Journal of Electroanalytical Chemistry 751 (2015) 75–79

Contents lists available at ScienceDirect

Journal of Electroanalytical Chemistry

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

Azithromycin-molecularly imprinted polymer based on PVC membrane for Azithromycin determination in drugs using coated graphite electrode

Muna A. Abu-Dalo [a,*], Nabil S. Nassory [a], Najwa I. Abdulla [b], Ismaeel R. Al-Mheidat [a]

[a] Jordan University of Science and Technology, Faculty of Science and Arts, Department of Chemistry, P.O. Box 3030, Irbid 22110, Jordan
[b] Chemistry Department, College of Education (Ibn Al-Haitham), University of Baghdad, Adamya, Baghdad, Iraq

ARTICLE INFO

Article history:
Received 23 October 2014
Received in revised form 21 May 2015
Accepted 22 May 2015
Available online 27 May 2015

Keywords:
Azithromycin
Molecular imprinted polymer
Coated graphite electrode
Binding capacity

ABSTRACT

Several molecular imprinted polymer (MIP) membranes for Azithromycin (Azin) coated on graphite electrodes were constructed based on PVC matrix. The Azin-imprinted polymers (MIP) were prepared by thermal polymerization using acrylic acid (AA) and 2-vinyl pyridine (VPY) as monomers, ethylene glycol dimethacrylate (EGDMA) as a cross linker in the presence of benzoyl peroxide (BPO) as an initiator. Two plasticizers di-butyl phosphate (DBP) and di-octyl phthalate (DOP) were used in this study. Electrode parameters such as Nernstian slopes, concentrations, pH and interferences were studied. The results of Azin-MIP electrodes, which based on AA and VPY as monomers with DBP plasticizer, show fully Nernstian slopes. For MIP electrodes using DOP plasticizer the slopes were 49.1 and 51.3 mV/decade, respectively. Excellent detection limits for the electrodes around 10^{-7} M were obtained. Life times of MIP were more than four months. The pH range for the electrodes from 3.0 to 8.0 shows no change in the electrode response and a response time around 30 s was noticed for low concentrations of Azin. The effect of some cations and neutral species interferences on electrode response was also studied. Standard addition method using graphite MIP electrode was applied for Azin determination in commercial tablets and capsules of Azin drug. The results obtained by the MIP electrode were compared with the official spectrophotometric method. The binding capacity between polymer of AA as a monomer and Azin as a template was also investigated.

1. Introduction

Molecular imprinted polymer (MIP) is a selective technique for binding sites of template with highly cross-linked polymers. The concept of molecular imprinted polymer involves the following steps: self-assembly of template and functional monomers to form covalent or non-covalent bonds, polymerization process, extraction of template and rebinding of analyte. MIP is prepared from reaction of a template, functional monomer, a cross linking monomer, and a polymerization initiator in solvent. The development of synthetic membranes with molecular imprinted functionality is an important approach for future functional separation or purification materials [1]. Cheong et al. [2] reviewed MIP for separation science. The reviews in recent ca. 10 years were categorized into several subgroups according to specified topics in separation science and different fields.

Azithromycin (Azithromax, Azithrocin, Zmax, Azin) is an azalide with the formula $C_{38}H_{72}N_2O_{12}$ (748.984 g/mol) and has been used to treat many different types of infections caused by bacteria, such as respiratory infections, skin infections, and air infections. It is also effective against certain sexually transmitted infections, such as non-gonococcal urethritis, chlamydia, and cervicitis. Recent studies have also indicated it to be effective against late-onset asthma but this finding is controversial and not widely accepted [3,4].

Four types of Azin sensors were fabricated by Al-Arfaj and Tohamy [5], PVC plastic membrane, coated wire, carbon paste and modified multi-wall carbon nanotube carbon paste. These electrodes based on the incorporation of Azin with phosphotungstic acid and exhibited Nernstian slopes ranged from 55.1 to 58.04 mV/decade and were used for the determination of Azin in pharmaceutical dosage and biological fluids.

Several papers were published concerning electrodes preparation based on drug molecular imprinted polymer in PVC matrix membranes, a PVC membrane based on metoprolol-MIP using graphite electrode [6], solid-state ISE based on molecular imprinted polymer and graphite electrode [7], diphenylamine [8], hydroquinone [9], aspirin [10], ascorbic acid [11], sertraline [12] and ciprofloxacin [13]. Several ionic imprinted polymers (IIP) were

* Corresponding author.
E-mail address: maabudalo@just.edu.jo (M.A. Abu-Dalo).

http://dx.doi.org/10.1016/j.jelechem.2015.05.030
1572-6657/

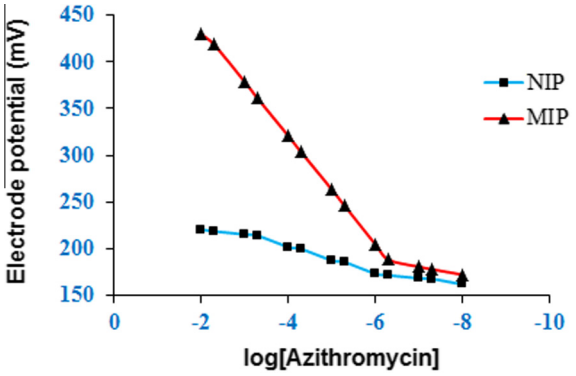

Fig. 1. Calibration curve of MIP and NIP (Azin + AA) graphite electrodes based on DBP plasticizer (membranes no. 1 and 2).

published such as; cadmium IIP [14], iron [15], dysprosium (III) [16] and thorium (IV) [17]. Dextromethorphan hydrobromide (DM) selective electrodes based on molecularly imprinted polymer in PVC have been constructed by Al-Mustafa et al. [18] and used for DM determination in pharmaceutical formulations.

Jayanna et al. [19] described a simple, sensitive, accurate, precise and economical visible spectrophotometric method for estimation of Azin in tablet formulation.

Peng et al. [20] have used cyclic voltammetry for the determination of Azin with ionic liquid-graphene and modified glassy carbon electrode. Azin produced an anodic peak at about 0.82 V and the method was successfully applied to determine the studied drug in the pharmaceutical dosage forms. Mallah et al. [21] developed a simple, rapid and economical method for Azin quantification in solid tablet by applying FTIR transmission spectroscopy. HPLC method has been developed and validated by Trivedi and Patel [22] to measure the amount of Azin in pharmaceutical formulation. Sayed et al. [23] developed spectrophotometric and conductivity methods for the estimation of Azin and other antibiotics in both pure and pharmaceutical forms. Sensitive and selective LC–MS methods were developed by Zuak et al. [24] and validated for the quantification of Azin in human plasma.

While accurate, these analytical approaches often require tedious sample preparations which include liquid extractions, and thus can be time consuming and expensive. The development of rapid and sensitive analytical methods for Azin determination is of importance because antibiotics are the most widely prescribed class of drugs and their environmental risks, which are associated with their use, are unknown. In this work, we report the development and application of sensitive and selective sensors for Azin by a thermal polymerization method. The developed sensors were very sensitive and selective indicating their potential use for Azin determination in pharmaceutical and environmental samples. The advantages of using molecular imprinted polymer (MIP) sensors in this application are the following: short response time, good stability, good sensitivity and selectivity, and long life time.

2. Experimental

2.1. Apparatus

All potentiometric measurements were made at room temperature with a millivolt-meter type PW 9421 conjugated with SCE as a reference electrode type K 401. The pH values were recorded using pH meter model BP 3001. The potential measurements were made with a moderate stirring at a sensitivity value of 0.1 mV. Construction of the electrode body and immobilization of Azin-MIP in the PVC matrix membrane have been done using the method given by Craggs et al. [25]. Centrifuge model Hermle-Z200A and UV/Visible spectrophotometer model 9423 UVG, Thermo Electron, USA have been used for method validation.

2.2. Reagents

The chemicals used were reagent grades with the highest purity and were used as received without further purification from Acros Organics (USA); acrylic acid (AA) purity (99.5%), 2-vinyl pyridine (VPY) (97%), benzoyl peroxide (BPO) (75%), ethylene glycol dimethacrylate (EGDMA) (98%), di-octyl phthalate (DOP) (99%), di-butyl phosphate (DBP) (99%) and methanol (99.8%).

HPLC grade of Tetrahydrofuran (THF) obtained from TEDIA company, Inc. (USA). Azithromycin (Azin) was a gift from a Jordanian pharmaceutical company. All aqueous solutions were made in deionized water with electrical conductivity of 0.1 $\mu S\,cm^{-1}$. Azin concentration for spectrophotometric method ranged from 0 to 20 ppm. $KMnO_4$ obtained from PS PARK LTD (UK), and K_2CO_3 obtained from MAY & BAKER LTD (ENGLAND).

A stock solution of Azin was freshly prepared daily by weighing an appropriate amount of the drug and dissolving it in 1:1 methanol–water, sonicated for 10 min. Working solutions were prepared by appropriate dilution with deionized water.

The Azithromycin tablets and capsules were purchased locally; Azro 500 mg tablets from Zentiva-Turkey, Azomycin 250 mg capsules from Julphar-U.A.E., Zomax 250 mg tablets from Hikma-Jordan and Zimax 250 mg capsules from Spimco-K.S.A.

2.3. Synthesis of the imprinted polymer

In a 50 mL screw cap glass test tube, 0.5 mmol Azin, 3.0 mmol (0.22 g) of the monomer (AA or VPY), 15 mmol (2.79 g) of the cross-linker EGDMA, 0.32 mmol of the initiator BPO and 4 mL of methanol were added. The solution was degassed for 10 min with high purity nitrogen and cured at 70 °C for 2 h. The polymer was dried and crushed and the template (Azin) was removed by repeated washing with 30% acetic acid in water. The polymer was dried at 60 °C for 24 h. The polymer was then ground and sieved and the particles with size 90–150 μm were collected and used in the preparation of the sensing membrane. The non-imprinted polymer (NIP) was made in the same way but without the template drug.

Table 1
Specific parameters of graphite electrode based on Azin MIP and NIP membranes.

Membrane no.	Electrode	Plasticizer	Slope (mV/decade)	R^2	Concentration range (M)	Detection limit (M)
1	MIP (Azin + AA)	DBP	57.1	0.9998	1×10^{-2}–5×10^{-7}	2.0×10^{-7}
2	NIP (Azin + AA)	DBP	12.2	0.9878	1×10^{-3}–1×10^{-6}	–
3	MIP (Azin + VPY)	DBP	54.2	0.9987	1×10^{-2}–5×10^{-6}	2.0×10^{-6}
4	NIP (Azin + Vpy)	DBP	25.1	0.9984	1×10^{-2}–5×10^{-5}	–
5	MIP (Azin + AA)	DOP	49.1	0.9996	1×10^{-2}–6×10^{-7}	5.0×10^{-7}
6	MIP (Azin + VPY)	DOP	51.3	0.9983	1×10^{-2}–2×10^{-6}	7.0×10^{-7}