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DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHODS FOR SIMULTANEOUS ESTIMATION OF PARACETAMOL AND ZALTOPROFEN IN BULK AND TABLET FORMULATION

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ABSTRACT: Two methods for simultaneous estimation of Paracetamol and Zaltoprofen in combined tablet dosage form have been developed. The first UV spectrophotometric method was a determination using the simultaneous equation method at 245 nm and 227 nm. The second UV spectrophotometric method is the Q – analysis (absorption ratio) method, which involves the formation of absorbance equation at 237.5 nm (isobestic point) and at 227 nm the maximum absorption of Zaltoprofen. The linearity ranges for Paracetamol and Zaltoprofen were 2 – 18 µg/ml and 2 – 18 µg/ml respectively. The accuracy of the methods was assessed by recovery studies was found to be 100.02 ± 0.467 and 99.87 ± 0.532 for simultaneous equation method and 99.82 ± 0.483 and 99.84 ± 0.512 for Q analysis (absorption ratio) method for Paracetamol and Zaltoprofen respectively. These methods are simple, accurate and rapid; those require no preliminary separation and can therefore be used for routine analysis of both drugs in quality control laboratories.

INTRODUCTION: Paracetamol and Zaltoprofen are available in tablet dosage form. Chemically, Paracetamol (PARA) is N acetyl-p-am inophenol and its structure is shown in **Fig. 1**. It has antipyretic and analgesic activity¹. Zaltoprofen (ZAL) (\pm)-2-(10, 11-dihydro- 10-oxodibenzo [b, f] thiepin-2-yl) propionic acid and its structure is shown in **Fig. 2**. Zaltoprofen (ZLT) is a non-steroidal anti-inflammatory drug, and has excellent effects even on post-surgery or post-trauma chronic inflammation.

It is used in the treatment of rheumatoid arthritis, osteoarthritis, and other chronic inflammatory Pain conditions⁶.

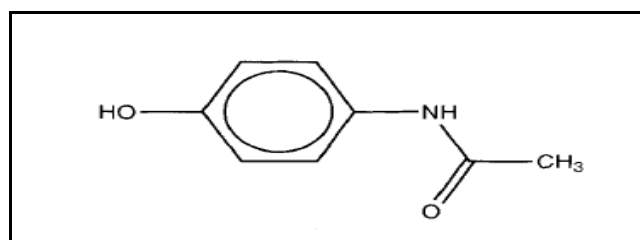


FIG. 1 STRUCTURE OF PARACETAMOL

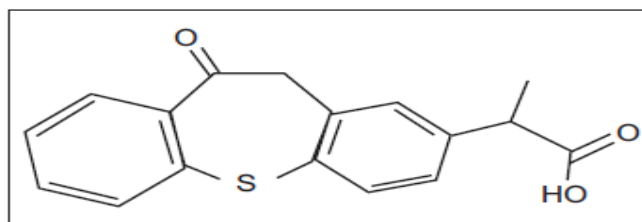


FIG. 2 STRUCTURE OF ZALTOPROFEN

QUICK RESPONSE CODE



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Literature survey reveals many analytical methods for determination of paracetamol such as UV Spectrophotometry, HPLC, and Capillary electrophoresis methods from pharmaceutical preparations¹⁻⁴. Few analytical methods for determination of Zaltoprofen using UV Spectroscopy and HPLC in pharmaceutical formulation have been reported⁵⁻⁹. However, there are no reported methods for simultaneous estimation of both drugs in combination.

This paper presents two simple, rapid, reproducible and economical methods for the simultaneous analysis estimation of both the drugs from pharmaceutical dosage form.

Experimental Work

Instruments & Chemicals

Pharmaceutically pure samples of ZAL were obtained as gifts from IPCA Lab Ltd. Mumbai & PARA of AR grade was purchased from Research Lab. Methanol AR grade (Research Lab) and distilled water (1:4) was used as solvent in the study. Double beam UV spectrophotometer Lab

India 3000 with a pair of 10mm matched quartz cells was used to measure absorbance of the resulting solution.

Preparation of standard stock solution:

Accurately 10 mg each of PARA and ZAL was weighed separately and transferred to two different 100ml volumetric flask. Each drug was dissolved by 10 min sonication in 20 ml methanol and then volume was made up to the mark with distilled water. The standard stock solutions (100µg/ml) were further diluted separately to obtain working standard of concentration 10µg/ml of PARA and ZAL each.

Study of spectra and selection of wavelengths;

Each working standard solution was scanned between the range 200-400 nm in 1 cm cell against blank. Maximum absorbing wavelength of PARA and ZAL were selected from spectral data and isobestic wavelength selected from overlain spectra of zero order. The λ max for PARA, ZAL and isobestic point was 245nm, 227nm and 237.5nm respectively.

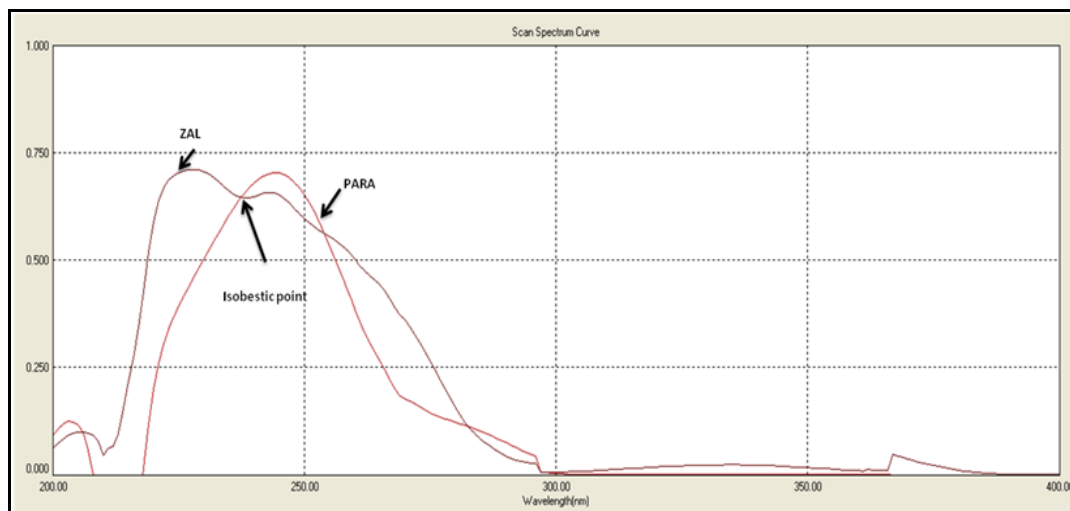


FIG. 3 OVERLAIN SPECTRA OF PARA AND ZAL

Method I:

In quantitative estimation of two components by simultaneous equation method, absorbances were measured at the maximum absorption wavelengths of two drugs. From the spectra of PARA and ZAL absorbances were measured at selected wavelengths i.e. 245nm (λ1) and 227nm (λ2) the maximum absorption of PARA and ZAL respectively. The absorptivity coefficients of each drug at both wavelengths were determined. The concentration of each drug in laboratory mixture

and tablet formulation was determined by substituting the absorbance and absorptivity coefficient in the following sets of equations.

$$C_x = \frac{A_1 a_{y2} - A_2 a_{y1}}{a_{x1} a_{y2} - a_{x2} a_{y1}} \dots \dots \dots \text{Eq. (i)}$$

$$C_y = \frac{A_1 a_{x2} - A_2 a_{x1}}{a_{y1} a_{x2} - a_{y2} a_{x1}} \dots \dots \dots \text{Eq. (ii)}$$

Where, A1 and A2 are absorbances of mixture at 245 nm and 227 nm respectively, ax1 and ax2 are absorptivities of PARA at λ_1 and λ_2 respectively and ay1 and ay2 are absorptivities of ZAL at λ_1 and λ_2 respectively. Cx and Cy are concentrations of PARA and ZAL respectively.

Method II:

In Q analysis method the absorbances were measured at the isobestic point and maximum absorption wavelength of ZAL. From overlain spectra of PARA and ZAL (**Fig.3**) absorbances were measured at the selected wavelengths i.e. 237.5nm (isobestic point) and at 227nm, the maximum absorption of ZAL. The absorptivity coefficients of each drug at both wavelengths were determined. The concentration of each drug in laboratory mixture and tablet formulation was determined by substituting the absorbance and absorptivity coefficients in the following sets of equations.

For PARA

$$C1 = \frac{Q0 - Q2}{Q1 - Q2} \times \frac{A}{a1}$$

For ZAL

$$C2 = \frac{Q0 - Q1}{Q2 - Q1} \times \frac{A}{a2}$$

Where,

$$Q0 = \frac{\text{Absorbance of sample at 237.5 nm}}{\text{Absorbance of sample at 227 nm}}$$

$$Q1 = \frac{\text{Absorptivity of PARA at 237.5 nm}}{\text{Absorptivity of PARA at 227nm}}$$

$$Q2 = \frac{\text{Absorptivity of ZAL at 237.5 nm}}{\text{Absorptivity of ZAL at 227nm}}$$

TABLE 1: LINEAR REGRESSION ANALYSIS OF CALIBRATION CURVES WITH THEIR RESPECTIVE ABSORPTIVITY VALUES

| Parameter | Method I | | Method II | |
|---------------------------------------|----------|---------|-----------|---------|
| | PARA | ZAL | PARA | ZAL |
| Beer's Law limit ($\mu\text{g/ml}$) | 2-18 | 2-18 | 2-18 | 2-18 |
| Correlation Coefficient (r) | 0.9998 | 0.9997 | 0.9995 | 0.9998 |
| Molar Absorptivity (Lit/mole/cm) | 8492.67 | 13796.2 | 9355.48 | 18401.4 |
| Slope | 0.048 | 0.045 | 0.065 | 0.059 |
| Intercept | 0.046 | 0.021 | 0.02 | 0.013 |
| LOD ($\mu\text{g/ml}$) | 0.7 | 0.5 | 0.9 | 0.8 |
| LOQ ($\mu\text{g/ml}$) | 2.5 | 1 | 2 | 1 |

A = Absorbance of sample at isoabsorptive point, a1 and a2 = Absorptivities of PARA and ZAL respectively at isoabsorptive point.

Procedure for analysis of tablet formulation:

Twenty tablets were accurately weighed and average weight was calculated. The tablets were triturated to a fine powder. An accurately weighed quantity of powder equivalent to 5 mg ZAL was dissolved in 20 ml methanol and sonicated for 50 min and volume was made up to 250ml by distilled water. The solution was filtered through Whatman filter paper No 41 and aliquot portion of filtrate was diluted to produce solution having concentration of $2\mu\text{/ml}$ of ZAL and $8.125\mu\text{/ml}$ of PARA. The absorbance of sample solution was measured at selected wavelengths and the concentrations of the two drugs were estimated using simultaneous equation method and absorbance ratio method. The analysis procedure was repeated six times and the results are depicted in **Table 1**.

Validation:

The methods were validated with respect to linearity, limit of detection (LOD), limit of quantification (LOQ), precision, accuracy and ruggedness. To study accuracy of the developed methods, recovery studies were carried out using standard addition method at three different levels. Percent recovery and low relative standard deviation for six replicates of sample solution was less than 2%, which met the acceptance criteria established for spectrophotometric methods.

Ruggedness of the proposed method was determined by analysis of sample solution prepared by proposed methods between different days. The percent relative standard deviation was found to be less than 2% showed ruggedness of the spectrophotometric methods. The results obtained are summarized in Tables.

TABLE 2: RESULTS OF RECOVERY STUDIES

| Level of Recovery % | Amount of pure drug added (mg) | | Simultaneous equation method % recovery | | Absorbance ratio method % recovery | |
|---------------------|--------------------------------|-----|---|--------|------------------------------------|--------|
| | PARA | ZAL | PARA | ZAL | PARA | ZAL |
| 80 | 8 | 4 | 100.09 | 100.61 | 100.74 | 99.52 |
| 100 | 10 | 5 | 99.47 | 98.82 | 100.22 | 100.37 |
| 120 | 12 | 6 | 100.51 | 100.23 | 98.51 | 99.63 |
| Mean % Recovery | | | 100.02 | 99.87 | 99.82 | 99.84 |
| SD* | | | 0.467 | 0.532 | 0.483 | 0.512 |
| CV** | | | 0.422 | 0.398 | 0.532 | 0.213 |

*Mean of six readings

TABLE 3: RESULTS OF ANALYSIS OF TABLET FORMULATION

| Drug | Label Claim (mg) | Simultaneous equation method % \pm SD (n=6)* | Absorbance ratio method % \pm SD (n=6)* |
|------|------------------|--|---|
| PARA | 80 | 100.37 \pm 0.231 | 100.51 \pm 0.123 |
| ZAL | 325 | 100.12 \pm 0.216 | 99.86 \pm 0.214 |

*Mean of six readings

TABLE 4: RESULTS OF INTERMEDIATE PRECISIONS

| Day | Method I % Label claim estimated (Mean \pm %RSD)* | | Method II % Label claim estimated (Mean \pm %RSD)* | |
|----------|---|-------------------|--|-------------------|
| | PARA | ZAL | PARA | ZAL |
| Intraday | 98.34 \pm 0.546 | 99.28 \pm 0.874 | 100.46 \pm 0.453 | 98.98 \pm 0.931 |
| Interday | 100.21 \pm 0.245 | 99.54 \pm 0.563 | 99.51 \pm 0.653 | 98.64 \pm 0.328 |

*Mean of six readings

RESULTS AND DISCUSSIONS: The overlain spectra of PARA and ZAL exhibit λ max of 245 nm and 227 nm for PARA and ZAL respectively which are quite separated from each other. Additionally one iso absorptive point was observed at 237.5 nm, this wavelength was selected for simultaneous estimation of PARA and ZAL for Q value analysis and it is assumed to be sensitive wavelength. Standard calibration curves for PARA and ZAL were linear with correlation coefficients (r) values in the range of 0.997 – 0.999 at all the selected wavelengths and the values were average of three readings with standard deviation in the range of 0.2465 – 0.7126.

The methods were repeated three times in a day and the average % RSD was found to be 0.546 for PARA and 0.874 for ZAL for method I and 0.453 for PARA and 0.931 for ZAL for method II. Similarly the method was repeated for three different days and average % RSD was found to be 0.245 for PARA and 0.563 for ZAL for method I and 0.653 for PARA and 0.328 for ZAL for method II. The accuracy of the methods was confirmed by recovery studies from tablet at three different levels of standard additions; recovery in the range of 98.51 – 100.74% justifies the accuracy of method.

CONCLUSIONS: The proposed UV spectrophotometric methods are a simple, accurate, precise, rapid and economical for the simultaneous estimation of PARA and ZAL in tablet dosage form. The proposed methods use inexpensive reagents, solvents and instruments that are available in laboratories. Hence, these methods can be conveniently adopted for the routine analysis in quality control laboratories.

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