FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF THE ETORICOXIB.

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ABSTRACT

The demand for mouth dissolving tablets has been growing during the last decade especially for elderly and children who have swallowing difficulties. Etoricoxib is a new non-steroidal anti-inflammatory drug (NSAID) with selective cox-2 inhibitory activity, selective inhibition of cox-2 provides anti-inflammatory and analgesic activity it is commonly used for osteo-arthritis, rheumatoid arthritis, primary dysmenorrhoea, post operative dental pain and acute gout. The main criteria for mouth dissolving tablets are to disintegrate or dissolve rapidly in oral cavity with saliva in 15sec to 60sec with need of water. The disintegrants used should fulfill the criteria by disintegrating the tablets in specified time limit.in the present investigation variety of super disintegrants like primogel, kollidone, Ac-Di-sol, L-HPMC, L-HPC, were selected and tablets were prepared by direct compression method in different concentration like 4% and 8%. The prepared tablets were evaluated for weight variation, hardness, friability, *in vitro* disintegration time, wetting time, *in vitro* dissolution study, etc. formulation f-9 shows the lowest disintegration time (44sec) and wetting time (52sec). *In vitro* dissolution studies revealed that formulation F-9 containning 8% L-HPC showed 97% drug release at the end of 20 min.

Keywords: Mouth dissolving tablets, *in vitro* disintegration time, wetting time, Etoricoxib.

INTRODUCTION

Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They are beneficial to swallowing tablets and capsules. Thus difficulty is particularly experienced by pediatric and geriatric patients. Various techniques such as freeze drying, sublimation, spray drying, moulding, mass-extrussion and direct compression method have been reported for preparation of mouth dissolving tablets.

Etoricoxib is an effective and selective cox-2 inhibitor with anti-inflammatory and analgesic properties. The poor water solubility of the drug give rise to difficulties in the formulation of dosage form leading to variable dissolution rate .hence it was selected as a model drug. In the present work an attempt has been made to prepare MDTs of etoricoxib using superdisintegrants in different concentrations.

MATERIALS AND METHODS

Etoricoxib was received as a gift sample from Alembic Pvt. Ltd., crosspovidone, croscarmellose, L-HPC, L-HPMC, primogel, were gift samples from Signet chemical Corporation, Mumbai. Mannitol, PVP K30, talc, magnesium stearate, HCl, were procured from Nice Chem., Cochin.

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Preparation of Etoricoxib tablets using direct compression

Weighed the Etoricoxib, superdisintegrants, mannitol, magnesium stearate, and talc accurately. All the materials were passed through 60 # screen prior to mixing. All the materials were transferred to glass mortar and triturated till it mixed uniformly. The resulting powder mixture was compressed into tablets using single punch tablet machine.

Evaluation of powder blend

Bulk density (D_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = M/ V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

Tapped density (D_t)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive

volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by

$$D_t = M / V_t$$

Where, M is the mass of powder
V_t is the tapped volume of the powder.

Angle of repose (θ)
The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder.

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\theta) = h / r$$
$$\theta = \tan^{-1}(h / r)$$

Where, θ is the angle of repose.
'h' is the height in cms
'r' is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel.

Carr's index (or) % compressibility
It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where, D_t is the tapped density of the powder and
D_b is the bulk density of the powder.

Hausner ratio
Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, Dt is the tapped density.
D_b is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Evaluation of mouth dissolving tablets
Weight variation
20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P

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

Friability (F)
Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Preweighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

In vitro disintegration time
The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Table 1: Formulation composition of Etoricoxib mouth dissolving tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Etoricoxib	60	60	60	60	60	60	60	60	60	60
Primogel	10	-	-	-	-	20	-	-	-	-
Ac-di-sol	-	10	-	-	-	-	20	-	-	-
Kollidone	-	-	10	-	-	-	-	20	-	-
L-HPC	-	-	-	10	-	-	-	-	20	-
L-HPMC	-	-	-	-	10	-	-	-	-	20
Mannitol	50	50	50	50	50	50	50	50	50	50
PVP K30	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5
Mg. Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2. 5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Lactose upto	250	250	250	250	250	250	250	250	250	250

Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$dl/dt = r\Upsilon\cos\theta/(4\eta l)$$

Where l is the length of penetration, r is the capillary radius, Υ is the surface tension, η is the liquid viscosity, t is the time, and θ is the contact angle. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37^{o}.

Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

In vitro drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile.

Dissolution test

USP 2 Paddle apparatus was used and paddle was allowed to rotate at 50 rpm. 0.1 N HCl (900 ml) was used as a dissolution medium.

Determination of amount of drug dissolved from tablets was carried out by UV 1601 spectrophotometer at 234 nm.

RESULTS AND DISCUSSION

Evaluation of the blend

Formula-tion code	Bulk density	Tapped density	Powder flow properties	Hausner ratio
F1	0.46	0.55	16.36	1.01
F2	0.45	0.54	16.66	1. 2
F3	0.46	0.55	16.52	1.19
F4	0.32	0.38	14.73	1.18
F5	0.45	0.52	18.75	1.15
F6	0.48	0.57	15.32	1.18
F7	0.47	0.57	17.42	1.21
F8	0.47	0.56	16.07	1.19
F9	0.45	0.54	16.14	1.21
F10	0.45	0.56	19.08	1.24

Table 3: Evaluation of the physical parameters of MDTs of Etoricoxib

Physical parameter of mouth dissolving tablets

Batch	Weight variation	Thick-ness (mm)	Hardness (kg/cm3)	Friability (%)
F1	Passes	4.52	3.7	0.41
F2	Passes	4.71	3.6	0.46
F3	Passes	4.55	3.6	0.46
F4	Passes	4.56	3.5	0.3
F5	Passes	4.87	3.8	0.3
F6	Passes	5.01	3.6	0.42
F7	Passes	4.83	3.5	0.49
F8	Passes	4.97	3.6	0.42
F9	Passes	4.87	3.5	0.35
F10	Passes	4.53	3.6	0.34

Discussion

In the present investigation, mouth dissolving tablets were formulated by direct compression method using various superdisintegrants such as kollidone, Ac-Di-sol, primogel, L-HPC, L-HPMC in different concentration like 4% and

Table 4: Physical parameter of mouth dissolving tablets

Batch	*In vitro* disintegration time (sec)	Wetting time (sec)	Drug release at 20 min	Assay (%)	Water abs. ratio
F1	88	93	76.28	99.18	83.365
F2	70	75	76.64	99.78	85.36
F3	63	78	81.99	98.12	95.78
F4	58	65	86.03	99.19	85.94
F5	120	130	73.00	98.00	85.83
F6	72	79	93.54	99.18	133.9
F7	57	65	95.57	98.25	67.73
F8	54	61	95.21	99.36	87.53
F9	44	52	97.21	98.98	84.53
F10	100	110	81.35	98.95	108.22

8%. Total ten formulations were prepared and evaluated for various parameters. Formulation F9 (8% L-HPC) showed minimum disintegration time, wetting time as compared to other formulation. Dissolution studies concluded that 97% of the drug was released at the end of 20min. The results showed that disintegration time was increased in the manner of L-HPC < Kollidone < Ac-Di-sol < Primogel < L-HPMC.

ACKNOWLEDGEMENT

Prof. B Jayakar, Principal, Vinayaka Missions College of Pharmacy, Salem, Tamilnadu for providing us the excellent facilities.

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