INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY, BIOLOGY AND CHEMISTRY

Research Article

Quantitative determination of Atenolol in tablets

Y. N. Zhuk and S. O. Vasyuk

Analytical Chemistry Department, Zaporizhzhya State Medical University, Ukraine.

ABSTRACT

In this investigation a visible spectrophotometric method for the quantitative determination of atenolol based on the absorbance of colored product of the reaction between atenolol and bromthymol blue in acetone medium at 402 nm measurement was developed. The optimal conditions for the quantitative determination of atenolol in the content of pharmaceutical drugs were established. The stoichiometric relationship coefficients between atenolol and bromthymol blue were determined. The proposed method is valid according to the validation requirements of Ukrainian Pharmacopeia. According to the experimental data, the technique can be correctly reproduced and it is suitable for routine quality control.

Keywords: Atenolol, quantitative determination, spectrophotometric method and bromthymol blue.

1. INTRODUCTION

Atenolol is antianginal, hypotensive and antiarrhythmic drug. It selectively blocks the β1-adrenergic receptors, without membrane-stabilizing action and intrinsic sympathomimetic activity.

Due to the extensive application of atenolol drugs in cardiology practice, development and validation methods for its quantitative determination is current problem today.

Spectrophotometric methods in the visible spectrum for the quantitative determination of atenolol in the composition of dosage forms described enough in the literature. Chloranilic acid[1], 4-chloro-7-nitro-2,1,3-benzoksadiazol[2], 2,3-dichloro-5,6-dytsiano-1,4-benzoquinon,2,4-dinitrophenol and 2,4,6-trinitrophenol[3, 4], sodium nitroprusside[5], ferroics and methyl orange[6] were used as reagents. Spectrophotometric methods in the UV spectrum for the quantitative determination of atenolol were described also[7-10]. But despite the many advantages presented UV spectrum determining methods are usually requiring increasing selectivity, and analysis in the visible spectrum based on the reactions that require special conditions and additional treatments such as extraction, pH adjustment or remote involvement expensive reagents. Other methods for the quantitative determination are described in literature too[11-14].

The proposed method is economical compared to the previously reported techniques. Moreover, this method is sensitive, simple, does not involve heating or extraction step, and free from usage of hazardous chemicals. Since inexpensive and easily available chemicals are used, the developed methods evidence low cost per analysis.

The aim of this work is development a simple, selective and sensitive spectrophotometric method for the quantitative determination of atenolol in drug dosage forms using bromthymol blue (BTB) as reagent.

2. RESEARCH MATERIALS AND METHODS

All chemicals and reagents used were of analytical or pharmaceutical grade.

2.1. Reagents

Pure atenolol substance was obtained from Ipco. Laboratories, (series 7271 AZRI), BTB was obtained from Pharmaceutical company's laboratory «Sinbias» (series 20081101), acetone was obtained from Lab-Scan, Poch, Ireland (series 4164/11).The dosage forms of atenolol were obtained from different firms – tablet «Atenobene» 100 mg (Ratiopharm, Germany, series M 30530), tablet «Atenolol-Zdorovie» 50 mg (Pharmaceutical company «Zdorovie», Ukraine, series 10214), tablet «Atenolol-Astrapharm» 100 mg (Pharmaceutical company «Astrapharm», Ukraine, series 010216).

2.2. Apparatus

Analytic Jena UV-visible spectrophotometer model

Specord 200 with 1 cm matched quartz cells, Kern electronic scales ABT-120-5DM, ultrasonic bath ELMASONICE60 H.

2.3. Assay procedure

The aliquots of the solution containing 0.18-0.28 mg of atenolol were transferred into a series of 10 ml calibrated flasks.1 ml of 0.1% BTB was added to each of the calibrated flasks and diluted to the mark with acetone.The contents were shaken well and left at room temperature for a minute. The absorbance of the yellow colored species was measured at 402 nm. 0.02% atenolol standard sample solution was used as comparison solution.

2.4. Assay procedure for dosage forms

Twenty tablets each containing 50 or 100 mg of atenolol were weighed accurately and pulverized. An amount of powdered tablet equivalent to 23 mg of atenolol was transferred into a 100 mL calibrated flask, 20 ml of acetone was added and shaken thoroughly for about 2–3 min. The content was diluted to the mark with acetone, mixed well and filtered through a filter paper to remove the insoluble matter. 1.00 ml of the filtrate was transferred into 10.00 ml volumetric flask, 1.00 ml BTB solution was added, diluted to the mark with acetone and analyzed using the procedure given above. The active substance content was calculated using the standard formulas[9].

3. RESULTS AND DISCUSSION

3.1. Optimum reaction conditions and absorption spectra

The choice of solvent for this reaction was based on the atenolol and sulfophthalein dyes solubility data, and on the experimental results. Experimentally was determined that acetone is the optimal solvent for this reaction. The reaction proceeds rapidly at room temperature, so temperature and time mode don't need correction in this case.

Atenolol reacts with BTB in acetone to give a soluble yellow colored ion-association complex which exhibits an absorption maximum at 402 nm. Presumably the ion-pair complex is formed due to atenolol excess electron density on the nitrogen atom and BTB donor proton. Under the experimental conditions, the reagent blank showed negligible absorbance as shown in Fig. 1.

3.2. The stoichiometric relationship coefficients

The stoichiometric relationship coefficients between atenolol and BTB were determined by isomolar series and molar ratio procedures[15].

The saturation curves analysis (Fig. 1) showed that break in curves was observed in ratio of components BTB – atenolol 1:1.

The results obtained by molar ratio procedure confirm the specified ratio (Fig. 2).

3.3. Determination of some validation characteristics

According to requirements of Ukrainian Pharmacopoeia the following validation characteristics as precision, linearity, accuracy and robustness were determined[16].

Linearity

Calibration graph was constructed by measuring the absorbance at six concentration levels which showed linear response of absorbance in relation to concentration of atenolol over the range of 1.8 – 2.8 mg/100 ml (Fig. 3)

Precision

Precision was determined from atenolol samples at three different concentrations in the calibration range in three replicates. In all cases confidence interval does not more than the maximum indeterminateness of analysis. The data is summarized in Table 2.

Accuracy

Accuracy was set for the drug dosage forms using standard addition method and suggested the high accuracy of the proposed method. Recoveries were found to be between 99.79 and 100.38% (Table 3).

Robustness

It was established that sample solutions are stable for at least 30 minutes, and addition±10% of BTB solution from the optimal to the sample solution has no effect on the absorbance value.

4. CONCLUSION

It was established that atenolol reacts with BTB at room temperature in acetone medium with absorbance maximum at 402 nm. The reaction is sensitive: the molar absorption coefficient is $1{,}97 \cdot 10^4$. The spectrophotometric determination procedure of atenolol in dosage form was developed. It was proved that procedure is valid.

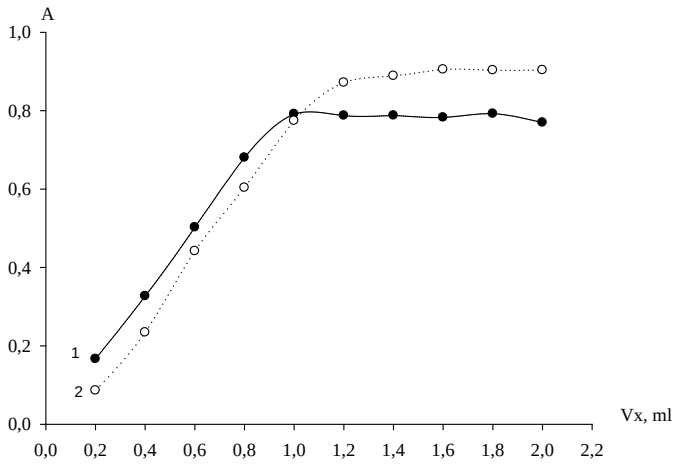

Fig. 1
The saturation curves: 1 – atenolol (BTB = const = 1 ml 0.0005 M); 2 – BTB (atenolol = const = 1 ml 0.0005 M)

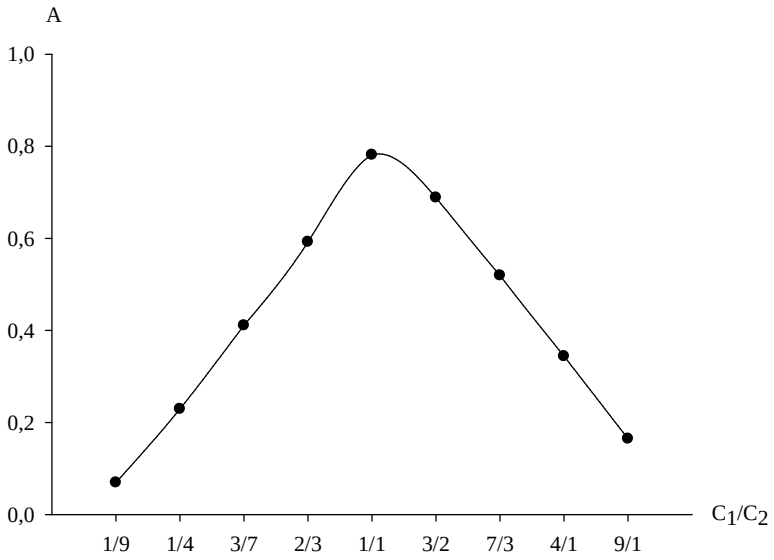

Fig. 2
The graph of the absorbance value as a function of isomolar solution composition (C_1 – 0,0005 M BTB solution, C_2 – 0,0005 M atenolol solution)

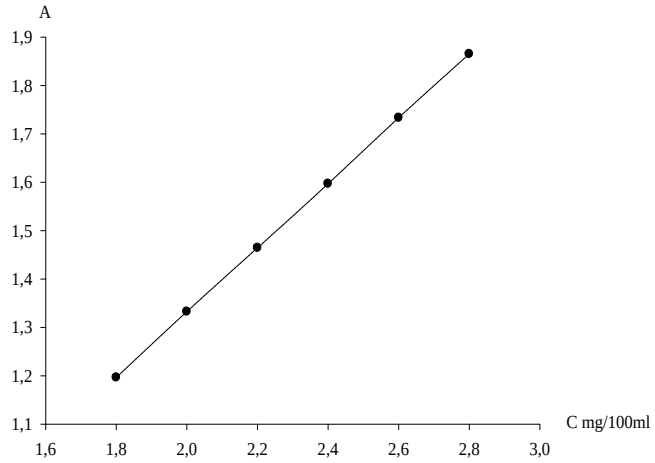

Fig. 3
Linear correlation between absorbance and concentration of atenolol

Table 1
Optical specifications and linear dependence parameters

Molar absorption coefficient, ε	19732
Sendel's coefficient, W_S	0.0135
Identification limit, Cmin (mkg/ml)	0.67
Equation of linear regression	Y = bX + a
Slope, b±(S_b)	0.6684±(0.0017)
Intercept term, a±(S_a)	-0.0058±(0.0039)
Residual standard deviation, $S_{x,o}$	0.00209
Correlation coefficient, r	1.000

Table 2
Precision determination results for atenolol dosage forms

Drug dosage form	$\overline{X}_{(n=9)}$	S	RSD%	Δ_x	Δ_{As}%
Atenobene» 100 mg	0.0987	8.33×10^{-5}	8.44×10^{-2}	1.55×10^{-4}	3.20
Atenolol-Zdorovie» 50 mg	0.0491	5.27×10^{-5}	0.107	9.80×10^{-5}	3.20
Atenolol-Astrapharm» 100 mg	0.0979	8.66×10^{-5}	8.85×10^{-2}	1.61×10^{-4}	3.20

Table 3
Accuracy determination results for atenolol dosage forms

Drug dosage form	$\overline{Z}_{(n=9)}$	S	Δ_Z	$\overline{Z} - 100$
Atenobene» 100 mg	99.79	2.82×10^{-2}	0.0525	0.21
Atenolol-Zdorovie» 50 mg	100.05	1.94×10^{-2}	0.0360	0.05
Atenolol-Astrapharm» 100 mg	100.38	3.48×10^{-2}	0.0647	0.38

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