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INNOVATIVE HYDROPHILIC MATRIX ENGINEERING FOR SUSTAINED DELIVERY OF OXCARBAZEPINE: A MECHANISTIC AND FUNCTIONAL PERFORMANCE EVALUATION

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Abstract: The oral route is a preferred method for systemic drug delivery because of its flexibility and patient compliance. This study focuses on developing sustained-release matrix tablets for oxcarbazepine to maintain stable plasma levels and reduce how often doses are needed. Seven formulations (F1–F7) were created using carbopol and chitosan as the main polymers. Pre-formulation studies used UV spectrophotometry to find a maximum absorbance at 256 nm in a pH 6.4 buffer. Compatibility tests with FT-IR and DSC showed the drug stayed in its pure state with no chemical interactions with the excipients. Pre-compression checks for bulk density, tapped density, and angle of repose showed that the powder had good to excellent flow properties. After compression, the tablets met standard requirements for thickness, weight variation, and friability, with drug content between 98.4% and 101.2%. Dissolution tests showed that nearly all the drug was released (90–100%) within 8 hours. Kinetic models showed the release followed first-order kinetics through a non-Fickian mechanism involving both diffusion and polymer relaxation. Stability tests for the F4 formulation showed it remained physically and chemically stable under normal and accelerated conditions for three months. These results show that matrix tablets are a cost-effective way to improve the delivery of oxcarbazepine.

Key words **- sustained release, oxcarbazepine, spectroscopy, Release kinetics**

1. INTRODUCTION

The oral route of administration remains the most popular and preferred method for systemic drug delivery within the pharmaceutical industry due to flexibility in design [1]. This prevalence is attributed to its ease of administration, patient compliance, and the adaptability of gastrointestinal physiology [2]. Traditional drug delivery systems are characterized by immediate release and repeated dosing which risk dose fluctuations [3]. Sustained release systems achieve a prolonged therapeutic effect by continuously releasing medication over an extended period [4]. These formulations allow for maintenance doses that provide an opportunity to prolong drug release and therapeutic activity [5]. Matrix tablets are a promising approach for extended-release therapy as they offer the lowest cost approach for solid dosage forms [6]. Matrix tablets are oral solid dosage forms where the drug is homogeneously dispersed or dissolved within polymeric matrices [7]. Polymers play a critical role in governance of release rates and mechanism, governing diffusion and erosion [8]. The release of drugs from hydrophilic matrices involves a complex interplay of dissolution, diffusion, and erosion mechanisms [9]. Ideal drugs for sustained release should have a biological half-life between 2 and 8 hours [10]. Uniform absorption from the gastrointestinal tract is essential for maintaining consistent therapeutic blood levels [11]. Biopharmaceutical selection parameters include drug molecular size, solubility, and partition coefficient [12]. Knowledge of the absorption mechanism from all GI segments is necessary for designing oral sustained release systems [13]. Matrix tablets can be formulated using simple methods like wet granulation or direct compression to maintain tablet hardness [14]. Matrix systems improve patient compliance by reducing dosing frequency and optimizing therapeutic outcomes [15]. Recent pharmaceutical technology trends have established matrix systems as a breakthrough in novel drug delivery [16]. The field has seen a remarkable increase in interest due to prohibitive costs of developing new drug entities [17]. The principal goal of sustained release forms is the improvement of drug therapy assessed by utility and side-effect reduction [18]. Rationale for SR includes stabilizing plasma levels and extending the duration of action for drugs with short half-lives [19]. Matrix tablets are popular because they can accommodate large drug doses while maintaining a simple formulation design [20].

1.1 ADVANTAGES OF SUSTAINED RELEASE FORMULATION

- Matrix tablets maintain constant plasma drug concentrations and sustain therapeutic action for prolonged time periods.
- These formulations maintain stable plasma drug concentrations while reducing dosing frequency.
- Sustained release improves patient compliance by reducing the frequency of dosing and minimizing fluctuations in drug levels.
- The goal of these systems is to reduce dosing frequency or increase effectiveness by localization at the site of action.
- Sustained release optimizes biopharmaceutical parameters to maximize therapeutic efficacy and reduce side effects.
- Rationale for development includes maximizing utility and stabilizing plasma level drug concentrations.
- Matrix drug delivery provides advantages such as increased safety margins for potent drugs and maximum drug utilization.
- Oral sustained release drug delivery provides constant delivery and better control of blood drug levels.
- These systems reduce "see-saw" fluctuations in systemic circulation and tissue compartments compared to conventional forms.
- Matrix tablets are commercially feasible sustained action dosage forms that utilize conventional facilities and accommodate large doses.
- These formulations are designed to maintain drug concentrations within the therapeutic window with minimum side effects.
- Sustained release technology results in shorter treatment periods and improved patient compliance.
- Formulations achieve optimized therapy by minimizing drug concentration fluctuations that cause adverse effects.
- Advanced drug delivery concepts focus on optimizing the biopharmaceutical and pharmacokinetic properties of active agents.
- The goal is more predictability and reproducibility to optimize the therapeutic effect with lower and less frequent doses.
- Matrix systems improve stability by protecting the drug from hydrolysis or other derivative changes in the GI tract.
- Controlled release delivery systems aim to provide precise dosing over a long duration.
- Formulating drugs into matrix cores stabilizes them against enzymatic degradation.
- Hydrophilic matrices are preferred due to simplicity, cost-effectiveness, and broad regulatory acceptance.
- Matrix technology allows for the stabilization of medical conditions through uniform and steady drug levels.

1.2 DISADVANTAGES OF SUSTAINED RELEASE TABLET

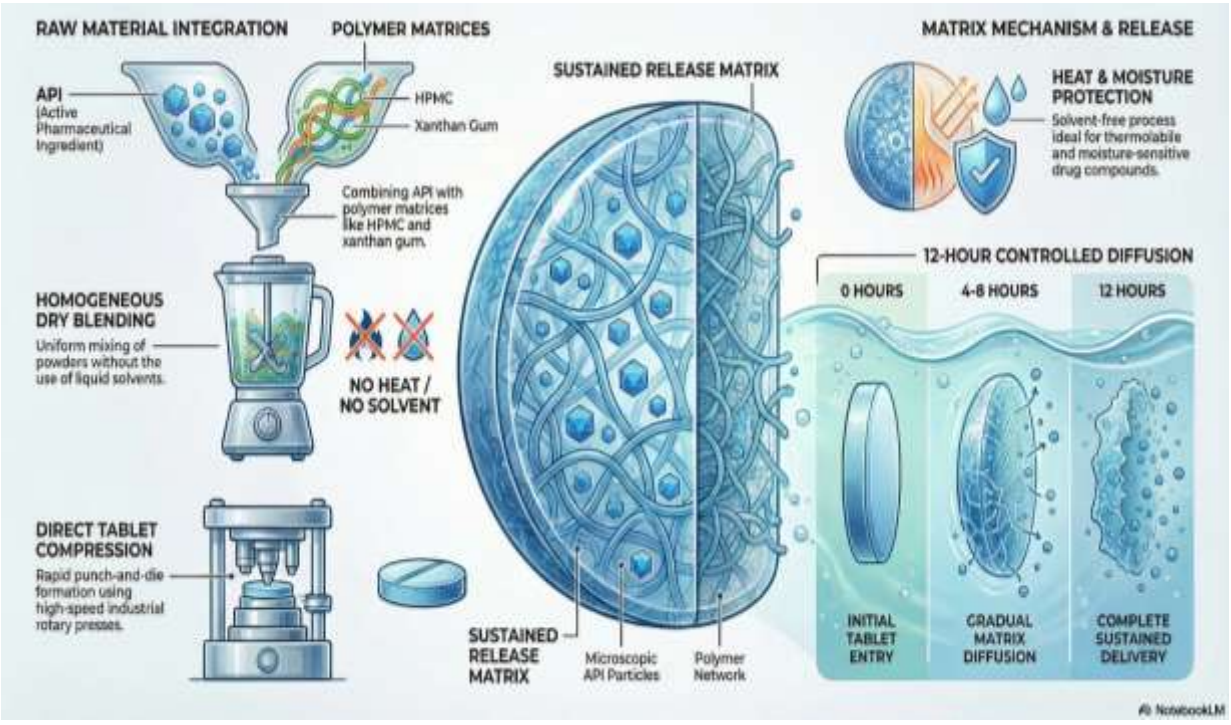
- Faulty matrix structure may lead to dose dumping, causing potentially toxic concentrations.
- Reduced potential for dose adjustment is a major drawback for fixed-release systems.
- The initial cost per unit dose is typically higher than conventional dosage forms.
- Poor in vivo and in vitro correlation makes predicting human performance difficult.
- Prolonging drug release may increase the potential for undesirable first-pass metabolism.
- Extensive patient education and counselling are required for proper administration.
- Delay in onset of action makes these forms inappropriate for acute medical conditions.
- Matrix tablets depend heavily on gastrointestinal residence time for effectiveness.
- Release can be affected by physiological factors like food intake and gastric motility.
- Achieving pure zero-order release is often difficult with standard matrix designs.
- Matrix skeletons (ghost matrices) must be recovered in feces, which can concern patients.
- SR preparations do not permit the prompt termination of therapy if adverse reactions occur.

- ❖ Systemic availability may be reduced compared to immediate-release conventional forms.
- ❖ Large doses required for certain drugs make the final matrix tablet too big to swallow.
- ❖ Poor candidate drugs include those with very short biological half-lives (<1hr).
- ❖ Drugs not effectively absorbed in the lower intestine are unsuitable for SR design.
- ❖ Quality control requirements for SR products are more extensive than for conventional tablets.
- ❖ It is difficult to deliver high molecular weight compounds through insoluble matrix barriers.
- ❖ Risk of toxicity increases if the delivery system fails internally.
- ❖ Not suitable for acute medical conditions where rapid dosage adjustment is needed.

2. GENERAL METHODOLOGIES FOR SUSTAINED RELEASE TABLET

2.1 Direct Compression Methodology

Direct compression is the simplest and most cost-effective method, where powdered materials are compressed directly without changing the drug's physical or chemical properties. The process involves mixing the active pharmaceutical ingredient (API) with polymers and other excipients to form a matrix, which is then tableted. This method is ideal for moisture-sensitive and thermolabile drugs as it avoids the use of heat and solvents.



2.2 Wet Granulation Methodology

Wet granulation involves blending the drug and polymeric retardants with a liquid binder (such as povidone or starch paste) to form a cohesive wet mass. This mass is then screened, dried, and compressed into tablets to enhance the flowability and compressibility of the mixture. This methodology is preferred for ensuring uniform drug distribution throughout the matrix.

2.3 Melt Granulation and Congealing

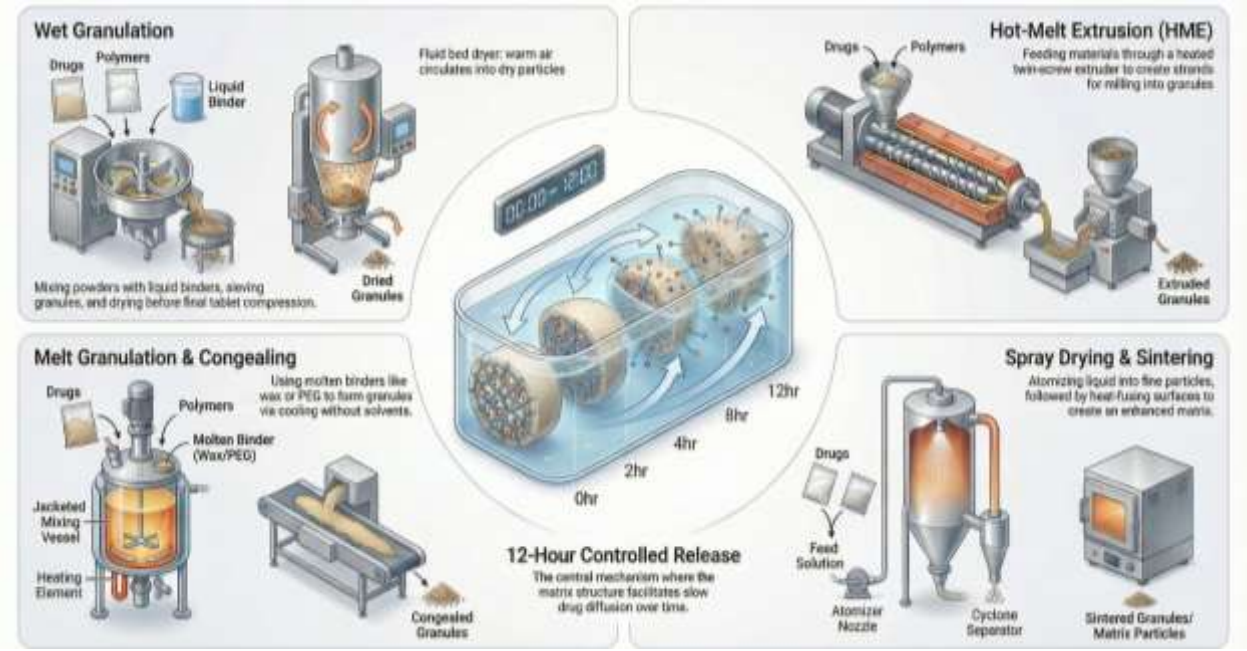
Melt granulation is a solvent-free technique utilizing a substance that melts at a relatively low temperature (such as carnauba wax or PEG) to act as a granulating agent. The molten binder is mixed with the drug and excipients, then cooled and compressed into tablets. This approach is particularly effective for formulating hydrophobic matrix systems.

2.4 Hot-Melt Extrusion (HME)

In hot-melt extrusion, a mixture of the drug, thermoplastic polymers, and processing aids is fed into an extruder where they are melted and mixed under heat and pressure. The resulting homogenous dispersion is forced through a die, cooled, and milled into granules. HME is a valuable technique for improving the solubility of poorly water-soluble drugs while maintaining a stable, sustained release.

2.5 Spray Drying and Sintering Techniques

Spray drying involves dissolving or dispersing the drug and polymer in a solvent, followed by rapid atomization into a heated drying chamber to produce fine encapsulated powder. Sintering is the bonding of adjacent particle surfaces in a mass of powder or a compact by applying heat below the melting point of its constituents, which is used to further stabilize and retard drug release.



3. RESEARCH EXPERIMENTAL WORK

3.1 Pre-Formulation Studies

3.1.1 Analytical method in the determination of Oxcarbazepine

The UV spectrophotometric method is developed by using the Shimadzu 1800 spectrophotometer for the analysis of the drug.

❖ **Preparation of 6.8 pH phosphate buffer solution**

A. A 0.2 M phosphate buffer was prepared using potassium dihydrogen phosphate and sodium hydroxide through a controlled neutralization process.
B. Initially, 50 ml of 0.2 M potassium dihydrogen phosphate stock solution was accurately measured using a pipette and transferred into a 200 ml volumetric flask. This solution serves as the acidic component of the buffer system.
C. Subsequently, 22.4 ml of 0.2 M sodium hydroxide solution was measured and added slowly to the flask with continuous gentle swirling to ensure proper mixing. This step results in partial neutralization and formation of a conjugate acid–base pair responsible for buffering action.
D. Finally, distilled water was added to the volumetric flask to make up the volume to 200 ml. The solution was mixed thoroughly by repeated inversion to obtain a uniform buffer solution.

❖ **Determination of λmax**

A. The determination of λmax of oxcarbazepine is carried out using UV–Visible spectrophotometry to identify the wavelength at which the drug shows maximum absorbance. The procedure is described below.
B. Initially, an accurately weighed quantity of oxcarbazepine is taken and dissolved in a suitable solvent such as methanol or a mixture of methanol and distilled water to prepare a standard stock solution of known concentration, for example 100 µg/ml. The solution is sonicated if necessary to ensure complete dissolution.
C. From this stock solution, a suitable aliquot is withdrawn and further diluted with the same solvent to obtain a working standard solution, typically in the range of 10 µg/ml.
D. The UV–Visible spectrophotometer is then switched on and allowed to stabilize. The instrument is calibrated using the selected solvent as a blank, filled in a quartz cuvette.
E. The prepared working standard solution is placed in the cuvette, and the absorbance is scanned over a wavelength range of 200 nm to 400 nm.
F. During the scan, the absorbance values are recorded, and a spectrum is obtained. The wavelength at which the maximum absorbance is observed is identified as the λmax of oxcarbazepine.
G. This λmax value is then used for further quantitative analysis of the drug.

❖ **Standard curve for Oxcarbazepine**

A. The standard calibration curve of oxcarbazepine was prepared by UV–Visible spectrophotometric method using the following experimental procedure.
B. An accurately weighed quantity of 100 mg of oxcarbazepine was transferred into a 100 ml volumetric flask. The drug was dissolved in a small quantity of 0.1 N sodium hydroxide with the aid of sonication to ensure complete solubility, and the volume was made up to 100 ml with the same solvent to obtain the primary stock solution having a concentration of 1000 µg/ml.
C. From this primary stock solution, 10 ml was pipetted out and transferred into another 100 ml volumetric flask, and the volume was adjusted up to the mark with 0.1 N sodium hydroxide to obtain a secondary stock solution of 100 µg/ml.
D. Aliquots of the secondary stock solution were then withdrawn and transferred into a series of 10 ml volumetric flasks to prepare working standard solutions of concentrations 5, 10, 15, 20, 25, and 30 µg/ml. The volume in each flask was made up to the mark using 0.1 N sodium hydroxide.
E. The UV–Visible spectrophotometer was switched on and allowed to stabilize. The instrument was calibrated using 0.1 N sodium hydroxide as the blank. The absorbance of each prepared solution was measured at 249 nm using a quartz cuvette.
F. A calibration curve was plotted by taking concentration in µg/ml on the x-axis and corresponding absorbance values on the y-axis. The linearity of the plot was used for quantitative estimation of oxcarbazepine.

3.1.2 Compatibility study using FT-IR

A. The compatibility study of oxcarbazepine with excipients was carried out using Fourier Transform Infrared (FT-IR) spectroscopy to evaluate possible physicochemical interactions during formulation development. This study is essential to ensure the stability and integrity of the drug in the presence of selected polymers and other formulation components.
B. Pure oxcarbazepine and its physical mixtures with excipients were subjected to FT-IR analysis. The physical mixtures were prepared by triturating the drug with individual excipients in suitable ratios, typically 1:1, using a mortar and pestle to ensure uniform mixing. These samples were stored in desiccators prior to analysis to avoid moisture interference.
C. For FT-IR analysis, the samples were prepared using the potassium bromide pellet method. A small quantity of the sample was mixed with dry potassium bromide and compressed into a transparent pellet using a hydraulic press. Alternatively, the samples could be analyzed directly using the attenuated total reflectance technique without pellet preparation.
D. The FT-IR spectra of pure oxcarbazepine, excipients, and their physical mixtures were recorded over a wavelength range of 4000 cm^{-1} to 400 cm^{-1} using an FT-IR spectrophotometer. The obtained spectra were carefully analysed to identify characteristic peaks corresponding to functional groups present in oxcarbazepine, such as N–H stretching, C=O stretching, aromatic C=C stretching, and C–O vibrations.
E. The spectrum of pure oxcarbazepine showed distinct and sharp peaks at specific wavenumbers, which serve as reference points. These characteristic peaks were then compared with those observed in the spectra of physical mixtures. The absence of significant shifts, disappearance, or broadening of these peaks in the mixtures indicates that there is no chemical interaction between oxcarbazepine and the excipients.
F. However, minor variations in peak intensity may be observed due to dilution effects or physical mixing, which are not indicative of incompatibility. The preservation of the drug's characteristic peaks confirms that the selected excipients are compatible with oxcarbazepine.
G. Thus, FT-IR analysis provides reliable evidence regarding drug–excipient compatibility and supports the selection of suitable formulation components for further development.

- **Procedure for FT-IR Compatibility study**

a) An accurately weighed quantity of the drug (approximately 3 mg) was taken and mixed with about 100 mg of potassium bromide, which was previously dried at 40–50°C to remove any moisture content. The mixing was carried out thoroughly using a mortar and pestle to obtain a uniform and fine powder mixture.
b) The prepared mixture was then transferred into a die cavity and compressed using a hydraulic press under a pressure of about 10 tons for a few minutes. This process resulted in the formation of a clear and transparent pellet suitable for infrared analysis.
c) The prepared pellet was carefully placed in the sample holder of the ft-ir spectrophotometer. The spectrum was recorded over a range of 4000 cm^{-1} to 400 cm^{-1} to identify the characteristic functional groups present in the drug.
d) The same procedure was repeated for all individual excipients used in the formulation, as well as for physical mixtures of drug and excipients. In case of physical mixtures, the drug and excipients were mixed in appropriate ratios before pellet preparation.
e) The obtained spectra of pure drug, excipients, and their mixtures were compared to detect any significant changes such as peak shifting, disappearance, or formation of new peaks, which could indicate possible drug–excipient interactions.
f) This method helps in confirming the compatibility of the drug with selected excipients prior to formulation development.

3.1.3 Compatibility study using Differential Scanning Calorimetry

A. Differential scanning calorimetry is a widely used thermal analysis technique for evaluating the compatibility of a drug with excipients in a formulation. In the case of oxcarbazepine, DSC helps in identifying possible physicochemical interactions by analysing changes in thermal behaviour such as melting point, crystallinity, and thermal transitions.
B. Oxcarbazepine, being a crystalline drug, exhibits a sharp and well-defined endothermic peak corresponding to its melting point in the DSC thermogram. This peak serves as a reference for assessing any interaction when the drug is mixed with excipients. During compatibility studies, the thermograms of pure drug, individual excipients, and their physical mixtures are compared.
C. If the drug is compatible with the excipients, the characteristic melting endotherm of oxcarbazepine remains intact with minimal or no shift in peak temperature. Slight variations in peak intensity may occur due to dilution effects or differences in heat capacity, which are generally not considered significant.
D. However, any major changes such as disappearance of the melting peak, broadening of the peak, or a significant shift in temperature may indicate possible interactions. These interactions could be due to chemical reactions, complex formation, or changes in the crystalline nature of the drug, such as conversion to an amorphous form.
E. DSC also helps in detecting polymorphic transitions, degradation, or incompatibility that may not be visible through other analytical techniques. This makes it an important tool in preformulating studies.
F. Overall, DSC provides valuable insights into the thermal stability and compatibility of oxcarbazepine with selected excipients, ensuring the selection of suitable components for stable and effective formulation development.

- **Procedure for DSC Compatibility study**

a) An accurately weighed quantity of pure oxcarbazepine was taken along with individual excipients and their physical mixtures for analysis. The physical mixtures were prepared by blending the drug with excipients in a suitable ratio, typically 1:1, using a mortar and pestle to ensure uniform mixing.
b) A small amount of each sample, usually between 2 to 5 mg, was weighed accurately and placed into clean and dry aluminium sample pans. The pans were then sealed properly using a crimping tool to avoid any loss of sample during the heating process.
c) An empty sealed aluminium pan was used as a reference. Both the sample pan and reference pan were placed in the differential scanning calorimeter.
d) The analysis was carried out under a nitrogen atmosphere to prevent oxidation, with a constant nitrogen flow maintained throughout the experiment. The samples were heated over a temperature range of approximately 25°c to 300°c at a controlled heating rate, generally 10°c per minute.
e) During the heating process, the instrument recorded the heat flow associated with thermal transitions, and thermograms were obtained for pure drug, excipients, and their mixtures.
f) The obtained thermograms were analysed and compared to observe any changes in the characteristic melting peak of oxcarbazepine. The presence or absence of peak shifts, disappearance, or formation of new peaks was used to assess compatibility between the drug and excipients.
g) The procedure was repeated if necessary to confirm reproducibility of the results.

Formula Code	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)
Oxcarbazepine	300	300	300	300	300	300	300
Carbopol	100	100	100	100	100	100	100
Chitosan	--	5	10	15	--	--	--
PVP K 30	5	5	5	5	5	10	15
Magnesium Stearate	3	3	3	3	5	5	5
Talc	2	2	2	2	3	3	3
Microcrystalline cellulose QS to	500	500	500	500	500	500	500

3.2 EVALUATION OF PRE-FORMULATION PARAMETERS

3.2.1 Melting Point

Melting point is defined as the temperature at which a solid substance changes into a liquid under atmospheric pressure. It is an important physical property used to assess the purity of a drug substance. A pure compound typically exhibits a sharp and narrow melting point range, whereas impurities tend to lower and broaden the melting range.

Melting point determination is useful in drug identification, compatibility studies, and selection of suitable excipients. It also provides insight into the thermal stability of the drug. Substances with low melting points may be more prone to degradation, while those with high melting points generally exhibit greater stability but may have lower solubility.

3.2.2 Angle of Repose

Angle of repose is the maximum angle formed between the surface of a pile of powder and the horizontal plane. It is an indirect measure of powder flowability.

It is calculated using the formula:

$\tan \theta = h / r$

where h is the height of the powder heap and r is the radius of the base.

A lower angle of repose indicates better flow properties, while a higher angle suggests poor flow. This parameter is particularly important in tablet manufacturing and capsule filling, where uniform flow of powder is essential.

3.2.3 Bulk Density

Bulk density is defined as the mass of powder divided by its bulk volume, which includes the spaces between particles. It provides information about the packing ability of the powder.

Bulk density influences the size of the container required for storage and transportation. It also plays a significant role in determining the final size and weight of dosage forms such as tablets and capsules. Factors such as particle size, shape, and moisture content can affect bulk density.

3.2.4 Tapped Density

Tapped density is the density attained after mechanically tapping a measuring cylinder containing the powder until little or no further volume change is observed.

It is calculated as the mass of powder divided by the tapped volume.

Tapped density provides information about the compressibility and consolidation behaviour of powders. It is widely used along with bulk density to evaluate flow properties and packing characteristics.

3.2.5 Carr's Compressibility Index (CI)

Carr's Compressibility Index is a measure of the compressibility of a powder and is an indicator of its flow properties. It is calculated using bulk density and tapped density.

Carr's Index = [(Tapped Density − Bulk Density) / Tapped Density] × 100

Lower values of Carr's Index indicate better flowability, whereas higher values suggest poor flow and high compressibility. This parameter is widely used in pharmaceutical formulation to assess the suitability of powders for processing.

3.2.6 Hausner's Ratio

Hausner's ratio is defined as the ratio of tapped density to bulk density. It is another parameter used to evaluate powder flow characteristics.

Hausner's Ratio = Tapped Density / Bulk Density

A value close to 1 indicates good flow properties, while higher values indicate poor flow and increased interparticle friction. Hausner's ratio is commonly used in conjunction with Carr's Index to assess powder behavior during formulation and processing.

3.3 EVALUATION OF POST-FORMULATION PARAMETERS

3.3.1 Diameter (mm) ± SD

The diameter of tablets is an important physical parameter that ensures uniformity in size and shape. It is usually measured using a calibrated Vernier caliper or digital micrometer. Consistent diameter is essential for proper packaging, handling, and patient acceptability.

The results are expressed as mean diameter along with standard deviation (SD), which indicates the variability among tablets. Minimal variation reflects uniform die filling and proper compression during tablet manufacturing.

3.3.2 Thickness (mm) ± SD

Tablet thickness is measured using a Vernier caliper or micrometer and is expressed in millimeters along with standard deviation. It depends on the size of the die, amount of fill, and compression force applied during tablet formation.

Uniform thickness is important for ensuring consistent appearance and proper packaging. Variation in thickness may indicate improper compression or inconsistency in granule flow.

3.3.3 Weight Variation (mg)

Weight variation test is performed to ensure uniformity of dosage units. A specified number of tablets (usually 20) are individually weighed, and the average weight is calculated.

Each tablet weight is compared with the average weight, and the percentage deviation is determined. The acceptable limits are specified in pharmacopeias such as the Indian Pharmacopoeia, depending on the average tablet weight.

This test ensures that each tablet contains an appropriate amount of drug substance

3.3.4 Hardness (kg/cm²)

Tablet hardness, also known as crushing strength, is the force required to break a tablet diametrically. It is measured using instruments such as Monsanto or Pfizer hardness testers.

Adequate hardness is necessary to withstand mechanical shocks during handling, packaging, and transportation. However, excessively hard tablets may affect disintegration and dissolution, leading to poor drug release.

The hardness is typically expressed in kg/cm².

3.3.5 Friability (%)

Friability test evaluates the ability of tablets to resist abrasion and mechanical stress. It is carried out using a Roche friabilator, where tablets are subjected to rotational movement.

After the test, tablets are dedusted and reweighed. The percentage weight loss is calculated using the formula:

Friability (%) = [(Initial Weight − Final Weight) / Initial Weight] × 100

A friability value of less than 1% is generally considered acceptable, indicating good mechanical strength.

3.3.6 Drug Content

Drug content analysis determines the amount of active pharmaceutical ingredient present in each tablet. It ensures uniform distribution of the drug within the formulation.

The test is usually performed by dissolving a specific number of tablets in a suitable solvent, followed by analysis using techniques such as UV spectroscopy or HPLC.

The drug content should fall within the specified pharmacopeial limits (generally 95–105% of the labelled claim), ensuring efficacy and safety of the dosage form.

3.3.7 In-vitro dissolution studies

In-vitro dissolution studies are performed to evaluate the rate and extent of drug release from a dosage form, particularly tablets, under standardized laboratory conditions. This test is essential for predicting the in-vivo performance of the drug and ensuring batch-to-batch consistency.

Dissolution testing is carried out using official apparatus specified in pharmacopoeias such as the Indian Pharmacopoeia, United States Pharmacopeia, and British Pharmacopoeia. The most commonly used apparatus include USP Apparatus I (basket type) and USP Apparatus II (paddle type).

In a typical procedure, the tablet is placed in a dissolution vessel containing a specified volume of dissolution medium (usually 900 mL), maintained at a constant temperature of 37 ± 0.5°C to simulate physiological conditions. The medium may be selected based on the drug properties and can include buffers of different pH (e.g., pH 1.2, 6.8, or 7.4) to mimic gastrointestinal environments.

The apparatus is operated at a predefined rotational speed (commonly 50–100 rpm depending on the method). At predetermined time intervals, samples are withdrawn from the dissolution medium and replaced with fresh medium to maintain sink conditions. The collected samples are filtered and analysed using suitable analytical techniques such as UV-visible spectroscopy or high-performance liquid chromatography (HPLC).

The amount of drug dissolved is calculated and expressed as a percentage of the labeled drug content. A dissolution profile is then constructed by plotting cumulative percentage drug release versus time. This profile helps in understanding the release kinetics and mechanism of drug release from the formulation.

In-vitro dissolution studies are crucial for:

- Evaluating the effect of formulation variables on drug release
- Ensuring quality control and batch uniformity
- Establishing in-vitro–in-vivo correlation (IVIVC)
- Supporting regulatory approval and product development

Acceptance criteria for dissolution are specified in pharmacopoeial monographs and depend on the type of dosage form. Generally, an immediate-release tablet is expected to release not less than a specified percentage (e.g., 75–85%) of the drug within a given time.

Overall, in-vitro dissolution testing is a vital tool in pharmaceutical development, providing critical information about drug release behaviour, formulation performance, and product quality.

3.4 MATHEMATICAL MODELLING OF DRUG RELEASE PROFILE

3.4.1 Zero Order Kinetics

Zero order kinetics describes a drug release mechanism where the drug is released from the dosage form at a constant rate, independent of its concentration. This type of release is ideal for maintaining a constant plasma drug concentration over time.

$$Qt = Q0 + k0t$$

where *Qt* is the amount of drug released at time *t*, *Q0* is the initial amount of drug in the solution (usually zero), and *k0* is the zero order release rate constant.

A plot of cumulative amount of drug released versus time yields a straight line for zero order kinetics. This model is commonly observed in controlled-release systems such as transdermal patches, osmotic systems, and matrix tablets designed for constant drug delivery.

The main advantage of zero order kinetics is that it provides a uniform drug release, minimizing fluctuations in drug concentration and improving therapeutic efficacy.

3.4.2 First Order Kinetics

First order kinetics describes drug release where the rate of release is directly proportional to the amount of drug remaining in the dosage form. As the concentration decreases, the release rate also decreases.

$$\log Qt = \log Q0 - (k \cdot t / 2.303)$$

where *Qt* is the amount of drug remaining at time *t*, *Q0* is the initial drug amount, and *k* is the first order rate constant.

A plot of log percentage drug remaining versus time gives a straight line. This model is commonly followed by conventional dosage forms such as immediate-release tablets and capsules.

First order kinetics indicates that drug release is concentration-dependent, leading to a rapid initial release followed by a slower release phase.

3.4.3 Higuchi's Model

Higuchi's model describes drug release from a homogeneous matrix system as a diffusion process based on Fick's law. It is one of the most widely used models for matrix-based drug delivery systems.

$$Q = kH \sqrt{t}$$

where *Q* is the amount of drug released at time *t* and *kH* is the Higuchi dissolution constant.

A plot of cumulative percentage drug release versus square root of time yields a straight line if the release follows Higuchi kinetics.

This model assumes that:

- The initial drug concentration is much higher than its solubility
- Drug diffusion occurs in one dimension
- The matrix swelling and dissolution are negligible

Higuchi's model is mainly applicable to porous matrix systems where drug release is controlled by diffusion through the matrix.

3.4.4 Korsmeyer–Peppas Model (Peppas Equation)

The Korsmeyer–Peppas model is a semi-empirical equation used to analyse drug release from polymeric systems when the mechanism is not well understood or when multiple release phenomena are involved.

$$Mt / M\infty = k \cdot t^n$$

where $Mt/M\infty$ is the fraction of drug released at time t, k is the release rate constant, and n is the release exponent that indicates the mechanism of drug release.

The value of n helps to characterize the release mechanism:

- $n = 0.5$ indicates Fickian diffusion
- $0.5 < n < 1$ indicates non-Fickian (anomalous) transport
- $n = 1$ indicates zero order (case II transport)
- $n > 1$ indicates super case II transport

A plot of log (fraction drug released) versus log time gives a straight line.

This model is widely used for polymeric drug delivery systems such as hydrogels, matrix tablets, and nanoparticles, where both diffusion and polymer relaxation may influence drug release.

4. STABILITY STUDIES

Stability studies are an integral part of pharmaceutical product development, conducted to evaluate the ability of a drug substance or drug product to maintain its identity, strength, quality, purity, and performance characteristics within specified limits throughout its shelf life. These studies provide critical information regarding the degradation behavior of the drug and help in establishing appropriate storage conditions, packaging systems, and expiry date.

Stability testing is performed in accordance with guidelines established by the International Council for Harmonisation, which harmonize global requirements for drug stability evaluation and ensure consistency in regulatory submissions.

4.1 Long-Term Stability Studies

Long-term stability studies are carried out under recommended storage conditions over an extended period to determine the real-time stability of the drug product.

Typical storage condition:

- 25°C ± 2°C / 60% RH ± 5% RH

For climatic conditions like India (Zone IVb), conditions may be:

- 30°C ± 2°C / 75% RH ± 5% RH

These studies provide actual shelf-life data and confirm the stability of the product under normal storage conditions.

4.2 Accelerated Stability Studies

Accelerated stability studies are performed under elevated stress conditions to predict long-term stability in a shorter duration. These conditions accelerate chemical degradation and physical changes.

Typical storage condition:

- 40°C ± 2°C / 75% RH ± 5% RH

These studies help in identifying degradation kinetics, formulation stability, and the effect of excipients on drug stability.

4.3 Intermediate Stability Studies

Intermediate stability studies are conducted when significant changes are observed during accelerated studies. These studies provide additional data to better understand the stability profile.

Typical storage condition:

- 30°C ± 2°C / 65% RH ± 5% RH

4.4 STORAGE CONDITIONS

- The selected formulations were subjected to a rigorous three-month stability study in accordance with the guidelines established by the International Council for Harmonisation. The formulations were carefully packed in wide-mouth glass bottles, tightly sealed to prevent contamination and moisture ingress, and further protected with aluminium foil to minimize the influence of external environmental factors such as light and humidity.
- Stability testing was carried out under two different storage conditions to simulate real-time and accelerated environments. The formulations were stored at 25°C ± 2°C with 60% ± 5% relative humidity, representing normal storage conditions, and at 40 °C ± 2°C with 75% ± 5% relative humidity, representing accelerated conditions.
- Throughout the study period, samples were periodically evaluated to monitor any changes in their physical and chemical characteristics. This systematic approach enabled a comprehensive assessment of the stability profile of the formulations, providing valuable insights into their shelf life, quality, and performance under varying environmental conditions.

5 RESULTS AND DISCUSSION

5.1 Preformulation study

Authentication of Oxcarbazepine

5.1.1 Organoleptic properties:

Sr.No.	Parameter	Reported	Observed
1.	Appearance	Crystalline	Crystalline
2.	Color	Whitish	Whitish
3.	Odor	Odorless	Odorless

5.1.2 Melting point of Oxcarbazepine

The MP was established using the capillary method & was found to be between 173- 175 °C, indicating that the powder sample of Oxcarbazepine is in its monograph-required pure state. It was noticed that the Melting point was within range:

Sr. No.	Sample	Reported	Observed
1.	Oxcarbazepine	215-216 °C	216°C

5.1.3 Lambda Max Determination of Oxcarbazepine

The lambda max of Oxcarbazepine was determined using a UV-Spectrophotometer and was found to be:

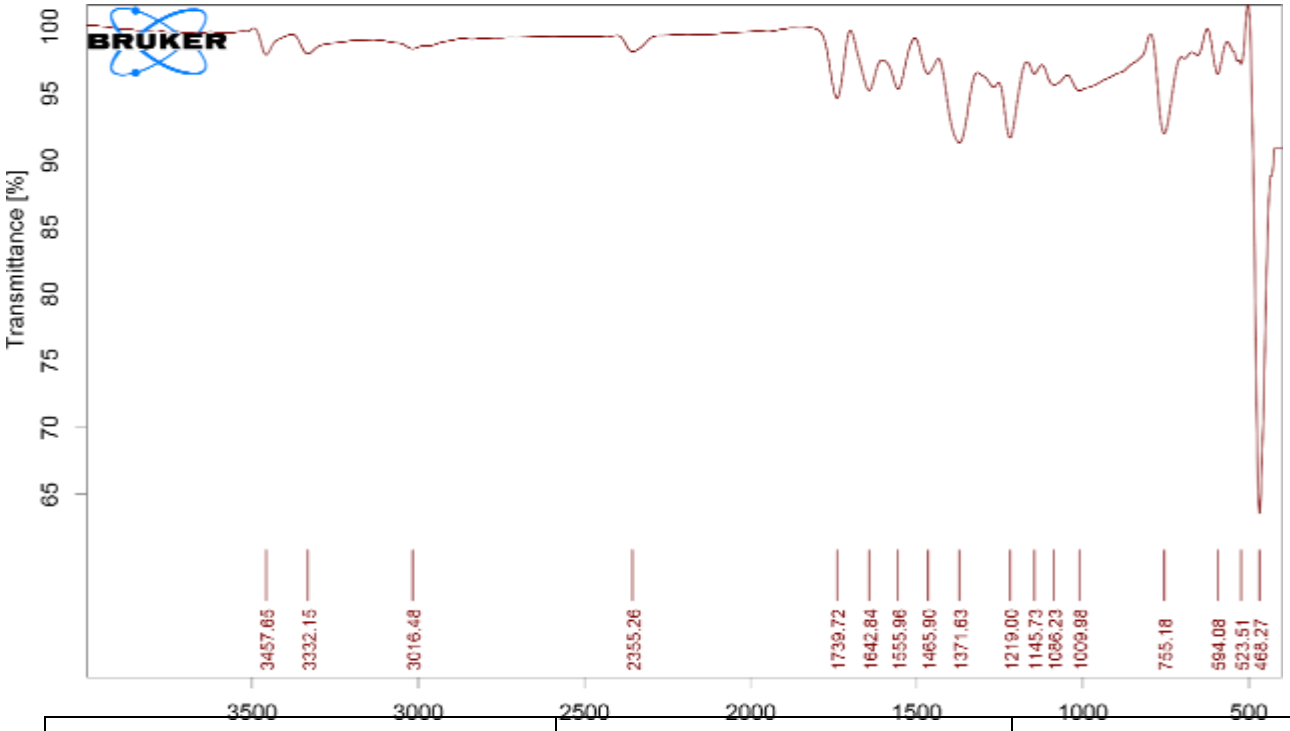
Lambda Max of Oxcarbazepine

Sr.No.	Solvent	λmax(nm)
1.	Phosphate Buffer 6.4	256

5.1.4 FT-IR Spectroscopy study

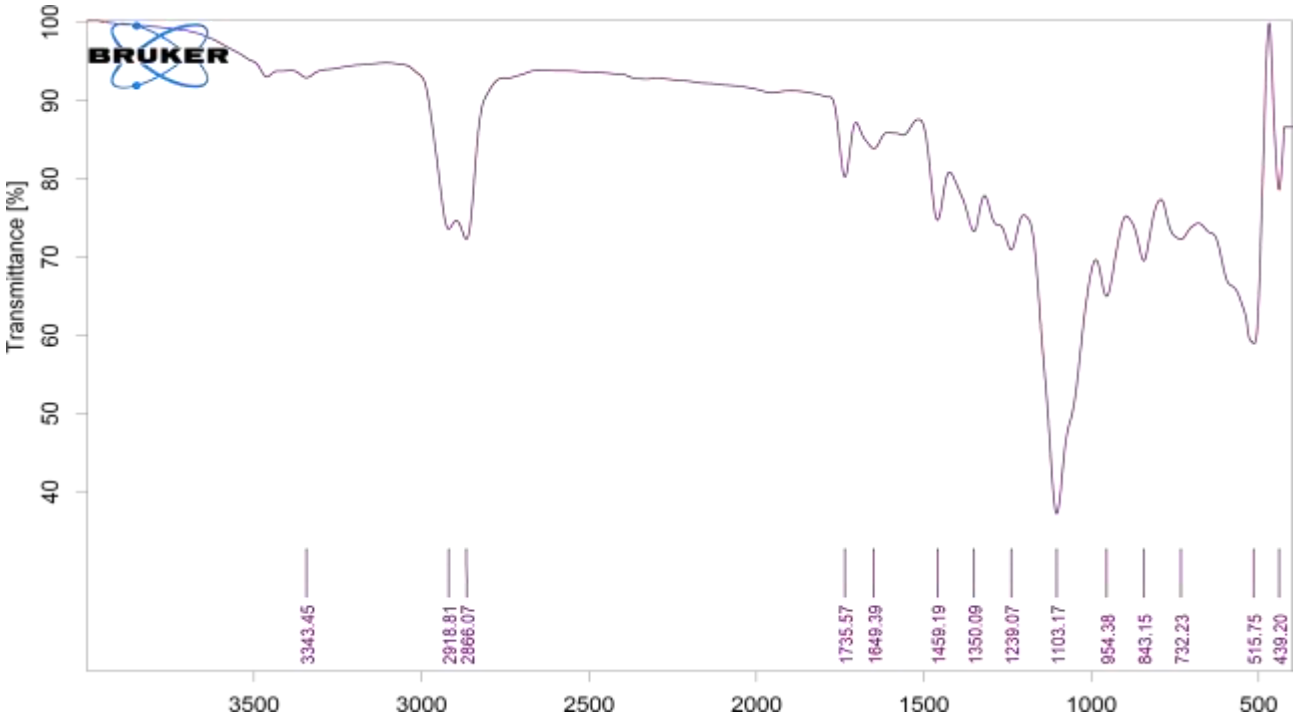
a. Oxcarbazepine

- Discussion



Peak Range (cm^{-1})	Observed Peak (cm^{-1})	Assignment
3500-3000	3457.65	NH_2 group of amides
1725-1705	1739.72	C=O ketonic group
1680-1630	1642.84	C=O of an amide group
1800-1600	1555.96	C=C in aromatic ring
1500-1400	1465.90	NH bending
1150-1050	1145.73	C-O stretching
3000-2850	3016.48	C-H stretching

b. Compatibility study

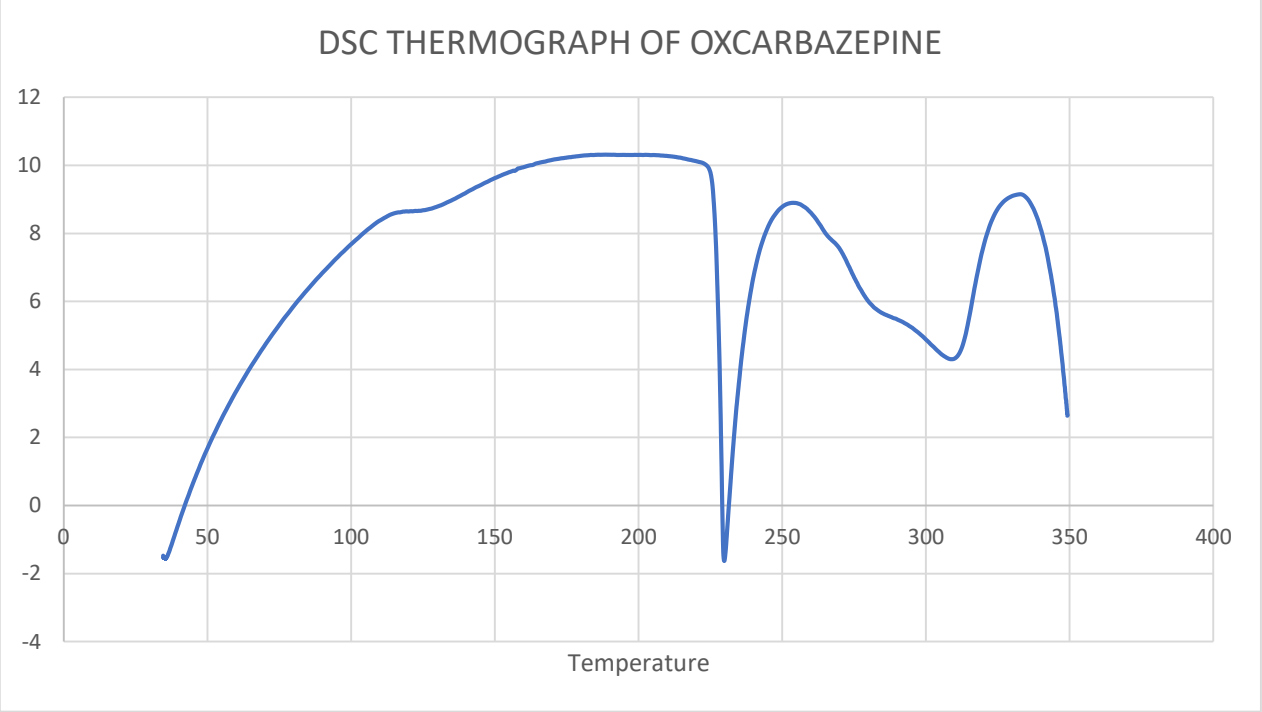


- Discussion

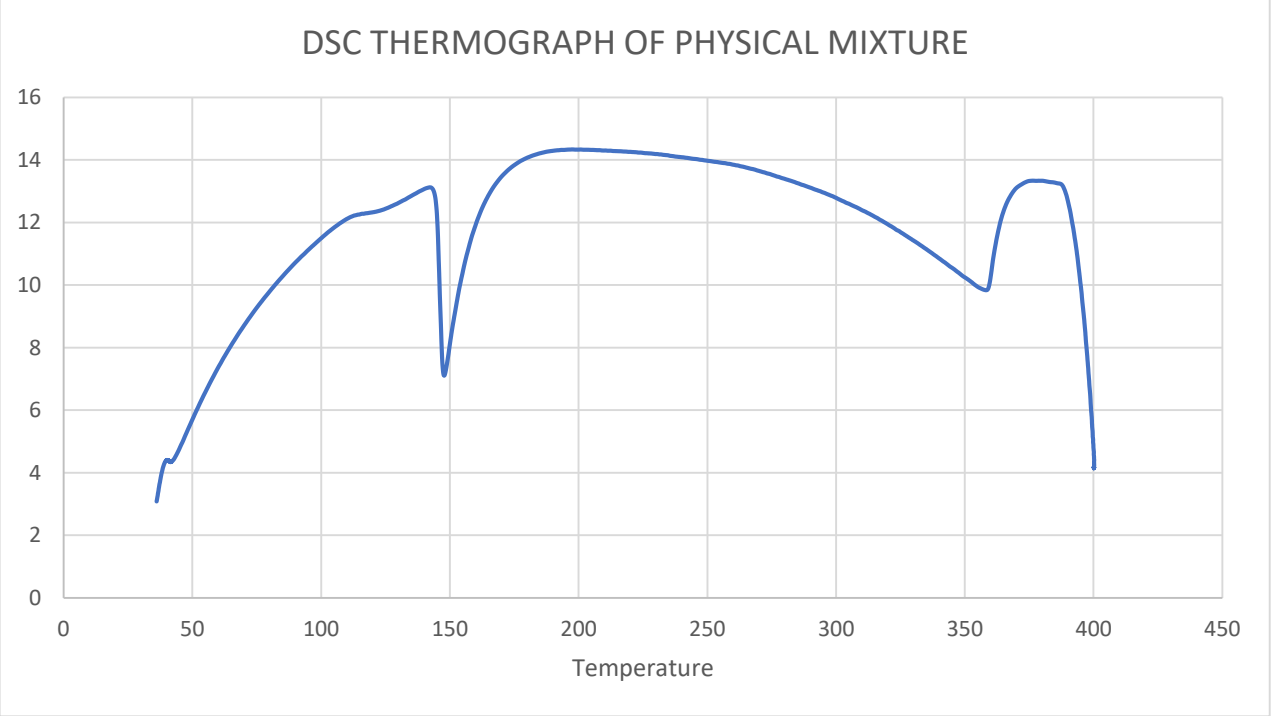
Peak Range (cm^{-1})	Observed Peak (cm^{-1})	Assignment
3500-3000	3343.45	NH_2 group of amides
3000-2850	2918.21	C-H stretching
2800-3000	2866.07	C-H Stretching (Methylene, Methyl)
1800-1600	1735.57	C=C in aromatic ring
1680-1630	1649.39	C=O of an amide group
1500-1400	1459.19	NH bending
1450-1350	1350.09	C-H Bending (Alkane, Aromatic)
1245	1239.07	P=O Stretching (Phosphomoyl Group)
1150-1050	1103.17	C-O stretching
800-600	843.15	OH bending (alcohols)

5.1.5 Differential Scanning Calorimetry Study

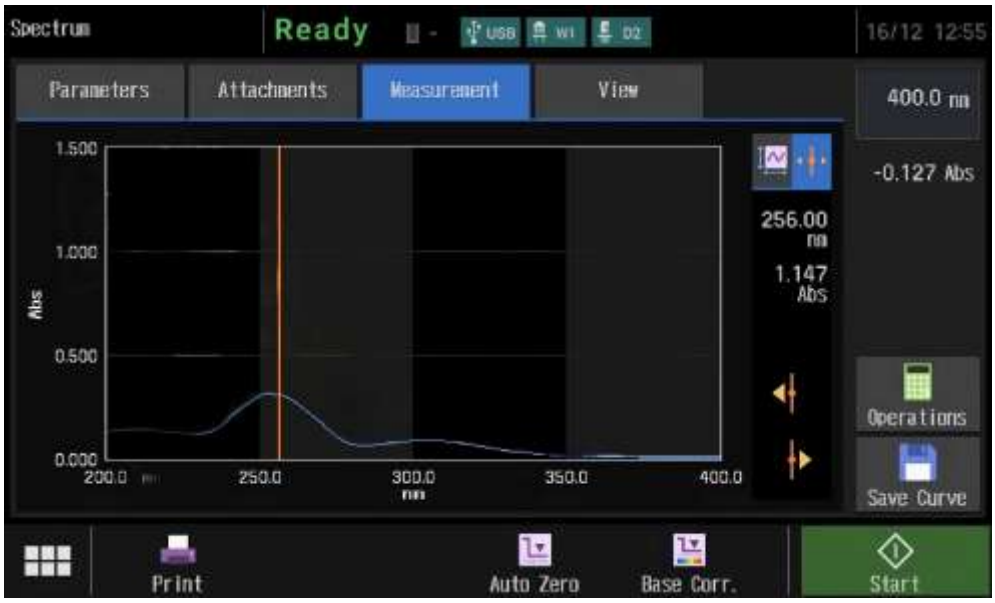
- Oxcarbazepine



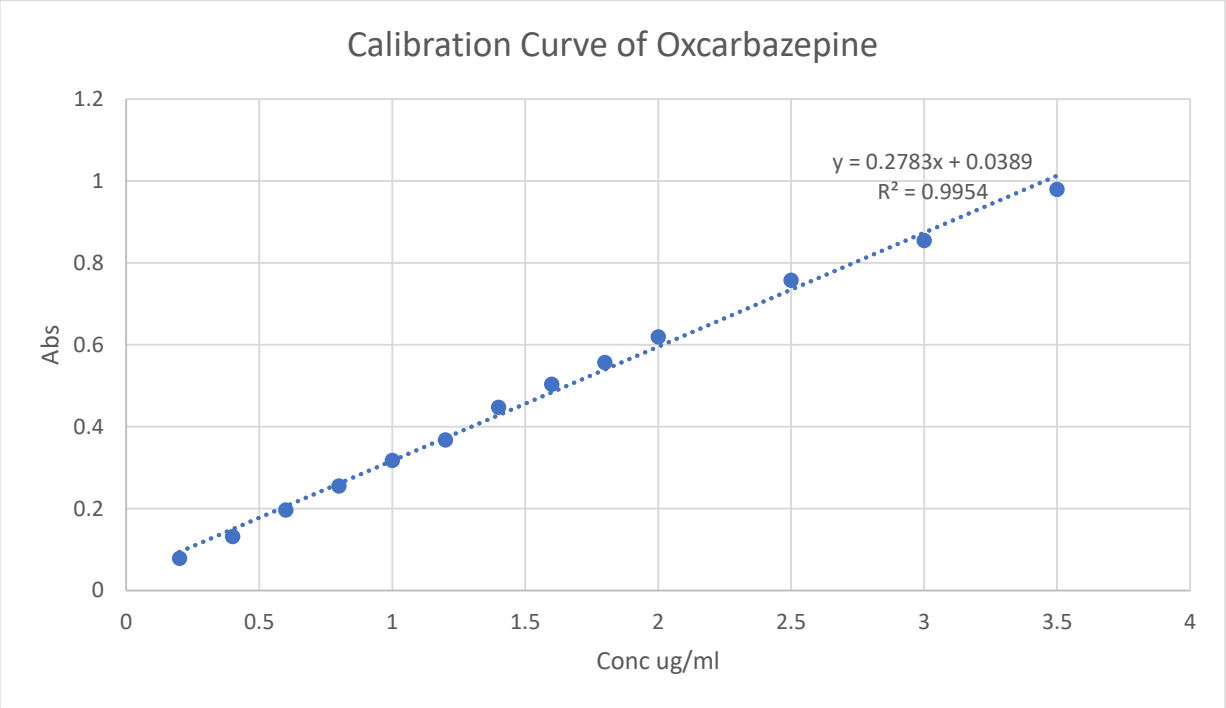
5.1.6 Compatibility study



5.1.7 CALIBRATION CURVE OF OXCARBAZEPINE



Conc.(µg/ml)	Absorbance
0.2	0.079±0.001
0.4	0.132±0.002
0.6	0.197±0.001
0.8	0.256±0.001
1	0.318±0.002
1.2	0.368±0.003
1.4	0.448±0.001
1.6	0.504±0.005
1.8	0.557±0.001
2	0.62±0.002
2.5	0.758±0.004
3	0.855±0.011
3.5	0.98±0.012



5.1.8 Evaluation of Pre-Formulation Parameters

Formulation	Bulk Density (Gm/Cc)	Tapped Density (Gm/Cc)	Carr's Index (%)	Hausner's Ratio	Angle Of Repose (°)
F1	0.372 ± 0.0011	0.408 ± 0.0024	7.45 ± 0.60	1.17 ± 0.0065	29.5 ± 0.40
F2	0.381 ± 0.0005	0.415 ± 0.0025	7.68 ± 0.50	1.05 ± 0.0060	25.5 ± 0.58
F3	0.386 ± 0.0014	0.420 ± 0.0005	7.30 ± 0.70	1.06 ± 0.0085	28.6 ± 0.30
F4	0.374 ± 0.0020	0.425 ± 0.0035	13.50 ± 0.75	1.08 ± 0.0050	27.6 ± 0.50
F5	0.358 ± 0.0016	0.458 ± 0.0028	17.10 ± 0.80	1.22 ± 0.0100	31.2 ± 0.12
F6	0.382 ± 0.0040	0.482 ± 0.0060	18.10 ± 0.110	1.25 ± 0.0020	28.0 ± 0.40
F7	0.384 ± 0.0080	0.435 ± 0.0120	10.50 ± 0.030	1.12 ± 0.0025	27.5 ± 0.40

Discussion

Bulk density and tapped density values for all batches are within a narrow range, suggesting uniform particle size distribution and good packing ability. Slight variations in tapped density indicate differences in compressibility among formulations. Carr's Compressibility Index (CI) values show that formulations F1–F3 (≈7–8%) exhibit excellent flow properties, while F4 and F7 (≈10–13%) indicate good flow. However, F5 and F6 (≈17–18%) suggest fair flow, indicating comparatively higher interparticle friction. Hausner's ratio further supports these findings. Values close to 1.0 (F2, F3) indicate excellent flow, whereas higher values in F5 and F6 (~1.22–1.25) suggest reduced flowability due to increased cohesiveness. Angle of repose values for all formulations (25°–31°) fall within the good to excellent flow range, with F2 showing the best flow (25.5°) and F5 showing slightly poorer flow (31.2°).

0.2 Post formulation result and discussion

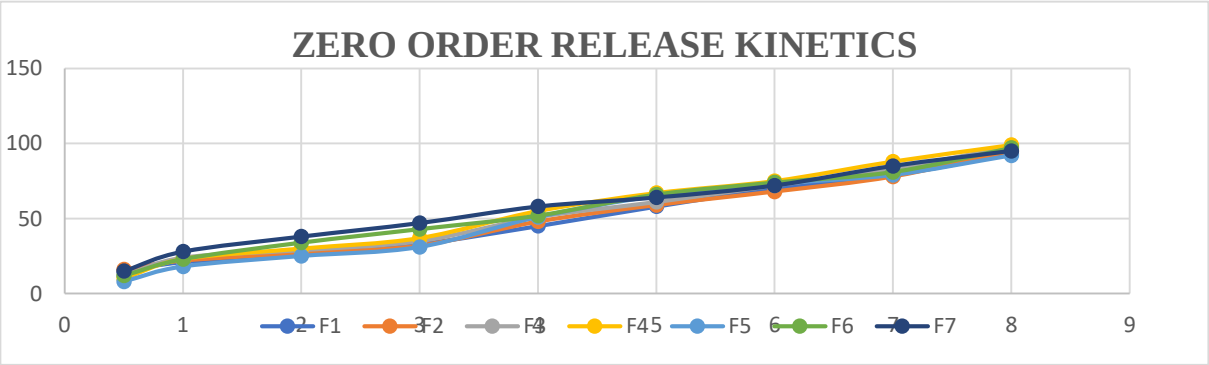
5.2.1 Post-Compression Evaluation Parameters

Formulation	Diameter (mm)	Thickness (mm)	Weight variation (mg)	Hardness (kg/cm²)	Friability (%)	Drug content (%)
F1	7.82 ± 0.012	3.85 ± 0.07	250.5 ± 0.20	7.8 ± 0.06	0.63 ± 0.008	98.5 ± 0.040
F2	7.80 ± 0.003	4.15 ± 0.02	253.5 ± 0.60	7.6 ± 0.03	0.55 ± 0.006	100.1 ± 0.030
F3	7.85 ± 0.007	4.25 ± 0.05	251.0 ± 0.50	8.2 ± 0.07	0.60 ± 0.030	98.4 ± 0.080
F4	7.83 ± 0.020	3.85 ± 0.08	249.0 ± 0.10	6.7 ± 0.04	0.75 ± 0.015	99.4 ± 0.070
F5	8.00 ± 0.014	4.00 ± 0.04	250.6 ± 0.30	7.0 ± 0.08	0.66 ± 0.070	99.2 ± 0.050
F6	7.95 ± 0.010	3.92 ± 0.06	248.8 ± 0.45	7.4 ± 0.04	0.72 ± 0.050	98.8 ± 0.060
F7	7.97 ± 0.015	4.18 ± 0.02	252.2 ± 0.50	6.6 ± 0.03	0.46 ± 0.009	101.2 ± 0.060

5.2.2 INVITRO DRUG RELEASE KINETICS

TIME	F1	F2	F3	F4	F5	F6	F7
0.5	15	16	12	10	8	12	15
1	21	22	24	23	18	23	28
2	26	27	29	30	25	34	38
3	33	32	35	37	31	43	47
4	45	48	51	55	51	52	58
5	58	59	61	67	65	66	64
6	70	68	72	75	73	74	72
7	79	78	83	88	79	81	85
8	93	95	98	99	92	97	95

Mathematical modelling of drug release profile

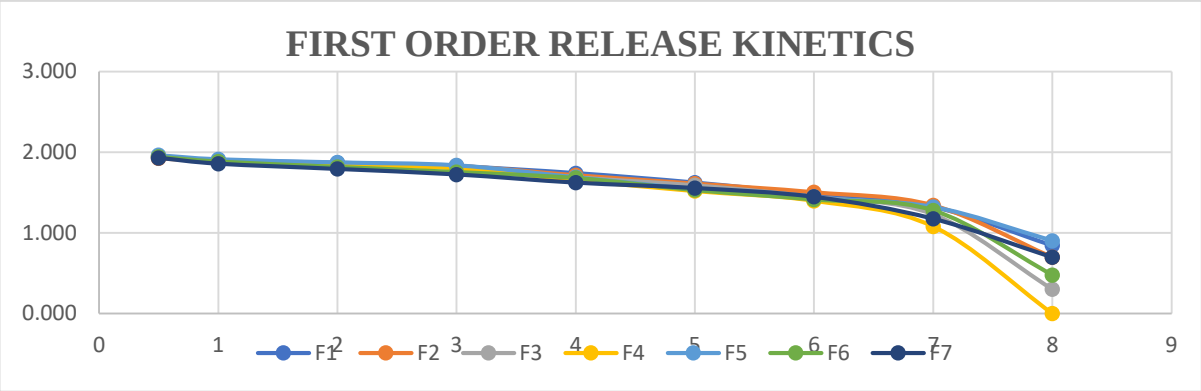


5.2.3 Zero order kinetics

- **Discussion**

➢ Mechanism of Release: Zero-order kinetics refers to a process where the drug release rate is constant over time, independent of the concentration of the drug remaining in the system. This is visually represented by the linear (straight-line) relationship seen in all seven formulations on the graph.

➢ Time and Percentage Release: The data is tracked over an 8-hour period. By the end of the 8th hour, all formulations (F1–F7) achieved a high cumulative drug release, ranging approximately between 90% and 100%.



➢ Comparison of Formulations: While all formulations follow a similar linear trend, there are slight variations:

1. Formulation F7 (dark blue line) shows a slightly higher release rate in the earlier stages compared to the others.
2. Formulation F5 (purple line) consistently shows the lowest percentage of release throughout the 8-hour duration.

➢ Significance: This type of release profile is ideal for controlled-release dosage forms, as it ensures a steady amount of the drug is maintained in the bloodstream over a prolonged period, rather than a rapid "burst" release .

5.2.4 First order kinetics

TIME	F1	F2	F3	F4	F5	F6	F7
0.5	1.929	1.924	1.944	1.954	1.964	1.944	1.929
1	1.898	1.892	1.881	1.886	1.914	1.886	1.857
2	1.869	1.863	1.851	1.845	1.875	1.820	1.792
3	1.826	1.833	1.813	1.799	1.839	1.756	1.724
4	1.740	1.716	1.690	1.653	1.690	1.681	1.623
5	1.623	1.613	1.591	1.519	1.544	1.531	1.556
6	1.477	1.505	1.447	1.398	1.431	1.415	1.447
7	1.322	1.342	1.230	1.079	1.322	1.279	1.176
8	0.845	0.699	0.301	0.000	0.903	0.477	0.699

Discussion

➢ Mechanism of Release: In first-order kinetics, the drug release rate is concentration-dependent. This means the amount of drug released per unit of time is proportional to the amount of drug remaining in the formulation. On this graph, this is shown as a downward trend representing the log of drug remaining over time.

➢ Time and Depletion: The study spans 8 hours. Most formulations show a relatively steady decline for the first 6 hours, followed by a sharp decrease in the drug remaining between hours 6 and 8.

➢ Comparison of Formulations:

○ Formulation F4 (light blue line) shows the most significant drop, reaching the zero point by the 8th hour, indicating near-complete depletion or release.

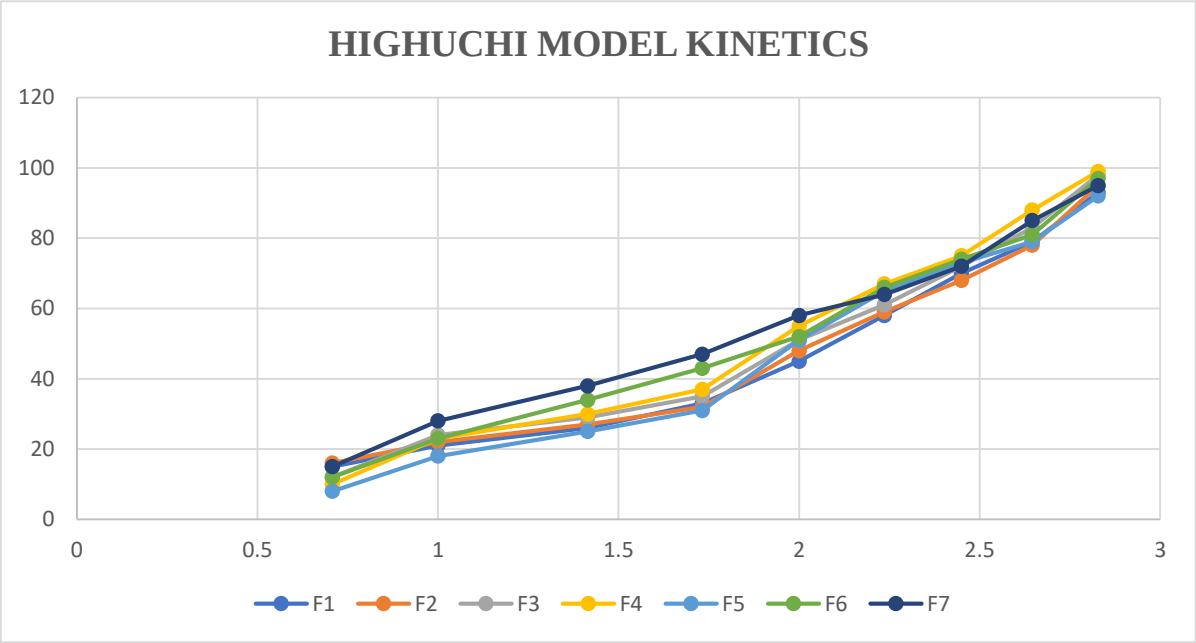
○ Formulation F5 (purple line) consistently stays higher than the other formulations, meaning it retains more drug for a longer period compared to the others.

○ Formulations F3 and F7 also show a very steep decline in the final two hours of the study.

➢ Significance: Unlike the Zero Order graph (Source 1), which showed a constant release rate, this graph shows that the release slows down as the drug concentration decreases. This model is commonly used to describe the release of water-soluble drugs from porous matrices.

5.2.5 Higuchi kinetic model

TIME	F1	F2	F3	F4	F5	F6	F7
0.707107	15	16	12	10	8	12	15
1	21	22	24	23	18	23	28
1.414214	26	27	29	30	25	34	38
1.732051	33	32	35	37	31	43	47
2	45	48	51	55	51	52	58
2.236068	58	59	61	67	65	66	64
2.44949	70	68	72	75	73	74	72
2.645751	79	78	83	88	79	81	85
2.828427	93	95	98	99	92	97	95



Discussion

➢ Model Significance: The Higuchi model is a mathematical formula used to describe drug release from a matrix system. In this model, the cumulative amount of drug released is plotted against the square root of time (represented on the x-axis).

➢ Release Mechanism: The lines for all formulations (F1–F7) are relatively linear. This linearity indicates that the drug release from these formulations is diffusion-controlled, which is the core principle of the Higuchi model.

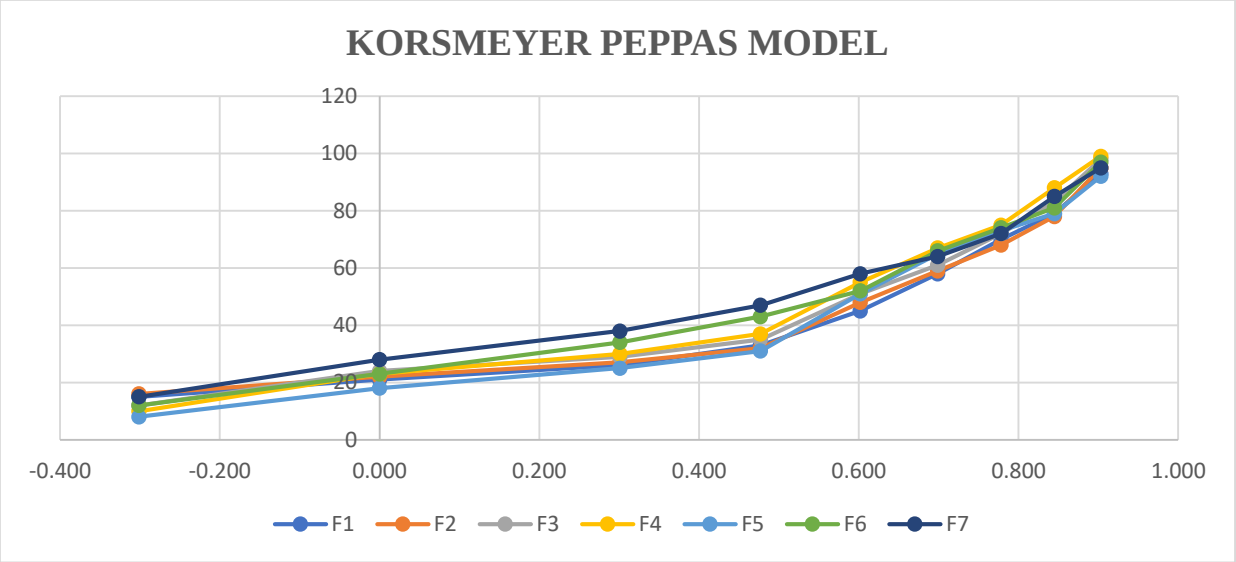
➢ Comparative Analysis:

1. Highest Release: Formulation F7 (dark blue line) consistently shows the highest cumulative release across most intervals, reaching nearly 100% at the final data point.
2. Lowest Release: Formulation F5 (magenta line) exhibits the slowest release rate compared to the others.
3. General Trend: While there are variations in the slopes (which represent the release rate constant, or K_H), all seven formulations follow a similar upward trajectory, suggesting that the basic mechanism of release is the same for all of them, regardless of the specific formulation changes.

5.2.6 Korsmeyer Peppas kinetic model

TIME	F1	F2	F3	F4	F5	F6	F7
-0.301	15	16	12	10	8	12	15
0.000	21	22	24	23	18	23	28
0.301	26	27	29	30	25	34	38
0.477	33	32	35	37	31	43	47
0.602	45	48	51	55	51	52	58

0.699	58	59	61	67	65	66	64
0.778	70	68	72	75	73	74	72
0.845	79	78	83	88	79	81	85
0.903	93	95	98	99	92	97	95



Discussion

- Comparison of Formulations: The graph evaluates seven distinct formulations, identified as F1 through F7.
- Release Trends: All seven formulations exhibit a consistent positive slope, meaning that the cumulative percentage of drug released increases over the recorded time intervals.
- Initial vs. Final Release:

1. At the starting phase of the study (indicated near the -0.300 mark on the x-axis), F7 shows a slightly higher initial release, while F5 appears to have the lowest.
2. By the end of the observed period (0.900 on the x-axis), all formulations converge, successfully achieving nearly 100% cumulative drug release.

- Linear Relationship: The data is plotted in a way that shows a relatively linear relationship for each formulation, which is typical for this model when using logarithmic scales to determine release kinetics.

Significance of the Model

- The Slope (n): The slope of these lines represents the release exponent (n), which characterizes the mechanism of drug transport (e.g., whether the drug is moving via simple diffusion, polymer swelling, or a combination of both).
- The Intercept (K): This relates to the release rate constant, which incorporates the structural and geometric characteristics of the delivery system.
-

- **Release exponent values and the release rate constant values of various formulations**

Batch	Zero order (R^2)	First order (R^2)	Higuchi's plots (R^2)	Korsmeyer-Peppas plots (R^2)	Korsmeyer-Peppas plots (N)	Best fit Model	Drug release mechanism
F_1	0.9285	0.981	0.9122	0.916	0.594	First order	Non-Fickian
F_2	0.966	0.971	0.8950	0.912	0.591	First order	Non-Fickian
F_3	0.917	0.984	0.9205	0.896	0.6081	First order	Non-Fickian
F_4	0.942	0.975	0.8931	0.895	0.577	First order	Non-Fickian
F_5	0.945	0.989	0.9570	0.911	0.491	First order	Non-Fickian
F_6	0.901	0.955	0.9032	0.926	0.7925	First order	Non-Fickian
F_7	0.895	0.986	0.9248	0.937	0.4845	First order	Non-Fickian

6 STABILITY STUDIES OF OXCARBAZEPINE SUSTAINED RELEASE TABLET

A. Results of stability studies for formulation F4 stored at 25ºC/60% RH

Storage period	Hardness (kg/cm²)	% Friability	Drug content (%)	% CDR
initial	8.2 ± 0.08	0.60 ± 0.10	99.5 ± 0.30	98.2 ± 0.28
after 1 month	7.9 ± 0.12	0.65 ± 0.25	98.5 ± 0.10	97.0 ± 0.35
after 2 month	7.8 ± 0.40	0.66 ± 0.18	98.0 ± 0.20	98.6 ± 0.38
after 3 month	7.6 ± 0.10	0.62 ± 0.10	97.5 ± 0.25	97.9 ± 0.40

A. Results of stability studies for formulation F4 stored at 40ºC/60% RH

Storage period	Hardness (kg/cm²)	% Friability	Drug content (%)	% CDR
initial	8.0 ± 0.06	0.58 ± 0.20	99.2 ± 0.30	98.8 ± 0.35
after 1 month	7.9 ± 0.05	0.62 ± 0.10	98.8 ± 0.20	98.1 ± 0.30
after 2 month	7.5 ± 0.07	0.64 ± 0.25	97.2 ± 0.28	97.8 ± 0.35
after 3 month	7.4 ± 0.06	0.66 ± 0.10	97.6 ± 0.35	96.9 ± 0.30

Discussion

The stability studies for formulation **F4** evaluate its physical and chemical integrity over a three-month period under two distinct conditions: 25°C/60% RH and 40°C/60% RH.

- From a physical perspective, the tablets showed minor changes. Hardness decreased slightly from 8.2 to 7.6 kg/cm^2 at room temperature and from 8.0 to 7.4 kg/cm^2 under accelerated conditions.
- However, % Friability remained consistently low, ranging between 0.58% and 0.66%, indicating that the tablets maintained their structural durability.
- Chemical stability was also robust. The drug content remained high, starting at 99.5% and only decreasing to 97.5% at 25°C. Even under the higher stress of 40°C, the drug content was maintained at 97.6% by the third month.
- Furthermore, the % Cumulative Drug Release (CDR) stayed above 97% across all tests, ensuring the formulation's performance remained consistent. Overall, the data suggests that formulation F4 is stable under both standard and accelerated storage conditions.

7 FUTURE ASPECTS

The future of sustained release drug delivery systems is centered on the continued evolution of matrix technology, which the sources identify as a breakthrough in pharmaceutical science. As the costs of developing new chemical entities become increasingly prohibitive, the pharmaceutical industry is expected to focus more heavily on optimizing existing drugs like oxcarbazepine through these advanced delivery systems. One significant area of growth involves the refinement of methodologies such as hot-melt extrusion and spray drying. These techniques are projected to play an essential role in enhancing the solubility of poorly water-soluble drugs while maintaining a stable, sustained release profile. Future research will likely target the achievement of a pure zero-order release profile, which remains a difficult challenge for current standard matrix designs. To achieve this, scientists may explore more complex hydrophilic matrices and polymeric retardants that can provide more precise control over the interplay of dissolution, diffusion, and erosion. There is also a significant opportunity to address current limitations, such as the difficulty of delivering high molecular weight compounds through insoluble matrix barriers. Information not explicitly in the sources: looking ahead, the integration of 3d printing for personalized medicine could allow for the creation of matrix tablets with internal geometries tailored to a specific patient's gastrointestinal transit time. Additionally, the development of stimuli-responsive polymers—which could trigger drug release based on specific ph changes or enzymatic presence—represents a promising frontier for increasing therapeutic efficacy. Furthermore, future developments will likely emphasize improving in-vitro and in-vivo correlations (ivivc) to better predict how these complex matrix systems will perform in the human body. This progress is vital to reduce the risk of dose dumping or treatment failure caused by physiological factors like food intake and gastric motility. Ultimate success in the field will depend on creating more predictable and reproducible systems that optimize therapeutic effects with lower and less frequent doses.

8 CONCLUSION

This research successfully demonstrates the development and evaluation of sustained release matrix tablets for oxcarbazepine, utilizing polymeric matrices such as carbopol and chitosan. Through rigorous pre-formulation studies, including ft-ir and dsc, it was confirmed that the drug remained in its pure state and was chemically compatible with the selected excipients. The physical properties of the formulations, including bulk density, tapped density, and angle of repose, indicated that the majority of the batches possessed good to excellent flow characteristics. Such results reflect uniform particle size distribution and good packing ability, which are essential for

consistent tablet manufacturing. Post-compression evaluations revealed that the tablets (f1–f7) maintained high drug content, ranging from 98.4% to 101.2%, and met standard requirements for hardness and friability. This ensures the tablets have the mechanical strength to withstand handling and transportation without compromising drug release. The in-vitro dissolution studies were particularly revealing, showing that all seven formulations achieved near-complete drug release—between 90% and 100%—over an 8-hour period. Mathematical modeling indicated that most formulations followed first-order kinetics and a non-fickian (anomalous) transport mechanism. This indicates that drug release was governed by a complex combination of diffusion and polymer relaxation. Notably, formulation f4 emerged as a highly stable candidate, maintaining its physical integrity and chemical potency even under accelerated stability conditions (40 degrees celsius and 60% relative humidity) for three months. By reducing dosing frequency and minimizing "see-saw" fluctuations in plasma levels, these sustained release systems offer a significant improvement in patient compliance and therapeutic outcomes compared to conventional immediate release forms. Overall, the study confirms that matrix tablets are a cost-effective, commercially feasible, and efficient method for delivering drugs with short biological half-lives.

9 REFERENCES

1. Abhishek OK, Verma S. A review - Sustained Release Drug Delivery Technology. World J Pharm Pharm Sci. 7(5): 250-260.

2. Loyd A, Nicholos G, Popvich HC. Solid Oral Modified-Release Dosage Forms and Drug Delivery System. Int J Pharm. 2009; 257-270.

3. Chien YW. Controlled and modulated-release drug delivery systems. In: Swarbrick J, Balyan JC. Encyclopedia of Pharmaceutical Technology. New York: Informa Health Care; 1990: 281-313.

4. Patnaik AN, Nagarjuna T, Thulasiramaraju TV. Sustained release drug delivery system: a modern formulation approach. Int J Res Pharm Nano Sci. 2013; 2(5): 586-601.

5. Bhargava A, Rathore RPS, Tanwar YS, et al. Oral sustained release dosage form: an opportunity to prolong the release of drug. Int J Adv Res Pharm Bio Sci. 2013; 3(1): 7-14.

6. Moghal M, Islam M, Ahmed I, et al. Development and optimization of sustain release matrix tablet of Ambroxol Hcl using central composite design. Indian J Pharm Educ Res. 2010; 44(1): 28-35.

7. Poddar RK, Rakha P, Singh SK, Mishra DN. Bioadhesive Polymers as a Platform for Drug Delivery: Possibilities and Future Trends. Res J Pharm Dosage Forms Technol. 2010; 2(1): 1-6.

8. Corti G, Cirri M, Maestrelli F, et al. Sustained-release matrix tablets of Metformin hydrochloride in combination with triacetyl-bcyclodextrin. Eur J Pharm Biopharm. 2008; 68: 303–309.

9. Chauhan MJ, Patel SA. A Concise Review on Sustained Drug Delivery System and Its Opportunities. Am J Pharm Tech Res. 2012; 2(2): 227-238.

10. Haresh M, Thimmasetty J, Ratan GN. Formulation Development and In-vitro Evaluation of Sustained Release Matrix Tablets of Risperidone. Inventi Impact Pharma Tech. 2013; 1: 28-34.

11. Hadi MA, Lokeswara VB, Pal N, Rao SA. Formulation and evaluation of sustained release matrix tablets of montelukast sodium. Int J Pharm. 2012; 2(3): 574-582.

12. Brahmankar DM, Jaiswal SB. Biopharmaceutics and Pharmacokinetics: Pharmacokinetics. 2nd ed. Delhi: Vallabh Prakashan; 2009: 399-401.

13. Pundir S, Badola A, Sharma D. Sustained release matrix technology and recent advance in matrix drug delivery system: a review. Int J Drug Res Tech. 2017; 3(1): 8.

14. Lachman L, Lieberman H, Kanig J. The Theory and Practice of Industrial Pharmacy. 3rd ed. Bombay: Verghese Publishing House; 1990.

15. Rao NG, Raj K, Nayak BS. Review on Matrix Tablet as Sustained Release. Int J Pharm Res Allied Sci. 2013; 2(3): 1-17.

16. Dikshit MK, Sharma V, Singh V. A Review on Sustained Release Matrix Tablets. Int J Health Adv Clin Res. 2023; 1(4): 76-79.

17. Bhagat VC, Awate PB, Kardile DP, et al. A Review on Sustained Release Drug Delivery and Sustained Release Matrix Tablets. J Coastal Life Med. 2023; 11: 1174-1190.

18. Kumar Sampath KP, Bhowmik D, Srivastava S. Sustained release drug delivery system potentials. Int J Pharm. 2010; 2: 751–754.

19. Wadher G, Satish B, Tukaram MK. Recent trend on Sustained drug delivery system. Int J Chem Pharm Sci. 2013; 4: 1–7.

20. Aulton ME. Aulton's Pharmaceutics - The Design and Manufacture of Medicine. 3rd ed. New York: Churchill Livingstone; 2007.

21. Kumar AR, Aeila ASS. Sustained Release Matrix Type Drug Delivery System: An Overview. World J Pharm Pharm Sci. 2019; 9(1): 470-480.

22. Kumar C, Sharma V, Ravindra N, Singh V. Sustained Release Matrix Tablets: A Comprehensive Review. Int J Health Adv Clin Res. 2024; 2(4): 24-28.

23. Mohaniya P, Modi D, Pawar R. A Review on Sustained Release Matrix Tablet. Int J Pharm Sci Med. 2024; 9(2): 52-58.

24. Karna S, Chaturvedi S, Agrawal V, Alim M. Formulation Approaches for Sustained Release Dosage Forms: A Review. Asian J Pharm Clin Res. 2015; 8(5): 46-53.

25. Pareek SP, Kumawat S, Sharma V, et al. Review on Sustained Release Technology. Int J Pharm Bio Sci Arch. 2019; 7(6): 29-38.

26. Gupta MM, Brijesh R. A Review On: Sustained Release Technology. Int J Ther Appl. 2012; 8: 18-23.

27. Shah N, Oza C, Trivedi S, et al. Review on Sustained Release Matrix Tablets: An Approach to Prolong the Release of Drug. J Pharm Sci Biosci Res. 2015; 5(3): 325-321.

28. Ratnaparkhi MP, Gupta JP. Sustained Release Oral Drug Delivery System - An Overview. Int J Pharma Res Rev. 2013; 2(3): 11-21.

29. Agarwal P, Akhtar S. A Comprehensive Review on Sustained Release Matrix Tablets: A Promising Dosage Form. Universal J Pharm Res. 2018; 3(6): 49-54.

30. Zalte HD, Saudagar RB. Review on Sustained Release Matrix Tablet. Int J Pharm Bio Sci. 2013; 3(4): 17-29.

31. Phad AB, Mahale NB, Chaudhari SR, Salunke KS. Matrix Tablet: As a Sustained Release Drug Delivery System. World J Pharm Res. 2014; 3(5): 1377-1390.

32. Dusane AR, Gaikwad PD, Bankar VH, et al. A Review on Sustain release technology. Int J Res Ayurveda Pharm. 2011; 2(6): 1701-1708.

33. Modi SA, Gaikwad PD, Banker VH, et al. Sustained Release Drug Delivery System. Int J Pharma Res Dev. 2011; 2(12): 147-160.

34. Vyas SP, Khar RK. Controlled drug delivery concept and advances. 2nd ed. Delhi: Vallabh Prakashan; 2012: 1-53.

35. Robinson JR, Lee VL. Controlled Drug Delivery: Fundamentals and Applications. 2nd ed. New York: Informa healthcare USA; 2009: 373-421.

36. Patel H, Panchal DR, Patel U, et al. Matrix Type Drug Delivery System: A Review. J Pharm Sci Biosci Res. 2011; 1(3): 143-151.

37. Kumar S, Kant S, Prashar B. Sustained release drug delivery system: a review. Int J Institutional Pharm Life Sci. 2012; 2(3): 356-376.

38. Jain D, Shukla SB. Formulation and Evaluation of Sustained Release Matrix Tablets of Isoniazid: A Comparative Aspect Based on Polymer. Inventi Rapid: NDDS 2011; 2(1).

39. Medisetti VK, Avasarala H, Ramesh KVRNS, et al. Formulation and Evaluation of Sustained Release Hydrophilic Matrix Tablets of Diclofenac Sodium using Natural Almond Gum. Inventi Rapid NDDS. 2012; (4): 1-6.

40. Prasad A, Issac J, Verma AK. Development of Sustained Release Cefpodoxime Matrix Tablets. Inventi Impact: NDDS. 2010; 1(2).

41. Pagar HB, Shinde UP, Barhate SD, et al. Formulation and Evaluation of Indomethacin Sustained Release Matrix Tablets. Inventi Rapid: NDDS. 2011; (4).

42. Madgulkar AR, Bhalekar MR, Warghade NS, et al. Preparation and Evaluation of Sustained Release Matrix Tablet of Nateglinide: Effect of Variables. Inventi Rapid: NDDS. 2011; 2(1).

43. Shanmugam S, Banthalarajan, Ayyappan T, et al. Formulation and evaluation of Sustained release matrix tablet of zidovudine using different polymer. Res J Pharm Dosage Form Technol. 2011; 3(1): 17-23.

44. Dunn CJ, Peters D. Metformin: a review of its pharmacological properties and therapeutic use in non-insulin-dependent diabetes mellitus. Drugs. 1995; 49: 721-749.

45. Hoffman A. Pharmacodynamics aspects of sustained release preparations. Adv Drug Delivery Rev. 1998; 33: 185-199.

46. Munday DC, Cox PJ. Compressed xanthan and karaya gum matrices: Hydration, erosion and drug release mechanisms. Int J Pharm. 2000; 203: 179-192.

47. Ali Alyahawi, Abdulmajed Alsaifi. Quality control assessment of different brands of ciprofloxacin 500 mg tablets in Yemen. Universal J Pharm Res. 2018; 3(4): 31-36.

48. Abdulmajed Alsaifi, Ali Alyahawi. Quality assessment of different brands of paracetamol tablets in Yemeni market. Universal J Pharm Res. 2018; 3(4): 42-47.

49. Venkatraman S, Davar N, Chester A. An overview of controlled release systems. Donald L Wise, Marcel Dekker Inc.; 2000; 2: 431-465.

50. Sujja AJ, Munday DL, Cox PJ, et al. Relationship between swelling, erosion and drug release in hydrophilic natural gum mini matrix formulations. Eur J Pharm Sci. 1998; 6(3): 207-217.

51. Nweje-Anyalowu PC, Anyalogbu EAA, White AJ. Design and evaluation of chronotherapeutic pulsatile drug delivery system of Cilnidipine. Universal J Pharm Res. 2017; 2(5): 18-22.

52. Boniferoni MC, Rossi S, Ferrari F, et al. Viscoelastic properties of gels. Int J Pharm Sci. 1995; 117: 41-48.

53. Shah Murad Mastoi, Azmat Ali, Hina Aslam, et al. Comparison of antidyslipiemic potential of 80 milligrams of Fenofibrate with 8 grams of Nigella sativa seeds daily. Universal J Pharm Res. 2017; 2(6): 50-52.

54. Patel KK, Patel MS, Bhatt NM, et al. An overview: extended release matrix technology. Int J Pharm Chem Sci. 2012; 1(2): 828.

55. Jaimini M, Kothari A. Sustained release matrix type drug delivery system: Review. J Drug Delivery Ther. 2012; 2(6): 142-148.

56. Igwe J Chibueze, Emenike IV, Oduola AR. Formulation and evaluation of Finasteride sustained-release matrix tablets using different rate controlling polymers. Universal J Pharm Res. 2016; 1(2): 25-31.

57. Oyeniran Taiwo Opeyemi, Obanewa opeyemi Adegbenro. Development and characterization of direct compressed matrix mini tablets of naproxen sodium. Universal J Pharm Res. 2018; 3(5): 7-11.

58. Kumar N, Roy Mahasweta, Kumar B, et al. Formulation and evaluation of sustained released metformin hcl tablet using natural polymers. Int J Pharmacy Pharm Res. 2016; 6(2): 217-237.

59. Prajapati B, Patel R, Patel D, et al. Metformin hydrochloride sustained release tablet using different matrixing tablet. e-Journal of Science and Technology (e-JST). 2013; 4(8): 61-72.

60. Saddam C Shaikh, Dnyaneshwar Sanap, Dipak V Bhusari, et al. Ibuprofen gastro-retentive floating tablets. Universal J Pharm Res. 2018; 3(4): 20-25.

61. Lapidus H, Lordi NG. Studies on controlled release formulations. Journal of Pharmaceutical sciences. 1968; 57:1292-1301.

62. Thomas Wai-Yip Lee, Joseph R Robinson. Controlled-release drug delivery system. In: Remington: The Science and Practice of Pharmacy. 20th ed. Vol 1. Baltimore: Lippincott Williams and Wilkins; 2000: 904-905.

63. Jain N.K. Controlled and Novel Drug Delivery. New Delhi: CBS Publisher; 2002: 676-698.

64. Sumati R, JK L, Poddar S. Formulation and evaluation of controlled release aspirin tablets. Indian J. Pharm. Sci. 2001; 63(2):110-3.

65. Lund W. The Pharmaceutical Codex - The principle and practice of pharmaceutics. 12th ed. London: The Pharmaceutical Press; 1994: 208-10.

66. Xuan Ding, Adam WG Alani, Joseph R. Robinson. Extended-Release and Targeted Drug-Delivery Systems. In: Remington: The Science and Practice of Pharmacy. 20th ed. Vol 1. Baltimore: Lippincott Williams and Wilkins; 2000: 946-951.

67. Salsa T, Veiga F, Pina ME. Oral controlled release dosage form. I. Cellulose ether polymers in hydrophilic matrices. Drug Develop. Ind. Pharm. 1997; 23: 929-938.

68. Sung KC, Nixon PR, Skoug JW. Effect of formulation variables on drug and polymer release from HPMC-based matrix tablets. Int. J. Pharm. 1996; 142: 53-60.

69. Basak S, Reddy JB, Mani LK. Formulation and release behavior of sustained release ambroxol hydrochloride HPMC matrix tablet. Indian J. Pharm. Sci. 2006; 68: 594-598.

70. Jamzad S, Fassihi R. Development of controlled release low dose class II drug-glipizide. Int. J. Pharm. 2006; 312: 24-32.

71. W. Mark Saltzman. Drug Delivery: Engineering principle for drug delivery, Controlled Drug Delivery Systems, Matrix Delivery Systems. New York: Oxford University Press; 2001: 245-246.

72. Siepmann J, Peppas NA. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Adv Drug Dev Rev. 2001; 48: 139-157.

73. Charman S, Charman W, Rathbone M, Hadgraft J, Roberts M. Modified Release Drug Delivery Technology. New York: Marcel Dekker; 2003: 129.

74. Borguist P, Korner A, Larsson A. A model for the drug release from a polymeric matrix tablets-effect of swelling and dissolution. J Controlled Release. 2006; 113: 216-225.

75. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of Release of solid drugs dispersed in solid matrices. J. Pharm. Sci. 1961; 52(1): 1145-9.