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Comprehensive study of the antidiabetic drug metformin and its transformation product guanylurea in Greek wastewaters

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ABSTRACT

Many pollutants such as pharmaceuticals and their transformation products (TPs) are not efficiently removed from wastewater treatment plants and enter into surface waters. The aim of this study was to investigate the occurrence and behavior of metformin, one of the most prescribed drugs worldwide, and its biological transformation product guanylurea, in eight wastewater treatment plants (WWTPs) of Greece. All WWTPs were equipped with conventional activated sludge treatment and the samples were taken from the influents and the effluents, over the four seasons of one year. The analytical method developed based on SPE followed by LC-UV/Vis-ESI/MS analysis, while positive findings were confirmed also by means of LTQ Orbitrap mass spectrometer. High polarity of both compounds led to the extraction with Oasis HLB and the use of the anionic surfactant SDS. The results showed that metformin dominated in the influents (bql-1167 ng/L), while guanylurea in the effluents (bql-627 ng/L) of the wastewater treatment plants, with Metformin/Guanylurea ratio ranging between 0.88 and 81.3 in the influents and between 0.005 and 0.78 in the effluents. Lack of a clear seasonal tendency in the occurrence and removal or formation was observed. Finally, an ecotoxicological risk assessment of metformin in effluent wastewaters took place by calculating the ratio between the environmental concentrations (MEC) and the predicted no effect concentrations (PNEC). Despite the fact that metformin presented low risk in all cases, an environmental concern is suspected for guanylurea since it is continuously released into the aquatic environment.

1. Introduction

In recent years, there have been a number of research articles and reviews dealing with the environmental occurrence, distribution and transport at national, European and worldwide scale of a vast array of pharmaceuticals in aquatic environment. In this light, many high production volume medicines like β-blockers, analgesics, antibiotics, lipid regulators, anti-inflammatories, and X-ray contrasts etc have been

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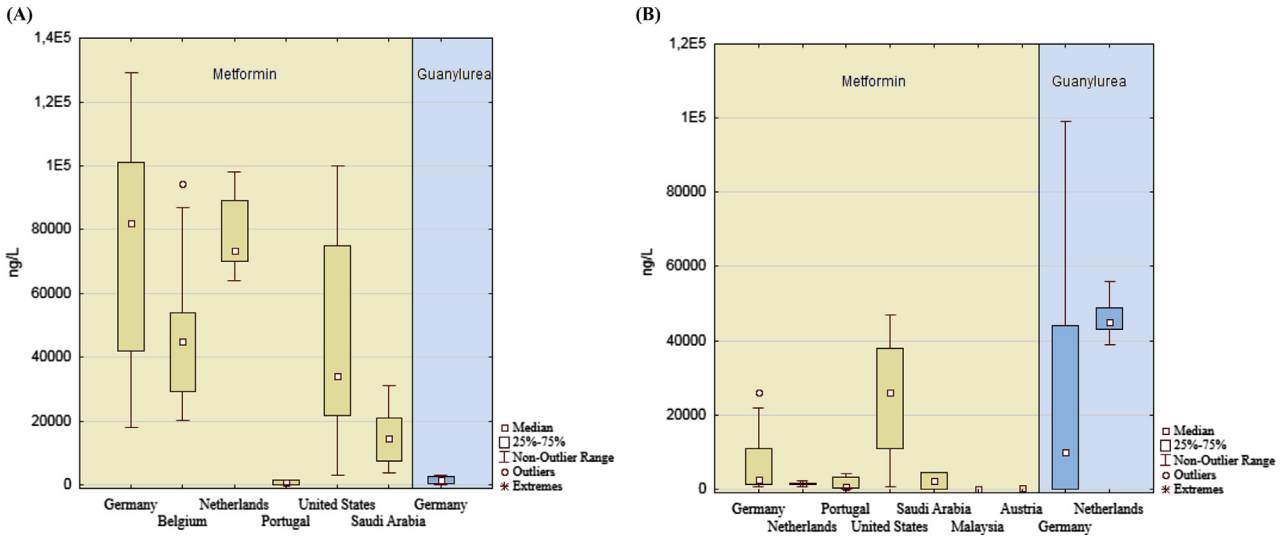

Fig. 1 – Concentration levels of metformin and guanylurea in (A) the influents and (B) the effluents of WWTPs, worldwide (Germany: Scheurer et al., 2009; Trautwein and Kümmerer, 2011; Scheurer et al., 2012; Belgium: Van Nuijs et al., 2010; Netherlands: Oosterhius et al., 2013; Portugal: Santos et al., 2013; United States: Blair et al., 2013b; Saudi Arabia: Shraim et al., 2012; Malaysia: Al-Odaini et al., 2010; Austria: Martín et al., 2012).

increasingly documented in groundwater, surface waters and wastewaters (Al-Qaim et al., 2014; Carmona et al., 2014; Gros et al., 2013; Kosma et al., 2010, 2014; Padhye et al., 2014; Stamatis et al., 2013; Stamatis and Konstantinou, 2013). However, antidiabetic drugs, which are among the most widely used pharmaceutical compounds, have received less attention. The number of people suffering from diabetes, a very common glucose-metabolic disease, accounts for more than 200 million on a worldwide scale. Hence, antidiabetic drugs are widely used for the treatment of this chronic disease and consequently, they are continuously being released into the environment through wastewater discharges from wastewater treatment plants. Interestingly, despite their high prescription rates and consumption volumes, up to date, little work has been conducted on the presence of antidiabetics in waters and wastewaters. Expectantly, the most attention has been given to metformin, which is the first line drug of choice used for the treatment of diabetes mellitus type II and is excreted non metabolized in the urine. In some countries metformin is in the top twenty list of prescribed, produced and environmentally loaded pharmaceutically active compounds and it is ranked number one in mass loading (1.10×10^6 kg/yr) (Dong et al., 2013). Its consumption increased in Netherlands and in Western Europe, with 26% between 2008 and 2012 and is expected to grow in the near future (ter Laak and Baken, 2014). Thus, not surprisingly, metformin has been detected in surface water, in concentrations up to 29 μg/L as well as in wastewater treatment plant influent and effluent up to 129 and 47 μg/L, respectively (Blair et al., 2013a, 2013b; ter Laak and Baken, 2014).

Until recently, relatively little work has been conducted on the environmental fate and distribution of metformin. Two recent works (Scheurer et al., 2012; Trautwein and Kümmerer, 2011), suggested that metformin is biologically transformed in activated sludge to the transformation product, known as guanylurea. Other studies demonstrated that because of their incomplete degradation and removal during wastewater treatment both compounds are expected in considerable amounts (up to several tens of mg/L) into effluents (see Fig. 1 & Fig.S1 (Supplementary Data)) and consequently into receiving waters. Furthermore, ter Laak and Baken (2014) reported that concentrations of metformin and guanylurea together, account for more than half of the total load of pharmaceuticals in surface waters. Due to the high environmental loading and the limited number of investigations on the environmental fate and occurrence of this group of bioactive compounds, increased knowledge is strongly recommended. Therefore, local research studies will be a key source of data to provide a better understanding of their behavior in wastewaters and water resources.

In view of the scarce data on the occurrence of antidiabetics in the aquatic environment, the aim of this work was: (1) to comprehensively investigate the simultaneous occurrence of metformin and its aerobic, bacterial dead-end TP, guanylurea, in eight WWTPs in Greece, by means of LC-UV/Vis-ESI/MS and LC-MS/LTQ Orbitrap systems, during one year monitoring program, (2) to evaluate the removal efficiencies across various types of WWTPs, (3) to provide a risk analysis in order to assess and compare the potential environmental risk of various types of wastewaters (hospital and municipal effluents) towards different aquatic organisms, (algae, daphnids, fish) through the calculation of risk quotients (Gros et al., 2010; Kosma et al., 2014; Valcárcel et al., 2011; Zhao et al., 2010).

To the present state of knowledge this is the first time that the simultaneous occurrence of these substances, is investigated in Greek aquatic environment and especially in conventional wastewater treatment plants. In addition, only a