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DEVELOPMENT AND EVALUATION FAST-DISSOLVING TABLET OF ETORICOXIB BY USING NATURAL DISINTEGRANT

MR. ASHOK KUMAR SHARMA[1], MR. MEHUL KUMAR CHOUDHARY[1], MR. PATEL SUNIL KUMAR1, MR. VIKAS GARG[1], DR. DEEPAK GODARA[2]

[1]*Associate Professor, Arya College of Pharmacy, Jaipur, Rajasthan*

[2]*Director Research, Bilwal Medchem and Research Laboratory Private Limited, Jaipur*

***Abstract*—Over the last 20 years, there has been a daily increase in demand for pills that dissolve quickly. The impact of natural superdisintegrants was compared to synthetic and conventional superdisintegrants in the fast-dissolving tablet formulation of etoricoxib in the suggested current project research. The NSAID etoricoxib is used to treat mild to moderate pain in a number of disorders, including osteoarthritis, and to lessen rheumatoid arthritis-related discomfort, swelling, and stiffness in the joints. Nine formulations of etoricoxib FDTs (fast dissolving tablets) were made in the current study employing superdisintegrants, which were then assessed and compiled according to the official guidelines and requirements. Four distinct superdisintegrants—natural superdisintegrants Fenugreek Powder, sodium starch glycolate, and cross carmelose sodium—were used to generate several formulations at three different concentrations (4%, 8%, and 12%) via the use of the direct compression technique. According to in-vitro dissolution investigations, formulation F2 exhibited the lowest disintegration time and 99.55% drug release after three minutes. The most stable formulations were also discovered to be the best ones, and in accordance with ICH guidelines, stability tests were conducted on the improved formulations.**

***Keywords*— Fast dissolving tablet, Natural Superdisintegrants, menstrual periods, Etoricoxib, Fenugreek powder, direct compression, dissolution time.**

I. INTRODUCTION

The tablet is the most popular solid dosage form due to its simplicity of self-administration, compact design, precise dosing, and ease of manufacture. One disadvantage of these traditional pills is that older and pediatric patients may have trouble swallowing them.1-2 The quick-dissolving pills dissolve in the mouth in a matter of seconds when they come into touch with saliva and don't need any extra water. Fast dissolving tablets (FDTs) provide the advantages of quicker start of action, better patient acceptability, and improved bioavailability.1-4

The powerful non-steroidal anti-inflammatory medication (NSAID) etoricoxib has analgesic, antipyretic, and anti-inflammatory properties. A cyclooxygenase-II (COX-II) selective nonsteroidal anti-inflammatory drug (NSAID) called etoricoxib is used to treat acute gout, primary dysmenorrhea, osteoarthritis,

postoperative tooth pain, and persistent low back pain. In addition, primary dysmenorrhea (painful menstrual periods) is treated with etoricoxib.

In the liver, it is rapidly metabolized in the first pass (around 90% of a dosage). Etoricoxib's bioavailability is lowered as a result. Since these medications have a first-pass metabolism action, they are used for fast-dissolving tablets.5–6

II. MATERIAL AND TECHNIQUE

Material: Cipla Ltd., Mumbai, got a gift sample of etoricoxib.

METHOD:

Etoricoxib fast-dissolving tablets were made by the direct compression technique. The required quantity of drug and excipients were taken for each formulation recommended by (Table No. 1) after pure drug and excipients were passed through #60 No. mesh. Using a mortar and pestle, the powdered medication, mannitol, and lactose were thoroughly combined while triturating continuously. After aspartame and super disintegrates were weighed and well combined for each batch, talc powder and magnesium stearate were added and thoroughly mixed. A ten station tablet punching machine was used to crush the combined mixture of medication and excipients. (Shakti Health Products). For every tablet formulation that was intended, a batch of 50 tablets of each formulation was made. Prior to tablet production or punching, compatibility studies (IR) and pre-compression characteristics such as Hauser's ratio, bulk density, taped density, compressibility index, and angle of repose were applied to the mixture blend of all suggested formulations.6-7

Studies on pre-formulation:- Angle of Repose (θ): The greatest angle that may exist between the powder pile's surface and the powder's horizontal plane is known as the angle of repose. As additional powder is added to the pile, it slides downward until the gravitational force and the mutual friction between the particles create a surface angle θ.8

Scientist Newman proposed the funnel technique to calculate the angle of repose. The following formula determines the angle of repose.Tan θ = h/rTan-1 h/r = θwhere h is the cone's height, r is its radius, and θ is its angle of repose.Bulk Density: Weight per unit volume is the definition of density. The mass of the powder divided by its bulk volume yields the bulk density, which is represented as gm/cm^3. Two varieties of bulk density exist.9.

Bulk density

The outcome is a light powder with a low bulk density because the particles are packed to leave big spaces between their surfaces.

This creates a hefty powder with a high bulk density as the smaller particles move in between the larger ones.

The ratio of the powder's total mass to its tapped volume is known as the "tapped density" (Dt). If there was a difference of less than 2% between these two volumes, the tapped volume was recorded and the powder was tapped 500 times to report the volume. It was stated as follows, with an expression in g/ml.

M/Vt = Dt

where Vt is the powder's tapped volume and M is the powder's mass.10

Carr's index, or compressibility percentage:

Powder flow qualities are determined using Carr's index. I=Dt−Db/Dt×100 gives the percentage expression for it.

where Dt is the powder's tapped density.

Moreover, the powder's bulk density is Db.11

Hausner Ratio:

An indirect measure of the features of easy powder flow is the Hausner ratio. The formula used to compute it is as follows:

Dt/Db is the Hausner ratio. where Db is the bulk density and Dt is the tapped density.

Better flow characteristics are indicated by a lower hausner ratio (<1.25) than by a greater one (>1.25).12

III. TABLET EVALUATION

In accordance with IP guidelines, every tablet of etoricoxib that was manufactured was assessed for the following parameters; the results of all of the calculations are shown in Table No.3.

WEIGHT VARIATION: Twenty Etoricoxib pills were chosen at random from each formulation, and their weights were recorded using Digital Balance for each tablet. The computed pills' average weight was determined to be within a normal range.15

HARDNESS: The Monsanto tablet harness tester, a tablet hardness testing device, was used to assess the Etoricoxib tablet's hardness.13

THICKNESS: For each planned formulation batch, the tablet's thickness was measured in millimeters using Vernier Calipers.14–15

FRIABILITY: Using a USP-type Roche fraibilator, the friability of a sample of twenty Etoricoxib tablets was determined. After reweighing the pills, the percentage of weight loss was computed and confirmed to be within the standard range.Initial Weight - Final Weight * 100 / Initial Weight = 16–17% Friability

Ratio of water absorption: A tiny Petri-plate (ID = 6.5 cm) holding 10 ml of water was filled with

a piece of tissue paper (12 cm X 10.75 cm) that had been folded twice. Every batch's tablet was laid down on the paper, and the number of seconds it took for the tablet to completely wet was recorded. For every batch, three randomized trials were conducted and the standard deviation was ascertained. After weighing the wet tablet, the water absorption ratio R was calculated using the formula $R = \{(Wa - Wb) / Wa\} \times 100$.

where Wa and Wb represented the tablet weights before to and after the research.18 Minutes of Wetting

Twofold folded tissue paper measuring 12 cm by 10.75 cm was put in a small Petri dish (ID = 9 cm) with 6 milliliters of pH 6.8 phosphate buffer. The time it took for the tablet to become completely wet was recorded after it was put on the paper. After selecting three tablets at random from each formulation, the average wetting time was recorded.

DISINTEGRATION STUDY: A disintegration test using 900 ml of distilled water at a temperature of (370C±20C) was conducted after choosing six Etoricoxib tablets. 19

DISSOLUTION STUDY: A 900 ml vessel containing PH 6.8 was taken, and the temperature was maintained at 37±0.50C in accordance with standard guidelines. The in-vitro dissolution study was conducted in the USP (United States Pharmacopeia) dissolution test apparatus type 2, known as the paddle dissolution apparatus. Phosphate buffer was used as the dissolution medium.20–21

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

Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Etoricoxib	30	30	30	30	30	30	30	30	30
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	40	40	40	40	40	40	40	40	40
Lactose	21	17	13	21	17	13	21	17	13
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

IV. 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

Drug Content in the Fast Dissolving Tablet of Etoricoxib

Parameters / **Formulation**	**Drug Content** Drug Content (mg per Tablet)	**% Drug % Drug % % 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

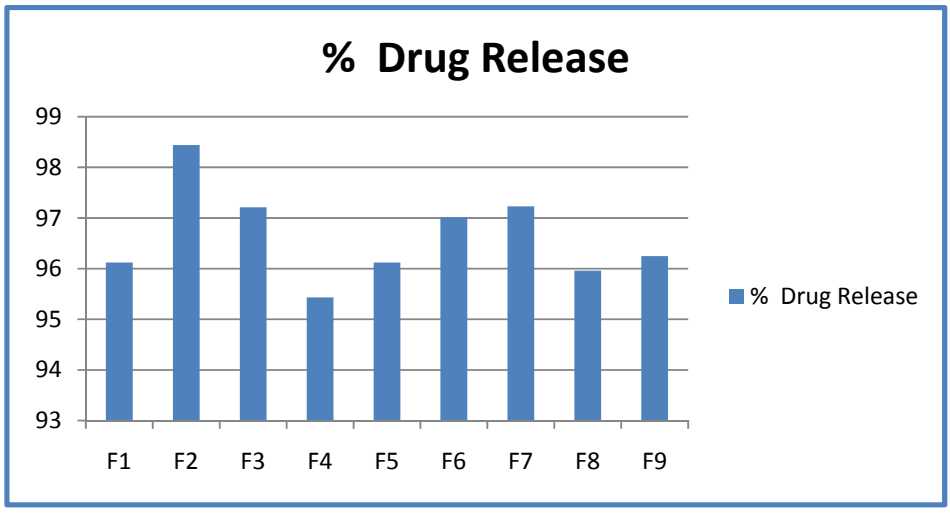

Fig.1. Drug Content in the Fast Dissolving Tablet of Etoricoxib

V. RESULTS AND DISCUSSION

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%).

VI. OUTCOMES

It was discovered that the blend of all formulas had an angle of repose between 20.44 and 23.58°. The range of the compressibility index was determined to be 16.99% to 26.60%. Every formulation exhibited acceptable flow characteristics. The range of 1.20 to 1.36 for Hausner's ratio suggested that all formulations had satisfactory flow characteristics. Weight fluctuation, thickness, and disintegration time (sec) are all within the acceptable range for all metrics. Based on all of the aforementioned findings, it was determined that formulation F2, which contains 8% fenugreek powder, had a superior formulation in terms of quick dissolving; nevertheless, formulation F2, which also contains 8% fenugreek powder, had a maximum percentage drug release of 98.44%.

RESULTS: The whole research suggests that the medication etoricoxib comes in fast-dissolving tablet form. Oral medication distribution may make use of natural superdisintegrants as pharmaceutical excipients. It was determined that the greatest percentage of drug release for formulation F2, including fenugreek powder, was 98.44%.

The study's findings indicated that natural superdisintegrants, such as fenugreek powder, outperformed synthetic superdisintegrants, such as sodium starch glycolate (SSG) and calcium carbimelose sodium (CCS). As a result, fenugreek powder can be used at higher concentrations due to its non-toxic, inexpensive, biodegradable, and side-effect-free qualities.

VII. 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.

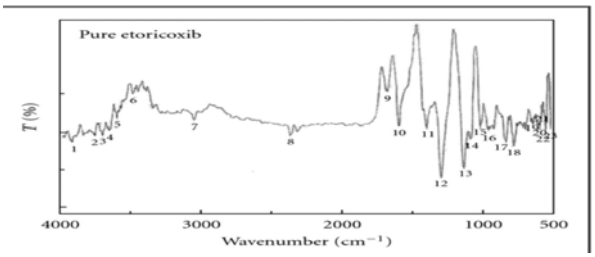

Fig. 2. IR spectra of Etoricoxib

Conflict of Interest

No conflict of interest to all authors.

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