

Can the digestion of polystyrene nanoplastics modulate their toxicological profile? Studies in three different human hematopoietic cell lines

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Plastic wastes released into the environment are degraded to micro-nano plastics (MNPLs) by the effects of physicochemical/biological processes. The main exposure route to MNPLs is via ingestion. Once MNPLs enter the human body they must pass through different compartments of the gastrointestinal tract that may affect their physicochemical properties and surface features. Thus, to effectively analyze the toxicity of MNPLs, the role of the digestion processes, must be considered. For this reason, this study aims to determine the influence of the *in vitro* digestive process on the toxicity of polystyrene nanoplastics (PSNPLs) in three different human leukocytic cell lines: Raji-B (B-lymphocytes), TK6 (lymphoblasts), and THP-1 (monocytes). The *in vitro* digestion process was performed on pristine polystyrene (dPSNPLs) and on its fluorescent counterpart (dFPSNPLs). Using transmission electron microscopy (TEM) and scanning electron microscopy (SEM) we have determined that all particles are spherically shaped, with similar appearance and sizes. Nevertheless, the digested particles show a relevant tendency to agglomerate. The hydrodynamic radius (measured by Dynamic Light Scattering, DLS), shows that digested particles have a larger hydrodynamic size, and the polydispersity index (PDI) indicates that the non-digested particles are more monodisperse. These results agree with the results of the Z-potential showing that the digested particles have less Z-potential.

Cell uptake was evaluated with the fluorescent polystyrene (FPSNPLs) and the digested version (dFPSNPLs) by flow cytometry and confocal microscopy. Results show that the three cell lines internalize more dFPSNPLs than FPSNPLs, at the same concentration. When cell viability was assessed, only moderate effects were observed at the highest concentration of dPSNPLs in TK6 at exposures lasting for 24/48 h. No intracellular ROS production was observed in any of the cell lines at 24/48 h and, finally, genotoxic damage induction was detected only at 24 h exposure in THP1 cells, and at the highest concentrations. No oxidative DNA damage was detected at any time and in any cell line.

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