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ANALYTICAL METHOD, DEVELOPMENT AND VALIDATION FOR EVALUATING REPAGLINIDE EFFICACY IN TYPE II DIABETES MELLITUS MANAGEMENT: A PHARMACEUTICAL PERSPECTIVE

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Abstract

An anti-diabetic drug called Repaglinide is used to treat type II diabetes. Repaglinide, a lipophilic medication with a short (1 h) half-life and little solubility in water is classified as a class II biopharmaceutical chemical (BCS) chemical. Only around 55% of drugs with a high metabolism in the first pass are bioavailable orally. Repaglinide's half-life is one hour, and because of first-pass metabolism, it is 56% bioavailable in the body. Repaglinide requires frequent dosage because its total daily dose is 16 mg (e.g., 4 mg four times day depending on meal patterns). Repaglinide transdermal patches were created to maintain medication release, enhance drug bioavailability, and increase patient compliance Transdermal patch of Repaglinide was prepared to sustain the release and improve bioavailability of drug and patient compliance. Different formulations were prepared by varying the grades of HPMC and concentration of PVP K30 by solvent casting method. The prepared formulations were evaluated for various parameters like thickness, tensile strength, folding endurance, % elongation, % moisture content, % moisture uptake, % drug content, in vitro drug release, in vitro permeation, and drug excipient compatibility.

Keywords: Repaglinide, Type II Diabetes, UV spectroscopy, FTIR.

INTRODUCTION

The largest and easiest to access organ of the body, the skin offers a potential route for medication delivery for systemic effects. Skin is divided into four layers, with the stratum corneum at the top serving as the most effective barrier against drug penetration and regulating the transdermal bioavailability of medications. To overcome the skin's natural barrier and deliver medication molecules with specific physicochemical properties to the systemic circulation, special transporters are therefore required. Transcutaneous administration of medications and vaccines is a practical substitute for oral and parenteral modes of administration. Hepatocytes can help prevent "first-pass" deactivation, lessen the risk of digestive discomfort, provide constant medication absorption over extended periods of time, and reduce drugging density, all of which improve adherence. The transcutaneous route has grown in popularity since ancient times because to its large external area and effects that facilitate drug administration. The most effective technique to arrange the drug administration is to avoid the skin because it is the most effective drug passage obstruction. It entails picking a method to deliver the dosage to the skin's surface. The

immersion of particles along the skin and circulation outside of the lungs is known as percutaneous absorption. Different drug delivery techniques have been developed for use on the skin. Drugs are primarily administered through the skin during cutaneous pharmacotherapy to produce local effects at the site of administration.

Repaglinide is a fast-acting, short-acting medication that works similarly to meglitinide but lasts an hour less, has a 50% lower bioavailability, and absorbs less well in the upper GI tract. As a result, it needs to be taken three to four times daily. All of these appearances make repaglinide a suitable candidate for the development of a gastro-retentive dosage form. The gastro-retentive mechanisms, which can fail in the gastric region for several hours, essentially cover the residence durations of drugs in the stomach. Long-term stomach retention improves bioavailability, reduces drug waste, and makes drugs that are hard to dissolve in an acidic environment more soluble. Another assertion made by such shippers is that local medication dispersion occurs into the stomach and proximal small intestine. Repaglinide reduces blood glucose absorption by promoting the release of insulin from beta cells in pancreatic islet tissue. This is stopped by a specific ion channel mechanism. Repaglinide blocks potassium efflux and adenosine triphosphate (ATP) potassium channels in the beta cell membrane. Depolarization and calcium influx are what cause insulin release. An antihyperglycemic drug for type II diabetes is repaglinide. In order to make repaglinide more soluble, an attempt was made to do so when making the transferosome.

MATERIALS AND METHODS

Materials Used - The repaglinide medicine was a gift sample from Medley Lab in Mumbai.

Instruments

The spectrophotometric measurements were performed using a laser-shot LBP-1210 Canon printer, an Intext LCD computer running Shimadzu UV PC software version 2.3, and a Shimadzu 1700 double-beam UV Visible spectrophotometer with a fixed slit width of 1 nm.

UV estimation For Repaglinide

Preparation of standard stock solution:

Repaglinide (1 mg) was precisely weighed and then transferred to a 1 ml volumetric flask. It was dissolved in methanol solvent, the volume was adjusted, and it was sonicated for five minutes. The drug's concentration in the resultant solutions is 1 mg/ml. The sample stock solution was further diluted using a solvent ratio to produce a sub-stock with a µg/ml range of 5 to 30. The blank solution in this case was methanol. After that, the solutions were scanned in a UV spectrophotometer between 400 and 200 nm.

Determination of wavelength of maximum absorption (λmax)

During the procedure firstly the blank solvent was run in the UV-Vis (Shimadzu, 1700) for baseline correction and scanning range was 200 to 800 (UV-Vis) nm to fix the maximum wave length. And later the dilution of the mid concentration was scanned and absorbance and wavelength were noted by UV spectrum.

1. Validation of the method

To develop a novel, convenient, economical, and cost-effective technique for the spectroscopic determination of Repaglinide, validation was carried out. The method's development and validation followed the analytical procedure in accordance with the ICH guidelines for the validation of analytical procedures in order to assess the analyte's ruggedness, robustness, linearity, accuracy, and precision.

a. Specificity

Specificity of the method was determined by the spectrum of isolated compound Repaglinide

b. Linearity

An analytical method, linearity is its ability to produce test results that are proportional to the concentration of the analytes within a given range in samples. The linearity of measurement was evaluated by analyzing different concentration of the solution of isolated compound Repaglinide. Calibration curves were built and the suggested technique was assessed in the respective statistical study by its correlation coefficient and intercept value calculated. For both the method, the Beer Lambert's concentration range was found to be 10-60 µg/ml.

c. Ruggedness study

The ruggedness of the method was determined by carrying out the analysis using two different concentrations and the respective absorbance was noted. Ruggedness of the methods was assessed by carrying out assay 3 reading with different analyst by using same equipment.

d. Robustness study

To determine the robustness, the same procedure was carried out by changing the temperature and the result was compared with the same previous procedure**.**

e. Precision

An analytical procedure& accuracy reflects the proximity of agreement (degree of scattering) between sequences of measurements acquired under the prescribed circumstances from the various sampling of the same homogeneous sample. Precision can be taken into account at three levels: repeatability, intermediate (intraday) precision and reproducibility (interday precision).

- **Intraday Precision:** Solutions containing 15 µg/ml of Repaglinidewere analyzed three times on the same day and %R.S.D was calculated**.**
- **Interday Precision:** Solutions containing 15 µg/ml of Repaglinidewere analyzed on three different successive days and %R.S.D was calculated**.**
- **Repeatability:** Method precision of the experiment was performed by preparing the standard solution of Repaglinide (15 µg/ml) for three times and analyzed as per the proposed method.

Fourier transmission Infra-Red Spectroscopy

FT-IR spectrum of Drug and excipient combination was recorded over the range of 4000 to 400 cm−1 by KBr pellet method using a FT-IR spectrophotometer. The KBr disc was prepared using 1 mg of each drug and drug + polymers in 100 mg of

spectroscopic grade KBr which has been dried using IR lamp. Both KBr and drug was mixed and subjected to hydraulic pressure to form disc. This disc was placed in FT-IR chamber. Infrared spectrum was recorded in the 4000 - 400 cm-1 region.

RESULT AND DISCUSSION

UV- visible spectrophotometer (1700- Shimadzu) is used to determine the lambda max (absorption maxima) of a substance. The lambda max of the Repaglinide was found to be 293.0 nm. This was well within the limits of the drug specification. The difference in the wavelength was admissible because it was permissible ±5 range.

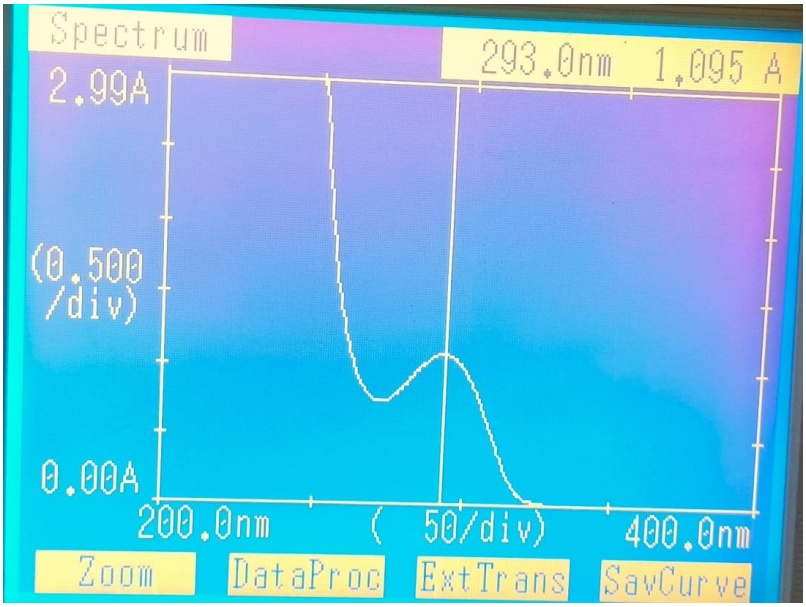

Figure 1: Lambda max of Repaglinide

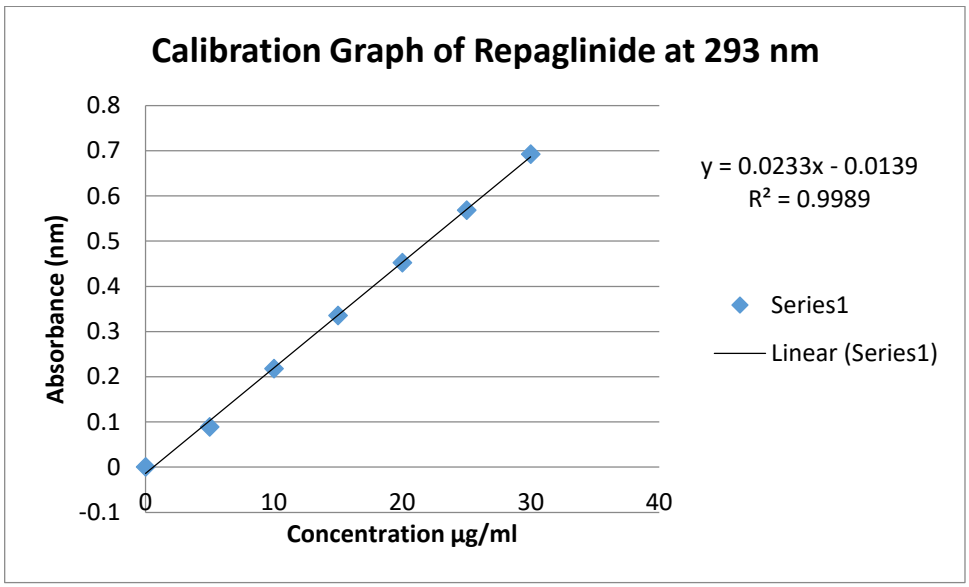

Figure 2: Calibration curve of Repaglinide

The linearity of the proposed method was established by least squares linear regression analysis of the calibration curve. The regression equation of **Repaglinide** was obtained by plotting absorbance versus concentration of **Repaglinide** in the range of 5-30 µg/mL. Six points calibration curve were obtained in a concentration range

from 5-30 µg/mL.for drug. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = = 0.023x - 0.013with correlation coefficient R^2 = 0.998.

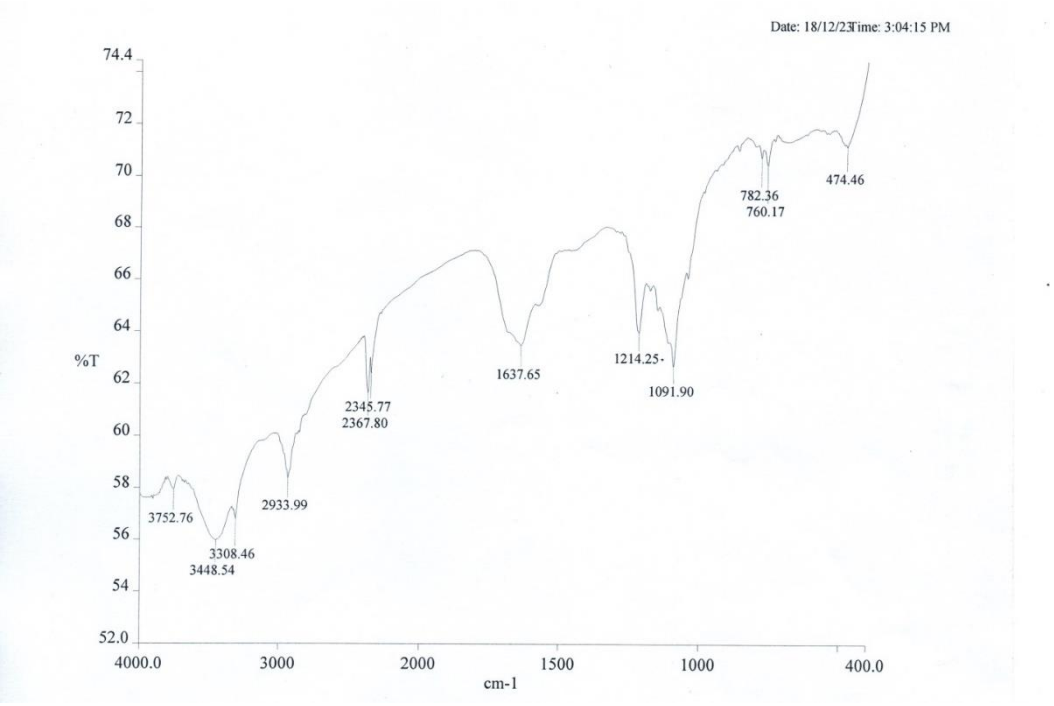

Figure 3: FTIR graph of Repaglinide

FTIR of the drug the analytical procedure is followed in doing FTIR tests. FTIR is used to examine the compatibility of medicinal excipients. Figure 1 shows the Repaglinide analysis of FITR.

Differential Scanning Calorimetric Studies: repaglinide melting point was found using DSC. The melting point of repaglinide is confirmed by a strong endotherm at **126 to 128 °C** in the DSC thermogram

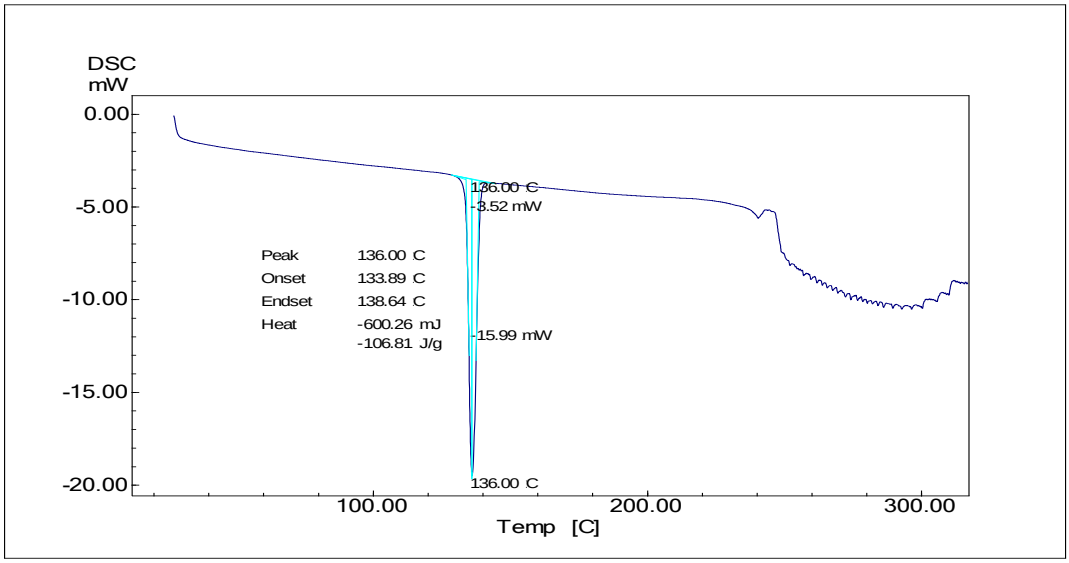

Figure 4: DSC thermogram of Repaglinide

Powder X-ray Diffraction Studies

Using P-XRD (Bruker, Germany), the crystallinity of the processed and unprocessed Rp samples was examined. All of the samples were placed into silicon wells before being scanned at a rate of 102T/min at a wavelength of 1.542 over the range of 5-500 at 2T.

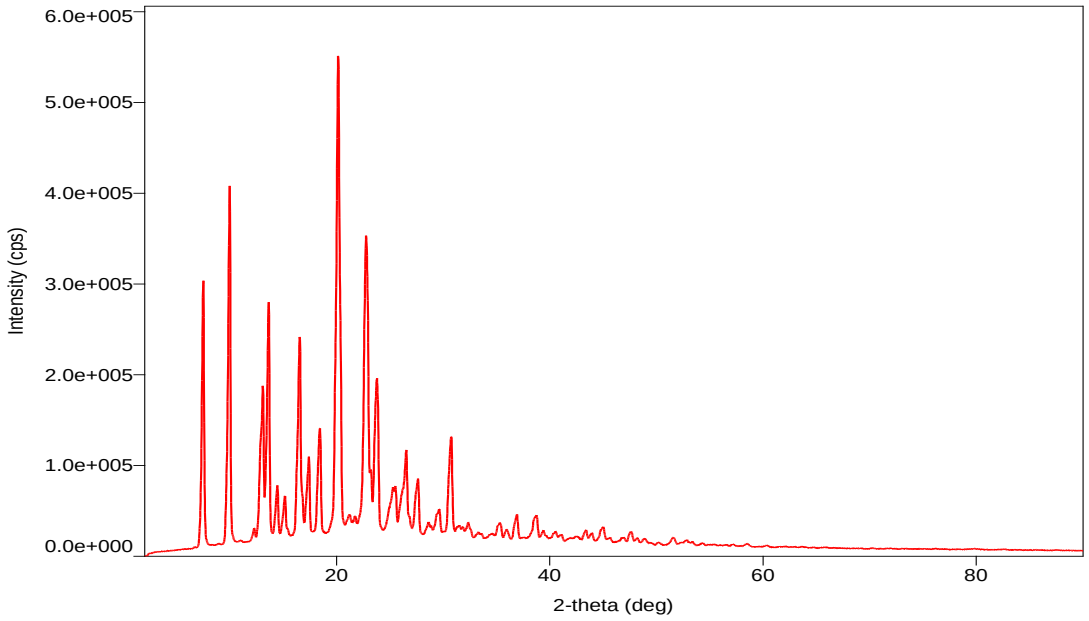

Figure 5: X-ray Diffraction Studies of Repaglinide

SUMMARY AND CONCLUSION

The present study was for Type II Diabetes mellitus. Repaglinide of poorly water-soluble drug, Repaglinide, having low bioavailability. The objective was to increase the dissolution ofdrugs and to improve patient compliance.

The formulation of Repaglinide with a smaller particle size canbe effectively produced by the thin film hydration method. The current investigation focused on Type II Diabetes Mellitus. Repaglinide has a low bioavailability and is not very water-soluble.

The goal was to improve patient compliance and increase drug dissolution. The formulation of Repaglinide with a reduced particle size can be successfully created using the thin film hydration process. The FTIR analysis used in this study reveals the presence of a potent Repaglinide peak.

Repaglinide's maximum dose has been established to be 242. A DSC A strong endotherm at 126 to 128 °C and an X-RD scan at 102 T/min at a wavelength of 1.542 over the range of 5-500 at 2 T are used to confirm the melting temperature of repaglinide.

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