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

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Agglomeration of nanomaterials (NMs) is a ubiquitous phenomenon and its dynamic behaviour throughout their life cycle poses a great challenge in assessing its impact on human health. 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 either agglomerates or individual/unbound particles. Two different sized titania particles, nano-TiO_2 (primary size 17 nm) and a sub-micron TiO_2 (117 nm) were selected for this study. Stable stock dispersions of non-agglomerated particles (median feret min size, 34 and 120 nm) and their respective agglomerates (137 and 309 nm) were prepared using a modified protocol published previously [3]. These dispersions were aerosolized and subsequently administered to human bronchial epithelial cell cultures (16HBE14o-) at the air-liquid interface [4,5], a procedure which is more realistic in terms of inhalation exposure. The cells were exposed to different doses of TiO_2 aerosols using electrostatic deposition. At the end of 4-hour exposure, the effects on cell membrane integrity (LDH release), metabolic activity (WST-1 reduction) and oxidative stress (glutathione depletion) were evaluated. Significant effects were observed only for nano-TiO_2. Non-agglomerated particles (34 nm) induced a dose dependent increase of LDH. Further, they decreased metabolic activity and glutathione levels at the highest dose tested. In contrast to unbound particles, agglomerates of nano-TiO_2 did not induce adverse effects although the deposited mass was similar. Similarly, exposure of cells to comparable doses of sub-micron TiO_2, either in the form of primary or agglomerated particles, also did not provoke toxicity. 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 particle size. In addition to acute cellular toxicity, other end points such as genotoxicity and altered gene expression are currently investigated.