Spectroscopic Investigations and *in silico D*eterminations of Nanocomplexes in Cancer Treatment

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BACKGROUND

This research delves into the spectral analysis of TiO2 nanoparticles (NPs) functionalized with 5,10,15,20-(Tetra-4-carboxyphenyl) porphyrin (TCPP). The investigation included UV-Vis absorption and Fourier transform infrared spectroscopy–attenuated total reflection (FTIR-ATR) assessments of the porphyrin and its complexes with TiO2 NPs. Furthermore, the study explored the effectiveness of generating singlet oxygen, a crucial element in photodynamic therapy.

Molecular Docking simulations were employed to predict the interaction between TCPP and receptors targeted in cancer treatment. The UV-Vis absorption spectra of the NP complexes exhibited discernible porphyrin bands, enabling the quantification of loaded porphyrins on TCPP-functionalized TiO2 NPs. FTIR-ATR analysis unveiled the creation of porphyrin-TiO2 complexes, indicating that TCPP adsorption onto TiO2 may involve pyrroles within the porphyrin ring or radicals within the porphyrin derivative.

While the quantum yield for generating singlet oxygen by TCPP-TiO2 NPs is slightly lower compared to unbounded porphyrins, the efficiency remains promising.

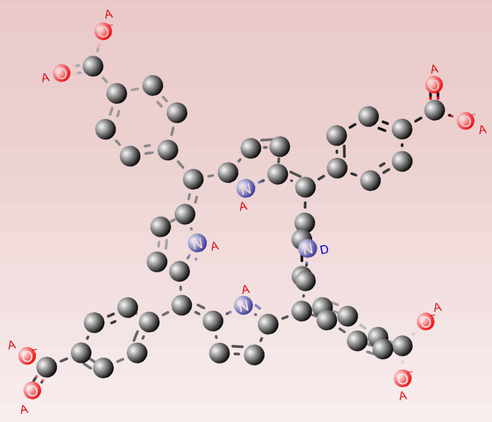
Through molecular docking studies involving several proteins targeted in melanoma treatment, like the A1 receptor and pro-caspase 3, TCPP displayed low binding energy, suggesting its potential interaction with these specific targets.

KEY FINDINGS

- Our predictions show that TCPP and pro-caspase 3 interact favourably in the following ways: conventional hydrogen-bound, carbon-hydrogen-bound, pi-anion, salt bridge in-teraction, and pi-alkyl. However, TCPP also forms an unfavourable negative-negative in-teraction with amino acid residue GLU43.
- The FTIR-ATR spectrum of TiO2-TCPP indicates characteristic TiO2 NP absorption bands and differences, suggesting TCPP binding to TiO2 via carboxylic acid radicals.
- The mean hydrodynamic size of TiO2 NPs was 559.1 nm, indicating the presence of aggregates in the samples, while TiO2-TCPP complexes showed a size of 1225.8 nm, suggesting the presence of larger aggregates and complex formation.
- The interaction between PS and TiO2, as well as energy transfer, is influenced by radicals serving as anchoring groups for porphyrins. Carboxyl groups, observed in the adsorption of TCPP on TiO2, enhance these interactions, potentially favoring the formation of OH radicals over 1O2.

TAKE-AWAY

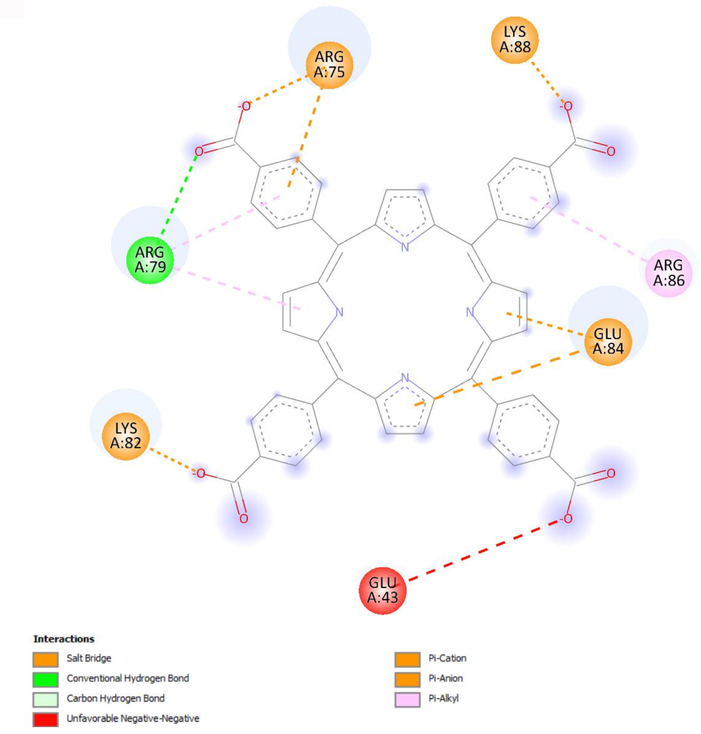
The conjugates of TCPP-TiO2 NPs hold promise as viable candidates for assessment in *in vitro* assays for photodynamic therapy.



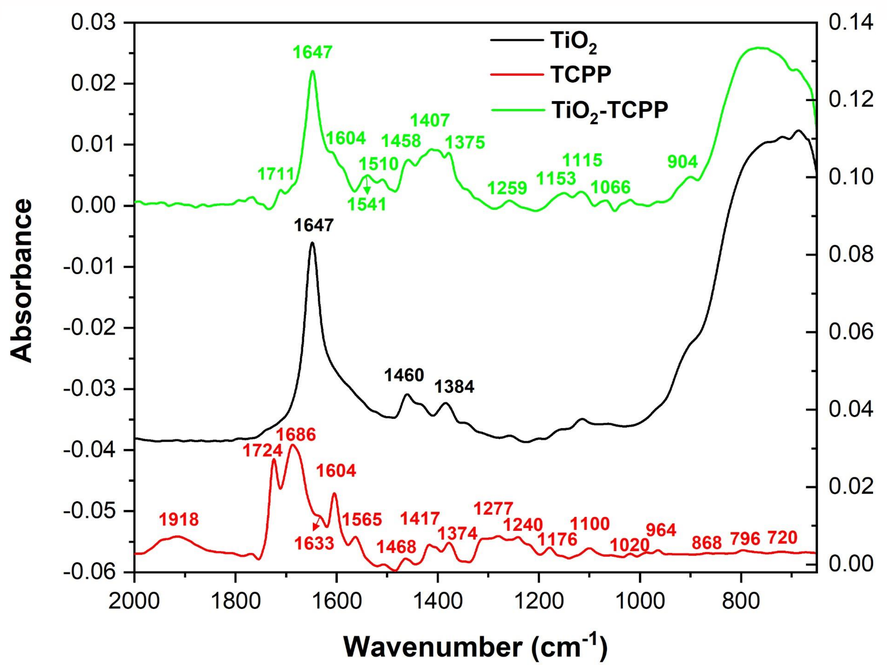
3D Structure of TCPP with highlighted donor and acceptor atoms with A for acceptor atoms and respective D for donors.

Lowest binding free energy predicted in kcal/mol and inhibition constant (K_I) predicted in nanomolar (nM).

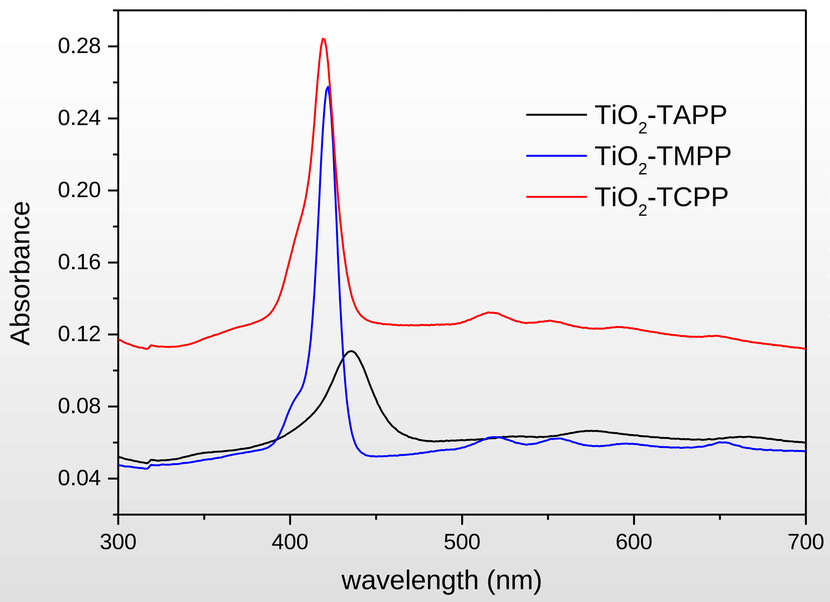
Target	ELFEB (kcal/mol)	K_I (nM)
Mcl-1	-7.55	2900
A1	-9.38	133.01
Bcl-B	-8.39	704.39
pro-caspase 3	-9.56	97.90
ML-IAP	-7.58	2770



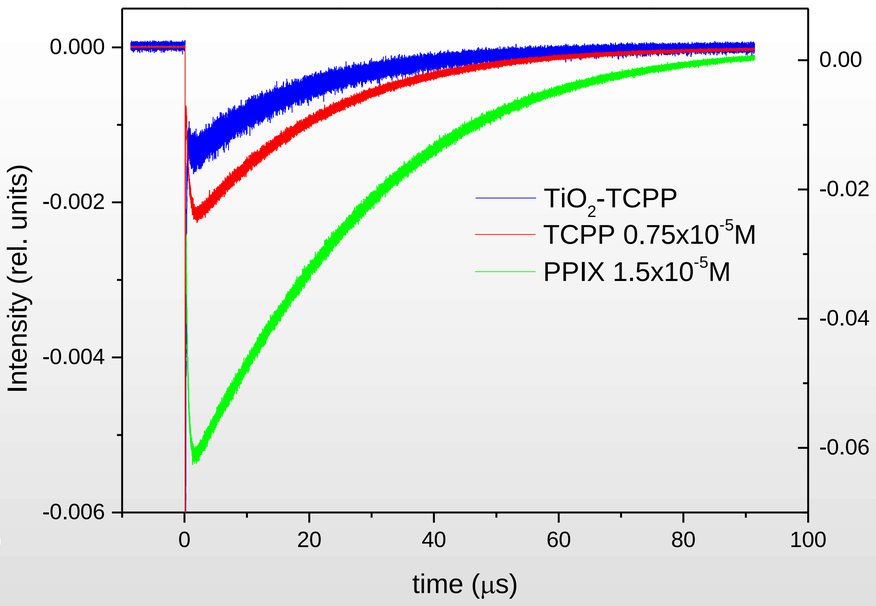
2D visualization of the interactions between TCPP and pro-caspase 3 amino acid residues. Green conventional H-Bond; orange Pi-Cation, Pi-Anion and Salt Bridge; pink Pi-Alkyl; red Unfavorable Negative-Negative.



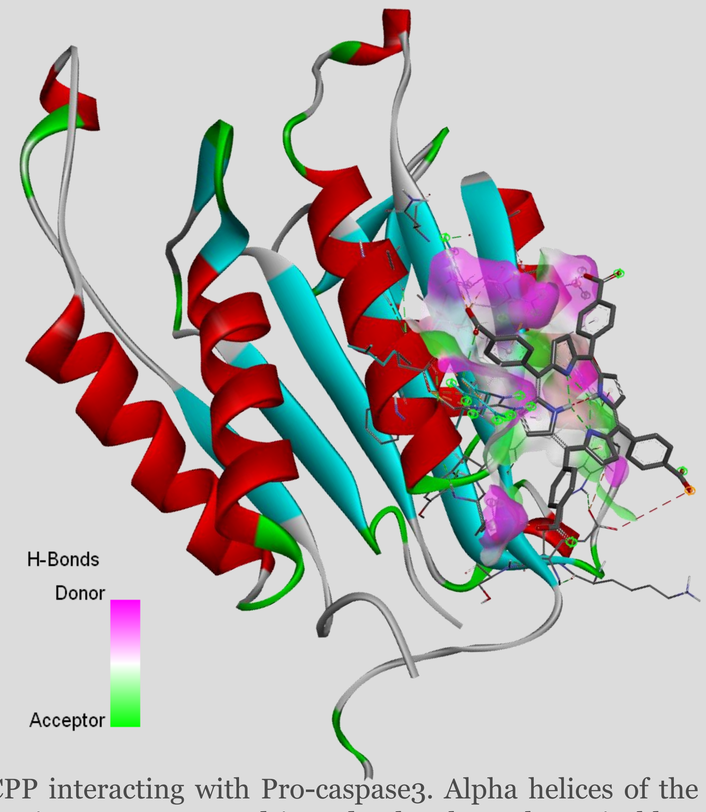
FTIR–ATR spectra of TiO2 NPs, TCPP, and TiO2 NPs loaded with TCPP. Left axis corresponds to the TiO2-TCPP spectrum, while right axis corresponds to TiO2 and TCPP spectra. The TiO2 spectrum is vertically translated.



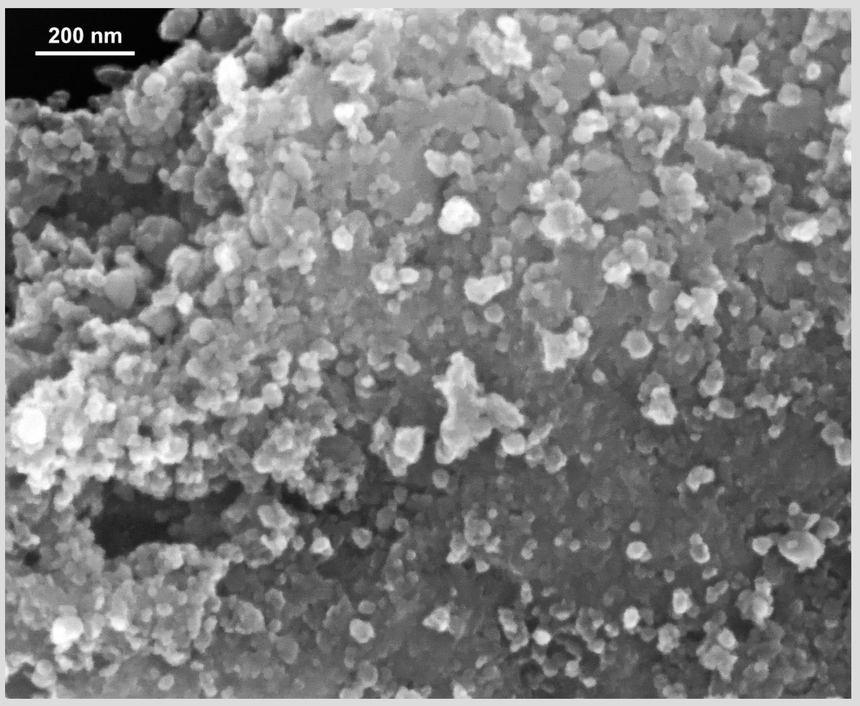
The absorption spectra of porphyrin-functionalized TiO2 nanoparticle suspensions and comparation with TAPP and TMPP derivatives.



Time-resolved phosphorescence signals for single oxygen generated by TCPP, and his conjugate with TiO2 in comparison with PPIX used as reference.



TCPP interacting with Pro-caspase3. Alpha helices of the protein are represented in red color, beta sheets in blue, turns in green, and random coil in grey



SEM image at 100,000× magnification of TiO2-TCPP sample. SEM analysis on TiO2-TCPP show that the particles are dispersed on a nanometer scale.

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