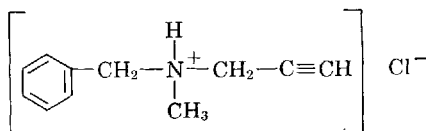


Qualitative and Quantitative Tests for Pargyline Hydrochloride

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.

N-METHYL-*N*-(2-propynyl)-benzylamine hydrochloride; $C_{11}H_{13}N \cdot HCl$; mol. wt. 195.69. The structural formula of pargyline hydrochloride may be represented as



Physical Properties.—Pargyline hydrochloride occurs as a fine white crystalline powder having a characteristic odor, m.p. 158–162° (U.S.P., class I). It is very soluble in water and freely soluble in alcohol. Pargyline hydrochloride sublimes slowly when maintained at temperatures approaching its melting range.

Identity Tests.—A 1 in 2,500 solution of pargyline hydrochloride in 0.1 *N* hydrochloric acid exhibits ultraviolet absorbance maxima at about 251, 257, 262 [absorptivity (*a*) about 1.55], and 268 μ , and absorbance minima at about 229, 253, 259, and 266 μ . The spectrum is shown in Fig. 1.

The infrared spectrum of a 0.5% dispersion of pargyline hydrochloride in potassium bromide, in a disk of about 0.82 mm. thickness is shown in Fig. 2.

Dissolve about 50 mg. of pargyline hydrochloride in 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).

Purity Tests.—Determine the water content of pargyline hydrochloride by the titrimetric (Karl Fischer) method: not more than 1% is found.

Char about 1 Gm. of pargyline 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 0.2%.

Determine the heavy metals content of pargyline hydrochloride by the U.S.P. heavy metals test, method II: the heavy metals limit for pargyline hydrochloride is 20 p.p.m.

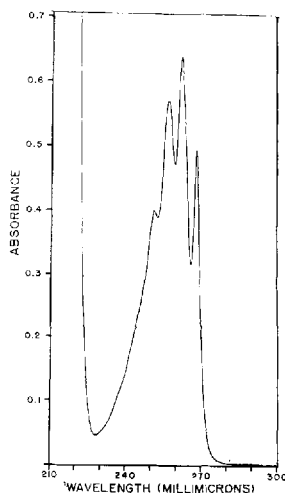


Fig. 1.—Ultraviolet absorption spectrum of pargyline hydrochloride in 0.1 *N* hydrochloric acid (400 mcg./ml.); Beckman model DK-2A spectrophotometer.

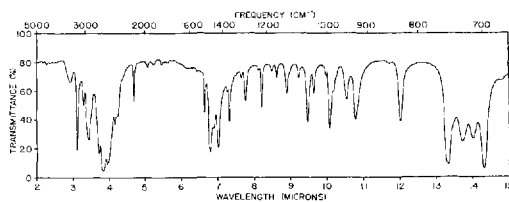


Fig. 2.—Infrared spectrum of pargyline hydrochloride in potassium bromide disk (0.5%); Perkin-Elmer model 21 spectrophotometer, sodium chloride prism.

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A solution of pargyline hydrochloride in water (1 in 10) is colorless and clear, except for some mechanical impurities which may remain in suspension.

Assay.—Acetylenic Group.—Transfer about 200 mg. of pargyline hydrochloride, accurately weighed, to a tall-form 200-ml. beaker and dissolve in 20 ml. of alcohol. Add 25 ml. of 0.1 *N* alcoholic silver nitrate (prepared by dissolving 8.5 Gm. of silver nitrate in 20 ml. of water and diluting to 500 ml. with alcohol), 50 ml. of 0.2 *M* alcoholic trishydroxymethylaminomethane (THAM), and mix. Titrate the mixture potentiometrically with 0.1 *N* alcoholic potassium hydroxide using glass and calomel electrodes. Each milliliter of 0.1 *N* alcoholic potassium hydroxide is equivalent to 9.785 mg. of $C_{11}H_{13}N \cdot HCl$. The amount of pargyline hydrochloride found is not less than 98.0% and not more than 102.0%.

Amine Group.—Transfer about 400 mg. of pargyline 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 titrate potentiometrically with 0.1 *N* acetous perchloric acid. Alternatively, add 2 drops of crystal violet T.S. and titrate to a green end point.¹ Each milliliter of 0.1 *N* perchloric acid is equivalent to 19.57 mg. of $C_{11}H_{13}N \cdot HCl$. The amount of pargyline hydrochloride found is not less than 98.0% and not more than 102.0%.

DOSAGE FORMS OF PARGYLINE HYDROCHLORIDE

Pargyline Hydrochloride Tablets

Identity Tests.—Transfer to a 100-ml. volumetric flask an amount of powdered tablets equivalent to about 40 mg. of pargyline hydrochloride. Add about 50 ml. of 0.1 *N* hydrochloric acid and shake mechanically for 15 min. Dilute to volume with 0.1 *N* hydrochloric acid, mix, and filter: the filtrate exhibits ultraviolet absorbance maxima and minima at the same wavelengths as a solution of pargyline hydrochloride reference standard in the same medium.

Assay.—Amine group.—Weigh and finely powder not less than 20 tablets. Transfer to a 125-ml. separator an amount of powder, accurately weighed, equivalent to about 40 mg. of pargyline hydrochloride. Add 30 ml. of water and 1 ml. of sodium hydroxide T.S. and extract with four 20-ml. portions of chloroform. Wash the combined chloroform extracts with 10 ml. of water and discard the water phase. Filter the chloroform extract through a pledget of purified cotton into a tall-form 200-ml. beaker and wash the cotton with 10 ml. of chloroform. Add 25 ml. of acetonitrile and titrate potentiometrically with 0.01 *N* perchloric acid in dioxane. Each milliliter of 0.01 *N* perchloric acid is equivalent to 1.957 mg. of $C_{11}H_{13}N \cdot HCl$. The amount of pargyline hydrochloride found is not less than 90.0% and not more than 110.0% of the labeled amount.

¹ If the indicator method is used, perform a blank titration and make any necessary correction.

DISCUSSION

U.S.P. and N.F. terminology for solubility, melting range, reagents, etc., have been used wherever feasible.

Pargyline hydrochloride² is a nonhydrazine monoamine oxidase inhibitor which acts as an antihypertensive.

Identity Tests.—The ultraviolet absorption spectrum of the extract obtained from commercial 10-mg. tablets compared qualitatively with that of Fig. 1 in the region of from 250–270 $m\mu$. Extraneous absorbance, due to unidentified tablet constituents, was present throughout the ultraviolet range but did not obscure the distinctive features of the pargyline hydrochloride spectrum.

Quantitative Methods.—The assay based on the acetylenic group in pargyline hydrochloride is similar to the assays provided in the N.F. XII monographs on ethchlorvynol and ethinamate. In the present assay, however, the titration with 0.1 *N* alcoholic potassium hydroxide determines the bound hydrochloric acid in addition to the acid released on formation of the silver acetylide. The bound acid may be determined independently by titration of a sample to which no silver nitrate has been added. Titration of the sample without the addition of THAM buffer results in extreme darkening of the solution as the titration progresses. This effect, which is believed to be due to a darkening of the precipitated silver chloride as well as the deposition of some silver oxide, is minimized in the buffered medium. The assay of pargyline hydrochloride gave an average value of $100.6 \pm 0.5\%$.³

Caution is to be observed in disposing of completed titration mixtures since silver acetylides are explosive when dry. The titration vessel should be flushed with water thoroughly prior to disposal. Occluded precipitates should be dissolved with nitric acid.

Attempts to employ this method for the direct determination of pargyline hydrochloride in the tablets proved unsuccessful. The voltage change in the vicinity of the end point was gradual, and the results obtained tended to be high (about 110% of label claim).

The nonaqueous titration of pargyline hydrochloride with perchloric acid gave an average value of $99.4 \pm 0.1\%$.³ With crystal violet indicator, the color change from turquoise to a definite green corresponded to the midpoint of the inflection in the potentiometric titration curve. Generally, the visual titration is not as advantageous as the potentiometric determination due to the fading of the indicator in the presence of the precipitate which forms during the titration. An additional drop of crystal violet T.S. as the end point is approached will aid in identifying the desired indicator change.

Extraction of the powdered tablets with chloroform followed by titration of the free base with perchloric acid gave an average value of $99.8 \pm 0.4\%$ ³ of the labeled amount of pargyline hydrochloride.

² Marketed as Eutonyl by Abbott Laboratories, North Chicago, Ill.

³ Maximum deviation from the mean value.