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An analytical framework on the leaching potential of veterinary pharmaceuticals: A case study for the Netherlands

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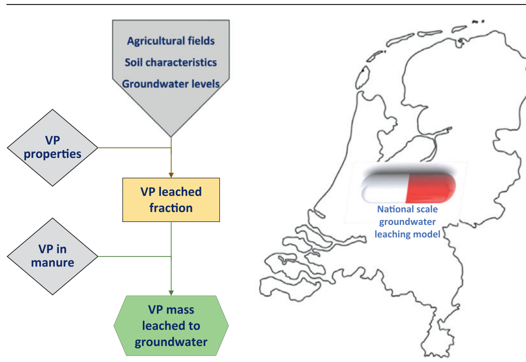
HIGHLIGHTS

- Oxytetracycline, Doxycycline, and Ivermectin are not prone to leaching to groundwater.
- Sulfadiazine and Flubendazole show limited and location specific leaching potential.
- Due to high leaching potential, Dexamethasone is prioritized for environmental risk assessment.
- For leaching to groundwater, substance environmental properties determine the importance of soil-applied quantities.
- The applied methodology and results may help policy makers to identify both relevant compounds and hotspots.

GRAPHICAL ABSTRACT



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ABSTRACT

Veterinary pharmaceuticals (VPs) residues may end up on the soil via manure, and from there can be transported to groundwater due to leaching. In this study an analytical framework to estimate the leaching potential of VPs at the national scale is presented. This approach takes soil-applied VPs concentrations, soil-hydraulic and soil-chemical properties, groundwater levels, sorption and degradation of VPs into account. For six commonly soil-applied VPs in the Netherlands, we assess quantities leached to groundwater and their spatial distribution, as well as the relative importance of processes that drive leaching. Our results for VPs Oxytetracycline, Doxycycline, and Ivermectin indicate that maximum quantities that may leach to groundwater are very low, i.e. $\ll 1$ μg/ha, hence spatial differences are not investigated. For VPs Sulfadiazine and Flubendazole we identify a few regions that are potentially prone to leaching, with leached quantities higher than 1 μg/ha. Leaching patterns of these two VPs are dominated by soil properties and groundwater levels rather than soil-applied quantities. For Dexamethasone, even though applied on the soil in much lower concentrations compared to other investigated VPs, spatially widespread leaching to groundwater is found, with leached quantities higher than 1 μg/ha. Due to the leaching affinity of Dexamethasone, variations in the soil-applied amounts have significant influence on the quantities leached to groundwater. Dexamethasone is

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highlighted as important for the future environmental risk assessment efforts. This study has shown that the leaching potential of VPs is not determined by one single parameter, but by a combination of parameters. This combination also depends on the compound investigated.

1. Introduction

Veterinary pharmaceuticals (VPs) are used to treat or prevent diseases of animals. Which specific VP is used varies per disease, animal sector and region (Berendsen et al., 2018). A prominent way by which VPs enter the environment is the excretion of urine and faeces from medicated animals and application of contaminated manure to agricultural land (Boxall et al., 2004). Thereafter, VPs may reach the groundwater due to leaching (Blackwell et al., 2009) and possibly affect water quality (Ostermann et al., 2013). Considering that groundwater is an important source of drinking water in Europe, and already high pollution pressures exerted by man-made chemicals on groundwater bodies (Rasheed et al., 2019; Sanchez-Gonzalez et al., 2013; Stuart et al., 2012; Tiktak et al., 2006; Wanner, 2021), identifying and quantifying VPs in groundwater is important. Many studies have confirmed presence of various VPs in groundwater (Lapworth et al., 2012; Mooney et al., 2020; Mooney et al., 2021), while some investigated environmental conditions that are relevant for VP leaching to groundwater (Gros et al., 2021; Pan and Chu, 2017). VP leaching to groundwater is mostly quantified through experiments and monitoring (Popova et al., 2013; Spielmeyer et al., 2017; Spielmeyer et al., 2020), whereas only few studies explored VPs leaching to groundwater through modelling (Di Guardo and Finizio, 2017). The lack of latter approaches represents a limitation in estimating the VPs pollution levels at e.g. national scales (Wohler et al., 2021). The advantage of a mechanistic modelling approach is that it is applicable to various environmental conditions and different types of VPs, whereas experimental efforts provide results for particular situations only. In addition, a model which estimates VPs leaching to groundwater could be useful for legislators and policy makers to identify environmental conditions and VP types that provide the highest environmental leaching potential in soil and groundwater systems. Therefore, modelling approaches could represent an important asset in determining the risk to the environment for these compounds.

In the Netherlands, manure from intensive livestock farming is spread onto arable land and grassland in considerable amounts. Consequently, together with Belgium, Netherlands shapes one of the highest nitrogen input regions in Europe (de Vries et al., 2021). Besides, applied manure may contain a broad range of VPs of different quantities, as detailed in Rakonjac et al. (2022). Dutch groundwater quality is systematically monitored and results affirm occurrence of VPs at diverse locations (van Loon et al., 2020). In addition, scientific studies confirm the presence of VPs in groundwater of different ages and at different depths (Kivits et al., 2018). However, information concerning the VP origin, travel time through the unsaturated zone, and impact of spatial variable conditions (e.g. soil characteristics) on the VP transport is highly lacking, thereby hampering a proper risk assessment of this group of compounds. To the best of our knowledge, so far only two Dutch studies (Hoeksma et al., 2020; Lahr and van den Berg, 2009) investigated spatially distributed modelling to evaluate the VP leaching to groundwater. In both cases, a pesticide-targeted model GeoPEARL (Tiktak et al., 2002) was used and the obtained results provided an aggregated national overview, whereas the details relevant for georeferenced local situations (fields) were not provided. This lack of local scale information limits the identification of groundwater vulnerable areas to VPs. Furthermore, both mentioned studies highlighted the large uncertainty in the input data, particularly in the estimated VP load. For these reasons, there is a need for an improved approach that will integrate the most detailed level of available data, but also takes into account the time processing efficiency of the calculations. The latter is especially relevant considering the number of VPs used in the Netherlands and yearly variations in their used quantities (Rakonjac et al., 2022).

Processes and conditions that affect VP leaching are similar to those involved for the leaching of many pesticides. Therefore, in this paper, we further elaborate on the analytical framework of van der Zee and Boesten (1991) concerning pesticide leaching to groundwater to estimate the VPs leaching towards phreatic groundwater. To quantify annual VPs loads, we use the VPs concentration in soil-applied slurry manure as derived in Rakonjac et al. (2022) and combine these with spatial allocation of manure soil-applied amounts which are given by the (national) model INITIATOR (Kros et al., 2019). Besides VP loads, we take into account local soil-hydraulic and soil-chemical properties, local groundwater levels, and VP environmental properties, to feed into the analytical model of van der Zee and Boesten (1991). Our approach is applied at a national scale to the Netherlands and provides spatially distributed quantification of VP leaching to groundwater at the spatial resolution of the field. According to our knowledge, this is the first VP-targeted approach to combine the abovementioned input data at local scale, resulting a time-efficient national scale model for assessing VP leaching to groundwater. Additional objective of this study is to provide suggestions on how to extend the analytical model with soil layering, and identify national hotspot (vulnerable) leaching locations, while considering soil and crop characteristics. This study further aims to determine the relative importance of various processes affecting VP leaching, and to distinguish them between the investigated VPs. Additionally, to address the influence of VP origin, we investigate the impacts of the VP loadings on leaching and the contribution of the different manure types. The framework proposed in this paper can be used to identify groundwater vulnerability from VPs at different spatial scales (local to national), thereby providing an important asset in environmental risk assessment of VPs.

2. Methodology

2.1. Leached fraction: conceptual model

To assess spatially distributed leaching for every field in the Netherlands we assume that each field can be represented by a hypothetical equivalent soil column. This column consists of several soil layers of varying thickness, and with an upper boundary at the soil surface, where the VP via manure is introduced (i.e. VP load), and a lower boundary at groundwater level, as illustrated in Fig. 1. Soil-hydraulic properties and organic matter content may vary per layer. The groundwater level is spatially variable and is assumed to be constant over time. After VP application on the soil surface, all layers above the phreatic water level contribute to the leaching. If the groundwater level is located within a particular soil layer (Fig. 1 - left) only the part above groundwater level is taken into account to calculate the leaching. If groundwater level is located below the lowest (known) layer, we extend that layer and its properties till the phreatic water level (Fig. 1 - right).

Referring for details of the derivations to van der Zee and Boesten (1991), we assume that the VP leached fraction of each soil layer, F [−], is defined as the exponent of (minus) the transformation rate times the residence time in the layer i, i.e.

$$F_i = \exp\left(-\frac{\mu_i * R_i * L_i}{v_i}\right) \tag{1}$$

where μ represents the first-order transformation rate of VP in the soil [T^{-1}], R is the retardation factor [−], L corresponds to the thickness of the soil layer [L], and v is the pore water velocity [L T^{-1}]. Note that Eq. (1) is based on the concept that both dissolved and adsorbed solute can degrade, where R reflects the solute travel time dependence on

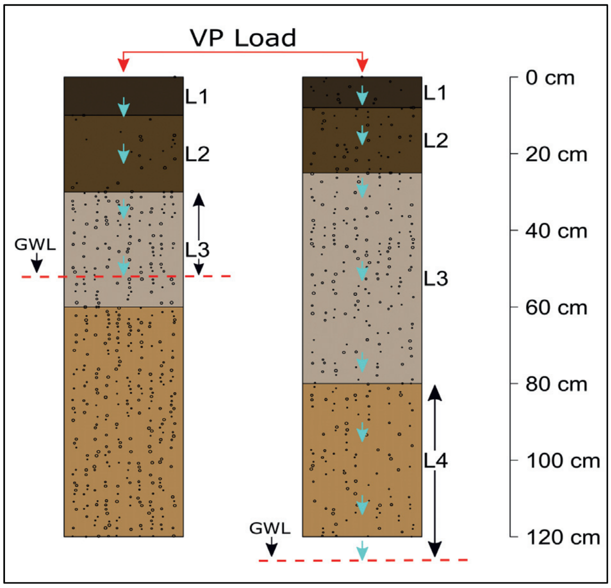

Fig. 1. Conceptual model visualization. Left soil column represents the case when groundwater level (GWL) is located within soil layer, while right soil column illustrates situation when GWL is below the lowest known soil layer. In both cases, soil layer thicknesses relevant for VP leaching are corrected (L3 and L4).

retarding processes such as sorption. A large R indicates that VP transport to groundwater will be retarded and VPs therefore reside in the soil for a longer time. R of a soil layer *i* is defined in the model as

$$R_i = 1 + \frac{\rho_i}{\theta_i} * f_{om,i} * K_{om,i} \tag{2}$$

where ρ represents the dry bulk density of the soil [$M\,L^{-3}$], θ is volumetric water fraction [$L^3\,L^{-3}$], f_{om} is mass fraction of organic matter [$M\,M^{-1}$], and K_{om} is coefficient for distribution over organic matter and water [$L^3\,M^{-1}$], which defines the sorption capacity of a VP. To calculate R and subsequently F, an estimation on pore water velocity, v, is needed. To pursue flow of water analytically, we assume a steady state situations, driven by excess precipitation. For this purpose, we recognise water flow rate as a specific discharge q [$L^3\,L^{-2}\,T^{-1}$] and calculate rates depending on annual precipitation, evaporation, and transpiration, which are obtained from the Royal Netherlands Meteorological Institute (KNMI). For the top soil layer, where root water uptake gradually diminishes the flow rate with increasing depth, we assume q driven by precipitation minus evaporation. Below the top layer, we account for the loss of transpiration water and the flow rate is therefore equal to precipitation minus evapotranspiration, and smaller than for the top layer. This implies that we assume that the crop transpiration water is taken from the upper layer.

For both the top soil and layers below, we then apply the Staring series approach which is used for deriving the standard soil-hydraulic characteristics (Heinen et al., 2020). Heinen et al. (2020) map soil types in the Netherlands and provide standard soil-hydraulic properties for 36 unique building blocks: 18 top soils and 18 subsoils. Each building block is described, among other things, with an average water-retention capacity and hydraulic conductivity. Then, depending on the soil layer and its properties we assume the previously calculated q to be equal to the hydraulic conductivity and from that we calculate hydraulic heads via Mualem equation (Mualem, 1976). We further use those as an input into van Genuchten equation (van Genuchten, 1980) to estimate the time-averaged volumetric water fraction θ. Finally, we calculate pore water velocities based on the Eq. (3). Details and equations about the above mentioned water flow estimation procedure are revealed in the Supplementary Material (SM1).

$$v_i = \frac{q_i}{\theta_i} \tag{3}$$

In addition to sorption, dissipation due to e.g. microbial degradation or other degradation processes has a significant impact on the leached fraction. Degradation kinetics might differ between the VPs and soil types (Berendsen et al., 2021), hence we use a pragmatic approach and assume first order degradation kinetics. Literature data on VPs half-lives in the soil, τ_0 [T], differs depending on e.g. the source (i.e. country/region), soil type and conditions (Cycon et al., 2019). We use VPs half-lives found in the literature and consider them as representative for the first (top) soil layers (Eq. (4)), but we are aware that field conditions may vary or have a gradient in depth (e.g. temperature) (van den Berg et al., 2016). To partly encompass for differences in biological activity, we assume that μ in the soil is proportional to organic matter content, and correct μ for the lower layers as given with Eqs. (4) and (5). This correction is also proposed for pesticides by Boesten and van der Linden (1991) and van der Zee and Boesten (1991).

$$\mu_1 = \frac{\ln(2)}{\tau_0} \tag{4}$$

$$\mu_i = \mu_1 * \left(\frac{f_{om,i}}{f_{om,1}}\right) \tag{5}$$

In line with van der Zee and Boesten (1991), we propose that leached fractions from all soil layers above the groundwater level affect the total VP leached fraction, F_{total} [−], of a hypothetical soil column. In a nutshell, when the VP fraction leached from a layer enters the next layer, it may further dissipate but partly also transport to the layers below. Together, they form a series of leaching layers as given in Eq. (6). This allows to include the impact per soil layer of which the properties vary.

$$F_{total} = \prod_{i=1} F_i \tag{6}$$

By coupling F_{total} with the soil-applied VP load per field (A [$M\,L^{-2}$]), we calculate the total VP leached quantity (T [$M\,L^{-2}$]) for each field, as given by

$$T = F_{total} * A \tag{7}$$

Details regarding A are provided in Section 2.3.

2.2. Parameterisation of the spatially distributed model

Spatially distributed data is taken from available datasets combined with geographic maps. Sources and adjustments are discussed hereafter. To spatially identify individual fields on which manure is applied, we use a geographic data shapefile from Dutch Crop Parcels Database (BRP, 2022), for the year 2017. The spatial scale of used BRP data is 1:25000. For obtaining soil properties, we use Soil Physical Unit Map (Wosten et al. (2013), spatial scale 1:50000) which provides the spatial distribution of different soil physical units in the Netherlands. Each unit has a schematic representation of the soil profile with affiliated soil layers (up to 7 and a soil depth of 120 cm). Soil-hydraulic and soil-chemical characteristics are associated with the individual soil layers on the basis of the Staring series approach. To estimate Dutch groundwater levels, we use a publicly available map with 19 groundwater level classes (spatial scale 1:50000) describing the average fluctuations of the groundwater level, and classes of highest and lowest levels (Knotters et al., 2018). However, the public (free) version of the mentioned map covers only 95 % of the BRP identified fields, particularly missing the fields located in higher and hilly areas of Limburg province and Veluwe region (5 %). For these regions we extrapolate the map (via the Raster Calculator tool in ArcGIS Pro) resulting in a good comparison with other publicly available data about Dutch groundwater levels. More details can be found in the SM2. Since our approach assumes a constant groundwater level per field, for each groundwater level class we derive the average of both the highest and lowest ranges and assume their mean value as a representative one. Finally, we identified for each field from BRP, the soil type and the averaged groundwater level. Identification was done based on the largest fraction of soil type/

groundwater level class per specific field. Based on the groundwater level and the soil type, soil-hydraulic and soil-chemical properties were derived for each field and per layer. Details and technical (software) procedures are provided in the SM3.

2.3. Estimation of VP loadings

The spatial distribution of VP loadings is significantly influenced by local manure application patterns. These local patterns depend on the amount and type of manure produced on nearby farms, the available area of agricultural land, the manure transport from farm to farm and optional manure processing and export. Manure application is confided by admissible nitrogen and phosphorus applications rates being regulated by the EU Nitrates Directive (de Vries et al., 2021; Kros et al., 2019). With regard to the Nitrates Directive 91/676/EEC (EC, 1991) the Netherlands as a whole is assigned as a vulnerable zone implying a strict maximum threshold for the use of animal manure of 170 kg N ha^{-1}. However, the EC has granted a derogation for the Netherlands implying a maximum application rate for dairy farm (>80 % grassland) ranging from 230 to 250 kg N ha^{-1}, depending on soil type and region. This results in considerable amounts of applied animal manure, on average ca. 200 kg N ha^{-1} and 70 kg P2O5 ha^{-1}. Nationally regulated, manure slurry is applied on the grassland between February and August, while on the arable land this is between February and September (RVO, 2022).

Distribution of manure in the Netherlands is calculated with the INITIATOR model (Kros et al., 2019). This model takes into account manure production on the individual farm, the manure sales outside the Netherlands and the manure utilization capacity, given the applicable N and P application standards. This makes it possible to distinguish between the effects of the generic (national) and the area-oriented (provincial) policy on the reduction of N deposition. The model is used to substantiate and evaluate Dutch manure and ammonia policy. INITIATOR simulates manure applied mass distribution [$M\,L^{-2}$] at the individual farm level, and we use predictions of the year 2017. We assume that this applied mass is equally distributed over all the fields associated with individual farms. For the most commonly soil-applied Dutch manure slurries (dairy cow, veal calf, pig), Rakonjac et al. (2022) estimated the VPs residue concentrations based on VPs usage, animal metabolism and manure storage practices, and prioritized these substances according to their residue potential (i.e. residue indicator). Based on that indicator, we select the VPs Oxytetracycline, Doxycycline, Sulfadiazine, Flubendazole, Ivermectin, and Dexamethasone for consideration in this paper. According to Rakonjac et al. (2022) those are the most frequently soil-applied VPs in the Netherlands, and they are prioritized in different slurries, as detailed in the Table 1. The mentioned study provided nationally averaged VPs soil-applied concentrations and not spatially distributed concentrations. As a first approximation of potential leaching of VPs we assume that those VPs concentrations are spatially constant and introduced everywhere in the Netherlands when being applied in manure types in which they are prioritized. To match with the available INITIATOR/BRP data, we use VPs concentrations for the year 2017. Accordingly, by multiplying the estimated VP concentration in a particular slurry manure type (Rakonjac et al., 2022) with the amount of corresponding slurry manure applied on each field in the Netherlands, we estimate the VP load distributed on the fields with each of the slurry manure types. Finally, the total soil-applied VP load on the field level (A, used in Eq. (7)) is obtained by summing the VP quantities present in all slurries applied on the particular field. National maps with soil-applied VP loads are given in SM4.

We estimate VPs properties (i.e. K_{om} and τ_0) for antibiotics based on the study done by Berendsen et al. (2021), who investigated two typical Dutch soils (sand and clay). Since our approach assumes one single value of K_{om} and τ_0 per substance in the top soils for the whole of the Netherlands, we average the reported values between two soils. For the targeted antibiotics, this approach is reasonable because measured values are quite similar (Berendsen et al., 2021). For other targeted VPs, due to data availability, we use different literature sources to estimate the VP properties. For Flubendazole we use K_{om} and τ_0 as in van der Linden et al. (2017), who reported an estimate based on the QSAR calculations. For K_{om} and τ_0 of Ivermectin we refer to the Veterinary Substances DataBase (VSDB) (Lewis et al., 2016). For Dexamethasone we use K_{om} as reported in the VSDB (Lewis et al., 2016), while we estimate τ_0 with the EPI Suite™ (EPA, 2022). Note that the VP sorption parameter is frequently provided in the literature as an organic carbon-water partition coefficient (K_{OC}), which is converted to K_{om} by multiplying with 0.58 (van den Berg et al., 2016).

3. Results and discussion

3.1. Leached quantities

After allocating a soil type, a groundwater level, and data from the INITIATOR model to each field of the BRP, in total 1,099,456 fields were available for analyses. We excluded part of the fields from further consideration: nature areas, fields that overlap with objects such as buildings, and fields that mismatch in the input maps. The latter is due to soil data originating from 2012, whereas manure data is from 2017, and therefore some discrepancies in identified fields are possible (e.g. reclamation of land close to sea). Among the available fields, 62.1 % are maize fields, 11 % are grassland fields, 5.3 % are fields used for grazing, 4.6 % are fields with summer barley, while the rest (17 %) are spread on 22 different crops as defined in BRP.

We calculated the total VP leached quantity, T, for all combinations of substances and manure types as indicated in the Table 1. Our calculations for Oxytetracycline, Doxycycline, and Ivermectin show that the maximum T that one field can have is 1.96E-38 mg/ha, 3.02E-52 mg/ha, and 3.77E-33 mg/ha, respectively, which is very low. These results suggest that combinations of properties and applied amounts for these particular VPs are not causing any relevant leaching. On the other hand, results for Sulfadiazine, Flubendazole, and Dexamethasone indicate some leaching at several locations in the Netherlands, with maximum T being 0.072 mg/ha, 2.91 mg/ha, and 0.63 mg/ha, respectively. However, distribution of T for Sulfadiazine and Flubendazole shows that the majority of the fields (>98 %) have T lower than 1 pg/ha, which we considered as the lower threshold for our mapping. For Dexamethasone this is significantly different with only 38 % of the fields having T lower than 1 pg/ha. Leaching maps of these

Table 1
Selected VPs, VP type, their properties, and concentrations in manure.

VP	Type	Cas no.	K_{om} [L/kg]	τ_0 [d]	C_{manure} [mg/ton][a]			
					Veal calf	Dairy cow	Dairy cow grazing	Pig[b]
Oxytetracycline	Antibiotic	79-57-2	869	8.5	**555.8**	**2.2**	**8.9**	**106.6**
Doxycycline	Antibiotic	564-25-0	1207	10	**1887.3**	*7.5*	*35.7*	**153.5**
Sulfadiazine	Antibiotic	68-35-9	2.4	0.8	**486.7**	**7.5**	**37**	*9.1*
Flubendazole	Antiparasitic	31430-15-6	650	89	*0*	*0*	*0*	**697.2**
Ivermectin	Antiparasitic	70288-86-7	8207	112	**0.6**	*0.2*	*0.8*	**4.1**
Dexamethasone	Hormone	50-02-2	139	120	*0.09*	**0.036**	**0.042**	**0.11**

[a] Italic (non-bold) numbers indicate that this VP is not prioritized in the particular manure type, and therefore not considered in our study. Prioritization is based on findings by Rakonjac et al. (2022) for the year 2017.

[b] Refers to a combined pig slurry (fattening pigs and sows).

three VPs are given in Figs. 2 and 3, while T distributions are revealed in the SM5.

As Fig. 2 reveals, for both Sulfadiazine and Flubendazole, fields with leached quantities larger than 1 pg/ha are located at the northern tip of Dutch province North Holland, on two Dutch islands, near the town of Lisse, and around river IJssel. In addition, in the case of Flubendazole some of these fields are located at the northern part of province Flevoland, and occasionally at some other regions.

For Sulfadiazine, all fields with leached quantities belonging to the highest defined category ($T > 1$ μg/ha) have a moderately fine sandy soil type. Typical profile of this soil type, as defined by Wosten et al. (2013), is: top soil layer of 5 cm ($f_{om} = 0.04$, $\rho = 1.43$ kg/L), 1st subsoil layer of 45 cm ($f_{om} = 0.002$, $\rho = 1.67$ kg/L), and 2nd deeper subsoil layer of 70 cm ($f_{om} = 0.002$, $\rho = 1.67$ kg/L). The average groundwater depth at these fields is 65 cm (median is 66 cm), meaning that groundwater level is typically located somewhere in the deeper subsoil layer.

For Flubendazole, 58 % of the fields with $T > 1$ μg/ha are located on moderately fine sandy soil, while 41 % are on (low loam)-sandy soil and 1 % on coarse sandy soil. Typical soil profile of (low loam)-sandy soil is: top soil layer of 6 cm ($f_{om} = 0.03$, $\rho = 1.47$ kg/L), 1st subsoil layer of 4 cm ($f_{om} = 0.012$, $\rho = 1.63$ kg/L), 2nd subsoil layer of 5 cm ($f_{om} = 0.018$, $\rho = 1.6$ kg/L), and 3rd subsoil layer of 105 cm ($f_{om} = 0.002$, $\rho = 1.68$ kg/L). Average groundwater depth at fields with $T > 1$ μg/ha on (low loam)-sandy soil is 137 cm (median is 145 cm), meaning that groundwater level is typically below the deepest known subsoil layer. For fields on moderately fine sandy soil, average groundwater depth is 88 cm (median is 81 cm). Typical soil profile of coarse sandy soil is represented with one soil layer of 120 cm ($f_{om} = 0.003$, $\rho = 1.54$ kg/L), while average groundwater depth at fields with T > 1 μg/ha is 73 cm (median is 67 cm).

Crop types among fields with T > 1 μg/ha, for both Sulfadiazine and Flubendazole, are similar to the national crop type distribution, where maize is the most frequent crop covering 69 % of Sulfadiazine fields and 31 % of Flubendazole. Except for floriculture, which is quite common among these fields with 17 % for Sulfadiazine and 22 % for Flubendazole and not so frequently observed at the national level (has only a national share of <2 %). Reason for this is that in the Netherlands soils adjacent to dunes are frequently transformed into fields for bulb cultivation. These soils are very prone to leaching due to sandy texture and low organic matter content, resulting in higher VP mobility, rapid drainage, and less sorption. Typically, these fields have shallow groundwater level (around 60 cm), which is sometimes kept constant to optimize the conditions for bulb cultivations. Note that we use average groundwater levels for calculations, whereas seasonal variations could result in even shallower levels and therefore pose higher risk for leaching. Furthermore, fields used for bulb cultivation are also noted as fields of concern for pesticide leaching to groundwater in the Netherlands (de Snoo and Vijver, 2012; Swartjes et al., 2016).

Unlike for the two previously discussed VPs, leached quantities of Dexamethasone higher than 1 pg/ha are distributed all over the Netherlands (681,655 fields, Fig. 3). The hotspot leaching locations (where $T > 1$ μg/ha) identified for Sulfadiazine and Flubendazole are also present for Dexamethasone but with addition of the northern parts of the provinces Friesland and Groningen, the province Zeeland, parts of Gelderland province, and southern Limburg. 21 % of fields with T > 1 μg/ha are situated on sandy soils, 66 % on clay soils, and 13 % on loamy soils, representing in total 36 different soil types as defined by Wosten et al. (2013) and detailed in SM6. In this case, we do not investigate groundwater depths for each of the 36 soil types but rather refer to groundwater map (see SM2) for regional impressions. Crop types distribution among fields with T > 1 μg/ha follows the national pattern where maize is the most spread (55 %), followed by grassland (10 %) and summer barley (7 %). Due to the much larger number of considered fields, the ones used for bulb cultivation are less common than for other two VPs, with presence of 3.5 %. Note that the differences between crop coverages among the three mentioned VPs are affected by the manure/crop application patterns, where e.g. Flubendazole is applied only in pig manure.

3.2. Discussion on parameters

Even though both compounds exhibit significantly different properties and concentrations in soil-applied manure (Table 1), calculations for Sulfadiazine and Flubendazole result in similar leaching patterns at the national scale. Sulfadiazine with its low K_{om} tends to be very mobile, but because of the low τ_0 it does not persist in the environment long enough to display widely spread leaching. On the other hand, Flubendazole is >100 times more persistent in the soil compared to Sulfadiazine, but it also has 270 times higher sorption coefficient. This means that it will reside in the soil for a longer time and therefore allows for degradation to occur.

For Sulfadiazine, leaching occurs mostly in fields with moderately fine sandy soil. Here, the top soil layer retards the leaching process for around 1.5 times ($R \approx 1.5$), while the 1st and 2nd subsoil layers retard for around 1.1 times. This seems reasonable because the top layer contains more organic matter, as explained earlier. Pore water velocity, v, in the three mentioned soil layers is estimated between 0.5 and 0.8 cm/day (top soil). Note

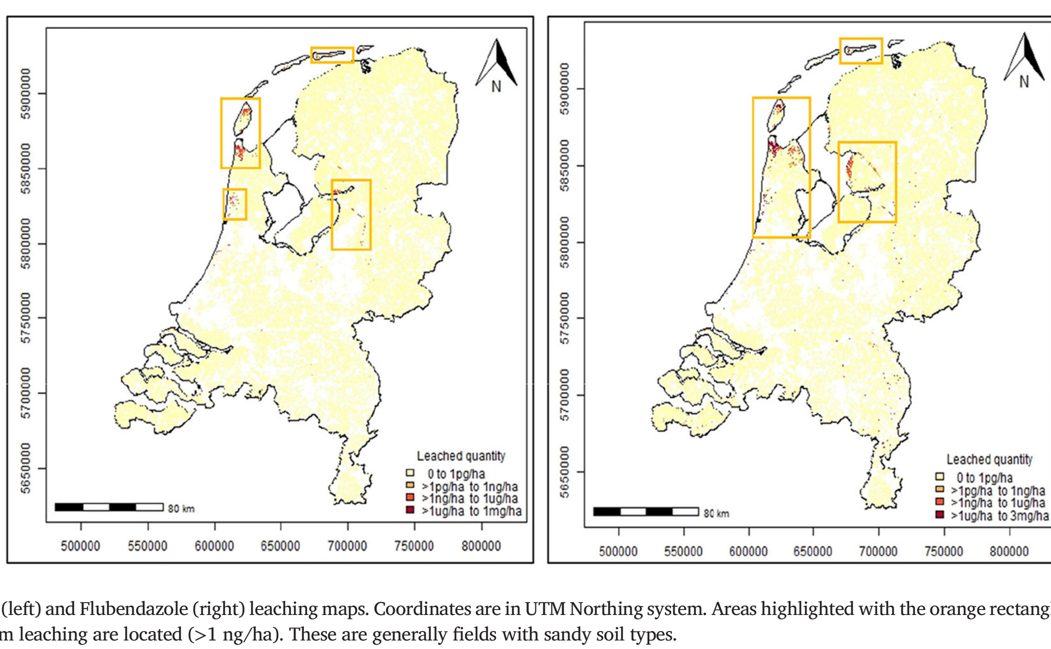

Fig. 2. Sulfadiazine (left) and Flubendazole (right) leaching maps. Coordinates are in UTM Northing system. Areas highlighted with the orange rectangles are the ones where fields with maximum leaching are located (>1 ng/ha). These are generally fields with sandy soil types.

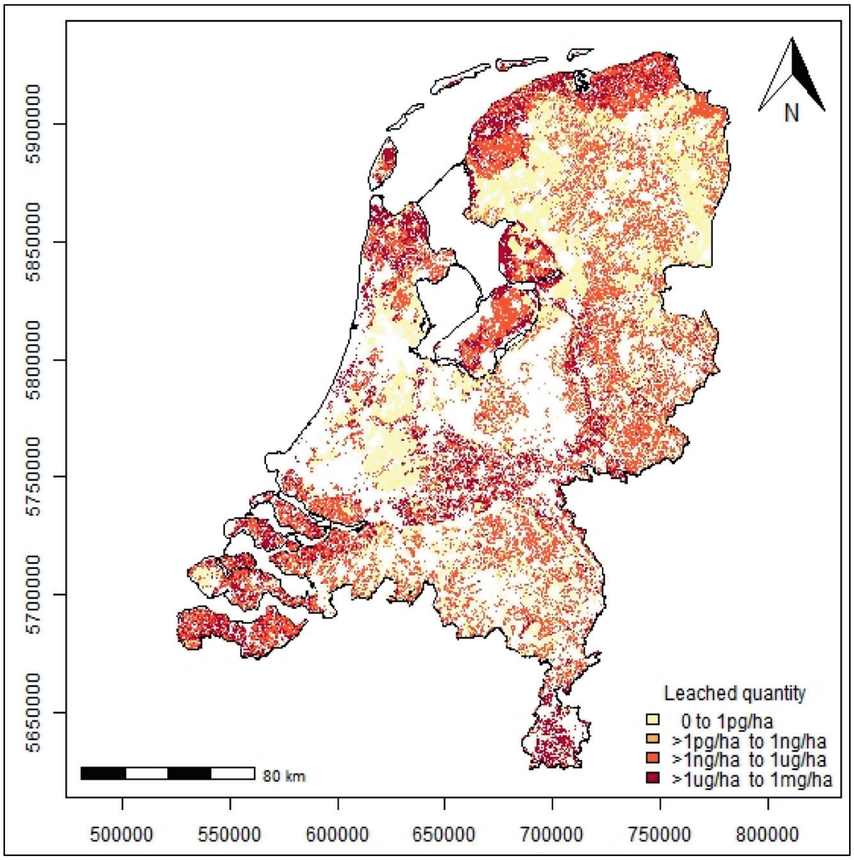

Fig. 3. Dexamethasone leaching map. Coordinates - UTM Northing.

that in reality due to spatial variability of water flow there might be a large number of different velocities, as addressed by van der Zee and Boesten (1991). The associated residence time of Sulfadiazine in the top soil layers of fields with moderately fine sandy soil is around 10 days, while in the deeper layers it could go up to 150 days. Residence times in the deeper soil layers are significantly influenced by the groundwater level which determines relevant soil layer thickness (Fig. 1).

When Flubendazole has a $T > 1\mu g/ha$, depending on the soil layer, R ranges between 12 and 156 for fields with moderately fine sandy soil, between 60 and 120 for fields with (low loam)-sandy soil, and is around 28 for fields with coarse sandy soil. The highest R values correspond to the top soil layers. The range of v values is larger compared to Sulfadiazine, ranging from 0.5 to 1.8 cm/day, where higher values correspond mostly to fields on coarse sandy soil. Residence times are between 30 and 2000 days, depending on the soil type and soil layer. This substantial increase in residence times compared to Sulfadiazine is in line with the larger sorption coefficient, K_{om}, in the case of Flubendazole (Table 1). This also indicates that the leaching processes of Oxytetracycline, Doxycycline, and Ivermectin allow for (almost) complete degradation before reaching groundwater.

Dexamethasone is applied on the soil in much lower concentrations compared to other investigated VPs (Table 1), but it frequently shows fields with $T > 1\mu g/ha$. This implies that the VP properties (K_{om} and τ_0) combined with the soil properties influence leaching to a larger extent rather than applied quantities. To further explore this for Dexamethasone, but also Sulfadiazine and Flubendazole, we analysed the values, patterns and distributions of T, F_{total} and A, based on all 1,099,456 fields.

Fig. 4 shows that Sulfadiazine ends up on the soil with around 2.5 times larger quantities than Flubendazole and around 4500 times larger quantities than Dexamethasone (x-axis middle figure). Still, it has the lowest T among the three (y-axis middle figure). The explanation for this is that the range of F_{total} values is around 100 times smaller compared to Flubendazole, and around 21,000 times smaller compared to Dexamethasone (x-axis left figure). Fig. 4 further shows (right vertical) that for all three VPs the largest quantities (A) are not applied on the fields with largest F_{total}, which is certainly something that reduces the possible leached mass. This means that the fields that are associated with a high leaching potential do not receive a high amount of Sulfadiazine, Flubendazole, or Dexamethasone.

Only in the case of Sulfadiazine, the field with the largest F_{total} is the one with the largest T (top-left figure). For leaching which is dominated by soil and substance properties above applied amounts, we expected to observe this also for the other substances. However, note that Flubendazole and Dexamethasone are not applied ($A = 0$) on the field with largest F_{total} (right vertical). Different leaching behavior between soil types is most notable with Dexamethasone, particularly on the fig. T vs F_{total}. Here, we observe three data accumulation zones, where the two on the right, with F_{total} around 0.10 and 0.25, group fields on moderately fine sandy soil and (low loam)-sandy soil, respectively. The same accumulation zones are visible on the fig. T vs A, where previously mentioned F_{total} values define the slope of the two linear zones. The reason for this clustering is caused by the different soil type parameters used to calculate F_{total}, where the ones related to the two mentioned soils are clearly in favor of relatively high leaching potential.

In our calculations we assumed Dexamethasone to be used in dairy cows and pigs only, and also this VP is considered to be used in all farms in the Netherlands. We assess the influence of manure application types on T as shown in Fig. 5. The impact of neglecting veal calves in the calculations for Dexamethasone is shown by comparing the red line (original calculation) and the blue dotted line (while including veal calves). A minor increase in A is indicated if veal calf manure is added. We therefore compare the hypothetical veal calve included A values with T. The results of this calculation can be found in the SM7. In principle, observed patterns are the same as without this manure type, but since applied amounts

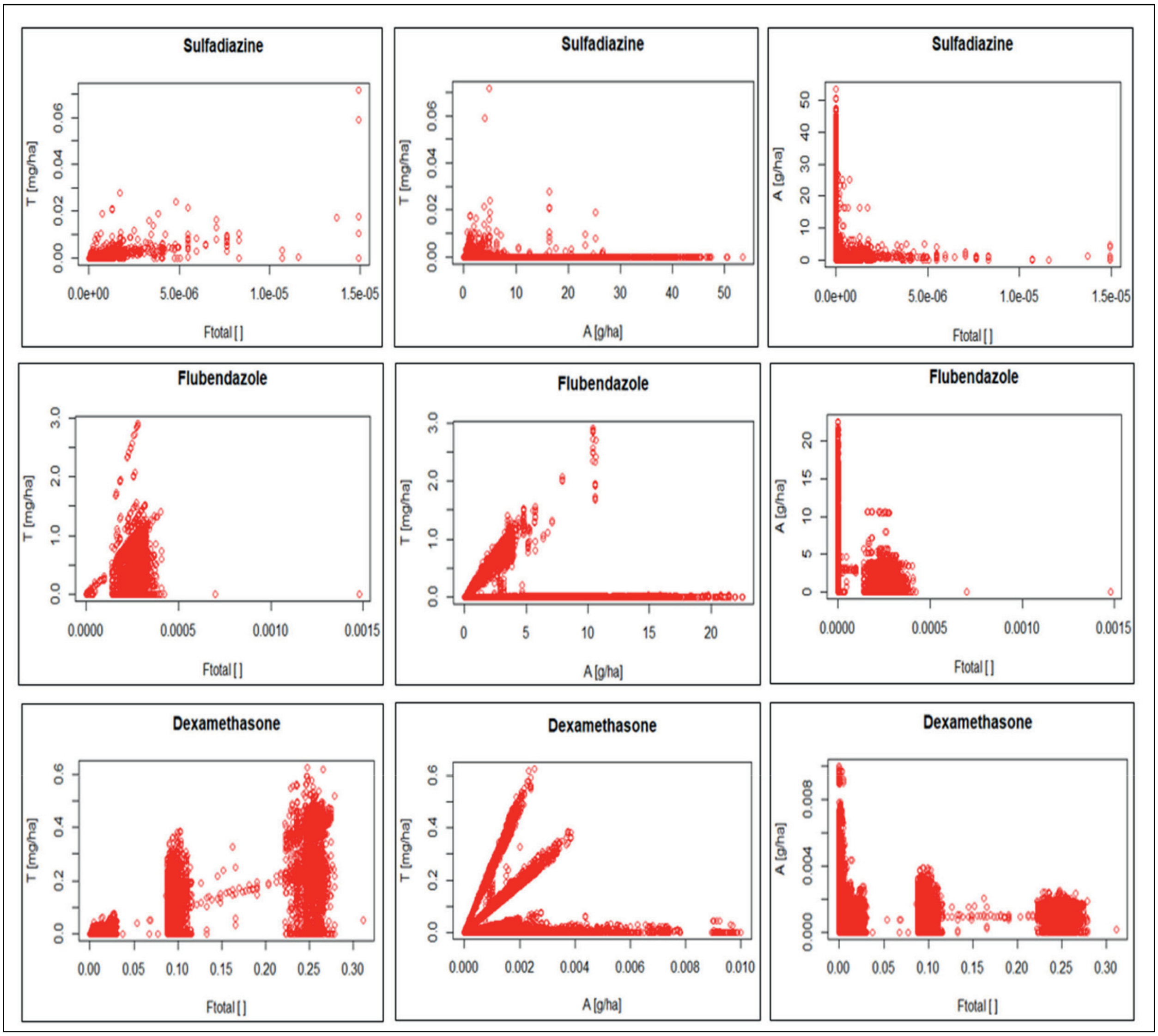

Fig. 4. Leached VP amount per field (T) compared to total VP leached fraction per field (F_{total}), T compared to applied VP amount per field (A), and A compared to F_{total}. Each dot represents one field of different size.

increased there is also an increase in leached quantities. This makes sense, because Dexamethasone is prone to leaching due to its properties, and therefore sensitive to changes in applied amounts. Note that this is not expected for other investigated VPs, because of the low leaching potential.

3.3. Uncertainties

To investigate leaching at the national scale, a number of assumptions have been made. To simulate VP transformation rate in the soil we disregarded the temperature dependence, which is considered to be one of the environmental factors with relatively high influence on pesticide transformation rates in the soil (van den Berg et al., 2016). The transformation rate of a pesticide increases sharply as the temperature increases. For calculations we used VP transformation rates from literature, usually experimentally determined for soils on a room temperature (20–25 °C). Soil temperatures in the Netherlands are known to vary with depth, per season, per region, per year, and are usually lower than 20 °C (Jacobs et al., 2011). This could imply that our assumed VPs transformation rates were overestimated and result in even higher leached fractions than calculated. However, considering that most VPs end up on the soil during spring and summer, when soil warms up, the eventual influence of temperature differences is minimized. Still, we recommend this to be explored in future work. Besides transformation rates, model parameters characterizing sorption are shown to have a significant influence on pesticide leaching to groundwater (Urbina et al., 2020), which we also observe for VPs in our model. However, for VPs these parameters vary a lot in the literature. Ideally, they should be estimated with respect to the soil type and environmental conditions, which is hardly available information.

In general, measured soil physical properties show already substantial in-field variation and heterogeneity. In addition, due to land management (ploughing, riding with tractors etc.) and weather conditions (heavy rainfall, droughts) soil structural changes might evolve affecting flow and transport processes. In particular top soils are prone to time-variant changes (compaction, soil crusting, development of shrinkage cracks in clay, peat and loamy soil, occurrence of macropores due to earthworm activity, water repellence, preferential flow etc.). This might result in substantial uncertainties.

Another important assumption is that all soil-applied yearly VP load is available for leaching. In general, this is probably not the case because part of the VP load might be affected by rainfall events and transported to surface water via fast flow routes (e.g. runoff, field drains). If this is the case, then our calculated leached quantities could be overestimated, particularly for VPs prone to leaching and due to their sensitivity on applied amounts, as discussed earlier for Dexamethasone.

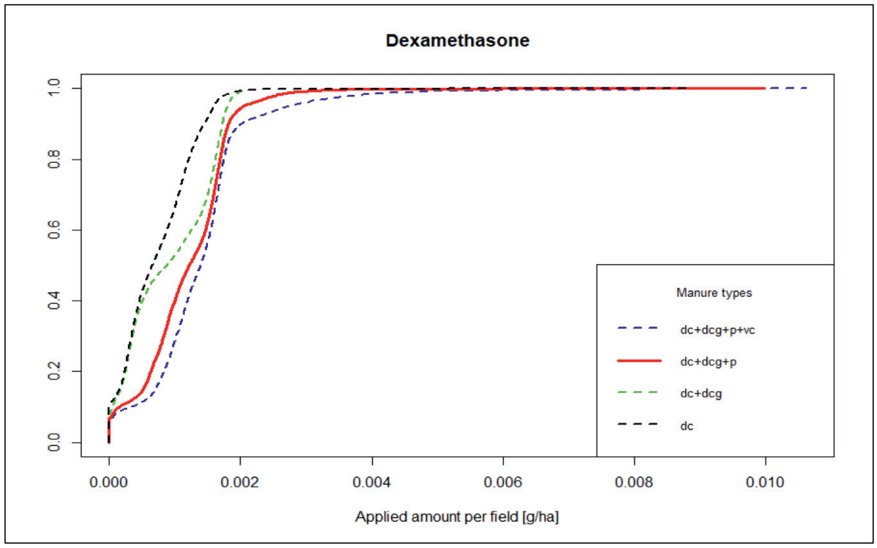

Fig. 5. Ascending cumulative distribution of applied amounts of Dexamethasone per field (A). dc-dairy cow, dcg-dairy cow grazing, p-pig, vc-veal calf. In this paper we considered application of Dexamethasone via dairy cows and pigs only. Veal calves were considered to have a minor contribution (see also Table 1). Our assumed case is represented with the red line.

Further, we assume that VPs are introduced per particular manure type everywhere in the Netherlands, which is probably not the case in reality. This assumption is a consequence of the available data on VP concentrations in manure, which are based on national averages. Considering our results, certain regions are more prone to leaching than others, hence assessing leaching with field specific input data might be relevant. Similarly, we assume national averages of precipitation and evapotranspiration to calculate water flow. This could be improved by taking into account regional weather data such as KNMI weather stations, and spatially connecting those with the appropriate regions. Assumption on constant groundwater levels is briefly explained earlier, but it is worth mentioning that eventual fluctuations in levels might be more relevant when looking at multiyear VP applications on soil. Some of the VP residues might persist in soil layers and be affected by those groundwater level fluctuations.

Note that the calculated leached mass (T) is an indication of potential groundwater concentrations, because of a number of assumptions which had to be made in order to create a national overview, and which are valid for both VP leached mass and VP concentration in groundwater. To assess whether the leached mass is objectively high and if it results in high groundwater concentration, it should be compared to the water flux evaluated at a certain depth in soil, which depends on the precipitation, soil/crop type, and local water management practices.

4. Conclusion

In this paper we quantified spatially distributed leaching of VPs to groundwater at the national scale, investigated the impacts of factors relevant for leaching, and identified locations vulnerable to leaching. Our model results showed that for the VPs Oxytetracycline, Doxycycline, and Ivermectin the maximum mass leached to groundwater is very low, i.e. $\ll 1$ μg/ha. These three VPs were prioritized as one of the most frequently soil-applied VPs in the Netherlands (Rakonjac et al., 2022), hence information on their very low leaching potential could be used in identifying their environmental pathways and impacts. For the VPs Sulfadiazine and Flubendazole we identified a few hotspot regions (Fig. 2) where the modelled quantities leached to groundwater were relatively high. These fields are located on sandy soils and have maize and floriculture as the most common crop types. Considering the leaching tendency, identified regions could be prioritized for future groundwater monitoring when targeting the VPs with similar environmental properties as Sulfadiazine and Flubendazole. On the other hand, our results for Dexamethasone indicated a widespread spatial distribution of fields where quantities leached to groundwater were relatively high (Fig. 3). Besides sandy soils, some of these fields also have clay and loamy soils. Based on the findings from an earlier study (Rakonjac et al., 2022), soil in the Netherlands is highly exposed to the application of Dexamethasone via different manure types. Therefore, being prioritized as spatially widespread in the two consecutive steps, i.e. application on the soil and leaching to groundwater, Dexamethasone warrants a closer examination when performing an environmental risk assessment of VPs.

Our results showed that the spatial patterns of VP leaching to groundwater were affected by many processes, and that the relative importance of those processes differed between the investigated VPs. When comparing the influence of the soil-applied VP masses (A) and estimated leached fractions (F_{total}) on the spatial distribution of calculated leached quantities (T), it was found that leaching patterns of Sulfadiazine and Flubendazole were dominated by F_{total} more than by A. For Dexamethasone this was also the case, but due to its high leaching potential, leaching patterns were found to be sensitive to changes in applied amounts. This implies that for assessing the factors with the highest influence on VPs leaching, a substance individual approach is probably the best option. Still, some generalization is possible regarding the leaching potential of VPs, as discussed in the following.

Even though we did not perform a targeted sensitivity analysis on the VP leaching potential with respect to degradation (τ_0) and sorption (K_{om}) parameters, indications from our study seem to be completely in agreement with the guidelines on groundwater exposure assessment proposed by the Organisation for Economic Co-operation and Development (OECD, 2013). Based on the experience with the PELMO model (Klein et al., 2000), which simulates the vertical movement of pesticides in soil, OECD advises that substances with a $K_{om} < 290$ L/kg and a $\tau_0 > 21$ d in soil may leach to groundwater and that the assessment of groundwater exposure must be performed. The only VP in our study which satisfies the mentioned thresholds is Dexamethasone (Table 1), and based on our results we also prioritized it for the leaching risk assessment compared to other investigated VPs. According to the OECD guidelines, substances with a $K_{om} > 290$ L/kg and τ_0 <21 d are not likely to leach to groundwater, which is indeed also an observation from our study (Oxytetracycline and Doxycycline). For the intermediate cases, when a substance has a $K_{om} < 290$ L/kg or a τ_0 >21 d, there are no specific OECD guidelines. In this case, for VPs we observed that some minor leaching could happen at the vulnerable (hotspot) regions, so location specific groundwater leaching assessment might still be needed.

CRediT authorship contribution statement

Nikola Rakonjac: Conceptualization, Methodology, Software, Writing.
Sjoerd E.A.T.M. van der Zee: Conceptualization, Methodology.
Louise Wipfler: Visualization, Writing - Review & Editing.
Erwin Roex: Visualization, Writing - Review & Editing.
C. A. Faúndez Urbina: Software.
Leen Hendrik Borgers: Data Curation, Software.
Coen J. Ritsema: Writing - Review & Editing.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.160310.

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