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Mass loading and removal of pharmaceuticals and personal care products, including psychoactive and illicit drugs and artificial sweeteners, in five sewage treatment plants in India

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ABSTRACT

Despite the high consumption of pharmaceuticals, mass loading and removal of these compounds in sewage treatment plants (STPs) in India have not been investigated. In this study, 43 pharmaceuticals and personal care products as well as 13 of their metabolites were analyzed in five domestic STPs (wastewater influent, effluent, and sludge) and in raw domestic sewage collected in open sewerage channels in residential areas in India. The mean concentrations of amphetamine in two of the five STPs (mean: 4300 ng/L and 4720 ng/L) were the highest ever reported for wastewater influents, globally. Among artificial sweeteners, saccharin was the most abundant compound in influents (mean: 303,000 ng/L, df: 100%), followed by cyclamate [3460 ng/L, detection frequency (df): 75%] and sucralose (1460 ng/L, df: 100%). Elevated mean concentrations of an antimicrobial (triclocarban = 6180 ng/L), analgesic (ibuprofen = 2320 ng/L), antihypertensive (atenolol = 3180 ng/L), illicit drug (amphetamine = 984 ng/L), and saccharin (419,000 ng/L) were found in the Cooum River in Chennai. The median removal efficiencies of pharmaceuticals and personal care products (PPCPs) ranged from 5% (norcocaine) to 100% (triclosan) for the five STPs. On the basis of the concentrations measured in influents, the mass loadings of PPCPs were estimated to range from 0.1 (norquetiapine) to 77,800 (saccharin) mg/d/1000 people. An estimated 2.55 kg of triclocarban, 3.24 kg of carbamazepine, 6.93 kg of amphetamine, and 252 kg of saccharin were discharged from a typical STP with an average flow rate of 20.7 million liters per day (serving a population of 325,000) in India.

1. Introduction

Pharmaceuticals and personal care products (PPCPs), released mainly through human excretion or flushed down the drain, are introduced into the sewage treatment plants (STPs) via the sewerage systems [1–3]. STPs are, in turn, a source of PPCPs to the environment, when effluents and sludge from the facilities are discharged to water bodies and farmlands [1]. The extent of environmental contamination by PPCPs is presumably significant in developing countries, where the capacity for the treatment of wastewater is far below the quantity of sewage generated by the populations. In India, only 31% of the total sewage produced (~38,254 million liters per day; MLD) in 908 cities, whose STPs serve a population of 258 million, was treated in 2008 [4]. Further, the existing STPs are not effectively utilized or maintained; ~39% of existing STPs do not comply with the prescribed environmental regulations prior to discharge of effluents into the streams. In many small towns and rural areas, STPs do not even exist. Thus, the environmental emission of PPCPs can be expected to be high in

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India; however, little is known on the occurrence and fate of PPCPs in sewerage systems and STPs in India [5].

India is a major global market for pharmaceuticals. The current market is valued at more than US $21.7 billion and is estimated to be US$36.7 billion in 2015 [6]. Apart from human excretion, industrial discharges can contribute to pharmaceutical contamination in the environment [7]. Few studies have reported the occurrence of select antibiotics and non-steroidal inflammatory drugs in wastewater [8–10], river water [11,12,5], and drinking water [8] in India. However, no earlier studies have reported the occurrence or removal of different classes of psychoactive pharmaceuticals, illicit drugs, or artificial sweeteners in STPs in India.

Estimation of mass loadings of PPCPs in a STP on the basis of prescription records may underestimate the actual load, as ~64% of Indian patients purchase medications without a prescription [11]. Based on the measured concentrations in wastewater, an estimated loading of antibiotics in a STP in India was reported to range from 15.4 to 1395 g/day [11]. Inadvertent use of antibiotics in India has led to an increase in the occurrence of drug resistant microorganisms (i.e., superbugs) in the Indian environment [13]. Further, little is known on the ecosystem level effects of PPCPs in the environment [14–16]. One study reported that tadpoles and zebrafish exposed to 0.2% effluents from STPs showed a 40% reduction in growth [17]. Another study showed that egg production was decreased in Japanese medaka (*Oryzias latipes*) following exposure to 0.5 mg/L of propranolol [18].

This is a pilot study to elucidate the occurrence and removal of 43 widely used PPCPs (two antimicrobials, four antibiotics, an antimycotic, four analgesics, an antihistamine, an antiplatelet, a UV-filter, a stimulant, two antischizophrenics, six sedative-hypnotics-anxiolytics, four antidepressants, four antihypertensives, eight illicit drugs, and four artificial sweeteners) and 13 of their metabolites in five STPs in India. In addition, PPCPs also were determined in raw sewage collected in open sewerage channels (i.e., ditches) near residential areas. The mass loadings of PPCPs to STPs, removal rates, and environmental emissions through the discharge of wastewater effluents and sludge were estimated based on the measured concentrations of PPCPs in limited samples of wastewater and sludge.

2. Materials and methods

2.1. Reagents and chemicals

Target analytes include two antimicrobials (triclosan and triclocarban), four antibiotics (sulfamethoxazole, trimethoprim, clindamycin, and lincomycin), an antimycotic (miconazole), four analgesics (ibuprofen, ketoprofen, codeine, and oxycodone), an antihistamine (diphenhydramine and its metabolite 2-diphenylmethoxy acetic acid), an antiplatelet (clopidogrel and its metabolite clopidogrel carboxylic acid), an UV-filter (oxybenzone), a stimulant (caffeine), two antischizophrenics (aripiprazole and quetiapine and their respective metabolites dehydro-aripiprazole and norquetiapine), six sedative-hypnotic-anxiolytics [alprazolam, α-hydroxyalprazolam (a metabolite of alprazolam), lorazepam, diazepam, oxydiazepam, nordiazepam, and carbamazepine], four antidepressants [venlafaxine, sertraline, norsertraline (a metabolite of sertraline), bupropion, citalopram, and *N*-desmethylcitalopram (a metabolite of citalopram)], four antihypertensives [verapamil, norverapamil (a metabolite of verapamil), diltiazem, desacetyl diltiazem (a metabolite of diltiazem), propranolol, and atenolol], eight illicit drugs [cocaine, three metabolites of cocaine (benzoylecgonine, cocaethylene/benzoylecgonine ethyl ester, and norcocaine), amphetamine, methamphetamine, methadone, EDDP (a metabolite of methadone: 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine), morphine, MDA (3,4-methylenedioxyamphetamine), MDEA (3,4-methylenedioxyethylamphetamine), MDMA (3,4-methylenedioxymethamphetamine)], and four artificial sweeteners (acesulfame, cyclamate, saccharin, and sucralose). Analytical standards of individual PPCPs and their metabolites, as well as corresponding isotopically labeled internal standards were purchased from commercial vendors, as described elsewhere [19–22]. The purity of all of the standards was ≥95%. All organic solvents (HPLC grade) and ammonium hydroxide (29.5% as ammonia) were purchased from Mallinckrodt Baker (Phillipsburg, NJ). Ultrapure water was prepared using a Milli-Q ultrapure system (Barnstead International, Dubuque, IA). All standard stock solutions were stored at −20° C.

2.2. Sample collection and preparation

Wastewater influent and effluent samples were collected from five STPs in India during July and August 2012: Saidpur (STP_{SP}), Beur (STP_{BU}), Coimbatore (STP_{CO}), Udupi (STP_{UP}), and Manipal (STP_{MP}). Saidpur and Beur are in Bihar state, Northern India, whereas Udupi and Manipal are in Karnataka state and Coimbatore is in Tamil Nadu state, Southern India. All STPs used activated biological treatment and received only domestic discharges. Aerobically digested sludge samples were collected from STP_{SP}, STP_{BU}, STP_{CO}, and STP_{UD}; however, samples from STP_{MP} was not be analyzed due to the lack of that sample. The activated sludge samples from all STPs were the combined sludge produced after primary and secondary treatments. Detailed information on STPs, including daily wastewater inflow, total treatment capacity, population served, and the sludge production rate are provided in Table 1. In addition to samples from STPs, raw sewage samples also were collected from sewerage channels near residential areas in Patna (Patna Sewage), Cooum River (two locations: at the Napier bridge near river mouth and at the mid-section near Spurtank Bridge, Chennai) and Sanganur Pallam (Mettupalayam Road, Coimbatore). A landfill leachate sample was collected from the Vellalore solid waste landfill facility in Coimbatore. All samples were collected as one-time grab samples in pre-cleaned 250 mL polypropylene bottles, shipped frozen to the laboratory in Albany, New York, and stored in a freezer at −20° C until extraction.

The detailed procedure for the extraction of wastewater and sludge has been described elsewhere [19–22]. Unfiltered wastewater samples (50 mL) were spiked with a mixture of labeled internal standards of the target analytes (25 or 50 ng) prior to

Table 1
Characteristics of five sewage treatment plants (STP) studied in India.

	Saidpur STP (STP_{SP})	Beur STP (STP_{BU})	Coimbatore STP (STP_{CO})	Udupi STP (STP_{UD})	Manipal STP (STP_{MP})
Inflow (capacity) (MLD)	19 (45)	20.9 (35)	22.5 (50)	2.0	2.0
Population served	350,000	275,000	350,000	10,000	12,000
Sludge production (tons/y ww)	60.7	67.0	12.0	–	–

Table 2
Concentrations of pharmaceuticals and their select metabolites in wastewater (ng/L) and sludge (ng/g dry wt) from Indian sewage treatment plants (STPs).

Analyte	LOQ	Saidpur STP			Beur STP			Coimbatore STP			Udupi STP			Manipal STP	
		Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent
Antischizophrenics															
QTP	0.5	36.8	ND	ND	20.8	6.32	1.20	24.8	16.6	4.39	13.8	ND	36.8	71.2	22.4
NQTP	5.0	1.87	4.04	3.93	6.78	ND	3.50	4.70	10.1	3.08	10.7	1.92	1.72	16.4	6.50
APPZ	0.5	ND	ND	4.26	4.20	ND	2.09	14.0	ND	0.99	ND	ND	3.98	ND	ND
DAPPZ	0.5	3.80	2.20	0.55	0.90	ND	ND	ND	ND	ND	ND	ND	2.31	ND	ND
Sedatives-hypnotics-anxiolytics															
LZP	0.5	ND	19.1	3.67	ND	27.4	ND	ND	24.4	15.0	23.6	8.24	5.21	19.8	41.8
APZ	5.0	10.1	6.94	ND	4.20	5.72	ND	ND	ND	0.92	ND	ND	0.59	6.98	2.52
AHA	5.0	ND	8.48	ND	ND	ND	ND	ND	ND	ND	ND	4.12	ND	ND	ND
DZP	1.0	6.80	8.20	1.49	4.46	47.0	ND	ND	ND	ND	6.66	24.6	ND	196	238
OXZP	1.0	ND	ND	ND	ND	ND	ND	25.0	38.2	0.79	ND	17.0	ND	13.7	17.0
NDZP	1.0	11.4	10.5	1.08	5.40	6.70	1.06	14.5	8.56	1.63	3.26	3.08	0.85	12.4	5.96
CBZ	1.0	82.2	88.0	3.02	270	236	7.88	840	900	18.8	22.0	147	13.4	726	318
Antidepressants															
VLF	0.1	30.6	6.70	4.49	10.3	7.96	10.9	138	105	132	9.30	7.26	8.04	46.2	29.4
BPP	0.5	ND	3.80	1.93	ND	ND	2.02	ND	ND	4.03	ND	ND	ND	ND	3.42
STL	1.0	5.33	ND	11.3	2.53	ND	17.6	87.0	59.8	58.3	10.6	ND	22.8	21.8	10.8
NSTL	10	116	55.6	ND	144	57.6	42.6	386	50.0	31.0	ND	ND	ND	ND	ND
CLP	1.0	ND	ND	26.4	7.16	ND	12.4	ND	9.46	6.39	16.4	14.7	9.70	31.8	29.8
DCLP	20	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Antihypertensions															
PPN	1.0	17.0	7.98	7.23	18.5	11.8	7.98	34.2	37.6	11.7	14.5	11.4	7.19	123	12.3
ANL	10.0	1010	197	ND	374	244	ND	2440	2500	21.1	192	16.3	ND	1910	772
DTZ	1.0	ND	ND	1.04	ND	ND	ND	ND	1.52	0.81	5.64	ND	0.90	1.39	1.53
DAD	0.5	6.40	3.02	0.78	1.04	1.82	ND	7.62	8.96	1.50	1.55	1.51	0.89	44.4	20.0
VPM	0.5	1.74	ND	ND	0.74	0.88	ND	ND	1.08	ND	ND	ND	ND	0.61	2.64
NVP	0.5	0.88	ND	1.53	ND	ND	0.78	4.04	1.46	0.55	ND	ND	ND	ND	ND
Antimicrobial															
TCS	10	450	ND	1200	145	ND	1220	2500	2500	1470	892	202	645	2440	ND
TCC	5.0	515	22.4	5620	933	457	6740	8880	5860	8460	1150	48.4	5570	2100	375
Antibiotic															
TMP	5.0	33.0	34.8	ND	90.8	38.0	ND	156	103	ND	160	ND	ND	35.6	2080
SMX	5.0	195	ND	ND	288	70.2	31.0	552	318	ND	414	228	ND	2260	296
CDM	5.0	5.16	48.0	2.03	18.3	6.96	6.72	27.2	17.5	48.5	49.6	63.8	80.6	1870	952
LCM	5.0	15.2	53.0	0.85	20.8	17.5	1.77	ND	3.92	1.50	226	187	47.3	148	43.0
Antimycotic															
MNZ	5.0	23.4	17.8	907	65.6	8.92	1230	1410	1020	927	46.0	ND	2770	894	17.0
Analgesics															
IPF	5.0	1130	ND	18.3	686	204	145	2140	1890	37.4	834	145	ND	4460	ND
CDN	5.0	182	56.8	ND	80.2	44.2	ND	214	208	26.6	62.6	37.2	17.4	242	38.0
OCD	5.0	4.0	ND	ND	ND	ND	ND	ND	ND	ND	21.6	ND	ND	ND	ND
KTP	5.0	39.6	23.4	ND	52.2	21.8	ND	ND	ND	ND	9.80	ND	ND	ND	5.04
Antihistamine															
DPH	0.5	83.0	35.0	156	34.8	24.6	179	112	108	54.5	144	52.4	39.0	130	91.2
DPMA	5.0	ND	32.0	ND	ND	23.2	ND	ND	ND	ND	50.6	ND	ND	ND	25.4
Antiplatalet															
CPG	1.0	34.0	2.52	ND	4.78	1.95	ND	172	191	203	5.08	ND	0.83	258	8.84
CPGC	1.0	202	149	ND	175	95.8	0.57	658	1540	18.4	173	84.0	1.85	712	1480
UV-filter															
OXB	20	ND	41.2	1.53	ND	ND	0.89	ND	ND	33.8	70.8	37.0	ND	85.6	ND
Stimulant															
CFI	10	22.8	19.0	1.53	16.0	1067	38.9	42500	51700	371	38100	ND	32.8	60500	389
Illicit drugs															
CCN	0.1	ND	17.0	ND	ND	ND	ND	32.4	55.6	ND	ND	ND	8.69	ND	ND
BEG	1.0	34.2	33.4	1.63	17.8	14.9	7.11	27.8	33.8	11.3	12.5	23.2	10.3	55.0	41.6
NCCN	0.5	36.4	34.4	ND	11.2	19.0	14.4	15.0	33.8	3.75	6.44	29.8	4.89	28.0	20.0
CCE	0.1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
MPH	0.5	189	ND	ND	ND	ND	ND	148	ND	ND	ND	ND	ND	141	ND
MTD	0.1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
EDDP	0.1	ND	ND	1.12	10.4	10.8	5.21	5.16	ND	ND	ND	2.58	ND	ND	ND
APT	0.5	238	2240	689	286	700	ND	760	558	ND	4300	ND	ND	4720	660

Table 2 (*Continued*)

Analyte	LOQ	Saidpur STP			Beur STP			Coimbatore STP			Udupi STP			Manipal STP	
		Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent	Sludge	Influent	Effluent
MAPT	0.5	10.9	498	41.8	153	304	7.62	42.4	ND	9.27	386	462	6.10	10.4	310
MDA	0.5	ND	ND	ND	440	1150	6.97	59.2	114	46.0	216	ND	ND	98.0	ND
MDMA	0.1	ND	21.8	ND	ND	ND	ND	23.0	29.0	ND	ND	ND	ND	ND	ND
MDEA	0.1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Artificial sweeteners															
SCH	5.0	369000	ND	4630	143000	6020	17900	315000	379000	33200	389000	ND	19200	299000	21100
ASF	5.0	ND	8.28	ND	57.6	51.2	8.81	72.8	389	26.2	62.4	63.8	12.3	85.4	157
CCM	5.0	ND	12.9	66.6	86.2	ND	301	8180	2220	460	3920	1670	544	5120	592
SCL	5.0	618	922	593	1060	1340	1870	1820	2440	1180	384	1540	101	3420	2460

df: detection frequency; LOQ: limit of quantitation; pharmaceutical metabolites are italicized.
AHA: α-hydroxyalprazolam, ANL: atenolol, APT: amphetamine, APPZ: aripiprazole, APZ: alprazolam, ASF: acesulfame, ASP: annual sludge production, BEG: benzoylecgonine, BPP: bupropion hydrochloride, CBZ: carbamazepine, CCE: cocaethylene/benzoylecgonine ethyl ester, CCM: cyclamate, CCN: cocaine, CDM: clindamycin, CDN: codeine, CFI: caffeine, CLP: citalopram hydrobromide, CPG: clopidogrel bisulfate, CPGA: clopidogrel carboxylic acid hydrochloride, DAD: desacetyl diltiazem, DAPPZ: dehydro-aripiprazole, DCLP: *N*-desmethylcitalopram hydrochloride, DZP: diazepam, DPH: diphenhydramine hydrochloride, DPMA: 2-(diphenylmethoxy) acetic acid, DTZ: diltiazem hydrochloride, EDDP: 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine, IPF: ibuprofen, KTP: ketoprofen, LCM: lincomycin, LZP: lorazepam, MTD: methadone, MAPT: methamphetamine, MDA: 3,4-methylenedioxyamphetamine, MDEA: 3,4-methylenedioxyethylamphetamine, MDMA: 3,4-methylenedioxymethamphetamine, MNZ: miconazole, MPH: morphine, NCCN: norcocaine, NDZP: nordiazepam, NQTP: norquetiapine hydrochloride, NSTL: norsertraline, NVP: norverapamil, OCD: oxycodone, OXB: oxybenzone, OxZP: oxazepam, PPN: propranolol, QTP: quetiapine fumarate, SCH: saccharin, SCL: sucralose, SMX: sulfamethoxazole, STL: sertraline hydrochloride, STP: sewage treatment plant, TCC: triclocarban, TCS: triclosan, TMP: trimethoprim, VLF: venlafaxine hydrochloride, VPM: verapamil hydrochloride.

extraction, mixed well, and allowed to equilibrate for ~30 min at room temperature. The samples were extracted by passage through Oasis® HLB 6 cm^3 (200 mg; Waters, Milford, MA) solid phase extraction (SPE) cartridges. The cartridges were conditioned with 5 mL of methanol and 5 mL of Milli-Q water prior to use. Wastewater samples were loaded at ~1 mL/min, and cartridges were allowed to dry for ~30 min under vacuum and then eluted with 6 mL of methanol followed by 3 mL of a mixture of acetone, methanol, and ethyl acetate (2:2:1 v/v/v). Cartridges also were eluted with 3 mL of methanol containing 5% ammonia. The eluents were combined and concentrated to ~100 μL under a gentle stream of nitrogen at 35° C using a TurboVap® Evaporator (Zymark Inc., Hopkinton, MA). The final volume of the extract was adjusted to 1 mL with methanol in an amber glass vial, and 10 μL of the extract was injected into high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS).

Sludge samples were analyzed by following the method described elsewhere [19,20]. Briefly, ~0.1 g of freeze-dried sludge was spiked with a mixture of internal standards (25 or 50 ng) prior to extraction and allowed to equilibrate for ~30 min at room temperature. Spiked sludge samples were vortex-mixed for 1 min and extracted with 6 mL of methanol:water mixture (5:3 v/v) using an ultrasonic bath (Branson® Ultrasonics 3510R-DTH; Danbury, CT) for 30 min. Extracts were centrifuged at 4500 × *g* for 5 min (Eppendorf Centrifuge 5804, Hamburg, Germany), and the supernatant was collected in a polypropylene tube. The extraction was repeated with 6 mL of methanol. The extracts were combined and concentrated to ~1 mL under a gentle stream of nitrogen. The concentrated extract was diluted with Milli-Q water to ~12 mL and purified by passage through Oasis® HLB (6 cm^3, 200 mg) cartridges, as described above for wastewater samples. The final volume of the extract was adjusted to 1 mL with methanol in an amber glass vial, and 10 μL of the extract was injected into HPLC–MS/MS for analysis.

2.3. Instrumental analysis

Target chemicals were analyzed using an API 2000 electrospray triple quadrupole mass spectrometer (ESI–MS/MS; Applied Biosystems, Foster City, CA, USA), interfaced with an Agilent 1100 Series HPLC system (Agilent Technologies, Santa Clara, CA, USA). Detailed information with regard to HPLC parameters, MS/MS parameters, including MRM transitions, analyte identification, quantification, and quality assurance, and quality control (QA/QC) protocols have been described elsewhere [19–22]. The continuing calibration verification standards that were injected before and after the wastewater and sludge samples showed recoveries at 100 ± 30%. The regression coefficients (r^2) for 6- to 10-point calibration standards (concentrations ranging from of 0.1 to 1000 ng/L for wastewater and 0.1 to 2000 ng/g for sludge), calculated by equal weighting quadratic regression, were ≥0.99 for all target analytes. Several procedural blanks were analyzed with wastewater and sludge samples. The measured concentrations of target analytes in procedural blanks were below the corresponding limit of quantification (LOQ). LOQs were determined as a minimum concentration of analytes in sample extracts that provide a signal to noise ratio ≥10. The concentrations of target chemicals in sludge are reported on a dry-weight basis unless stated otherwise.

A wastewater and a sludge sample were selected randomly for matrix spike (MS) and matrix spike duplicate (MSD) analyses. Target analytes and corresponding internal standards were each spiked at 25 and 50 ng, respectively, and were passed through the entire analytical procedure. The average recoveries of pharmaceuticals, psychoactive drugs, and illicit drugs in wastewater were 96 ± 20%, 98 ± 31%, and 91 ± 29%, respectively; the corresponding recoveries in sludge were 74 ± 32%, 61 ± 27%, and 55 ± 19%, respectively. The recoveries of triclosan, triclocarban, ibuprofen, sulfamethoxazole, codeine, miconazole, caffeine, and artificial sweeteners in wastewater and of triclosan, triclocarban, miconazole, and artificial sweeteners in sludge were not determined due to the high background concentrations of these compounds in samples.

2.4. Data analysis

The mass loadings, removal efficiency, and emissions of PPCPs in STPs were estimated using the following equations (Eqs. (1)–(3)), as reported by Subedi and Kannan [20].

$$\frac{\text{Mass load}}{1000 \text{ people}} = C_i \times F \times \left(\frac{1}{10^6}\right) \times \left(\frac{1000}{\text{population}}\right) \quad (1)$$

$$\%\text{Removal} = \left[\frac{(C_i - C_e)}{C_i}\right] \times 100\% \quad (2)$$

$$\left(\frac{\text{Emission}}{1000\ \text{people}}\right) = [(C_e \times F)] + (C_s \times \text{TSP})]\left(\frac{1}{10^6}\right)\left(\frac{1000}{\text{Population}}\right) \quad (3)$$

where C_i is the concentration of analyte in wastewater influent (ng/L), F is the daily flow of wastewater influent (L/d) over a 24-h period, population is the number of people served by the STP, mass load is the amount of individual pharmaceutical introduced into STP (mg/d/1000 people), C_e is the concentration of analyte in wastewater effluent (ng/L), C_s is the concentration of analyte in sludge (ng/g wet weight), TSP is the total sludge production (g/d wet weight), and emission/1000 people is the amount of pharmaceuticals discharged through wastewater effluent and sludge (mg/d/1000 people). The concentrations that were below the LOQ were substituted with 1/2-LOQ values for statistical analysis.

3. Results and discussion

A total of 41 target chemicals and 11 of their metabolites were detected in five STPs in India (Table 2). Among the several compounds analyzed, two illicit drugs [(methadone and 3,4-methylenedioxyethylamphetamine (MDEA)], a metabolite of cocaine (cocaethylene/benzoylecgonine ethyl ester), and a metabolite of citalopram (*N*-desmethylcitalopram) were not found in any of the samples analyzed. Concentrations of metabolites clopidogrel carboxylic acid and norsertraline were 4.0 and 5.1 times higher than the concentrations of corresponding parent compounds, clopidogrel and sertraline, respectively.

3.1. Antipsychotics in STPs

This is the first study to report the occurrence of psychoactive pharmaceuticals and their select metabolites in wastewater and sludge from STPs in India. Quetiapine and its metabolite norquetiapine were found in wastewater influents from all five STPs (Table 2). Quetiapine was among the most prescribed antipsychotic drugs in India [23] and the USA [24]. Moreover, quetiapine is typically prescribed at the highest dose (mean daily dose of ~365 mg in India) among various antipsychotic drugs in commerce [23]. The mean concentration of quetiapine (33.5 ng/L, df: 100%) in influents was 1.7 times higher than that reported in the USA, but 2.5 and ~100 times lower than that reported for centralized municipal STPs and wastewater from a psychiatric hospital in China, respectively [25].

India accounts for 27% of the total global production of benzodiazepine-type anxiolytics, which include lorazepam (1.2 tons), alprazolam (5.4 tons), diazepam (7.1 tons), and oxazepam (1.6 tons) in 2011 [26]. The mean concentration of diazepam (42.7 ng/L, df: 80%) and nordiazepam (9.4 ng/L, df: 100%) in influents were 2 times higher than that reported in Spain and the USA. Nordiazepam and oxazepam are available as pro-drugs and are formed as metabolites of diazepam. Therefore, the measured concentrations of oxazepam and nordiazepam in wastewater represent the drug residues excreted as a parent molecule and as metabolites of benzodiazepines [27]. Similar to that in two STPs in Canada [28], venlafaxine was found in all wastewater samples at the highest mean concentration (46.9 ng/L, df: 100%) among the antidepressants analyzed. Propranolol, atenolol, and desacetyl diltiazem (a metabolite of diltiazem) were found in all wastewater samples; the mean concentration of antihypertensive atenolol was 25 times higher than that of the antidepressant venlafaxine.

3.2. Illicit drugs in STPs

No earlier studies have reported on the occurrence of illicit drugs in wastewater samples from Indian STPs. Benzoylecognine and norcocaine, two major metabolites of cocaine, were found in 100% of influent samples at mean concentrations of 29.5 ng/L and 19.4 ng/L, respectively (Table 2). The mean concentration of BEG was 6–48 times lower than in wastewater influents from the UK [29], Canada [30], and the USA [20]. However, the latter three studies reported the concentrations of illicit drugs in 24 h composite samples of wastewater.

India has been reported as a major producer of amphetamine [31]. The mean concentrations of amphetamine in influents of STP_{UD} (4300 ng/L) and STP_{MP} (4720 ng/L) were the highest ever reported for this compound in wastewater. The mean concentration of amphetamine (2060 ng/L, df: 100%) in wastewater influents from five Indian STPs was 10 times higher than that reported in Spain [32], 15 times higher than that reported in the UK [29], and 125 times higher than that reported in Canada [34]. Amphetamine concentration in influents was ~2 times higher than in effluents; however, the concentration of methamphetamine in influents (121 ng/L, df: 100%) was ~4 times lower than that in effluents (480 ng/L, df: 100%).

The United Nation Office of Drugs and Crime reported that ~15 tons of heroin (equivalent to 3% of the global supply) are produced annually in India [33]. Heroin is rapidly metabolized to 6-monoacetyl morphine and to morphine [34]. However, the morphine concentration measured in wastewater was also contributed from therapeutic morphine as well as a metabolite of codeine [35]. The mean concentrations of morphine (160 ng/L) in influent from STP_{SD}, STP_{CO}, and STP_{MP} were similar to those reported in the USA [20]; the measured concentrations in Indian STPs were ~3 times higher than those from Spain [36] and ~2 times lower than those from the UK [29]. 3,4-Methylenedioxyamphetamine (MDA) was found only in influents from STP_{BU}, STP_{CO}, and STP_{MP} at a mean concentration of 203 ng/L.

3.3. Artificial sweeteners in STPs

All four ASWs were reported for the first time in this study in Indian wastewater samples (Table 2). In influents, saccharin was found at the highest mean concentration of 303,000 ng/L (df: 100%), followed by cyclamate (3460 ng/L, df: 75%) and sucralose (1460 ng/L, df: 100%). The distribution pattern of ASWs in India was different from that reported in other countries. In Germany, the pattern of ASWs found in wastewater was cyclamate > saccharin ~ acesulfame > sucralose [37], and in the USA, it was sucralose > saccharin > acesulfame [19]. In general, studies from European nations have shown the prevalence of cyclamate, acesulfame, and saccharin, whereas those from the USA have shown the predominance of sucralose in STPs. In Korean STPs, the distribution pattern of ASWs was aspartame > sucralose > acesulfame > saccharin > cyclamate [22].

Saccharin is the cheapest and the most widely used ASW in India [38]. The Prevention of Adulteration of Food Act in India permits 100 mg/kg of saccharin in carbonated drinks; however, other products, including pan masala, ice candy, and crushed ice, were reported to contain as high as 24,300 mg saccharin/kg [39,38]. The median concentration of saccharin in influent samples from India was 15 times higher than that reported in Spain [40], 20 times higher than that reported in the USA [19], and 38 times higher than that reported in China [41].

The mean concentration of cyclamate in influents from Indian STPs was 43 and 6 times lower than concentrations reported from Germany [37] and China, respectively [41]. The U.S. Food and Drug administration (FDA) banned cyclamate in 1970 from all foods due to its potential carcinogenic effects on experimental animals [42]. Due to their persistence, sucralose [43–45] and acesulfame [46,47] are used as tracers of wastewater contamination in groundwater, landfill leachate [48], and drinking water. However, relatively lower concentrations of sucralose (1460 ng/L, df: 100%) and acesulfame (56 ng/L, df: 80%) than other ASWs were found in influents of Indian STPs.

3.4. Miscellaneous pharmaceuticals in STPs

Antimicrobials (triclosan and triclocarban), antibiotics (sulfamethoxazole, trimethoprim, clindamycin, and lincomycin), an antimycotic (miconazole), analgesics (ibuprofen, codeine, and ketprofen), an antihistamine (diphenhydramine), an antiplatelet (clopidogrel), and a stimulant (caffeine) were found in all influent samples of Indian STPs (Table 2). The mean concentrations of antimicrobials were 1.77–33 times higher than the mean concentrations of antibiotics. The mean concentration of the antimycotic miconazole in influents was similar to that of the antibiotic clindamycin. Analgesics are widely used and are the largest group of over-the-counter drugs in India [49]. Analgesics ibuprofen (1200 ng/L), codeine, and ketoprofen were found at a ratio of 91:8:1 in influents from STPs in India. Singh et al. [10] reported a median concentration of 20.0 ng/L (as much as 26,500 ng/L) for ibuprofen and 40.0 ng/L for ketoprofen (as much as 16,200 ng/L) in wastewater from Ghaziabad, India. The mean concentration of codeine (156 ng/L, df: 100%) in our study was 2.3 times higher than that reported from Spain [36] but 8 times lower than that reported in the UK [29]. The mean concentrations of diphenhydramine and clopidogrel were 2.8 times higher than those reported in the USA.

3.5. PPCPs in open sewage channels in residential areas

A total of 35 PPCPs and 10 of their metabolites were found in raw wastewater collected from open sewage drains near residential areas (Table S1). The Cooum River flows through the Chennai metropolitan area (population = 8.9 M, the fourth largest city in India) and is a major receptacle of the city's untreated domestic sewage that eventually discharges into the Bay of Bengal [50]. Previous studies reported elevated concentrations of classic organic contaminants, such as pesticides in water and sediment from the Cooum River [51]. The concentrations of triclosan, triclocarban, sulfamethoxazole, miconazole, diphenhydramine, venlafaxine, sertraline, citalopram, amphetamine, saccharin, acesulfame, and cyclamate were 3–14 times higher in the Cooum River water at Napier Bridge near the river mouth at the Bay of Bengal than in the mid-section of the river. An antimicrobial (triclocarban = 6180 ng/L), an analgesic (ibuprofen = 2320 ng/L), a metabolite of antiplatelet (CPGC = 1370 ng/L), an antihypertensive (atenolol = 3180 ng/L), and an illicit drug (amphetamine = 984 ng/L) were the most abundant compounds in water from the Cooum River.

The mean concentration of benzoylecgonine, a metabolite of cocaine, in the Cooum River (26.1 ng/L) water was 3.5 times lower than that reported for wastewater-dominated rivers in Spain [32]; but 7 times higher than that reported for the River Po in Italy [52]. The mean concentration of amphetamine in the Cooum River water (631 ng/L) was 190 times higher than that reported for the rivers in the UK [53]. Similarly, saccharin (419,000 ng/L) and sucralose (2460 ng/L) were the two most abundant ASWs found in Cooum River water. These results suggest that high levels of PPCPs are discharged into the Bay of Bengal through the Cooum River. Triclocarban, ibuprofen, codeine, carbamazepine, and saccharin were found at high concentrations in another sewage channel in Coimbatore (Sanganur Pallam) and Patna, suggesting that local sewage drains are conduits of PPCPs to STPs and other waterbodies.

3.6. PPCPs in sewage sludge

A total of 21 pharmaceuticals, including antimicrobials, antibiotics, analgesics, antipsychotics, illicit drugs, and artificial sweeteners, were found in all treated sewage sludge (df: 100%) from four STPs (sludge was collected from only four STPs) (Table 2). The mean concentrations of triclocarban (6600 ng/g dw), triclosan (1140 ng/g dw), and miconazole (1460 ng/g dw) were the highest among the PPCPs analyzed in sludge. The mean concentrations of triclocarban and triclosan were 5.5 and 11 times lower, respectively, than in biosolids collected from 92 STPs in the USA as part of the U.S. EPA national sewage sludge survey [54]. Thus far, only four studies have determined ASWs in sewage sludge [55,56,40,22]. This is the first report of the occurrence of ASWs in sewage sludge from India. Saccharin, cyclamate, sucralose, and acesulfame were found in 75–100% of sludge samples at a mean concentration that ranged from 15.8 (acesulfame) to 18,700 ng/g dw (saccharin) (Table 1). The mean concentration of saccharin in Indian sludge was 113 times higher than that reported in Spain [40]; and the mean concentration of sucralose was 5.8–62 times higher than that reported in Spain [40] and Sweden [56]. The treated sewage sludge is primarily disposed on agricultural lands as manure and to a small extent as a landfill. The concentration of triclosan, triclocarban, miconazole, diphenhydramine, clopidogrel, oxybenzone, quetiapine, norquetiapine, sertraline, propranolol, benzoylecgonine, norcocaine, saccharin, and cyclamate in sludge from STP_{CO} were 1.1–45 times higher than in a landfill leachate collected from a landfill facility in Coimbatore (Table S1). However, the concentrations of caffeine, acesulfame, and sucralose in landfill leachate were 3.9 to 740 times higher than in sludge from STP_{CO} (Table S1).

3.7. Estimation of mass loads of pharmaceuticals to STPs

For the three large-scale STPs studied (average flow rate of 20.7 MLD, serving a population of 325,000), the mass loadings of pharmaceuticals calculated based on the concentrations in influent, daily sewage inflow, and the population served by the plant were in the order of: $STP_{CO} > STP_{BU} > STP_{SD}$ (Table 3). The mass loading of the antipsychotic carbamazepine (54 mg/d/1000 people) in STP_{CO} was found similar to that reported in the USA; however, the mass loadings of norsetraline (a metabolite of sertraline, 24.8 mg/d/1000 people) and atenolol (157 mg/d/1000 people) in STP_{CO} were 2 times higher than those reported in the USA. The mean mass loading of codeine (9.9 mg/d/1000 inhabitant) was similar to that reported in Spain [36], whereas that of amphetamine (27.7 mg/d/1000 inhabitant) was an order of magnitude higher than the values reported in Milan, Italy [35]. The mass loading we reported here can be expanded further to estimate the community-usage of select PPCPs [20], which can be of significant importance since ~64% of patients in India purchase medications without prescriptions [11]. It is worth to note that the mass loading of PPCPs measured in this study is an estimate, owing to the limited sample size (one-time grab sample).

The mass loading of saccharin in India was 1.8–4.4 times higher than that reported for Switzerland [46], Germany [37], and the USA [19]; however, mass loading of sucralose in India was 6.4–240 times lower than those reported in those three countries. In two small-scale STPs (STP_{UD} and STP_{MP}: average inflow = 2 MLD and population = 11,000), mass loadings of sulfamethoxazole,

Table 3
Mass loads of select PPCPs and their metabolites to sewage treatment plants in India, and their environmental emissions through wastewater effluent and sludge.

Analytes	Mass load (mg/d/1000 people)					Emission (mg/d/1000 people)				
	STP_{SD}	STP_{BU}	STP_{CO}	STP_{UD}	STP_{MP}	STP_{SD}	STP_{BU}	STP_{CO}	$^{*}STP_{UD}$	$^{*}STP_{MP}$
Antischizophrenics										
Quetiapine (QTP)	2.0	1.6	1.6	2.8	11.9	–	0.47	0.09	–	3.73
Norquetiapine (NQTP)	0.1	0.5	0.3	2.1	2.7	0.22	–	–	0.38	3.73
Aripiprazole (APPZ)	–	0.3	0.9	–	–	–	–	–	–	–
Dehydro-aripiprazole (DAPPZ)	0.2	0.1	–	–	–	0.12	–	–	–	–
Sedatives-hypnotics-anxiolytics										
lorazepam (LZP)	–	–	–	4.7	3.3	1.04	2.04	1.02	1.65	6.97
Alprazolam (APZ)	0.5	0.3	–	–	1.2	0.38	0.43	0.41	–	0.42
α-Hydroxyalprazolam (AHA)	–	–	–	–	–	0.46	–	1.13	0.82	–
Diazepam (DZP)	0.4	0.3	–	1.3	32.6	0.45	3.50	–	4.92	39.7
Oxazepam (OxZP)	–	–	1.6	–	2.3	–	–	0.81	3.40	2.83
Nordiazepam (NDZP)	0.6	0.4	0.9	0.7	2.1	0.57	0.50	1.35	0.62	0.99
Carbamazepine (CBZ)	4.5	20.1	54.0	4.4	121	4.78	17.6	57.6	29.3	53.0
Antidepressants										
Venlafaxine (VLF)	1.7	0.8	8.9	1.9	7.7	0.37	0.60	1.63	1.45	4.90
Bupropion (BPP)	–	–	–	–	–	0.21	–	–	–	0.57
Sertraline (STL)	0.3	0.2	5.6	2.1	3.6	–	0.01	0.64	–	1.79
Norsetraline (NSTL)	6.3	10.8	24.8	–	–	3.02	4.31	–	–	–
Citalopram (CLP)	–	0.5	–	3.3	5.3	0.01	0.01	1.00	2.95	4.97
Desmethyl citalopram (DCLP)	–	–	–	–	–	–	–	–	–	–
Antihypertensions										
Propranolol (PPN)	0.9	1.4	2.2	2.9	20.5	0.83	0.88	2.15	2.28	2.05
Atenolol (ANL)	54.8	27.9	157	38.5	319	10.7	18.2	59.7	3.25	129
Diltiazem (DTZ)	–	–	–	1.1	0.2	–	–	0.09	–	0.25
Desacetyl diltiazem (DAD)	0.3	0.1	0.5	0.3	7.4	0.16	0.14	0.28	0.30	3.33
Verapamil (VPM)	0.1	0.1	–	0.1	0.1	–	0.07	–	–	0.44
Norverapamil (NVP)	–	–	–	–	–	–	–	–	–	–
Antimicrobial										
Triclosan (TCS)	24.4	10.8	161	178	407	0.35	0.50	7.31	40.4	–
Triclocarban (TCC)	28	69.6	571	230	349	2.87	36.9	28.0	9.68	62.6
Antibiotics										
Trimethoprim (TMP)	1.8	6.8	10	32	5.9	1.89	2.83	1.74	–	347
Sulfamethoxazole (SMX)	10.6	21.5	35.5	82.8	377	–	5.25	8.38	45.6	49.3
Clindamycin (CDM)	0.3	1.4	1.7	9.9	311	2.61	0.52	2.71	12.8	159
Lincomycin (LCM)	0.8	1.5	–	45.1	24.6	2.88	1.31	0.10	37.4	7.16
Miconazole (MNZ)	1.3	4.9	90.4	9.2	149	1.24	1.17	0.72	–	2.83
Analgesics										
Ibuprofen (IPF)	61.2	51.1	138	167	743	0.01	15.3	35.6	29.0	–
Codeine (CDN)	9.9	6.0	13.8	12.5	40.3	3.08	3.29	11.7	7.44	6.33
Oxycodone (OCD)	0.2	–	–	4.3	–	–	–	–	–	–
Ketoprofen (KTP)	2.1	3.9	–	2.0	–	1.27	1.63	0.16	–	0.84
Antihistamine										
Diphenhydramine (DPH)	4.5	2.6	7.2	28.8	21.7	1.95	1.91	3.45	10.5	15.2
DPMA	–	–	–	10.1	–	1.74	1.73	3.41	–	4.23
Antiplatalet										
Clopidogrel (CPG)	1.8	0.4	11.1	1.0	43.0	0.14	0.15	2.07	–	1.47
CPGC	11.0	13.0	42.3	34.6	119	8.07	7.14	69.2	16.8	247
UV-filter										
Oxybenzone (OXB)	–	–	–	14.2	14.3	2.24	–	2.03	7.40	–
Stimulant										
Caffeine (CFI)	1.2	1.2	2730	7630	10100	1.04	79.6	230	–	64.8
Illicit drugs										
Cocaine (CCN)	–	–	2.1	–	–	0.92	–	–	–	–
Benzoylecgonine (BEG)	1.9	1.3	1.8	2.5	9.2	1.81	1.11	0.53	4.64	6.93
Norcocaine (NCCN)	2.0	0.8	1.0	1.3	4.7	1.87	1.42	0.88	5.96	3.33
Cocaethylene (CCE)	–	–	–	–	–	–	–	–	–	–
Morphine (MPH)	10.3	–	9.5	–	23.5	–	–	–	–	–
Methadone (MTD)	–	–	–	–	–	–	–	–	–	–
EDDP	–	0.8	0.3	–	–	–	0.81	–	0.52	–
Amphetamine (APT)	12.9	21.3	48.9	860	787	122	52.2	–	–	110
Methamphetamine (MAPT)	0.6	11.4	2.7	77.2	1.7	27.1	22.7	53.1	92.4	51.7
MDA	–	32.8	3.8	43.2	16.3	–	85.7	–	–	–

Table 3 (*Continued*)

Analytes	Mass load (mg/d/1000 people)					Emission (mg/d/1000 people)				
	STP_{SD}	STP_{BU}	STP_{CO}	STP_{UD}	STP_{MP}	STP_{SD}	STP_{BU}	STP_{CO}	$^{*}STP_{UD}$	$^{*}STP_{MP}$
MDMA	–	–	1.5	–	–	1.18	–	–	–	–
MDEA	–	–	–	–	–	–	–	–	–	–
Artificial sweeteners										
Saccharin (SCH)	20000	10700	20300	77900	49900	1.37	456	5550	–	3520
Acesulfame (ASF)	–	4.3	4.7	12.5	14.2	0.45	3.82	26.0	12.8	26.2
Cyclamate (CCM)	–	6.4	526	784	853	0.72	0.12	136	334	98.7
Sucralose (SCL)	33.5	79.0	117	76.8	570	50.2	101	246	308	410

Pharmaceutical metabolites are italicized; *the calculated emission was based only on the mean concentration of PPCPs in wastewater effluent (information on total amount of sludge produced was unavailable for these STPs).

ibuprofen, diphenhydramine, amphetamine, and saccharin were 5.3–30 times higher than those found in three large STPs.

3.8. Estimation of removal of PPCPs from STPs

The removal efficiencies of PPCPs were calculated based on the measured concentrations in influents and effluents (Eq. (2)). The median removal efficiencies ranged from 5% (norcocaine) to 100% (triclosan) for the five STPs (Fig. 1). However, clindamycin, lorazepam, diazepam, carbamazepine, verapamil, acesulfame, and sucralose showed negative removal efficiency in STPs. Microbial transformation of conjugated forms of drugs in the wastewater treatment processes can increase the residue levels of parent drugs in waste streams [57]. The removal rates of quetiapine (94%), venlafaxine (36%), sertraline (100%), and atenolol (62%) in Indian STPs were similar to those reported for STPs in the USA and Canada [28]. The seasonal as well as day-to-day variations in the removal efficiencies of PPCPs from STPs have been reported [58]. Therefore, it is important to note that the removal efficiencies of PPCPs reported in this study are based on the measured concentrations in a single grab sample [58]. Inefficient removal of select PPCPs can contaminate ground water and/or disrupt the endocrine system of aquatic species such as fish [59].

Metabolites of cocaine, benzoylecgonine and norcocaine, were poorly removed in STPs (≤16%); however, amphetamine, morphine, and MDA were removed at ≥86% (Fig. 1). Negative removal of some illicit drugs, particularly metabolic products, suggests enhanced transformation of parent/precursor compounds (or deconjugation of glucuronide) in STP processes [20]. Both saccharin and cyclamate were significantly removed from STPs, with an average removal efficiency of 96% and 81%, respectively (Fig 1). The average removal efficiency of saccharin found in our study was similar to that reported in Germany (>90%) [37] and China (97%) [41]. Acesulfame and sucralose showed negative removal efficiency, which was similar to that reported in Switzerland [46], China [41], Germany [37], and Sweden [56]. Sucralose is not liable for microbial degradation due to the

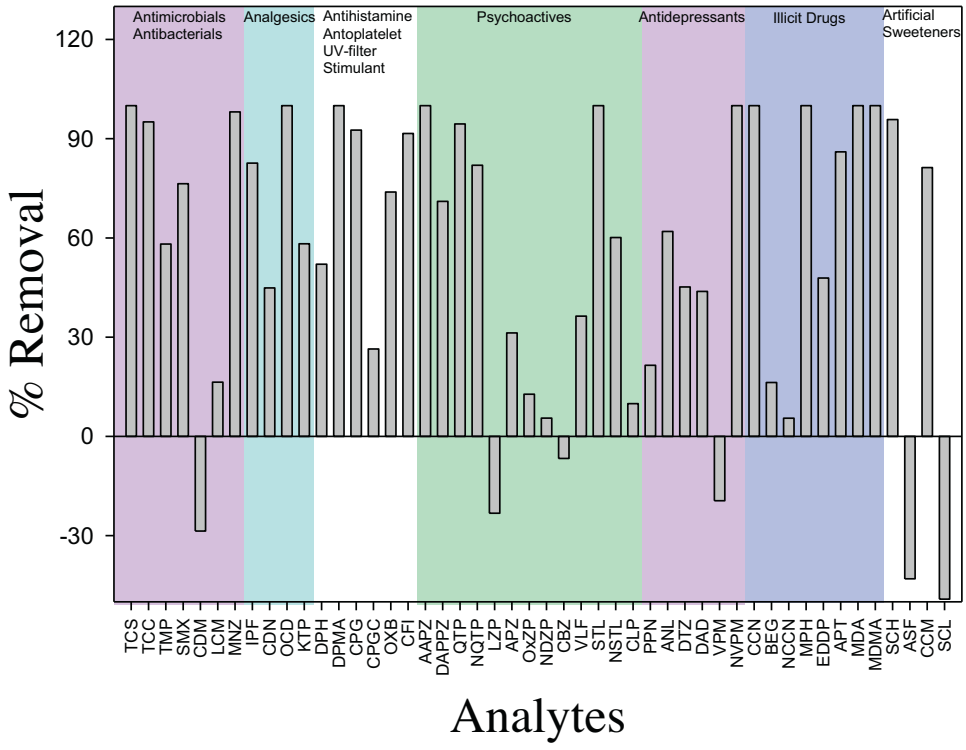

Fig. 1. The median removal efficiencies (%) of PPCPs from five sewage treatment plants in India.

presence of chlorine atoms [60,61]; however, no explanation is available to support the negative removal of acesulfame from STPs.

3.9. Estimation of environmental emission of PPCPs through STPs

The total mass of PPCPs discharged from STP effluents and sewage sludge was calculated based on the concentrations measured in effluents and sludge as well as on the daily discharge of effluents, total sludge production rate, and the population served by the STPs (Eq. (3)). The discharge/emission of carbamazepine was the highest (4.78–57.6 mg/d/1000 people) among several antipsychoactives analyzed, whereas atenolol (10.7–59.7 mg/d/1000 people) was the most highly discharged antihypertensive (Table 3). The environmental discharge rates of diphenhydramine and its metabolites were similar; however, the environmental discharge of a metabolite of antiplatelet CPGC was 33–60 times higher than that of its parent compound, clopidogrel. Overall, an average mass of 2.55 kg of triclocarban, 0.53 kg of sulfamethoxazole, 2.03 kg of ibuprofen, 12.5 kg of caffeine, 3.24 kg of carbamazepine, 3.60 kg of atenolol, 6.93 kg of amphetamine, and 4.17 kg of methamphetamine were discharged annually from a STP that serves an average population of 325,000 in India. This information can be used to extrapolate total annual emissions of PPCPs in India.

The estimated environmental emission of triclocarban was the highest among the antimicrobials and antibiotics analyzed, but it was two orders of magnitude lower than the emission of saccharin through STPs. Saccharin was found to be the most discharged (2000 mg/d/1000 people) ASW from STPs in India, followed by sucralose (132 mg/d/1000 people) and cyclamate (5.84 mg/d/1000 people). These values correspond to an estimated annual discharge of 252 kg of saccharin, 16.0 kg of sucralose, and 5.84 kg of cyclamate from a STP that serves an average population of 325,000 with an average inflow rate of ~21 MLD. However, the estimated annual discharge of ASWs from a STP (treatment capacity of 260,000 m^3/d) in China was found in a different order: 1600 kg of acesulfame followed by 26 kg of saccharin [41]. The U.S. EPA is assessing and regulating the presence of select pharmaceutical products in the environment as hazardous materials under the Resources Conservation and Recovery Act (RCRA) [62]. As an example, disposal of hazardous waste in municipal waste landfills, municipal incinerators, or medical waste plants is strictly prohibited under the RCRA. Similarly, European Union regulates the land application of sewage sludge to limit the risk of pollutants including PPCPs [63]. India regulates municipal wastewater, industrial wastewater, and chemical sludge produced from wastewater treatments under Hazardous (Management, Handling, and Transboundary Movement) Wastes Rules [64]. However, insufficient number of STPs, and proper maintenance of existing STPs, and overall lack on enforcement of regulations can result in high environmental emissions of PPCPs in India. Moreover, it is important to note that disposal of untreated sewage from hospitals, residential areas, and industries directly into surface waters in India can augment the estimated emission values for PPCPs [5]. The environmental emission of PPCPs to surface waters in India, as elucidated with the limited number of samples analyzed in this study, is a major concern, and further studies are needed to evaluate the effects of these chemicals on the ecosystems.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jece.2015.09.031.

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