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# FORMULATION AND EVALUATION OF CONTROL RELEASE TABLET OF REPAGLINIDE

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**Abstract:**

*This study focuses on the formulation and evaluation of sustained-release matrix tablets of Repaglinide, a drug widely used for the management of type 2 diabetes. Pre-formulation studies confirmed the physico-chemical properties of Repaglinide, including its melting point, solubility profile, and characteristic functional groups, ensuring the drug's compatibility for sustained-release formulation. Calibration curves in ethanol, methanol, and phosphate buffer (pH 6.8) exhibited strong linearity, facilitating accurate drug quantification. Pre-compression parameters, including angle of repose, bulk density, tap density, Carr's index, and Hausner ratio, demonstrated good flowability and compressibility. Post-compression evaluations indicated acceptable weight variation, friability, hardness, and uniform drug content across all formulations. In-vitro dissolution studies revealed that formulations F8 and F12 achieved prolonged drug release over 12 hours, with drug release rates of 84.91% and 99.92%, respectively. These results indicate that sustained-release matrix tablets of Repaglinide can be effectively formulated, offering a promising approach to enhance therapeutic efficacy and patient compliance in diabetes management.*

***Keywords:*** *Repaglinide, sustained-release tablets, type 2 diabetes, pre-compression parameters, post-compression parameters, in-vitro dissolution, drug release, matrix formulation.*

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## INTRODUCTION:

The formulation and evaluation of controlled-release tablets of Repaglinide aim to address the challenges associated with the management of type 2 diabetes mellitus (T2DM), a chronic condition characterized by elevated blood glucose levels due to insulin resistance and impaired insulin secretion. Repaglinide, a non-sulfonylurea oral hypoglycemic agent, is widely used to control postprandial blood glucose spikes in patients with type 2 diabetes. It works by stimulating insulin release from the pancreatic β-cells in a glucose-dependent manner, which helps in reducing the blood sugar levels after meals. Despite its efficacy, Repaglinide has a relatively short half-life of about 1 hour, requiring frequent administration to maintain consistent therapeutic effects. This frequent dosing, however, can lead to issues with patient compliance and fluctuations in blood glucose levels, hindering optimal disease control.

A controlled-release formulation of Repaglinide offers a solution to these issues by allowing for the sustained release of the drug over an extended period. By releasing the active ingredient gradually, a controlled-release system can maintain consistent therapeutic levels of Repaglinide in the bloodstream, reducing the peaks and troughs that often result in hypoglycemic episodes or suboptimal glucose control. The advantages of a controlled-release tablet include fewer doses per day, improved patient adherence, enhanced pharmacodynamic effects, and better management of blood glucose levels, all of which contribute to improved patient quality of life.
The drug profile of Repaglinide plays a crucial role in the development of controlled-release formulations. Repaglinide is highly lipophilic, has good oral bioavailability, and is primarily metabolized in the liver by the cytochrome P450 enzymes. Its pharmacokinetics show rapid absorption and elimination, which makes the drug a candidate for a controlled-release system. The challenge in formulating a controlled-release tablet lies in developing a system that effectively modulates the drug release rate to maintain therapeutic levels for an extended period, while ensuring stability and patient compliance.

Formulation strategies for controlled-release tablets of Repaglinide typically involve the use of matrix-based systems, where the drug is dispersed in a polymeric matrix, or coating-based systems, where the drug is surrounded by a controlled-release coating. Common excipients used include hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), which form gel-like structures upon contact with water, gradually releasing the drug. The selection of the right excipients and their concentrations is critical to achieving the desired release profile. The release rate is influenced by factors such as polymer type, matrix composition, and the manufacturing process, all of which need to be optimized to ensure consistent and controlled drug delivery.

Pre-formulation studies are essential to determine the solubility, stability, and compatibility of Repaglinide with the chosen excipients. These studies help identify the most suitable polymers and other formulation components that will enable controlled drug release while maintaining the integrity and stability of the tablet. During tablet preparation, methods like direct compression or wet granulation are typically employed, depending on the properties of the drug and excipients. The prepared tablets are then subjected to evaluation tests that include drug release studies (usually performed using a USP dissolution apparatus), mechanical strength testing, and stability testing to ensure that the formulation remains stable and effective under various conditions. The formulation of controlled-release tablets of Repaglinide represents a promising approach to improving the management of type 2 diabetes by providing sustained therapeutic effects, enhancing patient compliance, and ensuring better glycemic control. Through the careful design and optimization of the formulation, this research seeks to create a novel dosage form that can improve the overall treatment outcome for patients with type 2 diabetes mellitus.

## MATERIAL AND METHODS:

### MATERIALS:

The materials selected for the controlled-release tablets of Repaglinide include Repaglinide (API) from Microlabs Ltd, Hosur**.** Hydroxypropyl Methylcellulose (HPMC) from LOBA CHEM is used as a hydrophilic polymer to control the drug release. Eudragit 100 from COSMO CHEM is included to modify the release rate through its film-forming properties. Talc and Magnesium Stearate**,** both sourced from LOBA CHEM**,** serve as lubricants to prevent tablet sticking and enhance processing. Finally, Microcrystalline Cellulose (MCC) from LOBA CHEM acts as a binder and filler to ensure tablet integrity and consistency. These materials work together to optimize the formulation for sustained drug release.

### Pre-formulation Studies:

Preformulation studies are crucial in developing

stable and effective drug formulations. In this phase, the physical, chemical, and mechanical properties of Repaglinide were evaluated. The organoleptic characterization assessed its color, odor, and appearance. The melting point was determined using Thiele's tube apparatus, where the temperature at which Repaglinide melted was recorded. Additionally, the angle of repose was measured to assess the flow properties of the granules, where the height and radius of the granule heap were used to calculate the angle, helping to determine the frictional forces in the powder. These studies provide essential data for formulating a suitable dosage form.

**Determination of standard calibration curve:**
Repaglinide λmax in methanol was determined by scanning a 10 g/ml solution of Repaglinide in the region of 200-400 nm using a UV-visible spectrophotometer. The wavelength corresponding with the spectrum's peak was recorded.

**Standard Calibration Method Development of Repaglinide:**
The samples of the standard solution were scanned between 200-400 nm regions on Shimadzu 1800 UV spectrophotometer. There are 5 different stock solutions of the Repaglinide sample was prepared by dissolving 50 mg of drug in 50 ml of Distilled water, phosphate buffer solution pH 6.2, and phosphate buffer solution pH 7.4 respectively.

**Preparation of calibration curve for repaglinide:**
**Standard curve in 0.1N HCL by using U.V spectrophotometer Stock Sample Preparation:**
Accurately weighed 100 mg of drug was first dissolved in100 mL of 0.1N HCl in 100 mL of volumetric flask to make a concentration of 1000 µg/mL (primary stock solution). 5 mL of primary stock solution was pipetted out into 50 mL of volumetric flask and volume was adjusted with 0.1N HCL to make a concentration of 100µg/mL (secondary stock solution).

Sample Preparation: From the secondary stock solution pipette out 0.2, 0.4, 0.6, 0.8, 1.0 ml in to 10ml of volumetric flask and volume made up to with 0.1N HCl to give various concentrations such as 2, 4, 6,8,10 µg/mL were prepared for calibration curve. Standard curve was plotted by taking absorbance of secondary stock solutions in UV double beam spectrophotometer at 281 nm.

**Infrared Spectroscopy:**
Infra-red spectroscopy is one of the most widely used tools for purity analysis of drugs in pharmaceutical Industry. Fourier Transform IR spectra were recorded using Bruker Germany. IR spectrophotometer. KBr powder was used to prepare pellet for sampling. The scanning range was 4000- 40cm.

**Method of preparation of Control Release tablets:**
Wet granulation method has been employed to prepare tablet of Repaglinide using hydroxy propyl methyl cellulose and Micro crystalline cellulose, Eudragit Rs100 as polymers.

**Preparation:**
Control release tablets each containing 1mg of Repaglinide was prepared by wet granulation method (using isopropyl alcohol). All the ingredients except lubricants were mixed in the order of ascending weights and blended for 10 min in an inflated polyethylene pouch and then Repaglinide was added in this mixture then mixed for 2 min for uniform mixing. Granulation was done with binder solution of PVP which was previously dissolved in isopropyl alcohol, this damp mass passed through sieve #10. The granules were dried at 40ºC for 30 min. And then passed through sieve #22-44 and lubricants such as magnesium stearate and talc were mixed and then compressed it with 10-station rotary compression machine into 100mg tablet, to a hardness of 5-7kg/cm$^2$ using 6 mm punch.

**Table 1: Formulation for preparation control release tablet Repaglinide**

| Ingredients (mg) | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 | C11 | C12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Repaglinide** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Eudragit Rs100** | - | - | - | - | 30 | 40 | 15 | 60 | 15 | 20 | 25 | 30 |
| **hydroxy propyl methyl cellulose** | 30 | 40 | 50 | 60 | - | - | - | - | 15 | 20 | 25 | 30 |
| **Micro crystallinecellulose** | 66 | 56 | 46 | 36 | 66 | 56 | 46 | 36 | 66 | 56 | 46 | 36 |
| **Magnesium Stearate** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Talc** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| **Total** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**Evaluation:**

**Weight variation**

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance and the test was performed according to the official method.

**Hardness**

Tablet hardness (tablet crushing strength), the force required for breaking a tablet in a diametric compression of five tablets was measured using a Pfizer hardness tester.

**Friability**

Friability of the tablets was determined using Electro lab Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and re weighed.

**Drug content uniformity**

Ten tablets were weighed and powdered. An amount of the powder equivalent to 10mg of Repaglinide was dissolved in 100ml of pH 7.4 buffers, filtered, diluted suitably and analyzed for drug content at 243nm using UV-Visible spectrophotometer.

***In-vitro* drug release study**

*In-vitro* drug release study was carried out using a USP-23 rotating dissolution tester. The dissolution was measured at 37.0±0.5 ºC and 100rpm speed. Drug release from the tablets was studied in 900ml acidic medium (pH 1.2) for 2 hours, in alkaline medium (pH 7.4 phosphate buffer) for remaining hours end of the study. At predetermined time intervals, 5ml aliquots were withdrawn and replaced with the same volume of fresh solution. The amount of drug released was analyzed using UV-visible spectrophotometer at a λmax of 241nm.

## RESULT AND DISCUSSION:

**Physico-chemical Properties of Repaglinide:**

**Organoleptic Characterization:**

| Test | Specification/Limits | observations |
|---|---|---|
| Color | White to half-white powder | White powder |
| Odour | Odourless | Odourless |

**Determination of Melting Point:**

The melting point of Repaglinide was found to be 131℃. The reported value is 130-131℃. Hence, the given sample of Repaglinide is in close agreement with the reported value.

**IR Spectroscopy of the Drug:**

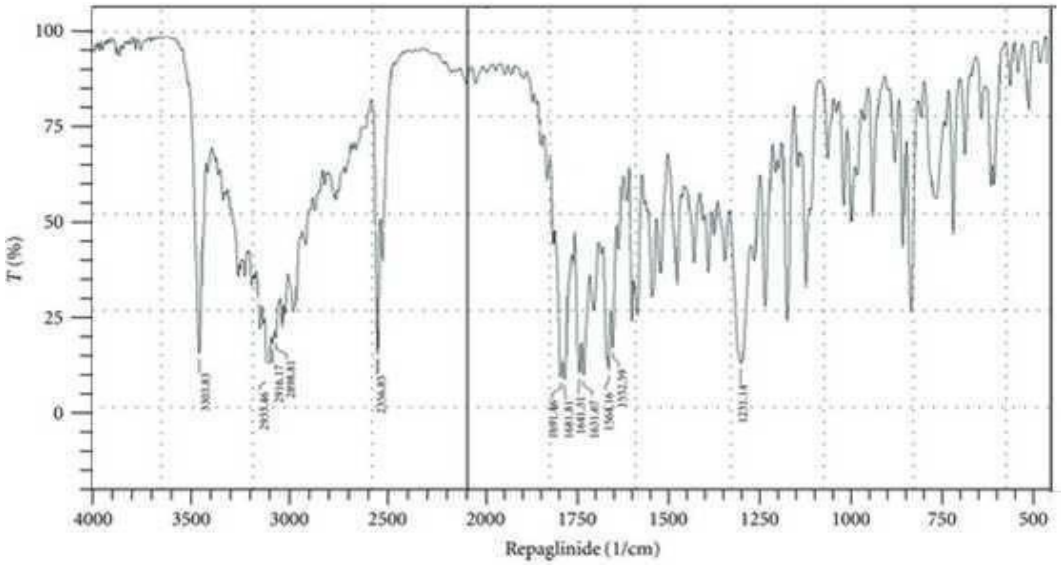
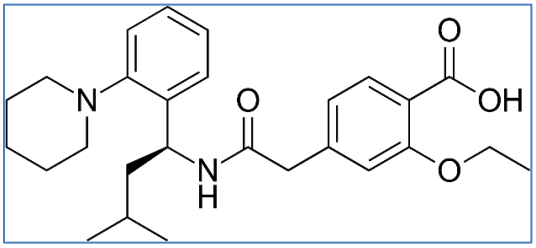
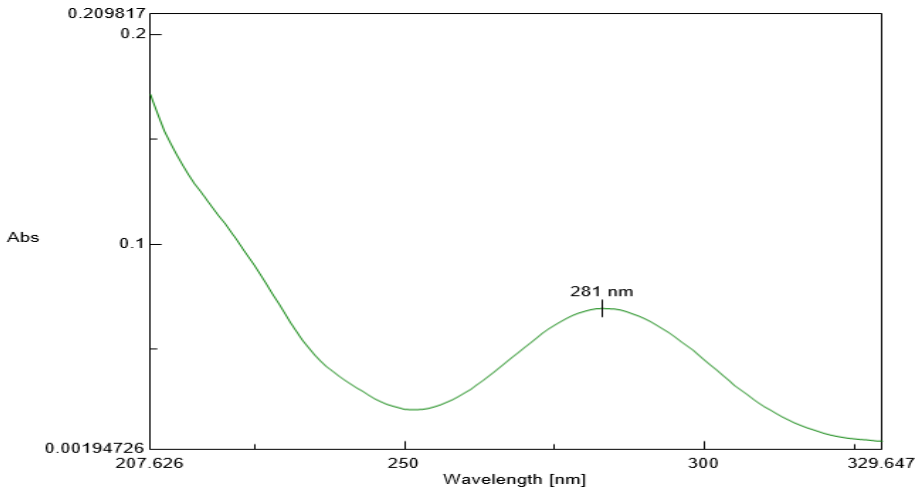



**Figure 1: FTIR spectra of Repaglinide Sample**




**Determination of λmax of Repaglinide:**
The spectrum of Repaglinide showed λmax at 281 nm it complies with reported value.




**Standard Calibration Curve of Repaglinide:**
**Calibration curve in ethanol:**
The UV spectrum of Repaglinide was obtained by scanning different concentration of Repaglinide in the range of 2-

20µg/ml between 200-400 nm using a UV Spectrophotometer (Shimadazu UV-1800). Absorbance of solution observed on UV spectrophotometer at 281 nm. Absorbance Vs Concentration graph plotted. It followed beers lamberts law.

**Table 2: Absorbance data of Repaglinide for calibration curve in ethanol**

| Concentration (µg/ml) | Absorbance at 281 nm |
|---|---|
| 2 | 0.176±0.001 |
| 4 | 0.219±0.002 |
| 6 | 0.375±0.0036 |
| 8 | 0.488±0.002 |
| 10 | 0.581±0.003 |
| 12 | 0.688±0.002 |

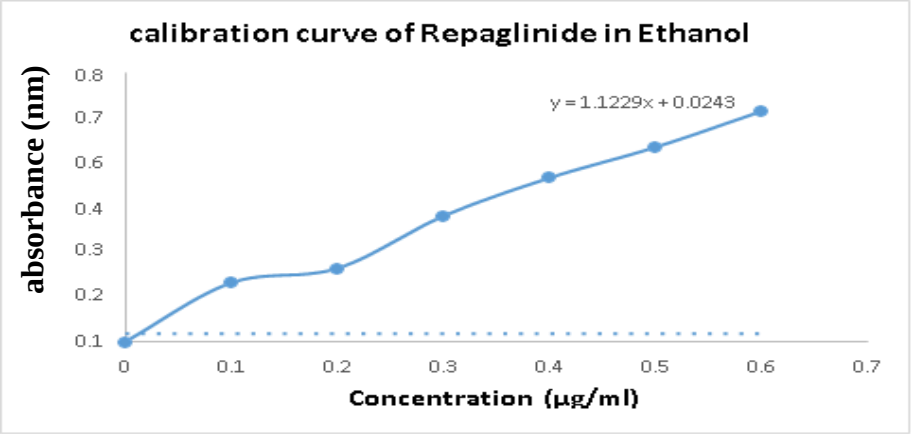



**Figure 2: Calibration curve in ethanol**

**Evaluation Parameter**

**Pre-Compression Parameters**

The following table 3 provides an overview of the pre-compression characteristics of Repaglinide controlled-release tablet formulations. The angle of repose (21.85°–30.94°) indicates good to excellent flow properties, while bulk density (0.134–0.199 g/cm³) and tap density (0.150–0.234 g/cm³) demonstrate adequate packing behavior. Carr's index values (6.71%–16.75%) and Hausner ratio (1.08–1.24) confirms that the formulations have satisfactory flowability and compressibility, ensuring consistency and efficiency in tablet production.

**Table 3: All the properties for Repaglinide Control Release Tablets**

| Formulation Code | Angle of Repose | Bulk Density (g/cm³) | Tap Density (g/cm³) | Carr's Index (%) | Hausner Ratio |
|---|---|---|---|---|---|
| **C1** | 30.61 | 0.190 | 0.206 | 7.71 | 1.09 |
| **C2** | 25.63 | 0.195 | 0.219 | 6.71 | 1.08 |
| **C3** | 21.85 | 0.177 | 0.192 | 13.52 | 1.15 |
| **C4** | 23.74 | 0.145 | 0.154 | 13.46 | 1.14 |
| **C5** | 24.77 | 0.135 | 0.174 | 14.25 | 1.24 |
| **C6** | 25.75 | 0.142 | 0.150 | 9.25 | 1.12 |
| **C7** | 26.52 | 0.164 | 0.192 | 16.75 | 1.09 |
| **C8** | 25.74 | 0.199 | 0.230 | 14.92 | 1.10 |
| **C9** | 22.56 | 0.134 | 0.234 | 13.25 | 1.20 |
| **C10** | 25.46 | 0.165 | 0.151 | 12.25 | 1.18 |
| **C11** | 23.74 | 0.145 | 0.219 | 11.52 | 1.16 |
| **C12** | 30.94 | 0.170 | 0.220 | 10.33 | 1.15 |

**Post-Compression parameters**

The following table 4 provides an overview of the post-compression parameters for Repaglinide controlled-release tablets, ensuring their quality and consistency. Weight variation across all formulations ranges from 100–104 mg, demonstrating uniformity in tablet weight. Friability values (0.665%–0.990%) fall within acceptable limits, confirming the tablets' resistance to breaking or chipping during handling. Hardness values, ranging from 4.6–6.7 kg/cm², indicate sufficient mechanical strength to withstand handling while ensuring proper drug release. Overall, the results validate that the formulations comply with standard requirements for controlled-release tablets.

**Table 4: The post-compression parameters of Repaglinide controlled-release tablets**

| Formulation Code | Weight Variation (mg) | Friability (%) | Hardness (kg/cm²) |
|---|---|---|---|
| **C1** | 100 | 0.891 | 5.6 |
| **C2** | 101 | 0.866 | 5.6 |
| **C3** | 103 | 0.921 | 5.6 |
| **C4** | 101 | 0.891 | 5.6 |
| **C5** | 100 | 0.901 | 6.7 |
| **C6** | 104 | 0.745 | 6.7 |
| **C7** | 100 | 0.665 | 6.7 |
| **C8** | 101 | 0.990 | 6.7 |
| **C9** | 100 | 0.930 | 4.6 |
| **C10** | 101 | 0.980 | 4.6 |
| **C11** | 100 | 0.865 | 4.6 |
| **C12** | 100 | 0.891 | 4.6 |

**Drug content uniformity:**

Ten tablets were weighed and powdered. An amount of the powder equivalent to 10mg of Repaglinide was dissolved in 100ml of pH 7.4 buffers, filtered, diluted suitably and analyzed for drug content at 241nm using UV-Visible spectrophotometer.

**Table 5: Drug content of Repaglinide Control Release Tablets**

| Formulation Code | Drug content |
|---|---|
| C1 | 97.32 |
| C2 | 95.14 |
| C3 | 96.00 |
| C4 | 93.26 |
| C5 | 98.55 |
| C6 | 96.45 |
| C7 | 96.15 |
| C8 | 94.22 |
| C9 | 95.55 |
| C10 | 98.22 |
| C11 | 97.66 |
| C12 | 96.42 |

All the formulations were evaluated for weight variation, hardness, friability and % drug content. The weight of the formulation varied from 100 to 104mg. Hardness of the tablets varied from 4.6 to 5.6kg/cm2. Friability of the tablets varied from 0.66 to 0.990% and drug content was found to be 93.26 to 98.55.

All formulation showed uniform hardness. The average percentage deviation of all parameters was found within the limit. The friability for all formulations was found below 1% indicating good abrasion resistance characteristics of tablets.

***In-Vitro* Dissolution Study:**

Dissolution study carried out. The study or 30 minutes, the results were illustrated in the tablebelow.

**Table 6: Dissolution Study of Repaglinide Control Release Tablets**

| Time (hr.) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 38.50 | 25.85 | 34.53 | 31.78 | 24.67 | 36.26 | 36.21 | 21.43 | 31.73 | 36.95 | 36.89 | 34.44 |
| 1.5 | 62.90 | 40.69 | 53.71 | 50.19 | 38.46 | 57.20 | 57.18 | 34.06 | 49.96 | 50.21 | 54.05 | 47.51 |
| 2 | 83.27 | 73.92 | 95.40 | 91.95 | 70.66 | 92.98 | 90.32 | 97.40 | 89.50 | 86.35 | 92.26 | 95.47 |

| Time (min) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **30** | 37.01 | 38.27 | 34.18 | 34.44 | 36.89 | 36.89 | 38.90 | 38.40 | 41.92 | 36.95 | 34.53 | 31.78 |
| **1** | 55.55 | 56.43 | 46.84 | 47.51 | 54.05 | 54.67 | 57.06 | 57.00 | 58.82 | 50.21 | 53.71 | 50.19 |
| **1.5** | 75.16 | 75.60 | 63.69 | 64.73 | 72.65 | 73.84 | 76.86 | 75.98 | 77.24 | 67.31 | 74.21 | 70.70 |
| **2** | 91.95 | 96.97 | 82.42 | 83.27 | 92.26 | 95.15 | 99.55 | 97.91 | 96.15 | 86.65 | 95.47 | 98.92 |

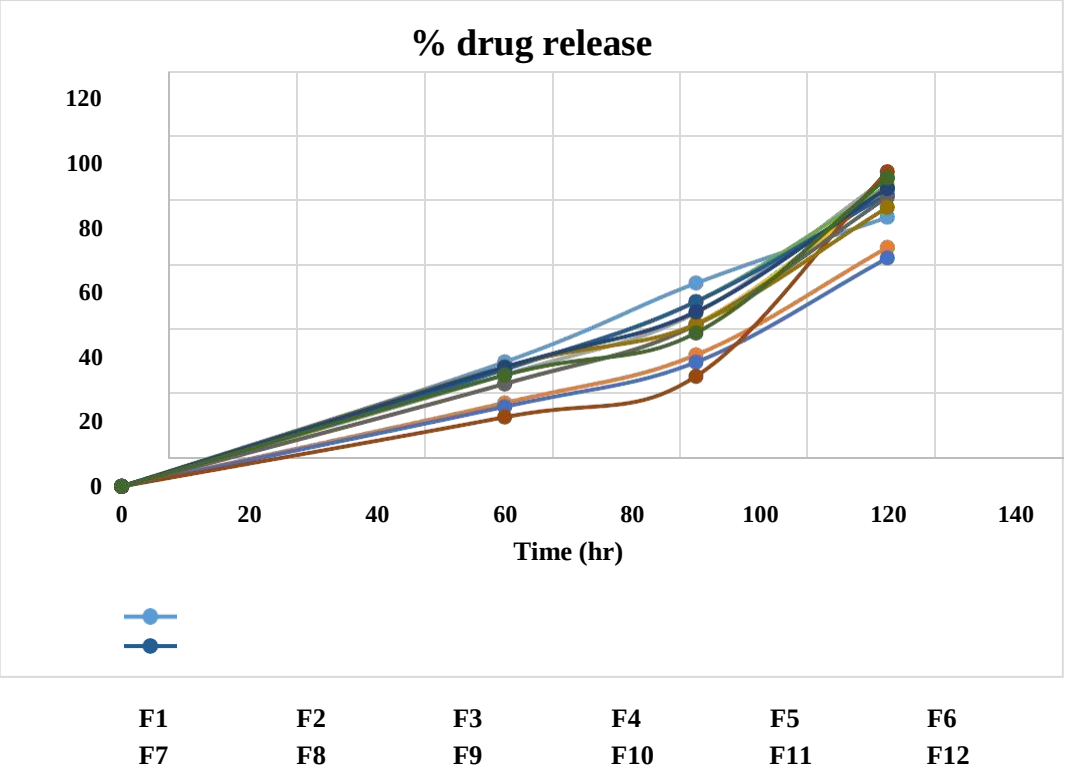



**figure 3: Drug Release**

## CONCLUSION:

In conclusion, this study successfully developed and evaluated sustained-release matrix tablets of Repaglinide, addressing the need for improved glycemic control in type 2 diabetes management. Comprehensive pre-formulation studies confirmed the physico-chemical properties of Repaglinide, including its organoleptic characteristics, melting

point, solubility profile, and FTIR spectrum, ensuring the integrity of the drug. Standard calibration curves demonstrated strong linearity in ethanol, methanol, and phosphate buffer (pH 6.8), validating accurate drug quantification methods.

Pre-compression parameters, including angle of repose, bulk and tap densities, Carr's index, and Hausner ratio, confirmed good flow and packing properties, ensuring efficient tablet manufacturing. Post-compression parameters, such as weight variation, friability, hardness, and drug content uniformity, indicated the tablets met the required quality standards. Notably, the in-vitro dissolution studies revealed that formulations F8 and F12 achieved prolonged drug release over 12 hours, with drug release rates of 84.91% and 99.92%, respectively, highlighting their suitability as sustained-release systems.

Overall, this study demonstrates the feasibility of formulating Repaglinide into sustained-release tablets, offering potential improvements in patient adherence and therapeutic efficacy in diabetes management.

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**AUTHORS CONTRIBUTIONS:**
All authors have contributed equally.

**CONFLICTS OF INTERESTS:**
All authors have declared no conflict of interest.

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