

Potential impact of pharmaceuticals on environmental health

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For much of the last thirty years, research on the effects of chemical pollution of the environment has focused almost exclusively on conventional "priority" pollutants. These pollutants are chemicals that have specific effects on organisms, such as the impacts that organotin compounds (used in antifouling paints on ships) are known to have on marine life. There is, however, another highly variable group of chemical compounds that have the potential to cause harm but which receive relatively little attention as possible environmental pollutants. These are pharmaceuticals, including both human and veterinary drugs, and even illicit (recreational) drugs.

Presence of pharmaceuticals in aquatic systems

Around the world, thousands of tons of pharmacologically active substances are used annually but surprisingly little is known about the ultimate fate of most drugs after their intended use. A large proportion of an administered dose (up to 90%) may be excreted, unchanged, while metabolites can be converted back to the active compound via bacterial action (Jones OAH, Voulvoulis N, Lester JN. Human pharmaceuticals in the aquatic environment: a review. *Environmental Technology* 2001;22:1383-94). In addition, the general public often disposes of unused medicines through the sewage system. From published occurrence data it seems likely that a large proportion of urban sewage is contaminated with drug compounds, differing only in the type and abundance of the substances present.

Recent studies have demonstrated that many pharmaceuticals are incompletely eliminated at sewage treatment plants. The existence of drugs in surface waters, groundwater and even marine systems has been confirmed at concentrations of high ng/litre to low µg/litre, rivalling the levels of some pesticides (Daughton CG, Ternes TA. Pharmaceuticals and personal care products in the environment: agents of subtle change? *Environmental Health Perspectives* 1999;107:907-42). Drug compounds disposed of in domestic refuse can end up in landfills, where they also pose a threat to surface and underlying groundwater. Furthermore, by contrast with more regulated pollutants — which often have longer environmental half lives — the continual introduction of drugs by sewage effluent may make them "pseudopersistent", with unknown consequences for aquatic organisms that may be subjected to continuous exposure.

The possible effects of the presence of drugs in aquatic systems are unknown and, consequently, in recent years they have been attracting increasing attention as potential pollutants. The fact that any commercially produced chemical may find its

way into the environment is not surprising in itself; the interesting point about pharmaceutical pollution is that it does not result primarily from manufacturing but rather from widespread and continual use, excretion, and improper disposal of both human and veterinary medicines.

Pharmaceuticals are potentially ubiquitous pollutants because they could be found in any environment inhabited by man. As yet, there is little evidence that pharmaceuticals are present in the environment in sufficient quantity to cause significant harm, though their use is expected to grow with the completion of the human genome project and the rising age of the population. Pharmaceuticals and their metabolites are more and more likely to be found in the receiving waters of areas adjacent to human activity and therefore further research in this area is warranted.

Determining the extent of the problem

With recent advances in analytical techniques (such as gas and liquid chromatography and mass spectrometry) detailed investigation has become possible (Ternes TA. Analytical methods for the determination of pharmaceuticals in aqueous environmental samples. *Trends in Analytical Chemistry* 2001;20:419-34). The data collected in studies to date, however, rarely provide information on the various processes that determine the fate of these compounds in the system under investigation; although drug substances receive considerable pharmacological and clinical testing during development, there is a severe paucity of data on the ecotoxicity of the majority of them.

A major concern so far has been that antibiotics found in effluent from sewage treatment plants may cause increased resistance among natural bacterial populations (Willis C. Antibiotics in the food chain: their impact on the consumer. *Reviews in Medical Microbiology* 2000;11:153-60). Many antibiotic-resistant isolates of microorganisms can be found in the environment and, although the subject remains controversial, the significant increase in the number of bacterial strains resistant to multiple antibiotics has often been attributed to the irrational use of antibiotics and the increase in discharges to wastewater. The three well-established mechanisms of gene transfer (conjugation, transduction and transformation) are all believed to occur in the aquatic environment; as a result, streams and rivers could provide a source and a reservoir of resistant genes as well as a medium for their spread. In addition, some non-target organisms (such as cyanobacteria) may be adversely affected by antibiotics, which could have an indirect, adverse effect on the aquatic food chain. In view of these concerns, guidelines for new pharmaceuticals have been introduced in

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Ref. No. 03-006189

the USA and a draft on the environmental risk assessment of new pharmaceuticals is proposed for the European Union. Neither of these pieces of legislation is likely to affect environmental levels of the large number of pharmaceutical products that are already licensed for use.

The problem is further complicated by the fact that exposure to only one drug or toxicant at a time is probably a rare event. Mixtures of only a few compounds have been shown to affect ecosystems in laboratory-scale studies, but what happens in the wider environment is unknown. Most organisms are continually exposed to a range of substances, with only slight temporal and spatial variations in concentration levels. Consequently, their tolerance limits will depend on the duration of exposure to chemical (and non-chemical) stressors, many of which share the same mechanism of action and whose effects may, as a result, be additive. Therefore, risk assessments that ignore the possible cumulative actions of pharmaceuticals will almost certainly lead to a significant underestimation of risk.

Care of water sources

Increasing demands on the world's water sources will be likely to lead to greater incidences of indirect and direct water reuse situations in the future. Drinking-water is a direct route to the human body, including for any drug compounds or other pollutants that may be present. Advanced water treatment technologies such as granular activated carbon (GAC) and reverse osmosis (RO) treatment can remove drugs from potable water to the extent that they are no longer detectable, but these processes are not universally applied. Municipal wastewater is never treated in this way because of a lack of suitable technology and the high economic investment required. Furthermore, the large numbers of different compounds that are released and the wide range of their properties and effects mean that comprehensive, large-scale monitoring programmes to test for the compounds would be extremely expensive and time-consuming.

Proposed action

As the full extent, magnitude, and ramifications of the presence of drugs in the aquatic environment are largely unknown, more research is required before a clear picture emerges of the true nature and importance of the problem. It would therefore be unwise to assert that these compounds are causing a significant environmental effect until conclusive evidence is available. To this end, the focus for the future should be on proper and sufficient science for establishing occurrence, exposure, susceptibility and effects, so that sound decisions can be made regarding human and environmental health.

When evaluating pharmaceuticals, the health benefits to humans must take precedence over any potential environmental damage. It may therefore be worthwhile to focus on reduction or elimination of problems at source, with the development of clearer labelling on medicinal products and better guidelines for the disposal of pharmaceutical compounds by patients and medical professionals. This approach would have the potential benefit of improved consumer health (by minimizing the intake of active substances) as well as reduced spending on health care. Given the enormous importance of the pharmaceutical industry both to human health and the economy, any increased controls could have significant economic and social ramifications. If pharmaceuticals do eventually prove to be problem pollutants, collaboration between the medical and environmental professions would be beneficial to both parties, since a large amount of research remains to be completed before a thorough understanding of this subject is available. ■

Acknowledgements

One of the authors (OAHJ) is grateful to the UK Engineering and Physical Sciences Research Council (EPSRC) for the award of a PhD scholarship.

Conflicts of interest: none declared.