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Chiral magnetic nanospheres resonance light scattering properties studies for selective determination of naproxen and phenylglycine enantiomers

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ABSTRACT

In this paper, a method for the analysis of the chiral compounds enantiomeric composition is reported. The method is based on different interaction of the chiral compound enantiomers with chiral modified nanospheres. Light scattering properties of the synthesized nanospheres in the presence and the absence of chiral compounds was chosen as the detection signal. A significant change in the scattering intensity of the nanospheres takes place by the addition of the mixture of the enantiomers of a chiral compound. The results showed that D-(+)-tryptophan modified magnetite nanospheres were very sensitive to (R)-(−)-naproxen and D-(−)-α-phenylglycine and its corresponding RRS signal greatly enhanced in the presence of these enantiomers and L-(−)-tryptophan modified magnetite nanospheres was sensitive to (S)-(+)-naproxen and L-(+)-α-phenylglycine. The proposed method is feasible for sensitive analysis of the model chiral compound in pure form as low as ng L^{-1} concentration levels. The results showed that the synthesized nanospheres have excellent enantioselectivity behaviour in the case of investigated model chiral compounds. The proposed procedure can be used as an efficient method for the precise and accurate enantiomeric composition analysis of the chiral compounds.

1. Introduction

A lot of chemical compounds used in pharmaceutical formulations feature one or more chiral centres. Each enantiomer of these chiral compounds exhibits different biological activities in living systems during biomedical and pharmacological processes. One enantiomer sometimes shows high toxicity while another is effective. Chemical analysis of chiral compounds, due to different physiological and therapeutic properties of their enantiomers, is the concern of science and technology researchers [1–3].

Methods currently available for the analysis of enantiomers are based either on separation techniques such as HPLC [4], capillary electrophoresis [5] and GC [6]; or spectroscopic methods such as circular dichroism [7], spectroflourometry [8], mass spectrometry [9], NMR [10], near infrared spectrometry [11], and room temperature phosphorescence [12]. Separation based techniques validity levels limited to the separation step(s) performance. Furthermore, these methods are expensive and not available in all laboratories. Chirooptical methods (i.e. optical rotatory dispersion and circular dichroism) are able of rapid enantiodiscrimination without the need of separation, but these methods suffer from relatively low sensitivity [1].

To overcome the above mentioned problems, this paper proposes that the enantiomer composition of a chiral compound could be determined by probing the different interaction of enantiomers with chiral nanospheres that lead to different significant resonance light scattering behaviours. This could be done through adding a selected chiral nanospheres (chiral compound modified nanospheres) to the chiral sample until a significant scattering intensity change is observed.

Resonance light scattering (RLS) has emerged as a powerful optical technique based on elastic light-scattering [13–15]. Due to the advantages of high sensitivity, rapidness, simplicity and convenience (using a common spectrofluorometer), RLS has attracted much more attention from analytical chemists and physicists [16]. Recently, RLS has been applied to determine inorganic ions [17], nanoparticles [18], proteins [19–21], nucleic acids [22], etc.

This paper reports a methodology for the enantiomeric ratio analysis of pure chiral compounds without using any separation step. This method could be applied for any type of chiral compounds with any composition variation. In this regard, (S)-(+)-naproxen (+NAP), (R)-(−)-naproxen (−NAP), L-(+)-α-phenylglycine (+PHY)

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and D-(−)-α-phenylglycine (−PHY) were chosen as model chiral compounds. Two type of chiral nanospheres, i.e. D-(+)-tryptophan modified magnetite nanospheres (+MNSs) and L-(−)-tryptophan modified magnetite nanospheres (−MNSs), were synthesized. Light scattering properties of the synthesized nanospheres in the presence and/or the absence of the model chiral compounds was followed by the aid of RLS technique. The results showed that +MNSs were very sensitive to −NAP and −PHY and its corresponding RLS signal greatly enhanced in the presence of these enantiomers. Whereas −MNSs were sensitive to +NAP and +PHY. Therefore, using the proposed method it can be feasible to sensitive analysis of the model chiral compound in pure form (in the absence of any other interfering chiral compound) as low as ng L^{-1} concentration levels.

2. Experimental

2.1. Reagents and materials

(S)-(+)-naproxen (+NAP), (R)-(−)-naproxen (−NAP), L-(+)-α-phenylglycine (+PHY), D-(−)-α-phenylglycine (−PHY), D-(+)-tryptophan and L-(−)-tryptophan were purchased from Sigma–Aldrich company (USA). All the other chemicals used were of analytical reagent grade or highest purity available and were purchased from Merck Company (Darmstadt, Germany). Double distilled water (DDW) was used throughout the work. All glassware were soaked in dilute nitric acid for 12 h and then thoroughly rinsed with DDW. The enantiomers stock solution was prepared in methanol and working standard solutions of different enantiomers concentrations were prepared daily by diluting the stock solution with DDW. Britton–Robinson universal buffer was used for pH adjustment of working solutions.

2.2. Apparatus

The size, morphology and structure of the nanospheres were characterized by transmission electronic microscopy (TEM, Philips-CMC-300 KV). The crystal structure of the synthesized nanospheres was determined by an X-ray diffractometer (XRD, 38066 Riva, d/G. via M. Misone, 11/D (TN) Italy) at ambient temperature. The magnetic properties of the synthesized nanospheres were measured with a vibrating sample magnetometer (VSM, 4 in. Daghigh Meghnatis Kashan Co., Kashan, Iran). The mid-infrared spectra of the synthesized nanospheres in the region 4000–400 cm^{-1} were recorded by an FT-IR spectrometer (Perkin-Elmer model Spectrum GX) using KBr pellets. A Metrohm model 713 pH-metre was used for pH measurements. A 40 kHz universal ultrasonic cleaner water bath (RoHS, Korea) was used. RLS measurements were performed with a Perkin Elmer (LS50B) luminescence spectrometer.

2.3. Preparation of magnetite nanospheres (MNSs) and silica coated magnetite nanospheres (SCMNSs)

MNSs were synthesized by the solvothermal reduction method with minor modifications [23]. $FeCl_3{\cdot}6H_2O$ (1.35 g, 5 mmol) was dissolved in ethylene glycol (40 mL) to form a clear solution, followed by the addition of sodium acetate (3.6 g) and polyethylene glycol (1.0 g). The mixture was ultrasonicated vigorously for 30 min and then refluxed at 180 °C for 8 h, and then allowed to cool down to room temperature. The black products were washed several times with ethanol and DDW water. Then dried at 60 °C for 6 h.

SCMNSs were prepared according to previously reported method with minor modifications [24]. Typically, 0.5 g of MNSs was dispersed in 60.0 mL ethanol and 10 mL of DDW water by sonication for 15 min, followed by the addition of 1.0 mL ammonium hydroxide (25%) and 3.0 mL tetraethoxysilane sequentially. The mixture was reacted for 12 h at room temperature under continuous stirring. The resultant product was collected by an external magnetic field, and rinsed consecutively six times with ethanol and DDW water. Finally, the obtained SCMNSs were dried under vacuum at 60 °C for 3 h.

2.4. Preparation of tryptophan modified SCMNSs

SCMNSs were modified by L- and/or D-tryptophan (named −MNSs and +MNSs, respectively), in similar procedures, in two steps (Scheme 1). In the first step, the surface of SCMNSs was modified by primary amine functional groups by the aid of 3-aminopropyltriethoxysilane reagent using below procedure: typically, 0.8 g of SCMNSs was dispersed in 60.0 mL ethanol and 10 mL of DDW by sonication for 15 min, followed by the addition of 1.0 mL ammonium hydroxide (25%) and 2.0 mL 3-aminopropyltriethoxysilane sequentially. The mixture was reacted for 12 h at room temperature under continuous stirring. The resultant product (NH_2-SCMNSs) was collected by an external magnetic field, and rinsed six times with ethanol and DDW water. Finally, the NH_2-SCMNSs obtained were dried under vacuum at 60 °C for 3 h.

In the second step, the NH_2-SCMNSs were tryptophan-functionalized by reacting with tryptophan in methanolic suspension with the aid of dicyclohexylcarbodiimide (DCC) condensation agent [25]. In a typical procedure, 0.4 g of D- or L-tryptophan were spread in 50 mL methanol at 50 °C and sonicated for 10 min. Then, to this solution, 0.4 g of DCC was added and the solution was stirred for several minutes. Finally 1.0 g of NH_2-SCMNSs was added to the above solution and the solution was stirred again for 24 h at 50 °C. The resultant product was collected by an external magnetic field, and washed to remove the unreacted molecules and the by-products with methanol and DDW water. Finally, the resultant nanospheres obtained were dried under vacuum at 60 °C for 12 h.

2.5. Resonance light scattering (RLS) measurements

RLS measurements were performed with a Perkin Elmer (LS50B) luminescence spectrometer with a 1.0 cm quartz cell, slit width = 10 nm, wavelength scan rate = 500 nm min^{-1}. The magnitude of RLS intensity was obtained by the synchronous scanning at $\lambda_{ex} = \lambda_{em}$ ($\Delta\lambda = 0$ nm). The relative RLS intensity (ΔI_{RLS}) was obtained by the difference between the assay system (I_{RLS}) and the reagent blank (I_0) at 454 nm, namely, $\Delta I_{RLS} = I_{RLS} - I_0$.

2.6. Overall route of the proposed technique for the determination of the model chiral compounds

RLS spectra of dispersed nanospheres were recorded with synchronous scanning at $\lambda_{ex} = \lambda_{em}$ and it was seen that the maximum wavelength of RLS spectra located at 454 nm. In order to selective and sensitive determination of each enantiomer of the selected chiral model compounds, firstly various factors that may potentially affect the scattering efficiency (optimized condition are given Table 1) were optimized using "one-at-a-time" method. Then the calibration curve was constructed for −NAP and/or −PHY using their signal enhancing effect on RLS signal of +MNSs (ΔI_{RLS}) as a function of the pure enantiomers concentrations. In the case of +NAP and +PHY similar route have been performed using their significant interaction with −MNSs.

3. Results and discussion

3.1. Characterization of the investigated nanospheres

Characterization test have been performed on D- and/or L-tryptophan modified MNSs. The results for both modified