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Preformulation Study of Propranolol Hydrochloride: A Foundation for Formulation Development

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Abstract. This preformulation study aimed to characterize the chemical and physical properties of propranolol hydrochloride, a commonly used beta-blocker drug, in order to provide essential information for the formulation design and development process. A key aspect of the study involved the preparation of a standard calibration curve using a methanol solution, which exhibited a high coefficient of determination (r^2) value exceeding 0.996, indicating a strong correlation between measured concentrations and absorbance values. The calibration curve demonstrated excellent adherence to the Beer-Lambert law within the conc. range of 4-20 mcg/ml, suggesting the reliability and suitability of the developed analytical approach for accurately quantifying propranolol hydrochloride in this range. The utilization of phosphate buffer of pH 6.8 as the medium for spectrophotometric measurements further supported the method's accuracy within the conc. range of 10-50 µg/ml. However, it is important to conduct compatibility studies between the drug substance and excipients to evaluate potential interactions that could impact product stability or performance. Overall, this preformulation study provides a solid foundation for the formulation development of propranolol hydrochloride, offering a well-established calibration curve, a robust quantification method, and highlighting the importance of excipient compatibility assessment.

Keywords: Preformulation study; Propranolol hydrochloride; Formulation development; Calibration curve; Excipient compatibility

INTRODUCTION

Cardiovascular diseases, including hypertension, angina pectoris, and arrhythmias, pose significant health challenges worldwide[1]. Propranolol, a non-selective beta-adrenergic antagonist, has emerged as a cornerstone medication in the treatment of these conditions. However, the limitations associated with its immediate-release formulations, such as frequent dosing requirements and fluctuations in drug concentrations, have prompted the development of sustained-release formulations[2].

Sustained-release formulations offer a promising solution by providing controlled and prolonged drug release, allowing for reduced dosing frequency while maintaining therapeutic drug levels within the desired range[3]. This approach not only addresses patient non-compliance but also enhances treatment efficacy and minimizes the occurrence of side effects[4].

In recent ages, there has been a rising interest in formulating propranolol into sustained-release tablets to overcome the limitations of immediate-release formulations[5]. The development of such formulations requires a systematic approach, encompassing the careful selection of excipients and formulation techniques to achieve the desired drug release profile[6].

This paper aims to explore the significance of sustained-release formulations for propranolol in cardiovascular therapy[7]. It will discuss the advantages of sustained-release formulations, including improved patient compliance, reduced side effects, and enhanced therapeutic efficacy[8]. Furthermore, it will delve into the critical considerations involved in formulating sustained-release tablets, such as excipient selection and formulation techniques[9].

By developing a well-designed sustained-release tablet formulation for propranolol, healthcare providers can offer patients a more convenient and effective treatment option, optimizing therapeutic outcomes and improving overall cardiovascular management[10].

MATERIALS AND METHODS:

Materials:

Propranolol hydrochloride (API): Pharmaceutical grade propranolol hydrochloride was obtained from a reputable supplier.

Excipients: Various excipients were selected based on their compatibility with propranolol and their ability to

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achieve sustained drug release. These may include hydrophilic polymers (e.g., hydroxypropyl methylcellulose, hydroxypropyl cellulose), release modifiers, diluents (e.g., lactose, microcrystalline cellulose), lubricants (e.g., magnesium stearate), and other necessary additives.

PREFORMULATION STUDY

Preformulation investigations, which characterise the physical and chemical characteristics of a medicinal material, are a crucial element of drug development. These studies offer critical information for the formulation design and development process. Propranolol hydrochloride is a commonly used drug in the class of beta-blockers, primarily used to treat hypertension, angina, and other cardiovascular conditions[11-13]. Here is an overview of the preformulation studies that could be conducted for propranolol hydrochloride:

Propranolol hydrochloride standard calibration curve preparation:

A calibration curve was constructed using a methanol solution to determine the concentration of Propranolol hydrochloride. The measurements were performed at a wavelength of 289 nm. The resulting calibration curve exhibited a high coefficient of determination (r2) value exceeding 0.996, indicating a solid correlation between the measured concentrations and the absorbance values. Additionally, the standard deviation (SD) was found to be low, indicating good precision in the measurements[14-15].

This analytical approach proves to be excellent for quantifying Propranolol hydrochloride concentrations within the range of 4-20 mcg/ml. The Beer-Lambert law, which explains the connection between the amount of a material that may be absorbed by a solution and the amount of that substance that is present in the solution, was found to be applicable in this range. The measured data, including the concentration values and corresponding absorbance values, can be found in Table 1. The relationship between concentration and absorbance is visually depicted in Figure 1.

ESTABLISHING A ROBUST CALIBRATION CURVE FOR PROPRANOLOL HYDROCHLORIDE: METHOD DEVELOPMENT AND VALIDATION

Spectral measurement

The propranolol HCl reference solution was subjected to spectral measurement using a UV-visible spectrophotometer. The scanning was performed in the wavelength range of 400 to 200 nm[16].

1.The Conventional Graphing Method

In this study, a spectrophotometric method was utilized for the estimation of Propranolol hydrochloride. The method involved measuring the absorbance of the drug at 290 nm in a phosphate buffer solution with a pH of 6.8[17].

Standard solutions were made by dissolving 100 mg of Propranolol Hydrochloride in 100 ml of phosphate buffer at pH 6.8 in a volumetric flask. The concentration of the resulting solution was adjusted to 1 mg/ml by diluting it further with phosphate buffer of pH 6.8.

A working stock solution with a concentration of 100 g/ml was obtained by diluting 10 ml of the prepared solution to 100 ml in phosphate buffer. Next, phosphate buffer with a pH of 6.8 was used to serially dilute the working stock solution to provide a range of concentrations from 10 to 50 g/ml.

Applying a Shimadzu 1400 double beam UV-visible spectrophotometer to the analysis, the dilutions were scanned between 400 and 200 nm to find the drug's max. As a blank for absorbance measurements at this wavelength, phosphate buffer at pH 6.8 was used to record the values of the dilutions.

Absorbance measurements were correlated with the concentrations of propranolol hydrochloride. The concentrations of Propranolol hydrochloride were plotted against the absorbance readings, yielding a calibration curve. Beer-law Lambert's was shown to be followed by the procedure between 10 and 50 ng/ml[18, 19].

2.The making of a phosphate buffer with a pH of 6.8

To prepare the pH 6.8 phosphate buffer solution, follow these steps:

1. Take out 50 millilitres of the potassium dihydrogen phosphate solution that has a concentration of 0.2 M.
2. Transfer the measured volume of the potassium dihydrogen phosphate solution into a 200 ml standard volumetric flask.
3. Add 22.4 ml of 0.2 M sodium hydroxide solution to the same flask containing the potassium dihydrogen phosphate solution.
4. After adding the sodium hydroxide solution, the total volume in the flask will not be at the desired mark yet.
5. To reach the desired volume, add distilled water to the flask in a methodical manner until the liquid level reaches the mark for 200 millilitres..
6. Mix the contents of the flask thoroughly to ensure homogeneity of the pH 6.8 phosphate buffer solution.

¬ Potassium dihydrogen phosphate, 0.2 M solution

To prepare a 0.2 M solution of potassium dihydrogen phosphate, follow these steps:

1. Accurately weigh 27.22 grams of potassium dihydrogen phosphate.

2. Dissolve the weighed potassium dihydrogen phosphate in distilled water.
3. Transfer the dissolved potassium dihydrogen phosphate into a 1000 ml volumetric flask.
4. Add distilled water to the flask gradually while swirling to make up the volume to 1000 ml.
5. Mix the solution thoroughly to ensure complete dissolution and homogeneity.

¬ Sodium hydroxide 0.2 M solution

To prepare a 0.2 M solution of sodium hydroxide, follow these steps:

1. Accurately weigh 8 grams of sodium hydroxide.
2. Dissolve the weighed sodium hydroxide in distilled water.
3. Transfer the dissolved sodium hydroxide into a 1000 ml volumetric flask.
4. Add distilled water to the flask gradually while swirling to make up the volume to 1000 ml.
5. Mix the solution thoroughly to ensure complete dissolution and homogeneity.

By following these steps, you will obtain a 0.2 M solution of sodium hydroxide in a 1000 ml volumetric flask.

RESULT:

Table 1: Calibration curve of Propranolol hydrochloride

S. No.	Concentration (µg/ml)	Absorbance (nm)
1	4	0.146
2	8	0.264
3	12	0.407
4	16	0.508
5	20	0.630

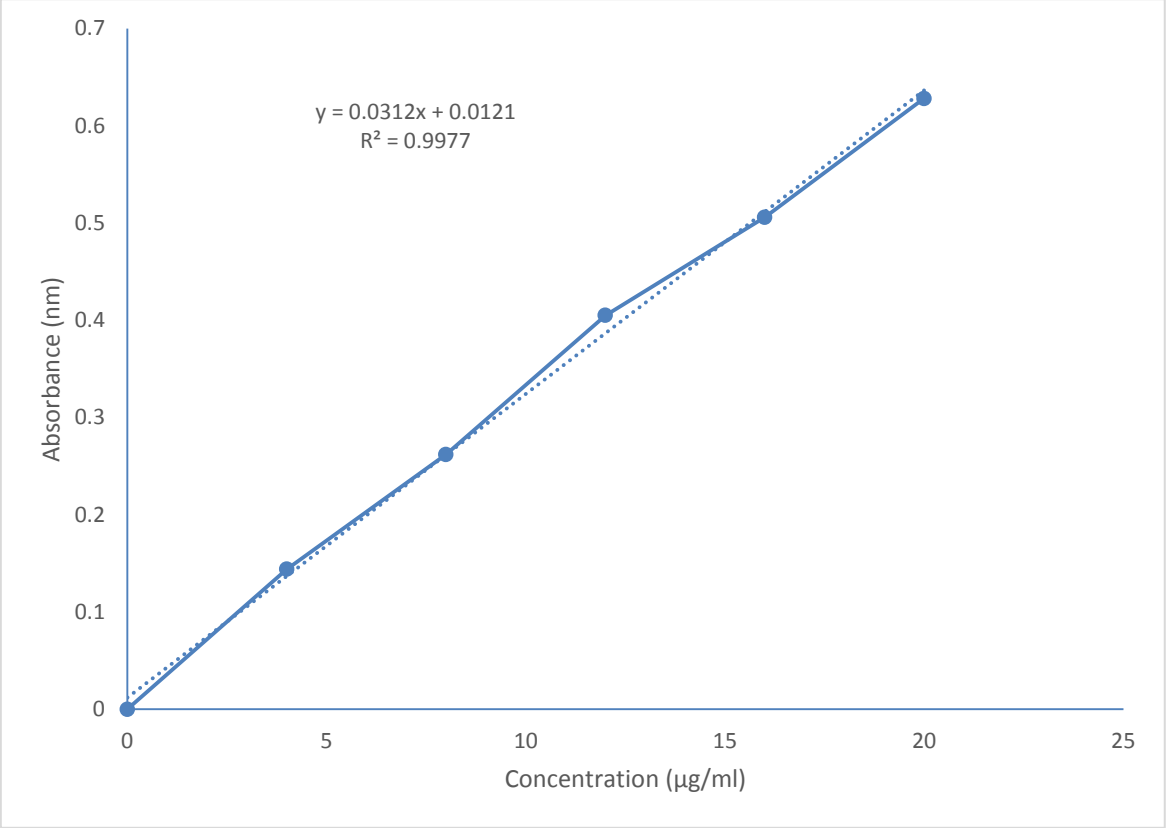

Fig. 1: Calibration curve of Propranolol hydrochloride

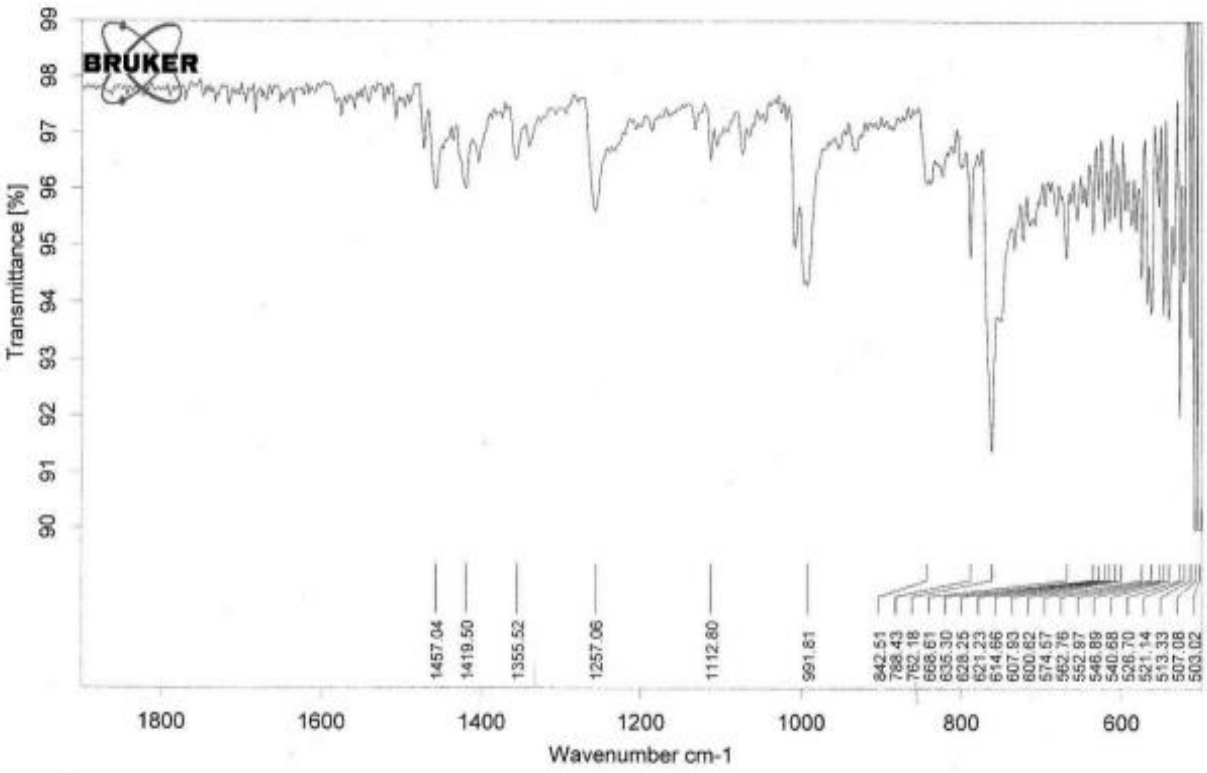

Fig. 2: FT-IR Spectrum of Propranolol hydrochloride

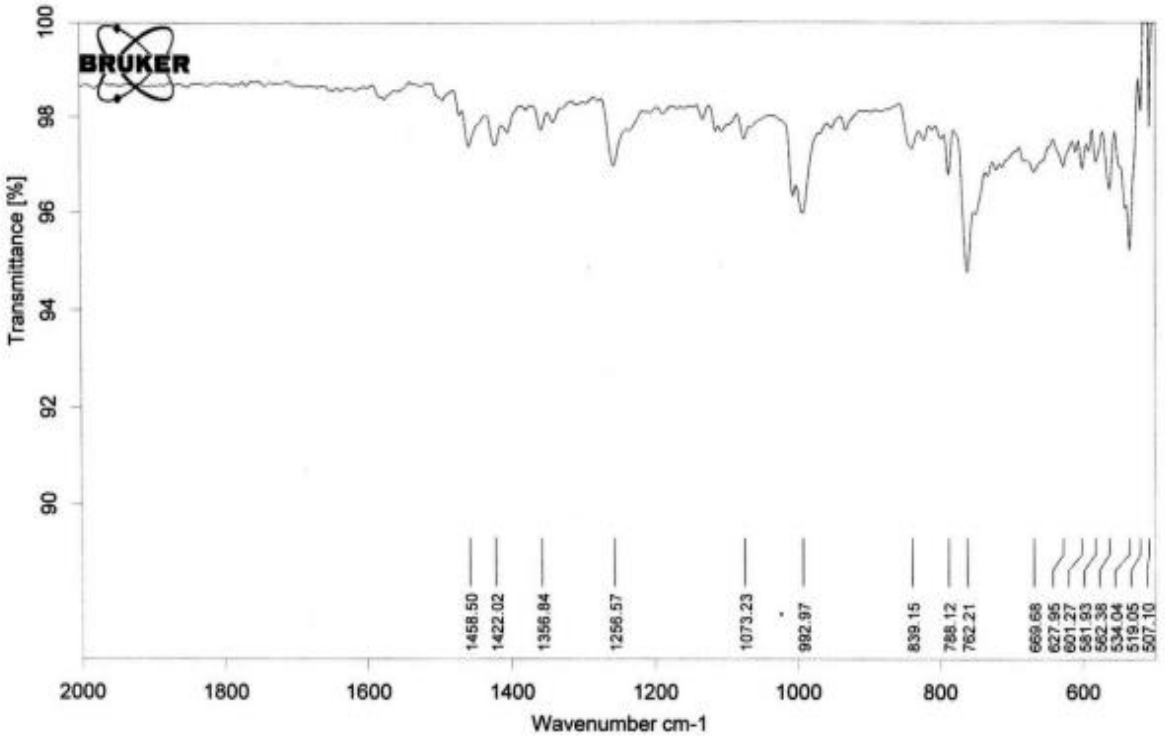

Fig. 3: FT-IR Spectrum of Propranolol hydrochloride + Lactose DCL 11

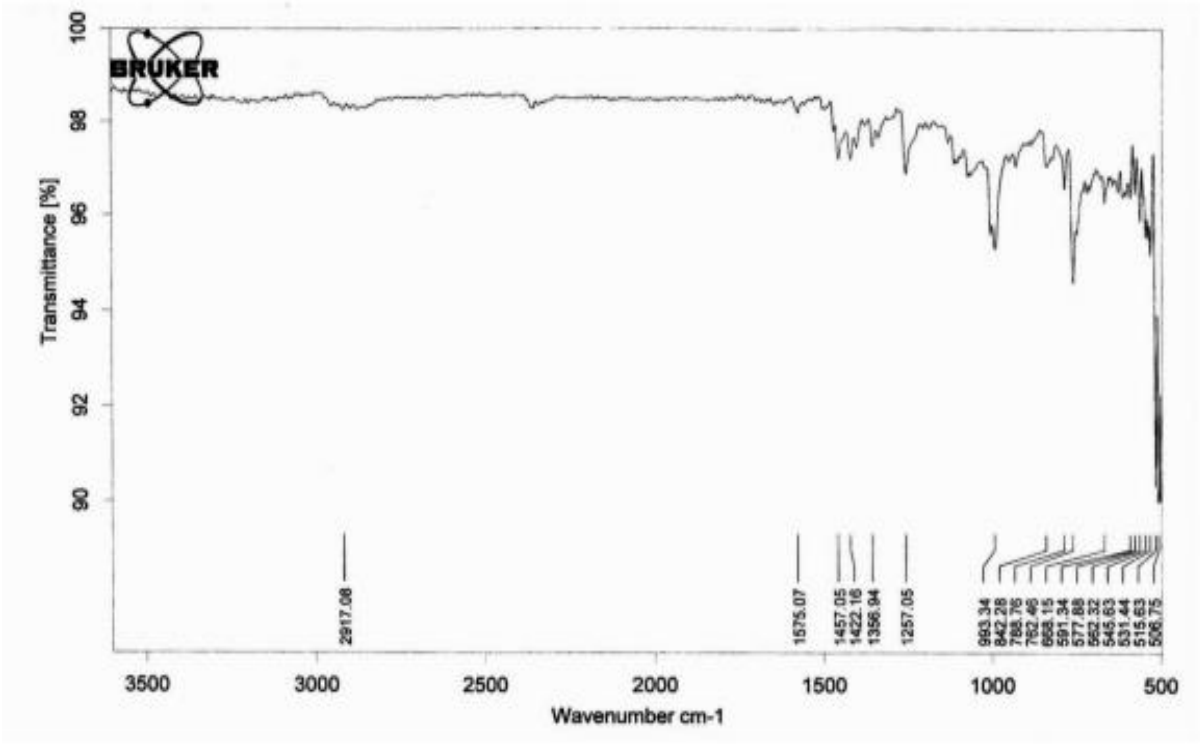

Fig. 4: FT-IR Spectrum of Propranolol hydrochloride + HPMC K4M

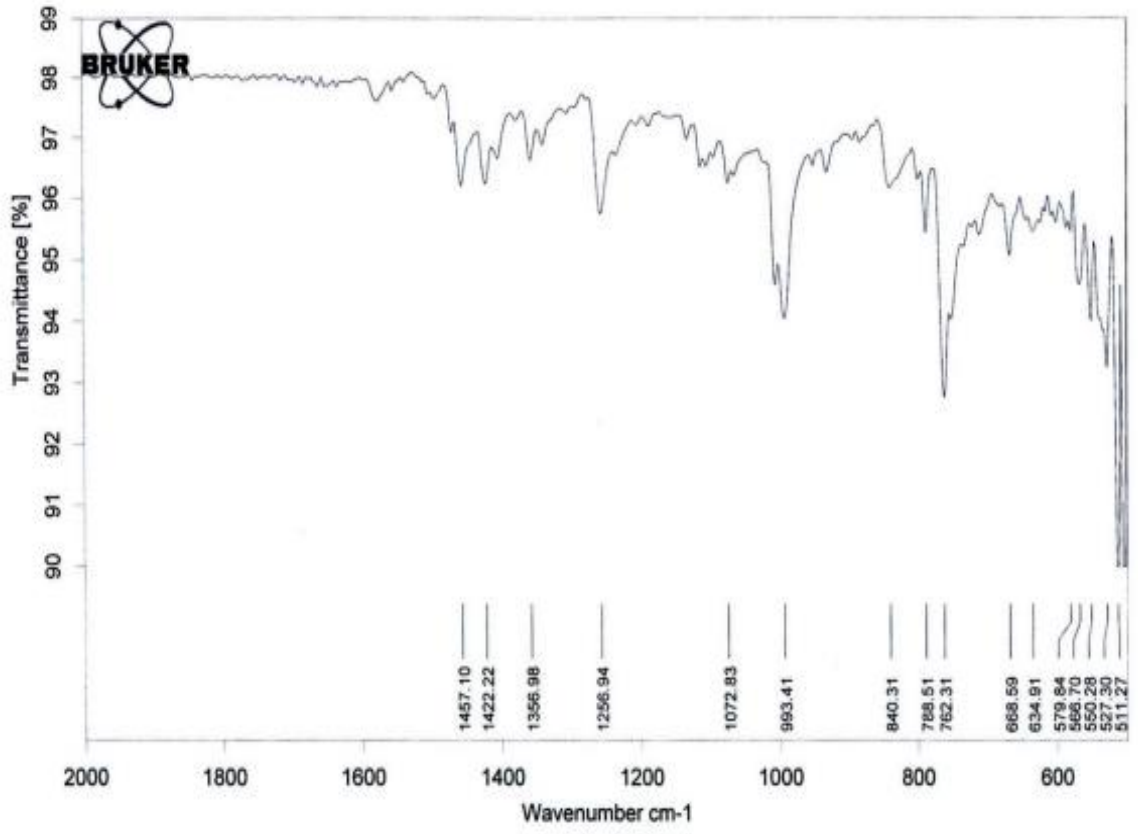

Fig. 5: FT-IR Spectrum of Propranolol hydrochloride + HPMC K100

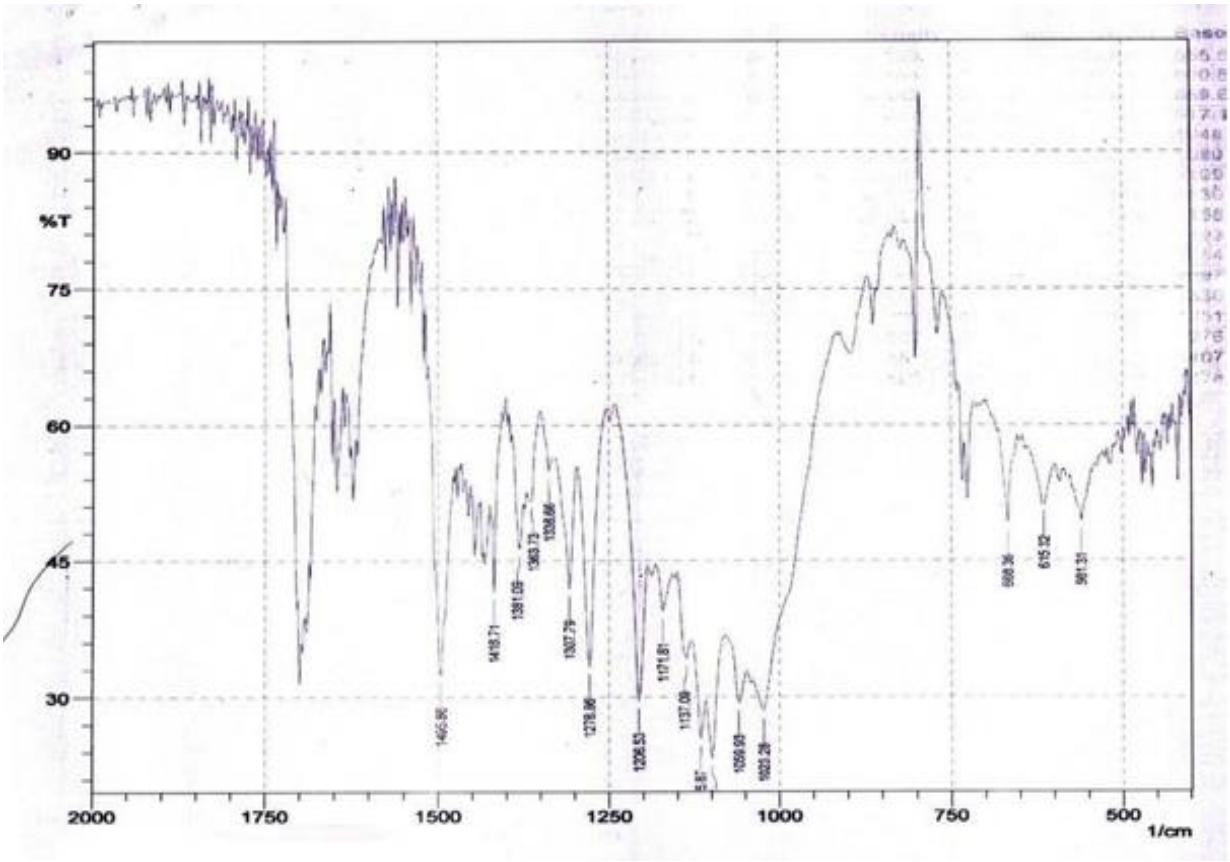

Fig. 6: FT- IR Spectrum of Propranolol hydrochloride + MCC pH 102

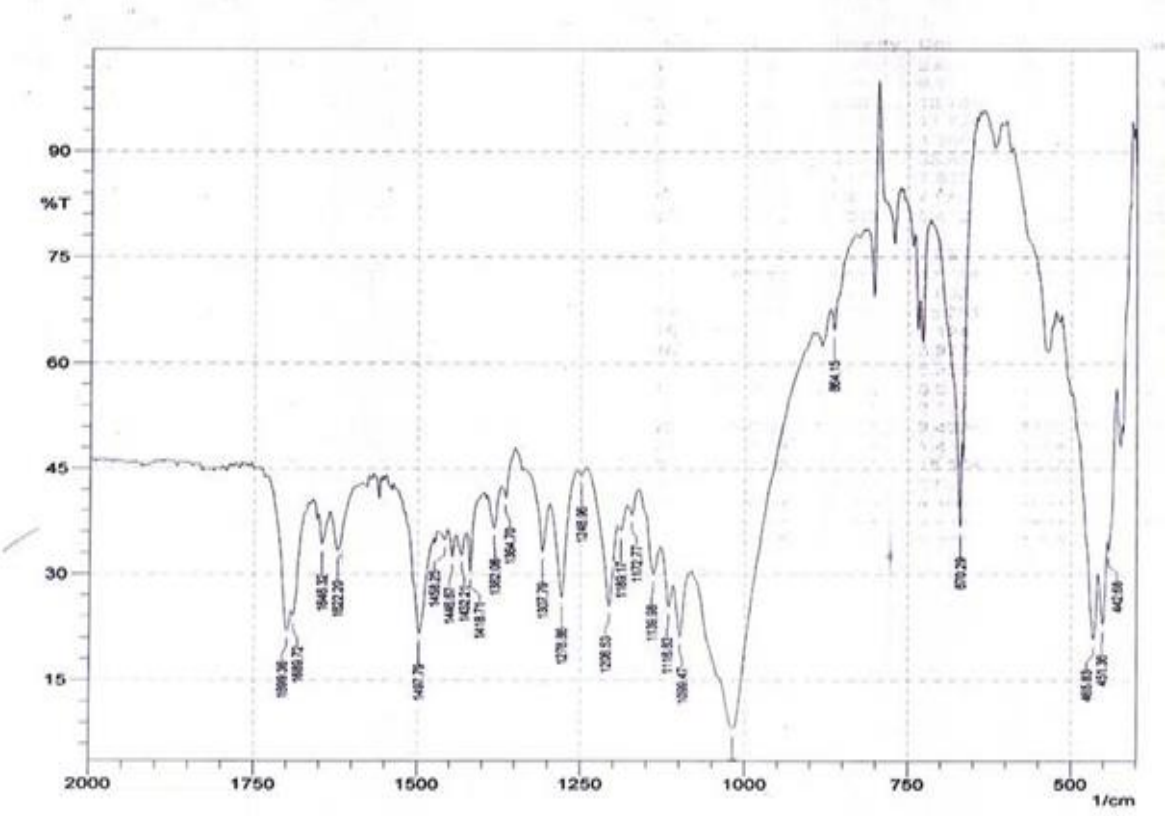

Fig. 7: FT-IR Spectrum of Propranolol hydrochloride + HPMC K100

DISCUSSION:

In this study, a preformulation study was conducted to characterize the physical and chemical properties of propranolol hydrochloride, a commonly used beta-blocker drug. The aim was to gather essential information for the formulation design and development process.

One important aspect of the preformulation study was the preparation of a standard calibration curve for propranolol hydrochloride using a methanol solution. The calibration curve exhibited a high coefficient of determination (r2) value exceeding 0.996, indicating a strong correlation between the measured concentrations and the absorbance values. The low standard deviation (SD) observed in the measurements further supports the reliability of the calibration curve.

The excellent performance of the calibration curve in following the Beer-Lambert law within the concentration range of 4-20 mcg/ml is noteworthy. This suggests that the developed analytical approach is suitable for accurately quantifying the concentration of propranolol hydrochloride in this range. The reliability and precision of this method make it a valuable tool for future drug analysis and formulation development.

The data presented in Table 1 and Figure 1 provide a comprehensive overview of the measured concentrations and corresponding absorbance values. These visual and numerical representations of the calibration curve facilitate easy interpretation and enable researchers to determine the concentration of propranolol hydrochloride in an unknown sample by comparing its absorbance to the calibration curve.

Furthermore, the use of phosphate buffer of pH 6.8 as the medium for the spectrophotometric measurements is a well-established approach. The method obeys Beer-Lambert's law within the concentration range of 10-50 µg/ml, demonstrating its suitability for accurate quantification of propranolol hydrochloride.

The inclusion of excipients in the formulation design is crucial to achieving sustained drug release and maintaining stability. However, information regarding the specific excipients selected and their compatibility with propranolol hydrochloride was not provided in this section. To ensure the success of the formulation process, it is essential to conduct compatibility studies between the drug substance and excipients to evaluate any potential interactions that could adversely affect product stability or performance.

Overall, the preformulation study conducted in this research provides a solid foundation for the formulation development of propranolol hydrochloride. The established calibration curve and method for quantifying the drug's concentration, along with the consideration of excipient compatibility, lay the groundwork for the subsequent formulation design and development steps in creating a stable and effective pharmaceutical product.

CONCLUSION

The preformulation study on propranolol hydrochloride has provided important information for the formulation design and development process. The calibration curve exhibited a strong correlation between measured concentrations and absorbance values, indicating its reliability and precision. The method is suitable for accurately quantifying propranolol hydrochloride within a specific concentration range. Compatibility studies with excipients are crucial for ensuring product stability and performance. Overall, the study has laid a solid foundation for formulation development, providing a calibration curve and method for quantification, as well as emphasizing the need for excipient compatibility assessment.

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