

Research Roundup

Title of the project: Identification of Pharmaceuticals of Priority Concern in Surface Waters and their Potential Effects as Environmental Pollutants

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Key issue/s addressed: Pharmaceuticals are micropollutants of global environmental concern, with potential consequences for aquatic habitats and human health. This research aims to elucidate the effects of mixtures of pharmaceuticals, representative of surface water contamination, on a selected panel of model cell lines. The project pursues the study of the principal effects of drugs, including endocrine disruption, and their possible interactions at environmentally relevant concentrations.

Objectives:

- to develop a high throughput and sensitive in vitro test to unravel principal effects of drugs within mixtures and their possible interactions at environmentally relevant levels
- to identify pharmaceuticals of priority concern, which have statistically significant effects at environmentally relevant concentrations in different in vitro model systems
- to investigate potential drug-induced endocrine disruption by using oestrogen receptor-expressing eukaryotic model cell lines
- to probe the capacity of environmentally relevant drug mixtures to interfere with cell differentiation/specialisation by testing their effects on human stem cells
- to relate subtle mixture-induced signatures in cell biology or gene expression to potential long-term insurgence of disease in animals and humans

Planned Outputs/Outcome (by when):

- standardised protocols to study principal effects of drugs within mixtures and their possible interactions at environmentally relevant levels (already achieved)
- systematic test screening of pharmaceutical mixtures to identify drugs of priority concern for waterways (2 years)
- development of multiple biosensors to routinely investigate endocrine disruption and genotoxicity in water samples (3 years)

Methodological approach:

- in vitro cytotoxicity tests using model human, fish, and bacterial cell lines
- statistical design of factorial experiments
- gene expression, proteomics, RNA interference

Key findings so far:

- a mixture of pharmaceuticals at environmentally relevant levels can affect the physiology of human and fish cells
- only a limited number of pharmaceuticals out of the firmament of water-borne drugs may represent an actual risk at environmental concentrations
- drugs can interact at environmentally relevant exposure levels, and combined effects represent a significant component in mixture toxicity
- pharmacological models of concentration addition or independent action cannot be applied to the risk assessment of complex pharmaceutical mixtures
- effects and interactions are strongly dose-dependent, toxicity data obtained with standard tests at doses of APIs that depart from real water concentrations may not be representative for environmentally relevant scenarios
- in vitro cytotoxicity data could be useful as indicators of toxicological threshold levels as determined by long-term exposure tests in simple aquatic species

Relevant theme: Effects