Effects of duloxetine and econazole on freshwater species towards individual and combined conditions

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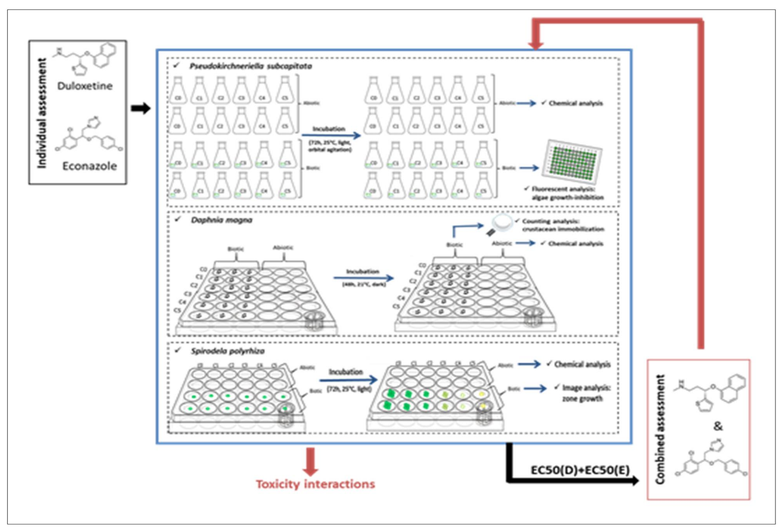
Introduction

The pharmaceutical compounds represent a diverse collection of over a thousand biologically active pharmaceuticals ingredients (APIs) used in human and veterinary medicine. Nowadays, the occurrence of pharmaceuticals in aquatic environments is a well-established issue and has become a matter of both scientific and public concern. However, there are still gaps in our knowledge on the fate and effects of these compounds in the environment. The available ecotoxicological data mainly focused on about 15 molecules, among them Paracetamol (analgesic), Ibuprofen and Diclofenac (nonsteroidal anti-inflammatory drugs), or fluoxetine (antidepressant) belong to the most studied pharmaceuticals. Many of the other drug classes are still poorly studied [1].

Evaluating API ecotoxicology is even more challenging due to uncertainties about appropriate dosages, durations of exposure, range of sensitive taxa, sensitivity of developmental stages, and toxicological endpoints [2]. A rigorous evaluation of environmental risk needs a revision of ecotoxicity data reported. More attention should be paid on the non-target organisms and the chiral nature of contaminants. More than 50% of pharmaceuticals in current use are chiral compounds. Enantiomers may exhibit differences in pharmacokinetics, pharmacodynamics and toxicity profile [3].

The aim of this study was to assess the toxicity of two chiral pharmaceuticals: the antidepressant Duloxetine and the antifungal Econazole. Toxicological profiles of both drugs was studied individually and combined, on three freshwater species—green algae *Pseudokirchneriella subcapitata, crustacean Daphnia magn*a, and aquatic plant *Spirodela polyrhiza.*

Materials and methods



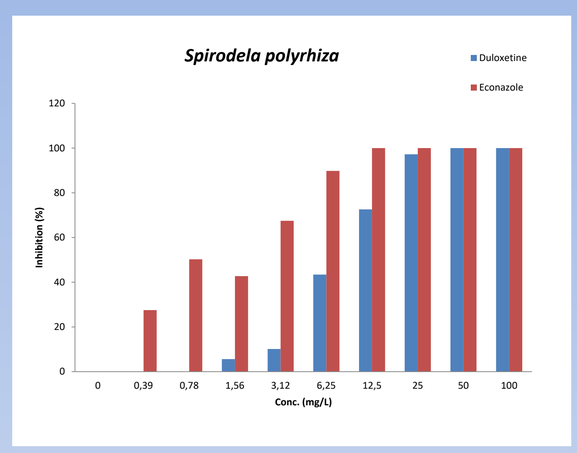
Bioassays:

- **End-points:** 72h algae growth-inhibition,
  48h crustacean immobilization
  72h duckweed growth-inhibition
- **Individual assesment:** APIs concentration ranged from 0.039 to 100 mg L−1.
- **Combined assesment**: based on EC50 values obtained for individual APIs
  Combination Index-isobologram method

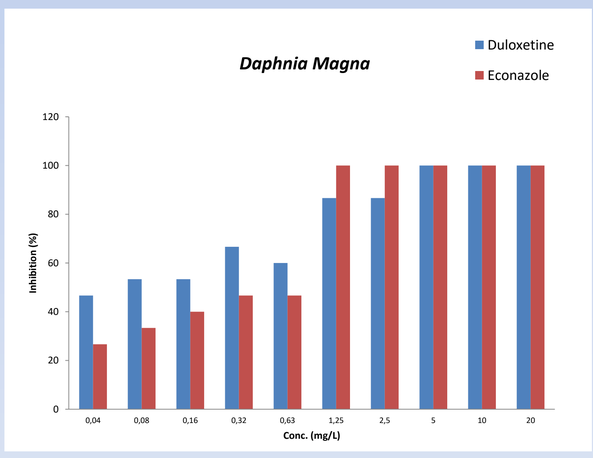
Physico-chemical characterization :

- **APIs analysis:** capillary electrophoresis (CD)
- **abiotic and biotic experiments**: effects of ligth irradiation and pH-dependence hydrolysis

Results and discussion



- ✓ Duloxetine and Econazole leading to growth reduction and significant changes in the morphology of the duckweed fronds of *S. polyrhiza*.
- ✓ Both pharmaceuticals caused significant damage in fronds showing a clear decoloration of leaves at high concentration.



- ✓ Short-term exposure produced drastic inhibition in green algae (data not show) and crustacean compare to aquatic plants.

Conclusions

The EC50 values obtained in this work permit to classify Duloxetine as toxic for crustacean and plants and very toxic for algae. In contrast Econazole can be considered as very toxic for all species studied. Results indicated that algae and crustacean were more strongly affected than the aquatic plants.

References

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