

**Title:** Environmental Impact of Ketoprofen on Key Freshwater Species: Insights on intra and inter-species response variability

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## Abstract

The ecotoxicological profile of ketoprofen (Kp) remains poorly explored. Therefore, this study aimed to provide a classification of the environmental hazard of Kp, firstly by determining the intraspecific tolerance of a laboratory-simulated cladoceran population; and secondly, by providing Kp effective concentrations (EC) for different freshwater species. The ECs were assembled into Species Sensitivity Distribution (SSD) curves to derive hazard concentrations that affect 5% of the population (HC<sub>5</sub>, probabilistic approach) and compared with the deterministic approach (lowest L(E)<sub>x</sub> divided by an assessment factor of 1000), for risk quotient determination.

Relatively to intraspecific tolerance, significant correlation (0.97) was found between daphnids baseline tolerance to copper and tolerance to Kp, a compound they had never been exposed to. This type of approach can help to outline more realistic environmental protection targets, since genetic diversity is the cornerstone of population resilience in the face of environmental change. Regarding interspecific variability, the results showed that the embryos of the fish *Danio rerio* were the most sensitive ecological receptors, while the green microalga *Raphidocelis subcapitata* was the most tolerant to Kp. The determined risk quotient was >1, meaning that Kp poses a risk to aquatic biota.

**Keywords:** pharmaceutical, nonsteroidal anti-inflammatory drugs, clonal lineages, hazard classification