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Spectrophotometric Estimation of Paracetamol in Bulk and Pharmaceutical Formulations

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Abstract: A new, simple and sensitive spectrophotometric method for the determination of paracetamol has been developed. The proposed method is based on the reaction of paracetamol with iron(III) and a subsequent reaction with ferricyanide in an hydrochloric acid medium to yield Prussian bluish green coloured product with a mixiumum absorption at 715 nm. There were no interferences observed from the common excipients present in the formulations. The method is successfully employed for the determination of paracetamol in various pharmaceutical preparations and the results have been statistically compared with those obtained by the official method.

Keywords: Spectrophotometry, Paracetamol, Iron(III), Potassium ferricyanide, Hydrochloric acid.

Introduction

Paracetamol (*N*-acetyl-*p*-aminophenol) is widely used as analgesic and antipyretic drug, together with caffeine, ibuprofen and diclofenac sodium. Several spectrophotometric methods have been reported for their determination. The majority of published methods for paracetamol depend on hydrolysis of the compounds leading to the formation of a Schiff base with a substituted benzaldehyde[1,2], or reaction with *o*-cresol[3], sodium nitroprusside[4], cerium(IV)[5] and oxidative coupling with m-cresol[6] and sodium iodylbenzoate[7]. Other spectrometric methods are based on indophenols blue formation[8-9], nitrosation and subsequent chelation[10], ultraviolet absorption[11] and its change with pH[12]. Most of these methods require lengthy treatments and lack the simplicity and sensitivity needed for routine analysis.

Sangavi *et al*[13] reported a colorimetric method for the hydrolysed product of the paracetamol with 1,2-naphthoquinone-4-sulphonate (NQS) in acid medium to form a Schiff base having an absorption maximum at 480 nm.

The present communication reports on the investigation for the use of iron(III) salts in the presence of ferricyanide as reagent for the spectrophotometric determination of paracetamol. No method has been found for dealing with the use of combinations of these two reagents.

This method offers the advantages of simplicity, specificity without the need of extraction or heating, besides having higher sensitivity range than most of the existing spectrophotometric methods. Moreover, this method is totally free from the twin disadvantages of critical acid or reagent concentration and instability of the coloured species.

Experimental

A JASCO model UVI DEC-610 UV-VIS spectrophotometer with 1.0 cm matched cells was used for electronic spectral measurements. Standard solutions of paracetamol (1000 µg/mL was prepared by dissolving 100 mg in distilled water and diluted to the mark in a 100 mL calibrated flask. A working standard solution of paracetamol containing 50 µg/mL was prepared by further dilution. A potassium ferricyanide solution (0.002 M), ferric chloride solution (0.1 M) and hydrochloride acid solution (5 M) were prepared in deionised water.

Aliquots of standard paracetamol solution were transferred into 10 mL calibrated flask, 2 mL of potassium ferricyanide and 0.4 mL of ferric chloride were added and the mixture was set aside for 10 min. Then 1.0 mL of hydrochloric acid was added, the contents were diluted to the mark with water and mixed thoroughly. After 20 min. the absorbance values at 715 nm were measured against a reagent blank and a calibrated graph was constructed.

Five tablets (commercial tablets) were powdered and weighed. An amount equivalent to 50 mg (for syrup and injection forms an appropriate volume of the samples) of paracetamol was taken and dissolved in distilled water and filtered if necessary. A suitable aliquot of this solution in individual paracetamol working range was treated as described in the procedure.

Results and Discussion

This method involves the oxidation of the drug with iron(III) and subsequent chelation with ferricyanide to form a Prussian blue coloured product. The factors affecting the colour development, reproducibility, sensitivity and adherence to Beer's law were investigated with paracetamol and listed in Table 1.

Table 1. Parameters for the spectrophotometric determination of paracetamol

Parameter	Paracetamol
Colour	Bluish Green
λ_{max},nm	715
Stability, min	10
Beer's law range, µg mL^{-1}	0.1 - 2.4
Molar absorptivity, L mol^{-1} cm^{-1}	$4.2160x10^4$
Sandell's sensitivity, µg cm^{-2}	0.0038
Limit of detection, µg mL^{-1}	0.03
Limit of quantification, mg mL^{-1}	0.08
Regression coefficient (r)	0.99789
Slope (a)	0.2806
Intercept (b)	0.0044
R.S.D, %	0.709
Range of error	0.708

Spectral characteristics

A bluish green complex is formed when paracetamol was allowed to react with iron(III) in the presence of ferricyanide in hydrochloric acid medium with maximum absorption as shown in Figure 1. The colourless reagent blank has practically negligible absorbance at this wavelength.

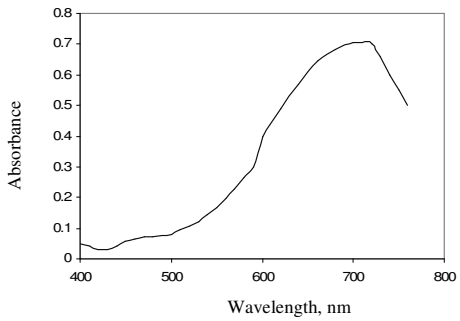

Figure 1. Absorption spectra of paracetamol by proposed method

Optimum conditions for complex formation

It was found that a 0.1 M solution of ferric chloride in the range of 0.3-0.5 mL and a 0.002 M solution of potassium ferricyanide in the range of 1.0-3.0 mL were necessary to achieve the maximum intensity of the product. The colour intensity decreases above the upper limit and below the lower limit. Therefore 0.4 mL of ferric chloride and 2.0 mL of ferricyanide were recommended for all measurements.

Dilution of the bluish green product with different solvents like water, methanol, ethanol, acetic acid, sulphuric acid and hydrochloric acid were tested. Results showed that hydrochloric acid gives clear blue colour with maximum intensity compared to acetic acid and sulphuric acid. It was found that hydrochloric acid in the range of 1.0-10.0 mL was necessary to get clear, stable colour. Therefore, a 1.0 mL volume of hydrochloric acid was recommended for all subsequent measurements.

Interference studies

A detailed study on the interference of different excipients were made, it was found that many of the cations, anions and other concomitant substance such as glucose, lactose, starch, talc *etc*., do not interfere in analysis and the tolerance limits of these and other ions are listed in Table 2.

Table 2. Effect of interfering ions and excipients on the determination of paracetamol

Compounds/ions added	Tolerance limit, ppm
Glucose	250
Lactose	150
Starch	100
Talc	100
Sodium Chloride	100
Sodium sulphate	200
Cadmium	300
Barium	100
Sulphite	100
Carbonate	100
Manganese	200
Calcium	200

Applicability of the method

The applicability of the method to assay pharmaceutical preparations was examined. To results of assay of available paracetamol preparations are summarized in Table 3. We prepared tablets of paracetamol in the laboratory and used for the assay. The results obtained compare favourably with the results obtained by the official method[14].

Table 3. Determination of paracetamol by the proposed method

Product	Composition, mg	Recovery (%, mean± R.S.D.)[b]	
		Proposed method	Official method
Dolo (syrup)[a] Paracetamol	500	101.00±1.01	100.3± 0.99
Crocin Drops[a] Paracetamol	150	100.7± 0.56	100.2± 0.99
Dolopar[a] Paracetamol	250		
Analgin	250	99.8± 1.07	99.4±1.1
Caffeine	250		
Phenacetin (laboratory made)	200	99.8 ± 0.78	99.7± 1.0
Flamar-P[a] Chlorzoxaone	250	99.8± 0.81	99.8 ± 0.81
Paracetamol	300		
H-Mol-75[a] Paracetamol	75	99.9± 1.14	99.8 ± 1.21
Benzyl alcohol Calpol[a] Paracetamol	500	101.3 ± 0.68	100.1± 0.65
Ibugesic Plus[a] Ibuprofen	200	102.5 ± 0.45	101.5 ± 0.73
Paracetamol	325		
Diclogesic[a] Diclofenac	50	101.3 ± 0.45	100.4 ± 0.49
sodium Paracetamol	500		
Pacimol[a] Paracetamol	500	102.1 0.98	99.9 0.53

[a]Trade name, [b]Average of five determinations, assayed as a percentage of label claim. R.S.D., relative standard deviation (n=5)

Conclusion

The method is found to be simple, economical, sensitive and rapid. The Statistical parameters and the recovery study data clearly indicate the reproducibility and accuracy of the method. The recommended procedure is well suited for the assay and evaluation of drugs in pharmaceutical preparations to assure high standard of quality control.

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