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QUANTITATION OF PROPRANOLOL HYDROCHLORIDE IN PHARMACEUTICAL DOSAGE FORMS BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT

A high-performance liquid-chromatography method for the quantitation of propranolol hydrochloride in pharmaceutical dosage forms (capsules, injections and tablets) has been developed. The method can also be used for contents uniformity as required by USP-NF. There is no interference from the excipients present and from hydrochlorothiazide which is often mixed with propranolol hydrochloride. The method is accurate, reproducible and precise with a percent relative standard deviation of 0.6 based on 5 readings. A sample decomposed with sodium hydroxide treatment showed about 9% potency and 2 new peaks in the chromatogram.

BACKGROUND

Propranolol hydrochloride is a beta-adrenergic receptor blocking drug and is used widely against hypertension.

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The USP-NF method[1] for the quantitation of propranolol hydrochloride is based on UV spectroscopy which is not a stability indicating assay method. The quantitation of propranolol hydrochloride in plasma using high-performance liquid chromatography (HPLC) has been reported[2,3]. Due to sensitivity requirements in plasma samples, a fluorophotometer was used for detection. An HPLC method[4] to quantify beta-blockers in tablets has been reported. This method was not applied to dosage forms which also contained hydrochlorothiazide, a very common ingredient present with propranolol hydrochloride.

The purpose of these investigations was to develop a high-performance liquid chromatography method based on UV detector which can be used to quantify propranolol hydrochloride in pharmaceutical dosage forms including in combination with hydrochlorothiazide and can also be applied for contents uniformity.

MATERIALS AND METHODS

Chemicals and Reagents: All chemicals and reagents were USP, NF or ACS grade and were used as received. Propranolol hydrochloride[5] (I) and verapamil hydrochloride[6] (II) were used without further purification. A high-performance liquid chromatograph[7], equipped with a multiple wavelength detector[8], a recorder[9] and digital cm integrator[10], was used.

Column: A nonpolar column[11] (30 cm long x 4 mm i.d.) consisting of a monomolecular layer of octadecyltrichlorosilane permanently bonded to silica gel was used.

Chromatographic Conditions: The mobile phase contained 43% V/V of methanol, 0.5% V/V of glacial acetic acid and 0.02M ammonium formate in water and the flow rate was 2.0 ml/minute. The detector was set at 270 nm and the sensitivity was 0.04. The temperature was ambient and the chart speed was 30.5 cm/hr.

Preparation of Solutions: The stock solutions of propranolol hydrochloride (1.0 mg/ml) in ∿0.02N HCl and verepamil hydrochloride (5.0 mg/ml) in water were prepared fresh daily. A standard solution was prepared by mixing 5.0 ml of the stock solution of I with 3.0 ml of the stock solution of verapamil hydrochloride (the internal standard) and bringing the volume to 50.0 ml with water. Solutions of other concentrations were prepared as needed.

Preparation of Assay Solutions: For tablets and capsules, ten tablets or contents of capsules (one tablet/capsule for contents uniformity) were ground to a fine powder, a portion representing 10.0 mg of I was weighed accurately and mixed with 4 ml of ∿0.5N HCl, 50 ml of water and 6.0 ml of the stock solution of verapamil hydrochloride. The mixture was stirred for 2-3 minutes, brought to volume (100.0 ml) with water and filtered. The first 15 ml of the filtrate was rejected and then collected for assay. For ampuls, a 2.5 ml quantity of the solution was mixed with 1.5 ml quantity of the stock solution of verapamil hydrochloride and brought to volume (25.0 ml) with water.

Assay Procedure: A 20 µl of the assay solution was injected into the chromatograph using the described conditions. For comparison, an identical volume of the standard solution was injected after the assay solution eluted.

Calculations: The results were calculated using

$$\frac{(Ph)_a}{(Ph)_s} \times 100 = \text{Percent of the label claim}$$

where $(Ph)_a$ is ratio of peak heights (propranolol/verapamil) of the assay solution and $(Ph)_s$ that of the standard solution of an identical concentration. Preliminary investigations indicated that ratio of peak heights versus concentrations were linear between 0.8 to 2.5 µg of I.

Decomposition of Propranolol Hydrochloride: A 6.0 ml quantity of the stock solution of I was mixed with 0.3 g of sodium hydroxide pellets in a 150 ml beaker and boiled on a hot plate (more water was added as needed). The mixture was cooled, pH adjusted[12] to ∿4 with ∿1N HCl and assayed after appropriate dilution with water.

RESULTS AND DISCUSSION

The results indicate (Table I and Figure 1) that the developed HPLC method can be used for the quantitation of propranolol hydrochloride in a variety of pharmaceutical dosage forms (tablets, capsules and injectables) including in combination with hydrochlorothiazide. The method is accurate, reproducible and precise with an average percent relative standard deviation of 0.6 based on 5 readings. The wavelength of 270 nm was preferred to improve the sensitivity of verapamil (the internal standard) which had poor absorption at 291.5 nm (the maxima for propranolol hydrochloride). Later on, in these investigations, it was determined that the sensitivity of method may be further improved by using 278 nm (the maxima for verapamil), rather than 270 nm. At this

TABLE 1

Propranolol Hydrochloride Assay Results

Contents of Tablet/Capsule/Injection/ Synthetic Mixture	Percent of the Label Claim Found
Propranolol hydrochloride 10 mg - pink tablets[a]	99.9
Propranolol hydrochloride 20 mg - blue tablets[a]	99.2
Propranolol hydrochloride 40 mg - green tablets[a]	100.2
Propranolol hydrochloride 80 mg - yellow tablets[a]	99.7
Propranolol hydrochloride LA 80 mg - capsules[a]	98.9
Propranolol hydrochloride 40 mg and hydrochlorothiazide 25 mg - organge tablets[b]	99.0
Propranolol hydrochloride 1 mg/ml - ampuls[a]	100.2
Propranolol hydrochloride 50 mg and hydrochlorothiazide 25 mg synthetic mixture[c]	99.8
Contents uniformity 10 mg tablets[a]	
Tablet 1	98.2
Tablet 2	102.2
Tablet 3	99.1
Tablet 4	98.7
Tablet 5	97.8
Tablet 6	101.7
Tablet 7	100.8
Tablet 8	101.2
Tablet 9	97.9
Tablet 10	98.9

[a]Ayerst Laboratories, New York, NY.

[b]Invamed, Inc., Fairfield, NJ

[c]Prepared by mixing both powders by the process of trituration.

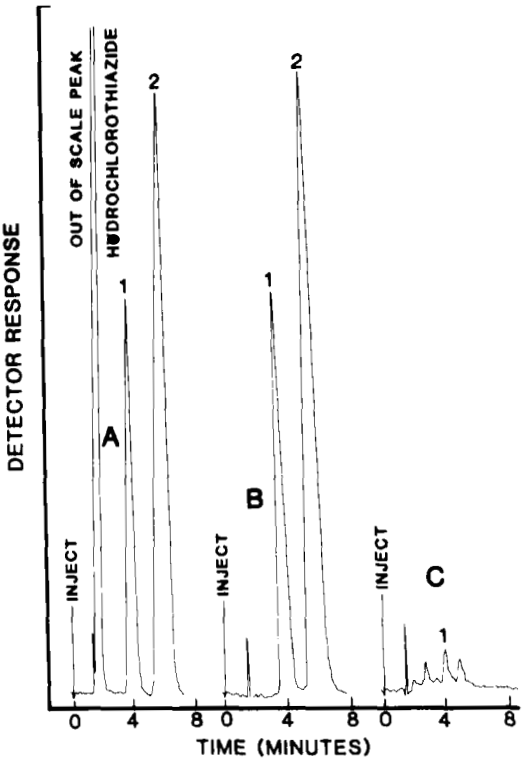

FIGURE 1

Sample chromatograms; Peak 1-2 are from propranolol hydrochloride and verapamil hydrochloride, respectively. Chromatogram A is a tablet containing 40 mg of I and 25 mg of hydrochlorothiazide; B from a standard solution and C from a decomposed sample (see text). For chromatographic conditions, see text.

wavelength also, the results were reproducible, precise and accurate. Also from Figure 1, it is obvious that the concentration of the internal standard may be reduced from 300 to 200 μg/ml, even at 270 nm.

There was no interference with the procedure from various excipients present in the dosage forms and from hydrochlorothiazide (Figure 1A) which is often mixed with I. Hydrochlorothiazide

separated completely from I. The method requires a very simple extraction procedure from tablets/capsules and can be used for the determination of contents uniformity as given in the USP-NF[1]. The method appears to be stability-indicating since a decomposed sample (see text) contained 8.7% of the label claim of propranolol hydrochloride and there were 2 new peaks (Figure 1C) in the chromatogram.

REFERENCES

1. "United States Pharmacopeia," 20th ed., "National Formulary," 15th ed., U.S. Pharmacopeial Convention, Inc., Rockville, MD, 1980, p. 684.
2. M.T. Rosseel and M.G. Bogaert, J. Pharm. Sci., 70, 688 (1981).
3. O.H. Drummer, J. McNeil, E. Pritchard and W.J. Louis, Ibid. p. 1030.
4. B.R. Patel, J.J. Kirschbaum and R.B. Poet, Ibid., 70, 336 (1981).
5. Ayerest Laboratories, New York, NY.
6. Knoll Pharmaceuticals, Whippany, NJ.
7. Waters ALC 202 equipped with U6K universal injector, Waters Associates, Milford, MA.
8. Schoeffel Spectroflow Monitor 770, Kratos Inc., Ramsey, NJ.
9. Omniscribe 5213-12, Houston Instruments, Austin, TX.
10. Autolab Minigrator, Spectra Physics, Santa Clara, CA.
11. Waters, μBondapak/C_{18}.
12. Beckman SS-3, Zeromatic pHmeter, Beckman Instruments, Irvine, CA.