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Received October 16, 1972.
Accepted for publication January 24, 1973.
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Kinetic Assay of Single Nitroglycerin Tablets

Keyphrases ☐ Nitroglycerin (single) tablets—kinetic assay, compared to compendial method ☐ Tablets, single nitroglycerin—kinetic assay, compared to compendial method ☐ Kinetic analysis—single nitroglycerin tablets, compared to compendial method

Sir:

Current interest in the stability of nitroglycerin tablets (1, 2) demonstrates the need for a simple, rapid, and precise single-tablet assay procedure for nitroglycerin. The present USP method (3) requires separation of the drug from potentially interfering substances by column chromatography followed by acid hydrolysis, which yields the nitrate ion, and subsequent spectrophotometric determination of nitrated phenoldisulfonic acid. Its complexity of manipulation does not permit this method to be rapid and efficient for the determination of nitroglycerin in single tablets. The GC (4) and polarographic (5) methods are accurate and specific but require extensive instrumentation. Simpler methods, such as that developed by Bell (6), are nonspecific; they can be subject to interference either by nitrate or nitrite ions.

The recent accelerated research activities in nitroglycerin formulations prompted us to report our preliminary data on a kinetic assay of nitroglycerin in tablets. This assay method is simple, rapid, and precise and appears to be superior to existing methods for the single-tablet assay of nitroglycerin.

Nitroglycerin has no significant UV absorption above 240 nm.; but in alkaline solutions, it degrades *via* a chromophoric intermediate which exhibits an absorption peak around 336 nm. For example, in 99% methanol and at a sodium hydroxide concentration of 0.03 *M*, the appearance and disappearance of peak intensity at 336 nm. (Fig. 1) can be ascribed to $A \rightarrow B \rightarrow C$ kinetics. The kinetic order, rate of degradation, and maximum peak absorbance are dependent on nitroglycerin and sodium hydroxide concentrations and solvent composition. A detailed description of the kinetics and mechanism of nitroglycerin degradation in alcoholic sodium hydroxide solutions will be presented elsewhere[1].

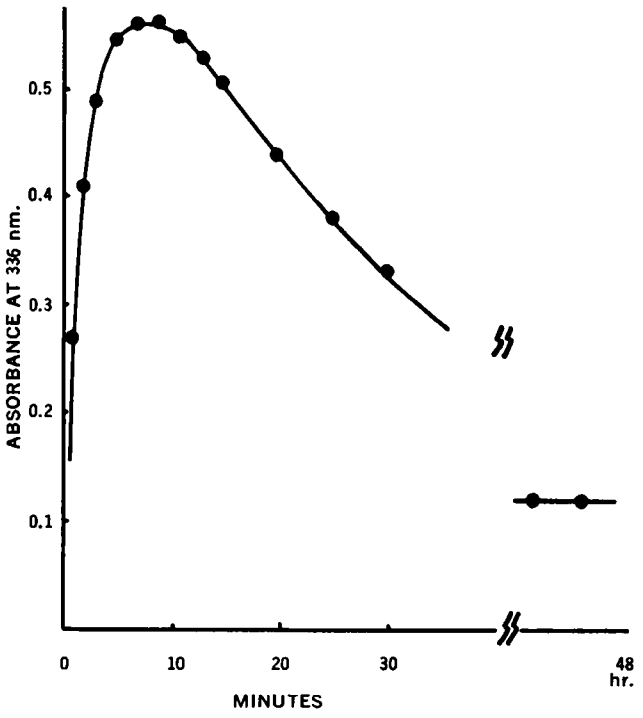

Figure 1—*Degradation of nitroglycerin as followed by absorbance change at 336 nm.; [nitroglycerin] ≃ 0.4 mg./3 ml. of reaction mixture; [sodium hydroxide] = 0.03* M; *solvent = 99% methanol; 25°.*

At a constant sodium hydroxide concentration and solvent composition, the observed maximum absorbance at 336 nm. was found to be a linear function of nitroglycerin concentration. A convenient system was 33% water in methanol and 0.033 *M* NaOH in the reaction mixture. The kinetic assay could be initiated either by placing 1 ml. of aqueous nitroglycerin solution or dissolving the sublingual tablet with 1 ml. of water directly in a 1-cm. cell, followed by addition of 0.05 *M* NaOH in methanol. The absorbance at 336 nm. was then followed until a maximum value was reached.

The validity of the present assay technique was checked against the official USP method. Different quantities of nitroglycerin tablets[2] and powders[3] were dissolved in water, and the solutions were assayed simultaneously by the USP and the kinetic methods. In the USP assay, 1-ml. aliquots of nitroglycerin solutions were mixed with the indicated amount of column material[4] and applied to the column. The same volume of nitroglycerin solution was used in the kinetic assay. Figure 2 shows a plot of absorbance maximum at 336 nm. as a function of the concentrations of nitroglycerin in the prepared solutions as determined by the USP method. The excellent linearity observed (correlation coefficient = 0.994 for 14 points) strongly testifies to the validity of the kinetic assay.

The slight positive intercept observed in Fig. 2 was apparently contributed by the tablet diluent (lactose)

[1] H.-L. Fung, P. Dalecki, and C. T. Rhodes, to be published.
[2] Eli Lilly & Co.
[3] One part of nitroglycerin plus nine parts of lactose USP, supplied by ICI America Inc., Atlas Chemicals Division, Wilmington, DE 19899
[4] Celite 545, Fisher Scientific Co., Fair Lawn, N. J.

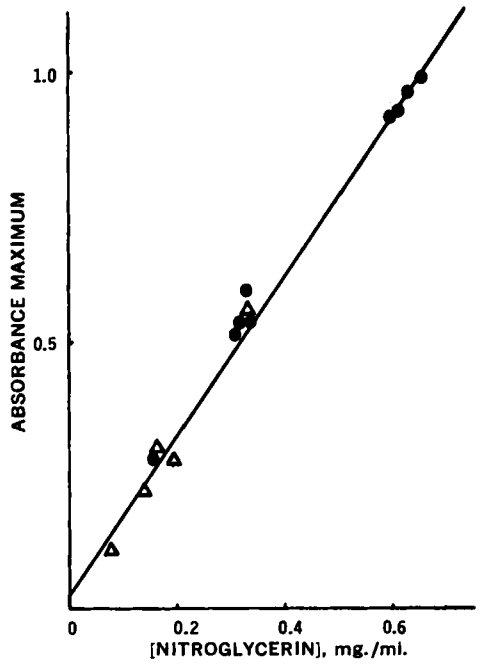

Figure 2—*Calibration of kinetic assay against USP method using solutions of nitroglycerin prepared from tablets (●) and powders (△).*

present, since a solution of lactose in the absence of nitroglycerin produced a similar blank reading. This small blank reading was constant during the time of the kinetic assay and did not appear to be sensitive to changes in lactose concentrations. Sodium nitrate and nitrite did not give observable absorbances under similar experimental conditions.

The kinetic assay described here appears to be specially suitable for content determination of nitroglycerin in single tablets. The tablet can be placed directly in a 1-cm. UV cell and immediately assayed, with minimal requirements of manipulative steps, reagents, and instrumentation. Its simplicity, accuracy, and ready adaptability to automation strongly recommend the kinetic assay for use in the quality control and formulation research of nitroglycerin dosage forms.

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Received January 3, 1973.
Accepted for publication February 7, 1973.
Supported in part by General Research Support Grant FR5-501RR-05454-10 from the General Research Support Branch, Division of Research Facilities and Resources, National Institutes of Health, Bethesda, MD 20014
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BOOKS

REVIEWS

Neuropharmacology and Behavior. By V. G. LONGO. W. H. Freeman, 660 Market St., San Francisco, CA 94104, 1972. 184 pp. 15 × 23.5 cm. Price $6.95.

This relatively brief book does not attempt to cover all aspects of psychotropic drugs. The author, by drawing on his own research in this field, has written a very readable and interesting book covering the discovery, development, and use of psychotropic drugs. It is divided into four chapters—Antipsychotic Drugs, Antidepressant Drugs, Tranquilizing Drugs, and Hallucinogenic Drugs. For the reader interested in a historical perspective or a good overview, this book is recommended.

Staff Review ■

International Drug Monitoring: The Role of National Centres. World Health Organization Report Series. World Health Organization, Geneva, Switzerland. (Available from American Public Health Association, 1015 18th St., N.W., Washington, DC 20036), 1972. 47 pp. 16 × 24 cm. Price $1.00.

The development of systems for detecting adverse drug reactions has recently received increased attention. This report offers guidelines on the methodology and organization of national detection centers and the role of such national centers in an international reporting system. Since resources vary from country to country, a flexible approach is stressed. Recommendations concerning the principal activities of national drug monitoring centers are given as well as suggestions relative to the means for carrying out these activities.

Staff Review ■

Automation and Management in the Clinical Laboratory. Edited by GEORGE E. WESTLAKE and JAMES L. BENNINGTON. University Park Press, Chamber of Commerce Building, Baltimore, MD 21202, 1972. 274 pp. 13.5 × 20.5 cm. Price $12.50.

Hospitals have been the subject recently of allegations of inefficiency and wastefulness. This book represents the updated and revised proceedings of a conference, held in May 1971, on effective management of clinical laboratories. This meeting attempted to apply industrial engineering techniques to the medical laboratory. Individuals from laboratory management and systems design discuss how the principles of industrial management, accounting, and engineering may be used to develop greater economy, reliability, accuracy, and speed of delivery in the clinical laboratory. Computerized laboratory systems are examined in terms of objectives,