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Original Research Article

FORMULATION AND EVALUATION OF RAPID DISSOLVING TABLETS OF DOMPERIDONE PREPARED BY SUBLIMATION, DIRECT COMPRESSION, AND MELT GRANULATION TECHNIQUES

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Name of Author:
Purushotam Yadav[1], Manmohan Sharma[2], Anil Ahuja[2] , Jyoti Devi[3]

Affiliation: *[1]Scholar, School of Pharmaceutical Studies, Dr. K. N. Modi University, Newai, Rajasthan*
[2]Professor, School of Pharmaceutical Studies, Dr. K. N. Modi University, Newai, Rajasthan
[3]Assistant Professor, School of Pharmaceutical Studies, Dr. K. N. Modi University, Newai, Rajasthan

Corresponding Author:
Purushotam Yadav, Manmohan Sharma, Anil Ahuja, Jyoti Devi

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Abstract: The present study aimed to formulate and evaluate rapid dissolving tablets (RDTs) of Domperidone to achieve rapid onset of action and improved patient compliance, particularly in pediatric and geriatric patients with swallowing difficulties. Domperidone, a dopamine D_2-receptor antagonist, was formulated into RDTs using three different manufacturing techniques: sublimation, direct compression, and melt granulation. The prepared formulations were evaluated for precompression parameters, tablet hardness, friability, disintegration time, wetting time, water absorption ratio, drug content uniformity, and in-vitro dissolution behavior. Among all formulations, tablets prepared by the sublimation technique exhibited superior performance due to the formation of a highly porous tablet matrix following sublimation of the volatile agent. The optimized sublimation batch (SB2) showed the shortest disintegration time (17.2 seconds), lowest wetting time (17.6 seconds), highest water absorption ratio (75.1%), and maximum drug release (99.5% within 45 minutes). Direct compression formulations showed acceptable mechanical strength and rapid disintegration, while melt granulation formulations demonstrated comparatively slower disintegration and dissolution due to denser granule formation. The study concludes that the sublimation technique is a simple and effective approach for developing rapid dissolving tablets of Domperidone with enhanced disintegration and dissolution characteristics, ensuring faster therapeutic action.

Keywords: Domperidone, Rapid dissolving tablets, Sublimation technique, Direct compression, Melt granulation.

INTRODUCTION

Domperidone is a dopamine D_2-receptor antagonist commonly used as an antiemetic and gastroprokinetic agent in the management of nausea, vomiting, and gastrointestinal motility disorders1. However, its limited aqueous solubility and slow dissolution from conventional oral tablets may delay the onset of therapeutic action. In addition, swallowing conventional tablets can be difficult for pediatric, geriatric, and dysphagic patients2.

Rapid dissolving tablets (RDTs) are designed to disintegrate quickly in the oral cavity without the need for water, offering improved patient compliance and faster drug release. The performance of RDTs largely depends on formulation composition and manufacturing technique, which influence tablet porosity, wetting, and disintegration behavior3,4.

Various techniques such as sublimation, direct compression, and melt granulation have been employed to enhance the disintegration and

dissolution characteristics of RDTs. Sublimation produces a highly porous tablet matrix, direct compression utilizes superdisintegrants for rapid tablet breakup, while melt granulation improves flow properties but may result in denser tablets5-7.

The present study focuses on the formulation and comparative evaluation of Domperidone rapid dissolving tablets prepared using sublimation, direct compression, and melt granulation techniques, with the objective of identifying an optimized formulation capable of providing rapid disintegration and enhanced dissolution for faster therapeutic action.

2. Objectives: To formulate rapid dissolving tablets of Domperidone using sublimation, direct compression, and melt granulation techniques.
• To evaluate and compare the prepared formulations for disintegration time, wetting behavior, and in-vitro dissolution.
• To identify an optimized formulation with rapid disintegration and maximum drug release.

MATERIALS AND METHODS

Domperidone was obtained from a standard pharmaceutical supplier. Camphor (subliming agent), lactose, mannitol, microcrystalline cellulose, crospovidone, croscarmellose sodium, polyethylene glycol 4000, magnesium stearate, talc, and other excipients of analytical grade were used for the formulation of rapid dissolving tablets.

4. Methods

A. Preparation of Rapid Dissolving Tablets (RDTs): Rapid dissolving tablets of Domperidone were prepared using three different formulation techniques—sublimation, direct compression, and melt granulation—to study the influence of manufacturing method on tablet porosity, disintegration, and dissolution8.

B.Sublimation Method (SB1–SB3): Domperidone was blended with lactose, mannitol, superdisintegrants (crospovidone and croscarmellose sodium), and camphor as a volatile subliming agent. The powder blend was mixed uniformly and lubricated with magnesium stearate and talc. Tablets were compressed using a single-punch tablet press. The compressed tablets were then placed in a hot air oven at 60 °C for 4–5 hours to sublimate camphor, creating a porous tablet structure that promoted rapid water penetration and disintegration9.

C. Direct Compression Method (DC1–DC3): Domperidone was mixed with directly compressible excipients such as mannitol and microcrystalline cellulose along with varying concentrations of superdisintegrants. The powders were passed through sieve #40, blended thoroughly, and lubricated with magnesium stearate. Tablets were compressed directly using a tablet compression machine, with formulation differences mainly in superdisintegrant type and concentration10,11.

D. Melt Granulation Method (MG1–MG3): Polyethylene glycol 4000 was melted at 55–60 °C and Domperidone was incorporated into the molten mass. Excipients were added gradually with continuous mixing until uniform granules were formed. The granules were allowed to cool, passed through sieve #40, dried, lubricated, and compressed into tablets. This method produced dense granules, influencing disintegration behavior10,12.

E. Evaluation of Powder Blends: Powder blends were evaluated for angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio to assess flow and compressibility10.

F. Evaluation of Tablets: Tablets were evaluated for appearance, weight variation, thickness, hardness, and friability. Disintegration time was measured using a USP disintegration apparatus in distilled water at 37 ± 0.5 °C. Wetting time and water absorption ratio were determined to assess tablet hydration behavior. Drug content uniformity was analyzed spectrophotometrically after dissolving tablets in 0.1 N HCl11.

G. In-vitro Dissolution Study: Dissolution studies were carried out using USP Type II (paddle) apparatus at 50 rpm in 900 mL of 0.1 N HCl maintained at 37 ± 0.5 °C. Samples were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically. Percent cumulative drug release was calculated and compared among formulations and with a marketed tablet12.

4.3 Evaluation of Powder Blends

4.3.1 Flow Properties: The powder blends were evaluated for:
• Angle of repose (static funnel method)
• Bulk and tapped density
• Carr's compressibility index
• Hausner's ratio
These parameters predict compressibility and flow characteristics critical for uniform die filling during tablet compression.

4.4 Evaluation of Tablets

4.4.1 Physical Parameters: Tablets were inspected for appearance, weight variation, hardness (Monsanto hardness tester), thickness (Vernier caliper), and friability (Roche friabilator at 25 rpm for 4 minutes).

4.4.2 Disintegration and Wetting Time

Disintegration time was measured using a USP disintegration tester in distilled water at 37 ± 0.5 °C.

Wetting time was determined by placing a tablet on tissue paper soaked in eosin-coloured water, and the time for complete wetting was recorded. These parameters predict patient acceptability and in-mouth dispersion performance13,14.

4.4.3 Water Absorption Ratio: Water absorption ratio (R) was calculated using:

$R = (W_1 - W_0) / W_0 \times 100$

where W_0 is the tablet weight before wetting and W_1 after wetting. This reflects tablet's porosity and hydrophilicity14.

4.4.4 Drug Content: Drug content uniformity was evaluated spectrophotometrically after dissolving powdered tablets in 0.1N HCl and filtering. Measurements were taken at the λmax of Domperidone13.

4.4.5 In-vitro Dissolution Studies: Dissolution testing was performed using USP Type II (paddle) apparatus at 50 rpm in 900 mL of 0.1N HCl maintained at 37 ± 0.5 °C. Samples were withdrawn at predetermined intervals (5–45 minutes), filtered, and analyzed spectrophotometrically. Cumulative drug release was calculated and compared with a marketed Domperidone tablet15.

RESULTS

5.1 Precompression Evaluation

All powder blends exhibited satisfactory flow and compressibility characteristics, indicating their suitability for tablet compression. The angle of repose values ranged between 24° and 29°, suggesting good flow properties. Bulk and tapped density measurements were consistent across all formulations.

Carr's compressibility index values were found to be in the range of 11–16%, while Hausner's ratio varied between 1.12 and 1.18, confirming good packing ability and uniform die filling. Sublimation blends showed slightly lower bulk density due to the presence of camphor particles, which later contributed to increased tablet porosity after sublimation. Melt granulation blends demonstrated excellent flow behavior owing to the formation of smooth, dense granules by the molten binder.

5.2 Post-compression Evaluation

The post-compression results of SB2, DC2, and MG2 are shown in Table 1. All formulations met the pharmacopeial limits for hardness, friability, and drug content. However, noticeable differences were observed in disintegration-related parameters due to the variations in formulation techniques.

Table 1. Post-compression parameters of optimized batches (SB2, DC2, MG2)

S. No.	Parameter	SB2	DC2	MG2
1	Hardness (kg/cm²)	2.7	3.0	3.4
2	Friability (%)	0.62	0.51	0.48
3	Disintegration Time (sec)	17.2	26.4	44.3
4	Wetting Time (sec)	17.6	28.1	46.7
5	Water Absorption Ratio (%)	75.1	67.3	55.4
6	Drug Content (%)	99.8	98.4	97.2

• SB2 showed the fastest disintegration (17.2 sec) and shortest wetting time (17.6 sec) among all batches. This is because sublimation created a more porous tablet structure, allowing quicker water entry. SB2 also had the highest water absorption ratio (75.1%), supporting its superior wetting and disintegration behaviour.

• DC2 performed moderately, with acceptable hardness and friability, but slower disintegration compared to SB2 due to lower porosity.
• MG2 showed the slowest disintegration (44.3 sec) and lowest water absorption ratio, which can be linked to its denser granules formed during the melt granulation process.

Overall, SB2 performed best in terms of tablet breakup, water uptake, and drug content, making it the optimized formulation for rapid dissolving tablets.

5.3 Dissolution Studies: Following table 2 indicates drug release at 45 minutes and a line graph showing percent drug release vs. time, where SB2 demonstrates fastest and highest release (99.5% at 45 minutes), followed by DC2 (94.2%), marketed tablet (92%), and MG2 (85.6%).

Table 2. % Drug Release at 45 minutes

S. No.	Formulation	% Release
1	SB2	**99.5%**
2	DC2	94.2%

3	MG2	85.6%
4	Marketed Tablet	92.1%

SB2 exhibited significantly faster dissolution ($p < 0.05$), attributed to highly porous structure, faster water penetration, and enhanced solubility due to β-cyclodextrin complexation.

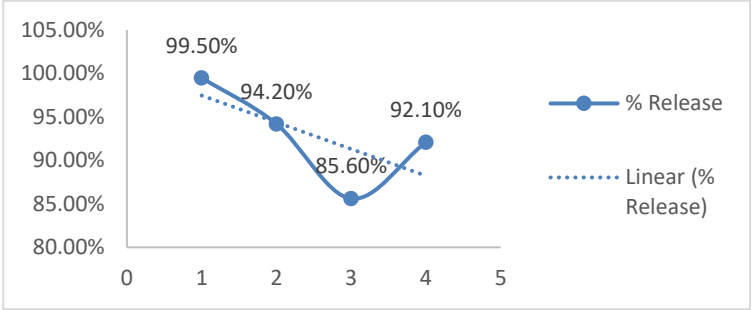

Figure 1: % Drug Release at 45 minutes

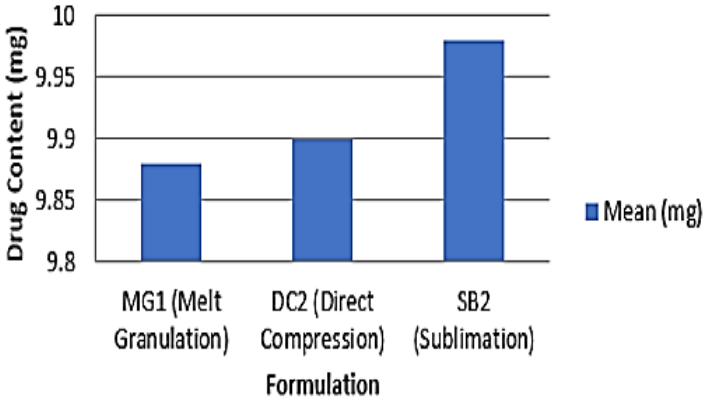

Figure 2: Drug content uniformity of tablets various formulations

5.4 Comparative Interpretation

• Sublimation > Direct Compression > Melt Granulation in terms of disintegration and dissolution enhancement.
• SB2 consistently outperformed other formulations across all evaluation parameters, making it the optimized batch.
• Melt granulation produced dense granules with lower porosity, explaining lower performance.
• Direct compression showed acceptable results but was inferior to the sublimation approach.

CONCLUSION

Rapid dissolving tablets of Domperidone were successfully formulated using sublimation, direct compression, and melt granulation techniques. Among all formulations, the sublimation-based batch SB2 showed the shortest disintegration time, highest water absorption, and maximum drug release due to its highly porous tablet structure. The study confirms that sublimation is an effective technique for developing Domperidone rapid dissolving tablets with enhanced disintegration and faster therapeutic action.

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Conflict of Interest

The authors declare no conflict of interest regarding the publication of this work.

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