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Zero order and First order Derivative Spectrophotometric Methods for determination of Baclofen in Pharmaceutical formulation

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Abstract: Simple, fast and reliable derivative spectrophotometric methods were developed for determination of Baclofen in bulk and pharmaceutical dosage forms. The solutions of standard and the sample were prepared in methanol. The quantitative determination of the drug was carried out using the zero order derivative values measured at 220 nm and the first order derivative values measured at 215 nm (n=6). Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Baclofen using 3-18 µg.mL-1 (r^2 = 0.9997 and r^2 = 0.9996) for zero order and first order derivative spectrophotometric method. All the proposed methods have been extensively validated as per ICH guidelines. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations. Developed spectrophotometric methods in this study are simple, accurate, precise, sensitive to assay of Baclofen in tablets.
Keywords: Baclofen, Derivative spectrophotometric, Zero order derivative spectrum, First order derivative spectrum.

1. INTRODUCTION

Baclofen is an orally administered synthetic antispastic agent or muscle relaxant[1]**.** It reduces spasticity in many neurological disorders like multiple sclerosis, amyotrophic lateral sclerosis, spinal injuries and flexor spasms but is relatively ineffective in stroke, cerebral palsy, rheumatic and traumatic muscle spasms and parkinsonism[2].It may act as an agonist at GABA-B receptors[3].

Baclofen is chemically β-(amino methyl)-4-chlorobenzene propanoic acid (Fig.1) and it is used as antispastic agent or muscle relaxant[4].The molecular formula of Baclofen is $C_{10}H_{12}ClNO_2$[5], the molecular mass of Baclofen is 213.67g/mol. It is freely soluble in water, 0.1N HCl and 0.1N NaOH, slightly soluble in methanol, very slightly soluble in ethanol[1]. It is official drug in I.P, B.P and U.S.P.[5,6,7] Literature survey reveals that, only bioanalytical methods by HPLC and few Spectrophotometric methods were found using human plasma and urine for the quantitative estimation of Baclofen in bulk drug and pharmaceutical formulations[8-13].

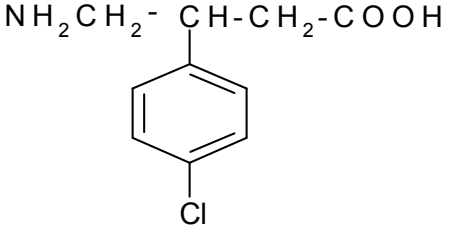

Figure 1. Chemical structure of Baclofen

2. EXPERIMENTAL

2.1. MATERIALS AND METHODS

Baclofen was a gift sample by Unicare Pvt. Ltd., Gujarat., India and was used without further purification. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals, India.

2.2. INSTRUMENTATION

For all the spectrophtometric methods, Shimadzu model 1700 double beam UV-VIS spectrophotometer with spectral bandwidth of 1.8nm, wavelength accuracy of 2 nm and a pair of 1 cm matched quartz cells of 10 mm optical path length was used.

2.3. PREPARATION OF STANDARD AND SAMPLE SOLUTIONS:

Stock solution of 1000 µg.mL-1of Baclofen was prepared in methanol, for zero order and first order derivative spectrophotometric analysis. The standard solutions were prepared by dilution of the stock solution with water in a concentration range of 3, 6, 9, 12, 15 and 18 µg.mL^{-1} with water for zero order and first order derivative spectrophotometric methods. Water was used as a blank solution.

2.3. ASSAY PROCEDURE:

A total of 20 tablets of Baclofen were opened and the contents were weighed and mixed. Accurately weighed and powdered. An aliquot of powder equivalent to the weight of 1 tablet was accurately weighed and transferred to volumetric flask and was dissolved in 100 ml of water and made up to the volume with water. The solutions were filtered through a 0.45 µm nylon filter and sonicated for about 15 min and then volume made up with water. This solution was filtered to remove any insoluble matter. The filtrate was collected in a clean flask. Appropriate dilutions were made to obtain 9 µg.mL^{-1} with water from stock solution for both zero order and first order derivative spectrophotometric methods. Figure 2.

3. RESULTS AND DISCUSSION

The zero order and first order derivative spectra for Baclofen were recorded at the wavelength of 220 nm and 215 nm respectively [**Fig. 2-3].**

3.1. LINEARITY AND RANGE:

Under the experimental conditions described, the graph obtained for zero order and first order derivative spectra showed linear relationship. Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were y = 0.04x + 0.0068 (r2 = 0.9997) at 220 nm for zero order derivative spectrophotometry and y = 0.002x + 0.004 (r2 = 0.9996) for first order derivative spectrophotometry. The range was found to be 3-18 µg.mL^{-1} for both zero order and first order derivative spectrophotometric methods. (**Table I).**

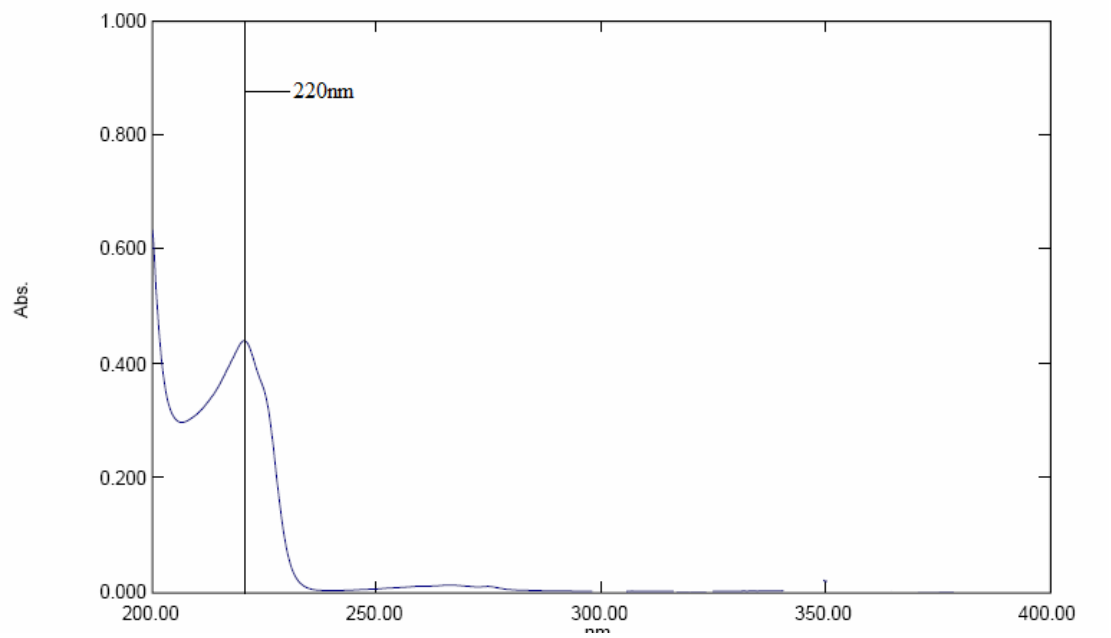

Figure 2. Zero order derivative spectrum of 9 µg.mL^{-1} Baclofen in water

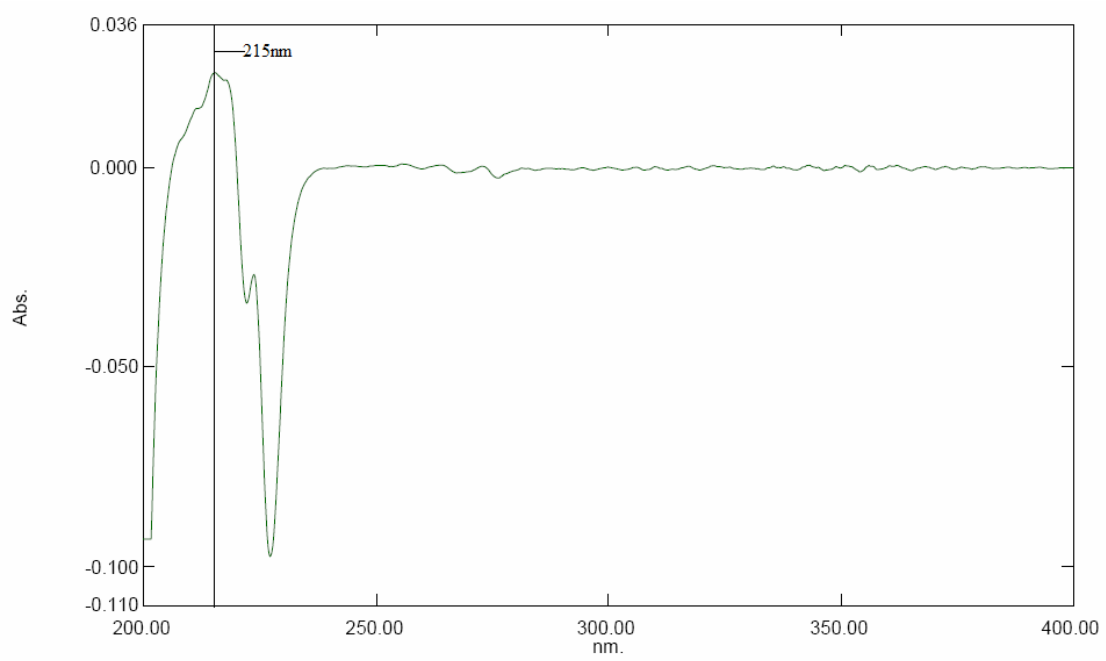

Figure 3. First order derivative spectrum of 9 µg.mL^{-1} Baclofen in water

Table I : Stastical data for the calibration graphs for determination of Baclofen by proposed methods

Parameters	Zero order derivative	First order dwrivative
Linearity range (3-18 µg.ml^{-1})	3-18	3-18
r ^{2}± S.D.	0.9997	0.9996

[a]n=6

Table II: Results of Intra and Inter Day Precision

Parameters	Intra Day Precision		Inter Day Precision	
	S.D	% RSD	S.D	% RSD
Zero derivative	0.0483	0.0482	0.7318	0.7347
First derivative	0.0406	0.0406	0.7164	0.7194

[a]n=6 [b]Average of one concentrations 9 µg.Ml^{-1}

Table III: Data of recovery studies

Actual concentration (µg.ml^{-1})	Observed concentration (µg.ml^{-1})	Recovery (%)	% RSD
Zero order derivative spectrophotometric method			
9	8.98	99.77	0.010
9.6	9.62	100.20	0.009
10.6	10.58	99.81	0.010
First order derivative spectrophotometric method			
9	9.03	100.33	0.010
9.6	9.57	99.68	0.009
10.6	10.59	99.90	0.010

Table IV : Assay results for the determination of Baclofen in pharmaceutical formulation

Parameters	Tablet brand name	Drug Content (%)	% RSD
Zero order derivative	Liofen 10mg	100.01	0.499
First order derivative	Liofen 10mg	99.93	0.377

[a]n=6, Average of three concentrations 9 μg Ml^{-1}

Table V : Summary of validation parameters

Parameter	Zero derivative method	First derivative method
Wavelength (nm)	220	215
Linearity range (μg.Ml^{-1})	3-18	3-18
Correlation coefficient	0.9997	0.9996
Limit of detection (μg.Ml^{-1})	0.039	0.952
Limit of quantitation (μg.ml^{-1})	0.120	2.886
Mean recovery %	99.86	99.97
Precision(%±RSD)		
repeatability	0.0482	0.7347
Inter day	0.0406	0.7194

3.2. PRECISION:

To determine the precision of the method, Baclofen solutions at a concentration of 9 μg.mL^{-1} were analyzed each six times for both zero order and first order derivative spectrophotometric methods. Solutions for the standard curves were prepared fresh everyday (**Table II).**

3.3. SENSITIVITY:

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations LOD = 3 x σ / S and LOQ = 10 x σ /S, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 0.039μg.mL^{-1} and 0.120 μg.mL^{-1} respectively for zero order derivative and The LOD and LOQ were found to be 0.952 μg.mL^{-1} and 2.886 μg. mL^{-1} for first order derivative methods respectively.

3.4. RECOVERY:

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of known amounts of Baclofen to reanalyzed solutions of commercial tablets (Table III).

3.5. ANALYSIS OF THE MARKETED FORMULATION:

There was no interference from the excipients commonly present in the tablets. The drug content was found to be 100.01% with a % R.S.D. of 0.14 and 99.93% with a % R.S.D. of 0.37 for zero order and first order derivative spectrophotometric methods respectively. It may therefore be inferred that degradation of Baclofen had not occurred in the marketed formulations that were analyzed by this method. The low % R.S.D. value indicated the suitability of this method for routine analysis of Baclofen in pharmaceutical dosage form (Table IV). The summary of the validation parameters is depicted in (Table V).

4. CONCLUSION

No UV or derivative spectrophotometric methods have been described for the determination of Baclofen. Therefore simple, fast and reliable derivative spectrophotometric methods were developed for the routine determination of Baclofen. The developed methods can be concluded as accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

5. ACKNOWLEDGEMENT

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