

SIMULTANEOUS ESTIMATION OF TIZANIDINE AND ACECLOFENAC IN BULK DRUG & TABLET FORMULATION BY Q-ANALYSIS AND AREA UNDER CURVE

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Accepted on: 22-02-2011; Finalized on: 28-04-2011.

ABSTRACT

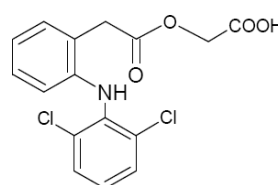
The present study deals with UV spectrophotometric method development & Validation for estimation of Tizanidine & Aceclofenac in bulk drug & tablet dosage form by Quantitative method & Area under curve method. First method is based on Q analysis/absorption ratio method using two wavelengths, 293 nm (isobestic point at which both the drugs exhibit absorbance) and 318 nm (λ_{max} of Tizanidine). Second method is based on Area under curve (AUC) method. For the second method the wavelength range 225 nm to 245 nm was selected for Aceclofenac and 262nm to 286 nm for Tizanidine. The Linearity of Tizanidine & Aceclofenac was found to be in the range Of 2-10 $\mu\text{g/ml}$ & 5-25 $\mu\text{g/ml}$ respectively. The % recovery of Tizanidine & Aceclofenac was found out to be 98-102 % respectively. The proposed method was validated as per ICH guidelines.

Keywords: Tizanidine, Aceclofenac, Q-Analysis, Area under curve.

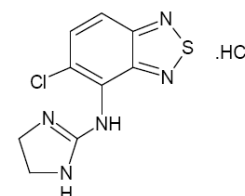
INTRODUCTION

Tizanidine Hcl [64461-82-1] [TZN] chemically is 5-chloro-N-(2-imidazolin-2-yl) 2,1,3-benzothiadiazol-4-yl-amine. Tizanidine is a short acting drug for the management of spasticity. It is an agonist at a 2-adrenergic receptor sites & presumably reduces spasticity by increasing presynaptic inhibition of motor neurons. Aceclofenac [89796-99-6] [ACF] chemically is 2-[2-[2-(2,6-Dichlorophenyl) amino phenyl]cetyl]oxyacetic acid which is used as an effective NSAID having pronounced analgesic, antipyretic, anti-inflammatory property. It is belonging to developed NSAIDS of arylacetic acid type & structurally related to diclofenac. Aceclofenac-tizanidine combination is more effective than aceclofenac alone and had a favourable safety profile in the treatment of acute low back pain and for rheumatic disorders. TZN & ACF is official in Indian Pharmacopoeia 2007 respectively¹⁻².

Aceclofenac is reported for spectrophotometric, RP-HPLC and simultaneous estimation with other combinations Similarly, Tizanidine also reported in combination with other drugs. Since no spectrophotometric method is reported for simultaneous estimation of Aceclofenac and Tizanidine in combination therefore, the present work, a successful attempt has been made to estimate both these drugs simultaneously by two simple UV spectrophotometric methods (Q-Analysis method and Area under curve method). The present paper describes a simple, accurate and precise method for simultaneous estimation of Aceclofenac and Tizanidine in combined tablet dosage form³⁻⁸.



Aceclofenac



Tizanidine HCl

MATERIALS AND METHODS

Solubility Studies

Tizanidine is soluble in water but aceclofenac is insoluble in water, hence various solvent systems were screened for simultaneous determination and methanol & phosphate buffer was selected as solvent system.

Instrumentation

The instrument used was Jasco double beam UV/Vis spectrophotometer model V- 530. Weighing was done on electronic balance (Contech precision balance CB- series).

Materials

TZN Hcl drug sample was kindly supplied by endoc pharma laboratories limited rajkot (Gujarat, India) and ACF drug sample was supplied by inventia health care (Mumbai, India) and were used without any further purification. Spectroscopic grade methanol was purchased from Thomas Beker chemicals. Assay was carried out on tablet dosage form labeled to contain 2 mg of TZN and 100 mg of ACF.

Preparation of Standard Stock Solutions

Standard stock solutions of TZN and ACF were prepared separately by dissolving 10 mg of each drug in 10ml of methanol to get standard stock solution of 1000 $\mu\text{g/ml}$

respectively by sonicating for 15 min and 1 ml was pipette out and further volume was made up to 10 ml with phosphate buffer to obtain concentration of 100 µg/ml. Further dilutions were made in phosphate buffer from stock solution to get concentrations of 2-10 µg/ml of TZN & 5-25 µg/ml of ACF. The standard solutions of both TZN & ACF were scanned in the range of 400-200 nm against solvent phosphate buffer and a spectrum was recorded.

Experimental Methods

METHOD I

Absorption ratio or Q-analysis method

In this method absorbances are measured at two wavelengths. One being the λ_{max} of Aceclofenac and other being a wavelength of absorptivity of the Tizanidine. Then absorbance of both drugs was recorded on selected wavelengths. Concentrations of Aceclofenac & Tizanidine were calculated by using following equations⁹.

$$C_{Acf} = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A_1}{ax_1} \dots\dots\dots (i)$$

$$C_{Tzn} = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A_1}{ay_1} \dots\dots\dots (ii)$$

Where, Q_m is ratio of absorbances A₁ and A₂ of mixture at λ₁ and λ₂ (isobestic point wavelength) Q_x is ratio of absorptivities ax₁ and ax₂ at λ₁ and λ₂. Q_y is ratio of absorptivities ay₁ and ay₂ at λ₁ and λ₂. C_{Acf} and C_{Tzn} are concentrations of Aceclofenac & Tizanidine.

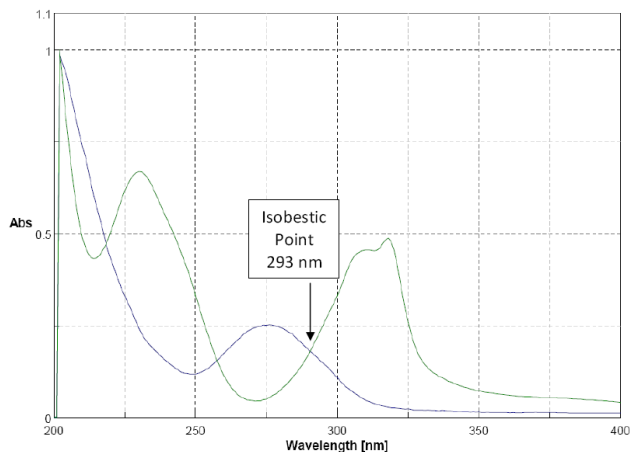


Figure 1: Overlain spectra for ACF & TZN showing isobestic point

METHOD II

Simultaneous equation using area under the curve method

In this method the overlain spectra of both drugs wavelength range of 225 nm to 245 nm for Aceclofenac and 262 nm to 286 nm for Tizanidine was selected for the analysis. The calibration curve of area vs concentration was plotted¹⁰.

By applying Cramer's rule and matrix method, concentration of Aceclofenac and Tizanidine can be calculated as,

$$C_{Acf} = \frac{X^{Tzn} \lambda_1 - \lambda_2 AUC \lambda_3 - \lambda_4 - X^{Tzn} \lambda_3 - \lambda_4 AUC \lambda_1 - \lambda_2}{X^{Tzn} \lambda_1 - \lambda_2 X^{Acf} \lambda_3 - \lambda_4 - X^{Tzn} \lambda_3 - \lambda_4 X^{Acf} \lambda_1 - \lambda_2} \dots\dots\dots (iii)$$

$$C_{Tzn} = \frac{X^{Acf} \lambda_1 - \lambda_2 AUC \lambda_3 - \lambda_4 - X^{Acf} \lambda_3 - \lambda_4 AUC \lambda_1 - \lambda_2}{X^{Tzn} \lambda_1 - \lambda_2 X^{Acf} \lambda_3 - \lambda_4 - X^{Tzn} \lambda_3 - \lambda_4 X^{Acf} \lambda_1 - \lambda_2} \dots\dots\dots (iv)$$

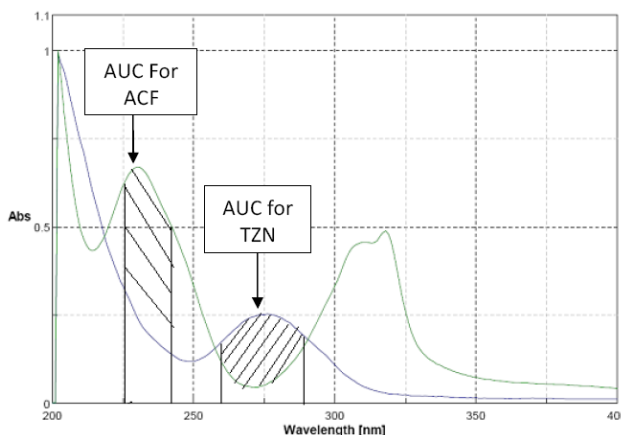


Figure 2: Overlain spectra for ACF & TZN showing Area under curve

Procedure for the Analysis of Tablet Formulation

Ten tablets containing label claim of 2 mg of TZN and 100 mg of ACF were weighed and finely powdered. Weight of the powder tablet was accurately weighed, transferred into a 100 ml flask, dissolved in methanol and this solution was sonicated for about 20 minutes then volume was made up to 100 ml with phosphate buffer and filtered to separate any insoluble matter. The clear solution obtained was diluted to get appropriate concentration. The concentrations of two drugs in the mixture were calculated using above equations.

Validation of UV Method

Validation of the UV method was done with respect to following parameters.

Linearity and range

The standard solutions were prepared by dilution of the stock solution with Phosphate buffer to reach a concentration range 5-25 µgml⁻¹ for Aceclofenac and 2-10 µgml⁻¹. The Absorbance was plotted against the corresponding concentrations to obtain the calibration graphs.

Accuracy

Recovery studies was carried out by applying the method to drug sample to which known amount of Aceclofenac and Tizanidine corresponding to 80, 100, 120% of label claim has been added (standard addition method).

Precision

The standard solutions of drug sample were prepared and analyzed. The tablet assay was performed to determine reproducibility and repeatability. The percentage relative standard deviation (RSD %) was found to be within limits.

RESULTS AND DISCUSSION

The present work provides an accurate rapid, sensitive method for the simultaneous analysis of TZN & ACF in bulk and tablet formulation. Linear relationships between drug concentrations were obtained over the range of at 2-10 & 5-25 µg/ml for TZN and ACF respectively. The correlation coefficient, slope and intercept obtained for each drug is as shown in Table 1. The proposed method was also successfully applied to a pharmaceutical formulation. The % assay was

found to be 100.63% for TZN and 99.37% for ACF. No interference was observed from the pharmaceutical adjuvants. Recovery studies results are tabulated in Table 2. For TZN percent recovery ranged from 98.66% to 99.72%, with RSD ranging from 0.216 to 0.320. For ACF, percent recovery ranged from 98.83% to 99.60%, with RSD ranging from 0.227 to 0.406. Hence, the proposed method was evaluated statistically and was validated in terms of precision, linearity and accuracy.

Table 1: The Method Was Validated As Per ICH Guidelines

Parameters	Method I		Method II	
	TZN (318nm)	ACF (293nm)	TZN (262 nm to 286 nm)	ACF (225 nm to 245)
Linearity range(µg/ml)	2-10 µg/ml	5-25 µg/ml	2-10 µg/ml	5-25 µg/ml
Correlation coefficient (r^2)	0.9959	0.9803	0.9973	0.9967
Interday	0.43	0.70	0.57	0.74
Intraday	0.63	0.50	0.74	0.60
Slope	0.099	0.0392	0.1251	0.0976
Intercept	0.075	0.1219	0.0138	0.0871

Table 2: Result of Recovery Studies

Level of recovery	Drug	Amt of Drug added µg/ml	Amt of drug std added µg/ml	Method I			Method II		
				% Recovery	S.D	% RSD	% Recovery	S.D	% RSD
80	ACF	100	99.50	99.86%	0.00097	0.2429	102.74%	0.00213	0.1691
80	TZN	2	1.5	100.06%	0.00101	0.04336	98.93%	0.00764	0.0386
100	ACF	100	98.75	99.75%	0.00065	0.1437	100.12%	0.0054	0.3883
100	TZN	2	2.03	100.12%	0.0008	0.0323	98.75%	0.0003	0.0145
120	ACF	100	101.05	99.77%	0.00110	0.2213	101.33%	0.0007	0.0466
120	TZN	2	1.10	100.11%	0.0006	0.0220	99.20%	0.0007	0.0298

Table 3: Analysis of Marketed Formulation

Parameters	Method I		Method II	
	Aceclofenac	Tizanidine	Aceclofenac	Tizanidine
Label claim (mg/Tab)	100 mg	2 mg	100 mg	2 mg
Drug content (%)	99.60 %	99.26 %	99.96 %	99.84 %

CONCLUSION

The results demonstrate that Q-Analysis and Area under curve employed enables quantitation of mixture of TZN and ACF with good accuracy and precision in bulk drug and pharmaceutical formulation. Thus, it can be easily and conveniently adopted for routine quality control analysis.

Acknowledgements: The authors are grateful to, the Principal and the Management of STES's Smt. Kashibai Navale College of Pharmacy, Kondhwa (BK) Pune. The authors are thank to Endoc pharma laboratories, Gujarat for providing gift sample of Tizanidine and Inventia health care, Mumbai for providing gift sample of Aceclofenac.

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