BUNDESINSTITUT FÜR RISIKOBEWERTUNG

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Oral Uptake of Micro- and Nanoplastics

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Recent Developments in Research and Risk Assessment

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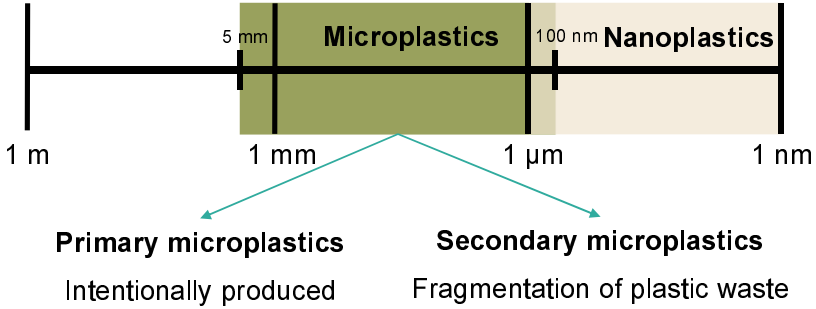
- Biochemist
- BfR, Department of Food Safety (since 2014)

- Main research focus:
  - Toxicology of micro- and nanoparticles
  - Uptake via the oral route
  - Cellular effects on intestine and liver

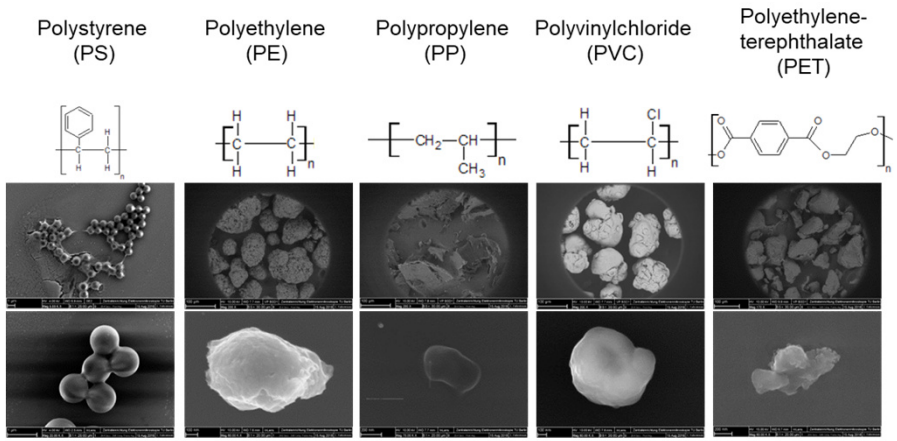
Microplastics: Material Challenges



Complex mixture:
Plastics does not equal plastics!

- early studies: mostly polystyrene, most available, monodisperse, with and without labeling or surface modifications
- other materials higher abundant, but only polydisperse powders
- no reference materials in small size range
- analytical methods have measuring limitations

- Method development necessary!



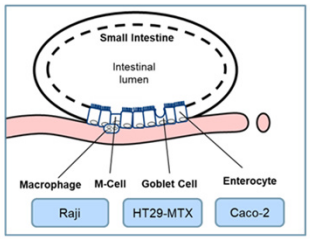
Material	Size (µm)	Surface -modification	Fluorescence	Size DLS (nm)	Image Analysis
Polystyrene (PS)	10	SO_4	●	✗	✓
	4	neutral / COOH / SO_4	●	3800 (± 430) ✓	✓
	1	COOH	●	871 (± 253) ✓	✓
	0.1	neutral / COOH / SO_4 / NH_2	NANO!	61.2 - 79.1 (± 0.6 - 0.8) ✓	✓
	0.02	COOH	NANO!	35 (±1.9) ✓	✓
Polyethylene (PE)	Powder		○	✗	✓
Polypropylene (PP)	Powder		○	✗	✓
Polyvinylchloride (PVC)	Powder		○	✗	✓
Polyethylene-terephthalate (PET)	Powder		○	✗	✓

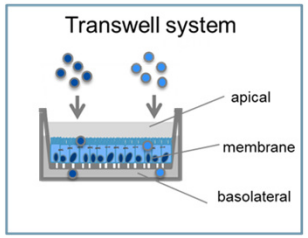
PhD-Project of Valerie Stock

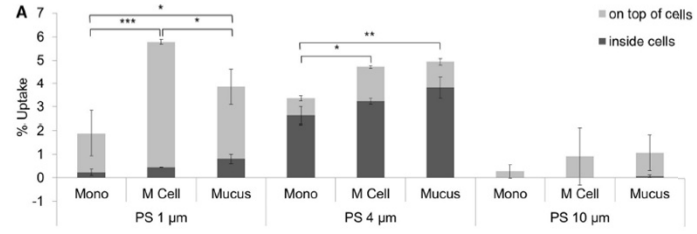
Cellular uptake analysis: Polystyrene …

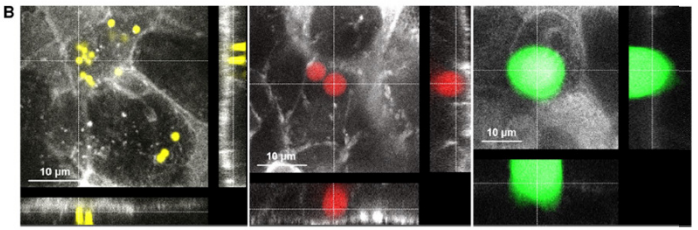
Size-dependent particle uptake

in vitro study









in vivo mouse study

- 28-day-oral diet study (HOTT-Reporter mice for oxidative stress)
- oral gavage: very low uptake, only in GI-tract organs
- no oxidative stress detected

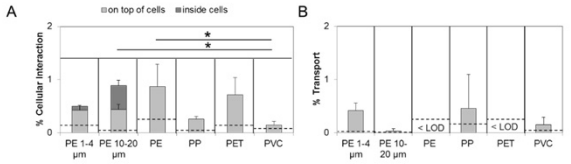
Stock, V.; Böhmert, L.; Lisicki, E.; Block, R.; Cara-Carmona, J.; Pack, L. K.; Selb, R.; Lichtenstein, D.; Voss, L.; Henderson, C. J.; Zabinsky, E.; Sieg, H.; Braeuning, A.; Lampen, A., Uptake and effects of orally ingested polystyrene microplastic particles in vitro and in vivo. Archives of toxicology 2019, 93 (7), 1817-1833.

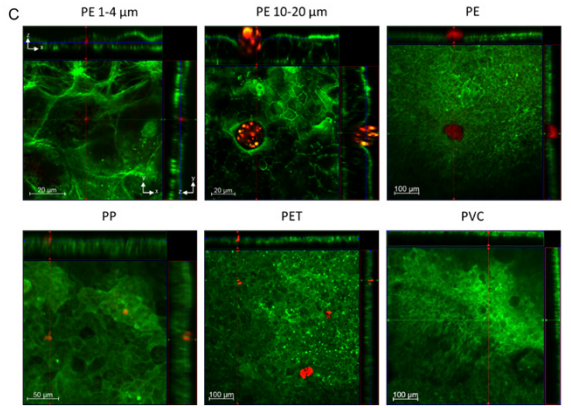
… and other Materials

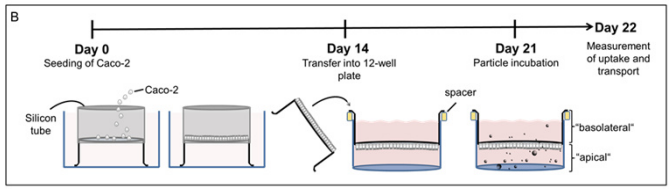
Material-specific particle uptake

Challenges:

- Higher polydispersity: broad size distribution
- No initial fluorescent label
  -> own labeling protocol
- PE, PP: Low density
  -> inverted cell culture model







Stock, V.; Laurisch, C.; Franke, J.; Dönmez, M. H.; Voss, L.; Böhmert, L.; Braeuning, A.; Sieg, H., Uptake and cellular effects of PE, PP, PET and PVC microplastic particles. Toxicology in Vitro 2021, 70, 105021

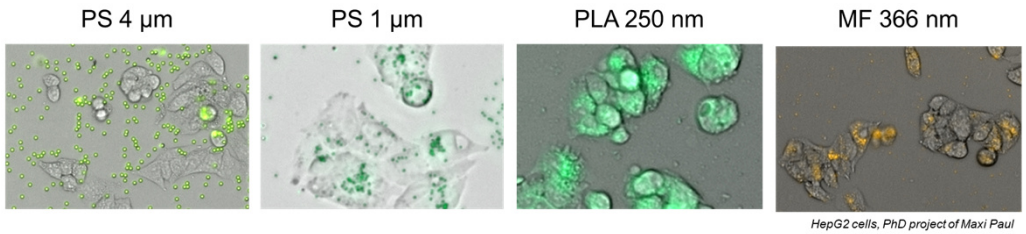
From Micro- to Nanoplastics

- Microplastics has been investigated intensively in recent years:
- Some assumptions:
  - Available exposure studies indicate low uptake:
    - Cellular uptake of particles > 1.5 µm very low
    - Often in non-edible organs, such as the intestinal tissue of fish
    - Systemic bioavailability unlikely.
  - Direct effects are low:
    - Material is supposed to be chemically inert.
    - Effects only in „overload“ situations measurable.

→ **Actual data indicates a low risk of accute toxicity via oral uptake**

  - but: Almost nothing is known about nanoplastics!
    - Analytical methods are reaching their limits
    - Reference materials are not available
    - Labeling, purification and utilization in cell systems challenging

- Essential differences in particle uptake between micro- and submicroparticles



HepG2 cells, PhD project of Maxi Paul

- Application of food-relevant materials
  - Extend the project from microplastics to submicron- and nanoplastics
- Uptake and transport studies
  - Detection and quantification methods
  - Fluorescence microscopy, Flow cytometry
- Cellular Effect studies
  - Signaling mechanisms, inflammation, immunology

Is there an unpredictable risk coming from submicro- and nanoplastics?

Apporaches for Risk Assessment / Summary

- State of knowledge:
  - Microplastics ubiquiteously present in food chain
  - Complex mixture of chemicals (polymer, additives, contaminants)

- Regulatory view:
  - Avaliable studies are not applicable for risk assessment yet
  - No validated quantification methods
  - Routine food control and monitoring not possible yet
  - Risk characterization unclear

- Data gaps:
  - Chronic exposure
  - Indirect effects
  - Nanoplastics
  - Method development ongoing for: Analytics, quantification and toxicological investigations