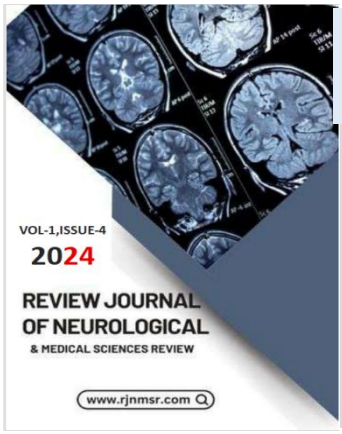

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Formulation Development And Evaluation Of Stable Rabeprazole Sodium Tablets

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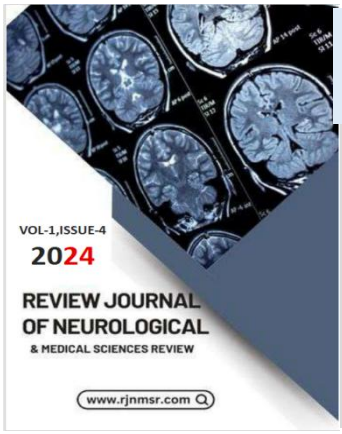
Abstract

Rabeprazole sodium, a proton pump inhibitor (PPI), is widely used to treat acid-related disorders such as gastroesophageal reflux disease (GERD) and peptic ulcers.



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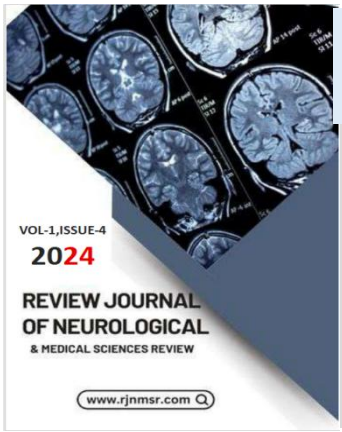
However, its poor stability in acidic environments and susceptibility to degradation present significant formulation challenges. The aim of this study was to develop and evaluate stable rabeprazole sodium tablets using different excipients and manufacturing techniques to optimize stability, dissolution, and overall tablet performance. Four formulations (F1, F2, F3, and F4) were prepared using direct compression (F1, F2) and wet granulation (F3, F4) techniques. Pre-formulation studies assessed powder flow properties, while post-compression evaluations included hardness, friability, weight variation, disintegration, and dissolution tests according to USP/BP standards. Stability testing was conducted under accelerated conditions (40°C ± 2°C / 75% ± 5% RH) for three months, with potency analysis using HPLC. Among all formulations, F1 (direct compression with zinc stearate) exhibited the most favorable properties, including optimal flowability (Carr's Index: 14.98%), rapid disintegration (4 min), high drug release (100.58% in 45 min), and excellent stability (98.90% drug retention after 3 months). Wet granulation formulations (F3, F4) showed higher hardness and lower dissolution rates, while formulations containing magnesium stearate (F2, F4) exhibited greater drug degradation over time. F1, prepared using direct compression with zinc stearate and magnesium oxide, proved to be the most stable and effective formulation, meeting all pharmacopeial standards for rabeprazole sodium tablets. This study highlights the advantages of direct compression in maintaining stability, improving dissolution, and ensuring ease of manufacturing, making it the preferred approach for commercial production. Future research could focus on coating technologies to further enhance drug protection and bioavailability.

Keywords: Rabeprazole sodium, direct compression, wet granulation, tablet stability, dissolution, formulation development.

Introduction

Rabeprazole sodium, a proton pump inhibitor (PPI), is widely used in the treatment of acid-related gastrointestinal disorders, including gastroesophageal reflux disease (GERD), duodenal ulcers, and Zollinger-Ellison syndrome (Bakheit et al., 2021). It functions by irreversibly inhibiting the H+/K+-ATPase enzyme in gastric parietal cells, leading to reduced acid secretion. However, rabeprazole sodium is highly unstable in acidic environments and susceptible to degradation due to hydrolysis, oxidation, and light exposure, which makes its formulation a significant challenge (Shen et al., 2020). Thus, the development of a stable and effective rabeprazole sodium tablet formulation requires careful selection of excipients and manufacturing techniques.

Solid oral dosage forms, particularly tablets, are the preferred method of drug delivery due to their ease of administration, precise dosing, and superior stability compared to liquid formulations (Sam et al., 2012). However, formulating a stable rabeprazole sodium tablet is complicated by its poor compressibility and sensitivity to moisture. The choice of formulation method plays a critical role in ensuring drug stability and bioavailability. Direct compression and wet granulation are the two most common techniques employed in tablet manufacturing. Direct compression offers advantages such as reduced processing steps and minimal exposure to



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moisture and heat, making it particularly suitable for moisture-sensitive drugs like rabeprazole sodium (Shangraw, 1989). In contrast, wet granulation enhances powder flowability and content uniformity but may expose the drug to conditions that accelerate degradation (Bandelin, 1989).

Excipients play a crucial role in the formulation of stable rabeprazole sodium tablets. Binders such as polyvinylpyrrolidone (PVP K-30) improve tablet integrity, while disintegrants like croscarmellose sodium enhance drug release (Kibbe, 2000). Lubricants, such as magnesium stearate and zinc stearate, influence tablet compression and stability. Studies have indicated that magnesium stearate may interact with rabeprazole sodium, leading to degradation, whereas zinc stearate provides better compatibility and stability (Rhee et al., 2008). Furthermore, the inclusion of alkalizing agents like magnesium oxide has been shown to enhance drug stability by creating a protective microenvironment around the active pharmaceutical ingredient (Ren et al., 2010).

To ensure formulation success, various quality control tests, including weight variation, hardness, friability, disintegration, and dissolution, must be performed in accordance with pharmacopeial standards (Patel et al., 2006). Additionally, accelerated stability testing under ICH guidelines is essential to predict the long-term stability of the developed formulation (Pokharana et al., 2018). Given the critical role of formulation techniques and excipients in determining the stability of rabeprazole sodium tablets, this study aims to develop and evaluate an optimized formulation using different excipients and manufacturing processes.

Materials and Methods

Materials

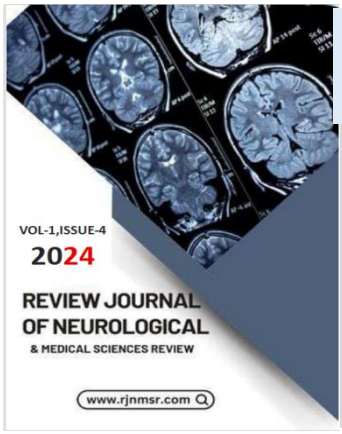
Rabeprazole sodium, the active pharmaceutical ingredient (API), was provided by Ferozsons Laboratories. Excipients used in the formulation included Avicel PH 112 (microcrystalline cellulose) as a filler, croscarmellose sodium as a superdisintegrant, zinc stearate and magnesium stearate as lubricants, talc and aerosil as glidants, magnesium oxide as an alkalizing agent, mannitol as a diluent, and PVP K-30 as a binder. Isopropyl alcohol (IPA) was used as a granulating solvent. All excipients were sourced from Usawa Pharmaceuticals and were of pharmacopeial grade (Kibbe, 2000).

Methods

Formulation of Rabeprazole Sodium Tablets

Four different formulations (F1, F2, F3, and F4) were prepared using direct compression and wet granulation techniques. The composition of each formulation varied based on the type of lubricant and excipient ratio to enhance stability and improve tablet properties (Patel et al., 2006).

Direct Compression (F1 & F2): The API and excipients were passed through a mesh (#20) sieve to ensure uniform particle size. Rabeprazole sodium was mixed with magnesium oxide and blended with other excipients in a double-cone mixer for 20 minutes. The final blend was compressed into tablets using a ZP-17 rotary tablet press with a 7.0 mm round bi-concave punch (Shangraw, 1989).



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Wet Granulation (F3 & F4): A binding solution of PVP K-30 in IPA was prepared and added to the dry mix of the API, mannitol, and primogel. The wet mass was granulated using a mesh (#10) sieve and dried in a tray dryer at 40–45°C. The dried granules were then blended with lubricants and compressed into tablets using the same rotary tablet press (Bandelin, 1989).

Pre-Formulation Studies

The flow properties of the powder blends were assessed using bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose (Muzzio et al., 2003). Drug-excipient compatibility was evaluated using Fourier-transform infrared (FTIR) spectroscopy by storing API-excipient mixtures at 40°C ± 2°C / 75% ± 5% RH for one month (Ren et al., 2010).

Evaluation of Tablet Properties

Post-compression quality control tests were performed as per USP and BP standards (Patel et al., 2006).

Weight Variation: Twenty tablets from each formulation were randomly selected, and individual weights were compared with the average weight.

Hardness & Friability: Hardness was measured using an ERWEKA TBH 125 hardness tester, and friability was assessed using an ERWEKA TA 100 friabilator at 25 rpm for 4 minutes.

Disintegration & Dissolution: Disintegration time was determined using a HOVERLABS disintegration apparatus in a simulated gastric fluid (pH 8.0). Dissolution studies were conducted using the USP Type II paddle method at 100 rpm in 900 ml of tris phosphate buffer at 37.0 ± 0.5°C, with drug release analyzed at 284 nm using a UV/Vis spectrophotometer (Cecil CE 7400) (Rhee et al., 2008).

Stability Studies

Accelerated stability testing was performed in accordance with ICH guidelines. Tablets were stored at 40°C ± 2°C / 75% ± 5% RH for three months, and samples were analyzed at 0, 1, 2, and 3 months for physical appearance, drug content, and dissolution using HPLC (Pokharana et al., 2018).

Results

The study evaluated the formulation and stability of rabeprazole sodium tablets using direct compression and wet granulation methods. The results include pre-formulation assessments, physicochemical characterization, dissolution testing, and stability analysis to determine the most suitable formulation.

Pre-Formulation Studies

Flow properties such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio were analyzed to assess the suitability of the powder blends for compression. The results are summarized in **Table 1**.

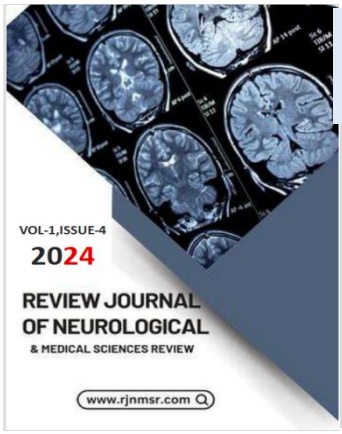

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Table 1. Flow Properties of Rabeprazole Sodium Powder Blends

Formulation	Angleof Repose (°)	BulkDensity (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner Ratio
F1	23.82	0.633	0.735	14.98	1.18
F2	23.62	0.631	0.739	15.77	1.19
F3	24.82	0.625	0.729	15.30	1.18
F4	24.91	0.630	0.724	15.99	1.16

F1 exhibited the best flowability, with the lowest Carr's index and Hausner ratio, indicating optimal compressibility for tablet formation.

Physicochemical Evaluation of Tablets

The hardness, friability, and disintegration time were assessed to ensure the mechanical integrity and rapid drug release of the tablets. **Table 2** presents the key physicochemical parameters.

Table 2. Hardness, Friability, and Disintegration Time of Rabeprazole Sodium Tablets

Formulation	Hardness (kg/cm²)	Friability (%)	Disintegration Time (min)
F1	4.52 ± 0.44	0.59	4
F2	4.84 ± 0.58	0.67	6
F3	5.86 ± 0.61	0.46	8
F4	5.94 ± 0.67	0.39	7

F1 exhibited an ideal balance of hardness and friability, ensuring durability while maintaining a rapid disintegration time.

Dissolution Studies

Dissolution tests were conducted using the **USP Type II paddle method**, and drug release was evaluated at **45 minutes**. The results are displayed in **Table 3**.

Table 3. Drug Release (%) at 45 Minutes

Formulation	Drug Release (%)
F1	100.58
F2	97.59
F3	87.99
F4	87.85

F1 demonstrated the highest drug release, meeting the USP requirement of **≥75% dissolution in 45 minutes**, confirming its superior bioavailability.

Stability Studies

Accelerated stability testing was conducted at **40°C ± 2°C / 75% ± 5% RH** over three months. **Table 4** summarizes the drug retention percentage over time.

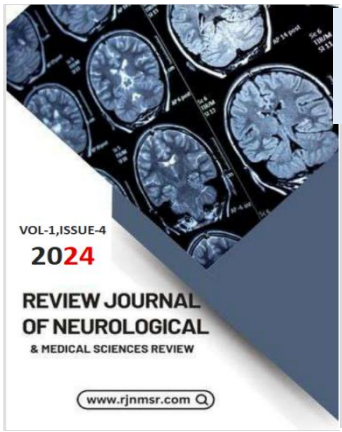

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Table 4. Drug Stability Over 3 Months (HPLC Analysis)

Formulation	Initial (%)	1 Month (%)	2 Months (%)	3 Months (%)
F1	100.00	99.85	99.52	98.90
F2	100.00	98.42	97.18	95.95
F3	100.00	96.80	94.75	92.50
F4	100.00	97.10	95.23	93.05

F1 retained **98.90%** potency after three months, making it the most stable formulation.

Discussion

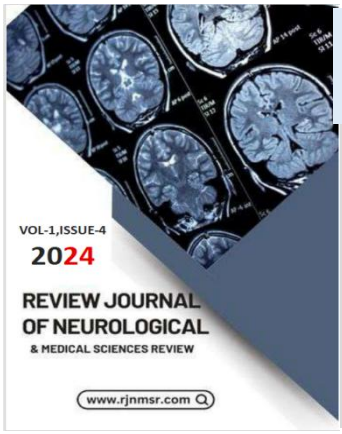
The development of a stable rabeprazole sodium tablet formulation requires careful selection of excipients and manufacturing techniques to ensure optimal flowability, mechanical integrity, dissolution, and long-term stability. The results of this study indicate that formulation F1, prepared using the direct compression method with zinc stearate as a lubricant, demonstrated superior properties compared to the other formulations.

Pre-formulation studies showed that F1 exhibited the best flow characteristics, with the lowest Carr's index (14.98%) and Hausner ratio (1.18), indicating excellent compressibility and minimal powder aggregation (Hickey & Giovagnoli, 2018). In contrast, the wet granulation formulations (F3 and F4) had slightly lower flowability, likely due to the presence of moisture in granules, which can lead to inter-particle adhesion (Muzzio et al., 2003). These findings align with previous research showing that direct compression enhances powder flow properties and simplifies manufacturing by reducing processing steps (Shangraw, 1989).

Physicochemical evaluations confirmed that all formulations met pharmacopeial standards, but F1 exhibited the most balanced mechanical properties. It had a hardness of 4.52 kg/cm², ensuring sufficient strength while maintaining a friability of 0.59%, well below the 1% USP limit (Chaturvedi et al., 2017). Wet granulation formulations (F3, F4) had higher hardness values, which may have contributed to prolonged disintegration times (Patel et al., 2006). The 4-minute disintegration time of F1 was significantly faster than the wet granulation formulations (7–8 minutes), indicating that the direct compression method allows for quicker tablet breakdown and drug release (Kibbe, 2000).

Dissolution studies further highlighted the advantages of F1, which achieved 100.58% drug release within 45 minutes, exceeding the USP requirement of ≥75% (Rhee et al., 2008). The rapid dissolution of F1 suggests that zinc stearate, as a lubricant, did not interfere with drug release, unlike magnesium stearate, which has been reported to reduce wetting and slow down dissolution (Babu et al., 2014). The wet granulation formulations (F3 and F4) exhibited slower dissolution rates, possibly due to stronger tablet compaction, which hindered water penetration (Surekha et al., 2013).

The stability studies revealed that F1 maintained 98.90% drug potency after three months, while F2, F3, and F4 exhibited significant degradation, particularly in



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formulations containing magnesium stearate. This aligns with literature findings that magnesium stearate can react with rabeprazole sodium, accelerating its degradation (Ren et al., 2010). The inclusion of magnesium oxide in F1 likely contributed to its stability by creating a local alkaline environment, protecting rabeprazole sodium from acid-mediated degradation (Shen et al., 2020).

Overall, these results suggest that direct compression using zinc stearate is the optimal formulation approach for rabeprazole sodium tablets. It offers advantages in ease of manufacturing, improved disintegration, faster drug release, and enhanced stability, making it suitable for commercial production. Future studies could explore coating technologies to further enhance the formulation's stability and bioavailability (Pokharana et al., 2018).

Conclusion

F1 (Direct Compression with Zinc Stearate) exhibited the best flowability, hardness, disintegration, dissolution, and stability. It is the optimal formulation for developing stable rabeprazole sodium tablets.

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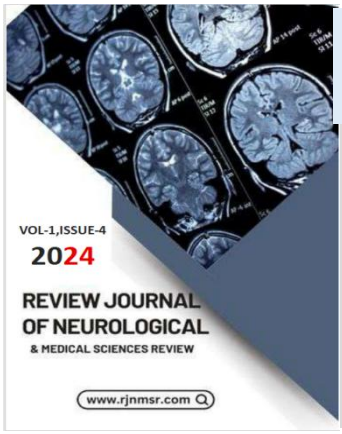

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