EMBRYOTOXICITY OF POLYMERS USED IN A NEW NANOTECHNOLOGICAL FORMULATIONS FOR THE PRODUCTION OF INSECT REPELLENT

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N, N-diethyl-m-toluamide (DEET) is the active ingredient used in several mosquito repellent formulations due to its effectiveness and low cost. Variable and unpredictable toxicity to DEET application has also been previously reported. The addition of organic solvents to the topical formulations has significantly improved DEET permeation to deeper skin layers, resulting in its systemic absorption. Therefore, novel strategies have been proposed, such as the encapsulation of DEET to polymeric nanometric systems. In this context, this study investigated the embryotoxicity of two polymers used in a new repellent formulation (polymer A: Polyoxyl 40 Hydrogenated Castor Oil and polymer B: Polyoxyl 15 Hydroxystearate) on zebrafish (*Danio rerio*) early-life stage. Polymeric systems were obtained by simple dispersion of the polymers in fish maintenance water. The fish embryo acute toxicity test (FET) was carried out according to OECD TG 236 (2013). Eight different polymer concentrations were tested in serial dilutions, ranging from 47 to 6000 mg/L for polymer A and 60 to 7500 mg/L for polymer B. Twenty fertilized eggs per concentration were exposed to 2 mL of polymer A, B or negative (maintenance water) and positive (3,4 - dichloroaniline at 4.5 mg/L) controls in triplicate. Lethal effects (coagulation of egg, lack of somite formation, lack of detachment of the tail, and lack of heartbeat) were assessed at 24, 48, 72, and 96-hours post-fertilization using a stereomicroscope. GraphPad Prism® version 5.0 was used for the statistical analysis. Both polymers induced significant lethal effects in concentration- and time-dependent ways, with $LC_{50\text{-}96h}$ of 670.4 mg/L and 134.1 mg/L for polymer A and B, respectively. These results indicated the polymer B was more toxic than polymer A. Therefore, it is essential to evaluate each constituent of new DEET-based formulations to predict or minimize possible toxic effects resulting from using them as an insect repellent.

Keywords: DEET, zebrafish, insect repellent, embryotoxicity.