Scientific Letters

Poster Communication 43

Crossing cellular boundaries: Functionalized nanoplastics and their impact on human neuroblastoma cells

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Abstract

Background: The detection of nanoplastics (NPs) in food, water, and air has intensified global concern regarding their environmental and health impacts [1,2]. Human exposure occurs unintentionally through ingestion, inhalation, or skin contact, raising questions about their interactions with biological systems, especially the nervous system [3–5]. Although accumulating data confirms the biological activity of NPs, the pathways underlying their neurotoxic potential — especially those shaped by surface functionalization — are still largely unresolved. **Objective:** This study investigates the neurotoxic effects of four polystyrene nanoplastics (PS-NPs): unmodified 50 and 100 nm PS-NPs and 100 nm amine- and carboxyl-functionalized PS-NPs, using the human SH-SY5Y neuronal cell line. **Methods:** SH-SY5Y cells were incubated with varying NP concentrations (1–500 µg/mL) for 24 or 48 hours. Before initiating cytotoxicity assays, the physicochemical features and medium stability of the particles were verified. The analysis focused on metabolic activity, ROS/RNS generation, nanoparticle uptake, and cellular or subcellular structural alterations. **Results:** Functionalized PS-NPs, notably amine-modified particles, induced higher toxicity than non-functionalized ones. Cell viability declined in a concentration- and time-dependent manner, with significant reductions observed at 200–500 µg/mL. Elevated ROS/RNS levels occurred for plain 100 nm and amine-functionalized NPs, with oxidative stress intensifying over time. Electron microscopy revealed marked subcellular damage — endoplasmic reticulum dilation, mitochondrial impairment, and Golgi disorganization — correlated with NP size, concentration, and surface chemistry. Surface-modified NPs exhibited enhanced internalization efficiency, with amine-functionalized variants demonstrating the highest accumulation within neuronal cells. Mechanistic analyses indicated activation of apoptosis, autophagy, and lysosomal dysfunction, strongest in cells exposed to functionalized PS-NPs. **Conclusions:** NP surface functionalization critically influences neurotoxicity, raising significant concerns about the long-term impact of NP exposure and its potential involvement in neurodegenerative disease processes.

Keywords: polystyrene nanoplastics; SH-SY5Y cell line; neurotoxicity; surface functionalization

Acknowledgments/Funding

This research was funded by PT national funds through the UID/50006 project and FCT/MCTES through the SALIVA+ project (DOI 705 10.54499/2022.08978.PTDC).

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