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Research Paper

Formulation And Evaluation of Sustained-Release Matrix Tablets Of Theophylline Using Hibiscus Esculentus Mucilage and Grewia Gum as Natural Polymeric Retardants

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ABSTRACT

The present study was aimed at the formulation and evaluation of sustained release matrix tablets of Theophylline using natural polymers, namely Hibiscus esculentus mucilage and Grewia gum, to achieve controlled drug delivery and improve therapeutic efficacy. Theophylline, a widely used bronchodilator, possesses a short biological half-life and narrow therapeutic index, necessitating the development of sustained release formulations to minimize dosing frequency and plasma concentration fluctuations. Preformulation studies confirmed the compatibility of the drug with selected excipients and suitability for formulation via the wet granulation method. A total of ten formulations (F1–F10) were prepared using varying concentrations of individual and combined polymers. The prepared tablets were evaluated for post-compression parameters such as weight variation, hardness, friability, thickness, and drug content, all of which were found to be within acceptable pharmacopeial limits. Swelling studies indicated that Hibiscus mucilage contributed to rapid hydration, whereas Grewia gum provided a robust gel barrier, and their combination exhibited a synergistic effect. In vitro dissolution studies demonstrated sustained drug release up to 12 hours, with the optimized formulation (F9) showing a controlled and reproducible release profile. Drug release kinetics revealed that the optimized batch followed zero-order and Higuchi models with a non-Fickian diffusion mechanism. Stability studies confirmed the formulation's robustness under accelerated conditions. In conclusion, the study highlights the potential of natural polymers in developing effective and stable sustained release formulations of Theophylline, offering improved patient compliance and therapeutic outcomes.

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INTRODUCTION

Solid oral dosage forms (i.e., Tablet and Capsule) are most favored class of drug delivery system administered by mouth. A tablet is a solid dosage form containing one or more active pharmaceutical ingredients (APIs) with or without excipients, compressed or molded into a defined shape. Tablets are the most commonly used oral dosage form due to their convenience, accuracy, and stability. Due to advancement in pharmaceutical technology, there is growing focus on creating sustained- release drug formulation for numerous medications.

The goal in designing sustained or controlled delivery systems is to reduce frequency of dosing or to increase the effectiveness of the drug by localization at the site of action, reducing the dose required, providing uniform drug delivery. These systems are particularly useful for drugs with a short biological half-life, those requiring frequent administration, or those that need to maintain steady plasma levels for optimal therapeutic activity.[1-2]

SUSTAINED RELEASE MATRIX TABLET:

A Sustained Release Matrix Tablet is a solid oral dosage form in which the drug is uniformly dispersed within a polymeric matrix. The matrix controls the rate of drug release through diffusion, erosion, or both mechanisms. Natural and synthetic polymers such as hydroxypropyl methylcellulose (HPMC), ethyl cellulose, guar gum, xanthan gum, and alginate are commonly used.

The main objective of sustained release matrix tablets is to maintain a constant plasma drug level for a prolonged period, reduce dosing frequency, and improve patient compliance. These tablets are especially suitable for drugs that require long-term therapy[3].

ADVANTAGES OF A SUSTAINED RELEASE (SR) DOSAGE FORM[4]:

Reduced dosing frequency – Fewer doses are required due to prolonged drug action.

Improved patient compliance – Convenient for patients, especially for chronic therapies.

Constant therapeutic effect – Maintains steady plasma drug concentration over time.

Minimized side effects – Avoids peaks and troughs associated with conventional dosing.

Better utilization of drug – Enhances bioavailability and therapeutic efficiency.

Reduced overall treatment cost – Due to fewer doses and better efficacy.

Improved stability of drug – Some sustained release forms protect the drug from degradation.

COMPARATIVE STUDY OF CONVENTIONAL AND SUSTAINED RELEASE MATRIX TABLET[5-6]

Table 1: Comparison of Conventional and Sustained Release Matrix Tablet

Parameter	Conventional Tablet	Sustained Release Matrix Tablet
Drug release	Immediate	Controlled / Prolonged
Dosing frequency	Frequent	Reduced
Patient compliance	Moderate	High
Therapeutic control	Variable	Steady
Formulation complexity	Simple	Complex
Cost	Low	Relatively high

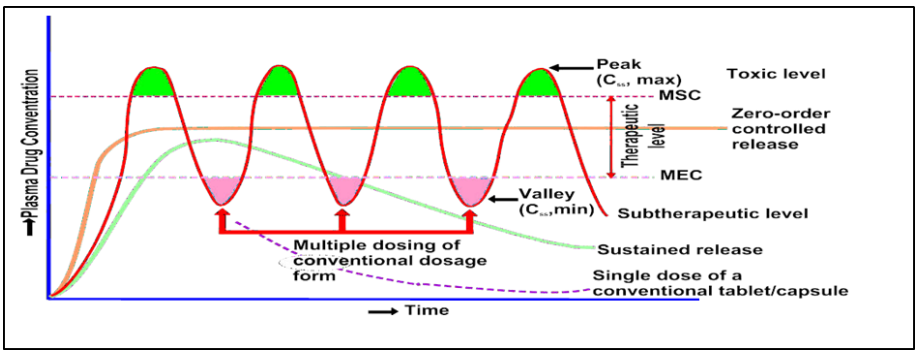


Fig. 1: A hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations. (MSC = maximum safe concentration, MEC = minimum effective concentration)[3]

CLASSIFICATION OF ORAL SUSTAINED/CONTROLLED RELEASE SYSTEMS[7]:

A) DIFFUSION CONTROLLED RELEASE SYSTEMS

In diffusion-controlled drug delivery system the dissolved drug diffuses through the polymeric barrier which act as the rate limiting membrane.

This is the basis of controlled drug delivery system.

The diffusion-controlled devices are formulated either by encapsulating the drug particle in a polymeric membrane or by dispersing the drug in a polymeric matrix.

1) Reservoir Devices Or Systems:

The drug core is surrounded by an inert polymeric membrane through which the drug diffuses at a controlled, constant rate over an extended period.

2) Matrix Systems

In this, drug is dispersed homogeneously in the matrix.

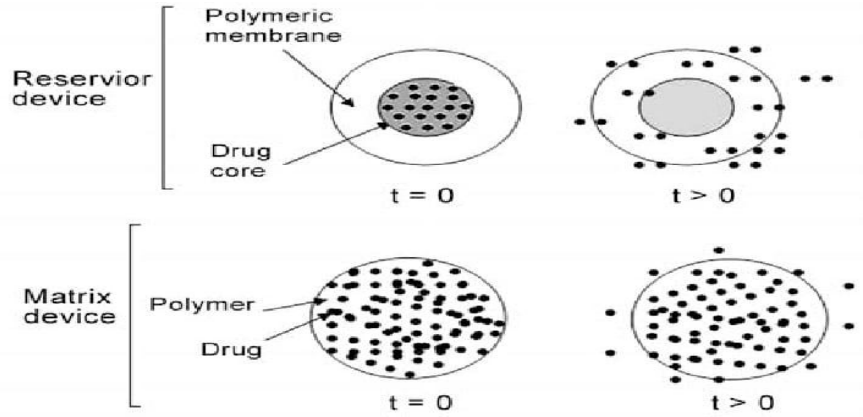


Fig. 2: Schematic Representation of Diffusion Type Reservoir device and Matrix device[6]

B) Dissolution Controlled Systems:

1) Encapsulation dissolution-controlled systems:

Particles, seeds, granules can be coated by techniques such as microencapsulation.

2) Diffusion and dissolution-controlled systems:

In a bio erodible matrix, the drug is homogenously dispersed in a matrix and it is released either by swelling controlled mechanism or by hydrolysis or by enzymatic attack.

RATIONAL OF THIS WORK:

Theophylline has a short half-life, requiring frequent dosing, which may reduce patient compliance; hence an SR formulation is necessary.

Matrix tablets provide a simple, cost-effective mechanism for achieving sustained drug release.

Natural polymers are biodegradable, biocompatible, and non-toxic, making them safer alternatives to synthetic polymers.

Hibiscus esculentus mucilage and Grewia gum exhibit excellent swelling, gel-forming, and viscosity-enhancing properties, which can effectively retard drug release.

Using plant-based polymers reduces formulation cost and enhances sustainability compared to synthetic polymers.

Natural mucilage and gums may improve patient safety by minimizing risk of adverse reactions associated with synthetic excipients.

Theophylline requires controlled release to maintain plasma concentration within the narrow therapeutic index, preventing toxicity.

Developing a natural polymer-based SR system contributes to green pharmacy and reduces environmental impact.

There is limited research combining these two natural polymers, providing novelty and scientific value.

The study may help establish an effective, stable, and economic natural polymer matrix for other sustained-release drug formulations in the future.

EXPERIMENTAL WORK:

MATERIALS:

The following materials collected for the experimental work done.

Table 2 : List of materials

SR.NO.	DRUG/EXCIPIENTS	GRADE	GIFTED/MFG.BY
1	Theophylline	AR	Glenmark Pharmaceuticals
2	Eudragit L100	AR	Merck, India
3	Colloidal Silicon Dioxide	AR	S.D. Fine Chemicals Ltd
4	HPMC	AR	Merck, India
5	Magnesium stearate	AR	S.D. Fine Chemicals Ltd
6	Microcrystalline cellulose	AR	S.D. Fine Chemicals Ltd
7	Lactose	AR	S.D. Fine Chemicals Ltd

Table 3 : List of polymer

Sr no.	POLYMER	ISOLATED FROM	Botanical name
1	Hibiscus esculentus Mucilage	Pods	*Botanical name :Abelmoschus esculentus* *Family: Malvaceae*
2	*Grewia Gum*	Leaf and seed	Botanical name :Grewia mollis Juss. Family: *Malvaceae*

HIBISCUS ESCULENTUS MUCILAGE OVERVIEW[8-9]:

Common Name: Okra

Scientific Name: Hibiscus esculentus

Source: The mucilage source from Hibiscus esculentus (okra) is primarily its immature fruit or pods, although other parts like the seeds and stem can also contain mucilage

Nature: natural, biodegradable, and non-toxic polysaccharide with a viscous, gellike nature.

Appearance: white to cream-colored amorphous substance.

EXTRACTION PROCEDURE[10-11]

1. Collection and Cleaning: Collect fresh okra fruits. Wash thoroughly with clean water to remove dust and impurities. Cut the fruits into small pieces (2–3 cm).
2. Extraction: Take the cut okra pieces in a beaker. Add distilled water in the ratio of 1:10 (w/v). Heat the mixture at 60–70°C for 1 hour, with continuous stirring. Allow the mixture to cool to room temperature. The okra pieces will release thick mucilage into the water.
3. Filtration: Filter the mixture through muslin cloth while still warm. Squeeze thoroughly to obtain maximum mucilage.
4. Precipitation of Mucilage: Add 3 volumes of acetone (or ethanol) to 1 volume of filtrate with continuous stirring. Mucilage will precipitate as a fibrous, jelly-like mass. Allow it to settle for 1 hour.
5. Collection and Washing: Separate the precipitated mucilage by decantation or filtration. Wash the mucilage with acetone to remove pigments and impurities.
6. Drying: The wet mucilage is spread uniformly on trays.

It Ican be dried using either of the methods below:

1)Oven Drying:

Dry at 40–50°C until constant weight (usually 24–48 hours).

Avoid temperatures above 60°C to prevent degradation.

2)Freeze Drying:

The wet mucilage is frozen and then lyophilized to get a fluffy, porous powder.

7. Powdering: After drying, the mucilage is powdered using mortar & pestle. It is passed through a 60-mesh sieve for uniformity. The final dried mucilage is stored in an airtight container in a cool, dry place

GREWIA GUM MUCILAGE OVERVIEW[12-14]:

Common Name: Grewia gum

Botanical Source: Grewia gum is botanically sourced from the inner stem bark, seeds and leaf of the Grewia Mollis plant.

Nature: a natural, edible polysaccharide gum extracted from the inner stem bark of the Grewia Mollis plant, a tropical shrub native to Africa

Appearance: varies from white to near-white powder for refined samples to a brown or brownish powder for those extracted via traditional methods. As a plant gum, its general appearance can range from yellow-cream to whitish, depending on the source and processing.

Odor/Taste: Grewia gum is both tasteless and odorless**.**

EXTRACTION PROCEDURE[18]

1. Collection and Cleaning of Grewia Gum: Collect the leaf and seeds from plant. Wash with tap water then distilled water and air-dry in shade. Grind dried material to coarse powder (sieve ~2 mm) with a grinder or mortar & pestle.
2. Extraction (water extraction):

Weigh & mix: Weigh powdered Grewia material (example 100 g). Add distilled water at 1:10 to 1:20 w/v (e.g., 100 g : 1–2 L). Choose higher water ratio for tougher material.

Hydration & stirring: Hydrate by stirring at room temperature for 2–4 hours

Precipitation:

Cool the aqueous extract (chilled if possible). Add chilled 95% ethanol slowly with gentle stirring in 3:1 to 4:1 (ethanol : extract) v/v ratio until turbidity/gel forms and gum precipitates. (If using acetone, similar ratio.)

Allow the mixture to stand 1–4 hours or overnight at 4 °C for complete precipitation.

3. Collection: Collect precipitated gum by vacuum filtration (Buchner funnel) or centrifugation (4,000– 6,000 rpm for 10–20 min). Decant supernatant carefully.

4. Washing: Wash precipitate with 70–80% ethanol (1–2 washes) to remove residual sugars, salts and solvent. Optionally wash with acetone for rapid drying.
5. Drying: Spread wet gum on trays and dry by either by Oven drying: 40–50 °C until constant weight (avoid >60 °C) OR Lyophilization (freeze-dry): preferred for best functional properties (porous, fluffy powder).
6. Powdering: Once fully dry, pulverize gently (mortar & pestle or mill) and sieve (mesh 60 or as required) to obtain uniform powdered gum.

IDENTIFICATION OF DRUG:

1. UV-Spectrophotometric Characterization[16-17]

The λmax of Theophylline was determined using a UV-Vis spectrophotometer. A stock solution (100 µg/mL) was prepared by dissolving 10 mg of drug in 100 mL of distilled water. A working standard (10 µg/mL) was scanned in the range of 200–400 nm against a water blank. The calibration curve was constructed by preparing a series of dilutions (2, 4, 6, 8, 10, 12, and 14 µg/mL) and measuring absorbance at the determined λmax.

2 Drug-Excipient Compatibility Studies (FTIR)

The chemical interaction between the drug and polymers was evaluated using FTIR spectroscopy (4000–400 cm^{-1}). Physical mixtures were blended with Potassium Bromide (KBr) and compressed into transparent pellets using a hydraulic press (6 tons). The spectra of the physical mixtures were compared with pure Theophylline and polymers to identify any significant shifts or disappearance of characteristic functional group peaks.

3 Preformulation Studies: The physical properties of the granules were evaluated to ensure optimum flow and compressibility.

Angle of Repose:

The angle of repose Tan θ was determined by the fixed-funnel method using the formula:

$\tan \theta = h/r$

$\theta = \tan^{-1}(h/r)$

Where h = Height of the pile, r = Radius of the pile.

Density and Compressibility Indices:

Bulk density and Tapped density were determined by measuring the volume of a weighed quantity of granules before and after mechanical tapping. These values were used to calculate the Compressibility Index (Carr's Index) and Hausner's Ratio:

- Carr's Index % = (Tapped density - Bulk density) / Tapped density X 100
- Hausner's Ratio = Tapped density / Bulk density

Table 4: Powder Flowability Classification Table

Flow Property	Angle of Repose (°)	Carr's Index (%)	Hausner's Ratio
Excellent	25–30	1.00 - 10.00	1.00–1.11
Good	31–35	11–15	1.12–1.18
Fair	36–40	16–20	1.19–1.25
Passable	41–45	21–25	1.26–1.34
Poor	46–55	26–31	1.35–1.45
Very Poor	56–65	32–37	1.46–1.59
Very, Very Poor	> 66	> 38	> 1.60

PREPARATION OF THEOPHYLLINE SUSTAINED-RELEASE TABLETS

The tablets were prepared using the wet granulation technique, as the natural polymers (Grewia gum and Hibiscus mucilage) exhibited poor flow properties under direct compression.

Granulation and Compression:

The drug and excipients were mixed using a geometric dilution pattern to ensure homogeneity. The mixture was then moistened with a suitable volatile solvent to form a coherent wet mass. This mass was screened through a specific mesh to produce granules, which were subsequently dried at a controlled temperature.The dried granules were lubricated and evaluated for pre-compression

parameters. Finally, approximately 300 mg of the lubricated blend was compressed into tablets using a single-punch tablet press equipped with 10×8 mm concave punches at a compression force of 1.5 N

FORMULATION OF THEOPHYLLINE SR MATRIX TABLETS

Sustained release tablets of Theophylline were prepared by direct compression using different natural polymers like, Hibiscus esculentus mucilage and Grewia gum by using individual and combination of above polymers.

Granules of Theophylline SR tablets were formulated by classic wet granulation by various proportions of Hibiscus esculentus mucilage and Grewia gum polymers with drug. The Theophylline was screened through sieve no. 40. The release retarding polymer namely Hibiscus esculentus mucilage, Grewia gum and additives namely PVP, microcrystalline cellulose, as diluent, magnesium stearate and talc as glidant with lubricant respectively were screened through sieve no. 60. The polymer and the drug were subsequently blended in a mortar by geometric progression for a time frame of 10-15 minutes. This mixture was processed then granulated with isopropyl alcohol, followed by sieving using 18# sieve. Obtained granules have been dried in hot air oven at 40ºC for 10-15 minutes. The dry granules have been combined with magnesium stearate and colloidal silicon dioxide and lactose monohydrate for further two minutes and compacted around 10mm standard. Concave punch.

INVESTIGATION OF VARIOUS GUMS AND ITS VARIABLE CONCENTRATION LEVELS

The natural gums including Hibiscus esculentus mucilage, Grewia gum and xanthan gum have been employed for the fabrication of tablets and their proportions in the formulations ranging from different ratios were employed.

PROCEDURE FOR PREPARATION OF MATRIX TABLET

A. Hibiscus esculentus mucilage formulations

Table 5: Composition of Hibiscus esculentus mucilage-based matrix tablets

Ingredients	F1(mg)	F2(mg)	F3(mg)
Theophylline	300	300	300
Hibiscus esculentus mucilage	50	100	150
Colloidal silicon dioxide	10	10	10
Lactose monohydrate	120	70	20
PVPK–30	10	10	10
Magnesium stearate	5	5	5
Talc	5	5	5

B. Grewia gum formulations

Table 6: Composition of Grewia gum-based matrix tablets

Ingredients	**F4(mg)**	**F5(mg)**	**F6(mg)**
Theophylline	300	300	300
Grewia gum	50	100	150
Colloidal silicon dioxide	10	10	10
Lactose monohydrate	120	70	20
PVPK–30	10	10	10
Magnesium stearate	5	5	5
Talc	5	5	5

C. Hibiscus esculentus mucilage + Grewia gum combinations

Table 7: Composition of Hibiscus esculentus mucilage + Grewia gum-based matrix tablets

Ingredients	F7(mg)	F8(mg)	F9(mg)	F10(mg)
Theophylline	300	300	300	300
Hibiscus esculentus mucilage	50	75	50	100
Grewia gum	50	75	100	50
Colloidal silicon dioxide	10	10	10	10
Lactose monohydrate	70	20	20	20
PVPK–30	10	10	10	10
Magnesium stearate	5	5	5	5
Talc	5	5	5	5

EVALUATION OF MATRIX TABLET[18-24]

Physical characterization of tablet:

Hardness: Measured using a Monsanto hardness tester. The force required to fracture the tablet was recorded in kg/cm² (n=3).

Thickness and Diameter: Determined using Vernier Callipers to ensure dimensional consistency.

Friability: Evaluated using a Roche friabilator. Ten pre-weighed tablets were rotated at 25 rpm for 4 minutes. The percentage friability was calculated as:

$$\%\ FRIABILITY = \frac{\text{INITIAL WT.} - \text{FINAL WT.}}{\text{INITIAL WT.}} \times 100$$

Weight Uniformity: Ten tablets were randomly selected and weighed individually. The average weight was calculated and compared against IP standards to ensure they fell within the permissible 7.5\% deviation for a 300 mg tablet.

Determination of Drug Content: Five tablets were crushed into a fine powder. An amount equivalent to 50 mg of Theophylline was extracted using phosphate buffer (pH 7.2). After filtration and suitable dilution, the drug content was analysed spectrophotometrically at 272 nm

In-Vitro Drug Dissolution Studies:

Drug release was monitored using a USP Type II (Paddle) dissolution apparatus (Lab India Analytical) at 37 ± 1°C and 50 rpm.

Media: 0.1N HCl (pH 1.2) for the first 2 hours, followed by phosphate buffer (pH 7.2) for the remaining 10 hours (900 mL total).

Sampling: 5 mL aliquots were withdrawn at 1-hour intervals for 12 hours, replaced with fresh medium, and analyzed via UV spectrophotometry. The Cumulative Percentage Drug Release (CPDR) was plotted against time.

Swelling Index (Water Uptake Study):

The hydration capacity of the natural polymer matrix was studied using 2% agar gel plates. Tablets were weighed (W_1) and placed on the gel surface at 37°C. At 4 and 8-hour intervals, tablets were removed, blotted dry, and re-weighed (W_2). The swelling index (SI) was calculated using:

$$SWELLING\ INDEX\ (\%) = \frac{W2 - W1}{W2} \times 100$$

Where, W1 = Initial weight of the tablet W2 = Final weight of the tablet

DETERMINATION OF DRUG RELEASE KINETICS

To evaluate the mechanism and pattern of drug release from the sustained-release matrix tablets, the *in vitro* dissolution data were fitted into various mathematical models. The Correlation Coefficient (R^2) was used to determine the best-fit model.

Zero-Order Kinetics: Describes systems where the drug release rate is independent of its concentration.

Plot: -Cumulative % drug released vs. Time.

Zero order release would be predicted by the following equation.

$A_t = A_o - K_o t$

Where,

A_t = Drug release at time't', A_o - Initial drug concentration, K_o- Zero order rate constant (hr^{-1})

First-Order Kinetics: Describes release proportional to the drug concentration remaining in the matrix.

Plot: - log cumulative % drug remaining vs. Time.

First order release would be predicted by the following equation

$\text{Log } C = \text{Log } Co - K_t/2.303$

Where, Log C –Amount of drug remained at time t, Log Co – Initial drug concentration, K – First order rate constant hr-1

Korsmeyer-Peppas Model: Used to analyze the release mechanism when the specific mechanism is unknown or when more than one type of release phenomenon is involved.

Plot: - Log cumulative % drug released vs. Log time

Equation: $M_t/M_a = Kt^n$

Where, Mt/Ma -The fraction of drug released at 't' K -Constant combining structural and geometrical properties of the drug

STABILITY STUDIES

Stability studies of pharmaceutical products were done as per ICH guide lines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.

Stability studies are important for the following reasons:

This is an assurance given by the manufacturer that the patient would receive a uniform dose throughout the shelf life.

The drug control administration insists on manufacturers on conducting the stability studies, identity, strength, purity and quality of the drug for an extended period of time in the conditions of normal storage.

Stability testing prevents the possibility of marketing an unstable product. Both physical and chemical degradation of drug can result in unstable product.

Method: Selected formulations were stored at different storage conditions at elevated temperatures such as 25C± 2C / 60% ± 5% RH, 30C ± 2C / 65% ±5% RH and 40C ± 2C / 75% ± 5% RH for 30 days. The samples were withdrawn at thirty days and checked for physical changes, hardness, friability, drug content and percentage drug release.

IDENTIFICATION OF DRUG

Standard calibration curve of Theophylline in pH 7.2 phosphate buffer. The absorbance maximum (λ max) of theophylline was found to be 272 nm. The UV spectroscopy of theophylline is shown in Figure 3. The standard calibration curve was shows good linearity with the r2 value $R^2 = 0.999$ as shown in Figure 4.

The correlation coefficient was calculated by linear regression analysis. The absorbances of the above concentration are shown in table 8.

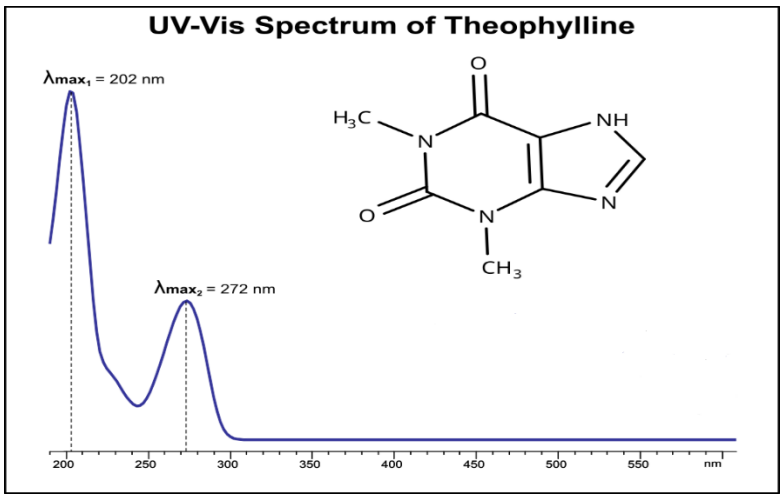


Figure 3: UV spectroscopy of Theophylline

Table 8: Standard calibration curve of Theophylline at pH 7.2

Concentration (mcg/ml)	Absorbance (272nm)
0	0.000
2	0.122
4	0.244
6	0.359
8	0.474
10	0.612
12	0.724
14	0.838

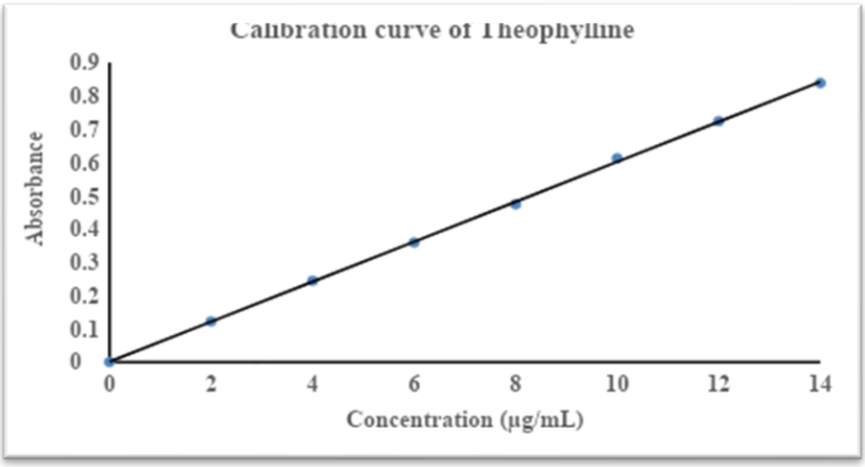


Figure 4: Standard graph of Calibration curve of Theophylline in pH 7.2 phosphate buffer (λmax 272 nm)

The standard calibration curve of Theophylline is shown in Figure 6.2. The standard calibration curve was shown good linearity with the r^2 value 0.9997**.**

FTIR study

Infrared spectroscopy is one of most powerful analytical method when it comes to the identification of existence of different functional groups involved in building up the molecule. It gives extremely well accountable spectral data on any change in the functional group features of a

pharmacological molecule happening while in the manufacturing of a formulation. IR Spectra of Theophylline and its formulations were acquired by KBr pellet technique using Shimadzu FTIR series model-8400S spectrometer in order to rule out drug-carrier interaction happening during the formulation process.

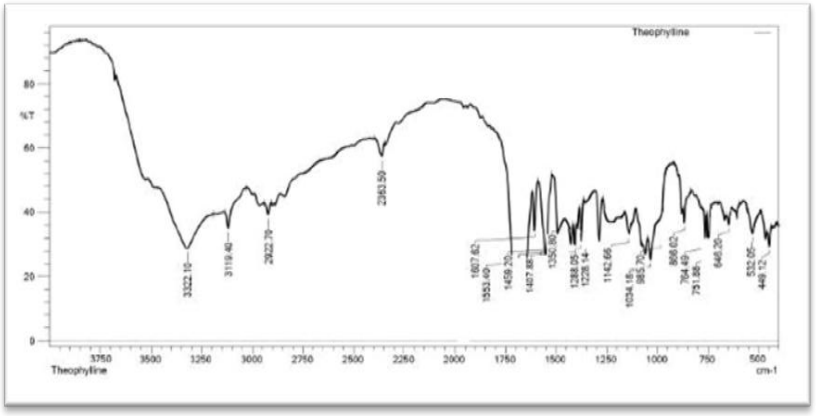


Figure 5: IR Spectra of (A) Theophylline (Pure drug)

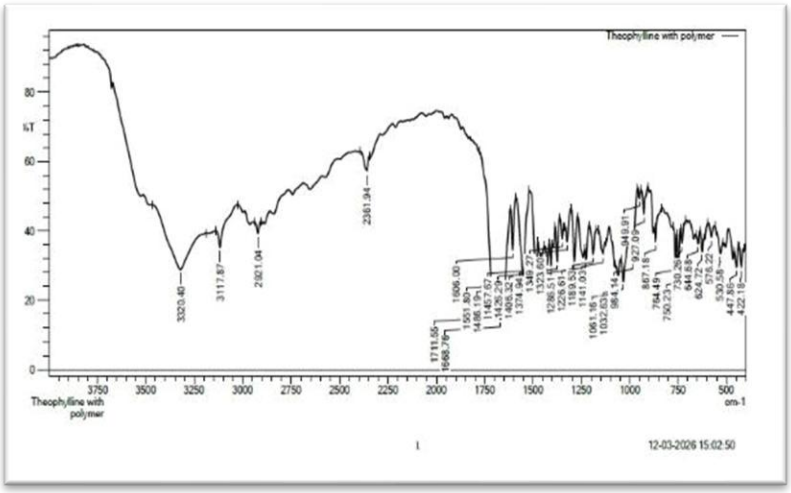


Figure 6: IR Spectra of (B) Optimized formulation F9

The FTIR spectrum of theophylline shows characteristic peaks such as a broad N–H stretching around ~3320 cm^{-1}, C–H stretching near ~2920 cm^{-1}, and a prominent C=O stretching peak in the region of ~1700–1650 cm^{-1}, confirming its imidazole-dione structure. Additional peaks between ~1550–1400 cm^{-1} correspond to C=N and C=C stretching, while the fingerprint region below 1300 cm^{-1} represents C–N stretching and ring vibrations. In the FTIR spectrum of theophylline with polymer, these characteristic peaks are retained with slight shifts and reduced intensity, indicating possible hydrogen bonding interactions. However, the absence of new peaks or disappearance of major peaks confirms that there is no significant chemical interaction, demonstrating compatibility of the drug with the polymer.

PRECOMPRESSION STUDIES:

EVALUATION OF TABLETS:

Table 9: Precompression parameters for Theophylline SR tablets

BatchNo.	Angle of Repose (°)	Bulk Density(g/ml)	Tapped Density(g/ml)	Carr's Index (%)	Hausner's Ratio
F1	25°03′	0.2745	0.3574	14.20	1.11
F2	25°31′	0.2868	0.3490	14.32	1.12
F3	26°54′	0.2723	0.3970	12.61	1.16
F4	27°08′	0.2675	0.3356	13.70	1.13
F5	26°02′	0.2569	0.3345	13.15	1.12
F6	25°87′	0.2745	0.3355	13.85	1.15
F7	24°60′	0.2770	0.3360	13.90	1.14
F8	24°67′	0.2820	0.3371	13.45	1.14
F9	25°14′	0.2842	0.3400	13.70	1.13
F10	25°20′	0.2814	0.3401	14.15	1.12

The angle of repose for the formulations F1-F10 has been estimated to be in the range 24°60′ to 27°08′ demonstrates good flow characteristics. Compressibility index for the formulations F1-F10 varied from 12.61% to 14.32% displaying the outstanding flow characteristics. Hausner's Ratio for the formulations F1-F10 found from 1.11 to 1.16 exhibiting excellent flow characteristics.

Table 10: Post compression parameters for Theophylline SR tablets

Batch.No	Weight Variation (%)	Friability (%)	Thickness (mm)	Hardness (Kg/cm^2)	Drug content (%)
F1	494±1.92	0.33	5.20±0.2	5.70	95.0
F2	490±2.04	0.32	5.22±0.2	5.94	96.0
F3	496±2.37	0.30	5.23±0.1	6.05	98.5
F4	501±1.25	0.34	5.22±0.1	5.80	98.5
F5	505±1.36	0.30	5.15±0.1	5.90	96.6
F6	503±1.23	0.27	5.17±0.1	6.10	94.6
F7	501±1.82	0.28	5.24±0.2	5.90	96.5
F8	510±1.49	0.25	5.20±0.3	6.10	99.5
F9	495±2.37	0.24	5.33±0.2	6.20	94.5
F10	510±1.91	0.25	5.23±0.1	6.10	97.2

Weight Variation (%)

The average tablet weights ranged from 490 ± 2.04 mg to 510 ± 1.49 mg, which falls within acceptable pharmacopeial limits (±5%). Lowest weight was observed in F2 (490 mg) whereas Highest weight was found in F8 & F10 (510 mg). It confirm Uniform weight variation across all batches and also good powder flow properties and proper die filling consistency. Slight increases in weight (F8, F10) are attributed to higher polymer content and reduced lactose, leading to differences in bulk density

Friability

Friability values ranged from 0.24% to 0.34%, well below the acceptable limit of 1%. Lowest

friability was found in formulation F9 (0.24%) whereas highest friability was seen in formulation F4 (0.34%). All formulations exhibited excellent mechanical resistance

Increasing polymer concentration in formulations F3, F6, F8 to F10 leads to decreased friability. This is due to stronger interparticle bonding and matrix formation

Thickness

Tablet thickness ranged from 5.15 ± 0.1 mm (F5) to 5.33 ± 0.2 mm (F9), reflecting good uniformity and consistent compression. A slight increase in thickness was noted in combination batches with higher polymer content; this is attributed to the low bulk density and swelling tendency of natural gums like Hibiscus and Grewia. Ultimately, the uniform thickness across all formulations confirms a reliable die fill and stable compression force during production

.Hardness

Theophylline SR tablets exhibited satisfactory mechanical strength, with hardness values ranging from 5.70 kg/cm² (F1) to 6.20 kg/cm² (F9). A direct correlation was observed between increased polymer concentration and tablet hardness, with Grewia gum contributing significantly due to its superior viscosity and binding capacity. Notably, all combination batches (F7–F10) demonstrated enhanced hardness, attributed to the synergistic effects of matrix formation between the polymers.

Drug Content

The drug content of Theophylline SR tablets ranged from 94.5% (F9) to 99.5% (F8), consistently meeting standard acceptance limits. These results confirm a uniform drug distribution across all formulations, with no significant degradation detected. Minor variations observed in certain batches were attributed to mixing efficiency and subtle polymer-drug interactions, ensuring the overall stability and potency of the tablets.

EFFECT OF POLYMER CONCENTRATION:

Hibiscus-Based Formulations (F1–F3):

n Theophylline SR tablets, increasing the Hibiscus mucilage concentration from 50 to 150 mg results in an increase in hardness from 5.70 to 6.05 kg/cm², a decrease in friability from 0.33% to 0.30%, and a slight increase in tablet thickness. While Hibiscus improves structural integrity through its swelling and binding properties, its moderate viscosity produces a relatively weaker matrix compared to formulations utilizing Grewia gum.

Grewia-Based Formulations (F4–F6):

In Theophylline SR tablets using increasing Grewia gum as natural polymer in the concentration range from 50 → 150 mg, Hardness was increasing from 5.80 → 6.10 kg/cm².Whereas friability was decrease in the range from 0.34 → 0.27%. It clearly confirms that Grewia gum provides strong gel-forming ability as well as better mechanical strength and more effective matrix formation.

Combination Formulations (F7–F10):

Increasing the polymer ratio in combination formulations F7–F10 resulted in higher hardness and lower friability, driven by a synergistic effect where Hibiscus mucilage promoted swelling and Grewia gum reinforced the gel barrier. Among these, F9 (Hibiscus:Grewia, 10:20) was identified as the optimized batch, exhibiting the highest hardness (6.20 kg/cm²), lowest friability (0.24%), and consistent weight and drug content. Ultimately, all formulations met pharmacopeial standards, confirming that the combination of these natural polymers—particularly in F9—provides the superior matrix integrity and

mechanical stability required for effective sustained Theophylline delivery.

IN VITRO DRUG RELEASE

All formulations of Theophylline SR tablets exhibited a controlled and extended release profile over 12 hours, confirming the suitability of natural polymers in sustaining drug release. It shows initial burst release observed in all batches due to surface drug that is followed by gradual and controlled release phase.

Hibiscus esculentus Mucilage gum

The release of medicines from the Hibiscus esculentus Mucilage gum matrix is mostly determined by the degree of swelling of the matrices. As the concentration of Hibiscus esculentus Mucilage gum increases in matrices from F1 to F3, swelling increases, and the rate of drug release varies depending on the matrices. Increasing Hibiscus mucilage slower drug release of theophylline as shown in table 11 and figure 7 However, due to moderate viscosity, matrix erosion is significant. Drug release mainly governed by the swelling with erosion mechanism. But the Hibiscus alone is not sufficient for strong sustained release of Theophylline

Table 11: In vitro drug release profile of Theophylline SR tablets F1 – F3 of Theophylline SR tablets

Time (hours)	BATCH NO.		
	F1	F2	F3
1	30.10	25.15	20.20
2	50.17	45.35	40.35.
4	70.24	65.20	60.15
6	85.35	80.10	75.20
8	95.78	92.30	88.40
10	100	98.35	95.60.
12	100	100	100

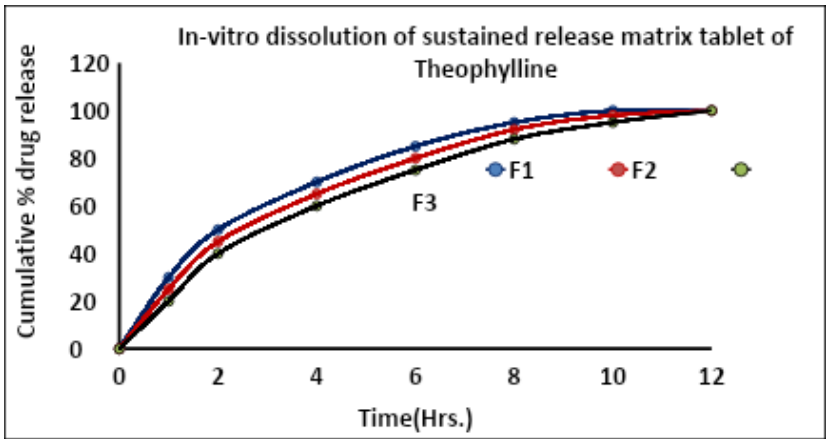


Figure 7 : In vitro drug release profile of F1 – F3 of Theophylline SR tablets

Grewia gum

The drug release of Theophylline from Grewia gum matrices is primarily determined by the degree of swelling and a significant erosion mechanism. Increasing the concentration of Grewia gum from F4 to F6 enhances the viscosity of the gel barrier, which effectively slows the drug release rate. Ultimately, Grewia gum functions as a more effective sustained-release polymer than

Hibiscus due to this superior viscosity, which maintains strong matrix integrity and controlled delivery.

Table 12: In vitro drug release profile of F4 – F6 of Theophylline SR tablets

Time (hours)	BATCH NO.		
	F4	F5	F6
1	22.40	18.90	15.40
2	42.55	35.50	30.55
4	62.10	55.10	50.70
6	78.35	70.40	65.60
8	90.25	85.50	80.60
10	96.45	93.30	90.70
12	100	100	98.80

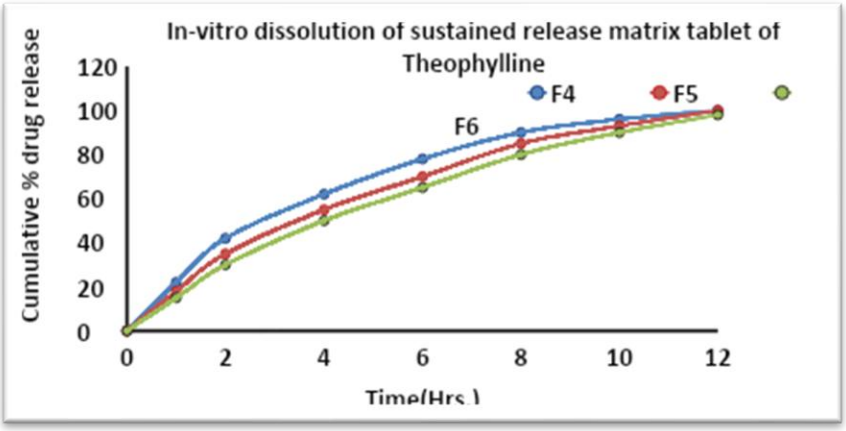


Figure 8: In vitro drug release profile of F4 – F6 of Theophylline SR tablets

Hibiscus esculentus Mucilage gum + Grewia gum Both *Hibiscus esculentus* and *Grewia* gum act as swellable polymers that form a gelatinous mass to regulate drug diffusion, with the hydrated gel layer thickness determining the release rate. Combination matrices (F7–F10) significantly reduce drug release compared to individual gums due to a synergistic interaction that forms a strong, elastic gel barrier. The most effective delay was observed in formulation F9 (10:20 ratio); however, deviating from this optimal concentration decreases synergistic efficiency and leads to faster drug release.

Table 13: In vitro drug release profile of F7 – F10 of Theophylline SR tablets

Time(hours)	Batch No.			
	F7	F8	F9	F10
0	0	0	0	0
1	20.10	18.50	15.30	22.30
2	38.45.	35.20	30.25	38.25
4	58.25	55.10	50.15	60.15
6	72.10	70.35	68.10	7530

8	86.45	85.10	8235	88.10
10	94.30	93.20	90.50	95.25
12	100	99.15	97.85	100

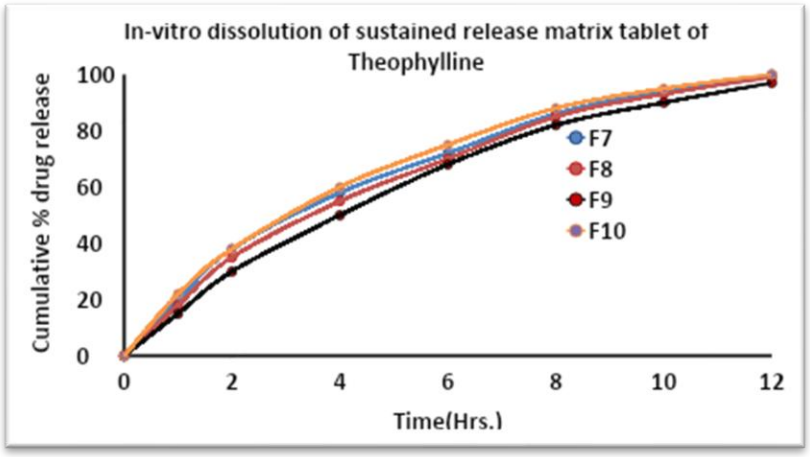


Figure 9: In vitro drug release profile of F7 – F10 of Theophylline SR tablets

Theophylline SR tablets sustained drug release over 12 hours, with combination formulations exhibiting a synergistic effect between the rapid hydration of Hibiscus and the robust matrix of Grewia. While Hibiscus-based batches showed faster release due to higher erosion, Grewia gum provided stronger retardation through a viscous diffusion barrier. Ultimately, F9 (10:20 Hibiscus: Grewia ratio) was identified as the optimized formulation for its controlled and reproducible drug release profile.

Swelling study

The release of drugs refile were dependent on expanding behaviour of the tablets. Swelling index increased with the amount of gain from the tablets increased proportionally according to the rate of hydration. Swelling index of chosen batch F3, F6, F7, F8, F9 and F10 had been calculated.

Table 14 : Swelling Index for of matrix tablets of Theophylline

Formulation	Time (Hours)	
	4	8
F3	0.68 ± 0.03	1.05 ± 0.05
F6	0.60 ± 0.02	0.95 ± 0.04
F7	0.65 ± 0.03	1.00 ± 0.04
F8	0.72 ± 0.04	1.12 ± 0.05
F9	0.66 ± 0.03	1.08 ± 0.04
F10	0.75 ± 0.04	1.15 ± 0.05

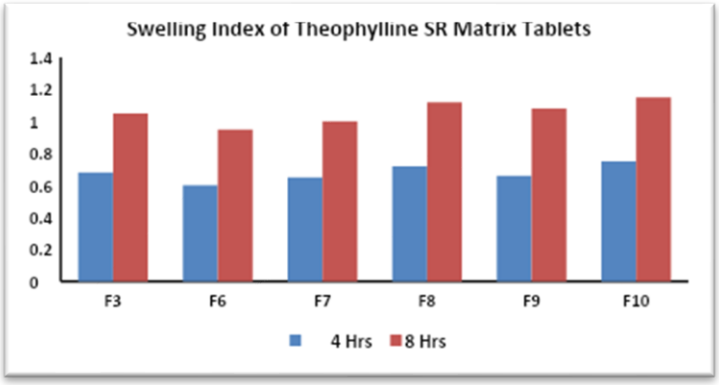


Figure 10: Swelling Index for matrix tablet of Theophylline

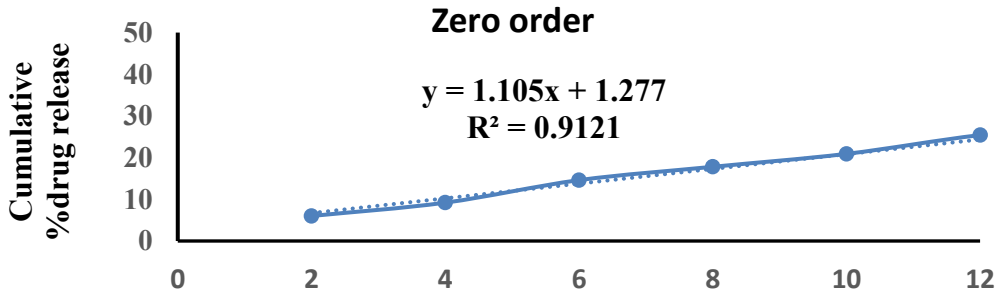


Figure 11: Zero order Kinetic plots

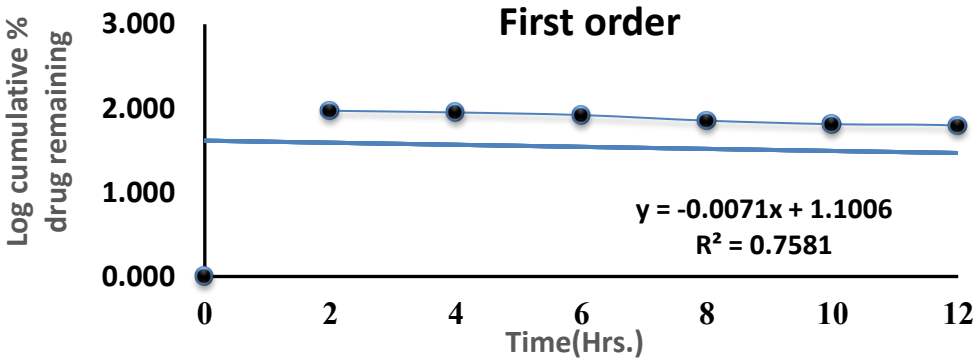


Figure 12: First order Kinetic plots

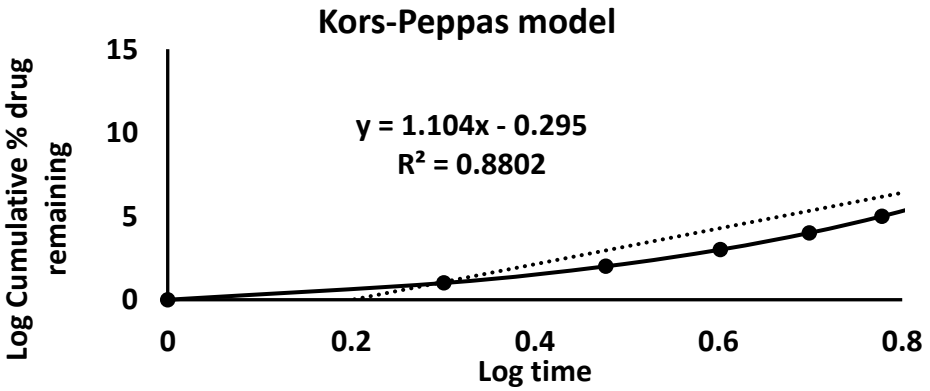


Figure 13: Kors-Peppas model plots

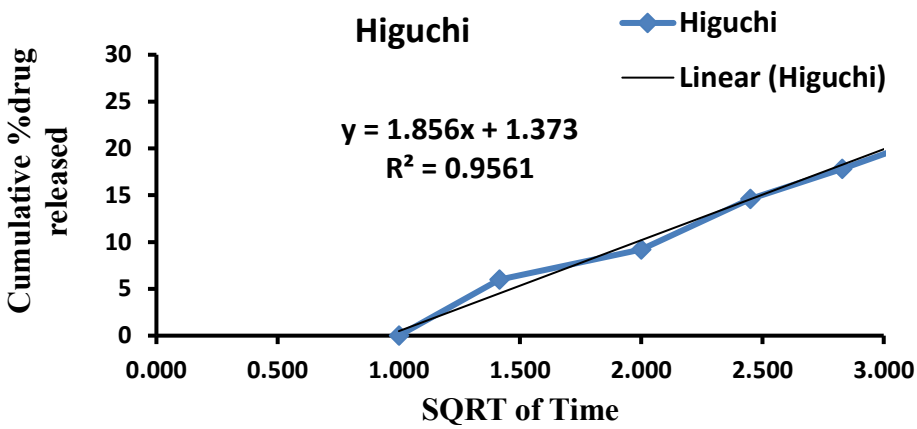


Figure 14: Higuchi Kinetic plots

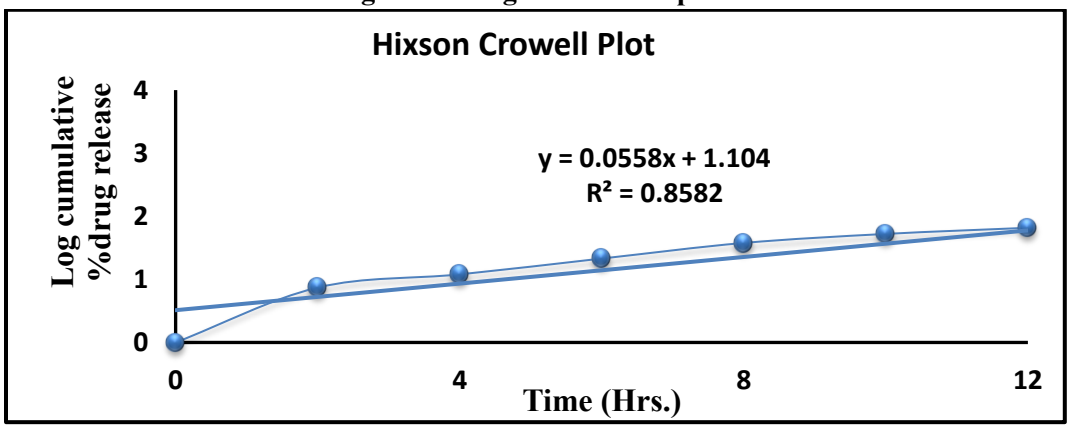


Figure 15: Hixson Crowell Kinetic plots

Table 15: Result of kinetic analysis of Theophylline SR tablet

Formulation	Zero order (R^2)	First order (R^2)	Higuchi kinetics (R^2)	Hixson Crowell (R^2)	Korsmeyer Peppas (R^2)
F9	0.7581	0.7581	0.9561	0.8582	0.8802

CONCLUSION

Theophylline, a common bronchodilator for asthma and COPD, faces clinical limitations due to its narrow therapeutic index and short biological half-life, which leads to frequent dosing and adverse reactions. To address this, a sustained release matrix tablet was developed using natural polymers—Hibiscus esculentus mucilage and Grewia gum—to maintain consistent plasma drug concentrations and improve patient compliance.

The study formulated ten batches (F1–F10), identifying Batch F9 as the optimized formulation. This batch utilized a synergistic combination of polymers to create a stable gel barrier, achieving a controlled drug release of approximately 50% at 4 hours and near-complete release by 12 hours. All formulations met pharmacopeial standards for weight, hardness, and drug content, with the natural polymers proving both biocompatible and effective in controlling diffusion.

Kinetic analysis confirmed that the optimized formulation follows zero-order kinetics and a non-Fickian release mechanism, governed by both diffusion and polymer erosion. Stability studies under ICH guidelines confirmed the formulation remains reliable over time. Ultimately, this research highlights the cost-effective potential of natural polymers in creating safe, efficient, and patient-compliant advanced drug delivery systems.

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