Extractive Spectrophotometric Determination of Atenolol in Pure and Pharmaceutical Formulations

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ABSTRACT

Two simple and sensitive extractive spectophotometric methods for the determination of Atenolol (ATN) in pure and pharmaceutical formulations with Bromo cresol green (BCG method A) and bromophenol blue (BPB, method B) are described. The methods are based on the formation of ion-association complexes of ATN with these dyes, which are extracted in to the chloroform and have absorption maximum at 420 nm .The methods are obey Beer's law and the precision and accuracy of the methods were checked by UV reference method.

INTRODUCTION: Atenolol (ATN), chemically known as benzene acetamide-4-[2-hydroxy -3-(1-methyl) amino –propoxy] is a hydrophilic β adrenergic blocking agent, widely used in the treatment of hypertension and certain types of cardiac arrhythmias [1]. It is official in IP[2] and BP[3] . The reported methods in the literature for the determination of ATN or fluorometry [4,8] UV Spectrophotometry [9-12] visible spectrophotometry [13-17] NMR Spectroscopy [18-19] HPLC [20-31] TLC [32] LC [33-34] and GC [35-37] Most of the reported visible spectrophotometric methods are less sensitive and more time consuming than the proposed methods.In contrast ,the extractive spectrophotometric technique provides a highly sensitive methods for determination of pharmaceuticals [38]. In the present communication, we are reporting a rapid, simple extractive spectrophotometric determination using a dyes bromo cresol green and bromo phenol blue.

The proposed methods are based on the formation of ion –association complexes with bromo cresol green and bromo phenol blue (λ max 420) and their complexes are quantitatively extracted into chloroform.

EXPERIMENTAL:

Preparation of Reagents: All the chemicals used were of reagent grade.

(i) **Bromo Cresol Green** (Loba, 0.1%, 1.433×10^{-3}M):100 mg of dye is dissolved in 100 ml of distilled water.

(ii) **Bromo Phenol Blue** (Loba, 0.1% 1.433×10^{-3} M):100 mg of dye is dissolved in 100 ml of distilled water.

STANDARD AND SAMPLE SOLUTIONS : A 1 mg ,ml^{-1} stock solution of pure ATN was prepared by dissolving 100 mg of the drug initially in 10 ml of 0.1 M Hcl and made up to 100 ml with distilled water to get 200 µg for ml.

Solutions of pharmaceutical formulations were prepared in the same manner as per pure samples and the insoluble residue was filtered, the filtrate was made up to volume with distilled water to obtain 1 $mg.ml^{-1}$ solution. The above solution was further diluted to the requisite concentrations for methods A and B for analysed as described under the procedures for pure samples.

INSTRUMENTATION: A Milton Roy spectronic 1201 and systronics 106 spectrophotometers with 1 cm matched quartz cells were used for all spectral and absorbance measurements. An Elico LI-120 digital pH meter was used for pH measurements.

PROCEDURES:

Method A: Aliquots 0.5 to 2.5 ml, 200 $\mu g/ml^{-1}$) of standard ATN solution were placed in a series of 125 ml separating funnels. The 6 ml of buffer solution (pH 3.5) and 2.0 ml of BCG solution were added to each separating funnel. The total volume of aqueous phase in each separating funnel was brought to 15 ml with distilled water .Then 10 ml of chloroform was added to each funnel and contents were shaken for 2 minutes .The two phases were allowed to separate and absorbance of the separated chloroform layer was measured at 420 nm against a reagent blank within the stability period (5 min-5 hrs) at laboratory temperature (28±5°C). The amount of drug was computed from calibration graph.

Method B: Aliquotos (0.5-5.0 ml 200 µ/ml) of standard ATN solution were placed in a series of 125 ml separating funnels and 6 ml of buffer (pH 2.5) and 2 ml of BPB were added to each separating funnel .The total volume of aqueous phase in each separating funnel was brought to 15 ml in each separating funnel with distilled water. Then 10 ml of chloroform was added to each funnel and the contents were shaken for 2 min. The two phases were allowed to separate and absorbance of the separated chloroform layer was measured at 420 nm against a reagent blank within the stability period (5 min-5 hrs) at laboratory temperature(28±5°C) The amount of drug was computed from calibration graph.

RESULTS AND DISCUSSION: The optical characteristics such as Beer's law limits molar extinction coefficient, sandal's sensitively correlation coefficient, slope and intercept data from linear least squares treatment and percent relative standard deviation (from six replicate samples) were presented in table-1.

Table 1 : Optical and regression characteristics, precision and accuracy of proposed methods for ATN

Parameters	Method A	Method B
λmax (nm)	420	420
Beer's law limits(μg.ml^{-1})	10 -50	20-100
Molar absorptivity(1 mole^{-1} –cm^{-1})	1.86×10^{3}	1.37×10^{3}
Sandell's sensitivity(μg cm^{-2}/0.001 Abs.unit)	1.42×10^{-1}	1.94×10^{-1}
Regression equation (y=a+bc) Slope(b) Intercept(a) Correlation coefficient(r) Relative standard deviation(%)* % Range of error (confidence limits) 0.05 level	 6.49×10-3 -8.0×10-4 0.9999 0.49 0.52	 5.19×10-3 -2.0×10-3 0.9998 0.28 0.30

Calculated from 6 determinations

The proposed methods have been applied to dosage forms (tables). The accuracy of the methods was ascertained by comparing the results from the proposed and reported methods. Statistically by the t- and F- tests and found not to differ significantly .To evaluate the validity and reproducibility of the method, known amounts of pure drug was added to previously analysed samples and the mixtures were analysed by the proposed methods and the results are incorporated in table 2. There is no interference of other ingredients present in the formulations.

Table 2: Assay of Atenolol in Pharmaceutical Formulations

Pharmaceutical formulations *	Labeled amount (mg)	Amount found by proposed method ** %		Found reference method (UV)[11]	% Recovery by proposed methods ***	
		METHO D A	METHOD B		METHOD A	METHOD B
Tablets ALOTEN 50	50	100.1±0.51 T=0.537 F=1.954	100.1±0.58 T=0.704 F=1.137	100.1±0.72	99.8±0.37	99.4±0.53
ALTOL	50	99.8±0.40 t=0.420 F=1.732	100.2±0.57 t=0.603 F=1.202	100.2±0.52	99.4±0.38	99.3±0.45
ANGITOL	25	99.6±0.61 t=0.644 F=2.046	99.6±0.60 t=0.633 F=1.976	99.9 ± 0.19	100.1 ± 0.47	99 ± 0.63
ATECARD	50	99.7 ± 0.49 t=5.05 F=1.236	99.5 ± 0.63 t=1.568 F=2.428	99.9 ± 0.19	99.0 ± 61	100.1 ± 60

* Formulations that are manufactured by four different pharmaceutical companies.

** Average ± standard deviation of six determinations the t- and F – values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confident limit, F-5.05, t=2.57

*** Recovery of 10 mg added to the pharmaceutical formulations (average of three determinations).

These results indicate that the proposed methods are simple rapid with reasonable precision and accuracy and applicable to various formulation of Atenolol.

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