Hazard identification and Risk characterization – micro and nano plastics in food and feed (draft)

6th May 2021, Ron Hoogenboom

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Hazards of micro- and nanoplastics

- Exposure via food and drinking water?
- Effects in gastrointestinal tract?
    - Including microflora?
- Uptake of particles resulting in systemic exposure?
- Effects in tissues and organs?
- Carriers of contaminants?
    - Which ones?
    - Relevant in comparison to other sources?

EFSA statement 2016

EFSA Journal

STATEMENT

ADOPTED: 11 May 2016

doi: 10.2903/j.efsa.2016.4501

Presence of microplastics and nanoplastics in food, with particular focus on seafood

EFSA Panel on Contaminants in the Food Chain (CONTAM)

EFSA statement 2016

Absorption data not available

- MPs <150 µm may be absorbed
- Absorption of MPs is likely limited, data indicate <0.3%.
  - Nanoparticle bioavailability in vivo <10%
  - Nanoparticle uptake in vitro <10%
  - Uptake size dependent, no simple correlation, different mechanisms
- Only MPs <1.5 µm may penetrate deeply into organs

EFSA statement 2016

Toxicity data

MPs could interact with the immune system, but not reported yet

- MP T-cell activation and uptake by macrophages (inhalation, injection) in vivo/in vitro

Data gaps

- Absorption and distribution data
- Metabolism and excretion data
- Tox data on effects of MPs
- Tox data on local effects of MPs on GI tract including microbiota

Review paper 2020

foods

MDPI

Review

Current Insights into Monitoring, Bioaccumulation, and Potential Health Effects of Microplastics Present in the Food Chain

Leonard W. D. van Raamsdonk [1,*], Meike van der Zande [1], Albert A. Koelmans [2], Ron L. A. P. Hoogenboom [1], Ruud J. B. Peters [1], Maria J. Groot [1], Ad A. C. M. Peijnenburg [1] and Yannick J. A. Weesepoel [1]

- Various aspects on analysis, occurrence, **uptake and toxicity**

Deng et al. 2017. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. Nature Scientific Reports. (159 times cited on 4-5-2021)

Study design

Oral gavage daily for 28 days.
2 sizes MPs: 5 and 20 µm (fluorescently labeled)

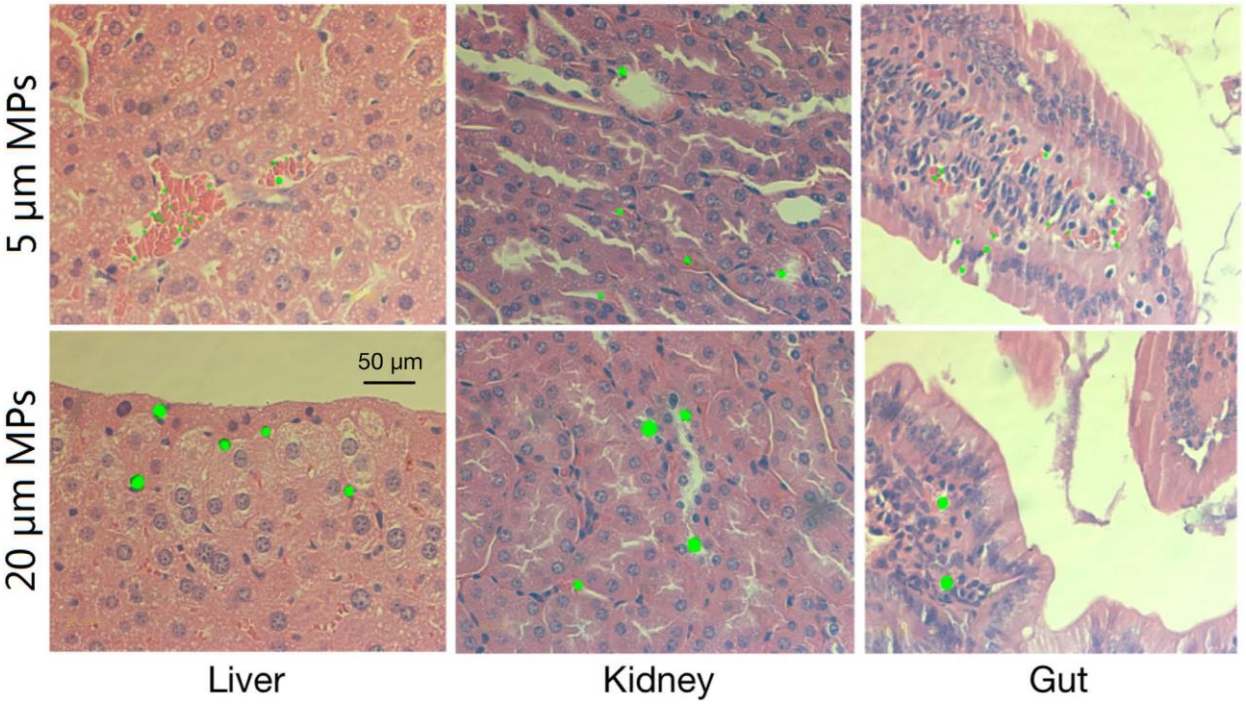
Bioavailability:

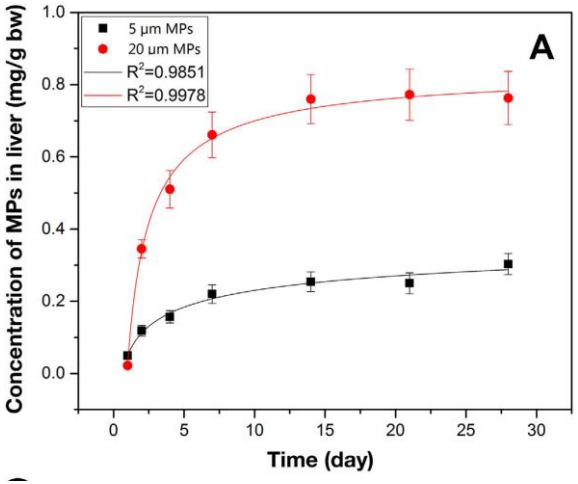
0.1 mg/day	(1.46 *10^6 MPs; 5 µm)	(2.27 *10^4 MPs; 20 µm)

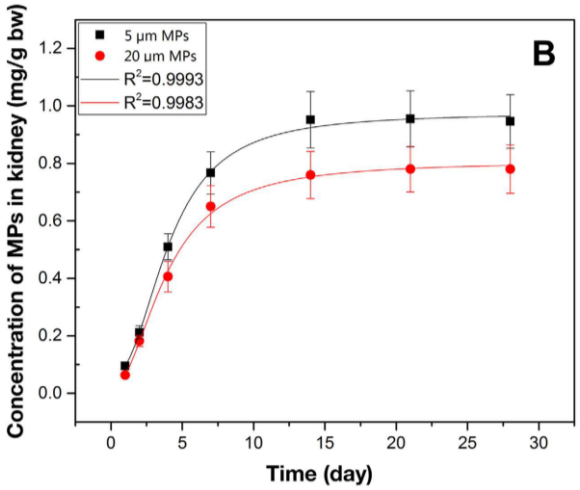
Effects:

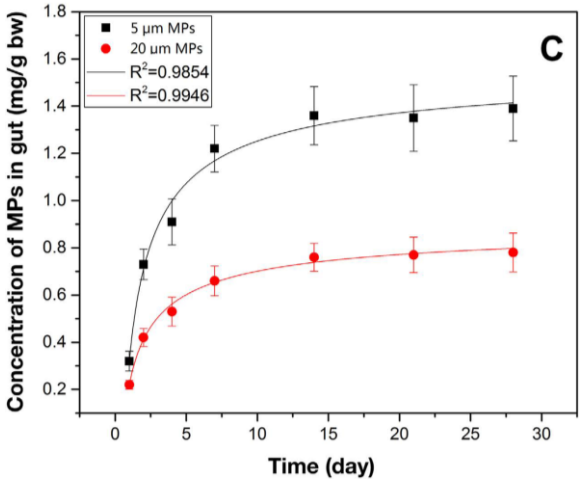
0.01 mg/day	(1 *10^5 MPs; 5 µm)	(2 *10^3 MPs; 20 µm)
0.1 mg/day	(1 *10^6 MPs; 5 µm)	(2 *10^4 MPs; 20 µm)
0.5 mg/day	(5 *10^6 MPs; 5 µm)	(1 *10^5 MPs; 20 µm)

Organs evaluated: liver, kidney, gut









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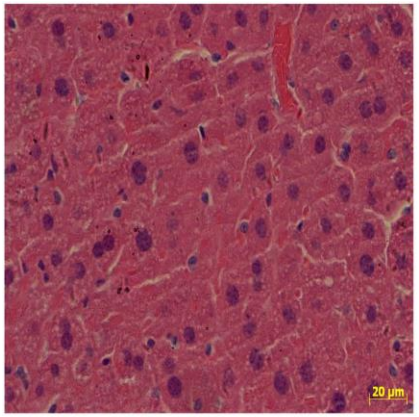
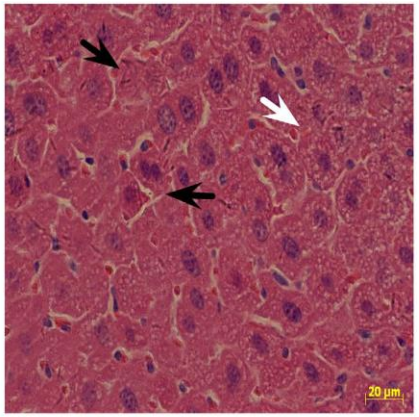
Deng et al., 2017

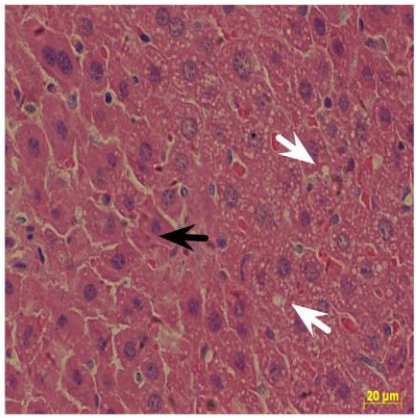
- Inflammation
- Lipid droplets
- Various blood parameters affected



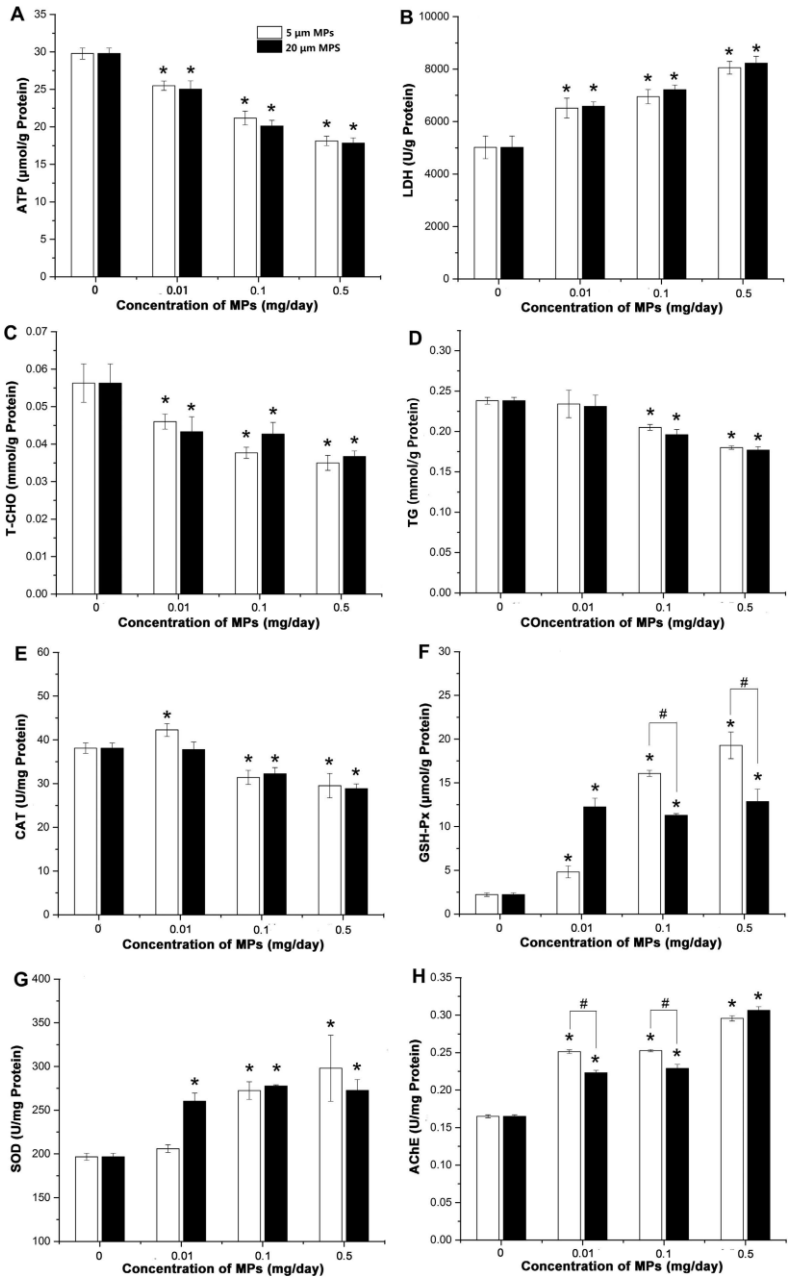
Control



5 μm MPs



20 μm MPs



Deng et al., 2017

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Major results

- Bioavailability
  - High accumulation (71% in gut, liver, kidney at day 4)
- Effects
  - Histology: liver inflammation and lipid droplets
  - Plasma markers:
    - ATP down, LDH up (energy disturbance)
    - Cholesterol and triglycerides down (lipid disturbance)
    - GSH and SOD up, CAD down (oxidative stress)
    - AChE up (neurotoxic responses)

Discussion in the literature by BfR

- Bioavailability
  - High accumulation (71% in gut, liver, kidney at day 4)
- Response to study:
  - BfR calculated clearance half life t1/2 = ~3 days
  - Would lead to ~100% bioavailability (highly unlikely)
  - EFSA report: Absorption is likely limited, data indicates <0.3%
  - EFSA report: Only MP <1.5 µm may penetrate deeply into organs

Discussion in the literature by BfR

- Effects
- Histology: liver inflammation and lipid droplets
  - BfR: no description of scoring (qualitative evaluation at best)
- Plasma markers
  - BfR points out that the SDs are very minor (unusual for serum data)

Alternative explanations

- Fluorescent label released from the particles?
  - But also particles observed
- Calculated concentrations in tissues not correct?
  - So time related increase
  - But lower levels that may still be relevant

Other studies (same group)

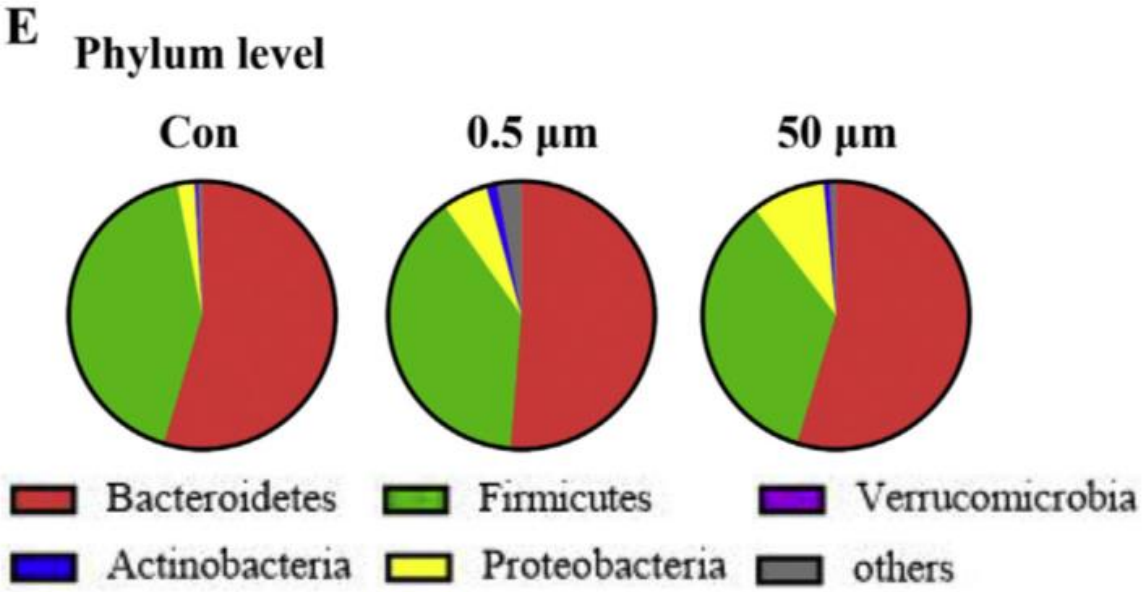
- Lu et al., 2018. Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. Science of the Total Environment
- Jin et al., 2019. Impacts of polystyrene microplastic on the gut barrier, microbiota and metabolism of mice. Sci Total Environ.
- Luo et al., 2019. Maternal exposure to different sizes of polystyrene microplastics during gestation causes metabolic disorders in their offspring. Environ poll.
- Luo et al., 2019. Maternal Polystyrene Microplastic Exposure during Gestation and Lactation Altered Metabolic Homeostasis in the Dams and Their F1 and F2 Offspring. Env Sci Tech.

Lu et al. (2018)

- Mice
  - Two sizes: 0.5 and 50 µm polystyrene MPs
  - Concentrations of 100 and 1000 µg/L (1.456×10^{10} and 1.456×10^{4} particles/L)
  - Exposure via drinking water for 5 weeks (how much water consumed?)
- Effects
  - Reduction in body, liver, and fat weight for high dose
  - Reduction in mucus production colon
  - Reduced liver and serum triglycerides and cholesterol

Lu et al. (2018)

- Composition microbiome changed at phylum and genus levels



- Effect on liver via effect on gut microbiota?

Stock et al., 2019. Uptake and effects of orally ingested polystyrene microplastic particles in vitro and in vivo. Archives of Toxicology.

- Male Hmox1 reporter mice (lacZ reporter gene under the control of the inflammation- and redox stress-sensitive heme oxygenase 1 promoter)
- Oral gavage for 28 days, 3x per week
- Fluorescently labeled MPs, 3 sizes: 1. 4 and 10 µm
  - 1 µm (4.55 × 10^7 particles)
  - 4 µm (4.55 × 10^7 particles)
  - 10 µm (1.49 × 10^6 particles)
- Duodenum, ileum and jejunum, testes, large intestine, lung, heart, spleen and kidneys

Stock et al. 2019: Results

- Some particles detected in the intestinal wall (not quantitative, concentration too low)
  - No particles detected in lung, heart spleen or kidneys
  - Data corroborate with EFSA report
- No inflammation and/or oxidative stress (histology and mouse model; fluorescence)
- Mice examined x days after last dosing: effect?

Other recent studies (not in review 2020)

- .....

Conclusions

- Absorption and effects of larger particles reported
  - Several studies
  - Results questioned
  - Data require thorough investigation
  - Repeat of studies?
- Unclear if high doses are relevant for humans
  - Need for more data on exposure
- Primarily polystyrene tested; studies with other types of plastics?

Acknowledgements

- Co-authors on the review paper
- Meike van der Zande for preparing the most of the slides
- EFSA for inviting me at this colloquium

Thank you for your attention

Questions?