ORIGINAL ARTICLE

HPLC as an assay method for the investigation of conditions of bisoprolol extraction by organic solvents

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Abstract

Introduction: Sample preparation is an important step in pharmaceutical analysis and is needed to improve the metrological characteristics of the analysis: Improving accuracy, reliability, correctness and reproducibility of the determination, expanding the range of values studied, accelerating the test, and reducing the error of the results of the analysis. The objective of this research was to select the optimal conditions for the extraction of bisoprolol fumarate by organic solvents from water solutions in dependence on pH solutions. **Materials and Methods:** The chromatographic analysis of bisoprolol fumarate performed on liquid chromatograph ACQUITY Arc System. **Results:** The extraction of bisoprolol fumarate by organic solvents from water solutions in dependence on pH solutions has been conducted. The quantitative determination of bisoprolol fumarate by high-performance liquid chromatography methods has been conducted. **Conclusion**: As a result of studies, we have found out that the optimal extragent is chloroform, which is extracted at pH 10 to 92.57% and methylene chloride is extracted at pH 10–90.08%. We have found that bisoprolol fumarate least extracted with hexane, so these conditions may be cleaned extracts from coextractives impurities.

Key words: Bisoprolol fumarate, extraction, high-performance liquid chromatography, organic solvents

INTRODUCTION

Bisoprolol is a synthetic, β1-selective (cardioselective) adrenoceptor blocking agent without significant membrane stabilizing activity or intrinsic sympathomimetic activity in its therapeutic dosage range. The chemical name of bisoprolol is 1-{4-[(2-isopropoxyethoxy) methyl] phenoxy}-3-(isopropyl amino) propan-2-ol. Any analytical definition includes the following steps: Sample preparation, proper chemical analysis, and statistical processing of the results of the analysis. Sample preparation is a complex of rational actions over the object of analysis to transform the test into a form acceptable for further analysis. Sample preparation is an important step in pharmaceutical analysis and is needed to improve the metrological characteristics of the analysis: Improving accuracy, reliability, correctness and reproducibility of the determination, expanding the range of values studied, accelerating the test, and reducing the error of the results of the analysis.[1-3] The nature of the sample preparation is determined by the nature of the sample and the analytical method used for further analysis. Depending on the nature, aggregate state, sample concentration, and method of analysis, various sampling procedures are used: Moisture removal, grinding, decomposition, dissolution, melting, elution, removal of the matrix, dilution, concentration, etc. For the purification of substances from impurities, as well as for the separation of mixtures of substances, extraction is used. This method is based on the different solubility of the substances

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in the suitable solvent, or in two non-mixing solvents.[4] Modern methods of isolating drugs from biological material based on the individual physicochemical properties of the compounds, so the choice of optimal conditions for isolation from biological objects, cleaning extracts of impurities are a pressing issue for improving existing and developing new methods of analytical and bioanalytical analysis for the studies pharmacokinetics and bioequivalence.[4,5,7]

Our aim was to select the optimal conditions for the extraction of bisoprolol fumarate by organic solvents from water solutions in dependence on pH solutions.

MATERIALS AND METHODS

Chemical and Reagents

The chemicals used in all experiments were obtained from Sigma (Barcelona, Spain) and Merck (Berlin, Germany), MEM (Hi-Media), bisoprolol fumarate, and dimethyl sulfoxide. All of other chemicals and reagents were obtained from Sigma-Aldrich**.**

The main quantitative measure of extraction is the degree of extraction (R) - the ratio of the extracted material to the total (initial) of the substance in the aqueous solution. Amount of API was determined experimentally using high-performance liquid chromatography (HPLC) method. We have chose organic solvents due their use in the pharmaceutical analysis of drugs for the isolation and purification of extracts from biological material such as hexane, chloroform, methylene chloride.

To investigate the degree of extraction of bisoprolol fumarate from aqueous solutions of organic solvents used standard solutions, which was prepared with concentrations. The standard solution concentration of bisoprolol fumarate is 10 µg/mL in 0.01 mol/L hydrochloric acid. Assay performed using previously developed conditions:[7-21] Research of bisoprolol fumarate extraction conditions with aqueous solutions of organic solvents was performed by the following procedure: The number of separating funnels made in 8.00 mL of buffer solutions and in 200 mL of standard solution of bisoprolol fumarate. To the resulting mixture was added 10.00 mL appropriate organic solvent. Mixtures shaken in separating funnel for 5 min and left for 10 min to separate the layers.

Organic layers were collected in a beaker and evaporated in a water bath to dryness, which was dissolved in 5 mL of ethanol, quantitatively transferred to a volumetric flask, and 10.0 mL of solvent was adjusted to the mark. Amount of API was determined experimentally using HPLC method. The experiment was performed 3 times for each pH studied for organic solvents. Need pH created using universal buffer Britona-Robinson (pH = 1.8) and 0.2 M sodium hydroxide from 2.0 to 12.0. The pH installed in the application of pH meter - pH 150 MI (2011, Russia).

Chromatography was performed on liquid chromatograph with spectrophotometric detector under the conditions, which are listed in Table 1.

RESULTS

The extractions of bisoprolol fumarate by organic solvents from water solutions in dependence on pH solutions were conducted. The different solvent extracted samples from the bisoprolol fumarate were analyzed using HPLC. For elaboration on the method, the chromatograms of the standard solution of bisoprolol fumarate [Figure 1], as well as the dependence on the intensity peaks on the retention time were obtained and analyzed.

DISCUSSION

HPLC is a versatile, robust, and widely used technique for the isolation of chemical products.[22] Currently, this technique is gaining popularity among various analytical techniques as the main choice for fingerprinting study.[23] To understand the purpose of HPLC analytical method, it is necessary to consider the applications of HPLC in pharmaceutical analysis there is wide variety of application throughout the processing of new drugs, from the initial drug discovery to manufacture of formulated products which will administer to the patients [24-26]

To find the appropriate HPLC conditions for separation of the examined drug, various reversed-phase columns, isocratic and gradient mobile phase systems were tried, and successful attempts were performed using a RP-C18 chromatographic column Symmetry C18 column (3.9 mm i.d. × 150 mm, 5 µm) and mobile phase composed of acetonitrile:phosphate buffer solution pH 7.0 in the ratio of 25:75 v/v, at a flow rate of 1.4 mL/min with λ_{max} at 226 nm. Under the described HPLC parameters, the respective compound was clearly separated and their corresponding peaks were sharply developed at reasonable Rt 2.09 min.

The results of the current study of bisoprolol fumarate degree of extraction of various organic solvents, depending on the pH clearly indicate that the extraction of the drugs takes place already almost in basic solutions.

Results of the present study are revealed in Figures 2-4 and indicate that bisoprolol fumarate is extracted with used organic solvents. The area of maximum extraction for most solvents is observed at pH 10. The obtained data testifies that the optimal solvents for the extraction of bisoprolol fumarate in the process of separating it from objects of biological origin are chloroform and methylene chloride. The amount of substance released by chloroform is 92.57% (at pH 10) and methylene chloride 90.08% (at pH 10).

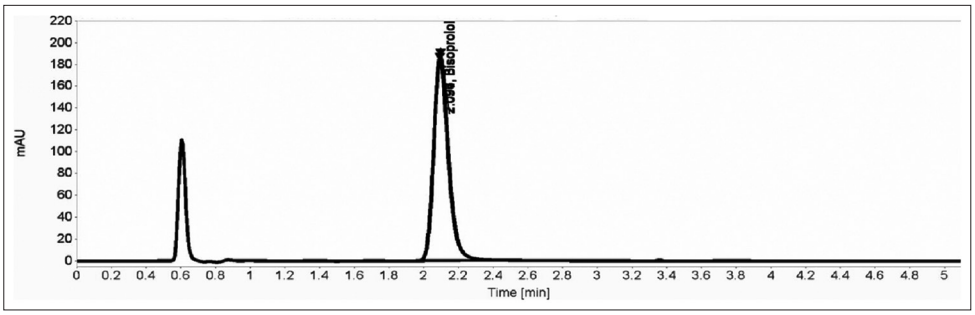

Figure 1: Representative chromatogram of bisoprolol fumarate using ultraviolet detection at 226 nm

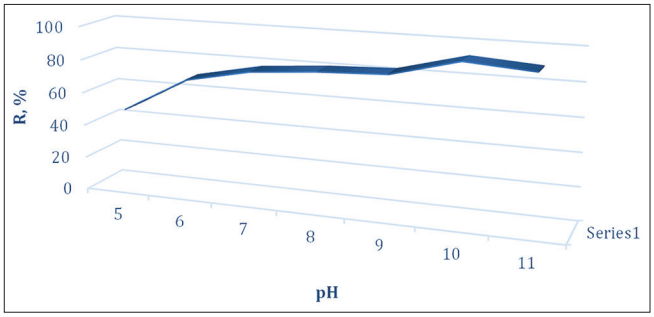

Figure 2: The dependence on the degree of extraction of bisoprolol fumarate on pH solutions and nature of organic solvents (chloroform)

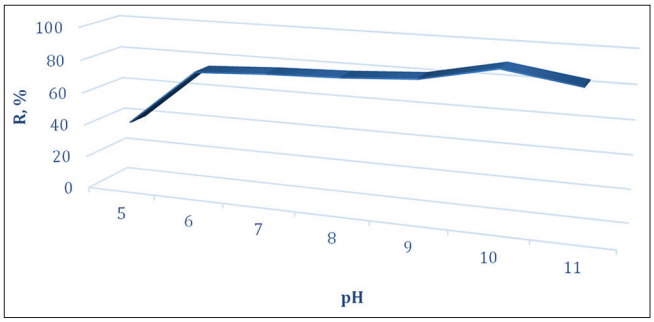

Figure 3: The dependence on the degree of extraction of bisoprolol fumarate on pH solutions and nature of organic solvents (methylene chloride)

Considering that hexane extracts very small amount of enalapril maleate from aqueous solutions, it can be used to purify aqueous extract containing the preparation.

CONCLUSION

The extraction of bisoprolol fumarate by organic solvents from water solutions in dependence on pH solutions has been conducted by RP-HPLC method. As a result of studies, we have found that the optimal extragent is chloroform, which is extracted at pH 10–92.57% and methylene chloride is extracted at pH 10–90.08%. We have found that bisoprolol fumarate least extracted with hexane, so these conditions may be cleaned extracts from coextractives impurities.

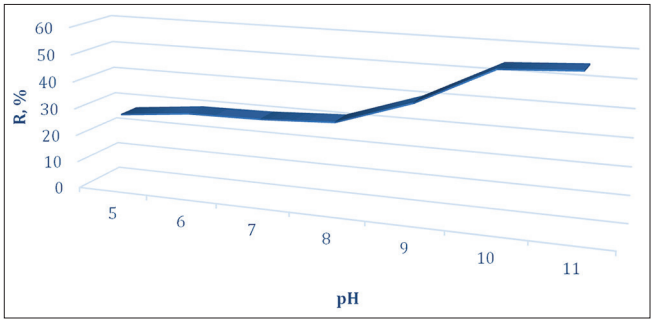

Figure 4: The dependence on the degree of extraction of bisoprolol fumarate on pH solutions and nature of organic solvents (hexane)

Table 1: Optimized chromatographic conditions

Parameter	Chromatographic conditions
Instrument	ACQUITY Arc System
Column	Waters Symmetry C18 column (3.9 mm i.d. × 150 mm, 5 μm)
Mobile phase	Acetonitrile: Phosphate buffer solution pH 7.0 (25/75, v/v)
Flow rate	1.4 mL/min
Detection wavelength	UV at 226 nm
Runtime	10 min
Column temperature	35°C
Volume of injection loop	10 μL
Retention time	2.09 min

UV: Ultraviolet

REFERENCES

1. Available from: https://pubchem.ncbi.nlm.nih.gov.
2. Namiesnik J, Szefer P. Preparing samples for analysis-the key to analytical success. Ecol Chem Eng S 2008;15:167-244.
3. Zala SP, Patel KP, Patel KS, Parmar JP, Sen DJ. Laboratory technique of purification and isolation. Int J Drug Dev Res 2012;4:41-55.
4. Clarke EJ. Isolation and Identification of Drugs in Pharmaceuticals, Body Fluids and Postmortem Material.

London: The Pharm.Press, Electr. Version; 2005.
5. Polyauk O, Logoyda L. The investigation of conditions of API from group of calcium channel blockers extraction by organic solvents by using high-performance liquid chromatography as assay method. Asian J Pharm Clin Res 2017;10:354-6.
6. Logoyda L, Korobko D, Oleshchuk O, Proniv T, Dmutriv M. A HPLC MS/MS method development and validation for the simultaneous determination of bisoprolol and enalapril in the present of enalaprilat in human plasma. Int J Appl Pharm 2018;10:54-9.
7. Arjun G, Sathis KD, Bindu MB, Naga MM, Ramalingam R, RavinderNath A. A simple HPLC method for quantitation of bisoprolol fumarate in tablet dosage form. Indian Drugs 2009;46:39-42.
8. Yadav SS, Rao JR. Simultaneous HPTLC analysis of bisoprolol fumarate and hydrochlorthiazide in pharmaceutical dosage form. Int J Pharm Pharm Sci 2013;5:286-90.
9. Joshi SJ, Karbhari PA, Bhoir SI, Bindu KS, Das C. RP-HPLC method for simultaneous estimation of bisoprolol fumarate and hydrochlorothiazide in tablet formulation. J Pharm Biomed Anal 2010;52:362-71.
10. Shaikh S, Thusleem OA, Muneera MS, Akmal J, Kondaguli AV, Ruckmani K. A simple and rapid high-performance liquid chromatographic method for the determination of bisoprolol fumarate and hydrochlorothiazide in a tablet dosage form. J Pharm Biomed Anal 2008;48:1055-7.
11. Patel LJ, Suhagia BN, Shah PB, Shah RR. Simultaneous estimation of bisoprolol fumarate and hydrochlorothiazide in tablet dosage form by RP-HPLC method. Indian J Pharm Sci 2006;68:635-8.
12. Vora DN, Kadav AA. Development and validation of a simultaneous HPLC method for estimation of bisoprolol fumarate and amlodipine besylate from tablets. Indian J Pharm Sci 2008;70:542-6.
13. Bozal B, Gumustas M, Dogan-Topal B, Uslu B, Ozkan SA. Fully validated simultaneous determination of bisoprolol fumarate and hydrochlorothiazide in their dosage forms using different voltammetric, chromatographic, and spectrophotometric analytical methods. J AOAC Int 2013;96:42-51.
14. Liliya L, Dmytro K, Olena S, Ihor B, Tamara K. Development of methodology for identification of captopril in medicines. Asian J Pharm 2016;10:168-71.
15. Logoyda L, Korobko D, Ivanusa I, Serhii K. Development of the methodology of the chromatographic determination of nifedipine in medicines. Asian J Pharm Clin Res 2017;10:149-52.
16. Logoyda L, Kondratova Y, Korobko D, Susla O, Soroka Y, Tsytsiura R. Youden's test of the chromatographic determination of captopril in pharmaceuticals. Int J Green Pharm 2017;11:188-91.
17. Logoyda L, Kondratova Y, Korobko D, Soroka Y. Development of UHPLC method for the determination of captopril in pharmaceutical dosage forms. Asian J Pharm Clin Res 2017;10:308-10.
18. Kondratova Y, Logoyda L, Voloshko Y, Abdel-Megied A, Korobko D, Soroka Y. Development and validation of HPLC-DAD method for the determination of bisoprolol in tablet dosage forms. Int J Appl Pharm 2017;9:54-9.
19. Logoyda L, Abdel-Megied AM, Kondratova Y, Trofimenko O, Korobko D, Dakhym I. Development and validation of HPLC method for the simultaneous determination of enalapril maleate in present of their impurities: Application to tablet analysis. Int J Appl Pharm 2018;10:98-102.
20. Cannell RJ. Natural Products Isolation. New Jersey: Human Press Inc; 1998. p. 165-208.
21. Fan XH, Cheng YY, Ye ZL, Lin RC, Qian ZZ. Multiple chromatographic fingerprinting and its application to the quality control of herbal medicines. Anal Chim Acta 2006;555:217-24.
22. Scheibe A, Krantz L, Gleixner G. Simultaneous determination of the quantity and isotopic signature of dissolved organic matter from soil water using high-performance liquid chromatography/isotope ratio mass spectrometry. Rapid Commun Mass Spectrom 2012;26:173-80.
23. Mohammadi B, Majnooni MB, Khatabi PM, Jalili R, Bahrami G. 9-Fluorenylmethyl chloroformate as a fluorescence-labeling reagent for derivatization of carboxylic acid moiety of sodium valproate using liquid chromatography/tandem mass spectrometry for binding characterization: A human pharmacokinetic study. J Chromatogr B Anal Technol Biomed Life Sci 2011;9:25-8.
24. Xu RN, Fan L, Rieser MJ, El-Shourbagy TA. Recent advances in high-throughput quantitative bioanalysis by LC-MS/MS. J Pharm Biomed Anal 2007;44:342-55.
25. Liliya L, Dmutro K, Stanislav S. Development of methods for identification of calcium channel blockers in medicines. Int J Res Ayurveda Pharm 2016;7(2):88-91.
26. Kondratova Y, Adebayo T, Logoyda L, Korobko D, Berdey I, Kuchmerovska T. Development of the methodology of the chromatographic determination of amlodipine in medicines. Int J Res Ayurveda Pharm 2016;7(4):32-35.