Multiple Approaches to Determine Toxicity of Micro and Nano-sized Titanium Dioxide Materials when Exposed to Human Red Blood Cells

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Abstract:
Introduction: The utility of engineered nanomaterials' is growing, particularly the titanium dioxide (TiO_2) polymorphs. TiO_2 is very useful for brightening paints, and coloring foods. Nano-sized TiO_2 is also useful for sunscreens, cosmetics, and can be utilized as a photocatalyst. However, the nanometer size and the large specific surface area of the TiO_2 materials are physicochemical characteristics which may contribute to human red blood cell (RBC) damage. Using RBCs as a cellular model, we have evaluated the effects of TiO_2 nanoparticle exposure to RBCs by quantifying oxidized glutathione, oxidized membrane vitamin E, hemolysis, hemoglobin adsorption, and cellular aggregation.

Results: Red blood cells are rich in the antioxidant glutathione (GSH). HPLC testing revealed that some TiO_2 materials have the ability to cause oxidation of GSH to the oxidized form, glutathione disulfide (GSSG). Due to surface area characteristics, some TiO_2 materials have the ability to adsorb protein (visualized as hemoglobin) to their surface. Additionally, some TiO_2 materials microscopically form red blood cell aggregates, significantly changing the red cell morphology. The aggregation data was quantified using a hemacytometer. Red blood cell membrane vitamin E was also measured by HPLC, and after exposure to these TiO_2 polymorphs, some materials caused vitamin E membrane oxidation. Some TiO_2 materials have the ability, through multiple different mechanisms, to cause hemolysis of the red blood cell.

Conclusions: Our results indicated that some of the TiO_2 polymorphs assayed contributed to red blood cell hemolysis via different mechanisms, whereas some polymorphs did not cause cellular damage. These data indicated that red blood cells can ultimately be hemolyzed by biological oxidative damage (BOD), intracellular oxidation of GSH to GSSG, oxidation of vitamin E in the RBC membrane, material adsorption to the RBC membrane, physical contact, or by a combination of these mechanisms.