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FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLETS OF PENTOXIFYLLINE

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Abstract:

The present study aimed to develop and evaluate sustained-release matrix tablets of Pentoxifylline using Hydroxypropyl Methylcellulose K4M (HPMC K4M) as a release-retarding polymer. Pentoxifylline has a short biological half-life and requires frequent administration, making it a suitable candidate for sustained-release delivery. Preformulation studies including organoleptic evaluation, solubility, melting point, UV spectrophotometric analysis and FTIR compatibility were performed. Seven formulations (F1–F7) were prepared by wet granulation using different concentrations of HPMC K4M. The prepared granules showed satisfactory flow and compressibility properties, while tablets exhibited acceptable weight variation, thickness, hardness, friability and drug-content uniformity. In-vitro dissolution studies demonstrated a concentration-dependent retardation of drug release with increasing HPMC K4M concentration. Formulation F5 was selected as the optimized formulation based on its satisfactory pharmaceutical characteristics and sustained-release profile. Kinetic analysis showed that drug release followed the Higuchi model predominantly, with diffusion, polymer relaxation and erosion contributing to the release mechanism.

Keywords: *Pentoxifylline, Sustained-release matrix tablet, HPMC K4M, Wet granulation, Drug release, Higuchi model, Diffusion, Matrix system.*

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1. INTRODUCTION:

Oral drug delivery remains one of the most widely accepted approaches for administering therapeutic agents because of its convenience, patient acceptability, ease of administration, and cost-effectiveness.[1] However, conventional immediate-release dosage forms may present several limitations, particularly when the drug has a short biological half-life. Rapid drug release followed by elimination can produce fluctuations in plasma drug concentration, requiring frequent administration to maintain the desired therapeutic effect. Such fluctuations may also influence treatment consistency and patient compliance. These limitations have encouraged the development of modified and sustained-release drug delivery systems capable of maintaining drug concentrations within the therapeutic range for a prolonged period.[2]

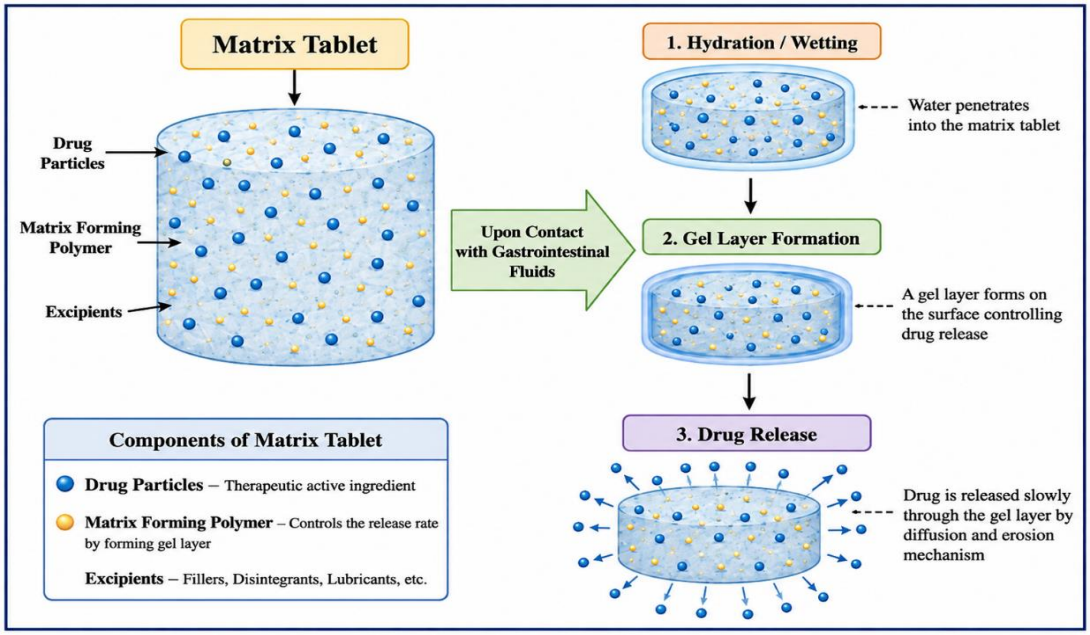

Figure 1. General Structure of a Matrix Tablet System

Sustained-release formulations are designed to release the drug gradually over an extended duration, thereby reducing dosing frequency and minimizing variations in plasma drug concentration. Among the different approaches, matrix tablets are widely investigated because of their simple formulation, ease of manufacturing, cost-effectiveness, and flexibility in controlling drug release.[3] In hydrophilic matrix systems, polymers such as hydroxypropyl methylcellulose (HPMC) hydrate in gastrointestinal fluids and form a viscous gel layer that controls drug diffusion and polymer erosion. The release pattern can be modified by varying the type and concentration of the polymer.[4]

Pentoxifylline is a methylxanthine derivative used mainly in the management of peripheral vascular disorders, particularly intermittent claudication. It improves blood rheology by increasing erythrocyte flexibility, reducing blood viscosity, and improving microcirculatory blood flow. The drug is rapidly absorbed after oral administration and undergoes extensive first-pass metabolism. Its short elimination half-life of approximately 0.4–0.8 h makes frequent administration necessary with conventional formulations.[5]

These pharmacokinetic characteristics make Pentoxifylline a suitable candidate for sustained-release formulation. Incorporation of the drug into a hydrophilic matrix containing HPMC K4M can provide prolonged drug release through swelling, diffusion, and erosion mechanisms. Such an approach may help maintain therapeutic drug concentrations, reduce dosing frequency, and improve patient compliance. Therefore, the present study focuses on the development and evaluation of Pentoxifylline sustained-release matrix tablets using an appropriate polymeric matrix system.[6]

2. MATERIALS AND METHODS:

2.1 Materials

Pentoxifylline was used as the active pharmaceutical ingredient for the development of sustained-release matrix tablets. Hydroxypropyl Methylcellulose K4M (HPMC K4M) was selected as the release-retarding polymer.[7] Microcrystalline Cellulose PH 102 (MCC) was used as diluent and dry binder, while magnesium stearate and talc were incorporated as lubricant and glidant, respectively. Sodium Starch Glycolate (SSG) was included at a low concentration to facilitate controlled hydration of the matrix. Isopropyl alcohol was used as the granulating solvent and distilled water was used

during analytical procedures. All materials were of pharmaceutical or analytical grade and were used as received. The major functions of the excipients were selected according to their contribution to powder flow, compressibility, matrix formation, lubrication and drug-release control.[8]

2.2 Instruments and Equipment

The formulation and evaluation studies were performed using calibrated laboratory instruments. An analytical balance was used for accurate weighing of materials, while a UV–Visible spectrophotometer was employed for drug estimation. FTIR spectroscopy was used for drug–excipient compatibility assessment. A USP Type II dissolution apparatus was used for in-vitro drug-release studies.[9] A Roche friabilator, Monsanto hardness tester and digital Vernier caliper were used for evaluation of friability, hardness and tablet thickness, respectively. A hot-air oven was used for drying the granules, and a rotary tablet compression machine was employed for tablet manufacture. A digital pH meter was also used during analytical investigations.[10]

2.3 Preformulation Studies

2.3.1 Organoleptic Evaluation

Pentoxifylline was examined for its physical appearance, colour, odour and general characteristics as a preliminary identification and quality assessment step. The observations were compared with reported pharmacopoeial characteristics.[11]

2.3.2 Solubility Study

The solubility of Pentoxifylline was investigated in distilled water, methanol, ethanol and phosphate buffer pH 6.8. An excess quantity of drug (100 mg) was added separately to 10 mL of each solvent and equilibrated at 37 ± 0.5°C with shaking at 100 rpm for 24 h. After equilibration, samples were allowed to stand, filtered through Whatman No. 1 filter paper and suitably diluted. Absorbance was measured at 274 nm using a UV–Visible spectrophotometer. The study was performed in triplicate, and solubility was calculated as the amount of dissolved drug per millilitre of solvent.[12]

2.3.3 Melting Point

The melting point of Pentoxifylline was determined by the capillary fusion method. Finely powdered drug was filled into a capillary tube and heated gradually at approximately 1–2°C/min near the expected melting range. The temperature at which the solid completely changed into a clear liquid was recorded. The determination was performed in triplicate and expressed as mean ± SD.[13]

2.3.4 Determination of λmax and Calibration Curve

A standard solution of Pentoxifylline was scanned in the UV region to determine its wavelength of maximum absorption. The selected wavelength was subsequently used for quantitative analysis. A concentrated standard solution was prepared and serially diluted to obtain different concentrations. The absorbance values were measured at the selected wavelength, and a calibration curve was constructed by plotting concentration against absorbance.[14]

2.3.5 Drug–Excipient Compatibility

Compatibility between Pentoxifylline and HPMC K4M was investigated using FTIR spectroscopy. Spectra of the pure drug and physical mixture of drug with polymer were recorded and compared. Characteristic functional-group peaks were examined for changes in position, disappearance or appearance of new peaks. Absence of significant spectral changes was considered indicative of compatibility.[15]

2.4 Formulation Development

Sustained-release matrix tablets were prepared using HPMC K4M as the principal release-retarding polymer. Seven formulations (F1–F7) were developed by maintaining Pentoxifylline at 400 mg per tablet while progressively increasing HPMC K4M from 40 to 160 mg. MCC was correspondingly adjusted from 135 to 15 mg to maintain a constant tablet weight of 600 mg. SSG was maintained at 10 mg, whereas talc and magnesium stearate were used at 5 and 10 mg, respectively. The formulation design therefore enabled investigation of the influence of increasing polymer concentration on drug-release behaviour.[16]

Table 1. Composition of Pentoxifylline Sustained-Release Matrix Tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7
Pentoxifylline	400	400	400	400	400	400	400
HPMC K4M	40	60	80	100	120	140	160
MCC PH 102	135	115	95	75	55	35	15
Sodium Starch Glycolate	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5
Magnesium Stearate	10	10	10	10	10	10	10
Total weight	**600**	**600**	**600**	**600**	**600**	**600**	**600**

2.5 Preparation of Matrix Tablets

The tablets were prepared by the wet granulation method. Pentoxifylline, HPMC K4M and MCC PH 102 were passed separately through a 40-mesh sieve and mixed thoroughly for approximately 10 min. Isopropyl alcohol (approximately 8–12 mL per batch) was gradually added with continuous mixing until a cohesive, non-sticky wet mass was obtained. The wet mass was passed through a 16-mesh sieve to produce uniform granules.[17]

The prepared granules were dried in a hot-air oven at 45 ± 2°C for approximately 30–45 min or until the moisture content was below 2% w/w. Dried granules were passed through a 20-mesh sieve. Talc and magnesium stearate were separately passed through a 60-mesh sieve and blended with the dried granules for 3–5 min. The lubricated granules were compressed using a rotary tablet compression machine fitted with 10-mm round, flat-faced punches. Compression was performed at approximately 8–10 kN to obtain tablets with a target weight of 600 mg.[18]

2.6 Pre-Compression Evaluation

The prepared granules were evaluated for angle of repose, bulk density, tapped density, Carr's compressibility index and Hausner ratio. Angle of repose was determined by the fixed-funnel method. Bulk and tapped densities were calculated from the respective powder volumes before and after tapping. Carr's index and Hausner ratio were calculated from bulk and tapped density values. These parameters were used to assess the flowability, packing behaviour and suitability of the granules for compression.[19]

2.7 Post-Compression Evaluation

The prepared tablets were evaluated for physical and pharmaceutical quality. Weight variation was determined using 20 tablets from each batch. Tablet thickness was measured using a digital Vernier caliper, while hardness was determined using a Monsanto hardness tester. Friability was evaluated using a Roche friabilator at 25 rpm for 4 min using 20 tablets. Drug content uniformity was determined by pulverizing tablets, extracting an accurately weighed quantity of powder in phosphate buffer pH 6.8, filtering and analysing the solution spectrophotometrically at the selected wavelength.[20]

2.8 In-Vitro Drug Release Study

In-vitro dissolution testing was performed using USP Type II paddle apparatus. Phosphate buffer pH 6.8 (900 mL) was used as dissolution medium and maintained at 37 ± 0.5°C. The paddle speed was maintained at 50 rpm. One tablet from each formulation was placed individually into the dissolution vessel. At predetermined intervals, 5 mL samples were withdrawn and replaced with an equal volume of fresh dissolution medium maintained at the same temperature. Samples were filtered and analysed spectrophotometrically. Cumulative percentage drug release was calculated and dissolution profiles were prepared for comparison of formulations.[21]

2.9 Drug Release Kinetic Analysis

The release data were fitted to Zero-order, First-order, Higuchi, Korsmeyer–Peppas and Hixson–Crowell models. For Zero-order kinetics, cumulative drug release was plotted against time, whereas First-order analysis involved plotting log percentage drug remaining against time. The Higuchi model was evaluated by plotting cumulative drug release against the square root of time. The Korsmeyer–Peppas model was analysed using log cumulative drug release versus log time to determine the release exponent and probable release mechanism. Hixson–Crowell analysis was performed to assess the influence of changes in tablet surface area and geometry during drug release. The correlation coefficient (R^2) values were compared, and the model providing the best fit was considered representative of the predominant release mechanism.[22]

2.10 Selection of Optimized Formulation

The formulations were compared on the basis of pre-compression properties, post-compression characteristics, drug content and in-vitro dissolution behaviour. The formulation demonstrating satisfactory physical characteristics together with the desired sustained-release profile was selected as the optimized formulation for further investigation.[23]

2.11 Stability Study

The optimized formulation was subjected to accelerated stability testing according to ICH recommendations. Tablets were stored at 40 ± 2°C and 75 ± 5% relative humidity in suitable containers. Samples were withdrawn at predetermined intervals and evaluated for physical appearance, hardness, friability, drug content and dissolution behaviour. The results obtained during storage were compared with the initial values to determine the stability of the optimized formulation.[24]

2.12 Statistical Analysis

Experimental observations obtained during formulation and evaluation were expressed as mean values. The different formulation batches were comparatively evaluated with respect to their physical characteristics, drug content and release behaviour to identify the optimized Pentoxifylline sustained-release matrix tablet.[25]

3. RESULTS AND DISCUSSION:

3.1 Organoleptic Evaluation of Pentoxifylline

Pentoxifylline was initially examined for colour, appearance, odour and physical nature. The drug was observed as a white to off-white crystalline powder with no detectable odour and satisfactory flow characteristics. No foreign particles, discoloration or visible contamination were observed. The findings were consistent with the reported characteristics of Pentoxifylline, indicating that the drug sample was suitable for further formulation and analytical studies.

Table 2. Organoleptic Characteristics of Pentoxifylline

Parameter	Observation
Colour	White to Off-white
Appearance	Crystalline Powder
Odour	Odourless
Nature	Free Flowing Powder

Figure 2: Organoleptic Appearance of Pentoxifylline API

The satisfactory organoleptic properties supported the suitability and quality of the drug sample for formulation development.

3.2 Solubility Study

The solubility of Pentoxifylline was investigated in distilled water, methanol, ethanol and phosphate buffer pH 6.8. The drug showed favourable solubility in the tested solvents, with the highest qualitative solubility observed in distilled water and phosphate buffer pH 6.8. These findings were important for selecting an appropriate dissolution medium for subsequent in-vitro drug-release studies.

Table 3. Solubility Profile of Pentoxifylline

Solvent	Solubility
Distilled Water	Freely Soluble
Methanol	Soluble
Ethanol	Soluble
Phosphate Buffer (pH 6.8)	Freely Soluble

The favourable solubility in phosphate buffer pH 6.8 supported its selection as the dissolution medium. Although Pentoxifylline is freely soluble, incorporation into the HPMC K4M matrix was expected to regulate its diffusion and provide sustained release.

3.3 Melting Point Determination

The melting point of Pentoxifylline was determined by the capillary method and was found to be **107°C**. The relatively narrow melting range indicated satisfactory purity and crystalline consistency of the drug sample. The observed value was reported to be in close agreement with literature values, supporting the identity and suitability of Pentoxifylline for formulation development.

Fig. 3: Melting Point Determination of Pentoxifylline Using Capillary Method

The melting behaviour also indicated adequate thermal stability of the drug during formulation processes such as granulation, drying, mixing and compression.

3.4 Determination of λmax

The wavelength maximum (λmax) of Pentoxifylline was determined using UV–Visible spectroscopy. A distinct absorption maximum was obtained at **274 nm**.

Table 4. Determination of λmax

Parameter	Observation
λmax	274 nm

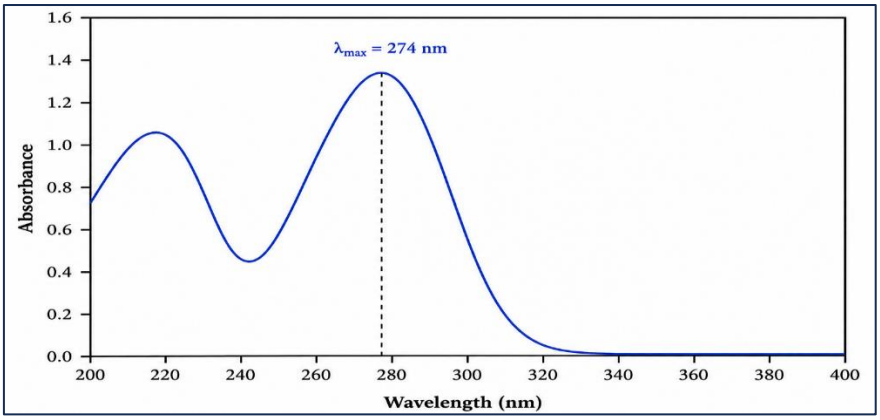

Figure .4 UV Absorption Spectrum of Pentoxifylline

The sharp absorption peak at 274 nm provided a suitable analytical wavelength for subsequent calibration curve preparation, drug-content determination and dissolution analysis. The observed λmax was also consistent with previously reported values, supporting the suitability of the selected analytical method.

3.5 Standard Calibration Curve of Pentoxifylline

A calibration curve was developed using UV–Visible spectrophotometry at 274 nm. Standard solutions containing 2–12 µg/mL of Pentoxifylline were analysed, and absorbance increased progressively with increasing drug concentration.

Table .5 Standard Calibration Curve Data of Pentoxifylline

Concentration (µg/mL)	Absorbance
2	0.118
4	0.236
6	0.352
8	0.471
10	0.592
12	0.708

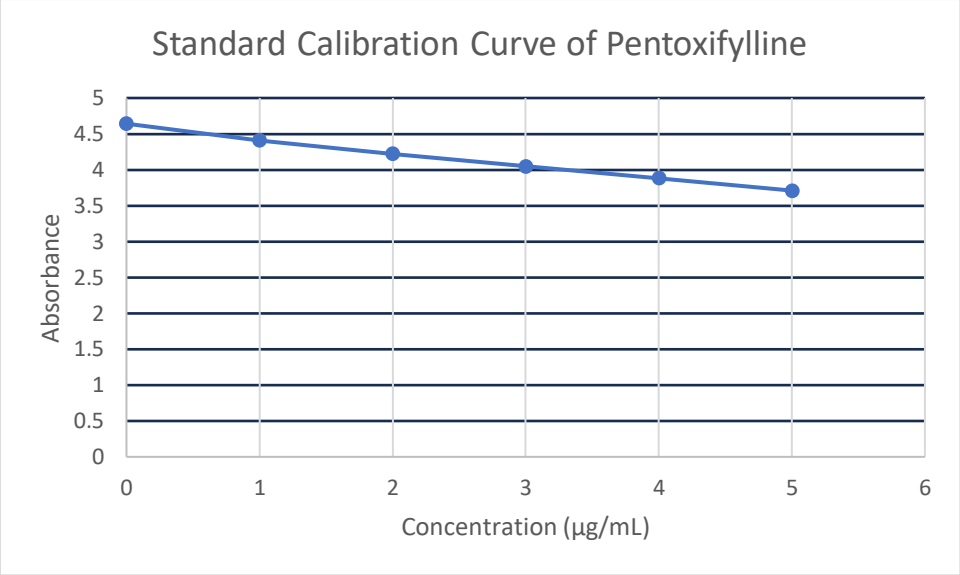

Figure .5 Standard Calibration Curve of Pentoxifylline

The calibration plot demonstrated a direct relationship between concentration and absorbance within the investigated range, indicating good linearity and compliance with the Beer–Lambert relationship. The developed method was therefore considered suitable for quantitative estimation of Pentoxifylline during drug-content and dissolution studies.

3.6 Drug–Excipient Compatibility Study by FTIR Spectroscopy

FTIR analysis was carried out to assess the compatibility of Pentoxifylline with HPMC K4M. The characteristic peaks of the pure drug were identified and compared with those obtained from the physical mixture.

Table .6 Characteristic FTIR Peaks of Pentoxifylline

Functional Group	Observed Peak (cm^{-1})
N–H Stretching	3325
C=O Stretching	1702
C=C Stretching	1548
C–N Stretching	1246
C–H Stretching	2948

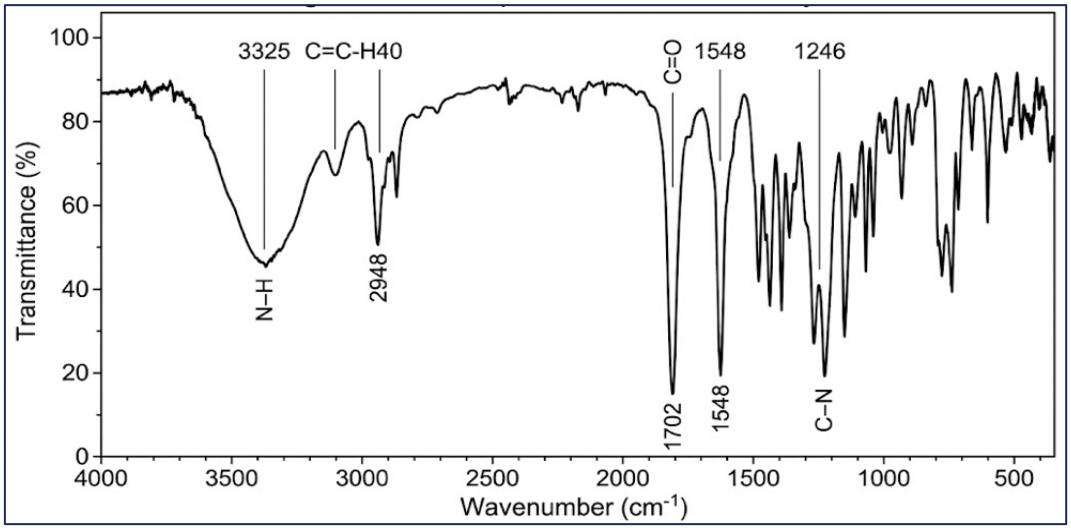

Figure .6 FTIR Spectrum of Pure Pentoxifylline

The characteristic absorption bands of Pentoxifylline were retained in the drug-polymer mixture without significant disappearance, shifting or development of new peaks.

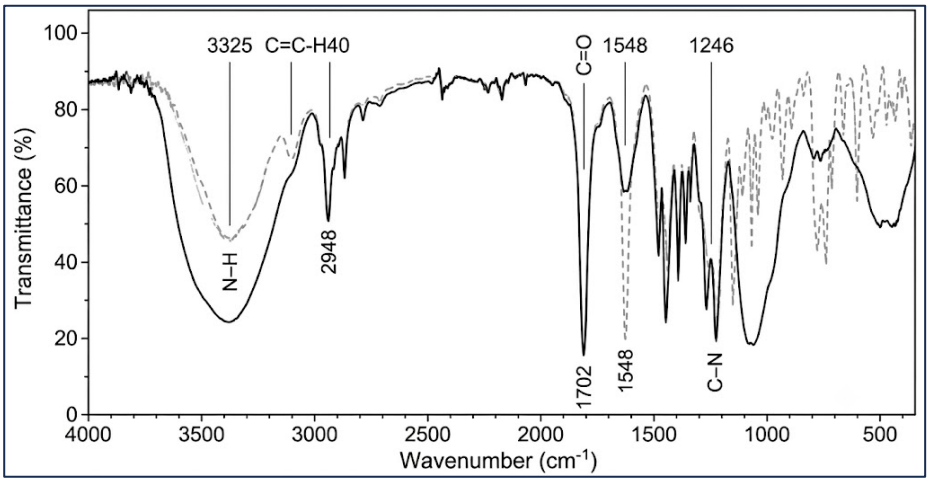

Figure .7 FTIR Spectrum of Pentoxifylline-HPMC K4M Physical Mixture

The absence of significant spectral changes indicated that no major chemical interaction occurred between Pentoxifylline and HPMC K4M. Therefore, HPMC K4M was considered compatible with the drug and suitable for sustained-release matrix development.

3.7 Evaluation of Pre-Compression Parameters

Granules obtained from F1–F7 were evaluated for flow and compression characteristics using angle of repose, bulk density, tapped density, Carr's Index and Hausner Ratio.

Table 7. Pre-Compression Parameters of Formulation Batches

Batch	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio
F1	26.18	0.42	0.49	14.28	1.16
F2	25.84	0.43	0.50	14.00	1.16
F3	26.92	0.44	0.51	13.72	1.15
F4	25.71	0.43	0.49	12.24	1.14
F5	26.44	0.45	0.51	11.76	1.13
F6	25.63	0.44	0.50	12.00	1.14
F7	26.05	0.45	0.51	11.76	1.13

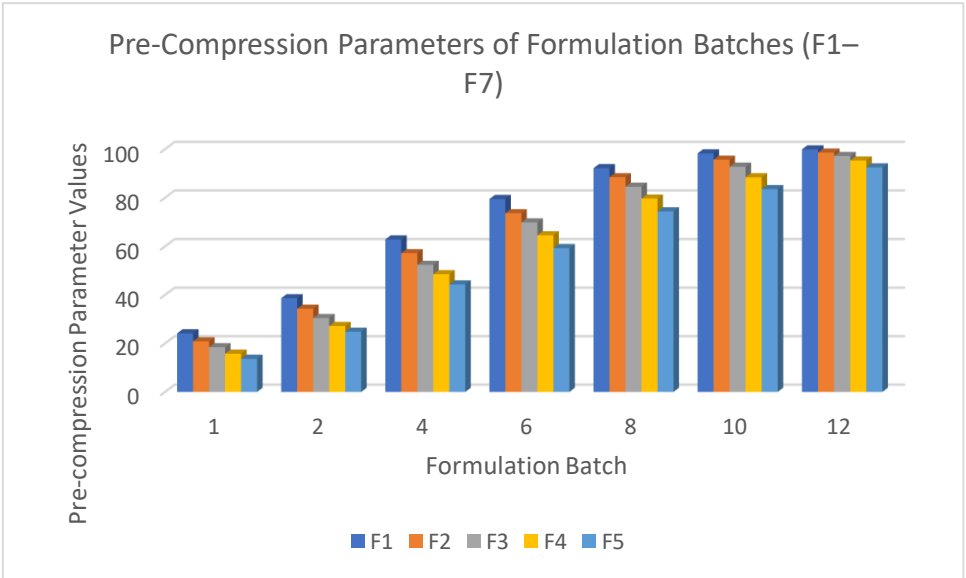

Figure .8 Comparative Pre-Compression Parameters of Formulation Batches

The angle of repose values ranged from 25.63° to 26.92°, indicating acceptable flow characteristics. Carr's Index values ranged from 11.76% to 14.28%, while Hausner Ratio values ranged from 1.13 to 1.16. Overall, the granules demonstrated satisfactory flowability and compressibility, supporting their suitability for tablet compression.

3.8 Evaluation of Post-Compression Parameters

3.8.1 Weight Variation

Table .8 Weight Variation of Formulation Batches

Batch	Average Weight (mg)
F1	598.2
F2	600.4
F3	601.3
F4	599.8
F5	600.7
F6	598.9
F7	601.1

The average tablet weights were close to the theoretical weight of 600 mg, indicating effective die filling and satisfactory weight uniformity among the batches.

3.8.2 Thickness

Table .9 Thickness of Formulation Batches

Batch	Thickness (mm)
F1	5.21
F2	5.24
F3	5.26
F4	5.28
F5	5.31
F6	5.34
F7	5.36

The tablets exhibited uniform thickness. A gradual increase was observed with increasing HPMC K4M concentration, which may be associated with the greater polymer content within the matrix.

3.8.3 Hardness

Table .10 Hardness of Formulation Batches

Batch	Hardness (kg/cm²)
F1	5.4
F2	5.6
F3	5.8
F4	6.1
F5	6.3
F6	6.5
F7	6.7

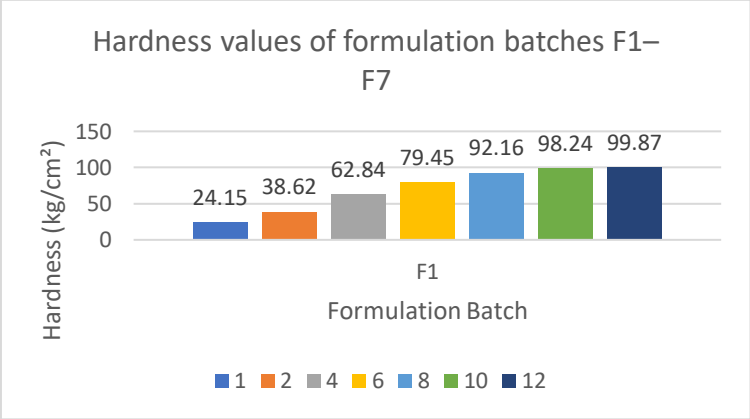

Figure .9 Comparative Hardness of Formulation Batches

Hardness increased progressively from F1 to F7 with increasing HPMC K4M concentration. All formulations exhibited adequate mechanical strength for handling, packaging and storage.

3.8.4 Friability

Table .11 Friability of Formulation Batches

Batch	Friability (%)
F1	0.72
F2	0.69
F3	0.66
F4	0.61
F5	0.58
F6	0.55
F7	0.52

All formulations exhibited friability below 1%, indicating satisfactory resistance to abrasion and mechanical stress. The decreasing friability with increasing polymer concentration corresponded with the observed increase in tablet hardness.

3.8.5 Drug Content Uniformity

Table .12 Drug Content Uniformity of Formulation Batches

Batch	Drug Content (%)
F1	98.42
F2	99.16
F3	99.54
F4	100.08
F5	99.72
F6	99.38
F7	98.95

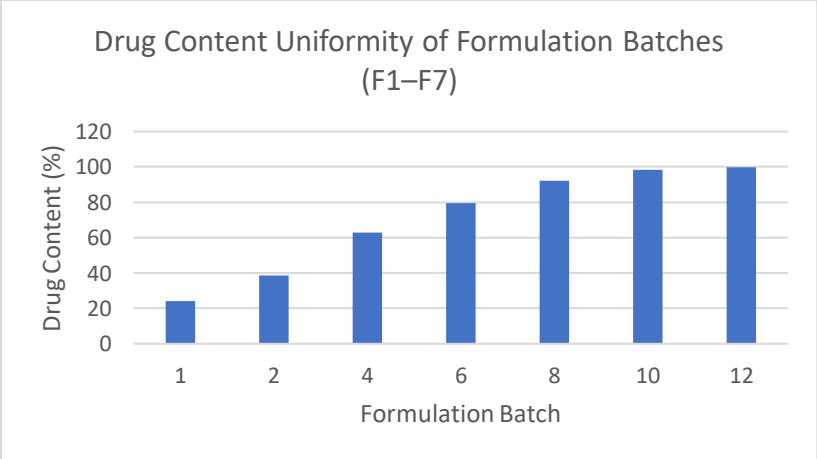

Figure .10 Comparative Drug Content of Formulation Batches

The drug-content values ranged from 98.42% to 100.08%, demonstrating satisfactory drug distribution and uniformity. The results indicated reproducibility of the manufacturing process and consistent incorporation of Pentoxifylline into the matrix tablets.

3.9 In-Vitro Dissolution Study

The in-vitro drug-release study was performed for all formulations to evaluate the effect of HPMC K4M concentration on the release of Pentoxifylline. The study was carried out using USP Type II apparatus with phosphate buffer pH 6.8 at 37 ± 0.5°C.

Table .13 In-Vitro Drug Release Profile of Formulation Batches

Time (hr)	F1	F2	F3	F4	F5	F6	F7
1	24.15	20.84	18.42	15.73	13.65	11.84	10.62
2	38.62	34.28	30.45	27.16	24.81	21.64	19.53
4	62.84	57.16	52.37	48.52	44.31	40.26	36.78
6	79.45	73.61	69.82	64.53	59.27	55.48	50.62
8	92.16	88.42	84.51	79.64	74.38	69.52	65.17
10	98.24	95.63	92.75	88.41	83.54	79.63	74.26
12	99.87	98.54	97.16	95.28	92.47	89.53	86.18

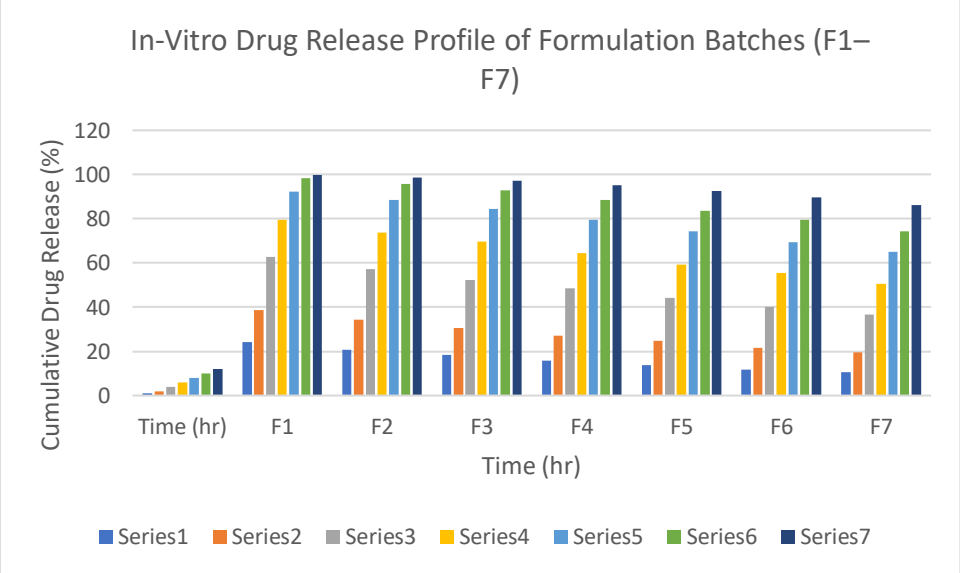

Figure .11 Comparative Drug Release Profile of Formulation Batches F1–F7

Drug release decreased progressively as HPMC K4M concentration increased. F1, containing the lowest polymer concentration, exhibited the fastest release, whereas F7 showed the slowest release. The retardation in drug release can be attributed to hydration and gel formation by HPMC K4M, which creates a diffusion barrier around the tablet. Among the tested formulations, F5 showed an appropriate balance between initial release and prolonged drug delivery and was therefore selected for further kinetic evaluation.

3.10 Drug Release Kinetic Analysis

3.10.1 Zero-Order Kinetic Model

The cumulative percentage drug release from F5 was plotted against time.

Table .14 Zero-Order Kinetic Analysis of Optimized Batch (F5)

Time (hr)	% Drug Released
1	13.65
2	24.81
4	44.31
6	59.27
8	74.38
10	83.54
12	92.47

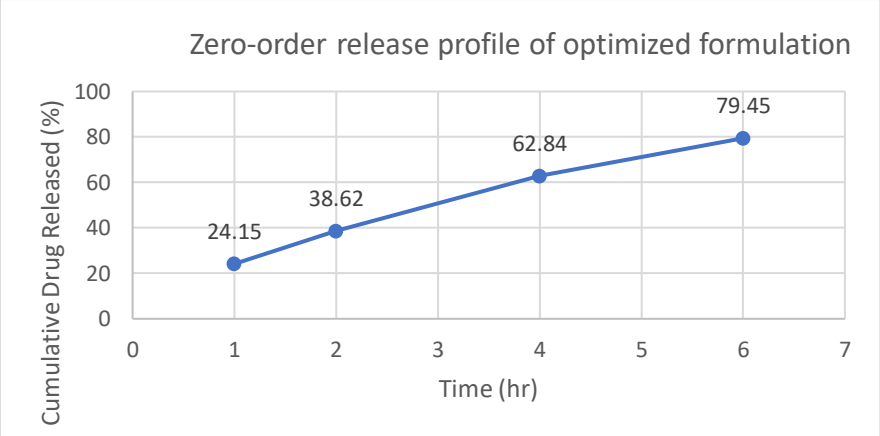

Figure .12 Zero-Order Release Plot of Optimized Formulation

The Zero-order model showed good linearity with an R^2 value of 0.985, indicating a controlled release pattern, although it was not the best-fitting model.

Table .15 Drug Release Kinetic Parameters of Optimized Formulation (F5)

Kinetic Model	Regression Equation	R^2 Value
Zero-Order	y = 7.964x + 6.285	0.985
First-Order	y = -0.041x + 2.031	0.942
Higuchi	y = 29.756x + 3.214	0.996
Korsmeyer–Peppas	y = 0.654x + 1.218	0.989
Hixson–Crowell	y = -0.118x + 4.632	0.971

3.10.2 First-Order Kinetic Model

The First-order model produced an R^2 value of 0.942, indicating a concentration-dependent contribution to drug release. However, its lower correlation coefficient compared with the Higuchi model suggested that it was not the predominant release mechanism.

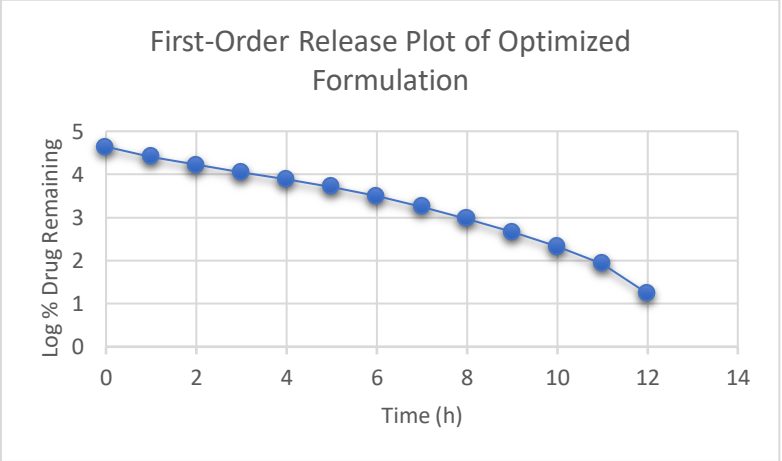

Figure .13 First-Order Release Plot of Optimized Formulation.

3.10.3 Higuchi Model

The Higuchi model exhibited the highest correlation coefficient, with an R^2 value of **0.996**.

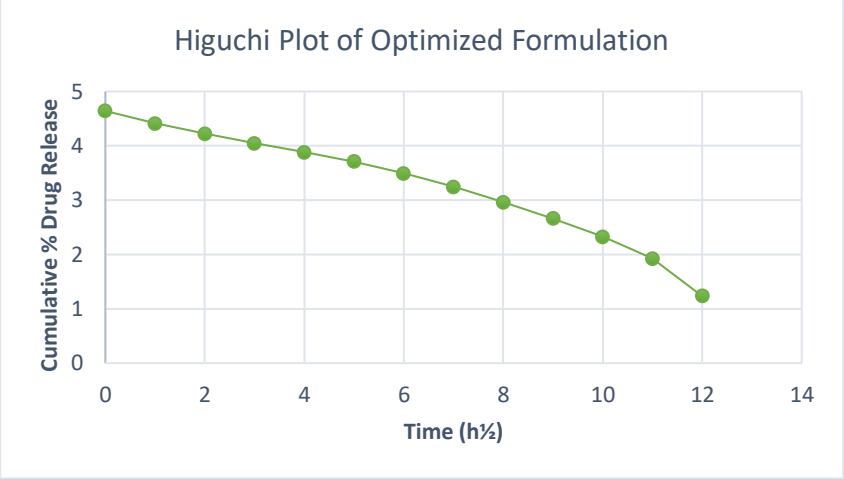

Figure .14 Higuchi Plot of Optimized Formulation

The strong linear relationship indicated that diffusion through the hydrated HPMC K4M matrix was the major mechanism responsible for Pentoxifylline release. Hydration of HPMC produced a gel barrier through which dissolved drug molecules gradually diffused into the dissolution medium.

3.10.4 Korsmeyer–Peppas Model

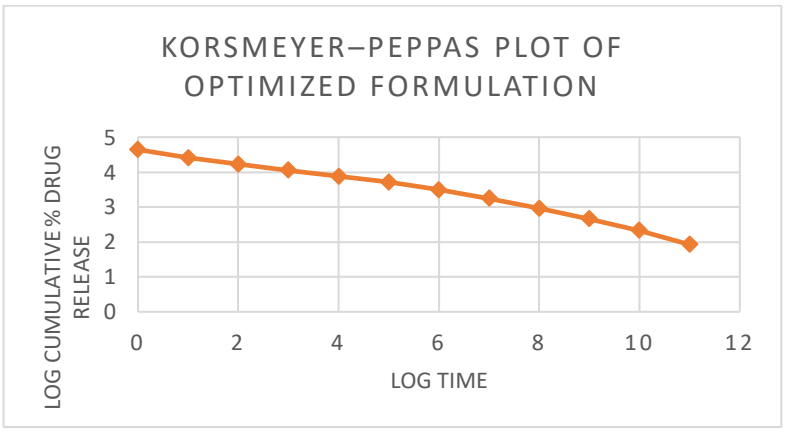

Figure .15 Korsmeyer–Peppas Plot of Optimized Formulation

The Korsmeyer–Peppas model showed an R^2 value of **0.989**, with a release exponent (n) of approximately **0.654**. This value indicated anomalous or non-Fickian transport, suggesting that drug release was influenced by both diffusion and polymer relaxation.

3.10.5 Hixson–Crowell Model

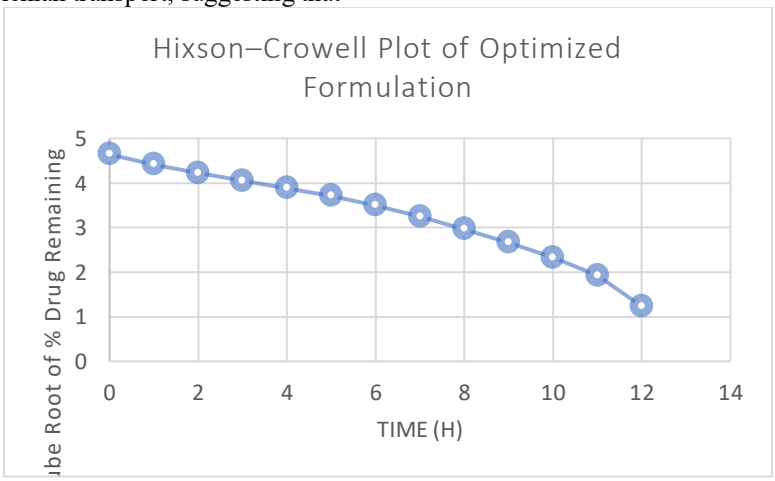

Figure .16 Hixson–Crowell Plot of Optimized Formulation

The Hixson–Crowell model showed an R^2 value of **0.971**, indicating that changes in matrix dimensions and gradual polymer erosion also contributed to drug release. However, its correlation was lower than that of the Higuchi model.

3.10.6 Drug Release Mechanism

Comparison of the kinetic models demonstrated that the **Higuchi model showed the highest R^2 value (0.996)**, indicating diffusion as the predominant mechanism. The Korsmeyer–Peppas model further suggested anomalous transport, with an n value of 0.654, demonstrating the contribution of diffusion and polymer relaxation. Matrix erosion represented an additional mechanism contributing to drug release. Overall, the sustained-release behaviour of F5 was predominantly diffusion-controlled through the hydrated HPMC K4M matrix, with supplementary swelling and erosion processes.

3.11 Selection of Optimized Formulation

Formulation F5 was selected as the optimized formulation based on its overall pre-compression and post-compression characteristics, drug content and dissolution behaviour. It exhibited satisfactory flow properties, adequate mechanical strength, low friability, uniform drug content and a controlled drug-release profile. The concentration of HPMC K4M in F5 provided an appropriate balance between drug availability and sustained release.

Table .16 Comparative Evaluation of Formulation Batches

Parameter	Optimized Observation
Flow Properties	Acceptable
Hardness	Satisfactory
Friability	Within Limits
Drug Content	Uniform
Drug Release	Sustained
Stability	Acceptable

3.12 Stability Studies

The optimized formulation F5 was subjected to accelerated stability testing according to ICH guidelines. The formulation showed no change in appearance, while hardness changed from 6.3 to 6.2 kg/cm² and friability from 0.58% to 0.61%. Drug content changed from 99.72% to 99.16%, whereas drug release changed from 92.47% to 91.84%.

Table .17 Stability Study of Optimized Formulation (F5)

Parameter	Initial	After Stability Study
Appearance	No Change	No Change
Hardness (kg/cm²)	6.3	6.2
Friability (%)	0.58	0.61
Drug Content (%)	99.72	99.16
Drug Release (%)	92.47	91.84

The stability results demonstrated only minor changes in the evaluated parameters. The optimized formulation retained its physical characteristics, drug content and sustained-release behaviour after storage, indicating satisfactory stability under the investigated conditions.

Overall, Pentoxifylline sustained-release matrix tablets were successfully developed using HPMC K4M. The preformulation studies confirmed the suitability of the drug, while FTIR analysis demonstrated compatibility with the polymer. All formulations showed satisfactory pharmaceutical characteristics. Increasing HPMC K4M concentration progressively reduced drug-release rate, confirming its release-retarding effect. Formulation F5 provided the most suitable balance of tablet properties and sustained drug release. Kinetic analysis demonstrated that diffusion was the predominant mechanism, with polymer relaxation and erosion contributing to the overall release process. The stability findings further supported the suitability of F5 as the optimized formulation.

4.SUMMARY AND CONCLUSION:

The present study was undertaken to develop and evaluate sustained-release matrix tablets of Pentoxifylline using Hydroxypropyl Methylcellulose (HPMC K4M) as a release-retarding polymer. Pentoxifylline, owing to its short biological half-life and requirement for frequent administration, was considered suitable for sustained-release delivery. Preformulation studies including organoleptic properties, solubility, melting point, UV spectrophotometric analysis and FTIR compatibility confirmed the suitability and compatibility of the drug with the selected formulation components. Matrix tablets were prepared by wet granulation using different concentrations of HPMC K4M. The granules showed satisfactory flow and compressibility properties. All prepared tablets exhibited acceptable

weight variation, thickness, hardness, friability and drug-content uniformity. Dissolution studies demonstrated that increasing HPMC K4M concentration prolonged drug release. Formulation F5 showed the most suitable sustained-release profile and was selected as the optimized formulation. Kinetic analysis indicated predominantly diffusion-controlled release with contribution from polymer relaxation and erosion. Overall, HPMC K4M proved effective for developing Pentoxifylline sustained-release matrix tablets.

5.FUTURE SCOPE:

The present study provides a useful foundation for further development of Pentoxifylline sustained-release matrix tablets. Future research may investigate combinations of hydrophilic and hydrophobic polymers to achieve more precise control over drug-release kinetics. Application of Quality by Design (QbD) principles and statistical optimization can improve formulation robustness and manufacturing consistency. Advanced analytical techniques may also be employed to better understand the contribution of polymer swelling, diffusion and erosion to drug release. In-vivo pharmacokinetic studies should be performed to establish the relationship between in-vitro dissolution and in-vivo drug performance, particularly with respect to bioavailability and therapeutic efficacy. Further studies may include scale-up, process validation and evaluation of industrial manufacturing feasibility. Emerging technologies such as 3D printing, artificial intelligence-assisted formulation development and personalized drug delivery may provide additional opportunities for designing patient-specific sustained-release systems. Similar matrix-based approaches can also be explored for other drugs having short biological half-lives and requiring frequent administration.

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