Impact assessment of a large panel of organic and inorganic micropollutants released by wastewater treatment plants at the scale of France

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Abstract

Micropollutants emitted by Human activities represent a potential threat to our health and aquatic environment. Thousands of active substances are used and go to WWTP through wastewaters. During water treatment, incomplete elimination occurs. Effluents released to the environment still contain part of the micropollutants present in the influents. Here, we studied the potential impacts on Human health and aquatic environment of the release of 261 organic micropollutants and 25 inorganic micropollutants at the scale of France. Data were gathered from national surveys, reports, papers and PhD works. The USEtox ® model was used to assess potential impacts. The impacts on Human health were estimated for 94 organic and 15 inorganic micropollutants and on aquatic environment for 88 organic and 19 inorganic micropollutants highlighting lack of concentration and toxicological data in literature. Some Polycyclic Aromatic Hydrocarbons and pesticides as well as As and Zn showed highest potential impacts on Human health. Some pesticides, PCB 101, βE2, Al, Fe and Cu showed highest potential impacts on aquatic environment.

Keywords

Persistent compounds, trace metals, pharmaceuticals, human health, aquatic environment, WWTP effluents

1. Introduction

Micropollutants are unwanted substances which presence in the environment at very low concentrations (ng to µg/L in aquatic environment) is mainly due to Human activities (industrial processes, agricultural practices, daily life activities). Even at low concentrations, they can have negative effects on living organisms due to their toxicity, persistence and bioaccumulation in the food chain.

Wastewaters contain a huge variety of organic and inorganic micropollutants that are more or less eliminated from water during wastewater treatments (Besha et al., 2017; Choubert et al., 2011; Clara et al., 2005; Michael et al., 2013) by sorption to sludge, volatilization or physicochemical/biological transformation (Alvarino et al., 2018; Grandclément et al., 2017). As the elimination from water is not complete (Carballa et al., 2004), effluents still contain part of the micropollutants present in wastewaters. Those micropollutants are thus emitted to environment with effluents and can impact aquatic environment and Human health.

Organic micropollutants have known effects on living organisms and Human beings, like carcinogenicity, endocrine disruption (Ahmed et al., 2017). Inorganic micropollutants may also have different effects on health depending on their form (Gwenzi et al., 2018): carcinogenicity, nervous system degradation, gastric troubles, dermal pathologies, etc.

As WWTP are converging point and disseminate a huge diversity of micropollutants, it is important to know the risks or impacts associated to these compounds on human health and aquatic environment.

One way to prioritize chosen micropollutants is to use concentrations in effluents which allows determining quantities emitted to the aquatic environment but the simultaneous use of emitted quantities and toxicity of micropollutants shows sometimes a different prioritization of micropollutants as poorly concentrated substances can show high toxicity (Oldenkamp et al., 2018).

The risk is usually evaluated with risk quotient using PEC/PNEC or MEC/PNEC ratios (PEC: Predicted Environmental Concentration, MEC: Measured Environmental Concentration and PNEC: Predicted No Effect Concentration) (Brus and Perrodin, 2017; Gunnarsson et al., 2019; Oldenkamp et al., 2018; Škrbić et al., 2018; Verlicchi et al., 2012; Yang et al., 2017). If the quotient is superior to one, it is considered that the micropollutant represent a risk meaning that the predicted or measured concentration in the environment is superior to the concentration with no effect. Difficulties come from obtaining PEC, MEC and PNEC. PEC is obtained considering dilution of the emitted concentration in the aquatic environment thus it does not consider potential transformation and sorption to sediment that limit bioaccessibility of micropollutants. MEC considered the real concentration in the aquatic environment; it is thus necessary to have measure campaigns to obtain this concentration; MEC furthermore cannot allow identifying source of emission as it corresponds to a resultant of many emissions (WWTP, agriculture, industries, air deposit, etc.). PNEC considers chronic or acute EC10, EC50 or NOEC corrected with a factor (/10 or /1,000) that considers the most sensitive species which implies uncertainties as only one species is thus considered. This approach is limited by the fact that micropollutants are studied one by one and the overall risk of all micropollutants cannot be estimated.

Another way to study the burden of micropollutants on Human health or aquatic environment is to use Life Cycle Assessment (LCA) tools. LCA allows to estimate the potential impacts of one or a set of micropollutants. Muñoz et al. (2008) used LCA tools to assess the potential impacts of micropollutants contained in influent and effluent of a WWTP. They showed that, over 98 micropollutants (Water Framework Directive substances and pharmaceuticals compounds), 15 (12 organic and 3 inorganic micropollutants) were identified with elevated risk in effluents for Human health, aquatic and terrestrial environments. More recently, Ortiz de García et al. (2017) used USEtox® characterization factors to evaluate the potential toxicological and ecotoxicological impacts of 49 pharmaceuticals and personal care products emitted by WWTP in Spain; contrary to risk assessment with PEC or MEC/PNEC ratios, they could give an impact score of the mixture of 49 compounds. Whatever the LCA model used to obtain characterization factors that convert emitted mass in potential impact, it considered a fate factor that takes into account transformation and sorption of micropollutants in aquatic environment and an exposure factor that gives the level at which humans and organisms are really exposed.

Here, we decided to use LCA tools to evaluate the potential impacts on Human health and aquatic environment of a mixture of micropollutants both organic and inorganic emitted by WWTP at the scale of France. The consensual USEtox® characterization factors were used. First, we selected a list of micropollutants according to the European Policy applied to France and we reviewed reports and papers on quantification of micropollutants, including pharmaceuticals, in French WWTP effluents. Then we evaluated the mean French concentrations of those substances in WWTP effluents with data collected in literature and given by industrial partners. Finally, potential impacts were evaluated by converting annual mass emitted in the environment with characterization factors obtained in USEtox® (Rosenbaum et al., 2008).

2. Material and methods

2.1 Micropollutants selection

The selection of reference lists was based on (i) European legislation applied to France that sets up monitoring of micropollutants in aquatic environments, (ii) studies that quantified all or part of these micropollutants and (iii) studies that highlighted hazards of emerging micropollutants which are not yet considered in legislation.

The European Water Framework Directive (WFD) and its modification set objectives for the preservation and restauration of the quality of surface water (freshwater and costal water) and groundwater. They give a list of substances and groups of substances that are priority substances or hazardous priority substances. For these substances, Environmental Quality Standards (EQS) set concentrations that cannot be exceeded in surface and groundwater. This implies the setting up of strategies to reduce or suppress emissions to the environment and the monitoring of these substances in aquatic environment.

In France, due to the WFD, an action of survey and reduction of hazardous substances in water (RSDE) started in 2002 with monitoring campaigns of emissions of 2,800 installations classified for the protection of the environment including wastewater treatment plants (WWTP). Results of this campaigns (INERIS, 2007) allowed to conclude that WWTP contributed in a non-negligible way and sometimes in significant way to the emission of priority substances and hazardous priority substances in aquatic environment. This first step lead to the setting up of a specific monitoring of WWTP effluents. Priority substances and hazardous priority substances were measured in the effluents of 760 WWTP with a nominal capacity equal or superior to 10,000 people equivalents (PE). Results confirmed previous emissions data.

Scientists also used the list of substances of the WFD for a quantification campaign of micropollutants in 15 WWTP effluents in France (Martin Ruel et al., 2012). They also add pharmaceutical compounds that were not considered in WFD, WWTP effluents being one of the main route of emission to the environment of such compounds.

We selected micropollutants listed in (i) the WFD (Directive 2008/105/CE, n.d.), (ii) the RSDE national action for survey and reduction of hazardous substances in water (INERIS, 2016) and (iii) the AMPERES French project in which micropollutants (WFD and pharmaceuticals) were analyzed in influents and effluents of 15 WWTP (Martin Ruel et al., 2012). Other micropollutants were selected according to the scientific expertise of industrial partners.

45 substances and families were identified as priority or hazardous priority substances in WFD. Individual substances were selected and substances included in families were added. Substances from the watch lists were also selected. Finally, 116 substances from the WFD and its watch lists were selected (112 organics and 4 inorganics).

94 substances came from the French RSDE survey; 35 new substances were added during the second stage of the action which was set up in August 2016, these micropollutants were also included in the list. Finally, as 66 substances were in common with the WFD, a list of 179 substances (134 organics and 15 inorganics) was selected.

128 substances were studied in the AMPERES project. 70 substances were in common with the previous list. A list of 237 substances was selected (212 organics and 25 inorganics).

The expertise allowed to add 48 substances to the list (pharmaceuticals compounds and additional polycyclic aromatic hydrocarbons of the US-EPA list not taken into account previously).

For imidaclopride, two forms were identified and quantified separately in studies. So, we decided to study the two forms thus it added one substance to the list.

Finally, a list of 286 substances was selected with 261 organic micropollutants and 25 inorganic micropollutants (the list is given in supporting information). This list included 87 pharmaceuticals (Pharma), 66 pesticides (Pest), 18 PolyChloroBiphenyls (PCB), 17

PolyChloroDibenzoDioxines and Furanes (PCDD and PCDF), 16 Polycyclic Aromatic Hydrocarbons (PAH), 8 AlkylPhenols (AP), 8 halogenated volatile organic compounds (HVOC), 8 HaloPhenols (HPh), 7 PolyBromoDiphenylEthers (PBDE), 4 BTEX (Benzene, Toluene, Ethylbenzene, Xylenes), 5 HexaBromoCycloDoDecanes (HBCDD), 4 organotins (OSn), 3 chlorobenzenes (ClBz) and 10 non classified substances (PFOS, bisphenol A, chloroalkanes, etc.).

2.2 Mass released in the aquatic environment

2.2.1 Volume of water

The volume of water released in the environment with WWTP effluents was estimated using daily flows arriving to WWTP considering that the amount of water arriving to WWTP was the same as the one of effluent. Flows were obtained on official website of French WWTP monitoring ("Portail d'informations sur l'assainissement communal - Accueil," n.d.). The flows of all WWTP were added and multiplied by 365 days to obtain the annual water volume discharged in the aquatic environment. We did not consider wet weather flows. The annual volume of effluent was estimated at 5,000,000,000 m^3.

2.2.2 Concentration and mass

Data were collected in the report of the French survey RSDE (INERIS, 2016), in the published data of AMPERES project (Bruchet et al., 2015), in 30 articles dealing with micropollutants in French WWTP effluents (Andreozzi et al., 2002; Bergé et al., 2012; Botta et al., 2009; Cargouët et al., 2004; Cavalheiro et al., 2017; Chiffre et al., 2016; Dagnac et al., 2005; Deycard et al., 2017; Dinh et al., 2017b, 2017a; Ferrari et al., 2004; Gabet-Giraud et al., 2014, 2010; Grandcoin et al., 2017; Janex-Habibi et al., 2009; Johnson et al., 2005; Labadie and Budzinski, 2005; Leclercq et al., 2009; Li et al., 2013; Mailler et al., 2016, 2015; Miège et al., 2009b, 2009a; Muller et al., 2008; Oberlé et al., 2012; Rabiet et al., 2006; Sablayrolles et al., 2011; Tamtam et al., 2008; Thiebault et al., 2017; Togola and Budzinski, 2007; Tran et al., 2015; Wiest et al., 2018), in 6 PhD reports dealing with French WWTP (Cladière, 2012; Coetsier, 2009; Gilbert-Pawlik, 2011; Mailler, 2015; Pasquini, 2013; Pomiès, 2013) or given by WWTP stakeholders.

Wet weather data as well as data from tertiary treatment were excluded. Data inferior to limit of quantification were estimated at half of the quantification limit as usually applied in environmental studies (INERIS, 2016).

Data were highly variable from one study to another which is consistent with local usage. Moreover, in many papers and reports, no information was given on location or analysis time. But we have chosen to tackle with this diversity of data, characterize it and take into account of the uncertainties rather than work on a single source of data. In order to do so and to avoid giving to much weight to the highest concentrations, mean concentration was estimated using geometrical mean; instead of arithmetical mean.

Furthermore, confidence intervals at 95 % were estimated allowing to show the accuracy of data; indeed, the lowest was the interval, the lowest was the variation of data. Considering variability of data above time and location with geometrical mean and confidence interval allowed estimation of mean value for a year and at the scale of France. For most of the molecules, there was a factor 2 between mean values and interval confidence boundaries which was much lower than the error on characterization factors (1 or 2 log). In view of all the uncertainties of what was available, we can only wish for a greater sharing of measured and consolidated data from WWTP with, for example, open data.

For each substance, a reliability index was estimated. If the proportion of data inferior to the limit of quantification was higher than 90 %, the index was set at 0. For some substances, only one concentration was found in literature or given by WWTP stakeholders, in that case, if the concentration was superior to quantification limit, the index was set at 1 and the error on the logarithm was estimated at 100 % (maximum error for substances with high number of found concentrations). In all other cases, the index was set at 1. This index allowed to eliminate data which were not reliable.

Considering that the estimated volume and the mean concentrations were representative of the whole France, mass released annually in the aquatic environment was estimated by multiplying each concentration by the volume. Mass was converted in kilograms or tons.

2.3 Impacts

Characterization factors were obtained from USEtox 2.1® (Hauschild et al., 2008; Henderson et al., 2011; Rosenbaum et al., 2011, 2008). Model was set to Europe and characterization factors were obtained for emissions in freshwater compartment. Characterization factors (CFs) were calculated in USEtox 2.1® through the following formula: CF = FF x XF x EF. FF was the fate factor indicating the residence time in the environment and was estimating with physicochemical properties for organic micropollutants or speciation for inorganic micropollutants. XF was the exposure factor *i.e.* the fraction of micropollutants in environment that was available for organisms. EF was the effect factor corresponding to the effect on aquatic environment (considering three trophic levels) or the effect on Human health. For Human toxicity CFs, USEtox 2.1® calculated the intake fraction (iF) *i.e.* the amount of micropollutants absorbed through air, water and food after emission in freshwater compartment. iF was equal to XF x FF.

LCA tool was preferred to PEC/PNEC or MEC/PNEC approach as we wanted to estimate potential impacts of each micropollutants and the overall impact of the mixture; furthermore, the use of this method allowed us determining the impact linked to WWTP emissions only.

Potential impacts were estimated by multiplying the mass with the characterization factor. According to USEtox® documentation (Fantke et al., 2017), impacts were different if there was 1 or 2 log difference for respectively organic and inorganic substances. Only the error due to the variation of concentrations was plotted but USEtox® error on impacts was also considered for results interpretation.

For Human health, the impact was expressed in DALY (Disability Adjusted Life Year) which represented the number of years lost with illness, handicap or premature death. It considered both carcinogenic and non-carcinogenic effects.

For aquatic environment, the impact was expressed in PDF.m^3.d (Potentially Disappeared Fraction integrated with volume and time).

The total impact for Human health or aquatic environment was calculated by summing all the impacts. No agonist or antagonist effects were considered.

When summing concentrations, mass or impacts, geometrical mean values were added and considered as the total mean. The error for the total mean was the sum of 95 % confidence intervals limits.

3. Results and discussion

3.1 Concentration and mass

3.1.1 Organic micropollutants

225/261 organic micropollutants (86 %) presented at least one concentration in literature and WWTP stakeholders' data. The 36 organic micropollutants without data were: (i) 17 PCDD/PCDF, (ii) heptabromodiphenylethers, (iii) 11 pesticides (methiocarbe, acetamipride, clothianidine, thiaclopride, thiametoxame, metaflumizone, triallate, cybutryne, DDT 24', DDD 44', DDE 44') and (iv) 7 pharmaceuticals (butylated hydroxytoluene, octyl methoxycinnamate, 4-epi-chlortetracycline, chlortetracycline, doxycycline, acetylsulfamethoxazole, azoxystrobine).

153/261 organic micropollutants (59 %) presented reliability index of 1: 123 had more than one available data and 30 had only one available data. Mean concentrations and masses were calculated for these 153 compounds. The reliability index allowed to eliminate substances poorly quantified with high limit of quantification such as methanol or hydrazine.

Concentrations ranged from 0.1 $ng.L^{-1}$ to around 5 $\mu g.L^{-1}$ (Table I). This underlined the high variety of concentrations. 75 % of the concentrations were below 0.1 $\mu g.L^{-1}$. Annual masses ranged between 0.5 kg to 26 tons. 75 % of the annual mass were below 0.6 tons. 15 compounds had concentrations/mass higher than the 90^{th} centile: (i) 9 pharmaceuticals (valsartan, irbesartan, ranitidine, hydrochlorothiazide, chlordiazepoxide, sotalol, furosemide, carbamazepine, atenolol) and (ii) NP1EC (nonylphenol ethoxyacetic acid), trichloromethane, tetrachloroethylene, dichloromethane, AMPA (aminomethylphosphonic acid) and DEHP (bis(2-ethylhexyl)phthalate). Pharmaceuticals concentrations in the French effluents were in accordance with the data in Europe (Verlicchi et al., 2012). Results highlighted that some pharmaceuticals have high emissions to the environment compared to other organic micropollutants; these high mass may be due to (i) high concentrations in wastewaters, (ii) low sorption to sludge, (iii) poor biodegradability, (iv) transformation in parent compounds of conjugated forms or (v) combination of these hypotheses. DEHP is a plasticizer used in many manufactured products (Wormuth et al., 2006). Tetrachloromethane, dichloromethane and tetrachloroethylene are chemicals used in many industries. AMPA is a transformation product of glyphosate and phosphonates present in washing powders and liquids (Grandcoin et al., 2017). NP1EC is a transformation product of nonylphenol polyethoxylates which are common surfactants used in many chemical products (Ying et al., 2002), and can no longer be used without authorization since July 2019 (REACH UE n° 999/2017 and 2020/171 annex XIV).

For some of these highest concentrated organic micropollutants, EQS were available: 1,650, 452, 2.5, 2.5 and 1.3 $\mu g.L^{-1}$ for dichloromethane, AMPA, carbamazepine, trichloromethane and DEHP respectively. In this study, estimated concentrations in effluents were 3.01 (2.81 – 3.21 range from – 95 % to + 95 % confidence interval), 1.12 (0.59 – 2.14), 0.40 (0.29 – 0.54), 0.58 (0.55 – 0.61) and 0.73 (0.69 – 0.77) $\mu g.L^{-1}$ for dichloromethane, AMPA, carbamazepine, trichloromethane and DEHP respectively. In this case, all effluent concentrations were lower than EQS. In French survey, it is considered that a substance should be monitored if concentration in effluent was above ten times its EQS (consideration of a mean dilution factor of 10 in the aquatic environment). Applying this rule, none of these molecules should be monitored.

Concentrations in French rivers were also found (survey from 1st of January 2015 and 31st of December 2018, http://www.naiades.eaufrance.fr/ consulted the 20th and 23rd of September 2019) for these 15 organic micropollutants. Mean concentrations were calculated with all obtained data with the same hypotheses as for WWTP effluents. When quantification frequency was lower than 10 % no mean concentration was calculated. All the mean concentrations found in rivers remained below the effluent ones but the ratio between those concentrations (effluent/river) is variable depending on the compounds, underlying that considering a common dilution factor to predict the concentration in the river from the effluent one may contribute to calculation error of the risk quotient. DEHP, AMPA, furosemide, carbamazepine and atenolol had concentrations in effluent 2 to 4 times higher than mean concentrations in rivers; sotalol, hydrochlorothiazide and irbesartan had concentrations in effluent 7, 11 and 16 times higher respectively than mean concentrations in rivers. Thus, WWTP may contribute in a significant way to occurrences in rivers; indeed, except AMPA which can also be emitted by agricultural emissions, all cited micropollutants originate from urban activities.

Those 15 compounds (10 % of the compounds) represented 70 % of the total mass of the 153 organic micropollutants: 48 % for the 9 pharmaceuticals and 22 % for the other 6 compounds.

The total mass of the 153 organic micropollutants released in the environment by French WWTP was around 147 tons (between 107 and 223 tons considering confidence intervals).

3.1.2 Inorganic micropollutants

A concentration was estimated for 24/25 (96 %) inorganic compounds (Figure 1). Thallium was searched in effluents but never quantified; it was not therefore considered. Concentrations ranged from 0.01 $\mu g.L^{-1}$ (mercury) to 159 $\mu g.L^{-1}$ (iron). The total mass released in the environment was around 1,892 tons (range 1,382 to 3,005 tons). Main contributors to the total mass were, in decreasing order: iron (42 %), boron (17 %), aluminum (10 %), zinc (9 %) and manganese (7 %).

Most of organic micropollutants are synthetic substances produced by Human activities (PAH are also produced by natural sources such as forest fire) but inorganic micropollutants are naturally present in the environment and increase of concentrations in environment compartments is also linked to Human activities; natural presence in water and non-biodegradability can explain that concentrations of inorganic micropollutants are generally higher than those of organic micropollutants. Mean concentrations estimated in this study in the effluent are close to environmental concentration (Salpeteur and Angel, 2010) and above French drinking water limits.

As for organic micropollutants, concentrations were compared to EQS and mean rivers concentrations for the highest concentrations in WWTP effluents. Only zinc has EQS, stated at 7.8 or 3.1 $\mu g.L^{-1}$ depending on water alkalinity. For some rivers, zinc should be monitored as its mean concentration in effluents was 35 (33 – 37 range) $\mu g.L^{-1}$ thus superior to ten times the lowest EQS.

Aluminum concentration in effluents was half of the mean concentration in rivers; iron and manganese concentration in effluents were close to rivers concentration; boron and zinc concentrations were respectively 6 and 20 times higher in WWTP effluents than in rivers concentrations. WWTP might only be a major contributor of inorganic micropollutants for boron and zinc which was in accordance with their use by human activities in urban areas.

3.2 Potential impacts of organic micropollutants

3.2.1 Human health

The impact on Human health of organic micropollutants was calculated with the 94 substances with characterization factors over the 261 selected organic micropollutants (36 %) and over the 153 organic micropollutants with estimated concentrations (61%). This was due to the lack of concentrations and/or characterization factors. Butylphenol, aspirin, ibuprofen, cimetidine, hydrochlorothiazide, βE2, caffeine and theophylline had characterization factors equal to 0. The impact on Human health was estimated with compounds representing 48 % of the characterized organic micropollutants mass.

Impacts ranged from 0 to 2 DALY (Figure 2 A) with a total average impact of 6 DALY. Main contributors were benzo(b)fluoranthene, benzo(k)fluoranthene, indomethacin, dicofol, indeno(1,2,3-cd)pyrene, pentabromodiphenylethers, dibenzo(a,h)anthracene and diclofenac with respective contributions of 28, 16, 15, 13, 12, 6, 3 and 1 % of the total impact (considering substances with at least 1 % contribution to the total impact). Those eight compounds represented only 4 % of the 94 characterized organic micropollutants mass but 94 % of the total potential impact on Human health. It is thus important not only to consider the mass released in the environment for prioritization but also toxicity as stated by Oldenkamp et al. (2018). Among these 8 compounds, 4 are PAH that are produced by human activities and natural sources and thus are ubiquist in environmental matrices. The 2 following compounds are already banned of use: dicofol is an acaricide forbidden since 2010 in France and pentabromodiphenylethers are a group of flame retardant forbidden since 2004 in France. Their low residual presence in WWTP effluents is thus relied to illegal use or persistence in the environment. Only indomethacin and diclofenac, both anti-inflammatory drugs are still used in France. Compounds with the highest potential impacts to Human health corresponded mainly to recognized carcinogenic ones (especially PAH and polybromodiphenylethers).

Muñoz et al. (2008) studied the impact on Human health of 98 micropollutants using a scenario in which they were emitted to soil (use for agricultural crop irrigation) with characterization factors coming from two different methods. First method, EDIP 97 (scores expressed in m^3) highlighted two substances with the highest impact on Human health: gemfibrozil and nicotine; 2nd method, USES-LCA (scores expressed in kg-DCB-eq), highlighted two others substances: 2,3,7,8-TCDD and hexachlorobenzene. In our study, nicotine was not considered, 2,3,7,8-TCDD and hexachlorobenzene were first selected but not taken into account due to non-available concentration data in French effluents. Gemfibrozil was characterized for Human toxicity and showed only around 0.01 % contribution to the total potential impact. Difference in results came from the LCA methods used for characterization factors calculation and from the choice of compartment in which emission is made and the exposure pathway via crops irrigated with treated effluent.

Ortiz de García et al. (2017) using a similar methodology based on LCA only studied pharmaceutical compounds. Over 49 substances, they were able to quantify the impact of 41 ones. The total impact, calculated considering their masses and characterization factors, was 36 cases which was 2 log higher than the 0.8 cases we found for our 94 substances (it was only possible to convert our results in cases). The total mass emitted to the environment is an explanation to the difference as it was 234 tons for their study and only 71 tons for ours. Considering only pharmaceuticals compounds of our study (46 substances), the total impact was 0.1 cases and the total mass was 37 tons confirming that the emitted mass is a critical point for the impact on Human health ; in our study, characterized pharmaceuticals represented 52 % of the total mass and around 14 % of the total impact meaning that other less concentrated compounds had high impacts on Human health due to high toxicity. If we considered only common pharmaceuticals compounds between both studies (16), their impact was one log higher than ours (Figure 3 A). In terms of mass released to the environment, only carbamazepine, diclofenac and sulfamethoxazole had same orders of magnitude; EE2 and trimethoprim had mass higher in our study with one log difference; for others, masses were lower in our study with one log difference for norfloxacine, azithromycine, ciprofloxacin, naproxen, alprazolam, βE2, fluoxetine, clarithromycin and ibuprofen and with 2 logs difference for acetaminophen and omeprazole. Those differences highlighted the need to consider geographical difference between countries. Some characterization factors were different between the two studies probably due to the update of USEtox® database except for naproxen, ciprofloxacin, trimethoprim, acetaminophen, sulfamethoxazole and norfloxacin with same order of magnitude. Trimethoprim and diclofenac had impact superior in our study with one log difference; ciprofloxacin, sulfamethoxazole and naproxen had similar impacts in both studies; for the other substances, impacts were lower in our study with 1, 2, 3 or 4 logs difference. For βE2 and ibuprofen, our database gave null characterization factor avoiding comparison. For substances with the same characterization factors, the difference between the two studies came from the emitted mass in aquatic environment. In accordance with available comparison, it meant that, probably due to difference in terms of use, pharmaceuticals' potential impacts to Human health could be strongly impacted by the mass emitted to the environment. Nevertheless, both studies showed low impact on Human health whatever the considered micropollutants were.

Other studies only evaluated the risk linked to the presence of organic micropollutants in drinking water. Hollender et al. (2018) searched more than 500 organic micropollutants in drinking water. They found 123 substances with concentrations above quantification limits and showed that there was no significant risk for the consumption of these water due to organic micropollutants presence (comparison of the measured concentrations with a threshold value of 0.1 µg.L^{-1} (Threshold of Toxicological Concern Approach)). Enault et al. (2015) compared the contribution of environmental micropollutants exposure (11 mineral elements and 73 organic micropollutants); they also showed a minor risk due to the consumption of drinking water due to poor exposure via water although some micropollutants (lead, non-dioxin-like polychlorobiphenyls, PFOA, PFOS) might have a non-negligible risk compared to air or food exposure. de Jesus Gaffney et al. (2015) showed with quotient risk analysis that 16 pharmaceuticals compounds (quantified over 31 searched ones) present in surface water, underground water and drinking water did not show an elevated risk to Human health. Although those studies concerned drinking water, it tended to confirm our results as contamination of drinking waters partly occurred because of WWTP emissions especially for compounds only used in everyday life such as pharmaceuticals.

In our study, the total impact of organic micropollutants released in aquatic environment through WWTP effluents on Human health was low due to (i) the absence of direct exposure to these molecules, (ii) the buffer role of the environment and (iii) the treatment steps before exposure (drinking water: ozonation, activated carbon treatments than can eliminate a huge part of organic micropollutants (Simazaki et al., 2015)).

3.2.2 Aquatic environment

Over the 153 organic micropollutants with estimated concentrations, 88 (58 %) had ecotoxicity characterization factors. The impact on aquatic environment was estimated with compounds representing 44 % of the organic micropollutants mass.

Impacts ranged from 13.10^3 to 49.10^9 PDF.m^3.d (Figure 2 B). Main contributors to the total impact (61.10^9 PDF.m^3.d) were cypermethrin, PCB 101, βE2, amoxicillin and aclonifen with respective contributions of 82, 12, 2 and 1 %. As cypermethrin had a very high score, we also included in the list with the highest impacts 1,2,5,6,9,10-HBCDD, boscalid, dicofol, isodrin and dichlorvos which had a least 1 % of the total impact calculated without cypermethrine; those 10 compounds represented around 2 % of the 88 organic micropollutants mass but 99 % of the total impact. Cypermethrin is a pesticide which use is limited in France. PCB 101 is an ubiquist polychlorobiphenyl forbidden since 1987 in France but highly refractory to degradation in the environment. βE2 is a natural hormone produced by humans and animals. It is a well know endocrine disruptor and this estrogenic effect has already been observed after discharged of treated water in river (Miège et al., 2009b); but this molecule presents also high ecotoxicity for aquatic environment which implies a high effect factor and a high impact calculated with our approach. By comparison, EE2, well-known to have higher endocrine disruption effect than βE2 (Jobling et al., 2006) had a lower potential impact because its ecotoxicity (expressed in the effect factor) was lower. Amoxicillin (beta-lactam from the aminopenicillin family) is a well-used antibiotic in France. 1,2,5,6,9,10-HBCDD is a flame retardant which use was progressively reduced since 2011 due to suspicion of endocrine disruption effect. Dicofol, isodrine and dichlorvos are pesticides which uses are forbidden in France; on the contrary, aclonifen and boscalid use is authorized in France (both pesticides). Among those main contributors, suspected endocrine disruptors were present (PCB, chlorinated pesticides, brominated flame retardant) (Matthiessen et al., 2018; Vilela et al., 2018) even if this effect is not considered in the effect factor used to calculate the ecotoxicity characterization factor.

For the ten compounds having the highest impacts on aquatic environment, we observed that the exposure factor had low influence on the potential impact as it was close to 100 % for all compounds. Thus, mass, fate factor and effect factor had the highest influence: the effect factor had a great influence as its contribution to the impact was between 45 and 72 %; the emitted mass and fate factor had similar contributions between 7 and 32 %. In that case, toxicity of the substances had more effect than the quantity released to the environment or the degradation potency of those molecules.

Other studies used Life Cycle Assessment tools to determine potential impacts of micropollutants emitted by WWTP on aquatic environment. Muñoz et al. (2008), with the study of one WWTP in Spain, showed that fluoxetine, triclosan and ciprofloxacin had greatest potential impacts on aquatic environment with both models they used; with EDIP97 model 2,3,7,8-TCDD had high contribution to the impact whereas USES-LCA model highlighted ibuprofen. In our study, fluoxetine, triclosan, ciprofloxacin and ibuprofen ranked, in decreasing order of contribution, at the 49^{th}, 30^{th}, 43^{rd} and 82^{nd} positions respectively. In our case, the molecules with highest impacts were not considered in (Muñoz et al., 2008); ibuprofen had low contribution in our study due to the difference of emitted mass and/or evaluation of characterization factor (not the same models). 2,3,7,8-TCDD was in our initial list but not considered due to lack of French concentration data in WWTP effluents. Nevertheless, its USEtox® characterization factor was among the highest meaning that even with probably low concentration in effluent (highly hydrophobic compound) its impact should be among the highest.

Ortiz de García et al. (2017) only studied pharmaceutical compounds. The total impact on aquatic environment of their 45 characterized pharmaceuticals was in same order of magnitude of our 88 substances total impact (respectively $1.4.10^{10}$ and $6.1.10^{10}$ $PDF.m^3.d$). The huge difference was the mass as already shown for Human toxicity (236 tons and 64 tons for 45 pharmaceuticals and 88 substances respectively). It proved that substances with very low concentrations can have a great impact on aquatic environment; contrary to the potential impact on Human health, taking into account other substances than pharmaceuticals was of great concern. When considering only our 37 characterized pharmaceuticals (38 % of the mass and 4 % of the impact), emitted mass and impact had one log less than Ortiz de Garcia's results; thus both results seemed consistent. It highlighted once more that geographical situation was very important when estimating potential impacts. Among the 45 substances, we had calculated the impact for the 19 substances in common (Figure 3 B). The total emitted mass was 70 and 10 tons for their study and ours respectively and the total impact was $1.3.10^{10}$ and $2.2.10^{9}$ PDF.m^{3}.d respectively. As already shown previously, mass emitted to the environment were different except for salicylic acid, estrone and norfloxacin (same order of magnitude). Contrary to toxicity characterization factors, only amoxicillin, clarithromycin, estrone and venlafaxine characterization factors were not in the same order of magnitude. Difference occurred for potential impacts on aquatic environment mainly due to the difference of emitted mass. In both studies, βE2, azithromycin and clarithromycin had very high potential impact. Hormone and antibiotics (macrolides) showed also high ecotoxicity.

Prediction of concentrations in aquatic environment crossed with estimation of ecotoxicity allowed also to study potential impacts on aquatic environment (Lindim et al., 2019). In their study, the bioavailable concentrations of 54 pharmaceuticals were predicted in different rivers thanks to fugacity model STREAM-EU and their ecotoxicity effect was evaluated in percentage of the total Potentially Affected Fraction (PAF) using EC_{50} of each substance. In their study, some pharmaceuticals with highest contribution to predicted toxic pressure were among the list of the most impacting pharmaceuticals in our study (diclofenac, EE2, erythromycin, ciprofloxacin).

Neale et al. (2015) coupled analytical tools and biological bioassays with mixture-toxicity modeling to *in vitro* effects of micropollutants to detected organic micropollutants in water. They showed that for some effect, few molecules contributed to a large amount of the impact which was in accordance with our findings.

Johnson et al. (2019) studied the change of wastewater treatment process on the biodiversity of macroinvertebrates in a river of the United Kingdom between 1970 and 2010. They studied the evolution of BMWP index (Biological Monitoring Working Party) and the SPEAR indexes (Species at Risk) during time in the river flow. One carbon filter was set up between 2008 and 2014 as tertiary treatment; during this period no significant impact on macroinvertebrates was noticed due to the use of activated carbon; the observed improvement of biodiversity was related to the improvement of oxygen levels during the whole study. Authors estimated that, in this case, pollutants present in WWTP effluent were not a great threat compared to other emissions such as agricultural ones.

Other articles confirmed our results showing an impact on aquatic environment. Richmond et al. (2018) analyzed pharmaceutical compounds in 190 aquatic insects' larvae and other aquatic invertebrates and riparian spiders. They showed possible bioaccumulation in aquatic organisms such as brown trout and terrestrial organisms (spiders and platypus consuming insects' larvae and insects). No effect of bioaccumulation was studied. Ojemaye and Petrik (2019) analyzed 15 organic micropollutants (pharmaceutical compounds, perfluoroalkyl compounds and compounds from chemical industry) in fish caught near Cape Town. Eleven molecules were detected at least in one body part of each fish. With risk quotient, results showed that micropollutants present in fish represent a potential risk to fish and Humans that consume them. Our results are in accordance with a low but real risk of the presence of organic micropollutants in aquatic environment: bioaccumulation and risk for organisms. Remaining question is that neither our study nor literature show the deleterious effect, if any, of bioaccumulation in aquatic organisms. Other studies, using mixture of micropollutants, showed cocktail effects but these studies were made in lab-control conditions with concentrations generally higher than in real environment (Cizmas et al., 2015; Elisabete Silva et al., 2002; Rajapakse et al., 2001; Thrupp et al., 2018).

Verlicchi et al. (2012) showed high risk of some pharmaceuticals in aquatic environment using PEC/PNEC method. Antibiotics (especially macrolides) in common in our studies were shown to have great impact or risk on the aquatic environment.

Bioaccumulation, endocrine disruption, and toxicity of micropollutants had been already observed and quantified in literature with different methods. Our results tended to confirm negative effects of micropollutants released by WWTP in aquatic environment. Many studies focused on emerging micropollutants such as pharmaceuticals. Here we highlighted potential impacts of recalcitrant and persistent compound and pharmaceuticals. Furthermore, literature and our study also proved that, whatever the method used to evaluate risk or impact, it is necessary to cross released or environmental concentration and ecotoxicity effect to determine negative effects of organic micropollutants on aquatic environment. High potential impacts of both persistent and emerging compounds imply that both source reduction and addition of tertiary treatment might have significant impact on the reduction of micropollutants burden to the aquatic environment.

3.3 Potential impacts of inorganic micropollutants

3.3.1 Human health

Over the 24 inorganic micropollutants with estimated concentrations, 15 (63 %) had Human toxicity characterization factors. Missing ones were for Fe, B, Al, Mn, Rb, Li, Ti, Co and U. Sn and Se had null characterization factors. The impact on Human health was estimated with compounds representing only 17 % of the inorganic micropollutants mass; indeed, highly concentrated compounds in effluents such as Fe and Al were not characterized.

Impacts ranged from 0 (Sn and Se) to 503 (As) DALY. As and Zn were the main contributors to the total impact of 818 DALY (Figure 4) with respective contributions of 62 and 29 %;

those two compounds represented 63 % of the 15 characterized inorganic micropollutants mass.

3.3.2 Aquatic environment

Over the 24 inorganic micropollutants with estimated concentrations, 19 (79 %) had ecotoxicity characterizations factors. Missing ones were for B, Rb, Li, Ti and U. The impact on aquatic environment was estimated with compounds representing 76 % of the inorganic micropollutants mass.

Impacts ranged from 1,595,278 (Hg) to 1,973,471,331,644 (Al) PDF.m^3.d. Al, Fe and Cu were the main contributors to the total impact of 2,858,392,569,287 PDF.m^3.d. (Figure 5) with respective contributions of 69, 15 and 12 %; those three compounds represented 69 % of the 19 characterized inorganic micropollutants mass.

It is difficult to conclude on the potential impacts of inorganic micropollutants on Human health and aquatic environment. Indeed, they are naturally present in the environment making difficult to assess the real effects due to the release by WWTP on aquatic organisms and Humans. If USEtox® provides characterizations factors for metals, they are considered as "interim" and should be interpreted with caution, as they present a high degree of uncertainty (Fantke et al., 2017).

4. Conclusions

286 substances were selected for this study and the potential impacts on Human Health and Aquatic environment were estimated only with 1/3 of the molecules (Figure 6).

Total potential impacts on Human health varied between 3 to 14 and 761 to 904 DALY for respectively organic and inorganic micropollutants. Total potential impacts on aquatic environment varied between 18 to 22 and 2 408 to 3 407 billions PDF.m^3.d for respectively organic and inorganic micropollutants. For toxicity and ecotoxicity, the potential impacts were calculated with little number of molecules over the ones that had been selected. This highlighted the lack of concentration data and characterization factors. The actual knowledge of the effects of micropollutants on Human health and aquatic environment is limited.

Our studies raised question about the solution to reduce organic micropollutants impacts on Human health and aquatic environment. Reduction or ban on using is preferred in France; here, we highlighted that ubiquitous micropollutants (PAH), forbidden (PCB) or natural ones (hormone) are still found in effluents and contributed to the calculated impact meaning that this solution is not appropriate for all the micropollutants. Tertiary treatments are another way to reduce amount release to the environment but we need to know if they are sufficient to reduce micropollutants with highest impacts and studies to prove that degradation products, if any, are not more toxic than parent compounds. Furthermore, we can also question the cost implied by the addition of tertiary treatments: we need to know if the available tertiary treatment options are effective to remove micropollutants and if they are cost-effective considering their cost and the decrease of impact. Our results raised questions about the impacts of inorganic micropollutants; indeed, they are naturally present in water, most of the concentrations in WWTP effluents are closed to river concentrations but estimated impacts showed high risk due to these substances.

USETox® is only based on chronic toxicity data and does not consider endocrine disrupting effect. Moreover, effects of nanomaterials, microplastics, resistance genes, etc. were not considered by this method but can represent a huge impact on human health and aquatic environment. However, this method could be used to compare different scenarii: addition of tertiary treatment, reduction of emission at the source, etc. Here, as a first step of potential impacts estimation, we focus on mean mass values at the scale of France. We know that there is a spatial and temporal variation of micropollutants emission (Lindim et al., 2019); one perspective is to use this kind of method at the scale of catchment basin, considering other emissions coming from agriculture or industries. Furthermore, other emissions on WWTP (air, sludge) can be studied with this method and compared to effluent emissions.

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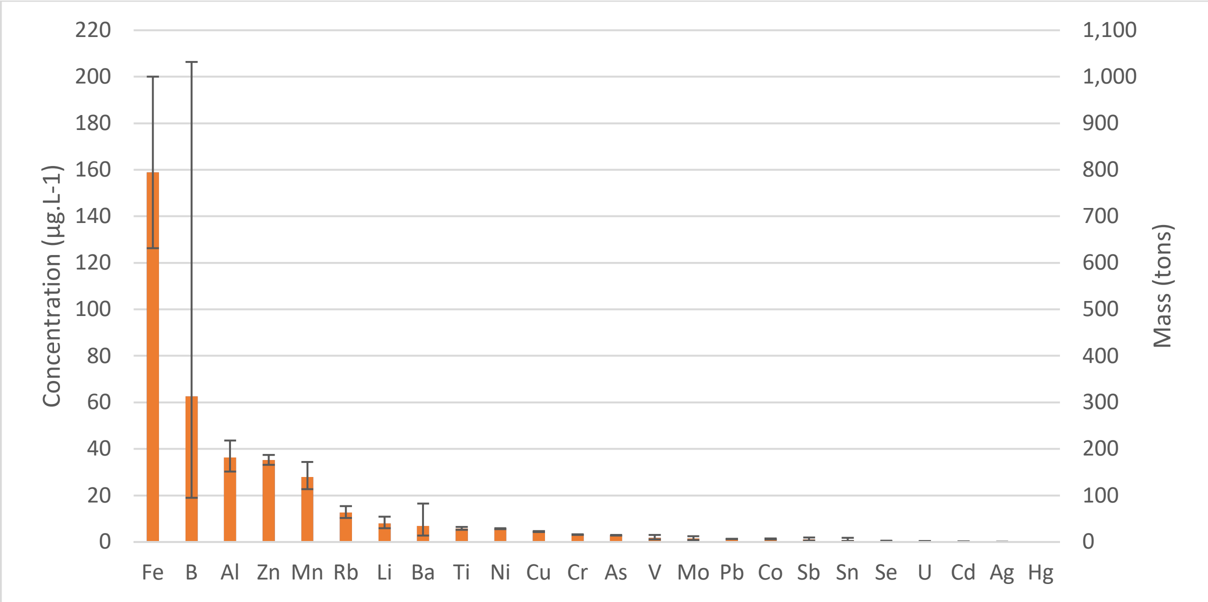


Figure 1. Concentration (left axis) and corresponding emitted mass in the environment calculated by multiplying the concentration with the one-year volume (right axis) of inorganic micropollutants in WWTP

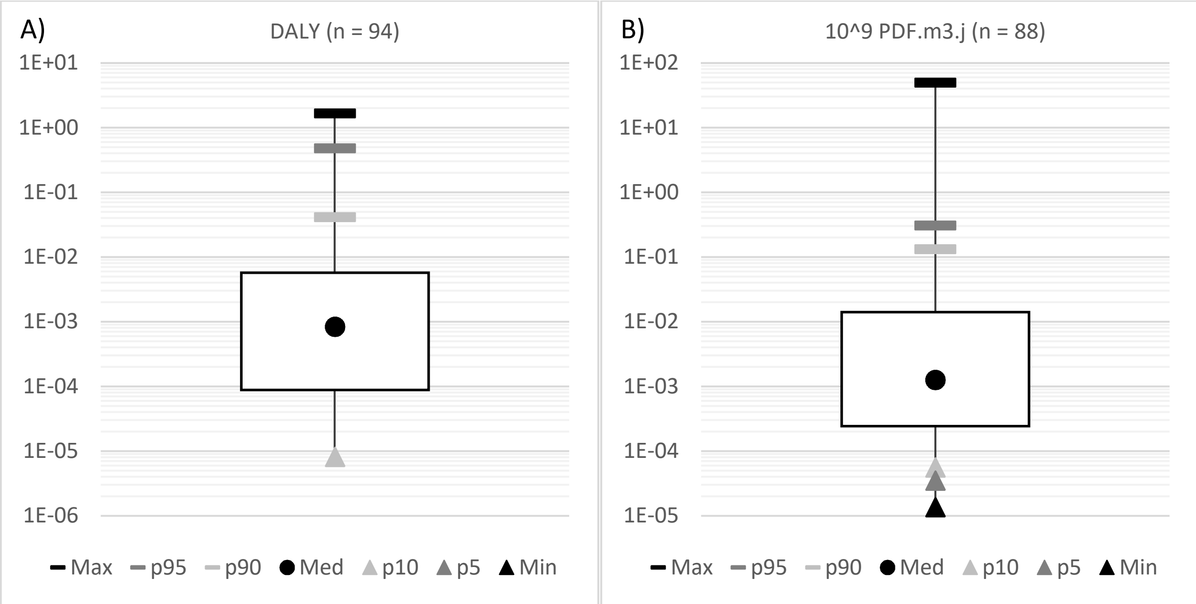
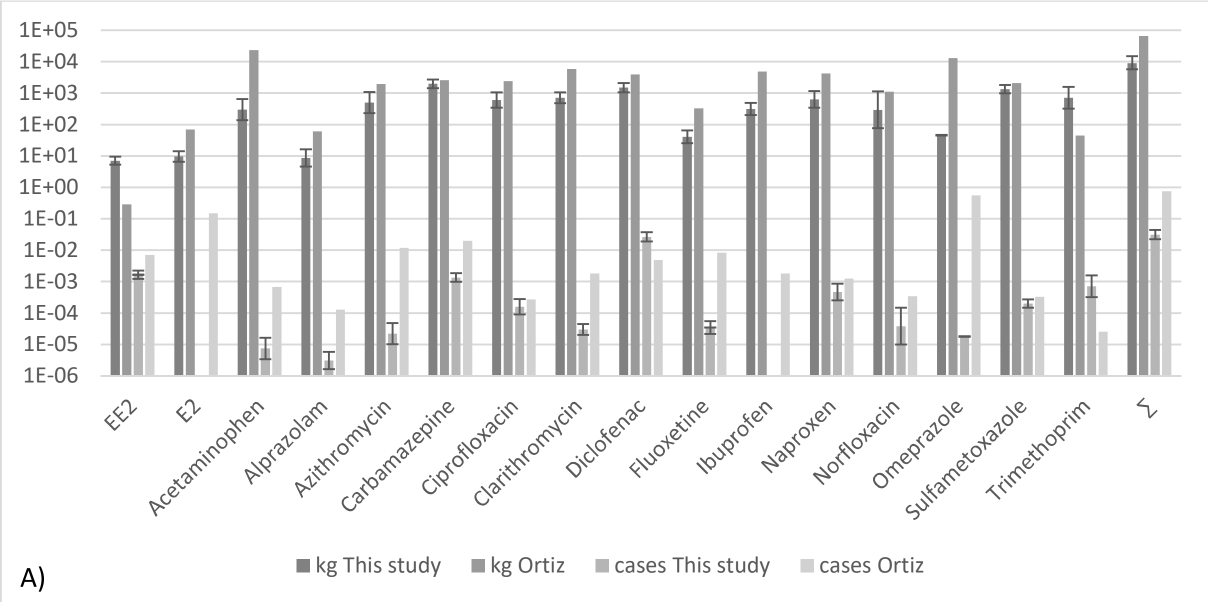


Figure 2. Distribution of the potential impacts on A) Human health of the 94/153 organic micropollutants with toxicity characterization factors and B) aquatic environment of the 88/153 organic micropollutants with ecotoxicity characterization factors; maximum (max), 95th percentile (p95), 90th percentile (p90), 3rd quartile, median (med), 1st quartile, 10th percentile (p10), 5th percentile (p5) and minimum are represented; DALY min and p5 are not represented because they are null and the data are represented in log scale



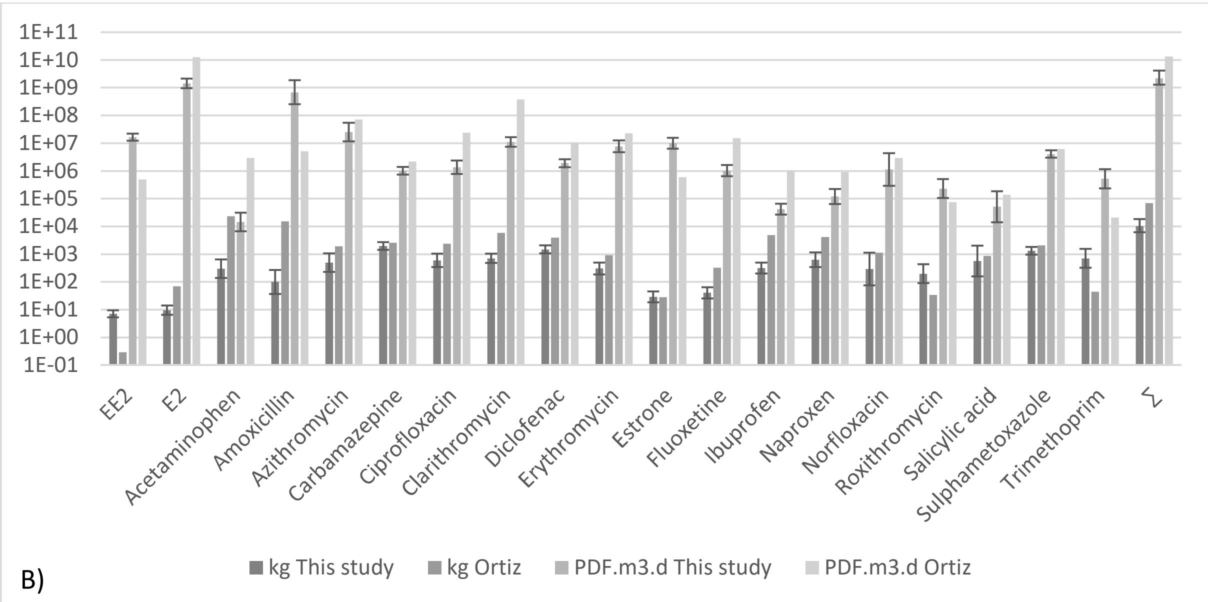


Figure 3. Comparison of masses and potential impacts for common pharmaceuticals of our study and Ortiz et al., 2019 study for A) Human health and B) aquatic environment

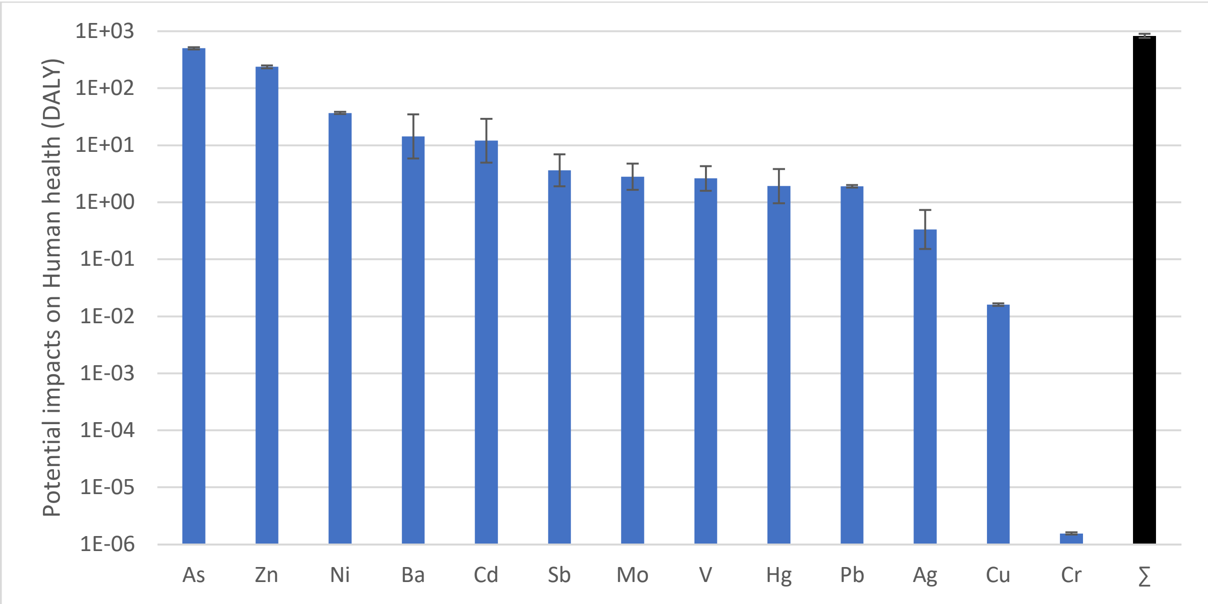


Figure 4. Potential impacts on Human health of the 15/24 inorganic micropollutants

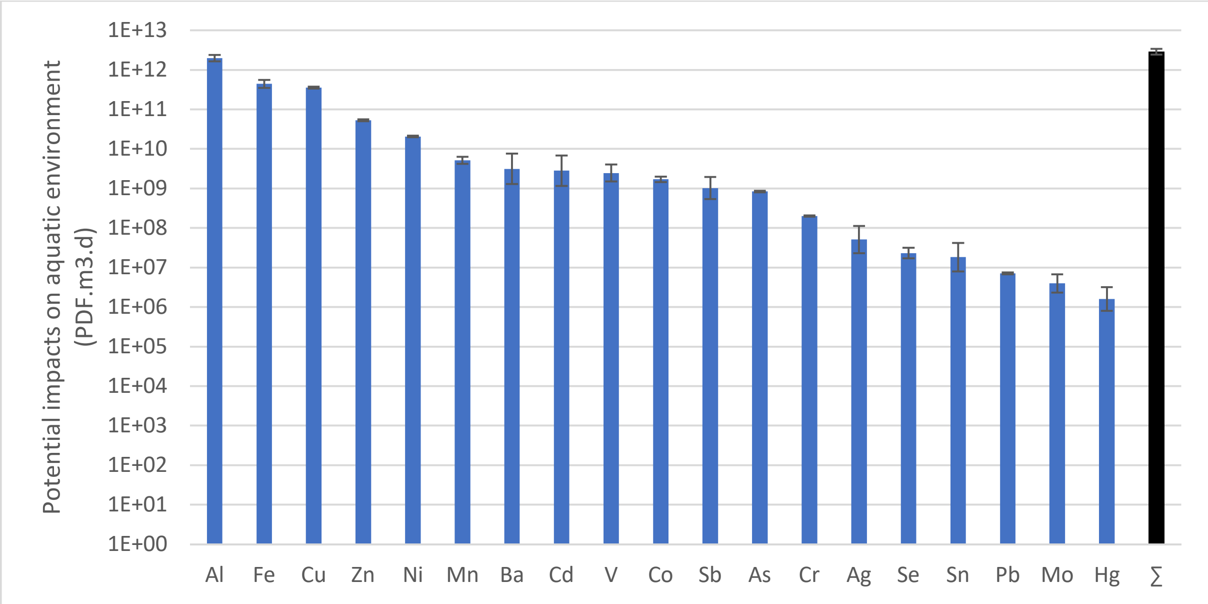


Figure 5. Potential impacts on aquatic environment of the 19/24 inorganic micropollutants

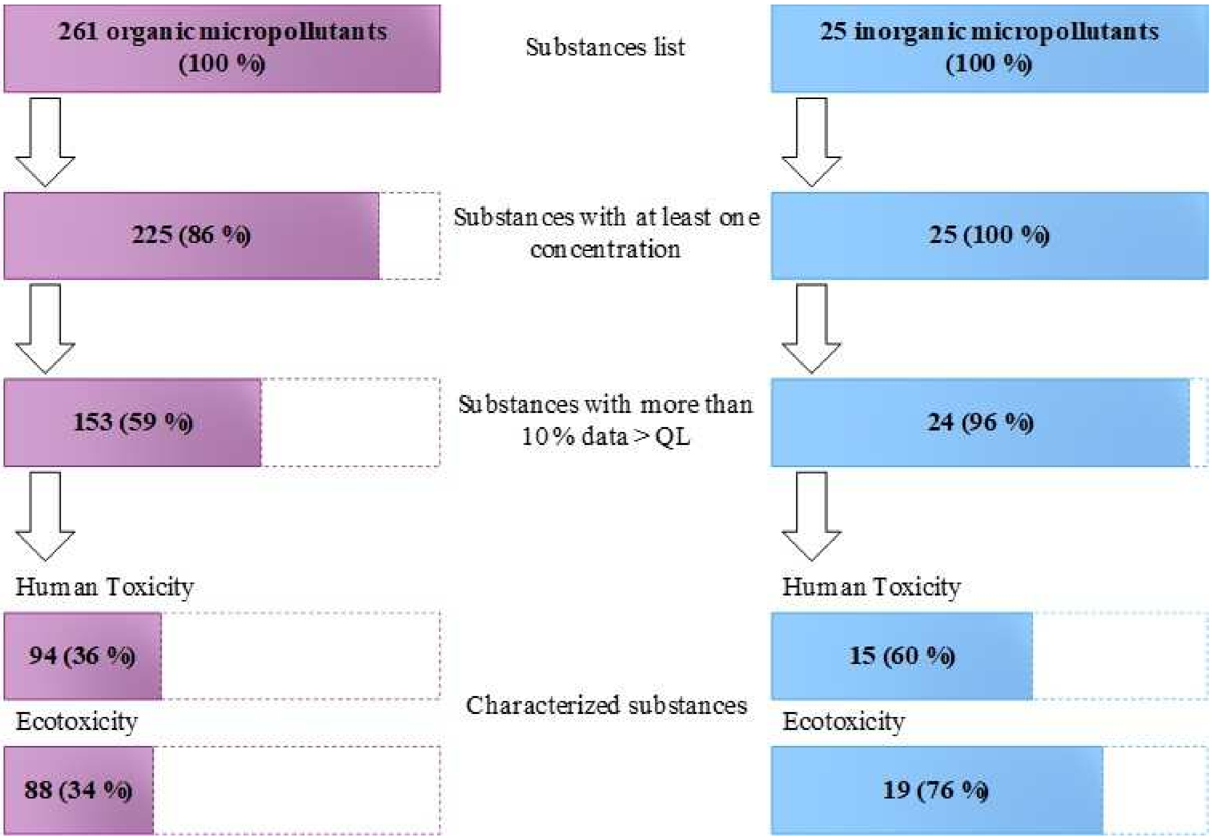


Figure 6. Synthesis of the study in number of molecules

Table I. Distribution of average concentrations and masses for the 153 organic micropollutants with measured concentrations in WWTP effluents

	Max	95th centile	90th centile	75th centile	50th centile	25th centile	10th centile	5th centile	Min
Concentration ($\mu g.L^{-1}$)	5,2	0,8	0,3	0,1	0,05	0,01	0,002	0,001	0,0001
Annual mass (tons)	26,1	3,9	1,5	0,6	0,27	0,04	0,010	0,006	0,0005

Graphical abstract