ISIS Report 02/10/12

Pharmaceutical Cocktails Anyone?

Widespread pollution of drinking water by unregulated discharges of pharmaceuticals is potentially damaging to health and the environment Prof. Joe Cummins

Pharmaceutical drugs in wastewater and drinking water

Pharmaceuticals are synthetic or natural chemicals found in prescription medicines, over-the-counter therapeutic drugs and veterinary drugs. The ubiquitous use of pharmaceuticals (both prescribed and over the counter) has resulted in the continuous discharge of pharmaceuticals and their metabolites into wastewater. They are introduced through sewage, which carries the excreta of individuals and patients who have used these chemicals, from uncontrolled drug disposal (e.g. discarding drugs into toilets) and from agricultural runoff in livestock manure. In addition, pharmaceuticals may be released into water sources in the effluents from poorly controlled manufacturing or production facilities.

Advances in the sensitivity of analytical methods have led to the detection of pharmaceuticals in wastewater, various water sources and some drinking-waters. Concentrations in surface waters, groundwater and partially treated water were typically less than 0.1 µg/l (100 ng/l), whereas concentrations in treated water were generally below 0.05 µg/l (50 ng/l).

The available data indicate that there is a substantial margin of safety between the very low concentrations of pharmaceuticals in drinking-water and the minimum therapeutic doses. Based on this finding, the World Health Organization (WHO) deems it unnecessary to develop formal contamination standard values for pharmaceuticals in its Guidelines for drinking-water quality; and concerns over pharmaceuticals in drinking-water should not divert water suppliers and regulators from other priorities for drinking-water safety, most notably microbial risks such as bacterial, viral and protozoan pathogens, and other chemical risks such as naturally occurring arsenic and excessive levels of fluoride [1, 2].

I will take issue with the WHO conclusion that drugs and their breakdown products are too low to impact human health. The drugs most frequently appear in drinking water as mixtures whose combined effect have not been considered by health authorities even though such mixtures have been shown to be biologically active in aquatic organisms as discussed in this article. (Synergistic effects due to mixtures of low concentrations of environmental pollutants are already well recognized, see [3] Super-Toxic Cocktails, *SiS* 43).

Among the drugs identified in water supplies are antibiotics, analgesics and anti-inflammatories, beta-blockers, hormones, statins, selective serotonin reuptake inhibitorsantiepileptic, diuretics, anti-asthmatics, antidepressants, antineoplastics, antipsychotics, stimulants, sedatives, and anticoagulants [4, 5].

Studies in the United States

A survey of groundwater samples from the United States showed that the antibiotic sufamethoxazole was detected (at a maximum concentration 1.11 micrograms per litre) in 23.4 % of 2000 samples at 25 sites across the country [6]. And pharmaceuticals including fluoxetine, an antidepressant and dehydronifedipine, an angina treatment, appeared in 4.3 % of the groundwater samples.

Surface drinking water sources from 49 sites across the US showed erythromycin-H_2O antibiotic in 8.1 % of the samples, along with carbamazepine anticonvulsant in 21.6% of the samples and the anti-histamine diphenhydramine an in 5.4 % of the samples. Other samples showed no contamination or smaller levels of the drugs. The levels of drugs found in the numerous samples were significant, ranging from 0.3 to 0.23 mg/L). Drugs or their breakdown products were detected in surface water levels ranging up to 176 ng/L in surface water , pre-treated surface water had somewhat reduced levels of the drugs ranging up to 147 ng/L. Drugs were not detected in treated surface water, but not considered threatening to human health [7].

Pharmaceutical compounds were detected at low concentrations in 2.3 % of 1 231 samples of groundwater used for public drinking-water supply in California. Samples were collected state-wide for the California State Water Resources Control Board's Groundwater Ambient Monitoring and Assessment (GAMA) Program. The drugs detected included acetaminophen (used as an analgesic, detection frequency 0.32 %, maximum concentration 1.89 μg/L), caffeine (stimulant, 0.24 %, 0.29 μg/L),carbamazepine (mood stabilizer, 1.5 %, 0.42 μg/L), codeine (opioid analgesic, 0.16 %, 0.214 μg/L), p-xanthine (caffeine metabolite, 0.08 %, 0.12 μg/L), sulfamethoxazole (antibiotic, 0.41%, 0.17 μg/L), and trimethoprim (antibiotic, 0.08%, 0.018 μg/L).

Groundwater from the Los Angeles metropolitan area had higher detection frequencies of pharmaceuticals and other anthropogenic compounds than groundwater from other areas of the state with similar proportions of urban land use. Half of the groundwater samples with detections of pharmaceutical compounds are from the Los Angeles metropolitan area. This primarily reflects the fact that the Los Angeles area is the largest urbanized area in the state. The median percentage of urban land use at sites with samples containing some modern groundwater in the Los Angeles area was 79%, while that of sites with samples containing some modern groundwater in the rest of the study (7%) was significantly lower. Also, artificially engineered recharge of waste water is far more prevalent in Los Angeles and has been employed longer than the rest of the state [8]. The relatively elevated levels of the drugs in groundwater are alarming. Engineered recharge of groundwater is essential in the United States but the process may lead to pollution of groundwater that is relatively free of microbes capable of remedying the pollution.

Studies from Europe

A study in the Netherlands monitored 17 common pharmaceuticals and 9 transformation products in sources including surface waters, pre-treated surface waters, river bank filtrates, groundwater samples affected by surface water and drinking waters. It detected 12 pharmaceuticals and 7 transformation products. Concentrations were generally highest in surface waters 176 ng/L, intermediate in treated surface waters and river bank filtrates and absent in produced drinking water except drinking water from river bank filtrates of phenazone. However, the concentrations of phenazone (an analgesic and antipyretic) and its environmental transformation product AMPH (at up to 35ng/L and 19ng/L respectively) were significantly higher in river bank filtrates, which is likely due to historical contamination. Fairly constant ratios were observed between concentrations of transformation products and parent pharmaceuticals [9]. In drinking water production, river bank filtration is used because it dampens peak concentrations of many dissolved components, substantially removing many micropollutants and removing, virtually completely, the pathogens and suspended solids. The production aquifer is not only fed by the river bank infiltrate but also by water percolating through covering layers. The Dutch study is important because transformation products of the drugs were measured. Such products may be as active as the parent drug or even highly toxic in comparison.

The Llobregat River in Spain receives treated waters from wastewater treatment plants, and serves as a source of drinking water for the city of Barcelona. Fifty-eight pharmaceuticals out of 74 monitored were detected in at least in one sample. In river water upstream, a majority of compounds were detected at low nanograms per litre levels. Downstream of discharge from tertiary effluents however, a few compounds were detected at levels higher than 100 ng/L, including acetaminophen (paracetomol), diclofenac (a non-steroidal anti-inflammatory drug), erythromycin (an antibiotic) and sulfamethazine (anti-microbial?). The total concentration of illicit drugs was found to be very low at both sampling sites (<50 ng L(-1)). The antibiotics ciprofloxacin and sulfamethoxazole in the river water were calculated to pose a significant threat to algae [10].

Singapore

Emerging organic contaminants (EOCs) occurring in urban runoff can negatively impact sensitive ecosystems and drinking water resources. The occurrence of 13 EOCs was characterized in the Marina Catchment, a large urban catchment approximately one-sixth the area of Singapore. The 13 EOCs included alkylphenol ethoxylate metabolites (APEMs), hormones, pharmaceuticals, bisphenol A (BPA), and a pesticide (fipronil). Several EOCs were present in the ng L(-1) range: chloramphenicol, 1-15 ng L(-1); ibuprofen, 2-76 ng L(-1); naproxen, 8-108 ng L(-1); BPA, 30-625 ng L(-1); fipronil, 1-72 ng L(-1); estrone, 1-304 ng L(-1) and estriol, 3-451 ng L(-1). The EOCs detected appear to enter canals and rivers from diffuse sources, possibly from runoff and leaking sewer lines. Estrone and estriol hormones exceeded literature-based Predicted No Effect Concentration (PNEC) values [11].

Great Lakes and Canada

An extensive survey undertaken by Dow Chemical Company of Midland, Michigan detected pharmaceutical compounds in 34 % of the surface water samples of the Great Lakes, including both prescription and non-prescription drugs, and most frequently at locations near to the point of discharge from wastewater treatment plants (WWTPs)or agricultural operations [12].

In August 2005, samples of surface water were collected at 10 sites along the Yamaska River basin in Quebec, which passes through important agricultural areas, and receives wastewater from several urban centres with populations up to 44 000. Several acidic drugs (naproxen, ibuprofen, gemfi brozil), neutral drugs (caffeine, carbamazepine, cotinine), and the sulfonamide antibiotic sulfamethoxazole were detected in the majority of the surface water samples. Acetaminophen (an acidic drug) was detected at only two sites, and sulfapyridine (sulfonamide antibiotic) was detected at only one site. Sulfamethoxazole and carbamazepine were present at the highest maximum concentrations of 578 ng/L and 106 ng/L, respectively [13].

A collaborative study was conducted in Calgary, Alberta [14]. A number of pharmaceuticals and endocrine-disrupting chemicals were detected in the WWTP effluents, at concentrations ranging from ng/L to several µg/L. Although these compounds were generally removed from WWTP effluents during treatment, some compounds such as carbamazepine were more persistent. Some target pharmaceuticals and endocrine-disrupting chemicals were detected at low ng/L levels in the surface and potable water. Currently, there is no evidence that small amounts of pharmaceuticals and endocrine-disrupting chemicals in Calgary's waterways can have a health impact on humans, but they may pose adverse chronic effects on aquatic life.

The Ontario Ministry of the Environment (MOE) conducted a survey in 2006 on emerging organic contaminants (EOCs) which included pharmaceuticals, hormones and bisphenol A .Seventeen sampling sites were selected from a cross-section of 17 drinking water systems that participate in the drinking water surveillance programme, which included 8 surface water sources from rivers; 7 from lake sources; and 2 from groundwater sources. The most frequently detected compounds (= 10%) in drinking water were carbamazepine, gemfibrozil, ibuprofen, and BPA; with their concentrations accurately determined using Integrated Database Management System (a database management system for mainframes) to be 4 to 10 times lower than those measured in the source water. The 13 most frequently detected compounds in over 10 % of the samples analysed in the source waters were: carbamazepine (50 %), gemfibrozil (33 %), BPA (22 %), ibuprofen (21 %), naproxen (21 %), lincomycin (19 %), sulfamethoxazole (18%), acetaminophen (11 %), monensin (11 %), and benzafibrate, trimethoprim, erythromycin and sulfamethazine (all at 10 %). Monensin, tylosin, tetracycline, erythromycin, enrofloxacin, lincomycin, roxithromycin and benzafibrate were detected in 2 to 9% of the drinking water samples. Carbamazepine was the most frequently detected compound in drinking water; it was in 25% of the samples from eight different sites, had a median, 95th percentile, and maximum value of 0.21, 37, and 601 ng/L, respectively [15].

The results of the MOE study are rather alarming but have been deemed not to be a matter of great concern by that Ministry. The report published in the journal *Science of the Total Environment* [15] did not identify the exact locations from which the drinking-water samples were collected. The journal editors seem to have failed to require the fundamental basis of science that experiments should be reported fully and truthfully. This is a serious abuse of science reporting which will allow bureaucrats and politicians to control and decide how and which data are to be used. Thirty three years ago, I criticized MOE and the journal *Environmental Mutagenesis* for publishing an article on mutagens in drinking water and failing to report the exact location from which samples were obtained. MOE should not have been allowed to continue a flagrant abuse of science. I am a taxpayer who pays taxes to finance such experiments, and I have learned that my very drinking water supplier Elgin water supplied samples for the study. The antibiotic erythromycin, to which I have a deadly allergy, was found at rather elevated levels in some drinking water sources and all of those sensitive to one or another of the pollutants should be informed about the contents of our drinking water. I am continuing to press MOE for the exact data on my home drinking water.

Biological activity of drinking water polluted with pharmaceuticals

Genotoxicity (DNA damage) poses a serious risk as it can lead to the development of cancers. Genotoxic potentials and the mechanisms of six pharmaceuticals frequently detected in surface water worldwide have been investigated using isogenic chicken cell lines. These pharmaceuticals include erythromycin, sulfamethazine, sulfathiazole, chlortetracycline, oxytetracycline, and diclofenac. The genotoxic effects of these pharmaceuticals were assessed through their effects on the growth kinetics of several mutant cell lines. The data indicate that the pharmaceuticals induce DNA damage that stalls DNA replication, resulting in chromosomal breaks as well as mutagenesis mediated by translesion DNA synthesis [15].

The use of antidepressants by pregnant women has been associated with autism. These and other unmetabolized psychoactive pharmaceuticals (UPPs) have also been found in drinking water from surface sources, providing another possible exposure route and raising questions about human health consequences. Gene expression patterns of fathead minnow fish treated with a mixture of three psychoactive pharmaceuticals (fluoxetine, venlafaxine & carbamazepine) in dosages intended to be similar to the highest observed conservative estimates of environmental concentrations were used to study gene expression. Microarray experiments, which simultaneously give an expression profile of many genes, were performed on brain tissue of fish exposed to individual pharmaceuticals and to a mixture of all three. Gene-class analysis testing for enrichment of gene sets involved in ten human neurological disorders was examined. Only sets associated with idiopathic autism were unambiguously enriched. UPPs induce autism-like gene expression patterns in fish. The findings suggest a new potential trigger for idiopathic autism in an overlooked source of environmental contamination [16].

Genotoxicity of effluent, before and after biodegradation, was evaluated *in vivo* in mouse bone marrow by assessing the percentage of cells bearing different chromosome aberrations. The results indicated that pharmaceuticals in wastewater included a mixture of organic compounds among which were celiprol (beta blocker), losartan (blood pressure control), enalapril (blood pressure control), buflomedil (enhanced blood circulation), losartan (blood pressure control) and carvedilol (cardiology drug); oseltamivir (anti-viral drug); sucralose and simvastatine (nutrition metabolism drug) and finally ciprofloxacin (antibiotic drug).The waste water showed a significant ability to induce DNA damage. In addition, the water induced a remarkable lipid peroxidation (LPO).The effect of chromosome aberration, as well as LPO, were significantly reduced after bioremediation of the polluted water [17].

The tissue distribution of selected serotonin reuptake inhibitors (SSRI) in brook trout exposed for 3 months to continuous flow-through primary-treated effluent before and after ozone treatment was assessed. Results showed that Na/K-ATPase activity was readily inhibited by exposure to municipal effluent before and, to a lesser extent, after ozone treatment. Moreover, the Na/K-ATPase activity was significantly and negatively correlated with brain tissue concentrations of fluoxetine ($r = 0.57$; $p < 0.03$), desmethylsertraline ($r = 0.84$; $p < 0.001$), and sertraline ($r = 0.82$; $p < 0.001$).This study reveals that SSRIs are readily available to fish and biologically active, corroborating previous findings on the serotonergic properties of municipal effluents to aquatic organisms [18]. Na/K-ATPase is an integral membrane enzyme that transports K^+ and Na^+ ions against the respective concentration gradients with the hydrolysis of ATP, and is associated with important physiological functions such as cell proliferation, volume regulation, and maintenance of the electrogenic potential of excitable tissues, i.e. muscle and nerves.

There is clear and substantive evidence that pharmaceuticals in water do impair aquatic organisms and the genotoxicity of both the pharmaceuticals and their breakdown products are likely to be injuring people and causing impairment of the nervous system.

Treatment to remove pharmaceuticals from drinking water

Constructed wetlands (CWs) are an attractive way to purify polluted water. They are low-cost wastewater treatment systems that have been used and studied for several decades in the treatment of urban sewage from small communities and several kinds of industrial wastewaters. These systems have proven to remove pharmaceuticals and personal care products (PPCPs). Microcosms of CWs were used to study PPCPs under a variety of soil and drainage conditions over a period of three years, and shown to be effective in remediating water polluted by PPCPs [19]. The effect of continuous and batch feeding on the removal of 8 pharmaceuticals (carbamazepine, naproxen, diclofenac, ibuprofen, caffeine, salicylic acid,ketoprofen and clofibric acid) from synthetic wastewater was studied in mesocosm-scale constructed wetlands (CWs) . Aquatic mesocosms, or experimental water enclosures, are designed to provide a limited body of water with close to natural conditions, in which environmental factors can be realistically studied . Batch feeding proved superior in removing pharmaceuticals from water [20].

Simultaneous *Escherichia coli* inactivation and oxidation of pharmaceuticals in simulated wastewater treatment plant effluents has been investigated using a photocatalytic treatment with titanium dioxide (TiO_2) in suspension or immobilised onto a fixed-bed reactor. TiO_2 is the naturally occurring oxide of titanium; it is a pigment used in white paint and has been studied a number of years for use in water purification. Both suspended and immobilised TiO(2) were able to simultaneously inactivate and oxidise both kinds of pollutants (bacteria and pharmaceuticals) [21].

Membrane filtration techniques, especially those using nanofiltration or reverse osmosis membranes, are among the most efficient and promising procedures for the removal of pharmaceutically active compounds from contaminated raw water sources. Despite higher operational costs, an increasing number of sewage or drinking water facilities are using membrane filtration as their final purification method. The results obtained from laboratory experiments, full-scale facilities, and mobile drinking water purification units all showed removal of pharmaceutically active compounds [22].

A high technology approach to removing pharmaceuticals is a novel methodology, termed 'capsular perstraction', which has been used to remove seven pharmaceuticals commonly found in water. The process involves the envelopment of pre-selected organic solvents within a porous hydrogel membrane to form liquid-core microcapsules, which effectively extracts a large range of compounds from the water. The results indicated rapid extraction of the seven compounds with variable efficiency. The simultaneous use of both dibutyl sebacate and oleic acid liquid-core microcapsules at a liquid volume ratio of only 4% (v/v) resulted in the following extractions within 50 minutes of capsule addition to contaminated water: furosemide 15%; clofibric acid 19%; sulfamethoxazole 22%; carbamazepine 54%; warfarin 80%; metoprolol 90% and diclofenac 100% [23].

Among the water purification methods mentioned above constructed wetlands may provide immediate relief for smaller communities. The TiO_2 photo catalyst method seems practical provided that it can be scaled up to large facilities. Membrane filtration is already employed in some countries. While capsular perstraction is still in the preliminary stages of commercialization, it may prove to be a major breakthrough.

To conclude

Much of the world's drinking water is polluted with pharmaceutical drugs or their breakdown products. WHO along with many water suppliers, maintain that the pharmaceutical pollution is not serious enough for concern even though the detrimental impacts of the exposure of aquatic organisms are well documented. The precautionary principle demands that the threat to human health and the environment should be acknowledged; and appropriate measures taken to remediate polluted water and to limit discharges from industrial sources.

Science is based on full and truthful reporting yet the Ontario Ministry of Environment choses to publish reports that cannot be independently corroborated because the exact locations of the drinking water sample collections are withheld. Journal editors should not allow this reprehensible practice to persist. The omission of information may well result in the life-threatening exposure of sensitive individuals to potent allergens or to chemicals such as those that cause autism.

WHO is seriously remiss in their role as guardian of the world's drinking-water supplies.

Addendum

I requested detailed information on the drugs polluting my home drinking water, which is supplied by the Elgin Primary Water Supply, Ontario, Canada, drawing water from Lake Erie. After a long delay, the Ontario Ministry of Environment provided detailed information on the polluting drugs. Three pharmaceutical drugs and a byproduct of plastic manufacture, bisphenol A, were detected in drinking water samples: carbamazide (an anti-epileptic) in 2 of 5 samples at around 3 ng/l, gemfibrozil (a lipid-regulating statin) in 2 of 5 samples at around 1.5 ng/l, and erythromycin (an antibiotic) in one of five samples at 116 ng/l; bisphenol A was detected in one of five samples at 56 ng/l [25].

Carbamazide was found to be toxic to algae at levels encountered in polluted environments [26]; it bio-accumulates in mussels and induces specific changes in gene transcription [27]. Water chlorination results in a chlorinated gemfibrozil that was more resistant to degradation and more toxic as anti- androgen than the parent drug [28]. Gemfibrozil caused embryo malformations in zebra fish [29]. Erythromycin was genotoxic in cutured chicken cells [30], and toxic to freshwater invertebrates and Medaka fish [31]. Bisphenol A was found to influence cell functions at levels well below that in the Elgin water supply [32]; it produced DNA adducts and modified the proteome in mice [33].

The Ontario Ministry of Environment study was conducted in 2005-2006 and published in 2011. There have been no major changes in drinking water treatment that will reduce trace chemical pollution since that study was completed. Certainly, further effort is needed to improve water treatment and to reduce the flow of pharmaceuticals into the environment.

Finally, those of us with known sensitivity to drugs such as erythromycin should be alerted to the drugs polluting our drinking water as soon as the finding is made.

References

1. World Health Organization (WHO) Information sheet: Pharmaceuticals in drinking-water 2012 http://www.who.int/water_sanitation_health/emerging/info_sheet_pharma...

2. WHO Pharmaceuticals in Drinking-water 2011 http://www.who.int/water_sanitation_health/publications/2011/pharmaceuticals_20110601.pdf

3. Saunders PT. Super-toxic cocktails.

4. Monteiro S, Boxall A. Occurrence and Fate of Human Pharmaceuticals in the Environment

in D.M. Whitacre (ed.), *Reviews of Environmental Contamination and Toxicology*, 202, DOI 10.1007/978-1-4419-1157-5_2, Springer Science +Business Media, LLC 2010

5. Brausch J, Connors K, Brooks B, Rand G. Human Pharmaceuticals in the Aquatic Environment: A Review of Recent Toxicological Studies and Considerations for Toxicity Testing in D.M. Whitacre (ed.), Reviews of Environmental Contamination and Toxicology 218, DOI 10.1007/978-1-4614-3137-4_1, © Springer Science+Business Media, LLC 2012

6. Barnes KK, Kolpin DW, Furlong ET, Zaugg SD, Meyer MT, Barber LB. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States--I) groundwater. *Science of the Total Environment* 2008, 402, 192-200

7. Focazio MJ, Kolpin DW, Barnes KK, Furlong ET, Meyer MT, Zaugg SD, Barber LB, Thurman ME. A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States--II) untreated drinking water sources. *Science of the Total Environment* 2008, 402, 201-16.

8. Fram MS, Belitz K. Occurrence and concentrations of pharmaceutical compounds in groundwater used for public drinking-water supply in California. *Science of the Total Environment* 2011, 409, 3409-17.

9. de Jongh CM, Kooij PJ, de Voogt P, Ter Laak TL.Screening and human health risk assessment of pharmaceuticals and their transformation products in Dutch surface waters and drinking water *Science of the Total Environment* 2012, 427-428, 70-7

10. López-Serna R, Postigo C, Blanco J, Pérez S, Ginebreda A, de Alda ML, Petrovic M, Munné A, Barceló D. Assessing the effects of tertiary treated wastewater reuse on the presence emerging contaminants in a Mediterranean river (Llobregat, NE Spain). *Environmental Science and Pollution Research* 2012, 19, 1000-12

11. Xu Y, Luo F, Pal A, Gin KY, Reinhard M. Occurrence of emerging organic contaminants in a tropical urban catchment in Singapore. *Chemosphere* 2011, 83, 963-9

12. Kle?cka G, Persoon C, Currie R. Chemicals of Emerging Concern in the Great Lakes Basin: An Analysis of Environmental Exposures in D.M. Whitacre (ed.), Reviews of Environmental Contamination and Toxicology, 207, DOI 10.1007/978-1-4419-6406-9_1, C Springer Science+Business Media, LLC 2010

13. Bérubé VE, Boily MH, DeBlois C, Dassylva N, Spear PA Plasma retinoid profile in bullfrogs, Rana catesbeiana, in relation to agricultural intensity of sub-watersheds in the Yamaska River drainage basin, Québec, Canada. *Aquatic Toxicololgy* 2005 26, 71, 109-20.

14. Chen M, Ohman K, Metcalfe C, Ikonomou M, Amatya P, Wilson J. Pharmaceuticals and Endocrine Disruptors in Wastewater Treatment Effluents and in the Water Supply System of Calgary, Alberta, Canada *Water Quality Research Journal of Canada* 2006, 41, 351 – 364

15. Kleywegt S, Pileggi V, Yang P, Hao C, Zhao X, Rocks C, Thach S, Cheung P, Whitehead B.Pharmaceuticals, hormones and bisphenol A in untreated source and finished drinking water in Ontario, Canada--occurrence and treatment efficiency. *Science of the Total Environment* 2011, 409, 1481-8

16. Liu X, Lee J, Ji K, Takeda S, Choi K. Potentials and mechanisms of genotoxicity of six

pharmaceuticals frequently detected in freshwater environment *Toxicology Letters* 2012, 211, 70-6.

17. Thomas MA, Klaper RD. Psychoactive pharmaceuticals induce fish gene expression profiles associated with human idiopathic autism. *PLoS One* 2012, 7, e32917. Epub 2012 Jun 6.

18. Ben Mansour H, Mosrati R, Barillier D, Ghedira K, Chekir-Ghedira L. Bioremediation of industrial pharmaceutical drugs. Drug & Chemical Toxicology. 2012 Feb 8. [Epub ahead of print]

19. Lajeunesse A, Gagnon C, Gagné F, Louis S, Cejka P, Sauvé S. Distribution of antidepressants and their metabolites in brook trout exposed to municipal wastewaters before and after ozone treatment--evidence of biological effects. *Chemosphere* 2011, 83, 564-71

20. Reyes-Contreras C, Hijosa-Valsero M, Sidrach-Cardona R, Bayona JM, Bécares E.Temporal evolution in PPCP removal from urban wastewater by constructed wetlands of different configuration: a medium-term study. *Chemosphere* 2012, 88, 161-7.

21. Zhang DQ, Gersberg RM, Zhu J, Hua T, Jinadasa KB, Tan SK.Batch versus continuous feeding strategies for pharmaceutical removal by subsurface flow constructed wetland. *Environmental Pollutants* 2012, 167, 124-31.

22. Pablos C, van Grieken R, Marugán J, Muñoz A.Simultaneous photocatalytic oxidation of pharmaceuticals and inactivation of Escherichia coli in wastewater treatment plant effluents with suspended and immobilised TiO(2).*Water Science & Technology* 2012, 65, 2016-23.

23. Heberer Tand Feldmann D. Removal of pharmaceutical residues from contaminated raw water sources by membrane filtration. Pharmaceuticals in the Environment 2008, Part V, 427-453, DOI: 10.1007/978-3-540-74664-5_27

24. Whelehan M, von Stockar U, Marison IW. Removal of pharmaceuticals from water: using liquid-core microcapsules as a novel approach. *Water Research* 2010, 44, 2314-24

25. Ontario Ministry of Environment Water Monitoring and Reporting Section Drinking Water Unit Data Summary for Pharmaceuticals in Water Survey For Raw Water and Treated Water Sample Locations as Monitored by the Drinking Water Surveillance Program Monitoring Period 2005 to 2006. Personal Communication August 2012

26. Zhang W, Zhang M, Lin K, Sun W, Xiong B, Guo M, Cui X, Fu R. Eco-toxicological effect of carbamazepine on Scenedesmus obliquus and Chlorella pyrenoidosa. *Environ Toxicol Pharmacol* 2012, 33(2), 344-52.

27. Contardo-Jara V, Lorenz C, Pflugmacher S, Nützmann G, Kloas W, Wiegand C. Exposure to human pharmaceuticals Carbamazepine, Ibuprofen and Bezafibrate causes molecular effects in Dreissena polymorpha. *Aquat Toxicol* 2011, 105(3-4), 428-37.

28. Bulloch DN, Lavado R, Forsgren KL, Beni S, Schlenk D, Larive CK. Analytical and biological characterization of halogenated gemfibrozil produced through chlorination of wastewater. Environ Sci Technol 2012, 46(10), 5583-9.

29. Raldúa D, André M, Babin PJ. Clofibrate and gemfibrozil induce an embryonic malabsorption syndrome in zebrafish. *Toxicol Appl Pharmacol* 2008, 228(3), 301-14

30. Liu X, Lee J, Ji K, Takeda S, Choi K.Potentials and mechanisms of genotoxicity of six pharmaceuticals frequently detected in freshwater environment.Toxicol Lett. 2012, 211(1), 70-6.

31. Ji K, Kim S, Han S, Seo J, Lee S, Park Y, Choi K, Kho YL, Kim PG, Park J, Choi K. Risk assessment of chlortetracycline, oxytetracycline, sulfamethazine, sulfathiazole, and erythromycin in aquatic environment: are the current environmental concentrations safe? *Ecotoxicology* 2012 Jun 19. [Epub ahead of print]

32. Welshons WV, Nagel SC, vom Saal FS. Large effects from small exposures. III. Endocrine mechanisms mediating effects of bisphenol A at levels of human exposure. *Endocrinology* 2006, 147(6 Suppl), S56-69.

33. Izzotti A, Longobardi M, Cartiglia C, D'Agostini F, Kanitz S, De Flora S. Pharmacological modulation of genome and proteome alterations in mice treated with the endocrine disruptor bisphenol A. *Curr Cancer Drug Targets* 2010, 10(2):147-54.

There are 2 comments on this article so far. Add your comment

Charles McEwan Comment left 2nd October 2012 20:08:11
A health worker a number of years ago indicated to me that there is a connection between the growth hormones used to speed up the growth of cattle and the rise of homosexuality in the population. She said it was well known in the medical profession but is not publicised due to reasons of political correctness. Do you have any information on this

Rory Short Comment left 3rd October 2012 18:06:59
We are an integral part of the biosphere and it in its turn is an integral part of the ecosphere. We evolved within the biosphere when it was in a particular state as was the ecosphere. It would therefore surely be sensible to compel anyone who wants to introduce a new substance into the ecosphere to test, to the fullest extent currently possible, for the substance's impacts on the bio and ecospheres before the introduction is authorised or not. Authorised substances would then be required to be re-evaluated on a regular basis using the latest technology and techniques. Surely the quality of human life should be the topmost priority not the monetary profits of some company.

Comment on this article

All comments are moderated. Name and email details are required.

Name

Email address

Your comments

Anti-spam question - just to prove you are human

How many legs does a spider have?

leave comments

The Institute of Science in Society, The Institute of Science in Society, 29 Tytherton Road, London N19 4PZ
telephone: **[+44 1908 696101] [+44 20 7272 5636]**

For email enquiries please see our contact details