RESEARCH ARTICLE

Ultra-high-performance Liquid Chromatography as an Assay Method for the Investigation of Conditions of Captopril Extraction by Organic Solvents

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Abstract

Introduction: In recent years, the principle and theory behind solvent extraction has gained wide acceptance as one of the new tools of modern pharmaceutical analysis. Analytical chemists have been using solvent extraction in the laboratory for many years for extracting molecular species from aqueous solutions by organic solvents. However, the requirements and objectives of an analytical procedure are quite different from those of a profit producing mill flow sheet. Depending on the nature, aggregate state, sample concentration and method of analysis, and various sampling procedures are used: Moisture removal, grinding, decomposition, dissolution, melting, elution, removal of the matrix, dilution, concentration, etc. The objective of this research was to select the optimal conditions for the extraction for captopril by organic solvents from water solutions in dependence on pH solutions. **Materials and Methods:** The chromatographic analysis of captopril performed on liquid chromatography ACQUITY Arc system. **Results:** The obtained data testify that the optimal solvents for the extraction of captopril in the process of separating it from objects of biological origin are chloroform and methylene chloride. The amount of substance released by chloroform is 91.48% (at pH 1), methylene chloride is 97.97% (at pH 1), and hexane is 69.65% (at pH 2). **Conclusion**: The extraction of captopril by organic solvents from water solutions in dependence on pH solutions has been conducted. As a result of studies, we have found that the optimal extragent is methylene chloride, which is extracted at pH 1–97.97% and chloroform is extracted at pH 1–91.48%.

Key words: Captopril, extraction, organic solvents, ultra-high-performance liquid chromatography

INTRODUCTION

In recent years, the principle and theory behind solvent extraction has gained wide acceptance as one of the new tools of modern pharmaceutical analysis. Analytical chemists have been using solvent extraction in the laboratory for many years for the extraction of molecular species from aqueous solutions by organic solvents. However, the requirements and objectives of an analytical procedure are quite different from those of a profit producing mill flow sheet. Depending on the nature, aggregate state, sample concentration and method of analysis, and 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 in the suitable solvent or in two non-mixing solvents.

Captopril [Figure 1] is an angiotensin-converting enzyme inhibitor used for the treatment of hypertension and some types of congestive heart failure. Captopril's main uses

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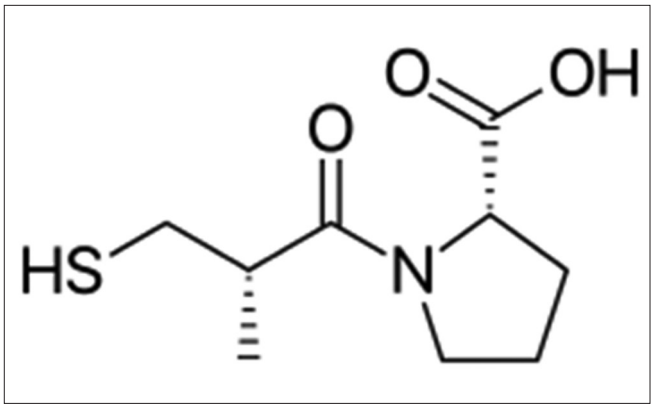

Figure 1: Chemical structure of captopril

are based on its vasodilation and inhibition of some renal function activities. These benefits are most clearly seen in (1) hypertension, (2) cardiac conditions such as congestive heart failure and after myocardial infarction, and (3) preservation of kidney function in diabetic nephropathy. A literature survey was conducted and several methods were reported for the investigation of conditions of some active pharmaceutical ingredients (API) extraction by organic solvents. However, no ultra-high-performance liquid chromatography (UHPLC) methods for the investigation of conditions of captopril extraction by organic solvents.[1,2]

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

MATERIALS AND METHODS

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 UHPLC method. We have chosen organic solvents due their use in the pharmaceutical analysis of drugs for the isolation and purification of extracts from biological material such as chloroform, methylenechloride and hexane.

Captopril was obtained as a gift from Ternofarm pharmaceuticals (Ternopil, Ukraine). HPLC grade methanol and trifluoroacetic acid were obtained from Merck pharmaceuticals.

To investigate the degree of captopril from aqueous solutions of organic solvents used standard solutions, which was prepared with concentrations: Standard solution concentration of captopril is 10 μg/ml in 0.01 mol/l hydrochloric acid. Assay performed using previously developed conditions.[3-8] Research of captopril 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 2.00 ml of standard solution of captopril; 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.

Collected organic layers 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 UHPLC 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. The pH installed in the application of pH meter - pH 150 MI (2011, Russia).

The chromatographic analysis of captopril performed on liquid chromatography ACQUITY Arc system.

Chromatography was performed on liquid chromatography with spectrophotometric detector using Fused-Core® technology Ascentis Express C18 column (4.6 150 mm).

Chromatographic analysis was carried out at ambient temperature (22°C–25°C). The compound was separated isocratically with a mobile phase consisting of methanol and 0.1% solution of trifluoroacetic acid (40/60, v/v) at a flow rate of 1.2 mL/min with injection volume 2 μL. The effluent was monitored spectrophotometrically at wavelength of 220 nm. Column temperature was 35°C.

RESULTS

For elaboration of the method, the chromatograms of the standard solution of captopril [Figure 2], as well as the dependence on the intensity peaks on the retention time were obtained and analyzed.

DISCUSSION

In previous studies,[3-8] specific, sensitive, and rapid HPLC methods had been developed and validated for the quantification of captopril in dosage forms and in human plasma. We have not found any study which shows optimal conditions for extraction of captopril by organic solvents from water solutions in dependence on pH solutions using UHPLC.

In this study, our first trials were directed to find optimal chromatographic conditions. Our objective of the chromatographic method development was to achieve a peak tailing factor <1.5, retention time in between 1 and 3 min, along with good resolution.[9-11] Ascentis express columns, based on Fused-core particle technology, provide more than twice the speed and efficiency of traditional columns at half the backpressure of sub-2-μm columns. This objective was obtained using mobile phase consisting of methanol and

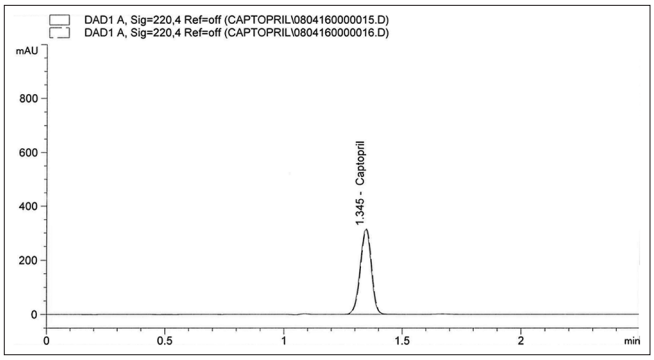

Figure 2: Chromatogram of the standard solution of captopril by ultra-high-performance liquid chromatography in terms of the quantification of captopril

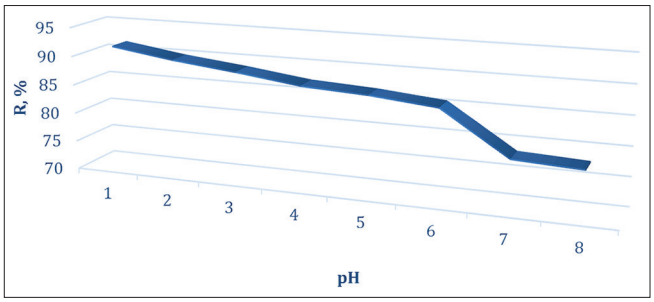

Figure 3: The dependence on the degree of extraction of captopril on pH solutions and nature of organic solvents (chloroform)

0.1% solution of trifluoroacetic acid (40/60, v/v). The mobile phase composition was optimized under the described conditions, the analyte peak was well defined, resolved, and free from tailing, the tailing factor was <1.5 for all peak. The elution orders were captopril (tR 1.345) at a flow rate of 1.2 mL/min.

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

Results of the study are shown in Figures 3-5 and indicate that captopril is extracted with used organic solvents. The area of maximum extraction for most solvents is observed at pH 1–2. The obtained data testify that the optimal solvents for the extraction of captopril in the process of separating it from objects of biological origin are chloroform and methylene chloride. The amount of substance released by chloroform is 91.48% (at pH 1), methylene chloride is 97.97% (at pH 1), and hexane is 69.65% (at pH 2).

CONCLUSION

The extraction of captopril by organic solvents from water solutions in dependence on pH solutions has been conducted. As a result of studies, we have found that the optimal extragent

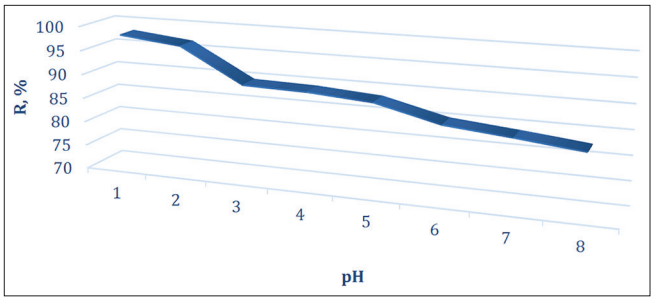

Figure 4: The dependence on the degree of extraction of captopril on pH solutions and nature of organic solvents (methylene chloride)

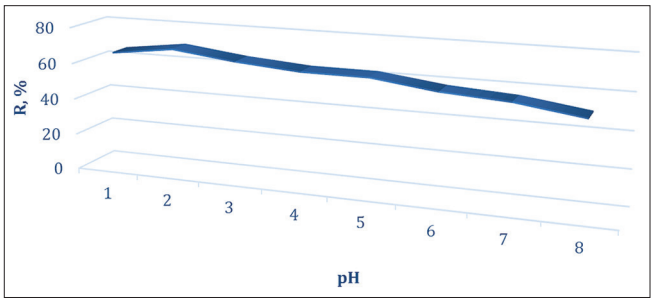

Figure 5: The dependence on the degree of extraction of captopril on pH solutions and nature of organic solvents (hexane)

is methylene chloride, which is extracted at pH 1–97.97% and chloroform is extracted at pH 1–91.48%.

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