

Evaluation of toxic effects caused by surfactants used in nano-medicine on the aquatic environment

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Surfactants are used in various fields such as personal care products and detergents. For the production of nano-formulations, surfactants are applied to change surface properties of nano-particles or to stabilize the colloidal system. Such nano-medicines could also enhance the specific accumulation of pharmaceuticals in tumor cells or increase the passage of physiological barriers such as the blood-brain-barrier. However, surfactants could also inhibit enzymes and cause the lysis of cells due to alteration of the cell membrane.

Surfactants used in nano-medicine can enter the aquatic environment via production or incorrect disposal where they can cause toxic effects and changes in behavior. Therefore, it is essential to examine possible negative effects of surfactants on the aquatic environment. The aim of this study is thus to identify surfactants which lead to the least negative effects in aquatic organisms. For this, the zebrafish embryo *Danio rerio* is used in the Fish Embryo Toxicity test (zFET). The following surfactants were tested: polyethylen-polypropylen glycole (here: Pluronic® F127 und Pluronic® F 68), polyoxyl-40 hydrogenated castor oil (Cremophor® RH40) and polyethylen-glycol-1100-mono(hexadecyl/octadecyl)-ether (Cremophor® A25).

For Cremophor® A25, an EC₅₀-value of 0,003 % was determined at 72 hours post fertilisation (hpf). Cremophor® A25 caused approximately 100 % mortality at a concentration of 0.05 % (72 hpf). At a concentration of 0.5 %, Cremophor® RH40 leads to 100 % mortality (72 hpf) and the EC₅₀-value was 0.037 % (72 hpf). Embryos which were exposed to Pluronic® F127 and Pluronic® F68 displayed sub-lethal deformations of the head, the tail and the chorda. The EC₅₀-values of Pluronic® F68 and Pluronic® F127 were 1.599 % and 2.389 %, respectively, at 72 hpf. Interestingly, the chorion of embryos exposed to Pluronic® F68 was deformed at the lowest concentration of 1.5 % within a few minutes after the start of exposure.

Based on the EC₅₀-values, we can conclude that Cremophor® RH40 and Cremophor® A25 cause one to two times higher toxic effects on aquatic organisms than the group of polyethylen-polypropylen glycole (Pluronic® F68 und Pluronic® F127). From an eco-toxic point of view, the polyethylen-polypropylen glycole are thus more appropriate for the production of nano-medicines.

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