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ABSTRACT

The use of down-the-drain products and the resultant release of chemicals may lead to pressures on the freshwater environment. Ecotoxicological impact assessment is a commonly used approach to assess chemical products but is still influenced by several uncertainty and variability sources. As a result, the robustness and reliability of such assessments can be questioned. A comprehensive and systematic assessment of these sources is, therefore, needed to increase their utility and credibility. In this study, we present a method to systematically analyse the uncertainty and variability of the potential ecotoxicological impact (PEI) of chemicals using a portfolio of 54 shampoo products. We separately quantified the influence of the statistical uncertainty in the prediction of physicochemical properties and freshwater toxicity as predicted from Quantitative Structure-Property Relationships (QSPRs) and Quantitative Structure-Activity Relationships (QSARs) respectively, and of various sources of spatial and technological variability as well as variability in consumer habits via 2D Monte Carlo simulations. Overall, the variation in the PEIs of shampoo use was mainly the result of uncertainty due to the use of toxicity data from three species only. All uncertainty sources combined resulted in PEIs ranging on average over seven orders of magnitude (ratio of the 90th to the 10th percentile) so that an absolute quantification of the ecological risk would not be meaningful. In comparison, variation in shampoo composition was the most influential source of variability, although less than compared to uncertainty, leading to PEIs ranging over three orders of magnitude. Increasing the number of toxicity data by increasing the number of species, either through additional measurements or ecotoxicological modelling (e.g. using Interspecies Correlation Equations), should get priority to improve the reliability of PEIs. These conclusions are not limited to shampoos but are applicable more generally to the down-the-drain products since they all have similar data limitations and associated uncertainties relating to the availability of ecotoxicity data and variability in consumer habits and use.

1. Introduction

A significant number of chemical products, including many personal care products, are commonly disposed down the drain after use. The resulting discharge of their constituent chemicals to receiving waters may lead to an increased ecotoxicological pressure on the receiving ecosystem (Brausch and Rand, 2011; Caliman and Gavrilescu, 2009; Petrie et al., 2015). Risk assessment is typically used to assess and manage the environmental safety of individual chemicals in products and help maintain aquatic ecosystems and the services they provide (United Nations, 2018). A number of methods have already been developed to assess the aggregate potential ecotoxicological impact of products such as the critical dilution volume, the use of an impact score, or so-called toxic units (Saouter et al., 2018; Swartz et al., 1995; Van Hoof et al., 2011). Such assessments may be used for product comparisons and in product design.

The assessment of the potential ecotoxicological impacts (PEI) of products requires quantitative information on emission, fate, and effects of their constituent chemicals (Brausch and Rand, 2011; Escher et al., 2011; Rosenbaum et al., 2008). Data on the environmental fate and ecotoxicological properties of individual chemicals is managed and collated by regulatory agencies such as the European Chemicals Agency

(European Chemicals Agency, 2015). However, the data in the REACH database is of variable quality and actual toxicity data is often limited for many chemicals (Saouter et al., 2017a; Saouter et al., 2017b). Quantitative Structure-Property Relationships (QSPRs), Quantitative Structure-Activity Relationships (QSARs), and Quantitative Structure Biodegradability Relationship (QSBR) methods are often used to fill data gaps in physicochemical properties as well as to predict the fate (e.g. biodegradability and adsorption) and the toxicity of chemicals (Golsteijn et al., 2014; Gramatica et al., 2016; Sarfraz Iqbal et al., 2013; US EPA, n.d.). Yet, the use of QSAR predictions introduces additional uncertainties in all properties derived from them (Golsteijn et al., 2012; Harbers et al., 2006; Van Zelm et al., 2007).

Besides uncertainty, the assessment of the PEI of down-the-drain products is also influenced by various sources of variability including differences in the composition and formats of products (e.g. different formulations), in consumer habits (e.g. amount used) (Escamilla et al., 2012), in the presence and design of wastewater treatment plants (WWTPs) (Luo et al., 2014), and in differences in environmental conditions (Kounina et al., 2014) (e.g. high precipitation rates and low freshwater depths will decrease the residence time of a chemical in the freshwater compartment). To our knowledge, no research has systematically assessed and compared the influence of the different sources of uncertainty and variability on the potential ecotoxicological impact of down-the-drain products. We chose to focus on shampoos as a model group of down-the-drain products because of their global use, the number of different formulations or product types on sale, and the availability of consumer habit information. Shampoos have also been considered in previous exposure modelling studies for similar reasons (Ernstoff et al., 2016).

Here, we present a method to quantify and compare the influence of various sources of uncertainty and variability on the PEI of a single use of a down-the-drain product, namely shampoo. Sources of uncertainty considered were the predictive reliability of QSPRs and QSARs to estimate physicochemical properties as well as toxicity and the sampling uncertainty due to the limited number of ecotoxicity data. Sources of variability included were the variability in WWTP characteristics, the spatial variability of environmental parameters, the chemical composition of the product, and the variability in the amount of product used per application.

2. Methods

2.1. Potential ecotoxicological impact

The potential ecotoxicological impact (PEI) of product use is defined in Eq. (1).

$$PEI_P = A_P \cdot \sum_{c=1}^{N} F_{mass,c,P} \cdot (1 - E_c) \cdot (FF_{c,r} \cdot XF_{c,r}) \cdot EF_c \qquad (1)$$

$PEI_P \rightarrow$ Potential ecotoxicological impact per capita use of product P [PAF*m^3*day/capita]

$A_P \rightarrow$ Per capita use of product P [g/capita]

$N \rightarrow$ Number of chemicals c contained in product P [dimensionless]

$F_{mass,c,P} \rightarrow$ Mass fraction of chemical c in product P [dimensionless]

$E_c \rightarrow$ Removal efficiency of chemical c by a WWTP [dimensionless]

$FF_{c,r} \rightarrow$ Fate factor of chemical c in region r [day]

$XF_c \rightarrow$ Exposure factor of chemical c in region r [dimensionless]

$EF_c \rightarrow$ Effect factor of chemical c [PAF m^3/g]

The PEI quantifies the potential impact on the freshwater environment of a single product use in terms of the potentially affected fraction (PAF) of species integrated over space (m^3) and time (day). PAF describes the fraction of species in an ecosystem exposed to environmental concentrations higher than a concentration at which they are affected at a specific level or not at all (Klepper et al., 1998). The PAF is derived from species sensitivity distributions (SSDs) based on observed effect

concentrations of different species and allows inference about the entire ecosystem (Posthuma et al., 2001). This definition aligns with the definition of the ecotoxicological impact assessment method in life cycle assessments (Hauschild and Huijbregts, 2015).

In brief, for a single product use, the potential impact on the freshwater environment is expressed as the sum of the potential impact of each chemical within the product. The amount of each chemical predicted to enter the freshwater environment was determined assuming treatment in an activated sludge wastewater treatment plant (WWTP). Any removal processes taking place during the use phase (e.g. volatilisation or skin penetration) were assumed to be small and omitted following current practices in environmental risk and impact assessment (European Commission Joint Research Centre, 2003; Kapo et al., 2016).

Removal efficiencies were estimated using the SimpleTreat programme version 4.0 (Struijs, 2014). We then applied the approach proposed in the USEtox model with 16 regionally specified conditions to describe a single chemical's fate in the environment (Rosenbaum et al., 2008; Saouter et al., 2018). For each chemical contained in a product and each geographical region modelled in USEtox, the amount of chemical released was multiplied by a fate factor (FF), quantifying the residence time of the chemical in freshwater, and an exposure factor (XF), taking into account that only a fraction of the chemical is freely available for uptake in organisms (Pennington et al., 2004). The FF and the XF are derived from the physicochemical properties of the chemicals. These properties namely describe whether the chemical is likely to volatilise (if its vapour pressure is high), sorb to soil (if its octanol-water partitioning coefficient is high while considering its ionic character), or degrade in any of the environmental compartment. The effect factor (EF), which reflects the average chemical's toxic potency, was quantified with Eq. (2) following Huijbregts et al. (2010).

$$EF = \frac{0.5}{HC50} \qquad (2)$$

where HC50 stands for the hazardous concentration affecting 50% of the freshwater species at a concentration above their EC50. The EC50 is the concentration where 50% of individuals show an effect. The EC50 values we considered described acute effects.

2.2. Uncertainty and variability

2.2.1. Overview

Table 1 lists the uncertainty and variability sources identified for the parameters of Eq. (1). More details are provided in the Supplementary Information (SI, S1).

2.2.2. Uncertainty

We chose to apply widely-accepted quantitative structure-property relationships (QSPRs) to estimate the uncertain chemical properties listed in Table 1 (Aronson et al., 2006; US EPA, n.d.). QSPRs are regression models relating structural properties of chemicals to some of their physicochemical properties. This way, we ensured a reproducible methodology and a consistent quantification of the different uncertainty sources for all chemicals included.

All physicochemical and environmental fate properties were estimated with the EPI Suite programme (EPA, 2012) except for pKa and K_{OC} values. The ACD Labs programme was used to estimate the pKa (ACD/Labs, 2017) because of its good performance (Liao and Nicklaus, 2009; Meloun and Bordovska, 2007). The K_{OC} was estimated following recommendations in ECETOC (2013), Franco and Trapp (2008) and Sablijc et al. (1995) and using the K_{OW} estimated from EPISuite. No uncertainty distribution was hereby assigned to the K_{OW} to avoid any double-counting.

The EF for each chemical was derived from ecotoxicity values (EC50s) estimated with three species-specific QSARs for *Pseudokirchneriella subcapitata*, *Daphnia magna*, and *Pimephales promelas*

Table 1

Uncertainty and variability sources influencing the quantification of the potential ecotoxicological impact included in this assessment. The section where each source is explained in more details is shown in the table. n.a. stands for not applicable.

Parameter	Uncertainty (Section 2.2.2)	Variability (Section 2.2.3)
A_P	n.a.	Inter-individual variability in product use habits
$F_{mass,c,P}$	n.a.	Each product formulation considered was used as the starting point to compute a set of PEI while varying the uncertain and variable parameters
$FF_{c.r}$	Vapour pressure at 25 °C (P_{vap}), solubility at 25 °C (Sol), organic carbon-water partitioning coefficient (K_{OC}), pKa (negative base-10 logarithm of the acid dissociation constant), and degradation rate constants in air (k_{degA}), water (k_{degW}), sediment (k_{degSd}), and soil (k_{degSl})	Spatial variability from the 16 regions implemented in USEtox
XF_c	pKa and organic carbon-water partitioning coefficient (K_{OC})	Spatial variability from the 16 regions implemented in USEtox
E_c	Vapour pressure at 25 °C (P_{vap}), solubility at 25 °C (Sol), organic carbon-water partitioning coefficient (K_{OC}), pKa, and degradation rate constants in wastewater (k_{degWW})	Technological variability between activated sludge wastewater treatment plants (WWTPs) (Franco et al., 2013)
EF_c	Ecotoxicity values; limited sample size	

respectively. The three species chosen cover three different trophic levels to align with recommendations in literature (Hauschild and Huijbregts, 2015; Huijbregts et al., 2010) and environmental risk assessment guidelines. QSARs developed specifically for personal care ingredients were used where possible and the resultant EC50 values are hereafter referred to as $EC50_{PeCP}$ (Gramatica et al., 2016). For chemicals outside the applicability domain of the personal care ingredient QSARs we used the ECOSAR estimation programme from the US EPA. This programme assigns a chemical to a class depending on its structure and estimates EC50 values using a class-specific QSAR ($EC50_{ECOSAR}$) (EPA, 2017). Whenever multiple $EC50_{ECOSAR}$ estimates were available per chemical and species type, the lowest value was selected.

In a next step, we assigned an uncertainty distribution to each uncertain parameter as summarised in Table 2.

When the training datasets were available (section a in Table 2), we quantified QSAR prediction uncertainty over the range of input values. If not available (section b in Table 2), we assumed a constant QSAR prediction uncertainty over the range of input values. Finally, some parameters required specific approaches (section c in Table 2). This was because the regression models were built on training data sets classified via expert judgment, i.e. degradation rate constants k_{degW}, k_{degSd} and k_{degSl}. For the biodegradation rates, we had to quantify the uncertainty assuming a standard deviation in the reported values. We hereby based our approach on values derived from experimental data collected in (Aronson et al., 2006). The procedures for the individual parameters are explained in more detail in the SI, S2.

Table 2

Parameters used to describe the uncertainty of the mean value of the physicochemical properties. $\bar{x}$ refers to the mean value of the property of interest, n is the size of the training data set, p stands for the negative 10-logarithm, log() refers to the 10-logarithm of the value in brackets. Values in Italic represent the estimated value provided by the estimation programme. *D. magna* stands for *Daphnia magna*, *P. subcapitata* for *Pseudokirchneriella subcapitata* and *P. promelas* for *Pimephales promelas*. DT50 stands for the biodegradation half-life in water.

a. QSAR training data set available

Property	$\bar{x}$	Uncertainty quantification	n	Estimation method
P_{vap}	$\log(P_{vap})$	(Mendenhall et al., 2009)	3037	(EPA, 2012), MPBVP Help
Sol	$\log(Sol)$	(Mendenhall et al., 2009)	817	(EPA, 2012), WSKOWWIN Help
K_{OC} acid	$\log(K_{OC})$	(Mendenhall et al., 2009)	62	(Franco and Trapp, 2008)
K_{OC} base	$\log(K_{OC})$	(Mendenhall et al., 2009)	66	(ECETOC, 2013)
K_{OC} neutral	$\log(K_{OC})$	(Mendenhall et al., 2009)	81	(Sablijc et al., 1995)
$EC50_{PeCPs}$	$pEC50$	(Mendenhall et al., 2009) and published mean squared errors.	72 D. magna 20 P. subcapitata 67 P. promelas	(Gramatica et al., 2014; Gramatica et al., 2016; Gramatica et al., 2013)

b. QSAR training data set not available – error in estimating mean value only

Property	$\bar{x}$	Uncertainty quantification	Estimation method
pKa	pKa	Standard deviation provided by estimation programme per chemical	(ACD/Labs, 2017) and Unilever internal documentation
k_{degA}		Standard deviation derived from the coefficient of variation of 0.4	(van Zelm and Huijbregts, 2013)
$EC50_{ECOSAR}$	$EC50$	Lognormal distribution following (Reuschenbach et al., 2008)	(EPA, 2017)
HC50	$\log(HC50)$	Standard deviation from estimated EC50 values	(Huijbregts et al., 2010)

c. Specific approaches

Property	$\bar{x}$	Uncertainty quantification	Estimation programme
DT50	$\log(median (DT50))$	Vary according to category (SI, S2)	(Aronson et al., 2006; Sarfraz Iqbal et al., 2013)
k_{degW}		Derived from degradation rate constant (DT50): $k_{degW} = \ln(2)/DT50$	
k_{degSd}		Derived from degradation rate constant (DT50): $k_{degSd} = \ln(2)/(DT50/9)$	
k_{degSl}		Derived from degradation rate constant (DT50): $k_{degSl} = \ln(2)/(DT50/2)$	
k_{degWW}		Derived from k_{degW}: $k_{degWW} = 30 \cdot k_{degW}$	(EPA, 2017)

2.2.3. Variability

Four sources of variability were considered in our study, two of which were quantified using continuous probability distributions and two were incorporated through computation of all possible scenarios. Inter-individual variability in the amount of product used per application was described using consumer use survey results (Ficheux et al., 2016). Technological variability between WWTPs was incorporated by assigning probability distributions to the technological parameters required in SimpleTreat, as described in Franco et al. (2013). These distributions describe actual design characteristics for WWTPs in Europe, but were applied to the WWTPs for all regions as a first approximation. These two variability sources together make up the initial variability. We further included variability in product composition and variability in environmental conditions by computing the PEI for each possible combination. This means that for each product composition, we varied the uncertain and variable parameters to derive a set of PEI. This was repeated per product composition for all world regions implemented. More details on the product chosen and the product compositions included as well as the selection procedure are given in Section 2.3. The 16 world regions described by Kounina et al. (2014) hereby represent different environmental conditions (e.g. different land area or mean freshwater depth).

2.2.4. Monte Carlo analysis

Uncertainty and variability were separately propagated into the PEI by means of a two dimensional Monte Carlo (2D MC) simulation, performed with the program R, Version 3.3.2 (R Core Team, 2016). Per product-region combination, a two-step iterative procedure was implemented: First, all variable input parameters were sampled and fixed (outer loop), followed by a Monte Carlo simulation with 1000 iterations over the uncertain input parameters (inner loop). This was then repeated 1000 times, each time with a new set of variable parameter values, but with the same 1000 uncertain parameter values. The variance found in the inner and outer loops then reflects the influence of uncertainty and variability, respectively (Fig. 1).

These variations were characterised using the uncertainty ratio (UR) and variability ratio (VR) defined in Eqs. (3) and (4). Exemplarily, for the uncertainty ratio, the 90th and 10th percentiles are taken from the curve representing the median, i.e. the 50th percentile of the variability

Fig. 1. Cumulative probability distributions derived from the 1000 uncertain iterations, each curve representing the outcome for a different set of variable input parameters. Only the 90th and 10th percentiles are represented (dashed grey curves) as well as the median (black curve). The spread between the curves (highlighted in blue) represents the variability ratio, while the spread within one curve (highlighted in orange) depicts the uncertainty ratio. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

distribution.

$$UR = \frac{P90_{p50\ variability}}{P10_{p50\ variability}} \tag{3}$$

$$VR = \frac{P90_{p50\ uncertainty}}{P10_{p50\ uncertainty}} \tag{4}$$

2.2.5. Parameter's importance analysis

The importance of uncertainty and variability in the continuous input parameters (chemical properties, product use, and WWTP characteristics) was investigated using Spearman correlation coefficients (ρ). For the variable parameters, these coefficients were computed over all 1000×1000 simulations run per product-region combination. The contribution of each parameter to the overall variation in the PEI (r) was computed per product-region combination using Eq. (5).

$$r_{V1} = \frac{\rho_{V1}^2}{\sum_1^p \rho_{Vi}^2} \tag{5}$$

For the uncertain parameters, ρ and r were computed per variable iteration per product-region combination for each chemical.

The influence of the categorical variables was assessed in a separate step. Geographical variability was quantified as the change in variation between the 16 different regions when the product formulation was fixed. Analogously, the change in variation of the PEIs between products was quantified by fixing the region assessed.

2.3. Case study data

2.3.1. Shampoo formulations

We based our analysis on a set of 54 Unilever shampoo formulations for which detailed information on the composition and properties of the organic chemicals was available (SI, S4). These 54 shampoo compositions described formulations from 20 different brands found in 13 different countries, and included regular as well as antidandruff shampoos.

The precise composition of each fragrance in every single shampoo was not disclosed and hence fragrances were modelled using the publicly available information on the fragrance composition provided by Unilever for 12 shampoos in the USA on the SmartLabel website (Grocery Manufacturers Association, 2017). Individual fragrance ingredients are disclosed by the producer only if they are present above 0.01% of the product formulation. The 12 fragrances were assigned by shampoo brand in non-US countries (e.g. Brand A fragrance composition in the USA was assigned to Brand A shampoo formulations in other countries). 31 shampoo formulations were from brands not present in the US, and were therefore randomly assigned one of the 12 fragrances. The weight fraction of each fragrance ingredient was derived by dividing the total fragrance weight fraction by the total number of ingredients.

2.3.2. Chemicals

We aimed to include as many chemicals as possible in the assessment of the environmental impact of the shampoos considered. However, some chemicals did not have clear SMILES notation and their properties could therefore not be predicted with the available QSARs. The shampoos containing chemicals with unclear or imprecise SMILES notation with expected toxicities higher than 100 mg/L (e.g. EC50 values < 100 mg/L) were excluded from the analysis because their potential ecotoxicological impact could not be considered adequately (14 in total). The toxicity threshold was set to 100 mg/L as it represents a concentration orders of magnitude higher than what can be expected for chemicals in freshwater environments with the exposure scenarios of these types of compounds. On the other hand, shampoos containing chemicals with unclear or imprecise SMILES notations but with
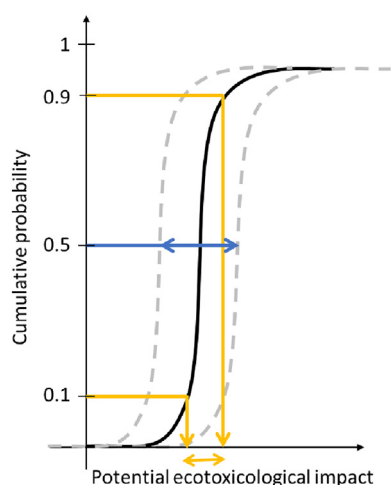
expected toxicities lower than 100 mg/L (e.g. EC50 values > 100 mg/L) were still considered in the analysis and the chemicals simply neglected from the ecotoxicological computation. The ingredients neglected were: plant extracts and oils, high molecular weight polymers, hydrolysed milk and animal proteins, vitamins, proteins and amino acids, honey, and yeast extract. Water was also neglected from the ecotoxicological impact computation. In addition, inorganic chemicals (K^+, N^+, O_2^-, SiO_2, Na^+, NH_4^+, Zn^{2+}, Cl^-, OH^-) were also neglected due to the lack of QSARs available to predict their fate and effect. The final total number of chemicals included was 102 (SI, S4).

2.3.3. Amount of shampoo used

The consumer use survey results gathered in France by Ficheux et al. (2016) were used to describe inter-individual variability in the amount of shampoo used per application. The aim was hereby to quantify the PEI of one use of shampoo somewhere in the world. From three candidate distributions, i.e. lognormal, gamma and Weibull, the lognormal distribution was found to be the best fit (SI, S3).

3. Results

Fig. 2 shows that the uncertainty ratio (P90/P10) of the PEI was on average around 7 orders of magnitude, but could range from nearly 4 to > 10 orders of magnitude depending upon the shampoo-region combination. The variability ratio of 3 orders of magnitude for the PEI of different shampoos within one region highlights the importance of the differences in shampoo formulation. In contrast, assuming 100% wastewater treatment, the variation in the median PEI between regions was relatively small: the highest median (for North Africa) was only 2 times larger than the lowest one (for North Australia) (SI, S5). This is also supported by the mean regional variability ratio of approximately 10 displayed in Fig. 2. The influence of the variable WWTP parameters and the variation in the amount of shampoo used per application was also small with a combined variability ratio of 8 (Fig. 2). Between both, the relative Spearman rank correlation coefficients showed that the influence of the variable WWTP parameters was nearly negligible (around 3.5%) compared to the variation in the amount of shampoo used per application (SI, S6).

In terms of their relative contribution to the PEI, the most important classes of ingredients were surfactants and fragrances followed by hair conditioning agents, antidandruff agents, and preservatives (Fig. 3). Fragrances, sequestrants, and hair conditioning agents, for their part, contributed largely to the variation in the final outcome as can be seen

by the long whiskers of these categories (Fig. 3).

The relative Spearman rank correlation coefficients showed that the uncertainty in the effect factor was the most influential, followed by the uncertainty in the removal efficiency from WWTPs, fate factor, and exposure factor (Fig. 4). Given the small differences in terms of importance analysis between regions, we present the contribution of the different parameters to the total variation in the PEIs for Europe only. The results for North Africa and North Australia are shown in the SI, S7. The uncertainty in the effect factor consists of uncertainty in the QSAR estimate itself as well as uncertainty resulting from the small number of data points available to derive it. We found that the small sample size was a particularly important source of uncertainty (SI, S8). We also observed that the uncertainty in the effect factors derived only from $EC50_{ECOSAR}$ was larger than when estimated from $EC50_{PeCP}$ only. In fact, it could span up to two orders of magnitude when all three EC50 values were estimated from ECOSAR whereas EFs estimated from $EC50_{PeCP}$ were always within the same order of magnitude (SI, S9).

The specific contribution of the physicochemical properties to the uncertainty in the PEI is shown in Fig. 5 by chemical function. Uncertainty in the biodegradation potential of fragrances and surfactants in water, sediment, soil, and wastewater had the largest influence on the uncertainty in the fate of the various chemical classes present in shampoo. As can be expected, the uncertainty in the solubility, degradation in air, and vapour pressure are more important for volatile ingredients, such as fragrances, than for surfactants.

4. Discussion

4.1. Variability sources of the potential ecotoxicological impact

The sources of variability assessed in our analysis included the amount of shampoo used, the shampoo composition, the WWTP's technological parameters, and the environmental conditions for 16 world regions specified in the USEtox model. While previous research highlighted the importance of consumer habits (amount of product used) when quantifying the potential ecotoxicological impact of personal care products (Escamilla et al., 2012), we found that variations between shampoo formulations were more important than differences in the amount of shampoo used per application. This even though the variability associated with differences in product formulation accounted for differences between products from a single manufacturer only. We could expect the variability associated with differences in product formulations to increase when considering other
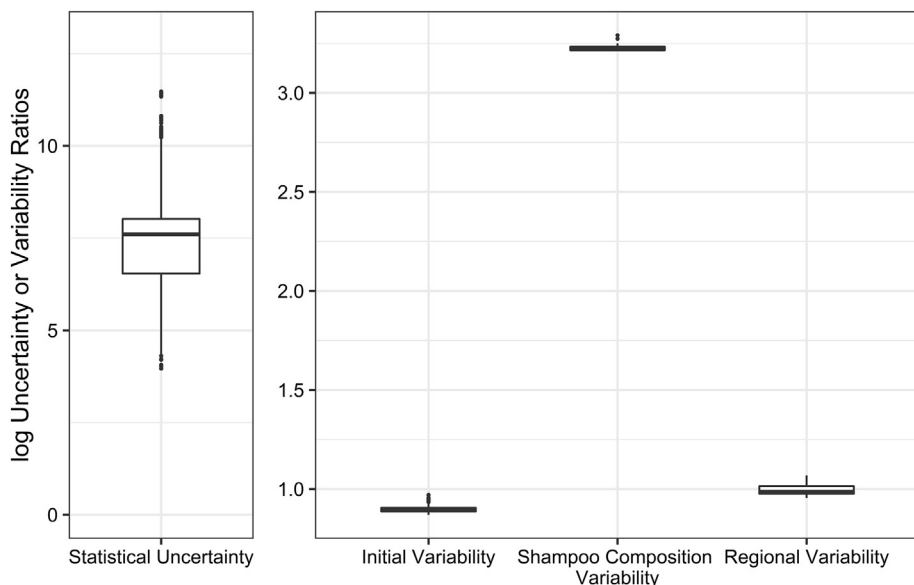

Fig. 2. Boxplots of the uncertainty (UR) and variability ratios (VR). The upper and lower line limits represent the 90th and 10th percentiles, while the box limits represent the 25th and 75th percentiles. The bold line is the median. The statistical uncertainty and initial variability correspond to the URs and VRs respectively computed per shampoo-region combination. The initial variability therefore considers the variability in the amount of shampoo used and the WWTP characteristics. In addition to the initial variability, the shampoo composition variability, describing the VRs computed per shampoo over all regions, also considers the variability in the shampoo composition, while the regional variability, describing the VRs computed per region over all shampoos, considers the initial variability and the variability between regions.
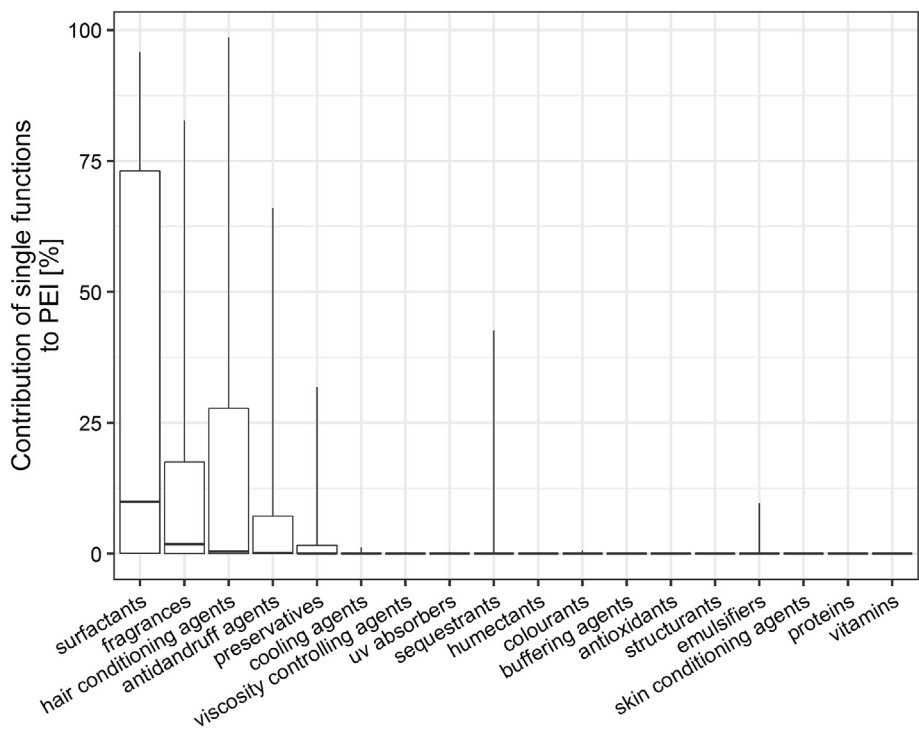
Fig. 3. Contribution of the chemicals' functions to the total potential ecotoxicological impact (PEI).
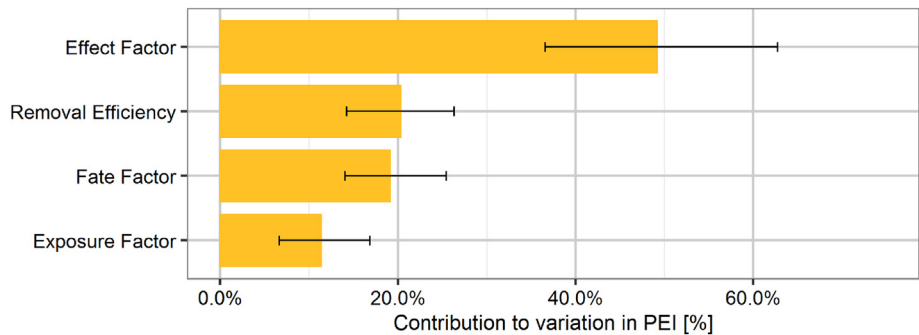

Fig. 4. Importance of the uncertain parameters for the overall variation in the potential ecotoxicological impacts (PEI) computed for Europe. The direction of the bar does not reflect the direction of the correlation. The whiskers represent the 10th and 90th percentile.
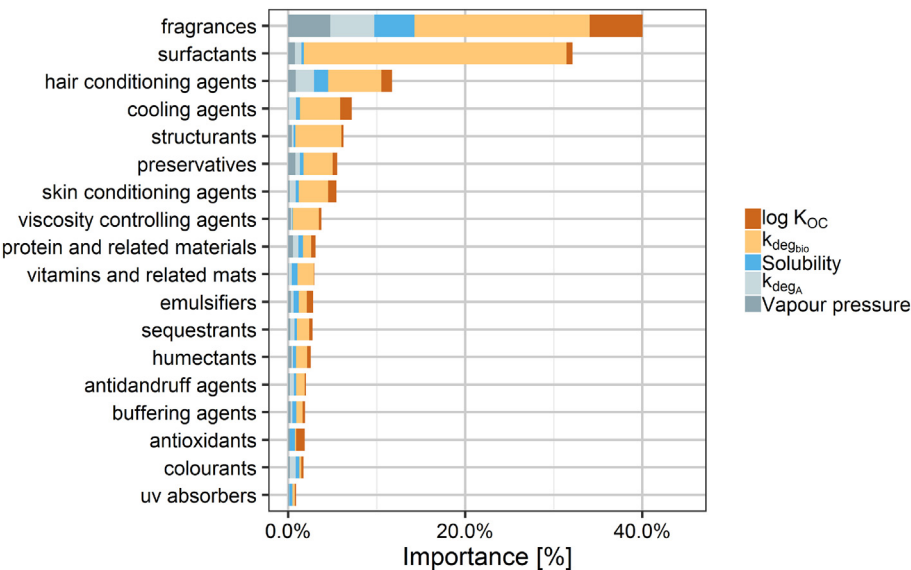

Fig. 5. Importance of the physicochemical properties per chemical's function for the uncertainty in the potential ecotoxicological impact, computed from the Spearman correlation coefficients available for Europe. K_{OC} is the soil organic carbon-water partitioning coefficient, k_{degbio} represent the biodegradation rate of the chemicals (in sediment, soil, water, and wastewater), and k_{degA} the degradation rate in air.

manufacturers' formulations. We also tested the sensitivity of our results to the assumption of equal weight fractions for all fragrance ingredients in a product using three scenarios. First, weight fractions were assigned randomly to the ingredients. Second, increasing weight fractions were assigned to chemicals with larger ecotoxicological value, and third, decreasing weight fractions were assigned to chemicals with larger ecotoxicological values. The difference in the derived PEI was smaller than 0.5 PAF m3 day/capita, much smaller than the observed ranges when the uncertainty and variability sources are included (SI, S10).

While the larger PEIs computed in North Africa compared to the smaller ones in North Australia are in line with how the fate of the chemicals is modelled in USEtox (Kounina et al., 2014) and reflect the longer water residence time to the sea for the first compared to the latter, the rather small influence of spatial variability across the 16 USEtox regions is surprising. Especially given that previous research has revealed its importance in life cycle assessments (Azevedo et al., 2013; Kounina et al., 2014). Some specificities of our study might have reduced the spatial variability's importance. For example, we used relatively large regions to assess the importance of spatial variability. Furthermore, Nijhof et al. (2016) showed a larger influence of the spatial variability on freshwater fate factors of persistent chemicals emitted to air and soil, while in our study we looked at chemicals that are not highly persistent and emitted down the drain to freshwater only. Also by assuming 100% connectivity to WWTPs we did not account for the actual differences in the extent of connectivity to WWTPs between the regions. However, changing the WWTP connectivity from 100 to 0% for a number of regions, meaning neglecting the removal of chemicals by WWTP prior entering the freshwater environment, only increased the mean PEIs by a factor of 2 (SI, S11). This in turn suggests that a more complete consideration of WWTP connectivity might have slightly increased the importance of spatial variation. Finally, because of the lack of available information, we could not refine the technological parameters of the WWTPs by region. However, we do not expect this to significantly affect the results given the small influence these parameters have on the total variation in PEI.

4.2. Uncertainty sources of the potential ecotoxicological impact

Besides variability, we also quantified the influence of uncertainty in the physicochemical and ecotoxicity values on the variation in the PEI. We showed that the variation in the PEI of the single use of a shampoo was dominated by the limited number of ecotoxicity data. This aligns with the findings of Harbers et al. (2006) and Bjorn et al. (2014). Both studies further highlighted the importance of uncertainty in ecotoxicological effects when quantifying the uncertainty in ecotoxicological impact of chemicals released into the freshwater environment. Van Zelm et al. (2007); van Zelm et al. (2008), and Golsteijn et al. (2014) also reported particularly uncertain effect factors of chemicals with a low number of species ecotoxicity data (n ≤ 3). Our research is consistent with these findings, since we showed that the uncertainty in the ecotoxicity QSAR estimates was not influencing the uncertainty in the EFs as much as the small number of species with ecotoxicity values available. However, we went a step further by showing that also when other sources of variability and uncertainty are considered, the uncertainty due to the limited number of species toxicity data is the dominant factor.

In assessing the total ecotoxicological impact of a shampoo formulation we assumed additivity of the individual chemicals ecotoxicity values (see Bjorn et al. (2014)). In the absence of known specific modes of actions for all the chemicals and assuming that all compounds will exhibit at least baseline toxicity at environmentally relevant concentrations, this assumption is considered justified in our case (SCHER et al., 2012). We noted a higher contribution from the chemical classified as hair conditioning agents, sequestrants, and surfactants to the overall uncertainty in the effect factors (> 10%). The main reason lies

in a combination of the higher weight fractions of these ingredients (especially surfactants), their increased occurrence in the products (especially sequestrants), and the large uncertainty of their effect factors. The latter is mainly due to the use of ecotoxicity values estimated with ECOSAR, which show larger uncertainty ranges than the QSARs from Gramatica et al. (2016). An additional word should be spent on the ecotoxicity of antidandruff agents. Given that their action is specifically anti-fungal and that no ecotoxicity values for fungi were available, the average toxicity of the antidandruff agents might have been underestimated. The large uncertainty of the derived effect factor does however likely account for such lack of knowledge.

Uncertainty in the fate properties of the chemicals also influenced the overall uncertainty in the PEI, be it through its fate factor or removal efficiency by WWTPs, as observed in e.g. Douziech et al. (2018). We identified the uncertainty in the biodegradation potential of chemicals as the most influential across all chemical function groupings. This aligns to previous research where the uncertainty in biodegradability was found to be large as well as its influence on the outcome of chemical impact assessments (Golsteijn et al., 2014; Huijbregts et al., 2000; Scholz et al., 2017; Wender et al., 2017). Aronson et al. (2006); Wender et al. (2017) also stressed the need for more accurate modelling of biodegradation processes. We should also mention that the uncertainty in biodegradation rates was not accounted for in the same way than for the other parameters. Deriving the uncertainty of the biodegradation rate directly from the QSAR fit would further improve our analysis. In addition, we showed that, depending on the chemical's function, different physicochemical properties influenced the spread in the computed PEI values. For example, the higher and wider range of the vapour pressure of fragrance ingredients compared to the one of surfactants, explains the greater importance of vapour pressure in the contribution from fragrance ingredients compared to surfactants.

Of all the groups of chemicals in shampoo, surfactants, used as cleaning agents, and fragrances contributed the most to the total PEI, followed by hair conditioning agents, antidandruff agents, and preservatives. These results are comparable with ecotoxicological assessments of representative or typical household care products (Dewaele et al., 2006; Golsteijn et al., 2015; Van Hoof et al., 2011) which like shampoos typically contain relatively high concentrations of surfactants and a range of fragrances ingredients. Our study is, however, one of the few underpinning this for shampoos in particular using actual formulations.

As stated in the methods section, to conduct a standardised assessment we only used predicted physicochemical and ecotoxicity values. This was necessary in order to evaluate all chemicals consistently (i.e. comparable datasets for all chemicals) and to avoid omitting chemicals with no or incomplete experimentally measured datasets. For the chemicals with available experimental properties and ecotoxicity data using only estimated ecotoxicity values may have led to an overestimation in the overall uncertainty. However, since the uncertainty in our results was mostly driven by the uncertainty in the effect factor which, in turn, is related to the use of toxicity data for only three species, the overall conclusions of our work are likely to apply whether or not species QSARs or test data are used. Even more so since for the majority of chemicals registered in Europe, ecotoxicity test data are only required for three species to establish safety using risk assessment. Despite the good performance of the used ecotoxicity QSARs, the representativity of the estimated ecotoxicity values is not known. A comparison to the available measured ecotoxicity values might have given a hint but was considered outside the scope of this paper.

4.3. Implications for current and future research

The aim of this work was to assess the influence of various sources of uncertainty and variability on a single use of personal care product. The results presented are specific for shampoo, but we expect that the conclusions can be generalised to other down-the-drain products. This

is because down-the-drain products have similar data limitations and associated variations related to the availability of ecotoxicity data and the inherent variability in consumer habits and use.

Our calculations do not include chemical removal processes in the showering phase, such as volatilisation and skin permeation. Current comparative ecotoxicological risk assessment practices of down-the-drain products neglect these removal processes, as the fraction removed during showering is expected to be relatively small for the majority of the chemicals, (< 2% (Csiszar et al., 2016)). Nevertheless, we recommend that future research should consider the removal processes in the use phase, including showering, as well as their uncertainty and variability when quantifying the environmental impact of down-the-drain products.

We clearly showed that with the current knowledge, a comparison of ecotoxicological results of life cycle assessments of products, for example, can only be informative if confidence intervals are included. A consistent communication of confidence intervals when such assessments are conducted is therefore recommended. Our results also indicate that the uncertainty in the effect factor drives the spread in the results the most, which is due to the use of a limited number of species. This highlights the need for additional ecotoxicological data either by testing a more diverse set of freshwater species, which may be costly, prohibited by a lack of standardised methods, or morally not accepted, or by using Interspecies Correlation Equations (ICE) (Raimondo et al., 2015). Our results suggest that estimated ecotoxicity values can compensate for a lack of experimental data without resulting in large uncertainty ranges. This was especially true when chemical-specific QSARs were used. A first step to reduce uncertainty and fill knowledge gaps in the PEI of personal care products would therefore be to develop QSARs with large applicability domains and increased reliability for additional specific freshwater species. In fact, extending the number of species even from three to four can reduce the uncertainty in the EF by orders of magnitude (see Van Zelm et al. (2007) and Golsteijn et al. (2012)). In addition, our results suggest that the uncertainty of PEIs could also be reduced by increasing the reliability of certain physicochemical properties of fragrances and surfactants. A second step to increase the reliability of PEI would consist in the improvement of the available methodologies for the estimation of the biodegradability of chemicals (Wender et al., 2017). An improvement of the reliability of these assessments is important to ensure that more meaningful conclusions can be drawn from comparative assessments of personal care products.

Finally, our approach can also be used to assess uncertainty and variability in the human health impact assessments of personal care products. The per capita use of a product, the chemical mass fraction in a product, the removal efficiency of a chemical by a WWTP, and the environmental fate factor of a chemical, as quantified in our analysis, are also relevant variables for assessing human health impacts (Ring et al., 2018). An additional modelling step quantifying the fraction of product volatilised or dermally adsorbed during use would further be necessary. In addition, uncertainty and variability in exposure and effect factors for humans would also need to be quantified. For instance, Ernstoff et al. (2016) showed that variable and uncertain parameters result in one to three orders of magnitude variation in product intake fractions (PiF) for shampoos from dermal intake and inhalation during use. Uncertainty in effect factors, as reported by Huijbregts et al. (2005), could be used for such an analysis as well.

5. Conclusion

The ability to reliably and meaningfully quantify the potential ecotoxicological impacts of products would aid their design and comparison. However, we have shown that if the various sources of uncertainty and variability are considered when calculating the PEI of down-the-drain products such as shampoos, no differences in impacts of each product's PEI can be observed. In addition, we showed that

research towards more accurate ecotoxicity estimation models (e.g. chemical-specific models) can be a way to reduce the uncertainty of these assessments. Nevertheless, in order to obtain more reliable outcomes, an increased number of ecotoxicity data is needed since most assessments are currently performed based on a limited number of species, which drives the uncertainty more than the source of the data. Including ecotoxicity values for more species either through more measurements or modelling techniques, like ICE, can therefore largely reduce uncertainty. Hereby, modelling techniques have the advantage of being less resource and time intensive. In terms of representativity of the derived ecotoxicity values, more research is necessary to assess the validity of the available QSARs and justify their increased use in such assessments. Finally, on-going efforts of regulating authorities to improve data quality (e.g. ECHA) should help standardise and correct the available data which in turn could be used to develop and improve predictive modelling approaches.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.01.080.

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