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Simultaneous Spectrophotometric Estimation of Atenolol and Hydrochlorothiazide in Tablet Dosage Forms

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Abstract: Two methods for the simultaneous estimation of atenolol and hydrochlorothiazide in combined tablet dosage form have been developed. The first method is the Q-analysis method, based on absorbance ratio at two selected wave lengths 232.0nm (Iso-absorptive point) and 270.0nm (λmax of hydrochlorothiazide).

The second method is the first order derivative spectroscopy using 214.0nm (zero cross for atenolol) and 241.0nm (zero cross for hydrochlorothiazide). The linearity was obtained in both the methods in the concentration range of 1-30µg/ml and 1-40µg/ml for atenolol and hydrochlorothizide, respectively. These methods are simple, accurate and results of analysis have been validated statistically and by recovery studies.

Key words: Atenolol, Hydrochlorothiazide, Q-analysis, Derivative spectroscopy.

Introduction:

Atenolol (ATN) chemically, 4-(2-.hydroxy-3-isopropyl aminopropoxy)-phenyl acetamide is a β-adrenoreceptor blocking agent, primarily used in hypertension, angina pectoris and myocardial Infraction. It mainly acts by inhibition of rennin release and angiotensin-2 & aldosterone production. It is reported to lack intrinsic sympathomimetic activity and membrane-stabilizing properties. The Indian pharmacopeia describes non-aqueous titration method for assay of atenolol.

Hydrochlorothiazide (HCTZ), 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide, which is widely used in antihypertensive pharmaceutical preparations, reduces active sodium reabsorption and peripheral vascular resistance. The review of the literature revealed that no method is yet reported for the simultaneous estimation of both the drugs in combined dosage forms. Present work describes two simple, accurate, reproducible, rapid and economical methods for simultaneous estimation of ATN and HCTZ in tablet formulation.

Experimental:

Instrumentation:

A double-beam shimadzu UV- 1800; UV-Visible spectrophotometer, spectral bandwidth of 2nm, wavelength accuracy ±0.5nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solution.

Materials:

Standard gift sample of atenolol and hydrochlorothiazide were provided by Cadila Pharmaceuticals Ltd, Ahmedabad. Combined dose of atenolol and hydrochlorothiazide tablets (ATEN-H, 50mg atenolol and 25mg hydrochlorothiazide; manufactured by Cadila HC), were purchased from local market.

Solvent:

Methanol of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The selection was made after

assessing the solubility of both the drugs in different solvents.

Preparation of standard Stock solutions:

Atenolol and hydrochlorothiazide (10mg each) were accurately weighed and dissolved separately in 10ml of methanol to give stock solutions (1000µg/ml). From the standard stock solution, 1ml each of ATN and HCTZ was taken in 10ml volumetric flask. Volume was made upto mark with methanol. Aliquot portion was appropriately diluted with methanol to get final concentration of 10 µg/ml (HCTZ) and 20 µg/ml (ATN) prepared respectively to give final concentrations and scanned between 200-400nm.

Method A (Absorbance ratio method):

In the absorbance ratio method, from the overlain spectra of both drugs (fig-1), wavelengths 232.0nm (Iso-absorptive point) and 270.0nm (λmax of hydrochlorothiazide) were selected for analysis. The calibration curves for atenolol and hydrochlorothiazide were plotted in the concentration range of 1-30µg/ml and 1-40µg/ml at both the wavelengths respectively. The absortivities values were determined for both the drugs at both the wavelengths. From the following set of equations the concentration of each component in sample was calculated,

$C\times=Qm-Qy/Qx-Qy \ .A_1/ax_1$ …… (1) and

$Cy=Qm-Qx/Qy-Qx \ .A_1/ay_1$ …….(2)

Where Cx=concentration of atenolol, Cy=concentration of hydrochlorothiazide, A_1=absorbance of sample at iso-absorptive wavelength 232.0nm, ax_1=absorptivity of atenolol at 232.0nm, ay_1=absorptivity of hydrochlorothiazide at 232.0nm, Qm=ratio of absorbance of sample solution at 232.0nm and 270.0nm, Qx=ratio of absorptivities of atenolol at 270.0nm and 232.0nm and Qy=ratio of absorptivities of hydrochlorothiazide at270.0nm and 232.0nm.

Method B (First order derivative spectroscopy method):

In first order derivative spectroscopy, solutions of atenolol(20µg/ml) and hydrochlorothiazide(10µg/ml) were prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400nm to 200nm.The absorption spectra thus obtained was derivatized in first order. The zero crossing wavelengths 214.0nm (zero cross for atenolol and 241.0nm (zero cross for hydrochlorothiazide) were selected for analysis. The calibration curves for atenolol and hydrochlorothiazide were plotted in concentration range of 1-30 µg/ml and 1-40 µg/ml at both the wavelength respectively.

Application of the proposed method for the determination of ATN and HCTZ in tablet dosage form:

Twenty tablets were weighed and average weight was calculated. The tablets were crushed into fine powder. Tablet powder equivalent to 25mg of HCTZ was transfered to 25ml volumetric flask and ultrasonicated for 10min .The volume was made upto the mark with methanol. The resulting solution was then filtered through a whatmann filter paper (No. 41). Aliquot portion was appropriately diluted with methanol to get final concentration of 10µg/ml and 20µg/ml of HCTZ and ATN respectively. The concentration of both ATN and HCTZ were determined by measuring absorbance of sample at 232.0nm, 270.0nm (method A) in spectrum mode and values were substituted in respective formulae to obtain the concentration. For method B concentration of ATN and HCTZ were determined by measuring the absorbance at 214.0nm, 241.0nm in first order spectrum mode. The results for tablet analysis were calculated and results for tablet analysis are shown table 1.

Validation:

The methods were validated with respect to linearity and accuracy.

Accuracy:

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels 80%, 100% and 120%. Percentage recovery by two methods was found in range of 98.12% to 99.99%.

Linearity:

The linearity was obtained in the concentration range of 1-30µg/ml and 1-40µg/ml for atenolol and hydrochlorothiazide respectively in both methods which obeys Beer-Lambert's law.

Table No:1 Results of analysis of tablet Formulation

Methods	Components	Label claim (mg/tab)	Amount found	Estimated label claim	SD	CV
A	ATN	50	49.6	99.20	0.3747	0.3772
	HCTZ	25	24.61	98.45	0.4596	0.4668
B	ATNZ	50	49.58	99.16	0.5232	0.5276
	HCTZ	25	24.76	99.04	0.5586	0.5640

Table No:2 Results of Recovery Studies

Level of Recovery (%)	Amount of pure drug added(µg/ml)		Method-A %recovery		Method-B %recovery	
	ATN	HCTZ	ATN	HCTZ	ATN	HCTZ
80	16	8	99.99	98.12	99.26	99.78
100	20	10	99.79	98.87	99.66	99.81
120	24	12	99.43	98.50	99.72	99.87
Mean % recovery			99.74	98.49	99.55	99.82
SD			0.2824	0.7458	0.5769	0.6152
CV			0.2831	0.7572	0.5795	0.6163

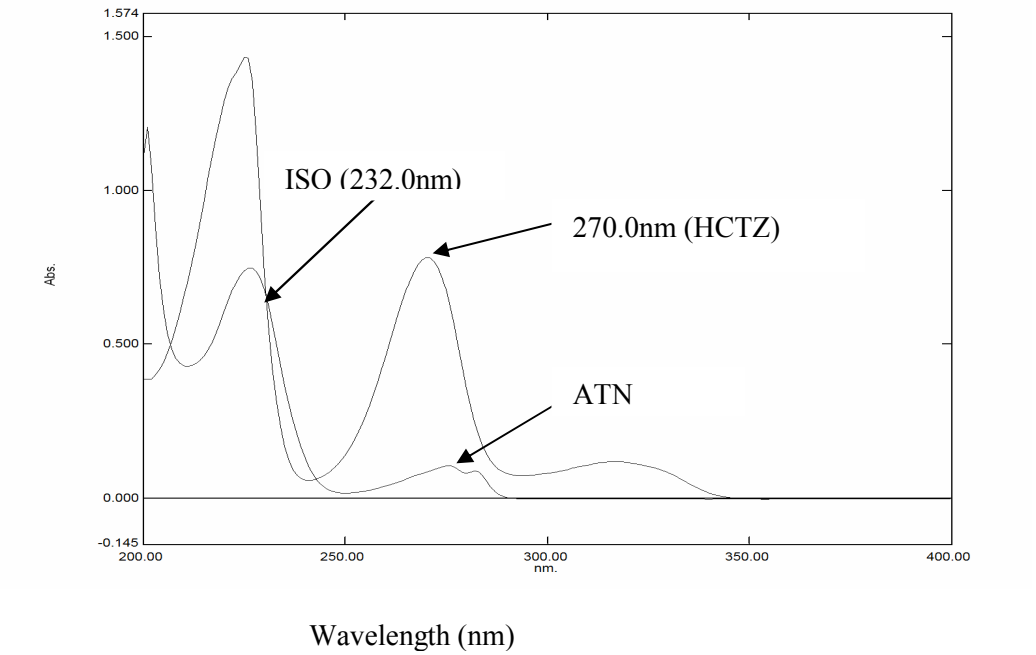
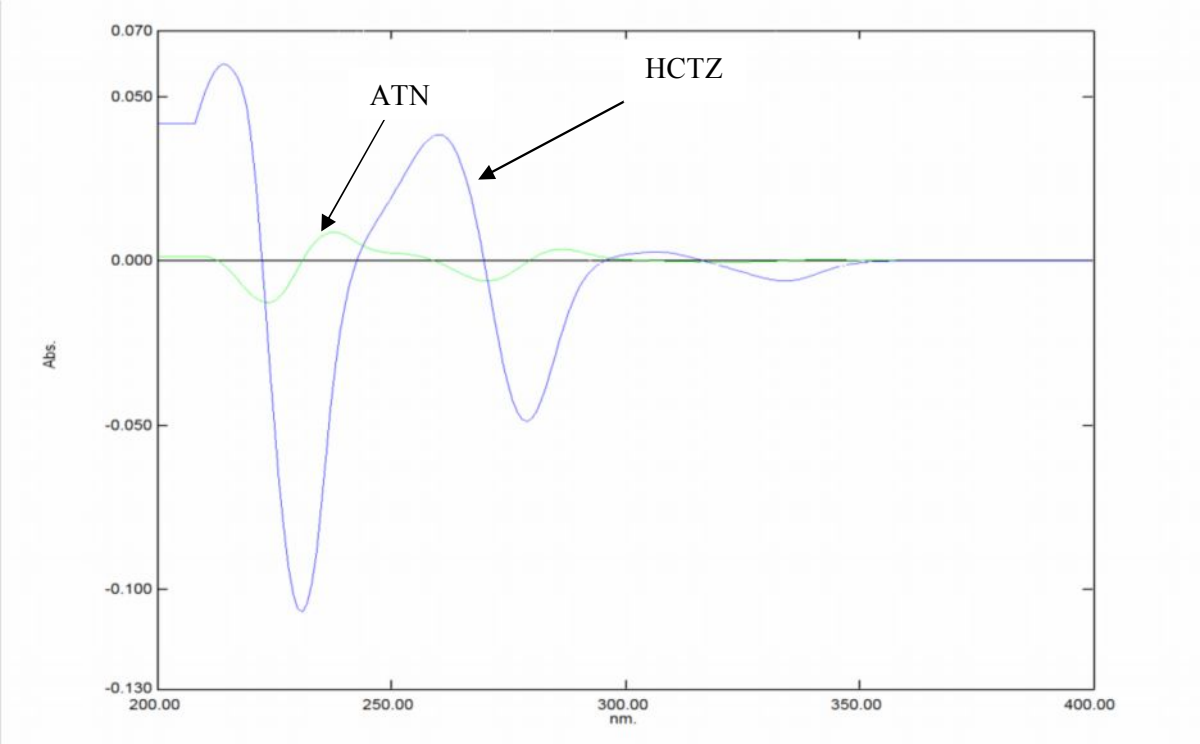


Fig.-1: Overlain Spectra of Atenolol(ATN) and Hydrochlorothiazide(HCTZ) in methanol.



Wavelength (nm)

Fig.-2: Overlain first derivative spectra of ATN and HCTZ in methanol.

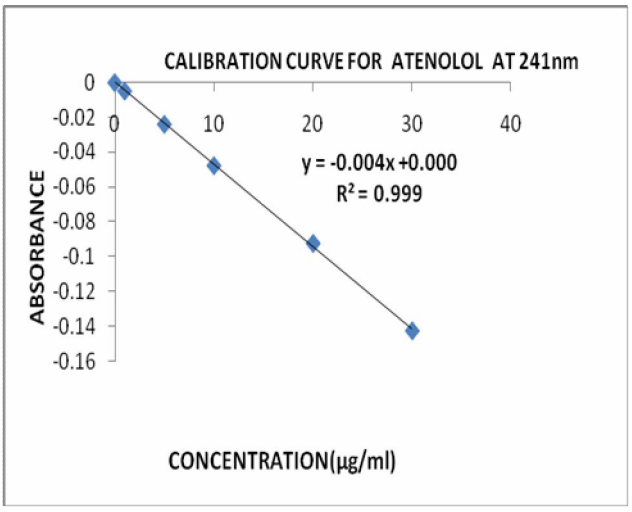


Fig-3: Calibration curve for ATN at 241nm by first derivative method

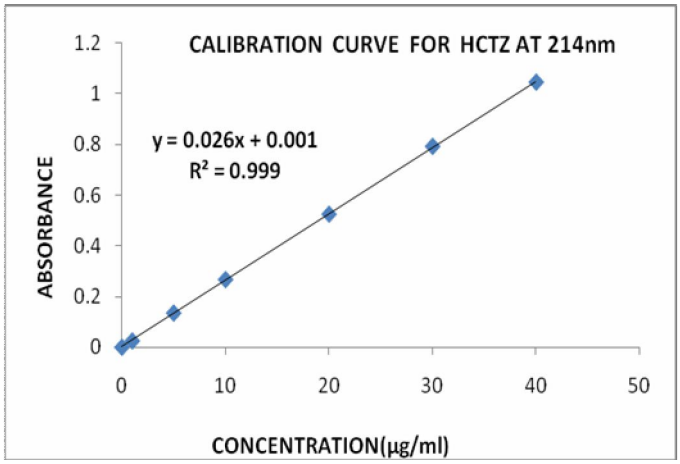


Fig-4: calibration curve for HCTZ at 214nm by first derivative method

Results and Discussion:

From the proposed method, it was found that atenolol and hydrochlorothiazide obeys linearity within the concentration range 1-30µg/ml and 1-40µg/ml respectively. Percentage label claim for ATN and HCTZ in tablet, by both the methods was found in the range of 98.45% to 99.20%. For method B, Coefficient of variation (CV) were calculated, which was found to be less than 2% indicating the method has good reproducibility. Accuracy of proposed methods was ascertained by recovery studies and results are expressed as %recovery. Percent recovery for ATN and HCTZ by both methods, was found in range of 98.12% to 99.99%, values of standard deviation and coefficient of variation were in range of 0.2824 to 0.7458 and 0.2831 to 0.7572 respectively indicating the accuracy of proposed method.

Conclusion:

Based on the results obtained, it is found that the proposed methods are accurate, precise, reproducible and economical and can be employed for routine quality control of atenolol and hydrochlorothiazide in combined dose tablet formulation.

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