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Formulation and Optimization of Fast Dissolving Tablets of Terbutaline Sulphate by Novel Co-Processing Technique

Atul Bopche[1], Dhanraj Vishwakarma[2], Dhruv Kumar Gupta[3], Gautam Kumar Verma[4], Harsh Patel[5], Harshit Singh[6], Hemant[7], Dr. Jagdish C. Rathi[8]

[1]*Assistant Professor, NRI Institute of Pharmaceutical Sciences, Bhopal, Madhya Pradesh, India*
[2-7]*UG Scholar, NRI Institute of Pharmaceutical Sciences, Bhopal, Madhya Pradesh, India*
[8]*Professor, NRI Institute of Pharmaceutical Sciences, Bhopal, Madhya Pradesh, India*

Abstract: ***Bronchial asthma demands rapid pharmacological intervention, yet conventional oral tablets of terbutaline sulphate, a widely used β₂-adrenergic bronchodilator are limited by slow disintegration and a delayed onset of action that can prove consequential during acute episodes. This study addresses that clinical gap through the formulation and optimization of fast dissolving tablets (FDTs) of terbutaline sulphate using novel co-processed superdisintegrants. Crospovidone and croscarmellose sodium were co-processed via solvent evaporation in varying ratios and incorporated into tablet formulations by direct compression. Three formulations (F1, F2, F3) were prepared with increasing superdisintegrant concentrations and evaluated for pre-compression parameters (angle of repose, bulk density, Carr's index, Hausner's ratio) and post-compression parameters (hardness, friability, weight variation, drug content, disintegration time, wetting time, and in-vitro dissolution). The optimized formulation, F3, stood out with a disintegration time of just 45 seconds and nearly complete drug release (99%) within 5 minutes, results attributable to the synergistic combination of crospovidone's wicking action and croscarmellose sodium's swelling capacity, both amplified by the intimate particle-level association achieved through co-processing. Accelerated stability testing (40°C/75% RH, 1 month) confirmed no clinically significant change in drug content or disintegration performance. These findings establish co-processed superdisintegrants as a practical and scalable strategy for developing high-performance FDTs, offering patients with asthma a faster, more accessible, and more effective dosage form.***

Keywords: Fast dissolving tablets, Terbutaline sulphate, Co-processing, Super disintegrants, Direct compression, Dissolution.

I. INTRODUCTION

Oral drug delivery is still the most preferred option to many, mainly due to its simple, affordable, and patient compatibility in most cases. But when you look at it practically, regular tablets don't always work that well for everyone [1]. A lot of people like pediatric and geriatric patients, or even those dealing with swallowing problems or breathing issues can struggle with taking tablets [2][3]. Also, conventional tablets don't always act quickly since they take time to break down, which delays the drug's effect [4]. Because of these drawbacks, fast dissolving tablets (FDTs) have gained significant attention. They're also called orally disintegrating tablets, as they dissolve in the mouth within seconds, without needing water. This makes them much easier to take, especially in situations where quick action is needed [5][6]. The fast breakdown mainly happens due to superdisintegrants. Crospovidone works by pulling water inside the tablet (kind of like capillary action), while croscarmellose sodium swells up when it absorbs water. Both together basically help the tablet break apart faster[7].

In recent times, FDTs have become quite popular, mostly because they can release the drug quickly and improve how patients stick to their medication. Different techniques like freeze-drying, spray drying, and sublimation have been explored for making these tablets. Still, direct compression is used more often since it's not complicated, costs less, and is easier to handle on a larger production scale[8][9].

One more thing that has come up in formulation work is co-processing. Instead of just blending excipients normally, this method combines them at a much finer level. Because of that, the final material tends to perform better and improves flow, compression properties, and disintegration also becomes quicker[10]. Some studies also mention that these combinations show a sort of synergistic behavior, meaning they work better together than alone. For example, when crospovidone and croscarmellose sodium are co-processed, the disintegration time is noticeably reduced compared to using them separately [11][12].

Terbutaline sulphate is a β_2-agonist used as a bronchodilator in conditions like asthma and COPD. It works well, but the usual tablets don't give very fast relief since they dissolve slowly [13]. So, turning it into a fast dissolving tablet using co-processed superdisintegrants is a practical way to get quicker drug release, which is especially important during sudden asthma symptoms [14].

II. CONCEPT AND RATIONALE OF CO-PROCESSING OF EXCIPIENTS

Co-processing represents a conceptually distinct departure from conventional excipient blending. Rather than combining materials through simple admixture, the technique integrates two or more excipients at the sub-particle level, generating a composite whose functional properties emerge from intimate physicochemical interactions between its components. This structural integration consistently yields performance advantages unachievable through physical mixing alone, including enhanced powder flowability, improved compressibility, accelerated disintegration, reduced segregation, and more homogeneous drug distribution within the tablet matrix [15].The selection of crospovidone and croscarmellose sodium as the co-processing pair was deliberate. Crospovidone facilitates disintegration via rapid capillary wicking, while croscarmellose sodium acts through pronounced volumetric swelling upon hydration [16][17]. When co-processed rather than physically blended, their complementary mechanisms are activated simultaneously and at full capacity, producing a synergistic disintegration response that substantially exceeds the performance of either agent used alone [18].

Bronchial asthma demands rapid pharmacological intervention, and the delayed onset of conventional terbutaline sulphate tablets a consequence of slow disintegration and dissolution represents a meaningful limitation during acute episodes [19]. Fast dissolving tablets address this directly by disintegrating upon salivary contact without requiring water, enabling earlier drug absorption when it matters most. Optimizing such a formulation, however, requires balancing disintegration efficiency against mechanical integrity conditions that typically work against each other [20]. Co-processing resolves this tension by intrinsically enhancing excipient performance, allowing rapid tablet breakdown without compromising hardness or friability [21].

III. MATERIALS AND METHODS

A. Materials

Table 1. Materials required for formulation of MDT of Terbutaline sulphate

Ingredient	Category / Function	Use in Formulation
Terbutaline sulphate	API (Active Pharmaceutical Ingredient)	Bronchodilator; provides therapeutic effect in asthma and COPD
Crospovidone	Superdisintegrant	Enhances rapid tablet disintegration via wicking (capillary action)
Croscarmellose sodium	Superdisintegrant	Promotes disintegration through swelling and water uptake
Mannitol	Diluent / Filler	Adds bulk, improves mouthfeel, and provides a cooling sensation
Magnesium stearate	Lubricant	Reduces friction during tablet compression and ejection
Talc	Glidant	Improves powder flow properties during manufacturing
Aspartame	Sweetener	Enhances palatability and taste masking
Distilled water / Ethanol	Solvent	Used during granulation or processing steps

All materials were of pharmaceutical grade.

B. Methodology

1) Preparation of Co-Processed Superdisintegrants

Crospovidone and croscarmellose sodium were mixed in ratios of 1:1 (CPS1), 1:2 (CPS2), and 2:1 (CPS3). Each blend (10 g) was wetted with 5 mL ethanol:water (1:1), granulated by passing through #40 mesh sieve, dried at 60°C for 2 hours, pulverized through #60 mesh, and stored in desiccators.

2) Formulation of Tablets

FDTs were prepared using direct compression. Formulations F1 (CPS1, 4% w/w), F2 (CPS2, 5% w/w), and F3 (CPS3, 6% w/w) were developed as per Table 1. All ingredients were sifted through #40 mesh, blended geometrically (20 min), lubricated with magnesium stearate/talc (5 min), and compressed using a single-punch rotary machine (8 mm flat-faced punches, 100 mg tablets).

Table 2: Formulation Composition (mg/tablet)

Ingredient	F1	F2	F3
Terbutaline sulphate	5	5	5
Co-processed SD	4	5	6
Mannitol	85	84	83
Aspartame	3	3	3
Mg stearate	2	2	2
Talc	1	1	1
Total	100	100	100

3) Pre-Compression Evaluation

Powder blends were assessed for angle of repose ($\theta = tan^{-1}(h/r)$ $\theta = \tan^{-1}(h/r)$), bulk density (mass/untapped volume), tapped density (after 100 taps), Carr's index ($(TD-BD)/TD \times 100$ $(TD-BD)/TD \times 100$), and Hausner's ratio (TD/BD).

4) Post-Compression Evaluation

Tablets (n=20) were tested for weight variation (IP limits), hardness (Monsanto tester), friability (% loss, Roche friabilator), thickness (vernier caliper), drug content (UV spectrophotometry at 276 nm), disintegration time (USP basket, 37°C in water), and wetting time (drop of water on dye paper).

5) In-Vitro Dissolution Study

Performed using USP Type II (paddle) apparatus in 900 mL phosphate buffer (pH 6.8, 37±0.5°C, 50 rpm). Samples withdrawn at intervals (0–30 min), analyzed at 276 nm.

IV. RESULTS AND DISCUSSION

A. Pre-Compression Results

All formulations exhibited good flow properties: angle of repose <30° (excellent), Carr's index ~15–16%, Hausner's ratio ~1.17–1.19 (Table 2). Co-processing improved flow over physical mixes due to reduced interparticle friction.

Table 3: Pre-Compression Parameters

Parameter	F1	F2	F3
Angle of repose (°)	28.5	27.2	26.8
Bulk density (g/cc)	0.52	0.54	0.55

Tapped density (g/cc)	0.62	0.65	0.66
Carr's index (%)	16.1	16.9	16.7
Hausner's ratio	1.19	1.20	1.20

B. Post-Compression Results

Table 4: Post-Compression Parameters

Parameter	F1	F2	F3
Weight Variation (mg)	150 ± 2	150 ± 1.5	150 ± 1
Hardness (kg/cm²)	3.2	3.5	3.8
Friability (%)	0.85	0.72	0.65
Thickness (mm)	3.1	3.2	3.3
Drug Content (%)	97.8	98.5	99.2

All tablets complied with IP standards. Friability was below 1%, indicating good mechanical strength. Drug content uniformity confirmed uniform drug distribution.

C. Disintegration and Wetting Time

Table 5: Disintegration and Wetting Time

Formulation	Disintegration Time (sec)	Wetting Time (sec)
F1	65	70
F2	55	60
F3	45	50

Disintegration time decreased with increase in co-processed excipient concentration. F3 showed fastest disintegration (45 sec) due to better swelling, Improved wicking action. Wetting time followed similar trend.

D. Dissolution Study

Table 6: Dissolution Study

Time (min)	F1 (%)	F2 (%)	F3 (%)
1	35	45	55
2	55	65	75
3	70	80	90
4	85	92	98
5	92	96	99

Drug release increased with an increase in superdisintegrant concentration. Co-processed excipients improved porosity, water penetration and tablet breakup. Out of all formulations, F3 showed Fastest disintegration, Maximum drug release and acceptable hardness. This indicates synergistic effect of crospovidone and croscarmellose sodium

E. Optimization

Table 7: Optimized Formulation (F3)

Parameter	Result
Disintegration Time	45 sec
Drug Release (5 min)	99%
Hardness	3.8 kg/cm²
Friability	0.65%

F. Stability Study

Table 8: Stability Study of Optimized Formulation (F3)

Parameter	**Initial**	**After 1 Month**
Appearance	No change	No change
Drug Content (%)	99.2	98.8
Disintegration Time	45 sec	48 sec

V. CONCLUSION

The present study successfully developed fast dissolving tablets of terbutaline sulphate using co-processed superdisintegrants (crospovidone and croscarmellose sodium) by direct compression. The co-processing approach improved flowability and compressibility of the powder blend, ensuring efficient tablet manufacturing. All formulations met pharmacopeial standards for hardness, friability, weight variation, and drug content, confirming good mechanical strength and uniformity.

An increase in the concentration of co-processed superdisintegrants significantly enhanced tablet performance. The optimized formulation F3 exhibited the best results, with rapid disintegration (45 seconds), reduced wetting time, and maximum drug release (99% within 5 minutes). This improved performance is attributed to the synergistic effect of crospovidone and croscarmellose sodium, combining wicking and swelling mechanisms to accelerate tablet breakup and dissolution.

Stability studies indicated no significant changes in the optimized formulation, confirming its reliability over time. Overall, the study demonstrates that co-processing of superdisintegrants is an effective and practical strategy for improving FDT performance, offering a patient-friendly dosage form with faster onset of action for the management of asthma.

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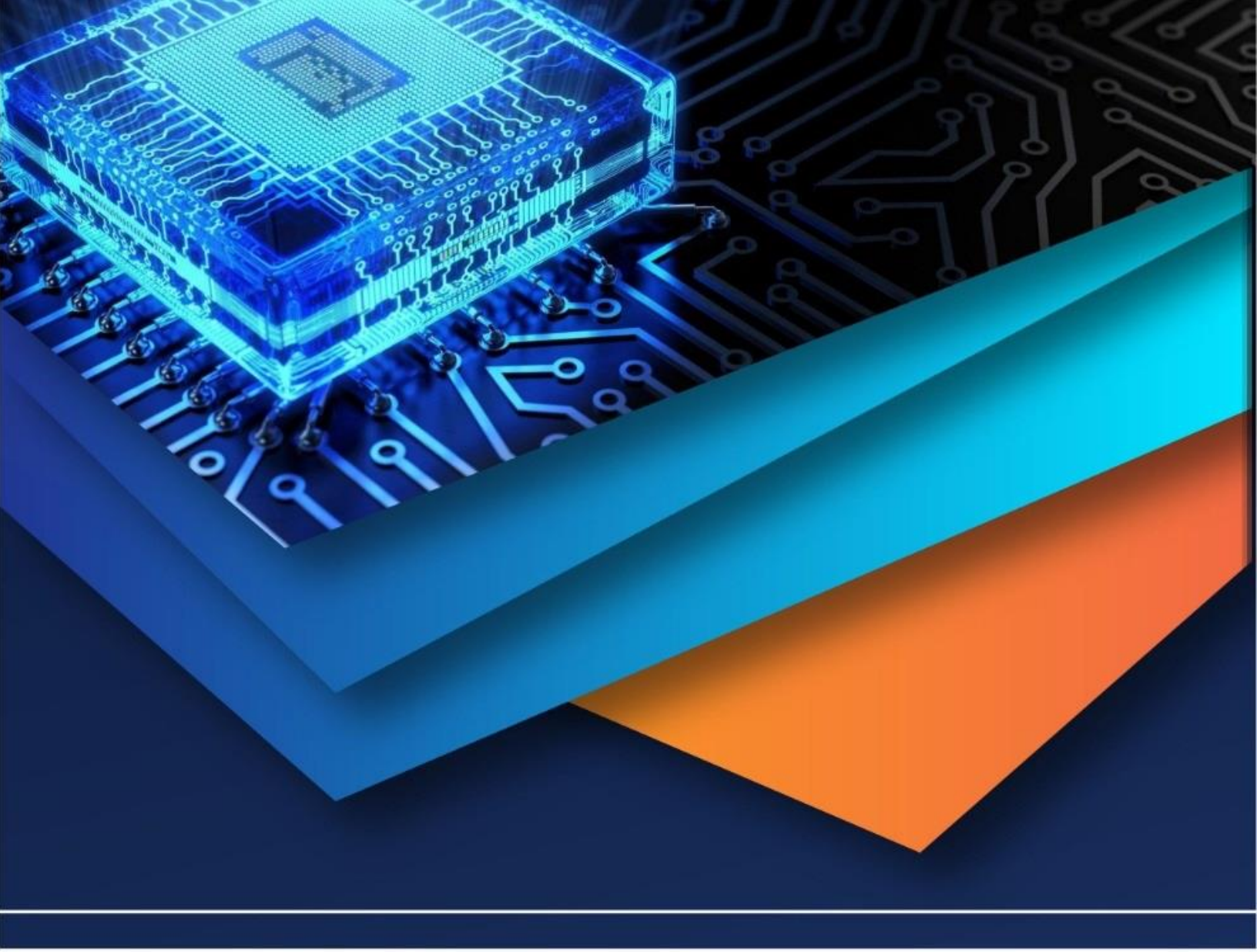

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