



# Fate of the drug chlorpromazine in river water according to laboratory assays. Identification and evolution over time of degradation products. Sorption to sediment



Juan J. Jiménez <sup>a, b, \*</sup>, Beatriz E. Muñoz <sup>c</sup>, María I. Sánchez <sup>c</sup>, Rafael Pardo <sup>a</sup>, María S. Vega <sup>a</sup>

<sup>a</sup> Department of Analytical Chemistry, Faculty of Sciences, Campus Miguel Delibes, University of Valladolid, Paseo de Belén 7, 47011 Valladolid, Spain

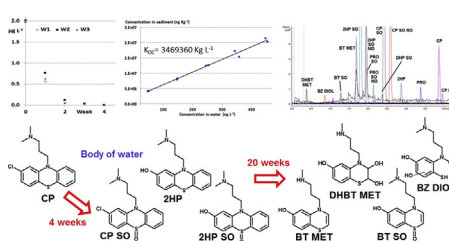
<sup>b</sup> I.U. CINQUIMA, Campus Miguel Delibes, University of Valladolid, Paseo de Belén 5, 47011 Valladolid, Spain

<sup>c</sup> Department of Analytical Chemistry, School of Industrial Engineers, University of Valladolid, Francisco Mendizábal 1, 47014 Valladolid, Spain

## HIGHLIGHTS

- Chlorpromazine is detected during 4 weeks when exposure to sunlight is limited.
- 16 degradation products tentatively identified from high-resolution MS/MS spectra.
- Oxidation, hydroxylation and breakdown of the promazine are degradation ways.
- Benzo[1,4]thiazin-6-ol derivatives are the main residues after 20 weeks.
- Sorption coefficient of chlorpromazine onto aquatic sediment is very high.

## GRAPHICAL ABSTRACT



## ARTICLE INFO

### Article history:

Received 6 May 2016

Received in revised form

25 July 2016

Accepted 29 July 2016

Handling Editor: Klaus Kümmerer

### Keywords:

Chlorpromazine

Degradation products

River water

Sorption coefficients

High-resolution mass spectrometry

## ABSTRACT

Toxic effects of the non-biodegradable drug chlorpromazine and its degradation products have been reported on microorganisms in aqueous media. Here, chlorpromazine degradation assays in forced and non-forced conditions have been done to know its persistence and degradation products in river water. Sunlight irradiation promotes the complete degradation of chlorpromazine ( $2 \mu\text{g L}^{-1}$ ) in less than 4 h, but if the exposure to sunlight is limited chlorpromazine is detected during 4 weeks in river water. Sixteen degradation products in surface water are described for first time after solid-phase extraction and analysis by ultra-pressure liquid chromatography/quadrupole time-of-flight/mass spectrometry; their structures are proposed from the molecular formulae of the fragment-ions observed in high-resolution tandem mass spectra. Hydroxylation and oxidation products such as chlorpromazine sulfoxide, 2-hydroxypropromazine and 2-hydroxypropromazine sulfoxide were predominant degradation products in the early stages; some benzo[1,4]thiazin-6-ol derivatives resulting from the breakdown of the phenothiazine core were the major and relatively stable products after 20 weeks under non-forced conditions. A degradation pathway of chlorpromazine in water is outlined. Moreover, it is shown that chlorpromazine is very strongly adsorbed on sediment while the degradation products that kept the promazine core have a notable capacity of sorption, too; sorption coefficients are calculated. Finally, a prediction about the

\* Corresponding author. Department of Analytical Chemistry, Faculty of Sciences, Campus Miguel Delibes, University of Valladolid, Paseo de Belén 7, 47011 Valladolid, Spain.

E-mail address: [jjimenez@qa.uva.es](mailto:jjimenez@qa.uva.es) (J.J. Jiménez).

toxicity of the degradation products in aquatic ecosystems suggests that some of them have toxicities similar, or even higher, than chlorpromazine.

© 2016 Elsevier Ltd. All rights reserved.

## 1. Introduction

Chlorpromazine (CP) is a lipophilic phenothiazine drug with antipsychotic and neuroleptic activity prescribed for the treatment of mental and behavioral disorders. It was introduced into psychiatry in the early 1950s, and nowadays, it is included in the World Health Organization's List of Essential Medicines which compiles the drugs needed in a basic health system. It has some veterinary uses, too.

There is some concern for the influence of the CP residues in the environment. Toxic and allergic effects on biomolecules, bacteria and protozoans have been observed in presence of CP residues and attributed to photochemical reactions involving the parent compound and its transformation products, whose composition is generally not well known (Nalecz et al., 2008; Viola and Dall'Acqua, 2006; Chignell et al., 1985; Trautwein and Kümmerer, 2012). Harmful effects on *Daphnia magna*, a biomarker of the health of the aquatic ecosystems, have also been reported (Oliveira et al., 2015) while the alteration of the microbial function of soil has been described (Gielen et al., 2011), too. Furthermore, a study of biological degradation of CP in water concluded that CP had to be classified as a non-biodegradable compound (Trautwein and Kümmerer, 2012).

Pharmaceutical compounds can reach the surface waters by different ways although the discharges from the wastewater treatment plants are usually the main introduction way. As regards CP only a manuscript has considered its analysis in wastewater effluents, it was not detected after the monitoring of effluents from five treatment plants (Borova et al., 2014). There are not data about its occurrence in surface waters.

In this context, some experiments have been conducted to estimate the degradation-rate of CP in river water and know its degradation products over time. Solutions of CP in river water were subjected to high temperature, and sunlight irradiation without any limitation, to force the degradation. Non-forced degradation involved the monitoring of residues in river water kept in glass container at room temperature, with or without added aquatic sediment; since glass absorbs partially UV radiation, the behavior of CP is thus comparable to that in a mass of water where the penetration of solar UV radiation is diminished with depth. Extracts of water samples were injected in an ultra-pressure liquid chromatographic system and the structure of the detected degradation products was tentatively elucidated from the molecular formulae estimated by high-resolution mass spectrometry (MS) and the interpretation of the fragments observed in high-resolution tandem mass spectrometry (MS/MS), proposing a degradation pathway. Furthermore, since a strong capacity of sorption of CP on sediment was observed, a sorption isotherm is presented while sorption coefficients for degradation products are calculated on the supposition that peak areas vary linearly with concentration. Finally, the possible toxicity of the identified degradation products is predicted by the TEST software (Toxicity Estimation Software Tool) developed by the US Environmental Protection Agency (EPA).

## 2. Experimental

### 2.1. Material and reagents

Water samples were collected from the rivers Pisuerga (pH value 7.8, chemical oxygen demand value  $4.6 \text{ mg L}^{-1}$ ), in the urban area of the city of Valladolid, and Tuerto (pH value 7.4, chemical oxygen demand value  $3.9 \text{ mg L}^{-1}$ ), in the rural area of the La Bañeza (León). A sediment sample (total organic carbon 1.2%; clay 11%, silt 44%, sand 45%) was collected from the river Pisuerga.

Cellulose nitrate disks, 0.20 and 0.45  $\mu\text{m}$  pore size, to filter water samples were obtained from Sartorius (Barcelona, Spain). Chlorpromazine hydrochloride (99% purity) was obtained from Sigma-Aldrich. 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).

Sodium hydroxide, potassium dihydrogen phosphate and sodium azide were purchased from Panreac. Oasis HLB cartridges (60 mg) were obtained from Waters and nitrogen for the LC-MS system was supplied by a gas generator from Zefiro (Vigonza, Italy). A vacuum centrifuge evaporator, Myvac model, was provided by Genevac (Ipswich, UK) and PK120 centrifuge by ALC (Winchester, VA, USA).

### 2.2. Degradation assays

Forced conditions are commonly applied to aqueous solutions to estimate the stability of environmental contaminants and foresee their degradation products in aquatic ecosystems. In addition to this strategy a simpler, although slower, approach was also adopted in this work to simulate the concurrent natural processes in a body of water. So, river water filtered through a 0.45  $\mu\text{m}$  pore-size cellulose nitrate disk was placed in a transparent and sodium calcium silicate glass container with air-tight seal, which was weekly open to collect a sample aliquot and replace the air inside in contact with the water surface. The container was placed within the laboratory at 18–21 °C and exposed to sunlight under the natural day-night cycle for 20 weeks, at which time the non-forced degradation assay was ended.

A volume of 2500 mL of river water placed in glass container was spiked with CP to achieve an initial concentration of  $2 \mu\text{g L}^{-1}$  in each degradation assay; aliquots of 25 mL were periodically collected, subjected to SPE and injected in the chromatographic system to follow the degradation of CP, look for degradation products and monitor them. Degradation experiments were made between the months of November and March with waters from the rivers Pisuerga (W1 sample) and Tuerto (W2 sample), and between January and May with water from the Pisuerga river (W3 sample). Simultaneously, the degradation on W1 sample was also studied in presence of sediment (SED sample), by adding river sediment to the container in a sediment to solution ratio of  $0.03 \text{ g mL}^{-1}$ , and in absence of sunlight (DARK sample) by coating the container with aluminum foil.

Furthermore, some degradation assays were done on W1

Download English Version:

<https://daneshyari.com/en/article/6306173>

Download Persian Version:

<https://daneshyari.com/article/6306173>

[Daneshyari.com](https://daneshyari.com)