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Colorimetric Determination of Paracetamol in Raw Material and in Pharmaceutical Dosage Forms

C O Usifoh[*a], *S A Adelusi* [a] *and R F Adebambo* [b]

[a] *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Benin, Benin City, Nigeria*

[b] *Department of Chemistry, Ondo State University, Ado-Ekiti, Nigeria*

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A rapid, accurate and simple method is proposed for the determination of p-acetaminophen (paracetamol) in raw material, tablets and syrups. The method is based on measuring the intensity of the yellow color that developed when acute acetaminophen is allowed to react with p-dimethylaminobenzaldehyde in 2M HCl after heating.
The color which absorbs in the visible region of λ 450nm is stable for several hours and the intensity is directly proportional to the concentration of the drug, that is, Beer-lambert law is obeyed. The method can be used to analyse paracetamol in raw material and in pharmaceutical dosage forms.

Key words: Paracetamol, Pharmaceutical dosage forms, P-dimethylaminobenzaldehyde.

Introduction

p-Aminoacetamidophenol (paracetamol) is a suitable substitute for aspirin, for its analgesic and antipyretic use in patients who are allergic to aspirin or when aspirin is contra indicated as in patients with gout or peptic ulcer (Abramson and Weissmann 1989; Insel 1996).

Since this drug is very important in our society, it is necessary to develop a simple and accurate method for its analysis in raw material and pharmaceutical dosage forms. Most of the colorimetric methods reported (Inamdar *et al* 1974) for the analysis of paracetamol in the literature are time consuming, costly and sometimes very complex and as a result specificity is sometimes lost (Davis *et al* 1974).

The present work has therefore proposed a colorimetric method for the analysis of paracetamol in raw material and pharmaceutical dosage forms.

Materials and Methods

Apparatus. Spectra were recorded on sp 800 spectrophotometer, using 1-cm cell.

a) Sample: Paracetamol B.P. grade powder from Nomagbon Pharmacy, was used as standard. Paracetamol tablets (500 mg) and syrups (120 mg 5 ml^{-1}) were collected from about six different manufacturers.

b) Raw material. PREPARATION OF SAMPLE SOLUTION: For stock solution of the standard solution, 1g of paracetamol was accurately weighed, dissolved in sufficient water and made up to 100ml in a standard volumetric flask to produce 1% solution of paracetamol.

*Author for correspondence

c) Reagents: 0.2% of p-dimethylaminobenzaldehyde in 95% alcohol, 2M Hydrochloric acid.

d) Development of the complex: A 10ml aliquot of the prepared solution of paracetamol (2mg ml^{-1}) was transferred into a test-tube and 2-ml of 2M HCl added and heated for 10 min. 5ml of 0.2% p-dimethylaminobenzaldehyde added, a yellow color resulted. The solution was cooled and made up to 20ml with distilled water. The absorbance of the solution was read at various wavelength in the visible range. A plot of the absorbance against the wavelength gave an absorption spectrum from which the wavelength or maximum absorption was determined.

e) Calibration curve: Serial dilution of the stock solution of paracetamol were made to obtain the concentrations in the range 1 to 5mg ml^{-1}. 10ml of each solution was treated as described under development of the complex. The absorbance of each solution was read at λ 450nm and a graph of absorbance plotted against the concentration.

e) Stoichiometric relationship: A continuous variation method was employed in the determination of the composition of the complex formed between paracetamol at 1 x 10^{-4}M and p-dimethylaminobenzaldehyde at 1.0 x 10^{-4}M. A series of standard solutions of paracetamol and p-dimethylaminobenzaldehyde in different complementary proportions totalling 20ml (from 0.20 to 20 + 0) inclusive were prepared. Each of the paracetamol standard solution is first heated for 10 min with 2ml of 2M HCl before the addition of the p-dimethylaminobenzaldehyde solutions. The solution were cooled and the absorbance read at λ 450nm against blanks prepared under the same conditions, but by replacing the p-dimethylaminobenzaldehyde solution with an equal volume of 95% ethanol.

f) Assay procedure: A 10ml aliquot of the sample of paracetamol is transferred into a test-tube and 2ml of 2M HCl added and heated for 10 min. 5ml of 0.2% of p-dimethylaminobenzaldehyde added, cooled and the absorbance read against another 10ml aliquot heated in the same manner but by replacing the p-dimethylaminobenzaldehyde with an equal volume of 95% ethanol

Results and Discussion

A characteristic yellow color, with an absorption maximum at λ 450nm developed when paracetamol was heated with 2ml of 2M HCl and 0.2% p-dimethylaminobenzaldehyde added. Fig. 1 shows the spectra of the reactants and the products of the reaction.

From this figure, it is evident that p-dimethylaminobenzaldehyde (curve C) and paracetamol (curve B) do not absorb at the same wavelength of λ 450nm as the complex (curve D). Therefore a difference colorimetric analysis is possible for the determination of paracetamol in pharmaceutical dosage forms. From Fig. 1, it follows that the difference in absorbance A is directly proportional to the concentration of paracetamol in the complex. Therefore a linear relation exists in which the Beers law is obeyed. This method is very useful in that, extraction from the tablet is not necessary. Moreover, it eliminates irrelevant absorption caused by excipients in the formulation.

Optimization of variables. a) Effect of concentration of p-dimethylaminobenzaldehyde: The optimum concentration of p-dimethylaminobenzaldehyde leading to a maximum intensity of color was found to be 0.04% in the prepared solution, which corresponds to 5ml of 0.2% p-dimethylaminobenzaldehyde reagent per 20ml of reaction mixture.

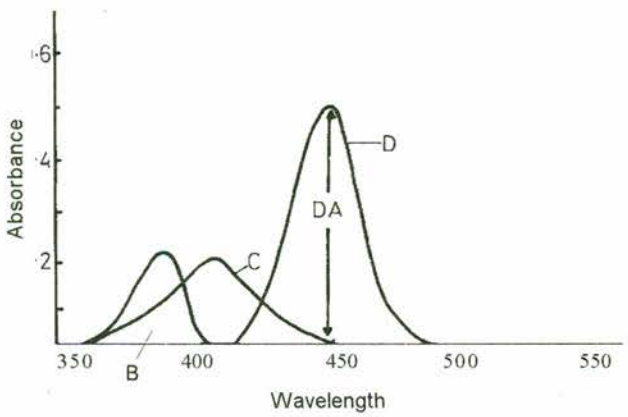


Fig 1. Absorption spectra of paracetamol in water (Curve B), p-dimethylaminobenzaldehyde in 95% ethanol (Curve C) and the chromogen (Curve D).

b) Effect of acid concentration: Volumes of 2M HCl ranging from 1-5 ml were treated with 10ml of the paracetamol solution and the highest absorbance was obtained at 2 ml 2M HCl.

c) Effect of reaction time (color stability): The yellow color formed instantaneously and the complex produced was found to be stable for several hours (Table 3) using the same concentration of paracetamol (10μg ml^{-1}) as earlier studied.

d) Quantification linearity of Beer-Lambert's Law plot: ACCURACY AND PRECISION. The Beer-Lambert's Law was obeyed when the absorbance at λ 450nm was plotted against concentration of paracetamol, the correlation coefficient of the calibration curve obtained is 0.9989. The method is reproducible and this was determined by running replicate samples, each containing 10 μg ml^{-1} of paracetamol in the final test solution. At this concentration level, the standard deviation did not exceed 1.5%.

Paracetamol to p-dimethylaminobenzaldehyde in the chromogen. The composition was found to be 1:1 ratio. The paracetamol in 2M HCl is hydrolysed whereby the acetamide group is converted to the amino group to give p-hydroxyaniline. The reaction of p-dimethylaminobenzaldehyde with

Table 1
Effect of concentration on color intensity absorbance at λ 450nm.

Concentration of p-dimethylaminobenzaldehyde	Concentration of paracetamol		
(%)	10μg ml^{-1}	15μg ml^{-1}	20μg ml^{-1}
0.01	0.210	0.470	0.628
0.02	0.250	0.485	0.635
0.03	0.270	0.487	0.658
0.04	0.350	0.495	0.667
0.05	0.310	0.495	0.660

Table 2
Effect of acid concentration on color intensity absorbance at λ 450nm

Volume of 2M HCl	Concentration of paracetamol		
(ml)	10μg ml^{-1}	15μg ml^{-1}	20μg ml^{-1}
1	0.15	0.28	0.33
2	0.35	0.68	0.83
3	0.31	0.58	0.79
4	0.28	0.36	0.36
5	0.22	0.33	0.52

Table 3
Stability of the color

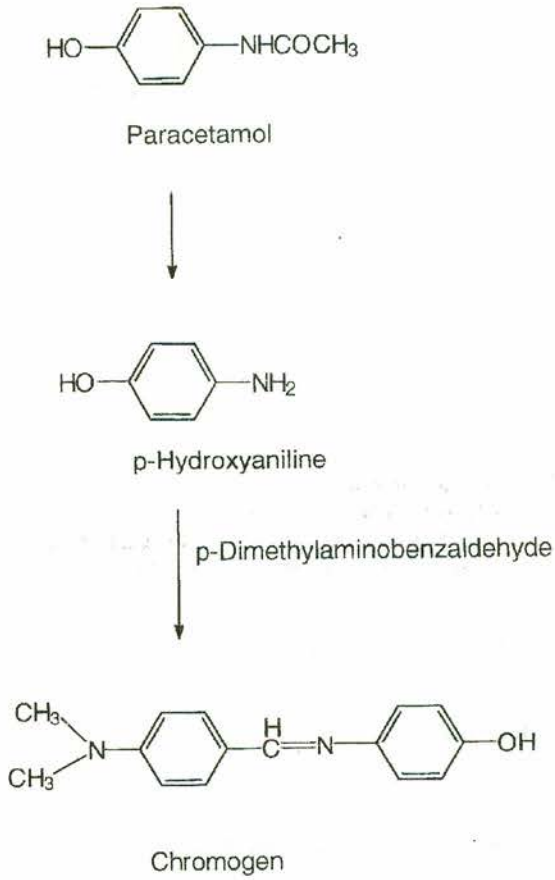
Time (h)	Absorbance
1/4	0.35
1/2	0.36
1	0.35
2	0.36
3	0.36
4	0.36
5	0.36
10	0.36
15	0.36
20	0.36
25	0.36
30	0.36
40	0.36
50	0.36

Table 4
The method for routine quality control analysis

Paracetamol sample	Amount taken	Recovery stated	Label strength	Recovery stated
Raw material	100	100.2±0.84		
Raw material	150	100.2±1.00		
Raw material	200	99.8±0.92		
Raw material	250	99.7±1.10		
Tablets A			500mg	98.9±1.02
B			500mg	99.5±0.93
C			500mg	100.1±1.02
D			500mg	99.7±1.03
E			500mg	100.1±0.99
Syrups F			120mg 5ml^{-1}	98.9±0.83
G			120mg 5ml^{-1}	99.5±0.93
H			120mg 5ml^{-1}	101.3±1.12
I			120mg 5ml^{-1}	99.3±1.04

the p-hydroxyaniline results in the elimination of water (as shown in the scheme 1) to form the chromogen which absorbs in the visible region of λ 450nm.

f) Interference: The method is very useful in the determination of paracetamol where there is no sulphonamide, or drugs containing aromatic amines since this will give similar reaction.



g) Application to the raw material: The suggested method was applied to the quantitative determination of paracetamol in raw material and dosage forms (Tablets and syrups). The data in Table 4 indicates the suitability of the method for routine quality control analysis.

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