Microplastics (MPs) are plastic particles smaller than 5mm. They have been detected in food and drinks, and interact with intestinal cells after weathering by digestive fluids. As we lack knowledge on how biological weathering of MPs affects intestinal cellular health, we investigated the impact of artificial stomach acid on MPs and on the MP-induced toxicity mechanisms, focusing on two particle sizes of polystyrene beads, 500 nm and 2 µm,. We used a Caco-2/HT29-MTX-E12 cell coculture model as a proxy of the human intestine.

This study demonstrates that a simplified cell culture model, bypassing traditional insert plates, enables the partial differentiation of Caco-2/HT29-MTX-E12 cells, facilitating high-throughput screening of microplastic (MP) effects. Using this model, we identified that larger, weathered MPs induce sub-cytotoxic membrane disruption and significantly alter lipid droplet formation compared to smaller, pristine MPs. Specifically, 2 µm MPs and weathered MPs exhibited a pronounced impact on the number and size of lipid droplets at 24 and 48 hours of exposure. We compared lipid droplet formation in cells with and without particle uptake, and were able to show mechanistic differences based on size, weathering and particle uptake. In general, intracellular localization of MPs differentially affected cellular pathways, with 500 nm MPs influenced internal cellular processes, while 2 µm MPs primarily interacted with the plasma membrane. Given the observed changes in mitochondrial morphology – including footprint, branch length, and network structure – we hypothesize a key role for mitochondria in mediating these effects.

To conclude, our findings reveal that MPs exert diverse cellular effects through size-dependent mechanisms, with larger particles primarily affecting membrane integrity and lipid metabolism, and smaller particles influencing intracellular and membrane-associated pathways, including mitochondrial dynamics.

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Polystyrene microplastics of varying sizes affect cell mechanisms depending on their uptake and weathering profile in Caco-2/HT29-MTX-E12 coculture

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