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DETERMINATION OF PROPRANOLOL CHLORIDE CONTENT IN GENERIC, SIMILAR AND MANIPULATED MEDICINAL PRODUCT BY ULTRAVIOLET-VISIBLE SPECTROPHOTOMETRY

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ABSTRACT

Propranolol Hydrochloride inhibits the stimulation of beta-adrenergic receptors (beta-1 and beta-2) present in the body such as the heart and blood vessels. It was the first successful beta-blocker developed, it is one of the most used drugs mainly in the treatment of hypertension, it is also indicated for the treatment and prevention of myocardial infarction, angina, cardiac arrhythmias, as well as migraine. However, this article aims to verify the Propranolol Hydrochloride content in Generic, Similar and Manipulated drug, by ultraviolet-visible spectrophotometry. It is an experimental research. Thus, the present research used Propranolol Hydrochloride in the Generic (G), Similar (S) and Manipulated (M) formulations. Propranolol hydrochloride content was determined using the UV-visible spectrophotometer method. Propranolol Hydrochloride tablets were purchased from a private pharmacy in Vitória da Conquista-Bahia. The results obtained in the analysis presented an average concentration of generic drug concentration 94.31%, similar 102.58% and manipulated 105.61%. According to the Brazilian Pharmacopoeia, the values must be between 90% and 110%. Thus, the drugs are suitable for consumption as the concentration content is within the required parameters.

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INTRODUCTION

Propranolol Hydrochloride is an antihypertensive drug, part of the National List of Essential Medicines (RENAME) of the Brazilian Ministry of Health. It is one of the drugs most used mainly in the treatment of hypertension, especially when it is associated with cardiovascular diseases such as angina pectoris, myocardial infarction and arrhythmias (Rigobello *et al*., 2013; Bylund, 2015; Guimarães, 2016). Propranolol hydro chloride is a non-selective beta-adrenergic receptor antagonist, interacts with equal affinity beta1 and beta 2 receptors, lacks intrinsic sympathomimetic activity and does not block alpha-adrenergic receptors (Hoffman; Lefkowitz, 1996; Bylund, 2015). Propranolol hydrochloride is completely absorbed after oral administration, and peak plasma concentrations occur between 1 and 2 hours after administration in fasting patients. The liver removes up to 90% of an oral dose, with an elimination half-life of 3 to 6 hours. Propranolol is widely and rapidly distributed throughout the body, with higher concentrations occurring in the lungs, liver, kidneys, brain and heart (ANVISA, 2015). Quality control of propranolol hydrochloride may be performed according methods available in the Brazilian Official Pharmacopoeia 4th edition, by ultraviolet-visible spectrophotometry method (Pharmacopoeia, 2001). Quality control is critical to ensure the quality of the drugs produced are within the required quality standards

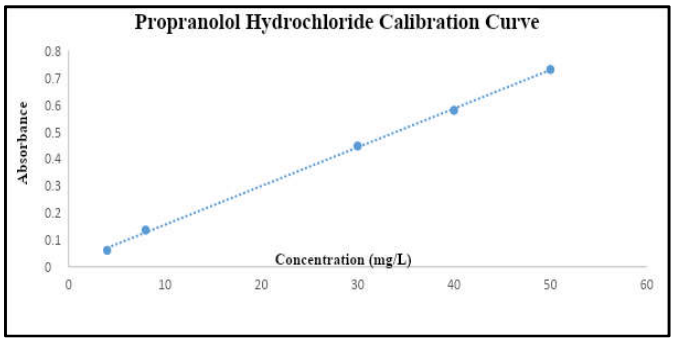
necessary to ensure product quality before they are released for sale or supply (Rocha *et al*., 3013; Asberg *et al*., 2016). Spectrophotometry is applied to Quality Control in the pharmaceutical industry and is of utmost importance to ensure the quality and safety of medicines, thus including Good Manufacturing Practices in Quality Assurance. Visible and ultraviolet spectrophotometry is one of the most commonly used analytical procedures to identify the active principle of drugs (Lemos *et al*., 2009). Spectrophotometric techniques are based on the absorption of electromagnetic energy by molecules that depend on both their concentration and their structure. According to the frequency range of the applied electromagnetic energy, absorption spectrophotometry can be divided into ultraviolet, visible and infrared, and can be used as a technique for substance identification and quantification (Pharmacopeia, 2010). However, this article aims to verify the Propranolol Hydrochloride content in Generic, Similar and Manipulated drug, by ultraviolet-visible spectrophotometry.

MATERIALS AND METHODS

This is an experimental research. Experimental research can be developed in the laboratory, where the researcher has control of variables and simulates situations that should be observed and analyzed. Normally, in experimental research the researcher compares different variables with the purpose of profiling, refuting hypotheses or approving theories (Oliveira, 2011). Thus, the present research used Propranolol Hydrochloride in the Generic (G), Similar (S) and Manipulated (M) formulations. Propranolol hydrochloride content was determined using the UV-visible spectrophotometer method. Propranolol Hydrochloride tablets were purchased from a private pharmacy in Vitória da Conquista-Bahia. The analysis was performed at the Quality Control / Physicochemical Laboratory, No. 20 of the Independent Faculty of the Northeast - FAINOR. The analytical reference standard for Propranolol Hydrochloride was obtained by a Highly Purified Manipulation Pharmacy located in the city of Vitória da Conquista. According to RDC No. 17 of 16 April 2010 and RDC No. 69 of 08 December 2014 a reference standard should be of the highest possible purity to be obtained and carefully characterized in order to ensure its identity, content, quality, purity and potency. Whose high degree of purity and authenticity have been demonstrated by analytical testing (Brasil, 2010; Brasil, 2014). The reagents used were methanol and distilled water. The materials employed were: analytical balance, volumetric flask, watch glass, beaker, gral and pistil mortar, spatula, glass stick, filter paper, buchner funnel, erlenmeyer, kitassate, pasteur pipette, spectrophotometer. Preparation of the standard solution is necessary to perform the procedure: exactly 20.00 mg of propranolol hydrochloride standard is weighed and transferred to a 100 mL volumetric flask. Distilled water (20 mL) was added and stirred for 10 min., Methanol (50 mL) was added and stirred for a further 20 min. The volume was completed with methanol and after filtration 10 mL of the filtrate was transferred to a 50 mL volumetric flask and the volume was methanol metered to a 0.04 mg mL-1 solution of propranolol hydrochloride (Pharmacopéia, 2001 Rigobello *et al*., 2013). Subsequent to the preparation of the sample solution: twenty units of each sample were ground and the amount of the powder equivalent to 20.00 mg propranolol hydrochloride was weighed in triplicate. Subsequently, the standard solution was prepared. Methanol was used as white (Pharmacopéia, 2001; Rigobello *et al*., 2013). Then take the absorbance reading on the spectrophotometer. The spectrophotometer (QUIMIS U2M) was selected to obtain IR spectra by selecting the wavelength 290 nanometers. The calibration curve was constructed using standards with the following concentrations: 5, 10, 15, 20, 25 and 30 mg/L. In the preparation of standards, 0.5 mL (5 mg / L), 1.0 mL (10 mg/L), 1.5 mL (15 mg/L), 2.0 mL (20 mg/L) were pipetted. 2.5 mL (25 mg/L) and 3.0 mL (30 mg/L) using a volumetric pipette and taking care to complete the volume of the 50 mL volumetric flask with methanol to the meniscus (Pharmacopéia, 2001; Rigobello *et al*., 2013). According to the IV Brazilian Pharmacopoeia (2001) the content of Propranolol Hydrochloride to be found in the tablets is a minimum of 90.0% and a maximum of 110.0%.

RESULTS AND DISCUSSION

Figure 1 below shows the data for the Propranolol Hydrochloride calibration curve. The calibration curve obtained, as seen in Figure 1, presents the R^2 present in the curve, which allows to estimate the quality of the curve. The curve can have a good linearity if it brings two or three nines after the comma, thus, the closer the R^2 of 1.0, presents an efficient linearity range (BRASIL, 2017). As can be seen in figure 1, the Propranolol calibration curve has a good linearity range with linear regression coefficient $R^2 = 0.9993$, which is within the required parameters (BRASIL, 2003). Linear regression analysis showed that the method presents a linear response, respecting the concentration range evaluated with a coefficient of determination above 0.99 (PONTES, 2009).



Source: Research Data.

Figure 1. Propranolol Hydrochloride Calibration Curve

Three drugs were used for the analysis, called Generic (G), Similar (S) and Manipulated (M), being used in triplicate each sample. After analysis by ultraviolet-visible spectro photometry, the following results were obtained: G - 94,31%; S -102.58% and M - 105.61%. Spectrophotometry is important in determining the amount of active ingredient contained in a drug. To be in accordance with the criteria established in the Brazilian Pharmacopoeia, the content of a drug must be within the specified range for tablets of 90% to 110% of the declared concentration (Pharmacopéia, 2001). After the analysis, it was observed that propranolol hydrochloride content obtained in the samples from the three classes (generic similar and manipulated) met within the limits, therefore, adequately met the specifications of the Brazilian Pharmacopoeia 4th edition. The data from this study are similar to the findings of PONTES (2009) in which all samples analyzed were within the standard required by the Brazilian Pharmacopoeia 4th edition. When the drug is within the recommended values according to the Brazilian Pharmacopoeia, they have

Table 1. Result of analysis of Generic Propranolol Hydrochloride samples

	Absorbance	[ ] = mg/L (Focused)	[ ] = mg/L (Diluted)	Bulk (g)	Content (%)	Average	Standard deviation
Generic (G)							
G1	0,251	16,67132867	83,35664336	8,335664336	83,35664336	94,31235431	14,93843354
G2	0,265	17,65034965	88,25174825	8,825174825	88,25174825		
G3	0,331	22,26573427	111,3286713	11,13286713	111,3286713		

Source: Research Data.

Table 2. Result of analysis of Propranolol Hydrochloride Similar samples

	Absorbance	[ ] = mg/L (Focused)	[ ] = mg/L (Diluted)	Bulk (g)	Content (%)	Average	Standard deviation
Similar (S)							
S1	0,302	20,23776224	404,7552448	40,47552448	101,1888112	102,5874126	2,126840046
S2	0,313	21,00699301	420,1398601	42,01398601	105,034965		
S3	0,303	20,30769231	406,1538462	40,61538462	101,5384615		

Source: Research Data.

Table 3. Result of analysis of samples of Manipulated Propranolol Hydrochloride

	Absorbance	[ ] = mg/L (Focused)	[ ] = mg/L (Diluted)	Bulk (g)	Content (%)	Average	Standard deviation
Manipulated (M)							
M1	0,258	17,16083916	85,8041958	8,58041958	85,8041958	105,6177156	18,80434187
M2	0,321	21,56643357	107,8321678	10,78321678	107,8321678		
M3	0,365	24,64335664	123,2167832	12,32167832	123,2167832		

Source: Research Data.

guaranteed content, quality, purity and potency, and may bereleased for sale. When the drug content is outside the recommended values, it poses a risk to the general population as adverse effects, which may evolve from ineffectiveness, toxicity or eventually death (Rigobello *et al*., 2013; Silva *et al*., 2017). According to Bridges (2009); Rigobello *et al*. (2013), the Determination of the content of the active ingredient makes it possible to check whether the amount of drug declared on the product label meets the specifications. Administration of a drug with an active ingredient concentration below the specified limit may lead to treatment failure, while above levels may result in adverse and / or toxic effects. Quality control is critical to ensure the quality of the drugs produced are within the required quality standards necessary to ensure product quality before they are released for sale or supply (Rocha *et al*., 3013; Asberg *et al*., 2016). Quality control is part of Good Manufacturing Practice (GMP), which should be conducted under the responsibility of a qualified person, fulfilled all stages of production of the drug, in order to avoid failures and detect product quality deviations capable of entail risks to the patient. Products can only be released for sale or supply when their quality is deemed satisfactory (Amorim *et al*., 2013; Rigobello *et al*., 2013; Rocha *et al*., 3013). Therefore, determining the quality of medications is an extremely important fact. Deviations in the recommended characteristics may pose serious health risks to patients and may even become a public health problem (Freitas *et al*., 2014).

Conclusion

From this analysis it is verified that Propranolol Hydrochloride (generic, similar and manipulated), presented a satisfactory result, since the concentration of the active principle were within the ideal parameters and recommended by the Brazilian Pharmacopoeia (2001). Given these results, quality control is of utmost importance to the pharmaceutical industries, and they perform tests and measurements that allow to approve or disapprove drugs and excipients before they are even available for manufacturing. Thus, the research contributes to the knowledge and warns of the importance of Quality Control for professionals, users / patients.

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