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MEDICINAL WATER? THE OCCURRENCE AND FATE OF PHARMACEUTICALS IN AQUATIC ENVIRONMENTS *A SHORT COMMUNICATION*

¿AGUA MEDICINAL? LA PRESENCIA Y EL TRANSPORTE DE COMPUESTOS FARMACÉUTICOS EN AMBIENTES ACUÁTICOS *BREVE COMUNICACIÓN*

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ABSTRACT

Although very little is known about the transport, fate and toxic effects of medical compounds in aquatic environments, the presence of these compounds in potable water sources can no longer be overlooked. We can argue that trace concentrations of drugs in the water is relatively a minor problem, however, the current and future demands on global potable freshwater supplies will probably lead to greater incidents of indirect and direct water-reuse situations at the local, regional, and cross-border levels. It is important to remark that the solution of this emerging ecological issue does not rely on new and better wastewater treatment technologies, but a new paradigm of responsibility and the understanding of the relations between anthropogenic actions and their ecological effects as well. The objective of this brief communication is to present the state of the art of research conducted in the last decade in Europe and United States concerning the presence of pharmaceuticals products in aquatic environments.

Keywords: pharmaceuticals, aquatic environments, wastewater treatment technologies, new paradigm.

RESUMEN

A pesar de que el conocimiento acerca del transporte, mecanismo de degradación y efectos tóxicos de compuestos farmacéuticos en el agua es aún escaso, la presencia de estos compuestos en diferentes fuentes de agua potable no debe ser desestimada. Podríamos esgrimir que la concentración de compuestos medicinales en el agua no es un problema relevante, sin embargo, la presente y la futura demanda global por fuentes de agua potable podría generar graves incidentes respecto al uso y reuso del agua tanto a nivel local y regional como transfronterizo. Es importante recalcar que esta problemática emergente no se resuelve al aplicar nuevas tecnologías para el tratamiento de aguas residuales; es necesario un nuevo paradigma donde el ser humano sea consciente de su responsabilidad ambiental así como de las relaciones entre sus actividades y los ecosistemas. Esta breve comunicación tiene como objetivo presentar el estado del arte de la investigación realizada en la última década en Europa y Estados Unidos concerniente a la presencia de compuestos farmacéuticos en cuerpos de agua superficial.

Palabras clave: compuestos farmacéuticos, ecosistemas acuáticos, nuevas tecnologías de tratamiento de aguas residuales, nuevo paradigma.

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1. Introduction

Research on the impact of chemical compounds has focused almost exclusively in convectional pollutants such as nutrients, heavy metals, pesticides, and sediments in the past three decades. Today, these compounds are less relevant for many first world countries because emissions have been substantially reduced through the adoption of appropriate legal measures and the elimination of many of the dominant pollution sources (Jones, 2005). In the last years, pharmaceuticals are an emerging environmental concern. These compounds are present in low concentration but might have the ability to cause harm. Accurate statistics about the production and consumption of the individual pharmaceutical compounds are not readily available because of privacy and industry competition issues. However, some crude estimates can be assembled based on the number of prescriptions that are handed out (Jjemba, 2008).

Since 1981, the pharmaceutical production trends have increased drastically in industrialized countries such as USA, Japan, Germany, France and the UK. The World Health Organization (2004) reported that the global sales of prescription and non-prescription medicines reached a total of US $316 billion in 2000. It is estimated that worldwide consumption of active compounds amount to some 100,000 tons per year (Kümmerer, 2004).

In the United States, consumer of more than the half of world´s medication, the most dispensed drugs registered 2.13, 2.82, 2.32 billion prescriptions in 2003, 2004, and 2005, respectively (Jjemba, 2008). The top 200 most prescribed drugs are sedatives, hypnotics, antipsychotics, antihypertensive, cardiovascular, and analgesics, which represent more than the 50% of the market. The worldwide medication's market is concentrated in a few therapeutic classes such as anti-ulcers, cholesterol and triglyceride reducers, antidepressants, antipsychotics, antihypertensive, and antibiotic drugs. These top therapeutic classes also reveal common problems and worldwide tendencies in our postmodern societies: daily stress, bad diet habits, increased of genetically modified food, and diseases with higher resistance to antibiotic treatments. The consumption and application of pharmaceuticals may vary considerable from country to country.

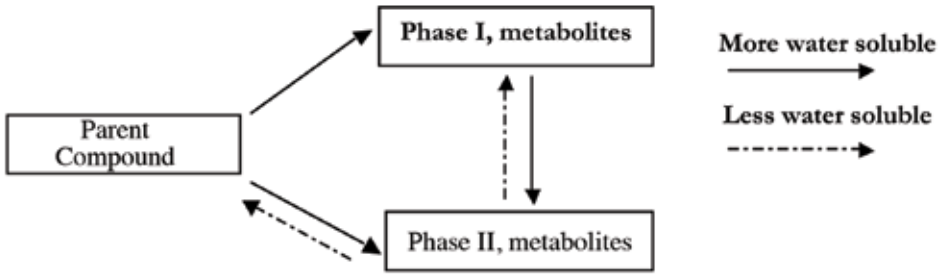
After application, some drugs are largely metabolized before they are excreted, while others are only moderately or poorly metabolized. Outdated medicines or their remains are sometimes disposed of down household drains. For example, Kümmerer (2004) reported that approximately one third of the total volume of pharmaceuticals sold in Germany is disposed of in the trash with household waste or down the drain. According to USA Today (2008), an investigation by Associated Press reported that antibiotics, anticonvulsants, mood stabilizers and sex hormones have been found in the drinking water supplies of at least 41 million USA citizens.

The objectives of this paper are: 1) to describe occurrence, fate, and eco-toxicity of pharmaceuticals; 2) to review the situation of pharmaceuticals in water supplies in Europe and United States; 3) to identify specific research/knowledge needs.

2. Occurrence and fate in the environment

Medical substances are developed with the intention of performing a biological effect. In fact, they often have the same type of physiochemical behavior e.g. lipophilic in order to be able to pass membranes, persistent in order to avoid the substance to become inactive before having a curing effect as other harmful xenobiotics (i.e. is a chemical which is found in an organism but is not normally produced or expected to be present in it) (Halling-Sørensen et al., 1998). For these reasons, the ultimate questions are: whether medical substances at low concentrations have any effects at all on organisms at different trophic levels? Are they persistent in the environment or may micro-organisms mineralize them?

Figure 1: An overview of the metabolization of parent compound into phase I and phase II metabolites. Source: Halling-Sørensen et al., 1998.



Most medical substances are metabolized to phase I or II metabolites (see Figure 1) before being retrieved from the body through the urine and may be exposed to the environment as such. **Phase I** reactions usually consist of oxidation, reduction or hydrolysis, and the products are often more reactive and sometimes more toxic than the parent drug. **Phase II** reactions change the physical chemical behavior of the substance because metabolisation always renders the metabolites more water soluble than the parent drug.

Pharmaceuticals may enter aquatic environments through several paths. Figure 2, shows sources, distribution, and sinks of these compounds in the ultimate water bodies. Active compounds present in manure will be not be discussed in this paper; nevertheless, they also represent an important non-point source pollution, especially for its potential to reach groundwater sources (F16) and surface water bodies (F15) via percolation and runoff, respectively.

In general, the fate of the medical substances may be divided in three principal possible fates: **i)** the substance is ultimately mineralized to carbon dioxide and water; **ii)** the substance is lipophilic and and not readily degradable so part of the compound will be retained in the sludge (F8); **iii)** the subtance is matabolized to a more hydrophilic form but still persistent and therefore it will pass throug the waste water treatment plant (F9) and end up in the receiving waters (F10) and may therefore affect the aquatic organisms if the metabolites are biologically active (F11).

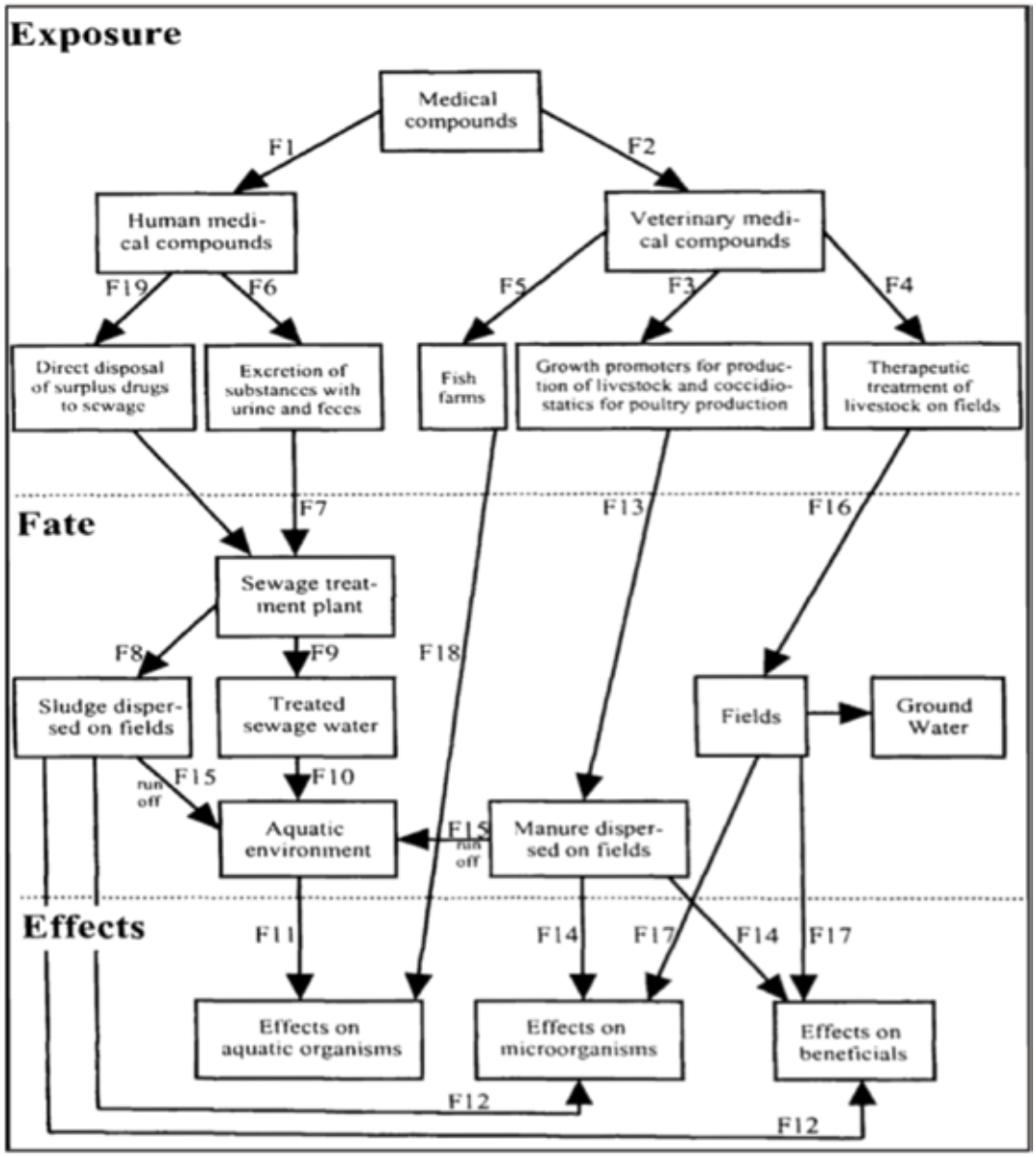
3. Eco-toxicity of pharmaceuticals on aquatic organisms

Reproductive and developmental abnormalities have been documented in aquatic organisms for several decades and recent increases in the reporting of diseases in aquatic organisms has caused concerns among scientists, managers, politicians and general public about deteriorating aquatic life (Jjemba, 2008). The active ingredients of medications have been selected or designed because of their activity against organisms. Thus it is to be expected that the following properties will be crucial for their environmental impact:

- effective against bacteria;
- effective against fungi;
- effective against (non) target higher organisms; and
- sometimes persistent.

Antibiotics have been detected in the effluent of pharmaceutical companies and hospitals in concentrations high enough, and sufficiently potent to cause adverse effects on wastewater bacteria (Hartmann et al., 1998; Farber, 2002). For most emerging contaminants, there is currently little information regarding their potential toxicological significance in ecosystems, particularly effects

Figure 2: Sources, distribution, and sinks of pharmaceuticals in the environment. Source: Halling-Sørensen et al, 1998.



from long-term, low-level environmental exposures. Table 1 shows a summary of toxic effects due to medical substances on different species from distinct trophic levels.

Table 1: Toxic effects of medical compounds.

Medical Compound or residue	Therapeutic use	Findings
Ibuprofen	Analgesic	Antibacterial activity
Streptomycin	Antibiotic	Prevent growth of blue-green algae
Chlortetracycline Oxytetracycline	Antibiotic	Prevent growth of pinto beans
Furazolidone	Medicated fish feed	Acute toxicity on crustaceans/copepods
Tinidazole	Prescribed against protozoa infections	Bacterial mutagens in the urine of patients in therapeutic treatment

Source: Modified from Halling-Sørensen et al, 1998.

4. Pharmaceuticals in water resources in Europe and United States

On the basis of the limited dataset, human drugs have only been detected in drinking water, with concentrations generally being in the ng/L range (Jones, 2005). In Europe, pharmaceuticals in water resources have been a matter of concern for three decades; extensive monitoring has been done, especially in Germany. Table 2 shows a review of the major findings of drugs in finished drinking water in several European countries and Canada.

In 1999 to 2000, the United States Geological Survey (USGS) studied the occurrence of 95 organic wastewater contaminants, including pharmaceuticals, personal care products, and other extensively used chemicals, such as detergent metabolites and insecticides. The study sampled 139 streams suspected to contain chemicals in 30 states. One or more compounds were found in 80 percent of the streams; about one-third of the streams had 10 or more chemicals. Generally, the concentrations were less than 1 μg/L. Many different chemicals in low

Table 2: Concentrations of pharmaceuticals found in finished drinking water.

Compound	Therapeutic group	Concentration (ng/L)	Country	Reference
Bezafibrate	Lipid regulator	27	Germany	Stumpf, 1996
Bleomycin	Anti-neoplastic	13	UK	Aherne, 1990
Clofibric acid	Lipid regulator	70	Germany	Stumpf, 1996
		165	Germany	Stan, 1994
		270	Germany	Heberer, 1997
		170	Germany	Heberer et al., 1996
		5.3	Italy	Zuccato, 2000
Carbamazepine	Anti-epileptic	24	Canada	Tauber, 2003

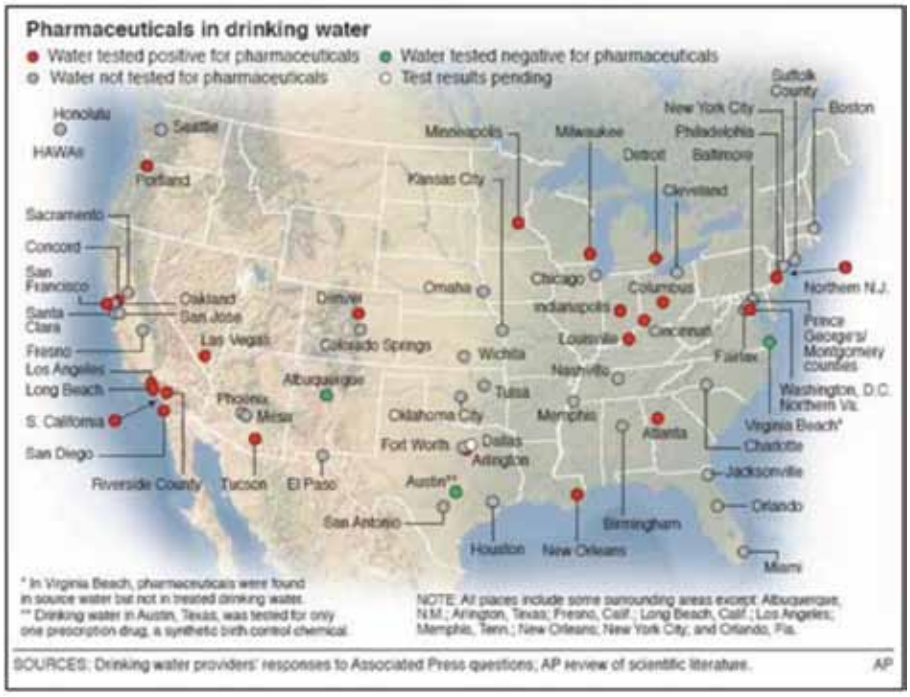
Compound	Therapeutic group	Concentration (ng/L)	Country	Reference
Diazepam	Psychiatric drug	10	UK	Waggot, 1981
Tylosin	Macrolide antibiotic, used as growth promoter for livestock	1.7	Italy	Zuccato, 2000
Phenazone	Analgesic and anti-pyretic	250	Germany	Zühlke, 2004
		400	Germany	Reddersen, 2002

Source: Modified from Jones, 2005.

concentrations commonly occurred downstream from areas of high urbanization and animal production in residential, industrial, and agricultural wastewaters. Although individual compounds were generally detected at low levels, total concentration of all organic wastewater contaminants in a single sample often exceeded 1 μg/L. (Buxton and Kolpin, 2002; Kolpin et al., 2002).

National reconnaissance has been done as well in groundwater, untreated drinking water sources, and streambed sediment. Recent local studies in metropolitan areas have shown that pharmaceuticals are present in finished drinking water. Figure 3 shows 23 cities where water contains at least one pharmaceutical compound.

Figure 3: Pharmaceuticals found in drinking water supplies within the United States: Source: Associated Press.



5. Conclusions: future research, knowledge needs, gaps, and further thoughts

The volume of pharmaceuticals that are used is expected to continue increasing worldwide as population density increases, per capita incomes rise, and new disease target groups as well as more potent compounds are identified (Jjemba, 2008). Therefore, the unintended consequences of pharmaceuticals in the environment cannot continue to be overlooked, and minimizing their impact is an enormous task that is not going to be accomplished easily. A list of topics that need to be addressed is shown below:

- Improving assessment of risks from pharmaceuticals in different trophic levels.
- Research on the effects of mixtures (in many cases drinking water is a cocktail of compounds, however studies have been only focused on the effects of individual substances).
- Research on the effects of chronic exposure to low doses.
- Nowadays, there is no regulation for pharmaceuticals. Thus, there is an urgent need to set a national primary drinking water regulation for pharmaceuticals.

Suggestions aside, it is highly important to make health care providers and patients aware of the medical and environmental consequences of our medication practices, including overprescribing. It also aims at minimizing pharmaceutical use by creating awareness about the linkages between human health and ecological health.

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