Colorimetric Assay Procedure for Dissolution Studies of Meprobamate Formulations

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Abstract □ A colorimetric analytical procedure applicable to N—H-containing compounds was employed in dissolution studies of meprobamate formulations. The method, which can be applied directly to the aqueous dissolution sample, gave results comparable to the official GC analytical procedure.

Keyphrases □ Meprobamate—colorimetric analysis for dissolution studies, compared to compendial methods □ Dissolution studies, meprobamate—development of applicable colorimetric method □ Colorimetry—meprobamate analysis in dissolution studies, compared to compendial methods

The dissolution test for meprobamate tablets in USP XVIII (1) specifies a GC procedure for analysis of drug in solution. This procedure requires extracting the active compound from the aqueous dissolution sample before analytical measurement. A colorimetric method that can be applied directly to the aqueous dissolution sample was employed in these laboratories. This method provided results consistent with those obtained using the compendia-recommended GC procedure. The colorimetric method utilized in this work was first reported by Ellis and Hetzel (2) for the determination of meprobamate in urine and was modified by Zappala and Simpson (3) for the determination of panthenol in multivitamin preparations.

EXPERIMENTAL

Dissolution—The dissolution of meprobamate from an experimental lot of meprobamate tablets was determined by the method described in USP XVIII (1). The aqueous samples obtained were analyzed for meprobamate in solution by both GC and colorimetric procedures.

Reagents—*Borate Buffer, 0.05* M—Dissolve 3.1 g. of reagent grade boric acid and 3.7 g. of potassium chloride in about 900 ml. of water. Adjust to pH 10.5 with 2 *N* NaOH and dilute to 1 l. with water.

Chlorinating Solution—Dilute a 5.25% sodium hypochlorite solution (Clorox) (1:30) with 0.05 *M* borate buffer. Prepare this solution daily and protect from light.

Acidified Phenol Solution—Use 0.5% phenol in 0.1 *M* hydrochloric acid.

Potassium Iodide Solution—Use 1.0% potassium iodide in distilled water. Prepare this solution daily and protect from light.

Colorimetric Procedure—Place 1 ml. of an aqueous solution containing 0.025–0.25 mg. meprobamate/ml. in a 50-ml. volumetric flask. Add 2 ml. of chlorinating solution, taking care to deliver the reagent directly into the solution without getting any on the neck of the flask. Swirl the solution, stopper the flask, and allow it to stand for 20 min. at room temperature. Add 2 ml. acidified phenol reagent, rinsing down the neck of the flask. Again, swirl the solution, stopper the flask and allow it to stand for 5 min. Add 1 ml. potassium iodide solution, and swirl the flask. After 15 sec., dilute the sample to the mark with absolute ethanol. Wait 15 min. and determine the absorbance at 358 nm. on a suitable spectrophotometer. A blank of 1.0 ml. of distilled water taken through the same procedure serves as reference.

Table I—Percent of Meprobamate in Solution at 30 Min. from Six Individual Dosage Units of an Experimental Tablet Formulation Determined by Two Methods

	Percent of Labeled Meprobamate in Solution	
	GC	Colorimetric
	84	88
	85	92
	94	88
	82	86
	88	90
	91	88
Average	87.3	88.7
Coefficient of variation	5.2	2.3

RESULTS AND DISCUSSION

The procedure as described was shown to adhere to Beer's law over the range of 0.025–0.25 mg. meprobamate. The precision of the analytical method was tested on a series of 10 replicate samples containing 0.25 mg. meprobamate/ml., and the coefficient of variation found was 1.54%.

The dissolution of meprobamate from a series of experimental and trade formulations of this compound employing a variety of common tablet excipients was evaluated by this procedure. In every case, the method was satisfactory and no analytical interference was observed. However, only one dosage unit was utilized in these studies with not less than 500 ml. of solvent. Therefore, the excipient concentration in the analytical sample was always small, with 0.07 mg./ml. being the maximum concentration attained.

It is obvious that interference will be encountered with products incorporating N—H-containing substances, either as excipients or active components. In such instances, appropriate separation techniques must be employed prior to analysis.

A dissolution test was completed on an experimental lot of tablets on which both the compendia-recommended GC and colorimetric analytical procedures were used (Table I). The average percent in solution for the GC procedure was 87.3%, with a coefficient of variation of 5.2%; the colorimetric method gave an average percent in solution of 88.7%, with a coefficient of variation of 2.3%.

Whereas the GC method requires an extraction step, with subsequent evaporation and redilution of the sample, the colorimetric assay has an advantage in that the aqueous sample can be analyzed directly.

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ACKNOWLEDGMENTS AND ADDRESSES

Received April 8, 1971, from the *Pharmacy Research and Development Division, Wyeth Laboratories, Radnor, PA 19087*

Accepted for publication August 30, 1971.

The authors thank Dr. Kenneth Dilloway for performing the GC analysis and Mr. Paul Polka for technical assistance.