

## **P158. Assessment of binary mixture toxicity of pharmaceuticals of environmental concern to aquatic organisms**

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Pharmaceutical products have been frequently detected in aquatic environments as mixtures. They may cause direct toxic effects to aquatic organisms and indirect effects on ecosystems, due to interactions which induce additive, synergistic or antagonistic effects. The classical mathematical models of concentration addition and independent action of pollutants have been extensively used for predicting the mixture effects of chemicals of environmental relevance. The objective of this study was to assess the binary mixture toxicity of pharmaceuticals: fluoxetine and propranolol; fluoxetine and sulfadiazine; fluoxetine and caffeine, in acute tests with *Daphnia similis* carried out based on ABNT/NBR standard methods. The prediction of the acute effects to binary mixture was performed considering the mentioned mathematical models and deviations of them (synergism/antagonism; concentration level-dependent or concentration ratio-dependent), using an automated Excel spreadsheet. For the mixture of propranolol + fluoxetine, the concentration addition model best described the mixture effects, which explained most of the variability of acute toxic responses. Through the concentration level-dependent, synergism at low doses and antagonism at high doses was pointed out. The concentration addition model better described the effects of the binary mixture of sulfadiazine + fluoxetine. Synergism related to the independent action model and an antagonism related to the concentration ratio-depend were identified. For caffeine + fluoxetine mixture, the concentration addition model described slightly better the effects of this binary mixture, synergism concentration level-dependent and dose ratio-dependent were identified. We can conclude that the nature of the interaction between the compounds of a mixture depends on effect level and on the ratio in which each one is applied. Major effects of the binary mixture were detected in the zone between the effects predicted by the evaluated models. The synergism/antagonism or additivity do not depend on the similarity/dissimilarity of the mode of action of the compounds of a mixture, showing a different behaviour respect to the theoretical assumptions.

**Palabras clave:** aquatic organisms, environmental pharmaceuticals, mixtures ecotoxicology, lethal effects.

**Área temática:** Pollutants of emerging concern and nanotoxicology.