Genotoxic and functional endothelial responses to nanoplastics: the role of physicochemical properties

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The vascular endothelium represents a critical biological interface for circulating micro- and nanoplastics (MNPLs) following systemic translocation. This thesis investigates MNPL-induced endothelial dysfunction using a primary human umbilical vein endothelial cell (HUVEC) model, integrating mechanistic and functional endpoints while systematically addressing the role of physicochemical properties. A progressive material strategy was implemented, beginning with well-defined polystyrene (PS) nanoplastics to dissect the effects of surface functionalization and nanoscale size (30–100 nm), and extending to environmentally relevant materials, including irregular polytetrafluoroethylene (PTFE) and real-life polyethylene terephthalate (PET) fragments derived from post-consumer bottles.

All tested nanoplastics were rapidly internalized; however, internalization efficiency did not predict biological impact. MNPL exposure induced a predominantly sub-lethal endothelial dysfunction phenotype characterized by intracellular cholesterol accumulation, impaired migration and angiogenesis, oxidative stress, DNA strand breaks, transcriptomic alterations, and IL-6 modulation. Surface functionalization emerged as a key determinant, with aminated PS exhibiting the highest toxicity despite lower uptake. Particle size modulated the magnitude and profile of responses, with 30 nm particles showing the most distinct transcriptomic signature. Environmentally realistic PET induced the strongest functional impairment.

Overall, MNPL-induced endothelial dysfunction occurs under sub-cytotoxic conditions and is strongly governed by surface chemistry, size, and environmental realism, underscoring the need to integrate physicochemical characterization into hazard assessment.

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