THE DEVELOPMENT AND VALIDATION OF AN ANALYTICAL METHOD FOR ASSESSING THE EFFECTIVENESS OF REPAGLINIDE IN THE MANAGEMENT OF TYPE 2 DIABETES MELLITUS

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Abstract

Type 2 diabetes is treated with repaglinide, an anti-diabetic medication. Repaglinide is a class 2 biopharmaceutical chemical (BCS) that is lipophilic, has a short half-life of one hour, and is note very soluble in water. Orally bioavailable medications comprise only around 55%of those having a high metabolism in the first run.

Repaglinide has an hourly half-life and is 56% bioavailable in the body due to first-pass metabolism. Repaglinide has a total daily dose of 16 mg, hence it needs to be taken frequently. Repaglinide transdermal patches were developed to improve drug absorption, sustain drug release, and boost patient adherence. Repaglinide transdermal patches were created to maintain medication release, enhance drug bioavailability, and increase patient compliance.

By changing the grades of HPMC and the concentration of PVP K30 using the solvent casting process, several formulations were created. A number of characteristics, including thickness, tensile strength, folding endurance, percentage elongation, moisture content, moisture uptake, percentage drug content, in vitro drug release, in vitro permeation, and drug excipient compatibility, were assessed for the producer formulations.

Keywords: *Repaglinide, type 2 diabetes, UV spectroscopy, FTIR*

Introduction

Repaglinide is short-acting, fast-acting drug that function similarly to meglitinide, but it absorbs less efficiently in the upper GI tract, lasts for only one hour, and has a 50% lower bioavailability. It must therefore be taken three to four time a day. Repaglinide is an appropriate choice for the creation of a gastro-retentive dosage form because of all of these appearances. The gastro-retentive mechanisms largely cover the durations of drug residence in the stomach, even if they can malfunction in the gastric region for several hours. Prolonged stomach retention increase bioavailability, decrease medication waste, and increases the solubility of medications that are difficult to dissolve in an acidic environment. These shippers also claim that local drug dispersion take place in the stomach and proximal small intestine.

By encouraging the release of insulin from beta cell in the islet tissue of the pancreas, repaglinide lowers the absorption of blood glucose. A certain ion channel mechanism block this. Repaglinide inhibits the beta cell membrane's adenosine triphosphate (ATP) potassium channel and potassium efflux. Insulin release is brought on by calcium influx and depolarization.

Repaglinide is an anti-hyperglycemic medication for type 2 diabetes. An attempt was made to increase the solubility of repaglinide during the transfersome-making process.

Material Used - A gift sample of repaglinide medication was obtained from Medley Lab in Mumbai.

Instrument -

A Shimadzu 1700 double-beam UV Visible spectroscopy with a fixed slit width of 1 nm, an Intext LCD computer running Shimadzu UV PC software version 2.3, and a laser-shot LBP-1210 Canon printer were used to produce the spectrophotometric observations.

UV estimation For Repaglinide

Preparation of standard stock solution:

After carefully weighing one milligram of repaglinide, it was added to a one milliliter volumetric flask. After dissolving it in methanol solvent and adjusting the volume, it was sonicated for five minutes. The resulting solution contain one milligram per milliliter of the medication. Using a solvent ratio, the sample stock solution was further diluted to create a sub-stock with a range of 5 to 30 µg/ml. Methanol served as the blank solution were then scanned between 400 and 200 nm in a UV spectrophotometer.

Determination of wavelength of maximum absorption

In order to rectify the baseline and fix the maximum wave length, the blank solvent was first run through the UV-Vis (Shimadzu, 1700) scanning range of 200 to 800 nm. Subsequently, the UV spectrum was used to scan the mid concentration dilution and record the wavelength and absorbance.

1. Validation of the method

Validation was done in order to create a new, practical, affordable, and efficient method for the spectroscopic determination of Repaglinide. In order to evaluate the analyte's ruggedness, robustness, linearity, accuracy, and precision, the technique was the analytical procedure and the ICH guideline for the validation of analytical procedures.

a. Specificity

The spectrum of the isolated molecule repaglinide was used to assess the method's specificity.

b. Linearity

The ability of an analytical method to yield test results that are proportionate to the analyte concentration within a given range in samples is known as linearity. The linearity of measurement was assessed by analyzing various concentration of the isolated compound rapaglinide solution; calibration curves were constructed, and the suggested technique was evaluated by its correlation coefficient and intercept value calculated in the corresponding statistic study; for both the method, the Beer Lamber's concentration range was found to be 10-60 µg/ml.

c. Ruggedness study

By doing the study using two distinct concentrations and noting the corresponding absorbance, the robustness

of the approach was confirmed. By using the same equipment and a different analyst to perform assay 3 reading, the robustness of the procedures was evaluated.

d. Robustness study

The same process was used with a temperature change to ascertain robustness, and the outcome was compared to the identical approach that had been used previously.

e. Precision

The degree of dispersion (or proximity of agreement) between sequences of measurements obtained under specified conditions from different samplings of the same homogenous sample is reflected in the accuracy of an analytical technique. Three levels of precision might be considered: reproducibility (interday precision), intermediate (intraday precision), and repeatability.

- Intraday precision

Three analysis of solution containing 15 µg/ml of repaglinide were performed on the same day, and the percentage R.S.D. was calculated.

- Interday precision

Repaglinide solution containing 15ug/ml were analyzed on three different successive days and % R.S.D. was calculated.

- Repeatability

The experiment's method precision was achieved by making the repaglinide standard solution (15 µg/ml) three times and analyzing it using the suggested procedure.

Fourier transmission intra-Red Spectroscopy

The FT-IR spectrum of using an FT-IR spectrophotometer, the drug and excipient combination was measured using the KBr pellet method over a range of 4000 to 400 cm-1. The 100 mg of spectroscopic grade KBr that had been dried under an infrared light were combined with 1 mg of each drug and drug plus polymers to create the KBr disc. To create a disc, the drug and KBr were combined and compressed using hydraulic pressure. This disc was put into the FT-IR detector. A recording of the infrared spectrum was made between 4000 and 400 cm-1.

Result and Discussion

A UV-visible spectrophotometer (1700-Shimadz) is used to measure a substance's absorption maximum, or lambda max. It was discovered that the Repaglinide's lambda max was 293.0 nm. This was comfortably inside medication specification's bounds. Since the wavelength difference was within the allowed +5 limit, was acceptable.

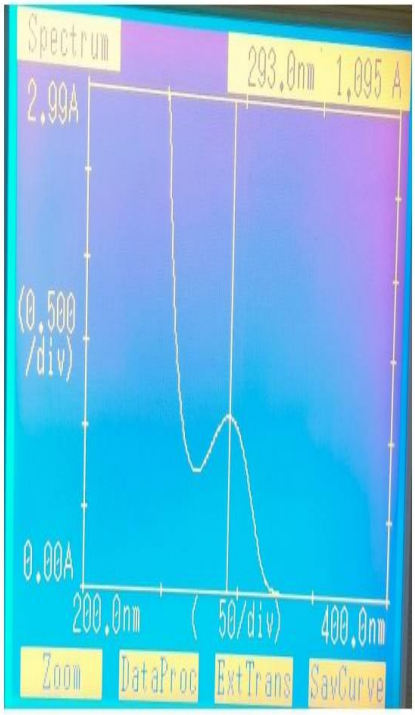

Figure 1 : Lambda max of Repaglinide

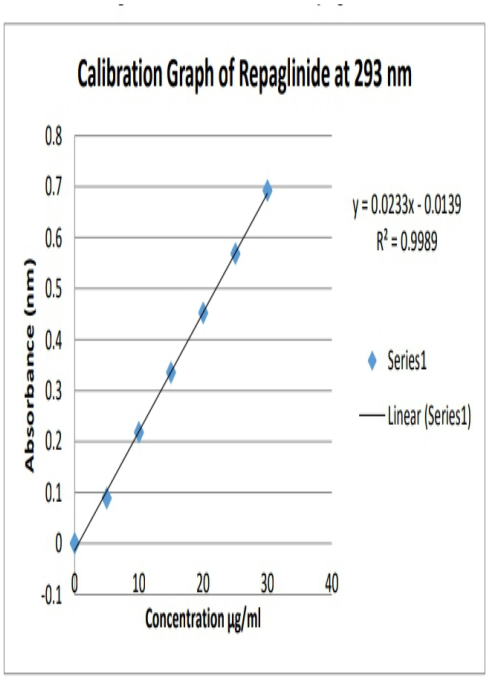

Figure 2 : Calibration curve of Repaglinide

By analyzing the calibration curve using least squares linear regression, the suggested method's linearity was demonstrated. Plotting absorbance against Repaglinide concentration in the range of 5-30 µg/mL yielded the Repaglinide regression equation. For the medication, a six-point calibration curve was obtained in the concentration range of 5-30 µg/ML. in the concentration range under research, the drug's reaction was determined to be linear, and the linear regression equation was y==0.023-0.013, with a correlation coefficient of R2= 0.998.

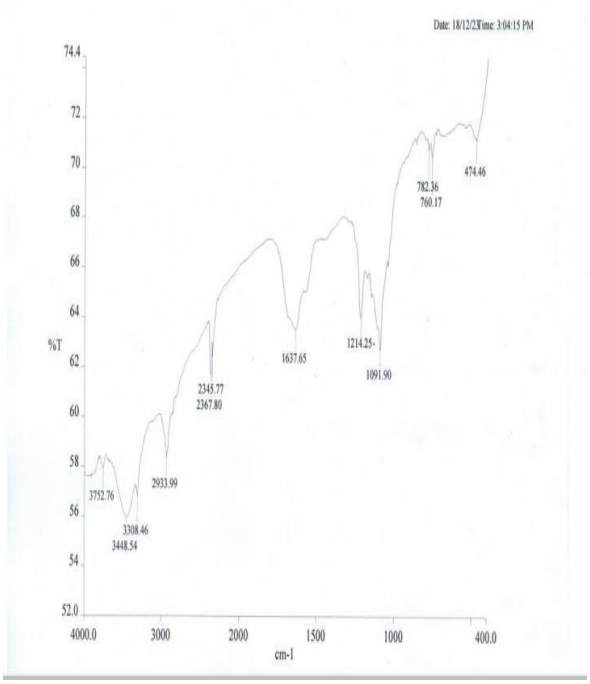

Figure 3 :FTIR graph of Repaglinide

When doing FTIR studies on drugs, the analytical protocol is adhered to. The compatibility of medicinal excipients is examined using FTIR. The FITR Repaglinide analysis is displayed in figure 1.

Differential Scanning Calorimetric Studies : DSC was used to determine the melting point of repaglinide. Repaglinde melting point is verified by a robust endotherm in the DSC thermogram at 126 to 128 °C.

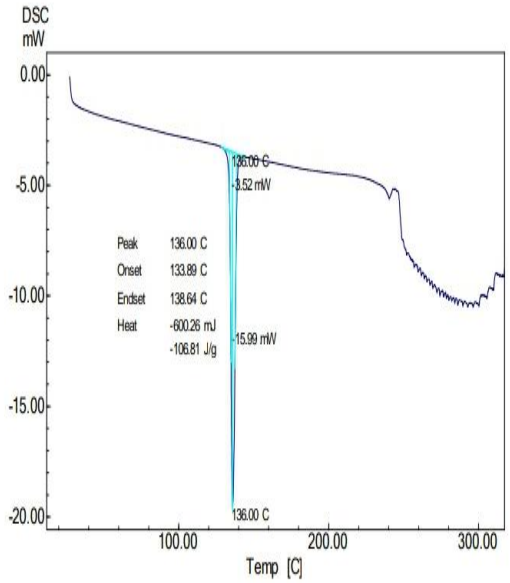

Figure 4 : DSC thermogram of Repaglinide

Powder X-ray Diffraction Studies

The crystallinity of the processed and raw Rp samples was investigated by P-XRD (Bruker, Germany). Prior to being scanned at a rate of 102T/min at wavelength of 1.542 over the range of 5-500 at 2T , each sample was put into a silicon well.

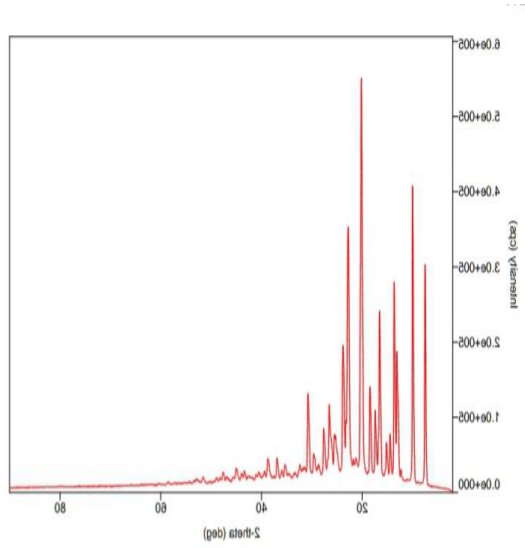

Figure 5 : X ray Diffraction studies of Repaglinide

Application of UV-visible spectroscopy

- Detection of impurities
  UV absorption spectroscopy is one of the best methods for determination of impurity in organic molecules.
- Quantitative analysis
  UV absorption spectroscopy can be used for the quantitative determination of compounds that absorb UV radiation
- Qualitative analysis
  UV absorption spectroscopy can characterize those types of compounds which absorbs UV radiation. Identification is done by comparing the changes can be observed.

SUMMERY AND CONCLUSION

Type ll diabetes was the subject of the current investigation. Repaglinide is a medication with low bioavailability and poor water solubility. Increasing drug dissolution and enhancing patient compliance were the goals. The thin film hydration process is an efficient way to manufacture repaglinide with lower particle sizes. The subject of the current study was type ll Diabetes Mellitus. Repaglinide is not particularly water soluble and has a limited bioavailability. Enhancing patient compliance and boosting medication dissolution were the objectives. The thin film hydration method can be used to effectively formulate Repaglinide with a smaller particle size. This study's FTIR analysis indicates the existence of a strong Repaglinide peak.

An X-ray dip at 102 T /min at a wavelength of 1.542 spanning the range of 5-500 at 2 T and a DSC A strong

endotherm at 126 to 128°C are used to confirm the melting temperature of repaglinide. The maximum dose of repaglinide has been determined to be 242.

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