C. R. Chimie 18 (2015) 914–928

Contents lists available at ScienceDirect

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Quick and simple formation of different nanosized charge-transfer complexes of the antibiotic drug moxifloxacin: An efficient way to remove and utilize discarded antibiotics

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ARTICLE INFO

Article history:
Received 20 March 2015
Accepted after revision 28 May 2015
Available online 20 August 2015

Keywords:
Moxifloxacin
Nanostructured materials
SEM
TEM
Nanoporous carbon

ABSTRACT

A quick and simple procedure for the synthesis of nanosized complexes of the drug moxifloxacin (MOX) is described. MOX nanoparticles were synthesized via charge-transfer (CT) interactions with the organic acceptors picric acid (PA), chloranilic acid (CLA) and chloranil (CHL). The structure and morphology of these nanoparticles were fully characterized using physicochemical techniques, such as UV–visible, IR, ^{1}H NMR and ^{13}C NMR spectroscopies, XRD, SEM, TEM, and elemental and thermal analyses. Notably, it has been found that the complexation of MOX with an organic acceptor leads to well-organized nanoparticles with a main diameter in the range of 10–20 nm. Interestingly, the direct carbonization of the complex containing the PA acceptor leads to nanoporous carbon material with uniform morphology. This method is an efficient way to remove and utilize discarded MOX antibiotic in other products.

1. Introduction

The study of nanostructured materials has become a popular area of research because of their unique physical and chemical properties. Furthermore, the charge-transfer (CT) or proton-transfer (PT) interactions between drugs or biological compounds and small molecular acceptors have attracted considerable interest because of their unique physical and chemical properties and wide range of applications [1–9]. The chemistry of these interactions is an important topic in pharmacology, chemistry, biology and medicine. Such interactions play crucial roles in many processes; therefore, understanding these interactions is important for understanding drug-receptor binding and the drug's mechanism of action as well as obtaining quantitative estimates of drugs [10–16]. To investigate these roles more fully, the physical and chemical properties of drug-acceptor complexes can be enhanced if the complexes are prepared on the nanoscale. For several years, we have investigated the synthesis, characterization and application of various CT and PT interactions [17–32]. As part of our continuing interest in this field, in this work, we sought to obtain nanoscale CT or PT complexes of the drug moxifloxacin (MOX) with various organic

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http://dx.doi.org/10.1016/j.crci.2015.05.019
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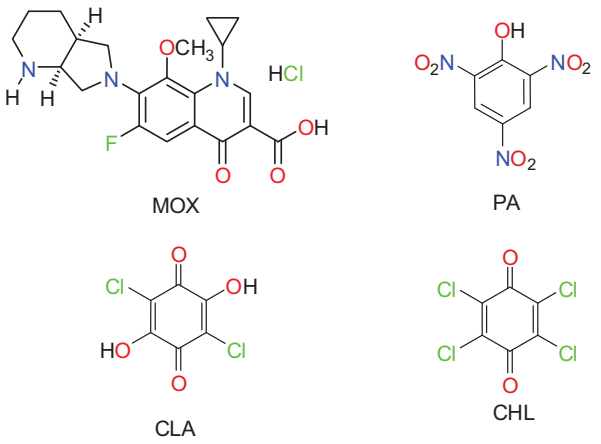

Fig. 1. (Color online.) The structure of drug moxifloxacin (MOX) and organic acceptors.

acceptors and to explore the benefits of CT interactions in removing and utilizing discarded amounts of this drug. MOX, or 1-cyclopropyl-7-(2,8-diazobicyclo[4.3.0]nonane)-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinoline carboxylic acid), is a fourth-generation fluoroquinolone antibiotic. Its structure is shown in Fig. 1. Currently, this drug is being extensively used in the treatment of respiratory system disease for its broad spectrum of antimicrobial activity against respiratory tract pathogens, including Gram-positive and Gram-negative organisms, anaerobic bacteria and atypical respiratory tract pathogens [33]. This work focused on the following objectives:

- synthesizing CT or PT nanoparticles of MOX with different organic acceptors (i.e. PA, CLA and CHL);
- verifying the complexation stoichiometry using CHN elemental analysis and spectrophotometric titrations;
- calculating the formation constant (K), molar extinction coefficient (ε) and other spectroscopic data using the Benesi–Hildebrand equations;
- characterizing the nanoparticles by elemental and spectroscopic data (UV–Vis, IR, ^{1}H and ^{13}C NMR);
- obtaining the thermal properties using TG analysis;
- determining the kinetic – thermodynamic parameters (i.e., E^{*}, A, ΔS^{*}, ΔH^{*}, and ΔG^{*}) using the Coats–Redfern and Horowitz–Metzger methods;
- observing and differentiating the microstructures of these nanoparticles using X-ray diffraction (XRD) and scanning electron microscopy (SEM) techniques;
- proving the nanometry using transmission electron microscopy (TEM);
- carbonizing the complexes to obtain a method for the removal of this antibiotic as porous carbon material.

2. Experiment and calculations

2.1. Chemicals and solutions

All the chemicals used were of analytical grade and were used as purchased. Moxifloxacin hydrochloride (MOX; $C_{21}H_{24}FN_3O_4{\cdot}HCl$; 437.89) was supplied by Sigma–Aldrich Chemical Co. (USA). The organic acceptors picric acid (PA; $C_6H_3N_3O_7$; 229.10), chloranilic acid (CLA; $C_6H_2Cl_2O_4$; 208.98) and chloranil (CHL; $C_6Cl_4O_2$; 245.88) (Fig. 1) were purchased from Merck (Darmstadt, Germany) and used without modification. HPLC-grade methanol was also purchased from Merck (Darmstadt, Germany). Standard stock solutions of the drug MOX and acceptors at a concentration of 5.0×10^{-3} M were freshly prepared prior to each series of measurements by dissolving precisely weighed quantities in a 100 mL volumetric flask. The stock solutions were protected from light. Solutions for spectroscopic measurements were prepared by mixing appropriate volumes of the MOX and acceptor stock solutions with the solvent immediately before recording the spectra.

2.2. Instruments

To ascertain the constituents, purity and compositions of the synthesized complexes, the carbon, hydrogen, and nitrogen contents were analyzed using a PerkinElmer 2400 series CHN microanalyzer (USA). The UV–Vis spectra were recorded in methanol over a wavelength range of 200–800 nm using a PerkinElmer Lambda 25 UV–Vis double-beam spectrophotometer with quartz cells. The path length of the cells was 1.0 cm. The infrared (IR) spectra of the solid products (as KBr discs) were acquired at room temperature using a Shimadzu FT–IR spectrophotometer (Japan) over the range of 4000–400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were collected on a Bruker DRX-250 spectrometer operating at 600 MHz. The measurements were performed at ambient temperature using DMSO-d_6 (dimethylsulfoxide, d_6) as the solvent and TMS (tetramethylsilane) as the internal reference. Thermogravimetric (TG) analysis was performed using a Shimadzu TGA–50H thermal analyzer (Japan) with standard platinum TG pans. The measurements were conducted at a constant heating rate of 10 °C/min over the temperature range of 25–600 °C in a nitrogen atmosphere using alumina powder as the reference material. The X-ray diffraction (XRD) profiles were obtained using a PANalytical X'Pert PRO X-ray powder diffractometer equipped with a Ge(III) secondary monochromator. Cu Kα_1 was employed as the radiation source, with a wavelength of 0.154056 nm. The samples were scanned with 2θ between 5° and 90°. The microstructure and morphology were analyzed by a scanning electron microscope (SEM, Quanta FEG 250 instrument). The instrument was operated at an accelerating voltage of 20 kV. The particle size was analyzed by transmission electron microscope (TEM, JEOL JEM-1200 EX II, Japan). The instrument was operated at an accelerating voltage of 60–70 kV.

2.3. Preparation of materials

2.3.1. Nanoparticle syntheses

A simple synthetic protocol was used for the preparation of nanostructured complexes of MOX. A typical procedure for the preparation is briefly described as follows. First, 2 mmol of MOX in a methanol solvent (20 mL) was added to 20 mL of a solution containing 2 mmol of the acceptor (either PA, CLA or CHL) in the same