

## Kinetics and toxicity of nanoplastics in *ex vivo* exposed human whole blood as a model to understand their impact on human health

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The ubiquitous presence of micro/nanoplastics (MNPLs) in the environment is considered of great health concern. Since MNPLs can cross both the intestinal and pulmonary barriers, their presence in the blood compartment is expected; consequently, understanding the interactions between MNPLs and human blood is required. In this study, to simulate more adequately the real exposure conditions, exposure was done on whole blood, and five different MNPLs: three polystyrene NPLs of around 50 nm (aminated, carboxylated, and pristine forms), together with two true-to-life MNPLs from polyethylene terephthalate (PET) and polylactic acid (PLA) of around 150 nm were used. Internalization was determined in white blood cells (WBCs) by confocal microscopy, once the different cell types (monocytes, PMNs, and lymphocytes), were sorted by flow cytometry. Reactive oxygen species (ROS) induction was determined in WBCs as well as the cytokine release in plasma. In addition, hemolysis, coagulation, and platelet activation were also determined. Results showed a differential uptake between WBC types with a higher internalization in monocytes. Regarding ROS, lymphocytes were those producing higher levels and with different NPLs. Cytokine releases were observed after exposures, with higher effects after PLA- and PS-NH<sub>2</sub>-NPL exposure. Hemolysis induction was observed after PS- and PS-NCOOH-NPL exposure, but no effects on platelet functionality were observed. Finally, it must be stated that this is the first study determining the effects of different NPL types on human whole blood and evaluating bloodstream toxicity.

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