Automated Assay of Single Tablets of Chloral Betaine

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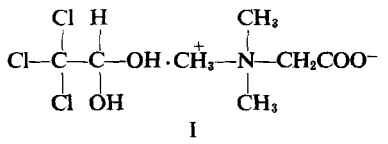
Abstract □ An automated analytical system was used to determine the amount of chloral hydrate in a single tablet. The intensity of a blue complex between chloral hydrate and quinaldine ethiodide in alkaline solution was a measure of its concentration in the tablet.

Keyphrases □ Chloral betaine tablets—automated colorimetric assay □ Chloral hydrate–quinaldine ethiodide complex—automated colorimetric assay of chloral betaine tablets □ Colorimetry—automated assay, chloral hydrate in chloral betaine tablets

Chloral betaine[1] (I) is a chemical complex of chloral hydrate and betaine. After ingestion, chloral betaine reduces to chloral hydrate, which is subsequently reduced to trichloroethanol, a potent hypnotic. Hence, it provides the recognized sedative and hypnotic effectiveness of chloral hydrate: induction of natural restful sleep, easy arousal, and minimal, if any, "hangover" (1).



I

Chloral betaine is usually assayed titrimetrically after basic hydrolysis (2). However, this procedure does not readily lend itself to automation. A colorimetric method for the determination of chloral hydrate (3) was found to be adaptable to automation.

Application of automated analyses to pharmaceutical preparations is well documented in the literature (4–6).

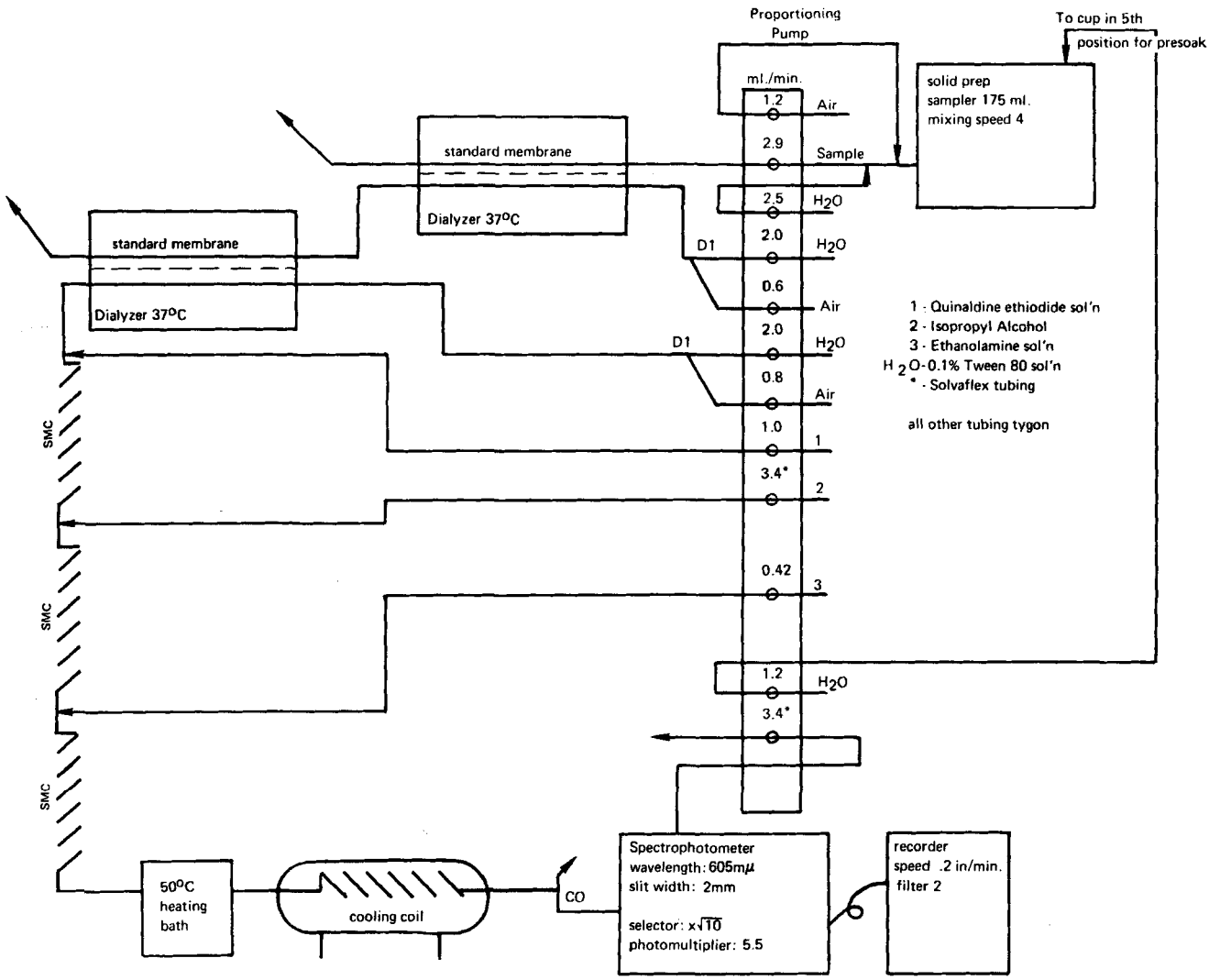


Figure 1—*Schematic diagram for chloral betaine, 500 mg., tablet analysis.*

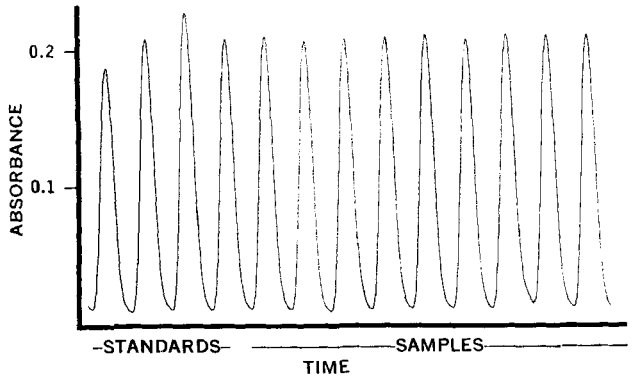


Figure 2—*Typical curves for chloral betaine standards and samples.*

The application of an automated colorimetric assay to single tablets of chloral betaine is now reported.

EXPERIMENTAL

Equipment—The analytical train consisted of the following Technicon[2] modules: (*a*) Solidprep sampler, (*b*) proportioning pump (model I), (*c*) dialyzer (model I), and (*d*) heating bath with 12.2-m. (40-ft.) coil, in conjunction with a spectrophotometer[3] using a microflow cell (9120 No. 5) and a recorder[4].

Reagents—The following were used: *Quinaldine Ethiodide Solution*—Quinaldine ethiodide[5] (1-ethylquinaldinium iodide) (0.75% w/v) in distilled water.

Ethanolamine Solution—Ethanolamine[6] (0.1 *M*) in distilled water.

Isopropyl Alcohol—Analytical reagent[7].

Water containing 0.10% polysorbate 80[8] was also used. Water was used as a diluent in the Solidprep sampler.

Standards—Aqueous solutions of chloral betaine were made up at three levels of concentration (78.1, 91.9, and 105.7 g./l.). Ten-milliliter aliquots of each solution were equivalent to 425, 500, and 575 mg. of chloral hydrate, respectively, when diluted with 175 ml. of water in the Solidprep sampler.

Samples—Production lots of tablets were used in this study. The theoretical content of each tablet was 870 mg. of chloral betaine (equivalent to 500 mg. of chloral hydrate).

Procedure—A schematic drawing of the automatic analyzer system is shown in Fig. 1. Each tablet was individually disintegrated in the presence of water. An aliquot of the resulting suspension was doubly dialyzed to remove extraneous solid matter and to dilute the sample further. The dialyzate was then reacted with quinaldine ethiodide and ethanolamine solutions and subsequently passed through the spectrophotometer where the intensity of the color at 605 nm. was measured and recorded (Fig. 2).

Tablets were sampled at a rate of 20/hr.

The standard solutions were analyzed several times during the day to check for any variation in absorbance. No significant variation was observed.

[1] Beta-Chlor, Mead Johnson Laboratories, Division of Mead Johnson and Co.
[2] Technicon Corp., Tarrytown, N. Y.
[3] Hitachi Perkin-Elmer model 139.
[4] Sargent model TR-05.
[5] Eastman Kodak.
[6] Matheson Coleman and Bell.
[7] Mallinckrodt.
[8] Tween 80, Atlas Chemical Industries, Inc., Wilmington, Del.

Table I—Statistical Results for Chloral Betaine Tablets

Lot	Mean, mg. Chloral Hydrate per Tablet	Coefficient of Variation, %
1	493	1.2
2	502	1.7
3	490	2.4
4	509	1.3
5	512	2.0
6	506	1.7
7	508	1.6
8	499	1.2

Calculation—The average absorbance for each standard was plotted *versus* tablet equivalent to give a standard curve. Reference to the standard curve for each sample yielded the milligrams of chloral hydrate per tablet.

DISCUSSION

Preliminary data indicated incomplete disintegration of the tablet in the Solidprep sampler due to tablet hardness. This problem was overcome by the addition of water to the sample cup at position five on the sampler tray, thus allowing for a 12-min. presoak in 3.6 ml. of water before sampling.

By using the described analytical system, the linearity of absorbance values obtained for standard solutions was satisfactory from 0 to 160% of declared tablet potency. Above 160%, negative deviations from the standard curve were observed, indicating the possibility of limiting concentrations of one or both colorimetric reagents.

RESULTS

Standard Curve—The average absorbance for each of the three standards was determined. A plot of the values gave a straight line in accordance with Beer's law.

Reproducibility of Standards—The reproducibility of the method was checked by the analysis of 30 standards (three levels of concentration). The coefficient of variation ranged from 1.1 to 1.7%.

Statistical Results—The results of eight lots of 50 tablets were evaluated. The data are presented in Table I.

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