Potential of existing in vitro methods for revealing potential hazards of micro-nanoplastics

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INTRODUCTION

The vast majority of micro/nanoplastics (MNP) particles in the environment derive from degrading (macro)plastic waste, abrasions of car tyres, synthetic textiles etc. Currently the exposure levels of micro-nanoplastic particles are unknown but even low concentrations combined with a repeated dosing can lead to an accumulation in human tissues if metabolising enzymes and excretion mechanisms are lacking. Such mixtures of polymers containing various additives/impurities with unique physico-chemical characteristics will make their safety assessment a challenge. Traditional test methodologies might not be sufficient to reveal potential hazards of nanoplastics and new combinations of tools and approaches will be necessary. In this scoping review, we have analysed the state of the art of intestinal in vitro models which can play a key role in the testing strategies of nanoplastics. our review of scientific literature demonstrated that the existing cellular models can only provide indications on a local toxicities and a potential uptake of MNPs

METHODOLOGY

By applying the principles of quick scoping reviews, we have highlighted main trends in the scientific literature that reports on intestinal toxicity assessments in vitro. The systematic screening by using a pre-established set of keywords resulted in a library of 2559 original articles and 68 reviews published between 2010 and March 2020. For the sake of clarity, we established four categories of cellular models (2D monocultures, co-cultures, organ-on-a-chip as well as organoids) while accepting an overlay between the categories and the fact that new advanced methods such as organoids and organ-on-a-chip require further validation and standardisation efforts. In a second step, we have analysed what kind of toxicological information relevant for hazard identification can be obtained from the various models. In parallel, we investigated to what extend in vitro models have already been used for assessing nanomaterials and MNPs.

RESULTS

More than 40 cell lines deriving from various intestinal tissues mainly Caco2, HT29, and HCT 116 cells are used for the identification of pharmacological-toxicological potential of drug candidates and chemicals including nanomaterials. The studies mainly focussed on the assessment of endpoints related to basal cytotoxicity, effects on membrane integrity and the uptake of nanomaterial. Advancing cell culture techniques e.g. based on microfluidic techniques or the use of stem cell-derived cell models, can further improve the physiological relevance of in vitro tests and allow the evaluation of additional toxicological mechanisms such as immunological reactions and metabolic imbalances. However, we have also identified methodological gaps, which might be relevant for the understanding of mechanisms leading to potential adversities of MNPs in the intestine. They include methods assessing potential for accumulation, leaching of additives/impurities and resulting long-term effects as well as cell-type specific toxicities. Finally, only a few in vitro studies investigated effects of MNPs on the microbiome.

DISCUSSION

The further increase of plastic pollution in the environment followed by a continuous breakdown of large plastic items into mixtures of small plastic debris having different compositions, sizes, shapes etc. calls for a strategic approach to fill knowledge gaps on potential risks associated to MNPs. The challenge for the scientific community to identify those physico-chemical properties that can have an impact on human health will require the use of new advanced methodologies since traditional toxicological standard testing regimes are expensive, laborious and might not be suitable for uncovering long term effects. In this study, we describe in vitro models and toxicological endpoints that are currently used for intestinal in vitro toxicity testing, and we propose a tiered testing strategy that could be used to assess MNPs.. In any case, the general lack of knowledge on potential hazards of polymers, the occurrence of MNPs as mixtures as well as the technical difficulties involved in detecting them and defining exposure levels requires more efforts to finally conclude on hazards, thresholds and risk mitigation strategies.