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TITLE:

Agglomeration state of titanium-di-oxide (TiO_2) nanomaterials influences the toxicity/biological responses in human bronchial epithelial cells at the air-liquid interface

ABSTRACT:

Agglomeration of nanomaterials (NMs) is a ubiquitous phenomenon and its dynamic behaviour throughout their life cycle poses the greatest challenge in assessing its human health impacts. While agglomerates are of prime importance in occupational exposure scenarios, their toxicological relevance remain poorly understood[1,2]. Therefore, the aim of this study was to compare the toxicity/biological responses induced by agglomerates with its unbound particle counterparts. A nano-TiO_2 (Primary size 16 nm) and a non-nano TiO_2 (112 nm) was selected for this study. Stable stock dispersions of unbound particles (median feret min size, 34 and 120 nm) and their respective agglomerates (137 and 309 nm) were prepared using modified Guiot and Spalla protocol[3]. These dispersions were aerosolized at the air-liquid interface[4], which is more realistic interms of inhalation exposure and human bronchial epithelial cell cultures(16HBE14o-) were exposed to different doses (by electrostatic deposition) of TiO_2 aerosols. At the end of 4-hour exposure, effect on membrane integrity (LDH), metabolic activity (WST-1) and oxidative stress induction (glutathione depletion) was evaluated. Significant effects were observed only for nano-TiO_2. Unbound particle dispersion of nano-TiO_2 (34 nm) induced a dose dependent increase of LDH (about 30% increase at the highest dose tested). Further, it induced about 30% decrease of metabolic activity and glutathione at the highest dose tested. The estimated deposited dose indicate that the dose was not a confounder of the differential toxicity observed. These results suggest that the agglomeration state of TiO_2 nanomaterials influences

the toxicity/biological responses at the air-liquid interface, depending on the primary size. Effect on other end points such as genotoxicity and mRNA expression are currently investigated.

KEYWORDS:

TiO_2 nanomaterials, agglomerates, air-liquid interface, human lung cells, toxicity

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