Research Article

Preformulation and compatibility study of Propranolol hydrochloride and herbal excipients

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Abstract

The objective of the present research work was preformulation study and physicochemical compatibility between synthetic drugs and their herbal excipients for advanced drug delivery. Propranolol HCl drug were selected as water soluble model drug, and where tamrind seed gum (TSG) and fenugreek seed gum (FSG) used as excipients. The preformulation study and physicochemical compatibility between synthetic drugs and herbal excipients studies were done by UV (Ultra-Violet Spectroscopy), Fourier transform infrared spectroscopy (FTIR), Thin layer chromatography (TLC) High Performance Liquid Chromatography (HPLC) and Differential Scanning Calorimetry (DSC). FTIR spectrophotometric graphs showed that there was no significant alteration occurred in position of functional groups in pure drugs and their herbal excipients with respect to their physical mixtures, represented that the characteristic peaks of drug appeared which showing that drug and their excipients was present as a crystalline form as well. The R_f values of the physical mixtures obtained from TLC study on the 0th and 30th day were approximately similar to the R_f values of the pure drug and herbal excipients. All of the experimental results and retention factor clearly validated that the synthetic-herbal drug combinations with pharmaceutical excipients are compatible with each other and can be utilized for successful development of different dosage formulations.

Keywords: Compatibility study, TLC, propranolol, Tamarind, Fenugreek

Introduction

Evaluation of preformulation and drug-drug-excipients compatibility is very vital part to recognize dosage formulation, and is stability as well as its reproducibility with ensured therapeutic efficacy (Shukla et al., 2024). Although supportive materials or excipients selected for dosage formulations have no pharmacological role, that inert in nature (Shukla et al., 2017). But the excipients may contribute in physical and chemical interface and produce serious degradation of active pharmaceutical ingredients with decrease dissolution rate and non uniformity of dose (Shukla et al., 2012). Over the decade, various methods have been developed to identify drug excipients compatibility. It's very essential to conduct such studies as a part of formulation development process (Garg et al., 2018; Khambete et al., 2021). Numerous sustained and controlled formulations have been developed for the increase patient acceptability, reduced frequency of dosing and reduced side effects (Garg et al., 2018; Khambete et al., 2021). These are formulation has been developed by many researchers with using natural polymers in place of synthetic polymers. Therefore, we were selected two model of drug one of water soluble propranolol HCl drug for the development of sustained release formulation with natural gum fenugreek and tamarind the objective of the present research work preformulation study, evaluating physicochemical compatibility between synthetic drugs and herbal excipients for advanced drug delivery. Propranolol drug were selected as model drug, and where tamrind seed gum (TSG) and fenugreek seed gum (FSG) as excipients (Garg et al., 2018, Khambete et al., 2021). These both of natural gum tamrind seed gum (TSG) and fenugreek seed gum

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respectively, traditionally both of gum has been used for treatment of diseases like as diabetic, hypertension, anti-obesity etc. Major the selection of these gums is easily availability and can be used commercial in future (Kumar et al., 2018; Sharma et al., 2018; Mourya et al., 2014; Bishnoi et al., 2018; Dubey et al., 2022; Dubey et al., 2021; Tiwari et al., 2024; Mehta et al., 2018; Shukla et al., 2017).

Materials and Methods

The selected drugs, Propranolol HCl were received as gift samples from Hiral Labs Limited, Uttarakhand, India Ltd., and Alembic Pharmacetical Limited, Vadodara, India Ltd., respectively.

Preformulation study of Propranolol HCl

Prior to formulation development, preformulation studies were carried out to determine physical and chemical properties of the drugs. The nature of the selected drug highly affects the processing parameters like method of preparation, loading efficiency, compatibility and pharmacokinetic response of the formulation. Preformulation studies are essential protocols for development of safe, effective and stable dosage form. The drugs were studied for the following parameters

Physical observation

The colour and odour of Propranolol HCl drug powders were observed organoleptically.

UV Calibration curve of Propranolol HCl

Standard curve of Propranolol HCl (PRP)

Determination of absorption maxima (λ-max) of propranolol HCl

Standard solutions (10µg/ml) of Propranolol HCl were prepared, in 0.1 N HCl, phosphate buffer pH6.8, and phosphate buffer pH 7.4. The prepared solutions were scanned on UV spectrophotometer for the determination of absorption maxima (λ-max).

Preparation of standard plot of propranolol HCl in 0.1N HCl (pH1.2)

10 mg of Propranolol HCl was dissolved in 100 ml of 0.1 N HCl to get stock solution of 100 µg/ml concentration. This stock solution was suitably diluted to get graded solutions in the range of 10-80µg/ml. The absorbance of each solution was determined by using UV spectrophotometer at wavelength of 287 nm (λ-max).

Preparation of standard plot in phosphate buffer (pH 6.8)

10 mg of Propranolol HCl was dissolved in 100 ml of phosphate buffer of pH 6.8 to get stock solution of 100 µg/ml concentration. This stock solution was suitably diluted to get graded solutions in the range of 10-80µg/ml. The absorbance of each solution was determined by using UV spectrophotometer at wavelength of 288 nm (λ-max).

Preparation of standard plot in phosphate buffer (pH 7.4)

10 mg of Propranolol HCl was dissolved in 100 ml of phosphate buffer of pH 7.4 to get stock solution of 100 µg/ml concentration. This stock solution was suitably diluted to get graded solutions in the range of 10-80µg/ml. The absorbance of each solution was determined by using UV spectrophotometer at wavelength of 288 nm (λ-max).

Determination of solubility

Solubility of Propranolol HCl was determined in distilled water, 0.1N HCl, and phosphate buffer of pH 7.4. An excess amount of drug was dissolved in 25 ml volumetric flask containing 25 ml of above solvents. Then flasks were agitated on a wrist shaker for 24 hrs at room temperature for two days. The aliquots were withdrawn and filtered through whatman filter paper. The filtrates were diluted with respective solvents and analysed on UV spectrophotometer (Shukla et al., 2025).

Melting point

Melting points of Propranolol HCl were determined, by taking the drug sample in small amount in a capillary tube closed at one end. Capillary tube containing drug was placed in melting point apparatus. The temperature at which the drug started melting and becomes liquid was noted as range (Kumar et al., 2024).

Partition coefficient

The partition coefficient study of Propranolol HCl was performed using n-octanol as the organic phase and distilled water as the aqueous phase. Accurately weighed 10 mg of drug was taken in the glass stoppered separating funnel containing 10 ml of n-octanol and 10 ml of water. The mixture was set aside for 24 hrs at room temperature with intermittent shaking. The two phases were separated and diluted. Thereafter, the drug concentration in aqueous phase and n-octanol phases was determined spectrophotometrically (Kumar et al., 2024, Mishra et al., 2019).

TLC method

Thin layer chromatography is an important analytical tool for the separation, identification. In this technique, the different compounds are separated by the different migration of solute between two phases, a stationary phase, and a mobile phase. The principle of separation is

adsorption and the stationary phase act as an adsorbent.

The solutions of drugs were prepared in ethanol. 5µl sample was taken by a capillary tube and spotted on the silica gel-G coated TLC plates at a distance of 2 cm above the end of plate. Acetonitrile: n-Butanol (50:50) was used as mobile phase was used as mobile phase for propranolol HCl. The plates were then placed in TLC chamber, (previously saturated with mobile phase).After development of chromatogram, the plates were removed and the spots were observed under the UV chamber at the wavelength 254nm. The R_f value were calculated and tabulated.

HPLC assay

For assessing the purity of drugs, assay of Propranolol HCl were carried out according to the process of Indian Pharmacopeia 2007 (Shukla et al., 2023; Shukla et al., 202 24).

Compatibility studies of drug and excipients

The FTIR spectra of the drug alone and in combination with different excipints were determined and studied for the presence of characteristic peaks of drug in presence of the excipiens (Shukla et al., 2023a; Shukla et al., 2023b; Shukla et al., 2020; Shukla et al., 2019a).

FTIR study

Drug-excipient compatibility was determined by using fourier-transform infrared spectroscopy (FTIR). FTIR spectra of the pure drug and physical mixture of the drug with the polymers were taken. The spectrum of the physical mixture of the drug with the polymer was compared to the spectra of the pure drug to detect the incompatibility. The study was carried out using Bruker (Shukla et al., 2019b, Shukla et al., 2019c).

Results and Discussion

Preformulation studies were carried out to determine physical and chemical properties of the drugs Propranolol HCl. The drugs were studied for the following parameters.

Physical observation

The colour of Propranolol HCl drug powders were visibly observed and found white crystalline powder and odour characteristic bitter in taste.

Melting point

Melting points of Propranolol HCl were determined, by taking the drug sample in small amount in a capillary tube closed at one end. Capillary tube containing drug was placed in melting point apparatus. The temperature at which the drug started melting and becomes liquid was noted as range (Kumar et al., 2024). It is one of the parameters for the determination of purity of drugs. In case of pure chemicals, melting points are very sharp and constant. The average melting point was noted 158-164^{0}C for the drug propranolol hydrochloride.

Standard curve of Propranolol HCl (PRP)

Calibration curve of Propranolol hydrochloride using HCl (pH 1.2)

The calibration curve of Propranolol HCl was prepared using 0.1N HCl pH 1.2, phosphate buffer, pH 6.8 and 7.4, by using Ultraviolet–visible (UV) spectroscopy. The absorbance was determined at 287 nm for different concentrations in the range of 10, 20, 30, 40, 50µg/ml as reported in table 2 and shown in figures 1 and 2. A high degree of correlation (R^2 = 0.999) was observed between the concentration of the drug solution and their respective absorbance obtain.

Calibration curve of Propranolol HCl using phosphate buffer (pH 6.8)

The calibration curve of Propranolol HCl was prepared in phosphate buffer, pH 6.8 by using UV spectroscopy. The absorbance was determined at 288 nm for different concentrations in the range of 10, 20, 30, 40, 50µg/ml as

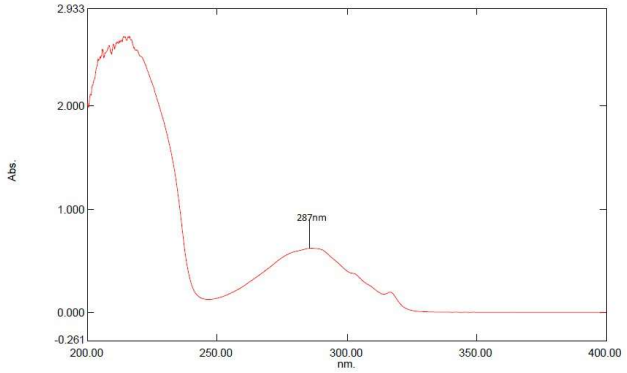

Figure 1. UV curve of Propranolol HCl using 0.1N HCl (pH 1.2)

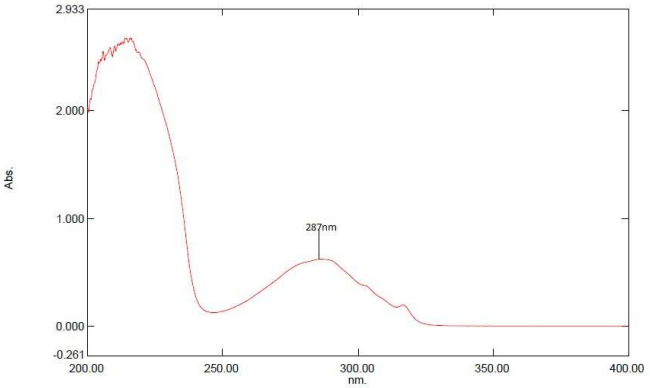

Figure 2. Standard curve of Propranolol HCl using 0.1N HCl (pH 1.2)

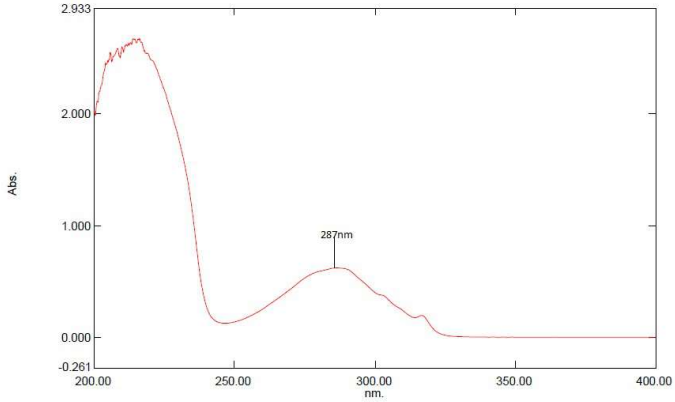

Figure 3. UV curve of Propranolol HCl using phosphate buffer (pH 6.8)

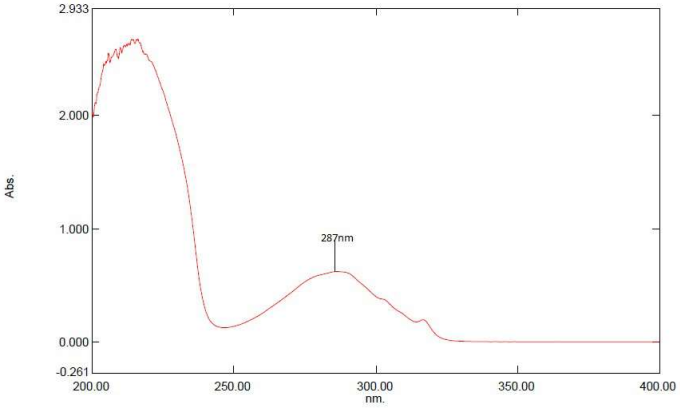

Figure 4. Standard curve of Propranolol HCl using phosphate buffer (pH 6.8)

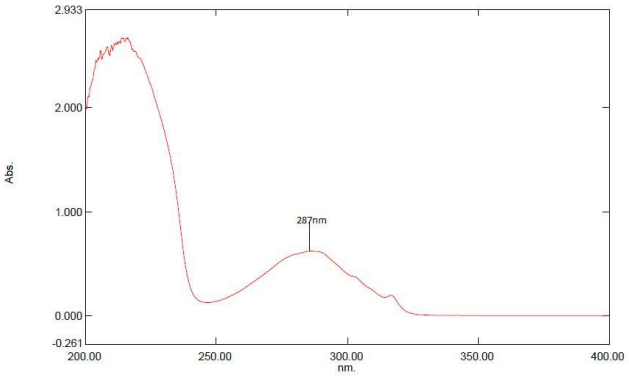

Figure 5. UV curve of Propranolol HCl using phosphate buffer (pH 7.4)

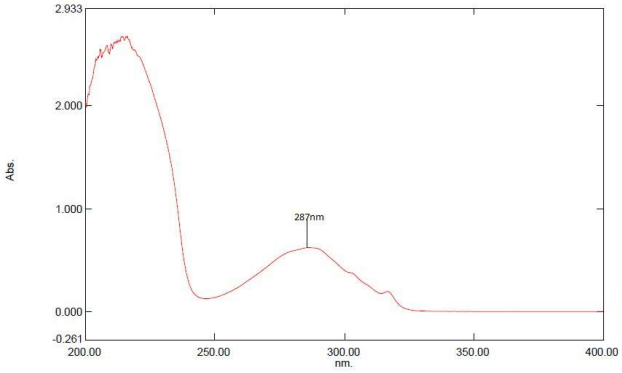

Figure 6. Standard curve of Propranolol HCl using phosphate buffer (pH 7.4)

reported in in figures 3 and 4. A high degree of correlation (R^2 = 0.996) was observed between the concentration of the drug solution and their respective absorbance obtained.

Calibration curve of Propranolol HCl using phosphate buffer (pH 7.4)

The calibration curve of Propranolol HCl was prepared in phosphate buffer, pH7.4 by using UV spectroscopy. The absorbance was determined at 288nm for different concentrations in the range of 10, 20, 30, 40, 50µg/ml as reported in shown in figures 5 and 6. A high degree of correlation (R^2 = 0.999) was observed between the concentration of the drug solution and their respective absorbance obtained.

Determination of solubility

Solubility of Propranolol HCl was determined in distilled water, 0.1N HCl, and phosphate buffer of pH 7.4. Results are shown in table 1.

Partition coefficient

The partition coefficient study of Propranolol HCl was performed using n-octanol as the organic phase and distilled water as the aqueous phase. Accurately weighed 10 mg of drug was taken in the glass stoppered separating funnel containing 10 ml of n-octanol and 10 ml of water. The mixture was set aside for 24 hrs at room temperature with intermittent shaking. The two phases were separated and diluted. Thereafter, the drug concentration in aqueous phase and n-octanol phases was determined spectrophotometrically (Mishra et al., 2019).

Partition coefficient studies are carried out to find out extent of drug transfer in the aqueous and the other non aqueous layer. Partition coefficient is the measurement of drug's lipophilicity and its ability to cross cell membranes. It is

Table 1. Solubility of propranolol hydrochloride

S.N	Solvent	Propranolol hydrochloride
1	O.1HCL pH1.2	138.27±.01 mg/ml
2	Distilled water	58.32±.04 mg/ml
3	Buffer pH 7.4	145.80±.02 mg/ml

defined as the ratio of unionized drug distributed between the organic and aqueous phase at equilibrium. Partition coefficient value of propranolol hydrochloride was found to be 1.56±.01.

TLC method

TLC of propranolol HCL was study. The solvent systems were selected as per Indian Pharmacopeia (I.P.). R_f value found 0.57 with single spot white color in ultraviolet light at 254. The solvent system was selected as per official monograph I.P. The R_f value was found 0.72, single violet and yellow-orange spot at 254. The results were shown in table 2 and figure 7.

$$\text{Partition coefficient} = \frac{\text{Amount of drug in octance layer}}{\text{Amount of drug in aqeous layer}}$$

HPLC assay

There under this process assay of propranolol HCL using HPLC solvent systems Buffer/ACN/Methanol 20:45:35. The propranolol HCl drug was found 99.59% pure. The results for both the drugs are shown in table 3 and chromatograms of drug shown in figure 8 (Kumar et al., 2018; Bishnoi et al., 2018).

Compatibility studies of drug and excipients

The FTIR spectra of the drug alone and in combination with different excipints were determined and studied for the presence of characteristic peaks of drug in presence of the excipiens. The FTIR spectra of drug (PRP) with and without excipients are shown in fig no. 9-12, respectively. The DSC

Table 2. TLC Chromatographic characteristics of propranolol hydrochloride

Drug	Mobile phase	R_f	Ultraviolet light at 254nm	Ultraviolet light at 365nm
PRP	Acetonitrile-n butanol 50:50	0.57	White color	White color

Figure 7. TLC of Propranolol HCl

Table 3. Assay of Propranolol HCl (HPLC method)

Drug	Mobile solvent	λ-max	Flow rate	Column	Result
Propranolol HCl	Buffer/ Acetonitrile /Methanol (20:45:35)	282nm	1ml/min	Column C18(250×4 .6mm)	99.59%

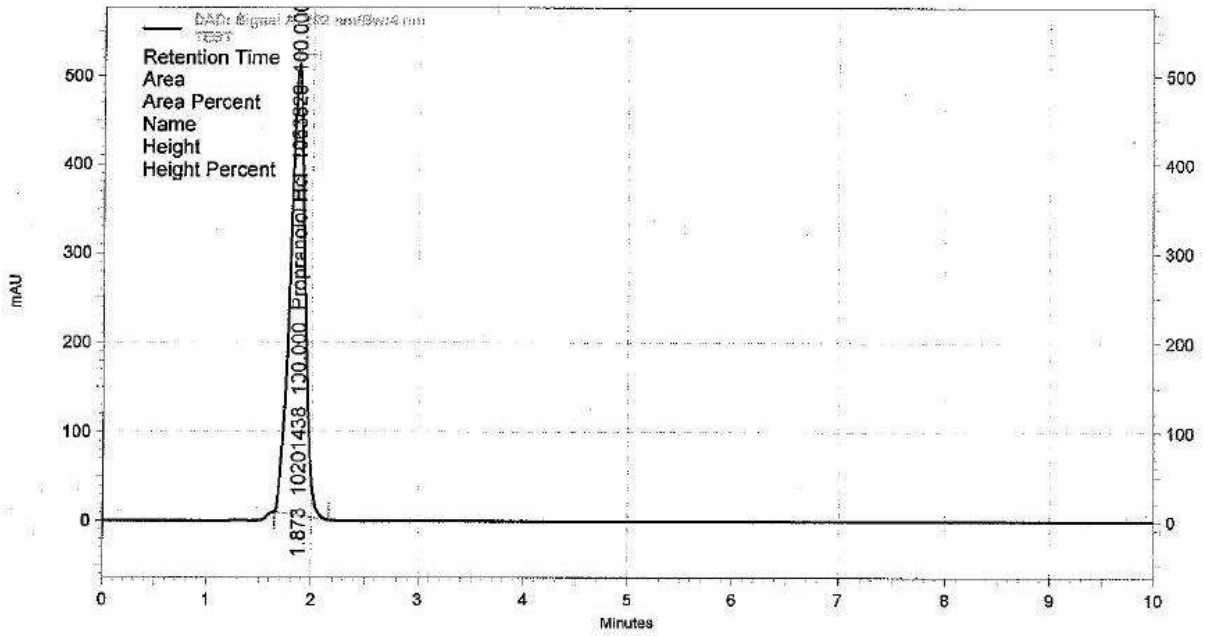

Figure 8. HPLC chromatogram of Propranolol HCl

thermo gram of pure drug Propranolol with excipients was recorded (DSC spectra of PRP 13) and (DSC spectra of PRP 14), respectively (Shukla et al., 2016; Shukla et al., 2017; Shukla et al., 2018; Shukla et al., 2019).

The FTIR spectra of propranolol hydrochloride with excipients showed characteristic peaks, and no any other peak is seen in spectra. The same characteristic peak was seen in the spectra of formulation. It indicates that the compatibility of drug (Propranolol hydrochloride) with excipients was good which has been used in bilayer and film coated tablet formulation.

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To ascertain any potential drug-gum interactions, another DSC was conducted. Thermograms revealed no drug-excipient interactions. A DSC was used to obtain the DSC curve for the pure medication PH at a heating rate of 1000 °C/min from 30 to 350 °C in a nitrogen environment (30 ml/minute) (Figure 13).

The temperature needed to melt the pure substances and the

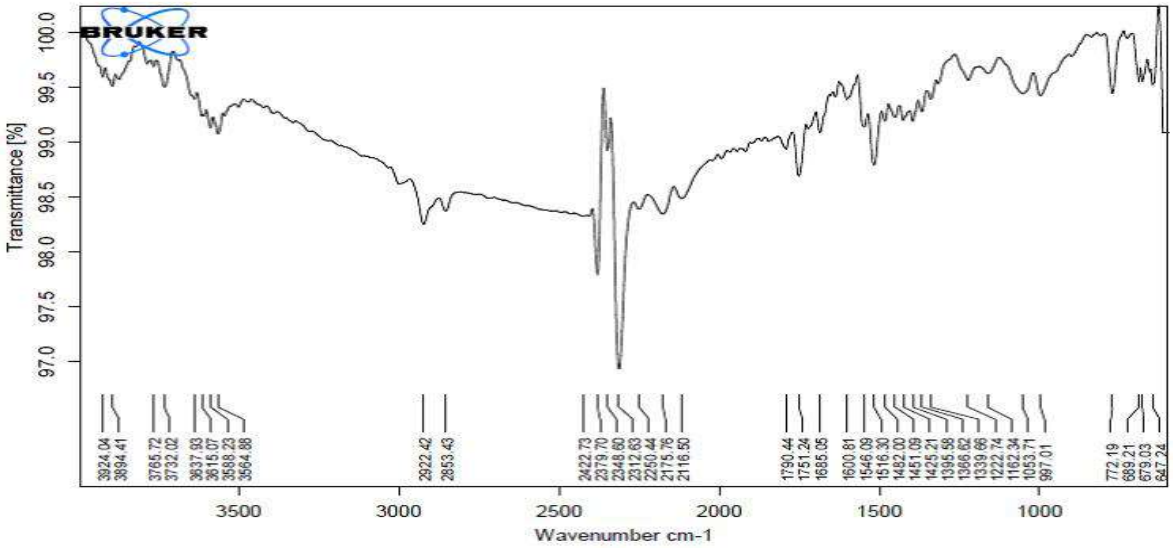

Figure 9. FTIR spectra of TSG

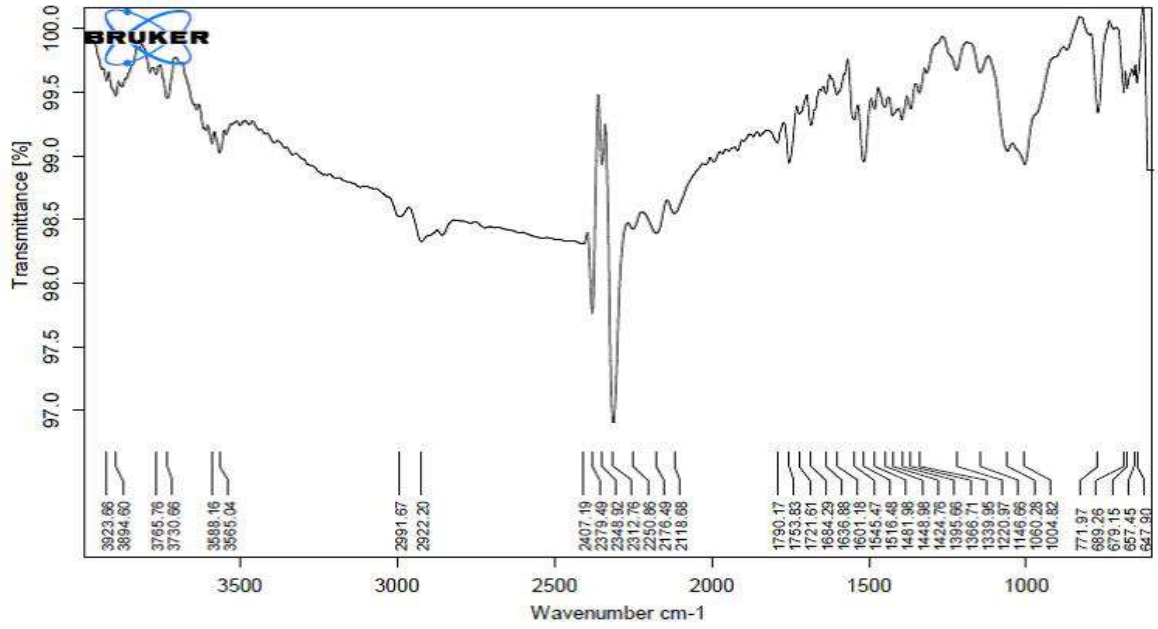

Figure 10. FTIR spectra of FSG

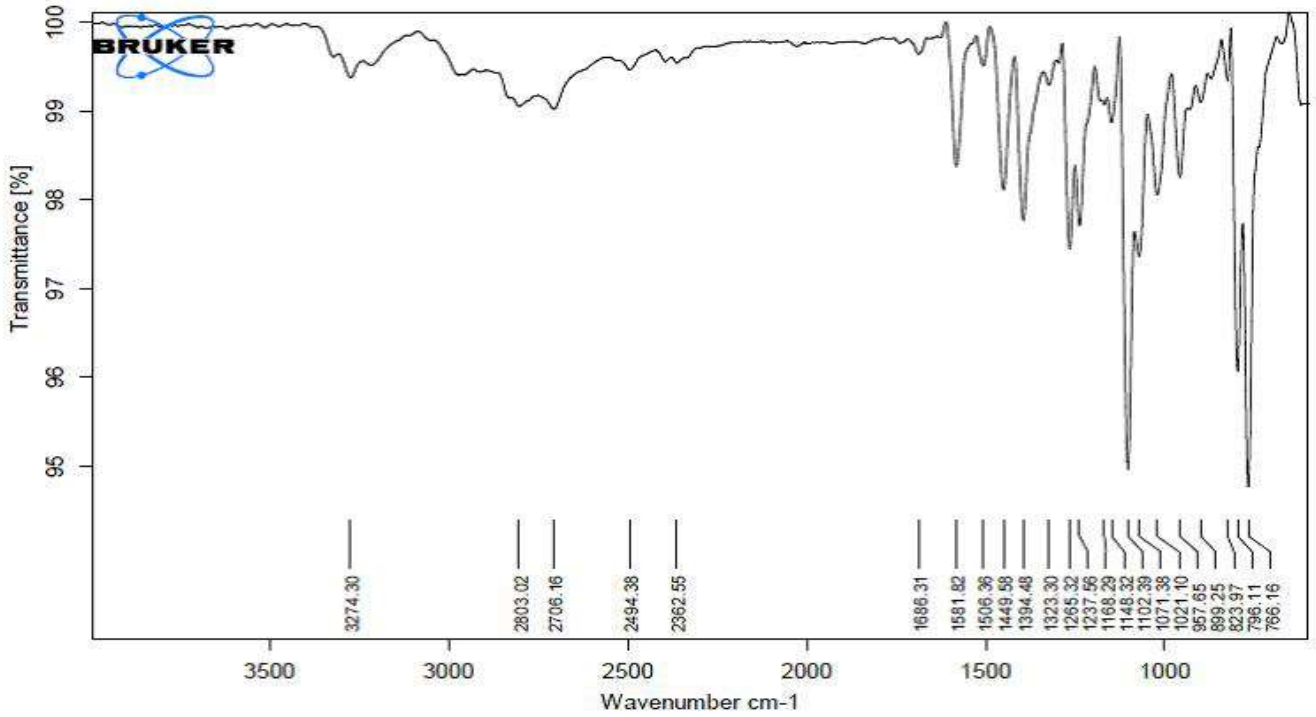

Figure 11. FTIR spectra of Propranolol HCl

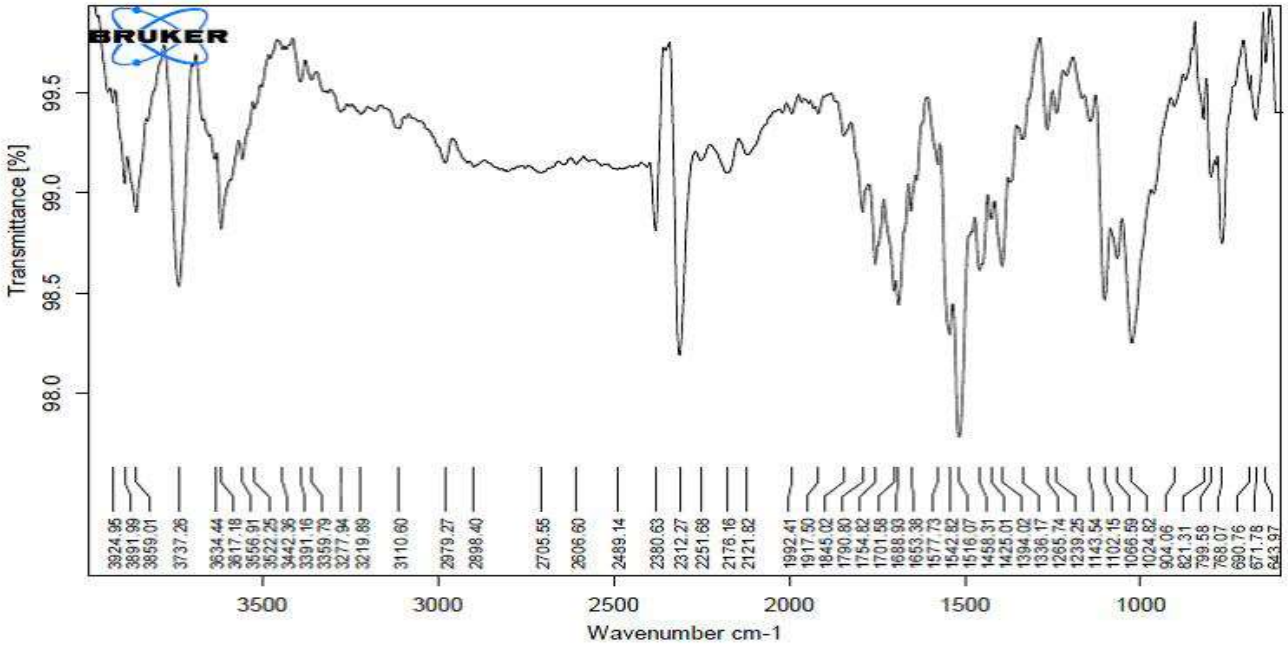

Figure 12. FTIR analysis of Propranolol HCl and excipients

physical mixes was determined by analyzing the obtained thermograms. The thermogram did not change from an endothermic to an exothermic state or vice versa. DSC results guarantee that medications and excipients are compatible. Figure illustrates the DSC thermogram of the medication PH with excipients figure 14.

All of the medications' distinctive peaks were seen. There was no chemical interaction between the medications and excipients, according to the results of FTIR and DSC (Shukla et al., 2020; Bishnoi et al., 2018; Bishnoi et al., 2019).

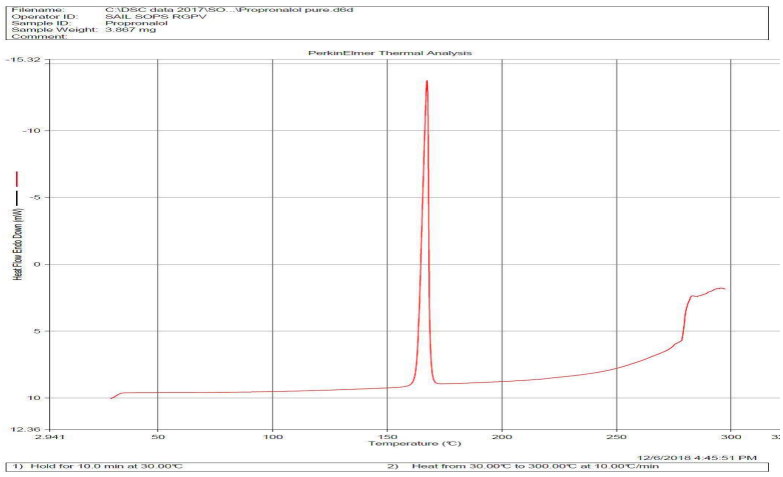

Figure 13. DSC spectrum of propranolol HCl pure

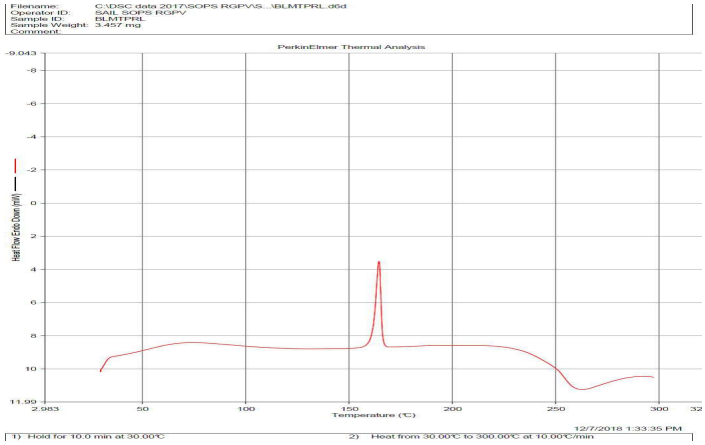

Figure 14. DSC spectrum of Propranolol HCl pure with excipients

Conclusion

The evaluation result data of Propranolol HCl study clearly represented no interaction between drug and their excipients were found. Therefore synthetic and natural drug combination is secure to formulate in a novel different dosage form. To recognize drug release example from novel delivery system, we will investigate for the development of different formulation in future.

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