

DESIGN, FORMULATION, AND EVALUATION OF FAST DISSOLVING ORAL FILMS OF ANALGESIC DRUGS ALONE AND IN COMBINATION THERAPY

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Abstract- Background: Etoricoxib is a selective cyclooxygenase-2 inhibitor used for the management of pain and inflammation. Conventional oral tablets may be inconvenient for patients who have difficulty swallowing and may not provide the rapid disintegration desired for fast-onset oral delivery. The supplied thesis investigated two rapid-release dosage forms: orally disintegrating tablets (ODTs) and mouth-dissolving films (MDFs).

Methods: Etoricoxib ODTs (F1–F9) were prepared by direct compression using microcrystalline cellulose, mannitol and crospovidone with taste-masking and lubrication excipients. MDFs (F1–F9) were developed by solvent casting using film-forming polymers, principally Pullulan, with PEG 400 as a plasticizer and additional formulation components. Preformulation, micromeritic, physicochemical, disintegration, drug-content, dissolution, FTIR, DSC and stability assessments were described in the thesis.

Results: The thesis-reported ODTs showed tablet weights of 244.5–245.4 mg, thickness of 3.16–3.20 mm, hardness of 3.6–5.1 kg/cm² and friability of 0.45–0.62%. Disintegration times were 12–24 s, with F5 at 14 s and F6 at 12 s. ODT drug content ranged from 92.1–99.2%, while 30-min drug release ranged from 72.4–98.1%. MDF thickness increased from 0.118 to 0.214 mm across F1–F9, and disintegration times ranged from 11–32 s. MDF drug content ranged from 91.8–99.8%, and 30-min drug release ranged from 86.4–99.7%. The thesis selected F5 as the optimized formulation for comparative discussion, although F6 showed the shortest disintegration time in both dosage-form series.

Conclusion: Both dosage-form approaches demonstrated rapid in-vitro disintegration and drug release in the thesis dataset. ODT F5 showed 14-s disintegration, 99.2% drug content and 98.1% release at 30 min, whereas MDF F5 showed 14-s disintegration, 99.8% drug content

and 99.1% release at 30 min. These findings support further experimental optimization, taste evaluation, long-term stability testing, scale-up and in-vivo performance assessment. Because selected values are explicitly described as illustrative in the thesis, final publication should use the original laboratory dataset and recalculated statistics.

Keywords: Etoricoxib; orally disintegrating tablet; mouth-dissolving film; Pullulan; crospovidone; direct compression; solvent casting; disintegration; drug release; oral drug delivery.

I. INTRODUCTION

Rapidly disintegrating oral dosage forms are designed to break down quickly in the oral cavity and can reduce the practical difficulties associated with swallowing conventional tablets.^[1] Orally disintegrating tablets and oral thin films are particularly relevant where administration without water, rapid dispersion and patient convenience are desirable. The thesis identifies pediatric, geriatric and dysphagic populations as important potential beneficiaries of such dosage forms.^[19]

Etoricoxib is a selective COX-2 inhibitor with analgesic, anti-inflammatory and antipyretic activity. The thesis reports a molecular formula of C₁₈H₁₅ClN₂O₂S, a molecular weight of approximately 358.8 g/mol, limited aqueous

solubility, a pKa of approximately 4.6 and a melting range around 135–140°C. Its limited aqueous solubility creates a formulation challenge because dissolution can influence the performance of an oral dosage form^[2,3].

The literature summarized in the thesis describes several strategies for rapid oral delivery, including direct compression, lyophilization, molding, spray drying and sublimation for ODTs, and solvent casting, hot-melt extrusion, semisolid casting, solid-dispersion extrusion and rolling for oral films. Previous etoricoxib studies cited in the thesis have investigated ODTs, mouth-dissolving films, inclusion complexes, superdisintegrants and polymeric film systems.^[4,5]

The present article condenses the thesis into a research-article structure and emphasizes the formulation-development logic, comparative performance of ODT and MDF systems, and the experimental observations reported in the supplied document.^[6,7]

II. AIM AND OBJECTIVES

The primary aim was to develop and evaluate fast-dissolving oral delivery systems of Etoricoxib with rapid disintegration and drug release, while improving the practical acceptability of oral administration.

- Develop nine Etoricoxib ODT formulations and evaluate their physicochemical and performance characteristics.
- Develop nine Etoricoxib mouth-dissolving film formulations by solvent casting.
- Evaluate drug content, disintegration/dispersion behavior and in-vitro drug release.
- Assess drug–excipient compatibility using FTIR and thermal behavior using DSC.
- Compare the optimized ODT and MDF formulations and identify areas for further optimization and validation.

III. MATERIALS AND METHODS

3.1 Materials

The thesis reports Etoricoxib as the active pharmaceutical ingredient. Major ODT excipients included microcrystalline cellulose PH 102, crospovidone, mannitol, sodium

saccharin, aspartame, talc and magnesium stearate. ^[12]The MDF system used Pullulan, HPMC E5 and PVA as film-forming polymers in the broader development work, with PEG 400, glycerol, propylene glycol, Tween 80, sodium saccharin, citric acid, flavor, ethanol and distilled water as formulation components^[8,9]

3.2 Preformulation and Analytical Evaluation

Preformulation included organoleptic examination, melting-point determination, differential scanning calorimetry, bulk and tapped density, Carr's compressibility index, Hausner ratio, angle of repose, solubility assessment and FTIR drug–excipient compatibility^[24,25] A UV-visible method was developed using a standard stock solution and serial dilutions. The thesis reports a working concentration range of 2–10 µg/mL and an experimentally identified λ_{max} of 345 nm^[10,11]

Table 1. Organoleptic characteristics of Etoricoxib

Parameter	Observation
Colour	White to off-white
Odour	Odourless
Appearance	Fine crystalline powder
Physical nature	Crystalline powder

Table 2. Micromeritic properties of the ODT powder blends.

Formulation	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)
F1	0.48	0.55	12.7	1.15	31.2
F2	0.49	0.56	12.5	1.14	30.5
F3	0.50	0.57	12.3	1.14	29.8
F4	0.49	0.56	12.5	1.14	30.2
F5	0.51	0.58	12.1	1.14	28.9
F6	0.52	0.59	11.9	1.13	28.1
F7	0.50	0.57	12.3	1.14	29.6
F8	0.51	0.58	12.1	1.14	28.6
F9	0.52	0.59	11.9	1.13	28.0

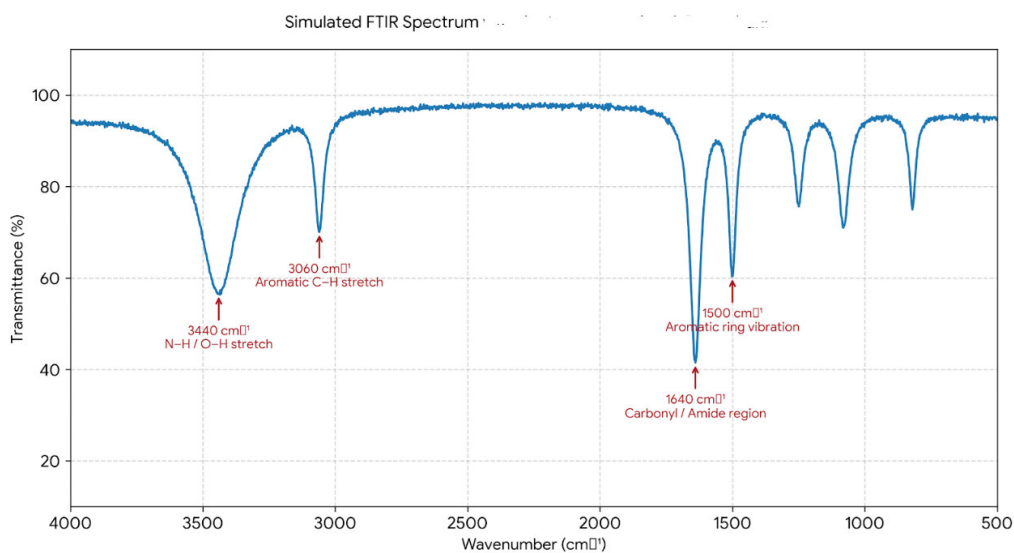


Figure 3. FTIR spectrum of Etoricoxib showing characteristic absorption bands.

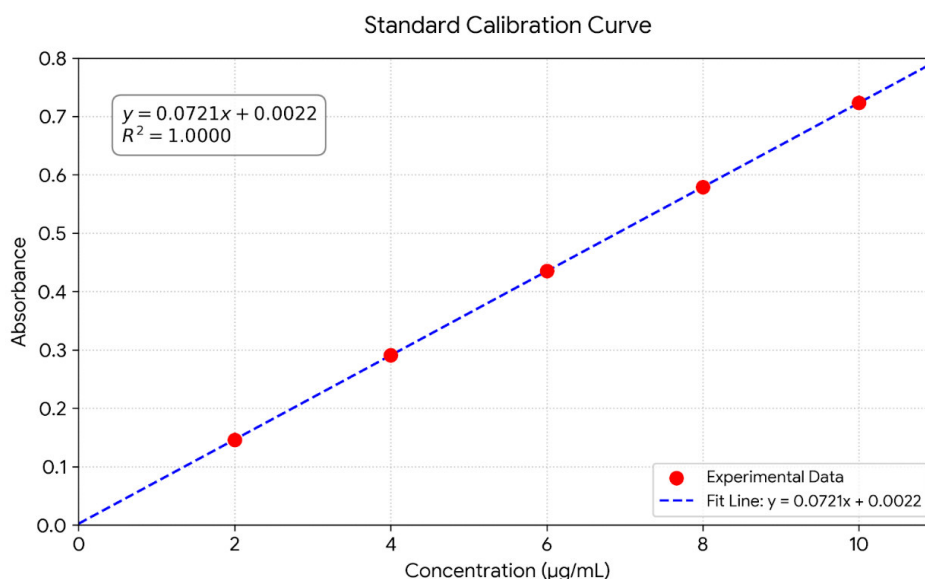


Figure 4. Standard calibration curve of Etoricoxib.

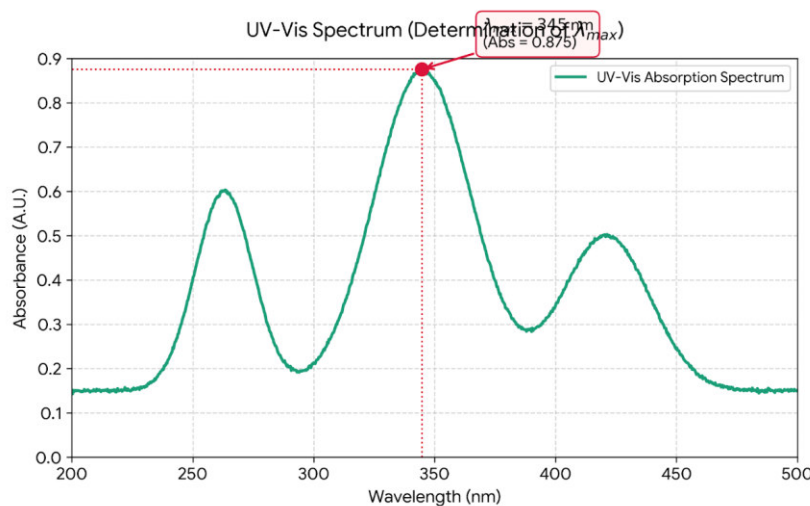


Figure 5. UV-visible absorption spectrum showing the reported λ_{max} of Etoricoxib.

3.3 ODT Preparation

For ODT preparation, Etoricoxib, filler, superdisintegrant and taste-masking excipients were weighed and sieved. The drug was geometrically mixed with a portion of

microcrystalline cellulose, followed by addition of the remaining excipients. Talc and magnesium stearate were added at the final blending stage. The lubricated blend was evaluated for flow and compressed into tablets of predetermined weight.

3.4 MDF Preparation

MDFs were prepared by solvent casting. The thesis describes hydration of Pullulan in distilled water under stirring, preparation of an Etoricoxib

dispersion/solution in ethanol, incorporation of plasticizer and other formulation components, removal of entrapped air, casting on a suitable surface and controlled drying. Film composition was varied across F1–F9.

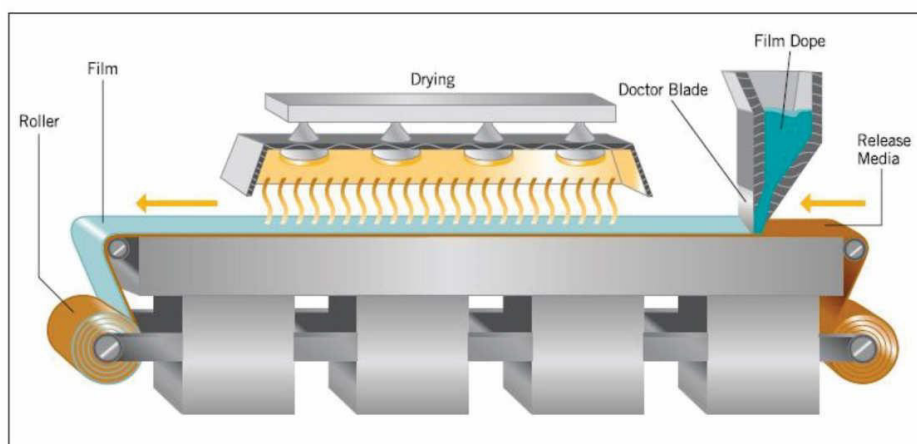


Figure 6. Solvent-casting system relevant to oral-film manufacture.

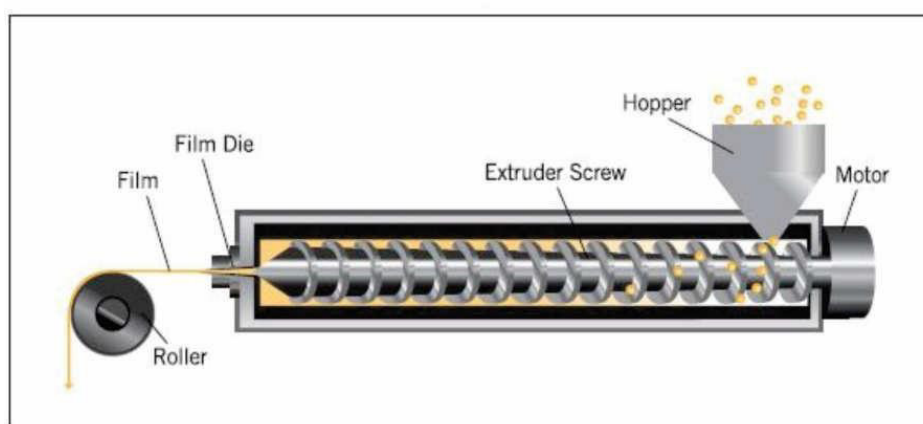


Figure 7. Film-extrusion system included in the thesis as an alternative oral-film manufacturing approach.

3.5 Evaluation of ODTs and MDFs

ODTs were evaluated for weight variation, thickness, hardness, friability, wetting time, water absorption, dispersion time, disintegration time, drug content and in-vitro drug release. MDFs were evaluated for appearance, thickness, folding endurance, dispersion/disintegration behavior, drug content and in-vitro release. Optimized formulations were additionally characterized by FTIR and DSC, and stability observations were reported.

For dissolution, the thesis describes a USP Type II paddle method for ODTs using 900 mL phosphate buffer pH 6.8 at $37 \pm 0.5^{\circ}\text{C}$ and 50 rpm, with sampling at predetermined intervals. Cumulative percentage drug release was calculated from the UV-visible calibration method.

IV. RESULTS AND DISCUSSION

4.1 Preformulation Findings

Etoricoxib was described as a white to off-white, fine crystalline, essentially odourless powder. The reported melting point was $135\text{--}139^{\circ}\text{C}$, supporting a defined crystalline thermal transition. Micromeritic assessment of the ODT blends showed bulk density of 0.48–0.52 g/mL, tapped density of 0.55–0.59 g/mL, Carr's index of 11.9–12.7%, Hausner ratio of 1.13–1.15 and angle of repose of $28.0\text{--}31.2^{\circ}$. These values were interpreted in the thesis as favorable for powder flow and direct compression.

The FTIR and DSC characterization indicated retention of characteristic Etoricoxib functional-group bands and modification/broadening of the characteristic thermal event without a new major transition. The thesis therefore interpreted the findings as absence of major drug–excipient incompatibility.

COMPARATIVE COMPATIBILITY AND SOLID-STATE CHARACTERIZATION OF ETORICOXIB FORMULATIONS

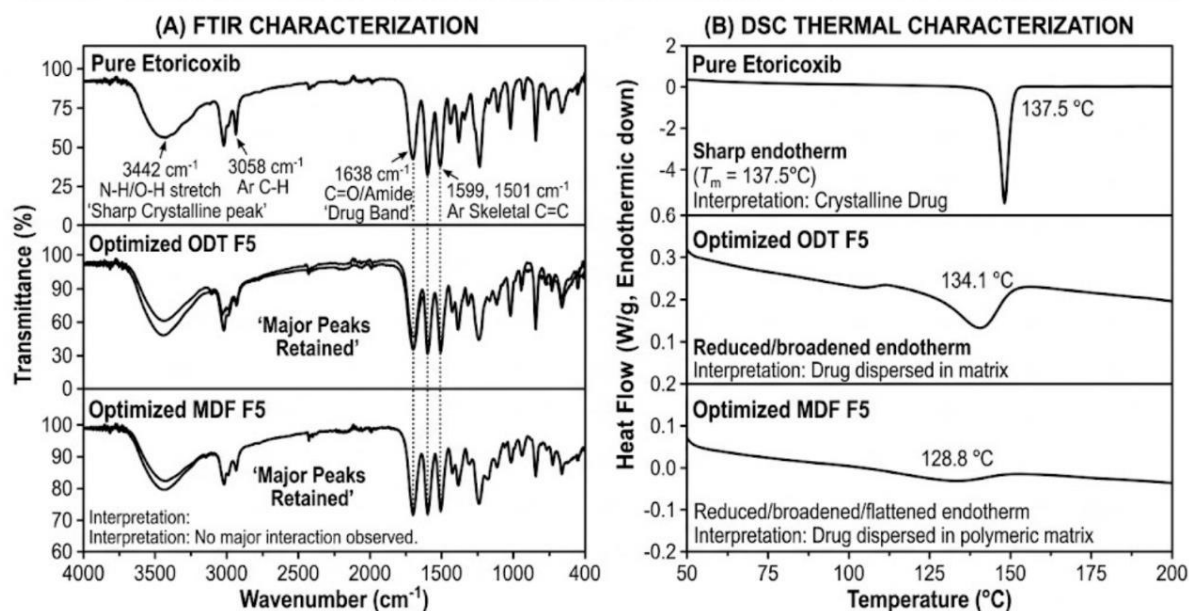


Figure 8. Comparative FTIR and DSC characterization of pure Etoricoxib and optimized formulations.

4.2 ODT Evaluation

Formula tion	Weig ht (mg)	Thickn ess (mm)	Hardn ess (kg/cm ²)	Friabil ity (%)	Wetti ng (s)	Water absorpt ion (%)	Dispers ion (s)	Disintegra tion (s)	Drug conte nt (%)	30- min relea se (%)
F1	245.4	3.18	3.6	0.62	28.4	39	25	24	92.1	72.4
F2	244.7	3.16	4.0	0.58	26.8	34	22	21	94.0	78.6
F3	245.1	3.17	4.3	0.54	24.7	31	19	18	96.2	84.3
F4	244.5	3.19	4.1	0.6	27.2	36	21	20	93.5	76.9
F5	245.0	3.17	4.8	0.48	23.1	27	15	14	99.2	98.1
F6	244.8	3.18	5.1	0.45	21.9	24	13	12	98.7	95.4
F7	245.3	3.2	4.2	0.57	25.9	33	20	19	95.0	82.7
F8	244.9	3.19	4.7	0.5	23.8	29	16	15	98.0	96.8
F9	245.2	3.18	5.0	0.46	22.5	25	14	13	98.4	97.3

ODT tablet weights were tightly grouped at 244.5–245.4 mg and thickness varied only from 3.16–3.20 mm. Hardness ranged from 3.6–5.1 kg/cm², while friability ranged from 0.45–0.62%. Wetting and dispersion became faster in formulations with greater crospovidone contribution, consistent with the wicking

mechanism described in the thesis. F6 had the shortest disintegration time (12 s), whereas F5 showed 14 s and the highest reported drug content (99.2%) and 30-min release (98.1%). The thesis selected F5 as the optimized ODT because optimization considered multiple quality attributes rather than disintegration time alone.

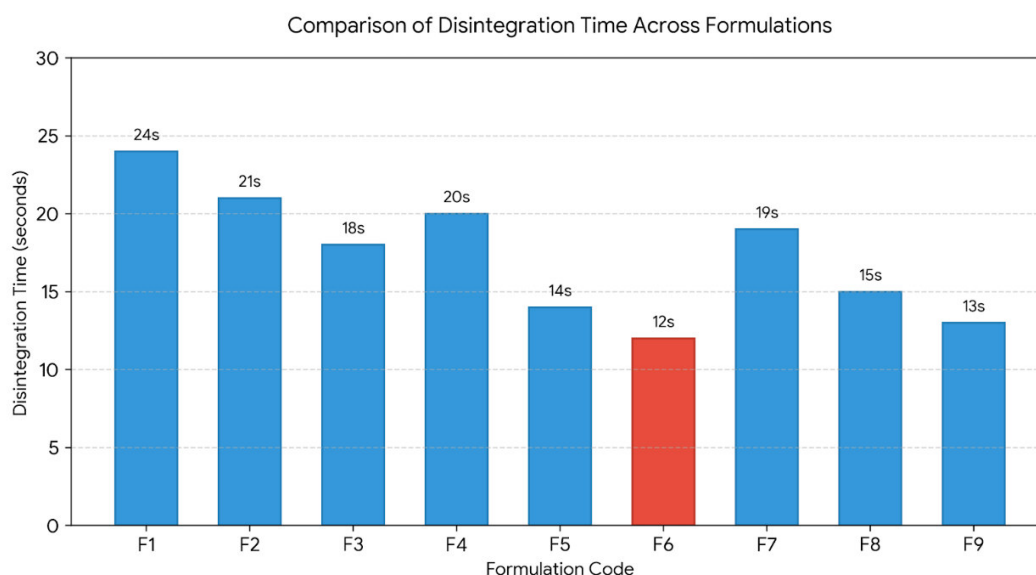


Figure 9. ODT disintegration time across F1–F9.

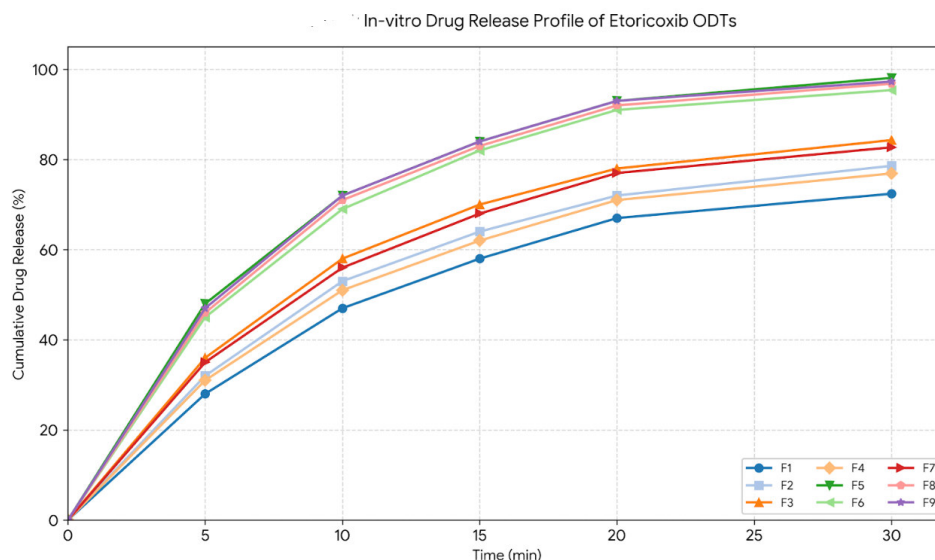


Figure 10. In-vitro drug-release profiles of Etoricoxib ODTs.

4.3 MDF Evaluation

Formulation	Thickness (mm)	Strength*	Handling loss (%)	Dispersion (s)	Disintegration (s)	Drug content (%)	30-min release (%)
F1	0.118	18	1.42	29	32	91.8	86.4
F2	0.121	20	1.21	25	28	93.7	90.2
F3	0.125	22	1.08	22	25	95.3	93.7
F4	0.162	23	1.17	24	27	94.3	91.8
F5	0.166	25	0.86	12	14	99.8	99.1
F6	0.17	27	0.74	10	11	99.5	99.7
F7	0.207	29	0.96	15	17	97.0	97.4
F8	0.211	30	0.79	11	13	99.0	99.0
F9	0.214	31	0.76	10	12	98.6	99.4

MDF thickness increased from 0.118 mm in F1 to 0.214 mm in F9, which the thesis associated with increasing Pullulan concentration. PEG 400

was described as contributing plasticization and flexibility. Disintegration times ranged from 11–32 s; F6 was fastest at 11 s, followed by F9 at 12

s and F8 at 13 s. F5 showed 99.8% drug content and 99.1% release at 30 min and was selected as

the optimized MDF for comparative analysis.

Formulation	Thickness (mm)	Strength*	Handling loss (%)	Dispersion (s)	Disintegration (s)	Drug Content (%)	Release 30 min (%)
F1	0.118	18	1.42	29	32	91.8	86.4
F2	0.121	20	1.21	25	28	93.7	90.2
F3	0.125	22	1.08	22	25	95.1	93.7
F4	0.162	23	1.17	24	27	94.3	91.8
F5	0.166	25	0.86	12	14	99.8	99.1
F6	0.170	27	0.74	10	11	99.2	99.7
F7	0.207	29	0.96	15	17	97.0	97.4
F8	0.211	30	0.79	11	13	99.0	99.0
F9	0.214	31	0.76	10	12	98.6	99.4

Figure 11. MDF formulation-evaluation data reproduced from the thesis.

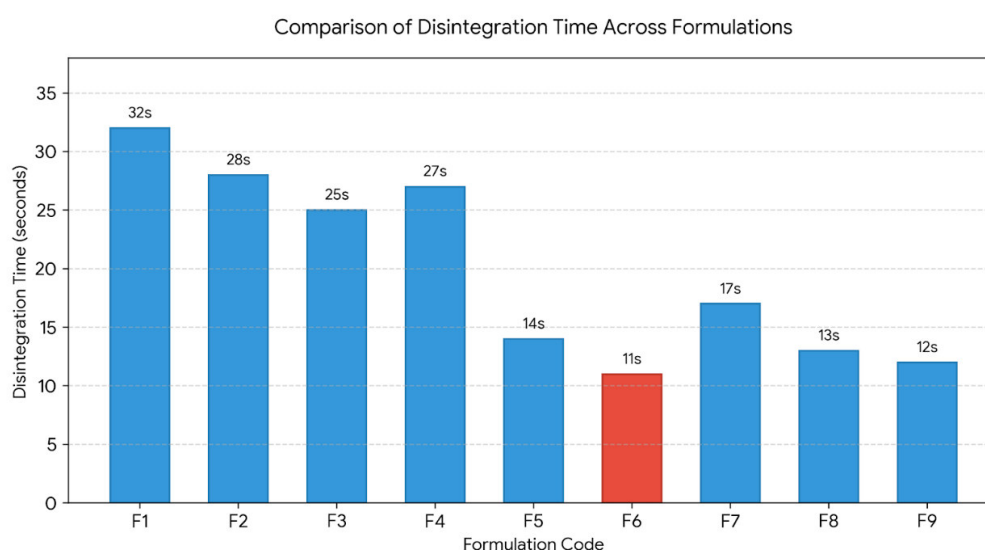


Figure 12. MDF disintegration time across F1–F9.

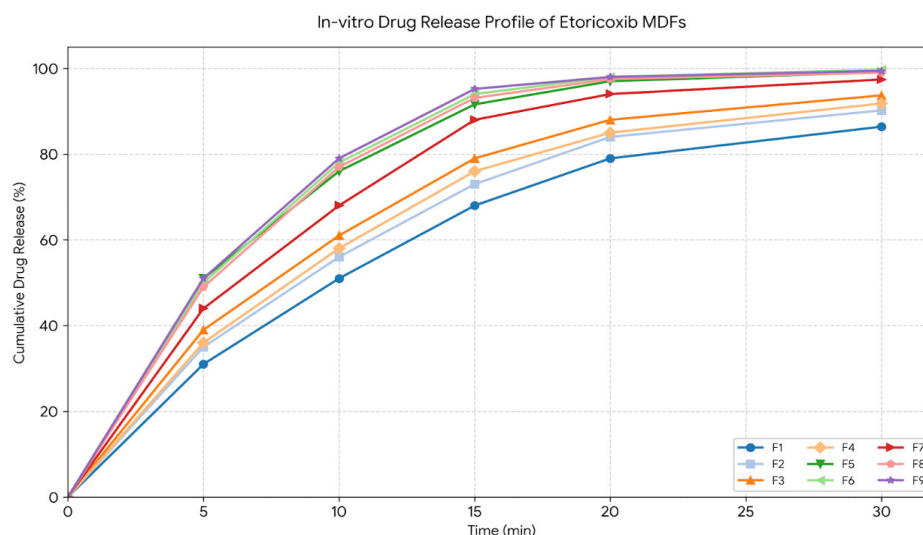


Figure 13. In-vitro drug-release profiles of Etoricoxib MDFs.

4.4 Comparative Evaluation of Optimized F5 Formulations

Parameter	ODT F5	MDF F5
Disintegration time	14 s	14 s
Dispersion time	15 s	12 s
Drug content	99.2%	99.8%
Drug release at 30 min	98.1%	99.1%
Physical integrity	Good	Good
Dosage form	Tablet	Thin film

The thesis reports broadly similar rapid disintegration for the optimized ODT and MDF, with both F5 formulations reaching 14 s. MDF F5 had slightly faster dispersion, higher drug content and marginally higher 30-min release in the reported dataset. The difference is consistent

with the formulation rationale that a thin film offers a large surface area for hydration. However, these observations remain in-vitro formulation findings and do not establish superior clinical efficacy or bioavailability.

4.5 Drug-Release Kinetics

Formulation	Model	R ²	N
ODT F5	Zero order	0.972	—

ODT F5	First order	0.989	—
ODT F5	Higuchi	0.976	—
ODT F5	Korsmeyer–Peppas	0.981	0.54
MDF F5	Zero order	0.965	—
MDF F5	First order	0.982	—
MDF F5	Higuchi	0.97	—
MDF F5	Korsmeyer–Peppas	0.986	0.61

The thesis reports the first-order model as the best fit for ODT F5 ($R^2 = 0.989$) and the Korsmeyer–Peppas model as the best fit for MDF F5 ($R^2 = 0.986$; $n = 0.61$). However, the thesis explicitly states that these kinetic calculations should be repeated using the complete original experimental dissolution dataset before final submission. Accordingly, these values should not be treated as publication-validated kinetic parameters without recalculation.

4.6 Stability

The supplied thesis includes an illustrative one-month stability dataset for optimized ODT F5. Drug content changed from 99.2% initially to 99.0% at one month; disintegration remained 14 s; reported 30-min release changed from 98.1% to 97.8%. The thesis also contains a narrative statement of a decrease to 97.2%, creating an internal inconsistency. Because the source itself labels the dataset illustrative and contains this discrepancy, the values should be reconciled against the original stability records before publication.

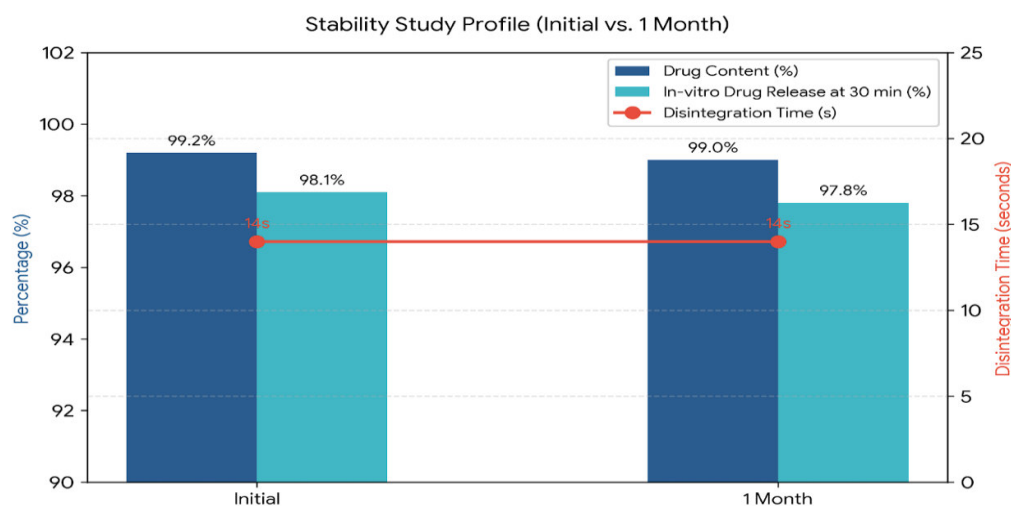


Figure 14. Stability profile reproduced from the thesis; values require confirmation against the original stability dataset.

V. DISCUSSION

The formulation results indicate that both dosage-form platforms can be engineered to achieve rapid oral disintegration. In the ODT system, crospovidone was central to rapid water uptake and matrix disruption. The ODT dataset shows a general reduction in disintegration time across formulations, with the lowest value observed for F6. Nevertheless, F5 provided a strong combined profile of mechanical properties, drug content and drug release, explaining its selection as the optimized formulation in the thesis.

In the MDF system, film geometry and polymer/plasticizer balance were key formulation variables. Increasing Pullulan was associated with increased film thickness, while

PEG 400 contributed flexibility. The rapid disintegration of F5–F9 is consistent with the film's thin geometry and rapid hydration. F5 was selected for comparative evaluation despite F6 showing the shortest disintegration time, again reflecting multi-parameter optimization rather than selection on a single response.

The compatibility findings are supportive but should be interpreted correctly. Retention of characteristic FTIR bands and the absence of a new major thermal event suggest that no major incompatibility was evident under the reported characterization conditions. They do not, by themselves, prove long-term chemical stability.

The drug-release profiles demonstrate rapid release in vitro, with the optimized F5 formulations approaching 98–99% release at 30

min in the thesis dataset. However, dissolution performance alone cannot establish improved clinical onset, bioavailability or therapeutic superiority. Those endpoints require appropriately designed pharmacokinetic, bioavailability/bioequivalence and clinical studies.

The most important limitation is data status. Several tables and narrative sections in the thesis explicitly describe values as illustrative or request recalculation using the original experimental readings. A journal submission should therefore replace any illustrative values with raw experimental data, replicate numbers, mean $\pm$ SD, statistical testing, validated analytical-method parameters, and complete stability results.

VI. CONCLUSION

The supplied thesis describes successful development of Etoricoxib ODT and mouth-dissolving film systems using direct compression and solvent casting, respectively. The reported formulations showed rapid disintegration, acceptable physical properties, high drug content in selected formulations and rapid in-vitro drug release. ODT F5 and MDF F5 were selected for comparative evaluation and showed 14-s disintegration, with 98.1% and 99.1% drug release at 30 min, respectively, in the thesis-reported dataset.

The work provides a formulation-development basis for rapid-release Etoricoxib delivery, but the publication-ready conclusion must be based on the original experimental records rather than the illustrative datasets identified in the thesis. Future work should prioritize validated analytical data, systematic Design of Experiments, taste/mouthfeel evaluation, long-term and accelerated stability, packaging studies, scale-up and appropriately designed in-vivo performance studies.

VII. FUTURE SCOPE

- Apply factorial Design of Experiments or Response Surface Methodology to quantify the effects of polymer, plasticizer and superdisintegrant concentrations
- Recalculate dissolution kinetics from the complete raw dissolution dataset and report confidence intervals/replicate variability.
- Perform systematic taste-masking and mouthfeel studies for Etoricoxib films.
- Conduct long-term and accelerated stability studies under defined ICH conditions.
- Investigate moisture-protective packaging and scale-up feasibility for the optimized film.
- Evaluate pharmacokinetics, bioavailability/bioequivalence and, where justified, clinical performance^[13,15]

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