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Review

# Transformation of pharmaceuticals during oxidation/disinfection processes in drinking water treatment

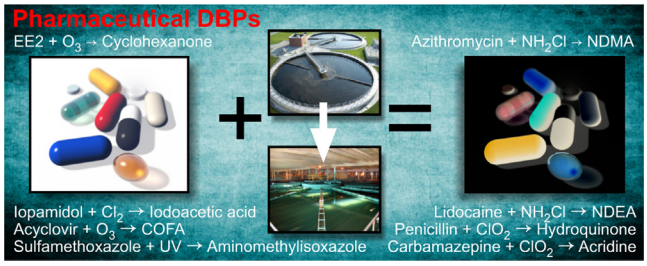
Cristina Postigo[a], Susan D. Richardson[b,*]

[a] Institute for Environmental Assessment and Water Research (IDAEA)—Spanish National Research Council (CID-CSIC), Barcelona, Spain
[b] Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, USA

## HIGHLIGHTS

- Review of transformation pathways of pharmaceuticals during disinfection processes.
- DBPs are formed with chlorine, chloramine, ozone, chlorine dioxide, UV, or UV/$H_2O_2$.
- Chlorine reacts with amine and reduced sulfur groups and activated aromatic systems.
- Chlorine dioxide and ozone react with electron-rich functional groups.
- Potential health effects are noted for some pharmacuetical DBPs when available.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Pharmaceuticals are emerging contaminants of concern and are widespread in the environment. While the levels of these substances in finished drinking waters are generally considered too low for human health concern, there are now concerns about their disinfection by-products (DBPs) that can form during drinking water treatment, which in some cases have been proven to be more toxic than the parent compounds. The present manuscript reviews the transformation products of pharmaceuticals generated in water during different disinfection processes, i.e. chlorination, ozonation, chloramination, chlorine dioxide, UV, and UV/hydrogen peroxide, and the main reaction pathways taking place. Most of the findings considered for this review come from controlled laboratory studies involving reactions of pharmaceuticals with these oxidants used in drinking water treatment.



*Abbreviations:* DBP, disinfection by-product; EE2, ethinylestradiol; GC, gas chromatography; HO•, hydroxyl radical; ICM, iodinated X-ray contrast media; LC, liquid chromatography; MS, mass spectrometry; NDMA, *N*-nitrosodimethylamine; NMR, nuclear magnetic resonance; MDMA, 3,4-methylenedioxymethamphetamine or ecstasy; MDA, 3,4-methylenedioxyamphetamine; MDEA, 3,4-methylenedioxyethylamphetamine.

* Corresponding author. Tel: +1 803 777 6932.
*E-mail address:* richardson.susan@sc.edu (S.D. Richardson).

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**Contents**



## 1. Introduction

Pharmaceuticals are important emerging contaminants, due to their presence in environmental waters (caused by incomplete removal in wastewater treatment or point-source contaminations) and potential estrogenic, antibiotic resistance, and other effects to wildlife and humans. Pharmaceuticals are introduced not only by humans, but also through veterinary use from livestock, poultry, and fish farming [1]. Increasingly, pharmaceuticals are being measured in drinking water, and recent studies are following their occurrence and fate "full circle", from wastewaters to river water to source water to finished drinking water. Examples include the measurement of antidepressants in Canada [2] and the United States [3], antibiotics in Australia [4], iodinated X-ray contrast media (ICM) in Germany [5], and a variety of other pharmaceuticals in the United States [6], Canada [7], Spain [8,9], and France [10]. Most of the time, pharmaceuticals are partially removed during wastewater treatment, after which their concentrations are reduced further in rivers as they are transported downstream of the wastewater treatment plant, due to continued dilution and biological degradation before entering drinking water sources. Because of these removal processes and dilution on the way to drinking water sources, pharmaceuticals are only occasionally detected in drinking water sources, just prior to disinfection. And when detected in source waters, pharmaceuticals generally are present at low ng/L levels [11].

Detecting pharmaceuticals in finished drinking water is even more uncommon because drinking water undergoes additional physical treatment (e.g., flocculation, sedimentation, filtration) and chemical disinfection (e.g., with chlorine, ozone, chloramines, or chlorine dioxide), such that pharmaceuticals are generally removed further by these processes, and few survive these additional treatments to remain in finished drinking water [12]. Even so, improved detection limits have enabled researchers to identify many pharmaceuticals in finished drinking water. For example, Benotti et al. [6] found 9 of their 17 target pharmaceuticals in finished drinking waters from the United States, Kleywegt et al. [7] found 17 of their 48 target pharmaceuticals in finished drinking waters from Canada, Vulliet et al. [10] found 18 of their 51 target pharmaceuticals in finished drinking waters in France, and Huerta-Fontela et al. [8] found 5 of their 55 target pharmaceuticals in finished drinking waters from Spain. Target pharmaceuticals from these studies included antibiotics, analgesics, anti-inflammatory drugs, antihistamines, β-blockers, β-agonists, lipid regulators, antidepressants and other psychiatric drugs, synthetic hormones and contraceptives, antiepileptics, cardiac drugs, and high blood pressure drugs.

Pharmaceuticals found most often in finished drinking water include carbamazepine, gemfibrozil, ibuprofen, atenolol, phenytoin, and hydrochlorothiazide. Levels as high as 601 ng/L of carbamazepine have been reported in finished drinking water [7], but levels of most pharmaceuticals are typically <10 ng/L.

While concentrations of pharmaceuticals in finished drinking water are generally considered too low for human health concern, there are now concerns about their disinfection by-products (DBPs) that can form in drinking water treatment. A key example includes the transformation of ICM in drinking water treatment. ICM are widely used for medical imaging, are administered at high doses (200 g/person/day), and are designed to be inert substances, with 95% eliminated in urine and feces unmetabolized [13]. ICM are not well removed in wastewater treatment, such that they occur among the highest levels of any pharmaceutical measured in rivers and streams (up to 100 μg/L) [14] and up to 2.7 μg/L in drinking water source waters [15]. ICM are not toxic in themselves (which is why they can be used at such high doses for medical imaging), but recent research has shown that they can be transformed by chlorine or monochloramine in drinking water treatment to form the most genotoxic and cytotoxic DBPs known (iodo-DBPs) [15–17].

Besides pharmaceuticals, other environmental contaminants can also form DBPs, and some of their transformation products have been shown to be toxic or estrogenic [18]. These contaminants include pesticides, personal care products, estrogens, bisphenol A, alkylphenol surfactants, and algal toxins. Most contaminant DBPs have been identified in controlled laboratory studies and not in