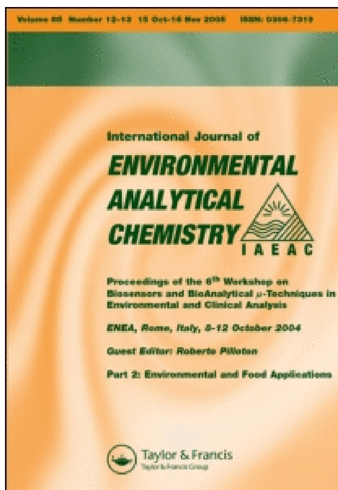
This article was downloaded by:
On: *18 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



International Journal of Environmental Analytical Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713640455

Colorimetric Determination of Tranexamic Acid with *p*-Dimethylaminobenzaldehyde

Mohamed E. Mohamed[a]; Hassan Y. Aboul-enein[a]
[a] Department of Pharamaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

To cite this Article Mohamed, Mohamed E. and Aboul-enein, Hassan Y.(1984) 'Colorimetric Determination of Tranexamic Acid with *p*-Dimethylaminobenzaldehyde', International Journal of Environmental Analytical Chemistry, 19: 1, 19 — 25
To link to this Article: DOI: 10.1080/03067318408077014
URL: http://dx.doi.org/10.1080/03067318408077014

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Intern. J. Environ. Anal. Chem., 1984, Vol. 19, pp. 19–25
0306-7319/84/1901-0019 $18.50/0
© 1984 Gordon and Breach, Science Publishers, Inc. and OPA Ltd.
Printed in Great Britain

Colorimetric Determination of Tranexamic Acid with *p*-Dimethylaminobenzaldehyde

MOHAMED E. MOHAMED and HASSAN Y. ABOUL-ENEIN†

Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia

Downloaded At: 20:26 18 January 2011

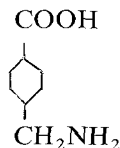
(*Received April 4, 1984; in final form May 26, 1984*)

Tranexamic acid condenses with *p*-dimethylaminobenzaldehyde giving a Schiff base of stable yellow colour exhibiting maximum absorption at 394 nm. The reaction proceeds in methanol and attains maximum colour development when heated at 100°C for 10 min. A linear relationship has been established between absorbance (A_{max}) and concentration over the range 0.5 to 3 $\mu g\,ml^{-1}$. When applied to tablets labelled to contain 500 mg each, the mean found was 99.1% ± 1.72. The results were comparable with those of the classical formol titration method for aminoacids.

KEY WORDS: Tranexamic acid, colorimetric determination, condensation with *p*-dimethylaminobenzaldehyde, pharmaceutical analysis.

INTRODUCTION

Tranexamic acid (trans-4-aminomethylcyclohexanecarboxylic acid) is a synthetic ω-aminoacid with useful anti-fibrinolytic properties.[1]



†Author to whom correspondence should be addressed.

A gas-chromatographic method using an electron capture detector was reported for its determination in biological fluids.[2] Recently Wahbi *et al.*[3] reported a spectrophotometric method of determination for tranexamic acid based on the formation of a complex with chloranil buffered at pH 9. The complex, formed as a result of $n \rightarrow \pi$ charge transfer,[4,5] is stable for about 10 min. The results obtained by Lin and Chen[5] suggest that the structure of the aminoacid plays an important role in the mechanism of the charge-transfer process, thereby influencing the stability of the aminoacid–chloranil complex.

In view of the fact that tranexamic acid possesses an amino functional group, it was deemed useful to develop a stable colorimetric method for its determination in authentic and tablet forms.

p-Dimethylaminobenzaldehyde has lead to numerous applications as an analytical reagent.[6] The reagent has been applied to the colorimetric determination of primary alkylamines, aminoacids, primary arylamines, nitroaromatic derivatives (reduced beforehand to amines) and indole derivatives.[7–9]

Downloaded At: 20:26 18 January 2011

EXPERIMENTAL

Apparatus, materials and reagents

a) A Varian DMS 90 double beam spectrophotometer with 1-cm quartz cuvettes was used.
b) Tranexamic acid: Authentic powder (Batch No. 60283) and 500 mg tablets (Cyklokapron®) Lot. No. 78391 were kindly donated by Kabi AB, Stockholm, Sweden.
c) Standard tranexamic acid stock solution: Prepared from authentic powder as $5\ \mathrm{mg\,ml^{-1}}$ in methanol.
d) *p*-Dimethylaminobenzaldehyde solution: Analar, product of BDH (Poole, England) freshly prepared as 0.1% w/v in methanol.

Methanol used as solvent was spectral grade, product of BDH (Poole, England).

General procedure

Prepare from the standard stock solution of tranexamic acid a more dilute solution containing 5 mg per 100 ml methanol. From this

dilute solution pipette 0.2–1.2 ml portions into six 10 ml test tubes. Add exactly 2.0 ml of *p*-dimethylaminobenzaldehyde solution to each test tube. Prepare a reagent blank. Mix and heat in boiling water for 10 min. Let all solutions cool to room temperature (20°C). Transfer quantitatively the contents of each tube into 20 ml calibrated flasks. Adjust to volume with methanol and measure absorbance in 1-cm cells at 394 nm.

Procedure for sample

Weigh 10 tablets accurately and calculate the mass per tablet. Powder five tablets and weigh accurately a quantity of powder equivalent to about 500 mg of tranexamic acid and transfer quantitatively into a 100 ml calibrated flask. Add 80 ml of distilled water and shake for 30 min. Adjust to volume with water, mix and filter rejecting the first few millilitres. Pipette 1.0 ml of the filtrate into 100 ml calibrated flask and complete to volume with methanol. Apply the general procedure to 1.0 ml of this solution. Calculate the amount of tranexamic acid from the calibration curve or from an equivalent linear equation.

Downloaded At: 20:26 18 January 2011

RESULTS AND DISCUSSION

p-Dimethylaminobenzaldehyde in methanolic solution reacts with tranexamic acid to form a Schiff base of stable yellow colour with maximum absorption at 394 nm (Figure 1). Under the experimental conditions employed, the absorbance (A) in 1-cm cells is linearly related to concentration $C\ \mu g\ ml^{-1}$ over the range 0.5 to $3\ \mu g\ ml^{-1}$, the linear equation being $A = 0.106C - 0.007$, with a correlation coefficient of 0.999 at 95% confidence limits. From the slope of the linear equation an estimate of 1.06×10^3 for $(A^{1\%}_{1\,cm})$ of tranexamic acid may be worked out. This value, being relatively high, confirms the sensitivity of the method.

To study the stoichiometry of the reaction the continuous variation method,[10] in which the total molar concentration is kept constant and the mole fraction of one of the components is plotted on the abscissa, has been applied. The ordinate scale represents the measured absorbance, A, of the complex since both tranexamic acid

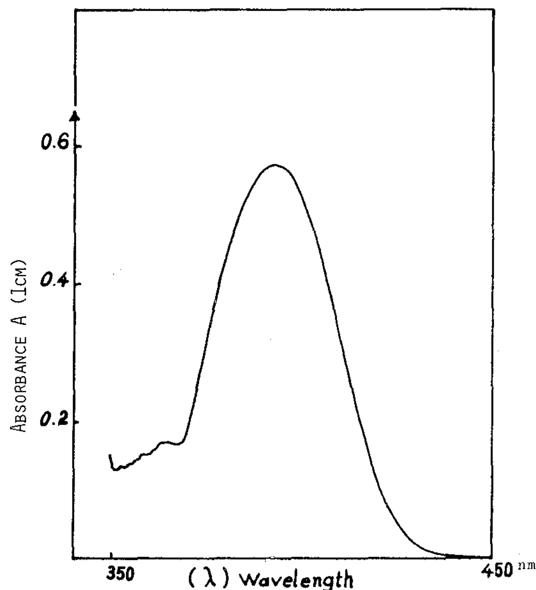


FIGURE 1 Absorption spectrum of the condensation product from tranexamic acid and *p*-dimethylaminobenzaldehyde.

Downloaded At: 20:26 18 January 2011

and *p*-dimethylaminobenzaldehyde do not absorb at 394 nm. It is apparent from Figure 2 that the molar ratio is to a good approximation 1:1, confirming that one molecule of tranexamic acid condenses with one molecule of *p*-dimethylaminobenzaldehyde.

The effect of temperature has been investigated, and it has been found that the reaction proceeds satisfactorily at 100°C. From Figure 3, the minimum heating time necessary for maximum colour production is 10 min.

The presence of acid (glacial acetic acid) did not have an effect on the rate of colour development. The volume of *p*-dimethylaminobenzaldehyde utilized for development of colour and the final dilution were selected such that the absorbance readings were maintained within a satisfactory range.

The proposed method has been applied to the analysis of tranexamic acid in commercial tablets, the results being compared with those obtained by the classical formol titration of aminoacids, which involves the addition of neutral formaldehyde solution to aqueous

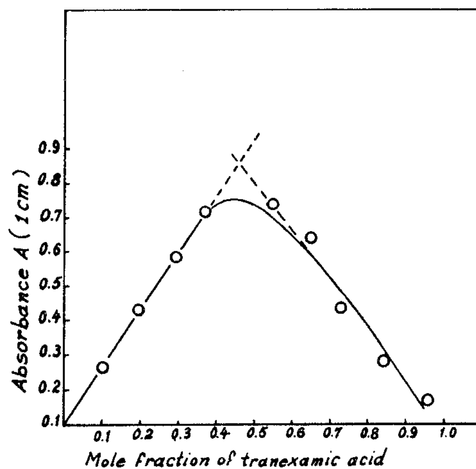


FIGURE 2 Continuous variation plot of concentrations of tranexamic acid and *p*-dimethylaminobenzaldehyde versus the absorbance of the condensation product.

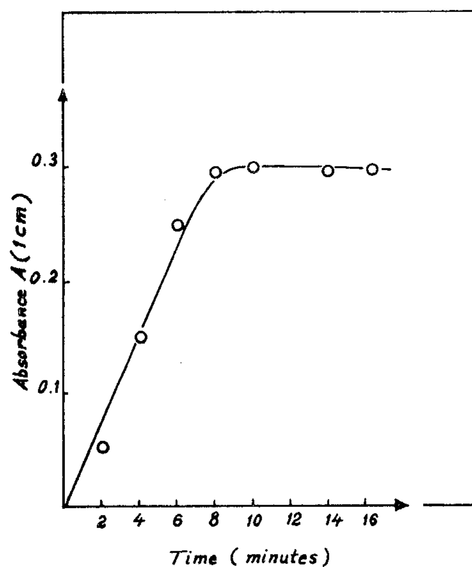


FIGURE 3 Development and stability of colour with time. (Conc. of tranexamic acid 2.5 $\mu g\, ml^{-1}$).

Downloaded At: 20:26 18 January 2011

solution of tranexamic acid and subsequent titration with 0.1 M NaOH using phenolphthalein indicator. Statistical comparison of the results of the proposed method with formol titration according to the *F*- and *t*-tests indicates a non-significant difference with regard to precision and accuracy (Table I). However, the method presented in this communication is more sensitive than the formol method. Moreover, the present method is as sensitive as the spectrophotometric method develooped by Wahbi *et al.*,[3] and is superior with regard to stability of the reaction product.

TABLE I
Determination of tranexamic acid tablets by the *p*-dimethylaminobenzaldehyde and formol titration methods.

Percentage found	
Colorimetry	Titration
97.8	96.5
101.0	99.3
97.4	98.5
101.1	100.7
97.6	97.6
99.7	100.5
Mean ± s.d. 99.1 ± 1.72	Mean ± s.d. 98.9 ± 1.60

F and t-tests

$F_{0.05}$	1.15 (5.05)[a]
$t_{0.05}$	0.21 (2.23)[a]

( )[a] significant levels.

Acknowledgements

The authors would like to thank Kabi AB, Kabi Blood Products Division, S-11287 Stockholm, Sweden, for providing an authentic sample of tranexamic acid, and the tablets analysed. In addition the authors extend their deepest thanks to King Saud University for offering the facilities to conduct this work.

References

1. L. Anderson, I. M. Nilsson, J. E. Nihlen, U. Hender, B. Granstrand and B. Melander, *Scand. J. Haematol.* **2**, 230 (1965).

Downloaded At: 20:26 18 January 2011

2. J. Vessman and S. Stromberg, *Anal. Chem.* **49,** 369 (1977).
3. A. M. Wahbi, E. A. Lotfi and H. Y. About-Enein, *Talanta,* in press (1984).
4. J. B. Birks and M. A. Slifkin, *Nature* **197,** 42 (1963).
5. B. Y. Lin and K. L. Cheng, *Anal. Chim. Acta* **120,** 335 (1980).
6. M. Pesez and J. Bartos, *Colorimetric and Fluorimetric Analysis of Organic Compounds and Drugs,* (Marcel-Dekker, Inc., New York, 1974), 1st ed., p. 200.
7. E. Sawicki and H. Johnson, *Chemist-Analyst* **55,** 101 (1966).
8. M. Pesez and J. F. Burtin, *Bull. Soc. Chim. Fr.* 1996 (1959).
9. P. Byron and J. H. Turnbull, *Talanta* **10,** 1217 (1963).
10. P. Job, *Ann. Chim.* **9,** 113 (1928); *Chem. Abstr.* **22,** 2120 (1928).

Downloaded At: 20:26 18 January 2011