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# Room Temperature Phosphorescence Determination of Propranolol in Pharmaceutical Formulations

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**Abstract** □ A simple, rapid, and specific procedure was used for the analysis of propranolol in pharmaceutical formulations. The procedure consisted of dissolving (diluting) appropriate quantities of preparations and standards in (with) a 2 *M* potassium iodide–ethanol–water solution, spotting 5 μl of each resultant solution onto filter paper disks, determining the phosphorescence intensities at room temperature, and comparing sample signal levels with those of standards. The results indicated that room temperature phosphorescence can be easily applied to the analysis of pharmaceutical formulations where active ingredients are generally contained in a wide variety of matrices.

**Keyphrases** □ Propranolol—room temperature phosphorescence determination in tablets and injections □ Phosphorescence—determination of propranolol in tablets and injections □ β-adrenergic agents—propranolol, room temperature phosphorescence determination, tablets and injections

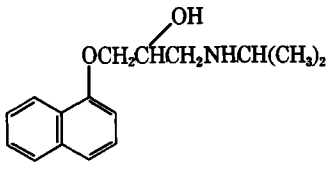
Propranolol hydrochloride, a β-adrenergic blocker, is commonly used for the treatment of nonacute hypertension, angina pectoris, and cardiac arrhythmias. With the patent on the only marketed product nearing its expiration, generic brands of propranolol will soon become available. Because generic manufacturers often use a variety of materials (diluents, binders, *etc.*) in their formulations, a specific procedure is needed for the quantitation of the active ingredient in the formulation.

The current USP procedure (1) for propranolol is cumbersome, and as a result, many pharmaceutical manufacturers are currently investigating fluorometry and high-performance liquid chromatography (HPLC) for quality control.

The present report describes a simple and rapid room temperature phosphorescence procedure applicable to the determination of propranolol in several pharmaceutical preparations. While room temperature phosphorescence has been shown to be analytically useful, real sample applications have been limited (2, 3). Overall, room temperature phosphorescence offers good selectivity with moderate sensitivity and detection power.

## EXPERIMENTAL

**Reagents**—Propranolol hydrochloride[1] (I) and hydrochlorothiazide[2] (II) were used as received. All pharmaceutical preparations were purchased through a local hospital pharmacy[3]. All other materials were of analytical reagent grade.



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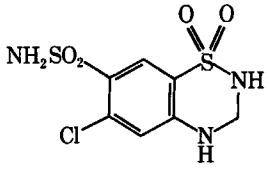

II

**Apparatus**—All room temperature phosphorescence measurements were made with a spectrophotofluorometer[4] fitted with a 150-W xenon arc lamp[5], a laboratory-constructed phosphoroscope (4) for bar, room temperature phosphorescence (5), and a potted photomultiplier tube[6]. A ratio photometer[7] supplied high voltage to the photomultiplier tube in addition to serving as a DC amplifier. All line voltages were regulated with an AC regulator[8].

**Standard and Sample Preparation**—A standard stock solution (400 μg/ml) was prepared by dissolving an accurately weighed portion of propranolol hydrochloride in a 2 *M* potassium iodide solution (ethanol–water, 50:50). Standard solutions (5, 10, 20, 50, 100, 200, and 300 μg/ml) were prepared daily by mixing appropriate volumes of the stock solution with the ethanolic solution. Samples were prepared for assay by dissolution–dilution in/with the ethanolic solution. For analysis of representative samples, 20 tablets were weighed and powdered with a mortar and pestle, and four portions (equivalent to 100 μg/ml of active ingredient in a total volume of 10 ml) were dissolved in the ethanolic solution. This procedure was repeated for each solid sample. For the analysis of liquid preparations, appropriate volumes (same equivalence as tablets) of the samples were diluted with the ethanolic solution. Four different test solutions were prepared for each pharmaceutical formulation; each test solution contained 100 μg/ml of active ingredient.

**Procedure**—Bar, room temperature phosphorescence analysis consisted of an aluminum bar, a cover plate with four holes (each ~0.64-cm diameter) and filter paper disks[9]. The filter paper disks were placed under the cover plate and the cover plate was tightened into place on the bar with four screws. Samples were spotted onto the paper disks in 5-μl vol-

[1] Ayerst Laboratories, New York, N.Y.: Inderal, propranolol hydrochloride; Inderide, propranolol hydrochloride with hydrochlorothiazide.
[2] Ciba Pharmaceutical Co., Summit, N.J.
[3] Pharmacy Stores, Shands Teaching Hospital, Gainesville, Fla.
[4] Aminco-Bowman SPF, American Instrument Co., Jessup, Md.
[5] Canrad-Hanovia, Newark, N.J.
[6] 1P21, Hamamatsu, Middlesex, N.J.
[7] American Instrument Co.
[8] Sorenson 1001, Norwalk, Conn.
[9] Grade 903, Schleicher & Schuell, Keene, N.H.

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**Table 1—Results for the Determination of Active Ingredients in Pharmaceutical Formulations [a]**

| Formulation, mg Active Ingredient/ Dosage Form | Concentration Found Experimental, μg/ml[b] | | Coefficient of Variation, % | Experimental Amount (mg) of Active Ingredient/ Dosage Form[c] |
|---|---|---|---|---|
| Propranolol | Mean | Range | | |
| 20 | 98 | 90–108 | 5.2 | 20 |
| 40 | 97 | 88–108 | 7.2 | 39 |
| 80 | 102 | 94–108 | 4.0 | 82 |
| 1 (injection 1-ml ampule) | 103 | 94–111 | 4.4 | 1 |
| Propranolol/Hydrochlorothiazide | | | | |
| 40/25 | 102 | 94–110 | 5.0 | 41 |
| 80/25 | 101 | 94–110 | 4.5 | 81 |

[a] All test samples were 100 μg/ml of active ingredient. [b] Calculated from 16 measurements of each of four samples. [c] Mean value calculated from 16 determinations of active ingredients in each of four weighed portions.

umes with a micropipet[10]. After spotting, the bar was slipped into the sample compartment (equipped with a phosphoroscope can with a chopping rate of 200 Hz) and the samples were allowed to dry for 7 min under a flow of dehumidified nitrogen gas (~20 liters/min). During the drying process, signals increased over a period of ~6 min at which time a plateau was reached for ~2 min. Measurements were made on this plateau. This procedure was repeated 16 times for each sample and standard. The excitation and emission wavelengths used in the analyses were 306 and 492 nm, respectively.

**Quantitation**—Quantitation was achieved by comparing the relative phosphorescence intensities of the samples with those of the standards. For the analyses, the linear range of the propranolol standard solutions extended from 20 to 300 μg/ml. Linear regression analysis gave the line $y = 0.725x - 7.34$ with a correlation coefficient of +0.999.

## RESULTS AND DISCUSSION

The results in Table I indicate that room temperature phosphorescence can be successfully applied to the determination of propranolol in pharmaceutical preparations. Precision studies with 16 determinations of each sample and standard gave coefficients of variation between 4 and 8%. While room temperature phosphorescence is well established as a method of analysis with great selectivity, its sensitivity generally lags behind that of other techniques.

Both propranolol and hydrochlorothiazide phosphoresce when 2 *M* NaOH is added to the ethanolic solution. However, because of the weaker phosphorescence signal of hydrochlorothiazide, it was not possible for it to be quantitatively determined in the prepared mixtures. Only propranolol appeared to phosphoresce when present in the ethanolic solution, and this component was analyzed in the prepared mixtures. Figures 1 and 2 illustrate what is spectrally observed without and with the addition of 2 *M* NaOH to the ethanolic solutions.

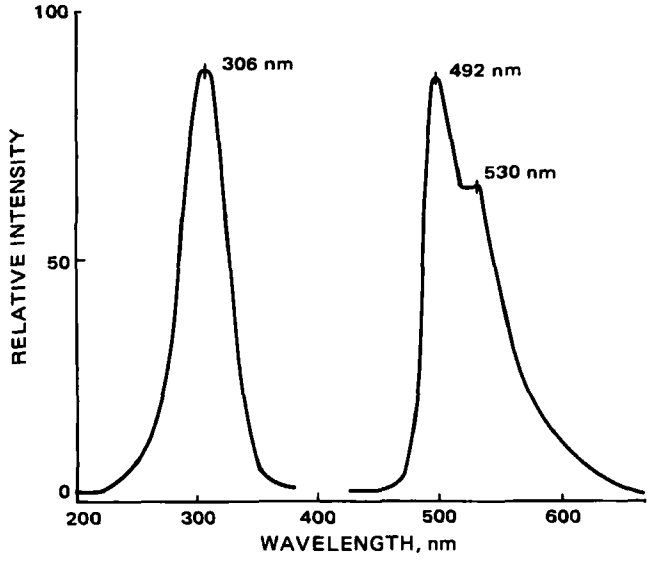


**Figure 1**—*Room temperature phosphorescence obtained from 100-μg/ml propranolol hydrochloride in an ethanolic solution and from a mixture of 100-μg/ml propranolol hydrochloride and 50-μg/ml hydrochlorothiazide.*

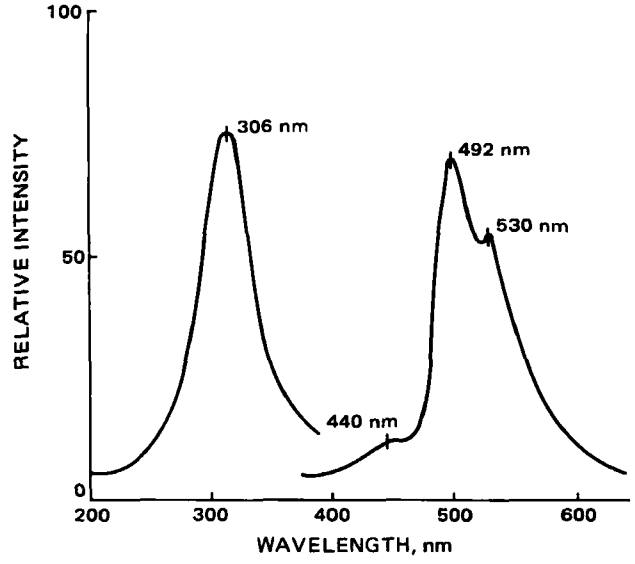


**Figure 2**—*Room temperature phosphorescence obtained from a mixture of 100-μg/ml propranolol hydrochloride and 50-μg/ml hydrochlorothiazide with 2 M NaOH in an ethanolic solution.*

The selectivity factor in room temperature phosphorescence was advantageous in that no compound other than propranolol appeared to phosphoresce. Because pharmaceuticals are proprietary in nature, no absolute assurance of any other species contributing to the phosphorescence of the sample can be given. It would be expected that those species in the formulations that may phosphoresce are minor constituents and are subsequently diluted when the sample is prepared for analysis. Thus, this procedure is reported to be quite simple and specific for the determination of propranolol in pharmaceutical formulations.

[10] SMI micro/pettor, Scientific Manufacturing Industries, Emeryville, Calif.

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