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ARTICLE *in* ENVIRONMENTAL SCIENCE AND TECHNOLOGY · FEBRUARY 2006

Impact Factor: 5.33 · DOI: 10.1021/es050991m · Source: PubMed

Environ. Sci. Technol. **2006**, *40,* 357−363

Removal of Pharmaceuticals in Sewage Treatment Plants in Italy

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A listing of "priority pharmaceuticals" for human use in Italy resulted in the selection of 26 pharmaceuticals, belonging to 11 therapeutic classes. They were analyzed by liquid chromatography−tandem mass spectrometry, their occurrence was assessed in six sewage treatment plants (STPs), and the loads and the removal rates (RR) were studied. Total loads ranged from 1.5 to 4.5 g/day/1000 inhabitants in influents and 1.0 and 3.0 g/day/1000 inhabitants in effluents. Total RR in STPs were mostly lower than 40%. Pharmaceuticals could be divided into three groups according to their behavior in STPs: one group with RR higher in summer than in winter, one group with RR similar in summer and winter, and a last group not removed. Last, we studied the distribution and fate of residual pharmaceuticals in the surface waters receiving the effluents of the STPs and identified degradation and sorption as the major factors affecting attenuation. Ciprofloxacin, ofloxacin, sulfamethoxazole (antibiotics), atenolol (cardiovascular drug), ibuprofen (antiinflammatory), furosemide, hydrochlorothiazide (diuretics), ranitidine (gastrointestinal drug), and bezafibrate (lipid regulator) were the most abundant residual drugs, thus those of environmental concern.

Introduction

About 1500 tons of pharmaceuticals were used in 2003 in Italy (*1*). Variable amounts, up to 95% of the administered dose (*2*, *3*), can be excreted unmetabolized in urine or stool and discharged into domestic wastewater. Unwanted or expired medications can be improperly disposed directly in wastewater. Several pharmaceuticals can therefore reach sewage treatment plants (STPs) in substantial amounts and, if they escape degradation or elimination through sludge, can be released into surface water. Moreover, several pharmaceuticals are excreted as conjugates and can release the active moiety by cleavage during treatment in STPs (*4*). The presence of several pharmaceuticals in STP effluents has been confirmed in Germany (*5*, *6*), The Netherlands (*7*), Switzerland (*8*), United Kingdom (*9*), France, Greece, Sweden and Italy (*10*), Spain (*11*) the United States (*12*, *13*), Canada (*14*), Brazil (*15*), and Australia (*16*). For the majority of drugs, removal by conventional biological treatments seems inefficient, since they are found in significant amounts in STP effluents and surface water. For instance, carbamazepine is described as a persistent compound, not degraded or adsorbed during wastewater treatments (*17*) or only barely degraded (*5*). However, for other compounds such as clofibric acid and bezafibrate, removal can reach 34−51% and 50−83%, respectively (*5*, *6*), while up to 90% of ibuprofen is apparently removed (*5*). The removal rate (RR) of pharmaceuticals in STPs can therefore vary and is potentially affected by several factors, such as the nature of the pharmaceutical, the treatment process employed, the age of the activated sludge, the environmental conditions such as the temperature and the light intensity, and the characteristics of the influent (*11*, *18*).

Biological filters and activated sludge are the most frequent secondary treatments, the latter probably more efficient for removal of pharmaceuticals (*6*). Tertiary treatments are seldom used because they are expensive but are under extensive investigation (*14*). Technologies such as flocculation, ozonation, advanced oxidation, membrane filtration (activated carbon adsorption), and photocatalysis (*19*−*23*) could improve the RR of pharmaceuticals in STPs soon. As recently suggested (*18*), prevention of pharmaceuticals entry in the aquatic ecosystem might be the best strategy for facing possible environmental problems. Larsen analyzed several processes to remove pharmaceuticals from wastewater and noted that a combination of biological treatments, high sludge residence time, and ozonation of the effluent seemed the most promising (*24*). However, the cost of such new technologies has still to be evaluated. STPs are currently still "hot spots" of environmental contamination, at least when dealing with pharmaceuticals for human use, and further research is needed to clarify their capacity to remove a wide range of active molecules and metabolites.

This paper reports results from a study carried out in Italy, in the framework of a national project, to assess efficiency and identify factors affecting the removal of pharmaceuticals in STPs. Twenty-six drugs belonging to various therapeutic classes, and two metabolites, were listed according to priority depending on predicted environmental loads. Occurrence and RR of these "priority pollutants" was monitored in six STPs in Italy, the seasonal variability was evaluated and, last, the distribution and fate of residual pharmaceuticals in the receiving surface waters was studied.

Experimental Section

Prioritization of the Pharmaceuticals. A preliminary selection identified the pharmaceuticals for human use most likely to cause environmental problems in Italy (Table 1). The selection involved ranking the predicted environmental loads of the active substances, calculated by multiplying sales figures by the rate of metabolism in man. We used official Ministry of Health prescription data (*1*) to estimate sales. By correcting for the percentage of excretion as the parent compound after administration in man, annual sales were converted to predicted environmental loads (*2*, *3*). The drugs with the highest predicted loads were considered for analysis in the environment.

A group of "historical" molecules (diazepam and carbamazepine, i.e., drugs already measured in the environment in Europe during occasional surveys and selected by a literature search) (*2*, *3*) were also included, together with a group of molecules with documented high biological activity, and thus potential toxicity despite a low environmental load, like estrogens and anticancer drugs (17α-ethinylestradiol, cyclo-

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10.1021/es050991m CCC: $33.50
Published on Web 11/25/2005

TABLE 1. List of "Priority Pollutants" (Including the Metabolites Clofibric Acid and Demethyl Diazepam and the Natural Estrogens 17β-Estradiol and Estrone)

therapeutic class		pharmaceuticals	therapeutic class	pharmaceutical
antibiotics for human use	macrolides–lincosamides	clarithromycin	cardiovascular	atenolol
		erythromycin		enalapril
		spiramycin	CNS drugs	diazepam
		lincomycin		carbamazepine
	quinolines	ciprofloxacin	diuretics	furosemide
		ofloxacin		hydrochlorothiazide
	pencillins	amoxycillin	estrogens	17α-ethinylestradiol
	sulfamides	sulfamethaxole	gastrointestinal	omeprazole
antibiotics for veterinary use	macrolides	oleandomycin		ranitidine
		tilmicosin	lipid regulators	bezafibrate
		tylosin	metabolites	clofibric acid
	tetracyclines	oxytetracycline		demethyl diazepam
anticancer		cyclophosphamide	natural estrogens	17β-estradiol
		methotrexate		estrone
antiinflammatory		ibuprofen		
bronchodilator		salbutamol		

FIGURE 1. Sewage treatment plants (STPs) sampled in Italy.

phosphamide, methotrexate). The natural estrogens 17β-estradiol and estrone were included in the list, to study the total estrogenic activity of the effluents. A group of frequently used veterinary drugs in Italy were also included (*2*, *3*), to assess the possible contribution of veterinary medicines. Two metabolites were considered: clofibric acid, the main metabolite of clofibrate, and demethyl diazepam, a metabolite of diazepam.

This process resulted in the selection of 26 pharmaceutical substances, belonging to 11 different therapeutic classes, and two metabolites.

Sampling Protocol. Six STPs were chosen in towns spread over different Italian locations, to assess the pattern of contamination on a national level (Figure 1). The STPs in Naples, Latina, and Cuneo were sampled in winter 2004 (January–March), those in Cagliari and Varese Lago in

TABLE 2. Characteristics of the STPs

STPs	population	flow rate (m^3/day)	type of waste treated	effluent discharge
Cagliari	270000	86700	domestic	Mediterranean Sea
Naples	840000	181000	domestic	Mediterranean Sea
Latina	45000	19000	domestic	Mediterranean Sea
Cuneo	140000	31000	domestic	River Po
Varese Olona	120000	23000	domestic	River Olona
Varese Lago	110000	40000	domestic and industrial	Lake Maggiore

summer 2004 (June−September), and the STP in Varese Olona was sampled in both seasons. The STPs were all equipped with pretreatment and primary and secondary treatment facilities, i.e., primary settling and activated sludge processes. Detailed information on "population equivalents", or "units of population connected" for the STPs mainly receiving domestic wastes, flow rates, and the type of waste received by each plant are reported in Table 2. We sampled the influents and the effluents of all the STPs for mass balance calculations. In Varese Olona we also sampled the river receiving the treated water. For each plant, 24-h composite samples of the influents and effluents were obtained by pooling water collected every 20 min by automatic sampling. All the plants were sampled in dry weather conditions. One sample of influent and one of effluent were collected from each plant. Composite samples of surface waters were obtained by pooling samples collected every 20 min during a period of 2 h. Timing the sampling took into account the residence time of the wastewater in the plant. Influents were collected from time 0, for 24 h, and effluents were sampled for 24 h with a delay determined by the retention time of the wastewater in the STP (18 h in the Varese Olona plant). Rivers were sampled starting 12 h after the beginning of the sampling of the effluents. The River Olona, receiving the effluent from the Varese Olona plant, was sampled in three sites, before the plant (site 0), 100 m after it (site 1), and 1000 m further down (site 2). The sampling sites were carefully chosen taking into account parameters, such as river flow rate (0.5 m^3/s) and deepness (0.15 m), to guarantee a complete mixing of the effluent in the river water.

Water samples (2 L each) were transferred into glass flasks and kept at +4 °C in the dark. Analysis were performed within 2 days. Before extraction, aqueous samples were filtered on a glass microfiber filter GF/A 1.6 μm (Whatman, Kent, U.K.). Particulate matter was collected on filters and dried before extraction. Water samples and particulate were subsequently analyzed for the presence of pharmaceuticals.

Analysis of the Pharmaceuticals. A specific multiresidue analytical method was set up to measure pharmaceuticals in waste and surface water (*3*, *25*). Briefly, the pharmaceuticals were measured by reversed-phase liquid chromatography−tandem mass spectrometry (HPLC−MS/MS), after combined extraction by two SPE columns, an Oasis MCX (60 mg, Waters Corp., Milford, MA) at pH 2.0 and a Lichrolut EN (200 mg, Merck, Darmstadt, Germany) at pH 7.0. A Luna C8 column 50 mm × 2 mm i.d., 3 μm particle size (Phenomenex, Torrance, CA) was used; the mass spectrometer was an Applied Biosystem−SCIEX API 3000 triple quadrupole ($Q_1q_2Q_3$) equipped with a turbo ion spray source (Applied Biosystems−Sciex, Thornhill, ON, Canada). Analysis was done in the multiple reaction monitoring mode, in positive and negative ionization mode. Three deuterated internal standards were used: salbutamol-d_3, for quantification of the pharmaceuticals analyzed in the positive ion mode, and ibuprofen-d_3 and 17β-estradiol-d_2 for compounds analyzed in the negative ion mode. Recoveries of the pharmaceuticals generally exceeded 70%, variability of the method was below 8%, and limits of quantification (LOQ) were lower than 1 ng/L, with few exceptions (amoxycillin 8.7 ng/L, 17β-estradiol 1.7 ng/L, and 17α-ethinylestradiol 4.8 ng/L).

TABLE 3. Loads in STP Influents and Effluents (Medians and Ranges of Six Plants)[a]

	load in influent (mg/day/1000 inh)		load in effluent (mg/day/1000 inh)	
pharmaceutical	median[b]	range[b]	median[b]	range[b]
amoxycillin	13	nd−88	nd	nd−68
atenolol	494	134−1029	281	155−966
bezafibrate	50	20−682	29	4−79
carbamazepine	12	nd−386	28	nd−422
cyclophosphamide	nd	nd	nd	nd−1
ciprofloxacin	259	120−507	97	37−271
clarithromycin	21	nd−46	55	nd−421
clofibric acid	nd	nd−25	0.4	nd−18
demethyl diazepam	1.1	nd−19	1.6	0.5−13
diazepam	0.4	nd−1.4	0.5	nd−1
enalapril	31	nd−61	1.2	nd−58
erythromycin	nd	nd−1	5	nd−161
17β-estradiol	nd	nd−4	nd	nd
estrone	5.4	nd−28	6.4	nd−20
17α-ethinylestradiol	nd	nd	nd	nd
furosemide	277	9−835	195	72−644
ibuprofen	122	nd−324	28	nd−162
hydrochlorothiazi de	354	58−845	415	55−745
lincomycin	3.4	nd−65	5.4	0.5−183
methotrexate	nd	nd−3	nd	nd
oleandomycin	nd	nd−0.2	nd	nd−0.8
ofloxacin	360	83−614	233	28−268
omeprazole	nd	nd	nd	nd
oxytetracycline	nd	nd	nd	nd
ranitidine	188	87−520	96	21−266
salbutamol	4.3	1−9	4	2−8
spiramycin	4.8	nd−47	35	12−418
sulfamethoxazole	65	nd−209	10	nd−304
tilmicosin	nd	nd	nd	nd
tylosin	0.1	nd−2	nd	nd−1.4

[a] The loads were normalized by the population equivalent of each plant and expressed as mg/day/1000 inhabitants. [b] nd, not detectable (below the LOQ).

The filters containing the particulate obtained by filtration of the aqueous samples were dried at room temperature and extracted three times with 20 mL of methanol under sonication. The supernatant was dried under an air stream, redissolved in 100 μL of 0.01% acetic acid in MilliQ water, and analyzed as described for the aqueous samples.

Results and Discussion

Pharmaceuticals in STPs. The prioritization procedure resulted in the selection of 26 pharmaceutical substances, belonging to 11 therapeutic classes (the "priority pollutants"). Two metabolites and the natural estrogens 17β-estradiol and estrone were also included in the list (Table 1).

Concentrations of the pharmaceuticals in STP influents and effluents were multiplied by the flow rates, to obtain loads for each of the six plants, and normalized for the population equivalent of the plants. Median and range of the load of each pharmaceutical, expressed in mg/day/1000 inhabitants, are reported in Table 3. Ciprofloxacin, ofloxacin, sulfamethoxazole, ibuprofen, atenolol, furosemide, hydrochlorothiazide, ranitidine, and bezafibrate were the most

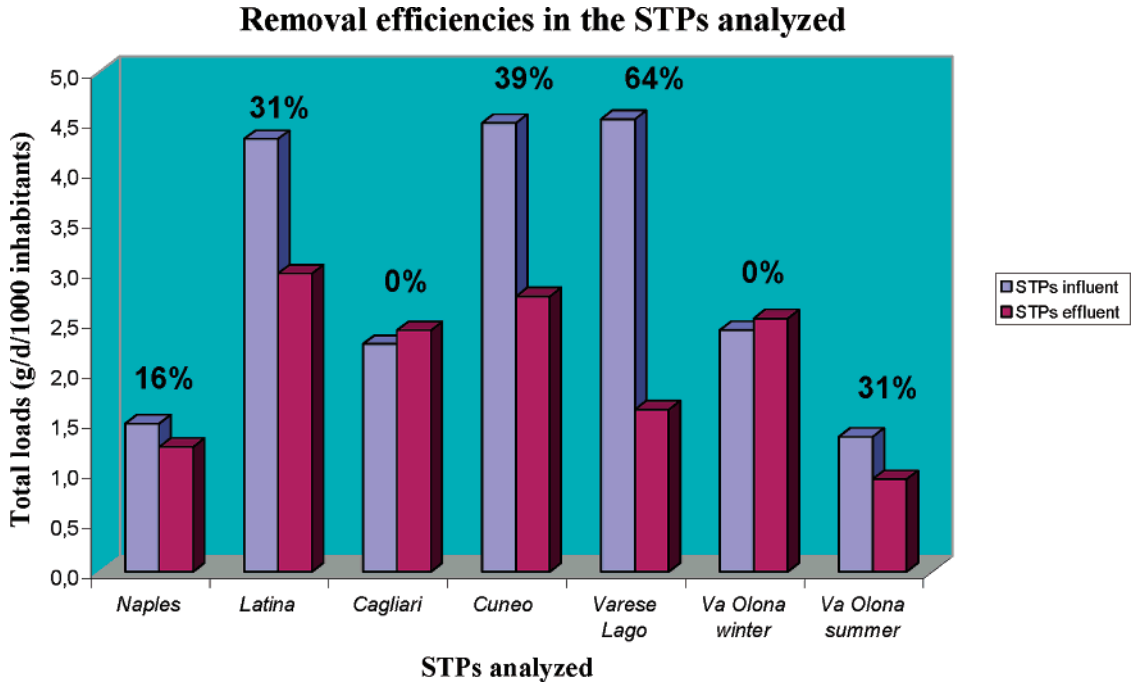

FIGURE 2. Removal rate in STPs. Total loads of the pharmaceuticals were normalized for population equivalents and expressed as g/day/1000 inhabitants.

abundant pharmaceuticals. Their median loads ranged from about 50 to 500 mg/day/1000 inhabitants in influents and from about 30 to 400 mg/day/1000 inhabitants in effluents, with peak values for atenolol exceeding 1 g/day/1000 inhabitants. These values are comparable with those described by Ternes in Germany (*5*) who reported loads in the same range as us for carbamazepine and clofibric acid but higher for bezafibrate and ibuprofen.

The STP effluents still contained pharmaceuticals that were therefore discharged in the receiving water. The total load (sum of the loads of the 26 pharmaceutical substances and the two metabolites) discharged through the STP effluents was in the range of 1−3 g/day/1000 inhabitants (Figure 2). Therefore about 60−180 kg of pharmaceutical substances reach surface waters this way every day in Italy.

Seasonal Variability. Total loads of the pharmaceuticals in STPs are reported in Figure 2. In STPs sampled in winter, (Naples, Varese Olona, Cuneo, and Latina) loads were, respectively, 1.5, 2.4, 4.5, and 4.3 g/day/1000 inhabitants in influents, and 1.2, 2.5, 2.7, and 3 g/day/1000 inhabitants in effluents. In STPs sampled in summer (Cagliari, Varese Lago, and Varese Olona) loads were 2.3, 4.5, and 1.3 g/day/1000 inhabitants in influents and 2.4, 1.6, and 1 g/day/1000 inhabitants in effluents.

A comparison between winter and summer loads could be done for the Varese Olona plant, which was the only one sampled in both the seasons. Differences were not statistically significant. However, in this plant, the total influent load in summer was about half that in winter (1.5 vs 3 g/day/1000 inhabitants), probably because of a higher RR (see below) and less use of pharmaceuticals, particularly antibiotics, in summer than winter. In fact, while for several pharmaceuticals the extent of contamination can be anticipated continuously during the year, for others seasonal variability can be expected. Table 4 reports winter and summer loads in the influent of the Varese Olona plant for the most abundant pharmaceuticals. Atenolol, furosemide, hydrochlorothiazide, and ranitidine had comparable loads in winter and summer, while ibuprofen, ciprofloxacin, ofloxacin, and sulfamethoxazole had lower loads in summer. This is consistent with their patterns of use, which is constant over the year for beta-blockers (atenolol), diuretics (furosemide and hydrochlorothiazide), and antiulcer drugs (ranitidine), but seasonal, with peaks in the winter, for antibiotics (ciprofloxacin, ofloxacin, and sulfamethoxazole) and anti-inflammatory (ibuprofen).

TABLE 4. Winter and Summer Loads of the Most Abundant Pharmaceuticals in the Varese Olona Influent

pharmaceuticals	winter loads (mg/day/ 1000 inh)	summer loads (mg/day/ 1000 inh)	difference (%)
atenolol	494	345	−30
furosemide	101	85	−16
hydrochlorothiazide	251	354	+40
ranitidine	87	128	+47
ciprofloxacin	490	259	−47
ibuprofen	122	20	−84
ofloxacina	373	84	−77
sulfamethoxazole	209	0	−100

Removal of Pharmaceuticals in STPs. The role of STPs in the removal of pharmaceuticals from wastewater was investigated by mass balance calculations. RR were calculated by comparing the load of each drug in influents and effluents in each plant. Considering the total loads, RR were generally less than 40%, with the exception of the plant in Varese Lago (64%) (Figure 2). In two plants (Varese Olona and Cagliari) the RR was zero. RR were 0%, 16%, 31%, and 39% in the four STPs sampled in winter and 0%, 31%, and 64% in those sampled in summer. When a comparison was possible (STP in Varese Olona), RR were higher in summer than winter (31% vs 0%), in line with a temperature-dependent increase of microbial activity (average temperatures 9.7 °C in winter and 18.6 °C in summer).

Table 5 reports medians and ranges of the RR for each pharmaceutical in the six plants, classified according to the season. Pharmaceuticals could be grossly divided into three groups. A first group had RR higher in summer than in winter and included amoxicillin (median of about 75% in winter and 100% in summer), atenolol (10% and 55%), bezafibrate (15% and 87%), enalapril (18% and 100%), furosemide (8%

TABLE 5. Winter and Summer Removal Rates (RR) in STPs

	winter RR (%)		summer RR (%)	
pharmaceutical[a]	median	range	median	range
amoxycillin	75	49−100	100	100
atenolol	10	0−21	55	36−76
bezafibrate	15	0−66	87	0−98
carbamazepine	0	0	0	0
ciprofloxacin	60	45−78	63	53−69
clarithromycin	0	0−24	0	0
clofibric acid	30	0−30	<0.36[b]	<0.36[b]
enalapril	18	4−31	100	69−100
erythromycin	0	0	0	0
estrone	0	0−29	0	0
furosemide	8	0−17	54	15−62
ibuprofen	38	25−72	93	0−100
hydrochlorothiazide	24	0−77	44	0−51
lincomycin	0	0	0	0
ofloxacina	43	0−62	57	33−66
ranitidine	39	0−76	84	72−89
salbutamol	0	0	0	0−12
spiramycin	0	0−11	0	0
sulfamethoxazole	17	0−84	71	71

[a] For cyclophosphamide, demethyl diazepam, diazepam, 17β-estradiol, 17α-ethinylestradiol, methotrexate, oleandomycin, omeprazole, oxytetracycline, tilmicosin, and tylosin, the RR could not be assessed because concentrations in influents or effluents were below the LOQ. [b] LOQ (<0.36) reported was referred to ng/L.

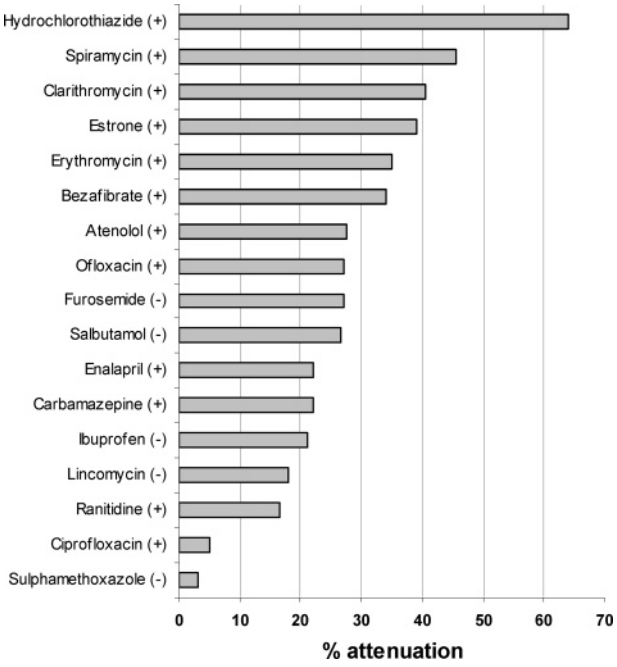

FIGURE 3. Percentage of attenuation in surface water (median values) and occurrence in the particulate (+ or −).

and 54%), ibuprofen (38% and 93%), ranitidine (39% and 84%), and sulfamethoxazole (17% and 71%). A second group had RR similar in summer and winter, and included ciprofloxacin (60%), hydrochlorothiazide (30%), and ofloxacin (50%), and a third group had a RR close to zero in both seasons, and included carbamazepine, clarithromycin, erythromycin, lincomycin, salbutamol, and spiramycin, plus estrone.

In our hands, the median RR for clofibric acid was 30%, similar to the values reported in the literature (*5*, *15*). For amoxycillin we found relatively high RR in STPs, in agreement with the low environmental stability described for this compound (*3*, *26*). The levels we report for bezafibrate, ibuprofen, and sulfamethoxazole are similar to those previously reported in Germany, Spain, and Brazil (*5*, *11*, *15*). For carbamazepine, our results are consistent with previous work describing the resistance of this molecule to treatments in STPs (*5*, *14*, *15*) and its prolonged persistence in the environment (*19*). In the STPs we studied, estrone was also not degraded, in agreement with previous reports (*9*, *11*, *16*). The fluoroquinolones ciprofloxacin and ofloxacin had similar RR in summer and winter of about 50−60%, in line with previous results, suggesting that their removal in STPs is mainly due to sorption on the sludge (*27*, *28*).

However, it must be taken into account that RR can be affected by the time proportional sampling method that can lead to a systematic inaccuracy of the influent loads. The typical 24-h dry flow pattern varies by a factor of 2 between night minimum and daily maximum, and the concentration variation is expected in a similar range. The consequence could be a systematic underestimation by 5−15% of the influent load, that could directly propagate to the estimated RR.

Residual Pharmaceuticals in Surface Waters. To study the presence and fate of pharmaceuticals in the environment after discharge from the STP, we analyzed samples of surface water of a river receiving the effluent. The River Olona, receiving the effluent from the Varese Olona STP, was sampled in three sites, before the plant (site 0), 100 m after it (site 1), and 1000 m further down (site 2), once in winter and once in summer. Loads were calculated by multiplying concentrations in surface water by the river's mean flow rate (about 0.5 m^3/s). For each pharmaceutical we calculated a percentage of "attenuation" as the difference in the load between site 1 and site 2, after correction for the background measured at site 0. STP effluents were analyzed on the same occasions. Since we found no seasonal differences in the percentage of attenuation in the river, data were pooled and expressed as medians (Figure 3). The fate of a compound in surface waters is affected by at least two major factors, degradation (biodegradation, photodegradation, and chemical degradation) and distribution (partition in different compartments, such as sorption or volatilization). To distinguish between these factors, we also measured pharmaceuticals in the particulate obtained by filtration of the surface water, adapting the analytical method used for aqueous samples. Since this method was not specifically designed for particulate, data were only expressed qualitatively (presence/absence of the pharmaceuticals).

The loads measured at site 1 were comparable to those in STP effluents.

Analyzing pharmaceuticals along the river and comparing values at sites 1 and 2 (about 1 km apart), we generally noted a higher percentage of attenuation (from 30% up to 60%) for molecules also found in the particulate (hydrochlorothiazide, bezafibrate, spiramycin, clarithromycin, estrone, and erythromycin), indicating that in this group both sorption and degradation might contribute to the attenuation (Figure 3). However, some of these molecules (spiramycin, clarithromycin, estrone, and erythromycin) were not significantly degraded in STPs, suggesting sorption as the major factor in their "disappearance" from surface water. A second group of compounds had a lower percentage of attenuation (<30%) and included molecules with documented environmental persistence and/or stability in water, like carbamazepine (*14*, *15*), atenolol (*29*), furosemide (*30*), enalapril (*31*), and ranitidine (*32*). Atenolol, carbamazepine, enalapril, and ranitidine were also detectable in the particulate (sorption was therefore considered important for their attenuation), while furosemide was not, possibly indicating a greater role for degradation. As already reported ofloxacin and ciprofloxacin were sorbed to the particulate (*27*, *28*), thus confirming sorption as important for their removal from wastewater. Ibuprofen, however, which is reported to be easily

TABLE 6. Summary of Loads and Removal Rates (RR) in STPs and Attenuation Rates and Residual Loads in Surface Water for the Most Abundant Pharmaceuticals

pharmaceutical	load in influent (mg/day/1000 inh)[a]	RR in STP (%)[a]	residual load in effluent (mg/day/1000 inh)[a]	attenuation in river (%)[a]	residual load in surface water (mg/day/1000 inh)[a]	occurrence in particulate (+/−)
atenolol	494	21	281	28	257	+
ofloxacin	360	57	233	27	94	+
hydrochlorothiazide	354	44	415	64	197	+
furosemide	277	15	195	27	66	−
ciprofloxacin	259	63	97	5	224	+
ranitidine	188	72	96	17	33	+
ibuprofen	122	55	28	21	35	−
sulfamethoxazole	65	24	10	3	122	−
bezafibrate	50	30	29	34	38	+
enalapril	31	69	1.2	22	6	+
clarithromycin	21	0	55	41	66	+
carbamazepine	12	0	28	22	28	+
erythromycin	5	0	5	35	3	+
spiramycin	5	0	35	46	30	+
salbutamol	4	0	4	27	2	−
lincomycin	3	0	5	18	4	−

[a] Median values.

degraded in the environment (4), was not detected in the particulate, suggesting a role for degradation. Sulfamethoxazole, which is degraded up to 70% in STPs (*11*), and salbutamol and lincomycin, which in our hands were not degraded at all, were not detected in the particulate, thus indicating a greater role for degradation.

The attenuation rates refer to a relatively short tract of river, only about 1 km. Several pharmaceuticals (those with high attenuation rates) can therefore be expected to be completely "removed" from surface water, by sorption, degradation, or a combination of both, within a few kilometers after reaching the river. Their presence in surface water therefore results from a continuous flow, entering the aqueous environment from several inlet points. For other more molecules (those with low attenuation rates) removal is likely to be complete only after several kilometers, or never. In this case some accumulation in surface water might occur.

Table 6 summarizes loads and RR in STPs and attenuation rates and residual loads in surface water of the most abundant pharmaceuticals. To provide a general view, effluents' median loads were calculated from the median loads measured in the influents, after correction for the RR in the STPs, using "general" medians, without taking into account seasonal differences. Loads in surface water were then estimated by correcting these values for the attenuation rate in surface water. This table thus lists the priority substances most likely to cause environmental problem in Italy. Ciprofloxacin, ofloxacin, sulfamethoxazole, atenolol, ibuprofen, furosemide, hydrochlorothiazide, ranitidine, and bezafibrate were the most important, with loads of 50−500 mg/day/1000 inhabitants in the influents and estimated residual loads, after removal in STPs and in the river, of 25−280 mg/day/1000 inhabitants, which give from 1.5 to 16 kg a day if we extrapolate this result to the whole of Italy.

In conclusion, we identified a group of pharmaceuticals with "priority" for the environment in Italy, studied their RR in some STPs, and estimated the loads discharged into surface water. These drugs belong to several therapeutic categories, such as antibiotics, antiinflammatory and cardiovascular drugs, diuretics, gastrointestinal drugs, and lipid regulators. The total amount of such pharmaceuticals discharged into the environment in Italy ranged between 60 and 180 kg/day. Seasonal variations in inputs were observed in the Varese Olona plant, with heavier loads in winter, probably due to higher consumption of antibiotics. Total RR by STPs were generally less than 40%, with a seasonal difference in the Varese Olona plant. Pharmaceuticals could be grossly divided into three groups according to their behavior in STPs: one group with RR higher in summer than in winter, one group with definite RR similar in summer and winter, and a last group not removed either in winter or summer. Last, the presence and distribution of residual pharmaceuticals in water samples and particulate suggested different roles of degradation and partition in the removal of the various substances from surface water.

Acknowledgments

This work was partially supported by the University and Scientific Research Ministry (MIUR) project prot. 2002098317 (2002). The authors are grateful to Dr. Cortelezzi and Sogeiva s.p.a. for technical assistance and collaboration.

Supporting Information Available

Two pages (S2−S3) with two tables: Table 1, chemical and biological parameters of influents and effluents of the Varese Olona STP in the year 2004; Table 2, single removal rate values for each drug in the STPs. This material is available free of charge via the Internet at http://pubs.acs.org.

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Received for review May 27, 2005. Revised manuscript received September 30, 2005. Accepted October 27, 2005.

ES050991M