ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Spectrophotometric Simultaneous Determination of Paracetamol and Aceclofeanc in Tablet Dosage Form.

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ABSTRACT

A simple, precise and accurate UV spectrophotometric method was developed for the simultaneous determination of Paracetamol and Aceclofenac in tablet dosage form. The method involved solving simultaneous equations based on measurement of absorbance at two wavelengths 247nm and 276nm. The proposed method was validated for linearity, accuracy and precision. The percentage recovery was found to be 99 - 101% for Paracetamol and 98 – 100% for Aceclofenac which indicates that the method was accurate and precise for simultaneous estimation of Paracetamol and Aceclofenac in tablets.

Keywords: Simultaneous equation method, Paracetamol, Aceclofenac

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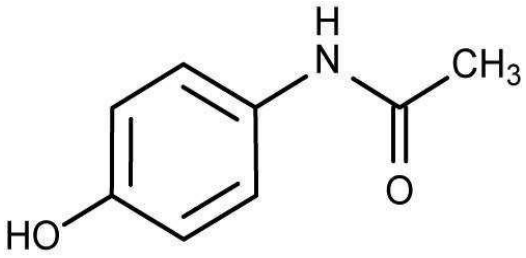
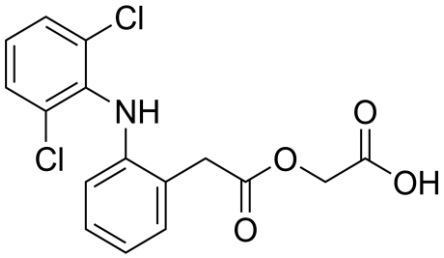
ISSN: 0975-8585

INTROCUCTION

Paracetamol (PCT) is chemically N - (4-hydroxyphenyl) acetamide and is used as analgesic and anti-pyretic agent. It has a narrow therapeutic index – the therapeutic dose is close to the toxic dose. Aceclofenac (ACF), {[2-(2`, 6`-dichlorophenyl) amino] phenyl acetoxyacetic acid} is a new phenyl acetic acid derivative with potent analgesic and anti-inflammatory properties with improved gastric tolerance. Literature survey reveals that various analytical techniques viz, Literature survey reveals that various analytical techniques viz, UV spectrophotometry, High performance liquid chromatography (HPLC) were reported for the analysis of PCT and ACF in pharmaceuticals. Few UV methods have been reported [1-9] for the simultaneous determination of PCT and ACF. Aim of present work was to develop simple, economical, rapid, precise and accurate method for simultaneous determination of Paracetamol and Aceclofeanc.



Paracetamol



Aceclofenac

EXPERIMENTAL

Chemicals and reagents:

PCT and ACF working standard were obtained from Glenmark (Mumbai, India), Tablets containing PCT (500mg) and ACF (100mg) were obtained from Unichem (Mumbai, India), AR grade methanol and acetonitrile were purchased from Baker (Mumbai, India).

Preparation of standard drug solution:

50mg of Paracetamol and 10 mg of Aceclofenac was separately weighed and transferred to a 50cm^3 volumetric flask. It was dissolved in a minimum quantity of methanol and then diluted up to the mark with methanol. The concentration of the solution obtained was 1000µg/mL for Paracetamol and 200 µg/mL for Aceclofenac. 10cm^3 of each of this solution was diluted to 100 cm^3 in a volumetric flask with methanol. The concentration of the solution obtained was 100µg/mL for Paracetamol and 20µg/mL for Aceclofenac.

Preparation of Sample solution:

Twenty tablets [AROFF PLUS] were weighed and average weight was calculated. These tablets were powdered and 0.0840gm of powdered tablet was taken in a 100 mL volumetric

flask, 10mL of methanol was added and sonicated for 20minutes and shaken by mechanical means for 20minutes at 250rpm. Further the solution was diluted with methanol. The solution was mixed and allows settled for 5 minutes. The solution was filtered through Whatman filter paper No 41. Then 2.5mL of the filtrate was diluted to 100mL with diluents and mixed. The concentrations obtained were 12.5 µg/mL of Paracetamol and 2.5 µg/mL of Aceclofenac. This sample solution was used for further determination.

Method in Brief

The present work describes an ultraviolet spectrophotometric method for the quantitative simultaneous determination of Paracetamol and Aceclofenac from its bulk drug and pharmaceutical preparation. Paracetamol and Aceclofenac absorb the radiation in the ultraviolet region. The Proposed ultraviolet spectrophotometric method is based on the measurement of absorbed ultraviolet radiations by both the analytes. The absorbance measurement was carried out at the λ_{max} of Paracetamol and Aceclofenac. Paracetamol shows maximum absorbance at 247nm wavelength while Aceclofenac shows at 276nm. The molar absorptivities of both the analytes were found at their respective λmax value. Using the molar absorptivities of both the analytes simultaneous equation was constructed and the concentration of analytes was determined. The proposed ultraviolet spectrophotometric method was subjected to statistical validation to determine its accuracy and precision.

Optimization of Experimental Conditions

The instrument used for the analysis of the samples is LAMBDA 25 UV/Visible Spectrophotometer, Range: 190 nm - 1100 nm, Bandwidth: 1 nm. The solvents that are commonly used in spectrophotometric analysis are water, dilute bases and organic solvents. Most of the drugs are soluble in organic solvents like methanol, acetonitrile etc. In the present study the drugs used are Paracetamol and Aceclofenac. Both the drugs are highly soluble in methanol. Other solvents were also tried but methanol gives higher $E_{1\%}$ Value.

Table 1: $E_{1\%}$ Value for Paracetamol and Aceclofenac

Solvent	Paracetamol		Aceclofenac	
	Conc. in µg/mL	**$E_{1\%}$**	Conc. in µg/mL	**$E_{1\%}$**
Methanol	12.5	**919.2**	2.5	**484**

From the above $E_{1\%}$ value data it has been found that methanol was chosen as a solvent for the preparation of solution as it gives higher $E_{1\%}$ value.

Spectral Characteristics

To find out the wavelength for maximum absorbance, standard solutions of Paracetamol and Aceclofenac in methanol was prepared in the given range of concentration. Paracetamol and Aceclofenac having the concentration from 5 µg/mL to 20 µg/mL and 1 µg/mL to 4.5 µg/mL respectively. The standard solutions of these analytes were scanned on

ISSN: 0975-8585

spectrophotometer from 200nm to 400nm against methanol as the regent blank. Paracetamol shows the maximum absorbance at 247nm wavelength and Aceclofenac shows at 276nm wavelength. The spectra of Paracetamol, Aceclofenac and overlain spectra for both analytes are as shown below.

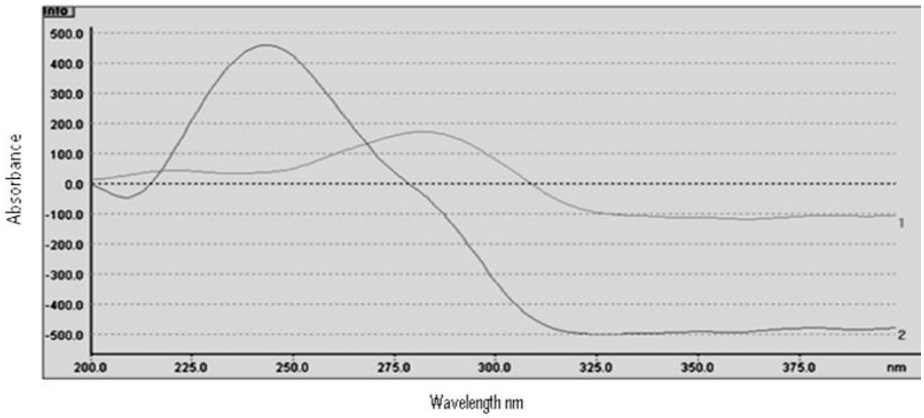


Figure 1: Overlain spectra of Paracetamol and Aceclofenac

Method Validation:

The method was validated as per ICH guidelines [13] for specificity, linearity, quantification limit, precision, accuracy, recovery and stability. Specificity was investigated by analyzing the blank diluents and samples of 100% level for any interference of the endogenous material at the absorbance of PCT and ACF. The linearity of the method was tested by taking several aliquots of standard solutions of PCT and ACF in 50mL volumetric flask and diluted upto the mark with solvent. The final concentration of PCT and ACF was 5-20 µg/mL and 1-4 µg/mL respectively.

The accuracy of the method was determined by recovery experiments. A standard addition method was employed for this experiment. A known quantity of each drug substance (PCT and ACF) corresponding to 0%, 10%, 20% and 30% of the label claim of each drug was added. The accuracy was expressed as a percentage of analytes recovered by the assay. In the present research work 2.5ppm sample solution was considered as 100% (0 level).

As a part of method validation, Intermediate precision was performed by carrying out the same assay procedure on a different instrument on a different day under similar experimental conditions. Robustness of the proposed method was determined by minor changes in the λmax of both the analytes.

RESULTS AND DISCUSSIONS

To develop rapid, low cost and sensitive UV method for simultaneous determination of PCT & ACF the optimized conditions were necessary. A study of overlain spectra of Paracetamol and Aceclofenac in methanol shows that at 247nm Paracetamol shows maximum absorbance

whereas Aceclofenac shows at 276nm. The overlain spectrum also shows that both the analytes shows considerable absorbances at their λmax values. Hence it was possible to construct simultaneous equation.

$$Cx = \frac{A_2 0.0185 - A_1 0.0480}{0.0205 \times 0.0185 - 0.0960 \times 0.0480}$$

and

$$Cy = \frac{A_1 \times 0.0205 - A_2 \times 0.0960}{0.0205 \times 0.0185 - 0.0960 \times 0.0480}$$

The study of the system suitability test showed that the operating system has given good results and verified the reproducibility of the method.

Validation

Linearity

Linearity of the method was tested from 40% to 160% of the targeted level of the assay concentration (12.5 µg/mL Paracetamol and 2.5 µg/mL Aceclofenac) for the two analytes. The standard solutions containing 5 – 12.5 µg/mL Paracetamol and 1.0- 4.0µg/mL Aceclofenac were prepared from the standard stock solutions of Paracetamol and Aceclofenac. Linearity test solutions were injected and analyzed in triplicate. The calibration graphs were plotted by using absorbance of the analytes against the concentration of the drug (in micrograms per milliliter). In the simultaneous determination, the calibration graphs were found to be linear for both the analytes in the mentioned concentration ranges. The regression equations for Paracetamol and Aceclofenac were found to be y = 0.081X + 0.143 and y = 0.039X + 0.020, and the correlation coefficients for the regression lines were 0.9990 and 0.9990, respectively.

Sensitivity

Sandell's sensitivity of Paracetamol and Aceclofenac was found to be sufficiently low. Table 2 shows that very less amount of both the drugs can be effectively detected by this method.

Table 2: Sensitivity Parameters for Paracetamol and Aceclofenac

Analyte	λ max (nm)	Molar absorptivity	Sandell's Sensitivity
Paracetamol	247	1.244×10^4 lit.mol^{-1} cm^{-1}	0.01215 µg/cm^3/cm^2
Aceclofenac	276	1.3814×10^4 lit.mol^{-1} cm^{-1}	0.02559 µg/cm^3/cm^2

Recover

The accuracy of the method was determined by the standard addition method at three different levels. The sample solution of 100% level was considered as a zero level and 10%, 20% and 30% of the standard drug of analytes were added respectively. Each determination was performed in triplicates. The accuracy was then calculated as the percentage of the standard

ISSN: 0975-8585

drug recovered by the recovery study. The recovery of Paracetamol and Aceclofenac from the standard mixture solution was found to be 99.13% -100.40% and 98.16-100.31% respectively. The recovery results show that Paracetamol and Aceclofenac could be quantified by this procedure simultaneously. The results are well within the acceptance limit and hence the method is accurate. Table 3 & 4 shows the % recoveries of PCT and ACF

Table 3: % recoveries of Paracetamol

Obs No	Levels in %	Absorbance		Initial amount in mg	Amt added in mg	Amt found in mg	% recovery
		at 247nm	at 276nm				
1	0%	1.250	0.349	12.5	0	12.497	99.98
2		1.253	0.351	12.5	0	12.521	100.17
3		1.254	0.350	12.5	0	12.537	100.30
1	10%	1.375	0.384	12.5	1.25	13.746	99.97
2		1.38	0.386	12.5	1.25	13.793	100.31
3		1.381	0.387	12.5	1.30	13.799	100.36
1	20%	1.505	0.420	12.5	2.50	15.047	100.31
2		1.498	0.421	12.5	2.50	14.963	99.75
3		1.507	0.422	12.5	2.60	15.06	100.40
1	30%	1.621	0.451	12.5	3.75	16.189	99.62
2		1.619	0.449	12.5	3.80	16.171	99.21
3		1.617	0.453	12.5	3.80	16.158	99.13
						Mean	99.96
						S.D	0.44
						%RSD	0.44
						Range of Recovery	99.13-100.40

Table 4: % recoveries of Aceclofenac

Obs No	Levels in %	Absorbance		Initial amount in mg	Amt added in mg	Amt found in mg	% recovery
		at 247nm	at 276nm				
1	0%	1.250	0.349	2.5	0	2.454	98.16
2		1.253	0.351	2.5	0	2.468	98.73
3		1.254	0.35	2.5	0	2.471	98.84
1	10%	1.375	0.384	2.5	0.25	2.702	98.26
2		1.38	0.386	2.5	0.25	2.726	99.11
3		1.381	0.387	2.5	0.26	2.744	99.78
1	20%	1.505	0.42	2.5	0.50	2.951	98.35
2		1.498	0.421	2.5	0.50	3.004	100.13
3		1.507	0.422	2.5	0.52	2.987	99.58
1	30%	1.621	0.456	2.5	0.75	3.260	100.31
2		1.619	0.455	2.5	0.76	3.246	99.88
3		1.617	0.453	2.5	0.76	3.210	98.47
						Mean	99.13
						S.D	0.77
						%RSD	0.78
						Range of Recovery	98.16-100.31%

ISSN: 0975-8585

Robustness

Robustness study shows that the proposed method was found to be robust where minor variation in wavelength could not alter the assay of the analytes.

As a part of method validation, Intermediate precision was performed by carrying out the same assay procedure on a different instrument on a different day. The experimental conditions kept same.

Table 5: Cumulative % RSD of Paracetamol & Aceclofenac in precision and Intermediate precision

Obs No	Paracetamol mg/tab	% LC Paracetamol	Aceclofenac mg/tab	% LC Aceclofenac
M.P 1	501.48	100.30	100.74	100.74
M.P 2	499.12	99.82	99.96	99.96
M.P 3	502.97	100.59	97.62	97.62
M.P 4	502.21	100.44	101.31	101.31
M.P 5	497.55	99.51	101.44	101.44
M.P 6	497.71	99.542	98.81	98.81
I.P 1	499.03	99.806	98.71	98.71
I.P 2	498.12	99.624	99.05	99.05
I.P 3	498.38	99.676	99.78	99.78
I.P 4	503.08	100.62	101.3	101.3
I.P 5	501.64	100.33	100.19	100.19
I.P 6	502.29	100.46	99.12	99.12
Mean	500.30	100.06	99.84	99.84
S.D.	2.161	0.432	1.214	1.214
Cumulative % RSD	0.432	0.432	1.216	1.216
Limits	NMT 2.00%		NMT 2.00%	

CONCLUSION

The UV method has proved to be simple, specific, precise and accurate and is suitable for simultaneous determination of Paracetamol (PCT) and Aceclofenac (ACF). The proposed method gives good results among these analytes. High percentage of recovery shows that the method is accurate.

ACKNOWLEDGEMENT

The author is thankful to Dr. K.V. Mangaonkar Principal, Sonopant Dandekar College Palghar, India for their support.

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