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CHARACTERIZATION AND SOLUBILITY STUDY OF THE DIABETES TYPE 2 DRUG REPAGLINIDE IN DIFFERENT SOLVENTS

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ABSTRACT:

Repaglinide (RPGD) is prescribed for the treatment of type 2 diabetes mellitus. It has excellent therapeutic potential due to its potency as a molecule; however, its variable bioavailability and low solubility in water constitute a limitation. For the purpose of characterizing RPGD, the methodology employs a variety of techniques, including melting point, solubility analysis in various solvents, UV spectrum, “Fourier transformed infrared spectroscopy (FTIR)”, and “differential scanning calorimetric (DSC)” analysis. In results, the melting point of RPGD was measured to be between 136 and 138 degrees Celsius. Tween 20, Oleic acid and methanol has higher solubility of repaglinide. Nevertheless, the methodologies employed to improve the solubility of RPGD could potentially be applied to other medications of a similar nature (BCS class-II). In conclusion, this study utilized a formulation strategies-based approach to increase the substance's weakly soluble in water, concentration RPGD.

Keywords: Repaglinide, solubility, drug, diabetes type 2

INTRODUCTION

Increasing the mobility of medications that are not easily soluble in water has been one of the greatest challenging elements of contemporary drug development. Low solubility in waters affects 35–40% of all newly discovered chemicals at the moment (Ansari, 2019). For formulation scientists, solubility is the most crucial factor among those that limit the bioavailability of oral products and impede drug development (Bhalani et al., 2022). The pharmaceutical industry conducts preformulation studies to characterize the drug material before proceeding to formulate a dosage form that is both pharmacologically effective and safe for human use (Gupta et al., 2018). Understanding how a medication dissolves in water and other biological fluids is crucial for predicting how it will be released from a certain dose form (Wen et al., 2015).

Many pharmaceutical companies are developing drug libraries in the millions owing to strategies for discovering medicines that incorporate genetics, robotics, reduction, high-volume evaluation, and computational chemistry knowledge. Despite efforts to improve the pharmacological activities of NCE during the drug discovery process, the drug's basic physicochemical qualities, such as its solubility, always suffer as a result (Patel et al., 2023). More and more drug compounds with low aqueous solubility are showing up in the R&D pipelines of drug companies with an emphasis on discovery. In spite of the fact that compounds formed by the aforementioned methods have excellent permeability properties in a variety of tissues, they may result in inadequate and variable global exposure, a delayed breakdown in biological fluids, and, eventually, less-than-ideal patient effectiveness, especially when taken orally. Poor solubility concerns and consequently reduced bioavailability affect not only the NCE but also several already available medicines in various formulations (Dixit et al., 2023).

T The ability of a material to become dissolved in a solution of solvent is referred to as "dissolving" at specific temperature and pressure conditions. Improving the solubility of a drug that is

inadequately soluble in water is among the most difficult aspects of contemporary drug development. Repaglinide (RPG) is a medication used for managing diabetes type 2 (Desai et al., 2023).

MATERIAL AND METHOD

UV spectrum of Repaglinide- The ultraviolet (UV)-visible spectroscopy has become the most important analytical instrument in the modern workplace.

Fourier transmission infrared (FT-IR) spectroscopy- The infrared spectra of the drug sample were acquired using a potassium bromide (KBr) pellet as the medium, with a resolution of 4 cm^{-1}, covering the wavelength range from 4000 to 400 cm^{-1}. The quantification of the major peaks was conducted using a Shimadzu FTIR-8400S spectrophotometer, Japan.

Melting point determination-The determination of the melting point is a vital physical characteristic utilized in the identification of the active pharmaceutical substance. The investigation of the melting point of Repaglinide was carried out utilizing the Veego digital melting point equipment, namely the VMP-DS model.

Solubility studies of Repaglinide by using standard curves-

Various pH buffers were made according to the guidelines provided by the Indian Pharmacopoeia. These buffers included acetate buffer with a pH of 1.2, phosphate buffer with a pH of 6.8, and phosphate buffer with a pH of 7.2:. Furthermore, experiments were carried out in a solution of "0.1 N hydrochloric acid (HCl)" and in pure water. The drug was introduced in surplus to a 10mL medium in distinct vessels that were placed in an ultrasonicator for a duration of 30 minutes. :Subsequently, the vessels were agitated for a period of 24 hours in a hot tub containing water kept at an appropriate temperature of 37 ± 0.5°C:. The suspension underwent filtration utilizing No. 40 Whatman filter paper. The dissolved drug content of itraconazole was measured using a spectrophotometric technique at a wavelength of 260 nm.

RESULT AND DISCUSSION

Authentication Study

Characterization of drug was carried out by Melting point method, IR spectra, UV spectrum and DSC Solubility.

U V Spectroscopy

After dispersing 10 milligrams of RPGD in a hundred milliliter of USP phosphate-buffered water with an acidity level of 1.2, a usual solution that contained 1000 mcg/mL was created and imaged between 400 and 200 nm in spectrum. At 243 nm, the highest possible absorbing was recorded, which corresponds to the reference UV spectrum. In Figure 1, the UV spectrum of purified RPGD is displayed.

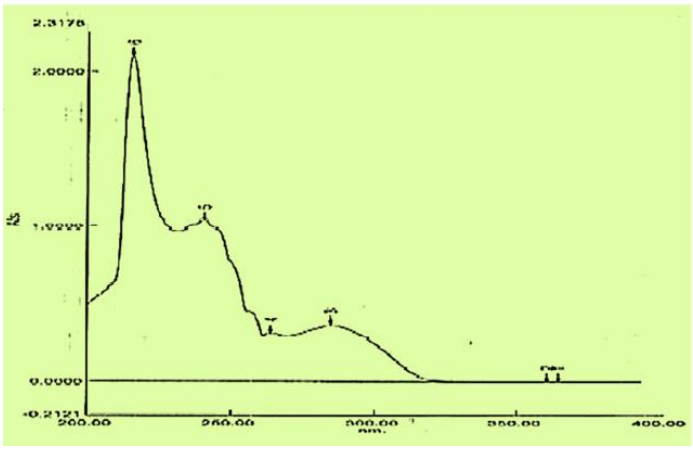

Figure 1: UV spectra of pure Repaglinide

FT-IR Spectrum

The **FT-IR** spectrum of a solid potassium bromide mixture was measured. Repaglinide's IR spectrum is depicted in Figure 4.2. Peaks observed are described in Table 8.

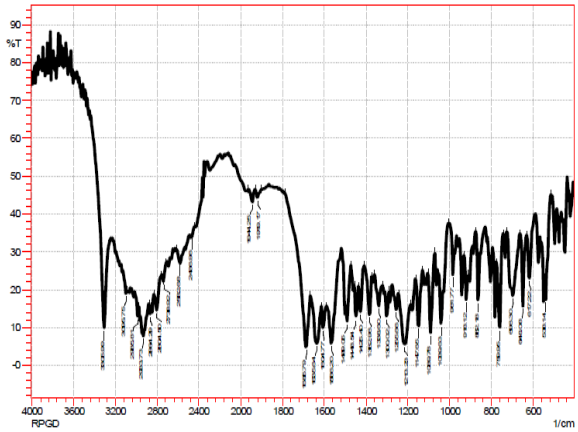

Figure 2: FT-IR spectrum of pure Repaglinide

In the spectrum produced for the received drug sample, the reported peaks of purified Repaglinide remained unaltered. This verifies that the obtained substance was not degraded and is therefore suitable for formulation. The peaks observed in the official spectrum and the spectrum of the received substance are compared in Table 1.

Table 1: "Principal peak and chemical group present in IR spectra of Repaglinide."

Observed Peaks (cm-1)	Official Peaks (cm-1)	Interpretation of Chemical group	Intensity
3310.95	3308.57	absorption of NH group	Strong
2935.90	2934.70	CH stretching	Strong

1688.75, 1635.71	1705, 1640.56	C=O Stretching	Strong
1554.69, 1491.04	1570.20, 1490.08	Aromatic Medium,	Strong
1605.99	1605.79	N-H Bending	Medium

Differential Scanning Calorimetry (DSC)

"Differential scanning calorimetry is often employed as the thermal analysis technique of preference in the pharmaceutical industry due to its capacity to provide comprehensive information on the physical and energetic characteristics of a substance. As depicted in Figure 2, RPGD has been demonstrated by differential scanning calorimetry at a scanning rate of 100C/min; it exhibits an abrupt melting endothermic peak at 134.03^0C" relative to its melting point. The reported maximum temperature ranged from 132 to 134^0C.

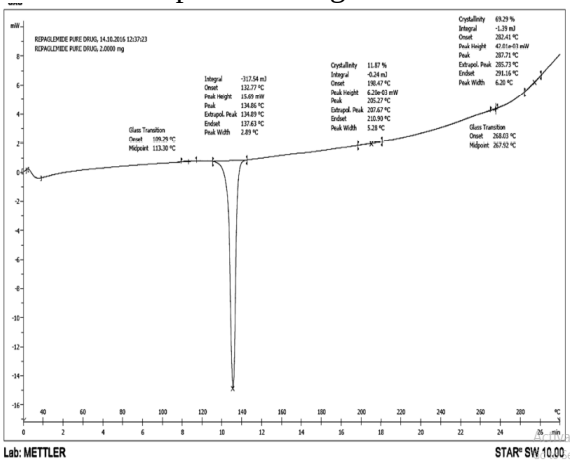

Figure 3: DSC spectrum of pure Repaglinide.

Melting Point Determination

Using a capillary tube, the drug's melting point was determined. In the laboratory, the melting point of RPGD was measured to be between 136 and 138 degrees Celsius. It was consistent with the "melting point reported in the literature (USP National Formulary, 2007)".

` Solubility determination

The solubility of RPGD was investigated using the saturation solubility methodology in various non-volatile liquids and pH solutions. The solubility data are displayed in Table 4.5 and Figure 4.7. y = 0.0795x + 0.0386 R^2 = 0.9887

Table 2: Solubility study of repaglinide in different solvents

Sr. No.	Solution	Concentration (mg/mL)
1.	Water	"0.0287 ± 0.0020"
2.	"pH 1.2 buffer"	"0.0535 ± 0.0011"
3.	"pH 3.0 buffer"	"0.0453 ± 0.0009"
4.	"pH 5.0 buffer"	"0.0352 ± 0.0010"
5.	"pH 7.0 buffer"	"0.0224 ± 0.0031"
6.	"pH 9.0 buffer"	"0.5782 ± 0.0262"
7.	Methanol	17 ± 1.62
8.	Tween-80	42.31 ± 2.14
9.	Propylene glycol	3.2 ± 0.87
10.	PEG 400	6.81 ± 0.63
11.	Castor oil	9.4 ± 0.92
12.	Oleic acid	23.11 ± 2.03

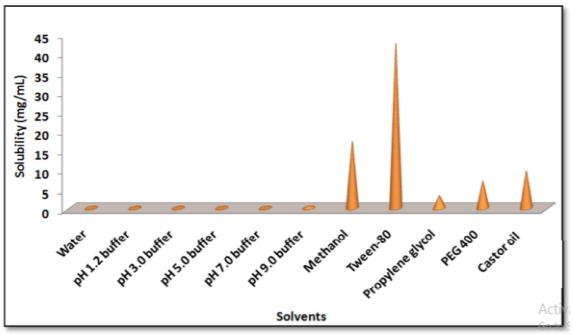

Figure 4: Solubility of repaglinide in different solvents.

CONCLUSION:

In conclusion, this study utilized a formulation strategies-based approach in order to increase a medication's relatively little soluble in water RPGD. Improving the solubility of a drug that is inadequately soluble in water is among the most difficult aspects of contemporary drug development. . This is primarily due to their enhanced solubility, cost-effectiveness, and industrial applicability".

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