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Research Article

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Spectrophotometric determination of paracetamol in syrup formulations using 2,4,6-trimethoxybenzaldehyde as a coupling agent

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ABSTRACT

A new, simple, sensitive and economical spectrophotometric method for the determination of paracetamol has been developed. The proposed method is based on the reaction of 2, 4, 6-trimethoxybenzaldehyde with hydrolyzed paracetamol (p- aminophenol) to yield a pinkish coloured product with a maximum absorption at 377 nm. There were no interferences observed from the common excipients present in the formulations. The method was successfully employed for the determination of paracetamol in syrup preparations and the results obtained compared favourably with the known official methods.

Key words: paracetamol, 2, 4, 6-trimethoxybenzaldehyde, spectrophotometric, syrup, determination.

INTRODUCTION

Paracetamol (p-acetamidophenol) is used extensively as an over the counter drug in the treatment of pain. It is marketed in different formulations (tablet, syrup and suppository); at times it comes with the combination of caffeine, ibuprofen and diclofenac sodium. Different official and unofficial methods abound for the analysis of paracetamol. Among other methods that could be used in the assay of paracetamol, spectrophotometric methods have also been reported. These depend on hydrolysis of the compound leading to the formation of a Schiff base with a substituted benzaldehyde, [1] or reaction with *o*-cresol, [2], sodium nitroprusside, [3] cerium(IV), [4] and oxidative coupling with *m*-cresol, [5] and sodium iodylbenzoate [6]. Other spectrometric methods are based on indophenols blue formation, [7], nitrosation and subsequent chelation [8] ultraviolet absorption and its change with pH [9]. Some of these methods require lengthy treatments and lack the simplicity and sensitivity required for routine analysis of the drug. There is need therefore, for a continual search for a cost-effective method that could be used for rapid assay of this common drug that is liable to counterfeiting. A simple, economical and effective method has been designed by treating the hydrolyzed paracetamol with 2, 4, 6-trimethoxybenzaldehyde. This method was used to analyze commercial paracetamol syrup.

EXPERIMENTAL SECTION

An SP 800 spectrophotometer with 1cm cell was used for the electronic measurement of the drugs.

Preparation of stock solution

For the preparation of stock solution, 1 g of paracetamol was accurately weighed into 100 mL volumetric flask and dissolved in sufficient distilled water and made up to the mark to produce 1% solution of paracetamol. 5 mL of 1% stock solution was pipetted into 50 mL volumetric flask and made up to the mark with distilled water to produce 0.1% solution. All other reagents were prepared according to British pharmacopoeia specification [10].

Establishment of volume of 2 M hydrochloric acid needed for reaction

Volumes of 2 M hydrochloric acid ranging from 1 to 5 mL were treated with 10 mL aliquot of 40 mg/mL paracetamol solution and heated for about 10 minutes. Excess (about 6 mL) of 0.2% 2, 4, 6-trimethoxybenzaldehyde in 95% ethanol was added and a pink colour was formed. The solution was cooled and made up to 20 mL with distilled water. The absorbance of the solutions was at 377 nm. The highest absorbance was obtained at 2 mL of 2 M hydrochloric acid as shown in table 1.

Establishment of volume of 0.2% of 2, 4, 6- trimethoxybenzaldehyde needed for reactions

Volume of 0.2% 2,4,6- trimethoxybenzaldehyde in 95% ethanol ranging from 1-5 mL were used ; 10 mL aliquots of 40 mg/mL solution of paracetamol were prepared and transferred to five different test tubes and 2 mL 2M hydrochloric acid was added in each test tube and heated for about 10 minutes. Different volumes of the aldehyde (1-5 mL) were added in each test tube and pink complex was formed. The solutions were cooled and made up to 20 mL with distilled water. The absorbance of the solutions was read at 377 nm and the highest was at 5 mL as shown in table 2.

Establishment of reaction time

10 mL aliquots of 40 mg/mL solution of paracetamol were prepared and transferred to three different test tubes. 2 mL of 2 M hydrochloric acid was added in each test tube and heated for 5, 10, 15 minutes respectively. 5 mL of 0.2% 2, 4, 6- trimethoxybenzaldehyde in 95% ethanol was added to each test tube and pink complex was formed. The solutions were cooled and made up to 20 mL with distilled water. The absorbance of solutions was read and the highest absorbance was at 10 minutes as shown table 3.

Complex development/ determination of maximum wavelength

10 mL aliquot of paracetamol solution (40 mg/mL) was prepared by taking 0.4 mL of 0.1% paracetamol solution into 10 mL volumetric flask and was made up to 10 mL with distilled water. It was transferred into a test tube; 2 mL of 2 M hydrochloric acid was added and heated for 10 minutes to aid hydrolysis of paracetamol so as to yield p-aminophenol. 5 mL of 2, 4, 6- trimethoxybenzaldehyde in 95% ethanol was added and a pink complex was formed. The solution was cooled and made up to 20 mL with distilled water. A reference solution was used to zero the spectrophotometer. It was treated as in complex development but paracetamol was not included. This is a variation of the method employed by Usifoh *et al.*, [11] where all was added to reference preparation except the aldehyde.

The absorbance of the solution was read at various wavelengths in the visible range (Table 4). A plot of absorbance against the wavelength of maximum absorption was determined.

Calibration curve

Serial dilution of the stock solution of paracetamol were made to obtain 0.1% solution, which was used to prepare the following concentrations; 20 µg/mL, 40 µg/mL, 60 µg/mL, 80 µg/mL and 100 µg/mL. The absorbance of each solution was read at 377 nm, and a graph of absorbance plotted against the concentration to obtain the calibration curve (Beer-Lambert curve)

Assay of various samples of paracetamol syrup

Different brands - A, B, C, and D of paracetamol syrup were used. The label claim on each sample is 120 mg/5 mL. They were all analyzed at 40 µg/mL and 60 µg/mL; the concentrations were prepared as follows;

5 mL of 120mg/5mL solution was taken and made up to 10mL with distilled water in a 10mL volumetric flask to obtain 10 mL of 12 mg/mL solution. 1mL of the solution was taken and made up to 10 mL with distilled water in a 10 mL volumetric flask to obtain 10 mL of 1.2mg/mL. 1mL of the resulting solution was taken and made up to 10 mL with distilled water in a 10 mL volumetric flask to obtain 0.12 mg/mL solution. From this 40 µg/mL and 60 µg/mL solutions were prepared.

Percentage content determination

Percentage content determination was done by comparing the absorbance of test sample with that of standard preparation

A_T/A_S x 100%

Where A_T = absorbance of test sample,
A_S = absorbance of standard preparation.

RESULTS AND DISCUSSION

Paracetamol is the most commonly used drug for its analgesic and antipyretic properties, both in adults and children. It is an important drug in the society and occurs in different pharmaceutical forms - syrups, tablets and suppositories. In this work, only syrups were considered. Paracetamol syrup is often administered to children than any other drug and it is most likely to be counterfeited than any other over the counter (OTC) drugs. This is the basis for this investigation.

Table 1: Volume of 2M hydrochloric acid used for reaction

Concentration of paracetamol(µg/mL)	Volume of 2M hydrochloric acid	Absorbance
40	1	0.049
40	2	0.056
40	3	0.042
40	4	0.033
40	5	0.027

Table 2: Volume of 0.2% 2, 4, 6- trimethoxybenzaldehyde used in the reaction

Concentration of paracetamol (µg/mL)	Volume of 0.2% 2,4,6- trimethoxybenzaldehyde	Absorbance
40	1	0.022
40	2	0.037
40	3	0.041
40	4	0.046
40	5	0.053

Table 3: Optimum time for reaction

Concentration of paracetamol (µg/mL)	Hydrolysis time (minutes)	Absorbance
40	5	0.31
40	10	0.055
40	15	0.049

Table 4: Wavelength of maximum absorption for 40 µg/mL

Wavelength	Absorbance
360	0.024
365	0.032
370	0.044
375	0.049
376	0.051
377	0.055
378	0.052
379	0.047
380	0.040
390	0.026
400	0.018

Low concentrations (in µg/mL) were used because at high concentrations, the colour intensity of paracetamol solution interfered with light absorption. Different volumes of 2 M hydrochloric acid were treated as in the development of complex and the solution that gave the highest absorbance was found to be 2 mL. Various volumes (1-5 mL) of 0.2% 2, 4, 6 - trimethoxybenzaldehyde were treated as in complex development, the volume that gave the highest absorbance value was found to be 5 mL. The time for complete hydrolysis was found to be 10 minutes.

10 mL aliquot (40 µg/mL) of paracetamol solution was treated as in complex development and absorbance was read by various wavelengths and the wavelength of maximum absorption was found to be 377 nm. Various concentrations of paracetamol (20, 40, 60, 80 and 100 µg/mL) were prepared and the absorbance of each solution was read at 377 nm and the calibration curve was plotted accordingly. With respect to Beer-Lambert plot, the percentage contents of various samples of paracetamol syrup (A-D) were determined. The quantity of the drug was ascertained in terms of the percentages using values stated in the British pharmacopoeia (B.P) [10] as standards. B.P states that paracetamol content should lie between 95.0 - 105.0% of the stated amount. All the samples used for the assay except sample B met the B.P specification of the percentage content. The percentage content of sample B was found to be 53.30% which is far below the B.P specification. Based on this method employed for the assay of the syrup preparations, this sample B was found to be substandard.

Table 5: Percentage composition of the different brand of paracetamol syrups

Sample	40 µg/mL	60 µg/mL
A	97.50	96.67
B	55.00	53.30
C	102.50	103.30
D	97.50	98.30

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