

Biomolecular changes in cervical cancer cells by non-stabilised and albumin-stabilised colloidal N-TiO₂ nanoparticles: SR FTIR spectroscopical approach

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The presented research focuses on the intracellular changes induced by N-doped TiO₂ (N-TiO₂) nanoparticles (NPs) in cancer therapy, using cervical cancer as a model system. Uncovering the underlying intracellular mechanisms and the interplay between various signalling pathways that lead to cell death and the elimination of cancer cells is essential. A general approach to beat cancer and minimise severe side effects is to apply controlled and targeted therapy. Among other techniques, photodynamic therapy is promising, as it uses light to externally activate a drug with photosensitising properties and control tumour elimination. To increase efficiency, applying NPs as drug carriers or as photosensitisers (PSs) is advantageous [1]. TiO₂ NPs are promising as carriers and PSs due to their good photo-catalytic properties. On the other hand, due to its wide gap, only photoactivation with UV light is possible. Doping of TiO₂ with different elements, such as nitrogen [2] can change its bandgap, allowing its activation with visible light.

Our approach to assessing biomolecular changes is through applying Synchrotron Radiation Fourier Transform Infrared Spectroscopy (SR FTIR). This method, known for its high photon flux, allows us to understand intracellular biomolecular changes in cervical cancer cells (HeLa) caused by pristine N-TiO₂ and N-TiO₂ stabilised by bovine serum albumin (BSA-N-TiO₂). The high spatial resolution and precision of SR FTIR increase the accuracy of the research. It can be performed on whole cells and tissues immobilised on a CaF₂ carrier, providing a detailed assessment of biomolecular intracellular changes both qualitatively and quantitatively in different regions of cells. These involve changes in lipids, nucleic acids and proteins. Our results demonstrate that stabilising N-TiO₂ with BSA induces different structural changes in the proteins compared to pristine N-TiO₂. These changes are more expressed in the vibrational region of β -sheets, whereas both NPs cause changes in the area of α -helices. In addition, significant changes in the nucleic acid region were also detected in treated cells compared to the control. In summary, by using SR FTIR, we have demonstrated significant biomolecular changes in cells treated with N-TiO₂ and BSA-N-TiO₂, implying that the stabilisation of NPs with serum albumins plays a role in controlling the NPs' cellular action.

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References

- [1] Nešić, M., Žakula, J., Korićanac, L., Stepić, M., Radoičić, M., Popović, I., Šaponjić, Z., Petković, M. Light controlled metal-drug delivery system based on the TiO₂ nanoparticles and Ru-complex. *J. Photochem. Photobiol. A: Chemistry*, 347(2017)55-66
- [2] Ansatri, S.A., Khan, M.M., Ansari, M.O., Cho, M.H. Nitrogen-doped titanium dioxide (N-doped TiO₂) for visible light photocatalysis. *New J. Chem.*, 40(2016)3000-3009.