

Spectrophotometric Estimation and Validation of Atenolol in Tablets by Hydrotropic Solubilisation.

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Abstract

Hydrotropic solubilization is a technique that is used to improve the solubility of poorly water soluble drugs. Various hydrotropic agents like urea, sodium benzoate, sodium acetate, nicotinamide were utilized in enhancing the aqueous solubility. In this study, 5M urea solution was employed to estimate the amount of atenolol present in bulk form and its pharmaceutical tablets by spectrophotometric estimation. The solubility of pure atenolol in distilled water was found to be 9.34mg/ml, whereas in 5M urea solution it was found to be 21.4mg/ml. A marked increase in solubility of Atenolol in the hydrotropic solution was observed. Atenolol showed maximum absorbance at the wavelength of 225nm. It obeyed Beer-Lambert' law in the concentration range of 4-20 µg/ml. Atenolol estimation can be done within 24 hours without any detrimental effect on drug stability. It was evident that there was good correlation between the amount of drug estimated and the label claim. The estimated label claim was found to be 99.33±0.333mg by this method. The recovery studies revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method. The co-efficient of variation were less than 1.0% which confirmed good intermediate precision for the proposed method. The low values of LOD and LOQ, 0.3664µg/ml and 0.4071µg/ml respectively indicated good sensitivity of proposed method. Thus the proposed method is new, simple, environmentally friendly, accurate and cost-effective which can be successfully employed in routine analysis of atenolol in tablets.

Key Words

Hydrotrophy, Atenolol, Urea, Spectrophotometry

Introduction

Hydrotrophy is the term that has been used to designate the increase in aqueous solubility of various poorly water-soluble compounds in concentrated solutions of hydrotropic agents due to the presence of large amount of additives¹. Hydrotropes are a class of chemical compounds which affect an increased aqueous solubility by several folds to certain solutes which are sparingly soluble in water under normal conditions. This hydrotrophy technique is considered to be a potentially and industrially attractive technique since the observed increase in solubility is much higher than the other solubilization methods. Easy recovery of dissolved solute and possible re-use of hydrotrope solutions makes this method the most attractive one particularly at industrial levels³. Organic solvents that are used to solubilize poorly water soluble drugs suffer from major drawbacks of high cost, toxicity and volatility.

Concentrated aqueous hydrotropic solutions of sodium benzoate, niacinamide, sodium citrate, sodium glycinate and urea have been utilized to enhance aqueous solubility of insoluble and slightly soluble drugs and also in routine analysis of pharmaceutical formulations². Atenolol is a β-blocker, is prescribed widely in diverse cardiovascular diseases, e.g. hypertension, angina pectoris, arrhythmias, and myocardial infarction. Atenolol is a sparingly soluble in water, having low partition coefficient^{5,6}. The purpose of this study was aimed at developing a new, simple, accurate, environmental friendly, cost effective, safe, sensitive spectrophotometric estimation of atenolol in tablet dosage form using 5M urea as hydrotropic solution.

Materials and Method

Shimadzu UV/Visible recording spectrophotometer (model-UV-1601) with 1cm matched silica cells was employed. Atenolol drug sample was purchased from Yarrow chem. Products Ltd, Mumbai. Tablets of atenolol were purchased from the local market.

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All other chemicals and solvents used were of analytical grade.

Experimental

Preliminary solubility studies of the drug

Solubility of atenolol was determined by saturation aqueous solubility method in 5M urea and distilled water. An excess amount of drug was added to the 100ml beakers containing 5M urea and distilled water. The beakers were shaken for 12 hours at $28\pm 1^{\circ}\text{C}$. The solutions were filtered through Whatman filter paper #41, and the resulting filtrates were suitably diluted and analyzed spectrophotometrically at 225 nm against solvent blank⁷.

Preparation of standard stock and calibration curve

The standard stock solution of atenolol was prepared by dissolving 100mg of drug in 100 ml of 5M urea. From this solution 5ml of solution was diluted to 50ml with distilled water to get a solution containing $100\mu\text{g/ml}$ and was scanned in the UV range of 400-200 nm to determine the λ max of the drug. The λ max of atenolol was found to be 225 nm. Five working standard solutions for the drug having concentration 4,8,12,16 and 20 $\mu\text{g/ml}$ was prepared with distilled water from the stock solution. The absorbances of resulting solutions for the drug were measured at wavelength of 225nm and a calibration curve was plotted to get the linearity and regression equation.

Analysis of atenolol in tablets using 5M urea

Twenty tablets were weighed and powdered. Powder equivalent to 100 mg atenolol was transferred to a 50 ml volumetric flask containing 40 ml of 5M urea solution. The flask was shaken for about 5 min to solubilize the drug. Then volume was made up to the mark with distilled water. Solution was filtered through Whatman filter paper #41. Filtrate was divided into two parts, A and B. Part A was kept at room temperature for 24 hours to check the effect on stability of drug in presence of urea and also to note precipitation, if any, during this period. Part B filtrate was appropriately diluted with distilled water and absorbance was measured at 225 nm against solvent blank and drug content was calculated. After 48 hours, filtrate of part A was also appropriately diluted with distilled water and analyzed for drug content. There was no precipitation in the filtrate in 48 hours.

Validation of the proposed method

Recovery studies

Tablet powder equivalent to 100mg of atenolol was transferred to a 50 ml volumetric flask containing 40 ml of 5M urea solution. Pure atenolol drug sample (20 mg) was added to the volumetric flask. The flask was shaken for 5 minutes to solubilize the drug. Then solution was filtered through Whatman filter paper #41. The filtrate was diluted with distilled water appropriately and absorbance was measured at 225nm against corresponding reagent blank. Drug content was calculated and percent recovery was calculated. Similar procedure was repeated using 40 mg and 80 mg of pure atenolol as spiked concentration. The drug contents were determined and percent recoveries were estimated.

Precision

Precision was determined by studying the repeatability and intermediate precision. The standard deviation, coefficient of variance and standard error were calculated for the drug.

Inter- day and Intra- day precision

The intra-day concentration of the drug was calculated on the same day at an interval of one hour, whereas the inter day concentration of drug was calculated on three different days within the laboratory conditions.

Linearity

Appropriate dilutions of standard stock solutions were assayed as per the developed method. The Beer- Lambert's concentration range was found to be 4-20 $\mu\text{g/ml}$ for atenolol in 5M urea solution.

Limit of detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ of atenolol by the proposed method were determined using calibration standards. LOD and LOQ were calculated as $3.3\sigma/S$ and $10\sigma/S$, respectively, where S is the slope of the calibration curve and σ is the standard deviation of response⁸.

Results and Discussion

The results of solubility studies indicated that aqueous solubility of atenolol was enhanced in hydrotropic solution of 5M urea as compared to solubility in distilled water. The solubility of pure atenolol in distilled water was found to be 9.34mg/ml, whereas in the 5M urea solution, the solubility was found to be 21.4mg/ml. There was a

marked increase in solubility of atenolol in 5M urea. So it was decided to employ this solution of 5M urea in the analysis of the tablet formulation. A part of the solution was kept at room temperature for 24 hours to check the effect on stability of drug in presence of urea and for precipitation. The study revealed that estimations of atenolol can be done within 24 hours without any detrimental effect on drug stability. The Beer-Lambert's concentration range was found to be 4-20 µg/ml for atenolol at the wavelength of 225 nm. The drug showed good regression value at this wave length. It was evident that there is good correlation between the amounts estimated and the label claim. The estimated label claim was found to be 99.33 ± 0.333 mg and low values of standard error (Table 1). Accuracy and reproducibility of the proposed method were further confirmed by the recovery studies. The results of recovery studies revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method (Table 2). The values of LOD and LOQ, 0.3664 and 0.4071 were observed to be low and it indicated good sensitivity of the proposed method. Repeatability results indicated the precision under the same operating conditions over a short interval time and inter- assay precision. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter-day precision study for the method co-efficient of variation were not more than 1.0% indicates good intermediate precision.

Conclusion

It is thus concluded that the proposed method is a new, simple, cost effective, accurate and precise method. This method can be successfully adopted for routine analysis of atenolol in tablet dosage form.

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Table 1: Results of analysis of tablet formulations of atenolol.

Tablet formulation	Drug	Label claim (mg)	% Label claim Estimated* (mean \pm S.D.)	Standard error
Commercial Tablet I	Atenolol	100	99.33 \pm 1.252	0.333

*Average of three determinations

Table 2: Results of recovery studies.

Formulation	Amount of Atenolol tablet powder	Amount of pure atenolol added (mg)	% recovery estimated* (mean \pm S.D.)	Standard error
Commercial Tablet I	100	20	101.33 \pm 0.7638	0.4410
	100	40	100.73 \pm 0.4359	0.2517
	100	80	100.47 \pm 0.4676	0.2700

*Average of six determinations

Table-3: Optical characteristics data and validation parameters.

Parameters	Values for Atenolol
Working λ_{max} (nm) in 5M Urea	225 nm
Beer's law limit (μ g/ml)	4-20
Molar Absorptivity	10.57x 10 ³
Correlation coefficient*	0.9995
Intercept*	0.0016
Slope*	0.0393
LOD* (μ g/ml)	0.3664
LOQ* (μ g/ml)	0.4071
Intra-day* (precision) (Co-eff. of variation)	0.2789
Inter-day*(precision) (Co-eff. of variation)	0.1317
Robustness	Robust

*Average of six determinations
