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Simultaneous Estimation of Atenolol and Chlorthalidone as Bulk and In Tablet Dosage Form Using Uv- Spectrophotometry

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Abstract: *A simple, accurate, precise, economical and reproducible UV Spectrophotometric method has been developed for the simultaneous estimation of Atenolol and Chlorthalidone in bulk and in combined tablet dosage form. The stock solutions were prepared in methanol followed by further required dilutions with methanol. The absorbance maxima of Atenolol and Chlorthalidone were found to be 225nm & 284nm respectively. Beers law obeyed the concentration range of atenolol is 10 µg mL^{-1} to 60 µg mL^{-1} & chlorthalidone is 30 µg mL^{-1} to 140 µg mL^{-1}. The results of analysis were validated statistically and by recovery studies. The % RSD for the recovery study was less than 2. The proposed method can be effectively applied for the simultaneous estimation of these two drugs in bulk & combined dosage forms.*

Keywords: *UV spectrophotometric method; atenolol; chlorthalidone and simultaneous estimation.*

I. Introduction:

Atenolol chemically, 2-[4-{(2RS)-2-hydroxy-3-[(1-methylethyl)amino]propoxy}phenyl] acetamide (fig. 1) is a selective β_1 receptor antagonist, a drug belonging to the group of beta blockers , a class of drugs used primarily in cardiovascular diseases. The chemical works by slowing down the heart and reducing its workload. Atenolol does not pass through the blood-brain barrier thus avoiding various central nervous system side effects.[1] Atenolol is primarily used for hypertension, anginapectoris &myocardial infarction. I mainly act by inhibition of renin release and angiotensin-II (AT-II) and aldosterone production. Chlorthalidone chemically 2-chloro-5-(1-hydroxyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl) benzene-1-sulfonamide (fig. 2) is widely used in antihypertensive pharmaceutical preparations, reduces active sodium reabsorption and peripheral vascular resistance. Chlortalidone is a diuretic drug used to treat hypertension. It is described as a thiazide diuretic. Compared with other medications of the thiazide class, chlorthalidone has the longest duration of action but a similar diuretic effect at maximal therapeutic doses. It is often used in the management of hypertension and edema.

Literature survey reveals that there are several analytical methods for the estimation of atenolol and chlorthalidone individually or in combination with other drugs. Although the combination use of atenolol & chlorthalidone is continuously increasing, there is no UV method for the determination of these drugs in combined dosage form. Hence the aim of my study is to develop and validate a simple, precise, accurate, selective UV method for the estimation of atenolol and chlorthalidone in combined dosage form.

II. Methods And Materials:

Materials:

Atenolol, Chlorthalidone, Methanol, Acetonitrile, 0.1N HCl,0.1N NaOH ,Water, formulation TENOCLOR (Atenolol 25mg, Chlorthalidone 12.5mg), Shimadzu UV–Visible spectrophotometer (model UV-1800) with matched quartz cells.

Selection of solvent and wavelength (λ max):

The absorbance of the both drugs i.e. atenolol and chlorthalidone was found to be maximum in methanol solvent compared to other solvents, the λ max of atenolol and chlorhalidone was fixed as 225nm and 284nm respectively.

Preparation of Atenolol Stock Solution:

Standard atenolol stock solution was prepared by dissolving 100 mg of drug in methanol and volume make up to 100 ml with methanol to get concentration about of 1 mg/ml (1000 µg mL^{-1} stock solution). From stock solution take 1ml of this solution was taken and diluted to 10ml with methanol to get final concentration of 100 µg mL^{-1}.

Preparation of Clorthalidone stock solution:

Standard chlorthalidone stock solutions were prepared by dissolving 100mg drug in methanol and volume make up to 100ml with methanol to get concentration of 1mg/ml solutions. (1000µg mL^{-1}). From stock

solution take 1ml of this solution was taken and diluted to 10ml with methanol to get final concentration of 100µg mL^{-1}.

Preparation of Linearity curve:

To construct Beer's law plot for atenolol and chlorthalidone different aliquots of atenolol (1-6ml) with different concentrations (10, 20, 30, 40, 50 and 60 µg mL^{-1}) and chlorthalidone (3-14ml) with different concentrations (30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130 and 140 µg mL^{-1}) were prepared by serial dilutions with methanol. Mixed standard solutions were prepared from working standard solutions of the two drugs. Then absorbance of the solutions was measured at 225nm for atenolol and 284 nm for chlorthalidone, respectively. Both these drugs obeyed linearity individually and in mixture with the concentration range of 10-60 µg mL^{-1} for atenolol and 30-140 µg mL^{-1} for chlorthalidone.

Preparation of Test Solutions and Estimation of atenolol and chlorthalidone in Tablet formulations:

For analysis of commercial formulations of tablets, 10 tablets were weighed, powdered and accurately weighed the equivalent to 25 mg of atenolol and 12.5mg of chlorthalidone, which was transferred into 100 ml volumetric flask and in methanol and make up to 100ml with methanol, filtered and further diluted with methanol to get the concentrations within the linearity range of respective drugs and measured the absorbances at 225 nm for atenolol and 284 nm for chlorthalidone fig. 4, respectively. Then the amount of drug present in the formulations was calculated using calibration curve. The results were shown in table-5.

Recovery studies:

The recovery studies were carried out at three different levels i.e. 50%, 100% and 150% level. To ensure the reliability of the above method, recovery studies were carried out by mixing a known quantity of standard drug with the pre analysed sample formulation and the contents were reanalyzed by the proposed method. The percentage recovery was found and shown in table-2.

III. Results And Discussion:

From the optical characteristics of the proposed method, it was found that the drug obeys linearity within the concentration range of 10-60 µg mL^{-1} for Atenolol and 30-140 µg mL^{-1} for Chlorthalidone. From the results it was found that the % RSD is less than 2% which indicates that the method has good reproducibility. From the results shown in accuracy table-2 it was found that the percent recovery values of pure drug from the preanalysed solutions of formulations were in between 98.3% -100.16%, which indicates that the method is accurate and which reveals that commonly used excipients and additives present in the pharmaceutical formulations did not interfere in the proposed method. The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routine determination of Atenolol and Chlorthalidone in bulk samples and pharmaceutical formulations.

IV. Conclusion:

A convenient and rapid UV method has been developed for simultaneous estimation of Atenolol and Chlorthalidone in available dosage form. The assay provides a linear response across a wide range of concentrations. Low intra-day and interday % RSD coupled with excellent recoveries. Hence, this method can be easily and conveniently adopted for routine analysis of Atenolol and Chlorthalidone in pure form and its dosage forms.

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Table No: 1 Linearity and correlation coefficient

	Atenolol	Chlorthalidone
Linearity µg mL^{-1}	10 – 60	30 – 140
Correlation coefficient (r)	0.999	0.998

Table No: 2 Recovery studies

Drug	% Recovery	Amount added µg mL^{-1}	Amount recovered µg mL^{-1}	% Recovery	% *RSD
Atenolol	50	12.5	12.42	99.36	0.342
	100	25	24.85	99.4	0.145
	150	37.5	37.47	99.92	0.426
Chlorthalidone	50	6.25	6.39	98.3	0.263
	100	12.5	12.52	100.16	0.521
	150	18.75	18.43	99.62	0.336

* = three estimations

Table No: 3 Precision studies

Drug	**Concentration µg mL^{-1}**	**Intra-day Precision (n=3)**	**Inter-day Precision (n=3)**
		% RSD	**%RSD**
Atenolol	50	1.01	0.38
Chlorthalidone	40	0.57	0.36

Table No: 4 LOD and LOQ

PARAMETERS	ATENOLOL	CHLORTHALIDONE
Limit of detection (LOD) µg mL^{-1}	4	10
Limit of quantification (LOQ) µg mL^{-1}	10	30

Table No: 5 Analysis of formulation

Drug name	Amount labeled (mg/tablet)	Amount estimated (mg/tablet)	% Label claim	% *RSD
Atenolol	25mg	24.42	97.68	0.365
Chlorthalidone	12.5mg	12.19	97.52	0.524

*= three estimations

Table No: 6 Summary of validation parameters for proposed methods

Parameters	Atenolol	Chlorthalidone
Linearity	10-60 µg mL^{-1}	30-140 µg mL^{-1}
Linear regression Intercept (c)	0.032	0.004
Slope(m)	0.032	0.005
Correlation Coefficient	0.999	0.998
Limit of Detection (LOD)	4 µg mL^{-1}	10 µg mL^{-1}
Limit of Quantification (LOQ)	10 µg mL^{-1}	30 µg mL^{-1}
Precision(%RSD) Intraday(n=3)	1.01	0.57
Interday(n=3)	0.38	0.36

Fig. 1: Atenolol

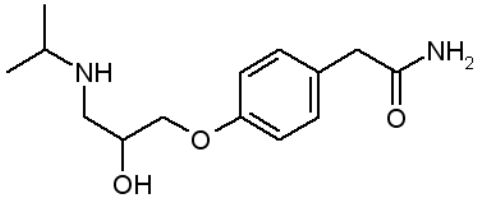

Fig. 2: Chlorthalidone

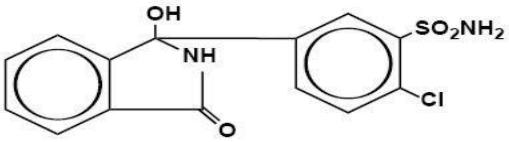

Fig. 3: Overlain spectrun of standard Atenolol and Chlorthalidone

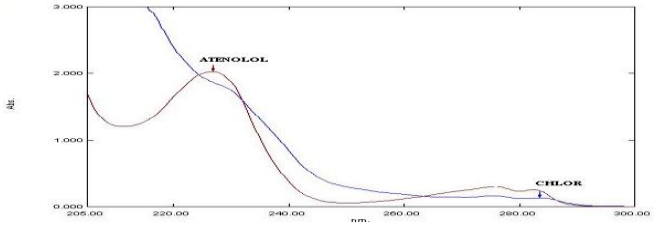

Fig.4:SpectraofAtenololand Chlorthalidone formulation