Health and ecological risk assessment to emerging contaminants (pharmaceuticals, personal care products, and artificial sweeteners) in surface and groundwater (drinking water) in the Ganges River Basin, India

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1. Introduction

Several pharmaceuticals and personal care Products (PPCPs) as well as artificial sweeteners (ASWs) are known as contaminants of emerging concerns due to their frequent detection in environmental samples (Brack et al., 2012; Petrie et al., 2014). Often, residues of these contaminants are collected in wastewater effluents after their consumption and due to their low removal in wastewater treatment plants (WWTPs), these compounds enter freshwater ecosystems. In several cases where WWTPs are not existing, these substances enter the aqueous environment directly following human and veterinary excretion and municipal wastewater effluents. Their environmental (i.e. in soils and aquatic environment) occurrence has been pointed as a direct indicator of wastewater-derived pollution (Kümmerer and Henninger, 2003), especially some ASWs such as sucralose and acesulfame K that are highly soluble and stable in the environment. During the last two decades, numerous studies have documented the occurrence of PPCPs and ASWs in wastewater and recipient water from many regions (Boxall et al., 2012; Sui et al., 2015; Y. Yang et al., 2017). Presence of the pharmaceuticals in groundwater could foster the dissemination of antibiotic resistance genes, which may interact with human intestinal flora and spread the resistance determinants, potentially impacting the human health (Szekeres et al., 2018). On the other hand, irrigation using water containing pharmaceuticals could imply that crops may take up these compounds, being another route of human exposure (Miller et al., 2016).

As some of the PPCPs are biologically active at low concentrations and have potential to accumulate in aquatic organisms (Brausch and Rand, 2011; Lillicrap et al., 2011; Tanoue et al., 2015), occurrence of these contaminants in drinking and irrigation water may pose health concerns and a water management challenge in many regions. Areas suffering drinking water scarcity and poor wastewater management are particularly sensitive to emerging contaminants. This is typically the case of developing countries with transitional economies, growing urban populations, insufficient pollution control infrastructures, and subject to frequent draught periods.

The pharmaceutical sector in India has seen a large growth in the last few decades and now ranks globally 3rd by volume, accounting 10% of the global pharmaceutical production (Department of Pharmaceuticals. Government of India, 2018). Increasing access to therapeutic drugs, use of veterinary drugs in intensive animal farming and industrially-processed food, and feeds represent drivers of high emission of PPCPs and ASWs to recipient waters as well as, potentially, in drinking water resources. Water resources scarcity, poor or absent wastewater management and high demand for irrigation water can also result in transferring a significant contaminant load to farms and possibly in the food production chain. Data supporting this hypothesis in developing countries including India are rare as monitoring of contaminants of emerging concern is not implemented on a routine base due to high cost and needs of in-place capacity.

In India, increasing demand for drinking water, poor management of available water resources, and unreliable water supply due to both anthropogenic and climate factors cause a virtually chronic water crisis (Natarajan et al., 2016; Thatte, 2018). While the protection of available drinking water resources from pollution is crucial, the process of building resilience in safe drinking water supply still requires essential base-line information. Only eight studies have monitored PPCPs in river water and two in groundwater in India, while no study monitored ASWs (Balakrishna et al., 2017; Fick et al., 2009; Philip et al., 2018). Available studies from India describe the results of local surveys, while works with a larger spatial breadth are still missing.

In this study, we examined the presence of selected PPCPs and ASWs in the surface and groundwater in the largest river basin in India, the Ganges River Basin (GRB). It is home of about 7% of the global human population and several industries are located within the watershed. For the last few decades, several mega-cities and semi-urban areas in the GRB have been experiencing serious water pollution issues and drinking water supply scarcity (Chakraborti et al., 2018; Natarajan et al., 2016). More than 60% of the irrigated agriculture and 85% of the drinking water supplies depend on the groundwater resources in India (World Bank, 2010) and contamination of groundwater aquifers may turn into a potential threat to the health of millions of people in India. The specific objectives in this study are to: (1) assess the contamination profile of selected PPCPs and ASWs in the Ganges River water acting as recipient of municipal wastewater (partially or mostly untreated) and groundwater resources in its proximity, and (2) evaluate the human health and ecological risks associated with existence of PPCPs and ASWs in drinking water and river water, respectively.

2. Materials and methods

2.1. Description of study area and sampling

The Ganges River is the largest river in India and along with the Brahmaputra and Meghna Rivers the third largest in the world in terms of water discharge. Along the 2 525 km long course in India, the Ganges crosses a steep environmental and socioeconomic gradient. Its average annual discharge is 12 400 m^3/s and the hydrological basin covers 861 452 km^2 (MoWR, 2014; UNESCO, 1971). Surface water and groundwater resources of the GRB are extensively used to support the livelihood of 43% of the Indian population through irrigation, provision of drinking water and of water for industrial purposes, ultimately contributing to 40% of India's gross domestic product. There are around 764 industries and 36 class I cities (population > 100 000) situated along the Ganges River (Narain, 2014). An estimated 1.4×10^6 m^3/day of mostly untreated domestic wastewater and 0.26×10^6 m^3/day of industrial sewage are discharged into the Ganges River and its tributaries (Natarajan et al., 2016). Along the Ganges River channel, there are about 27 chemical plants including production of fertilizers, pesticides, and pharmaceuticals which generate about 98×10^3 m^3/day of wastewater. Chemical industries along with sugar and pulp industries generate 79% of the total industrial wastewater along the Ganges River (CPCB (Central Pollution Control Board), 2013).

The GRB can be divided into three reaches representing different ecological and socioeconomic conditions: the Himalayan Reach (HR, mostly rural and semiurban population), Middle Reach (MR, mostly urban, growing cities and industries), and Lower Reach (LR, mostly semirural and rural, and industries). River water and groundwater samples were collected from 9 locations (4 in the HR, 2 in MR, and 3 in LR) (figure 1). To capture local contamination patterns, samples upstream and downstream of major cities were collected from 5 of the 9 locations (namely UK, KP, VS, PT, and FK, see figure 1 caption for location legend). In total, 14 sampling sites were included. Groundwater was collected from handpumps (used as drinking water sources) by local communities. Sampling locations for groundwater were positioned within 5 km from the Ganges River. Sample collection took place during February–April 2014 in dry weather conditions (defined as no rain in the previous 24 h and less than 2 mm in the previous of 48 h (Tran et al., 2014). Collected samples were kept in an icebox and transported to The Energy and Resources Institute (TERI) laboratory where they were temporarily stored frozen until they were shipped (cooled at 4 °C) to the Research Centre for Toxic Compounds in the Environment (RECETOX) laboratory for chemical analysis. Further details about the sampling campaign are provided in supplementary data (Table S1) and in a previous work (Sharma et al., 2016).

Figure 1. Sampling locations in the GRB. Sampling locations are: UKU/D = Uttarkashi upstream/downstream, DAK = Devprayag along Alaknanda River, DBG = Devprayag along Bhagirathi River, DGR = Devprayag along Ganges River, KPU/D = Kanpur upstream/downstream, VSU/D = Varanasi upstream/downstream, PTU/D = Patna upstream/downstream, FKU/D = Farakka upstream/downstream, GSR = Ganga Sagar.

2.2. Sample preparation and extraction

Collected water samples were stored in RECETOX laboratories at –25° C until analysis and processed in agreement with previous work (Sharma et al., 2016). All samples and procedural blanks were filtered prior to the extraction (70 mm Whatman GF/C filter with pore size 1.2 µm) and spiked with 20 µL of surrogate standard (C13 caffeine; 400 ng/mL, used for recovery control). The extraction was performed using solid phase extraction column (Waters® Oasis HLB 6cc/150mg). Cartridges were conditioned with 4 mL of 0.1% ammonium hydroxide in methanol, 4 mL of methanol, and 4 mL of Milli-Q water. Water samples (pH adjusted to 2 – 3) were loaded into the pre-conditioned cartridge at a flow rate ranging between 3 and 6 mL/min under moderate vacuum. After extraction, cartridges were dried for 30 minutes under vacuum in a protected atmosphere and washed with acetate buffer (4 mL, 0.025M). Pharmaceuticals and artificial sweeteners were eluted with 4 mL methanol into the falcon tubes and concentrated to about 250 µL (exactly weighted) using a gentle stream of nitrogen in TurboVap II (Caliper LifeSciences, USA) concentrator. Prior to the analysis, two aliquots of each extract (10 and 50 µL) were diluted with ammonium acetate in water (5mM) to get a final volume of 100 µL and the content of either 10% (for ASWs and PPCPs ionized with ESI+) or 50% (for PPCPs ionized with ESI–) of methanol in the sample to reach the initial mobile phase content use for different target method.

2.3. Target compounds and chemical analysis

In total, 12 pharmaceuticals (acetaminophen, atenolol, caffeine, carbamazepine, ciprofloxacin, clofibric acid, diclofenac, hydrochlorothiazide, ibuprofen, ketoprofen, naproxen, and sulfamethoxazole), three personal care products (diethyltoluamide (DEET), triclocarban, triclosan) and five artificial sweeteners (acetsulfamate K, aspartame, cyclamate, saccharine, sucralose) were analyzed in the collected river and groundwater samples. The selection of these PPCPs and ASWs in this study was based on their popularity in selected previous studies from India and in other countries, and their availability on the Indian market. In addition, selection of PPCPs and ASWs for analysis was also influenced by the availability of analytical methods used in the trace laboratories of RECETOX where the collected samples were processed and analyzed.

ASWs were separated using an ultra-performance liquid chromatograph (UPLC ACQUITY, Waters®, Milford, MA, USA) equipped with BEH C18 (100x 2.1 mm, 1.7 µm, 130 Å) column (Waters, Milford, MA, USA). Both water and methanol used as mobile phases contained 0.1% formic acid. Gradient elution with an initial content of 10% of methanol was applied and the final content of methanol (90%) was reached in 5 minutes. The flow rate of the mobile phase was 0.4 mL/min. The injection volume was 10 µL per individual sample. Before the next separation, the column was equilibrated using the initial composition of the mobile phase for 3 minutes. The mass spectrometer (Xevo TQS, Waters®, Milford, MA, USA) was operated in negative ion mode (ESI-). Quantification of analytes was based on an external calibration using freshly prepared

standards with a range of 0.05–500 ng/mL (10 points). The mass-labelled standard (sucralosse-d3) was used for matrix effects evaluation and sucralose quantification.

For the analysis of the first fraction of the PPCPs (acetaminophen, atenolol, caffeine, carbamazepine, ciprofloxacine, DEET, diclofenac, sulfamethoxazole), the same column as used for the ASWs was used with methanol and water as mobile phase, both containing 0.01% formic acid and 0.1M ammonium acetate. The separation gradient, flow rate of mobile phase and injected volume were as described above for ASWs. The mass spectrometer was operated in positive ion mode (ESI+). Quantification of analytes was based on an external calibration using freshly prepared standards (10 points) with a range of 0.02–100 ng/mL (0.002-10 ng/mL for carbamazepine). The mass-labelled standards (paracetamol-d4 and sulfamethoxazole-d4) were used for matrix effects evaluation.

The second fraction of PPCPs (clofibric acid, hydrochlorothiazide, ibuprofen, ketoprofen, naproxen, triclocarbon, triclosan) was separated using an Xterra C18 (100 x 2.1 mm, 3,5µm) column (Waters, Milford, MA, USA). Water containing 0.1% acetic acid and 0.1% ammonium acetate and a mixture of methanol and acetonitrile (50:50) were used as mobile phases. The initial gradient was set at 40:60 organic:water, in ten minutes the content of the organic mixture was increased up to 100 percent (hold for 2 min). The flow rate of the mobile phase was 0.2 mL/min. The injection volume was 10 µL per individual sample. Before the next run, the column was equilibrated using the initial composition of the mobile phase for 4 minutes. The mass spectrometer was operated in negative mode (ESI−). Quantification of analytes was based on an external calibration using freshly prepared standards (10 points) with a range of 0.1 – 500 ng/mL. The mass labelled standards (ibuprofen-d3 and 13C6-triclosan) were used for matrix effects evaluation. Mass-labelled standards were added to the extracts prior to the instrumental analyses and were used for matrix control. If the response of mass-labelled standards dropped below the threshold (60% of response in calibration) the samples were diluted and re-analyzed to minimalize the matrix effects.

2.4. Quality assurance/quality control (QA/QC)

To ensure no significant contamination occurred during transport of samples, travel blanks were analyzed during a pilot study prior to the campaign. Travel blanks were obtained from a previous sampling campaign (in which marine water samples originating from pristine open ocean areas in the South Atlantic were collected). These were transferred in the same type of bottles and travel conditions used for the field campaign in this study and transported sealed during several days using commercial courier-express services. Concentration of PPCPs and ASWs measured in the travel blanks (n=3) (reported in (Brumovský et al., 2017)) were similar to those measured in laboratory procedural blanks, suggesting no significant contamination occurred during transport. Travel blanks results are provided in Table S4.

Procedural blanks (n=3; SPE cartridges without any loaded samples) were processed under identical laboratory conditions as the field samples and used to control potential contamination during analysis. In addition, to control LC-MS instrument sensitivity, a QA/QC sample was analyzed after each batch of 10 samples.

Method detection limits (MDLs) were calculated as the average of the individual compounds signals in the procedural blanks plus 3 times their standard deviation (SD). These signals were considered significant if they exceeded a threshold of 3 in the signal-to-noise ratio. For analytes which were not detected in blanks, MDLs were calculated as the concentration in samples with a signal-to-noise ratio equal to 3. The MDL values calculated from the procedural blank contamination were then compared with those obtained from the signal to noise ratio in the samples and the highest were chosen. The average MDLs (Table S7) were found between 0.06–15.0 ng/L and 0.5–2.0 ng/L for PPCPs and ASWs, respectively. The final results were blank-corrected using the average concentration of the target compounds in the procedural blanks. Reported concentrations of PPCPs and ASWs were not corrected for recovery. Concentrations of target analytes in procedural and field blanks are provided in Table S4. Recovery tests (n=10) were performed using spiked Milli-Q water with addition of target analytes at levels 20–200 ng/L (Table S5). Recoveries of most compounds ranged from 54% to 125%. In contrast, low but consistent recoveries were observed for acetsulfamate K (28±6%) and cyclamate (20±4%).

Measures for quality assurance and control have been described in detail by Brumovský et al. (Brumovský et al., 2017) and are also reported in the SI.

2.5. Estimation of human health and ecological risk

We estimated the worst-case scenario of potential health risk of the detected PPCPs in the groundwater (i.e. drinking water) along the Ganges River. We calculated an age-dependent risk quotient (RQ) for each detected PPCP by dividing the maximum measured concentration in the groundwater (MC_{GW}) by the corresponding age-dependent drinking water equivalent level (DWEL) (Eq. 1). Age-specific assessment of exposures has been previously used to reduce uncertainty in risk assessment (de Jesus Gaffney et al., 2015; Leung et al., 2013; Yun Ya Yang et al., 2017).

$$RQ = \frac{MC_{GW}}{DWEL} \quad \text{..... (1)}$$

Often, it is easier to convert the acceptable daily intake (ADI) into a corresponding water concentration, such as DWEL, so that the comparison of chemical concentrations measured in drinking water to ADIs is simpler. The DWEL was estimated for seven age categories (from 1 year to >21 years of age) by using equation 2.

$$DWEL = \frac{ADI(or\ RSD)*BW}{DWI*AB*FOE} \quad \text{..... (2)}$$

Where ADI (µg/kg/day) is the acceptable daily intake or risk specific dose (RSD) for noncarcinogenic and carcinogenic effects, respectively. Values of ADI (or RSD) for each detected PPCP and ASW were adopted from the literature (Leung et al., 2013; Yun Ya Yang et al., 2017) (Table S9). BW is the median body weight (kg) of age-specific groups (Table S10), DWI is the daily drinking water intake (L/day) of age-specific groups (Table S10), AB is the gastrointestinal absorption rate assumed to be 1, and FOE is related to the frequency of exposure (350 days/365 days)(de Jesus Gaffney et al., 2015; Yun Ya Yang et al., 2017). A RQ value greater than 1 indicated the possibility of human health risk. A RQ value between 0.2 and 1 calls for more detailed assessment, whereas RQ ≤0.2 is considered of no appreciable concern to human health (Schriks et al., 2010; Yun Ya Yang et al., 2017).

The ecological risk assessment was performed by calculating RQ for the detected PPCPs and ASWs in the river water, as described in a previous publication (Yun Ya Yang et al., 2017). It was calculated by dividing the maximum river water concentration (MC_{RW}) for each PPCP and ASW by the corresponding predicted no effect concentration (PNEC) for three classes of aquatic organisms (i.e. algae, *Daphnia Magna*, and Fish) (Eq. 3).

$$RQ = \frac{MC_{RW}}{PNEC} \quad \text{(3)}$$

PNEC was calculated as:

$$PNEC = \frac{EC_{50} \text{ or } LC_{50}}{AF} \quad \text{(4)}$$

Where the EC_{50} (effective concentration, reducing a biological process by 50%) or LC_{50} (lethal concentration, killing 50% the organisms) was obtained from the literature or by using the US EPA Ecological Structure Activity Relationship (ECOSAR v1.10) model. For PPCPs or ASWs (namely: atenolol, caffeine, ciprofloxacin, hydrochlorothiazide, cyclamate, saccharine, sucralose), more than one toxicity values (EC_{50}/LC_{50} value) were available from ECOSAR model. For these contaminants, baseline toxicity values were chosen as a precaution measure. A summary of the EC_{50}/LC_{50} values is provided in the Table S12. AF, a standard assessment factor with a value of 1000, was introduced to account for extrapolation from intra- as well as inter-species variability in sensitivity (Hernando et al., 2006). Risk to aquatic organisms was subsequently classified into three categories: Low risk (RQ<0.1), moderate risk (0.1<RQ<1), and high risk (≥1) (de Souza et al., 2009; Hernando et al., 2006).

3. Results

3.1. Distribution of PPCPs and ASWs in the Ganges River water

Of the 15 target PPCPs, 14 were detected in the Ganges River water at one or more sampling sites. Atenolol and ibuprofen were detected at only one sampling site, while clofibric acid was not detected at any sampling site. Caffeine, DEET, and ketoprofen were detected with 100% detection frequency. The sum of detected PPCPs in the river water ($\sum PPCPs_{RW}$) at the monitored sampling sites ranged between 54.7–826 ng/L. The highest $\sum PPCPs_{RW}$ was found in the lower

reach of the Ganges River. The highest concentration among the PPCPs was found for caffeine (743 ng/L), followed by ketoprofen (107 ng/L). High concentrations of caffeine were found at sampling sites in Himalayan reach. Except caffeine, the other PPCPs were generally higher in the middle and lower reach of the Ganges River compared to the Himalayan reach. At local level, as expected, concentrations of PPCPs were generally higher at the downstream sites of major cities such as Kanpur, Varanasi, and Patna. Concentrations of the frequently detected PPCPs in the Ganges River water are depicted in figure 2A and presented in Table S7.

Of the five ASWs, only three (cyclamate, saccharine, and sucralose) were detected in the Ganges River water at more than one sampling sites. Cyclamate and sucralose were detected with 79% frequency. The highest concentration among these frequently detected ASWs was found for saccharine, followed by sucralose and cyclamate. In river water, concentrations of saccharine and sucralose ranged between 2.4–85 ng/L and 0.5–24 ng/L, respectively. Concentrations of saccharine and sucralose clearly peaked in the middle and lower reach of the Ganges River. Concentrations of cyclamate ranged between 0.2–1.2 ng/L with elevated concentrations in the Himalayan and lower reach. Acetsulfamate K was detected only at one location in the lower reach. The sum of detected ASWs in river water ($\sum ASWs_{RW}$) at monitored sampling sites ranged between 0.2–102 ng/L. Similar to $\sum PPCPs_{RW}$, the highest $\sum ASWs_{RW}$ was detected at downstream of Patna in the lower reach. Concentrations of ASWs detected in the Ganges River water are depicted in figure 2B and presented in Table S8.

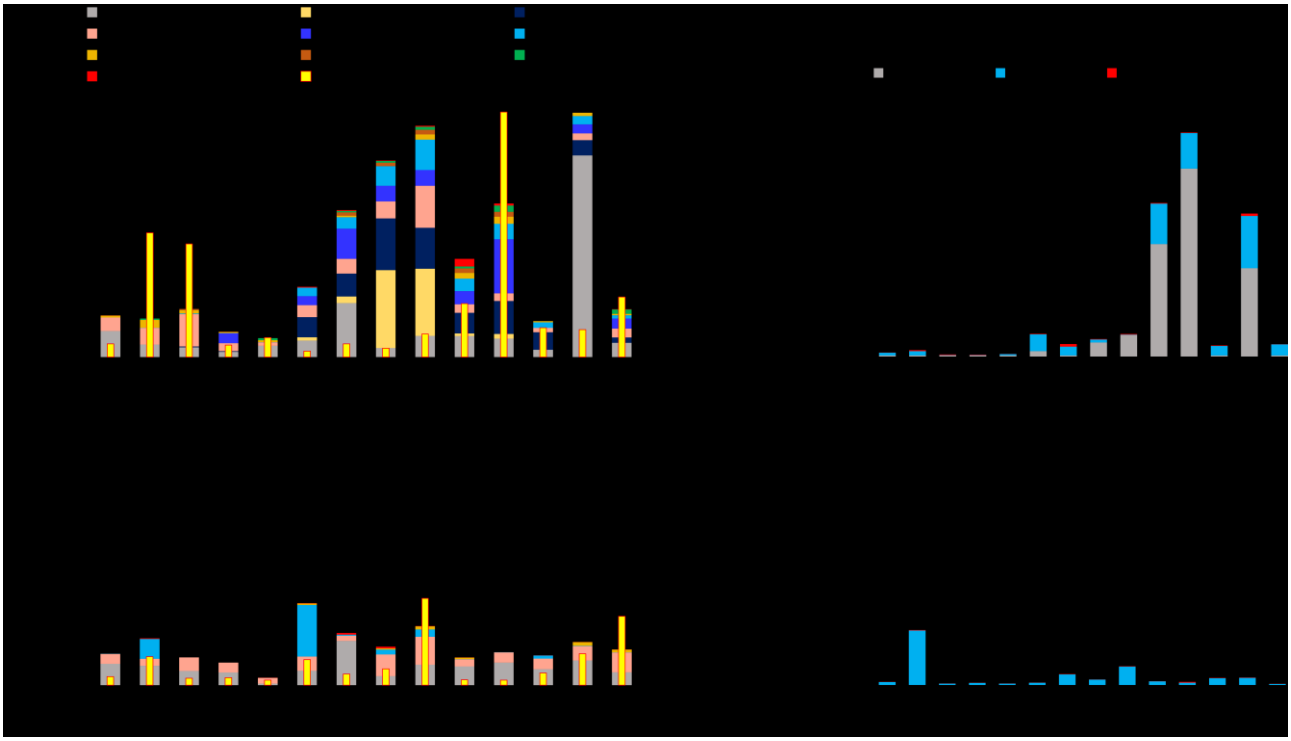

Figure 2. Panels A and C depict concentrations of frequently PPCPs in the Ganges River water and groundwater from the vicinity of the river channel, respectively. Caffeine is displayed by yellow bars corresponding to the secondary y-axis and it is not part of stacked bars in panels A and C. Panel B and D depict concentrations of frequently detected ASWs in Ganges River water and in groundwater from the vicinity of the river channel, respectively.

3.2. Distribution of PPCPs and ASWs in groundwater

Thirteen out of the 15 target PPCPs were detected in the groundwater at one or more sampling sites. Atenolol and clofibric acid were not detected at any sampling sites. Similar to river water, caffeine and DEET were detected with 100% frequency. The sum of detected PPCPs in groundwater ($\sum PPCPs_{GW}$) ranged between 34–293 ng/L, with elevated concentrations observed in the middle and lower reaches of the Ganges River. $\sum PPCPs_{GW}$ were about a factor of 2 (geometric mean) lower than those found in the river water. However, at few sampling sites, $\sum PPCPs_{GW}$ was found higher than the $\sum PPCPs_{RW}$. Similar to the river water, highest concentrations in groundwater were detected for caffeine, ranging from 15–262 ng/L. Other elevated PPCPs in groundwater were ibuprofen (<MDL–49.4 ng/L), carbamazapine (<MDL–27.2 ng/L), and ketoprofen (<MDL–23.4 ng/L). Unlike river water, PPCPs in groundwater did not consistently display higher concentrations in wells located downstream the major cities. Concentrations of selected PPCPs in the groundwater along the Ganges River are depicted in figure 2C and presented in Table S7.

Similar to river water, cyclamate and sucralose in groundwater were detected at more than one sampling site. Sucralose was detected in groundwater with 100% frequency and ranged between 0.5–25 ng/L. Groundwater concentrations of cyclamate ranged between <MDL–0.26 ng/L. Results for cyclamate have however been taken cautiously due to poor recoveries (Table S5). The detection frequency of sucralose in groundwater was higher than that in the river water, whereas that of cyclamate was 50% and lower than that observed in river water (78%). Interestingly, similar to river water, acetsulfamate K was detected in groundwater only at one location in the Himalayan reach. The sum of detected ASWs in the groundwater ($\sum ASWs_{GW}$) ranged between 0.5–27 ng/L. Except for one sampling site (UKD) in the Himalayan reach, levels of detected ASWs in groundwater were elevated in the middle and lower reaches of the Ganges River. Concentrations of ASWs in the groundwater are depicted in figure 2D and presented in Table S8.

Generally, it is expected that PPCPs and ASWs with low $\log K_{ow}$ would have a tendency to be present in groundwater, but in this study, no clear relationship was observed between $\log K_{ow}$ and either the frequency of detection of PPCPs and ASWs or their concentrations in groundwater.

Pairwise/Dependent ANOVA was used for testing differences in concentrations of frequently detected PPCPs and ASWs in both river and groundwater in the three different reaches of the Ganges River. These PPCPs and ASWs selected for ANOVA were acetaminophen, DEET, caffeine, carbamazepine, sulfamethoxazole, ketoprofen, hydrochlorothiazide, triclocarban, cyclamate, and sucralose. Pairwise ANOVA was chosen because of possible overlaps in PPCP and ASW contamination sources to the river and groundwater. Significant differences ($p<0.05$) between concentrations in the three reaches were observed for carbamazepine ($p=0.004$), sulfamethoxazole ($p=0.008$), and sucralose ($p=0.050$). Carbamazepine was significantly higher in both river and groundwater in the middle reach of the Ganges River. Similarly,

sulfamethoxazole was significantly higher in river water in the middle reach of the Ganges River, but not in the groundwater. Sucralose was found significantly higher in the river water in the lower reach of the Ganges River, but not in ground water.

3.3. Human health and ecological risk

We provide first estimations of age-specific RQs based on the maximum detected groundwater concentrations of PPCPs in the GRB as a worst-case scenario of human exposure. For all detected PPCPs, DWELs for all age groups ranged from 4.8 µg/L (for carbamazepine, 1–2 years age group) to 12.8 mg/L (for acetaminophen and 16–21 years age group) and RQs ranged from 1.5×10^{-7} (for acetaminophen, 16–21 years age group) to 0.0021 (for carbamazepine, 16–21 years age group) (Table S11). The PPCPs with higher RQs were carbamazepine, ciprofloxacin, ketoprofen, caffeine, ibuprofen, and triclosan (figure 3A, Table S11). Among different age groups, children (1–11 years) had higher RQs than adolescents (11–21 years) and adults (>21 years). Overall, RQs of all detected PPCPs were <1, implying that the detected PPCPs in groundwater in the present study do not pose a risk to human health through drinking water consumption.

The RQ values (based on PNECs from Table S12) for ecological risk due to PPCPs and ASWs in river water are presented in Figure 3B and Table S13. For some of the PPCPs and ASWs noticeably high RQs were calculated, mainly for algae. For example, the RQ of caffeine as high as 49.5 was observed for three different aquatic organisms. Similarly, the RQs of triclocarban and triclosan ranged from 0.03 to 0.3 and 0.01 to 3.9, respectively. Among ASWs, the RQ values up to 0.1 were observed for sucralose, particularly for algae. The RQs for freshwater invertebrates (except for daphnia from triclocarbon) and fish were generally lower than 0.1, implying negligible risk of acute/chronic toxicity to these aquatic organisms.

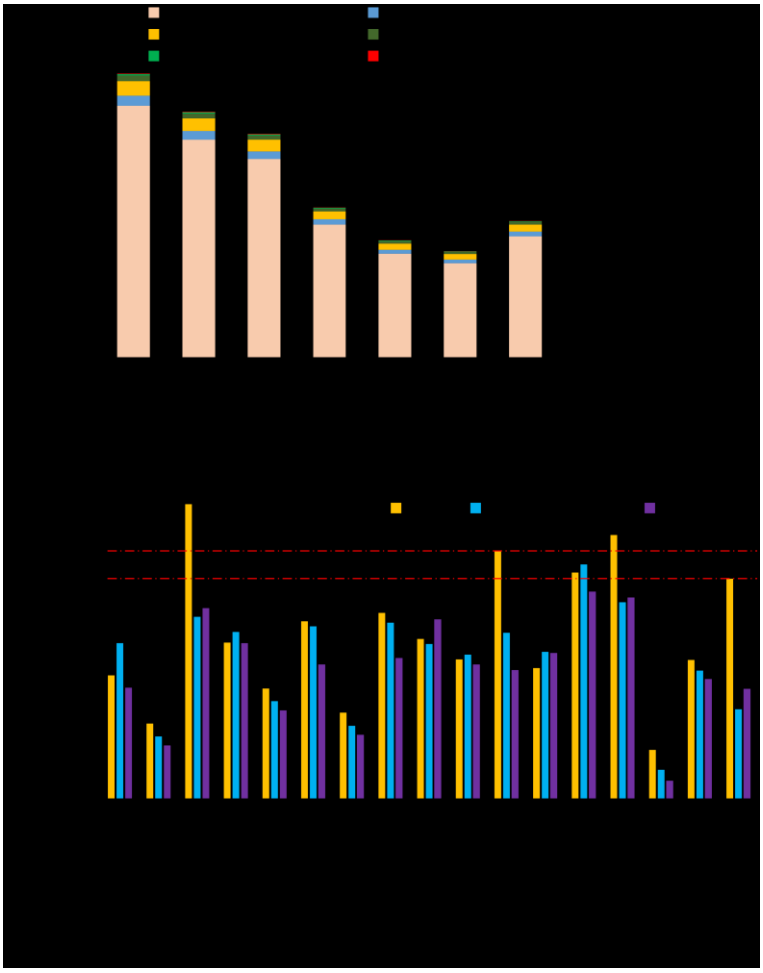

Figure 3. Panel A shows the human health life-stage RQs for some of the PPCPs in the drinking water (groundwater). Panel B shows the risk quotients (on a logarithmic scale) for PPCPs and ASWs in the river water with respect to acute toxicity for algae, daphnia, and fish.

4. Discussion

This is the first study reporting concentrations of PPCPs and ASWs in river and groundwater resources in the GRB. Previously, only eight studies have reported data on PPCPs in rivers from India (Balakrishna et al., 2017). Among them, only one study determined the fate and occurrence of some commonly used antibiotics in the Yamuna River in Delhi, a tributary of the Ganges (Mutiyar and Mittal, 2014). The other seven studies reported PPCPs concentrations in rivers from southern India. Similarly, studies determining levels of PPCPs in groundwater in India are scarce, only two studies reported concentrations of selected pharmaceuticals in Indian groundwater (Fick et al., 2009; Jindal et al., 2015), despite the fact that groundwater accounts for over 85% of drinking water supplies in India (World Bank, 2010). To the best of our knowledge no previous study focused on ASWs in rivers or groundwater in India. Two earlier studies reported data on ASWs in WWTPs in India (Anumol et al., 2016; Subedi et al., 2015).

The present study shows that many PPCPs and ASWs are ubiquitous in both river and groundwater wells in proximity of the main river channel. Concentrations of selected PPCPs (diclofenac, ibuprofen, ketoprofen, naproxen) measured in this study were in similar ranges to

those reported in southern Indian rivers (Shanmugam et al., 2014). However, concentrations of ciprofloxacin in the Ganges River were up to 6 orders of magnitude lower than those found in the Isakavagu-Nakkavagu Rivers and in southern India (ciprofloxacin: 10–2500 µg/L) and in the Yamuna River (<1.44 µg/L) (Fick et al., 2009; Mutiyar and Mittal, 2014). In the present study, triclosan in river water ranged between <MDL–5.4 ng/L and had concentrations higher than MDL at only three sampling sites, whereas triclosan concentrations were found up to three order of magnitude higher in rivers in southern India (Ramaswamy et al., 2011). Concentrations of ciprofloxacin and diclofenac in the groundwater in the present study were up to 3 orders of magnitude lower than those observed in wells located villages of southern- and northern-India (Fick et al., 2009; Jindal et al., 2015).

In a global context, various studies have reported levels of PPCPs and ASWs in river and groundwater in North America, Europe, and Asia (Ebele et al., 2017; Kuroda et al., 2012a; Liu and Wong, 2013; Sui et al., 2015). River water concentrations of 14 PPCPs in the present study were up to one order of magnitude lower than those detected in the Qing and Liangshui Rivers in China (276–6 109 ng/L) (Dai et al., 2016), and in same range of those detected in the Túria River in Spain (average 50 ng/L) (Carmona et al., 2014). The median concentrations of sucralose were 1 140 ng/L in the Pearl River delta (Yuan Yuan Yang et al., 2017a), 2 orders of magnitude higher than those detected in river water in the present study. Similarly, up to 3 orders of magnitude higher concentrations of sucralose were detected in the Haihe River, China (Gan et al., 2013). Noticeably higher levels of cyclamate (0.12 – 0.67 µg/L) compared to the present study were detected in the Haihe River, China (Gan et al., 2013). Similarly, higher levels of cyclamate and sucralose were detected in European rivers (Lange et al., 2012). Although concentrations of PPCPs and ASWs in the present study were lower than those in many other regions, mass loadings of some of the PPCPs and ASWs in the Ganges River can be substantially higher or similar to those found in developed countries (Spoelstra et al., 2013) due to the enormous river water discharges of the Ganges.

Concentrations of PPCPs in the groundwater along the Ganges River were found to be either lower or in ranges of those detected in various other countries (Sui et al., 2015). For example, groundwater concentrations of sulfamethoxazole (MDL–4.13 ng/L) detected in this study were up to two orders of magnitude lower than those detected in groundwater in vicinity of municipal landfills in Guangzhou, China (29–125 ng/L) (Peng et al., 2014) and in range of those detected in groundwater from the Jianghan Plain (<0.8 ng/L) (Tong et al., 2014). Groundwater concentrations of ibuprofen in this study were in the same range as detected in Serbia and Canada (Gottschall et al., 2012; Petrović et al., 2014), while one order of magnitude lower than those reported in Spain, China, and Germany (López-Serna et al., 2013; Peng et al., 2014; Wolf et al., 2012). Groundwater concentrations of ASWs in the present study were up to three orders of magnitude lower than those reported in Canadian groundwater along streams (cyclamate<23 ng/L and sucralose<24 µg/L) (Van Stempvoort et al., 2011). Although, groundwater

concentrations of sucralose found in this study were higher than those detected in Singapore (Tran et al., 2014), China (<9.6 ng/L) (Gan et al., 2013).

Selected PPCPs (ketoprofen, DEET, acetaminophen, and caffeine) and one ASW (cyclamate) in the Ganges River water in the pristine Himalayan reach (at Uttarkashi) were found similar to those in the densely populated and industrialized middle and lower reach of the Ganges River. This might be due to the overlap of sampling campaign in Himalayan reach with the tourism season. This part of the river also has religious importance and hosts millions of people coming for pilgrimage between April and October. A recent study has elucidated the impact of tourism on levels of PPCPs in Alpine rivers (Mandaric et al., 2017). Moreover, the sampling locations in the Himalayan reach are also the only towns in the region providing health care services and weekly grocery shopping for residents of hundreds of nearby villages.

There are various possible sources of PPCPs and ASWs in the Ganges River water, including direct discharge of domestic and industrial wastewater in to the river. There are 764 industries (including chemical, dairy, food and beverage, and sugar) along the main channel of Ganges and its tributaries, which discharge about 501 million liters per day (MLD) of wastewater. In addition, 36 class-I and 14 class-II cities along the Ganges River discharge a total 2 601.3 MLD wastewater into the Ganges River. Total wastewater discharge at the sampling locations in the Himalayan reach is about 3.46 MLD which is 2 orders of magnitude lower than that at the sampling locations in middle and lower reaches (Kanpur: 598 MLD, Varanasi: 410 MLD, and Patna: 233 MLD) (CPCB (Central Pollution Control Board), 2013). In addition to these canalized wastewater sources, many household along the river banks discharge wastewater directly. In this study, we did not find any significant correlation of river water concentrations of PPCPs and ASWs with either wastewater discharges volumes into the Ganges River through major drains or population inhibiting within 20 km from sampling locations.

Possible sources of PPCPs and ASWs in the groundwater in vicinity of the Ganges River could be bank infiltration, irrigation through Ganges River water followed by leaching to the groundwater, leakage from septic tanks (or unpaved septic tanks) and leaching from landfills (e.g. many of which, in India, may illegally receive hospital waste, expired pharmaceuticals, etc.), flaws in sewage disposal practices, and unpaved drainage system. The intensity of these sources could vary during the wet and dry seasons depending on the magnitude and direction of infiltration. Several studies have previously used selected PPCP and ASW as markers of wastewater contamination. Caffeine, carbamazepine, acesulfame, sucralose, cyclamate, etc. have been indicated as appropriate wastewater indicator substances (Kuroda et al., 2012; Seiler et al., 1999; Yuan Yuan Yang et al., 2017b). In the present study, ketoprofen, DEET, and caffeine among PPCPs in river and groundwater and sucralose among ASWs in groundwater were detected with 100% detection frequency. These substances can be considered as appropriate indicators of wastewater contamination in surface and groundwater in the GRB.

This is the first study which provides estimates of health and ecological risks associated to PPCPs and ASWs in river and groundwater in India. Results of this study show that all detected PPCPs individually posed no considerable human health concern. However, as previously suggested, co-exposure to the PPCP cocktail have different implications for risk estimation (Backhaus and Karlsson, 2014). It has also to be noted that this assessment focuses only on a limited number of PPCPs, thus, the presence of other PPCPs and other emerging and legacy contaminants together should be considered in future studies. Compared to no appreciable risk to human health, moderate risks associated with some of the PPCPs were observed for aquatic organisms (i.e. algae and *Daphnia magna*). Previous studies also highlighted moderate risks associated with some of the PPCPs (namely: sulfamethoxazole and triclocarban) for aquatic organisms in other regions of the world (Du et al., 2017; Tamura et al., 2012; Yun Ya Yang et al., 2017).

5. Conclusion

This study shows that both surface and groundwater in the GRB are contaminated by PPCPs and ASWs, which are markers of wastewater contamination. Interestingly, some of the PPCPs and ASWs were detected in the river and groundwater at sampling locations in the pristine Himalayas. Previous studies have already shown contamination by other emerging and legacy contaminants in surface and groundwater from the Ganges River basin (Sharma et al., 2016, 2015). In this study, no considerable human health risk and moderate ecological risk associated to PPCPs and ASWs were estimated. However, health and environmental risk from exposure to a large mixture of emerging and legacy pollutants may be of concern, especially because river water (from the Ganges River and its tributaries) and groundwater are the important sources of drinking water and agricultural production for 600 million Indians living in the GRB. In recent years, a few studies have reported serious health problems associated to contaminated water in the Ganges River (Chakraborti et al., 2018). Due to increasing population, urbanization and shifting lifestyle standards from traditional to contemporary, we can expect higher exposure levels in the future, unless appropriate water and waste management solutions will take place. Results reported in this study are a useful baseline for planning and assessing efficacy of possible future pollution control measures as part of the Indian white paper on Ganges protection and restauration.

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