and imparts a cooling sensation when sucked or chewed to improve better taste F4 show unpleasant taste because the amount of mannitol is very low.

As illustrated in Figure 2 the dissolution profile for all formulation F1,FII,FIII,FIV and F At the following time intervals 5, 10,15, 20 ,25, 30 minute indicate good release where more than 70% of the drug was release at the first five minute.

CONCLUSION

We can conclude thatcroscarmellose , sodium starch glycolate and povidone considerably affect the various parameters such as waiting time, disintegration time, and percentage friability.

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تحضير وتقييم تركيبية دوائيه للميبيلوكسكام على شكل أقراص ذائبة في الفم

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ملخص

تهدف الدراسة الى تطوير وتقيم أقراص ذائبة في الفم لصنف الميلوكسكام وتعتبر طريقة ذوبانية الادوية في الفم وامتصاصها من التطورات الجديدة التي تستخدم كبديل للادوية التي لها مشاكل في القناة الهضمية سواء كان الامتصاص اوفي تاثرها بالاس الهيدروجيني او الاستقلاب المبكر وتعتبر طريقة تعاطي الادوية فمويا افضل وأكثر الطرق يعتبر الميلوكسكام من المسسكات غير الاسترودبة التي تعمل تثبيط للمساعد الانزيمي (COXI)

الطريقة: تم غمل خمس تراكيب مختلفة لصنف الميلوكسكام وتم عمل اختبارات تقييم للتراكيب الخمس وكانت التركيبة الخامسة هي افضل التراكيب حيث كانت نتائج الاختبارات كتالي :

حيث كانت الهشاشة (0.65%)وهي اقل من (1%) وكان زمن الابتلال 5.5 ثانية وكان زمن تفتت القرص (18) ثانيه بينما اوضحت دراسة الذوبانية التي تم خلال نصف ساعة ان اكثر من75%من الدواء يذوب في الخمس الدقائق الاولى وكانت نسبة المادة الفعالة في القرص هي 99.1% وهي ضمن المدى المحددمن قبل دستور الادويه (90 - 110)