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Development of Chronomodulated Pulsatile Drug Delivery Systems for Improved Therapeutic Efficacy of Antidiabetic Agents

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Abstract:

The present investigation was undertaken to develop and assess a film-coated oral tablet of Epalrestat intended for the treatment of diabetes mellitus. Preformulation investigations, including solubility studies, melting point determination, Fourier-transform infrared (FTIR) spectroscopy, and UV spectrophotometric analysis, were carried out to evaluate the physicochemical characteristics of the drug and its compatibility with the selected excipients. Core tablets were formulated using the direct compression technique with appropriate pharmaceutical excipients.

The prepared formulations were examined for key physicochemical parameters such as weight variation, hardness, thickness, friability, disintegration time, and drug content. Among the developed batches, formulation F6 demonstrated satisfactory evaluation results and was therefore selected as the optimized formulation for film coating. The coated tablets exhibited adequate mechanical strength, consistent drug content, and a controlled drug release profile. *In-vitro* dissolution studies indicated that more than 90% of the drug was released within 60 minutes. The findings suggest that the developed film-coated Epalrestat tablet possesses acceptable Preformulation and evaluation characteristics and may be suitable for oral drug delivery.

Keywords: Epalrestat, Film-coated tablets, Preformulation studies, Evaluation parameters, Controlled drug release.

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I. INTRODUCTION

The mechanism of drug delivery plays a crucial role in ensuring that the active pharmaceutical ingredient reaches the appropriate site, at the desired time, and in the required concentration to achieve the intended therapeutic effect[1]. Conventional oral drug delivery systems, such as immediate-release tablets, often fail to maintain consistent plasma drug levels, which may result in frequent dosing and an increased incidence of adverse effects[2]. To address these limitations, advanced drug delivery systems have been developed to deliver drugs at predetermined rates and times, thereby improving therapeutic efficacy and patient compliance[3]. Among these advancements, Pulsatile Drug Delivery Systems (PDDS) have attracted considerable attention for the management of diseases governed by circadian rhythms.[4] Unlike sustained-release dosage forms, PDDS are designed to release the drug rapidly and completely after a specific lag time, producing a single pulse of drug release[5]. This strategy is particularly advantageous for chronic metabolic disorders such as diabetes mellitus, where blood glucose levels exhibit predictable fluctuations over a 24-hour cycle[6]. Clinical evidence suggests that hepatic glucose production and insulin resistance are elevated during the early morning hours, a phenomenon known as the dawn phenomenon, which leads to fasting hyperglycemia[7]. Consequently, conventional antidiabetic medications administered at bedtime may fail to provide adequate glycemic control during this critical period[8].

A pulsatile drug delivery approach can be tailored to release antidiabetic agents, such as Epalrestat, during the early morning hours, thereby minimizing nocturnal hypoglycemic events and improving overall glycemic control[9]. Among various technologies used to design PDDS, the film coating method is widely preferred due to its ability to form a uniform polymeric membrane, excellent mechanical stability, and precise control over coating thickness[10]. Recent advancements in time-controlled oral dosage forms have highlighted the efficiency of tailored polymeric barriers to achieve sudden, post-lag phase drug release[11]. The system generally consists of a fast-disintegrating core tablet containing the antidiabetic drug and super disintegrants[12], which is subsequently wrapped in a functional, pH-dependent or time-controlled film coating layer (such as Eudragit) to regulate the precise lag time before drug liberation[13]. The primary objective of the present study is the development and evaluation of a pulsatile drug delivery system for an antidiabetic drug[14] using the film-coating approach to achieve a site-specific and time-controlled release pattern[15], thereby offering a more effective chronological approach to diabetes management.

II. Material and Methods

Materials

Epalrestat was obtained from Micro Labs Limited. (Bangalore, India), microcrystalline cellulose, lactose, sodium starch glycolate, magnesium stearate, hydroxypropyl methylcellulose (HPMC E5 LV Premium), ethyl cellulose and methanol were obtained from Loba Chemie Pvt. Ltd. (Mumbai, India); Eudragit L100 was obtained from Evonik (Essen, Germany); and ethanol (99.9%) was obtained from Changshu Hongsheng Fine Chemical Co., Ltd. (Jiangsu, China). All

excipients were of standard pharmacopoeia grade and all chemical reagents used for analysis were of analytical grade.

Preformulation Study

Solubility Study

The solubility behavior of Epalrestat was evaluated to obtain preliminary information required for formulation development. The study was carried out using a conventional shake-flask technique, which is widely adopted for qualitative solubility assessment during Preformulation studies.

An excess quantity of the drug was introduced into separate, tightly closed vials containing predetermined volumes of different solvents, including distilled water, methanol, chloroform, dichloromethane, dimethyl sulfoxide (DMSO), and phosphate buffer solutions of pH 1.2, 6.8, and 7.4. The mixtures were initially vortex-mixed to ensure uniform dispersion and subsequently placed on a mechanical shaker at ambient temperature (approximately 25 °C) for 24 hours to allow equilibrium to be attained.

After completion of the equilibration period, the samples were filtered to eliminate any undissolved drug particles. The clarity of the filtrates was visually inspected, and the solubility of the drug was qualitatively categorized as soluble or sparingly soluble based on the volume of solvent required for dissolution, in accordance with pharmacopoeial guidelines (IP/USP)[16].

Melting Point Determination

The melting point of Epalrestat was determined in order to assess the purity and thermal characteristics of the drug substance. A small amount of the powdered drug was filled into a thin-walled capillary tube sealed at one end. The capillary tube was then positioned in a Theil's melting point apparatus.

The temperature was gradually increased, and the point at which the drug sample completely transformed from solid to liquid state was carefully observed and recorded. The melting point obtained was compared with reported literature values to confirm the identity and purity of the drug[17].

Partition Coefficient Study

The partition coefficient of Epalrestat was determined to evaluate its lipophilic–hydrophilic balance, which is an important parameter influencing drug absorption and formulation behavior. The study was performed using the n-octanol and aqueous phosphate buffer system.

Equal volumes of n-octanol and phosphate buffer were transferred into a separating funnel. A known quantity of the drug was added to the biphasic system, and the mixture was shaken vigorously for 10 minutes to facilitate drug distribution between the two phases. The system was then allowed to stand undisturbed for 24 hours to achieve complete phase separation.

Following equilibration, the aqueous and organic layers were carefully separated and centrifuged at 2000 rpm for 10 minutes to remove any suspended particles. The drug content in each phase was quantified using a UV–Visible spectrophotometer at the respective λ max of the drug. The partition coefficient was calculated as the ratio of drug concentration in the n-octanol phase to that in the aqueous phase[18].

FTIR Analysis

Fourier Transform Infrared (FTIR) spectroscopy was employed to examine possible interactions between Epalrestat and the selected excipients. A small quantity (approximately 2–3mg) of each sample was thoroughly blended with spectroscopic-grade potassium bromide (KBr). The mixture was then compressed using a hydraulic press to obtain clear pellets. The prepared pellets were scanned in the infrared region ranging from 4000 to 400 cm^{-1} at an appropriate resolution. The obtained spectra of excipients were carefully compared with that of pure Epalrestat to identify any potential chemical incompatibility[19].

UV-Spectrophotometric Analysis

A primary stock solution of Epalrestat (1000 µg/mL) was prepared by dissolving an accurately weighed quantity of the drug (10 mg) in phosphate buffer (pH 6.8) and making up the volume to 10 mL in a volumetric flask. From this solution, an aliquot of 1 mL was further diluted to 10 mL with the same buffer to obtain a working standard solution of 100 µg/mL. The working solution was scanned in the wavelength range of 200–400 nm using a UV-Visible spectrophotometer, with phosphate buffer as blank, to determine the maximum absorbance wavelength (λmax), which was observed at 390 nm[20-22].

Calibration solutions were prepared by transferring suitable volumes (0.1–1.0 mL) of the working standard into 5 mL volumetric flasks and diluting with phosphate buffer to obtain concentrations of 2–20 µg/mL. Absorbance measurements were carried out at 390 nm in triplicate, and the mean absorbance values were used to construct the calibration curve[23,24].

Preparation of Core Tablets

Core tablets containing Epalrestat were manufactured using the direct compression technique as reported in the literature[25]. Various formulations (F1–F6) were designed, and their compositions are presented in **Table 1**. Precisely weighed quantities of Epalrestat, microcrystalline cellulose, lactose, ethyl cellulose, HPMC, Eudragit, and sodium starch glycolate were individually passed through sieve no. 40 and blended uniformly for 20 minutes. [26]. Magnesium stearate, previously sieved separately, was added to the blend and mixed further for 10 minutes to ensure uniform distribution[27].

The final powder blend was compressed using a rotary tablet compression machine equipped with suitable punches to produce core tablets weighing 355 mg[28,29].

Table 1. Formulation of Core Tablets of Epalrestat (F1–F6)

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Epalrestat	50	50	50	50	50	50

Microcrystalline cellulose	120	120	120	120	–	–
Lactose	100	100	100	100	100	100
Ethyl cellulose	78	68	58	48	–	–
HPMC	–	–	–	–	38	28
Eudragit	–	–	–	–	12	22
Sodium starch glycolate	10	20	30	40	50	60
Magnesium stearate	5	5	5	5	5	5

Note: All values in mg per tablet.

Equipment Used for Tablet Compression

Tablet compression was performed using a single-station manual tablet compression machine fitted with round concave punches and dies. The powder blend was manually compressed to obtain tablets of consistent weight and thickness. Compression force was optimized to achieve tablets with sufficient hardness and mechanical stability. The prepared tablets were visually inspected for surface imperfections and stored in airtight containers for subsequent evaluation studies **(Fig. 1).**

Fig. 1: Tablet compression machine used for the preparation of core tablets by direct compression method.

Selection of Optimized Formulation

Formulation F6 was chosen as the optimized core tablet based on its satisfactory mechanical strength, consistent thickness, and friability below 1%, indicating acceptable tablet integrity. Therefore, formulation F6 was considered suitable for further coating studies **(Fig.2)**.

Tablet coating

The compressed tablets were coated using a manual spray coating technique in a laboratory-scale conventional coating pan at the Pharmaceutics Laboratory, School of Pharmacy, Shri Shankaracharya Professional University (SSPU), Bhilai, India.

The coating process was performed to study the effect of different coating levels on drug release behavior. Tablets were coated to achieve 5%, 10%, and 15% weight gain.

Although the coating solution was applied manually using a spray gun, the overall process was carried out in a rotating pan coating setup, ensuring uniform exposure of tablets to the coating solution and controlled drying conditions **(Fig.2)**.

Fig. 2: Laboratory-scale pan coating apparatus used for manual spray coating of tablets.

Coating solution

The coating solution consisted of ethyl cellulose (95%) as the film-forming polymer and dibutyl phthalate (5%) as a plasticizer. The solution was prepared as a 6% w/v mixture using acetone and propan-2-ol in a 50:50 v/v ratio.

All the chemicals used were of analytical grade and procured from Loba Chemie Pvt. Ltd. (Mumbai, India).

Coating conditions

Coating was carried out at an inlet air temperature of 30–35 °C with a pan speed of 25 rpm. The spray rate was maintained at 2–2.5 g/min using a spray nozzle of 1.0 mm diameter. Coated tablets were dried at room temperature after achieving the desired weight gain **(Fig.3)**.

Fig. 3: Representative image of polymer-coated tablets of the optimized formulation F6 after completion of the coating process.

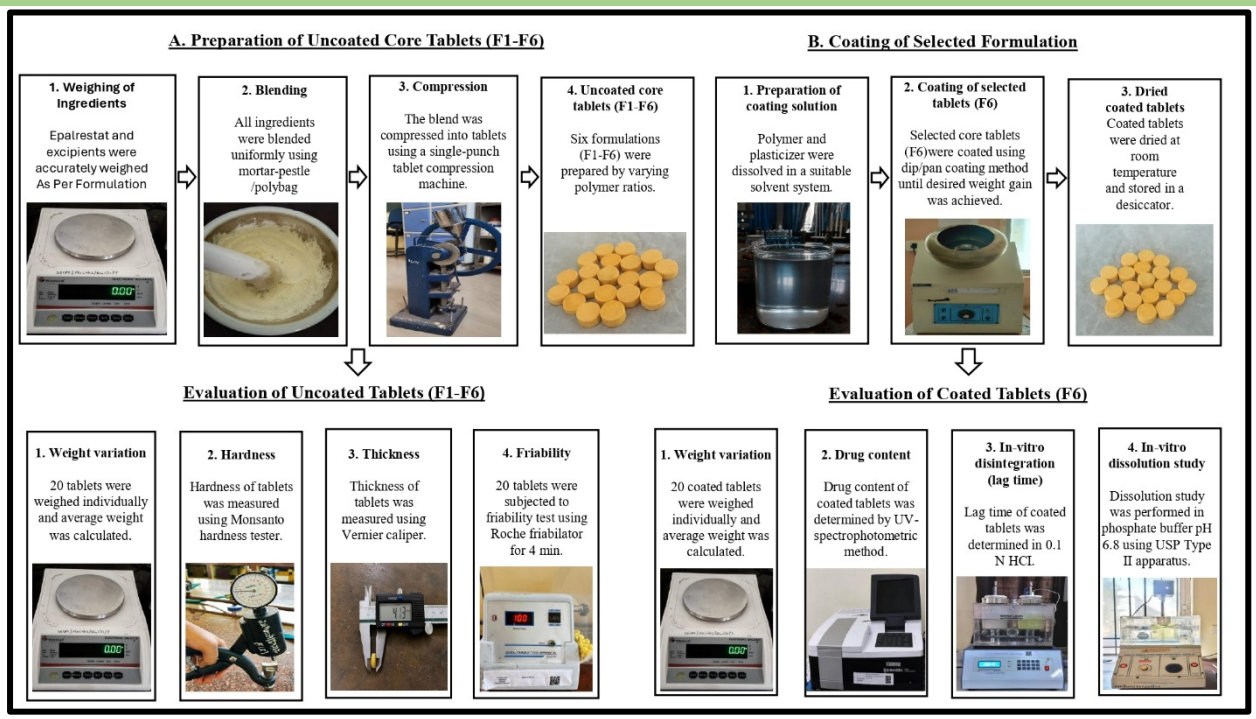

Fig. 4: Schematic representation of the preparation of uncoated core tablets (F1–F6), coating of the optimized formulation (F6), and evaluation of uncoated and coated tablets.

III. Evaluation of Tablets

Weight Variation Test

The average weight of twenty tablets selected at random was calculated. Each tablet was weighed individually, and the percentage deviation of individual tablet weight from the mean value was determined to evaluate uniformity of weight[30].

Weight variation (%) = (Individual tablet weight − Average tablet weight) / Average tablet weight × 100

Hardness Test

Tablet hardness was evaluated using a Monsanto hardness tester. From each formulation batch, three tablets were randomly selected and individually tested for crushing strength. The average hardness value obtained from these measurements was calculated and recorded[31].

Thickness

Tablet thickness was determined using both a micro-screw gauge and a vernier calliper. For each formulation batch, three tablets were randomly selected, and their thickness was measured individually. The obtained values were recorded and used for further evaluation[32].

Friability Test

The friability of the prepared tablets was assessed using a Roche Friabilator. The instrument consists of a rotating drum that permits the tablets to fall freely from a height of approximately six

inches during each rotation. The test was conducted for a duration of four minutes at a rotational speed of nearly 25 rpm.

Twenty tablets were accurately weighed prior to the test to obtain the initial weight and then placed in the Friabilator. After completion of the test, the tablets were removed, carefully dedusted using a soft muslin cloth, and reweighed to determine the final weight (W)[33].

This test evaluates the mechanical strength of tablets and their resistance to abrasion, breakage, and surface damage during handling, packaging, and transportation. Tablets exhibiting friability values below 1% were considered acceptable.

The percentage friability was calculated using the following formula:

Friability = [(Initial weight - Final weight) / Initial weight] × 100

Disintegration Test

The disintegration time of the tablets was determined using Disintegration Test Apparatus (Electrolab, Model 1901), as illustrated in the figure. Six tablets from each formulation batch were individually placed into the tubes of the apparatus. The test was performed using distilled water maintained at a temperature of 37.0 ± 0.5 °C.

The time required for complete disintegration of each tablet was recorded using a digital stopwatch. Complete disintegration was defined as the stage at which no palpable mass or solid residue remained on the screen of the apparatus. The experiment was carried out in triplicate, and the mean disintegration time was calculated and reported[34].

Drug Content Assay

The tablets were finely powdered using a mortar and pestle, and a quantity of powder equivalent to 10 mg of the drug was accurately weighed. The weighed sample was dissolved in methanol to obtain a stock solution. From this solution, aliquots ranging from 0.1 to 1.0 mL were withdrawn and diluted up to 5 mL with buffer solution to achieve concentrations between 2 and 20 µg/mL[35].

The prepared samples were analyzed using a UV–Visible spectrophotometer (Shimadzu UV-1780) at the selected wavelength. A standard solution of the pure drug at the same concentration was also analyzed under identical experimental conditions[36].

The percentage drug content was calculated using the appropriate formula, and the assay was performed in triplicate for each formulation batch.

Dissolution Study (*In-vitro* Study)

In-vitro dissolution studies were carried out using USP Apparatus-II (paddle method). The dissolution medium consisted of 900 mL of phosphate buffer with pH 6.8. The tablet was placed in the dissolution vessel containing the buffer, and the apparatus was operated under standard test conditions.

Samples of the dissolution medium were withdrawn at predetermined time intervals of 5, 10, 15, 30, 45, and 60 minutes. After each withdrawal, an equal volume of fresh phosphate buffer (pH 6.8) was added to maintain sink conditions. The collected samples were suitably diluted and analyzed using a UV–Visible spectrophotometer, and the cumulative percentage drug release was calculated.

The dissolution study was performed for both coated and uncoated tablets under identical experimental conditions to facilitate comparison of their drug release profiles[36,37].

IV. Results and Discussion

Preformulation Study

Solubility Study

The solubility study revealed that the drug is soluble in chloroform, dichloromethane, methanol and DMSO, whereas it is sparingly soluble in water and phosphate buffer solutions of pH 1.2, 6.8 and 7.4. This indicates that the drug shows better solubility in organic solvents compared to aqueous media **(Table 2)**.

Table 2: Solubility study

S. No.	Solvents	Solubility
1.	Water	Sparingly soluble
2.	Chloroform	Soluble
3.	Di-chloroform	Soluble
4.	Methanol	Soluble
5.	DMSO	Soluble
6.	Phosphate buffer pH 1.2	Sparingly soluble
7.	Phosphate buffer pH 6.8	Sparingly soluble
8.	Phosphate buffer pH 7.4	Sparingly soluble

Melting Point

The value of observed melting point range is given in the table below along with the reported melting point range **(Table 3)**.

Table 3: Observed Melting Point of Epalrestat

Parameter	Reference value	Experimental value	Final value
Melting point	210–217 °C	213 ± 0.58 °C 215 ± 0.58 °C 215 ± 0.58 °C	215 ± 0.58 °C

Mean ± SD, n = 3

Fig.5: Melting Point Apparatus Model 931

The experimental melting point of Epalrestat was found to be 21 ± 0.58 °C, which lies within the reported range of 210–217 °C, indicating the purity of the drug sample **(Fig.5)**[38].

Partition Coefficient

The partition coefficient study showed that Epalrestat preferentially distributed into the octanol phase as compared to the aqueous phase. The log P value of Epalrestat was found to be 2.7 ± 0.41 (mean ± SD, n = 3), indicating that the drug possesses lipophilic nature. The obtained value was found to be in good agreement with reported literature values of Epalrestat, confirming its physicochemical suitability for formulation development **(Fig.6)**[39].

Fig.6: Separating funnel showing aqueous and n-octanol phases.

Preformulation Compatibility Study (FTIR Analysis)

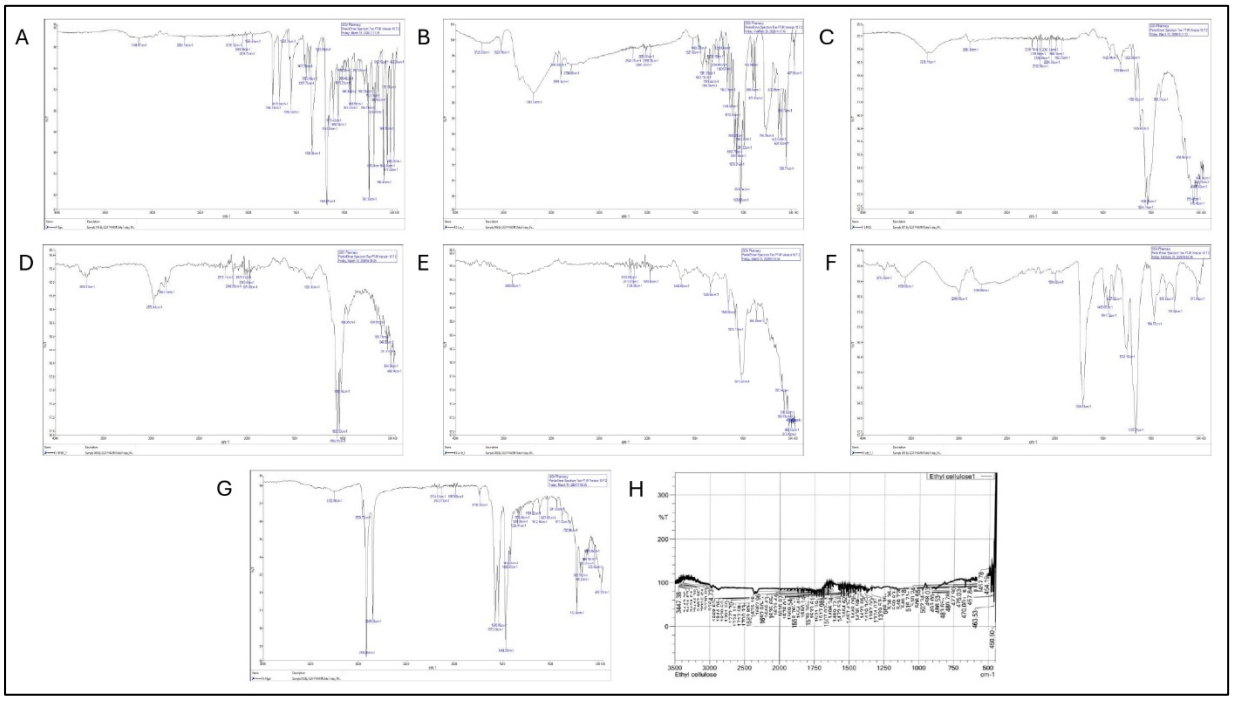

Fig.7: FTIR of (A) Epalrestat (B) Lactose (C) MCC (D) HPMC (E) SSG (F) Eudragit (G) Magnesium Stearate (H) Ethyl Cellulose

FTIR spectroscopy was performed as a key component of the Preformulation study to establish the fundamental chemical fingerprint of pure Epalrestat and to examine its theoretical compatibility with the selected excipients proposed for formulation development, namely Lactose, MCC, HPMC, SSG, Eudragit, Magnesium Stearate, and Ethyl Cellulose.

The FTIR spectrum of the pure active pharmaceutical ingredient (API), Epalrestat, exhibited well-defined and sharp characteristic absorption peaks corresponding to its major functional groups. Prominent peaks were observed at approximately 3300 cm^{-1}, attributed to –NH stretching vibrations; 2920 cm^{-1}, associated with aliphatic C–H stretching; 1715 cm^{-1}, indicative of carbonyl (C=O) stretching; 1600 cm^{-1}, corresponding to aromatic C=C stretching; and 1240 cm^{-1}, related to C–N stretching vibrations.

The FTIR spectra of the individual excipients were analyzed and compared with that of the drug. The comparison confirmed that the characteristic peaks of Epalrestat remained intact and clearly distinguishable in the presence of each excipient. No significant peak shifting, disappearance, or formation of new peaks was observed, indicating the absence of any chemical interaction or degradation. This observation suggests satisfactory physical and chemical stability of the drug with the selected excipients.

Overall, the FTIR compatibility study confirms that Epalrestat is compatible with Lactose, MCC, HPMC, SSG, Eudragit, Magnesium Stearate, and Ethyl Cellulose. The findings support the

suitability of these excipients for use in the subsequent development of a stable oral drug delivery system **(Fig. 7)**.

UV-Spectrophotometric Analysis

Determination of λ max (UV Spectrophotometric Analysis)

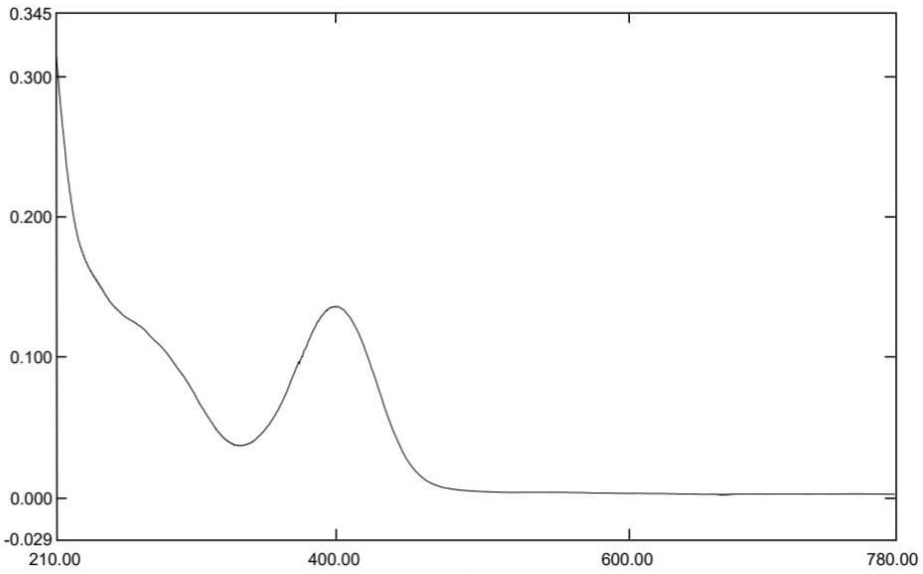

Fig.8: UV absorption spectrum of Epalrestat in phosphate buffer pH 6.8 showing λ max at 390 nm

The UV absorption spectrum of Epalrestat in phosphate buffer pH 6.8 revealed a distinct maximum absorbance at 390 nm, which was selected as the λ max for further analytical studies **(Fig. 8)**.

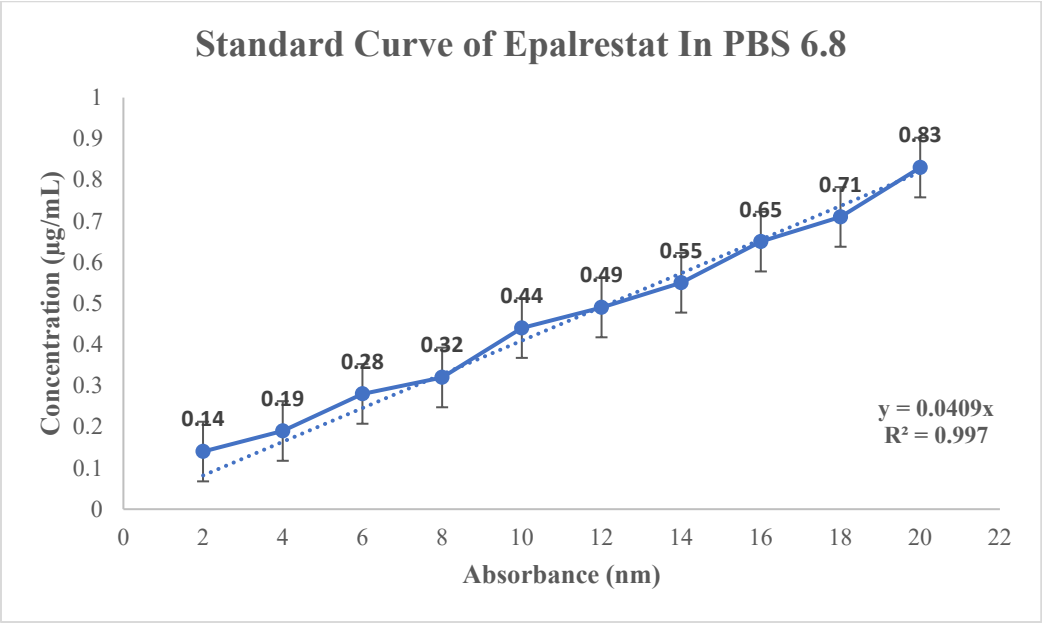

Fig. 9: Calibration curve of Epalrestat in phosphate buffer pH 6.8 at 390 nm

A calibration curve was constructed by plotting absorbance against concentration in the range of 2–20 µg/mL at 390 nm. The curve demonstrated good linearity with a regression equation of y = 0.0409x and a correlation coefficient (R^2) of 0.997, confirming adherence to Beer–Lambert's law **(Fig. 9)**[40].

The UV-spectrophotometric method was developed to evaluate the λ max and linearity of Epalrestat in phosphate buffer pH 6.8. The drug exhibited maximum absorbance at 390 nm, which is consistent with values reported in the literature, thereby validating the appropriateness of the selected wavelength for quantitative analysis. The calibration curve displayed excellent linearity within the concentration range of 2-20 µg/mL, with a high correlation coefficient (R^2 = 0.997), indicating a strong relationship between absorbance and concentration.

The reproducibility and clarity of absorbance values further demonstrate that phosphate buffer pH 6.8 serves as a suitable solvent system for the UV analysis of Epalrestat. Consequently, the developed method is reliable and appropriate for drug estimation during formulation development and *In-vitro* drug release studies[24,29].

Evaluation of Uncoated Core Tablets

Table 4: Evaluation of Uncoated Core Tablets (F1–F6)

S.N.	Formulation	Hardness (kg/cm²)	Thickness (mm)	Friability (%)
1	F1	3.2 ± 0.2	4.12 ± 0.04	1.25
2	F2	3.6 ± 0.3	4.09 ± 0.03	1.08
3	F3	4.0 ± 0.2	4.15 ± 0.05	0.95
4	F4	4.3 ± 0.3	4.11 ± 0.04	0.88
5	F5	4.6 ± 0.2	4.14 ± 0.03	0.76
6	**F6**	**4.9 ± 0.2**	**4.13 ± 0.04**	**0.62**

Mean ± SD, n = 3

All uncoated core tablet formulations (F1–F6) were evaluated for hardness, thickness, and friability. Hardness increased progressively from F1 to F6, while friability values decreased and remained within acceptable pharmacopoeial limits. Tablet thickness was found to be uniform across all formulations **(Fig.10; Table 4)**.

Table 5. Evaluation of Coated Tablets (Optimized Formulation F6)

S.N.	Formulation	Hardness (kg/cm²)	Thickness (mm)	Friability (%)
1	F6	5.4 ± 0.3	4.48 ± 0.05	0.58

Mean ± SD, n = 3

After coating, formulation F6 showed a slight increase in hardness and thickness due to the presence of a polymeric coating layer. Friability remained below 1%, confirming that the coating process did not adversely affect tablet strength **(Fig.10; Table 5)**.

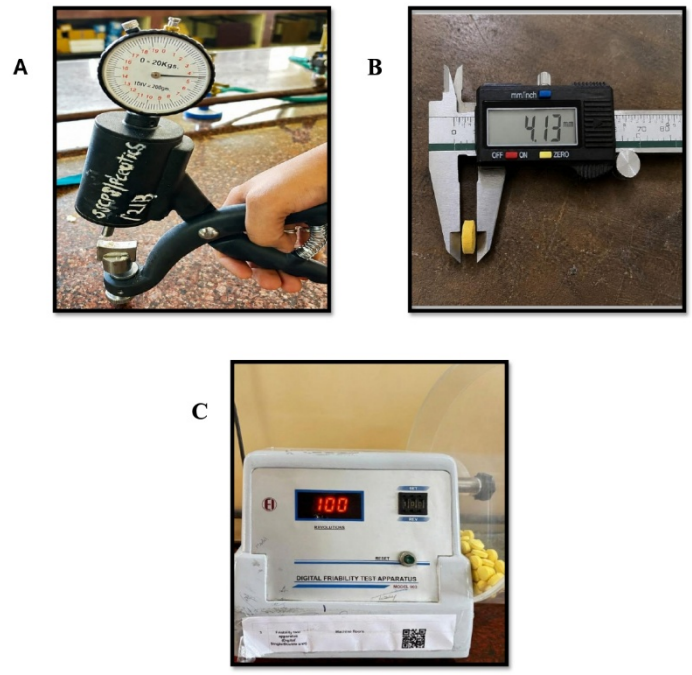

Fig.10: (A) Hardness testing of tablet using Monsanto hardness tester B) Measurement of thickness of tablets using digital vernier calliper (C) Digital Friability Test Apparatus (Roche Friabilator)

Weight Variation Study

The weight variation test was performed for the optimized uncoated core tablets and coated tablets of formulation F6 to evaluate uniformity of tablet weight

Table 6. Weight Variation of Uncoated and Coated Tablets (F6)

S.N.	Formulation	Average weight (mg)	Pharmacopoeial limit
1.	Uncoated F6	355 ± 4.2	±5%
2.	Coated F6	390 ± 5.1	±5%

Mean ± SD, n = 3

Both uncoated and coated tablets of formulation F6 complied with pharmacopoeial limits for weight variation. The uncoated tablets showed uniform weight distribution, indicating consistent die filling. A slight increase in average weight was observed in coated tablets due to the deposition of the coating layer **(Table 6)**.

Disintegration Test

The disintegration time of the coated tablets (F6) was found to be 28.6 ± 0.7 min. The increased disintegration time compared to uncoated core tablets may be attributed to the presence of a polymeric coating layer, which delayed the penetration of the dissolution medium. This confirms the integrity of the coating and its role in controlling tablet disintegration **(Fig.11; Table 7)**.

Table 7. Disintegration time of coated tablets (Optimized formulation F6)

S.N.	Formulation	Disintegration time (min)
1.	F6	28.6 ± 0.7

Mean ± SD, n = 3

Fig. 11: Disintegration test apparatus showing the disintegration behavior of film-coated pulsatile Epalrestat tablets in distilled water maintained at 37 ± 0.5 °C

Drug Content Assay

Table 8: Drug content of coated tablets (F6)

S.N.	Sample	Absorbance	Drug content (%)
1.	Tablet 1	0.407	97.6
2.	Tablet 2	0.414	98.4
3.	Tablet 3	0.401	96.9
4.	Tablet 4	0.419	99.1
5.	Tablet 5	0.409	97.8
6.	Tablet 6	0.416	98.6

The drug content assay was performed to determine the uniformity of Epalrestat distribution within the coated tablets of formulation F6. The percentage drug content of individual tablets was calculated based on UV absorbance values obtained from the tablet solutions and compared with the standard drug solution. The results are expressed as mean ± standard deviation **(Table 8)**.

***In-vitro* Dissolution Study**

Table 9. *In-vitro* drug release profile of Coated Epalrestat tablets (F6)

S.N.	Time (min)	Absorbance	Cumulative % Drug Release
1.	5	0.223	22.6
2.	10	0.299	30.3
3.	15	0.373	37.8

4.	30	0.537	54.4
5.	45	0.821	83.2
6.	60	0.903	91.4

The dissolution study of the selected coated formulation (F6) was performed utilizing a phosphate buffer medium maintained at pH 6.8. Absorbance values were converted into percentage drug release using the previously constructed calibration curve **(Table 9)**.

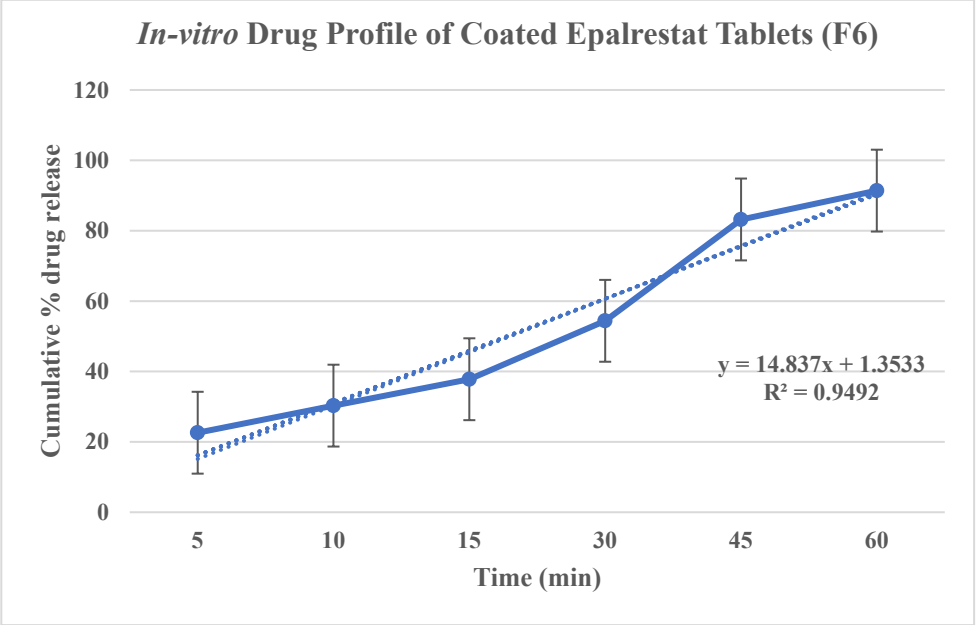

Figure 12: Coated Epalrestat tablets *In-vitro* drug release profile (F6).

Each data point represents the mean value obtained from triplicate measurements **(Fig.12)**.

Fig. 13: USP Apparatus II (Paddle method) used for *In-vitro* dissolution study.

V. Conclusion

The present study successfully developed and evaluated film-coated Epalrestat tablets using the direct compression method followed by polymer coating. Preformulation studies confirmed

the suitability and compatibility of the drug with the selected excipients. Among all formulations, F6 showed satisfactory hardness, thickness, friability, and drug content, and was selected as the optimized formulation. The coated tablets exhibited good physical characteristics and an immediate drug release profile, achieving more than 90% drug release, $y = 14.837x + 1.3533$, $R^2 = 0.9492$, and % Drug release *In-vitro* drug profile of coated Epalrestat tablets (F6) within 60 minutes. The results indicate that the developed formulation is a promising oral drug delivery system for Epalrestat and may contribute to improved therapeutic efficacy and patient compliance in the management of diabetes mellitus.

CRediT Authorship Statement

CRediT Authorship Statement: **Saket Singh Rajput** contributed to manuscript review and editing. **Neelam** was involved in reviewing and editing the manuscript. **Derhu Jangde** contributed to the preparation of the original draft and was responsible for visualization, validation, and software-related tasks. **Prince Nikhil Rathore** contributed by providing resources and performing formal analysis. **Suman Shrivastava** was responsible for data curation, methodology development, and conceptualization of the study. **Swarnali Das Paul** was involved in software handling and validation. **Rashmi Madhariya** supervised the study, contributed to investigation, resource support, formal analysis and prepared the final draft of the manuscript after critical review for publication.

Conflict of Interests

The authors affirm that the work described in this publication was not influenced by any known competing financial interests or personal ties.

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