

ECOTOXICOLOGICAL EFFECTS OF PHARMACEUTICAL CHEMICALS ON AQUATIC ORGANISMS

Gheorghe Stefania, Irina Lućaciu, Iancu Vasile, Jana Petre, Rozalia Grumaz

National Research and Development Institute for Industrial Ecology - INCD ECOIND, 90-92 Panduri Avenue, 050663 Bucharest - 5, Romania, ecoind@imedecoind.ro

ABSTRACT

The scientific researches have show that the pharmaceutical ingredients are frequently present in the environment aquatic component (surface water). This result has conducted at a regulatory mobility and scientific concerns for potentially environment impact assessment of active biologically pharmaceutical compounds. Within this context and according with REACH Regulation, the present work assessed the aquatic acute toxicity (LC_{50} / EC_{50}) for the most abundantly used pharmaceuticals from the class of analgesics (ibuprophen, diclophenac, acetaminophen, naproxen, ketoprophen and indometacin), carbamazepine and caffeine. The acute toxicity biotests were conducted on fresh water fish (*Cyprinus carpio* sp. - a common species from Romanian surface waters), crustacean (*Daphnia magna* sp.) and luminescent bacteria (*Vibrio fischeri* sp.). To comply the OECD/ISO methodology, the testing procedure have followed the biological parameters: mortality, behavior and physiological modifications (for fish); immobilization and reproduction inhibition (for crustacean); inhibition and stimulation (for luminescent bacteria). Analytical control of test solutions concentrations was performed through HPLC-UV method - ECOIND methodology.



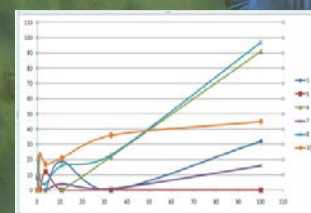
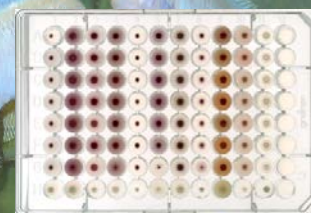
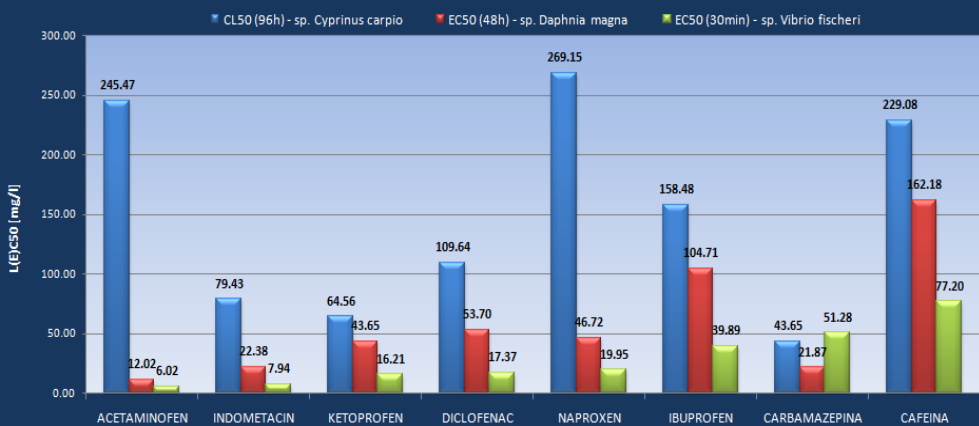
METHODS

ACUTE LETHAL TOXICITY BIOASSAYS (Romanian standard SR 13126/1994 or OECD method-C01). Determination of the mean Lethal Concentration which determine the death of half from the test organisms (fish *Cyprinus carpio*) - LC_{50}

DAPHTOXKIT F™ acute toxicity test with the freshwater crustaceans *Daphnia magna* and *Daphnia pulex* sp., according to OECD 202 and ISO 6341:1996. Assays are based on immobility or mortality of the test organisms, with calculation of the EC_{50} or LC_{50} .

MICROTOX - acute toxicity test with liquid-dried luminescent bacteria according to DIN EN ISO 11348-2. The measuring unit is the natural light output (luminescence) of the microorganisms *Vibrio fischeri* sp.

MICROBIAL ASSAY FOR RISK ASSESSMENT (MARA) - eukaryote bacteria) at toxic compounds. - a multi-species toxicity test based on responses of the n microorganisms (prokaryote s and eukaryotes)



CONCLUSIONS

According to EPA norms and National regulations for chemicals toxicity classification, the acute toxicity tests on fish have showed:

- The pharmaceutical chemicals acetaminophen, diclophenac, naproxen, ibuprophen and caffeine don't have any harm on aquatic organisms - fish *Cyprinus carpio* sp. The indometacin, ketoprophen and carbamazepine have a LC_{50} (96h) <100mg/l - toxic for fish with possibility to induce long-term effect.

- All test farmaceutical chemicals may have a toxic effect on *Daphnia magna* sp., except the ibuprophen and caffeine wich have a EC_{50} (48h) >100mg/l.

- All farmaceutical chemicals test on *Vibrio fischeri* sp. inhibit the bacteria luminiscence and we consider that induce a toxic effect on these bacteria, except the carbamazepine and caffeine wich have a EC_{50} (48h) >50mg/l.

- The carbamazepine and caffeine have a slow microbial toxicity show through MARA test (MTC 16h =>50 mg/l)

- Concerning the visual physiological aspect and behavior of test aquatic organisms we observed equilibrium lost, inactivity at stimulus, without changes of extern organs, in case o fish and lent swim and immobilization in case of *Daphnia*. Much details concerning sub lethal effects and long term effects we will obtain after chronic exposure of fish in the next researches.

