



## POLY(LACTIC ACID) PLASTICS CONTAMINATION (PLASTINATION): ORGAN INJURIES AND UNDERLINING MOLECULAR MECHANISMS: EVIDENCE FROM IN VIVO ZEBRAFISH MODEL

Marta A. Szychlinska<sup>1</sup>, Federica Scalia<sup>2</sup>, Martina Di Marco<sup>3</sup>, Giusy Vultaggio<sup>3</sup>, Maria Denise Amico<sup>3</sup>, Fabiano Capparucci<sup>4</sup>, Carmelo Iaria<sup>4</sup>, Marianna Marino<sup>5</sup>, Erwin Pavel Lamparelli<sup>5</sup>, Giovanna Della Porta<sup>5</sup>, Francesca Rappa<sup>3</sup>, Antonella Marino Gammazza<sup>3</sup>, Rosario Barone<sup>3</sup>, Antonino Testa<sup>6</sup>, Rosaria Meccariello<sup>7</sup>, Antonietta Santoro<sup>5</sup>, Francesco Cappello<sup>3</sup>

<sup>1</sup>Department of Precision Medicine in Medical, Surgical and Critical Care (MEPRECC), University of Palermo, Italy; <sup>2</sup>Department of Medicine and Surgery - Kore University of Enna, Italy; <sup>3</sup>Department of Biomedicine, Neuroscience and Advanced Diagnostics (BIND), University of Palermo, Italy; <sup>4</sup>Department of Chemical, Biological, Pharmacological and Environmental Sciences, University of Messina, Italy; <sup>5</sup>Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Italy; <sup>6</sup>Department of Biological and Pharmaceutical Environmental Sciences and Technologies, University of Campania "Luigi Vanvitelli", Caserta, Italy; <sup>7</sup>Department of Movement and Wellness Sciences, Parthenope University of Naples, Italy

The PLASTAMINATION project represents a comprehensive scientific effort to address a critical gap in environmental toxicology: the biological impact of biodegradable plastics. While traditional petroleum-based plastics are well-documented for their persistence and degradation into harmful microplastics (MPs) and nanoplastics (NPs), bioplastics like poly-lactic acid (PLA) are often marketed as "environmentally sustainable." However, this project highlights a sobering reality: in sub-optimal conditions, these biodegradable materials undergo fragmentation processes similar to fossil-based plastics, producing NPs that may pose significant risks to both aquatic ecosystems and human health. The project's primary objective was to assess the toxicity of PLA-NPs using both in vitro and in vivo models. Research focused on human dermal fibroblasts (HDF) to study uptake via contact, as well as zebrafish (*Danio rerio*) and rat models to simulate ingestion and systemic exposure. To ensure scientific consistency, the UNISA unit produced standardized PLA-NP suspensions, ensuring all units worked with particles of similar physical characteristics. The project was successfully concluded with significant findings contributed by various research units. The UNIPA unit conducted experiments using two different batches of PLA-NPs of varying sizes, testing them on early-stage larvae, juveniles, and sexually active adult zebrafish. These studies used polystyrene (PS) MPs as a negative control. The results indicated that PLA-NPs, similar to fossil-based plastics, triggered toxicity evidenced by increased cellular stress markers and physiological alterations<sup>1</sup>. A critical discovery was the correlation between particle size and toxicity. The study proved that

smaller-sized PLA-NPs had a significantly higher internalization capacity. This was observed in both the HDF cell lines and the developing zebrafish, suggesting that smaller particles possess a greater potential for systemic harm. As the investigation progressed to chronic toxicity, researchers investigated long-term molecular mechanisms across various organs. The findings highlighted that the gastrointestinal system was a major site of accumulation, where PLA-NPs caused the disruption of the intestinal barrier and alterations to the mucus layer. Further damage was analyzed across the brain, liver, and reproductive organs and gametes. Additionally, the project evaluated the antioxidant plant *Lemna minor* as a potential anti-toxic agent within the aquatic culture systems. Ultimately, the PLASTAMINATION project provided essential evidence that the "sustainable" label of bioplastics does not exempt them from environmental risk. The results underscored that PLA NPs internalize in a size- and concentration-dependent manner, causing physiological damage and organ-specific alterations that mirror the hazards of traditional, fossil-based plastic pollution.

*The experiments were conducted as part of the PRIN project "Plastic Contamination by Poly(Lactic Acid) (PLASTAMINATION): organ lesions and underlying molecular mechanisms", MUR, PRIN-PNRR2022 CODE NUMBER: P2022AA47Y-CUP: B53D23032060001.*

### Reference

Scalia F, Capparucci F, Amico MD, et al. Toxic effects of biodegradable polylactic acid nanoplastics on developing zebrafish (*Danio rerio*). *Sci Rep* 2025;15:38145.