www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2016; 5(6): 31-33

www.thepharmajournal.com
Received: 06-04-2016
Accepted: 07-05-2016

YN Zhuk
Analytical Chemistry
Department Zaporizhzhya State Medical University, Ukraine.

SO Vasyuk
Analytical Chemistry
Department Zaporizhzhya State Medical University, Ukraine.

Correspondence
YN Zhuk
Analytical Chemistry
Department Zaporizhzhya State Medical University, Ukraine.

Spectrophotometric determination of betaxolol in pure form and pharmaceuticals

YN Zhuk and SO Vasyuk

Abstract
A new spectrophotometric method for the quantitative determination of betaxolol in pharmaceutical formulations, such as tablets, has been developed. This method is based on the formation of yellow complex as a result of the reaction between betaxolol and bromocresol green (3',3",5',5"-tetrabromo-m-cresolsulfophthalein) with maximum absorption at 408 nm in acetone. 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: betaxolol, spectrophotometric determination, bromocresol green.

Introduction
Modern cardiology impossible without drugs of β-blockers, which are more than 30 names at present day. The need to include these drugs to the program of cardiovascular diseases treatment is obvious: the β-blockers have taken a strong position in the prevention of complications and in the pharmacotherapy of hypertension, ischemic heart disease, congestive heart failure, metabolic syndrome and other cardiovascular problems.
The one of the representatives of this drugs group is betaxolol hydrochloride – the selective β-blocker prolonged action that blocks most β1-adrenergic receptors. Shows hypotensive effect and prevents high blood pressure associated with physical activity, emotional stress and other factors [1].
In the literature described different methods for the quantitative determination of betaxolol hydrochloride in dosage forms.
B. N. Suhagia proposes the spectrophotometric determination of betaxolol hydrochloride in substance and dosage forms [2]. In this case betaxolol is oxidized with sodium periodate, to liberate formaldehyde, which is determined in situ, using acetyl acetone in the presence of ammonium acetate. A yellow coloured chromogen was obtained having absorption maxima at 405 nm. Other methods of betaxolol hydrochloride spectrophotometric determination were described also [3, 4]. American, British and European Pharmacopoeia recommend the acid-base titration method in non-aqueous media with potentiometric fixation endpoint for the substance of betaxolol hydrochloride [5-7]. For dosage forms of these drug in the American Pharmacopoeia described the HPLC with UV detection at 273 nm.
The extensive use of betaxolol drugs in pharmaceutical practice needs to improve existing and develop new methods of the quantitative determination of the active ingredient in the composition of dosage forms. The literature review shows that quantitative determination of betaxolol hydrochloride by spectrophotometry described enough.
In view of this, the aim of our work is development a sensitive, simple, cost effective and valid spectrophotometric methods for the quantitative determination of betaxolol hydrochloride in dosage forms using bromocresol green as reagent.

The research objectives
- ✓ determine the optimal conditions of photometric reaction between betaxolol and BCG;
- ✓ calculate the sensitivity fundamentals of the reaction;
- ✓ establish the stoichiometric relationship coefficients between betaxolol and BCG;
- ✓ work out the procedure of quantitative determination of betaxolol in pharmaceutical preparations;
- ✓ validate the developed procedure.

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

The research objects: tablets «Betac» 20 mg (Medochemie LTD, Cyprus, series E9E032MF), tablets «Locren» 20 mg (Sanofi-Winthrop Industrie, France, series 5T008), tablets «Betacor» 20 mg (Kiev vitamin factory, Ukraine, series 41015).

Reagents and solvents: pure betaxolol substance (Kiev vitamin factory, Ukraine, series BTX 872), BCG (Pharmaceutical company's laboratory «Sinbias», series 47), acetone (Lab-Scan, Poch, Ireland, series 4164/11).

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.

Assay procedure

The aliquots of the solution containing 0.165-0.275 mg of betaxolol were transferred into a series of 10 ml calibrated flasks. 2 ml of 0.5% BCG 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 408 nm. 0.02% betaxolol standard sample solution was used as comparison solution

Assay procedure for dosage forms

Twenty tablets each containing 20 mg of betaxolol were weighed accurately and pulverized. An amount of powdered tablet equivalent to 22 mg of betaxolol 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, 2.00 ml BCG 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 [8].

Results and discussion

Optimum reaction conditions and absorption spectra

For the purpose of the optimal reagent selecting to development of betaxolol hydrochloride quantitative determination procedure were compared the spectra of the reaction products of investigated substance with excess of the most common sulphophthalein dyes. The selection criterion was the absorption maximum. Reaction with BCG was the most sensitive (Fig. 1). The reagent amount was determined experimentally.

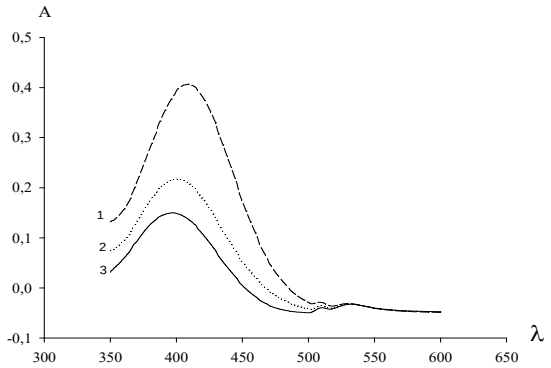

Fig 1: The absorption spectra of the reaction product between betaxolol and BCG (1), BCP (2), BTB (3)

The choice of solvent for this reaction was based on the betaxolol 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.

The stoichiometric relationship coefficients

The stoichiometric relationship coefficients between betaxolol and BCG were determined by isomolar series and molar ratio procedures [8].

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

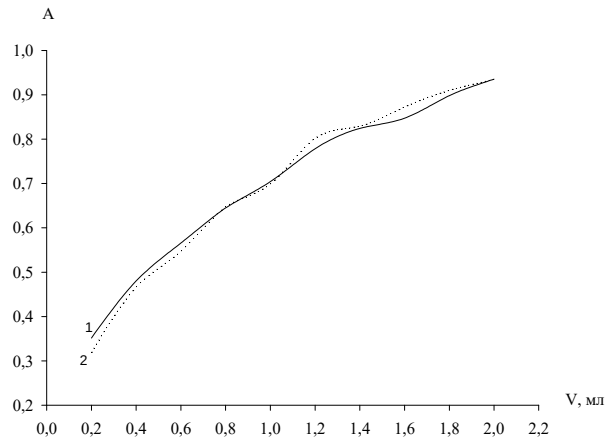

Fig 2: The saturation curves: 1 – betaxolol (BCG = const = 1 ml 0. 002 M); 2 – BCG (betaxolol = const = 1 ml 0.002 M)

The results obtained by molar ratio procedure confirm the specified ratio (Fig. 3).

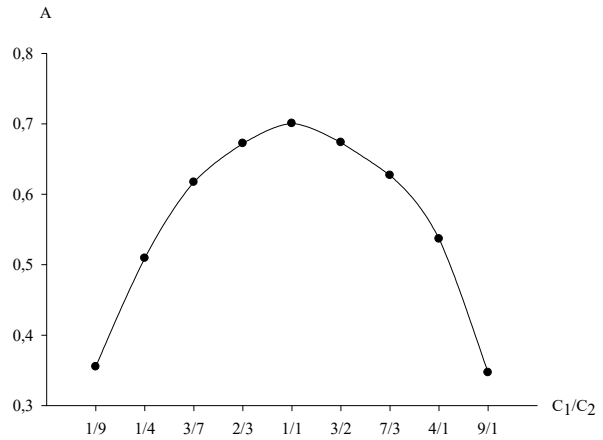

Fig 3: The graph of the absorbance value as a function of isomolar solution composition (C_1 – 0,002 M BCG solution, C_2 – 0,002 M betaxolol solution)

Determination of some validation characteristics

According to requirements of Ukrainian Pharmacopoeia the following validation characteristics as precision, linearity, accuracy and robustness were determined [9].

Linearity. Calibration graph was constructed by measuring the absorbance at five concentration levels which showed linear response of absorbance in relation to concentration of betaxolol over the range of 1.65 – 2.75 mg/100 ml (Fig. 4).

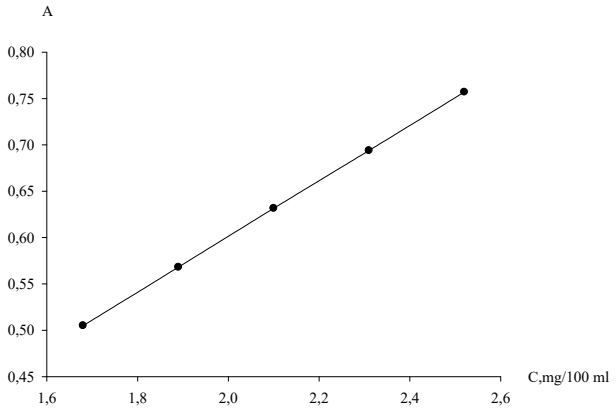

Fig 4: Linear correlation between absorbance and concentration of betaxolol

Table 1: Optical specifications and linear dependence parameters

Molar absorption coefficient, ε	10786
Sendel's coefficient, W_S	0,0285
Identification limit, Cmin (mkg/ml)	1,42
Equation of linear regression	Y = bX + a
Slope, b±(S_b)	0,3000±(0,0005)
Intercept term, a±(S_a)	0,0012±(0,0010)
Residual standard deviation, $S_{x,o}$	0,001
Correlation coefficient, r	1,000

Precision. Precision was determined from betaxolol 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.

Table 2: Precision determination results for betaxolol dosage forms

Drug dosage form	$\overline{X}$ (n=9)	S	RSD%	Δ_x	%
«Betac» 20 мг	0,0199	$1,22 \cdot 10^{-4}$	0,613	$2,27 \cdot 10^{-4}$	3.20
«Locren» 20 мг	0,0199	$1,59 \cdot 10^{-4}$	0,797	$2,96 \cdot 10^{-4}$	3.20
«Betacor» 20 мг	0,0201	$1,01 \cdot 10^{-4}$	0,502	$1,88 \cdot 10^{-4}$	3.20

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 99.92 and 99.98% (Table 3).

Table 3: Accuracy determination results for betaxolol dosage forms

Drug dosage form	$\overline{Z}$ (n=9)	S	Δz	$\overline{Z} - 100$
«Betac» 20 мг	99,97	$1,32 \cdot 10^{-2}$	0,0245	0,03
«Locren» 20 мг	99,92	$7,82 \cdot 10^{-3}$	0,0145	0,08
«Betacor» 20 мг	99,98	$8,33 \cdot 10^{-3}$	0,0155	0,02

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

Conclusions

It was established that betaxolol reacts with BCG at room temperature in acetone medium with absorbance maximum at 408 nm. The reaction is sensitive: the molar absorption coefficient is 10786. The spectrophotometric determination procedure of betaxolol in dosage form was developed. It was proved that procedure is valid.

Reference

1. Mashkovskiy MD. The pharmaceutical drugs. 2000; 1:606.
2. Suhagia BN, Shah SA, Rathod IS. Spectrophotometric estimation of Betaxolol Hydrochloride in bulk powder and its dosage forms. Indian Journal of Pharmaceutical Science. 2006; 68(2):267-269.
3. Yazbi Fawzy A El, Mahrous Mohamad E, Hammud Hassan H. Sensitive Spectrophotometric Methods for Estimation of Betaxolol and Imidapril Hydrochloride in Bulk Powder and in their Single Dosage Forms. International Journal of Applied Chemistry. 2008; 4 (Issue 2):119-141.
4. Sidharth Patil M, Vinod Panchal S, Ramchandra Chilkawar N. Development of validated UV spectrophotometric method for estimation of betaxolol hydrochloride in bulk and pharmaceutical dosage form. International Journal of Pharmaceutical Research and Bio-Science. 2013; 2(Issue 5):404-413.
5. United States Pharmacopeia 26. – USP Convention Inc. – Rockville, 2003.
6. European Pharmacopoeia. – 8th ed. – Strasbourg, France: Council of Europe, 2013, 3655.
7. British Pharmacopeia. – Her Majesty's Stationery Office. – London, 2000.
8. Bulatov MI, Kalinkin IP. Practical guide of photometric analysis methods. Edn 5, Chemistry, Leningrad, 1986, 432.
9. Ukrainian State Pharmacopoeia. Edn 1, Add 2, Scientific-expertise officinal center, Kharkiv, 2008, 620.