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Occurrence, sources and risk assessment of fluoroquinolones in dumpsite soil and sewage sludge from Chennai, India

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A R T I C L E I N F O

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A B S T R A C T

Soil and sludge are major reservoirs of organic compounds such as fluoroquinolones (FQs) which are broad-spectrum antibacterial agents. Hence, we monitored three major FQs, namely, ciprofloxacin (CIP), norfloxacin (NOR), and ofloxacin (OFL), in surface soil from two major dumpsites and dry and wet sludge from sewage treatment plants in Chennai city. The mean concentration of FQs in soil and sludge samples were 20 μg/g and 26 μg/g, respectively. Nearly 50% of the total FQs in dumpsite soil was contributed by CIP followed by NOR (32%) and OFL (13%). Similarly, CIP was the major contributor in sludge samples followed by NOR and OFL. The concentration of FQs was two folds higher in wet sludge than dry sludge most likely indicating that water solubility of these compounds might play an important role for elevated level of FQs in wet sludge. Solid waste from pharmaceutical industries, households, and sludge from wastewater treatment plants were expected to be the major source of FQs in dumpsite soil. Predicted risk assessment using soil to water migration concentrations via surface run off indicated high risk to aquatic organisms. However, risk quotient (RQ) was found less to earthworm in most of the soil samples. The findings from this study might help in future policies on disposal of household antibiotics in the solid waste stream.

1. Introduction

Solid waste dumping sites are regarded as a major source of new and emerging contaminants such as antibiotics (Musson and Townsend, 2009). Use and improper disposal of antibiotics allow a significant amount of their release into the environment and enhances the possibility of antibiotic resistance (Baquero et al., 2008). Antibiotics can end up in dumpsites via multifarious pathways viz., household waste, expired and unused medicines from pharmacies and hospitals, solid waste from pharmaceutical industries, and sludge from wastewater treatment plants (WWTP).

Fluoroquinolones (FQs) are a wide range of antibacterial agents that work by selectively inhibiting the synthesis of bacterial DNA. Due to its good oral absorption, FQs have become the third-largest consumed antibiotics in the world, accounting for 17% of the global market (Hamad, 2010), of which 13% is from India (Van Boeckel et al., 2014). The antibiotic market in India is 2.2 billion USD, which is 16.8% of the total sale of pharmaceuticals (Mehta et al., 2016). FQs contribute up to 25% of the total antibiotic consumption in India, with the highest proportional antibiotic consumption of 3.75 defined daily dose/1000 inhabitants per day (Farooqui et al., 2018). The three major FQs, ciprofloxacin (CIP), norfloxacin (NOR), and ofloxacin (OFL), are licensed for human administration. The global value of CIP was the highest (1.3 billion dollars), followed by OFL (900 million dollars) (Nakata et al., 2005).

FQs are considered highly harmful to plants, algae, and bacteria, as well as hazardous to fish and crustaceans (An et al., 2010). FQs in both humans and animals have been reported to cause neonatal changes in bone development, tendons and articulation cartilages (Stahlmann, 2003).

Once administered, some percentage of the drug is metabolized and absorbed by the body and the remaining is excreted, mostly in the pharmaceutically active form (Spiteller et al., 2009). FQs are found to be largely excreted in unchanged form in urine (up to 32%) and feces

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(up to 25%), thereby finding their way majorly in hospital waste and municipal discharges (Osinska et al., 2016). The reduction of FQs in WWTPs are about 88–92%, which is mainly due to the adsorption of these compounds on sewage sludge (Golet et al., 2003). The sludge collected from WWTP operations may be directly applied on land (Sukul and Spiteller, 2007) and presence of FQs in topsoil samples were reported where such contaminated sewage was used as fertilizer (Golet et al., 2003).

The unused and expired medicines from households and hospitals as well as waste from drug manufacturing sites, are disposed in the dumpsites. The first federal policy was established in the United States in 2007 which recommend the consumers to discard the unused medicines in household trash by mixing with an inert substance (Glassmeyer et al., 2009). In India, unused medicines are considered as hazardous substances but a large number of drugs are disposed into dumpsites through household waste due to lack of regulations. Substantial amount of FQ solid formulations have been detected in landfills and a study on US landfill revealed a CIP content of 6500 mg which is equal to 2.3 mg of CIP per kg of waste (Musson and Townsend, 2009). Although there is a paucity of data on FQs in landfill soils, other antibiotics such as oxytetracycline (100.9 ± 141.81 μg/kg), tetracycline (63.8 ± 37.7 μg/kg), and sulfamethoxazole (47.9 ± 8.1 μg/kg) were reported from China (Song et al., 2016). Once disposed in municipal solid waste, FQs may undergo adsorption, degradation, or move in leachate and if the landfill has no effluent collection, it reaches the groundwater. Surface and ground water contamination may occur due to leaching or runoff (Musson and Townsend, 2009). The highest contents of NOR (21 ± 0.31 μg/L) and OFL (23 ± 0. 37 μg/L), were detected in Shanghai landfill leachate (You et al., 2018). Concentrations of OFL up to 9.1 ng/L (mean) were found in groundwater near a landfill in Guangzhou, China (Peng et al., 2014).

Biodegradation and photo degradation are the two main natural mechanisms of FQ degradation in solid matrices. The soil microorganism can degrade some of the antibiotics in few days (Burkhardt and Stamm, 2007) while some antibiotics have higher half-lives and can therefore persist in soil (Marengo et al., 1997; Rosendahl et al., 2012). A variety of photo-transformation products were formed due to photodegradation of FQs in solid matrices (Speltini et al., 2012; Sturini et al., 2010). Besides, most antibiotics are highly non-volatile and polar, preventing their escape from the soil once released (Hernando et al., 2006).

Chennai is a fast-growing city with a population growth of 48% (2011–2019) and is the highest per capita generator of waste in the country (0.71 kg/day). Kodungaiyur and Perungudi are the two main dumpsites in Chennai, located in densely populated suburbs at a distance of 10 km north and south, respectively, from the city centre. The dumping grounds receives a total of 5400 tonnes/day of solid waste, which also includes approximately 10,000 kg of biomedical waste from 730 hospitals in the city. Open burning of dumped waste in these two dumpsites was previously found to be an important source of certain plasticizers, bisphenol A, polycyclic aromatic hydrocarbons (Chakraborty et al., 2019), polychlorinated biphenyls, dioxins and furans (Chakraborty et al., 2018). Given the data gap, it is of prime importance to study the occurrence of pharmaceutically active compounds such as FQs in dumpsite soil and sludge owing to their high sorption tendency to soil and sludge. These field observations are useful in the search for selective antibiotic concentration in various matrices, with the ultimate aim to inspire and guide antibiotic pollution management (Rutgersson et al., 2014). Hence, the main objectives of this work were to study (i) the zone-wise distribution of CIP, NOR, and OFL in the surface soil of two major municipal dumpsites in Chennai city viz., Kodungaiyur and Perungudi (ii) the occurrence of CIP, NOR and OFL in the dry and wet sludge from WWTPs, (iii) predicted risk associated with FQs in soil and (iv) regulatory framework for pharmaceutical waste management in India.

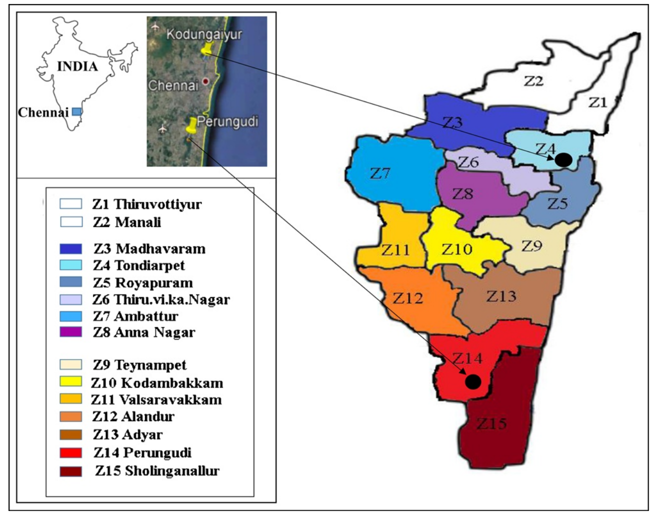

Fig. 1. Zonal designation of Chennai city representing distinct zones for collection and disposal of solid waste in Kodangaiyur and Perungudi dumpsites.

2. Materials and methods

2.1. Study area and sample collection

Chennai city is situated in the southern part of India and has a population of 10.5 million. The city occupied an area of 174 sq.km before 2011 and has expanded by adding nearby municipalities into the city limits resulting in a combined area of 426 sq.km after 2011. The main solid waste disposal method in the city is open dumping (Swati et al., 2008). For this purpose, the city is divided into 15 zones. The two major municipal solid waste dumping sites are Kodungaiyur dumpsite (KDS) in the north and Perungudi dumpsite (PDS) in the southern part of the city. The 15 zones of the city and two dumpsites are shown in Fig. 1. KDS and PDS receive 2600–2800 and 2400–2600 tonnes of waste/ day, respectively. A total of forty-one composite surface soil (KDS = 31; PDS = 10) samples were collected from a depth of 0–20 cm using a stainless scoop pre cleaned with hexane. Sampling points and zone wise separation of both the dumping sites are shown in Fig. 2(a) and (b). Sampling site details are given in the Supplementary Information Table S1.

Dry and wet sludge samples were collected from three wastewater treatment plants (WWTPs), out of these, two are located near to KDS and one near to PDS. Two sludge (one wet and one dry) samples from each treatment plant (n = 6) were collected. Wet sludge represents the sludge from the secondary settling tank, and dry sludge represents the sludge from the drying beds. All the samples were stored at −20 °C before extraction.

2.2. Chemicals and reagents

High purity (99%) analytical standards of ciprofloxacin (CIP), norfloxacin (NOR), and ofloxacin (OFL) were purchased from Sigma-Aldrich, USA. $^{13}C_3$ caffeine was obtained from Cambridge Isotope Laboratories, USA. Methanol, acetone, hexane (HPLC grade), citrate buffer, disodium EDTA, hydrochloric acid, disodium phosphate (Na_2HPO_4), and citric acid were used for extraction. Milli-Q Gradient A10 water purification system was used to obtain milli-Q-water.

2.3. Soil and sludge sample extraction and clean-up

Soil samples were air-dried and extracted according to the method given elsewhere (Luo et al., 2011). Briefly, 5 g of air-dried samples were weighed, transferred into centrifugal tubes. Each sample was spiked with $^{13}C_3$ caffeine (20 ng) as a surrogate standard. 30 mL of extraction

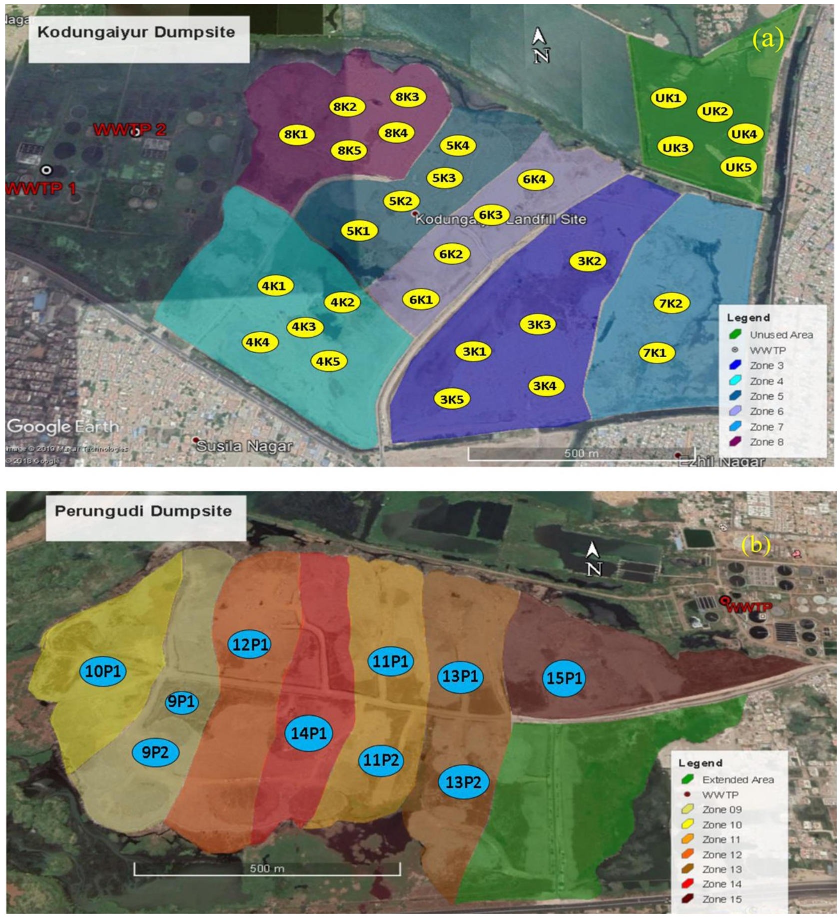

Fig. 2. Sampling locations at different zones in (a): Kodungaiyur dumpsite and (b): Perungudi dumpsite.

buffer (15 mL of methanol (MeOH), 5 mL of 0.1 M disodium EDTA (Na_2-EDTA), and 10 mL of citrate buffer was added to 5 *g* of soil. The samples were vortexed for 1 min, followed by 15 min of ultra-sonication at 40 kHz. Further, the samples were centrifuged at 8800 rpm for 5 min, and 25 mL of supernatant was collected. The procedure was repeated three times, and the pooled supernatants were reduced to 2 mL using a rotary evaporator. The sample was then filtered using a 0.22 μm micro-syringe filter and stored at −4 °C until analysis by high performance liquid chromatography (HPLC).

Sludge samples were extracted with the method given elsewhere (Dorival-Garcia et al., 2013). Briefly, 0.5 *g* of air-dried samples were extracted using 5 mL of extraction buffer solution (MeOH/McIlvaine buffer 50:50 (v/v), pH = 3) using ultrasonication for 15 min at 75% amplitude. The extracts were centrifuged at 4500 − 5000 rpm for 30 min. The supernatant was then transferred into a round bottom flask and evaporated to dryness in a rotary evaporator. 2 mL of MeOH was added and were then filtered through 0.22 μm syringe filters and stored at −4 °C until HPLCanalysis.

2.4. Instrumental analysis

Shimadzu LC-20AD HPLC system equipped with an LC10ADVP binary pump (Shimadzu, Japan) and Rheodyne 7725 injection valve furnished with a 20 μL loop was used for quantification. The samples were separated with the Phenomenex C18 column (RP, 250 × 4.6 mm, 5 μm) using methanol (B): water (0.1% formic acid) (A) with a ratio of 80:20 as mobile phase in a gradient system. The gradient program started with 20% of A and gradually increased to 40% in 7 min, followed by returning to initial composition in 3 min, which was maintained for 18 min. The total run time was 28 min. The column was maintained at room temperature. The flow rate was set at 0.8 mL/min and the injection volume was 20 μL. Detection was carried out at a wavelength (λ) of 280 nm using an SPD-M20A photodiode array detector. Lab Solution Software (Version 7.1, Shimadzu) was used to process the data. Three fluroquinolones (FQs) analysed were: ofloxacin (OFL), norfloxacin (NOR) and ciprofloxacin (CIP).

2.5. Total organic carbon analysis

Total organic carbon (TOC) for each sample was analysed by using the loss on ignition method. Briefly, soil samples were dried in the oven at 105 °C followed by combustion in a muffle furnace for 2 h at 360 °C. The weight before and after combustion was noted to calculate TOC.

2.6. Quality assurance and quality control

The calibration curve of the standard antibiotics was prepared by analyzing the standard solutions of 7, 15, 30, 60, 125, 250, and 500 μg/L. The correlation coefficient of the calibration curve for each FQs were 0.999. For every set of 7 samples one method blank was run. Blank samples did not show any compound above the detection limit. Range of recovery percentage of $^{13}C_3$ caffeine varied between 85–105%.

2.7. Risk assessment

The risk to the terrestrial compartment, especially to the soil were reported by very few studies (Gao et al., 2008). Because of the lack of toxicity of FQs in soil, calculating the risk quotient (RQ) was a challenge. Since bioaccumulation, bioavailability, and toxicity are closely related to the pore water concentrations, an equilibrium partitioning method was adopted by converting soil concentration into pore water concentration and further calculating the RQ value in soil (Wu et al., 2014).

The risk quotient of each soil sample was calculated using Eq. (1).

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

Where MEC is the measured environmental concentration (µg/g), $PNEC_{soil}$ is the predicted no-effect concentration in soil. An equilibrium partition approach (European Commision 2003; Martín et al., 2012) was used to obtain $PNEC_{soil}$ from $PNEC_{water}$ using Eq. (2).

$$PNEC_{soil} = PNEC_{water^*}\, K_d \quad (2)$$

Where $PNEC_{water}$ is the predicted no-effect concentration (ng/L) in water and Kd is the soil water partition coefficient.

$PNEC_{water}$ values were derived from various studies conducted according to European technical guidance document on risk assessment (European Commission, 2003) and are derived from the acute toxicity, effective concentration (EC), non-observed effect concentration (NOEC) divided by assessment factor. According to European Commission., 2003, the following ranking criterion was used to assess the data. RQ > 1 indicates high risk, RQ < 0.1 indicates low risk and RQ between 0.1 and 1 indicates medium risk.

2.8. Statistical analysis

Box-whisker plots and other statistical analysis were done using SPSS version 20 software. Pearson correlation coefficient was used to check the linear fitting and correlation between the parameters at a significant level of 0.05.

3. Results and discussion

3.1. General discussion

Distribution of three FQs in surface soil and sludge samples from KDS and PDS are shown in Figs. 3 (a2), (b2), and 4 . Higher concentration of FQs in soil samples (Table S2) suggest that the antibiotics are disposed from the households in the solid waste stream act as a potential source of these emerging contaminants in the dumpsite soil. The factors affecting the persistence of FQs in soil and sludge are photostability, adsorption and binding capability, degradation rate, and leaching into the water. Depending upon the properties of soil and sorption coefficient (K_d) of FQs, the percentage of adsorption of FQs may vary. Total organic carbon (TOC) in the soil samples (Table S1) did not show any correlation with the concentration of FQs thereby suggesting a recent source as was observed in urban soil of Beijing, China (Gao et al., 2015). Furthermore, the lack of correlation with TOC might be due to the adherence of FQs to the soil mineral and metal oxides, thereby interfering with the relationships (Carrasquillo et al., 2008). The utilization of sewage sludge from WWTPs as manure for livestock or fertilizers can intensify strong adsorption of FQs in the agricultural soil.

CIP contributed to 55% and 75% of the total FQs in dumpsite soil and sludge samples of Chennai city, respectively. The highest concentration of CIP might be due to its higher half-life (2310 ± 1155 days) (Walters et al., 2010) in soil and lower log octanol-water partition (log Kow) coefficient (0.28) (Table S3). CIP molecule contains one –COOH, one –C = O, one $-CONH_2$, and one $-N(CH_3)_2$, which contributes to its strong adsorption to soil. Furthermore, due to the higher K_d value of FQs compared with other antibiotics, FQs tend to accumulate in the soil, thereby exhibits lower mobility in soil. The heterocyclic ring's strong chemical stability renders higher persistence of these compounds, and relatively higher solubility enhances their environmental diffusion (Sturini et al., 2010). The prevalence of CIP over NOR and OFL could be due to its high production and consumption rate in India (Kotwani and Holloway, 2011). Previously, a higher concentration of CIP over NOR and OFL was observed in wastewater effluent from 90 drug manufacturing industries in India (Larsson et al., 2007).

3.2. Zone-wise distribution

Out of the 15 zones in the city, solid waste from zones 3–8 are dumped in KDS and 9–15 are dumped in PDS. Zone 1 and 2 have separate dumpsites. Solid waste from each zone is dumped in the specific area of dumpsite representing respective zones in the city (Fig. 1). All three FQs, CIP, NOR, and OFL, were ubiquitously present in all the soil samples. The concentration of FQs varied between 2 µg/g and 126 µg/g (61 ± 46 µg/g; Avg ± SD) (Table 1). Most of the values were between 1–10 µg/g (20–76%) and 10–50 µg/g (24–83%). Less than 12% of the samples were between 50–100 µg/g and less than 5% of the samples were above 100 µg/g. The average concentration of CIP (34 µg/g) is two folds higher than NOR (19 µg/g) and four folds higher than OFL (8 µg/g).

Due to the unavailability of reports on FQs from dumpsite soil, the concentration in the present study was compared with surface soil concentrations from vegetable farmland, urban soil, and soil amended with manure and sludge (Table 2). The present concentrations were found to be about 1000 times higher than those reported from studies conducted in greenhouse vegetable production bases in Beijing, China, organic vegetable bases in northern China and organic vegetable farms in southern China (Li et al., 2015, 2014; Li et al., 2011). Average concentration of FQs in this study (19 µg/g NOR and 34 µg/g of CIP) was comparable with the levels found in poultry litters from Brazil (4.5 µg/g NOR and 2 µg/g of CIP) (Leal et al., 2012). The concentration of NOR was 35 times higher than the concentration found in manure and soil amended with manure from Malaysia (Ho et al., 2012). The difference in type and concentration levels of FQs observed in India and other countries might reflect that dumpsite soil can accumulate FQs generated from household disposal unlike conventional sources such as manure and sludge.

3.2.1. KDS

KDS is located in the northern part of Chennai city. In KDS 269 acres of land is used for solid municipal waste dumping with people residing within one km surrounding the dumpsite. The waste coming to KDS is extended over an area of 178 sq. km covering 837,031 households with a population of 34 lakhs and 39 pharmaceutical companies as shown in Fig. 3(a1).

OFL, NOR, and CIP were ubiquitously present in all the surface soil samples. The highest average concentration was observed for CIP (33 µg/g ± 26; avg ± S.D), followed by NOR (19 µg/g ± 14), and OFL (8 µg/g ± 6) (Figure S1). A sample from the unused site exhibited the highest concentration (126 µg/g) with greater than 50% contribution from CIP. The mean concentration of CIP, NOR, and OFL was 1.2 times higher in unused sites than the other sites, most likely due to the dumping of WWTP sludge in this area. Sludge is an important reservoir for FQs, especially for CIP due to its high octanol carbon partition coefficient (Koc = 61,000) (Tolls, 2001). Furthermore, owing to high-water solubility, FQs may reach such low-lying unused areas during the rainy season. Previous studies have reported a higher concentration of water-soluble antibiotics during high flood season, mainly due to surface runoff contribution (Li et al., 2014; Jiang et al., 2011). Interestingly, the concentration of FQs in the unused area was 1.2 times higher than the sludge collected from KDS. This might be due to a combined effect of runoff from the entire area or due to the presence of some original active pharmaceutical ingredient (API) (Musson and Townsend, 2009). In the used areas, the highest mean concentration of Σ_3FQs was observed in zone 3 (72 µg/g, Madhavaram). Zone 3 contributed up to 25% of Σ_3FQs from the used area in KDS. Almost three fourth of the Σ_3FQs stemmed from CIP followed by NOR and OFL as observed in other sites. It is noteworthy that among other zones, zone 3

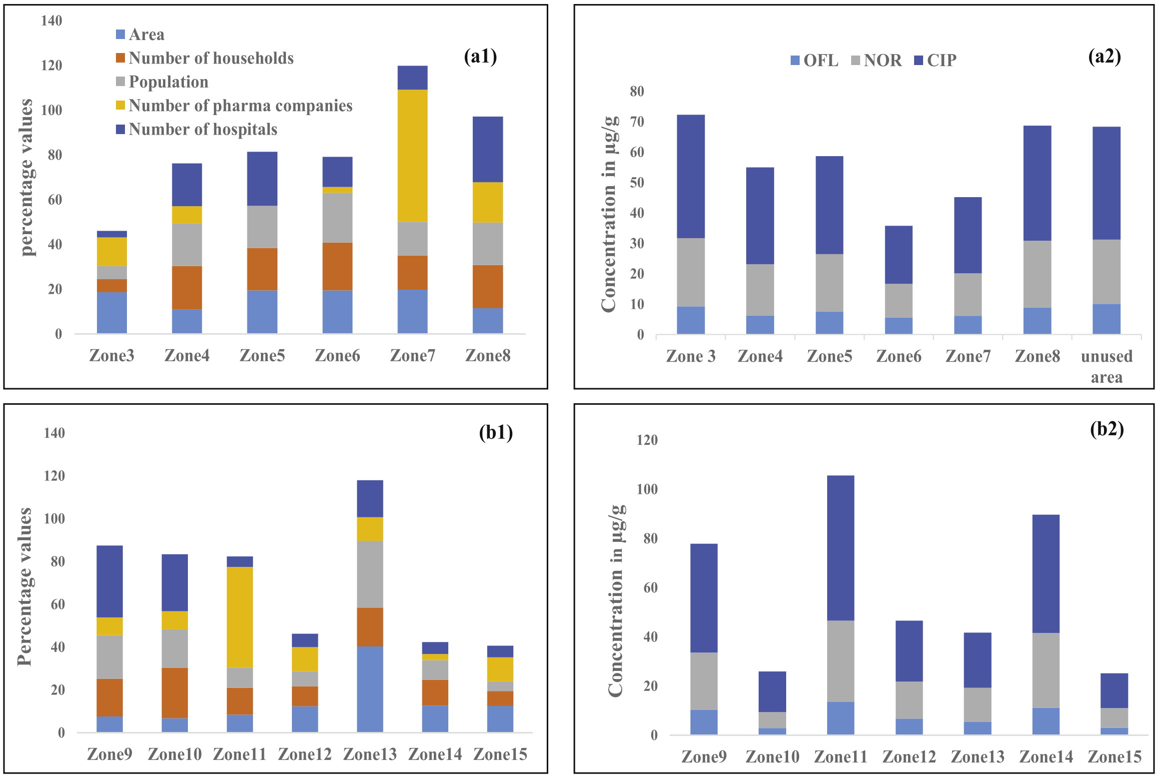

Fig. 3. Zone wise distribution of population, area and the number of hospitals, pharmaceutical and household with the corresponding levels of fluoroquinolones in Kodungaiyur dumpsite (a1 and a2) and Perungudi dumpsite (b1 and b2).

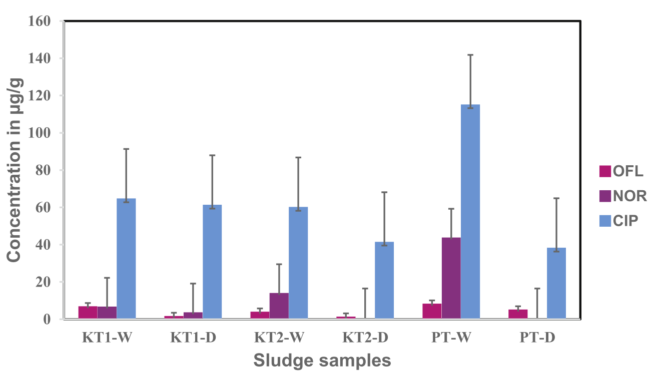

Fig. 4. Error plots showing the concentration of ofloxacin (OFL), norfloxacin (NOR) and ciprofloxacin (CIP) in wet and dry sludge samples from the wastewater treatment plants.

Table 1
Concentration range of three major fluoroquinolones viz., ofloxacin (OFL), norfloxacin(NOR) and ciprofloxacin (CIP) in dumpsite soil samples.

Compounds	OFL(µg/g)	NOR(µg/g)	CIP(µg/g)	Σ FQNs(µg/g)
Minimum	2.48	6.46	11.32	20.54
Maximum	33.15	70.96	126.29	230.40
Mean	8.05	19.11	33.94	61.10
Median	6.08	13.97	24.74	44.96
Standard deviation	6.12	14.09	26.21	46.21
Coefficient of Variation (%)	75.99	73.74	77.23	75.63
Percentage Distribution (%)				
1.0–10 µg/g	76	20	0	0
10–50 µg/g	24	73	83	66
50–100 µg/g	0	7	12	20
> 100 µg/g	0	0	5	15

has the lowest population density as well as authorized pharmaceutical companies. Therefore, it is suspected that the elevated concentrations may be due to the unauthorized sorting facilities occupied in this area, revealing a defection in the source.

Interestingly, areas with higher population density as well as hospitals such as zone 8 (Anna Nagar) contributed to 19% of total FQs in KDS indicating waste from households could be a possible source in city's open municipal dumpsite as observed elsewhere (You et al., 2018). It is noteworthy that surface soil collected from zone 5 (Royapuram) contributed to 20% of the total FQs in the present study. Royapuram has the highest density of hospitals (approximately 94). Hospital waste can act as an important source of FQs in India, especially CIP, NOR, and OFL (Diwan et al., 2009). Hence the high concentration of FQs in zone 5 could be due to the large floating population in Chennai, mainly coming for various medical reasons.

3.2.2. PDS

PDS is located in the southern part of Chennai city. The Perungudi dumping ground is low lying, poorly drained and occupied by extensive areas of permanently wet and seasonally inundated marshy land. The solid waste is collected from seven different zones (zone 9–15) in the city and dumped in PDS. The mean concentrations of FQs is shown in Figure S2. The total area from where the waste is collected to dump in PDS is 339 sq km and it consists of 710,717 households with a population of 37 lakhs and 36 pharmaceutical companies. (Fig. 3(b1). Similar to KDS higher average concentration of CIP (36 µg/g ± 25) was observed in PDS (20 µg/g ± 13) followed by NOR and OFL (8 µg/g ± 6).

The highest mean concentration of FQs was observed in zone 11 (CIP-59.14 µg/g, NOR-32.95 µg/g, OFL-13.52 µg/g). Zone 11 contributed to 33% of Σ_3FQs from PDS. The absence of strict regulations for the disposal of waste from pharmaceutical industries might be the reason for the high concentration of FQs in this zone as 23 percentage of pharmaceutical industries in Chennai city are concentrated in this zone.

Table 2
Comparison of average fluoroquinolones concentration in this study and different studies across the globe on varied soil types.

Antibiotic	Concentration (μg/kg)	Type of soil	Location	Reference
Ciprofloxacin	253	Green house soil	Beijing	Li et al. (2015)
	9342	Manure	Beijing	Li et al. (2015)
	21	Open field	Beijing	Li et al. (2015)
	119.8	Vegetable farm land	Pearl River Delta, China	Li et al. (2011)
	53	Agricultural field amended with poultry manure	Turkey	Uslu et al. (2008)
	450 ± 100	Agricultural field amended with sludge	Zurich	Golet et al. (2003)
	5.87 ± 3.85	Peri-urban soil	China	Zhao et al. (2019)
	2800	Manure	Austria	Martínez-Carballo et al. (2007)
	370	Open field	Austria	Martínez-Carballo et al. (2007)
	60	Manure	Turkey	Karci and Balcioğlu (2009)
	50	Agricultural field amended with poultry manure	Turkey	Karci and Balcioğlu (2009)
	100 – 4300	Manure	Northern China	Hu et al. (2010)
	0.65 – 2.13	Poultry litter	Brazil	Leal et al. (2012)
	10.3 – 30.1	Vegetable farm land	Northern China	Hu et al. (2010)
	ND-42	Vegetable farm land	Southern China	Wu et al. (2014)
	33.94 (μg/g)	Dumpsite soil	Chennai, India	This study
Norfloxacin	69	Green house soil	Beijing	Li et al. (2015)
	2187	Manure	Beijing	Li et al. (2015)
	24	Open field	Beijing	Li et al. (2015)
	150.2	Vegetable farm land	Pearl River Delta, China	Li et al. (2011)
	16.5	Manure	France	Salvia et al. (2015)
	350 ± 100	Agricultural field amended with sludge	Zurich	Golet et al. (2003)
	30.7 – 1885.9	Manure	Malaysia	Ho et al. (2012)
	17.6 – 95.7	Agricultural field amended with poultry manure	Malaysia	Ho et al. (2012)
	6.59 ± 3.51	Peri-urban soil	China	Zhao et al. (2019)
	0.8 – 4.5	Poultry litter	Brazil	Leal et al. (2012)
	0.14-17.9	Vegetable farm land	Southern China	Wu et al. (2014)
	19.11(μg/g)	Dumpsite soil	Chennai, India	This study
Ofloxacin	1.8	Manure	France	Salvia et al. (2015)
	230 – 15700	Manure	Northern China	Hu et al. (2010)
	0.6–1.6	Vegetable farm land	Northern China	Hu et al. (2010)
	8.05(μg/g)	Dumpsite soil	Chennai, India	This study

Although FQ concentration in landfills is not available, the average concentration of FQs in PDS is comparable with levels of other antibiotics such as penicillin (120.52 ± 22.33 μg/g), amoxicillin (76.62 ± 15.3 μg/g) and metronidazole (50.08 ± 48.34 μg/g) in landfill sites of Ghana (Borquaye et al., 2019). However, average levels in the present study was thousand folds higher than oxytetracycline (100.9 ± 141.81 μg/kg), tetracycline (63.8 ± 37.7 μg/kg), and sulfamethoxazole (47.9 ± 8.1 μg/kg) from China (Song et al., 2016). FQs were found up to a concentration of 6.5 mg/L (CIP) in freshwater from a lake in India, mainly due to the discharge of effluents from pharmaceutical companies (Fick et al., 2009).

Similar to zone 8 in KDS, zone 9 (24% of Σ_3FQs) in PDS was also found with an elevated concentration of FQs and it is noteworthy that both of the zones have the highest number of hospitals. Previous studies conducted in the hospital wastewater in India reported the presence of FQs and CIP in all the samples and showed the highest concentration of 236 μg/L (Diwan et al., 2009).

Zone 10 and zone 15 contributed the least, accounting to 4% of the Σ_3FQs. The number of hospitals in zone 10 and zone 15 is 93 and 15, respectively. Most of the multispecialty hospitals are located in zones 5, 8, and 9 and contributed to 20%, 19%, and 24%, respectively of the Σ_3FQs where we can expect floating population who stays in the city for medical treatment. Zone 14 contributed to 22% of the Σ_3FQs in PDS, which is comparable with zone 3 (25%) in KDS. Both the zones (3 and 14) has less number of hospitals and smaller population yet showed elevated range of FQs. This observation is most likely associated with the dumping of unauthorized pharmaceutical waste in these zones of Chennai city. A study conducted in Brazil found a relationship between pharmaco-pollution and household waste medicine and stated that hospitals and other health care facilities were not the main source of antibiotic contamination in municipal sewage but rather the human population was the major contributing factor (Pereira et al., 2017). The population is responsible for 75% discharge of antibiotics in Germany and the United States and 70% in the United Kingdom (Schuster et al., 2008).The pharmaceutical industry is a source of antibiotics pollution in developing nations. A study conducted in soil, sediment and groundwater near a pharmaceutical industry in India reported 915 ng/L of total FQ in groundwater and a maximum of 1.9 μg/g of CIP in soil and 54 μg/g in sediment (Rutgersson et al., 2014).

3.3. Levels and compositional profile of fluoroquinolones in dry and wet sludge samples

Sludge can act as the main reservoir for FQs due to its sorption properties. FQs have a high affinity towards solids which favor sorption to sewage sludge, thus showing high levels in sewage sludge. FQs were detected in all the wet and dry sludge samples except NOR, which was absent in two dry samples. The pervasive usage of FQs in human medication can be linked to the occurrence of these compounds in sewage (Golet et al., 2002). After medication, the non-metabolized part of these compounds enters the WWTPs leading to elevated levels of antibiotics in wastewater. The worldwide average concentrations of FQs in sludge have been given in Table 3. Previous studies from India also reported the presence of FQ in wastewater influent and effluent samples (Diwan et al., 2009).

Similar to dumpsite soil samples, in sludge samples the maximum contribution of FQs was from CIP followed by NOR and OFL. The higher contribution of CIP than other second-generation quinolones might reflect the consumption pattern in the subcontinent (Kotwani and Holloway, 2011; Farooqui et al., 2018). The concentrations of FQs in wet and dry sludge samples are shown in Fig. 4. The highest concentration of CIP was detected in wet sludge samples collected from the Perungudi treatment plant (114 μg/g).

The activated sludge process is the main secondary treatment process in all the three treatment plants from where the sludge was collected. The two Kodungaiyur WWTPs have a capacity of 110 and 80

Table 3
Global comparison of average fluoroquinolones concentration in sludge samples with this study.

Antibiotic	Concentration(μg/kg)	Country	Reference
Ciprofloxacin	3148	France	Salvia et al. (2015)
	3500 ± 300	Zurich	Golet et al. (2003)
	206.1	Gran Canaria	Montesdeoca-Esponda et al. (2012)
	2420	Zurich	Golet et al. (2002)
	285	China	Li et al. (2013)
	1600-11,000	Sweden	Östman et al. (2017)
	46 (μg/g)	India	This study
Norfloxacin	2055	France	Salvia et al. (2015)
	3300 ± 100	Zurich	Golet et al. (2003)
	5280	China	Chen et al. (2013)
	5399	China	Li et al. (2013)
	13.4	Gran Canaria	Montesdeoca-Esponda et al. (2012)
	2.56(μg/g)	India	This study
Ofloxacin	8492	France	Salvia et al. (2015)
	24,760	China	Chen et al. (2013)
	2686	China	Li et al. (2013)
	2.79(μg/g)	India	This study

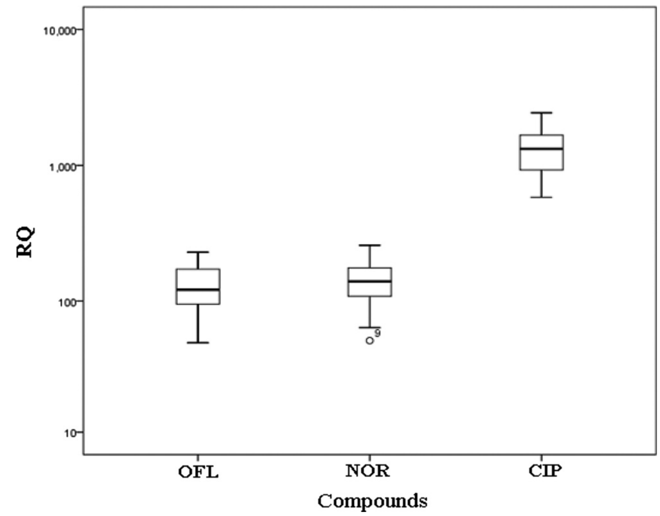

Fig. 5. Box whisker plots showing the range of the estimated risk quotients for ofloxacin (OFL), norfloxacin (NOR) and ciprofloxacin (CIP) in dumpsite soil of Chennai city.

million litres per day (MLD) respectively. WWTP at Perungudi treats 60 MLD of wastewater per day. Biological treatment such as activated sludge process fails to degrade the antibiotics, which causes the presence of high residues in sewage sludge. The reduction of FQs in the wastewater treatment plant is about 89%, which is mainly due to the adsorption of these compounds on to sludge. Dry sludge was collected from sludge drying beds, which are exposed to the atmosphere, and the annual average temperature in Chennai city is around 28.6 °C. The percentage reduction of FQ compounds after drying is given in Table S4. When comparing concentrations of FQs in wet and dry sludge, NOR was completely removed from two samples (KT2 and PT) after drying, and there is a maximum reduction of 67.3% for CIP in one sample (PT). The average removal percentage of OFL after drying is 89%. Hence it can be inferred that in the presence of sunlight, photodegradation might have reduced the FQs concentration in sludge samples. During drying process, water soluble FQs in wet sludge might get degraded in presence of sunlight to some extent since the photodegradation of FQs in solid matrix is slower than in water (Lai and Lin 2009). Experimental studies with FQs spiked in soil showed considerable reduction of the compounds in presence of sunlight (Speltini et al., 2011). Biodegradability of FQs is very less, but photodegradation reduces the FQ levels in the environment. Several studies suggested that the possible removal mechanism of FQs in WWTP is sorption to sludge rather than biodegradation (Conkle et al., 2010; Golet et al., 2003). With the high distribution coefficient (K_d, solid) of these compounds, the mobility of FQs reduces in the soil thereby decreasing the risk of leaching into the groundwater although their persistence in the soil for a longer time cannot be neglected. Sludge is used as fertilizer in agricultural farmland and dumped in low lying or unused areas; thus, it acts as a secondary source of contamination.

4. Risk assessment

The occurrence of FQs in soil can affect the composition and behaviour of microbial communities in the soil due to their longer residence time (Girardi et al., 2011). High levels of FQs were reported from different parts of the world, mainly in poultry litters and agricultural soil with poultry litter application (Leal et al., 2012). A study conducted in broiler manure and soil amended with this manure also reported high levels of FQs (Ho et al., 2012). But all those studies were conducted on the samples which were excreted from the animal body after metabolization. The high sorption of FQs in soil often decreases the acute toxicity in terrestrial ecosystems at lower concentrations, but natural processes such as wind and water erosion may sweep such pollutants into the aquatic environment that leads to aquatic species toxicity (Riaz et al., 2018). In this study, the area from where the soil samples were collected is exposed to direct disposal of pharmaceuticals. During monsoons surface run-off can cause transportation of such emerging contaminants to the nearby canals or rivers ending up in the sea. So, it is inevitable to study the ecotoxicological risk assessment of these antibiotics in the environment. Hence soil concentrations were converted into pore water and the possible risk was assessed. The $PNEC_{water}$ and $PNEC_{soil}$ calculations of FQs are given in Table S5. The calculated RQ values are given in Table S6.

In this study, all the RQ values obtained for aquatic organisms were above 1. OFL, NOR, and CIP might pose a high risk to bacteria like luminescent marine bacteria and *cyanobacterium* (Fig. 5). RQ values ranged from 49 to 2442, which are very high compared with other studies in soil (Wu et al., 2014). A study conducted on earthworm exposure to CIP reported that it could grow normally in sands spiked with CIP solution of concentration 33 mg/kg. (Wen et al., 2011). The mean concentration of FQs from all the sampling points from this study was 20 μg/g indicating medium or low risk to earthworm. However, few zone displayed high risk (RQ > 1) due to higher mean concentration of CIP (zone 3, zone 8, unused area, zone 9, zone 11 and zone 14). It is understood that plants can uptake FQs from the soil, suggesting a possible route for direct human exposure by ingestion of FQs. In crops, OFL concentration was measured up to 3.6 μg/kg, where the soil was fertilized with manure. (Hu et al., 2010)

However, the most recognized health risk associated with exposure to environmental antibiotics are not direct effects but rather risks to promote the evolution and spread of resistance in pathogenic bacteria. Several studies have reported the occurrence of antibiotic resistance genes (ARGs) in dumpsite soil (Song et al., 2016; Borquaye et al., 2019). The resistance in the indigenous bacteria may increase by selective pressure or by horizontal gene transfer due to the introduction of antibiotic-resistant bacteria into the soil (Wu et al., 2017).

5. Regulatory framework for pharmaceutical waste management in India

The increased production and consumption of antibiotics in the last two decades developed a concern about the fate and effects of these compounds in the environment. There is a lot of confusion about the right way of disposal of drugs, as many of the countries do not have standard protocols for disposing of medicines (Tong et al., 2011). A study conducted in Ghana reported that 80% of the respondents and 60% of the pharmacies routinely dispose of their pharmaceutical waste along with household trash (Osei-djarbeng et al., 2015). Since 1971, Sweden has an existing reverse distribution system run by a major pharmacy wholesaler in conjunction with the state pharmaceutical association, and their policy states that the medicinal goods have to be returned to pharmacies where it is incinerated and the residue is disposed off in landfills (Tong et al., 2011). In India, most of the unused medicines are disposed along with household waste. The two major pathways through which the antibiotics enter into the environment are (i) excretion after ingestion (ii) disposal of unwanted antibiotics along with trash from household as well as pharmaceutical industries.

The disposal of pharmaceutical waste is mentioned in Hazardous Waste (Management, Handling, and Transboundary Movement) Rules, 1989 in India. But most of the people, industrialists, and small clinics are not well aware of these rules. There is no proper documentation for unused medicines in a common household. Lack of awareness among the people is the reason for direct disposal. It is high time for India to start a new program to collect unused medicines instead of disposing it along with the solid waste collection system.

6. Conclusion

Over one microgram per gram level of OFL, NOR, and CIP were detected in all the dumpsite soil and sludge samples with a minimum and maximum concentrations of of 3 μg/g and 126 μg/g, respectively. Elevated levels of FQs in dumpsite soil can be reasoned with improper disposal of pharmaceutical waste into the solid waste dumping site. Sludge, which contains a high amount of FQs, is also disposed of in these dumpsites. A small percentage of FQs are removed during the drying process due to photo-degradation. Owing to the high half lives of these compounds FQs tend to persist in the soil. The presence of these compounds in the soil can change the soil microbiology, and resistance power of microorganisms might develop in due course of time. Therefore, this work suggests the importance of proper disposal methods for pharmaceutical solid waste and sewage sludge. We suggest that the segregation of waste can be implemented at household level which can ultimately play an important role in proper disposal of unused antibiotics.

CRediT authorship contribution statement

Sija Arun: Writing - original draft, Investigation, Data curation, Visualization. **R. Mohan Kumar:** Investigation, Formal analysis, Validation. **Jairaj Ruppa:** Investigation, Formal analysis. **Moitraiyee Mukhopadhyay:** Investigation, Writing - review & editing. **K. Ilango:** Resources. **Paromita Chakraborty:** Conceptualization, Funding acquisition, Investigation, Methodology, Resources, Supervision, Writing - review & editing.

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 material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.etap.2020.103410.

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