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Spectrophotometric Determination of Chlorpromazine in Pharmaceutical Dosage Forms

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Abstract □ A rapid and convenient spectrophotometric method for the determination of chlorpromazine hydrochloride and its unit dosage forms is described. Extensive separation and extraction of the active ingredient are not required. The microsensitive color response (λ_{max}, 520 mμ) with Van Urk's reagent is the basis of the analytical technique. The results are reproducible.

Keyphrases □ Chlorpromazine dosage forms—analysis □ Colorimetric analysis—spectrophotometry □ Van Urk's reagent—color formation

Chlorpromazine hydrochloride (CPZH), a phenothiazine derivative, is a widely used psychopharmacological agent. Chlorpromazine hydrochloride and some of its unit dosage forms are official in BP 1968 (1), USP XVII (2), and Ph.I. (3). A number of gravimetric, titrimetric, opticometric, electrometric, and chromatographic methods for the quantitative determination of phenothiazines have been reported in the literature, each one claiming individual advantages. These have been reviewed by Blazek (4), Blazek *et al.* (5), and Gyenes (6). Blake and Agarwal (7) recently reported a photometric titration of phenothiazines with ceric sulfate. The current pharmacopeias recognized nonaqueous titrimetry for determining the drug, while the unit dosage forms containing the drug—*viz.*, tablets, injections, *etc.*, are determined by methods based on the UV absorption properties of the phenothiazine base. However, these methods involve a series of extractions of the active ingredient from the unit dosage forms.

The authors have observed that a color ($\lambda_{max.}$, 520 mμ) results when CPZH is treated with Van Urk's reagent. The color-producing reaction with phenothiazines has not been previously reported in the literature. This investigation is primarily directed toward the evaluation of the observed novel reaction as a quantitative measure of chlorpromazine in its various dosage forms.

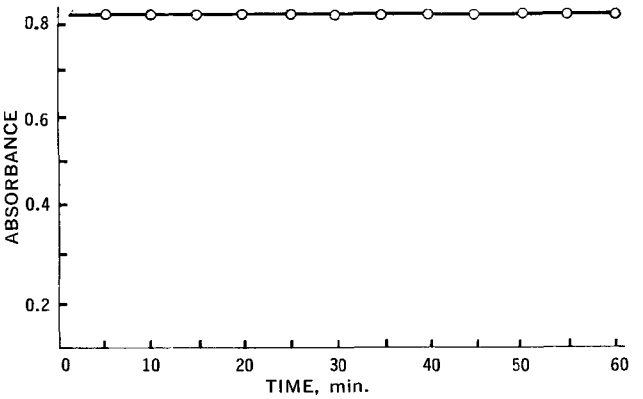

Figure 1—*Effect of time on the stability of color with Van Urk's reagent and CPZH.*

EXPERIMENTAL

Instrumentation—Beckman DU spectrophotometer (1-cm. cell) was used.

Materials—Van Urk's reagent, BP 1968 (8), was used. Chlorpromazine hydrochloride and the various dosage forms were obtained from commercial sources. All reagents were analytical grade. Glass-distilled water was used throughout this work.

Standard Reference Solution—Chlorpromazine hydrochloride (50 mg.), previously dried, in distilled water (250 ml.) was used.

Sample Preparation—*Tablets*—Twenty tablets were weighed and reduced to a fine powder. An accurately weighed portion of the powder, equivalent to 50 mg. of the drug, was transferred to a 250-ml. volumetric flask. The flask was shaken thoroughly for 10–15 min. after adding 100 ml. of water and was made to volume. The contents of the flask were filtered.

Injections—An equivalent volume, representing 50 mg. of the drug, was measured and diluted with water to 250 ml.

Suppositories—Suppositories representing 100 mg. of the drug were placed in a 500-ml. volumetric flask and melted by heating on a

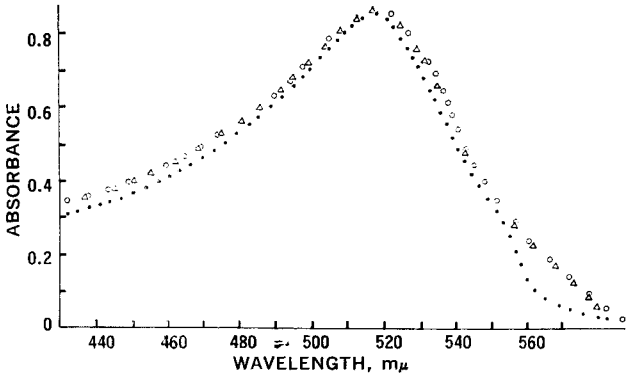

Figure 2—*Effect of water-soluble inert diluents on the absorption maxima. Key: . . ., CPZH and lactose and sucrose; ○, CPZH and acacia or tragacanth; and △, CPZH.*

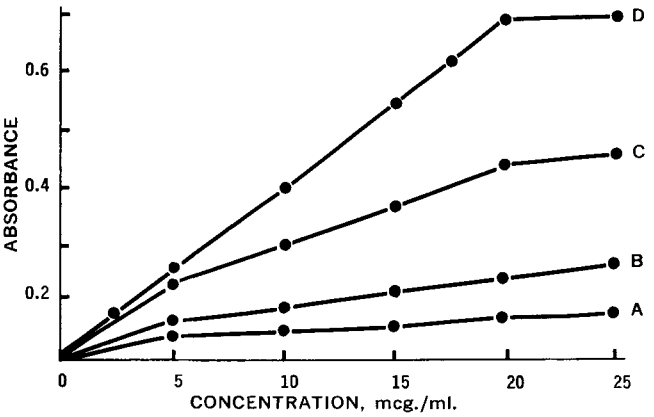

Figure 3—*Effect of volume of Van Urk's reagent on absorbance. Key: volume of reagent: A = 1 ml.; B = 2 ml.; C = 3 ml.; and D = 4 ml.*

steam bath. Hot water (100 ml.) was added; the solution was shaken and finally made to volume with water. Following filtration, the filtrate was used for the assay.

Syrup—A volume of syrup representing 50 mg. of the drug was diluted with water to 250 ml.

Method—A 0.1–0.5-ml. aliquot of the sample solution, prepared as previously described, was treated with 4 ml. of Van Urk's reagent, shaken, and made to a known volume with water. The intensities of the colors developed by the sample solution and by the chlorpromazine standard, treated simultaneously with the reagent, were measured at 520 mμ against the reagent blank.

RESULTS AND DISCUSSION

The color produced in the reaction is stable for at least 60 min. (Fig. 1); the presence of 0.5 mg. of the commonly used inert diluents —acacia, tragacanth, lactose, and sucrose—did not interfere (Fig. 2). The most suitable slope of the calibration curve and the maximum color intensity were obtained with the use of 4 ml. of the reagent with 0.1–1.0 ml. of the standard solution in a total volume of 10 ml. (Fig. 3). For a constant volume of Van Urk's reagent, an increase in the concentration of CPZH up to 20 mcg./ml. produced an increase in color intensity. Color generation under standard conditions obeyed Beer's law between 5–20 mcg./ml. (0.165–0.7 absorbance, respectively, at 520 mμ) (Fig. 3). The mean absorbance of 10 replicates from one solution to another was noted. The standard deviation was found to be ± 0.005.

The data in Table I indicate that quantitative recoveries were obtained for the unit dosage forms and that the results were in good agreement with the official methods. The reported procedure has the advantage that it does not require the preliminary extraction of the active ingredient. The effect of decomposition products on the recovery of the parent compound has not been evaluated. The procedure allows for a simple, rapid, and accurate determination of small quantities of chlorpromazine.

Table I—Analysis of Unit Dosages Containing CPZH

Dosage Form[a]	Labeled Amount per Unit, mg.	Method BP 1968, % R[b]	Method USP XVII, % R	Proposed Method, % R
Tablet	50.00	101.00[c]	102.00[c]	102.00 ± 0.4[d]
Injection	27.90	99.30	102.10	102.10 ± 0.4
Syrup	5.58	98.60	98.60	98.60 ± 1.0
Suppositories	111.60	Not official	98.80	98.60 ± 0.6
Control CPZH	50.00	100.40	100.40	100.40 ± 0.2

[a] Dosage forms analyzed for two different labeled amounts; one only is given. [b] % R represents the percentage recovery. [c] Average of at least three determinations by official method. [d] Standard deviation based on at least four determinations.

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