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Environmental risk assessment of selected pharmaceuticals in Turkey

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ABSTRACT

In this study, environmental risks of selected pharmaceuticals were investigated to assess potential hazards. Ciprofloxacin, Clarithromycin, Cefuroxime axetil, antibiotics, Benzalkoniuman antiseptic, Paracetamol, an analgesic, and Naproxen, an anti-inflammatory, were selected due to their high rate of usage in Turkey. Ciprofloxacin was found to have the highest risk due to its high PEC/PNEC ratio (28.636). Benzalkonium, Paracetamol and Clarithromycin have a potential to cause environmental hazards. The biodegradation and biological concentration factors (BCF) of the drugs were also determined using EPA/STWIN and EPA/BCFWIN programs. The results illustrated that these pharmaceuticals are nonbiodegradable in wastewater treatment plants. The BCFs of Benzalkonium and Clarithromycin were found to be very high, 70.790 L/kg and 56.490 L/kg, respectively. It was suggested that alternative treatment methods other than biological ones should be investigated for these pharmaceuticals because of their low biodegradability. Also, unnecessary use of antibiotics is supposed to be discouraged to reduce environmental hazards.

1. Introduction

Pharmaceuticals reach aquatic environments by hospital wastewaters, domestic wastewaters, wastewaters from pharmaceutical manufacturing facilities and disposal of unused medicines. Many drugs are disposed of without being highly metabolized in bodies and as a result of this, biologically active forms are mixed with water bodies (Buhner, 2002; Boxall and Breton, 2003). A study by Kummerer (2001) showed that pharmaceuticals used for anesthesia were discarded without being metabolized by a ratio of 90% (Kummerer, 2001). Pharmaceuticals which are not metabolized by the body usually are the least biodegradable drugs (Stuer-Lauridsen et al., 2000). Thus, these drugs cause bioaccumulation in aquatic and terrestrial environments (Halling-Sorensen et al., 1998). In addition, pharmaceutical active ingredients not metabolized by human and animals reach sewage systems and thereby, municipal wastewater treatment systems. So, they discharged to receiving environment without treatment. Table 1 shows concentration of these pharmaceuticals in aquatic environments in some countries worldwide.

Several studies on the biodegradation of pharmaceuticals in activated sludge wastewater treatment plants indicated that many of these pharmaceuticals are nonbiodegradable (Kummerer et al., 1997, 2000; Halling-Sorensen et al., 1998; Kummerer, 2001; Jones et al., 2002; Sebastine and Wakeman, 2003). Since nonbiodegradable pharmaceuticals are discharged directly to the receiving environments, environmental risk assessments of pharmaceuticals are essentially needed (Kummerer et al., 1997, 2000; Halling-Sorensen et al., 1998; Jones et al., 2002; Sebastine and Wakeman,

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Table 1 – Pharmaceuticals concentration in various water sample.

Pharmaceutical	Sample	Location	Concentration (ng/L)	References
Naproxen	Urban wastewater influent	Canada	1730–6030	Lee et al. (2005)
Naproxen	Urban wastewater influent	Sweden	3650–3800	Stumpf et al. (1999)
Naproxen	Hospital wastewater	Taiwan	698–915	Lin and Tsai (2003)
Naproxen	Urban wastewater influent	Spain	109–455	Hernando et al. (2006)
Paracetamol	Yeraltı suyu	USA	380–425	Barnes et al. (2008)
Paracetamol	Urban wastewater influent	Korea	13046–56944	Choi et al. (2008)
Paracetamol	Hospital wastewater	Spain	500–29000	Jones et al. (2005)
Ciprofloxacin	Hospital wastewater	Switzerland	3000–87000	Hartmann et al. (1998)
Ciprofloxacin	Urban wastewater influent	Canada	382–481	Lee et al. (2007)
Benzalkonium	River Water	Spain	1100–9700	Francisco et al. (2003)
Benzalkonium	Urban wastewater effluent	Spain	100–1100	Francisco et al. (2003)
Benzalkonium	Urban wastewater influent	Spain	4300–43000	Francisco et al. (2003)
Clarithromycin	Urban wastewater effluent	Germany	240	Hirsch et al. (1999)
Clarithromycin	Spring Water	Germany	260	Hirsch et al. (1999)
Cefuroxime Axetil	Hospital wastewater	Spain	24.04	Gros et al. (2013)
Cefuroxime Axetil	Urban wastewater influent	Spain	22.90	Gros et al. (2013)
Cefuroxime Axetil	Urban wastewater effluent	Spain	26.90	Gros et al. (2013)
Cefuroxime Axetil	River Water	Spain	5.48	Gros et al. (2013)

2003). To assess the environmental risks of pharmaceuticals, Predicted Environmental Concentration (PEC) of the pharmaceuticals, the Predicted Noeffective Environmental Concentration (PNEC) and PEC/PNEC ratios are generally used (Halling-Sorensen et al., 1998; Webb, 2000; Jones et al., 2002; Stockholm County Council, 2012; Sebastine and Wakeman, 2003; Kummerer, 2004; Remtsma and Jekel, 2006). If the PEC value of a pharmaceutical is below 0.01 μg/L, tests and researches of this pharmaceutical are not required. If PEC value is between 0.01 and 0.1, the PEC/PNEC ratio should be investigated. If the PEC/PNEC > 1, this pharmaceutical has serious risks to the environment and the investigation of this pharmaceutical is crucial (Sebastine and Wakeman, 2003). Alternatively, another method to specify the pharmaceutical risks is the City Council Stockholm. According to this method, the risk is specified as (Stockholm County Council, 2012):

Insignificant, if PEC/PNEC < 0.1
Low, if PEC/PNEC in the range of 0.1 to 1
Moderate, if PEC/PNEC in the range of 1 to 10
High, if PEC/PNEC > 10

The aim of this study is to investigate the risk assessments of the most commonly used pharmaceuticals having active ingredients with high PEC values. Ciprofloxacin, Clarithromycin, Cefuroxime axetil, antibiotics, Benzalkonium, an antiseptic, Paracetamol, an analgesic, and Naproxen, an anti-inflammatory, were selected due to their high rate of usage in Turkey. Only potential environmental risks of antibiotics have been studied in Turkey (Turkdogan and Yetilmezsoy, 2009). The biodegradability and BFCs of these drugs have not been investigated yet. The current study inspected not only antibiotics but also some other selected drugs carrying environmental risk hazards. The biodegradation potential and BFCs of these pharmaceuticals were studied as well.

2. Materials and methods

The pharmaceuticals chosen in this study are classified as the most widely used in Turkey according to the pharmaceutical industry special expert commission report (T.S.P.O., 2006).

First, the predicted environmental concentrations (PEC) of these pharmaceuticals were calculated; then, their ineffective environmental concentrations (PNEC) were determined based on the literature. Finally, the environmental risks were evaluated according to the PEC/PNEC ratios. In addition, biodegradation capabilities and biological concentration factors (BCF) of these pharmaceuticals were determined by the EPA's EPI Suite interface. Also, the octanol–water partition coefficients of the pharmaceuticals, log K_{ow} values, were determined and K_d values were calculated using the EPA's EPI Suite interface to verify absorption properties of these pharmaceuticals on surfaces (US EPA, 2001).

PEC values were found using Eq. (1) (EC, 1994; Stuer-Lauridsen et al., 2000; Jones, 2002).

$$\text{PEC (mg/L)} = \frac{A \times (100 - R)}{365 \times P \times V \times V \times 100} \quad (1)$$

where A: the amount of annual use of pharmaceuticals (to determine the amount of annual use of pharmaceuticals, data in the table of domestic demand projection in the pharmaceutical industry special expert commission annual report were used (T.S.P.O., 2006); R: removal rate before mixing with the water bodies (adjusted to 0 (Jones et al., 2002)); P: The number of people living in Turkey (75627384 (T.S.Ia 2013)); V: The amount of wastewater produced per person per day (182 L/person/day, (T.S.I b 2013)); D: Environmental dilution factor (usually 100) (EC, 1994; Stuer-Lauridsen et al., 2000; Jones, 2002). Also, to determine the biological treatability of pharmaceuticals in wastewater treatment plants, EPA/EPI Suite interface STWIN program was used, and to find out the bioconcentration factors (BCF) and the log K_{ow} values the BCFWIN and KOWWIN programs were applied, respectively (US EPA, 2001; Jones et al., 2002; Sebastine, 2003). K_d values were calculated using the following formula to decide the adsorption capacity of pharmaceuticals (Dobbs et al., 1989).

$$K_d = 0.58 + 1.14 \log \log K_{ow} \quad (2)$$

where K_{ow}: octanol/water partition coefficient.