Indian Journal of Chemistry
Vol. 25A, August 1986, pp. 789-790

Spectrophotometric Determination of *p*-Aminophenol & Acetaminophen through Schiff Base Formation & Subsequent Chelation

M S MAYADEO* & R K BANAVALI

Department of Chemistry, Ramnarain Ruia College, Matunga, Bombay 400 019

Received 7 *February* 1984; *revised* 30 *November* 1984; *re-revised and accepted* 6 *September* 1985

p-Aminophenol and its derivative acetaminophen have been estimated using a spectrophotometric method based on schiff base formation and its subsequent chelation. Chelate formed is stable in chloroform, obeys Beer's law and has been used for the determination of *p*-aminophenol and acetaminophen in some pharmaceutical formulations.

A number of methods have been proposed for the estimation of *p*-aminophenol and acetaminophen[1-4]. However, most of these methods are not sufficiently sensitive. Some indirect methods based on diazotisation or nitrosation of the reagents and their subsequent chelation with metal ions have also been proposed[5-7].

Estimation of *p*-aminophenol and acetaminophen via schiff base formation on condensation with 4-nitro, and 2,4-dinitrobenzaldehydes[8], 1,2-naphtoquinone-4-sulphonate[9], homophthaldehyde[10], vanillin[11], anisaldehyde[12], *p*-dimethylaminocinnamaldehyde[13] and *p*-dimethylaminobenzaldehyde[14] have also been reported.

In the present note the reactions of *p*-aminophenol and acetaminophen (hydrolytic product) with 2-hydroxy-5-phenylbenzaldehyde and subsequent chelation with copper(II) ion have been adopted for the determination of *p*-aminophenol and acetaminophen in some commercial preparations.

All the reagents were of AR grade. AR grade acetic acid, hydrochloric acid, 98% ethyl alcohol and redistilled chloroform were used as and when necessary.

A Beckman DU ultraviolet and visible spectrophotometer with 1 cm silica or glass cells, and an Elico *p*H meter, model LI-15, were used.

Hydrolysed acetaminophen solution

Acetaminophen (50 mg) was added to 10 ml of 15% hydrochloric acid and refluxed for 30 min. The solution was cooled and diluted to 100 ml with alcohol. This solution contained 500 μg/ml of hydrolysed acetaminophen.

Proposed procedure :

p-Aminophenol

Aliquots of standard solutions of *p*-aminophenol (0.1 ml to 1.6 ml of ethanolic solution containing 500 μg/ml) were taken in a series of separating funnels. Ethanol was added to make the final volume to 2.0 ml. To this, 2 ml of an ethanolic solution of 2-hydroxy-5-phenylbenzaldehyde containing 5 mg/ml were added. After mixing and allowing the solution to stand for 5 min, 10 ml of chloroform was added and contents were stirred. To the above mixture, copper sulphate reagent (10 ml, 2.4 mg/ml) was added and the whole solution was shaken vigorously. Chloroform layer was allowed to separate. It was then collected in a 50 ml volumetric flask after passing through a plug of sodium sulphate (anhydrous). The aqueous layer was further extracted by adding 10 ml of chloroform and collected in the same flask and finally diluted to 50 ml. Similarly reagent blank was prepared omitting *p*-aminophenol. The absorbance values were measured at 385 nm against the reagent blank. Absorbance values against reagent blank when plotted against the concentrations of *p*-aminophenol gave a straight line passing through origin and obeyed the Beer's law for the concentration range 2 μg ml^{-1} to 14 μg ml^{-1}.

Acetaminophen

In a series of separating funnels 2 ml of an ethanolic solution of 2-hydroxy-5-phenylbenzaldehyde (5 mg/ml) were taken. To these, fixed aliquots of hydrolysed acetaminophen were added (0.1 ml to 1.6 ml). Then ethanol was added to adjust the total volume to 4.0 ml. To this mixture 1.0 ml of 1 *M* sodium acetate was added. After mixing and allowing to stand for 5 min, chloroform (10 ml) was added and contents were shaken. To the above mixture 10 ml of copper sulphate reagent (*p*H 5.5 to 6.0) were added and whole solution was shaken vigorously and chloroform layer was allowed to separate. It was then collected in a 50 ml volumetric flask after passing through a plug of sodium sulphate (anhydrous) and the volume was made up in the same manner as mentioned in the case of *p*-aminophenol.

Similarly reagent blank was prepared adding all the reagents as above except the hydrolysed acetaminophen solution.

Absorbance values were measured at 385 nm using reagent blank. The graph obtained by plotting absorbance against concentration gave a straight line passing through the origin and obeyed Beer's law for

concentration range 2 $\mu g\ ml^{-1}$ to 20 $\mu g/ml^{-1}$ of acetaminophen.

Preparation of assay solutions for commercial sample analysis

Tablets (20) were powdered and weighed. An amount equivalent to 50 mg of acetaminophen was taken and subjected to hydrolysis using 15% hydrochloric acid. It was then diluted to 100 ml to get 500 mg/ml solution. It was then filtered and the first portion of the filtrate (approx. 1.0 ml) was discarded. The filtrate was then treated in accordance with the general procedure described earlier.

In the case of syrups, a known aliquot volume was diluted with water to get the desired concentration suitable for use in the general procedure.

The proposed method was applied to available marketed formulations and the results were compared with the labelled claims. The following ingredients were found to be non-interfering.

Analgin I.P. 250 mg/tab (B), caffeine I.P. 25 mg/tab (B), oxyphenbutazone I.P. 100 mg/tab (C), diazepam I.P. 2.5 mg/tab (C,D), phenylbutazone I.P. 100 mg/tab (D), chloropheniramine maleate U.S.P. 2 mg/tab (E), codeine phosphate 11 mg/tab (F), phenylphrine hydrochloride 5 mg/tab (E). (B, C etc. represent the notation letter given to the different formulations).

To evaluate the accuracy and precision of the proposed method, recovery studies were done using different formulations. Various parameters such as relative mean deviation, standard deviation, coefficient of variance and also confidence limit values were calculated. It was found that proposed method is quite accurate and precise (Table 1). The recommended method cannot be applied to formulations containing other amino, carbonyl (aldehyde) and metal ions (magnesium trisilicate).

Table 1—Summary of the Results Obtained from the Various Formulations of Acetaminophen

Formulation	Labelled amount (mg)	Amount found (mg)	Percentage recovery	Std. deviation	Coeff. of variance
Tablet A	500	501.85	99.73	0.05	0.57
Tablet B	250	246.80	99.80	0.04	0.50
Tablet C	250	250.52	99.52	0.04	0.50
Tablet D	250	247.85	99.89	0.02	0.20
Tablet E	500	503.10	99.89	0.02	0.25
Tablet F	500	494.35	100.09	0.02	0.21
Syrup S_1	125	122.26	99.89	0.02	0.32

References

1 Inamdar M C, Gore M A & Mehta R C, *Indian J Pharm*, **36** (1974) 7.

2 Deodhar R D, Shastri M R & Mehta R C, *Indian J Pharm*, **35** (1973) 120.

3 Devis D R, Fogy A G, Thorburn Burns D & Wragg J B, *Analyst*, **99** (1974) 12.

4 Kaito Tsunnetoshi & Sagara Kazahiko, *Yakugaku Zasshi*, **94** (1974) 639.

5 Saied F Belal, Abdel - Hady Elsayed, M Elwaliely A & Abdine H, *J Pharm Sci*, **68** (1979) 750.

6 Abdel - Salam Mohamad Korany Mohamad A, *Egypt J Pharm Sci*, **18** (1977) 29.

7 Saied F Belal, Abdel - Hady Elsayed, M Elwaliely A & Abdine H, *Analyst, London*, **104** (1979) 919.

8 Kulatz's Evangelas Zarb, Irena, *J Pharm Sci*, **65** (1976) 71.

9 Sanghavi N M & Pai M G, *Eastern Pharm*, **17 (198)** (1974) 53.

10 Sakano Toshiyaki Amo Tameguki, *Yokugaku Zasshi*, **94** (1974) 639.

11 Vaughan J B, *J Pharm Sci*, **58** (1969) 469.

12 D'Souza A A & Shenoy K G, *Can J Pharm Sci*, **3** (1968) 90.

13 Inoue T, Tot Suzawa M, Lee S C & Ishii T, *Eisci Kagaku*, **21** (1975) 313, *Analyst Abstr*, **31** (1976) 1E29.

14 Sanghavi N M & Vishwasrao D R, *Indian J Pharm*, **35** (1973) 172.