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Chemical composition of propranolol determined by IR spectroscopy

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Abstract
In this article, we determined the composition of propanolol using FTIR spectroscopy using a Shimadzu Prestige-21 FTIR spectrophotometer. Propanolol contains absorption bands between wavelengths 3286 and 771cm^{-1}. The functional groups that make up propanolol are: OH, α-substituted naphthalene, carboxymethyl chitosan.

Keywords: Propranolol, IR spectroscopy, composition

Introduction

Propranolol, the active substance in this medicine, belongs to the class of non-selective beta-blockers and is indicated for: high blood pressure; prophylaxis of angina pectoris attacks; long-term treatment after acute myocardial infarction; treatment of heart rhythm disorders: sinus tachycardia, supraventricular tachyarrhythmias (paroxysmal tachycardia, atrial flutter and fibrillation, junctional tachycardia), ventricular arrhythmias (extrasystoles, ventricular tachycardia); it is the drug of choice in arrhythmias of sympathoadrenergic pathogenesis; pheochromocytoma (in association with alpha-blockers); cardiovascular disorders in hyperthyroid patients; hypertrophic cardiomyopathy; migraine; essential tremor; anxiety states due to sympathoadrenergic hyperactivity, accompanied by tachycardia, palpitations, blood pressure oscillations, tremor, etc [1, 5].

Do not take Propranolol: if you are allergic to propranolol hydrochloride or any of the other ingredients of this medicine, if you have had anaphylactic-type reactions in the past; if you have bronchial asthma and chronic obstructive pulmonary disease; if you have uncontrolled heart failure; if you have cardiogenic shock, if you have marked arterial hypotension; if you have sinus bradycardia (< 50 beats/min); sinus node disease (including sino-atrial block); atrioventricular block of the second and third degree; if you have Raynaud's phenomenon and other peripheral vasospastic disorders.

Treatment with propranolol should not be discontinued abruptly in patients with ischemic heart disease, as it may lead to serious cardiac rhythm disorders, acute myocardial infarction or sudden death; doses are reduced gradually. Long-term administration of propranolol may cause an increase in triglycerides and, to a lesser extent, an increase in serum cholesterol; the clinical significance of the increase in plasma lipids is not specified. In patients with vasculospastic angina (Prinzmetal), propranolol, like other beta-blockers, is not the medication of choice. It can be added to other antianginal drugs when these are not sufficiently effective. In patients with therapeutically controlled heart failure, treatment should be initiated with low doses that can be gradually increased under medical supervision.

In the event of symptomatic bradycardia (< 55 beats/min), the propranolol dose should be reduced.

Due to the negative dromotropic effect, beta-blockers should be administered with caution in patients with first-degree atrioventricular block [6, 12].

In patients with pheochromocytoma, alpha-blocker treatment should be instituted before beta-blocker administration to prevent the risk of increased blood pressure.

In the elderly, treatment should be initiated with low doses and under close medical supervision.

Caution is recommended in establishing doses in patients with hepatic and renal insufficiency.

In diabetics, blood glucose monitoring is recommended; certain signs and symptoms that may indicate a hypoglycemic reaction may be masked (e.g. tachycardia, palpitations, sweating).

The use of propranolol in patients with unstable diabetes requires caution. When initiating treatment with beta-blockers in patients with psoriasis, it should be borne in mind that cases of worsening of the disease during treatment have been reported.

In patients with a history of severe anaphylactic reactions, especially to iodinated contrast agents, as well as in those undergoing desensitization treatment, the administration of beta-blockers may constitute an aggravating factor and have an antagonistic effect to adrenaline.

Although treatment with beta-blockers reduces the risk of arrhythmias, myocardial ischemia and hypertensive surges, during general anesthesia, the inhibition of compensatory sympathoadrenergic reactions favors hypotensive accidents during anesthesia. When beta-blocker treatment cannot be interrupted (e.g. in coronary patients), it is recommended to protect against vagal dominance by administering atropine; general anesthetics that depress the heart should be avoided. It is recommended to inform the anaesthetist if the patient is under treatment with beta-blockers. If this treatment must be interrupted, a 48-hour break is sufficient for the re-emergence of the response to catecholamines. The risk of anaphylactic reactions must be taken into account.

If beta-blockers are administered to patients with liver cirrhosis and digestive bleeding, the blood count, hematocrit and hemoglobin should be checked regularly.

In case of thyrotoxicosis, beta-blockers may mask cardiovascular signs in hyperthyroid patients.

Athletes should be warned that propranolol and other beta-adrenergic blockers are included in the list of doping substances.

Propranolol contains lactose monohydrate. If your doctor has told you that you have an intolerance to some sugars, please ask him before using this medicine.
In particular, tell your doctor if you are taking: amiodarone, propafenone, quinidine, disopyramide - used to treat heart rhythm disorders; halogenated anesthetics - used to induce anesthesia; diltiazem, verapamil, methyldopa, clonidine, reserpine - used to lower excessive blood pressure; tricyclic antidepressants, neuroleptics and baclofen – used in some psychiatric disorders; non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids – used to treat inflammation; insulin or oral antidiabetics – recommended for the treatment of diabetes; cimetidine – recommended for the reduction of excessive gastric secretion, lidocaine – used as a local anesthetic, phenobarbital – used to treat seizures, rifampicin – recommended for the treatment of some infections, magnesium, aluminum and calcium compounds.
Beta-blocker treatment, including propranolol, should be discontinued, if possible, before radiological investigations with iodinated contrast agents due to the risk of severe adverse reactions.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine.
Propranolol crosses the placental barrier. Animal studies have not shown teratogenic effects. Clinical experience has not shown teratogenic or malformative effects in pregnant women treated with propranolol.
Newborns whose mothers were treated antepartum with propranolol may experience hypotension, bradycardia, respiratory distress, hypoglycemia.
Beta-blockers can be administered during pregnancy. Treatment close to the date of birth requires careful monitoring of the newborn (control of heart rate and blood glucose) during the first 3-5 days of life.
Beta-blockers are excreted in breast milk. Since the risk of bradycardia and hypoglycaemia in the infant has not been evaluated, either discontinuation of treatment or discontinuation of breast-feeding should be considered.
Propranolol has no influence on the ability to drive or use machines.
Propranolol contains lactose monohydrate. If your doctor has told you that you have an intolerance to some sugars, contact your doctor before taking this medicine.
Always take this medicine exactly as your doctor or pharmacist has told you. Talk to your doctor or pharmacist if you are not sure.
Like all medicines, this medicine can cause side effects, although not everybody gets them.
The following side effects have been reported with propranolol: tiredness, cold extremities, slow heartbeat, nausea, vomiting, diarrhoea, stomach pain, insomnia, nightmares [13, 17].

Materials and methods

Materials

Propranolol hydrochloride was received from Kimia Farma (Jakarta, Indonesia). Carboxymethyl chitosan (CMCh), hydrochloric acid, magnesium stearate, CMC-Na, xanthan gum and lactose, buffer phosphate 7.2. All the other chemicals used were of analytical grade.

Instrumentation

Tablets were prepared using single punch tablet compression machine (Reickermann Korsch,
Germany). Infrared spectra were recorded with Shimadzu Prestige-21 FTIR Spectrometer.

Fig 1: Shimadzu Prestige-21 FTIR Spectrometer

Results and discussions

As shown in Fig. 2, propranolol hydrochloride gives peaks in IR spectrum nearby at 2962 cm $^{-1}$ due to the presence of a secondary amine group, 3286 cm^{-1} due to the hydroxyl group (secondary), the aryl alkyl ether displays a stretching band at 1103 cm^{-1} and the peak at 771 cm^{-1} due to α-substituted naphthalene [7]. Carboxymethyl chitosan gives peaks in IR spectrum nearby 3441 cm^{-1} due to the hydroxyl group. The IR spectra of the physical mixture showed broadening of peaks at 3325 cm^{-1} due to the extensive hydrogen bonding. Major frequencies of functional groups of pure propranolol hydrochloride remained in physical mixture containing excipients. Hence, there was no major interaction between the propranolol hydrochloride and excipients used in the study. Mentioned evidences thus lead to the conclusion that changes seen are as a result of physical interaction between the propranolol hydrochloride and excipients.

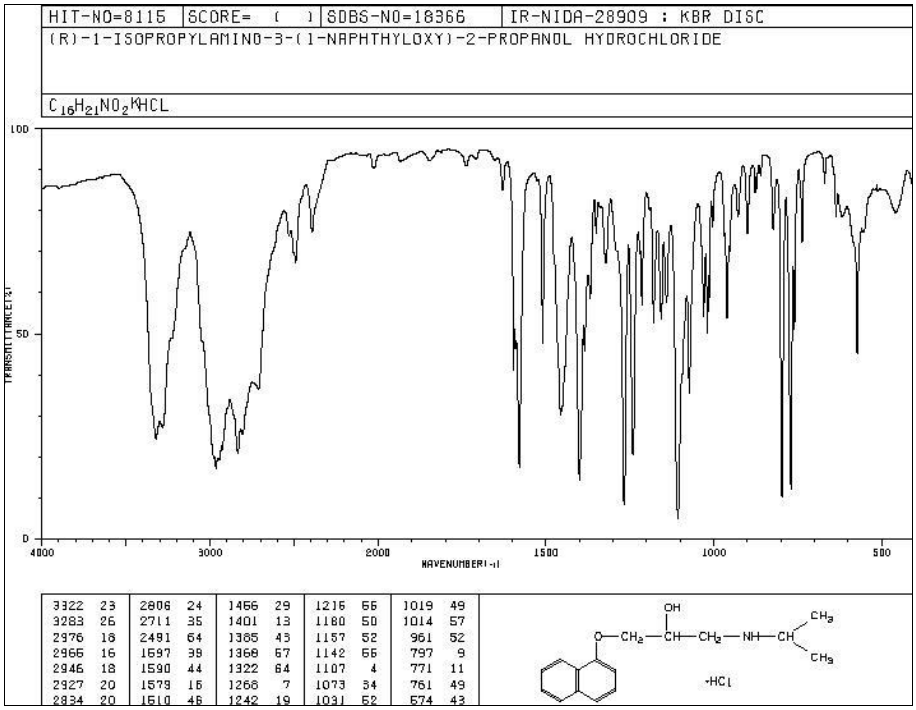

Fig 2: Spectrul IR al propanololului

Conclusions

Propranolol, the active substance in this medicine, belongs to the class of non-selective beta-blocking drugs and contains absorption bands between wavelengths 3286 and 771cm^{-1} and the functional groups that make up propranolol are: OH, α-substituted naphthalene, carboxymethyl chitosan.

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