FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLET OF NICOTINAMIDE DRUG

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ABSTRACT

The objective of this research was to formulate and evaluate sustained release (SR) tablets of nicotinamide to overcome limitations associated with its short biological half-life and frequent dosing. Nicotinamide, a water-soluble derivative of vitamin B3, plays a critical role in energy metabolism and cellular functions but exhibits rapid absorption and elimination, necessitating multiple daily doses. To enhance patient compliance and maintain therapeutic plasma concentrations, sustained release formulations were developed using natural and synthetic polymers. Pectin, ethyl cellulose, and hydroxypropyl methylcellulose (HPMC) were employed as release-retarding agents. Wet granulation was selected as the manufacturing method to ensure uniformity and compressibility. Six formulation trials (F1–F6) were designed with varying polymer concentrations and evaluated for pre-compression parameters, post-compression quality attributes (weight variation, hardness, friability, and drug content), and in vitro dissolution behavior using USP apparatus II in phosphate buffer (pH 6.8). Compatibility studies confirmed no interaction between drug and excipients. Swelling index and dissolution studies indicated that polymer concentration significantly influenced drug release kinetics. Among the batches, F6 exhibited an optimized release profile, achieving approximately 97.6% cumulative drug release over 11–12 hours, demonstrating effective sustained release properties. Stability studies conducted under accelerated conditions confirmed the robustness of the optimized formulation without significant changes in physical or chemical characteristics. The study concludes that the combination of pectin, ethyl cellulose, and HPMC in appropriate ratios can effectively control nicotinamide release, reducing dosing frequency and improving therapeutic efficacy. This approach provides a promising strategy for the development of sustained release formulations for highly soluble drugs.

Keywords: Nicotinamide, sustained release, wet granulation, pectin, ethyl cellulose, HPMC, dissolution.

1. INTRODUCTION

Nicotinamide, also known as niacinamide, is a water-soluble amide form of vitamin B3, derived from nicotinic acid and essential for various metabolic functions including energy production, DNA repair, and cellular signaling [1]. It serves as a precursor for nicotinamide adenine dinucleotide (NAD) and its phosphate form (NADP), which are vital coenzymes in numerous redox reactions [2]. Dietary sources of nicotinamide include meat, fish, nuts, legumes, and fortified cereals, and its deficiency leads to pellagra, a condition characterized by

dermatitis, diarrhea, and dementia [3].Therapeutically, nicotinamide is employed in both nutritional supplementation and pharmacological interventions. It has demonstrated benefits in dermatological disorders such as acne and rosacea due to its anti-inflammatory properties [4], potential neuroprotective effects in neurodegenerative diseases [5], and improvement of insulin sensitivity in metabolic syndrome and type 2 diabetes [6]. Moreover, its role in lipid modulation has been explored in hyperlipidemia management [7]. Despite these benefits, the pharmacokinetics of nicotinamide—marked by rapid absorption (Tmax 0.5–2 h) and short elimination half-life (~50 minutes)—necessitate frequent dosing to maintain therapeutic levels [8]. This frequent administration may result in fluctuating plasma concentrations, reduced patient compliance, and increased risk of adverse effects [9] .Sustained release (SR) drug delivery systems are designed to prolong the therapeutic activity of drugs by maintaining steady plasma concentrations within the therapeutic window over extended periods [10]. For nicotinamide, SR formulations can minimize peak–trough fluctuations, enhance therapeutic efficacy, reduce dosing frequency, and improve patient adherence [11].

Sustained release can be achieved through various formulation strategies, including hydrophilic matrix systems, hydrophobic coatings, osmotic pumps, and polymeric drug–excipient complexes [12]. In the case of nicotinamide, polymers such as pectin and ethyl cellulose have been studied for their ability to control drug release through gel formation and diffusion barriers, respectively[13,14].The biopharmaceutical classification of nicotinamide as a Class I drug (high solubility, high permeability) favors its incorporation into sustained release systems [15]. However, the challenge lies in modulating its rapid dissolution to achieve the desired release kinetics without compromising bioavailability [16]. Preformulation studies, including drug–excipient compatibility assessments, are crucial in selecting appropriate excipients and optimizing formulation parameters [17]. Previous studies have demonstrated that matrix-based sustained release tablets of niacin and nicotinamide can provide controlled drug release over 12–20 hours using hydrophilic and hydrophobic polymers in varying ratios [18]. However, formulation variables—such as polymer concentration, binder type, and granulation technique—significantly influence the dissolution profile [19]. In the present study, wet granulation was employed as the manufacturing method, with the aim of achieving an optimized sustained release profile using pectin and ethyl cellulose as primary release-retarding agents [20].The objective of this research was to formulate and evaluate sustained release nicotinamide tablets with improved pharmacokinetic performance, enhanced patient compliance, and acceptable physicochemical stability, while ensuring bioequivalence to

innovator formulations [21]. The study encompasses preformulation evaluation, formulation trials, in vitro dissolution studies, and stability assessments to establish a robust and reproducible dosage form.

2. MATERIALS AND METHODS

2.1 Materials and Instruments Used

The study utilized high-quality pharmaceutical excipients and standard laboratory instruments to ensure reproducibility and reliability of results. Nicotinamide was selected as the active pharmaceutical ingredient (API), obtained from Modern Industries. Other excipients included pectin, ethyl cellulose, crosspovidone, microcrystalline cellulose (MCC), lactose, magnesium stearate, and talc, all procured from reputable sources such as Lobachemie, Lab Fine Chem, and Pune Chem Laboratory [22]. Analytical-grade reagents and chemicals were used throughout the study. The instruments used included a precision weighing balance (Wensar™), UV-Visible spectrophotometer (Shimadzu), dissolution test apparatus (USP Type II, Electrolab), hardness tester, friability tester, hot air oven (Classic Scientific), stability chamber (Thermolab), and rotary tablet compression machine (Rimek). All equipment was calibrated prior to use to ensure accuracy [23].

2.2 Preformulation Studies

Preformulation studies were performed to evaluate the physicochemical properties of the API and to ensure its compatibility with the selected excipients.

Bulk and Tapped Density:

Approximately 370 mg of nicotinamide was passed through a 25# sieve and carefully transferred to a 100 mL graduated cylinder. The bulk volume was noted, and bulk density was calculated as the ratio of mass to bulk volume. The same sample was tapped at a fixed rate of 300 drops per minute until a constant volume was obtained, and the tapped density was calculated as the ratio of weight to tapped volume [24].

Hausner’s Ratio and Compressibility Index (Carr’s Index):

These parameters were calculated using bulk and tapped density values to assess flow properties. A Hausner’s ratio below 1.25 and a compressibility index between 5–15% indicated good flow properties, whereas higher values indicated poor flow.These parameters were calculated using bulk and tapped density values to assess flow properties. A Hausner’s ratio

below 1.25 and a compressibility index between 5–15% indicated good flow properties, whereas higher values indicated poor flow [25].

Angle of Repose:

The angle of repose was determined using the fixed funnel method, where a known quantity of drug powder was allowed to flow through a funnel to form a conical pile. The angle (θ) was calculated using the ratio of pile height to base radius [26].

Particle Size Distribution:

Sieve analysis was performed using standard sieves ranging from 20# to 140#, with 100 g of the API placed on the uppermost sieve and shaken for 3 minutes. The retained material was weighed to determine the particle size distribution [27].

Moisture Content:

Loss on drying (LOD) was assessed using a moisture analyzer set at 105°C for 5 minutes, and the percentage loss was calculated as the difference between initial and final weight [28].

Solubility Studies:

The solubility of nicotinamide was evaluated in various pH buffers (6.0–8.0) and distilled water. Approximately 250 mL of each medium was prepared, and the drug was sonicated for 30 minutes to ensure proper dissolution [29].

2.3. UV SPECRAL ANALYSIS [30-34]

A) Preparation of standard solution of phosphate buffer 6.8 (0.2 Molar of) potassium dihydrogen phosphate):Taking 27.218gm of potassium dihydrogen phosphate dissolved in H2O. Dilute upto 1000ml. That's made 0.2 molar of potassium dihydrogen phosphate.

B) Preparation of 0.2 Molar of sodium hydroxide: Weigh 8gm of sodium hydroxide and dissolve in water and dilute upto 1000 ml into the 1000ml of beaker.

C) For taking 7 PH of buffer: Pipette out 250ml of potassium dihydrogen phosphate and 145.5ml of sodium hydroxide into in one beaker volume makeup upto 1000ml.

D) Determination of wavelenghth (ג max):For determination of ג max of the drug candidate, standard solution was prepared and scanned over complete UV range (i.e.200-800) using shimatzu UV-Visible spectrophotometer(European pharmacopeia 20000 dissolution media guidance is described in

Table 01: Dissolution Media

Parameter	Description
Dissolution Apparatus	USP II (Paddle)
Media	7 pH buffer
Volume	900ml
Speed	50 rpm
Time points	1,3,6,9,12 hours
Temperature	37±0.5°C

Table 02: Innovators product details

Particulars	Observations
Brand	Alertonic
Country of origin	U.S
Dosage form	Sustained release
Manufactured by	Allergan, Inc.
Label claim	370mg
Appearance	White tablet-shaped
Category	Vitamin
Average weight(mg)	500mg
Hardness	42 ± 10 N
Dimensions	Length: 8-16mm Breadth: 3-6mm Thickness: 7.70-7.75
Assay	NLT 95% to NMT 105% of label claim
Content Uniformity	NLT 95% to NMT 105% of label claim

Dissolution study	Dissolution was performed using USP apparatus 2 (paddle in) at 37°C in, a) 0.1 N HCL at 50rpm for 8 hours b) pH 7 phosphate buffer for 12 hours
Inactive ingredients	a) Tablet core: Lactose, magnesium stearate, talc
Storage condition	Store at room temperature at 37°c
Pack	Strips of tablets, Protect from moisture. Tablets can be dispensed without desiccants for upto 6 weeks.

2.4 Drug excipients compatibility study [35-37]

Pharmaceutical incompatibilities are generally referred to as changes in the physical, chemical, and therapeutic properties of a dosage form resulting from the interaction of the API with excipients or other components of the drug product. A wide variety of factors influence the nature and extent of drug excipients interactions. These factors include the physico-chemical properties of the drugs and the excipient interactions, relative ratios and proximity of this components in the formulation, and other processing and environment factors. Drug excipients compatibility study ratio used for study are given

Table 03: Drug Excipients compatibility

Sr.no.	Physical Mixture	Drug: Excipients	Initial description
1.	API	1	White color powder
2.	API: Pectin	1:0.5	White beige color powder
3.	API: ethyl cellulose	1: 0.5	White color powder
4.	API: Crosspovidone	1: 0.3	White color powder
5.	API: MCC	1: 0.3	White color powder
6.	API: Lactose	1:0.4	White color powder
7.	API: magnesium stearate	1:0.25	White color powder
8.	API: talc	1:0.25	White color powder

2.5 Formulation Trail [38-40]

Formulation in the pharmaceutical industry involves creating a medication product by combining chemicals for therapeutic effects. It considers drug pharmacokinetics, administration routes, dose forms, stability, and shelf life. Preformulation research, formulation development, and optimization are common processes. The initial formulation is evaluated for safety, efficacy, and stability, ensuring its effectiveness.

2.5.1 Trial 1

AIM: To take feasibility trail of sustained released nicotinamide tablet

Working formula for trail R1 is discussed in

Table 04: Composition of Sustained Release Nicotinamide Tablet (Trial F1) Using Wet Granulation Method

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Nicotinamide	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Sustained release polymer(pectin)	260	260	26.0
Binder solution				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00

4.	Weight of dry granules(mg	380.00	380.00	38.9
Extra granular material				
5.	Mcc	30	30	3
6.	Crosspovidone	3	3	0.3
7.	Lactose	50	50	5
8.	Magnesium stearate	3	3	0.3
9.	Talc	2	2	0.2
Total weight		88.00	88.00	8.8

Procedure

All ingredients were carefully dispensed according to the formulation sheet. The active pharmaceutical ingredient (API) was first sifted through a 25# ASTM sieve to ensure uniform particle size. A binder solution was prepared by mixing water and isopropyl alcohol in a 1:9 ratio. The required excipients were taken in a mortar, and the binder solution was gradually added, mixing thoroughly to achieve a uniform consistency.

The flow properties of the resulting powder blend were assessed to ensure suitability for further processing. The API and binder solution were mixed in the mortar for one minute, followed by kneading for 20 seconds to form a wet mass. This wet mass was then granulated and passed through a 20# ASTM sieve. The obtained granules were dried in a hot air oven for 20 minutes to remove residual moisture.

Once drying was completed, magnesium stearate and talc were added as lubricants to the granules. The granulated mixture was again sifted through an 18# ASTM sieve to achieve uniformity. After this, the granules were prepared for tablet compression.

Tablets were compressed using a 12 mm punch, and their weight was recorded. Following compression, disintegration testing was carried out to evaluate the performance of the tablets.

Observation

All the coated tablets were physically evaluated for their appearance and texture. The tablets were uniformly formed, with a smooth surface and proper coating. A functional coating of 7% was found to effectively retard the dissolution profile of the drug, playing a crucial role in ensuring delayed release.

Conclusion

The study concluded that reducing the polymer concentration may help achieve satisfactory results while maintaining the desired dissolution profile. Further evaluation is necessary to confirm whether the process parameters significantly influence the dissolution behavior of the drug.

2.5.2 TRIAL 2

Aim: To take trial of sustained released tablet of using natural excipients like pectin.

Working formula for trial 2 of formulation 2

Table 05: Dispensing sheet for batch F1

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Anti-inflammatory	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Ethyl cellulose and pectin	260	260	
Binder solution				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00

4.	Weight of dry granules(mg	380.00	380.00	38.0
Extra granular material				
5.	MCC	40	40	4
6.	Crosspovidone	3	3	0.3
7.	Lactose	40	40	4
8.	Magnesium stearate	3	3	0.3
9.	Talc	2	2	0.2
10.	Total weight	88.00	88.00	8.8

Procedure:

The formulation process began with the dispensing of all ingredients according to the specified composition sheet. The active pharmaceutical ingredient (API) was first sifted using a 25# ASTM sieve to ensure uniform particle size. A binder solution was prepared by combining water and isopropyl alcohol in a 1:9 ratio. All excipients were taken in a mortar, and the prepared binder solution was added gradually while mixing thoroughly to form a homogenous mass.

The flow properties of the powder blend were then evaluated to assess its suitability for further processing. The API and binder solution were mixed in the mortar for one minute, followed by kneading for approximately 20 seconds to achieve uniform granulation. The damp mass obtained after granulation was passed through a 20# ASTM sieve and subsequently dried in a hot air oven for 20 minutes to remove residual moisture.

Once drying was completed, magnesium stearate and talc were incorporated as lubricants into the granulation. The mixture was then passed through an 18# sieve to ensure uniformity. The prepared granules were compressed into tablets using a 12 mm punch, and each tablet was weighed to maintain consistency.

Following compression, a disintegration test was conducted to evaluate the tablets' performance. Physical evaluation revealed that the coated tablets exhibited a smooth texture, proper formation, and satisfactory coating. It was observed that a 7% functional coating

effectively retarded the drug dissolution profile, indicating its critical role in achieving delayed drug release.

In conclusion, the study suggested that reducing the polymer concentration may enhance the dissolution profile while maintaining desired formulation characteristics. Further evaluation is necessary to determine the extent to which the process parameters influence the drug's dissolution behavior.

2.5.3 Trial 3

Table 06: Dispensing sheet for batch F3

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Anti-inflammatory	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Pectin and ethyl cellulose	144+ 144	288	28.8
Binder solution				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00
4.	Weight of dry granules(mg	380.00	380.00	38.9
Extra granular material				
5.	MCC	20	20	2
6.	Crosspovidone	3	3	0.3

7.	Lactose	35	35	3.5
8.	Magnesium stearate	2	2	0.2
9.	Talc	3	3	0.3
Total weight		63.00	63.00	6.3

Procedure:

All the ingredients required for the formulation were accurately dispensed as per the formulation sheet. The active pharmaceutical ingredient (API) was initially sifted using a 25# ASTM sieve to achieve uniform particle size. For the binder solution preparation, all the required excipients were placed in a mortar, and a binder solution consisting of water and isopropyl alcohol in a 1:9 ratio was gradually added. The mixture was thoroughly blended to ensure uniform wetting of the components.

Following this, the flow properties of the powder blend were evaluated to confirm its suitability for granulation. The API and binder solution were then mixed in the mortar for one minute, followed by kneading for 20 seconds to form a wet mass. This wet mass was granulated and passed through a 20# ASTM sieve, after which it was dried in a hot air oven for 20 minutes to remove residual moisture completely.

Once drying was completed, magnesium stearate and talc were added as lubricants to the granules, and the mixture was again passed through an 18# sieve to achieve uniform granule size. The prepared granules were then subjected to compression using a 12 mm punch to form tablets, and their weight was checked to ensure uniformity.

Finally, the disintegration test was carried out to assess the performance of the compressed tablets.

Observations

The coated tablets were evaluated visually for their physical appearance and were found to be well-formed with a smooth texture and uniform coating. It was observed that a 7% functional coating effectively retarded the dissolution profile of the drug. The functional coating played a significant role in ensuring delayed release characteristics, which are essential for the intended formulation purpose.

Conclusion

The study indicated that reducing the polymer concentration resulted in less effective control over the drug release profile. This highlights the critical role of both the polymer concentration and the coating process in achieving the desired dissolution behavior of the drug.

2.5.4 Trail 4

Table 07: Dispensing sheet for batch F4

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Anti-inflammatory	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Pectin and ethyl cellulose	152+152=304	304	30.4
Binder solution(20 % + 8%)				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00
4.	Weight of dry granules(mg	380.00	380.00	38.9
Extra granular material				
5.	MCC	3	3	0.3
6.	Crosspovidone	3	3	0.3
7.	Lactose	35	35	3.5

8.	Magnesium stearate	3	3	0.3
9.	Talc	2	2	0.2
Total weight		46.00	46.00	4.6

Procedure:

The required ingredients were first dispensed according to the formulation sheet. The active pharmaceutical ingredient (API) was passed through a 25# ASTM sieve to ensure uniform particle size. A binder solution was prepared by mixing water and isopropyl alcohol in a ratio of 1:9. All the excipients were taken in a mortar, and the prepared binder solution was gradually added, followed by thorough mixing.

The flow properties of the powder blend were then evaluated to ensure proper compressibility and flow behavior. The API and binder solution were further mixed in the mortar for one minute, followed by kneading for 20 seconds to form a damp mass suitable for granulation.

This damp mass was wet milled using a 20# ASTM sieve, after which the wet granules were placed in a hot air oven for 20 minutes to remove residual moisture. Once dried, magnesium stearate and talc were added as lubricants and blended with the granules. The granulation was then passed through an 18# sieve to ensure uniformity.

The granules obtained were ready for tablet compression. Tablets were compressed using a 12 mm punch, and their weights were checked for uniformity. Following compression, a disintegration test was conducted to evaluate the tablets' disintegration behavior.

Observation

All coated tablets were physically examined for their appearance and coating uniformity. The tablets were well-formed, with a smooth texture, and the coating process was effective. A slight increase in the quantity of the sustained-release polymer was noted, which played a crucial role in controlling the drug release. Functional coating was found to be essential in achieving delayed drug release.

Conclusion

A batch with a 10% functional coating on the tablets was prepared to evaluate its influence on the dissolution profile of the drug. The study indicated that the coating process significantly impacts the release characteristics of the formulation.

2.5.5 Trail 5

Table 08: Dispensing sheet for batch F5

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Anti-inflammatory	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Pectin and Ethyl cellulose	113+ 185= 298	298	29.8
Binder solution				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00
4.	Weight of dry granules(mg	380.00	380.00	38.9
Extra granular material				
5.	MCC	10	10	1
6.	Crosspovidone	2	2	0.2
7.	Lactose	35	35	3.5

8.	Magnesium stearate	3	3	0.3
9.	Talc	2	2	0.2
Total weight		52.00	52.00	5.2

Procedure:

The formulation process began with dispensing all the required ingredients according to the specified formulation sheet. The active pharmaceutical ingredient (API) was first sifted through a 25# ASTM sieve to ensure uniform particle size and remove any coarse particles.

A binder solution was prepared using water and isopropyl alcohol in a 1:9 ratio. The binder was incorporated into the dry ingredients placed in a mortar, and the mixture was thoroughly blended to achieve a uniform consistency. The powder blend was mixed for one minute, followed by a kneading process lasting 20 seconds to form a damp mass suitable for granulation.The granulated mass was then wet milled using a 20# ASTM sieve to achieve the desired particle size. The wet granules were subjected to drying in a hot air oven for 20 minutes to remove moisture completely. Once dried, magnesium stearate and talc were added as lubricants to improve flow properties and prevent sticking during compression. The dried granules were then passed through an 18# sieve to ensure uniform granulation before proceeding to the compression stage.Tablet compression was performed using a 12 mm punch, and the weight of each tablet was monitored to ensure uniformity. Following compression, the tablets underwent a disintegration test to assess their structural integrity and performance.

Observation

The tablets were evaluated for their physical appearance and were found to be well-formed with a smooth surface and uniform coating. The functional coating, applied at 7%, effectively retarded the dissolution profile of the drug, demonstrating its role in controlled release. Natural polymers, such as pectin, along with ethyl cellulose, were used in varying quantities to optimize the release characteristics. The functional coating played a significant role in achieving delayed drug release, ensuring controlled and sustained drug delivery.

Conclusion

The process effectively produced smooth, well-coated tablets with satisfactory results. The functional coating significantly influenced the dissolution profile of the drug, demonstrating its importance in achieving delayed release. The study highlighted the role of the manufacturing process and coating composition in determining the final performance of the tablet formulation.

2.5.6 Trail 6

Table 09: Dispensing sheet for batch F6

Batch Process: Wet granulation				
Batch: F1				
Sr.no.	Ingredient	Quantity(mg/tab)	Quantity(g/batch)	%w/w
		370	720	
Dry mix				
1.	Anti-inflammatory	370	370	37.00
2.	Weight of dry mix(mg)	370	370	37.00
3.	Pectin, ethyl cellulose and HPMC	70+ 120+ 120=310	310	31.0
Binder solution				
2.	Isopropyl alcohol	9.00	9.00	0.9
3.	Purified Water	1.00	1.00	1.00
4.	Weight of dry granules(mg	380.00	380.00	38.9
Extragranular material				
5.	Mcc	3	3	0.3

6.	Crosspovidone	2	2	0.2
7.	Lactose	30	30	3
8.	Magnesium stearate	3	3	0.3
9.	Talc	2	2	0.2
Total weight		41.00	41.00	4

Procedure:

The formulation process began by dispensing all the ingredients as per the specified quantities mentioned in the formulation sheet. The active pharmaceutical ingredient (API) was initially sifted through a 25# ASTM sieve to achieve uniform particle size. For the preparation of the binder solution, all the required ingredients were taken in a mortar, and a binder solution consisting of water and isopropyl alcohol in a 1:9 ratio was gradually added while mixing thoroughly to ensure homogeneity.

The flow properties of the prepared powder blend were then calculated to assess its suitability for further processing. The API was mixed with the binder solution in the mortar for one minute, followed by kneading for 20 seconds to form a wet mass suitable for granulation. This wet mass was then passed through a 20# ASTM sieve for wet milling to achieve proper granule size. The sifted granules were subjected to drying in a hot air oven for 20 minutes to remove all residual moisture.

After drying, magnesium stearate and talc were added as lubricants to the granules to improve flow properties and reduce friction during tablet compression. The lubricated granules were then passed through an 18# ASTM sieve to achieve uniform granulation. The final granules were compressed into tablets using a 12 mm punch. Each tablet was weighed to ensure uniformity of weight.

Following compression, a disintegration test was performed to evaluate the integrity of the tablets.

Observation

All the coated tablets were evaluated for their physical characteristics. The tablets exhibited a smooth texture, uniform appearance, and proper coating. The incorporation of the new

sustained-release polymer played an essential role in controlling the release rate of the drug. The functional coating was observed to be significant in achieving delayed release properties.

Conclusion

It was concluded that the addition of an extra concentration of polymer may provide more satisfactory results. Further investigation is needed to evaluate the influence of this modification on the dissolution profile of the drug to ensure optimal sustained-release performance.

2.6 Release profiles comparison

In vitro dissolution studies can play an important role in the assessment of the impact of formulation, quality assurance, simplifying certain supervisory determinations (eg. lack of effect of minor formulation modifications), and can be valuable for back characterization of the products.A model-independent mathematical method was developed by Moore and Flanner for comparison of dissolution profiles using two factors, fl and f2.The factor f2, known as the similarity factor, measures the closeness between the two profiles:

$$\text{F2} = 50 \times LOG\{[1 + (\frac{1}{n}) \sum_{t=1} n\,(\text{R-}T)^2]^{-0.5} \times 100$$

where, n is the number of time points, R, and T, are the dissolution value of the reference and test product at time t, respectively (Xie, et al, 2015).

Specifically, being an empirical and fixed limit, the similarity limit of f2 102 (P50) is not justified by any mechanistic or biopharmaceutical 103 reasons, and the range of f2 is from 1 to 100 and it is not sym104 metric about zero.The factor, f1, is the average % difference over all time points in the amount of test brand dissolved as compared to the reference brand. The f1 value is 0 when the test and the reference profiles are identical and increases proportionally with the dissimilarity between the two profiles[41-43].

2.7. Stability testing

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions [44].

2.8. Stress Testing

Stress testing of the drug substance can help identify the likely degradation products. which can in turn help establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used. The nature of the stress testing will depend on the individual drug substance and the type of drug product involved. Stress testing is likely to be carried out on a single batch of the drug substance. It should include the effect of temperatures (in 10°C increments (e.g., 50°C, 60°C, etc.) above that for accelerated testing), humidity (e.g., 75% RH or greater) where appropriate, oxidation, and photolysis on the drug substance

2.9. Testing Frequency

At the accelerated storage condition, a minimum of three time points, including the initial and final time points (e.g., 0, 3, and 6 months), from a 6-month study is recommended. Where an expectation (based on development experience) exists that results from accelerated studies are likely to approach significant change criteria, increased testing should be conducted either by adding samples at the final time point or by including a fourth time point in the study design.

2.10. Storage Conditions

In general, a drug substance should be evaluated under storage conditions (with appropriate tolerances) that test its thermal stability and, if applicable, its sensitivity to Visture. The storage conditions and the lengths of studies chosen should be sufficient R cover storage, shipment, and subsequent use (ICH Q1 (R2), 2003) [45].

3. RESULTS AND DISCUSSION

3.1 API Characterization

The specification of API were established with in-house controls. The API used for the specifications had been characterized by different physicochemical tests as given below

Table 10: Physicochemical Characterization of Nicotinamide API

Parameter	Results
Bulk Density	0.707gm/ml
Tapped density	0.838gm/ml
Carr’s Index	15.63%

Hausner's Ratio	1.185
Angle of repose	Good flow

Observation: API complies as per the specification. Based on the above data it was concluded that the API has good flow property.

3.2. Drug excipient compatibility study data

Table 11. Physical Observation of drug excipients compatibility

Sr.no.	Physical Mixture	Drug: Excipients	Initial description	37°C !st Week	2nd week	3rd week
1	API	1	White color powder	NC	NC	NC
2	API: Pectin	1:0.5	White-beige color powder	NC	NC	NC
3	API: Ethyl cellulose	1:0.5	White color powder	NC	NC	NC
4	API: Crosspovidone	1:0.3	White color powder	NC	NC	NC
5	API: Mcc	1:0.3	White color powder	NC	NC	NC
6	API: Lactose	1:0.4	White color powder	NC	NC	NC

7	API: Magnesium stearate	1:0.25	White color powder	NC	NC	NC
8	API: Talc	1:0.25	White color powder	NC	NC	NC

NC= No Change

Observation from table , it was concluded that there was no significant interaction between drug and excipients. All the selected excipients were suitable to use for formulation of sustained released tablet.

Post compressional parameters of the formulated SR tablets

3.3. Flow Properties:

Table 12. Flow properties

Formulation	Average weight	Thickness(mm)
F1	720.2±0.500	6.14±0.015
F2	720.9±0.527	6.28±0.009
F3	720.2±0.707	6.28±0.010
F4	720.3±0.881	6.29±0.010
F5	720.4±0.500	6.25±0.014
F6	720.7±0.527	6.29

Table:13 Post-Compression Parameters of Nicotinamide Sustained Release Tablets

Formulations	Hardness(KP)	% Friability	% Drug content
F1	12.75±0.105	0.163	98.58
F2	12.87±0.138	0.092	97.61
F3	12.77±0.115	0.144	95.87
F4	12.86±0.091	0.145	98.22
F5	12.86±0.121	0.131	100.65
F6	12.71±0.147	0.197	100.91

3.4. Swelling index of nicotinamide tablets

Table 14: Swelling index of nicotinamide tablets

Time (hours)	F1	F2	F3	F4	F5	F6
0	0	0.0	0.0	0.0	0.0	0.0
1	85.72	96.0	83.5	82.7	105.7	114.2
2	92.96	113.7	106.1	108.1	128.0	160.4
3	149.2	153.5	147.6	148.4	155.5	187.4
4	160.8	165.3	164.7	173.7	178.6	197.0
5	171.9	188.6	184.3	188.5	193.3	216.1
6	194.3	190.2	190.3	189.7	200.1	226.7
7	201.2	203.1	202.0	202.6	209.9	239.8
8	214.1	215.0	210.5	209.2	216	254.3

Table 15: Swelling index of nicotinamide

Time (hours)	F1	F2	F3	F4	F5	F6
0	0.0	0.0	0.0	0.0	0.0	0.0
1	21.5	17.1	24.0	21.4	22.0	22.1
3	39.0	36.4	44.9	39.0	40.6	39.9
6	57.6	54.7	69.1	57.7	58.7	61.2
9	71.7	65.2	88.2	71.6	71.9	77.5
12	83.5	77.4	96.4	82.2	83.1	91.3

3.5. Parameter of uncoated formulations

Table16: Parameter of uncoated formulations

Formulation	Uncoated formulations
Pure drug	0.5502
F1	0.7782
F2	0.9174
F3	0.9424
F4	0.1777
F5	0.4795
F6	0.8174

3.5. Parameter of Coated formulations

Table 17: Parameter of Coated formulations

Formulations	Coated formulations
Pure drug	0.5502
F1	0.7782
F2	0.9174
F3	0.9424
F4	0.4964
F5	1.0721
F6	0.8174

3.6. Percent cumulative drug release of selected formulations

Table 18 : Percent cumulative drug release of selected formulations

Formulation	% Cumulative drug released		
code	Before coating	After coating	After stability study
F2	97.3% in 9 hours	99.6% in 12 hours	97.4% in 6 hours
F5	99.2% in 11 hours	99.8% in 7 hours	96.7% in 9 hours
F6	96% in 10 hours	97.6% in 11 hours	97.61% in 12 hours

Determination of wavelength 262nm(ג max) of API by UV- Spectrophotometer and Calibration curve

3.7. Calibration curve of drug X in distilled water

Table 19: Calibration curve of drug X in distilled water

Concentration (µg/ml)	Absorbance
10	0.308
20	0.542
30	0.821
40	1.092
50	1.269

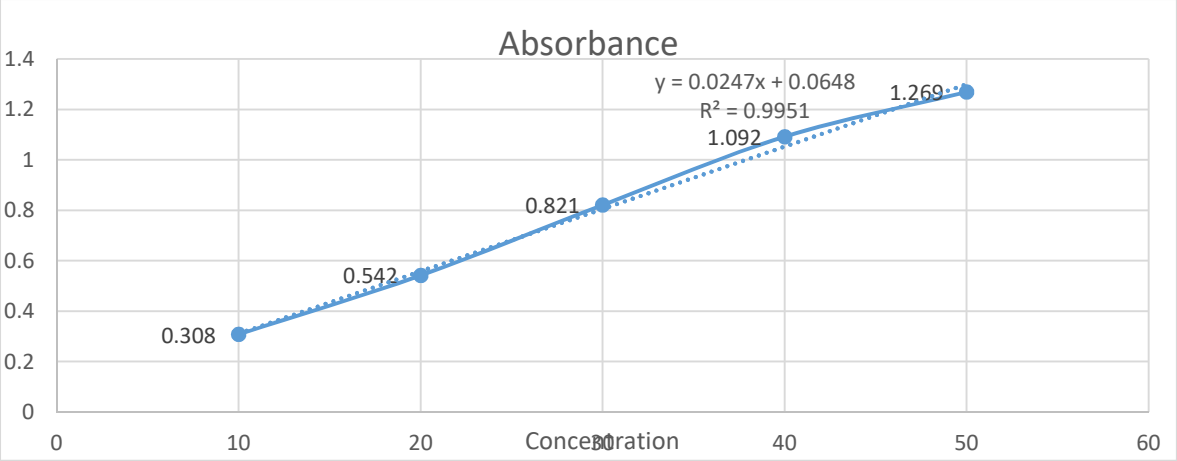


Fig 01. Calibration Curve of Nicotinamide drug in distilled water

Observation: Stock solution preparation and concentration of solution used for calibration curve are described as table no. , the excel plot obtained after uv analysis is described.

3.8. Calibration curve of drug X in phosphate buffer pH 6.8

Fig 20. Calibration curve of drug X in phosphate buffer pH 6.8

Concentration(µg/ml)	Absorbance
20	0.298
40	0.556
60	0.872
80	1.164
100	1.450

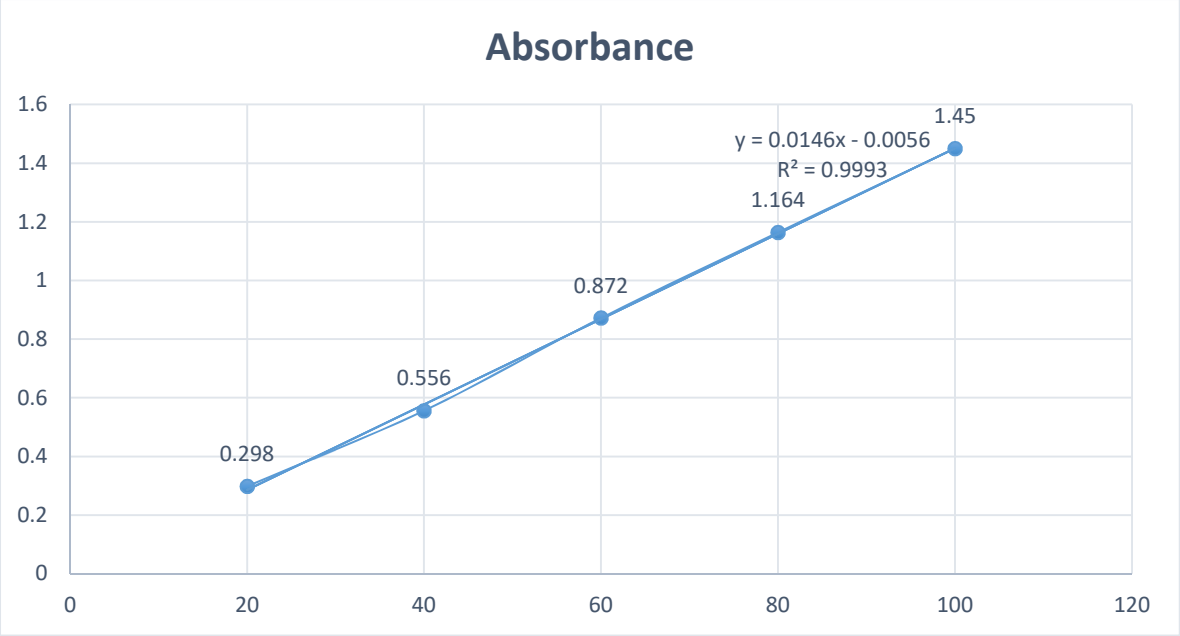


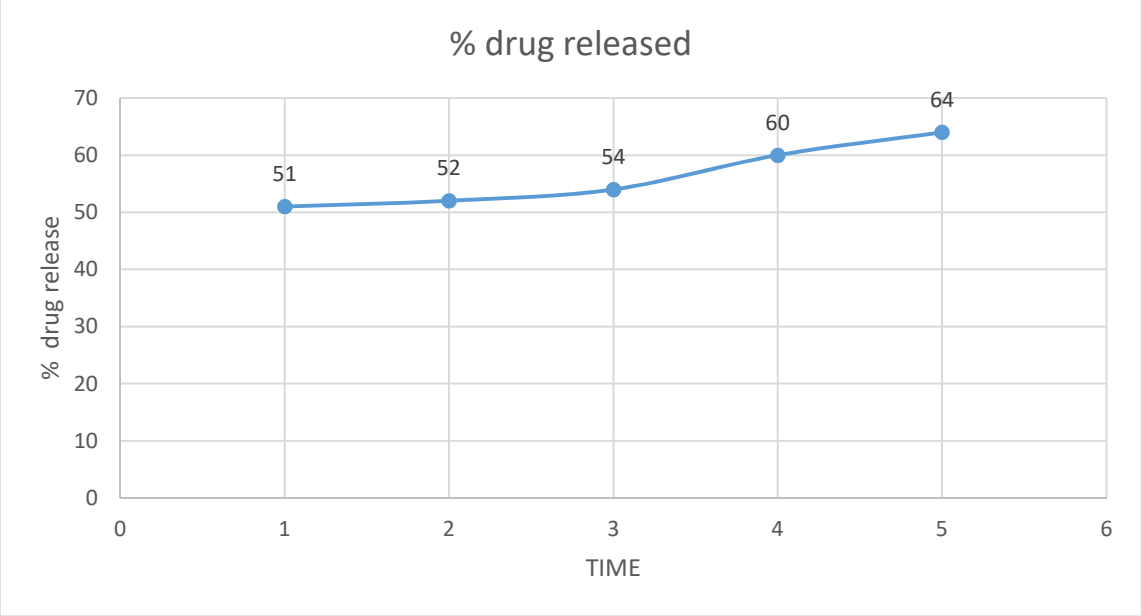
Fig 02. Calibration Curve of Nicotinamide drug in phosphate buffer pH6.8

Observation: Stock solution preparation and concentration of solution used for calibration curve are described.in table ,in figure the excel plot obtained after uv analysis is described.

3.9. Dissolution Result:

3.9.1. Dissolution results of Reference listed drug (RLD drug):

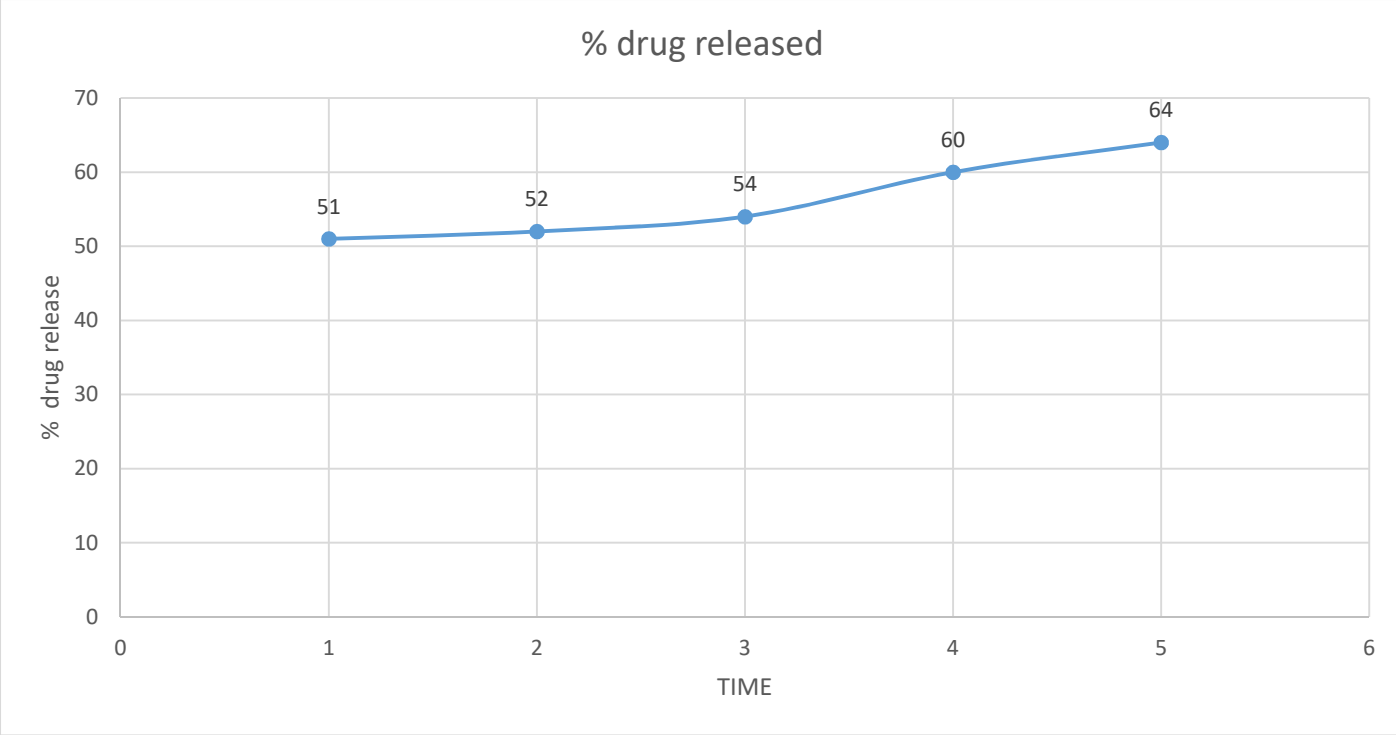
Sr.no.	Time	% drug release
1.	T1	53
2.	T2	55
3.	T3	58
4.	T4	62
5.	T5	64.8



Observation: Table and figure , concludes that RLD was completely released in dissolution media. Excel plot gives the % drug release in graphical form.

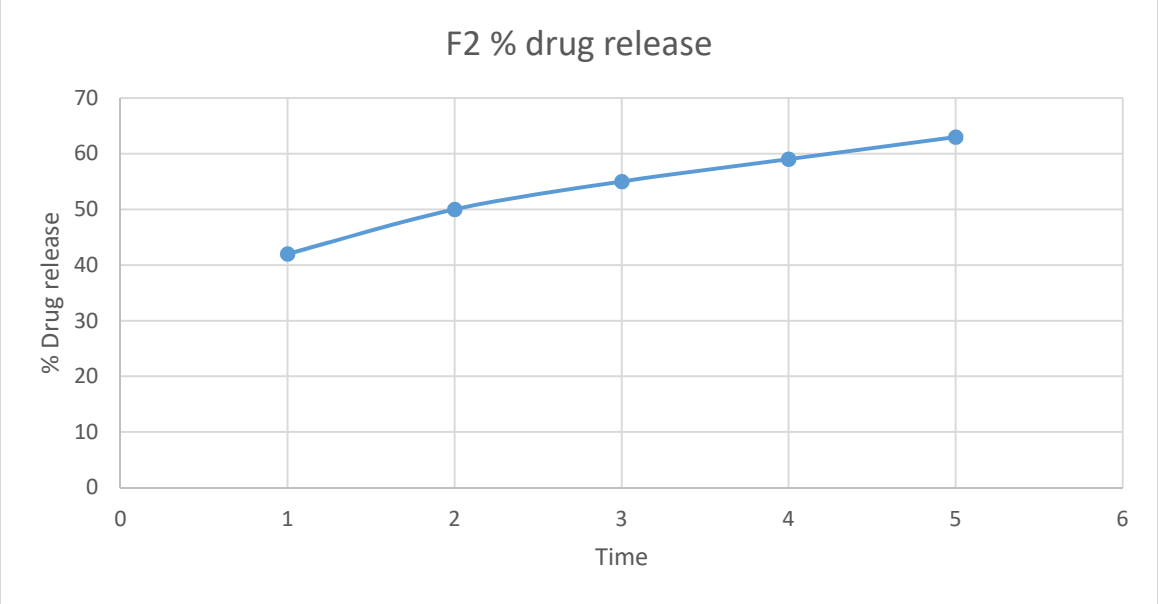
3.9.2. Dissolution results of RLD(f1):

Sr.no.	Time	% drug release
1.	T1	53
2.	T2	55
3.	T3	58
4.	T4	62
5.	T5	64.8



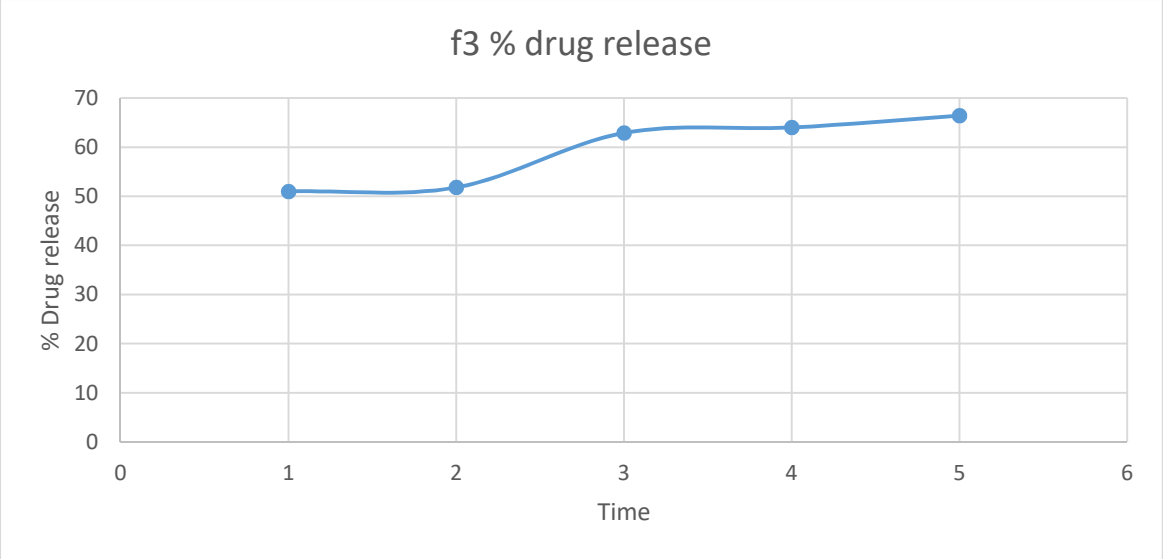
3.9.3. Dissolution results of RLD(f2):

Sr.no.	Time	% drug release
1.	T1	42
2.	T2	50
3.	T3	55
4.	T4	59
5.	T5	63



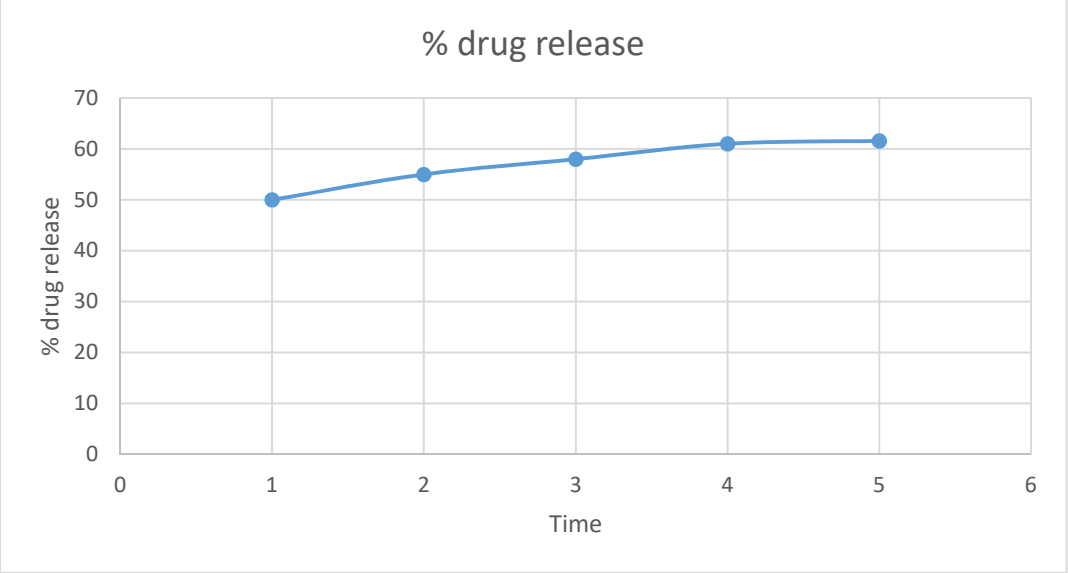
3.9. 4 Dissolution results of RLD(f3):

Sr.no.	Time	% drug release
1.	T1	51
2.	T2	51.8
3.	T3	62.9
4.	T4	64
5.	T5	66.4



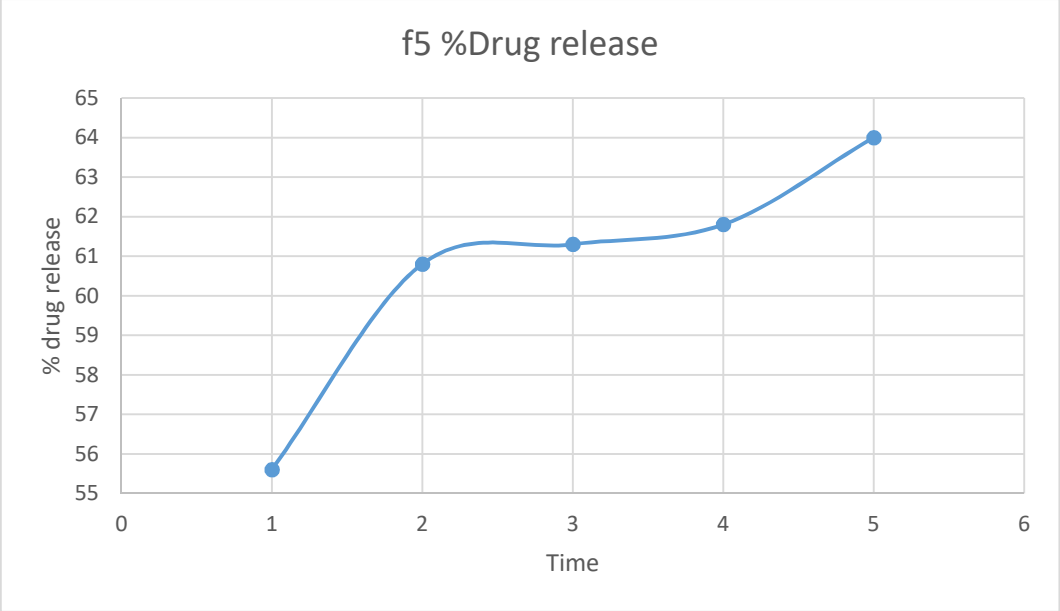
3.9. 5. Dissolution results of RLD(f4):

Sr.no.	Time	% drug release
1.	T1	50
2.	T2	55
3.	T3	58
4.	T4	61
5.	T5	61.6



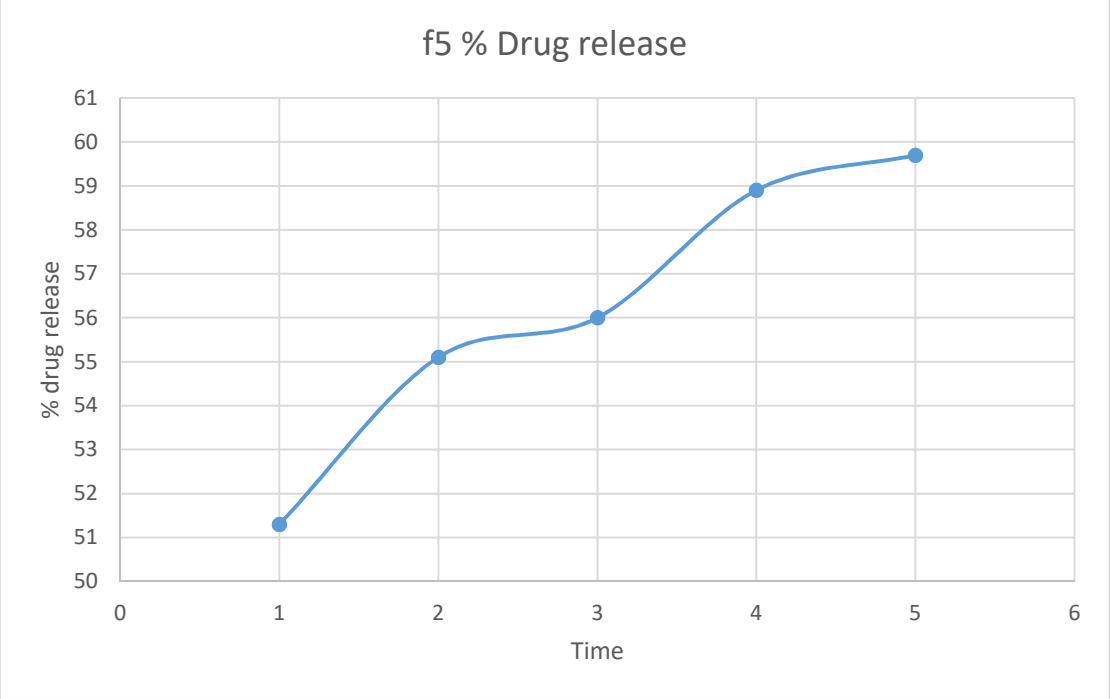
3.9.6. Dissolution results of RLD(f5):

Sr.no.	Time	% drug release
1.	T1	55.6
2.	T2	60.8
3.	T3	61.3
4.	T4	61.8
5.	T5	64

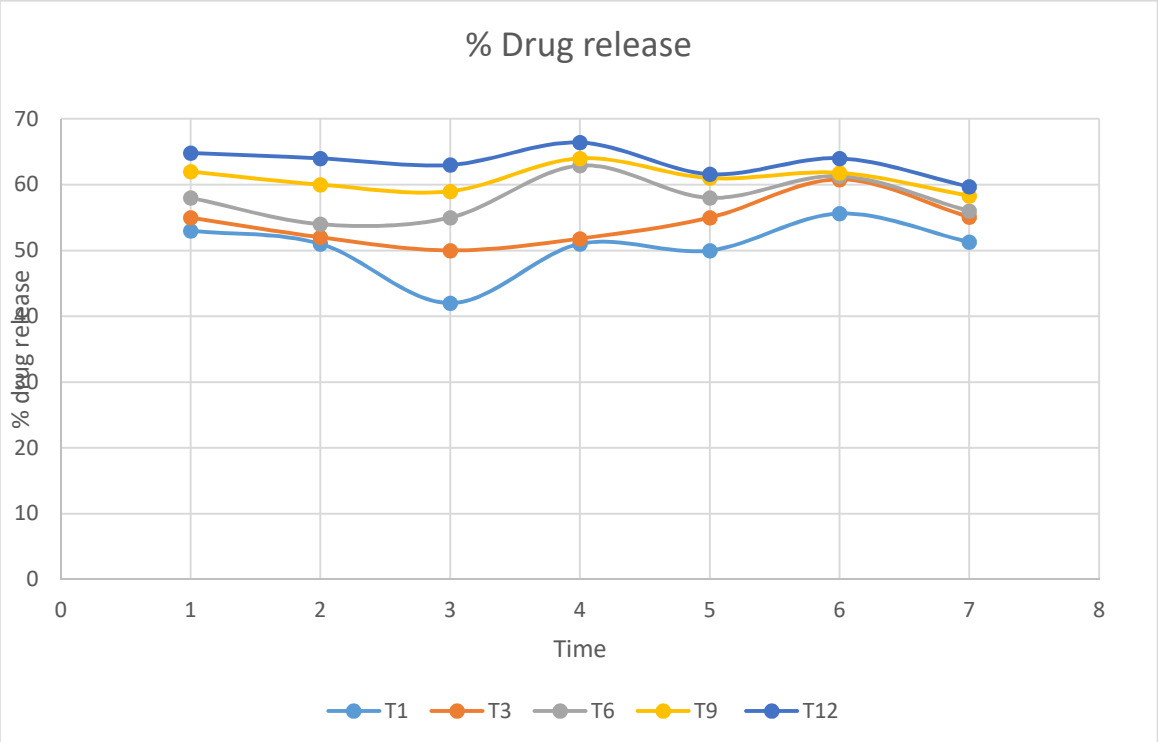


3.9.7. Dissolution results of RLD(f6):

Sr.no.	Time	% drug release
1.	T1	51.3
2.	T2	55.1
3.	T3	56
4.	T4	58.3
5.	T5	64.8



3.9.8. Comparative Dissolution profile of trail batches and RLD



Observations: The comparative figure , shows the all the dissolution results in one single plot. This plot shows that drug release profile if trail was comparable the RLD. F4 couldn't match with RLD.

DISCUSSION

The sustained release tablets of nicotinamide were successfully formulated using a wet granulation technique, with pectin and ethyl cellulose serving as the primary release-retarding polymers. Preformulation studies confirmed the good flow properties of the API, with a bulk density of 0.707 g/ml, tapped density of 0.838 g/ml, Hausner's ratio of 1.185, and Carr's index of 15.63%, indicating suitability for direct processing. Compatibility studies showed no significant interaction between the drug and excipients, ensuring formulation stability. Among the trials conducted (F1–F6), variations in polymer concentration and functional coating significantly influenced swelling behavior, drug release, and post-compression parameters. Trial F5 exhibited optimal results with a drug content of 100.65%, friability of 0.131%, and hardness of 12.86 KP, achieving 99.8% cumulative drug release over 7–11 hours. Coating played a critical role in modulating the release profile, as batches with 7–10% functional coating demonstrated better sustained release compared to uncoated formulations. Swelling index studies indicated that increased polymer ratios enhanced matrix integrity and controlled drug diffusion, particularly in formulations F5 and F6. Stability studies confirmed no significant changes in drug release or physical characteristics over the testing period. Overall, the optimized formulation achieved prolonged drug release, reduced dosing frequency, and improved potential patient compliance compared to conventional nicotinamide tablets.

CONCLUSION

The present research successfully formulated and evaluated sustained release tablets of nicotinamide with the aim of improving its pharmacokinetic performance, minimizing dosing frequency, and enhancing patient compliance. Various formulation trials (F1–F6) using wet granulation were conducted with natural and synthetic polymers, primarily pectin and ethyl cellulose, as release-retarding agents. The preformulation studies confirmed the suitability of excipients, and drug–excipient compatibility studies indicated no significant interactions. Among the trials, formulations with optimized polymer ratios demonstrated satisfactory hardness, friability, drug content, and swelling index. In vitro dissolution studies revealed that selected formulations, particularly F2, F5, and F6, achieved a controlled drug release profile up to 12 hours, closely matching the reference listed drug (RLD). Coating percentage and polymer concentration were found to significantly influence the drug release kinetics, highlighting their critical role in sustained release performance. Stability studies further confirmed the formulations' physicochemical stability under accelerated conditions. Overall,

the study established a robust formulation approach for nicotinamide sustained release tablets, ensuring consistent therapeutic levels, reduced dosing frequency, and improved patient adherence. Future work may involve in vivo pharmacokinetic studies and scale-up optimization to validate clinical performance and commercial viability.

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