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Spectrophotometric determination of paracetamol in pharmaceutical preparation using heterocyclic coupling agent

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ABSTRACT

A fast, sensitive and simple spectrophotometric method is described for determination of paracetamol. The method is based on the hydrolysis of the amide to amino group followed by diazotization and coupling reaction with 8-quinolinol. The resulting coloured azo dyes exhibit maximum absorption at 498nm. The experimental conditions were optimized and Beer's law was obeyed over the applicable concentration ranges of 1-25μg/ml. The common excipients used as additives in pharmaceutical preparations do not interfere with the determination. Results from the analysis of pure paracetamol and its commercial tablets by the proposed method agree well with the reported method.

KEYWORDS

Paracetamol;
Diazotization;
8-Quinolinol;
Spectrophotometry;
Pharmaceutical preparations.

INTRODUCTION

Paracetamol (4-acetamidophenol, acetaminophen, PA) is an analgesic and antipyretic derived from phenacetin. It is widely used (alone or associated with other active substances such as caffeine) due to the lack of gastric upsets often associated with other analgesics such as acetylsalicylic acid[1].

So, the accurate determination of PA in pharma ceutical preparations and biological fluids has appeared especially attractive. For its measurement, many methods have been developed, such as fluorometry [2-3], chemiluminescence[4], electrochemical method[5-7], liquid chromatography[8-15], capillary electrophoresis[16], Ion chromatography[17], near infrared spectroscopy [18-19], sequential injection system[20] and spectrophoto metric methods[21-30].

This report describes a new spectrophotometric method, simple, fast, and reliable for the determination of PA in either pure form or in its pharmaceuticals formulations.

The scientific novelty of the present work is that the reagents used in both methods are easily available and the chemistry of these reagents is already well established. The reactions involved with these reagents are simple, rapid and sensitive in their range of determination compared with other established methods.

MATERIEL AND METHODS

Instrumentation

A Perkin Elmer UV-visible spectrophotometer type lambda 20 version(1.01) with 1.0cm matched cells was used.

Reagents

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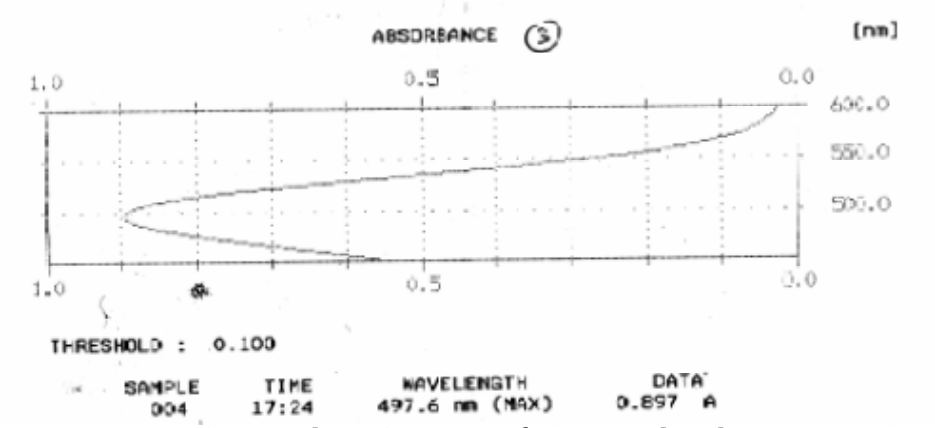


Figure 1 : Absorption spectra of paracetamol product

All chemicals used were of analytical-reagent grade. 8-quinolinol and sodium hydroxide were purchased from Merck, Sodium nitrite and sulfamic acid were purchased from Fluka. Deionized water was used to prepare all solution and in all experiments.

Solutions

Accurately weighed (50mg) PA was transferred to a 100ml beaker containing 30ml of 20% hydrochloric acid and refluxed for 30 min. The solution was cooled and diluted to volume with water. The working standard solution of the hydrolysis PA containing 50µg ml^{-1} was prepared by further dilution.

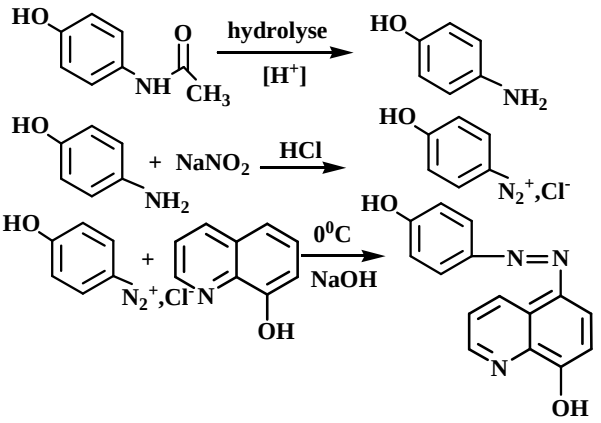
A 1% 8-quinolinol solution in HCl 0.1N is prepared in amber-glass volumetric flasks. A 2% sodium nitrite solution, a 4% sulfamic acid solution and 5% sodium hydroxide solution were prepared separately in Deionised water in amber-glass volumetric flasks.

Procedure

Aliquots of standard solution of PA were transferred into a 20ml calibrated flask. 2ml of HCl 1N was added, cool in an ice bath and 2ml of 2% $NaNO_2$ was added with swirling. The solutions were allowed to stand for 5min and then 2ml of 4% sulfamic acid solution was added. The solutions were swirled and allowed to stand for 5min. Add 2ml of 1% 8-quinolinol. After 5min, made up to the mark with 5% of NaOH solution.

Procedure for assay of pharmaceutical tablets

Twenty tablets were powdered and mixed thoroughly. An amount equivalent to 50mg of PA was taken and subjected to hydrolysis using 30ml of 20% hydrochloric acid. The filtrate was made up to 100ml and aliquots of this solution were treated as described above for pure sample.



SCHEME 1 : Reaction sequence for the formation of red-break colored product

RESULTS AND DISCUSSION

The spectrophotometric method for the determination of PA is based on the hydrolysis of the amide to amino group with hydrochloric acid followed by diazotization and coupling with 8-quinlinol to form the red-break colored product.

Spectral characteristics

The absorption spectra of the red-break colored product with λ_{max}=498nm is presented above. The reagent blank has practically negligible absorption at this wavelength (figure1)

Reaction mechanism

The stochiometric equation derived is illustrated in SCHEME 1.

TABLE 1 : Parameters for the spectrophotometric determination of paracetamol

Parameters/characteristics	Paracetamol
Colors	Red-break
λmax (nm)	498
Stability(in days)	3
Beer's law range (μg ml^{-1})	1 - 25
Molar absorptivity (l mol^{-1} cm^{-1})	4,02 10^3
Regression equation(y)[a]	
Slope (a)	0.0279
Intercept (b)	0.0097
Correlation coefficient	0.9965
R.S.D. (%)[b]	0.57

[a]y=ax+b where x is the concentration of paracetamol in μgml^{-1}; [b]relative standard deviation (n=5).

TABLE 2 : Determination of paracetamol in presence of excipients

Excipients	Amount (mg)	Recovery of paracetamol, (± RSD)[a]
Lactose	30	99.8 ± 1.1
Povidone	40	99.2 ± 0.95
Starch	40	99.4 ± 0.7
Sodium starch glycolate	10	99.4 ± 0.85
Sodium saccharinate	20	100.1± 0.33
Glucose	30	100.4±0.68
Magnesium stearate	20	100.3± 1.2
Aspartame	40	99.6 ±1.14

[a]average of five determination, R.S.D., relative standard deviation

TABLE 3 : Assay of paracetamol in pharmaceutical preparation

Product	Label claim (mg)	Recovery of paracetamol, (± RSD)[a]
Doliprane®500	500/tablet	99.5 (±1.3)
Doliprane®1000	1000/tablet	99.8 (±1.6)
Algik® 500	500/tablet	101.2(±1.2)
Algik® 500	500/oral suspension	98.6 (±2.1)
Xalgik® 400	400/tablet	97.2 (±1.9)
Dolamine®500	500/tablet	98.4 (±2.3)
Parantal®500	500/tablet	99.1 (±2.3)
Parantal®80	500/tablet	100.3(±2.3)

[a]average of five determination, R.S.D., relative standard deviation

Optimization of reaction conditions

The factors affecting color development, reproducibility, sensitivity, and conformity with Beer's law investigated. It was found that (0.5-3)ml of HCl 1M, (1-4)ml of 2% $NaNO_2$ solution, (1-4)ml of 1% 8-quinolinol solution was necessary to achieve maximum color intensity. The excess of nitrite sodium could be removed by the addition of 1ml of 4% sulfamic acid solution. An excess of sulfamic acid has no effect on the color intensity of the formed product.

Quantification

Beer's law is obeyed over the PA concentration range of 1-25μg/ml.

The proposed procedure is validated by determination optical parameters, which are listed in TABLE 1.

Interference

The effects of various substances that often accompany PA in pharmaceutical preparations were studied. Majority of the common excipients do not interfere in the present method. The results are listed in TABLE 2.

Application

The application of the method to assay pharmaceutical preparation was examined. The assay of PA, singly and in various combinations is shown in TABLE 3.

The excellent recoveries obtained indicate the absence of any interference from the excipients.

CONCLUSION

The method is found to be simple, economical, selective and more sensitive than most of the spectrophotometric methods reported. The statistical parameters and recovery data study clearly indicate the reproducibility and accuracy of the method. Analysis of the authentic samples containing paracetamol showed no interference from the common excipients. Thus the method can be adopted for routine analysis in quality control laboratories.

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