COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COT)

Potential risks from exposure to microplastics: Update on literature

Introduction

1. A scoping paper was presented to the COT in October 2019 (TOX/2019/62)[1] on the potential risks from exposure to microplastics, it summarised two reports from authoritative bodies. Firstly, the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM) statement on microplastics in food, with particular focus on their presence in seafood in 2016 (EFSA, 2016). Secondly, the World Health Organisation (WHO) report on microplastics in drinking-water published in 2019 (WHO, 2019). To date, no evaluations have been made of risks from inhaling microplastics, however, a 2018 narrative review by Gasperi et al., (2018) was also summarised. Furthermore, the scoping paper described developments in the literature since the EFSA statement in 2016.

2. This paper is intended to provide an update on the literature since October 2019 when the scoping paper was first presented.

Search strategies

3. The following search strategies were combined to identify literature relevant to the exposure and toxicity of microplastics to humans. Pubmed, Science Direct and Google Scholar databases were searched using single words or combinations of terms as described in Annex A. Reports and assessments by other authoritative bodies were appraised and relevant literature cited within these reports were identified.

Environment and Climate Change Canada and Health Canada (ECCC and HC)

4. The government bodies of Environment and Climate Change and Health Canada published a draft science assessment of plastic pollution in January. 2020[2]. An executive summary is provided in the following paragraphs.

5. It was estimated that 1% of plastic waste (29,000 tonnes in which plastic packaging was the biggest contributor) enters the environment in Canada, this value is anticipated to increase over time. Microplastics were defined as particles ≤5 µm.

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[1] Discussion paper available at: https://cot.food.gov.uk/sites/default/files/tox201962microplastics.pdf.
[2] The full report can be downloaded at: https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/draft-science-assessment-plastic-pollution.html.

6. It was concluded that humans may be exposed to microplastics via the ingestion of foodstuffs (including bottled water), as well as through the inhalation of indoor and outdoor air, however, data concerning the human health effects is limited.

7. The epidemiological data available from microplastic-related industries (e.g. synthetic textiles, nylon flock and polyvinyl chloride; PVC) identified increases in adverse respiratory effects including airway lesions and fibrosis, decreased pulmonary function, wheezing, bronchitis *etc*. Despite these associations, no firm conclusion could be drawn by ECCC and HC on human health effects of exposures to plastic particulates or fibres since confounding variables such as co-exposures with other workplace hazards could contribute to the observed effect.

8. A review by DeMatteo et al., (2012) on the epidemiological evidence of health effects in women working in plastics manufacturing and processing industries was identified to be relevant by ECCC and HC, however, it was noted that microplastics were not specifically addressed. The study identified associations with this specific occupational exposure and the manifestation of breast cancer, spontaneous abortion, and infertility. As mentioned, microplastics were not specifically addressed and therefore it was not clear if the observed adverse health effects were directly correlated to microplastic exposure or exposure to other substances utilised in the production of plastics.

9. Other epidemiological studies on exposure to polyurethane dust in polyurethane foam workers showed no increases in lung or respiratory tract cancer (Sorahan & Pope, 1993; Mikoczy et al., 2004; Pinkerton et al., 2016). Conversely, exposure to plastic dusts in pattern and model makers, showed an increase in lymphocytopenia[3], but no exposure-response relationship was observed.

10. Although some associations between high exposure levels have been linked with adverse effects in laboratory animals and humans (in an occupational setting; as described above) have been reported, their relevance to the general population is unknown, as extrapolation from high-dose occupational exposures to lower doses is difficult in the absence of data on health effects at lower concentrations. Furthermore, the studies did not evaluate the impact of dose-response on the health outcomes and the observed workers may have had co-exposures to other chemicals associated with adverse health effects (e.g. catalysts, additives *etc*).

11. Effects observed in animal studies were associated with the exposure pathway, i.e. for oral gavage effects on the digestive system were reported, whilst exposures following inhalation resulted in respiratory tract effects. It was, however, highlighted regardless of the route exposure (mentioned above), the movement of a small fraction of microplastic particles to lymphatic or systemic tissues have been observed. Overall, the ECCC and HC concluded that in the available animal studies, there were no dose-response relationship observed in mortality, survival time, behaviour, clinical observations or tumour incidence from inhalation exposures.

[3] Lymphocytopenia: is the condition of having abnormally low levels of lymphocytes (white blood cells) in the blood.

12. In terms of the risks from sorbed[4] and chemically bound (*e.g.* persistent organic pollutants) and unbound chemicals (*e.g.* monomers) on plastic particles, current literature suggests that, while the transport of chemicals *via* plastic is possible, the impact to biota is limited and international reviews carried out by EFSA (2016), Food and Agriculture Organisation (2017) and WHO (2019), as detailed in TOX/2019/62[5], indicate that there is likely a low health concern for human exposure to chemicals from ingestion of microplastics from food or drinking water.

13. With regards to the presence and formation of biofilms on the surface of microplastics particles, the ECCC and HC indicated that there is currently no indication that this would impact human health. Despite limited data, it is anticipated that drinking water treatment processes have the ability to inactivate biofilm-associated microorganisms.

14. To conclude, the ECCC and HC are in the view that under the precautionary principle, further action is needed to reduce the presence of macro- and microplastics that end up in the environment.

15. The following research needs were recommended in order to carry out a human health risk assessment; development of standardised methods for sampling, quantifying, characterising, and evaluating the effects of macro- and nanoplastics, studies to further understand the effects of microplastics exposure in human and the environment, and lastly, expanding and development consistent monitoring efforts to include poorly characterised compartments such as soil.

Other published reviews

16. Hale et al., (2020) published a global health perspective with the following three key points. Firstly, the sources, behaviour, fate and effects of microplastics are directly linked to their plastic product and macro-debris precursors, as well as the nanoplastics into which they fragment. Secondly, the inadequacy of sampling and characterisation methods of microplastics were highlighted as an important area that required further development. Lastly, the plastic problem must be regarded as a global and multi-media phenomenon and should not be regarded in a single context e.g. as a pollutant in the marine environment.

17. They concluded that exposure to particles <20 µm can compromise feeding, metabolic processes, reproduction and behaviour in animals, however, further investigations are required to draw definitive conclusions on human health effects.

18. The recommended solutions include improving globally based pollution prevention, development of biodegradable polymers and additives, and reducing consumption/expanding plastic reuse.

19. Rodrigues et al., (2019) reviewed the current literature on the impacts of plastic products used in daily life on the environment and human health. They characterised the most common plastic materials widely utilised by humans by its

[4] Sorbed (*adj*) taken into and retained in another substance.
[5] Discussion paper available at: https://cot.food.gov.uk/sites/default/files/tox201962microplastics.pdf.

polymer type (Table. 1) and complied the environmental and human health hazards of these polymers including the impacts of monomers, additives (Table. 2), degradation products (Table. 3) and adsorbed contaminants based on a literature review.

20. It was concluded that, PVC was the most toxic polymer type used daily (monomer and additives); it was found that additives were more toxic than monomers to both human and the environment, whilst the most toxic additives were benzene, phthalates and lead stabilisers.

Table. 1 – lists the chemical and morphological characterisation of 43 plastic products widely used in everyday life (reproduced from Rodrigues et al., 2019).

Plastic	Source	Polymer type	Shape
Plastic cup	Supermarket	PS	Fragment
Water bottle cap 1, 2, & 3		PE	Fragment
Water bottle cap 4		PP	Fragment
Yoghurt bottle cap		PE	Fragment
Milk bottle cap		PP	Fragment
Beverage bottle cap 1, 2, & 3		PE	Fragment
Liquid yoghurt		PE	Fragment
Solid yoghurt		PS	Fragment
Water bottle 1, 2, & 3		PET	Fragment
Water bottle 4		PP	Fragment
Beverage bottle 1, 2, & 3		PET	Fragment
Food packaging 1, 2, & 3		PP	Fragment and film
Milk box		PE	Fragment and fibre
Drinking straws		PP	Fragment
Toilet paper packaging		PE	Fragment
Toothpaste		PE/PET	Fragment
Handwash packaging		PET	Fragment
Alcohol packaging		PE	Fragment
Garbage bag		PE	Film
Supermarket bag		PE	Film
Cleaning product packaging		PE	Fragment
1, 2, & 3 Cleaning product packaging		PP	Fragment
4 & 5 Cleaning product packaging		PET	Fragment
6 Cotton swab box		PP	Fragment
Cotton swab		PP	Fragment
Pipe		PVC	Fragment
Styrofoam	Industry	EPS	Foam
Fishing net	Fishing shop	PA	Fibre
Fabric	Fabric store	PET	Fibre
Rope	Supermarket	PP	Fragment

Abbreviations: EPS; expanded polystyrene, PA; polyamide, PE; polyethylene, PET; polyethylene terephthalate, PP; polypropylene, PS; polystyrene and PVC; polyvinyl chloride.

Table. 2 – Impacts, monomers and additives associated to a hazard level based on the European Union's Classification, Labelling and Packaging Hazard Class and Lithner et al., 2011 (reproduced from Rodrigues et al., 2019).

Hazard level	Impacts	Monomers/Additives	Associated polymers
Very low	Flammable liquid and vapour	Styrene/Chlorobenzene; Acetic acid	PS, EPS, HIPS, HDPE, PA6
	Highly flammable liquid and vapour	n-hexane; Heptane; Toluene; Cyclohexane; Isooctane; Di-tert- butyl Peroxide; Benzene; Ethanol; Isopentane; Ethylbenzene; Pentane	PP, HDPE, HIPS, LLDPE, LDPE, PET, EPS
	Extremely flammable gas	Propylene; Ethylene; 1-butene; Vinyl chloride/Iso-butene; 1,3- butadiene	PP, HDPE, LLDPE, LDPE, PVC, HIPS
Low	May cause respiratory irritation	ε-caprolactam; Hexamethylenediamine/p-benzoquinone; Dipotassium peroxodisulphate; Diammonium peroxodisulphate	PA6, PA6.6, PA6.10, PS, PVC
	Skin corrosion/irritation	Styrene; ε-caprolactam/n-hexane; Heptane; Toluene; Cyclohexane; Isooctane; Benzene; p-benzoquinone; Dipotassium peroxodisulphate; Diammonium peroxodisulphate	PS, EPS, HIPS, PA6, PP, HDPE, LLDPE, LDPE, PVC
	Serious eye damage/eye irritation	Styrene; ε-caprolactam; Adipic acid/ Dibenzoyl peroxide; Benzene; p-benzoquinone; Dipotassium peroxodisulphate; Diammonium peroxodisulphate	PS, EPS, HIPS, PA6.6, PA6, LDPE, PVC
	Harmful if swallowed, inhaled and/or in contact with skin	Ethylene glycol; ε-caprolactam; Hexamethylenediamine; Styrene/2,2'-dimethyl-2,2'-azodipropiononitrile; Dipotassium peroxodisulphate; Diammonium peroxodisulphate; Hydrogen peroxide; Heat stabilisers (lead); Chlorobenzene; Ethylbenzene	PET, PA6, PA6.6, PA6.10, PS, EPS, HIPS, HDPE, PVC, LDPE
	Drowsiness or dizziness	Ethylene/ n-hexane; Heptane; Toluene; Cyclohexane; Isooctane; Isopentane; Pentane	PP, HDPE, HIPS, LLDPE, EPS
	Harmful to aquatic life with long-term effects	2,2'-dimethyl-2,2'-azodipropiononitrile	LDPE, PS, PVC
Medium	Ingestion, inhalation and/or dermal toxicity	Methanol; p-benzoquinone	PP, HDPE, PS, LDPE, PET, PA6.6, PA6.10
	Severe skin burns and eye damage	Hexamethylenediamine/ Titanium tetrachloride; Acetic acid; Phosphoric acid; Hydrogen peroxide	PA6, PA6.6, PA6.10, PVC, PP, HDPE, LLDPE, PA12

	Suspected of carcinogenicity	Fuels; Antimony trioxide	HDPE, PET
	Suspected of damaging fertility	n-hexane; Heat stabilisers (lead; Cadmium); Benzyl butyl phthalate	PP, HDPE, PVC

	Suspected of damaging the unborn child	Toluene; Heat stabilisers (Cadmium)	HDPE, HIPS, PVC
	Damage to organs through prolonged repeated exposure	n-hexane; Toluene; Benzene; Heat stabilisers (lead; Cadmium)	PP, HDPE, HIPS, LDPE, PVC
	May be fatal if ingested and inhaled	n-hexane; Heptane; Naphtha; Toluene; Cyclohexane; Isooctane; Benzene; Isopentane; Pentane	PP, HDPE, HIPS, LLDPE, LDPE, HDPE, EPS
	Very toxic to aquatic life	Heptane; Cyclohexane; Isooctane; Zinc oxide; p-benzoquinone; Heat stabilisers (lead; Zinc powder; Cadmium); Benzyl butyl phthalate	PP, HDPE, LLDPE, PS, PVC, PET
	Toxic to aquatic life with long-term effects	n-hexane; Chlorobenzene; Isopentane; Pentane	PP, HDPE, LLDPE, EPS
High	Fatal if inhaled	Heat stabilisers (Cadmium)	PVC
	Suspected of germ cell mutagenicity		
	Damage to organs	Methanol	PP, LDPE, PET, PA6.6, PA6.10
	Very toxic to aquatic life with long-term effects	Heptane; Cyclohexane; Isooctane; Zinc oxide; Heat stabilisers (lead; Zinc powder; Cadmium), Benzyl butyl phthalate	PP, HDPE, LLDPE, PS, PVC, EPS, LDPE, PET
	Allergic skin reaction	Dibenzoyl peroxide; Dipotassium peroxodisulphate; Diammonium peroxodisulphate	LDPE, PS, EPS, PVC
	Respiratory difficulties/asthma symptoms/allergy	Dipotassium peroxodisulphate; Diammonium peroxodisulphate	PS, PVC
Very high	Carcinogenicity	Vinyl chloride/ Benzene; 1,3–butadiene; Naphtha; Heat stabilisers (Cadmium)	LDPE, HIPS, PVC, PP
	Germ cell mutagenicity	Benzene; 1,3–butadiene; Naphtha	LDPE, HIPS, PP
	Damage fertility and/or the unborn child	Heat stabilisers (lead); Benzyl butyl phthalate	PVC

Abbreviations: EPS; Expanded polystyrene, HIPS; High-impacted polystyrene, LDPE; Low-density polyethylene, LLDPE; Linear-low-density polyethylene, PA; Polyamide, PA 6; Polyamide 6, PA 6.6; Polyamide 6.6, PA 6.10; Polyamide 6.10, PA 11; Polyamide 11, PA 12; Polyamide 12, PE; Polyethylene, PET; Polyethylene terephthalate, PP; Polypropylene, PS; Polystyrene, PVC; Polyvinyl chloride.

Table. 3 – risk assessment of degradation products obtained after abiotic degradation processes (reproduced from Rodrigues et al., 2019).

Polymer	Degradation products	Hazard level
Polypropylene (PP)	C_3-C_{15} saturated hydrocarbons	NF
	Acetlyaldehyde	Medium
	Acetic acid	Medium
	Acetone	Low
	Formaldehyde	Very high
	Butanone	Low
	Methanol	High
	Ethanol	Very low
	Butanol	Low
	Furan	Very high
	Benzoic acid*	Medium
	Tetrahydrofuran*	Low
	Propanoic acid**	NF
	Dimethylfuran**	NF
Polyethylene (PE)	Formaldehyde	Very high
	Acetaldehyde	Medium
	Acetic acid	Medium
	C_3-C_{15} saturated hydrocarbons	NF
	Ethanol*	Very low
	Ethoxypropanol*	NF
	Furan*	Very high
Polyethylene terephthalate (PET)	Monomers	Low
	Acetaldehyde	Medium
Polystyrene (PS)	Monomer	Medium
	Ethylbenzene	NF
	Acetaldehyde	Medium
	Benzaldehyde	Low
	C_3-C_{16} saturated hydrocarbons*	NF
	Acrylaldehyde**	High
	Acetophenone**	Low
Polyamide (PA)	Monomer (ε-caprolactam)	Low
	Acetaldehyde	Medium
	Methacrylaldehyde	NF
	Ethanol	Very low
	Acetic acid	Medium
	C_3-C_9 saturated hydrocarbons	NF
	Benzene	Very high
	Hydrogen cyanide	High
Polyvinyl chloride (PVC)	Formaldehyde	Very high
	Acetaldehyde	Medium
	Methyl methacrylate	High
	Acetic acid	Medium
	C_3-C_5 saturated hydrocarbons	NF
	Methylethylacetone*	NF
	Methylvinylacetone*	NF
	Ethanol*	Very low
	Ethylhexanol*	NF
	C_6-C_{13} saturated hydrocarbons*	NF
	Hydrogen chloride**	Medium
	Benzene**	Very high
	Toluene**	Medium

Abbreviations: NF; Not found. *; degradation products only found on industrial sites. **; degradation products only found in a laboratory setting.

21. Groh et al., (2019) presented a database of chemicals associated with plastic packaging, which included chemicals used during manufacturing and/or present in final packaging articles (~60% of all plastic packaging is used for food and beverages, other applications include healthcare, cosmetics, consumer, household, apparel, and shipment packaging). The compiled databased consists 906 chemicals likely associated with plastic packaging and 3,377 substances that are possibly associated. With reference to the harmonised hazard classifications assigned by the European Chemicals Agency and the Classification, Labelling and Packaging Regulation (EC No. 1272/2008); 63/906 ranked highest for human health hazards and 68/906 for environmental hazards, 7 were identified as persistent, bio-accumulative, and toxic, or very persistent, very bio-accumulative, and 15 were endocrine disrupting chemicals. The authors were in the opinion that the most hazardous chemicals identified in this list should be assessed in detail and potential candidates for substitution.

22. Verla et al., (2019) carried out a review of the literature with the following 5 objectives: to summarise the concentrations of toxic chemicals sorbed on microplastics (*e.g.* heavy metals and hydrophobic organic contaminants), to evaluate their spatial distribution regarding adsorbed contaminant, to discuss plausible mechanisms by which microplastics adsorb or desorb toxic chemicals in the environment, to discuss the implications of their occurrence in air, water and soil media, and to discuss the impact of ingested microplastics to human health. An executive summary of each objective is provided in the following paragraphs.

23. The conclusions on quantified concentrations of toxic chemicals sorbed on microplastic surfaces is hereby summarised. Microplastic particles from heavily polluted areas were found to contain higher levels than those form less polluted areas. The toxic contaminant concentrations were reported up to 38,800 µg/g for heavy metals and 101,000 ng/g for organic pollutants. The degradation stages of plastic were found to be a factor in determining the concentration present on the microplastic particle, since aged (those which are discoloured and yellowed) particles were found to have higher concentrations of contaminants. Additives used in plastics were of potentially toxic substances (n=~300) and have the ability to migrate internally to the plastic surface. Additives were further shown to influence the concentrations on toxic chemicals sorbed from the environment; they increase it. The quantification of toxic chemicals was achieved by spectroscopic techniques following extraction *via* weak acidification, aqua regia extraction[6] or through a Soxhlet apparatus for extraction of organic pollutants. A total of 12 metals, 1 halogen, and 15 groups of organic pollutants have been reported in literature (*Table. 4*). Only a few studies reported the concentrations of toxic chemicals in African marine environments (Ghana, Mozambique and South Africa), and none were reported for Nigeria.

24. The conclusions on adsorption and desorption mechanisms are hereby summarise. There is currently no accurate information regarding this topic, although, it is thought that hydrophobic adsorption, biofilm assisted adsorption and additives may play a role. Poly-parameter linear free energy relationship and novel film-pose

[6] Aqua regia is a mixture of nitric acid and hydrochloric acid. It has the ability to dissolve gold and platinum.

mass transfer models were reported to be the best methodology in studying adsorption mechanisms of toxic chemicals, in which the major parameter is the partition or sorption coefficient. Various factors were found to influence desorption mechanism kinetics which were split into three categories: the microplastic matrix (composition/type of plastic, degradation stage, structure, binding energies, the presence of biofilm growth and surface properties), the release medium (pH, temperature, ligand concentration, concentration gradient, ionic strength and salinity) and the properties of the pollutant (solubility, redox state, interaction with the matrix, charges and stability).

Table. 4 – tabulates the contaminant type and the associated substances identified in literature (extracted from Verla et al., 2019).

Contaminant type	Substance name
Metal	Aluminium, arsenic, cadmium, chromium, cobalt, copper, iron, magnesium, nickel, lead, titanium, zinc.
Halogen	Bromine
Organic pollutant	Polyaromatic hydrocarbons, polychlorinated biphenyls, dichlorodiphenyltrichloroethane and related compounds, perfluorinated compounds, perfluoroalkyl substances, aliphatic hydrocarbons, bisphenol A, nonylphenols, octylphenols

25. The conclusions on implications of the presence of microplastics in the environment are hereby summarised. In terms of environmental impacts, exposure of microplastics to marine and soil organisms resulted in harmful effects (e.g. false satiety leading to a loss of energy, decreasing fertility etc.), however, it must be noted that these effects are dependent on the microplastic particle type, concentration and size.

26. In term of human implications, it was concluded that it is unclear whether exposure will result in adverse effects, however, the impact may potentially due to physical, chemical or microbial interactions.

27. The authors recommended that further research is required to understand the sources of toxic chemicals whether they are inherent to the plastic particle, from the ambient environment, or acting synergistically. There is also a need to investigate whether microplastics act as sinks or sources of metals and hydrophobic organic contaminants, the possibility of microplastics acting as vectors and their possible effects to organisms, the role of biofilm formation in adsorption of chemicals from the ambient environment, characterising the most common microplastic type in soils, and their effects in plants and humans.

Analytical methods

28. Schwaferts et al., (2019) critically reviewed the methods for: analyte extraction and pre-concentration from various environmental matrices, separation of the nanoplastic into specific size fractions, light scattering techniques and various types

of microscopy to characterise particle fractions, and chemical identification of particles to validate the obtained data.

29. It was highlighted that there is a current methodological gap in for the analysis of submicro and the nanoplastic range (<1µm-1 nm) (Fig. 1), where considerations must be taken into account for particle size distribution or morphology and the chemical identity.

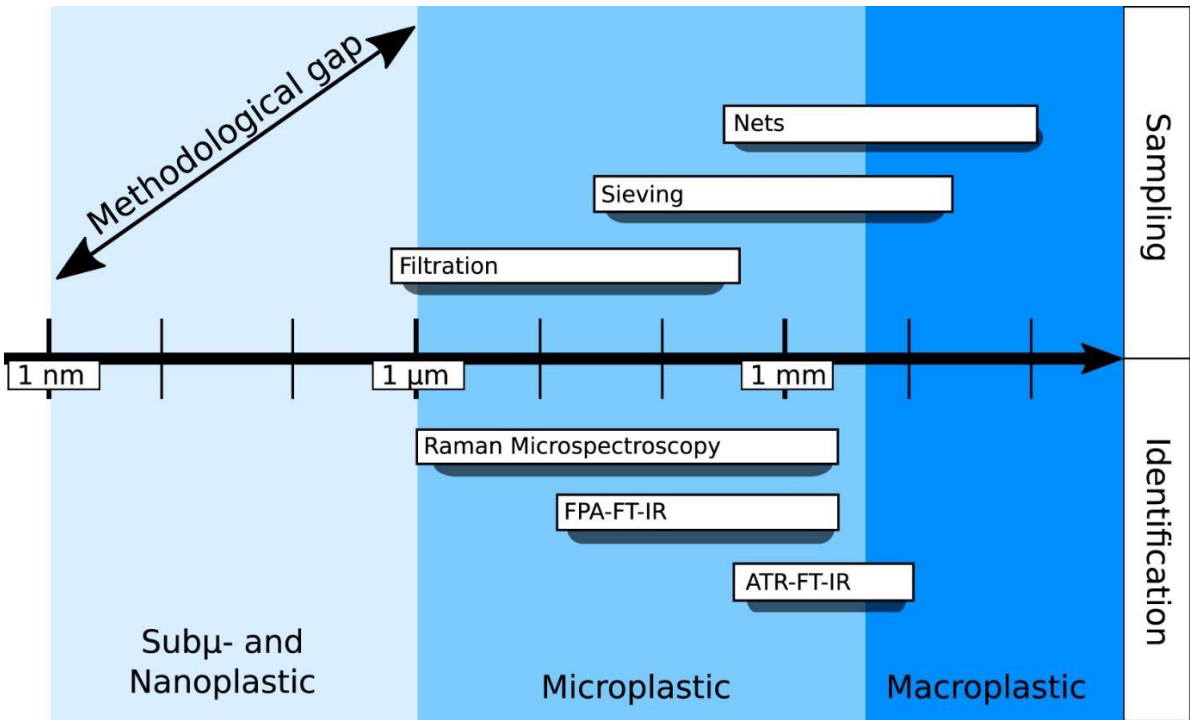

Figure. 1 – describes the available sampling and identification methodologies for macro and microplastic particles, whilst there is a methodological gap for submicro and nanoplastic particles. Abbreviations: FPA-FT-IR; Focal Plane Array Fourier-Transform Infrared Spectroscopy, ATR-FT-IT; Attenuated Total Reflection Fourier-Transform Infrared Spectroscopy (reproduced from Schwaferts et al., 2019).

30. Available techniques that have been utilised in the field of engineered nanoparticles and microplastic analysis have the potential to be transferred to plastic particles in the nanometre range, however, it must be noted that there will be a need to adapt the analytical protocol to the sample and the required information by selecting appropriate techniques. All in all, it is necessary to select and combine techniques that provide minimal amount of data to answer the analytical question.

31. The authors proposed a roadmap for the whole analytical process that considers cost efficiency, speed and methods that are able to have high throughput screening capacity (Fig. 2).

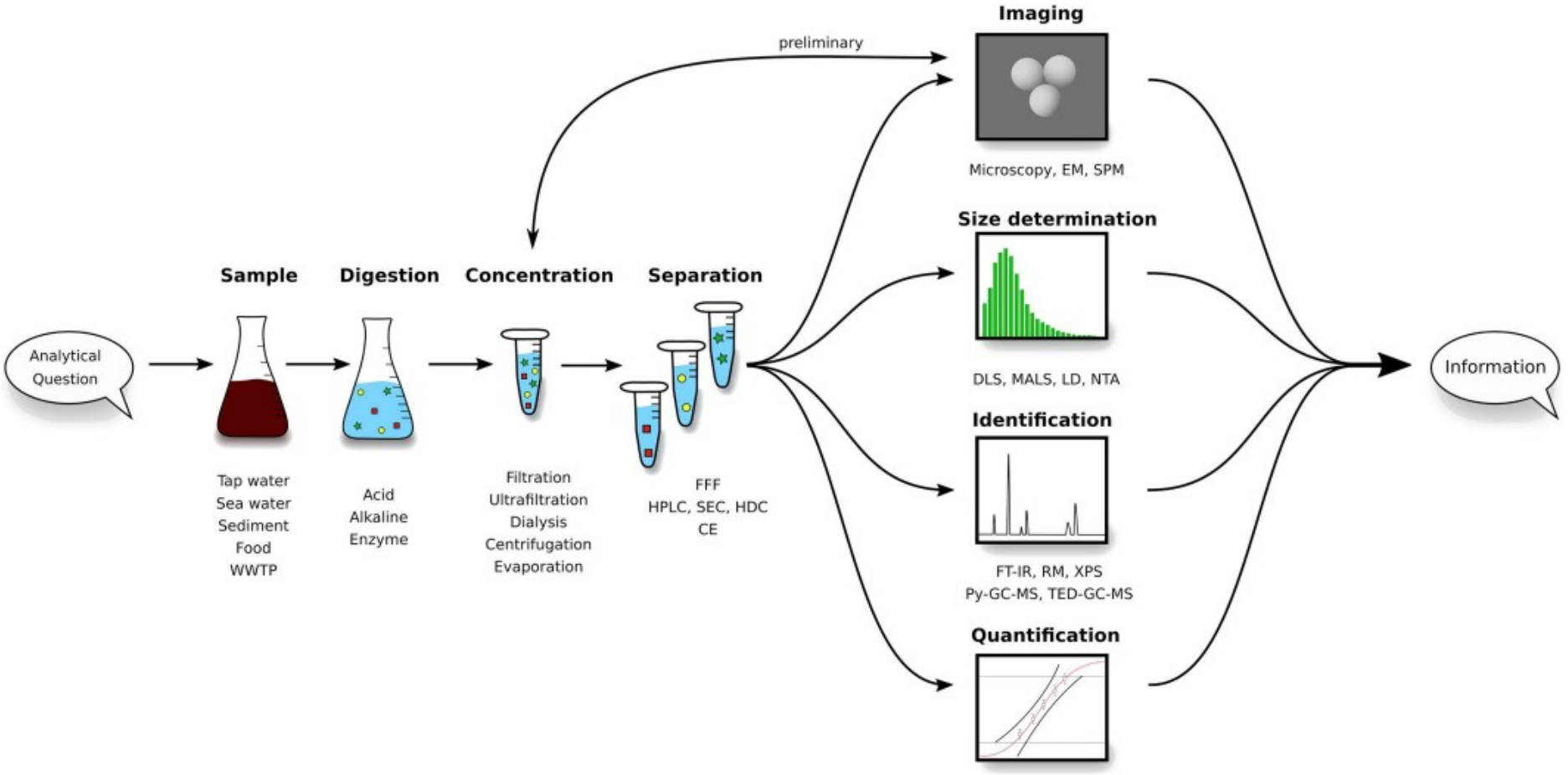

Figure. 2 – describes the roadmap for the analytical process of submicrometre and nanoplastic particles proposed by Schwaferts *et al*., 2019. Abbreviations: WWTP; Waste Water Treatment Plant, FFF; Field Flow Fractionations, HPLC; High Performance Liquid Chromatography, SEC; Size Exclusion Chromatography, HDC; Hydrodynamic Chromatography, CE: Capillary Electrophoresis, EM; Electron Microscopy, SPM; Scanning Probe Microscopy, DLS; Dynamic Light Scattering, MALS; Multi-angle Light Scattering, LD; Laser Diffraction, NTA; Nanoparticle Tracking Analysis, FT-IR; Fourier-Transform Infrared Spectroscopy, RM; Raman Microspectroscopy, XPS; X-ray Photoelectron Spectroscopy, Py-GC-MS; Pyrolysis Gas Chromatography Mass Spectroscopy, TED-GC-MS; Thermal Extraction Desorption Gas Chromatography Mass Spectroscopy (reproduced from Schwaferts *et al*., 2019).

Toxicity

In vivo

Repeated dose toxicity

32. Park *et al*., (2020) (journal pre-proof) administered polyethylene microplastics (PE-MPs) (0.125, 0.5 and 2 mg/day/mouse) by oral gavage to ICR mice (10 mice/sex/dose) for 90 days. This was performed according to a protocol approved by the Korea Institute of Toxicology.

33. An additional study was also performed to screen the effects of the PE-MPs on reproduction and development. Five mice/sex/dose were mated from the 80th to the 89th day after dosing. All male mice were sacrificed at day 90, whilst the female mice were continuously dosed during the lactation period and sacrificed on day 21 post-partum, together with the pups. Non-pregnant female mice were sacrificed on the final necropsy.

34. Clinical observations, haematological, transmission electron microscopy (TEM), and histopathological analyses were performed.

35. The physicochemical properties of the PE microplastics were as follows: they were modified to contain acid and hydroxy groups, had irregular surfaces, and the approximate diameter size was 17 µm (suspended in drinking water as a stock solution of 10 mg PE-MPs/mL) and were serially diluted prior to dosing.

36. The clinical observations were as follows in the F0 generation: body weight gain was significantly different in dosed male mice compared to the control at 15.8 g, 13.4 g (0.125 mg/day), 13.5 g (0.5 mg/day) or 14.8 g (2 mg/day). No statistical significance in body weight was observed for dosed female mice. There was no significant difference in water and food consumption between the control and dosed groups during the experimental period.

37. As for haematological changes, neutrophils in the blood increased in male mice when compared to the control group (~177% of control at 2 mg/day dose), whereas the number of white blood cells and the relative proportion of lymphocytes decreased (~75% and ~83% of control at 2 mg/day dose, respectively).

38. PE-MPs were not taken-up into the stomach epithelial cells, however, minimal hypertrophy[7]/hyperplasia[8] were observed in the mucosal layer (chief and parietal cells, as well as other cell types) surrounding the glandular stomach of dosed mice. The abdominal aorta and fallopian tubes were also notably expanded in dosed groups (data not shown).

39. Effects on the immune response were also noted on the F0 generation. Migration of granules to mast cell membranes, a PE microplastic-like material and degranulated granules were observed in the stomach of dams at the 2 mg/day dose

[7] Hypertrophy: the enlargement of an organ or tissue from the increase in size of its cells.
[8] Hyperplasia: the enlargement of an organ by an increase in the reproduction rate of its cells.

group. Additional abnormalities were observed in TEM analysis, this included the accumulation of several organelles within the nucleus and mitochondria in the spleens from the same dams. The ratio of T helper cells (CD^{4+}) to T cytotoxic cells (CD^{8+}) increased with the dose, additionally the proportion of mature dendritic cells ($CD11b^{-}/CD11^{+}$) decreased in a dose dependent manner. Lastly, the concentration of IgA significantly increased in the blood of dosed mice when compared to the control at 7.9 ng/mL, 6 ng/mL (0.125 mg/day), 15.8 ng/mL (0.5 mg/day) and 40.3 ng/mL (2 mg/day). The concentrations of IgE, IgG and IgM.

40. Results on the effects of reproduction following PE-MPs administration are hereby presented. All female mice in the control and the highest dose group (2 mg/day) (n=5/dose) became pregnant, whilst one mouse in the 0.125 and 0.5 mg/day dose groups were not pregnant. Treatment-related adverse effects were not observed in any of the dams during the gestation or lactation period. Five pups (n=4 in the 0.5 mg/day group and n=1 in 2 mg/day group) died at day 1 after birth. The number of live births per dam and body weight of pups (within 6 hours after birth) in the highest dose group were significantly decreased when compared to the control group at 12.6 and 14.6, respectively for live births and 1.46 g and 1.51 g, respectively for body weight of pups. The sex ratio (male/female) of the offspring was also altered by PE exposure, however, this tendency was not dose dependent.

41. The effects on the F1 generation are hereby summarised. No further dose-related deaths of offspring were noted from day 2 to day 21 after birth. The average post-natal day 4 and necropsy weights are presented in Table. 5.

Table. 5 – The average post-natal and necropsy weights of F1 mice generation (extracted from Park et al., 2020).

Dose group (mg/day)	Weight at post-natal day 4 (g)	Necropsy (g)
Control	2.77	15.45
0.125	2.47	16.9
0.5	2.31	16.29
2	0.33	15.59

42. The proportion of T cells within the spleen from the female pups of F0 dosed at 2 mg/day decreased compared to control, while the proportion of CD^{4+} cells increased in both sexes of pups. The maturation of dendritic cells was notably inhibited in male pups, whereas it was increased in the female pups.

43. To conclude, the authors proposed that the no-adverse-effect-level of PE-MPs is lower than 60 mg/kg bw/day for a 90-day repeated dose oral toxicity and 15 mg/kg bw/day for the reproductive and developmental toxicity.

In vitro

Cytotoxicity

44. Cortés et al., (2020) evaluated the effects of polystyrene nanoparticles (PS-NPs) on human intestinal epithelial Caco-2 cells, which were either fluorescently labelled (0.04-0.09 µm) or non-fluorescently labelled (0.05-0.1 µm) PS-NPs. The following endpoints were analysed as indicators of nanotoxicity including cytotoxicity, reactive oxygen species (ROS) increase, genotoxicity, DNA oxidative damage and increase in the expression of stress-related genes (haemoxygenase-1; HO1[9], superoxide dismutase 2; SOD2, and glutathione S-transferase P; GSTP1, heat shock protein 70; HSP70[10], and inflammatory response genes; interleukin (IL): IL-1β and IL-8).

45. Caco-2 cells were exposed to PS-NPs for 24 and 48 hours at 0, 25, 50, 100, 125, 150, 175 and 200 µg/mL.

46. No cytotoxic effects were observed until the 150 µg/mL concentration and, the highest dose (200 µg/mL) induced a mild cytotoxic effect, both at 24 and 48 hours, reaching relative survival values of 80%. TEM imaging showed that fluorescent PS-NPs were easily up taken by Caco-2 cells in a concentration dependent manner, with greater accumulation at higher exposures. In addition, they were also detected inside the cell nuclei, independent of the concentration tested, even at the lowest concentration of 1 µg/mL, the fluorescent PS-NPs reached the nucleus.

47. At 1 µg/mL, PS-NPs induced the appearance of dark, electron-dense structures in the perinuclear regions, which were also visible at higher exposure concentrations where higher accumulations of electron-dense vacuoles and lysosomes were found.

48. The mitochondrial membrane potential tended to significantly increase in the samples exposed to PS-NPs after 24 hours, however, despite this observation the levels of mitochondrial ROS did not change after the tested exposure concentrations.

49. The genotoxic and oxidative DNA damage was assessed by the alkaline comet assay. The percentage of DNA in the tail of Caco-2 cells exposed to PS-NPs was not significantly higher than those observed in untreated cells. Chromosome damage was tested by FCMN assay, PS-NPs was not able to induce significant changes in the frequency of micronuclei on the exposed Caco-2 cells.

50. As for gene expression analysis, only HO1expression showed significant changes post administration of PS-NPs for both exposure times. HSP70 expression was significantly changed after 48 hours of exposure. Neither the expression of IL-1β nor IL-8 showed significant changes after the exposure to PS-NPs.

[9] Haeme-oxygenase 1 (HO1): Haeme-oxygenase is an enzyme that catalyses the degradation of haem.
[10] Heat shock protein 70 (HSP70): forms a group of molecular chaperones that assist in the folding of nascent proteins. It also targets misfolded proteins for degradation and transport across biological membranes.

51. To summarise, PS-NPs did not exert significant toxic effects on undifferentiated Caco-2 cells, independent of the exposure time (24 or 48 hours), however, changes in the levels of HSP70 were observed mainly in exposure for 48 hours. In spite of the absence of toxicity, PS-NPs were internalised cellularly in a concentration-dependent manner, after 24 hours of exposure >80% of the cells have internalised fluorescent PS-NPs.

52. The authors concluded that although human intestinal Caco-2 cells were able to uptake and internalise PS-NPs, the related biological effects detected were not statistically significant in range of 1-100 µg/mL.

Genotoxicity

53. Poma et al., (2019) investigated the cytotoxic, proliferative and genotoxic effects of PS-NPs (particle size: 100 nm, diameter: 0.100 mm, density: 1.05 gr/cm^3) on the human fibroblast Hs27 cell line.

54. The cytotoxic effects were detected by the MTT[11], Trypan Blue and ROS detection assays. The genotoxic effects were evaluated by the cytokinesis-block micronucleus (CBMN) assay[12]. Cells were assessed following exposure for 4, 24, and 48 hours at different concentrations: 5, 25 and 75 µg/mL.

55. Compared to the control cells, the data at 4 hours showed significant viability increase at the 75 µg/mL dose (~33%). Post-24 hours the same dose again was statistically significant from the control, however, at 48 hours this was not observed. At this time point, the 5 µg/mL dose showed ~20% increase. The observed viability trends were disregarded by the authors since it was not dose dependent.

56. In terms of proliferative effects, a decrease was not a significant decrease regardless of the concentration at 4 hours, however, differences were observed after 24 hours; cells exposed at the highest dose showed a sudden decrease from ~85,000 to ~75,000 cells at 48 hours. It was hypothesised that the trend of the growth curve was influenced by the tendency of the PS-NPs to aggregate.

57. As for ROS production, increases were observed within the first 30 minutes of PS-NPs exposure especially at the 5 and 25 µg/mL dose concentrations.

58. The CBMN showed DNA damage, resulting in the increased formation of micronuclei and nuclear buds, at the highest dose (75 µg/mL); ~12 micronuclei/1,000 binucleated cells and ~155 nuclear buds/total cells were observed.

59. It was concluded that, PS-NPs induces oxidative stress which subsequently resulted in DNA damage in the human fibroblast Hs27 cell line.

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[11] MTT assay: dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT) is a colourimetric assay for assessing cell metabolic activity.

[12] Cytokinesis-block micronucleus assay (CBMN): is a genotoxicity assay that provides simultaneous information on the different types of chromosomal damage *e.g.* chromosomal breakage, rearrangements, and gene amplification.

Immune response

60. The following paragraphs are of not direct relevance to non-intentional exposure to microplastics (*i.e.* clinical setting), however, the historical data provides an insight in the immune response resulting from exposure to microplastic particles.

61. Rader et al., (1999) examined the effect of PE spheroid particles (~1 µm) on cytokine release by THP-1 human monocytic leukaemia cells (MLC). Cells were exposed to concentrations ranging from 0.8 – 400 x 10^8 particles using a rotation device was utilised to mimic in the *in vivo* situation near arthroplasties[13], thus maintaining relevant contact between floating PE particles and MLC during incubation (6 hours; 15 rotations/min). The tests were carried through twice.

62. Cells were characterised by fluorescence-activated cell sorter scan of CD14[14]. Cell culture supernatants were analysed for IL-1β, IL-8, and tumour necrosis factor-α (TNF-α).

63. Secretion of TNF-α was not found to be influence by rotation, whilst the levels of IL-1β and IL-8 increased by a factor of 30 when compared to the control group. Significant TNF-α release was not observed till the particle concentration reached 48-80 x 10^8/10^6 MLC, measuring 640 pg/mL (~300 fold). At 108 x 10^8 PE particles, a decline of TNF-α release was seen, which preceded a decrease in cell survival.

64. A similar observation was seen for IL-1B, at 0.8 and 48 x10^8 exponential release was detected (20-fold increase), after which there was a decrease preceding cell death. The secretion pattern of IL-8 was similar to the release of IL-1β, up to 4,000 pg/mL at 0.7 x 10^8 particle concentration.

65. At concentrations higher than 400 x 10^8 PE particles/ 10^6 MLC; 90% cell death was observed. It was concluded that TNF-α release in response to PE particles and human MLC was more marked compared to the relative stimulation of the secretion of IL-1β and IL-8.

66. Green et al., (1998) evaluated the *in vitro* response of C3H murine peritoneal macrophages to PE particles (0.21, 0.49, 4.3, and 7.2 µm) and PE resin (mean size 88 µm) at volume (µm)^3 to cell number ratios of 100:1, 10:1, 1:1 and 0.1:1 for 24 hours. Levels of IL-6, IL-1β and TNF-α were determined by enzyme-linked immunosorbent assays. A cell viability test was also performed by MTT assay.

67. PE particles were found to stimulate primary macrophages producing elevated levels of IL-6 (0.49 and 4.3 µm particles at 100:1 ratio produced 2.41 and 3.15 units, respectively; n=3), IL-1β (0.49, 4.3 and 7.2 µm particles at 100:1 ratio produced 1.87, 1.85 and 1.06 units respectively; n=3) and TNF-α (0.49, 4.3 and 7.2 µm particles at 100:1 ratio produced 33.3, 35.58 and 16.46 units respectively; n=3), *in vitro*. The volume and size of particles are critical factors in macrophage activation, the most biologically active being 0.3-10 µm. The largest PE resin particle (88 µm) and the smallest PE particle (0.21 µm) did not induce the release of the

[13] Arthroplasty is the surgical reconstruction or replacement of a joint.
[14] CD14: surface antigen that is preferentially expressed on monocytes/macrophages.

tested osteolytic cytokines above control levels. This was hypothesised to be the inability of the macrophage to phagocytose large particles.

68. As for cell viability, the mean optical densities for the treatment group were not significantly different from the control group, which suggest that PE particles did not affect the macrophage cell viability.

69. The authors concluded that based on the results the critical size range for macrophage activation by PE particles may well extend below than 0.5 µm, since particles with a mean size of 0.49 µm stimulated high levels of IL-6, IL-1β and TNF-α.

Degradability

70. Stock *et al*., (2020) analysed the impact of gastrointestinal passage using artificial saliva, artificial gut simulated fluid and artificial intestinal fluid on the physical characteristics of PE, PP, PVC, PET and PS. Scanning electron microscopy (SEM) and subsequent image analysis were utilised to characterise microplastic particles.

71. SEM analysis of undigested particles and their particle diameters are shown in *Fig. 3*. PS was monodisperse and spherical, PE was polydisperse, porous and roundish in shape, PP was polydisperse shred-shaped, whilst PVC and PET were smooth and roundish. All particle diameters were in the range of 1-200 µm. The average particle size for the plastic particles were: PS; 3.8 µm, PE; 90.1 µm, PP; 67.1 µm, PVC; 136.5 µm and PET; 60 µm.

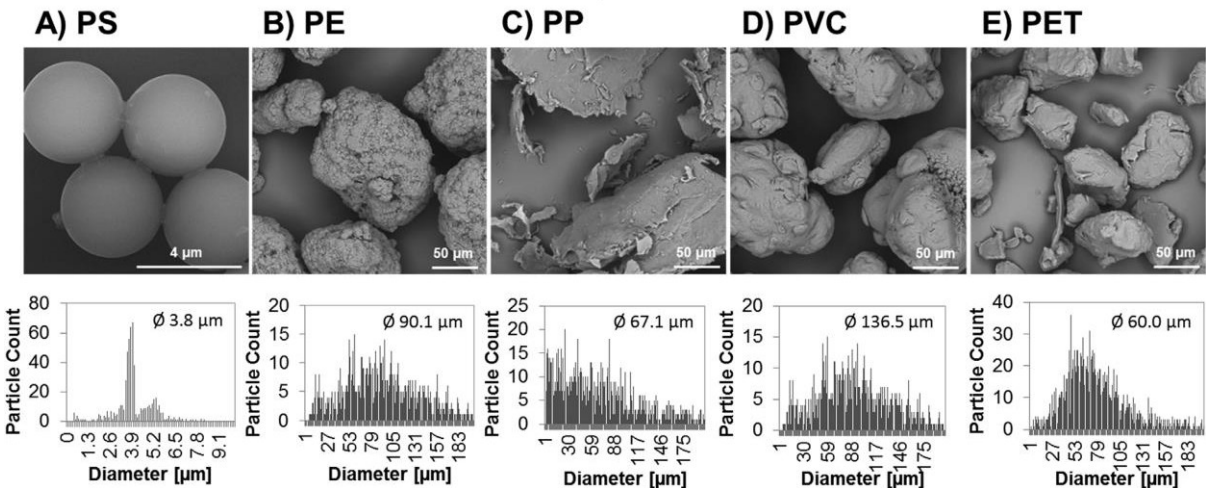

Figure. 3 – Scanning electron microscopic images of (A) polystyrene, (B) polyethylene, (C) polypropylene, (D) polyvinyl chloride and (E) polyethylene terephthalate microplastics. The size distribution of at least 80 plastic particles, are also provided as determined by image analysis are presented as histograms with mean diameters (reproduced from Stock *et al*., 2020).

72. Results for artificial *in vitro* digestion, showed changes in both shape and size of tested particles (especially PS particles). The particle diameters increased up to 20 µm through the different digestion steps. Marked changes for other plastic types

were not observed, with only few being deposited on the particle surface. Furthermore, the formation of protein coronas[15] were observed.

73. Based on the results, it was concluded that there was a high resistance of all plastic particles to the artificial digestive fluids tested, eluding that the main stages of the human gastrointestinal tract do not decompose the particles.

In silico

74. Jeong & Choi (2019) proposed a putative adverse outcome pathway (AOP) applicable to microplastic management to understand microplastic toxicity. A literature review carried out in January 2019 identified 46 publications on microplastic toxicity using Google Scholar. These were matched with toxicity mechanisms and apical endpoints to a key event (KE) and an adverse outcome (AO) information from the AOP Wiki database[16].

75. Six were applicable to both human health an ecotoxicity using model species that include zebrafish (*Danio* rerio) and roundworm (*Caenorhabditis elegans*). Only three publications discussed human health implications using *in vitro* human cell lines and *in vivo* mice studies. Various toxic effects were observed but the most common endpoints were oxidative stress-related endpoints including ROS generation, oxidative stress, and a mitogen-activated protein kinase signalling pathway.

76. Forty-three studies were confirmed with 21 KEs; the most common being oxidative stress (30.2%), ROS formation (14%), inhibition of acetylcholinesterase (11.6%), increase in inflammation (4.7%) and lipid peroxidation (4.7%). The most commonly used type of microplastics in these studies were PS (79.1%) and PE (16.3%). The animal models were mice (25.6%) and zebrafish (14%).

77. The most abundant AO was increased mortality (34.1%), growth reduction (22.7%), feeding inhibition (15.9%) and reproductive failure (11.4%). These studies used six microplastic types; PS (41%), PE (27.9%), PP (14.8%), and PVC (9.8%). *Daphnia magna* was the commonly used test species (22.2%), few studies investigated AO using model species relevant for human health toxicity (13.3%).

78. A schematic diagram of the putative AOPs for microplastics is shown in *Fig. 4.*

79. Based on the results, the authors suggest that the molecular initiating event was ROS formation and the AOs were increasing mortality, decreasing rates of growth, and reproduction failure, however, it was acknowledged that there were a limited number of studies available on microplastic toxicity mechanism and evidence between the relationship between KEs were not sufficient. Thus, further research is required to revise the putative AOP.

[15] Protein corona: is referred to as the layer of bound or adsorbed proteins around micro and nanoplastic particles.
[16] The AOP database can be found at: https://aopwiki.org/.

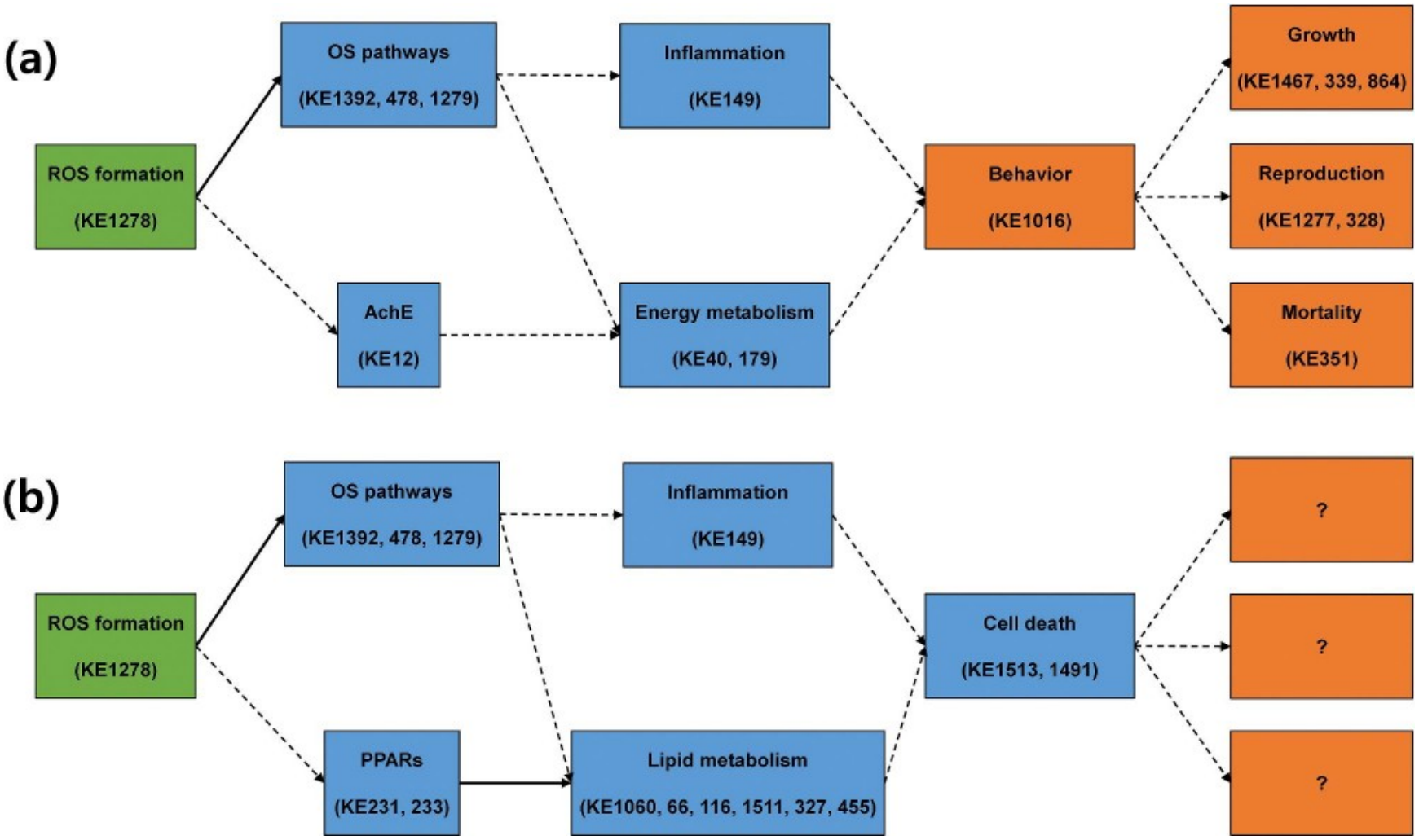

Figure. 4 – a schematic flowchart of the putative AOP for ecotoxicity (a) and human health implications (b) developed by Jeong & Choi (2019). Green boxes: molecular initiating events, Blue boxes: Key events, Orange boxes: Adverse outcomes. Solid lines: strong evidence, Dashed lines: weak evidence. Abbreviations: AChE; Acetylcholinesterase, AO; Adverse Outcome, PPARs; Peroxisome proliferator-activated receptor, ROS; Reactive Oxygen Species (reproduced from Jeong & Choi, 2019).

Environmental models

80. Berber (2019) assessed the acute toxicity of PS-MPs (1 µm) on *Daphnia magna* (n=20/dose) according to OECD Test Guideline 202. The PS-MPs concentrations were: 50, 100, 200, 400, 800, 1,600 and 3,200 µg/mL, the exposure was 48 hours. The lethal concentration 50 (LC_{50}) was calculated when the *Daphnia* was immobile (non-swimming for 15 seconds).

81. In conjunction, the genotoxicity of PS-MPs (1 µm) on Neocaridina davidi (cherry shrimp) (n=20/dose) was assessed by the Comet assay. The PS-MPs concentrations were: 200, 400, 800 and 1,600 µg/mL, the exposure was 24 hours.

82. The LC_{50} value was determined to be 808.97 µg/mL. The tail length, tail intensity and tail moment were increased in shrimp exposed to PS-MPs compared to the control (except in the lowest dose tested; 200 µg/mL).

Exposure

83. Prata et al., (2020) reviewed the environmental exposure to microplastics and presented an overview on possible human health effects. They summarise that exposure may occur by ingestion, inhalation, and dermal contact due to the presence of microplastics in the in consumer personal products, foodstuffs and air. In all biological systems, exposure may cause particle toxicity, with oxidative stress, inflammatory lesions and increased uptake or translocation. Due to the persistence of plastic particles, immune cells are overloaded which subsequently may lead to chronic inflammation and increase the risk of neoplasia[17]. Microplastics may also release their constituents (leachants such as phthalates and bisphenol A), absorbed chemicals (*e.g.* persistent organic pollutants) and pathogenic organisms. *Fig. 5* presents the potential pathways of exposure and particle toxicity for microplastics in the human body.

84. The authors concluded that although there is currently no evidence for widespread human health risk, there is a need to understand the effects of microplastic exposure (<10 µm). The toxicokinetic/toxicodynamic modelling of rats of 5 and 20 µm PS predicts higher bioaccumulation in the liver, and that the overall human threshold concentration of 5.1-53.3 mg/g bw (Yang *et al*., 2019), which corresponds to an estimated minimum human exposure to induce effects (using the most sensitive biomarker) of > 7.7 g (considering the average human liver weight) or 357 g (considering the average adult weight of 70 kg). The authors thought that this level of exposure is unlikely to occur, however, further research is needed to fill data gaps in order to perform a risk assessment.

[17] Neoplasia is the presence or formation of new, abnormal growth of tissue.

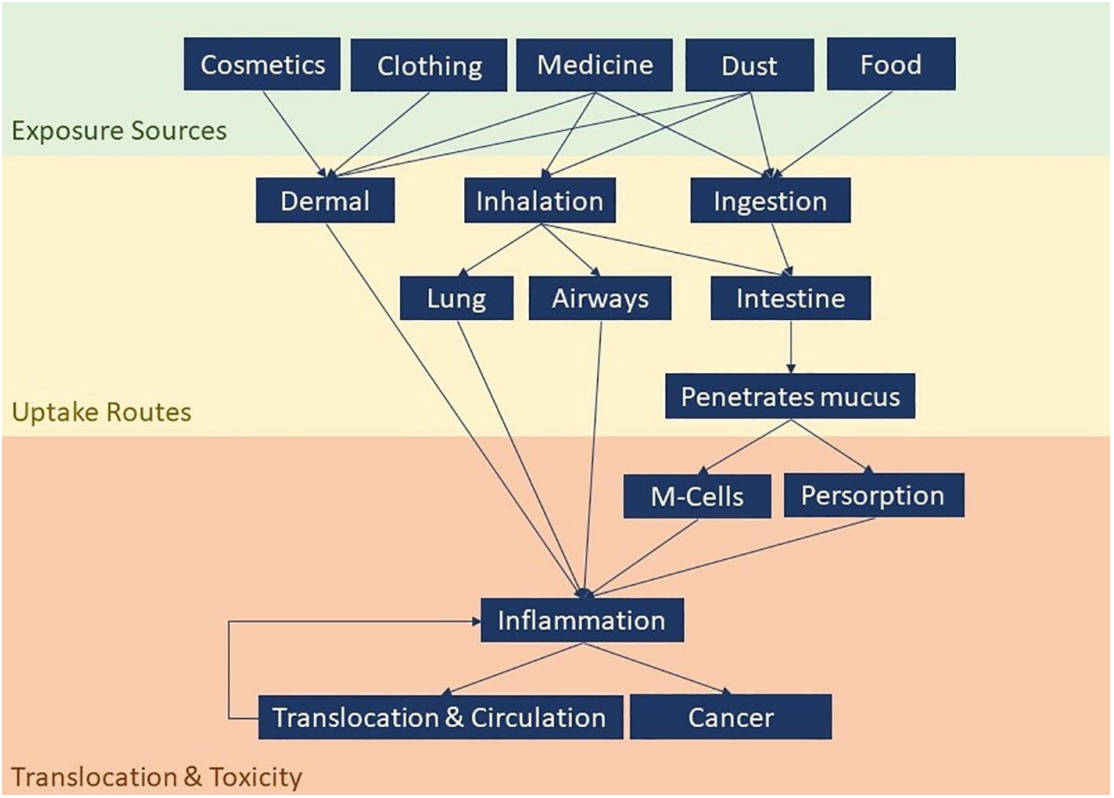

Figure. 5 – a flow chart diagram that shows the potential pathways of exposure and resulting particle toxicity for microplastics in the human body (reproduced from Prata et al., 2020).

86. Vianello et al., (2019) simulated human exposure to indoor airborne microplastics using a breathing thermal manikin. Three apartment environment types were investigated in Aarhus, Denmark during November and December 2017. The first apartment was a new lightweight building construction (A1), while the second and the third apartment (A2 and A3) were part of a two typical Danish brick building. All apartments consisted of four rooms: bedroom, bathroom, kitchen and a living room.

87. Measurements were performed in a sitting position at a table (~110 cm), with a respiration frequency and volume flow of 14.26/minute and 0.82 L/min, respectively (based on male respiration rate). The sampling period was 24 hours that included periods with and without human activity, thus the sampled air volume per sample (n=3/location) was 16.8 m^3. Note that three procedural blanks samples were also taken and analysed to monitor potential sources of contamination affecting the analysis.

88. Samples were analysed through Focal Plane Array-Fourier Transform-Imaging-Micro-Spectroscopy followed by automatic analyses down to particles of 11 µm in size by MPhunter software[18].

[18] MPhunter is a freeware program developed at Aalborf University in collaboration with Alfred Wegener Institute, for automated detection of microplastics from Fourier Transform-Imaging-Micro-Spectroscopy chemical imaging datasets.

89. All samples were contaminated with microplastics, with concentrations ranging between 1.7-16.2 particles/m^3. The average was 9.3 particles/m^3. The highest exposure concentration was measured in A3, corresponding to an inhalation rate of 11.3 microplastics/hour. Based on this, it was estimated that an average male person doing light activity would potentially inhale up to 272 microplastics over a 24-hour period.

90. Synthetic fragments and fibres accounted for ~4% of total identified particles, while non-synthetic particles of protein and cellulose constituted 91%, and 4%, respectively. Polyester was the predominant polymer in all samples (81%), then polyethylene (5%), and nylon (3%). Microplastics were typically of smaller size than non-synthetic particles. It was suggested that cellulose materials came mainly from paper and cotton products, whilst protein-based materials were associated with shed skin.

91. Inter-location and intra-location variations were observed. Differences in building materials, furniture type, cleaning procedures, and other activities in the apartment were associated with inter-location variations, whilst intra-location variations were thought to be related to activities happening during the sampling, which could have temporarily modified the particle concentration in the indoor air (*e.g.* opening of windows, loss of particles during the transfer of the sample from the filtration membrane to the analytical substrate *etc.*).

92. The authors concluded that microplastics constitutes a non-negligible fraction of respirable and ingestible indoor airborne particulates, and thus cannot be ruled out as having negative impacts on human health.

Secretariat
March 2020

Abbreviations

AChE	Acetylcholinesterase
AO	Adverse Outcome
AOP	Adverse Outcome Pathway
ATR-FT-IT	Attenuated Total Reflection Fourier- Transform Infrared Spectroscopy
CBMN	Cytokinesis-block micronucleus assay
CE	Capillary Electrophoresis
CONTAM	Panel on Contaminants in the Food Chain
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
DLS	Dynamic Light Scattering
DNA	Deoxyribonucleic acid
ECCC	Environment and Climate Change Canada
EFSA	European Food Safety Authority
EM	Electron Microscopy
EPS	Expanded polystyrene
FFF	Field Flow Fractionations
FPA-FT-IR	Focal Plane Array Fourier-Transform Infrared Spectroscopy
FT-IR	Fourier-Transform Infrared Spectroscopy
GSTP1	Glutathione S-transferase P
HC	Health Canada
HDC	Hydrodynamic Chromatography
HIPS	High-impacted polystyrene
HO1	Haemoxygenase-1
HPLC	High Performance Liquid Chromatography
IL	Interleukin
KE	Key Event
LC_{50}	Lethal concentration 50
LD	Laser Diffraction
LDPE	Low-density polyethylene
LLDPE	Linear-low-density polyethylene
MALS	Multi-angle Light Scattering
MLC	Human monocytic leukaemia cells
MTT	Dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide
NTA	Nanoparticle Tracking Analysis
OECD	Organisation for Economic Co-operation and Development
PA	Polyamide
PA 11	Polyamide 11
PA 12	Polyamide 12
PA 6	Polyamide 6
PA 6.10	Polyamide 6.10

PA 6.6	Polyamide 6.6
PE	Polyethylene
PE-MPs	Polyethylene microplastics
PET	Polyethylene terephthalate
PP	Polypropylene
PPARs	Peroxisome proliferator-activated receptor
PS	Polystyrene
PS-NPs	Polystyrene nanoparticles
PVC	Polyvinyl chloride
Py-GC-MS	Pyrolysis Gas Chromatography Mass Spectroscopy
RM	Raman Microspectroscopy
ROS	Reactive Oxygen Species
SEC	Size Exclusion Chromatography
SEM	Scanning Electron Microscopy
SOD2	Superoxide dismutase 2
SPM	Scanning Probe Microscopy
TED-GC-MS	Thermal Extraction Desorption Gas Chromatography Mass Spectroscopy
TEM	Transmission Electron Microscopy
TNF-α	Tumour necrosis factor α
WHO	World Health Organisation
WWTP	Wastewater Treatment Plant
XPS	X-ray Photoelectron Spectroscopy

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COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COT)

Potential risks from exposure to microplastics: Update on literature

Details of literature search carried out by the Secretariat at the Food Standard (FSA)

Relevant literature was obtained from reviews published by authoritative bodies, as described in paragraph 3 of the discussion paper. In addition, searches for further literature relating to the toxicity of micro and nanoplastics were carried out utilising the search terms below. The literature searches were performed by the Secretariat at the FSA, with a limit of publication date ranging from 2019-current.

Search terms

“Microplastics OR Nanoplastics &”

Toxicity
Toxicokinetics
Absorption
Distribution
Metabolism
Excretion
Acute Toxicity - oral
Sub(chronic)tox/ carcinogenicity
Human exposure
Human health effects
Risk assessment
Genotoxicity
Reproductive toxicity
Developmental toxicity
Immunotoxicity
Neurotoxicity
Inhalation toxicity
Endocrine effects
Food
Soil
Water - drinking-water, bottled water, water treatment plants
Air/aerial – atmospheric fallout
Bioaccumulation/retention
Europe
United Kingdom - UK
Sorption of environmental chemicals - metals, POPs, pharmaceuticals, microbes
Leachates
Biomonitoring
Biofilm