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Pharmaceutical Active Compounds Contamination and Seasonal-Based Ecotoxicity Assessment of the Yamuna River for the Delhi stretch

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Abstract: Yamuna River is the only river in Delhi. This results in heavy reliance on Yamuna to meet Delhi Water demands. This has prompted several research works covering physicochemical, biological, heavy metal concentration, emerging pollutant occurrence, and their risk assessment. This study investigated occurrence, seasonal variation (pre-monsoon, monsoon, and post-monsoon), and risk assessment posed by 7 PhACs at five sampling locations along a 22 km stretch of Yamuna River in Delhi. The samples were collected and analysed in pre-monsoon, monsoon, and post-monsoon seasons. The seven PhACs, comprised of 2 antibiotics (Ciprofloxacin; CIP, sulfamethoxazole; SMZ), 2 NSAIDs (Paracetamol; PCM, Ketoprofen; KPF), 1 anxiety control (Lorazepam, LOR), 1 anticonvulsant (Carbamazepine; CBZ) and 1 statin (Fluvastatin; FUT). The PhACs range of occurrence across three seasons was PCM 75-589 ng L^{-1}, KPF 31-238 ng L^{-1}, CBZ 11-192 ng L^{-1}, LOR 62-462 ng L^{-1}, CIP 48-192 ng L^{-1}, SMZ 192-1534 ng L^{-1}, and FUT 0-421 ng L^{-1}. The seasonal occurrence was in the order of post-monsoon> pre-monsoon> monsoon. PCM, CBZ FUT posed a negligible ecotoxicological risk, LOR posed a low-medium risk, and ketoprofen, ciprofloxacin, and sulfamethoxazole posed high risks. Based on the risk index, all seasons have high ecological risk at every sample point. Discharges of untreated sewage and insufficient and inefficient treated wastewater are the primary contributors of PhACs in the Yamuna River. This study concludes that existing WWTPs need drastic upgrades. Policies and measures should also be developed to prevent untreated wastewater from reaching the Yamuna River. This necessitates further studies to investigate processes suitable for installing and treating wastewater along the longitudinal section of the drain and assess their technical feasibility.

Keywords: Yamuna River, wastewater discharge, pharmaceutical compounds, ecotoxicity

1. Introduction

Water quality and its assessment have become a normal routine for the sustainable maintenance of water resources (Singh Sankhla et al. 2022a). The focus of water quality studies has shifted from physicochemical parameters to biological parameters, from heavy metal concentration to emerging pollutants, in recent years (Mishra et al. 2023a). Delhi's population needs 4086 MLD (million litres per day) of water to meet the daily requirements of its population (Singh Sankhla et al. 2022a). Delhi relies heavily on River Yamuna to meet its water demand. However, 80% of the water demand is estimated to transform into wastewater after use (Parween et al. 2021). This renders Delhi producing 3268 MLD of wastewater each day.

Delhi consists of three drainage basins to properly dispose of the generated wastewater, i.e., trans-Yamuna, Barapullah and Najafgarh, covered by 201 major and minor drains (Khan et al. 2023). Another classification of drains is termed as major Delhi drains, comprising 14 drains. Further adding to the already grieved pollution of the river Yamuna, Delhi is home to several healthcare facilities that ensure the good health of its residents. This has led to concerns, both at research and government levels, about investigating and improving the water quality of Yamuna.

The concern over surface water bodies contamination from PhACs is increasing, leading to several rivers being investigated in various countries. The primary source of pharmaceutical compounds in the surface water body has been linked to wastewater treatment plants (WWTP) (V. Singh & Suthar 2021). This is linked to the fact that upon intake of PhACs, they are excreted in wastewater, which goes to WWTP for treatment. However, since WWTPs are not designed specifically for PhAC removal, they enter an environment with effluent from WWTP. Additionally, leakage from septic tanks and sewers allows for directly discharging PhACs into the environment. Keeping in lieu of the worldwide trend, water quality in surface water bodies is also a growing trend in India, including river Yamuna (Lalwani et al. 2020).

Table 1. Literature on water quality assessment of Yamuna River and its flood basin

Parameter	Study/ Analysis	Reference
Organic micropollutants	Occurrence of organic micropollutants in Yamuna River	(Mishra et al. 2023b)
Lead and Nickel	Assessment of climate on prevalence of lead and nickel in Yamuna River	(Singh Sankhla et al. 2022b)
Ciprofloxacin, paracetamol, Carbamazepine, …. 16 compounds	Studies occurrence of pharmaceuticals, compounds, personal care products and hormones in Yamuna River for a stretch of 575 km from Delhi Okhla barrage to Agra city	(Biswas & Vellanki 2021)
BOD, COD, E. Coli	Impact of COVID-19 Lockdown on Yamuna River within Delhi	(Patel et al. 2020)
Antibiotic resistant genes	Metagenomic study of the occurrence of antibiotic resistance genes in sediments	(Das et al. 2020)
Carbamazepine, coliforms, and ESBL resistant bacteria and respective genes	Transfer of antibiotic resistance to river Yamuna from sewage	(Lamba et al. 2020)
Fe, Mn, Zn, Cr, Ni, Cu, Pb, Co, As, Cd	Assessment of soil biological activities and risk from irrigation with heavy metal loaded Yamuna River water	(P. Singh et al. 2020)
Ni, Cd, Pb, Co, Mn, Cr, Fe, Cu, As, Zn	Heavy metal distribution, pollution, health risk and ecological assessment due to trace metal in Yamuna River floodplain	(Aithani et al. 2020)
Ca^{2+}, Mg^{2+}, SO_4^{2-}, Cl^-, HCO_3^-	Alluvial River Yamuna hydrogeochemical characterisation in northern India	(Kaur et al. 2019)
Physicochemical parameters and heavy metals	Evaluation of pollution load in Yamuna River	(Yadav & Khandegar 2019)
Total coliform, carbapenem resistant bacteria, and three integron	Wastewater-borne carbapenem resistance across Delhi in 12, hospitals, 12 sewage treatment plants, 20 sewers and 5 locations along the Yamuna River	(Lamba et al. 2018)
Ketoprofen, paracetamol, carbamazepine, lorazepam….9 compounds	Ecological risk assessment and fate of pharmaceutical compound in Yamuna River	(Mutiyar et al. 2018)
Amoxicillin, carbenicillin, aztreonam, ceftazidime & cefotaxime	Pandrug and Heavy metal analysis for resistance among E. Coli in Yamuna River	(Azam et al. 2018)
Fe, Cu, Zn, Ni, Cr, Pb, Cd	Environmetrics and indexing-based analysis of heavy metal contamination of Yamuna River	(Bhardwaj et al. 2017)
Fecal coliform & Fecal streptococci	Microbial point & non-point source pollution of Yamuna River	(Jamwal et al. 2011)
BOD, COD & Total Coliform	Analysed water quality of the Yamuna River	(Upadhyay et al. 2011)
C, Cr, Fe, Ni & Physicochemical parameters	Heavy metal enrichment and contamination assessment of river Yamuna in Haryana stretch	(Kaushik et al. 2009)
DO & BOD	QUAL2E application for the Yamuna River water quality modelling	(Paliwal et al. 2007)
Cu, Pb, Zn & Cd	Eco-toxic assessment of metal ions in the Yamuna River	(Jain 2004)

River Yamuna has also been investigated in terms of its water quality. The previous studies focussed on organic load and bacteriological pollution of Yamuna River water. Recently, studies have concentrated on emerging micropollutants. Mutiyar et al. (2018) have investigated 9 PhACs compounds in the Yamuna River. Biswas & Vellanki (2021)investigated PhACs in Yamuna River based on summer and post monsoon occurrence at a 573 km distance starting from Lower Himalaya, crossing Delhi and Uttar Pradesh. Mutiyar et al. (2018) had earlier studied PhACs occurrence in the Yamuna River for the Delhi stretch, but no seasonal variation was considered. Also, the sampling points were not determined specifically, as there are 17 drains in Delhi emptying into the waters of the Yamuna River. However, the surface water bodies need characterisation based on annual hydrological variations (Mandaric et al. 2019).

Hence, this study considers the seasonal variation of the Yamuna River for its Delhi stretch. The objectives of this study are: 1. Assess PhACs occurrence in River Yamuna, 2. To analyse seasonal variation during pre-monsoon, monsoon, and post-monsoon seasons, and 3. Ecotoxicity assessment of PhACs in the river water.

2. Data and Method Used

2.1. Study area

Delhi is among four metropolis cities of India situated between 22.38°N and 77.13°E. Delhi lies in the Indo-Gangetic plain, covering an area of 1483 km^2. River Yamuna is a perennial river originating from the Himalayas that traverses 296 km in the distance before finally flowing into Delhi (Yamuna Basin Organisation 2018). The total length of River Yamuna in Delhi is 48 km, of which 22 km lies in the main capital, and the rest passes through the National Capital Region. This stretch is so significant that out of 5 segments of the Yamuna River, the Delhi stretch is defined as a separate segment per India's central water commission (Supplementary Table S5). It is a perennial river that provides potable water to Delhi and receives sewage from sewage treatment plants and drains (Mutiyar et al. 2018). Delhi is largely developed on the western banks of the Yamuna River, but a boom in the economy also led to its development on the eastern banks. The total catchment area of the Yamuna River in Delhi is only 0.4%, i.e., 1485 km^2 (Yamuna Basin Organisation 2018).

2.2. Sampling Site

Sampling locations in this study were located in between Wazirabad-Okhla barrages. In total, five sampling locations were selected, including the two barrages. The first sampling location was at Wazirabad barrage (S1); the other four locations were downstream from the first location. The second location was at Wazirabad Khyber Pass drain (S2), the third location was at Delhi Gate drain (S3), the fourth location was at Maharani Bagh drain (S4), and the fifth location was at Okhla Barrage (S5). The sampling location details are presented in Table S6 in supplementary tables. Wazirabad barrage was selected as a reference point to determine the difference in pollution load attributed to various drains (Mutiyar et al. 2018). Okhla barrage was identified to calculate the total pollution load incurred by the Yamuna River from Delhi alone compared to the Wazirabad barrage (Biswas & Vellanki 2021). Both locations have also been selected for the very purpose in previous studies (Biswas & Vellanki 2021, Kumar Dubey & Parmar 2014, Patel et al. 2020, Upadhyay et al. 2011). Hence, five sampling sites in this study can represent the water quality of the Yamuna River in Delhi. Sampling Location of River Yamuna in this study is presented in Fig. 1.

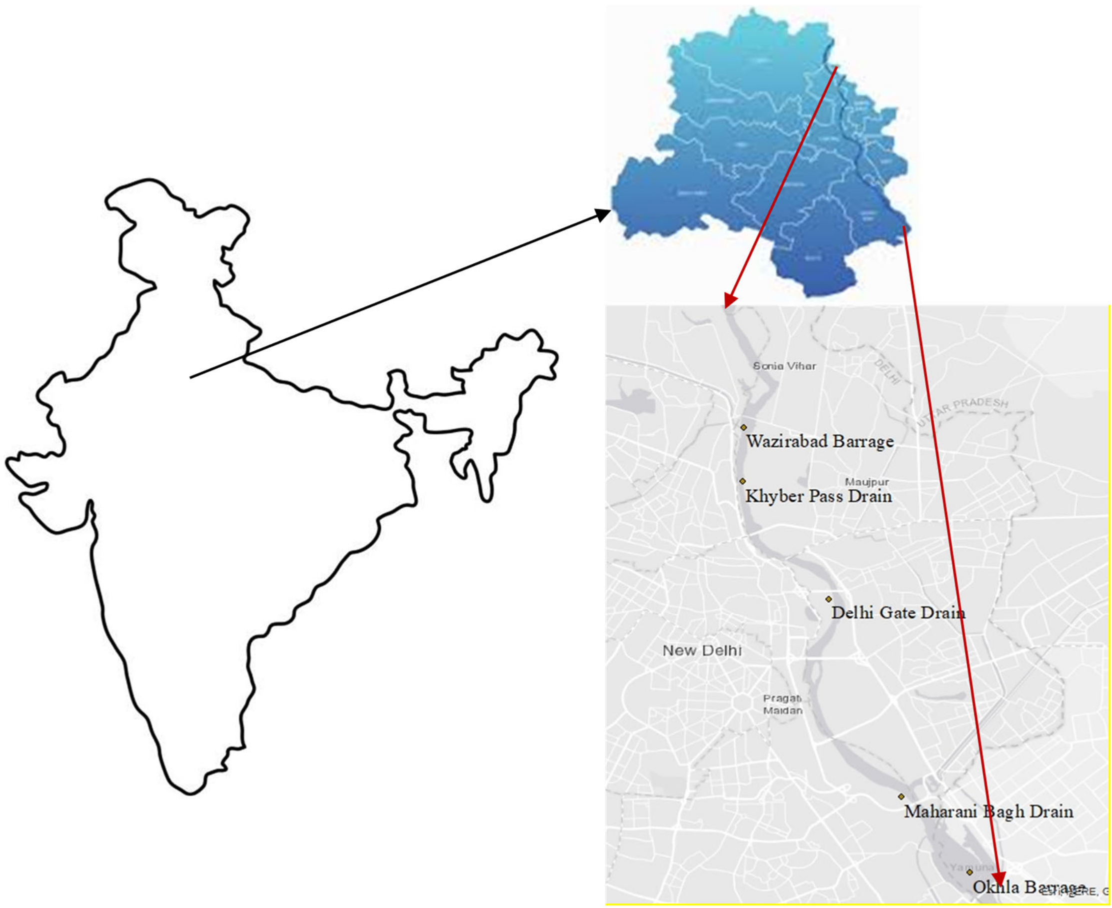


Fig. 1. Study area with sampling location along the course of River Yamuna for Delhi stretch starting from Wazirabad Barrage and ending at Okhla Barrage

2.3. Sample Collection

Grab-composite water samples were collected for analysis. The water samples were collected at a depth of 0.4 m below the surface of the water level. Each grab sample comprised 150-200 ml, which was combined to make a 500 ml sample at each water collection interval. Three grab samples of 500 ml were collected at an interval of 8 hours for 24 hours. Then, the grab samples were combined to obtain a composite sample of 1500 ml. The samples were collected thrice a year: pre-monsoon (April), monsoon (July), and post-monsoon (November). Three samples for each location at each time duration were obtained. The mean values of the three samples are presented in this study. The physio-chemical, biological parameters and pharmaceutical residues have been analysed thrice a year. The pollution is expected to be lowest in the monsoon season because rain is the source of fresh water, leading to dilution of the pollutant, followed by pre-monsoon and post-monsoon. To prevent light interference, water samples were obtained in brown bottles. All the glassware was washed with detergent, dried at 110°C for 2 hours, and rinsed with deionised water (Im et al. 2020a). The collected water samples were stored in ice containers before being transferred to the laboratory. In the laboratory, collected samples were stored at 4°C and brought to room temperature 24 ± 2°C. The p-value test was used in this study to determine the statistical significance of the target compounds analysed.

2.4. LC-MS (Liquid Mass chromatography-mass spectrometry)

All the samples analysed were tested against blanks with no PhACs concentration to prevent contamination during sampling analysis and extraction which was also adopted by Singh & Suthar (2021). A sample of volume 10 µL was injected in the C18 column (1.7 mm particle size & 150 x 1.0 mm). In mobile phase A (0.1% formic acid in ultrapure water) and in mobile phase B (0.1% formic acid in methanol), gradient mode was employed for a flow rate of 0.4 mL min^{-1}. The gradient method adopted was in lieu of Im et al. (2020). The operating conditions are scan time (300 ms), mass range (100-400 aum), nebuliser pressure (35 psi), capillary current (3500 v) and gas flow 8 l min^{-1}. Two ionised pairs and retention time were compared with respective standard compounds to identify PhACs. The PhACs analysed in this study are presented in Table. 2.

Table 2. Selected pharmaceuticals analysed in water samples of the Yamuna River

CAS Number	Pharmaceutical	Code	Min	Max	Mean	Std. Deviation
298-46-4	Carbamazepine	CBZ	61.06	589.50	180.5473	139.20470
856-49-1	Lorazepam	LOR	22.94	238.64	80.2253	65.28888
723-46-6	Sulfamethoxazole	SMZ	0.00	192.06	60.5987	53.34638
93957-54-1	Fluvastatin	FUT	51.34	468.93	185.4907	131.47287
85721-33-1	Ciprofloxacin	CIP	0.00	192.05	92.4020	54.93703
22071-15-4	Ketoprofen	KTF	122.43	1534.00	487.1280	413.95661
103-90-2	Paracetamol	PCM	0.00	421.00	127.2813	109.49915

2.5. Ecological Risk Assessment

Ecological risk assessment is necessary as the release of PhACs into the environment highly impacts its consumers. Ciprofloxacin causes swelling of muscles around bones, which means the tissue connecting muscles with bones swells up, and the contact strength and reflex are highly reduced (Timofeeva et al. 2022). Paracetamol is widely used to bring down body temperature. However, its overdose can lead to damage to the liver, which can be fatal and irreversible (ECHA CHEM Database 2023). Sulfamethoxazole, besides its required positive effect on the human body, causes many side effects. Diarrhoea, dizziness, sore throat, bloating, unpleasant breathing, etc., are known side effects (Online Drug Bank 2024). Ketoprofen is commonly used to relieve pain, viz. muscle pain, cramps, dental pain, etc. Its side effects may also lead to symptoms similar to SMZ, including drowsiness, nausea, constipation, upset stomach, headache, etc. (Clinic 2024). Hence, it should be clearly understood if these compounds are present in the environment and how much they can affect the ecosystem. This necessitates the extent of risk their presence in the water bodies poses.

Ecological risk assessment is an approach to assess the impact of exposure to chemicals on the ecosystem. Risk Quotient is a commonly used approach (Singh & Suthar 2021). RQ has been widely used in ecological risk assessment of pharmaceuticals (Zhang et al. 2020). The RQ for each PhAC was calculated against MEC (measured environmental concentration, ng L^{-1}) concerning PNEC (predicted-no-effect-concentration, ng L^{-1}) as presented in Eq. 1. The effective or lethal concentration (EC_{50} or LC_{50}) of individual PhACs was divided by value of 1000 to obtain the PNEC value of PhACs concerned (Sharma et al. 2019, Ginebreda et al. 2010). PNEC values for pharmaceuticals were obtained from Aa van der et al. (2001), Mendoza et al. (2016) and Pereira et al. (2020). Zhang et al. (2020) have taken MEC as the maximum environmental concentration, while Na et al. (2019) have preferred MEC as an average or reasonable maximum concentration at 95% UCLs and 95% UFL. This study has taken the mean of three sample values as MEC to evaluate RQ.

$$RQ = \frac{MEC}{PNEC} \quad (1)$$

3. Result and Discussion

3.1. Pharmaceuticals occurrence in Yamuna River

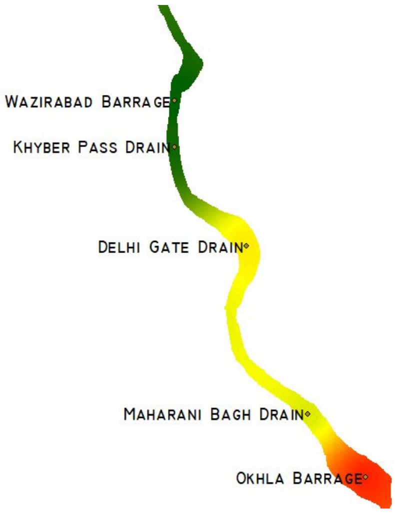
The PhACs proportion concentration and spatial distribution at sampling points are presented in Fig. 2. The occurrence of antibiotics in water bodies is a major concern attributed to their capacity to develop resistance in microbes. Also, they are intended to alter the metabolism and biological activities of the human body to provide relief to patients and thereby may cause a similar effect on the biodiversity of the receiving environment (Aimee K. Murrayet et al. 2021, Lamba et al. 2020). Wazirabad barrage water samples served as reference samples as they are the entry point of Yamuna in Delhi territory. The river pollution load was expected to increase with discharge from 14 drains that discharge into the Yamuna River in the Delhi stretch up to Okhla Barrage. Out of seven PhACs, two antibiotics (CIP, SMZ), two analgesics (KTF, PCM), one anticonvulsant (CBZ), and one anxiety control (LOR) were categorically analysed. Fig. 2 presents the spatial distribution of the seven PhACs in Yamuna River water at the five sampling sites. Based on the concentration occurrence of PhACs, it was in the order of SMZ >PCM >LOR >CIP >CBZ >KTF >FUT at Wazirabad Barrage. During monsoon season, Ketoprofen and Lorazepam also fell below detection limits (BDL). At Okhla barrage, at the exit of Delhi, the occurrence of PhACs changed to SMZ >LOR >PCM >KTF >CBZ >SUT >CIP. Mishra et al. (2023b) have also indicated that PhACs are the most prevalent constituent in the Yamuna River among organic micropollutants. The concentration of PCM, SMZ, & FUT increased at every sampling point in the Yamuna River with respect to distance. KTF and LOR concentration increased at SP2, SP4, and SP5, but 20% and 48% decreases were observed at SP3, respectively. Only CIP saw a decrease in concentration by 15% at SP2. The p value again validates this. The p value ≤ 0.01 indicated a significant relationship between the targeted compounds. The p value of ≤ 0.01 for PCM, SMZ and KUT indicated significant relationship between them at sampling point SP2, SP3 SP4 and SP5. Similarly, p value ≤ 0.01 for KTF and LOR presented their strong relationship at SP sampling point SP2, SP4 and SP5, while the same compounds had p value > 0.01 at SP3 and indicated no significant relationship. Similarly at sampling point SP2 the CIP concentration was observed to be decreasing which was corresponding to, p value >0.01 indicates no significant relationship between CIP and other targeted compounds at SP2 station.

Antibiotics accounted for an average of 48.6%, with a range of 40-54% of all PhACs. SMZ contributed 65-80% of the total load from two antibiotics, while CIP constituted only 20-35%. SMZ values were between 112-1734 ng L^{-1}. CIP ranged between 38-400 ng L^{-1}. In another study of the Ganges River, India, antibiotics were reported to constitute only 8% of the total PhACs load (Singh & Suthar 2021). Also, Biswas & Vellanki (2021) observed that CIP ranges between 60-240 ng L^{-1} in the Yamuna River. In the Han River of South Korea, 6-27.9 ng L^{-1} concentration of sulfamethoxazole has been observed. Bagnis et al. (2020) have also reported a high occurrence and concentration of antibiotics in the Nairobi River, Kenya. Park & Jeon (2021) have reported lower proportions of antibiotics in the Nakdong River, Korea waters. The high concentration in river water samples indicates the prevalence of infectious diseases in the river basin (White et al. 2019).

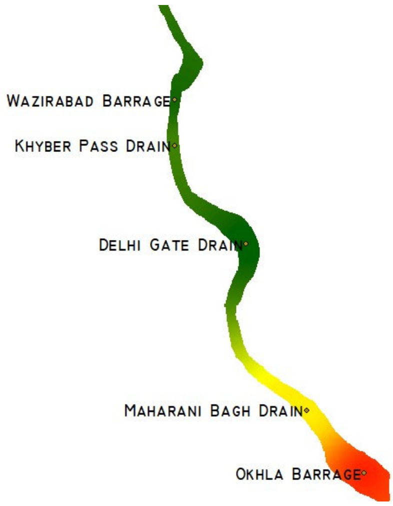
NSAIDs (paracetamol and Ketoprofen) are the most commonly used to suppress various kinds of pain (Guiloski et al., 2017; Yang et al., 2019). NSAIDs, on average, formed 24% of the total PhACs load in the Yamuna River. Paracetamol was in higher concentration than Ketoprofen, which was 65-579 ng L^{-1}. Ketoprofen contributed 0-245 ng L^{-1} and 0-75 ng L^{-1} of NSAIDs load in the Ganga River, India and the Lis River, Portugal (Singh & Suthar 2021, Paíga et al. 2016). Paracetamol has been reported to be present at 34.4 ng L^{-1} concentration in the Danube River (Kondor et al. 2020). NSAIDs were prevalent in the river Thames over three times the standard limits, but Ketoprofen was below the permissible limits attributed to 100% removal in WWTPs as it is highly biodegradable (White et al. 2019).

CAB is used for the control of seizures and pain and is among the most commonly studied PhACs (Cantwell et al. 2018, K'oreje et al. 2018, Kondor et al. 2020, Mandaric et al. 2017, Na et al. 2019, Sharma et al. 2019, Su et al. 2021, Zhang et al. 2020). CAB concentration in this study was between 16-183 ng L^{-1} with 100% detection frequency. CAB was prevalent at a concentration of 880 ng L^{-1} in the muscles of fish species in the Uruguay River with 92% detection frequency (Rojo et al. 2019). The high sorption capacity of CAB in fish is attributed to its property of low water solubility, moderate hydrophilic nature, and low biodegradability. These properties prevent its photodegradation and biodegradation (Mandaric et al. 2019). Paíga et al. (2016) analysed Lis River water samples, found 24-219 ng L^{-1} concentration, and confirmed its occurrence was owing to effluents from WWTPs.

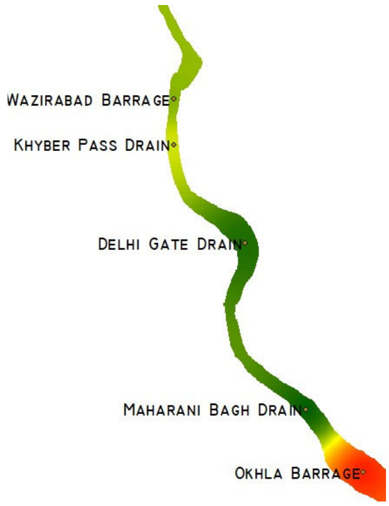
LOR is known to calm the brain and nerves and is thereby highly used in short-term treatment of insomnia, anxiety relief, and preoperative sedation (Singh & Suthar 2021). LOR was detected in the Garonne River estuaries and was in the range of 0.6-7 ng L^{-1} (Aminot et al. 2016). The concentration of LOR in the waters of The Yamuna River was 61-468 ng L^{-1}. LOR was not detected among fish species in the investigation of national rivers and streams in the USA (Huerta et al. 2018). But in the Uruguay River, it was prevalent at 730 ng L^{-1} concentration in fish species (Rojo et al. 2019). Fluvastatin is prescribed to reduce the risk of stroke and heart attack. The detection frequency was 80% at an average of three seasons. The FUT range of occurrence in waters of Yamuna was between 0-421 ng L^{-1}. Rezka & Balcerzak (2015) has reported 4.5-90 ng L^{-1} concentration of Fluvastatin in the aquatic environment.



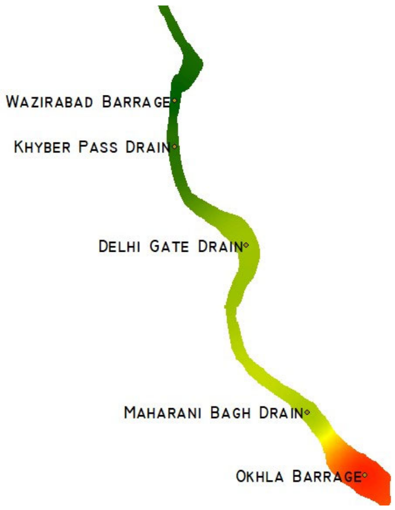
Paracetamol-PrM **(a)**



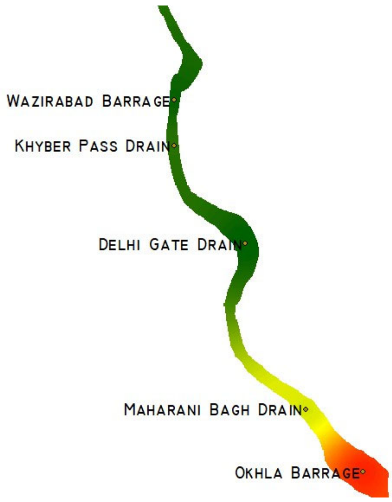
Ketoprofen-PrM **(b)**



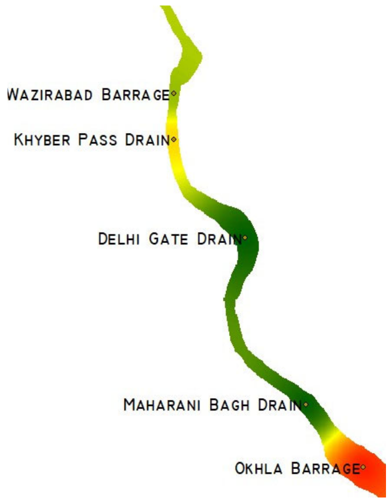
Carbazepam-PrM **(c)**



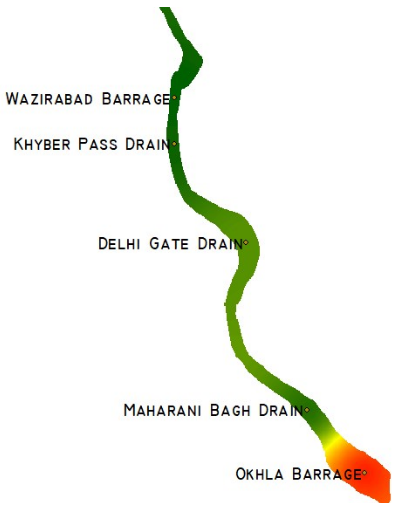
Paracetamol-M **(d)**



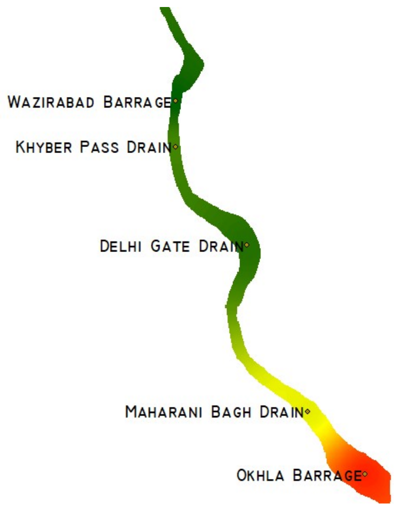
Ketoprofen-M **(e)**



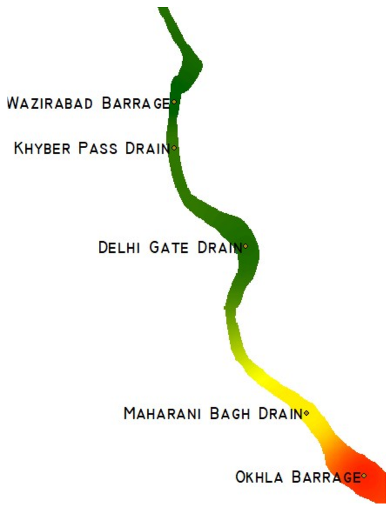
Carbazepam-M **(f)**



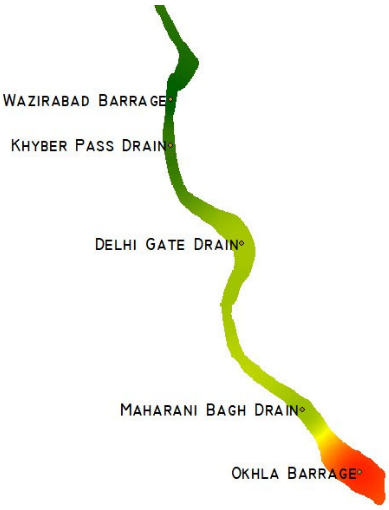
Paracetamol-PM **(g)**



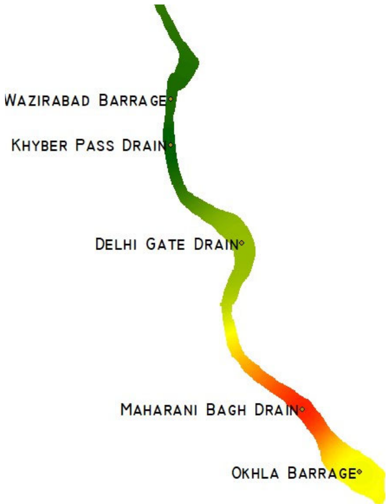
Ketoprofen-PM **(h)**



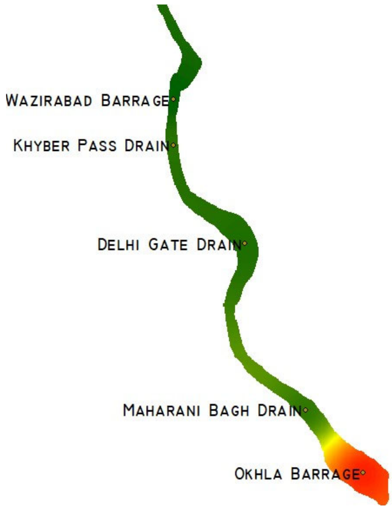
Carbazepam-PM **(i)**



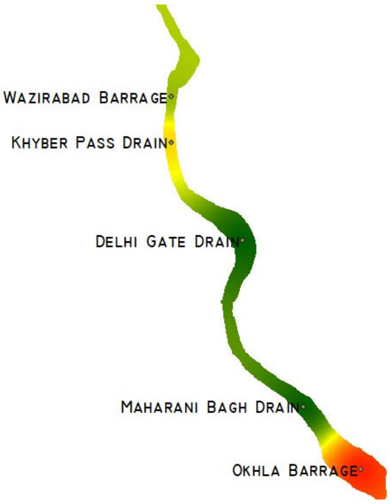
Lorazepam-PrM **(j)**



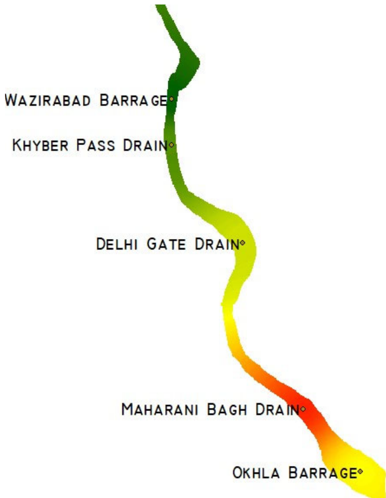
Ciprofloxacin-PrM **(k)**



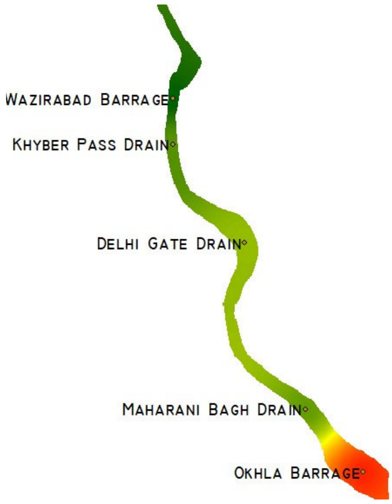
Sulfamethoxazole-PrM **(l)**



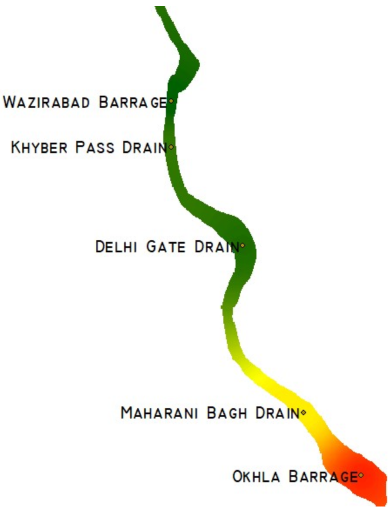
Lorazepam-M **(m)**



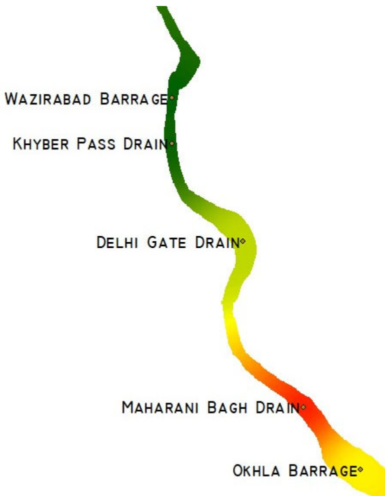
Ciprofloxacin-M **(n)**



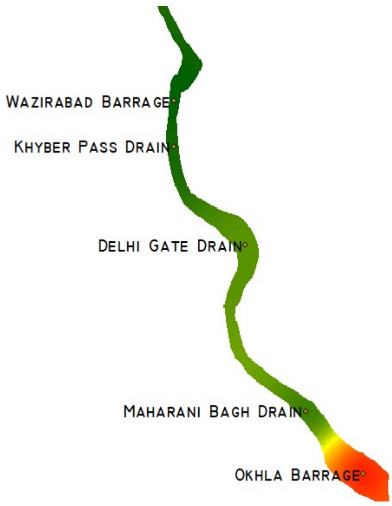
Sulfamethoxazole-M **(o)**



Lorazepam-PM **(p)**



Ciprofloxacin-PM **(q)**



Sulfamethoxazole-PM **(r)**

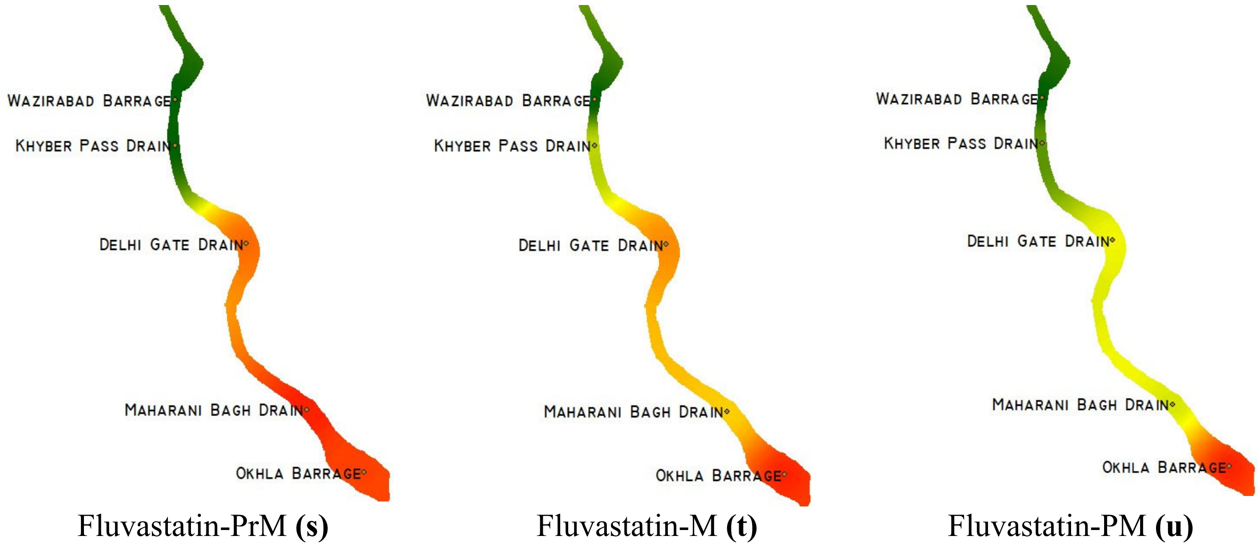


Fig. 2. Spatial distribution of PhACs in Delhi stretch of Yamuna River. The range is defined on 0-1000 ng L^{-1} to compare on a similar scale as Indian Standards yet define no standard values. (PrM = Pre-monsoon, M = Monsoon, and PM = Post Monsoon, for better presentation proportion of river Yamuna has been adjusted, Green = 0-250 ngL^{-1}, Yellow 250-500 ngL^{-1}, Orange = 500-750 ngL^{-1}, Red = 750-1000 ngL^{-1})

3.2. Seasonal variation in pharmaceutical concentration in water of river Yamuna

The PhACs concentration is presented in Fig. 3 for Pre-monsoon, monsoon and post-monsoon seasons. In premonsoon-monsoon season, antibiotics were reduced by 1-35% & 18-29% for CIF and SMZ, respectively. NSAIDs decreased concentration by 2-24% & 0-42% for PCM and IBF. CAB, LOR, and SIT concentrations also reduced in range of 0-37%, 5-40%, and 20-51%, respectively. The zero values indicate that the PhACs are below the detection limit. The reduced concentration in the monsoon season compared to pre-monsoon and post-monsoon is attributed to runoff waters entering The Yamuna River (Patel et al. 2020). During the monsoon season, river Yamuna reaches the highest flood level, which increases the volume of water in the river many times compared to pre-monsoon and post-monsoon seasons. The volume of water increases significantly; however, the concentration of PhACs does not increase proportionally, indicating dilution as the primary reason. CIF has been found in higher concentrations during summer and also in the Yamuna River passing through Agra city (Biswas & Vellanki 2021). In the Jilin Songhua River, PhACs were found in relatively higher concentration during the ice breakup period, i.e., when the weather changed to warmer conditions (Zhang et al. 2020). Daneshvar et al. (2010) also reported the highest PhACs concentration for Swedish-river lake system water samples during summer.

During the monsoon to post-monsoon season, the variation was consistent with that of pre-monsoon to monsoon season. In the absence of precipitation and resulting runoff, it was expected to see an increase in PhACs concentration at all locations. Similar results were observed for most of the samples. However, for SP3 and SP4 for PCM concentration, a decrease of 11 and 30% was observed. IBF was reduced by 18% at SP1. LOR concentration decreased by 7% at SP4, CIF by 36% (SP1) and SMZ by 14% (SP2). Except for these, all other concentrations for PhACs at all sample points were found to increase: antibiotics (13-76%), NSAIDs (25-86%), CAB (6-66%), LOR (6-41%), and LUT (10-77%). White et al. (2019) have also found higher antibiotic concentrations during winters in the Thames River, UK. It must be noted that PhACs general occurrence was post-monsoon>pre-monsoon>monsoon. A similar trend was also observed in the River Ganga, where PhACs concentration during winter was higher than in summer (Singh & Suthar 2021). Hence, from the literature, we get results that are both similar and contrary to our results based on seasonal variations of PhACs in river water. This is attributed to the temperatures prevailing in the river waters at the sampling time. Paíga et al. (2016) also reported this, cited from previous literature that predominant elimination processes (bioremediation and sorption) in surface water bodies are temperature dependent. Jilin Songhua River, China, and Sweden river lake system had higher PhACs concentrations in summer. But the temperature in both countries in summer is around 20+°C. However, 40+°C is observed during pre-monsoon season in Delhi. And 20+°C is observed during post-monsoon season. Again, this is the ambient air temperature. Only when sample temperature is reported can this hypothesis be further validated.

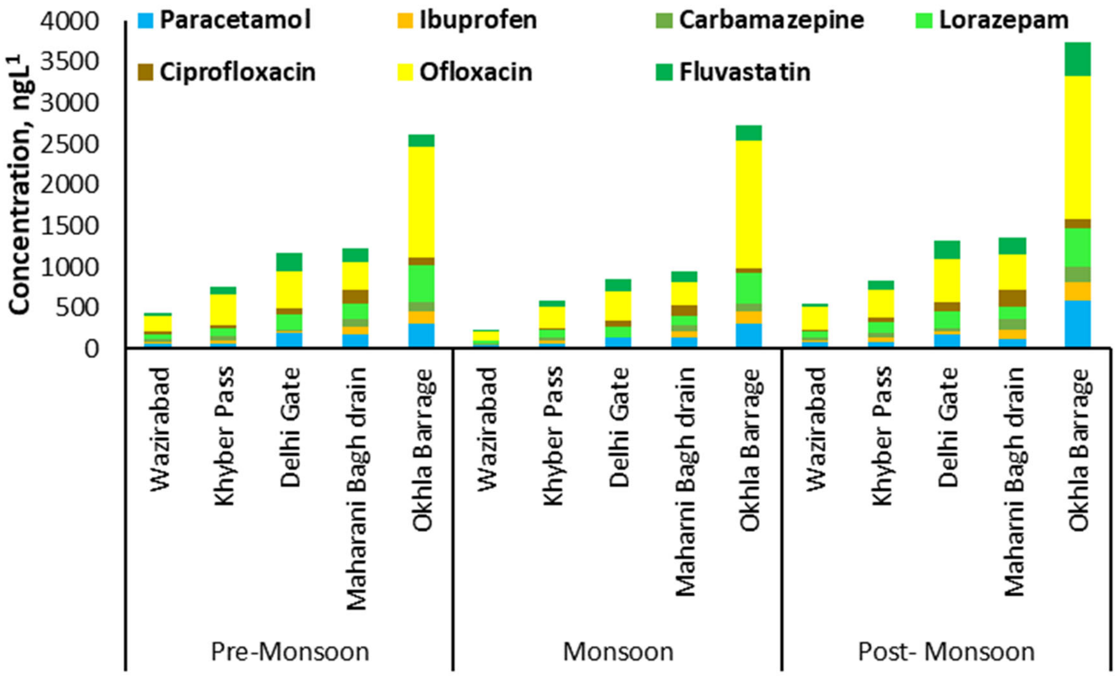


Fig. 3. Comparison of cumulative concentration of PhACs at a sampling point in the Yamuna River

The variation in PhACs concentration during monsoon and non-monsoon periods is not as high as anticipated. These points to two significant factors that may affect the result. First, the sampling procedure adopted so far is ineffective in presenting the real-time river scenario. Second, the discharge of wastewater is significant in River Yamuna. When it enters Delhi at Wazirabad Barrage, the Yamuna River is already laden with PhACs. In seasonal variation, no high variation was detected because the samples were obtained close to shore manually. Hence, samples from across the width of The Yamuna River were not obtained and were not reported in previous studies as well (Biswas & Vellanki 2021, Samson et al. 2019, Singh & Suthar 2021, Yadav & Khandegar 2019). This arises from the fact that no organised boat service operates in the Yamuna River. Samples were taken from the boat for the Danube River (Kondor et al. 2020). The occurrence of PhACs in surface water bodies has been attributed to effluent from WWTPs (Cantwell et al. 2018, Huerta et al. 2018, Im et al. 2020b, Mandaric et al. 2019, Su et al. 2021).

However, before accounting for the wastewater discharge into the Yamuna River its annual flow condition needs to be assessed. About 80% of the Yamuna River flow occurs in the monsoon (July to September) season, while the rest of the 20% of the flow makes up for the rest of the nine months (October to June). The Yamuna River's annual mean flow is about 13.9 BCM (billion cubic meters). Of these, 9.5 BCM is extracted for irrigation and drinking until Delhi leaves only 4.4 BCM for river flow. Again, when this flow reaches Wazirabad Barrage, it is reported to release about 3.8 BCM during the monsoon season, leaving 0.3 BCM for the remaining 9 months as river flow (Vikram Soni & Shashank Shekhar 2013).

Fig. 4 presents the amount of wastewater in MLD (million litres per day) discharged into the River Yamuna along the Delhi stretch. The relation of PhACs with WWTPs holds for developed countries where 100% of wastewater is treated before discharge into the environment. Also, the 100% removal of PhACs was not reported in any study. The presence of PhACs in river water can also be attributed to the absence of WWTPs, i.e., wastewater is released into the environment without treatment (Paíga et al. 2016). However, problems in developing countries worsen as all raw sewage/wastewater does not reach WWTPs. The reasons are economic constraints and lack of infrastructure. Even if both are resolved, technical feasibility is a major constraint. Old urban areas generally develop without a controlled development plan. Not only are urban development byelaws overruled, but there is no wastewater discharge plan at all.

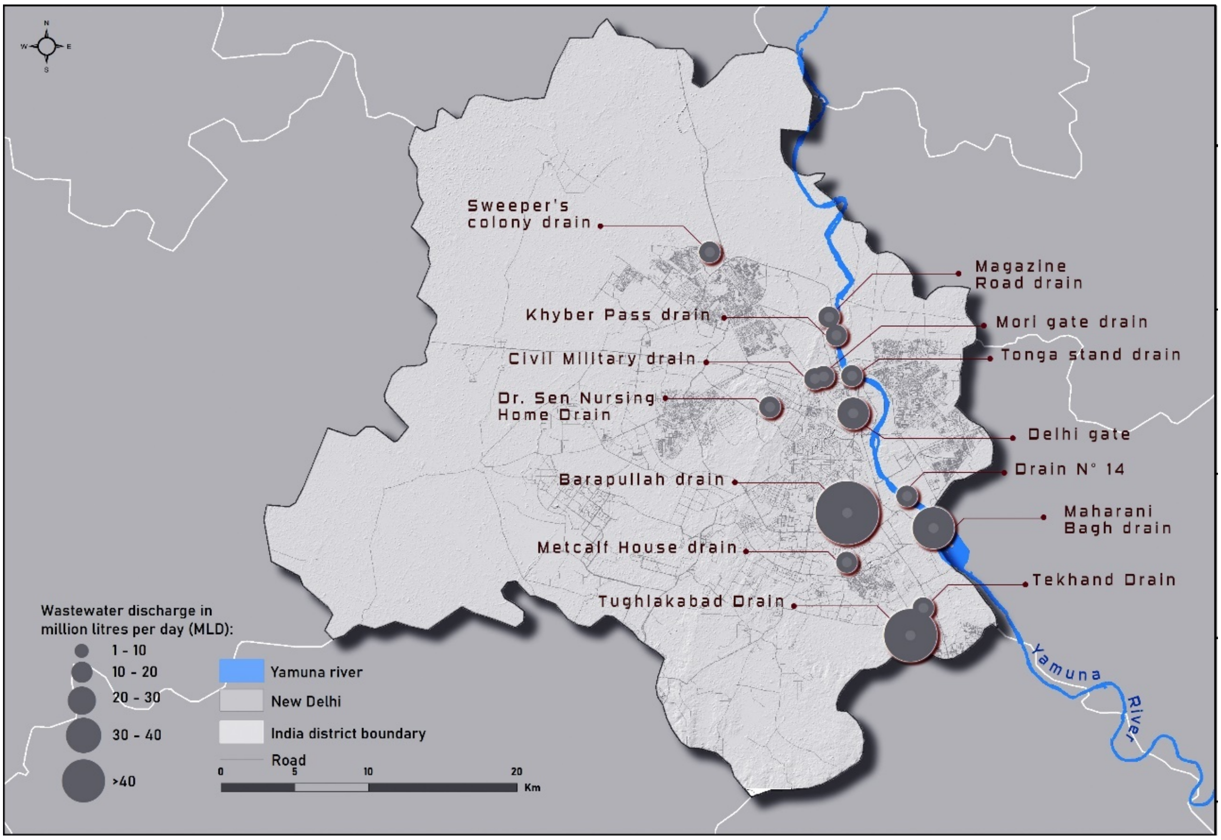


Fig. 4. Wastewater discharge in million litres per day (MLD) from various drains in Delhi

Delhi has installed forty-one wastewater treatment plants to treat its raw sewage. Only twenty-four are functional, while two are running over capacity, nine are running under capacity, and six are not functional. Even if all forty-one WWTPs are fully operational, 512 MLD of wastewater reaches The Yamuna River without any treatment as it is technically not feasible. Additionally, this 512 MLD data is obtained with the difference in the total sewage generated in Delhi against the total treatment capacity installed in Delhi. However, actual utilisation of operational and non-operational capacity only adds to this untreated sewage volume. If total generated sewage is taken as 100% (3330 MLD), then the total treatment capacity of Delhi's WWTPs is 86% (2896 MLD), out of which 81% (2715 MLD) is the operational capacity. This is again reduced to 72% (2712 MLD) of the actual utilisation of WWTPs, and this treatment capacity is again reduced by 5% (90 MLD) owing to non-operational WWTPs. Again, the treatment processes employed in existing WWTPs are old and cannot keep up with the merging pollutants (Supplementary Table S7). For example, 26 WWTPs' secondary treatment was comprised of an activated sludge process, and 2 still used extended aeration (Gupta et al. 2018). This makes up almost one-third of the total sewage generation in Delhi. Hence, WWTPs need maintenance, upgradation, and rehabilitation, and infrastructure needs to be developed to ensure that 100% of wastewater reaches WWTP before its discharge into the Yamuna River.

This explains the small variation of PhACs concentration in The Yamuna River during monsoon and non-monsoon seasons. The flow variation during monsoon is up to 12 times higher than in non-monsoon season. However, the PhACs concentration variation in pre-monsoon and post-monsoon seasons is up to 1.8 times only. The 512 MLD per day of untreated sewage discharge into the Yamuna River means it makes up 45% of the total flow. Hence, the dilution capacity is very low, and the concentration of PhACs changes slightly. Regarding 80% of flow during monsoon season, the study suspects that since the sampling has been done on the side of the discharge of drains, the homogenous mixing of pollutants in river water could not occur. Hence, slight variation was observed compared to the variation in flow during monsoon season.

Collecting all wastewater generated in Delhi and taking it to a wastewater treatment plant is not only an economic strain but also not feasible. This is based on the fact that Delhi, an old city of India, underwent urbanisation centuries ago. Urban development has kept up well with modern times, but little attention has been paid to sewer system development. This led to the non-connectivity of old drainage systems to modern sewage systems. The only solution is a complete reconstruction of the old drainage system, which is financially and technically humongous and has been ruled out by the governing agencies. The authors suggest, from their experiences of other cities in India like Lucknow and Varanasi, a parallel sewer system along the bank of the

Yamuna River that stretches across the Delhi stretch and installing a wastewater treatment plant to treat the collected water. This will ensure that no single drop of wastewater reaches the Yamuna River before treatment. Compared to the already ruled-out options, this is a much more feasible and cheaper option that renders its sustainable restoration plan for restoring the Yamuna River water quality.

3.3. Ecological risk

A preliminary risk assessment was used to estimate potential hazards from individual PhACs in terms of Risk Quotient (RQ). This assessment was also carried out in other studies under different headings: ecotoxicological risk assessment (Mutiyaret al. 2018, Im et al. 2020), environmental risk assessment (Pereira et al. 2020) and preliminary risk assessment (Zhang et al. 2020). Environmental pollutants have been linked to increased carcinogenic risk (Kiani et al. 2021). Environmental pollutants can also lead to the deterioration of the quality of food and herbs consumed daily (Shokri et al. 2022). Similarly, pharmaceutical compounds tend to alter and modify metabolism, which may have a degrading impact on the ecosystem, especially the aquatic environment, which is the first to receive contaminated wastewater (Shamsollahi et al. 2019). The RQs of individual PhACs are presented in Fig. 5 for pre-monsoon, monsoon, and post-monsoon seasons. RQ < 0.01 infers no risk from compound upon exposure, RQ >0.01 and <0.1 have low risk (green colour) from the corresponding PhACs, RQ >0.1 and <1 pose medium risk (yellow-orange colour) and RQ >1 present high risk (red colour). SIT, SMZ, PCM, and LOR pose high risks at every sample point and in all three seasons. IBF, except for point S5, posed a medium risk. CIP and CAB were in the range of no risk to medium. Individual RQ was in the medium to no risk range for 4 of the 8 PhACs. The summative RQ, i.e., RI (∑RQ), was >1 for all points in every season considered in this study, as depicted in the right column in colour in Fig. 5. Even if RI is not considered SIT, SMZ, LOR and PCM pose a serious threat to the environment. In other studies covering rivers of Southern India, RQs values up to 1500 were reported for the Tamariparani river, the Kaveri river and the Velar river. (Mutiyar et al. 2018) In river Ganga, RQ for CIP, IBF and SMZ were <1 (Singh & Suthar 2021). Even if RQ < 1, they may threaten invertebrates and algae (Zhang et al. 2020). The impact of PhACs on the aquatic environment is presented in Supplementary Table S6.

4. Conclusion

This study evaluated the occurrence of seven pharmaceutical compounds in the Yamuna River, and its variation in three seasons (pre-monsoon, monsoon and post-monsoon). Also, the ecological risk posed by these pharmaceutical compounds was estimated. PhACs were found to be present in The Yamuna River before its entry in the Delhi stretch and meeting any of drains at Wazirabad Barrage (paracetamol, 75 ngL^{-1}, ketoprofen 35 ngL^{-1}, carbamazepine 42 ngL^{-1}, lorazepam 63 ngL^{-1}, ciprofloxacin 56 ngL^{-1}, and sulfamethoxazole 193 ngL^{-1}). As hypothesised, the pharmaceutical compound concentration in the river increased on average while crossing the urban areas and meeting different drains (paracetamol increased from 82 ngL^{-1} at Najafgarh drain, 210 ngL^{-1} at Nala no. 12, 185 ngL^{-1} at Barapullah downstream and 321 ngL^{-1} at Okhla barrage). Similar trends were observed for the rest of the targeted compounds. The seasonal variation was relevant and in line with the expected dilution or reduced concentration of pharmaceutical compounds during monsoon season. Ecotoxicity assessment found high risks from the pharmaceutical compound analysed in water samples. The two antibiotics, i.e., sulfamethoxazole and ciprofloxacin, were to have risk quotient value >1. Also, ketoprofen risk quotient value >1 for all 5-sampling locations. The lower dilution and variation in pharmaceutical compound concentration were attributed to the significant amount of untreated sewage discharged into the Yamuna River.

Hence, this study suggests procurement of river water samples not only along the downstream length but also along the cross-sectional length of the river at every given sample point. This will ensure a homogeneous river water sample. On river banks, concentration may be high, as wastewater from drains did not mix homogeneously with river water. Also, this study highlighted that most studies have focussed on western banks of the Yamuna River and 14 major drains. However, drainage basins on eastern banks have been neglected in previous studies. Also, this study found that the discharge of wastewater from drains is not the source of the problem alone. Inefficient and insufficient wastewater treatment plants and technical feasibility are significantly responsible. Hence, future work must include investigating processes suitable for removing pharmaceutical compounds from wastewater. Based on the results of this study, it is highly recommended that the water quality of the Yamuna River be regularly monitored. The results of this study can be used to adopt mitigation policies and measures to improve overall Yamuna River water quality. Further research is required to assess the pharmaceutical compound concentration from each wastewater treatment plant effluent and identify the source of untreated sewage that is being discharged into the river Yamuna to propose possible solutions. Also, the presence of pharmaceutical compounds in surface water calls for investigation into pharmaceutical compound occurrence in groundwater in Delhi, for which further studies are required.

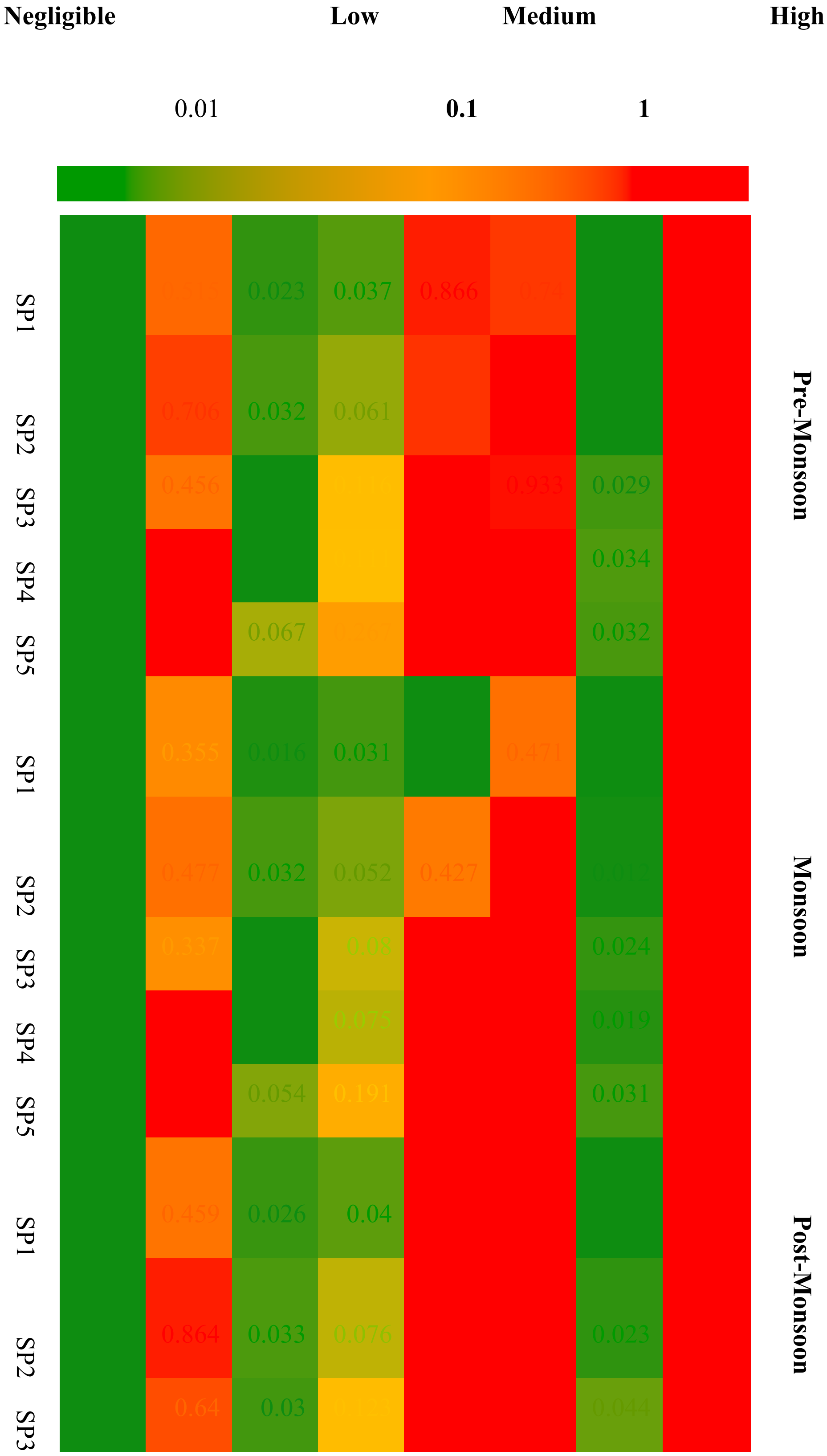


Fig. 5. RQs of individual PhACs at five sampling points during Pre-monsoon, monsoon and post monsoon season

Statements and Declarations

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Competing interests

The authors declare no competing interests.

Availability of data and materials

The data that support the findings of this study are available from [Roohul Abad Khan] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [Roohul Abad Khan].

Animal research

Not applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

Ethical Approval

Not applicable

Additional information

Correspondence and requests for materials should be addressed to R.A.K

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