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Forced and long-term degradation assays of tenoxicam, piroxicam and meloxicam in river water. Degradation products and adsorption to sediment

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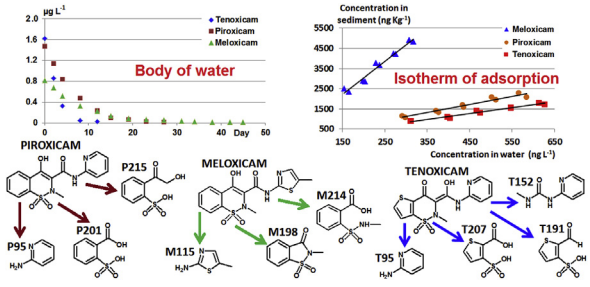
HIGHLIGHTS

- Tenoxicam, piroxicam and meloxicam are not persistent in river water.
- The degradation rate increases in this order: meloxicam, piroxicam, tenoxicam.
- Sunlight promotes their degradation and yields many degradation products.
- Most degradation products arise from the breakdown and oxidation of their moieties.
- The three oxicams have certain capacity of adsorption on a river sediment.

GRAPHICAL ABSTRACT



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ABSTRACT

The fate of the pharmaceutical drugs tenoxicam, piroxicam and meloxicam in river water is evaluated here for first time. So, biological, photochemical and thermal degradation assays have been conducted to estimate their degradation rates and know their degradation products. Results indicated that the direct sunlight irradiation, without any protection, promoted a fast degradation of the oxicams while the chemical reactions in solution were less important. The biological degradation in water was negligible except for tenoxicam in whose case its influence was scarce. When the exposition of river water to sunlight was partially limited and kept under the natural day-night cycle, as occurs inside a body of water, tenoxicam, piroxicam and meloxicam (at 2 μg L^{-1}) were detected during a period of 15, 27 and 45 days, respectively. Residues were monitored by ultra-pressure liquid chromatography/quadrupole time-of-flight/mass spectrometry after solid-phase extraction and several degradation products were found (10 for tenoxicam, 9 for piroxicam and 7 for meloxicam) and monitored over time. Their structures were proposed from the molecular formulae and fragmentation observed in high-resolution tandem mass spectra; the nature of the transformation products found in the long-term resulted to be very variable for each oxicam. Furthermore, the degradation in presence of river sediment was also monitored over time, with some differences being noted; the adsorption coefficients of the compounds on sediment were

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calculated, meloxicam exhibited a higher sorption capacity. The ecotoxicity of the different compounds in aquatic ecosystems was predicted, too.

1. Introduction

The presence of pharmaceutical drugs in surface waters and sewage, which is the main introduction source of these drugs in the environment, has been revealed in many publications since the beginning of the 21st century. So, the stability of some drugs in aqueous medium has been studied to foresee their degradation and persistence in surface water. Among these microcontaminants are tenoxicam, piroxicam and meloxicam, which are non-steroid anti-inflammatory drugs prescribed for the treatment of painful musculoskeletal disorders. There is much information in the scientific bibliography about their pharmacokinetics but very few manuscripts have considered their possible occurrence in surface water. In this way, piroxicam has been detected in average concentrations of 103 and 15 ng L^{-1} in effluent wastewaters and surface waters (Petre et al., 2016), and in concentrations lower than 32 ng L^{-1} for 5 out of 17 samples collected in the Danube basin river (Chitescu et al., 2015). In other work, meloxicam was detected in the influent of a wastewater treatment plant at a concentration of 1.8 μg L^{-1} but it was not detected in the effluent (Zhao et al., 2014). There are no data for tenoxicam.

The behavior of piroxicam and meloxicam in aqueous solution has been assessed in some works in order to test their stability in pharmaceutical preparations. Thus, it has been stated that meloxicam is stable in water at room temperature for at least 7 days (Ingrao et al., 2013) and that both compounds are insensitive to alkaline hydrolysis under reflux while they are decomposed at acidic pH (Bandarkar and Vavia, 2009; Suntornsuk et al., 2005). In other work it is remarked that piroxicam and meloxicam in water-acetonitrile solution are labile compounds under hydrolytic, oxidative and photoneutral conditions besides describing some degradation products (Modhave et al., 2011). Various degradation products arisen from biological processes are known for tenoxicam, piroxicam and meloxicam; they are found in plasma, urine and feces of human or animal origin and, mainly, they are hydroxylated derivatives of the three oxicams (Aberg et al., 2009; Dell et al., 1984; Grude et al., 2009; Marland et al., 1999; McKinney et al., 2004; Milligan, 1992; Ródenas et al., 1998; Wasfi et al., 2001). A microbial transformation of meloxicam by fungi isolated from soil has been reported, too (Prasad et al., 2009).

Reliable information about the fate of the three oxicams in surface water and especially about their long-term fate in non-forced conditions is not available. In this context, river water spiked individually with each oxicam at trace level was subjected to degradation studies in this work to ascertain the importance of the chemical, photochemical and biological processes in their degradation in surface water. Moreover, their behavior in a body of water over time under non-forced conditions has also been simulated. Water aliquots were analyzed by ultra-pressure liquid chromatography/quadrupole time-of-flight/mass spectrometry, and the structures of the degradation products found have been tentatively elucidated from the molecular formulae and fragmentation observed in high-resolution tandem mass spectra. The evolution of the degradation products was also monitored over time to estimate their occurrence and propose a degradation pathway. In addition, the adsorption capacity of the oxicams on a sediment was evaluated by calculating the corresponding adsorption coefficients and ecotoxicities were predicted.

2. Experimental

2.1. Material and reagents

Water samples were collected from the rivers Pisuerga (pH value 7.8, chemical oxygen demand value 4.6 mg L^{-1}), in the urban area of the city of Valladolid, and Tuerto (pH value 7.4, chemical oxygen demand value 3.9 mg L^{-1}), in the rural area of the La Bañeza, province of León. A sediment sample (total organic carbon 1.2%; clay 11%, silt 44%, sand 45%) was collected from the river Pisuerga. Cellulose nitrate disks from Sartorius (Barcelona, Spain) were used: river water was filtered through 0.2 μm pore-size disks for the estimation of adsorption coefficients, through 3 μm pore-size disks to carry out biodegradation experiments, and through 0.45 μm pore-size disks for other degradation experiments.

Tenoxicam, piroxicam and meloxicam (99% purity) were obtained from Sigma-Aldrich (St. Louis, MO, USA). LC-MS grade methanol, acetonitrile and formic acid were supplied by Panreac (Barcelona, Spain) and ultrapure water was obtained from a Milli-Q plus apparatus (Millipore, Milford, MA, USA). Analysis-grade sodium hydroxide, potassium dihydrogen phosphate and sodium azide were purchased from Panreac. Oasis HLB cartridges (60 mg) for solid-phase extraction were purchased from Waters (Milford, MA, USA) and PTFE disposable syringe filter units, 0.20 μm pore size, were obtained from Scharlab (Barcelona, Spain). A vacuum centrifuge evaporator, Myvac model, was provided by Genevac (Ipswich, UK), a PK120 centrifuge by ALC (Winchester, VA, USA) and a Promax 2020 reciprocating platform shaker by Heidolph (Germany).

2.2. Biological degradation

2.2.1. Aerobic degradation

Biological degradation assays were carried out individually for each compound with water from the river Pisuerga (pH 7.8) which was spiked to achieve a concentration of 2 μg L^{-1} for each analyte. A volume of 50 mL of river water was transferred into a 100 mL Erlenmeyer flask, which was then coated with aluminum foil to avoid exposure to sunlight but allowing the exchange of air with the atmosphere. An analyte control solution was similarly prepared in ultrapure water (pH 7.8 adjusted with NaOH) containing 0.02% (*W/V*) sodium azide as a biocide. Water blanks were prepared as well. Samples were run in parallel; flasks were shaken in a reciprocating shaker at a rotation speed of 130 r min^{-1} for 5 weeks, within a temperature range of 18–21 °C. Aliquots (5 mL) were collected each week and subjected to analysis. Evaporation water losses were periodically restored by addition of water of the same type. All biological experiments were carried out in duplicate.

2.2.2. Anaerobic degradation

River water (pH 7.8) spiked at 2 μg L^{-1} was placed in 15 mL vials, completely filled to avoid the presence of air in the headspace. The vials were closed, protected from light by coating them with aluminum foil and kept in a temperature range of 18–21 °C. Control solutions with analyte in ultrapure water (pH 7.8 adjusted) containing 0.02% sodium azide, and the corresponding blanks, were