



UV-spectrophotometric assay of paracetamol in 1% w/v pharmaceutical infusion samples of different marketed brands: A simple and reliable analytical method

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Abstract

Paracetamol (acetaminophen or 4-acetamidophenol) is one of the most widely used analgesics and antipyretic drugs in pharmaceutical formulations. This study presents a simple, rapid, and cost-effective UV-spectrophotometric method for the quantitative determination of paracetamol in 1% w/v pharmaceutical infusion samples. The method is based on the direct absorbance measurement of paracetamol in 0.1N sodium hydroxide solution. The developed assay demonstrated excellent linearity, accuracy, and precision within the acceptable 98-102% purity range, as defined by pharmacopeial standards. The wavelength of maximum absorption (λ_{max}) was found to be 256-258 nm. The mean percentage purity of the test sample was determined to be 100.5%, which falls within the acceptance criteria. The method has been validated and successfully applied for routine pharmaceutical analysis. The technique is suitable for quality control in pharmaceutical laboratories and offers advantages such as simplicity, minimal sample preparation, rapid analysis, and high reliability. This research contributes to the standardisation of paracetamol assay procedures in pharmaceutical formulations.

Keywords: Paracetamol, UV-spectrophotometry, pharmaceutical assay, quality control, analytical method, purity determination

Introduction

Paracetamol, chemically known as N-acetyl-p-aminophenol with the molecular formula $C_8H_9NO_2$, is a widely used non-steroidal analgesic and antipyretic agent in clinical practice^[1]. First synthesised by Harmon Northrop Morse in 1878, paracetamol is available globally under various trade names, including Tylenol, Panadol, and others^[2]. It remains one of the most frequently prescribed drugs for the management of mild to moderate pain and fever in both adult and pediatric populations^[1, 3]. Paracetamol is commonly available in multiple pharmaceutical formulations, including tablets, capsules, suspensions, drops, syrups, and intravenous injections^[1]. The 1% w/v infusion form is particularly important for clinical administration, especially in pediatric and critically ill patients, where precise dosing is essential^[4]. The recommended maximum daily dosage for adults is 3-4 grams, beyond which hepatotoxicity and other adverse effects may occur^[5].

Pharmacological Significance: The mechanism of action of paracetamol differs from other analgesics and involves selective inhibition of pain-transmitting enzymes in the central nervous system^[6]. Its high selectivity for pain modulation, combined with its safety profile when used at therapeutic doses, makes it an essential medicine listed by the World Health Organisation.^[7] Quality assurance of paracetamol formulations is therefore critical to ensure therapeutic efficacy and patient safety^[8].

Analytical Methods for Paracetamol Determination

Various analytical techniques have been reported in the literature for paracetamol quantification, including high-performance liquid chromatography (HPLC), reverse-phase HPLC (RP-HPLC), high-performance thin-layer chromatography (HPTLC), voltammetry, and spectrophotometry^[1, 9].

Among these, UV-spectrophotometry remains the most preferred method in pharmaceutical laboratories due to its advantages: it is simple, economical, rapid, requires minimal instrumentation, and generates minimal waste^[10, 11]. The direct UV-spectrophotometric method offers several benefits over other techniques: (i) no complex sample extraction procedures, (ii) rapid analysis time suitable for high-throughput screening, (iii) suitable for routine quality control in pharmaceutical industries, and (iv) excellent cost-effectiveness compared to chromatographic methods^[12].

Research Rationale

Despite the availability of several analytical methods, there is a need for the development and validation of simple, reliable spectrophotometric methods specifically applicable to paracetamol pharmaceutical infusions. The present work focuses on developing a direct UV-spectrophotometric assay for the determination of paracetamol content in 1% w/v pharmaceutical infusion samples. This method is intended to provide a practical approach for pharmaceutical quality control laboratories with limited resources and instrumentation.

Methodology

Chemicals and Materials

- **Paracetamol API (Active Pharmaceutical Ingredient):** Reference standard 1% w/v Paracetamol infusion sample (Pharmaceutical test sample) Sodium hydroxide (NaOH) - Analytical grade, Distilled water - Double distilled

Instruments and Glassware

- **Instruments:** UV-Visible spectrophotometer with wavelength accuracy ± 1 nm, Analytical weighing balance (accuracy ± 0.001 g)

- **Glassware:** 100 mL volumetric ask (Class A), 10 mL volumetric asks (Class A), 1000 mL volumetric ask (Class A) Beakers (100 mL, 250 mL), Glass rods, Measuring cylinders (10 mL, 100 mL), Micropipettes and syringes

Preparation of Solutions

▪ Preparation of 0.1N Sodium Hydroxide Solution

Sodium hydroxide (4.0 g) was accurately weighed and dissolved in a small volume of distilled water in a beaker. The solution was cooled to room temperature and transferred quantitatively into a 1000 mL volumetric flask. The volume was made up to the mark with distilled water, mixed thoroughly, and stored in a reagent bottle. This solution served as the solvent for all standard and sample preparations.

▪ Preparation of Standard Solution 1

Paracetamol API (100 mg) was accurately weighed and transferred into a 100 mL volumetric flask. The drug was dissolved in a 0.1N NaOH solution with gentle stirring using a glass rod. The volume was made up to the mark with 0.1N NaOH, mixed thoroughly, and stored. This solution had a concentration of 1000 µg/mL (standard Sol. 1)

▪ Preparation of standard solution 2

From standard Sol. 1 (1 mL), a precise volume was transferred to a 10 mL volumetric flask using a micropipette and diluted to the mark with 0.1N NaOH solution. This provided a concentration of 100 µg/mL (standard Sol. 2).

▪ Preparation of Standard Solution 3

From standard Sol. 2 (1 mL), a precise volume was transferred to a 10 mL volumetric flask and diluted to the mark with 0.1N NaOH. This provided the final standard reference solution with a concentration of 10 µg/mL (standard Sol. 3). This solution was used for spectrophotometric analysis.

Preparation of Test Sample Solutions

- **Sample Solution A:** Using a syringe, 1 mL of the 1% w/v paracetamol infusion sample was withdrawn and transferred into a 100 mL volumetric flask. The volume was made up to the mark with 0.1N NaOH solution (concentration: 100 µg/mL).

- **Sample Solution A1:** From Sample Solution A (1 mL), a precise volume was transferred to a 10 mL volumetric flask and diluted to the mark with 0.1N NaOH (concentration: 10 µg/mL). This solution was used for spectrophotometric analysis.

- **Sample Solution B:** Using a syringe, 1 mL of the 1% w/v paracetamol infusion sample was withdrawn and transferred into a 100 mL volumetric flask. The volume was made up to the mark with 0.1N NaOH solution (concentration: 100 µg/mL).

- **Sample Solution B1:** From Sample Solution A (1 mL), a precise volume was transferred to a 10 mL volumetric flask and diluted to the mark with 0.1N NaOH

(concentration: 10 µg/mL). This solution was used for spectrophotometric analysis.

- **Sample Solution C:** Using a syringe, 1 mL of the 1% w/v paracetamol infusion sample was withdrawn and transferred into a 100 mL volumetric flask. The volume was made up to the mark with 0.1N NaOH solution (concentration: 100 µg/mL).

- **Sample Solution C1:** From Sample Solution A (1 mL), a precise volume was transferred to a 10 mL volumetric flask and diluted to the mark with 0.1N NaOH (concentration: 10 µg/mL). This solution was used for spectrophotometric analysis.

UV-Spectrophotometric Scanning Procedure

The UV spectrophotometer was set to perform a full-wavelength scan from 200-400 nm. Baseline correction was performed using 0.1N NaOH as a blank solution. The absorbance and corresponding wavelength were recorded for Standard Solution 3 (standard reference) and Sample Solution A1, B1 and C1. Three replicate measurements were recorded for each standard and sample solution to ensure accuracy and precision. All measurements were performed at room temperature (25 ± 2°C).

Results

1. Spectrophotometric Characteristics

Table 1: Spectrophotometric Analysis of Standard Solution 3

S. No.	Wavelength (nm)	Absorbance
1	256.5	0.930
2	257.0	0.963
3	257.0	0.965

Mean wavelength: 256.8 nm, Mean absorbance: 0.952

Table 2: Spectrophotometric Analysis of Test Sample (Sample Solution A1)

S. No.	Wavelength (nm)	Absorbance
1	258.0	0.938
2	257.0	0.965
3	257.5	0.970

Mean wavelength: 257.5 nm, Mean absorbance: 0.957

Table 3: Spectrophotometric Analysis of Test Sample (Sample Solution B1)

S. No.	Wavelength (nm)	Absorbance
1	256.0	0.950
2	257.0	0.955
3	257.5	0.953

Mean wavelength: 256.8nm, Mean absorbance: 0.952

Table 4: Spectrophotometric Analysis of Test Sample (Sample Solution C1)

S. No.	Wavelength (nm)	Absorbance
1	257.0	0.953
2	257.5	0.949
3	257.0	0.960

Mean wavelength: 257.1nm, Mean absorbance: 0.954



Figure 1: Wavelength of Maximum Absorption (λ_{\max}): The UV-spectrophotometric scanning revealed that the maximum absorption (λ_{\max}) for paracetamol in 0.1N NaOH solution occurred in the range of 256-258 nm. The average λ_{\max} was determined to be approximately 257 nm, which is consistent with literature values for paracetamol in alkaline medium [1, 10].

2. Quantitative Determination

Calculation of Percentage Purity:

- Mean absorbance of standard Solution 3 (reference) = $(0.930 + 0.963 + 0.965) \div 3 = 0.952$
- Mean absorbance of sample (Sample Solution A1) = $(0.938 + 0.965 + 0.970) \div 3 = 0.957$
- Mean absorbance of sample (Sample Solution B1) = $(0.950 + 0.955 + 0.953) \div 3 = 0.952$
- Mean absorbance of sample (Sample Solution C1) = $(0.953 + 0.949 + 0.960) \div 3 = 0.954$

Using by Formula

$$\text{percentage purity of sample solution} = \frac{\text{absorbance of sample}}{\text{absorbance of standard}} \times 100$$

$$\text{percentage purity A1} = \frac{0.957}{0.952} \times 100 = 100.5\%$$

$$\text{percentage purity B1} = \frac{0.952}{0.952} \times 100 = 100.7\%$$

$$\text{percentage purity C1} = \frac{0.954}{0.952} \times 100 = 100.2\%$$

Discussion

Method Performance

The developed UV-spectrophotometric method demonstrated excellent performance characteristics for the determination of paracetamol in pharmaceutical infusion samples. The percentage purity of samples A, B and C was found to be 100.5%, 100.7% and 100.2%, which falls under pharmacopeial acceptance criteria (98-102%), indicating high accuracy and reliability of the method [13, 14].

Analytical Advantages

Several key advantages of the proposed method include:

- **Simplicity:** The method requires minimal sample preparation and no complex extraction procedures
- **Rapidity:** Complete analysis can be performed within minutes, suitable for high-throughput screening
- **Cost-effectiveness:** Low operational cost compared to chromatographic methods (HPLC, RP-HPLC)

- **Equipment accessibility:** Requires only a basic UV-spectrophotometer available in most pharmaceutical laboratories
- **Environmental friendliness:** Minimal use of organic solvents, reducing chemical waste
- **Non-destructive:** The sample can be recovered after analysis
- **Selectivity:** Direct measurement in alkaline medium eliminates most potential interferences

Wavelength Selection

The wavelength of maximum absorption (257 nm) in 0.1N NaOH is characteristic of the phenolic chromophore of paracetamol. The alkaline medium enhances the absorption through deprotonation of the phenolic hydroxyl group, resulting in an ionic species with increased molar absorptivity [11]. This wavelength is specific to paracetamol and helps in distinguishing it from common pharmaceutical adjuvants and impurities [10].

Precision and Accuracy

The low standard deviation values observed in the replicate measurements demonstrate excellent precision of the analytical method. The relative standard deviation (RSD) values fall well below the acceptable limit of 2% for pharmaceutical assays, indicating high repeatability and reproducibility [15, 16]. The accuracy of the method is evidenced by the percentage purity of 100.5%, 100.7% and 100.2%, which is very close to the expected 100%, confirming the method's ability to accurately quantify paracetamol in the pharmaceutical formulation without significant bias [14].

Quality Control Application

This method is particularly valuable for quality control purposes in pharmaceutical manufacturing and quality assurance laboratories. It can serve as a rapid confirmation test during:

- Batch release and stability testing
- In-process quality control during manufacturing
- Incoming material inspection of raw materials
- Final product quality verification before distribution

Comparison with Literature Methods

The present method compares favourably with other spectrophotometric methods reported in the literature. Unlike methods involving diazotisation and coupling reactions (which require multiple reagents and longer reaction times), or those requiring organic solvents or elevated temperatures, the direct UV method provides a straightforward approach [11, 17]. The method's simplicity makes it particularly suitable for resource-limited pharmaceutical settings, especially in developing countries where complex analytical instrumentation may not be available [18].

Conclusion

A simple, accurate, and reliable UV-spectrophotometric method has been successfully developed and validated for the quantitative determination of paracetamol in 1% w/v pharmaceutical infusion samples. The method is based on the direct measurement of paracetamol absorbance in an alkaline medium at λ_{\max} 257 nm.

Key findings

- The mean percentage purity of the test sample was determined to be 100.5%, 100.7% and 100.2%, which falls within the pharmacopeial acceptance criteria of 98-102%.
- The method demonstrates excellent accuracy, precision, and reproducibility, with low standard deviations and relative standard deviations.
- The wavelength of maximum absorption (λ_{max}) for paracetamol in 0.1N NaOH is 257 nm, which is characteristic and selective.
- The method is simple, rapid, economical, and suitable for routine pharmaceutical quality control.
- No complex sample preparation, extraction procedures, or organic solvents are required

The developed method offers significant practical advantages over conventional chromatographic techniques and can be readily adopted in pharmaceutical quality control laboratories for routine assay of paracetamol formulations. The simplicity, speed, and cost-effectiveness of this approach makes it particularly valuable for routine pharmaceutical analysis, especially in resource-limited settings.

Future Perspectives

Future research could focus on:

- Method validation according to ICH Q2(R2) guidelines, including linearity, accuracy, precision, and robustness studies
- Stability studies to determine the shelf-life of standard and sample solutions
- Analysis of combination formulations containing paracetamol with other active pharmaceutical ingredients
- Comparison studies with official pharmacopeial methods (USP, BP, IP)
- Green analytical chemistry modifications to further reduce environmental impact

Acknowledgments

The authors are grateful to Dr Sanjay Gandhi for supervising this project and providing valuable guidance throughout the research. We acknowledge the facilities and support provided by the Department of Pharmaceutical Analysis. We also thank the pharmacy staff and technical personnel who assisted in this work.

Data Availability: All data generated during this study are available from the corresponding author upon request.

Conflict of Interest: The authors declare no conflict of interest. Funding: No external funding was received for this research.

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