Controlled pro-oxidant action of $(Gd,Y)VO_4:Eu^{3+}$ nanocrystals through delayed ROS generation

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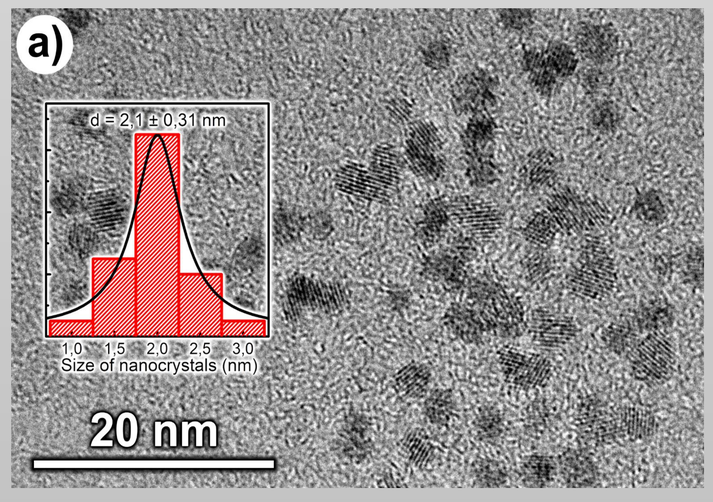
Abstract

A significant challenge in traditional photodynamic therapy (PDT) is its dependence on oxygen to generate singlet oxygen ($^1O_2$). Because solid tumors often exhibit hypoxia, the efficacy of classical PDT is frequently compromised. In contrast, the generation of hydroxyl radicals (•OH) presents a superior alternative for cancer treatment, as these radicals can be produced directly from water molecules rather than dissolved oxygen. This study focuses on $(Gd,Y)VO_4:Eu^{3+}$ orthovanadate nanocrystals (NCs) that exhibit controlled pro-oxidant action by generating •OH in a delayed manner, after UV pre-irradiation in the absence of continuous external stimuli.

The $(Gd,Y)VO_4:Eu^{3+}$ NCs (~2.1 nm) possess a high density of oxygen vacancies (V_O) and structural defects. Under UV pre-irradiation, photo-induced holes are created. Instead of immediate recombination, these holes are captured by localized metastable levels formed by the scattering potentials of the oxygen vacancies. These trapped holes eventually migrate to the surface of the NCs and react with water molecules to produce hydroxyl radicals long after the light source has been removed.



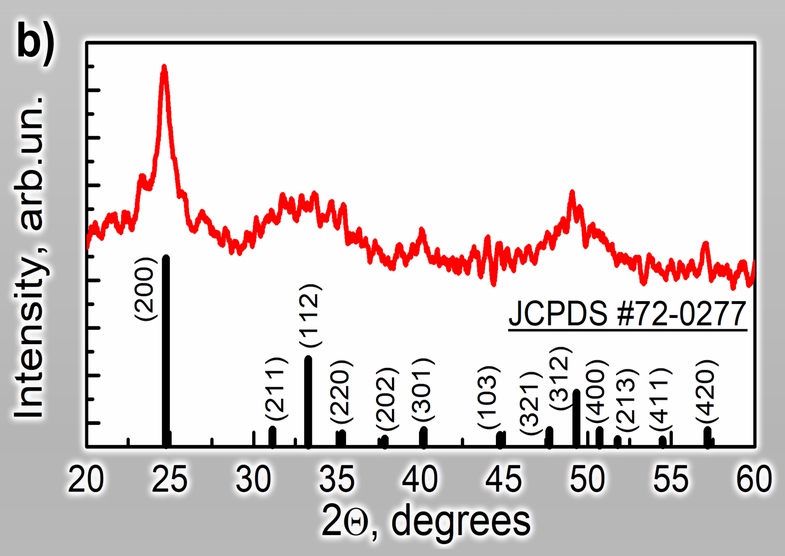


Fig.1. TEM image (a) and X-ray diffraction pattern (b) of $(Gd,Y)VO_4:Eu^{3+}$ NCs

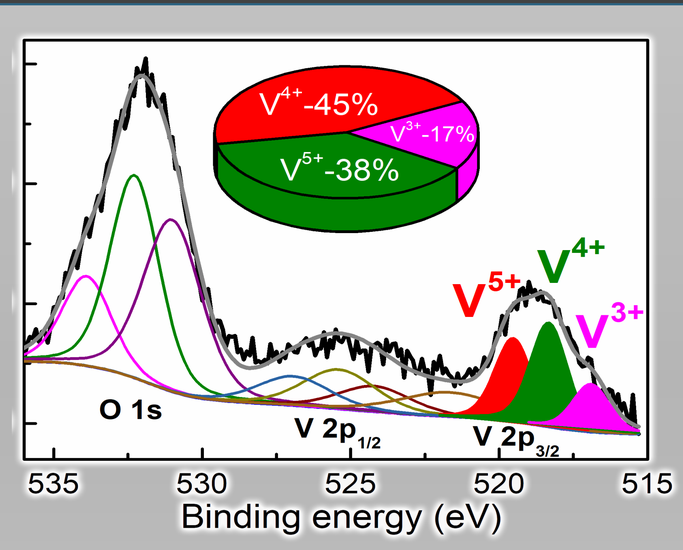


Fig.2. XPS of $(Gd,Y)VO_4:Eu^{3+}$ NCs

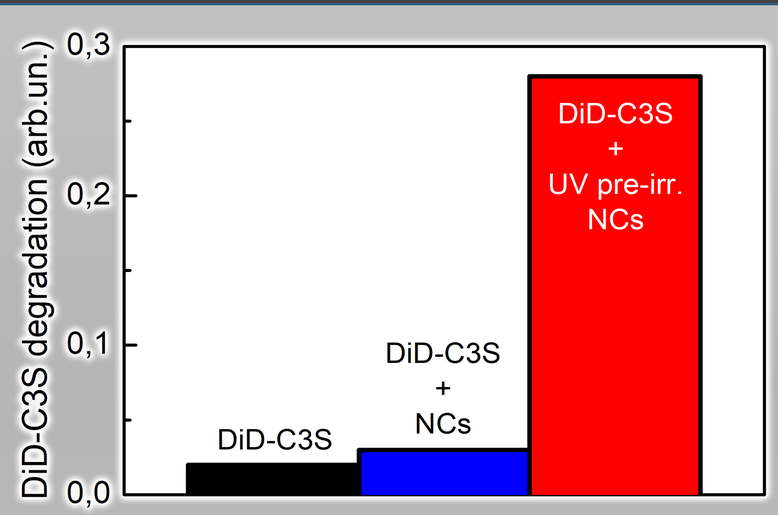


Fig.3. DiD-C3S degradation in water solutions containing $(Gd,Y)VO_4:Eu^{3+}$ NCs

Experiment

The delayed generation of •OH radicals after UV pre-irradiation in the dark was confirmed using several analytical techniques:

1) Luminescence spectroscopy: using coumarin as a fluorescent probe, which reacts with •OH to form highly fluorescent 7-hydroxycoumarin.
2) EPR spectroscopy: using DMPO as a spin trap, which reacts with •OH to form DMPO-OH adducts.
3) Overall pro-oxidant activity: the oxidative capacity was further evidenced by the degradation of DiD-C3S dye in solutions containing UV pre-irradiated NCs.

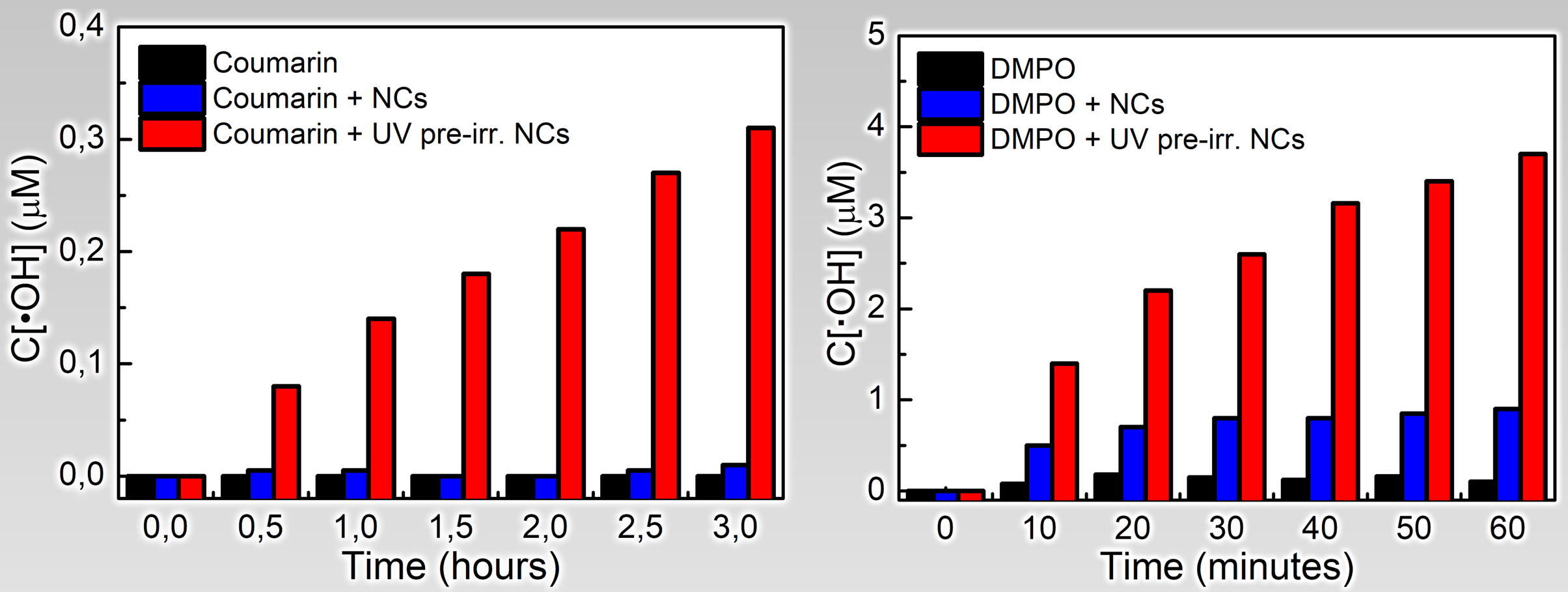


Fig.4. •OH generation in water solutions containing $(Gd,Y)VO_4:Eu^{3+}$ NCs: left - luminescence spectroscopy, right - EPR spectroscopy

Conclusions

The ability to trigger and then sustain the release of •OH radicals provides a unique mechanism for controlled pro-oxidant action. By bypassing the need for high oxygen concentrations and continuous irradiation, $(Gd,Y)VO_4:Eu^{3+}$ NCs offer a promising strategy for the treatment of hypoxic malignant cells, potentially overcoming the limitations of oxygen-dependent therapeutic modalities.

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