Semiautomated Determination of Mandelic Acid as Benzaldehyde in Content Uniformity Testing of Methenamine Mandelate Tablets

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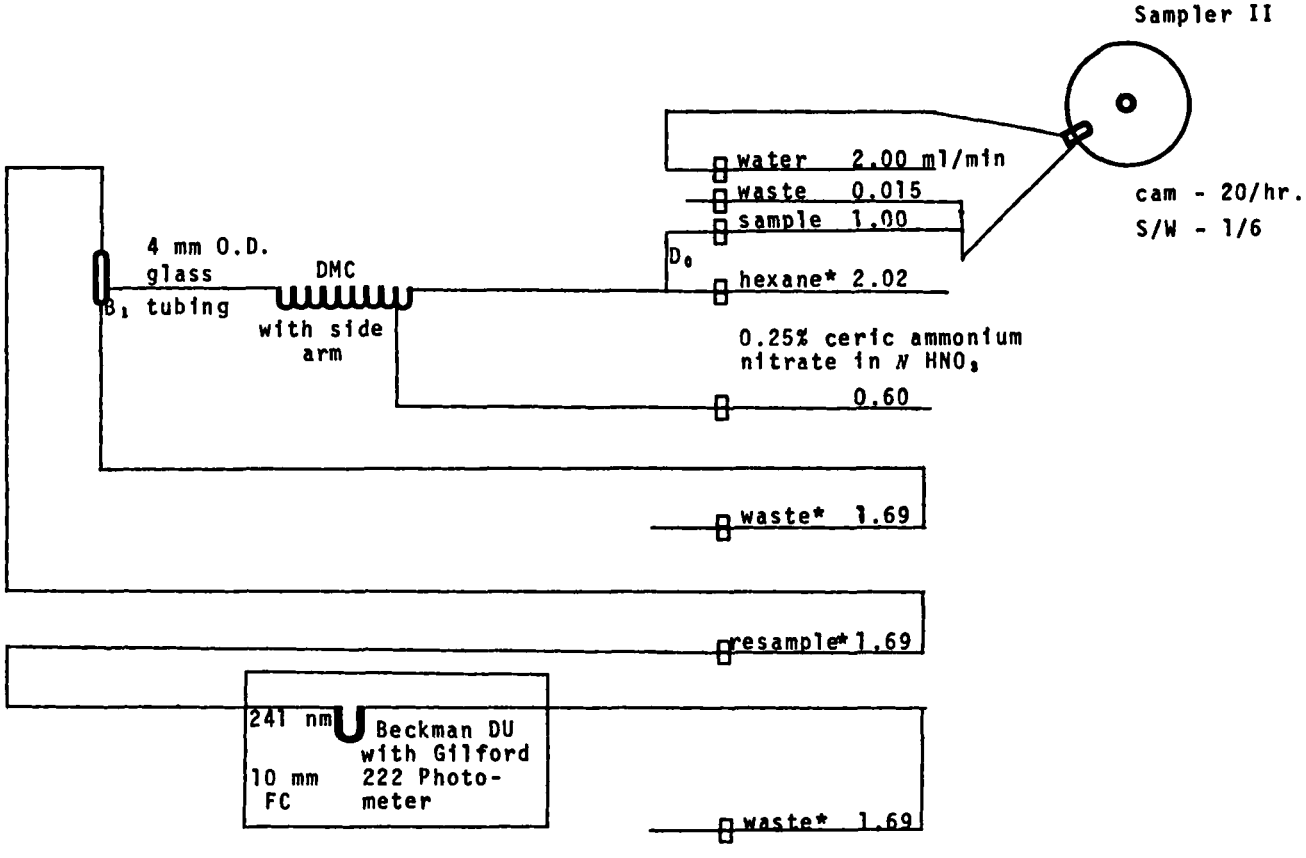
Abstract □ A semiautomated method for the determination of the mandelic acid component of methenamine mandelate tablets is described. A programmed cam rate of 20 samples/hr., excellent recoveries, and relative standard deviations of about 1.5% were obtained. Benzaldehyde, formed by ceric-ion oxidation of the arylglycolic acid, is determined in the system described.

Keyphrases □ Methenamine mandelate tablets—semiautomated spectrophotometric determination of content uniformity, mandelic acid as benzaldehyde □ Tablet content uniformity, methenamine mandelate—semiautomated spectrophotometric determination □ Content uniformity, methenamine mandelate tablets—semiautomated spectrophotometric determination □ Arylglycolate ester drugs, content uniformity—semiautomated spectrophotometric determination □ UV spectrophotometry—determination of content uniformity for methenamine mandelate tablets

Dow *et al.* (1) provided an autoanalytic method for methenamine mandelate tablets based on colorimetry of formaldehyde released from the methenamine moiety of the drug. An alternative method based on the mandelic acid component, which is potentially useful for control of a number of different drugs, is presented here.

Chafetz (2) described a method for spectrophotometric determination of mandelic acid and other arylglycolic acids as benzaldehyde or aryl ketones formed by oxidation with ceric ion. This method is used in the NF XIII (3) for assay of oxyphencyclimine hydrochloride tablets and for content uniformity determina-



Scheme I—Flow diagram: methenamine mandelate content uniformity manifold

tion of homatropine methylbromide tablets (4). Cerimetric titration methods using the same chemistry have been described for methenamine mandelate formulations (5) and for homatropine hydrobromide (6). Automation of the spectrophotometric method is described here, wherein 20 units of methenamine mandelate tablets can be determined in an hour.

EXPERIMENTAL[1]

Materials—Methenamine mandelate USP, 0.25% ceric ammonium nitrate in 1 *N* nitric acid, and hexane were used.

Assay—*Standard Preparation*—Transfer about 100 mg. of methenamine mandelate USP [previously assayed by direct cerimetric titration (2)], accurately weighed, to a 100-ml. volumetric flask and dilute to volume with distilled water. Further dilute 10.0 ml. to 100.0 ml. with water to obtain a concentration of about 100 mcg./ml.

Assay Preparation—Transfer one tablet to the jar of the blender, add exactly 100.0 ml. of distilled water, and blend for about 15 sec. With a disposable pipet, withdraw a portion of the sample and completely rinse the cap and the sides of the jar. Blend the sample for an additional 45 sec. Dilute the solutions to a final concentration of about 100 mcg. methenamine mandelate/ml.

Procedure—Assemble the apparatus as shown in Scheme I. Allow the recorder and spectrophotometer to stabilize for at least 30 min. and charge the reagent lines. Insert the 20/hr. sample cam with a 1:6 sample–wash ratio, place 2-ml. sample cups in the sampler, and arrange so that duplicate assays are obtained for each tablet and each 10-assay preparation is bracketed with a standard preparation. Set the recorder on the 50-mv. scale, adjust the wavelength of the spectrophotometer to 241 nm., and adjust the absorbance meter to an absorbance of 1.200 and the ratio switch on the power supply to 0.25.

Calculations—For a 1-g. tablet, milligrams per tablet = $A_u/A_s \times 10C$; for a 0.5-g. tablet, milligrams per tablet = $A_u/A_s \times 5C$; and for a 0.25-g. tablet, milligrams per tablet = $A_u/A_s \times 2.5C$; where A_u and A_s are the absorbance of the sample and standard, respectively, and C is the weight, in milligrams, of standard taken.

RESULTS AND DISCUSSION

A 0.25% solution of ceric ammonium nitrate in 1 *N* nitric acid was sufficient for reproducible oxidation of methenamine mandelate in the concentration range employed. Adherence to Beer's law was demonstrated over a concentration range of from 50 to at least 150 mcg./ml.

Methenamine mandelate tablets[2] USP (declaring 1, 0.5, and 0.25 g./tablet) were assayed. Recoveries of added methenamine mandelate in six replicate assays of each formulation by the automated method were 99.8 ± 1.27% for the formulation declaring 1 g./tablet, 99.4 ± 1.38% for the formulation declaring 0.5 g./tablet, and 99.2 ± 1.87% for the formulation declaring 0.25 g./tablet.

SUMMARY AND CONCLUSIONS

A rapid, sensitive, and repetitive semiautomated method has been described for determination of the content uniformity of methenamine mandelate tablets. Excellent recovery data were obtained for methenamine mandelate added at the 0.25-, 0.5-, and 1-g./tablet levels. On the basis of previous work on spectrophotometric determination of arylglycolate ester drugs (2), it is expected that the method could easily be extended to the content uniformity determination of the tablet preparations of clidinium bromide, glycopyrrolate, homatropine methylbromide, mepenzolate bromide, oxyphencyclimine hydrochloride, and penthienate bromide in NF as well as to unofficial drugs with similar structure.

REFERENCES

(1) M. L. Dow, C. E. Wells, and T. G. Smith, Method No. 6, in "Drug Autoanalysis Manual," 2nd ed., R. F. Heuermann, Ed., FDA National Center for Drug Analysis, St. Louis, Mo., 1972.

(2) L. Chafetz, *J. Pharm. Sci.*, **53**, 1192(1964).

(3) "The National Formulary," 13th ed., Mack Publishing Co., Easton, Pa., 1970, p. 513.

(4) *Ibid.*, p. 346.

(5) L. Chafetz and C. A. Gaglia, Jr., *J. Pharm. Sci.*, **55**, 854 (1966).

(6) L. Chafetz and R. E. Daly, *ibid.*, **57**, 1977(1968).

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[1] A Waring blender equipped with a liter glass jar, a Sargent SRLG recorder, a Beckman DU spectrophotometer modified with a Gilford 222 photometer and equipped with an elevated cell chamber cover and automated apparatus (Technicon AutoAnalyzer, Technicon, Inc., Tarrytown, N. Y.), which included a sampler (Sampler II) and a proportionating pump (Proportionating Pump I) were employed.

[2] Mandelamine tablets, Warner-Chilcott Laboratories, Division of the Warner-Lambert Co.