FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF AN ANTI-PARKINSON DRUG

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Abstract

The present study focused on the formulation and evaluation of sustained release matrix tablets of Selegiline using HPMC K15M as a hydrophilic polymer by the wet granulation method. Pre-formulation studies confirmed the suitability and stability of the drug for sustained release formulation development. Powder blends showed good flowability and compressibility, while all prepared tablets complied with pharmacopoeial limits for physical evaluation parameters such as hardness, friability, weight variation, and thickness. In-vitro drug release studies demonstrated sustained release of Selegiline over 12 hours, with polymer concentration effectively controlling drug release. Among all formulations, F4 showed the most satisfactory sustained release profile comparable to the marketed formulation. Stability studies confirmed that the optimized formulation remained stable under accelerated conditions. Overall, the study concluded that Selegiline sustained release matrix tablets can be successfully developed using HPMC to achieve prolonged drug release and improved therapeutic efficacy in Parkinson's disease management.

Keywords: *Selegiline; Sustained Release Matrix Tablets; HPMC K15M; Wet Granulation; Controlled Drug Release; Parkinson's Disease.*

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1. Introduction

Parkinson's disease is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra of the brain, leading to symptoms such as tremors, rigidity, bradykinesia, and postural instability (Katzung, 2021). It is one of the most common neurological disorders affecting elderly individuals and significantly impacts quality of life. The treatment of Parkinson's disease primarily focuses on restoring dopaminergic activity in the brain through anti-Parkinson drugs that improve motor function and reduce disease-associated complications (Rang et al., 2019).

Selegiline is a selective monoamine oxidase-B (MAO-B) inhibitor widely used in the management of Parkinson's disease. It acts by inhibiting the enzymatic breakdown of dopamine, thereby prolonging dopaminergic activity and improving symptomatic control (Brunton et al., 2018). However, conventional oral dosage forms of Selegiline require frequent administration due to its short biological half-life and extensive first-pass metabolism, resulting in fluctuating plasma drug levels and reduced patient compliance. Hence, the development of a sustained release dosage form is beneficial for maintaining therapeutic drug concentrations over an extended period while minimizing dosing frequency and side effects (Vyas & Khar, 2012).

Sustained release matrix tablets are among the most widely used controlled drug delivery systems because of their simplicity, ease of manufacturing, cost-effectiveness, and ability to provide prolonged drug release (Aulton & Taylor, 2018). In matrix systems, the drug is dispersed within a polymeric network that controls drug release through diffusion, swelling, and erosion mechanisms. Hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC) are extensively used in sustained release formulations due to their excellent swelling and gel-forming properties (Lachman et al., 2013). Upon contact with gastrointestinal fluids, HPMC hydrates rapidly to form a viscous gel layer around the tablet, which effectively controls drug diffusion and release (Colombo et al., 2000).

The present study was undertaken to formulate and evaluate sustained release matrix tablets of Selegiline using HPMC K15M as the matrix-forming polymer by the wet granulation method. The formulation was designed to achieve prolonged drug release, improve therapeutic efficacy, and enhance patient compliance in the management of Parkinson's disease. Various formulations with different drug–polymer ratios were prepared and evaluated for pre-compression parameters, post-compression characteristics, swelling

behavior, in-vitro drug release, and stability studies to identify the optimized sustained release formulation (Siepmann & Peppas, 2012).

2. Methodology

2.1 Procurement and Authentication of Materials

Selegiline and required excipients were procured from reliable, certified suppliers to ensure quality and purity. Hydrophilic polymers like HPMC and other pharmaceutical-grade materials were authenticated through physical evaluation and standard tests. Drug purity was confirmed using UV spectrophotometry, and all materials complied with IP, USP, and BP specifications before use.

2.2 Pre-Formulation Studies

Pre-formulation studies were conducted to assess the physicochemical properties of the drug, including solubility, stability, and compatibility. These evaluations provide essential information for selecting suitable excipients and formulation methods, ensuring the stability, efficacy, and performance of the final dosage form.

2.2.1 Physicochemical Characterization of Drug

Physicochemical characterization of the drug was carried out to evaluate key properties such as melting point, solubility, partition coefficient, and moisture content. These parameters help understand the drug's nature and its influence on formulation and development.

2.2.1.1 Melting point determination

The melting point of Selegiline was determined using the capillary method to assess its purity and identity. A powdered sample was heated in a melting point apparatus, and the temperature range from initial melting to complete liquefaction was recorded. The test was performed in triplicate, and the average value was compared with reported data to confirm purity and suitability for formulation.

2.2.1.2 Solubility studies

Solubility studies of Selegiline were performed by adding excess drug to different solvents and buffer systems, followed by shaking until equilibrium was achieved. The solutions were filtered, suitably diluted, and analyzed using UV–Visible spectrophotometry. The solubility data helped in understanding the drug's dissolution behavior and supported the selection of appropriate formulation strategies and excipients.

2.2.1.3 Partition coefficient

The partition coefficient of Selegiline was determined using the shake-flask method with n-octanol and water to evaluate its lipophilicity. After equilibration and phase separation, the drug concentration in the aqueous phase was analyzed by UV–Visible spectrophotometry,

and the organic phase concentration was calculated. The partition coefficient was obtained as the ratio of concentrations in n-octanol and water, providing insight into the drug's hydrophilic–lipophilic balance for formulation design.

2.2.1.4 Moisture content

The moisture content of Selegiline was determined by the loss on drying (LOD) method to assess water content, which may affect stability and compressibility. A known quantity of drug was dried in a hot air oven at 105 °C until constant weight, cooled in a desiccator, and reweighed. The loss in weight was used to calculate percentage moisture content. This parameter ensures drug stability and suitability for formulation development.

2.3 Flow Properties of Powder Blend

The flow properties of the powder blend were evaluated prior to compression to ensure uniform die filling and consistent tablet quality. Parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio were determined to assess flow behavior and compressibility.

2.3.1 Angle of repose

The angle of repose is used to evaluate powder flow properties before compression, influencing die filling and tablet quality. It reflects interparticle friction and flowability. It was determined by the fixed funnel method, where powder forms a cone and the angle is calculated using $\theta = \tan^{-1}(h/r)$. Lower values indicate good flow, while higher values suggest poor flow.

2.3.2 Bulk density

Bulk density is a key parameter used to assess the packing ability and flow behavior of a powder blend. It is defined as the ratio of the mass of powder to its bulk volume before tapping and reflects how particles are arranged in the powder bed. It was determined by weighing a known quantity of powder and transferring it into a graduated cylinder without tapping, followed by recording the initial volume. Bulk density was calculated using the formula:

$$\text{Bulk Density} = \text{Weight of powder} / \text{Bulk volume.}$$

This parameter helps in evaluating powder compressibility and supports further flow property studies such as Carr's index and Hausner ratio.

2.3.3 Tapped density

Tapped density is used to evaluate the packing ability and compressibility of a powder blend after mechanical tapping. It is defined as the ratio of powder mass to the volume occupied after tapping and reflects particle consolidation behavior. It was determined by placing a

known quantity of powder in a graduated cylinder and tapping it mechanically until a constant volume was obtained. The final volume was recorded, and tapped density was calculated using the formula:

Tapped Density = Weight of powder / Tapped volume.

This parameter helps assess packing efficiency and is used for calculating Carr's index and Hausner ratio to evaluate flow properties.

2.3.4 Carr's index

Carr's Index, also known as compressibility index, is used to evaluate the flowability and compressibility of a powder blend based on bulk and tapped density values. It reflects interparticle interactions and packing behavior, which influence tablet compression. It was calculated using the formula:

Carr's Index (%) = [(Tapped density – Bulk density) / Tapped density] × 100.

Lower values indicate good flow properties, while higher values suggest poor flow due to increased cohesiveness, helping determine suitability of the powder blend for tablet formulation.

2.3.5 Hausner ratio

Hausner ratio is used to assess the flow properties and cohesiveness of a powder blend based on bulk and tapped density. It indicates how easily the powder flows during tablet compression. It was calculated using the formula:

Hausner Ratio = Tapped density / Bulk density.

Values close to 1 indicate good flow, while higher values indicate poor flow due to increased interparticle friction. Generally, a value below 1.25 suggests acceptable flow for tablet formulation.

2.4 Formulation Development

Formulation development was carried out to prepare sustained release matrix tablets of Selegiline aimed at achieving prolonged drug release and maintaining therapeutic levels over an extended period. It involved selection of suitable polymers and excipients, optimization of formulation variables, and preparation of tablets using an appropriate method to ensure desired physical properties and controlled release behavior.

2.4.1 Selection of Polymer and Excipients

Suitable polymers and excipients were selected to control drug release and ensure formulation stability. HPMC was used as the matrix-forming polymer due to its swelling and gel-forming properties, which help regulate sustained drug release. Diluents like MCC or lactose increased bulk, PVP K30 acted as a binder, magnesium stearate served as a lubricant,

and talc improved flow. All excipients were pharmaceutically compatible with Selegiline, ensuring a stable and effective sustained release formulation.

2.4.2 Preparation of Sustained Release Matrix Tablets

Sustained release matrix tablets of Selegiline were formulated to provide controlled and prolonged drug release. A hydrophilic matrix system using HPMC was selected due to its swelling and gel-forming properties, which regulate drug diffusion. The tablets were prepared by wet granulation to improve flow, compressibility, and uniform drug distribution within the formulation.

2.4.3 Preparation of Hydrophilic Matrix Tablets using HPMC

Selegiline sustained release matrix tablets were prepared by the wet granulation method using HPMC as the matrix-forming polymer. Accurately weighed drug, polymer, and excipients were sieved and mixed uniformly, followed by granulation using PVP K30 solution. The wet mass was sieved, dried, and re-sieved to obtain uniform granules. Lubricants and glidants were then added, and the blend was compressed into tablets using a tablet compression machine to obtain sustained release matrix tablets.

Table 1: Formulation of Selegiline Sustained Release Matrix Tablets

Formulation	Selegiline (mg)	HPMC K15M (mg)	Microcrystalline Cellulose (mg)	Lactose Monohydrate (mg)	PVP K30 (% w/v in binder)	Magnesium Stearate (mg)	Talc (mg)	Total Weight (mg)
F1	10	50	70	30	5	3	2	170
F2	10	60	65	30	5	3	2	175
F3	10	70	60	30	5	3	2	180
F4	10	80	55	30	5	3	2	185
F5	10	90	50	30	5	3	2	190
F6	10	100	45	30	5	3	2	195
F7	10	110	40	30	5	3	2	200
F8	10	120	35	30	5	3	2	205
F9	10	130	30	30	5	3	2	210
F10	10	140	25	30	5	3	2	215

2.5 Optimization of Formulation Parameters

Optimization of formulation parameters is a key step in developing sustained release matrix tablets to achieve desired physical properties and controlled drug release. Variables such as

drug–polymer ratio, compression force, and tablet weight were systematically evaluated and adjusted to obtain an optimal formulation with suitable tablet characteristics and sustained release behavior.

2.5.1 Drug–polymer ratio

The drug–polymer ratio is crucial in sustained release matrix tablets as it controls drug diffusion through a gel barrier. Selegiline and HPMC were used in varying ratios (F1–F10), while other excipients remained constant. The formulations were prepared by wet granulation, evaluated, and subjected to in-vitro release studies. Lower polymer levels resulted in faster release, whereas higher levels slowed release due to a thicker gel layer. The optimum ratio was selected based on balanced drug release and acceptable tablet properties.

2.5.2 Compression force

Compression force is a key parameter affecting tablet strength, porosity, and drug release. Selegiline granules were compressed at varying forces and evaluated for hardness, friability, weight variation, thickness, and drug release. Lower forces produced softer, fragile tablets, while higher forces increased hardness but slowed drug release due to reduced porosity. An optimum force was selected to achieve balanced mechanical strength and sustained release.

2.5.3 Tablet size and weight

Tablet size and weight are critical for ensuring uniformity, compressibility, and consistent drug release. Selegiline tablets were prepared using fixed punches to maintain size, and composition was adjusted for uniform weight. Post-compression evaluation confirmed minimal variation. Consistency in these parameters ensures uniform drug content and predictable release, making them essential for effective sustained release formulations.

2.5.4 Method of preparation (wet granulation)

The wet granulation method was used to improve flow, compressibility, and content uniformity for sustained release matrix tablets of Selegiline. The drug, HPMC, and diluents were sieved and mixed uniformly, followed by addition of PVP K30 binder solution to form a damp mass. This mass was sieved, dried, and re-sieved to obtain uniform granules, which were then blended with lubricants and glidants before compression into tablets using a rotary tablet press. Proper granulation and drying ensured uniform particle size, good mechanical strength, and consistent sustained release performance across batches.

2.6 Evaluation of Prepared Tablets

2.6.1 Physical Evaluation

2.6.1.1 Weight variation

Weight variation is a key quality control test used to ensure uniformity of tablet weight within a batch, indirectly confirming consistent drug content and formulation quality. For Selegiline sustained release tablets, 20 tablets were randomly selected, individually weighed, and compared with the average weight to determine deviation. The results were evaluated against pharmacopoeial limits based on tablet weight categories. Compliance within acceptable limits confirms uniform granule distribution, proper mixing, and consistent compression, ensuring reliable therapeutic performance and batch-to-batch reproducibility.

2.6.1.2 Thickness and diameter

Tablet thickness and diameter are important physical parameters that ensure uniformity, mechanical strength, and consistent drug release. For Selegiline sustained release tablets, 10 tablets were randomly selected and their thickness and diameter were measured using a vernier caliper. The average values were calculated and compared to individual readings to assess uniformity. Consistent dimensions indicate proper die filling and compression, while variations may reflect processing issues such as poor flow or uneven granule distribution, making these parameters essential for quality control and reproducibility.

2.6.1.3 Hardness

Tablet hardness (crushing strength) was evaluated to assess the mechanical integrity of Selegiline sustained release tablets Ten tablets were randomly selected and measured using a Monsanto hardness tester, and the force required to break each tablet was recorded. The average hardness was calculated and assessed against the desired range. Adequate hardness ensures resistance to handling and transportation while maintaining appropriate drug release. It is influenced by compression force, binder level, and granule properties, making it an important quality control parameter for ensuring consistency and reproducibility of the formulation.

2.6.1.4 Friability

Friability was evaluated to determine the mechanical strength of Selegiline sustained release tablets and their resistance to abrasion during handling and transport. Twenty tablets were weighed (W_1), subjected to 100 revolutions in a friabilator at 25 rpm for 4 minutes, then de-dusted and reweighed (W_2). Friability was calculated using the standard formula. Values below 1% indicate acceptable mechanical stability, while higher values suggest poor binding or inadequate compression. Low friability ensures tablet integrity and uniform drug content throughout handling and use.

2.6.1.5 Swelling Index Study

The swelling index study was performed to evaluate the water uptake and swelling behavior of Selegiline sustained release matrix tablets. Tablets were weighed (W_1) and immersed in phosphate buffer pH 6.8 at 37 ± 0.5°C. At specific time intervals, tablets were removed, blotted, and reweighed (W_2). The swelling index was calculated using the standard formula. This study helps assess gel formation by HPMC, which controls drug release. Swelling behavior depends on polymer concentration and formulation composition, ensuring effective sustained release while maintaining tablet integrity.

2.7 In-Vitro Drug Release Studies

In-vitro drug release studies were conducted to evaluate Selegiline release from sustained release matrix tablets using a USP Type II (paddle) apparatus in phosphate buffer pH 6.8 at 37 ± 0.5°C. Samples were withdrawn at fixed intervals, analyzed by UV spectrophotometry, and replaced with fresh medium to maintain sink conditions. The release profiles of formulations (F1–F10) were compared to identify the optimized batch and understand release kinetics.

2.8 Stability Studies as per ICH guidelines

Stability studies were conducted to assess the effect of temperature, humidity, and light on the physical, chemical, and drug release properties of Selegiline sustained release matrix tablets, in accordance with International Council for Harmonisation Q1A (R2) guidelines. The optimized formulation was stored under accelerated (40 ± 2°C/75 ± 5% RH) and long-term (25 ± 2°C/60 ± 5% RH) conditions. At specified intervals, tablets were evaluated for appearance, hardness, friability, thickness, weight variation, drug content, and in-vitro drug release. The studies confirmed stability in terms of mechanical strength, drug content, and sustained release behavior, supporting the product's shelf-life, safety, and therapeutic efficacy.

3. Results

3.1 Pre-Formulation Studies

3.1.1 Physicochemical Characterization of Drug

3.1.1.1 Melting point determination

The melting point of Selegiline was determined to evaluate its purity and identity. It was found to be 124–126 °C, closely matching reported literature values. The narrow range indicates good purity and crystalline nature, with minimal impurities. This confirms the authenticity and suitability of the drug for the development of sustained release matrix tablets.

Table 2: Melting point

Crude Drug	Melting Point (°C)
Selegiline	124–126

3.1.1.2 Solubility studies

The solubility of Selegiline was evaluated in various solvents to support formulation development. It showed low solubility in distilled water (0.5 mg/mL), indicating poor aqueous solubility, while exhibiting high solubility in methanol (12.0 mg/mL) and ethanol (10.5 mg/mL). In phosphate buffers, moderate solubility was observed (0.8 mg/mL at pH 6.8 and 1.0 mg/mL at pH 7.4). Based on these results, phosphate buffer pH 6.8 was selected as the dissolution medium for in-vitro drug release studies.

Table 3: Solubility of Selegiline in Various Solvents

S. No.	Solvent	Solubility (mg/mL)	Solubility Description
1	Distilled Water	0.5	Sparingly soluble
2	Methanol	12.0	Freely soluble
3	Ethanol	10.5	Soluble
4	Phosphate Buffer pH 6.8	0.8	Slightly soluble
5	Phosphate Buffer pH 7.4	1.0	Slightly soluble

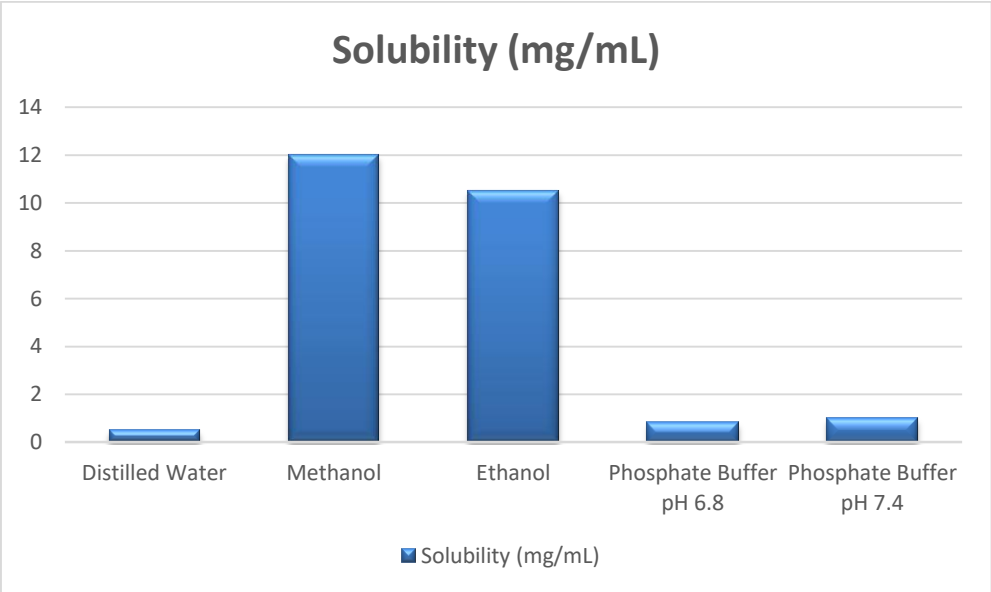

Fig 1: Solubility

3.1.1.3 Partition coefficient

The partition coefficient of Selegiline was determined using an n-octanol/water system to assess its lipophilicity. The obtained value (P = 12.11) indicates a strong affinity for the organic phase, confirming its lipophilic nature. This property supports its ability to permeate biological membranes and makes it suitable for sustained release matrix formulations, enabling gradual drug diffusion and effective absorption.

Table 4: Partition Coefficient of Selegiline

Drug	Solvent System	Partition Coefficient (P)
Selegiline	n-Octanol / Water	12.11

3.1.1.4 Moisture content

The moisture content of Selegiline was determined by the loss on drying (LOD) method and found to be 0.77%, indicating low water content. This low moisture level supports good stability, flow, and compressibility, making the drug suitable for formulation. Hence, Selegiline is appropriate for the development of sustained release matrix tablets without significant risk of moisture-related issues.

Table 5: Moisture Content of Selegiline

Sample	Moisture Content (%)	Remarks
Selegiline	0.77	Low, suitable for formulation

3.2 Flow Properties of Powder Blend

3.2.1 Angle of repose

The angle of repose was evaluated to assess the flow properties of Selegiline powder blends. Values for formulations F1–F10 ranged from 27.5° to 28.3°, indicating good flowability (below 30°). This ensures uniform die filling, consistent tablet weight, and proper drug distribution. The results were comparable to the marketed tablet (27.9° ± 0.11), confirming that the blends were suitable for tablet compression and efficient manufacturing.

Table 6: Angle of Repose of Selegiline Powder Blends (F1–F10)

Formulation / Sample	Angle of Repose (°)
F1	27.5 ± 0.12

F2	28.0 ± 0.15
F3	27.8 ± 0.10
F4	28.2 ± 0.14
F5	27.9 ± 0.11
F6	28.1 ± 0.13
F7	27.6 ± 0.09
F8	28.3 ± 0.16
F9	27.7 ± 0.10
F10	28.0 ± 0.12
Marketed Tablet	27.9 ± 0.11

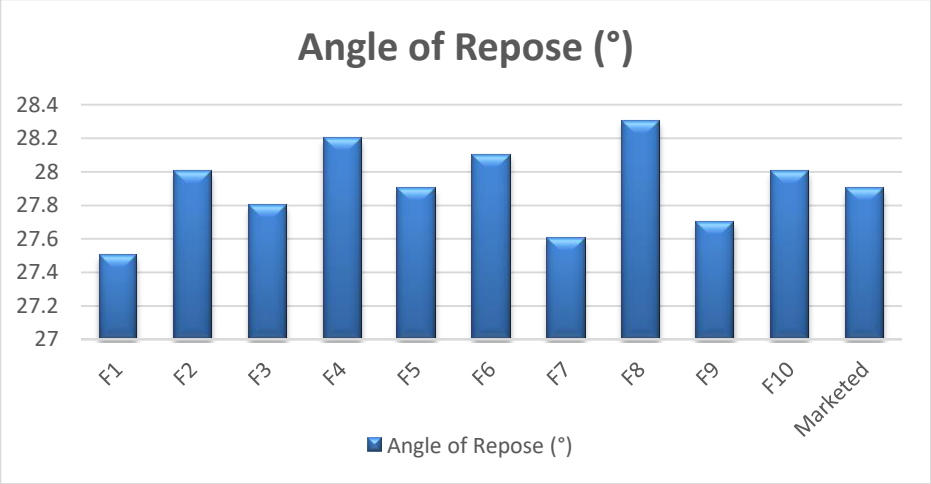

Fig 2: Angle of Repose (°)

3.2.2 Bulk density

The bulk density of Selegiline powder blends was evaluated to assess packing and flow properties before compression. Values for formulations F1–F10 ranged from 0.47 to 0.50 g/mL, indicating uniform packing and good flow behavior. The consistency among formulations suggests similar particle size distribution, and the values were comparable to the marketed tablet (0.49 ± 0.01 g/mL). Overall, the blends showed suitable properties for tablet compression.

Table 7: Bulk Density of Selegiline Powder Blends (F1–F10)

Formulation	Bulk Density (g/mL)
F1	0.48 ± 0.01
F2	0.49 ± 0.01
F3	0.47 ± 0.01

F4	0.50 ± 0.01
F5	0.48 ± 0.01
F6	0.49 ± 0.01
F7	0.47 ± 0.01
F8	0.50 ± 0.01
F9	0.48 ± 0.01
F10	0.49 ± 0.01
Marketed Tablet	0.49 ± 0.01

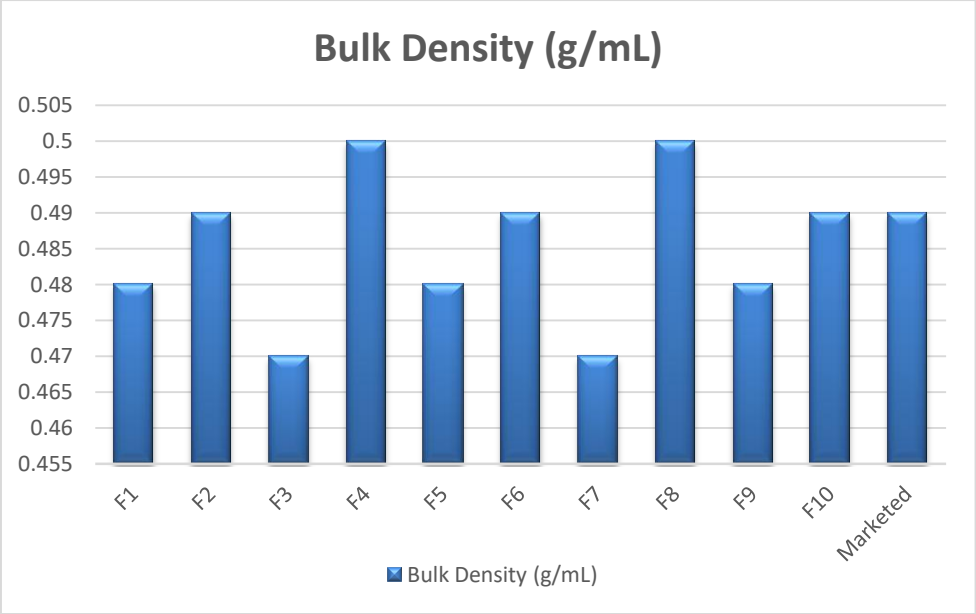

Fig 3: Bulk Density (g/mL)

3.2.3 Tapped density

The tapped density of Selegiline powder blends was evaluated to assess packing and compressibility before compression. Values for formulations F1–F10 ranged from 0.55 to 0.58 g/mL, indicating moderate packing ability. The uniformity across formulations suggests consistent particle size and consolidation behavior. These values were comparable to the marketed tablet (0.57 ± 0.01 g/mL), confirming suitability for tablet compression.

Table 8: Tapped Density of Selegiline Powder Blends (F1–F10) Compared with Marketed Tablet

Formulation	Tapped Density (g/mL)
F1	0.56 ± 0.01
F2	0.57 ± 0.01
F3	0.55 ± 0.01

F4	0.58 ± 0.01
F5	0.56 ± 0.01
F6	0.57 ± 0.01
F7	0.55 ± 0.01
F8	0.58 ± 0.01
F9	0.56 ± 0.01
F10	0.57 ± 0.01
Marketed Tablet	0.57 ± 0.01

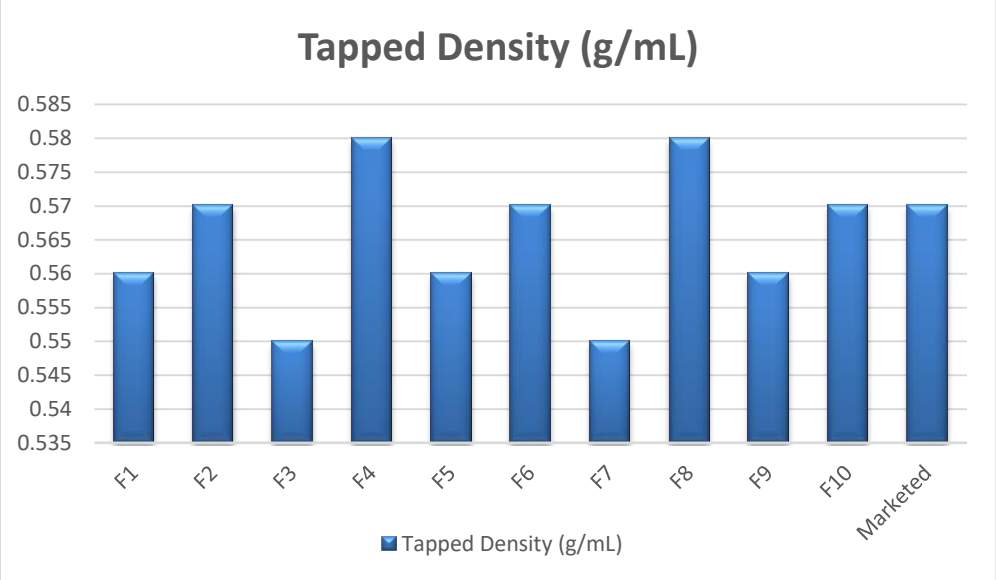

Fig 4: Tapped Density (g/mL)

3.2.4 Carr's index

Carr's index of Selegiline powder blends was evaluated to assess compressibility and flow properties. Values for formulations F1–F10 ranged from 13.8% to 14.6%, indicating good flowability. The uniform results suggest consistent compressibility and packing behavior, essential for efficient tablet compression. These values were comparable to the marketed tablet (14.1 ± 0.4%), confirming suitability for sustained release matrix tablet formulation.

Table 9: Carr's Index of Selegiline Powder Blends (F1–F10) Compared with Marketed Tablet

Formulation	Carr's Index (%)
F1	14.3 ± 0.5
F2	14.0 ± 0.4
F3	14.5 ± 0.5

F4	13.8 ± 0.4
F5	14.2 ± 0.5
F6	14.1 ± 0.4
F7	14.6 ± 0.5
F8	13.9 ± 0.4
F9	14.2 ± 0.4
F10	14.0 ± 0.4
Marketed Tablet	14.1 ± 0.4

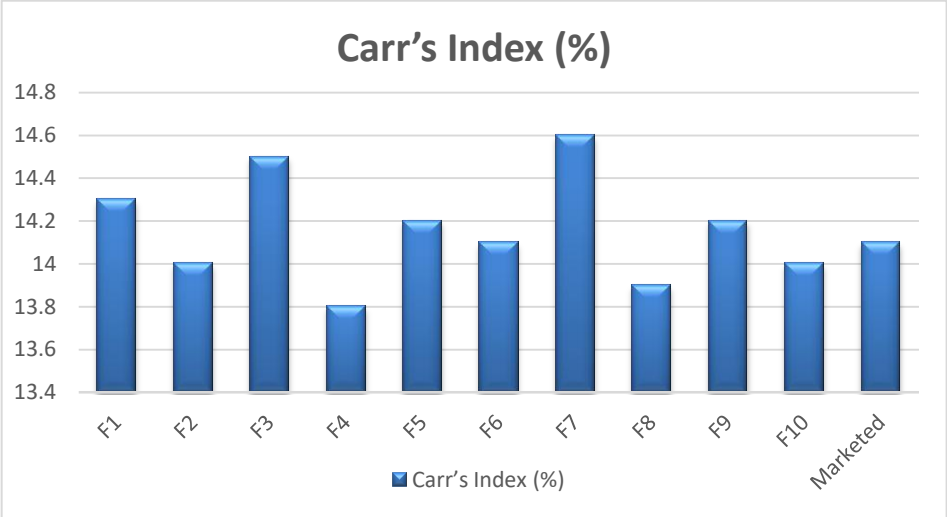

Fig 5: Carr's Index (%)

3.2.5 Hausner ratio

The Hausner ratio of Selegiline powder blends was evaluated to assess flow and cohesiveness. Values for formulations F1–F10 ranged from 1.16 to 1.17, indicating good flowability (less than 1.25). The results suggest low cohesiveness and efficient die filling. These values were comparable to the marketed tablet (1.16 ± 0.01), confirming suitability for tablet compression and sustained release formulation.

Table 10: Hausner Ratio of Selegiline Powder Blends (F1–F10) Compared with Marketed Tablet

Formulation	Hausner Ratio	Flow Property
F1	1.16 ± 0.01	Good
F2	1.16 ± 0.01	Good
F3	1.17 ± 0.01	Good
F4	1.16 ± 0.01	Good
F5	1.17 ± 0.01	Good
F6	1.16 ± 0.01	Good
F7	1.17 ± 0.01	Good

F8	1.16 ± 0.01	Good
F9	1.17 ± 0.01	Good
F10	1.16 ± 0.01	Good
Marketed Tablet	1.16 ± 0.01	Good

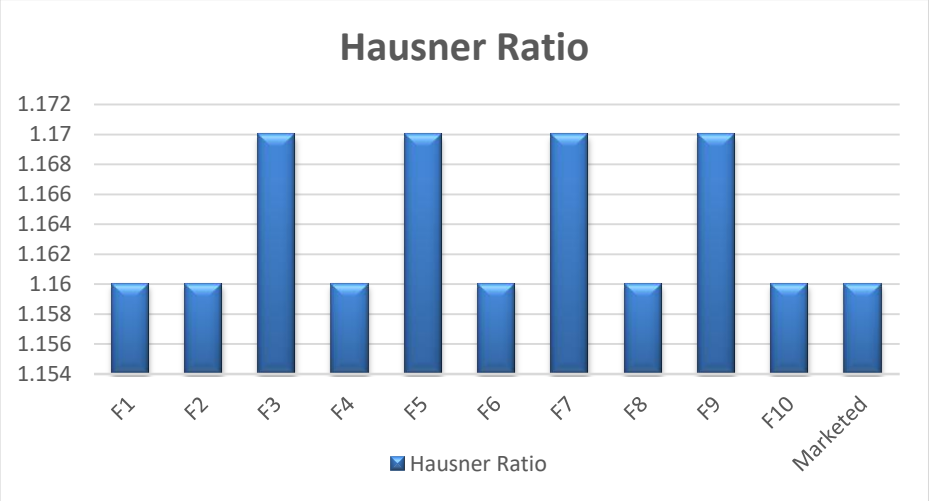

Fig 6: Hausner Ratio

3.3 Optimization of Formulation Parameters

3.3.1 Drug–polymer ratio

The effect of drug–polymer ratio on Selegiline release was studied using formulations F1–F10 with varying HPMC concentrations. Drug release after 12 hours ranged from 64.5% to 92.5%, showing a strong influence of polymer content. Lower polymer levels (F1–F2) resulted in faster release due to a thinner gel layer, while higher concentrations (F3–F10) progressively slowed release by forming a thicker, more viscous barrier. Formulation F9 exhibited an optimal sustained release profile. Overall, increasing polymer concentration effectively retarded drug release, highlighting its key role in controlling release kinetics.

Table 11: Effect of Drug–Polymer Ratio on Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	Drug:Polymer Ratio	Cumulative % Drug Release at 12 h	Remarks / Release Profile
F1	1:0.5	92.5 ± 1.2	Faster release, thin gel layer
F2	1:0.75	88.7 ± 1.3	Slightly slower release
F3	1:1	85.2 ± 1.1	Controlled release begins

F4	1:1.25	81.5 ± 1.0	Sustained release improving
F5	1:1.5	78.0 ± 1.2	Better sustained release
F6	1:1.75	75.3 ± 1.1	Prolonged drug release
F7	1:2	72.0 ± 1.0	Slower release, thicker gel
F8	1:2.25	69.5 ± 1.2	Further sustained release
F9	1:2.5	66.8 ± 1.1	Optimal sustained release
F10	1:2.75	64.5 ± 1.0	Very slow release, maximum gel effect

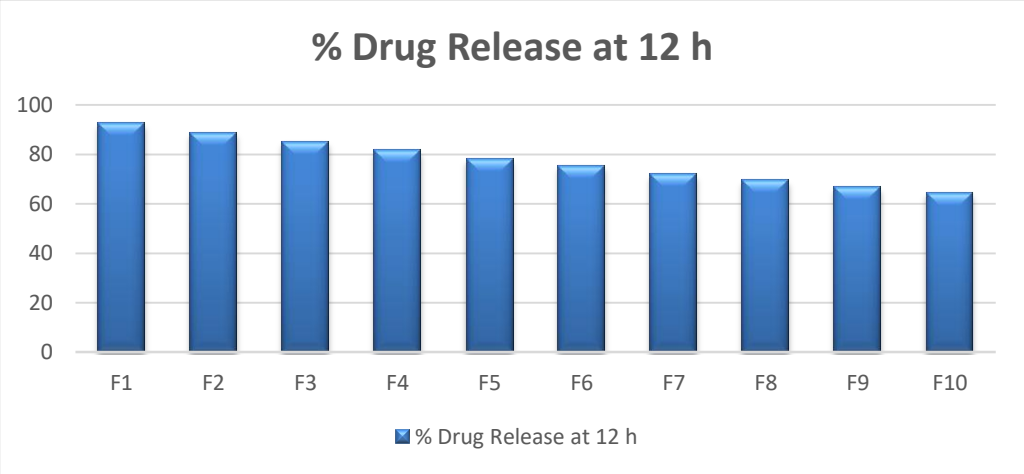

Fig 7: % Drug Release at 12 h

3.3.2 Compression force

The effect of compression force (4–13 kN) on Selegiline matrix tablets showed a significant impact on hardness, friability, and drug release. Lower force (4 kN) produced weak tablets with low hardness and high friability, while moderate force (5–8 kN) improved mechanical strength and reduced friability. Higher forces (9–13 kN) further increased hardness but slowed drug release due to reduced porosity. Formulation F5 (8 kN) showed optimal properties with good strength and controlled release, indicating that compression force must be carefully optimized.

Table 12: Effect of Compression Force on Selegiline Sustained Release Matrix Tablets

Formulation	Compression Force (kN)	Hardness (kg/cm²)	Friability (%)	Cumulative Drug Release at 12 h (%)	Remarks

F1	4	3.5 ± 0.2	1.25 ± 0.05	90.8 ± 1.3	Soft tablets, higher friability
F2	5	4.1 ± 0.2	0.98 ± 0.04	88.6 ± 1.2	Acceptable strength
F3	6	4.8 ± 0.3	0.82 ± 0.03	86.9 ± 1.1	Improved hardness
F4	7	5.4 ± 0.2	0.70 ± 0.03	84.7 ± 1.0	Good mechanical strength
F5	8	5.9 ± 0.3	0.62 ± 0.02	82.5 ± 1.1	Optimum compression
F6	9	6.3 ± 0.3	0.58 ± 0.02	80.9 ± 1.0	Slightly slower release
F7	10	6.8 ± 0.2	0.54 ± 0.02	79.4 ± 1.1	Reduced porosity
F8	11	7.1 ± 0.3	0.50 ± 0.02	77.6 ± 1.0	Hard tablets
F9	12	7.4 ± 0.3	0.48 ± 0.02	75.9 ± 1.0	Slower drug release
F10	13	7.8 ± 0.4	0.45 ± 0.02	74.3 ± 1.1	Very hard tablets

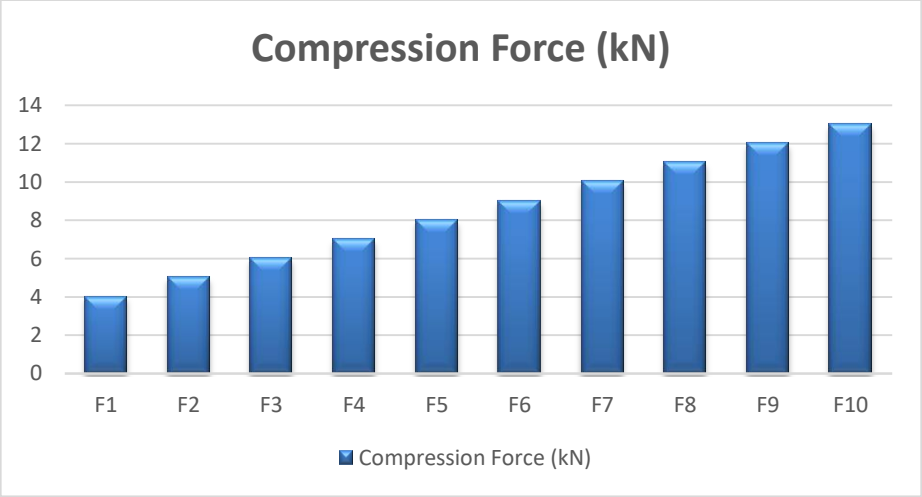

Fig 8: Compression Force (kN)

3.3.3 Tablet size and weight

The average weight and thickness of Selegiline matrix tablets were evaluated for uniformity. Formulations F1–F10 showed weights of 298–302 mg and thickness of 3.45–3.54 mm, within acceptable limits. The minimal variation indicates good flow and compressibility, ensuring consistent tablet size and quality. Results were comparable to the marketed tablet (300 ± 1.9 mg; 3.48 ± 0.04 mm), confirming suitability for further evaluation.

Table 13: Tablet Weight and Thickness of Selegiline Sustained Release Matrix Tablets

Formulation	Average Tablet Weight (mg)	Thickness (mm)

F1	298 ± 2.1	3.45 ± 0.05
F2	300 ± 1.9	3.48 ± 0.04
F3	301 ± 2.0	3.50 ± 0.05
F4	299 ± 1.8	3.47 ± 0.04
F5	300 ± 2.2	3.52 ± 0.05
F6	302 ± 2.0	3.54 ± 0.05
F7	301 ± 1.9	3.51 ± 0.04
F8	300 ± 2.1	3.49 ± 0.05
F9	299 ± 1.8	3.46 ± 0.04
F10	300 ± 2.0	3.50 ± 0.05
Marketed Tablet	300 ± 1.9	3.48 ± 0.04

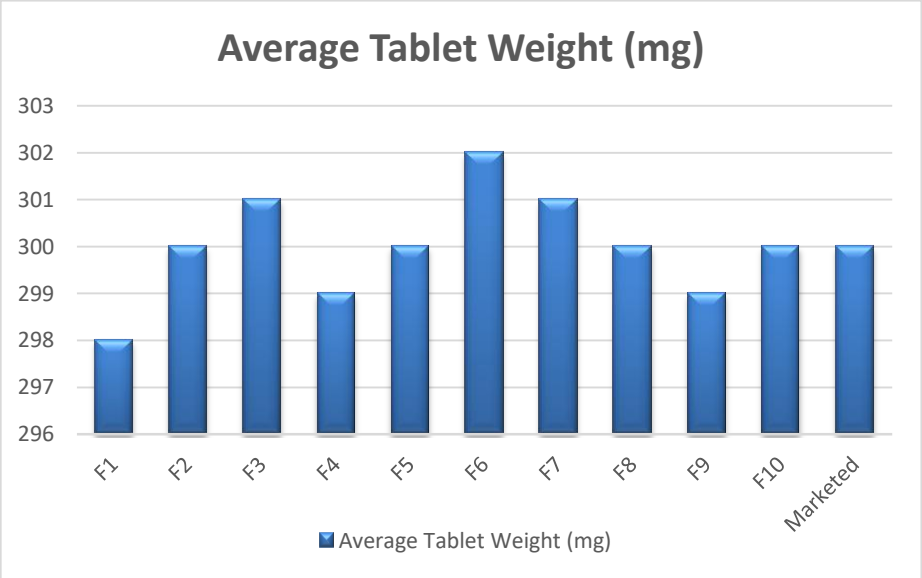

Fig 9: Average Tablet Weight (mg)

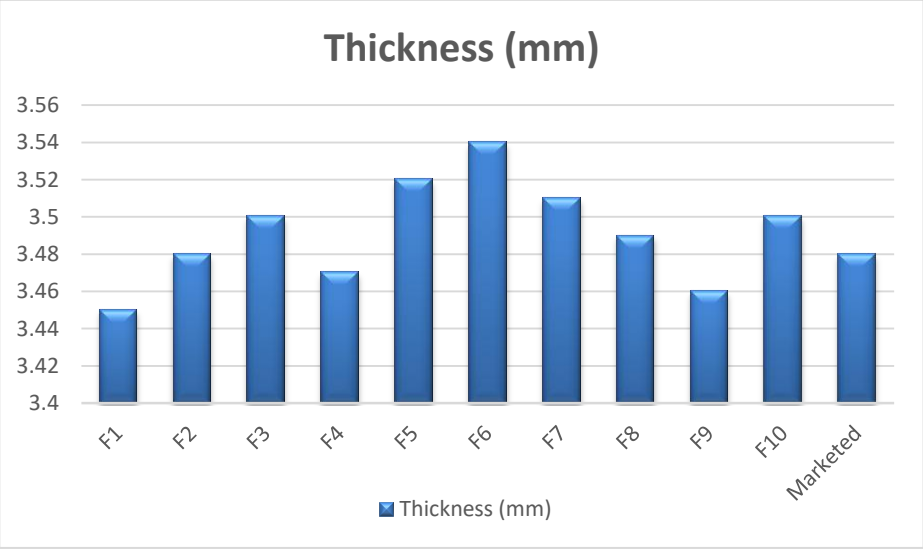

Fig 10: Thickness (mm)

3.3.4 Method of preparation (wet granulation)

The wet granulation method was successfully used to prepare Selegiline sustained release matrix tablets. It produced uniform, free-flowing granules with good flowability and compressibility. Pre-compression parameters were within acceptable limits, enabling smooth compression without defects. The tablets showed consistent weight, thickness, hardness, and low friability. Overall, the method yielded stable and uniform tablets suitable for further evaluation.

3.4 Evaluation of Prepared Tablets

3.4.1 Physical Evaluation

3.4.1.1 Weight variation

The weight variation test showed that Selegiline tablets (F1–F10) had an average weight of 298–302 mg, with deviations of 0.66% to 0.80%, well within the pharmacopoeial limit (±7.5%). This indicates excellent weight uniformity, uniform die filling, and good flow properties. The results were comparable to the marketed tablet, confirming consistent dosage accuracy and compliance with quality standards.

Table 14: Weight Variation of Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	Average Weight (mg)	% Deviation	Pharmacopoeial Limit	Result
F1	298 ± 2.3	0.77	±7.5 %	Pass
F2	300 ± 2.1	0.70	±7.5 %	Pass
F3	301 ± 2.0	0.66	±7.5 %	Pass
F4	299 ± 2.2	0.74	±7.5 %	Pass
F5	300 ± 2.4	0.80	±7.5 %	Pass
F6	302 ± 2.1	0.69	±7.5 %	Pass
F7	301 ± 2.0	0.66	±7.5 %	Pass
F8	300 ± 2.3	0.77	±7.5 %	Pass
F9	299 ± 2.2	0.74	±7.5 %	Pass
F10	300 ± 2.1	0.70	±7.5 %	Pass
Marketed Tablet	300 ± 2.0	0.66	±7.5 %	Pass

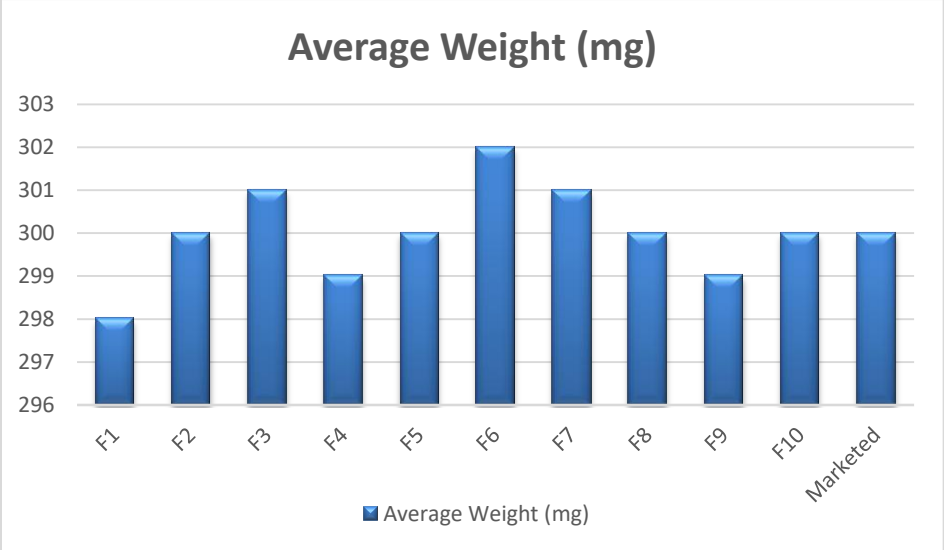

Fig 11: Average Weight (mg)

3.4.1.2 Thickness and diameter

The thickness and diameter of Selegiline tablets were evaluated for size uniformity. Formulations F1–F10 showed thickness of 3.45–3.54 mm and diameter of 8.00–8.04 mm, indicating consistent compression and die filling. The values were comparable to the marketed tablet (3.48 ± 0.04 mm; 8.01 ± 0.03 mm), confirming good dimensional uniformity and suitability for further evaluation.

Table 15: Thickness and Diameter of Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	Thickness (mm)	Diameter (mm)
F1	3.45 ± 0.05	8.02 ± 0.03
F2	3.48 ± 0.04	8.01 ± 0.04
F3	3.50 ± 0.05	8.03 ± 0.03
F4	3.47 ± 0.04	8.00 ± 0.03
F5	3.52 ± 0.05	8.02 ± 0.04
F6	3.54 ± 0.05	8.04 ± 0.03
F7	3.51 ± 0.04	8.02 ± 0.03
F8	3.49 ± 0.05	8.01 ± 0.04
F9	3.46 ± 0.04	8.00 ± 0.03
F10	3.50 ± 0.05	8.02 ± 0.04
Marketed Tablet	**3.48 ± 0.04**	**8.01 ± 0.03**

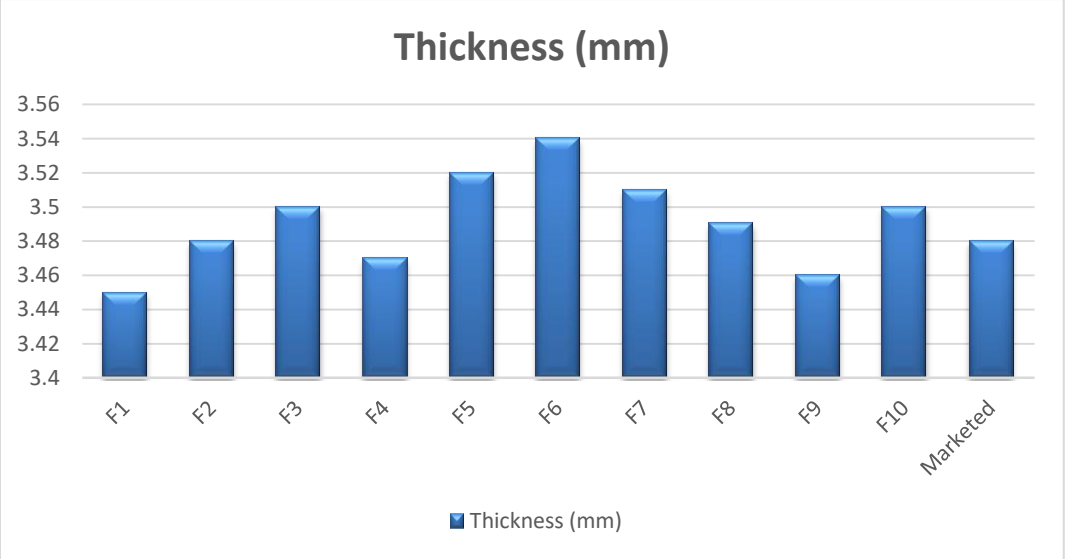

Fig 12: Thickness (mm)

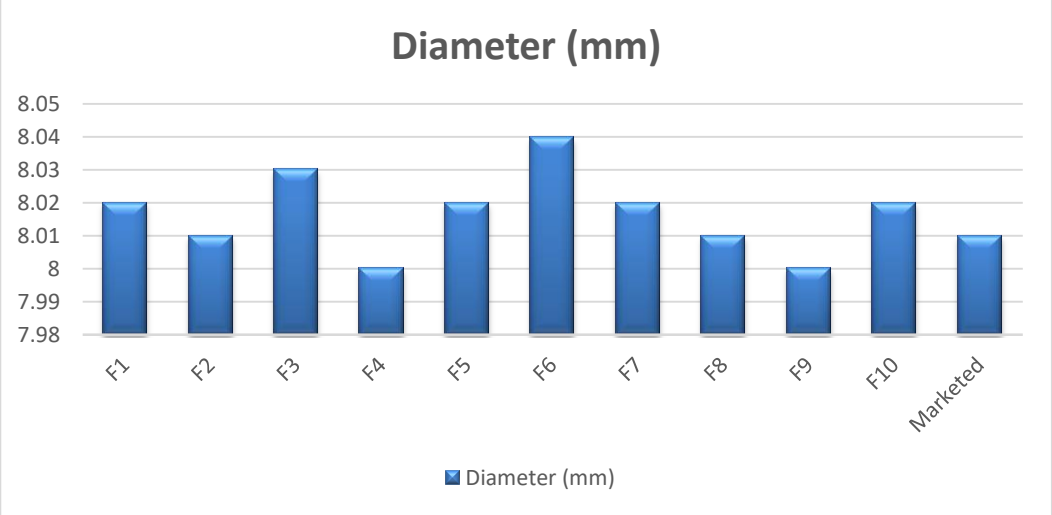

Fig 13: Diameter (mm)

3.4.1.3 Hardness

The hardness of Selegiline matrix tablets ranged from 5.4 to 7.2 kg/cm², indicating adequate mechanical strength for sustained release formulations. The variation may be due to differences in polymer concentration and compression force. The values were comparable to the marketed tablet (6.5 ± 0.20 kg/cm²), confirming good stability and suitability for further evaluation and controlled drug release.

Table 16: Hardness of Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	Hardness (kg/cm²)
F1	5.4 ± 0.21
F2	5.6 ± 0.18
F3	5.8 ± 0.20
F4	6.0 ± 0.22

F5	6.2 ± 0.19
F6	6.4 ± 0.23
F7	6.6 ± 0.20
F8	6.8 ± 0.24
F9	7.0 ± 0.22
F10	7.2 ± 0.21
Marketed Tablet	**6.5 ± 0.20**

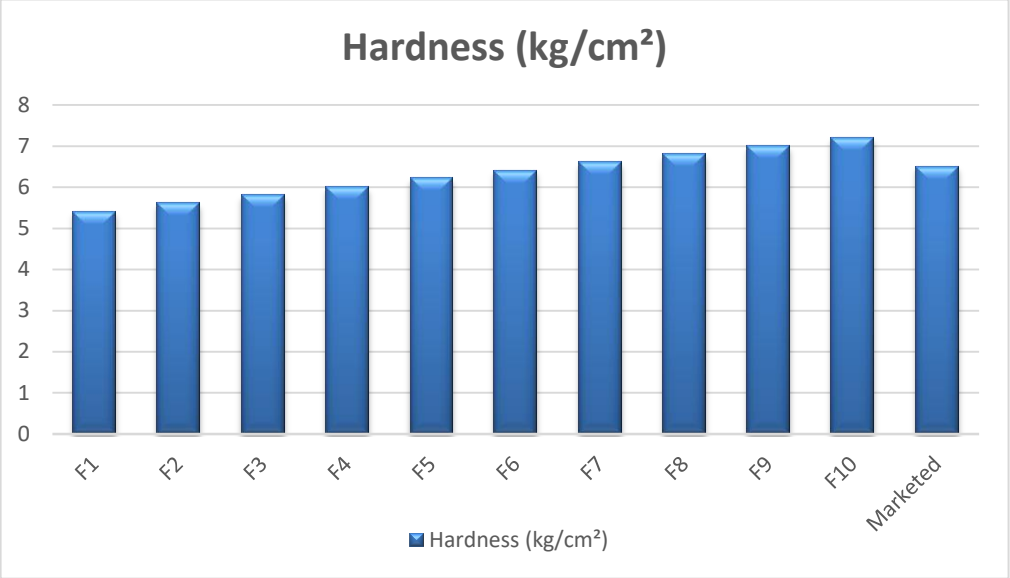

Fig 14: Hardness (kg/cm²)

3.4.1.4 Friability

The friability of Selegiline matrix tablets ranged from 0.49% to 0.66%, well within the acceptable limit of ≤1%. This indicates good mechanical strength and resistance to abrasion. The values were comparable to the marketed tablet (0.49%), confirming that the tablets are robust and suitable for handling, packaging, and further evaluation.

Table 17: Friability of Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	Initial Weight (g)	Final Weight (g)	Friability (%)	Result
F1	6.02	5.98	0.66	Pass
F2	6.01	5.97	0.66	Pass
F3	6.03	5.99	0.66	Pass
F4	6.02	5.99	0.50	Pass
F5	6.04	6.01	0.49	Pass
F6	6.05	6.02	0.49	Pass
F7	6.03	6.00	0.50	Pass
F8	6.04	6.01	0.49	Pass
F9	6.02	5.99	0.50	Pass

F10	6.05	6.02	0.49	Pass
Marketed Tablet	6.03	6.00	0.49	Pass

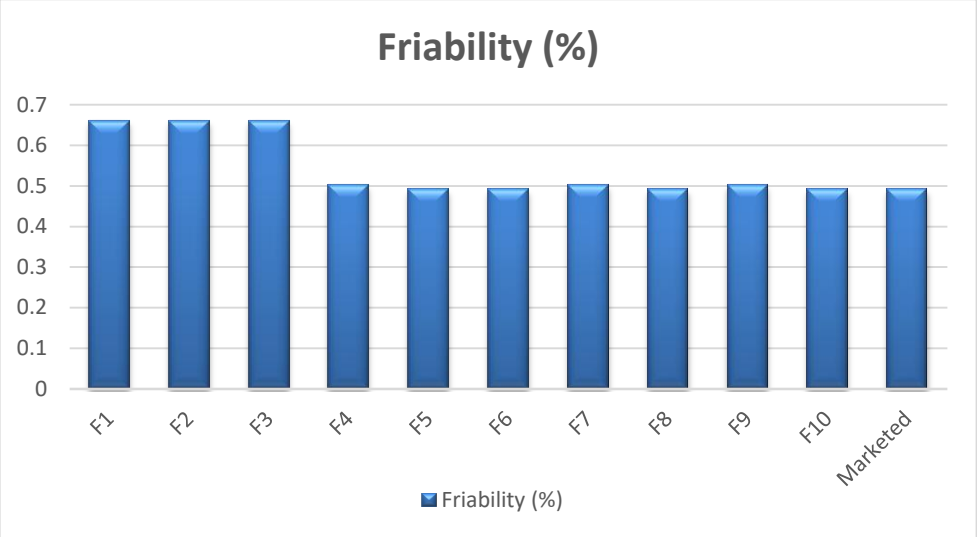

Fig 15: Friability (%)

3.5 Swelling Index Study

The swelling index study of Selegiline matrix tablets in phosphate buffer (pH 6.8) showed a progressive increase in swelling over time, indicating effective hydration and gel layer formation. Swelling ranged from 38–56% at 1 hour to 90–128% at 8 hours. Higher polymer concentrations resulted in greater swelling due to thicker gel barrier formation, which helps control drug diffusion. Overall, the results confirm suitable swelling behavior for sustained and controlled drug release.

Table 18: Swelling Index of Selegiline Sustained Release Matrix Tablets (F1–F10)

Formulation	1 hr (%)	2 hr (%)	4 hr (%)	6 hr (%)	8 hr (%)
F1	38 ± 1.5	52 ± 1.8	68 ± 2.0	81 ± 2.2	90 ± 2.4
F2	40 ± 1.6	55 ± 1.9	71 ± 2.1	85 ± 2.3	95 ± 2.5
F3	42 ± 1.7	58 ± 2.0	75 ± 2.2	88 ± 2.4	98 ± 2.6
F4	44 ± 1.8	61 ± 2.1	78 ± 2.3	92 ± 2.5	102 ± 2.7
F5	46 ± 1.9	64 ± 2.2	82 ± 2.4	96 ± 2.6	106 ± 2.8
F6	48 ± 2.0	67 ± 2.3	86 ± 2.5	100 ± 2.7	110 ± 2.9
F7	50 ± 2.1	70 ± 2.4	90 ± 2.6	104 ± 2.8	115 ± 3.0
F8	52 ± 2.2	73 ± 2.5	94 ± 2.7	108 ± 2.9	120 ± 3.1
F9	54 ± 2.3	76 ± 2.6	98 ± 2.8	112 ± 3.0	124 ± 3.2

F10	56 ± 2.4	80 ± 2.7	102 ± 3.0	116 ± 3.2	128 ± 3.3

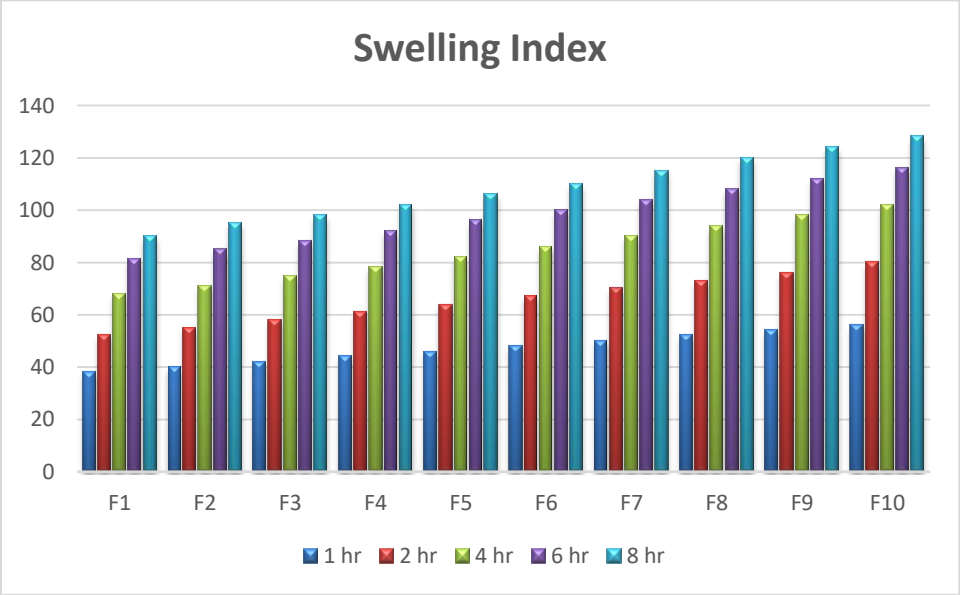

Fig 16: Swelling Index

3.6 In-Vitro Drug Release Studies

The in-vitro drug release study of Selegiline matrix tablets (F1–F10) showed a controlled release over 12 hours, with cumulative release ranging from 72% to 98%. F1 exhibited the fastest release due to low polymer content, while higher polymer formulations (F8–F10) showed slower release due to a thicker gel barrier. Formulations F4–F6 provided a balanced release profile comparable to the marketed tablet (88% at 12 hours). Overall, increased polymer concentration effectively retarded drug release, confirming suitability for sustained release delivery.

Table 19: In-Vitro Drug Release Profile of Selegiline Sustained Release Matrix Tablets

Time (hr)	F1 (% release)	F2 (% release)	F3 (% release)	F4 (% release)	F5 (% release)	F6 (% release)	F7 (% release)	F8 (% release)	F9 (% release)	F10 (% release)	Marketed (% release)
0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0
1	18 ± 1.3	16 ± 1.2	15 ± 1.1	14 ± 1.0	13 ± 1.0	12 ± 1.0	11 ± 1.0	10 ± 1.0	9 ± 1.0	8 ± 1.0	11 ± 1.1
2	30 ± 1.5	28 ± 1.4	26 ± 1.3	24 ± 1.2	22 ± 1.2	20 ± 1.1	18 ± 1.1	17 ± 1.0	16 ± 1.0	14 ± 1.0	19 ± 1.2
4	48 ± 2.0	45 ± 1.9	42 ± 1.8	40 ± 1.7	37 ± 1.6	35 ± 1.5	33 ± 1.5	31 ± 1.4	29 ± 1.3	27 ± 1.2	34 ± 1.7
6	63 ± 2.2	60 ± 2.1	57 ± 2.0	54 ± 1.9	50 ± 1.8	48 ± 1.7	45 ± 1.6	43 ± 1.5	41 ± 1.5	39 ± 1.4	47 ± 1.9

8	78 ± 2.4	74 ± 2.3	70 ± 2.2	67 ± 2.1	63 ± 2.0	60 ± 1.9	57 ± 1.8	55 ± 1.7	52 ± 1.6	50 ± 1.5	61 ± 2.0
10	90 ± 2.5	86 ± 2.4	82 ± 2.3	78 ± 2.2	74 ± 2.1	70 ± 2.0	67 ± 1.9	64 ± 1.8	61 ± 1.7	58 ± 1.6	75 ± 2.2
12	98 ± 2.6	95 ± 2.5	92 ± 2.4	90 ± 2.3	87 ± 2.2	84 ± 2.1	81 ± 2.0	78 ± 1.9	75 ± 1.8	72 ± 1.7	88 ± 2.3

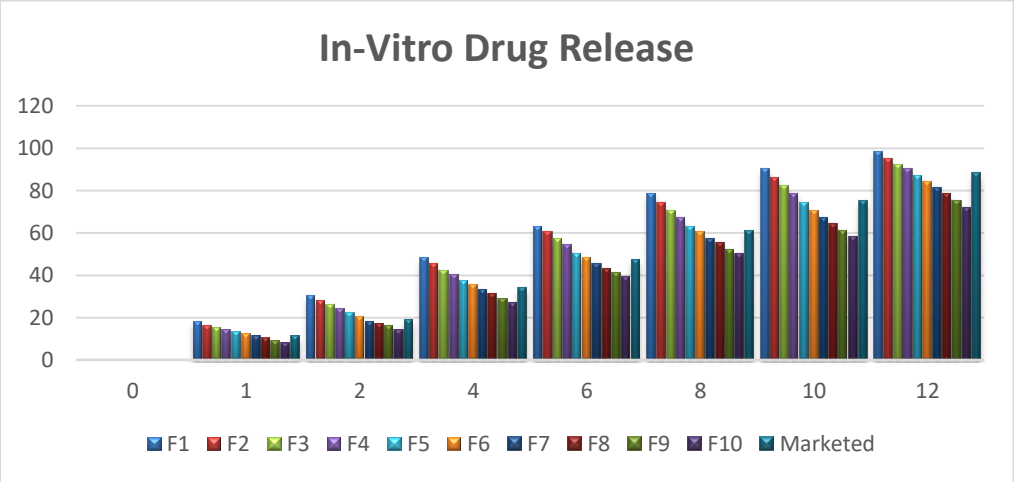

Fig 17: In-Vitro Drug Release

3.7 Stability Studies as per ICH guidelines

The accelerated stability study of optimized formulation F4 (40 ± 2°C/75 ± 5% RH, 3 months) showed no significant changes in physical appearance, weight, thickness, hardness, friability, drug content, or drug release. Minor variations remained within acceptable limits, with drug release slightly changing from 90% to 88% at 12 hours. Overall, F4 demonstrated good physical and chemical stability, confirming its suitability for long-term use.

Table 20: Accelerated Stability Study of Optimized Selegiline Matrix Tablets (F4)

Parameter	Initial	After 1 Month	After 2 Months	After 3 Months
Appearance	White, smooth tablets	No change	No change	No change
Average Weight (mg)	299 ± 2.2	300 ± 2.1	298 ± 2.3	299 ± 2.2
Thickness (mm)	3.47 ± 0.04	3.46 ± 0.05	3.47 ± 0.05	3.48 ± 0.04
Hardness (kg/cm^2)	6.0 ± 0.22	5.9 ± 0.20	5.8 ± 0.21	5.8 ± 0.23
Friability (%)	0.50	0.52	0.54	0.55
Drug Content (%)	99.2 ± 0.8	98.9 ± 0.9	98.5 ± 1.0	98.1 ± 1.1
% Drug Release at 12 hr	90	89	89	88

4. Conclusion

The present study successfully developed and evaluated sustained release matrix tablets of Selegiline using HPMC as a hydrophilic matrix-forming polymer by the wet granulation method. Pre-formulation studies confirmed the purity, stability, and suitability of the drug for sustained release formulation development, while powder blend evaluations demonstrated good flowability and compressibility suitable for tablet compression. All prepared formulations complied with pharmacopoeial standards for physical parameters such as weight variation, hardness, friability, thickness, and dimensional uniformity, indicating good mechanical strength and tablet quality. The swelling index study confirmed effective hydration and gel barrier formation by HPMC, which played a major role in controlling drug release. In-vitro drug release studies demonstrated that increasing polymer concentration effectively prolonged drug release over 12 hours, with formulation F4 showing the most balanced sustained release profile comparable to the marketed formulation. Stability studies conducted according to ICH guidelines revealed no significant changes in physical characteristics, drug content, or release behavior under accelerated conditions, confirming the stability of the optimized formulation. Overall, the study concluded that HPMC-based sustained release matrix tablets of Selegiline can be successfully formulated to provide controlled drug release, improved patient compliance, and prolonged therapeutic efficacy in the management of Parkinson's disease.

5. Acknowledgement

The authors sincerely thank all researchers and institutions whose work contributed to this review.

6. Conflict of Interest

The authors declare that they have no conflict of interest related to this work.

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