Journal of Chromatography B, 1021 (2016) 221–228

Contents lists available at ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/chromb

Determination of roxithromycin from human plasma samples based on magnetic surface molecularly imprinted polymers followed by liquid chromatography-tandem mass spectromer.

Jie Ding [a,*], Fengshuang Zhang [b], Xiaopan Zhang [b], Long Wang [b], Changjia Wang [c], Qi Zhao [b], Yang Xu [b], Lan Ding [b], Nanqi Ren [a]

[a] State Key Laboratory of Urban Water Resource and Environment, Harbin Institute of Technology, 202 Haihe Road, Harbin 150090, China
[b] College of chemistry, Jilin University, 2699 Qianjin Street, Changchun 130012, China
[c] Jilin Provincial Health Department Key Laboratory for Infectious Disease, Department of Hepatology, People's Hospital of Jilin Province, Changchun 130021, China

ARTICLE INFO

Article history:
Received 23 March 2015
Received in revised form 17 July 2015
Accepted 1 August 2015
Available online 4 August 2015

Keywords:
Magnetic molecularly imprinted polymers
Surface molecularly imprinted polymers
Roxithromycin
Human plasma
Liquid chromatography–tandem mass spectrometry

ABSTRACT

In this paper, a simple and reproducible method for the determination of roxithromycin in human plasma samples is proposed. The surface magnetic molecularly imprinted polymers (MMIPs) were utilized as sorbent. Roxithromycin was used as imprinted compound. The experimental results showed that the MMIPs had high affinity and selectivity toward roxithromycin. The extraction process was carried out in a single step by mixing the extraction solvent, MMIPs and human plasma samples by vortex. When the extraction process was completed, the MMIPs adsorbed the analyte were separated from the sample matrix by an external magnet due to the magnetism. The analyte eluted from the MMIPs was analysed by liquid chromatography-tandem mass spectrometry. Some main factors affecting the extraction of roxithromycin such as the amount of MMIPs, extraction solvent, extraction time, washing and elution conditions were optimized in this study. The calibration curve obtained by analyzing matrix-matched standards showed excellent linear relationship ($r^2 = 0.9997$) in the concentration range of 10–1000 ng mL^{-1}. The limit of detection and quantification obtained were 3.8 and 9.8 ng mL^{-1}, respectively. The relative standard deviations of intra- and inter-day obtained were in the range of 3.9 %–5.5 % and 2.9 %–4.6 % with the recoveries ranging from 86.5 % to 91.5 %.

1. Introduction

Roxithromycin is a semi-synthetic 14-membered ring macrolide antibiotic, which is derived from erythromycin [1]. Roxithromycin is more effective than other macrolides for a wide range of infections and has been clinically used for the treatment of respiratory infections [2,3] . After oral dosing a very high concentration of roxithromycin is achieved in pulmonary, prostatic, and tonsillar tissues [4] . Therefore, it is necessary to establish a simple and effective method for the determination of roxithromycin in biological fluids such as human plasma.

Recently, a variety of analytical methods have been published for the determination of roxithromycin, such as liquid chromatography (LC) with fluorescence and UV absorbance detection [5–9], fluorimetry [10], spectrophotometric detection [11], fluorescence detection [12] and mass spectrometric detection [13–15]. Compared with the methods above, LC with tandem mass spectrometry (LC-MS/MS) is the most selective and sensitive technique for identification and quantification of roxithromycin [16–19] .

Because of the relatively low concentrations of roxithromycin and the inherent complexity of the plasma samples, the preconcentration and clean-up steps are necessary for the reliable determination of these compounds, prior to their analysis. Nowadays, the papers which have reported that the conventional sample preparation techniques for the determination of roxithromycin in plasma was liquid–liquid extraction [20,21], column-switching [20] or solid phase extraction (SPE) [22,23] and so on. SPE is the most commonly used technique for clean-up and preconcentration of the analytes in human plasma samples. In an SPE procedure, a desired adsorbent is an important factor to obtain good recovery, high enrichment factor and reduce the interfer ing substances for detection of analytes. Consequently, the adsorbents with good adsorption efficiency, highly stability and selectivity should be developed.

* Corresponding author. Fax.: +86 0451 86282193.
E-mail address: dingjie123@hit.edu.cn (J. Ding).

http://dx.doi.org/10.1016/j.jchromb.2015.08.001
1570-0232/

Molecularly imprinted polymers(MIPs) are of particular interest because of the high selectivity to target molecules. In the reported preparation methods, such as emulsion [24], precipitation [25,26], suspension and multistep swelling polymerization [27], film graft imprinting [28] and surface imprinting[29], surface imprinting technique is welcome because the binding sites situated at the surface of the polymers. This special structure could show many advantages, such as high selectivity, enhanced adsorption, more accessible sites, fast mass transfer and binding kinetics [30]. In addition, it have been reported that the molecule imprinted polymers synthesized by surface imprinting technology could exhibit controllable size, regular shape, better mechanism intensity, and good reuse performance which are much better than the traditional imprinting materials [31–35].

The molecularly imprinted polymers for erythromycin have previously been synthesized by precipitation polymerization [36] and have been used as adsorbent for the solid-phase extraction of erythromycin from pig muscle and chicken muscle [37,38]. Roxithromycin is derived from erythromycin. It was reported to be absorbed rapidly with the long elimination half time, giving higher plasma levels than erythromycin [5].Therefore, it is important to establish a method to determine the concentration of roxithromycin in human plasma. To the best of our knowledge, no method has been reported for the separation and determination of roxithromycin in human plasma based on MMIPs.

In recent years, because of the rapid and easy sample preparation procedure and the great potential for applications, magnetic separation technique has received much considerable attention. If the magnetic separation technique and the SPE are combined together, the new technique is magnetic SPE (MSPE). The new technique has been often reported in application due to the rapid and easy sample preparation procedure [39]. If some magnetic components are encapsulated into MIPs, the resulting composite polymer, magnetic MIPs (MMIPs) will have not only magnetically susceptible characteristic but also selectivity for the guest molecule [40].

In this work, the MMIPs with roxithromycin as imprinted compound was synthesized and used as adsorbents for the extraction of roxithromycin from human plasma samples, followed by LC–MS/MS analysis. After mixing the extraction solvent, MMIPs and human plasma samples by vortex, the MMIPs adsorbing target analyte can be separated from the sample matrix by an external magnet. Compared with conventional method, the sample pretreatment procedure has been simplified and the time consuming use of column has been avoided. In addition, this method showed high extraction recovery and sensitivity, which revealed great potential for analysis of some complex samples.

2. Experimental

2.1. Reagents and chemicals

The standard of roxithromycin (99.8%) was purchased from National Institute for the Control of Pharmaceutical and Biological Products(Beijing, China). It chemical structure is shown in Fig. 1a. Chromatographic grade methanol and acetic acid were obtained from Fisher (Pittsburgh, PA, USA). Ethylene glycol dimethacrylate (EGDMA) was purchased from Sigma–Aldrich (St. Louis, MO, USA). Methacrylic acid (MAA), isopropanol, tetramethylsilane (TEOS), silane coupling agent trimetoxysilylpropylmethacrylate (KH570), ammonia, iron (II) chloride tetrahydrate ($FeCl_2{\cdot}4H_2O$), iron (III) chloride hexahydrate ($FeCl_3{\cdot}6H_2O$), oleic acid, polyvinylpyrrolidone (PVP), azobisisbutyronitrile (AIBN) and formic acid were obtained from Guangfu Fine Chemical Research Institute (Tianjin, China). Methanol, ethanol and acetic acid were purchased from Beijing Chemical (Beijing, China). These reagents are analytically pure.

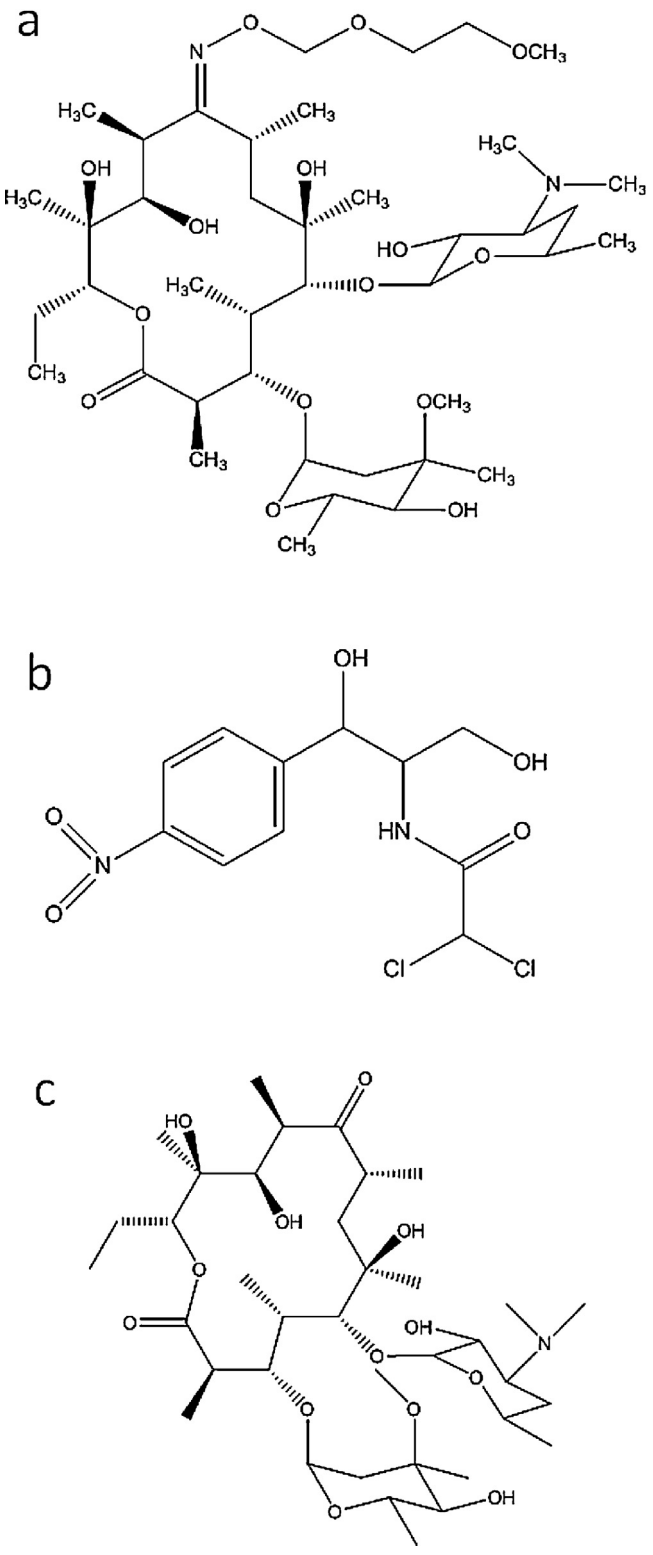

Fig. 1. Chemical structure of roxithromycin (a), chloramphenicol (b) and erythromycin (c).

The deionized water with resistivity of 18.2 MΩ cm^{-1} was obtained from a Milli-Q water system (Millipore, Billerica, MA, USA). And other analytes were purchased from National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China) and were analytically pure.

A stock solution of roxithromycin (1.0 mg mL^{-1}) was weekly prepared by dissolving roxithromycin in deionized water and