
SBPMat
B-MRS
SOCIEDADE BRASILEIRA
DE PESQUISA EM MATERIAIS
SALVADOR
XXIII B-MRS Meeting 2025
September 28th to October 2nd
BRICS
Brasil 2025

Toxicity of Titanium Dioxide Nanoparticles Assayed in Dynamic and Static Biomimetic Endothelial Cell Systems

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Titanium dioxide nanoparticles (TiO_2NP) have several applications in modern industry and medicine, primarily cosmetics. When TiO_2NP is in contact with the organism, it can enter the bloodstream and reach several organs, causing inflammatory reactions and cell distress, which can be pathogenically relevant. We used a microchip fabricated in polyester-toner [1] as a dynamic model to mimic a blood vessel to investigate the effects on endothelial cells and the toxicity mechanism, which could lead to pathogenicity. The confluence of human venous endothelial cells (HUVEC) inside the microchip under a constant perfusate flow containing various concentrations of TiO_2NP indicates the level of toxicity. The results were compared to a static system (cell culture plates) under the same stress but no flow. The effect of TiO_2NP on proliferation, death, and related responses to an inflammatory process, such as vascular endothelial growth factor (VEGF) and superoxide anion production, was evaluated. The results demonstrated that TiO_2NP induced apoptosis and necrosis and inhibited cellular proliferation by reducing VEGF expression. Also, TiO_2NP induced HUVEC activation associated with oxidative stress related to inflammatory processes. The experiments in a microchip environment demonstrated the influence of dynamics in cellular responses to TiO_2NP, suggesting that dynamic models mimicking blood vessels can represent, more realistically, what happens *in vivo*. Therefore, TiO_2NP may cause inflammation in a dose-dependent manner in HUVEC, indicating that endothelial cell-TiO_2NP interactions can be pathologically relevant.

Acknowledgements
CNPq 422380/2021-0

References
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