SHORT COMMUNICATION

Nano-sized Amitriptyline (AT) imprinted polymer particles: Synthesis and characterization in Silicon oil

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Abstract

Amitriptyline hydrochloride is a highly permeable active pharmaceutical ingredient (API). The function of these drugs is to block the reuptake of the neurotransmitters, norepinephrine and serotonin in the central nervous system. The nano-sized Amitriptyline (AT) imprinted polymer particles were synthesized successfully. The nanoparticles were characterized by Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM) and thermal gravimetric (TG) methods. AT-imprinted polymer was prepared using suspension polymerization in silicon oil with AT as template, Methacrylic acid (MAA) as functional monomer and ethylene glycol dimethacrylate (EGDMA) as cross-linker. As illustrated in SEM images, it is possible to obtain real nano-sized molecular imprinted polymer particles (around 80 nm) with approximately spherical shapes, through the methods and techniques presented and discussed in this study. Thermal analyzes indicated that, an abrupt weight loss for nano-sized MIP was observed at 310°C. This mass loss can be attributed to the loss of nano-sized MIP chain degradation.

Keywords: *Amitriptyline; FT-IR; Nano-sized molecularly imprinted polymer; SEM; TG.*

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INTRODUCTION

Amitriptyline hydrochloride is a highly permeable active pharmaceutical ingredient (API) [1]. It is a tricyclic antidepressant drug most commonly approved for the treatment of major depression [2]. This drug is chemically basic and is in the form of hydrochloride salt (pKa 9.4) in the market [3]. The function of these drugs is to block the reuptake of the neurotransmitters, norepinephrine and serotonin in the central nervous system [4]. Molecularly imprinted polymers (MIPs) have attracted great interest in recent years [5]. During the preparation of MIPs, three-dimension structure cavities were generated after polymerization and template extraction [6, 7]. As the cavities were complementary in size, shape and chemical functionality to that of templates, MIPs possess excellent recognition ability toward template molecules, and these specific binding affinities between the multifunctional MIPs and the target molecule have proven to be valuable for a variety of separation purposes in environmental remediation [8, 9].

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So far, synthesized MIPs have been widely used as selective sorbents in different methods such as solid phase extraction (SPE) [10, 11], solid phase microextraction (SPME) [12, 13], stir barsorptive extraction (SBSE) [14,15], and dispersive liquid-liquid microextraction (DLLME) [16]. They are used as biosensors as well [17-20]. In these techniques, organic solvents are used to extract the analyte from the MIP, pre-concentrate, and analyze it. In this study, we report the synthesis of nano-sized AT imprinted polymer particles were using suspension polymerization in silicon oil nanoparticles that used for example in determination of drugs.

EXPERIMENTAL

Amitriptyline hydrochloride was from Daropakhsh.Co. (Tehran, Iran). And Methacrylic acid (MAA) as functional monomer and ethylene glycol dimethacrylate (EGDMA) as cross-linker and 2,2-azobisisobutyronitrile (AIBN) as initiator were purchased from Merck Chemical Company. Methanol, acetone, acetic acid, sodium hydroxide and all the other chemicals used in this study were of analytical reagent grade obtained from Merck (Germany). Doubly distilled water was used throughout the experiments. The whole procedure and structural characterization of nano-sized AT imprinted polymer particles have been investigated by FTIR, SEM and TGA. The FTIR spectrum was recorded with a model Perkin Elmer spectrum RX1 of Fourier transform infrared spectrometry using a KBr pellet. The SEM pictures were recorded with KYKY Model EM 3200 instrument at the accelerating voltage of 25 kV. Thermo gravimetric analyzer (TG) was used to determine thermal stability of the synthesized AT-imprinted polymer using a TA instrument, Q-5000 model.

Nano-sized MIP preparation

In order to prepare the MIP nanoparticles, UA suspension polymerization in silicon oil was applied. Then, 0.08 mmol of AT, 4.6 mmol of MAA, 9 mmol of EGDMA and 0.02 g of AIBN were dissolved in 5 ml of methanol. Then, 45 ml of silicon oil was purified by a nitrogen gas stream for 10 min. The pre-polymerization mixture was added to silicon oil and then dispersed at 800 rpm for 15 min. Then, the mixture was further mixed by an ultrasonic mixer in order to break the suspended polymerizable droplets into smaller ones [19]. This step lasted about 15 min. Finally, the obtained mixture was put into a water bath and its temperature was fixed at 67°C, for 12 h. The synthesized particles were filtered and washed with petroleum ether and toluene several times. In order to extract AT and the remaining monomers from the polymer networks, the particles were washed with methanol. To extract the AT from the polymer networks, the particles were washed with methanol/acetic acid (90:10, v/v) for 24 h. The MIP was then dried at 40 °C for 1 h.

RESULTS AND DISCUSSION

FT-IR analysis

The resulting MIP was characterized by FTIR. The IR spectra of the unleached AT imprinted polymers were recorded using KBr pellet method (Fig. 1). Except for the regions of~1500-1700cm^{-1},

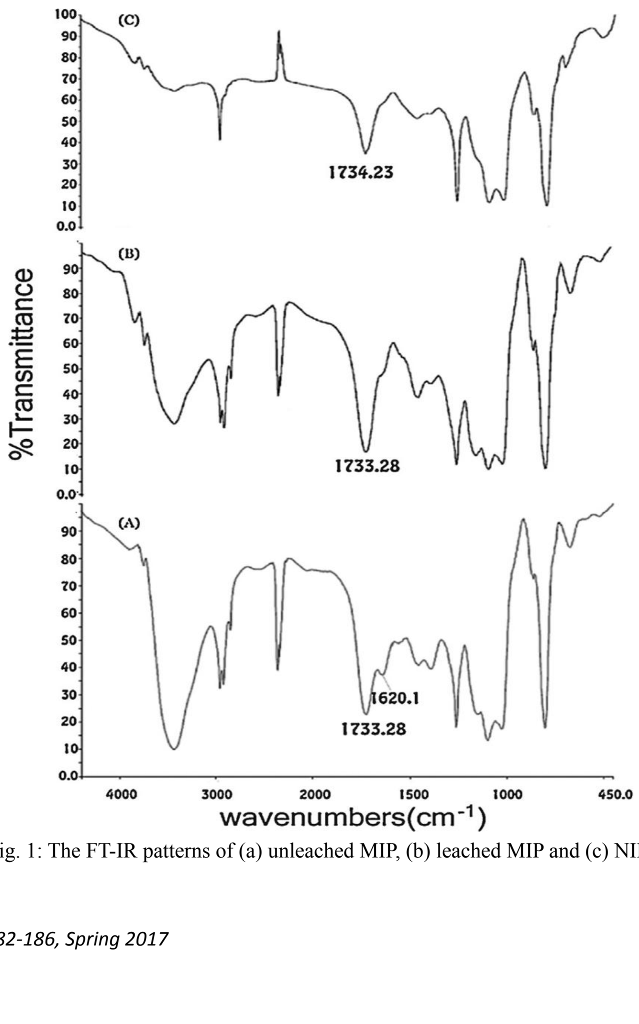

Fig. 1: The FT-IR patterns of (a) unleached MIP, (b) leached MIP and (c) NIP.

no other significant differences were observed among the FT-IR spectra of the polymers which were meticulously examined in all recorded regions.

Fig. 1(a, b and c), illustrate the FT-IR spectra of the unleached MIP, leached MIP, and also NIP respectively. The perceived strong stretching vibration band ~1733cm^{-1} is due to the –C=O of carboxylic acid group of methacrylic acid, which are mostly located at the polymeric particle surface. This band can be observed in all of the polymers examined. However, in the region of 1500–1700cm^{-1} for NIP, there are no bands observed. For the unleached MIP at the previously discussed region of (~1620cm^{-1}), a band is clearly noticed, which is considered the result of the –C=O, linked to AT, via coordination bonding. Since these kinds of –C= O groups are mostly located at the interior parts of MIP particles, they are not as strong as the bands at ~1721cm^{-1}. The observations show that MIP washing and AT removal result in considerable reduction of the vibration band height of the –C= O coordinated to AT. These observations and examined evidences prove the presence and efficient interaction of the selective recognition sites in the MIP particles which are produced in the course of the imprinting procedure.

Morphology of samples

Fig. 2 shows the scanning electron microscopy (SEM) image of nano-sized MIP. The sizes of the synthesized polymer particles are at nano-scale range. The SEM images represented in Fig. 2 show the MIP particles produced via suspension polymerization in silicon oil.

As illustrated in these images, it is possible to obtain real nano-sized MIP particles (around 80 nm) with approximately spherical shapes, through the methods and techniques presented and discussed in this study.

Thermo gravimetric analyze

Fig. 3 shows the TGA thermograms of nano-sized MIP. The thermogram of pure nano-sized MIP shows that the mass loss begins at around 60◦C and continued up to 90◦C and stable up to 230°C. An abrupt weight loss for nano-sized MIP was observed at 310°C . The initial mass loss is due to the loss of water molecules, the next mass loss can be attributed to the loss of nano-sized MIP chain degradation.

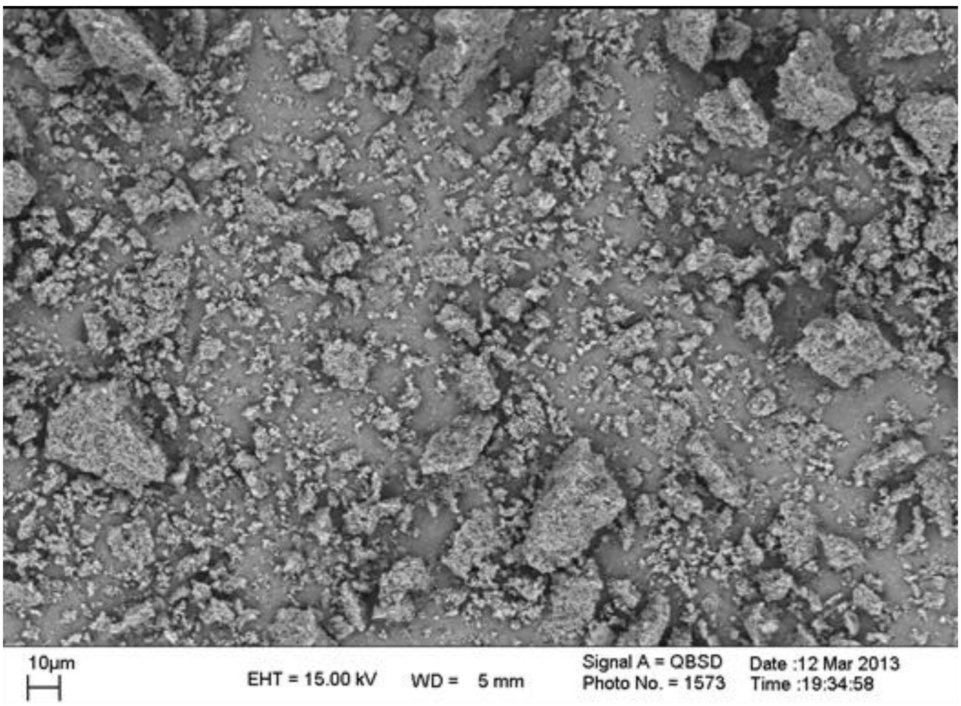

Fig. 2: Scanning electron microscopy images of the nano-sized AT imprinted polymer.

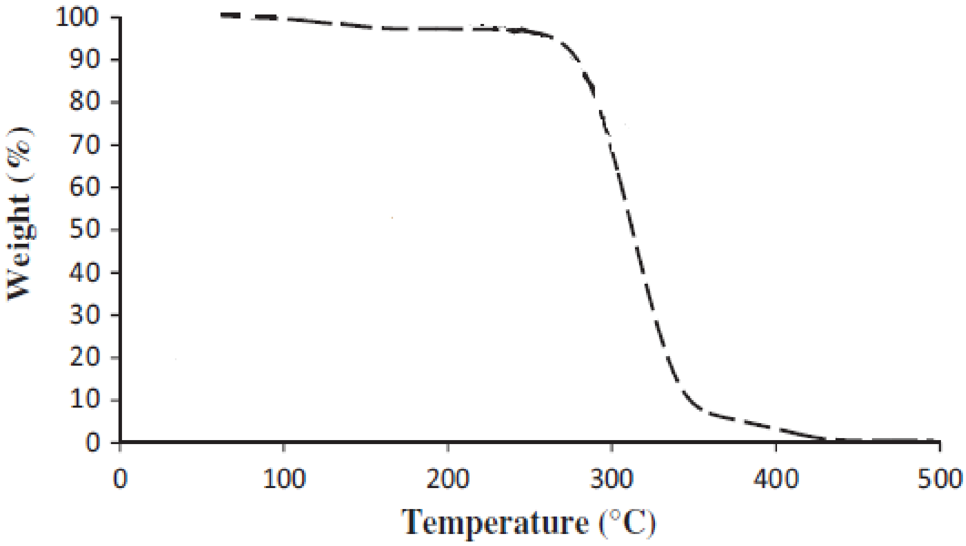

Fig. 3: TGA thermograms of nano-sized MIP.

CONCLUSIONS

The nano-sized AT imprinted polymer particles were synthesized using suspension polymerization in silicon oil and characterized by FT-IR, SEM and TG methods. FT-IR results and examined evidences prove the presence and efficient interaction of the selective recognition sites in the MIP particles which are produced in the course of the imprinting procedure. As illustrated in SEM images, it is possible to obtain real nano-sized MIP particles (around 80 nm) with approximately spherical shapes, through the methods and techniques presented and discussed in this study.Thermal analyzes indicated that, an abrupt weight loss for nano-sized MIP was observed at 310 °C .

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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