Environmental Risk Assessment of the pharmaceutical diclofenac: an approach to potential impacts in aquatic systems

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Introduction

Pharmaceuticals are emerging pollutants, these compounds are found in the environment in the ng/L- µg/L, and therefore they have been undetectable until now with modern analytical techniques (Santos et al., 2010).

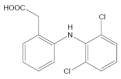

Figure 1. Molecular structure of diclofenac
Source: Jiskra (2008)

Diclofenac is a widely used pharmaceutical that was reported as the causal agent of outbreaks in populations of three species of vultures (*Gyps bengalensis*, *Gyps indicus,* and *Gyps tenuirostris*), that have declined by more than 97 % and are now classified as critically endangered . This example might will be the worst ever case of poisoning of wildlife by a chemical (Sumpter, 2010). Since this discovery, an increasing body of research has investigated the ecotoxicological effects of diclofenac on non-target organisms, and has mainly focused on acute effects on aquatic organisms. However pharmaceuticals are expected to produce effects after chronic exposure at low concentrations (Halling-Sorensen et al., 1998).

Aims

1. Assessing the risks of diclofenac in the aquatic environment
2. Finding out the best management options to avoid the risk

Methodology

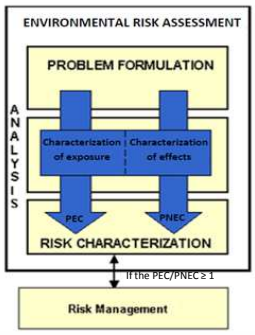

Figure 2. Risk assessment framework for the aquatic environment of pharmaceuticals.
Source: modified from Webb (2001)

So as to assess the risks and the management, data from existing literature was recompiled following the scheme on the left. Furthermore:

- The PEC (predicted environmental concentration) was compared to the MEC (measured environmental concentration) to ensure its robustness
- The PNEC was obtained by dividing the lowest effect concentration (LOEC) for the most sensitive species with an appropriate safety factor

All the data was consulted at platforms such as web of knowledge or google scholar

Characterization of exposure

- Drug use : about 940 tons are estimated to be consumed globally on an annual basis (Zhang et al., 2008)

- Behaviour in the environment:

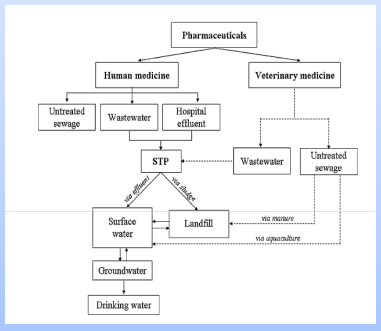

Figure 3. Possible pathways of pharmaceuticals in the environment **Source**: Santos et al. (2010)

- The most direct entry of diclofenac to aquatic environments is through discharges of sewage treatment plants (STPs) effluents
- Removal rates in STPs are highly variable (between 0-80%) (Jiskra, 2008)
- The two major sinks identified for diclofenac are photodegradation and biodegradation

Characterization of effects

- Acute effects:

Compound	Test-species	Test-type	Ecotoxicity data
Diclofenac	Bird, vulture	LOAEL, dietary intake, renal failure	0.007 mg/kg
	Vibrio fischeri (bacteria)	EC_{50}, 30 min	11.45 mg/L
	Vibrio fischeri (bacteria)	EC_{20}, Tox.Alert, 15 min	13.5 mg/L
	Vibrio fischeri (bacteria)	EC_{50}, Microtox	13.7 mg/L
	Pseudokirchneriella subcapitata = *S. capricornutum* (green algae)	NOEC, 96 h, growth	10 mg/L
	Pseudokirchneriella subcapitata = *S. capricornutum* (green algae)	LOEC, 96 h, growth	20 mg/L
	Daphnia magna	EC_{50}, 48 h	224.3 mg/L
	Ceriodaphnia dubia (crustacean)	EC_{50}, 48 h	22.7 mg/L
	Ceriodaphnia dubia (crustacean)	NOEC, 7 days, reproduction	1.0 mg/L
	Ceriodaphnia dubia (crustacean)	LOEC, 7 days, reproduction	2.0 mg/L
	Brachionus calyciflorus (rotifer)	NOEC, 48 h, reproduction	12.5 mg/L
	Brachionus calyciflorus (rotifer)	LOEC, 48 h, reproduction	25 mg/L
	Danio rerio (zebrafish)	NOEC, 10 days, ELS	4 mg/L
	Danio rerio (zebrafish)	LOEC, 10 days, ELS	8 mg/L
	Desmodesmus subspicatus (green algae)	EC_{50}, 72 h, (sodium salt)	72 mg/L
	Daphnia magna	EC_{50}, 48 h, (sodium salt)	68 mg/L
	Lemna minor (aquatic vascular plant)	EC_{50}, 7 days, growth	7.5 mg/L

Table 1. Acute ecotoxicity data for diclofenac. **Source**: modified from Carlsson et al. (2006)

- Chronic effects: cytological alterations in *Oncorhynchus mykiss at* 1g/L diclofenac = LOEC

	Liver	Kidney	Gills
Diclofenac	++ (collapse of cellular compartmentation, glycogen reduction, membrane material, dilation and vesiculation of ER, increased amount of macrophages)	+++ (glomerulonephritis with thickened basal lamina, shortening of pedicels and retraction from basal lamina, necrosis of endothelial cells, hyaline droplet degeneration)	+++ (epithelial lifting, pillar cell necrosis, hyperplasia and hypertrophy of chloride cells)

Table 2. Chronic effects tested in liver, kidney, and gills (+++ heavy reactions and/or destruction of organ; ++ strong reaction
Source: Triebskorn et al. (2004)

Risk characterization

PEC (µg/L)	MEC (µg/L)	PNEC (µg/L)	PEC/PNEC
0.05	0.08-1.4	0.01	5

Table 3. values obtained for PEC, MEC, PNEC and risk quotient
Source: own elaboration from data obtained from Santos et al. (2010)

A risk is expected because PEC/PNEC > 1

Management

Legislation:

Article 16 of the Water Framework Directive requires the European Commission to identify priority substances among those presenting significant risk to the aquatic environment, and to set EU Environmental Quality Standards (EQS)

Diclofenac was proposed to be added to the priority list, but Members of European Parliament rejected the purpose of establish an EQS for pharmaceuticals

Depuration in water treatment plants:

Advanced oxidation processes by means of combining different highly oxidizing agents, such as H_2O_2/ozone or UV/ozone, can provide the best removal rate for diclofenac (99,9%).

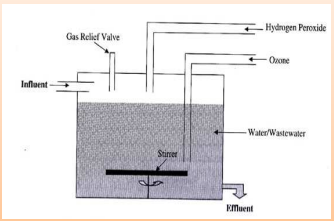

Figure 4. Design of an advanced oxidation process reactor.
Source: Ijemba (2008)

Conclusions

- Environmentally relevant concentrations of diclofenac are able to impair the normal physiology of fishes. In addition, mixture with other pharmaceuticals and toxicity of metabolites and transformation products of diclofenac is recommended to make a more fiable ERA.
- To ensure an appropriate management of the risk of diclofenac, policies more respectful with environment and advanced treatmeant in STPs should be carried out.

References:

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