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Original Research Article

DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLET OF ETORICOXIB BY USING NATURAL SUPERDISINTEGRANT (FENUGREEK POWDER)

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Abstract

The demands for fast dissolving tablets have received ever increasing day by day during the last two decade. In the proposed present project study, the effect of natural Superdisintegrants was compared with synthetic Super disintegrants and conventional Super disintegrants in the of fast dissolving tablet formulation of Etoricoxib. Etoricoxib NSAID is used for the treatment of mild to moderate pain in various conditions like (osteoarthritis) and reducing pain, swelling, and joint stiffness caused with rheumatoid arthritis. In the present work 9 formulations of FDT (Fast dissolving tablet) of Etoricoxib were prepared by using Super disintegrants was evaluated and compiles with the official parameters and specifications. Various formulations were prepared using four different superdisintegrsnts namely natural superdisintegrats Fenugreek Powder, sodium starch glycolate, cross carmelose sodium with three concentrations (4%, 8%, 12%) by direct compression method. Formulation F2 showed the lowest disintegration time and in-vitro dissolution studies recorded that formulation F2 showed 99.55% drug release at the end of 3 minutes. The best formulations among these were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline.

Keywords: Fast dissolving tablet, Natural Superdisintegrants, Etoricoxib.

INTRODUCTION

The tablet is most widely used solid dosage form because of its convenience in term of self-administration, compactness, dose accuracy and ease in manufacturing. Over this one drawback of these conventional tablets is difficulties in swallowing by pediatric and geriatric patients.[1-2] The fast dissolving tablets that dissolving in few seconds in the mouth when they come with contact with saliva without requirement of any additional water. The advantage of FDT (Fast dissolving tablet) is onset of action, higher patient acceptance, and increased bioavailability.[1-4] Etoricoxib is the potent non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, antipyretic and analgesic actions. Etoricoxib is a cyclooxygenase-II (COX-II) selective NSAID used in the treatment of rheumatoid arthritis, osteoarthritis, postoperative dental pain, chronic low back pain, acute gout and primary dysmenorrhea. Etoricoxib is also used for

the treatment of primary dysmenorrheal (painful menstrual periods).

It undergoes rapid first-pass metabolism in the liver (approximately 90% of a dose). This leads to lower bioavailability of Etoricoxib. Such drugs shows first-pass metabolism effect, so the drug is selected for fast dissolving tablet.[5-6]

MATERIAL AND METHOD

Material

Etoricoxib was received as gift sample by Cipla. Ltd., Mumbai, Magnesium stearate used were procured from Rescue Laboratories, Jaipur, Fenugreek powder was gifted by Ayursatva, Madhya-Pradesh, Asparteme used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

Method

Fast dissolving tablet of Etoricoxib were prepared by using direct compression method. Pure drug and excipients were passed through # 60 No. mesh, required amount of drug and excipients were taken for every formulation suggested by (Table No. 1). The powdered drug, Mannitol and Lactose were mixed uniformly with continuous trituration using mortar and pestle. Then weighed quantity of super disintegrates and aspartame taken for each formulation and properly mixed, finally magnesium stearate and talc powder were added and mixed well. The mixed blend of drug and excipients were compressed using 10 station tablet punching machine. (Shakti pharmaceuticals**)**. A Batch of 50 tablets of each formulation was prepared for all the designed tablet formulations. Before the tablet preparation /punch the mixture blend of all designed formulations were subjected to compatibility studies (IR) and pre-compression parameters like- Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.[6-7]

Pre-formulation studies:

Angle of Repose (θ):

Angle of repose is defined as, the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder. When more quantity of the powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force [8]

The angle of repose is determined by the funnel method suggested by scientist Newman. Angle of repose is determined by the following formula

$\tan \theta = h/r$

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

Where θ = Angle of repose, r = Radius of the cone, h = height of the cone

Bulk Density:

Density defined as weight per unit volume. Bulk density can be defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/ cm^3. There are two types of bulk density. [9]

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density

High bulk density, here the smaller particles shift between the large particles resulting in heavy powder of high bulk density.

Tapped Density (Dt):

It was the ratio index of total mass of the powder to tapped volume of the powder. Volume was reported by tapping the powder for 500 times and the tapped volume was recorded, if the difference

between these two volumes was less than 2%. It was expressed in g/ml and was given as following,

Dt= M/Vt

Where, M is the mass of powder, Vt is the tapped volume of the powder.[10]

Carr's index (or) % compressibility:

Carr's index results powder flow properties. It is expressed by percentage and is given by:

I=Dt−Db/Dt×100
Where, Dt denotes the tapped density of the powder

And Db is the bulk density of the powder.[11]

Hausner ratio:

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

Hausner ratio=Dt/Db Where, Dt show the tapped density, Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).[12]

Evaluation of tablet: -

All prepared tablets of Etoricoxib were evaluated for the following parameters as per IP guideline; all the calculations are represented in the table No.3

Weight Variation: -

Twenty tablets of Etoricoxib formulation were selected randomly from each of the formulation and weighted individually using Digital Balance for their weight data. The average weight of the tablets calculated was found in standard range.[15]

Hardness: -

Hardness of the Etoricoxib tablet was measured with the tablet hardness testing apparatus known as Monsanto tablet harness tester.[13]

Thickness: -

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.[14-15]

Friability: -

The friability of the Etoricoxib tablet, a sample of twenty tablets was measured using USP type Roche fraibilator. The tablets reweighed and percentage weight-loss was calculated, was found in standard range.[16-17]

%Friability= InitialWeight−Final Weight * 100/ Initial Weight

Water absorption ratio:

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet of every batch was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three random trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation

$R = \{(Wa - Wb) / Wa\} \times 100$

Where, Wa and W_b were weights of the tablets after and before study.[18]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and than the average wetting time was noted.

Disintegration Study: -

Disintegration time study was carried out by selecting 6 tablets of Etoricoxib and performed disintegration test using 900 ml D.W. at temperature (370C±20C). [19]

Dissolution Study: -

The In-vitro for the dissolution study was carried out in the USP (United state pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at 37±0.50C as per standard guidelines.[20-21]

Table No. 1: Formulation of fast dissolving tablet of Etoricoxib:

Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Etoricoxib	60	60	60	60	60	60	60	60	60
Fenugreek Powder	4	8	12	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	4	8	12	-	-	-
Cross carmellose Sodium	-	-	-	-	-	-	4	8	12
Aspartame	1	1	1	1	1	1	1	1	1
Flavour	1	1	1	1	1	1	1	1	1
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mannitol	10	10	10	10	10	10	10	10	10
Lactose	21	17	13	21	17	13	21	17	13
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

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RESULT AND DISCUSSION: -

Table No. 2: Pre-compression parameters of Etoricoxib FDTs

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibility Index (%)	Angle of Repose
F_1	0.391± 0.02	0.511±0.01	1.30±0.04	23.48± 0.05	20.65± 0.08
F_2	0.392± 0.02	0.521±0.01	1.32±0.02	24.76± 0.03	20.44± 0.01
F_3	0.395± 0.01	0.512±0.01	1.29±0.01	22.85± 0.01	20.66± 0.02
F_4	0.401 ± 0.01	0.490±0.02	1.22±0.02	18.16± 0.01	21.86 ± 0.02
F_5	0.412 ± 0.15	0.502±0.03	1.21±0.04	17.92± 0.02	21.77 ± 0.01
F_6	0.425 ± 0.02	0.512± 0.02	1.20±0.01	16.99± 0.01	21.33 ± 0.02
F_7	0.378 ± 0.06	0.515± 0.01	1.36±0.02	26.60± 0.03	23.09± 0.03
F_8	0.379 ± 0.04	0.513± 0.02	1.35±0.03	26.12± 0.02	23.58± 0.03
F_9	0.391 ± 0.02	0.505± 0.01	1.29±0.01	22.57± 0.01	22.72± 0.01

Table No. 3: Post-Compression parameters of Etoricoxib FDTs:

Parameters / Formulation	Thickness (mm)	Weight (mg)	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
F_1	3	97.05±0.55	3.05±0.15	0.58±0.84	45±0.01	15±1
F_2	3	98.57±0.78	3.02±0.01	0.62±0.25	35±0.02	14±2
F_3	3	98.01±0.11	3.25±0.09	0.69±0.17	40±0.01	16±1
F_4	3	97.02±0.25	3.24±0.12	0.65±0.16	45±0.02	21±1
F_5	3	98.01±0.11	3.22±0.01	0.62±0.12	40±0.03	22±2
F_6	3	101.05±0.15	3.23±0.10	0.68±0.32	42±0.01	18±2
F_7	3	102.01±0.15	3.32±0.05	0.67±0.13	44±0.02	19±2
F_8	3	100.50±0.04	3.40±0.09	0.65±0.23	42±0.03	22±2
F_9	3	101.02±0.22	3.45±0.18	0.58±0.19	43±.0.4	17±1

Table No. 3: Drug Content in the fast-dissolving tablet of Etoricoxib

Parameters Formulation	Drug Content (mg per Tablet)	% Drug Content
F_1	96.12±0.015	96.12
F_2	98.44±0.031	98.44
F_3	97.21±0.015	97.21
F_4	95.43±0.010	95.43
F_5	96.12±0.025	96.12
F_6	97.01±0.021	97.01
F_7	97.23±0.018	97.23
F_8	95.96±0.015	95.96
F_9	96.25±0.012	96.25

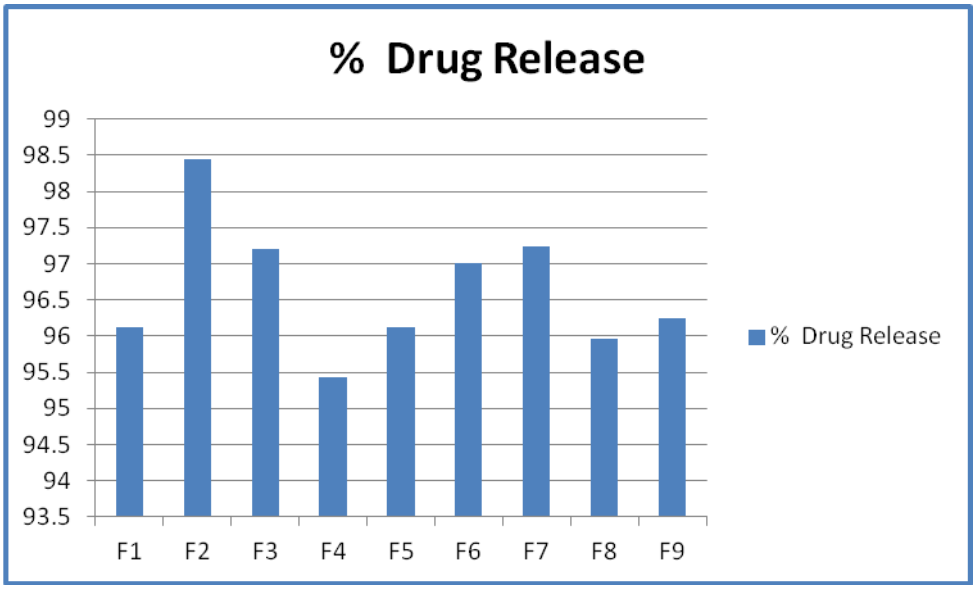

Figure: Drug Content in the fast-dissolving tablet of Etoricoxib

The angle of repose for the entire formulations blend was found to be in the range 20.44 to 23.58°. Compressibility index was found to be in the range 16.99 % to 26.60 %. All formulations showed good flow properties. Hausner's ratio was found to be in the range 1.20 to 1.36 and that indicated that all formulation has good flow properties. All parameters show weight variation, thickness, Disintegration time (sec) within standard limit. From all the above observations it was concluded that the formulation F2contain Fenugreek powder 8% found to be better formulation in terms of rapid dissolution and but maximum percentage drug release was

found 98.44% of formulation F2, with Fenugreek Powder (8%).

CONCLUSION:

It can be concluded from the whole study that fast dissolving tablets of Etoricoxib drug. Natural Superdisintegrants can be used as pharmaceutical excipients for oral drug delivery. It was concluded formulation F2 maximum percentage drug release was found 98.44%, with Fenugreek Powder.

From the study, it was concluded that Natural Superdisintegrants like Fenugreek Powder showed better disintegrating property over the synthetic super disintegrate like, SSG (Sodium starch glycolate) and CCS (Crosscarmelose Sodium)

Hence the Fenugreek Powder can be used at higher concentration at it has advantage of being non-toxic, low cost,
biodegradable and biocompatible with no side effect.

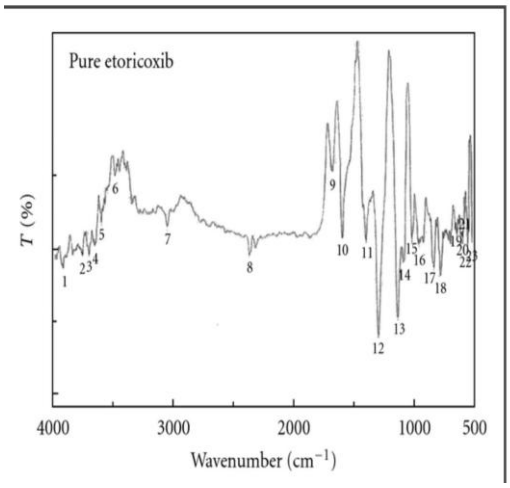

Figure 1: IR spectra of Etoricoxib

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