University of Kadiz, Spain

Erasmus Mundus Joint Master in Water Coastal Management

Tools for general environmental quality assessment: Risk assessment of contamination by caffeine, ibuprofen, carbamazepine and novobiocin

Supervisor: Prof. Dr. Laura Martin Diaz

Sobir Kodirov

1. Introduction

The environmental impact of pharmaceuticals and personal care products (PPCPs) is largely speculative. PPCPs are substances used by individuals for personal health or cosmetic reasons and the products used by agribusiness to boost growth or health of livestock. PPCPs have been detected in water bodies throughout the world [2].

The issue is that we lack a global view of what happens when these medicinal products are discharged into the environment, and further characterisation of possible exposure routes for humans is necessary. Residues of various types of medicinal products (hormones, anti-cancer, antidepressants, antibiotics, etc.) have been detected in the various compartments of the environment, which raises the question whether this represents a risk for exposed plants, animals and microbes, or for humans [3].

2. Calculation of environmental risk of the selected substances:

Acute bioassays were carried out by using: bacterium Vibrio fischeri (marine water), microalgae Isochrysis galbana (marine water), Pseudokirchneriella subcapitata (freshwater) and sea urchin Paracentrotus lividus. The table shows different values of measured environmental concentration (MEC) for each substance, concentrations affecting 50% of the sample size (EC_{50}) or half maximal inhibitory concentration (IC_{50}). The predicted no effect concentrations (PNEC) which represent the limits below which no adverse effects of exposure in an ecosystem are measured, they were calculated such as the EC_{50} values were divided by the assessment factor of 1000 (since it's an acute toxicity test with single-species data).

3. Result

The lowest PNEC value derived from lowest IC_{50}/EC_{50} of all test pharmaceuticals was found in *P.lividus (*48 h) toxicity test, followed by *P.lividus*

(1h) , *I.galbana* (96h), *P.subcapitata* (96h) *and V.fisheri* (15 min) (Table 1.). This might be the highest ecological risk, consequently.

Pharmaceuticals	IC_{50} / EC_{50} (mg/L)					Predicted no effect concentration (PNEC) (mg/L)				
	V.fisheri (15mins)	*P.subcapitata (96h)*	*I.galbana (96h)*	*P. lividus(1h)*	*P.lividus (48h)*	*V.fisheri (15mins)*	*P.subcapitata (96h)*	*I.galbana (96h)*	*P. lividus (1h)*	*P.lividus(48h)*
CAF	19600	500	405.7	3050	0.0002	19.6	0.5	0.4057	3.05	0.0000002
IBU	800	500	86.01	2065	0.00001	0.8	0.5	0.08601	2.065	0.00000001
CBZ	25200	500	500	10000	0.00001	25.2	0.5	0.5	10	0.00000001
NOV	400	500	72.8	670	0.001	0.4	0.5	0.0728	0.67	0.000001
CAF = Caffeine; IBU = Ibuprofen; CBZ = Carbamazepine;and NOV = Novobiocin										

Table 1. IC_{50}/ EC_{50} and PNCE of selected drugs for different species

The highest environmental risk was found in *P.lividus* species 48h toxicity test for different concentration of MEC of Caffeine (Table 2); Ibuprofen (Table 3); Carbamazepine and Novobiocin (Table 4). That means this species is most sensitive to caffeine among the test organisms. On the other hand *V. fisheri* showed less sensitivity. It was observed environmental risk for every pharmaceutical in each toxicity test of different species.

Caffeine	MEC ((mg/L)	MEC / PNEC				
		V.fisheri (15mins)	*P.subcapitata (96h)*	*I.galbana (96h)*	*P. lividus(1h)*	*P.lividus(48h)*
01	0.01	0.00051	0.02	0.024649	0.003279	50000.00*
02	0.07	0.003571	0.14	0.172541	0.022951	350000.00*
03	0.09	0.004592	0.18	0.221839	0.029508	450000.00*
04	0.16	0.008163	0.32	0.39438	0.052459	800000.00*
05	0.25	0.012755	0.5	0.616219	0.081967	1250000.00*
06	1.90	0.096939	3.8*	4.683263*	0.622951	9500000.00*
07	3.60	0.183673	7.2*	8.873552*	1.180328*	18000000.00*
08	4.42	0.22551	8.84*	10.89475*	1.44918*	22100000.00*
09	6.00	0.306122	12.00*	14.78925*	1.967213*	30000000.00*
10	10.00	0.510204	20.00*	24.64876*	3.278689*	50000000.00*
11	12.00	0.612245	24.00*	29.57851*	3.934426*	60000000.00*
12	13.90	0.709184	27.80*	34.26177*	4.557377*	69500000.00*
13	22.20	1.132653*	44.40*	54.72024*	7.278689*	111000000.00*
14	293.00	14.94898*	586.00*	722.2085*	96.06557*	1465000000.00*
"*" indicates the risk and need for a deeper assessment						

Table 2. Risk assessment of Caffeine drugs determined in different organisms at different level of MEC

Ibuprofen	MEC ((mg/L)	MEC / PNEC				
		V.fisheri (15mins)	*P.subcapitata (96h)*	*I.galbana (96h)*	*P. lividus(1h)*	*P.lividus(48h)*

01	0.01	0.00051	0.02	0.024649	0.003279	50000.00*
02	0.01	0.00051	0.02	0.024649	0.003279	50000.00*
03	0.01	0.00051	0.02	0.024649	0.003279	50000.00*
04	0.03	0.001531	0.06	0.073946	0.009836	150000.00*
05	0.05	0.002551	0.10*	0.123244	0.016393	250000.00*
06	0.15	0.007653	0.30*	0.369731	0.04918	750000.00*
07	0.30	0.015306	0.60*	0.739463	0.098361	1500000.00*
08	0.50	0.02551	1.00*	1.232438*	0.163934	2500000.00*
09	0.70	0.035714	1.40*	1.725413*	0.229508	3500000.00*
10	0.80	0.040816	1.60*	1.9719*	0.262295	4000000.00*
11	1.00	0.05102	2.00*	2.464876*	0.327869	5000000.00*
12	1.30	0.066327	2.60*	3.204338*	0.42623	6500000.00*
13	2.10	0.107143	4.20*	5.176239*	0.688525	10500000.00*
14	2.30	0.117347	4.60*	5.669214*	0.754098	11500000.00*
15	2.60	0.132653	5.20*	6.408676*	0.852459	13000000.00*
16	3.00	0.153061	6.00*	7.394627*	0.983607	15000000.00*
17	6.30	0.321429	12.60*	15.52872*	2.065574*	31500000.00*
18	7.10	0.362245	14.20*	17.50062*	2.327869*	35500000.00*
19	10.10	0.515306	20.20*	24.89524*	3.311475*	50500000.00*
20	20.00	1.020408*	40.00*	49.29751*	6.557377*	100000000.00*
21	24.60	1.255102*	49.20*	60.63594*	8.065574*	123000000.00*
"*" indicates the risk and need for a deeper assessment						

Table 3. Risk assessment of Ibuprofen drugs determined in different organisms at different level of MEC

Carbamazepine	MEC ((mg/L)	MEC / PNEC				
		V.fisheri (15mins)	*P.subcapitata (96h)*	*I.galbana (96h)*	*P. lividus(1h)*	*P.lividus(48h)*
01	0.03	0.001531	0.06	0.073946	0.009836	150000.00*
02	0.04	0.002041	0.08	0.098595	0.013115	200000.00*
03	0.07	0.003571	0.14	0.172541	0.022951	350000.00*
04	0.10	0.005102	0.20	0.246488	0.032787	500000.00*
05	0.10	0.005102	0.20	0.246488	0.032787	500000.00*
06	0.10	0.005102	0.20	0.246488	0.032787	500000.00*
07	0.10	0.005102	0.20	0.246488	0.032787	500000.00*
08	0.13	0.006633	0.26	0.320434	0.042623	650000.00*
09	0.16	0.008163	0.32	0.39438	0.052459	800000.00*
10	0.44	0.022449	0.88	1.084545*	0.144262	2200000.00*
11	0.63	0.032143	1.26*	1.552872*	0.206557	3150000.00*
12	0.75	0.038265	1.50*	1.848657*	0.245902	3750000.00*
13	0.70	0.035714	1.40*	1.725413*	0.229508	3500000.00*
14	0.87	0.044388	1.74*	2.144442*	0.285246	4350000.00*
15	0.95	0.048469	1.90*	2.341632*	0.311475	4750000.00*
16	1.10	0.056122	2.20*	2.711363*	0.360656	5500000.00*
17	1.50	0.076531	3.00*	3.697313*	0.491803	7500000.00*
18	1.50	0.076531	3.00*	3.697313*	0.491803	7500000.00*
19	2.30	0.117347	4.60*	5.669214*	0.754098	11500000.00*
20	4.00	0.204082	8.00*	9.859502*	1.311475*	20000000.00*
21	6.30	0.321429	12.60*	15.52872*	2.065574*	31500000.00*
Novobiocin						
01	0.33	0.016837	0.66	0.813409	0.108197	1650000.00*
"*" indicates the risk and need for a deeper assessment						

Table 4. Risk assessment of Carbamazepine and Novobiocin drugs determined in various organisms with different levels of MEC

4. Discussion and Conclusion

The use of human and veterinary pharmaceuticals is increasing. Over the past decade, there has been a proliferation of research into potential environmental impacts of pharmaceuticals in the environment [4].

Firstly, it is almost impossible to stop or rapid reduce the amount of pharmaseuticals which are discharging to the environment. That means the pharmaseuticals should be as environmentally friendly as it's possible.

Secondly, current prospective risk assessments are based on individuals exposed to a single pharmaceutical under relatively benign laboratory conditions. In reality, animals are exposed to cocktails of chemicals, including pharmaceuticals and multiple environmental stressors, which can interact synergistically, additively or antagonistically [4].

And the last but not least, it's time to focus on the issue globally not just regionally or locally. There is no consideration of rapidly developing society on assessing the impact of pharmaceuticals. Therefore in developing World the pharmaceuticals will increase even more quickly.

References

1. http://www.ntn.org.au/wp/wp-content/uploads/2015/05/NTN-Pharmaceutical-Pollution-in-the-Environment-2015-05.pdf
2. https://en.wikipedia.org/wiki/Environmental_impact_of_pharmaceuticals_and_personal_care_products
3. http://www.greenfacts.org/en/pharmaceuticals-environment/
4. http://rsbl.royalsocietypublishing.org/content/9/4/20130492