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Mixture Toxicity of Anthelmintic Drugs to Water Flea (*Daphnia Magna)*

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Extended Abstract

The issue of pharmaceutical residues in the environment has been a growing concern in recent years, since these substances have been regularly detected in aquatic and terrestrial environments. Although their concentrations are quite low (around the µg/L and ng/L levels), they are continuously released are presently being classified as emerging environmental contaminants (Horvat et al., 2012; Petrovic & Barcelo 2007).

Two anthelmintic drugs belonging the group of benzimidazoles (flubendazole and fenbendazole) were chosen, as they are widely used in veterinary practice in order to treat diseases in agriculture, aquaculture and also in human medicine. These substances are designed to exhibit a specific pharmacological action (inhibition of the formation of microtubules) and data concerning their toxicity is available (Danaher et al., 2007). However they may also have unknown effects on important non-target organisms while the state of knowledge concerning the ecotoxicity of these compounds is scant. Nevertheless flubendazole and fenbendazole have been found to exhibit acute effects (at ng/L level concentrations) on an important test organism – the water flea (*Daphnia magna*). This was first reported by (Hoechst-Roussel Agri-Vet Company 1995; Oh et al., 2006) and later confirmed in our studies (data not published).

Since these substances do not occur in natural media as single, isolated substances but together with other compounds, usually of the same family or type - this study is focused on determining the effects of mixtures of the two selected veterinary drugs and considering possible synergistic-antagonistic effects (Kolpin et al., 2002). The ecotoxicity tests with *D. magna* were carried out with respect to internationally accepted OECD Guideline 202, which describes the procedure of an acute (24 and 48 hour) immobilization assay. Mixtures of pharmaceuticals were applied to the test procedures in concentrations related to their individual toxic effects. Furthermore since a complete view of the exposure and risk posed by these pollutants is impossible to ascertain using only ecotoxicological tests (García-Galán et al., 2009) - analytical techniques (HPLC) were applied to determine the exact concentrations of target compounds, thus enabling us to define their stability in the tests systems. The results were considered with regard to predictions based on the well-established concept of concentration addition (CA), which applies to mixtures of substances with a similar mode of action.

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