Tablets have been marketed in which meprobamate was combined with other active ingredients. The following substances have been examined and found to produce no interference in the determination of meprobamate: amphetamine sulfate, hydrochlorothiazide, dexamethasone, pentaerythritol tetranitrate, benactyzine hydrochloride, and aspirin.

Carisoprodol and mebutamate were analyzed by the same procedure. Their NMR spectra are also shown in Fig. 1. Unlike meprobamate, two peaks are produced at 3.8 p.p.m. Further differences may be noted in the area of 0.8 to 1.4 p.p.m. Preliminary work shows the accuracy to be of the same order as for meprobamate.

The speed, accuracy, and specificity of the NMR method make it useful as a rapid procedure that can provide both a quick and conclusive identification and an assay having an accuracy of about 1–2%.

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Qualitative and Quantitative Tests for Prilocaine Hydrochloride

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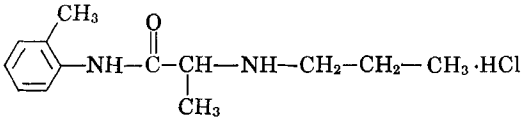
Provisional, unofficial monographs are developed by the Drug Standards Laboratory, in cooperation with the manufacturers of the drug concerned, for publication in the *Journal of Pharmaceutical Sciences*. The ready availability of this information affords discriminating medical and pharmaceutical practitioners with an added basis for confidence in the quality of new drug products generally, and of those covered by the monographs particularly. Such monographs will appear on drugs representing new chemical entities for which suitable identity tests and assay procedures are not available in the published literature. The purity and assay limits reported for the drugs and their dosage forms are based on observations made on samples representative of commercial production and are considered to be reasonable within expected analytical and manufacturing variation.

2-(PROPYLAMINO) - *o* - PROPIONOTOLUIDIDE HYDROCHLORIDE; $C_{13}H_{20}N_2O \cdot HCl$; mol. wt. 256.78. The structural formula of prilocaine hydrochloride may be represented as:



Physical Properties—Prilocaine hydrochloride occurs as a white, odorless crystalline powder with a bitter taste, m.p. 166–169° (USP class I). It is freely soluble in water and in alcohol, slightly soluble in chloroform, very slightly soluble in acetone, and practically insoluble in ether.

Identity Tests—The infrared spectrum of a 0.5% dispersion of prilocaine hydrochloride in potassium bromide, in a disk of about 0.82 mm. thickness, is shown in Fig. 1.

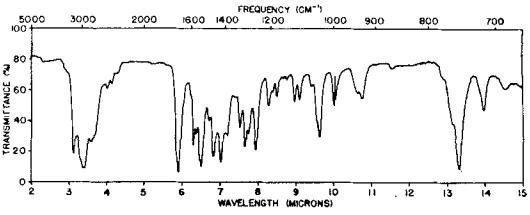


Fig. 1—Infrared spectrum of prilocaine hydrochloride in potassium bromide disk (0.5%); Perkin-Elmer model 21 spectrophotometer, sodium chloride prism.

Dissolve about 100 mg. of prilocaine hydrochloride in about 3 ml. of water, add ammonia T.S. until basic, and filter. Acidify the filtrate with diluted nitric acid, and add 1 ml. of silver nitrate T.S.: a white precipitate forms, which is insoluble in diluted nitric acid, but soluble in ammonia T.S. (presence of chloride).

Transfer about 300 mg. of prilocaine hydrochloride to a separator and dissolve in 5 ml. of water. Add 4 ml. of ammonia T.S. and extract with four 15-ml. portions of chloroform, filtering the extracts through paper. Evaporate the combined

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extracts on a steam bath with the aid of a current of air: the oily residue responds to the following tests.

Dissolve about 100 mg. of the free base in 1 ml. of alcohol, add 10 drops of cobaltous chloride T.S., and shake for 2 min.: a bright green color develops, and a fine precipitate is formed.

Dissolve about 100 mg. in a mixture of 5 ml. of water and 1 ml. of diluted nitric acid, warming if necessary to effect solution. Add 3 ml. of mercuric nitrate T. S., and heat nearly to boiling: the solution turns yellow or yellow-green.

Purity Tests—Dry about 1 Gm. of prilocaine hydrochloride, accurately weighed, at 105° for 4 hr.: it loses not more than 0.3% of its weight.

Char about 1 Gm. of prilocaine hydrochloride, accurately weighed, cool the residue, add 1 ml. of sulfuric acid, heat cautiously until evolution of sulfur trioxide ceases, ignite, cool, and weigh: the residue does not exceed 0.1%.

Dissolve about 200 mg. of prilocaine hydrochloride in 10 ml. of water, add 2 ml. of diluted hydrochloric acid, and 1 ml. of barium chloride T.S.: no turbidity is produced (absence of sulfate).

Dissolve about 200 mg. of prilocaine hydrochloride in 20 ml. of water, add 2 ml. of diluted hydrochloric acid and saturate the solution with hydrogen sulfide: no color or precipitate results (absence of heavy metals).

Assay—*Chloride*—Transfer about 200 mg. of prilocaine hydrochloride accurately weighed, to a 125-ml. conical flask, and dissolve in 10 ml. of water. Add 10 drops of potassium chromate T.S. and titrate with 0.1 *N* silver nitrate to a red-brown end point. Each milliliter of 0.1 *N* silver nitrate is equivalent to 3.546 mg. of chloride (Cl). The chloride content is not less than 13.4% and not more than 14.2%.

Prilocaine Hydrochloride—Transfer about 500 mg. of prilocaine hydrochloride, accurately weighed, to a tall-form 200-ml. beaker, and dissolve in 50 ml. of glacial acetic acid. Add 10 ml. of mercuric acetate T.S. and 2 drops of crystal violet T.S., and titrate with 0.1 *N* acetous perchloric acid to a blue-green end point. Perform a blank determination, and make any necessary correction. Each milliliter of 0.1 *N* perchloric acid is equivalent to 25.68 mg. of $C_{13}H_{20}N_2O \cdot HCl$. The amount of prilocaine hydrochloride found is not less than 99.0% and not more than 101.0%.

DOSAGE FORMS OF PRILOCAINE HYDROCHLORIDE

Prilocaine Hydrochloride Injection

Physical Properties—Prilocaine hydrochloride injection is a sterile aqueous solution with methylparaben present as a preservative. The pH of the solution is adjusted between 6.0 and 7.0 with sodium hydroxide.

Identity Tests—Transfer to a separator a volume of injection equivalent to about 300 mg. of prilocaine hydrochloride, and proceed as directed under the bulk drug beginning with "Add 4 ml. of ammonia T.S . . . ."

Assay—Transfer to a separator an accurately measured volume of prilocaine hydrochloride injection equivalent to about 200 mg. of prilocaine hydrochloride. Add 2 ml. of sodium hydroxide T.S. and extract with four 25-ml. portions of chloroform, filtering each portion through chloroform moistened paper into a titrating beaker. Concentrate the filtrate to about 10 ml. on a steam bath with the aid of a current of air, add 40 ml. of glacial acetic acid, 2 drops of crystal violet T.S., and titrate with 0.1 *N* acetous perchloric acid to a blue-green end point. Perform a blank determination, and make any necessary correction. Each milliliter of 0.1 *N* perchloric acid is equivalent to 25.68 mg. of $C_{13}H_{20}N_2O \cdot HCl$. The amount of prilocaine hydrochloride found is not less than 95.0% and not more than 105.0% of the labeled amount.

DISCUSSION

USP and NF terminology for solubility, melting range, reagents, *etc.*, has been used wherever feasible.

Prilocaine hydrochloride,[1] synthesized by Lofgren and Tegner (1), is a local anesthetic agent whose potency is comparable to lidocaine but whose toxicity is significantly reduced (2, 3). It is intended for use in infiltration and regional anesthesia, therapeutic nerve blocks such as intercostal and paravertebral blocks, and blockades of major nerve trunks *via* the peridural and caudal routes. Prilocaine hydrochloride is administered by injection and is available in 1, 2, 3, and 4% solutions. Prilocaine hydrochloride was formerly known by the generic name propitocaine hydrochloride.

Identity Tests—The reaction of prilocaine and mercuric nitrate to produce a yellow or yellow-green color differentiates the compound from anesthetics derived from *p*-aminobenzoic acid which turn red or orange. The free base isolated by chloroform extraction from alkaline solution can be reacted with methanesulfonic acid in anhydrous ether for identification. The methanesulfonate (mesylate) salt so obtained recrystallized from dehydrated alcohol–isopropyl ether (1,3) melts between 168–171°.

Quantitative Tests—Determination of chloride content by the Mohr method gave an average value of 13.8 ± 0.1%.[2] The theoretical value for the chloride content is 13.81%. The halide salt can be determined by many conventional methods of analysis for ionizable chloride.

Nonaqueous titration of prilocaine hydrochloride with perchloric acid gave an average value of 100.2 ± 0.3%.[2] The isolation of prilocaine base from the 1% injection and subsequent titration gave an average value of 100.4 ± 0.5%[2] of the labeled amount of prilocaine hydrochloride. Analyses of the 2, 3, and 4% injections yielded recoveries corresponding to 99–100% of label declaration.

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[1] Marketed as Citanest by Astra Pharmaceutical Products, Inc., Worcester, Mass.
[2] Maximum deviation from the mean value.