The Fate and Effects of Human Pharmaceuticals in the Aquatic Environment

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Abstract

There is relatively little known about the fate of human pharmaceuticals once they are released into the aquatic environment and what adverse impacts these compounds have on exposed aquatic organisms. Both of these factors are essential in defining the potential risk pharmaceuticals pose in the aquatic environment.

For this project up to 14 human therapeutic agents were selected as representative compounds to assess both their fate and effects within model aquatic systems. Considering sediments often serve as a repository for aquatic contaminants, the interaction of the selected pharmaceuticals with sediment was assessed. The sorption of the selected pharmaceuticals was found to be highly variable. Furthermore, the solution pH and ionic strength, due to Ca^{2+}, were found to exert a large degree of influence on the extent of sorption observed. These solution parameters, among others, may therefore make it difficult to predict the fate of pharmaceuticals, in terms of their association with sediments, using standardised assessment methods alone.

There is an extensive pool of knowledge on pharmaceuticals, in terms of their pharmacological profile, so their distribution within the human body (using the volume of distribution or V_D) was compared with their distribution within a sediment / water system (using the partition coefficient or K_d). The correlation between the V_D and K_d indicated this relationship provided a reasonable basis for estimating the distribution of drugs within the test sediment / water systems. This finding suggests that further exploration of the use of pharmacological data in understanding the potential fate of pharmaceuticals in aquatic systems is warranted.

The extent of the pharmaceuticals respective desorption values was also found to be highly variable within a standard test system. Further analysis on the desorption of carbamazepine, an anti-epileptic drug, was undertaken using an isotopic dilution technique. Observations from the isotopic dilution study indicated that both contact time with sediment and the quality of organic carbon could play an important role in the potential for sediments to irreversibly sorb carbamazepine present in aquatic systems. The desorption hysteresis observed for the other pharmaceuticals also indicates considerable effort is still required to address the issue of whether sediments can be a means of reducing exposure of pharmaceuticals to aquatic organisms (a "sink") or a means of increasing exposure to sediment-dependent organisms (a "source").

The necessity for further work on investigating the role that sorption with sediments may play in the fate and effects of human pharmaceuticals was highlighted by a series of ecotoxicological assays in both sediment and solution-only systems. Sediment-dwelling freshwater midges, *Chironomus tepperi*, were exposed to carbamazepine in both short- and long-term assays. Wet weight was found to be significantly reduced during short-term assays, while the development of *C. tepperi* larvae was found to be significantly inhibited when exposed to spiked sediment, over a longer exposure period. For these assays, the aqueous phase may have been a more important route of exposure of carbamazepine for the midges.

This study has indicated that sediments are likely to play an important role in the fate of pharmaceuticals and, subsequently, their effects. However, considerably more effort is required to assess the role sediments have and how this knowledge can be linked with current regulatory ecological risk assessments.

Abbreviations

ACR	acute:chronic ratio
ANOVA	analysis of variance
ASM	Australian statistics on medicines
ATC	anatomical therapeutic catagory
ATL	atenolol
ATP	adenosine triphosphate
BSA	bovine serum albumin
Ca	calcium
C_{aq}	aqueous concentration of drug
CAF	caffeine
CBZ	carbamazepine
CEC	cation exchange capacity
CH_3CN	acetonitrile
CHOOH	formic acid
CIM	cimetidine
C_s	solid phase concentration of drug
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CV	coefficient of variation
DCF	diclofenac
DDD	defined daily dose
DIL	diltiazem
DMI	desipramine
DPH	diphenhydramine
dpm	disintegrations per minute
E-value	isotopically exchangeable value
EC	electrical conductivity
EC50	concentration where 50% effect observed relative to control
EE2	17α-ethynylestradiol
EMEA	European medicines agency
ERA	ecological risk assessment
FDA	food and drug administration
FLX	fluoxetine
g	gravities
GC	gas chromatography
H	hysteresis index
HPLC	high pressure (or performance) liquid chromatography
I	ionic strength
IBU	ibuprofen
IMI	imipramine
K_d	partition coefficient
K_f	Freundlich coefficient
K_{OC}	partition coefficient normalised to organic carbon content of sediment
K_{OW}	octanol-water partition coefficient
LC50	concentration where 50% lethality observed relative to control
LOD	limit of detection
LOEC	lowest observable effect concentration
LOQ	limit of quantitation

LSC	liquid scintillation counting
MDL	method detection limit
MHW	moderately hard water
Milli-Q	ultrapure water (18.2 $M\Omega cm^{-1}$)
ML	minimum limit of detection
MS	mass spectrometry
NaCHOO	sodium formate
Na^+/K^+-ATPase	sodium/potassium adenosine triphosphatase
NMR	nuclear magnetic resonance
NSAID	non-steroidal antiinflammatory drug
OC	organic carbon
OECD	Organisation for Economic Cooperation and Development
OTC	over-the-counter
OUB	ouabain
PAC	paracetamol
PDA	poly diode array
PEC	predicted environmental concentration
P_i	inorganic phosphate
pK_a	acid dissociation constant
PRL	propranolol
PTFE	polytetrafluoroethylene
QA	quality assurance
QC	quality control
SEI	sucrose/ethylenediaminetetraacetic acid/imidazole
SPE	solid phase extraction
SSRI	selective serotonin re-uptake inhibitor
TGA	Therapeutic Goods Administration
UV	ultraviolet
V_D	volume of distribution
WHO	World Health Organisation
WWTP	wastewater treatment plant

Acknowledgements

Having come to the end of writing this thesis, I cannot remember a longer period of constant introspection, waging a meditative conflict with my egos and their various opinions of interpreting scientific information. I am not sure if my inner critic or narcissist would have emerged the victor but I have no doubt either of these scenarios would have eventuated if not for the guidance and support that I was able to rely on. So, to briefly turn my attention away from my angst-ridden musings, I would like to pay tribute to the following people who were an unfailing social web, who provided the necessary and highly appreciated guidance, advice, support and coping mechanisms, licit or otherwise.

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PhD students hold a fairly cynical theory they are merely cheap labour. However, compared with the highly competent technicians who seemed to roam the laboratories

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Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in a university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Publication arising from this thesis

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