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FT-IR STUDY BETWEEN PROPRANOLOL HYDROCHLORIDE AND PHARMACEUTICALLY ACCEPTABLE EXCIPIENTS IN PHYSICAL MIXTURE

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Abstract: Propranolol hydrochloride (propranolol HCl) is a nonselective β-adrenergic blocking agent widely used for hypertension, angina pectoris, and many other cardiovascular disorders treatment. Fourier transform infrared spectroscopy (FT-IR) is a simple, rapid, and inexpensive method that was used to predict the drug-excipients interactions. Base on their frequent use in preformulation six pharmaceutically acceptable excipients: lactose, magnesium stearate, talcum, corn starch, microcrystalline cellulose pH 102 (avicel® pH 102), and sodium starch glycolate (explotab®) were mixed with propranolol HCl using simple physical technique in an agate mortar with pestle for approximately 5 min. The mixture samples were prepared by mixing propranolol HCl and each pharmaceutically acceptable excipients in a ratio of 1:1, 1:2, and 1:3 w/w. The FT-IR spectra showed the main peaks of propranolol HCl at 3270-3209, 2962-2715, 1250, and 802 cm^{-1} were secondary of hydroxyl group, secondary of amine group, aryl alkyl ether, and substituted naphthalene, respectively. Propranolol HCl and pharmaceutically acceptable excipients had not been interacting in their physical mixtures. The increasing of amount ratio of pharmaceutically acceptable excipients obviously increased the intensity of main peak of each pharmaceutically acceptable excipients around 1600-1000 cm^{-1}.

Keywords: Fourier transform infrared spectroscopy, Pharmaceutically acceptable excipient, Propranolol HCl

บทคัดย่อ: โพรพราโนลอล ไฮโดรคลอไรด์ เป็นยายับยั้งตัวรับเบต้าอะดรีเนอจิกแบบไม่เจาะจง ยานี้ใช้รักษาความดันโลหิตสูง ปวดเค้นหน้าอก และโรคทางระบบหลอดเลือดและหัวใจอื่น ๆ ฟูเรียร์ทรานฟอร์มอินฟราเรดสเปกโทรสโกปีเป็นวิธีที่ง่าย เร็ว และถูกที่ใช้สำหรับทำนายการเกิดปฏิกิริยาระหว่างยาและสารช่วย สารช่วยที่เป็นที่ยอมรับทางเภสัชกรรมทั้ง 6 ชนิด ที่ใช้บ่อยสำหรับการตั้งตำรับ คือ แลคโตส แม็กนีเซียม สเตียเรท ทัลคัม แป้งข้าวโพด ไมโครคริสตอลลีนเซลลูโลส เกรด pH 102 (avicel® pH 102) และ โซเดียมสตาร์ชไกลโคเลท (explotab®) ถูกนำมาผสมกับยาโพรพราโนลอล ไฮโดรคลอไรด์โดยวิธีการผสมทางกายภาพอย่างง่ายในโกร่งผสมเป็นเวลา 5 นาที สารผสมตัวอย่างถูกเตรียมโดยใช้อัตราส่วนระหว่างโพรพราโนลอล ไฮโดรคลอไรด์และสารช่วยที่เป็นที่ยอมรับทางเภสัชกรรมเพียงชนิดเดียว คือ 1:1 1:2 และ 1:3 โดยน้ำหนัก ฟูเรียร์ทรานฟอร์มอินฟราเรดสเปกโทรสโกปีแสดงพีคหลักของโพรพราโนลอล ไฮโดรคลอไรด์ที่ตำแหน่ง 3270-3209 2962-2715 1250 และ 802 cm^{-1} ของการแทนที่ในตำแหน่งที่ 2 ของหมู่ไฮดรอกซิล การแทนที่ในตำแหน่งที่ 2 ของหมู่เอมีน อาริล อัลคิล อีเธอร์ และการแทนที่ของแนฟทาลีน ตามลำดับ โพรพราโนลอล ไฮโดรคลอไรด์และสารช่วยที่เป็นที่ยอมรับทางเภสัชกรรมไม่เกิดปฏิกิยากันจากการผสมทางกายภาพของตัวอย่างเหล่านี้ การเพิ่มปริมาณของสารช่วยที่เป็นที่ยอมรับทางเภสัชกรรมจะเพิ่มความเข้มของพีคหลักของสารช่วยที่เป็นที่ยอมรับทางเภสัชกรรมชนิดนั้นๆ ในย่าน 1600-1000 cm^{-1}

คำสำคัญ ฟูเรียร์ทรานฟอร์มอินฟราเรดสเปกโทรสโกปี สารช่วยที่เป็นที่ยอมรับทางเภสัชกรรม โพรพราโนลอล ไฮโดรคลอไรด์

INTRODUCTION

Propranolol hydrochloride (propranolol HCl) is a nonselective β-adrenergic blocking agent widely used for hypertension, angina pectoris, and many other cardiovascular disorders treatment. It has low molecular weight of 295.81 g/mol. Although it is well absorbed in the gastrointestinal tract, it has a low bioavailability about 15%-23% as a result of extensive first-pass metabolism (Cid et al., 1986, Patel et al., 2007). The buccal route can avoid the hepatic first-pass effect, improve the bioavailability of propranolol HCl, and reduce the dose of propranolol hydrochloride (Amores et al., 2014, Patel et al., 2007).

The drug–excipient compatibility is an important stage in preformulation for the pharmaceutical dosage form development. Because of the interaction between drugs and excipients: both physical and chemical interactions can initiate, propagate, or participate in chemical or physical interactions with drug compounds that effect on chemical nature of drug, the stability of pharmaceutical dosage form, and bioavailability of drugs and, consequently, their therapeutic efficacy and safety (Fathima et al., 2011, Tiţa et al., 2011b). Moreton, 2006 proposed three main components for development of pharmaceutical dosage forms: properties and limitation of active drug, properties and limitation of excipients, and advantage and limitation of development method (Moreton, 2006). Previous publications report the study of drug–excipient compatibility such as ibuprofen (Tiţa et al., 2011b), indomethacin (Tita et al., 2014), ketoprofen (Tiţa et al., 2011a), acetaminophen (Tomassetti et al., 2005), venlafaxine(Bernardi et al., 2009), norfloxacin (Oliveira et al., 2009), and lapachol (Lira et al., 2007).

However, propranolol HCl was not reported the drug–excipient compatibility and interaction in pure drug mixed with each pharmaceutically acceptable excipients. Thus, the aim of this work was to study the interaction between propranolol HCl and each pharmaceutically acceptable excipients: lactose, magnesium stearate, talcum, corn starch, microcrystalline cellulose pH 102 (avicel® pH 102), and sodium starch glycolate (explotab®). The drug-excipient preparation was prepared by physical mixture in an agate mortar with pestle for approximately 5 min with different ratio of propranolol HCl and each pharmaceutically acceptable excipients. Fourier transform infrared spectroscopy (FT-IR) technique was used to predict the interaction of theses preparations.

MATERIALS AND METHODS

Materials

Propranolol HCl powder, BP2005 grade was purchased from Chang zhou Yabang Pharmaceutical Co., Ltd., China. All pharmaceutically acceptable excipients i.e., lactose, magnesium stearate, talcum, corn starch, microcrystalline cellulose pH 102 (avicel® pH 102), and sodium starch glycolate (explotab®) were commercial grade.

The physical mixtures preparation

The w/w different ratios (1:1, 1:2, and 1:3) of propranolol HCl and each pharmaceutically acceptable excipients were studied the probability of observing any interaction. Propranolol HCl powder was homogeneously mixed with each pharmaceutically acceptable excipients i.e., lactose, magnesium stearate, talcum, corn starch, microcrystalline cellulose pH 102 (avicel® pH 102), and sodium starch glycolate (explotab®) in different w/w

ratios (Table1). The simple physical was mixed in an agate mortar with pestle for approximately 5 min.

FT-IR study

The interaction of propranolol HCl and each pharmaceutically acceptable excipients were determined by the FT-IR spectrometer (model: Nicolet 6700, DLaTGS detector, Thermo Scientific, USA.). The FT-IR study used the spectrophotometric-grade potassium bromide (KBr) because of the KBr is completely transparent to Infrared radiation, but is hygroscopic. It might showed the broad spectrum for water absorption bands around 3333 cm^{-1} and 1640 cm^{-1}. Thus, before to use, it should be oven dried overnight at 110°C to eliminate moisture interference. After that, the 1.5 mg dry sample powder was mixed with 200 mg dry KBr. Then, the mixture was ground into a fine powder using an agate mortar before being compressed into a KBr disc sample. The characteristic peaks were scanned and recorded over a wavenumber region of 4000 - 400 cm^{-1} at a resolution of 4 cm^{-1} with 16 scans.

Table 1. The ratio composition of propranolol HCl and pharmaceutically acceptable excipients

Formulas	Ingredients	Ratio
PE1	Propranolol HCl : Lactose	1 : 1
PE2	Propranolol HCl : Lactose	1 : 2
PE3	Propranolol HCl : Lactose	1 : 3
PE4	Propranolol HCl : Magnesium stearate	1 : 1
PE5	Propranolol HCl : Magnesium stearate	1 : 2
PE6	Propranolol HCl : Magnesium stearate	1 : 3
PE7	Propranolol HCl : Talcum	1 : 1
PE8	Propranolol HCl : Talcum	1 : 2
PE9	Propranolol HCl : Talcum	1 : 3
PE10	Propranolol HCl : Corn starch	1 : 1
PE11	Propranolol HCl : Corn starch	1 : 2
PE12	Propranolol HCl : Corn starch	1 : 3
PE13	Propranolol HCl : Avicel® pH 102 (microcrystalline cellulose pH 102)	1 : 1
PE14	Propranolol HCl : Avicel® pH 102 (microcrystalline cellulose pH 102)	1 : 2
PE15	Propranolol HCl : Avicel® pH 102 (microcrystalline cellulose pH 102)	1 : 3
PE16	Propranolol HCl : Explotab® (sodium starch glycolate)	1 : 1
PE17	Propranolol HCl : Explotab® (sodium starch glycolate)	1 : 2
PE18	Propranolol HCl : Explotab® (sodium starch glycolate)	1 : 3

RESULTS AND DISCUSSION

The propranolol HCl and pharmaceutically acceptable excipients were homogeneous preparation. The interaction between drug and pharmaceutically acceptable excipients was checked by IR spectra which compared to pure propranolol HCl and those pharmaceutically acceptable excipients (Figure 1-6). The main peak of propranolol HCl, $C_{16}H_{21}NO_2 \cdot HCl$, was 3270-3209, 2962-2715, 1250, and 802 cm^{-1} represented of secondary of hydroxyl group, secondary of amine group, aryl alkyl ether, and substituted naphthalene, respectively.

Figure 1, lactose, $C_{12}H_{22}O_{11}$, shows the broad peak at 3240 cm^{-1} due to the presence of stretching vibration of a hydroxyl group, hydroxyl groups of crystal water display the weak

peak of bending vibration at 1650 cm^{-1}, 1018 cm^{-1} due to the asymmetric stretching vibration of C-O-C in the glucose and galactose.

Figure 2, magnesium stearate revealed the presence of sharp peaks to the presence of stretching vibration of a alkane group at 2946-2838 cm^{-1} and stretching vibration of carbonyl group at 1527-1481 cm^{-1}.

The IR spectrum of talcum, $3MgO{\cdot}4SiO_2{\cdot}H_2O$, characteristically revealed the little sharp absorption peak at 3672 cm^{-1} due to the stretching vibration of hydroxyl group without a hydrogen bond and the strong absorption peak at 1014 cm^{-1} due to the stretching vibration of Si-O (Figure 3).

Corn starch, $(C_6H_{10}O_5)_n$ made from maize grain that showed the strong peak of -OH stretching vibration at 3270 cm^{-1}, C-O stretching and C-O-H bending at 1326 cm^{-1}, C-O-C bending, C-O-H bending, and C-O stretching at 987 cm^{-1} (Figure 4).

Avicel® pH 102, also known as microcrystalline cellulose grade pH 102, is a purified partially depolymerized cellulose with shorter, crystalline polymer chains prepared by treating alpha cellulose. It consists of linear chains of β-1,4-D anhydroglucopyranosyl units (Thoorens et al., 2014). Figure 5 shows the broad peak at 3240 cm^{-1} represented the hydroxyl group and 1049 cm^{-1} represented the C-O-C bending.

Explotab®, also known as sodium starch glycolate, is sodium salt form of a cross-linked carboxymethyl ether of starch or of carboxymethyl ether, which made from rice, potato, wheat, or corn origin. The main peaks of Explotab® are showed in Figure 6 which fund the broad peak at 3270 cm^{-1} due to the presence of stretching vibration of a hydroxyl group and sharp peak at 1002 cm^{-1} due to the presence of C-O-C bending.

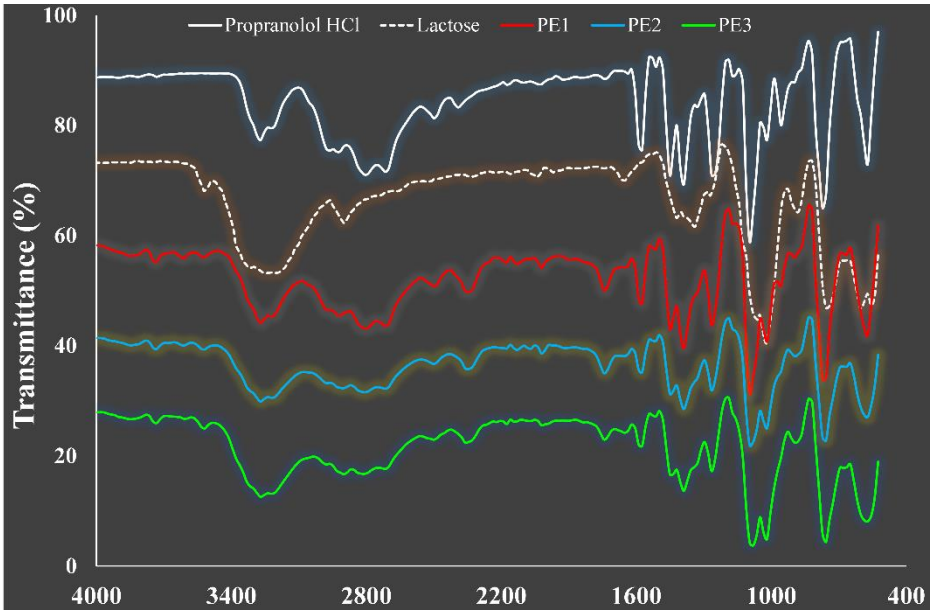

Figure 1. FT-IR spectra of propranolol HCl and lactose with different ratio physical mixture

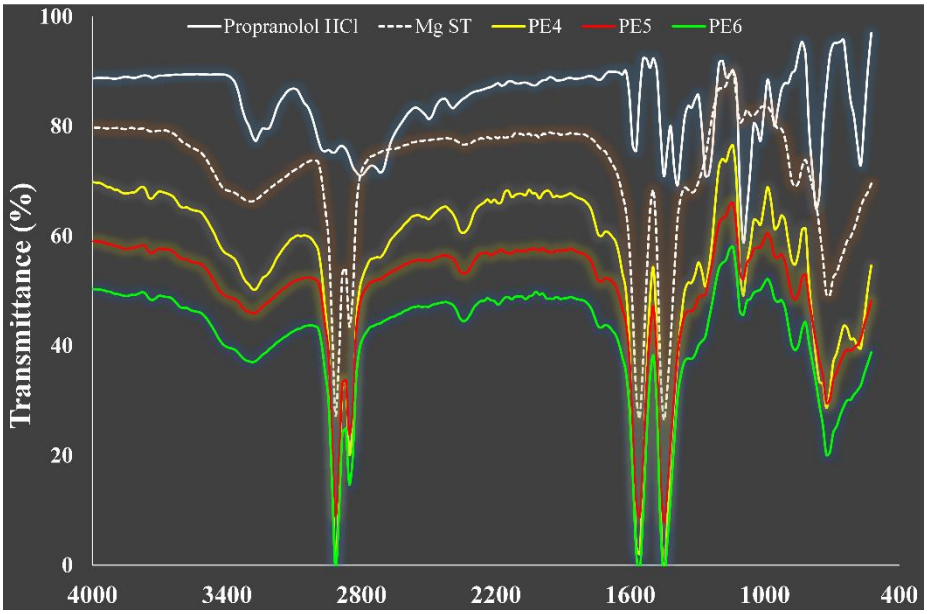

Figure 2. FT-IR spectra of propranolol HCl and magnesium stearate with different ratio physical mixture

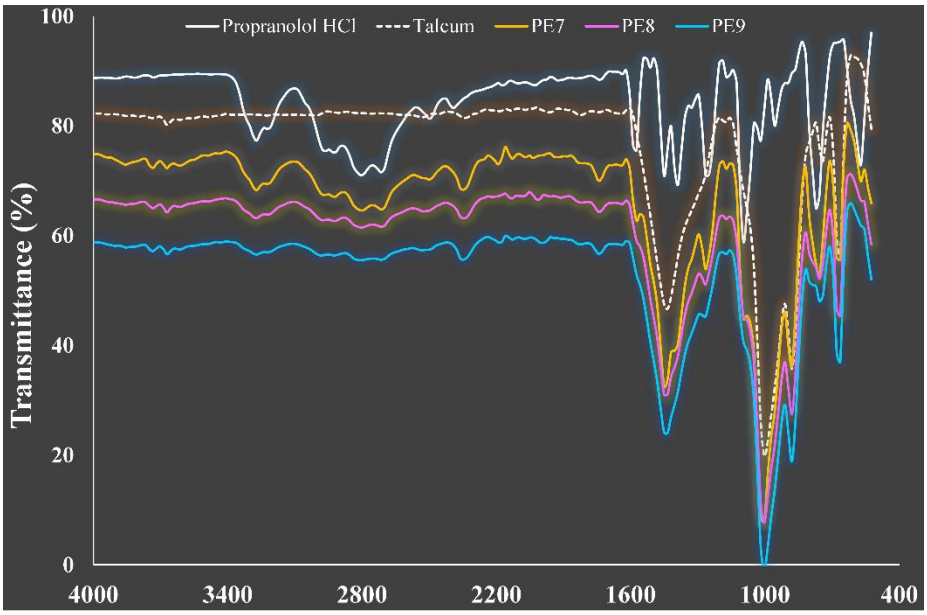

Figure 3. FT-IR spectra of propranolol HCl and talcum with different ratio physical mixture

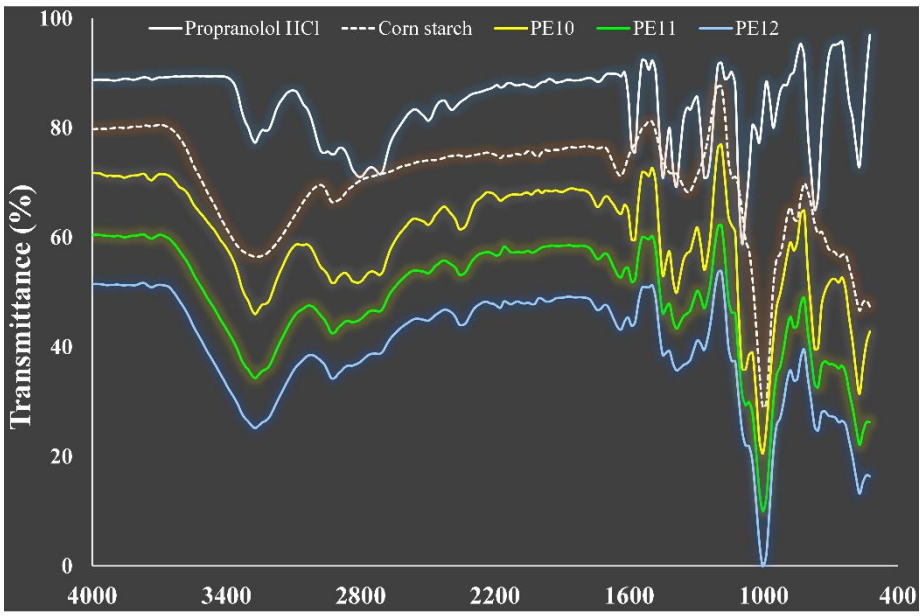

Figure 4. FT-IR spectra of propranolol HCl and corn starch with different ratio physical mixture

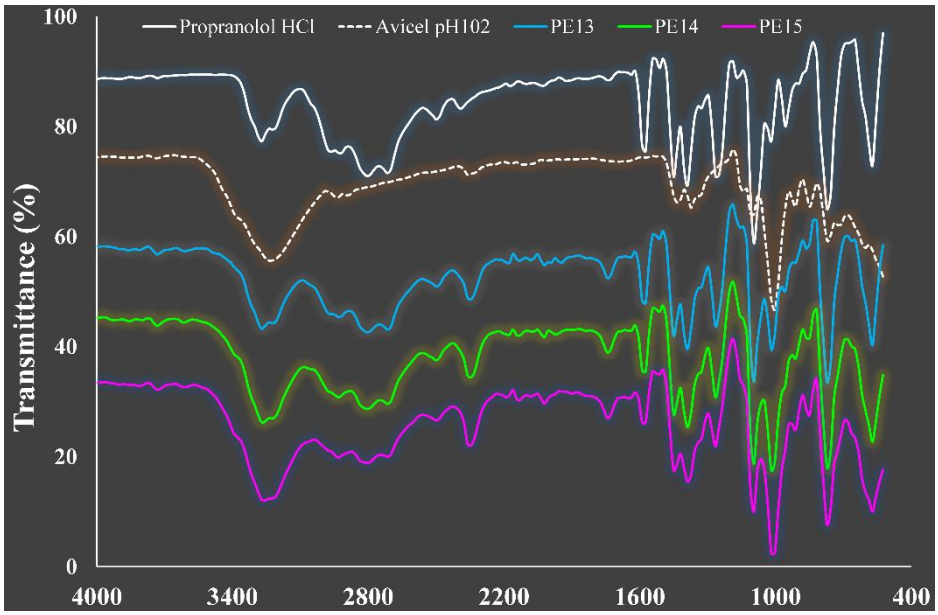

Figure 5. FT-IR spectra of propranolol HCl and avicel® pH 102 with different ratio physical mixture

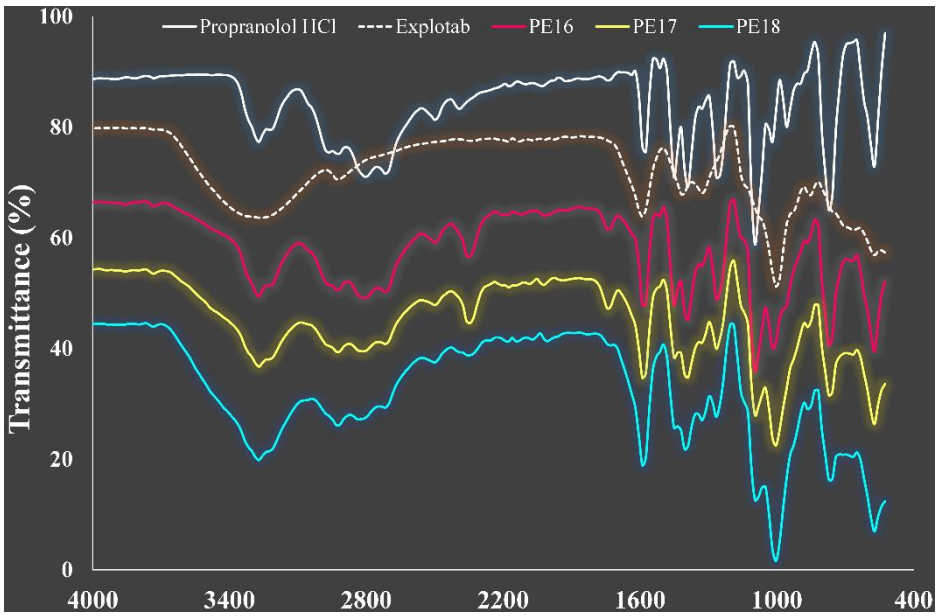

Figure 6. FT-IR spectra of propranolol HCl and explotab® with different ratio physical mixture

As the results, when propranolol HCl was mixed with each pharmaceutically acceptable excipients i.e., lactose, magnesium stearate, talcum, corn starch, microcrystalline cellulose pH 102 (avicel® pH 102), and sodium starch glycolate (explotab®), the IR spectra showed the all main peaks of both propranolol HCl and each pharmaceutically acceptable excipients. In addition, we found that the increasing of intensity of sharp main peak when increased each pharmaceutically acceptable excipients amount ratio in their physical mixture. The main functional groups of propranolol HCl were found in physical mixture containing different pharmaceutically acceptable excipients; therefore, there was no major interaction between the propranolol HCl and all pharmaceutically acceptable excipients used in the research (Figure 1-6).

CONCLUSION

The propranolol HCl was homogeneously mixed with different pharmaceutically acceptable excipients by physical mixtures in an agate mortar with pestle for approximately 5 min. We found the main peaks of propranolol HCl were of secondary of hydroxyl group, secondary of amine group, aryl alkyl ether, and substituted naphthalene at 3270-3209, 2962-2715, 1250, and 802 cm^{-1}, respectively in all physical mixture containing different pharmaceutically acceptable excipients. In addition, when pharmaceutically acceptable excipients amount ratio increased, the intensity of IR spectra were obviously found the increasing of main peak of each pharmaceutically acceptable excipients around 1600-1000 cm^{-1}. Therefore, the interaction between propranolol HCl and different pharmaceutically acceptable excipients was confirmed by FT-IR that had no major interaction in their physical mixtures. However, in the future study, the compatibility of these physical mixtures will be studied by thermal analysis.

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