Environmental Toxicology and Chemistry—Volume 41, Number 11—pp. 2700–2707, 2022
Received: 26 March 2021 | Revised: 29 May 2021 | Accepted: 25 July 2022

Environmental Toxicology

Adsorption of Individual and Mixtures of β-Blockers and Copper in Soils and Sediments

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Abstract: The (bio)availability of pharmaceuticals at solid/water interfaces is governed by their sorption, which determines their concentrations in groundwaters and surface waters in contact with biota, and can be affected by the presence of other contaminants such as metallic trace elements likely to compete for adsorption sites and form complexes with pharmaceuticals. We studied the adsorption of the pharmaceuticals propranolol and sotalol—two β-blockers—on one soil and one sediment using batch experiments to assess their (bio)availability. The influence of contact time, pH, and concentration was studied. As in the real environment these contaminants are not alone but in mixtures, and they were studied alone, simultaneously added, and in the presence of Cu^{2+}, which is known to form coordination complexes with propranolol and sotalol, but their presence in mixtures did not alter their adsorption properties. Sotalol was more mobile in water and thus more bioavailable for organisms than propranolol. The mobility in surface waters of both β-blockers and thus their bioavailabity for organisms is more important than their risk of transfer to groundwater during rainwater infiltration and to surface water due to runoff. *Environ Toxicol Chem* 2022;41:2700–2707. © 2022 The Authors. *Environmental Toxicology and Chemistry* published by Wiley Periodicals LLC on behalf of SETAC.

Keywords: Mobility; Retention; Pharmaceutical; Propranolol; Sotalol; Mixture

INTRODUCTION

β-Blockers are a class of pharmaceuticals widely used for the treatment of cardiovascular disorders such as heart rhythm disturbances, ischemic heart, or high blood pressure. They are also illegally used to enhance sport performances by decreasing the cardiac frequency and reducing tremors (Amendola et al., 2000). After excretion, these pharmaceuticals are not totally removed in wastewater treatment plants (WWTPs), and thus they are widely encountered in the environment, especially in soils and waters originating from WWTP effluents and sludges used as soil amendments and/or soil irrigation (water reuse; Xu et al., 2019). In addition, soil leaching and water run-off can release pharmaceuticals into groundwaters and surface waters (Farré et al., 2008) where adsorption/desorption at soil and sediment surfaces is a major process governing their distribution, mobility, and bioavailability, leading to a potential ecotoxic risk because they are considered to be endocrine-disruptive compounds in aquatic organisms (Huggett et al., 2002; Massarsky et al., 2011).

Among β-blockers, propranolol and sotalol are often detected in environmental solid phases (0.3–0.8 ng/g for propranolol and 20 ng/g for sotalol; Verlicchi & Zambello, 2015) because they present generally a high tendency to adsorb onto sediments (Lin et al., 2010; Yamamoto et al., 2009), soils (Drillia et al., 2005; Maszkowska et al., 2014), and sludges (Maurer et al., 2007). Despite their adsorption behavior, they are also frequently present in WWTP effluents and surface waters in the ng–µg/L range (Godoy et al., 2015), where they display a noticeable persistence higher than 100 days (Ramil et al., 2009). In this context, propranolol displays a high bioaccumulation in aquatic organisms such as crucian carp (Liu et al., 2015) and algae (Ding et al., 2015), and induces effects on different aquatic organisms (fish, freshwater crustacean, microalgae; Huggett et al., 2002; Massarsky et al., 2011). Several studies comparing the toxicity of β-blockers (propranolol, atenolol, metropolol, nadolol) on various organisms (algae, water flea, duckweed, fish, crustacean) showed that propranolol presented a higher acute toxicity than the other β-blockers toward the tested organisms (Cleuvers, 2005; Godoy et al., 2015; Huggett et al., 2002). The higher toxicity of propranolol could

This article contains online-only Supporting Information.

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Published online 28 July 2022 in Wiley Online Library (wileyonlinelibrary.com).
DOI: 10.1002/etc.5448

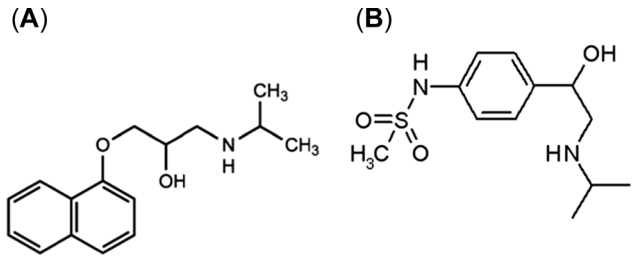

FIGURE 1: Structures of propranolol (**A**) and sotalol (**B**).

be explained by its higher octanol/water partition coefficient (K_{ow}) and the fact that propranolol is a strong membrane stabilizer (Liu et al., 2009). With a hazard quotient (predicted environmental concentration/predicted no effect concentration) higher than 1, propranolol was identified as a compound with a possible ecological risk for waters (Gabet-Giraud et al., 2014; Godoy et al., 2015; Mendoza et al., 2015).

In the environment, a given contaminant is not present alone but in mixture with others. In the literature, only few studies report the adsorption behavior of pharmaceutical mixtures, including β-blockers (Godoy et al., 2015; Mioduszewska et al., 2016; Vasquez et al., 2014), whereas their simultaneous presence may affect their mobility, bioavalability, and thus their ecodynamics. For example, metoprolol adsorbed onto soils decreased the mobility of cyclophosphamide and ifosfamide (Mioduszewska et al., 2016). Among contaminants, metallic trace elements such as Cu are ubiquitous in soils, sediments, and water bodies, and are known to affect pharmaceutical mobility in soils (Graouer-Bacart et al., 2013, 2015; Guaita et al., 2011). Because β-blockers can form coordination complexes with Cu (Bontchev et al., 2003; Gölcü et al., 2004; Viera et al., 2009), it is important to take into account its influence on their behavior in the environment in mixture conditions. To our knowledge, such studies are missing in the literature.

In the present study, the adsorption properties of two β-blockers (propranolol and sotalol) singly and simultaneously present were investigated to study the influence of their co-presence on their mobility and availability at solid/water interfaces. The influence of Cu as another class of co-contaminant in the mixtures was also studied.

MATERIALS AND METHODS

Materials and reagents

All chemicals were used without further purification. Propranolol hydrochloride, 1-iso-propylamino-3-naphthyloxy-propan-2-ol (purity 99.5%), and sotalol hydrochloride, 4-(1-hydroxy-*N*-isopropylaminoethyl)methane sulfonanilide (purity 98.5%; Figure 1) were purchased from VWR. Copper sulfate, $CuSO_4.5H_2O$ (Normapur) was obtained from Prolabo. The stock solutions of propranolol (1 mmol/L; 259.3 mg/L), sotalol (1 mmol/L, 272.4 mg/L), and Cu (1 mmol/L; 63.5 mg/L) were prepared in distilled water. Hydrochloric acid (HCl) and potassium hydroxide (KOH; Normadose) were purchased from Prolabo and acetonitrile (HiPerSolv CHROMANORM) from VWR.

For adsorption experiments, soil and river sediment were collected in the Champagne-Ardenne region (France). The soil and the sediment were collected in the 5–20 cm horizon, using a shovel for the former and a bottom gripper, a special stainless-steel device, for the latter. They were dried at 40 °C for 24 h, sieved under 2 mm, and characterized for particle size distribution (without decarbonation), pH, cation exchange capacity (CEC), organic carbon, and $CaCO_3$ contents according to French and International standard methods, following NF X31-107 (Association Française de Normalisation [AFNOR], 2003), International Organization for Standardization (ISO) 10390 (AFNOR, 2005), X31-130 (AFNOR, 1999), ISO 14235 (AFNOR, 1998), and ISO 10693 (AFNOR, 1995).

The main physicochemical properties of the soil and the sediment selected for adsorption experiments are presented in Table 1. The sediment had a sandy texture with a very low organic carbon content (0.4%) and CEC value (2.3 cmol/kg), and the soil had a loamy texture displaying a organic carbon content (1.9%) and a CEC value (8.8 cmol/kg) approximately four times higher than the sediment. Both had an important content of carbonates (50%), and as a result were basic solids (pH = 8.8 and 8.3 for the sediment and the soil, respectively).

Prior to adsorption experiments, the initial concentrations of propranolol, sotalol, and Cu in the studied solids were determined after a step of solvent-assisted extraction for both pharmaceuticals and after a mineralization step for Cu. The solvent extraction and mineralization steps were carried out using a Thermo Scientific Ethos EASY microwave (Milestone). The concentrations of sotalol and propranolol were then measured using high-performance liquid chromatography (HPLC) and the Cu concentration was determined by inductively coupled plasma atomic emission spectroscopy (ICP-OES; see *Adsorption experiments*). The concentrations of sotalol and propranolol were below the detection limit. Copper (<50 μg g^{-1}) was negligible compared to the concentrations added in adsorption experiments (from 0.78 to 16.3 mg g^{-1}).

Adsorption experiments

Adsorption experiments were carried out using the batch procedure at room temperature (20 °C), at natural soil/sediment pH, and using a solid content of 40 g/L. They were

TABLE 1: Main physicochemical properties of the solid samples

	pH	CEC (cmol/kg)	OC (%)	Silt (%)	Sand (%)	Clay (%)	Carbonates (%)
Soil	8.3 ± 0.1	8.8 ± 0.8	1.9 ± 0.2	41 ± 5	36 ± 2	23 ± 3	50 ± 3
Sediment	8.8 ± 0.1	2.3 ± 0.3	0.4 ± 0.1	5.0 ± 0.6	93 ± 4	2.0 ± 0.3	50 ± 2

Percentages of organic carbon (OC) and carbonates are expressed as a weight percentage of dry whole solid, whereas percentages of sand, silt, and clay (textural analysis) are expressed as weight percentages of dry mineral solid. The errors correspond to $n = 3$ replicates.

performed for each β-blocker singly added in batches (propranolol or sotalol) and for mixtures of both β-blockers simultaneously added at a molar ratio of 1 to 1 propranolol to sotalol. To avoid photodegradation of the β-blocker(s) the batches were covered with aluminum foil and the experiments were conducted in dark conditions. Controls containing the β-blocker(s) in the absence of solid were also prepared to check the absence of degradation and/or retention on vessels during the duration of the experiments. All the experiments were duplicated.

Solid hydration was preliminary ensured by suspending 1 g of solid in 20 ml of distilled water per batch during 24 h before adding the β-blocker(s) and adjusting the volume to 25 ml with distilled water. Then, the suspensions were continuously shaken for adsorption experiments (using a wrist arm shaker at 500 rpm from Ingenieurbüro CAT). Three types of adsorption experiments were carried out: kinetic experiments (variable contact time), variable β-blocker(s) concentration, and experiments as a function of pH.

For kinetic experiments, the β-blocker(s) solution was added to reach a final concentration of 50 μmol/L in each batch before shaking for a contact time varying from 15 min to 28 h (15, 30 min, 1, 2, 3, 4, 5, 6, 8, 15, 21, 24, 28 h).

The experiments as a function of pH were carried out for an introduced concentration of β-blocker(s) of 50 μmol/L. The pH was adjusted to a fixed value ranging between 5.5 and 9.5 by dropwise addition of 0.1 M HCl or 0.1 M KOH and the suspensions were shaken for the time necessary to reach the adsorption equilibrium (time predetermined by kinetic experiments).

The experiments with variable β-blocker(s) concentration were carried out with an introduced concentration of propranolol and/or sotalol ranging from 3 to 60 μmol/L (0.78–15.6 and 0.82–16.3 mg/g for propranolol and sotalol, respectively). The suspensions were stirred for the time necessary to reach the adsorption equilibrium. The distribution coefficient (K_d) values were determined in the isotherm linear part using an ordinary linear square regression according to the linear model corresponding to Equation (1), where q_{eq} and C_{eq} are the adsorbed amount on the solid and the remaining concentration in solution at equilibrium, respectively.

$$K_d = \frac{q_{eq}}{C_{eq}} \quad (1)$$

To study the influence of Cu(II) on both β-blockers' adsorption, experiments were conducted as described above by simultaneously adding propranolol, sotalol, and Cu(II) at a molar ratio equal to 1-to-1-to-1.

For each type of adsorption experiment, after shaking, the suspensions were filtered through a 0.22 μm cellulose acetate membrane. The remaining concentrations in solution of propranolol and/or sotalol were quantified using a 1260 infinity HPLC system from Agilent Technologies, consisting of a quaternary pump and a photodiode array detector. A mobile phase containing acetonitrile (A) and ultra-pure water (ALPHA Q 18 MΩ/cm) with orthophosphoric acid (0.5%; B) was used to elute the analytes (20 μl injection volume) in isocratic condition on a reverse-phase Agilent Pursuit XRs 5 C18 column (5 μm × 250 × 3 mm). Propranolol and sotalol were eluated at a flow rate of 0.65 ml/min, with 25%/75% and 5%/95% (v/v) A/B, respectively. Both β-blockers were detected at 230 nm. In the case of experiments carried out in presence of Cu, the remaining concentrations of Cu in the samples were measured by ICP-OES using an iCAP 6300 duo plasma emission spectrometer (Thermo Scientific) in axial mode. Yttrium was used as internal standard and $\lambda = 324.754$ and 327.396 nm were selected for Cu. The limits of detection and quantification were equal to 5 and 17 nmol/L, respectively.

RESULTS AND DISCUSSION

Propranolol and sotalol adsorption when singly present

Kinetic experiments were conducted to determine the time required to reach the adsorption equilibrium on the soil or the sediment for propranolol and sotalol when singly present (Figure 2). For all the systems, the adsorption process was quite

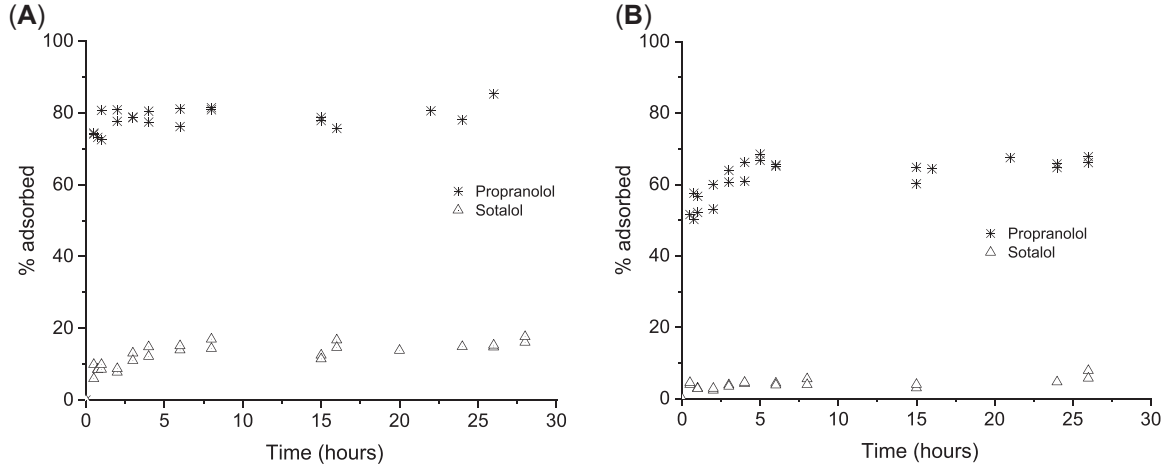

FIGURE 2: Adsorption kinetics of propranolol and sotalol on the soil (**A**) and on the sediment (**B**): $[propranolol]_0 = [sotalol]_0 = 50$ μmol/L, $T = 20$ °C, pH_{solid}, solid concentration = 40 g/L.

rapid (<7 h). On both solids, the adsorbed amounts of propranolol were more than five times (13 times for the sediment) greater than those of sotalol (80% of propranolol vs. 15% of sotalol adsorbed onto the soil, and 66% of propranolol vs. 5% of sotalol adsorbed onto the sediment for an introduced concentration of 50 μmol/L). On the one hand, propranolol displays a much higher value of log K_{ow} than sotalol (3.5 vs. 0.2), which favors hydrophobic interactions onto organic matter. On the other hand, the speciation of both contaminants is different as a function of pH: propranolol possessing one pK_a value (9.5) can be cationic or neutral, whereas sotalol possessing two pK_a values (8.2 and 9.8) can be cationic, zwitterionic, or anionic (Ramil et al., 2009). Thus, at the pH values of the studied solids, propranolol was mainly cationic (94% at soil pH and 83% at sediment pH) whereas sotalol was mainly zwitterionic (55% at soil pH and 74% at sediment pH) with a lower proportion of cationic species than propranolol (43% at soil pH and 19% at sediment pH; Figure 3). In a previous study, we evidenced that a cation exchange mechanism was preponderant for propranolol adsorption (Smith et al., 2018), thus the higher proportion of cationic species in the case of propranolol was in favor of greater adsorbed amounts compared to sotalol. Consequently, the two properties cited above (log K_{ow} and pK_a values) related to the hydrophobic and ionizable characters of the β-blockers are well in accordance with a more favorable adsorption of propranolol compared to sotalol. Finally, the greater adsorbed amounts measured in the soil compared to the sediment for both β-blockers can be explained with the solid properties because the soil displayed higher organic carbon content (1.9%) and CEC value (8.8 cmol/kg) than the sediment (0.4% organic carbon and CEC = 2.3 cmol/kg; Table 1): the organic carbon content is in favor of hydrophobic interaction with organic compounds, and the organic carbon content and the CEC value are generally both in favor of cationic species adsorption. Moreover, the sediment was more basic (pH = 8.8) than the soil (pH = 8.3; Table 1), translating, for both β-blockers, to a lower proportion of cationic species in the case of the sediment (94% at soil pH and 83% at sediment pH

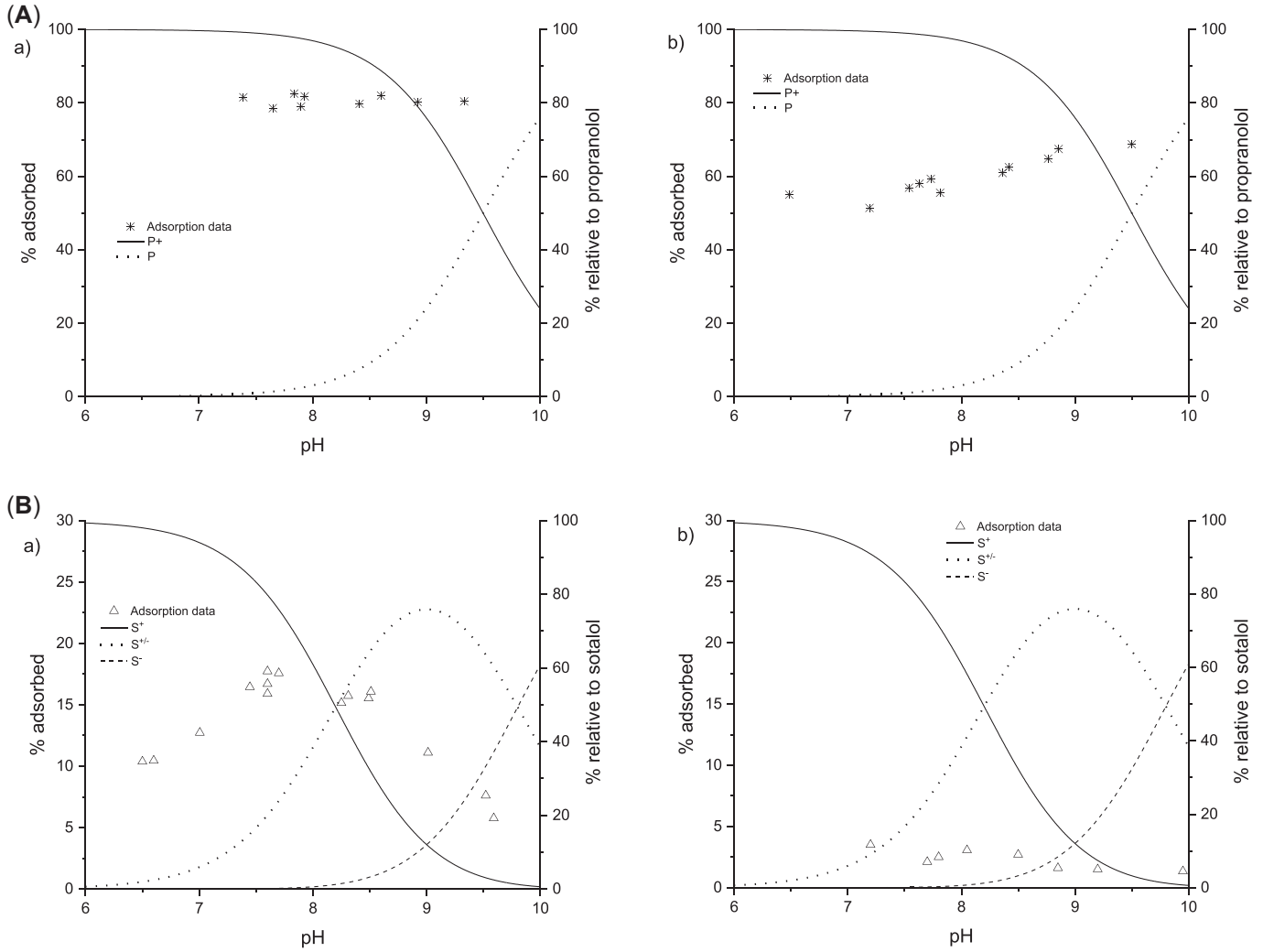

FIGURE 3: Adsorption of propranolol (**A**) and sotalol (**B**) as a function of pH on the soil (**a**) and on the sediment (**b**): $[propranolol]_0 = [sotalol]_0 =$ 50 μmol/L, $T = 20$ °C, solid concentration = 40 g/L. The distribution curves of the different sotalol or propranolol species in solution are superimposed to adsorption data and correspond to the right *y* axis (in % of the total sotalol or propranolol concentration). Lines (solid and dotted/dashed) show calculated percentages of cationic, zwitterionic, and anionic species based on the Hendersen–Hasselbalch equation.

for propranolol; 43% at soil pH and 19% at sediment pH for sotalol), and thus to a decrease of adsorbed amounts by cation exchange. These three soil properties (organic carbon content, CEC, and pH values) can therefore easily explain the adsorption behavior of sotalol and propranolol on the studied soil and sediment.

As highlighted above, pH value is an important parameter that may affect the adsorption of pharmaceuticals, especially if their speciation is pH dependent, as in the case of propranolol and sotalol displaying one and two pK_a values, respectively. The adsorption curves of propranolol and sotalol as a function of pH (from 6 to 9.5) onto the soil and the sediment are reported in Figure 3 for an introduced concentration of 50 μmol/L. In the case of propranolol onto the soil, no significant influence of pH was noticed on adsorbed amounts despite the decrease in the proportion of cationic species with increasing pH. For the sediment, one can notice a slight increase of adsorbed amounts with increasing pH between 7.5 and 9.5, while in this pH range the proportion of neutral propranolol increased at the expense of the cationic species. Hence, hydrophobic interactions would contribute substantially to propranolol adsorption. This assumption was supported by the much lower CEC value of the sediment compared to the soil, which can explain the lesser contribution of cation exchange in propranolol adsorption on the sediment, and thus a slight increase of adsorption at more basic pH. Unlike propranolol, sotalol adsorption onto the soil showed a marked pH dependence (Figure 3B): the adsorbed amounts increased from pH 6.5 to 7.7, and decreased significantly above pH 7.7. Between pH 6.5 and 7.7, the proportion of cationic sotalol decreased (from 98% to 75%) to the benefit of the zwitterionic form for which the proportion increased (from 2% to 24%). In parallel, an increase of pH generally leads to more negatively charged surface sites onto minerals and organic matter due to their deprotonation, in favor of electrostatic attraction with positive charges, and may explain adsorption improvement. Above pH 7.7, the proportion of sotalol cationic species decreased below 75% while that of the anionic species increased and that of the zwitterionic species increased until pH 9 then decreased at more basic pH values: the apparition of negative species could explain the drop in adsorption. Finally, the adsorption of both β-blockers as a function of their concentration was studied to plot the adsorption isotherms for both solids and determine the corresponding adsorption constants (Figure 4). Adsorption isotherms of the four studied β-blocker/solid systems were relatively linear and thus were well fitted with the linear model, enabling the determination of the distribution coefficient K_d as adsorption constant. The obtained K_d values (Figure 4) confirmed the conclusions drawn from adsorption kinetic experiments: (1) propranolol was by far more retained onto the soil and the sediment than sotalol because K_d values were much higher for propranolol (82.0 and 51.0 L/kg for the soil and the sediment, respectively) than for sotalol (5.2 and 0.7 L/kg for the soil and the sediment, respectively), and (2) the retention of both β-blockers was more important on the soil than on the sediment (82.0 and 5.2 L/kg for the soil compared to 51.0 and 0.7 L/kg for the sediment). These observations are in accordance with previous studies reporting higher adsorbed amounts of propranolol onto soils than sediments (Maszkowska et al., 2014; Yamamoto et al., 2009) and of propranolol than sotalol onto sediments (Burke et al., 2013; Ramil et al., 2009). Adsorption constants are used to predict the behavior of contaminants at solid/water interfaces and, classically, the greater the constant value, the less the contaminant is considered mobile and available for water compartments and organisms. Hence, (1) sotalol is more mobile in water and more bioavailable for organisms than propranolol, and (2) for both β-blockers, the risk of mobility in surface waters governed by their behavior at sediment/water interfaces, and thus their bioavailabity for aquatic organisms is more important than their risk of mobility in groundwater during rainwater infiltration and in surface water due to runoff, as well as their bioavailability for soil organisms, which is governed by their behavior at soil/water interfaces. However, these statement should be taken

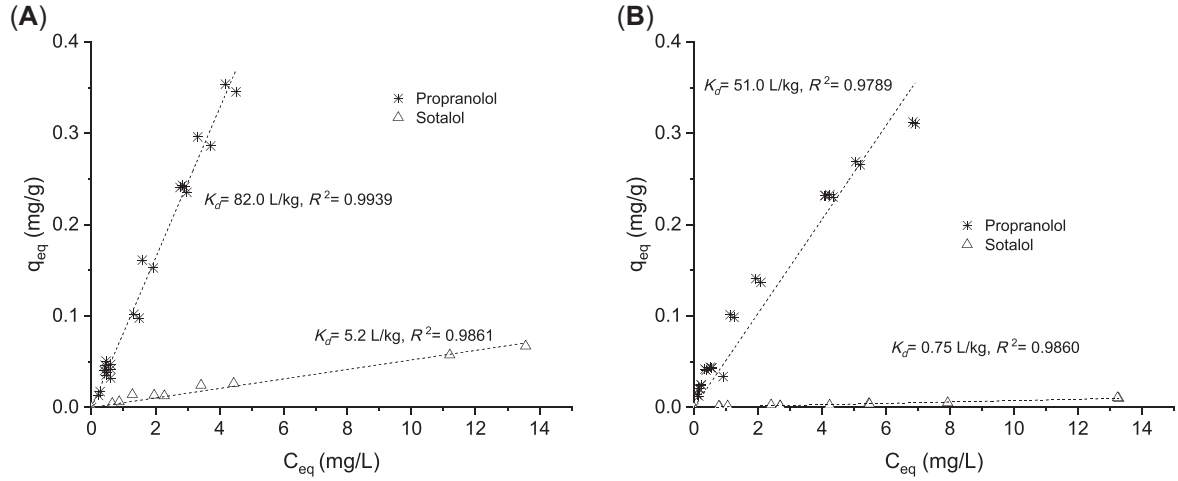

FIGURE 4: Adsorption isotherms of propranolol and sotalol on the soil (**A**) and the sediment (**B**), fitted with the linear model enabling the determination of the K_d adsorption parameter. $T = 20\,°C$, pH_{solid}, solid concentration = 40 g/L. q_{eq} = adsorbed amount on the solid; C_{eq} = the remaining concentration in solution at equilibrium.

with caution because these conclusions should be confirmed with a wide range of soils and sediments.

Adsorption of propranolol and sotalol present in mixture

In the environment, pharmaceuticals are not present as isolated species but occur in mixtures with other contaminants from various families, including pharmaceuticals. Their presence in mixtures can modify their behavior at solid/water interfaces and thus affect their mobility and their bioavailability. Contaminants, for example, can compete for the same adsorption sites, interact together by complex formation to form new species with their own behavior, and adsorbed contaminants can also modify surface properties such as surface sites (Graouer-Bacart et al., 2013; Guaita et al., 2011; Morel et al., 2014; Smith et al., 2018). In this context, we investigated the co-adsorption of propranolol and sotalol, that is their adsorption when they are present in mixtures, as it is the case in the environment (Xu et al., 2019). These experiments were conducted in exactly the same conditions as the experiments presented above by adding a single addition, but instead by adding them simultaneously.

The adsorption kinetic curves for both β-blockers are reported in Figure 5 and are superimposed on the ones obtained in the case of kinetic curves for single addition chemicals. Clearly, their presence in a mixture altered neither the shape of the curves, nor the adsorption equilibrium time, nor the adsorbed amounts at equilibrium. Experiments as a function of β-blocker concentration led to plotting the adsorption isotherms in Figure 6, which are compared to the ones resulting of their single addition. There was no significant influence of the mixture on propranolol and sotalol adsorption because the isotherms were almost superimposed, as attested by the K_d values which, for both β-blockers, were rather similar whether present alone or in mixtures: 77.0 (compared to 82.0) and 46.0 (compared to 51.0) L/kg for propranolol onto the soil and the sediment, respectively; 5.7 (compared to 5.2) and 0.67 (compared to 0.75) L/kg for sotalol onto the soil and the sediment, respectively. This negligible influence can be explained by the isotherm shape of both pharmaceuticals, which was linear at the studied concentrations (in the range 2–60 μmol/L). In these conditions, the soil and sediment surfaces are far from being saturated. In addition, the adsorbed amounts of sotalol were very low compared to those of propranolol. Consequently, even if propranolol and sotalol were retained on the same surface sites, there was no competition in their co-adsorption. Thus, the mobility of propranolol in the environment remains the same when it occurs alone and in mixture with sotalol. As indicated above, the presence of contaminants from other families can alter the adsorption behavior of pharmaceuticals, as is the case for metallic cations able to form complexes with them. For example, adsorbed amounts of enrofloxaxin, flumequine, and sulfamethoxazole were increased in the presence of Cu(II) due the formation of ternary surface complexes (Graouer-Bacart et al., 2013; Guaita et al., 2011; Morel et al., 2014). Copper(II), being ubiquitous in the environment, is present in water, soil, and sediment compartments (Arenas-Lago et al., 2014; Dang et al., 2020; Doré et al., 2019). In unpolluted soils, it is found in the range 2–85 ppm and far more in polluted soils. It is thus likely to be present in these matrices simultaneously with propranolol and sotalol. Because the existence of the complexes Cu(II)-propranolol and Cu(II)-sotalol was previously reported in solution and solid state (Bontchev et al., 2003; Gölcü et al., 2004; Viera et al., 2009), we also investigated the influence of Cu(II) on propranolol and sotalol adsorption. Otherwise, Cu(II) is classically greatly retained onto soils and sediments (Dang et al., 2020; Fagnano et al., 2020), which could compete with both pharmaceuticals for adsorption sites. In this goal, we studied the adsorption of the three contaminant mixtures (propranolol, sotalol, and Cu) simultaneously added in the same conditions as the mixture of both β-blockers. For both solids, the presence of Cu in the mixture had no influence on propranolol and sotalol adsorption (data not shown), and thus did not modify the K_d values. Consequently, there was no competition between the three contaminants for adsorption sites and the formation of ternary surface complexes did not seem to take place during the

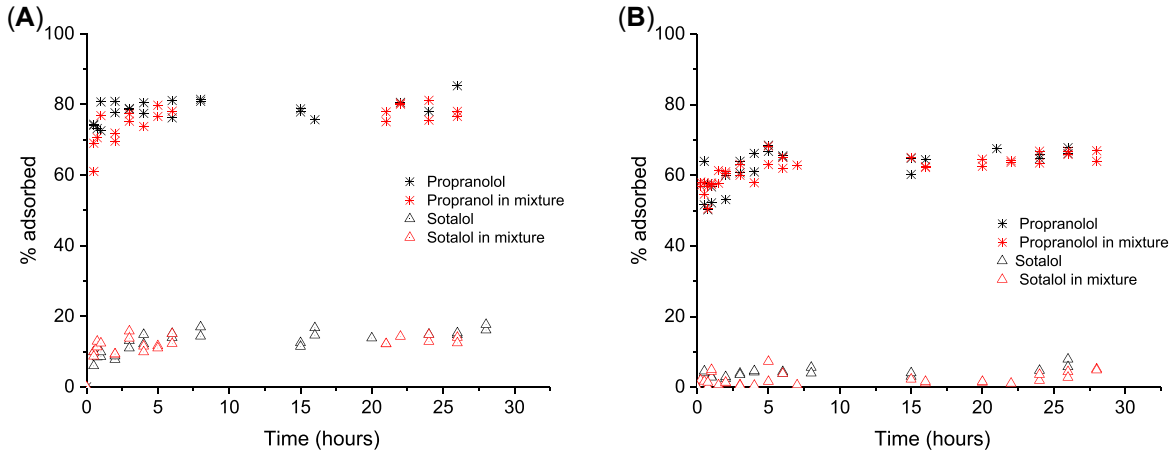

FIGURE 5: Adsorption kinetics of propranolol and sotalol on the soil (**A**) and on the sediment (**B**). β-blocker singly added in black and β-blockers in mixture in red. $[propranolol]_0 = [sotalol]_0 = 50$ μmol/L, $T = 20$ °C, pH_{solid}, solid concentration = 40 g/L.

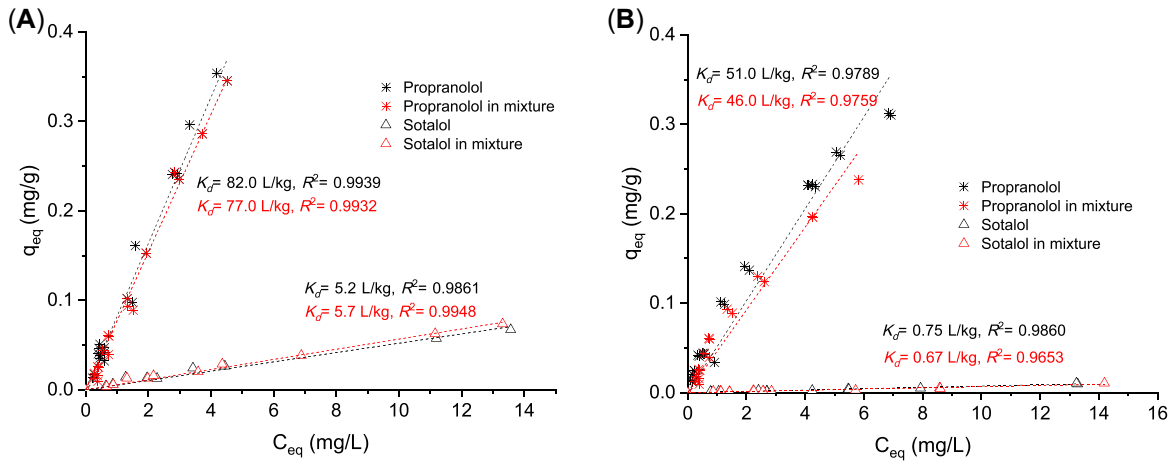

FIGURE 6: Adsorption isotherms of propranolol and sotalol on the soil (**A**) and on the sediment (**B**) fitted with the linear model enabling the determination of K_d adsorption parameter. β-blocker singly added in black and β-blockers in mixture in red. $T = 20\,°C$, pH_{solid}, solid concentration = 40 g/L.

sorption process (at least not to an extent that significantly influenced sorption).

CONCLUSIONS

According to adsorption experiments, propranolol is much more retained on solid surfaces than sotalol, indicating the greater availability and mobility of the latter. The retention of both β-blockers was greater on soil than on sediment, which evidenced a higher β-blocker availability and mobility at sediment/water interfaces than at soil/water interfaces in environmental conditions comparable to those of the soil and sediment investigated in the present study. These adsorption behaviors were in accordance with the differing speciation of both pharmaceuticals as a function of pH and with a cation exchange adsorption mechanism. No competitive effect was highlighted because the presence in a mixture of these pharmaceuticals did not affect these adsorption behaviors, even in presence of Cu, which is known to interact with them by coordination complex formation.

It is important to note that the present study was conducted at laboratory scale (40 g L^{-1} of soil/sediment and few hours of contact time for adsorption experiments but respecting the adsorption equilibrium time) in well-controlled conditions, which allows us to better understand the involved processes. It is thus difficult to extrapolate to the field scale where the surface area (many hectares) and time scale (many decades) involved are higher. Field experiments, which are unambiguously more environmentally relevant, involve several uncontrolled parameters, preventing a full understanding of the fate of contaminants, hence laboratory experiments such as those conducted in the present study remain vital for elucidating the processes and mechanisms occurring.

Supporting Information—The Supporting Information is available on the Wiley Online Library at https://doi.org/10.1002/etc.5448.

Acknowledgment—The authors would like to thank the French Seine-Normandy water agency for providing useful information for the present study. A. Destrebecq is acknowledged for ICP-OES analysis. The present study was carried out within the TrEcoPolEm project with the help of Champagne-Ardenne Region grant to R-M. Smith.

Author Contributions Statement—**Rose-Michelle Smith**: Investigation; Visualization; Writing—original draft. **Stéphanie Sayen**: Conceptualization; Methodology; Supervision; Resources; Writing—review and editing. **Emmanuel Guillon**: Conceptualization; Methodology; Supervision; Resources; Funding acquisition; Writing—review.

Data Availability Statement—Data, associated metadata, and calculation tools are available in the Supporting Information and from the corresponding author (stephanie.sayen@univ-reims.fr).

REFERENCES

Amendola, L., Molaioni, F., & Botrè, F. (2000). Detection of beta-blockers in human urine by GC-MS-MS-EI: Perspectives for the antidoping control. *Journal of Pharmaceutical and Biomedical Analysis*, *23*, 211–221. https://doi.org/10.1016/S0731-7085(00)00271-5

Arenas-Lago, D., Andrade, M. L., Lago-Vila, M., Rodriguez-Seijo, A., & Vega, F. A. (2014). Sequential extraction of heavy metals in soils from a copper mine: Distribution in geochemical fractions. *Geoderma*, *230–231*, 108–118. https://doi.org/10.1016/j.geoderma.2014.04.011

Association Française de Normalisation. (1995). *NF ISO 10693. Qualité du sol - Détermination de la teneur en carbonate - Méthode volumétrique*. Association Française de Normalisation.

Association Française de Normalisation. (1998). *NF ISO 14235. Qualité du sol - Dosage du carbone organique par oxydation sulfochromique*. Association Française de Normalisation.

Association Française de Normalisation. (1999). *NF X31-130. Qualité du sol - Méthodes chimiques - Détermination de la capacité d'échange cationique (CEC) et des cations extractibles*. Association Française de Normalisation.

Association Française de Normalisation. (2003). *NF X31-107. Qualité du sol - Détermination de la distribution granulométrique des particules du sol - Méthode à la pipette*. Association Française de Normalisation.

Association Française de Normalisation. (2005). *NF ISO 10390. Qualité du sol - Détermination du pH*. Association Française de Normalisation.

Bontchev, P. R., Ivanova, B. B., & Mehandjiev, D. R. (2003). Binuclear complexes of copper(II) with the antihypertensive drugs salbutamol and sotalol. *Bulgarian Chemical Communications*, *35*, 21–24.

Burke, V., Treumann, S., Duennbier, U., Greskowiak, J., & Massmann, G. (2013). Sorption behavior of 20 wastewater originated micropollutants in groundwater—Column experiments with pharmaceutical residues and industrial agents. *Journal of Contaminant Hydrology*, *154*, 29–41. https://doi.org/10.1016/j.jconhyd.2013.08.001

Cleuvers, M. (2005). Initial risk assessment for three beta-blockers found in the aquatic environment. *Chemosphere*, *59*, 199–205. https://doi.org/10.1016/j.chemosphere.2004.11.090

Dang, D. H., Layglon, N., Ferretto, N., Omanović, D., Mullot, J.-U., Lenoble, V., Mounier, S., & Garnier, C. (2020). Kinetic processes of copper and lead remobilization during sediment resuspension of marine polluted sediments. *Science of the Total Environment*, *698*, 134120. https://doi.org/10.1016/j.scitotenv.2019.134120

Ding, J., Lu, G., Li, S., Nie, Y., & Liu, J. (2015). Biological fate and effects of propranolol in an experimental aquatic food chain. *Science of the Total Environment*, *532*, 31–39. https://doi.org/10.1016/j.scitotenv.2015.06.002

Doré, E., Deshommes, E., Laroche, L., Nour, S., & Prévost, M. (2019). Lead and copper release from full and partially replaced harvested lead service lines: Impact of stagnation time prior to sampling and water quality. *Water Research*, *150*, 380–391. https://doi.org/10.1016/j.watres.2018.11.076

Drillia, P., Stamatelatou, K., & Lyberatos, G. (2005). Fate and mobility of pharmaceuticals in solid matrices. *Chemosphere*, *60*, 1034–1044. https://doi.org/10.1016/j.chemosphere.2005.01.032

Fagnano, M., Agrelli, D., Pascale, A., Adamo, P., Fiorentino, N., Rocco, C., Pepe, O., & Ventorino, V. (2020). Copper accumulation in agricultural soils: Risks for the food chain and soil microbial populations. *Science of the Total Environment*, *734*, 139434. https://doi.org/10.1016/j.scitotenv.2020.139434

Farré, M., la, Pérez, S., Kantiani, L., & Barceló, D. (2008). Fate and toxicity of emerging pollutants, their metabolites and transformation products in the aquatic environment. *TrAC, Trends in Analytical Chemistry*, *27*, 991–1007. https://doi.org/10.1016/j.trac.2008.09.010

Gabet-Giraud, V., Miege, C., Jacquet, R., & Coquery, M. (2014). Impact of wastewater treatment plants on receiving surface waters and a tentative risk evaluation: The case of estrogens and beta blockers. *Environmental Science and Pollution Research*, *21*, 1708–1722. https://doi.org/10.1007/s11356-013-2037-7

Godoy, A. A., Kummrow, F., & Pamplin, P. A. Z. (2015). Occurrence, ecotoxicological effects and risk assessment of antihypertensive pharmaceutical residues in the aquatic environment—A review. *Chemosphere*, *138*, 281–291. https://doi.org/10.1016/j.chemosphere.2015.06.024

Gölcü, A., Yücesoy, C., & Serin, S. (2004). Synthesis and characterization of metal complexes of acebutolol. Atenolol, and rpopranolol antihypertension drugs. *Synthesis and Reactivity in Inorganic Metal-Organic Chemistry*, *34*, 1259–1275.

Graouer-Bacart, M., Guillon, E., & Sayen, S. (2015). Adsorption of enrofloxacin in presence of Zn(II) on a calcareous soil. *Ecotoxicology and Environmental Safety*, *122*, 470–476.

Graouer-Bacart, M., Sayen, S., & Guillon, E. (2013). Macroscopic and molecular approaches of enrofloxacin retention in soils in presence of Cu(II). *Journal of Colloid and Interface Science*, *408*, 191–199. https://doi.org/10.1016/j.jcis.2013.07.035

Guaita, D. P., Sayen, S., Boudesocque, S., Guillon, E. (2011). Copper(II) influence on flumequine retention in soils: Macroscopic and molecular investigations. *Journal of Colloid and Interface Science*, *357*, 453–459. https://doi.org/10.1016/j.jcis.2011.01.097

Huggett, D. B., Brooks, B. W., Peterson, B., Foran, C. M., & Schlenk, D. (2002). Toxicity of select beta adrenergic receptor-blocking pharmaceuticals (B-blockers) on aquatic organisms. *Archives of Environmental Contamination and Toxicology*, *43*, 229–235. https://doi.org/10.1007/s00244-002-1182-7

Lin, A. Y.-C., Lin, C.-A., Tung, H.-H., & Chary, N. S. (2010). Potential for biodegradation and sorption of acetaminophen, caffeine, propranolol and acebutolol in lab-scale aqueous environments. *Journal of Hazardous Materials*, *183*, 242–250. https://doi.org/10.1016/j.jhazmat.2010.07.017

Liu, J., Lu, G., Zhang, Z., Bao, Y., Liu, F., Wu, D., & Wang, Y. (2015). Biological effects and bioaccumulation of pharmaceutically active compounds in crucian carp caged near the outfall of a sewage treatment plant. *Environmental Science: Processes & Impacts*, *17*, 54–61. https://doi.org/10.1039/C4EM00472H

Liu, Q.-T., Williams, T. D., Cumming, R. I., Holm, G., Hetheridge, M. J., & Murray-Smith, R. (2009). Comparative aquatic toxicity of propranolol and its photodegraded mixtures: Algae and rotifer screening. *Environmental Toxicology and Chemistry*, *28*, 2622–2631. https://doi.org/10.1897/09-071.1

Massarsky, A., Trudeau, V. L., & Moon, T. W. (2011). β-blockers as endocrine disruptors: The potential effects of human β-blockers on aquatic organisms. *Journal of Experimental Zoology Part A Ecological Genetics and Physiology*, *315A*, 251–265. https://doi.org/10.1002/jez.672

Maszkowska, J., Stolte, S., Kumirska, J., Łukaszewicz, P., Mioduszewska, K., Puckowski, A., Caban, M., Wagil, M., Stepnowski, P., & Białk-Bielińska, A. (2014). Beta-blockers in the environment: Part I. Mobility and hydrolysis study. *Science of the Total Environment*, *493*, 1112–1121. https://doi.org/10.1016/j.scitotenv.2014.06.023

Maurer, M., Escher, B. I., Richle, P., Schaffner, C., & Alder, A. C. (2007). Elimination of β-blockers in sewage treatment plants. *Water Research*, *41*, 1614–1622. https://doi.org/10.1016/j.watres.2007.01.004

Mendoza, A., Aceña, J., Pérez, S., López de Alda, M., Barceló, D., Gil, A., & Valcárcel, Y. (2015). Pharmaceuticals and iodinated contrast media in a hospital wastewater: A case study to analyse their presence and characterise their environmental risk and hazard. *Environmental Research*, *140*, 225–241. https://doi.org/10.1016/j.envres.2015.04.003

Mioduszewska, K., Maszkowska, J., Białk-Bielińska, A., Krüger, O., Kalbe, U., Liberek, B., Łukaszewicz, P., & Stepnowski, P. (2016). The leaching behavior of cyclophosphamide and ifosfamide from soil in the presence of co-contaminant—Mixture sorption approach. *Science of the Total Environment*, *54*(Part A), 915–922. https://doi.org/10.1016/j.scitotenv.2015.11.002

Morel, M.-C., Spadini, L., Brimo, K., & Martins, J. M. F. (2014). Speciation study in the sulfamethoxazole-copper-pH-soil system: Implications for retention prediction. *Science of the Total Environment*, *481*, 266–273. https://doi.org/10.1016/j.scitotenv.2014.02.040

Ramil, M., El Aref, T., Fink, G., Scheurer, M., & Ternes, T. A. (2009). Fate of beta blockers in aquatic-sediment systems: Sorption and biotransformation. *Environmental Science and Technology*, *44*, 962–970.

Smith, R.-M., Sayen, S., Nuns, N., Berrier, E., & Guillon, E. (2018). Combining sorption experiments and time of flight secondary ion mass spectrometry (ToF-SIMS) to study the adsorption of propranolol onto environmental solid matrices—Influence of copper(II). *Science of the Total Environment*, *639*, 841–851. https://doi.org/10.1016/j.scitotenv.2018.05.118

Vasquez, M. I., Lambrianides, A., Schneider, M., Kummerer, K., & Fatta-Kassinos, D. (2014). Environmental side effects of pharmaceutical cocktails, *Journal of Hazardous Materials*, *279*, 169–189. https://doi.org/10.1016/j.jhazmat.2014.06.069

Verlicchi, P., & Zambello, E. (2015). Pharmaceuticals and personal care products in untreated and treated sewage sludge: Occurrence and environmental risk in the case of application on soil—A critical review. *Science of the Total Environment*, *538*, 750–767. https://doi.org/10.1016/j.scitotenv.2015.08.108

Viera, I., Gómez, M. A., Ellena, J., Costa-Filho, A. J., Migliaro, E. R., Domínguez, L., & Torre, M. H. (2009). Synthesis, structural characterization and ex vivo biological properties of a new complex [Cu(propranolol)$_2$]·2H$_2$O, a potential beta-blocker. *Polyhedron*, *28*, 3647–3653. https://doi.org/10.1016/j.poly.2009.07.064

Xu, J., Sun, H., Zhang, Y., & Alder, A. C. (2019). Occurrence and enantiomer profiles of β-blockers in wastewater and a receiving water body and adjacent soil in Tianjin, China. *Science of the Total Environment*, *650*, 1122–1130. https://doi.org/10.1016/j.scitotenv.2018.09.086

Yamamoto, H., Nakamura, Y., Moriguchi, S., Nakamura, Y., Honda, Y., Tamura, I., Hirata, Y., Hayashi, A., & Sekizawa, J. (2009). Persistence and partitioning of eight selected pharmaceuticals in the aquatic environment: Laboratory photolysis, biodegradation, and sorption experiments. *Water Research*, *43*, 351–362. https://doi.org/10.1016/j.watres.2008.10.039

