

Assessment of the genotoxicity of a titanium dioxide nanomaterial using a combination of *in vitro* and *in vivo* assays

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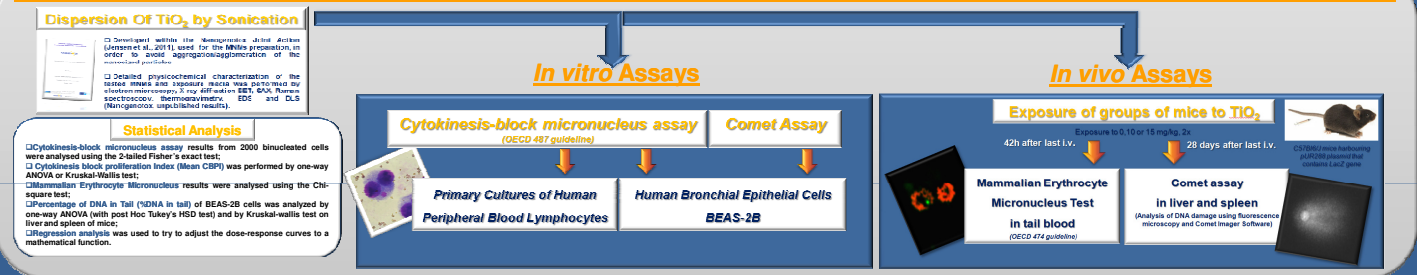
BACKGROUND

Human exposure to manufactured nanomaterials such as titanium dioxide (TiO₂), often used in sunscreens and cosmetics, has increased worldwide. Their specific properties, such as size and high surface area/mass, render them attractive for many applications, but may also be associated to higher toxicity in biological systems and adverse health effects.

OBJECTIVES

To analyse the potential genotoxic effects of a well-characterized TiO₂ nanomaterial, correlating *in vitro* and *in vivo* effects.

MATERIALS & METHODS



RESULTS

In vitro Assays

Comet Assay

- Significant induction of DNA damage (3-fold increase) at doses 32, 64 and 128 µg/cm² for %DNA in tail ($p = 0.005, 0.002$ and 0.002 , respectively)
- No dose-dependent relationship

Cytokinesis-block micronucleus assay

- No chromosome breaks or loss were induced by TiO₂
- No impairment of cells proliferation ability, as measured by CBPI
- Significant increase in micronucleated binucleated cells (MNBC) frequency at concentration of 125 µg/ml ($p = 0.038$)
- Cell cycle progression (measured by CBPI) showed no significant decrease following exposure of lymphocytes

In vivo Assays

Comet Assay

No significant induction of DNA damage in liver and spleen, measured by the % of DNA in tail, was observed after 28 days exposure to TiO₂.

Mammalian Erythrocyte Micronucleus test

No significant induction of micronuclei was observed neither in mature (ERY) nor immature (RET) blood erythrocytes after 42h exposure to TiO₂.

CONCLUSIONS

- Different results were obtained *in vitro* depending on the assay: DNA damage was observed in BEAS-2B cells, but no significant clastogenic/aneugenic events were observed neither for BEAS-2B nor for human primary lymphocytes.
- In vivo* assays (two endpoints in the same animal) revealed negative results for both endpoints tested.
- The data obtained for micronuclei analysis suggest a good comparability between the *in vitro* and *in vivo* outcomes, pointing to the absence of genotoxic effects following exposure to this TiO₂ nanomaterial at the dose levels tested.
- However, somewhat different genotoxicity outcomes concerning comet assay *in vitro* and *in vivo* may reflect tissue-specific effects affecting, e.g., cellular uptake of the nanomaterial.