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DOES GREEN SYNTHESIS SHAPE THE EPIGENETIC RESPONSE TO TIO_2 NANOPARTICLES?

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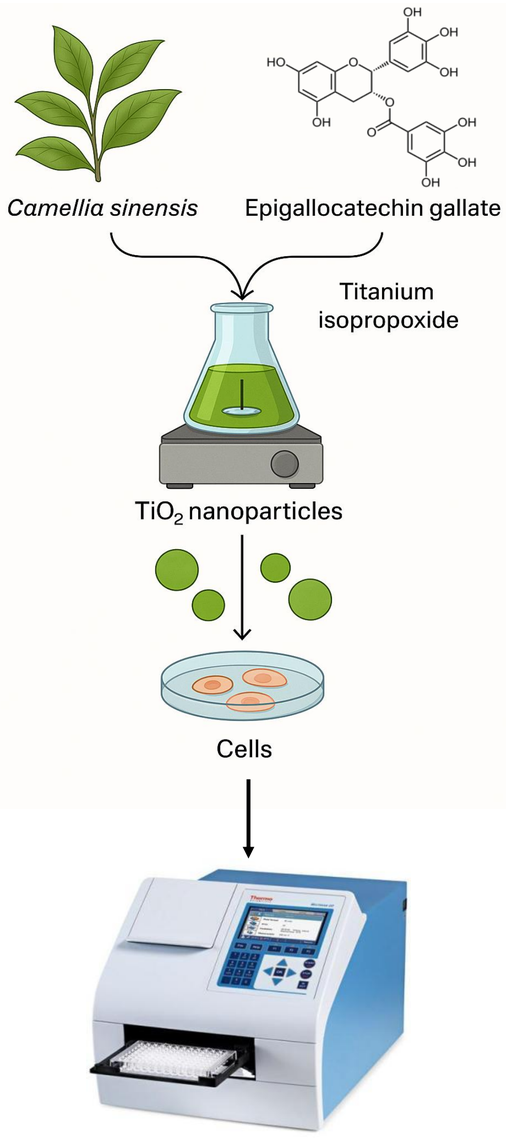
INTRODUCTION

- Titanium dioxide nanoparticles (TiO_2 NPs) are widely used in a variety of industrial and biomedical applications due to their unique physicochemical properties. As their production and use continue to increase, concerns have also grown regarding their potential impact on human health and the environment. This has led to growing interest in green synthesis approaches, which use naturally derived compounds to produce NPs in a more sustainable and environmentally friendly manner.
- Beyond their conventional toxicological effects, NPs can also induce epigenetic alterations, including changes in histone modifications that regulate chromatin structure and gene expression. These epigenetic changes are recognized as early molecular events associated with nanotoxicity and may provide insight into the biological effects of different NPs formulations.
- In this context, ***the present study aimed to compare the in vitro epigenetic responses induced by TiO_2 NPs obtained using the chemical as well as the green synthesis method in the presence of epigallocatechin-3-gallate (EGCG), the major catechin found in green tea (Camellia sinensis)***.

Camellia sinensis



MATERIALS AND METHODS

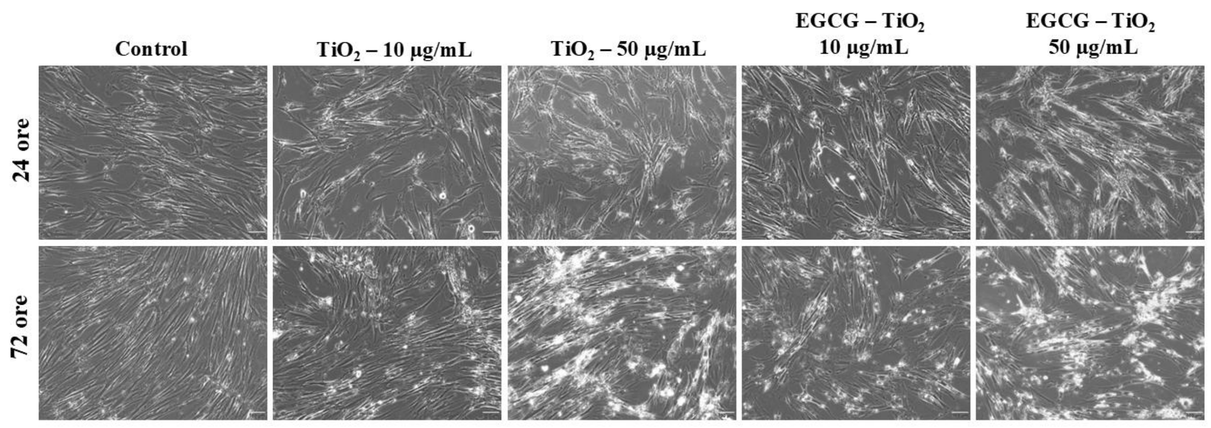
The chemical TiO_2 NPs were prepared by hydrolyzing titanium isopropoxide in distilled water. For the green synthesis route, the procedure was replicated in the presence of an aqueous 1 mM solution of epigallocatechin gallate (EGCG), acting as stabilizing agent.

The *in vitro* cytotoxic effects were evaluated on human pulmonary fibroblasts (MRC-5 cell line) through multiple parameters, including cell viability (MTT assay) and membrane integrity (LDH release), following exposure to TiO_2 NPs at concentrations of 10 and 50 µg/mL for 24 and 72 hours.

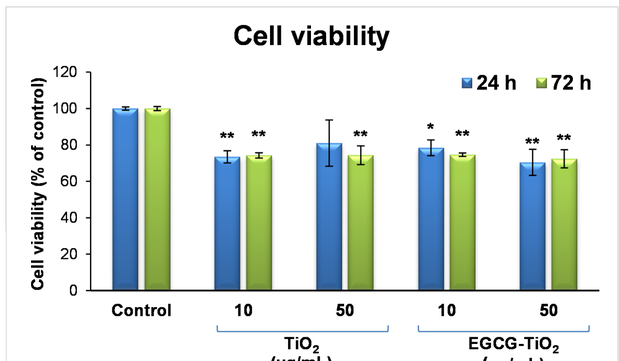
Epigenetic changes were assessed for the higher dose (50 µg/mL) and longest time exposure (72 hours). Different histone H4 modifications were measured by ELISA multiplex.

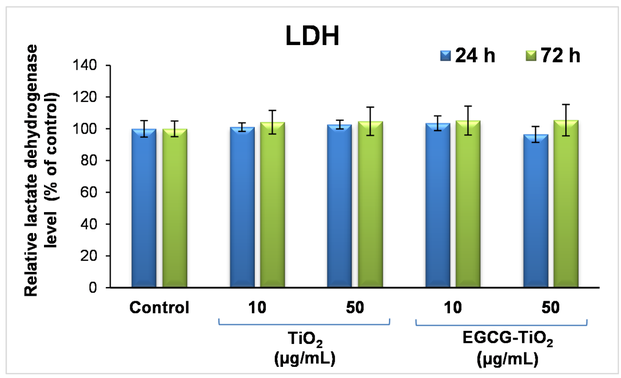
RESULTS AND DISCUSSION

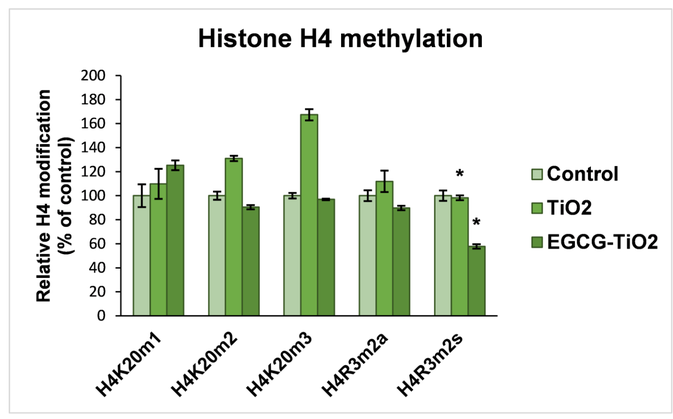
► Following exposure of MRC-5 lung fibroblasts to 10 and 50 µg/mL TiO2 NPs for 24 and 72 h, it was observed that both types of NPs induced a decrease in cell viability (up to 30%), with no significant differences between the two doses or time exposure intervals.



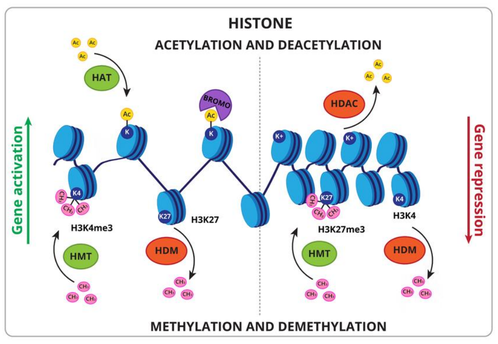
Representative images of phase contrast microscopy revealing cellular morphology of MRC-5 after 24h and 72 h of incubation with photocatalysts. Scale bar: 100 µm.



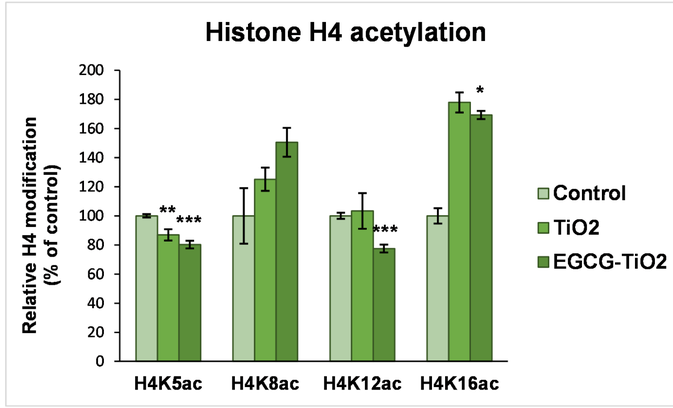


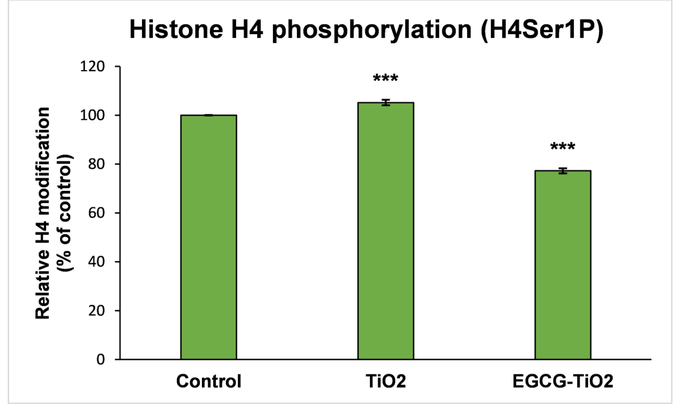


► Our results showed that chemical and EGCG-mediated green TiO_2 NPs induced distinct patterns of histone modifications in MRC-5 lung fibroblasts. Chemical TiO_2 predominantly increased H4K20 methylation and slightly enhanced H4Ser1 phosphorylation, whereas green TiO_2 shifted the response toward changes in histone acetylation, with decreased H4K5 and H4K12 acetylation, as well as increased H4K16 and H4K18 acetylation. Notably, the green NPs attenuated the methylation and phosphorylation changes induced by chemical TiO_2.



Histone modifications are associated with gene activation and gene repression (Cadavid et al., 2023)





CONCLUSIONS

✓ These findings highlight histone modifications as sensitive biomarkers of nanoparticle exposure and suggest that synthesis route can influence the epigenetic response to TiO_2 NPs.

References

1. Cadavid IC, Balbinott N, Margis R. Beyond transcription factors: more regulatory layers affecting soybean gene expression under abiotic stress. *Genet Mol Biol.* 2023, 46, e20220166.