# Switching of pro/antioxidant action of $GdYVO_4:Eu^{3+}$ nanoparticles by UV pre-irradiation

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## Motivation

❖ Despite the progress in tumor early diagnostics and improved treatment approaches observed in last years, cancer remains a major public health problem worldwide giving the second leading cause of death. Unfortunately, conventional anti-cancer treatments such as radiation- and chemotherapy have many disadvantages including high toxicity, effects on healthy cells, tissues and organs and variety of side effects, etc. That is why, a search of novel effective approaches for cancer treatment remains the challenge for human society in 21th century.

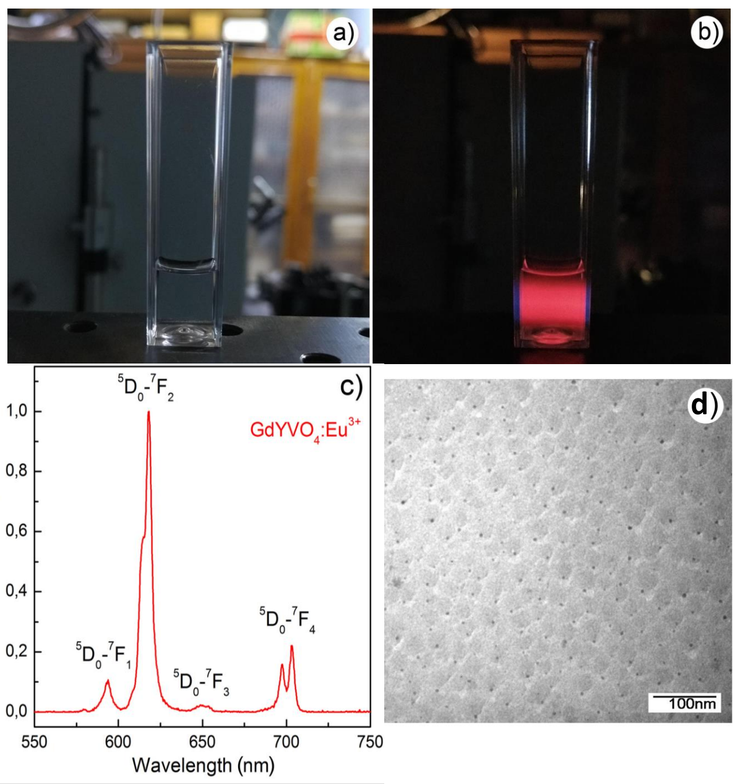
❖Reactive oxygen species (ROS) are redox active species containing oxygen, such as superoxide ($O_2^{\bullet-}$), hydroxyl radical ($^{\bullet}OH$), hydrogen peroxide ($H_2O_2$), and singlet oxygen ($^1O_2$), playing a key role in cell functionality.

❖In cancer cells, the level of ROS is maintained close to the threshold of cell death. Therefore, cancer cells are more sensitive to further ROS modulation and different strategies based on both ROS inducing and reducing have been proposed using various materials including nanoparticles (NPs): size, surface properties and concentration of defects in NPs affect sufficiently both pro- and antioxidant activities responsible for their antibacterial activity. Moreover, the presence of oxygen vacancies ($V_O$) and other structural defects is responsible for charge carriers storage and ROS generation in darkness that makes such materials prospective for various biomedical applications as antimicrobial and anticancer agents.

❖Rare-earth orthovanadate NPs ($ReVO_4:Eu^{3+}$) a bright example of nanomaterials with a multi-modal action.

***In this work will been shown that pro- or antioxidant activity of $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs in different biological environments can be controlled by NPs pre-irradiation with UV light or storage in the dark conditions before the experiments.***

## Synthesized nanoparticles




❖ Synthesized $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs were in a form of water colloidal solutions (pH = 7.4 – 7.8) transparent in transmitted light and exhibiting bright red fluorescence at UV-light irradiation, characteristic for $Eu^{3+}$ ions (Fig. a, b).

❖ The fluorescence of $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs is governed by the $Eu^{3+}$ ions and results from transition within their f–electron configuration with the main contribution of the $^5D_0$–$^7F_{2,4}$ forced electric dipole transitions and weaker $^5D_0$–$^7F_{1,3}$ magnetic dipole transitions (Fig. c).

❖ $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs are spherical particles with an average diameter ~ 2 nm as was revealed by the TEM micrograph (Fig. d)

## Pro-/antioxidant activity evaluation

1 mL of NPs water colloidal solutions was irradiated with UV light during 90 min using a 250 W mercury lamp and a band pass filter of 205–315 nm. Another 1 mL of the NPs water colloidal solution was stored in the dark for 4 days minimum.

**Ascorbic acid (AA)** is a well-known antioxidant and free-radical scavenger, i.e. an electron donor molecule, which reacts with ROS and free radicals eliminating them via electron transfer reaction. AA is the effective ROS scavenger, in particular, $O_2^{\bullet-}$, $^{\bullet}OH$, $H_2O_2$, and $^1O_2$.

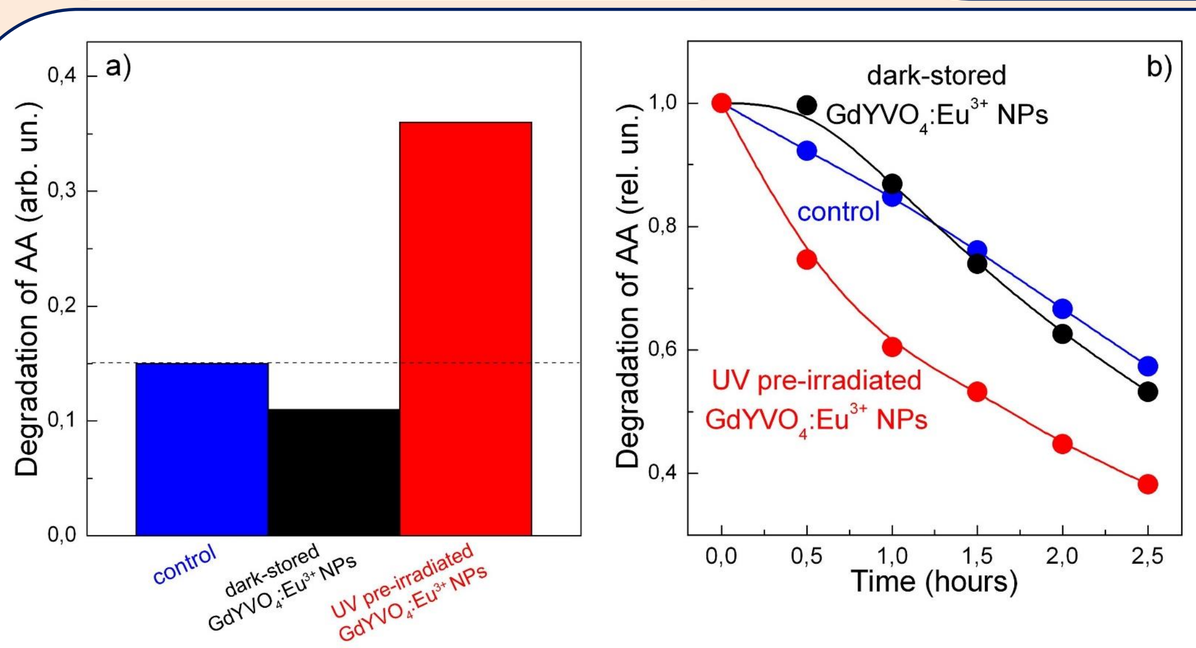
❖ UV-irradiated or dark-stored NPs solutions were mixed with a 1 mL of the AA water solution (0.02 g $L^{-1}$).

❖ The AA oxidation was estimated by the decrease of the characteristic absorption band ($\lambda_{max}$ = 265 nm) measured at different time intervals. As a control, an AA water solution without NPs was used.

**Lipid membranes of living cells** are known to be one of the main ROS target. Lipid oxidation by $O_2$ molecules takes place via a set of radical chain reactions with the production of various ROS and free radicals.

❖ 100 μL of the PC liposome suspension was mixed with 100 μL of NPs water solution (0.2 g $L^{-1}$). For lipid autoxidation test, the obtained PC-NPs suspensions were kept in a heat chamber (t=65°C) for 48h, whereas for studying the lipid oxidation at direct UV-irradiation, the suspensions were placed in quartz cuvettes (10x10 mm) and irradiated with UV light for different time intervals.

❖ The relative concentration of conjugated dienes formed in a water solution was estimated by measuring the absorbance of the suspensions at characteristic wavelength 234 nm. As a control, the suspension without NPs was taken.




*AA oxidation in water solutions containing 0.02 g $L^{-1}$ $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs measured after 30 min (a) and in different time intervals (b)*

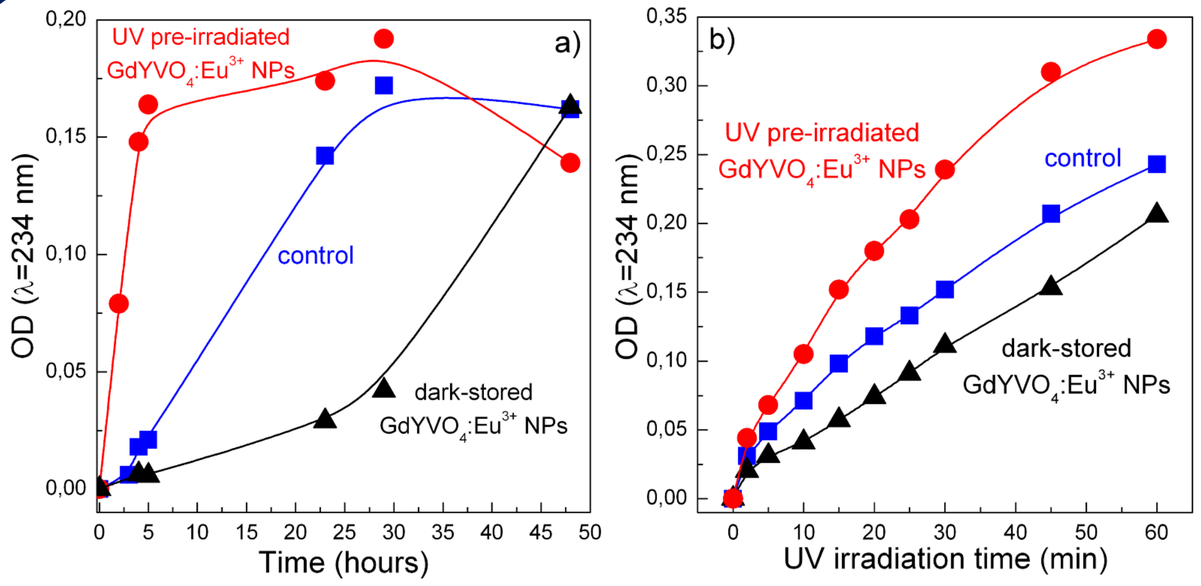
➢ **UV pre-irradiated NPs reveal strong pro-oxidant effect** (Fig. a) increasing the AA oxidation behavior. The faster oxidation of AA could be associated with the reducing ROS, such as $^{\bullet}OH$ and $O_2^{\bullet-}$, formed in the solution in dark conditions via reaction of captured $e^-$ and $h^+$ with $O_2$ and $H_2O$ adsorbed at the surface of NPs:

$$^3O_2 + e^- \text{ (captured)} \rightarrow O_2^{\bullet-}$$
$$H_2O + h^+ \text{ (captured)} \rightarrow {}^{\bullet}OH$$

➢ In time, when capture levels in $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs are depleted, the rate of AA oxidation slows down and becomes equal to that in the solution without NPs (Fig. b).

➢ $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs, which were **stored in the dark** before the experiment, being added to the AA solution **inhibit the process of AA oxidation** at the first stage (up to 30 min). This effect can be explained by the presence of $V^{4+}$–$V_O$–$V^{4+}$ sites in $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs and electron-donating property of $V^{4+}$ ions.

➢ After about 1 hours (Fig. b), $V^{4+}$ ions will be oxidized to $V^{5+}$, so $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs act neither as ROS scavengers, nor as ROS producers.




*Effects of dark-stored or UV-light pre-irradiated $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs on PC lipid autoxidation at t=65 ℃ (a) and oxidation initiated by UV-irradiation, t=23 ℃ (b)*

➢ **UV-light pre-irradiated NPs reveal strong pro-oxidant effect** increasing of lipid oxidation at the expense of $^{\bullet}OH$ generation (Fig. a).

➢ **Dark-stored NPs reveal strong anti-oxidant activity** inhibiting PC lipid oxidation in the first hours after experiment beginning. ROS formed during lipid oxidation are eliminated via the reaction with a participation of electrons stored at $V^{4+}$.

➢ When ROS scavenging mechanism is run out due to $V^{4+}$ oxidation to $V^{5+}$, fast lipid oxidation is detected with the rate similar to that in the solution without NPs.

➢ **Pro-** and **anti**oxidant effects of $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs can be observed even at direct irradiation of lipid suspensions containing NPs (Fig. b).

➢ UV-light pre-irradiated NPs increase the lipid oxidation due to their photocatalytic action, whereas dark-stored ones decrease the lipid oxidation due to ROS scavenging mechanism, which predominates in NPs at the first stage of NPs irradiation.

**We can conclude that small gadolinium-yttrium orthovanadate $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs (d=2nm) possess redox activity, i.e. ability to produce or scavenge ROS, and this redox activity can be triggered by altering conditions of NP pre-treatment. Light-triggered redox activity of $Gd_{0,7}Y_{0,2}VO_4:Eu^{3+}$ NPs makes them promising for biomedical applications such as radiotherapy, which will ensue a new approach in malignant cell treatment.**