Formulation and Optimization of Fast Dissolving Tablets of Etoricoxib Using Solid Dispersion Technique

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doi.org/10.64643/IJIRTV12I12-202899-459

***Abstract*—Fast Dissolving Tablets (FDTs) of Etoricoxib were formulated and optimized using solid dispersion technique with superdisintegrants Crospovidone and Croscarmellose Sodium. Etoricoxib, a selective COX-2 inhibitor (BCS Class II drug), suffers from poor aqueous solubility leading to delayed onset of action. Five formulations (F1–F5) were prepared by solid dispersion method with varying concentrations of superdisintegrants. All formulations were evaluated for precompression and postcompression parameters. Formulation F3 containing 9 mg Crospovidone demonstrated superior performance with disintegration time of 21 seconds and drug release of 99.9% within 30 minutes. Accelerated stability studies at 40°C ± 2°C / 75% ± 5% RH for 3 months confirmed stability of the optimized formulation. The results indicate that fast dissolving tablets of Etoricoxib can be successfully developed using solid dispersion technique, offering rapid onset of analgesic action and improved patient compliance.**

***Index Terms*—Etoricoxib, Fast Dissolving Tablets, Crospovidone, Croscarmellose Sodium, Solid Dispersion, Superdisintegrants, BCS Class II.**

I. INTRODUCTION

Oral drug delivery is the most widely accepted and preferred route for administration of pharmaceutical dosage forms because of convenience, patient acceptance, non-invasive nature, ease of manufacturing, and cost effectiveness. Despite these advantages, conventional oral solid dosage forms possess certain limitations, especially in patients who experience difficulty in swallowing, including pediatric, geriatric, bedridden, and dysphagic patients.

Fast Dissolving Tablets (FDTs) are novel oral solid dosage forms that disintegrate rapidly in saliva within seconds, without the need for water. According to the USFDA, an orally disintegrating tablet is "a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." FDTs provide rapid onset of action, improved patient compliance, and enhanced bioavailability, making them ideal for drugs requiring quick therapeutic action.

Etoricoxib is a selective COX-2 inhibitor belonging to the class of NSAIDs, widely prescribed for pain, inflammation, osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. It belongs to BCS Class II, characterized by low aqueous solubility and high membrane permeability, which limits its dissolution and onset of action in conventional tablets. Formulation of Etoricoxib as FDTs using solid dispersion technique can overcome this limitation by improving wettability, dissolution rate, and providing rapid analgesic effect.

II. AIM AND OBJECTIVES

A. Aim

To formulate and optimize Fast Dissolving Tablets of Etoricoxib to improve disintegration time, dissolution rate, onset of action, and patient compliance using suitable superdisintegrants through Solid Dispersion Technique.

B. Objectives

1. To formulate Fast Dissolving Tablets of Etoricoxib using Solid Dispersion Technique with Crospovidone and Croscarmellose Sodium as superdisintegrants.
2. To evaluate precompression parameters: angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio.

3. To evaluate postcompression parameters: weight variation, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, and drug content.
4. To perform in-vitro dissolution studies and optimize the best formulation based on minimum disintegration time and maximum drug release.
5. To conduct accelerated stability studies for the optimized formulation according to ICH guidelines.

III. DRUG PROFILE

Etoricoxib is a selective cyclooxygenase-2 (COX-2) inhibitor that selectively inhibits COX-2 enzyme while sparing COX-1 activity, thereby reducing pain and inflammation with lower gastric toxicity. It is classified under BCS Class II with poor aqueous solubility (Molecular Formula: C18H15ClN2O2S; Molecular Weight: 358.84 g/mol; Melting Point: 136–138°C).

Table I: Physicochemical Properties of Etoricoxib

Sr. No.	Parameter	Description
1	Drug Name	Etoricoxib
2	Category	NSAID (COX-2 Inhibitor)
3	Molecular Formula	C18H15ClN2O2S
4	Molecular Weight	358.84 g/mol
5	Appearance	White to off-white powder
6	Solubility	Poorly soluble in water
7	Melting Point	136–138°C
8	Half-life	~22 hours
9	BCS Classification	Class II
10	Bioavailability	~100%

Table II: Pharmacokinetic Parameters of Etoricoxib

Sr. No.	Parameter	Value
1	Bioavailability	~100%
2	Tmax	1–2 hours
3	Protein Binding	92%
4	Half-life	~22 hours
5	Route of Metabolism	Hepatic (CYP3A4)
6	Excretion	Urine and feces

IV. MATERIALS AND METHODOLOGY

A. Materials

Table III: Drug and Excipients Used

Sr. No.	Material	Category	Supplier
1	Etoricoxib	Active Pharmaceutical Ingredient	Yarrow Chem Products, Mumbai
2	Crospovidone	Superdisintegrant	Signet Chemical Corporation, Mumbai
3	Croscarmellose Sodium	Superdisintegrant	Loba Chemie Pvt. Ltd., Mumbai
4	Mannitol	Diluent	SD Fine Chemicals Ltd., Mumbai
5	Microcrystalline Cellulose	Binder/Filler	FMC Biopolymer, USA
6	Aspartame	Sweetener	HiMedia Laboratories, Mumbai
7	Talc	Glidant	Nice Chemicals Pvt. Ltd., Kerala
8	Magnesium Stearate	Lubricant	Merck Specialities Pvt. Ltd., Mumbai

B. Formulation Design

Five formulations (F1–F5) were designed using Etoricoxib (60 mg/tablet) with varying concentrations of superdisintegrants. The total tablet weight was maintained at 202 mg for all batches.

Table IV: Formulation Table (mg/tablet)

Sr. No.	Ingredients	F1	F2	F3	F4	F5
1	Etoricoxib	60	60	60	60	60
2	Crospovidone	3	6	9	-	-
3	Croscarmellose Sodium	-	-	-	6	9
4	Mannitol	80	77	74	77	74
5	Microcrystalline Cellulose	50	50	50	50	50
6	Aspartame	5	5	5	5	5
7	Talc	2	2	2	2	2
8	Magnesium Stearate	2	2	2	2	2
9	Total Weight (mg)	202	202	202	202	202

C. Solid Dispersion Preparation Method

Accurately weighed Etoricoxib and PEG 6000 were taken in required proportions. PEG 6000 was melted at 55–60°C in a porcelain dish. The drug was slowly incorporated into molten PEG with continuous stirring until uniform dispersion was obtained. The mixture was rapidly cooled at room temperature, solidified, pulverized using mortar and pestle, passed through sieve no. 60, and stored in desiccator until further use.

D. Tablet Compression

The solid dispersion was blended with Mannitol, MCC, Aspartame, and Crospovidone/Croscarmellose Sodium. Talc and Magnesium Stearate were added as glidant and lubricant respectively. The final blend was compressed on a tablet punching machine to obtain tablets of 202 mg.

V. EVALUATION PARAMETERS

A. Precompression Parameters

Angle of Repose ($\theta = \tan^{-1}(h/r)$), Bulk Density ($\rho b = M/Vb$), Tapped Density ($\rho t = M/Vt$), Carr's Compressibility Index (CI = [(TD–BD)/TD] × 100), and Hausner's Ratio (HR = TD/BD) were determined for all powder blends.

B. Postcompression Parameters

Weight Variation (n=20, IP limits), Thickness (Vernier caliper), Hardness (Monsanto hardness tester, kg/cm²), Friability (Roche friabilator, 25 rpm, 4 min; limit <1%), Wetting Time (tissue paper/petri dish method), Water Absorption Ratio, Disintegration Time (USP disintegration apparatus, 37±0.5°C; limit ≤60 sec for FDTs), Drug Content Uniformity (UV spectrophotometry; limit 95–105%), and In-vitro Dissolution Study (USP Type II paddle method, 900 ml phosphate buffer pH 6.8, 50 rpm, 37±0.5°C).

VI. RESULTS AND DISCUSSION

A. Precompression Parameters

Table V: Precompression Evaluation Results

Batch	Angle of Repose (°)	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio
F1	28.12 ± 0.15	0.42 ± 0.02	0.49 ± 0.01	14.28 ± 0.12	1.16 ± 0.01
F2	27.45 ± 0.18	0.43 ± 0.01	0.50 ± 0.02	14.00 ± 0.10	1.15 ± 0.02
F3	26.30 ± 0.12	0.44 ± 0.02	0.50 ± 0.01	12.00 ± 0.15	1.13 ± 0.01
F4	27.90 ± 0.20	0.42 ± 0.01	0.49 ± 0.02	14.10 ± 0.18	1.16 ± 0.01
F5	26.80 ± 0.14	0.43 ± 0.02	0.49 ± 0.01	12.24 ± 0.14	1.14 ± 0.02

The angle of repose for all formulations ranged from 26.30° to 28.12°, indicating good to excellent powder flow. Carr's index values (12.00–14.28%) and Hausner's ratio (1.13–1.16) confirmed good

compressibility and flowability of all powder blends, suitable for direct compression.

B. Postcompression Parameters

Table VI: Postcompression Evaluation Results

Parameter	F1	F2	F3	F4	F5
Weight Variation (mg)	201 ± 2.1	202 ± 1.8	201 ± 1.5	202 ± 1.6	201 ± 1.7
Thickness (mm)	3.12 ± 0.04	3.14 ± 0.03	3.16 ± 0.05	3.15 ± 0.04	3.13 ± 0.03
Hardness (kg/cm²)	3.1 ± 0.2	3.2 ± 0.1	3.3 ± 0.2	3.1 ± 0.1	3.2 ± 0.2
Friability (%)	0.82 ± 0.04	0.75 ± 0.03	0.62 ± 0.02	0.71 ± 0.03	0.66 ± 0.02
Wetting Time (sec)	42 ± 2	35 ± 2	24 ± 1	31 ± 2	27 ± 1
Water Absorption Ratio (%)	68 ± 2	74 ± 3	86 ± 2	79 ± 2	83 ± 3
Disintegration Time (sec)	48 ± 2	38 ± 1	21 ± 1	33 ± 2	26 ± 1
Drug Content (%)	97.2 ± 0.4	98.4 ± 0.3	99.1 ± 0.2	98.2 ± 0.4	98.8 ± 0.3

All formulations complied with pharmacopoeial limits. Friability (<1%), hardness (3.1–3.3 kg/cm²), and drug content (97.2–99.1%) were satisfactory. Formulation F3 with 9 mg Crospovidone showed the lowest wetting time (24 sec), highest water absorption ratio (86%), and fastest disintegration time (21 sec), attributable to the superior capillary action and wicking mechanism of Crospovidone at higher concentration.

C. In-vitro Dissolution Study

Table VII: In-vitro Dissolution Study – Cumulative % Drug Release

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
5	42.1	55.4	68.2	51.3	60.1
10	58.3	71.5	84.4	67.2	76.3
15	70.5	82.6	96.8	79.1	88.2
20	82.4	91.3	99.2	88.4	94.6
25	90.1	96.4	99.8	93.5	97.1
30	96.2	98.5	99.9	97.4	99.0

Formulation F3 exhibited maximum drug release of 99.9% within 30 minutes, significantly higher than F1 (96.2%) and F4 (97.4%). The enhanced dissolution was attributed to higher concentration of Crospovidone, rapid swelling, increased surface area, and improved water penetration into the tablet matrix via solid dispersion.

D. Stability Study of Optimized Batch F3

Table VIII: Stability Study Results – Optimized Formulation F3 (40°C ± 2°C / 75% ± 5% RH)

Parameter	Initial	After 3 Months	Inference
Appearance	White, smooth tablets	No change	Stable
Hardness (kg/cm²)	3.3 ± 0.2	3.2 ± 0.1	Acceptable
Friability (%)	0.62 ± 0.02	0.65 ± 0.03	Within limit
Drug Content (%)	99.1 ± 0.2	98.7 ± 0.3	Within limit
Disintegration Time (sec)	21 ± 1	23 ± 1	Acceptable
Drug Release (%)	99.9	99.1	No significant change

The optimized formulation F3 remained stable under accelerated conditions. No significant changes were observed in any parameter, confirming the physical and chemical stability of the formulation according to ICH Q1A(R2) guidelines.

VII. CONCLUSION

Fast Dissolving Tablets of Etoricoxib were successfully formulated using solid dispersion technique with Crospovidone and Croscarmellose Sodium as superdisintegrants. Among all five

formulations, F3 containing 9 mg Crospovidone was identified as the optimized formulation, exhibiting the shortest disintegration time of 21 seconds and maximum drug release of 99.9% within 30 minutes. All precompression and postcompression parameters were within acceptable pharmacopoeial limits. The accelerated stability studies confirmed stability of the formulation over 3 months at 40°C ± 2°C / 75% ± 5% RH. The developed Fast Dissolving Tablet formulation of Etoricoxib may serve as a promising alternative to conventional oral tablets for rapid analgesic and anti-inflammatory action with improved patient compliance, particularly for pediatric, geriatric, and dysphagic patients.

ACKNOWLEDGMENT

The authors sincerely thank the Principal and staff of BSS's Tatyaraoji More College of Pharmacy, Omerga, Maharashtra, for providing laboratory facilities and support throughout this research work.

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