Visible light-responsiveness of the nanocarrier/drug complex based on the TiO2 nanoparticles and Ru complex

M. Matijević[1], M. Stepić[1], M. Radoičić[2], M. Petković[1] and M. D. Nešić[1]

[1]Center for Light-Based Research and Technologies COHERENCE, Department of Atomic Physics, Vinča Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia

[2]Department of Radiation Chemistry and Physics, Vinča Institute of Nuclear Sciences - National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia

BACKGROUND

TiO2 nanoparticles (NPs) have great potential for implementing photodynamic therapy (PDT) as a part of drug delivery therapeutical systems [1]. However, high bandgap energy (3.2 eV) of TiO2 requires harmful UV light for photo-stimulation. Thus, to allow the responsiveness of TiO2 NPs in the visible range, we have modified TiO2 surface with Ru complex (cis-dichlorobis (2,2'-bipyridyl-4,4'-dicarboxylic acid)ruthenium(II) (Ru(dcbpy)2Cl2) forming the nanocomposite systems (NCSs). Moreover, Ru(dcbpy)2Cl2 has a pronounced cytostatic effect on the cancer cells [2], acting as a medicament in the photo-active NCSs. Hence, we have examined the cytotoxic effect on the cancer cells of the combined therapy of visible light and NCSs.

METHODS

- NCSs tested in this work were fabricated from colloid TiO2 NPs and TiO2 prolate nanospheroids (PNSs).
- The optical bandgaps of the synthesized NCSs were calculated by Tauc's equation:

$$(\alpha h\nu)^n = a(h\nu - E_g)$$

where α is the absorption coefficient, hν is photon energy, a is the absorption constant, and n indicates indirect (n = ½) or direct (n = 2) allowed transitions. The bandgap energy (Eg) is determined using the optical absorption coefficient α from the experimental absorbance. Eg values are obtained by extrapolating the curve's linear region to the abscissa (α = 0).

- We assessed the photocytotoxicity to the HeLa cell line. The cells were treated with NCSs, TiO2 and Ru(dcbpy)2Cl2 and incubated for 2h. Then, the photostimulation was delivered by the green light (532 nm) with three power levels (3, 13, and 22 mW) for 5 min.

RESULTS

The successful binding of the Ru(dcbpy)2Cl2 to the TiO2 NPs was confirmed and presented in our previous works [3, 4].

The UV-Vis spectra of NCSs have a similar appearance with the characteristic peaks at the same position, Fig. 1. More precisely, both NCSs' spectra show distinctive sharp TiO2 peaks at 350 nm due to the transitions of electrons from the valence band (VB) to the conduction band (CB) and short humps at 413 and 562 nm, resulting from Ru(dcbpy)2Cl2 adsorption on the surface of TiO2 NPs. These values clearly indicate that the synthesized NCSs are visible light active.

The evaluated bandgap of pure anatase TiO2 is 3.30 eV Fig. 2. (c). The Ru(dcbpy)2Cl2, on the other hand, energy gap values are: 3.7 eV due to inter-ligand π → π* transition, and 2.6 and 2.0 eV, corresponding to the metal to ligands charge transfer (dπ → π*), Fig. 2. (a). Finally, for the NCS, the energy gaps values are: 3.9, 2.7, and 2.1 eV, Fig. 2. (a). The reduced bandgap value of 2.7 eV, confirmed the visible light activity of the NCSs [5].

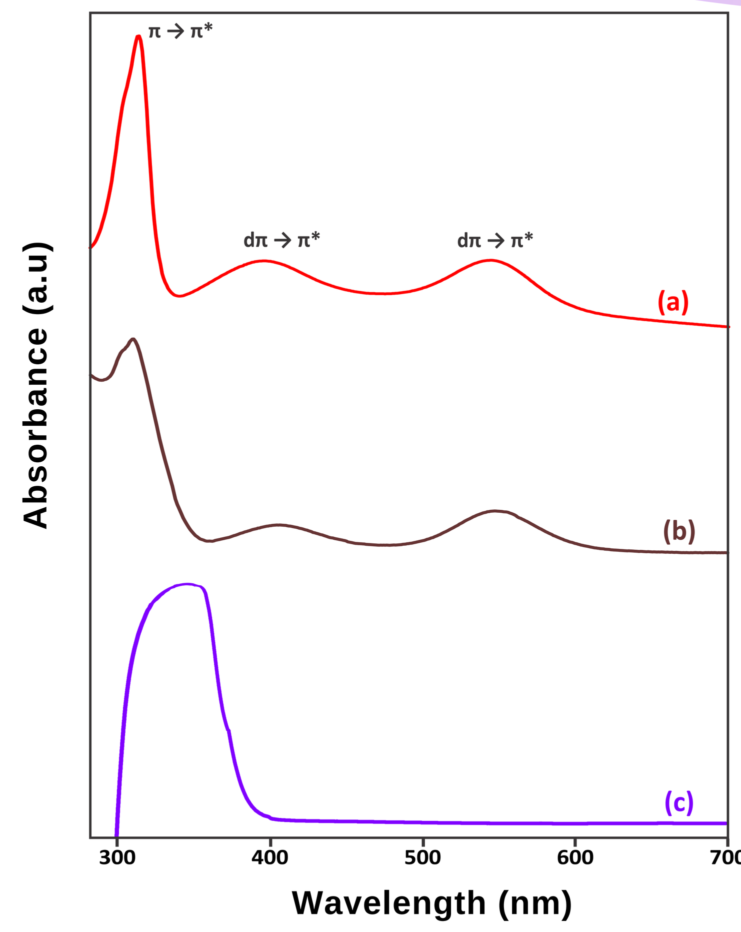

Fig. 1. UV-Vis spectra Ru(dcbpy)2Cl2 (a), NCS (b) and TiO2 (c).

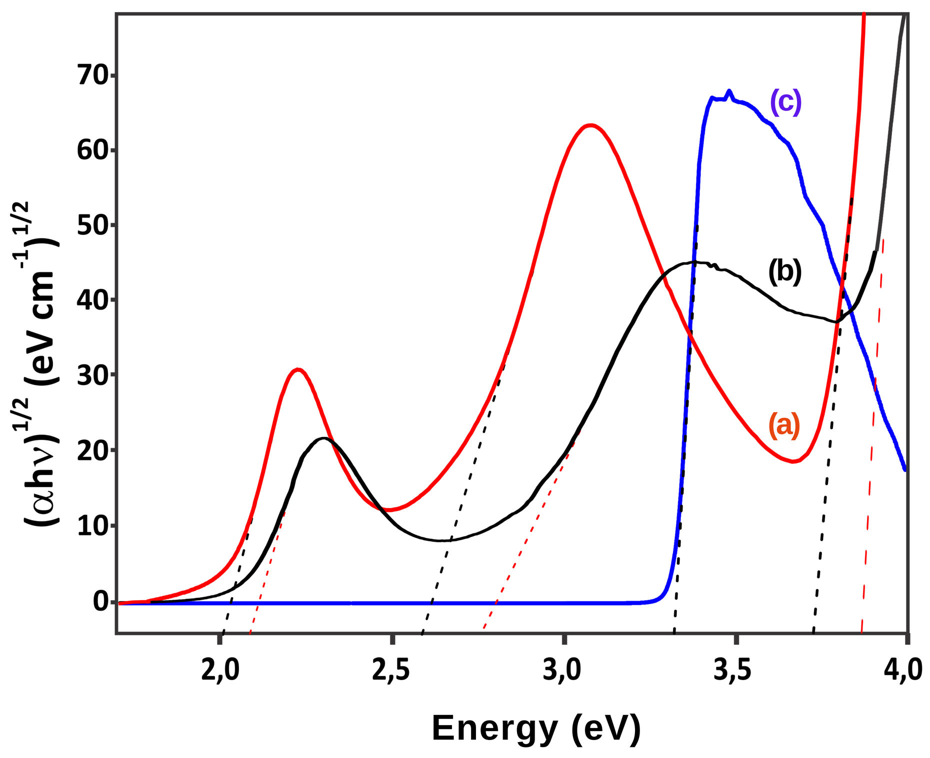

Fig. 2. The optical bandgaps for Ru(dcbpy)2Cl2 (a), NCS (b) and TiO2 (c) calculated by the Tauc plot method for indirect-allowed transitions.

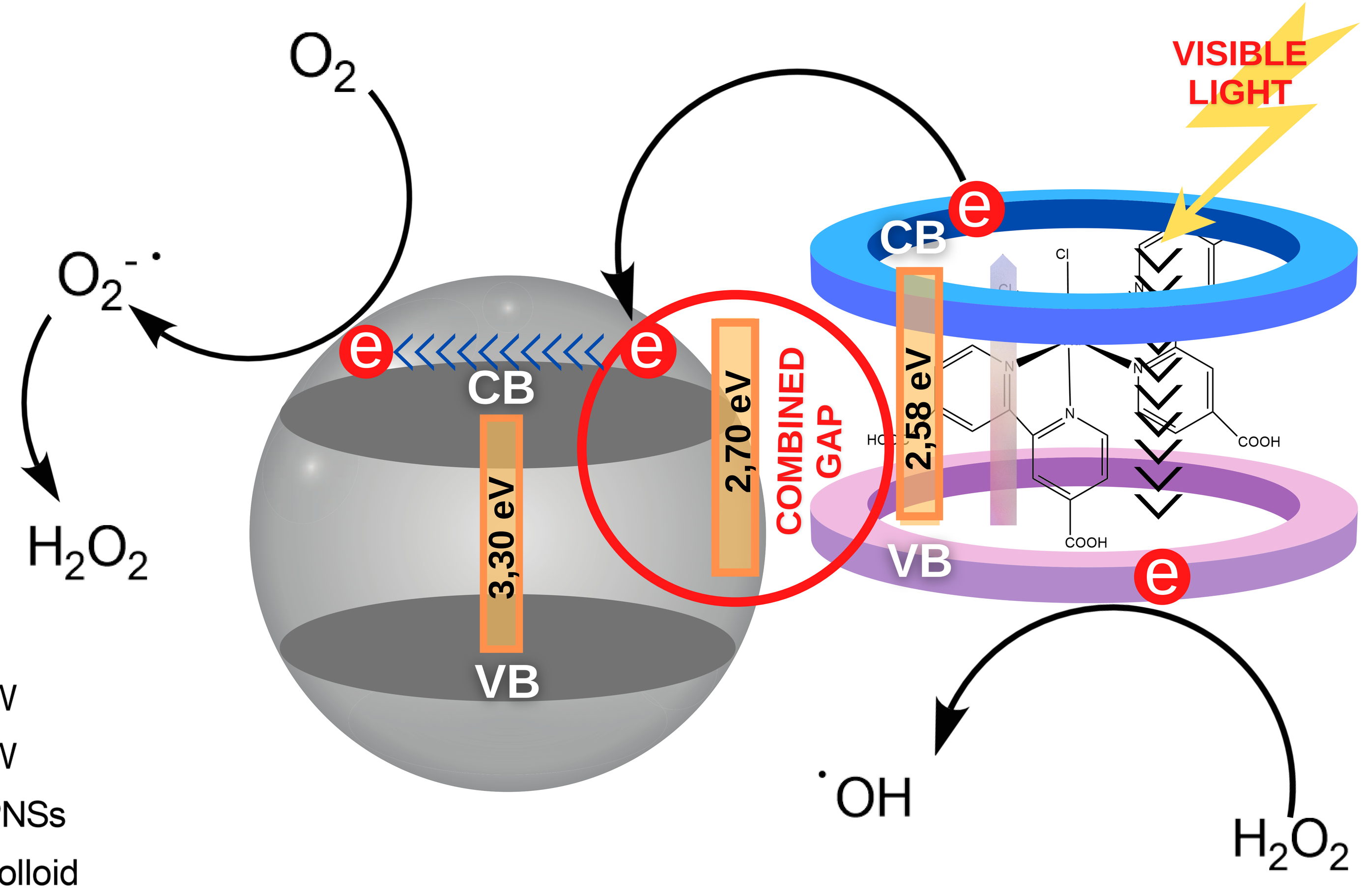

Fig. 3. The NCS' bandgap (of 2.7 eV) and the possible mechanism of ROS formation after NCS activation with visible light.

The blue ring represents CB, the purple ring represents VB of Ru(dcbpy)2Cl2, whereas the grey sphere represents TiO2 NP with its CB and VB (darker grey circules).

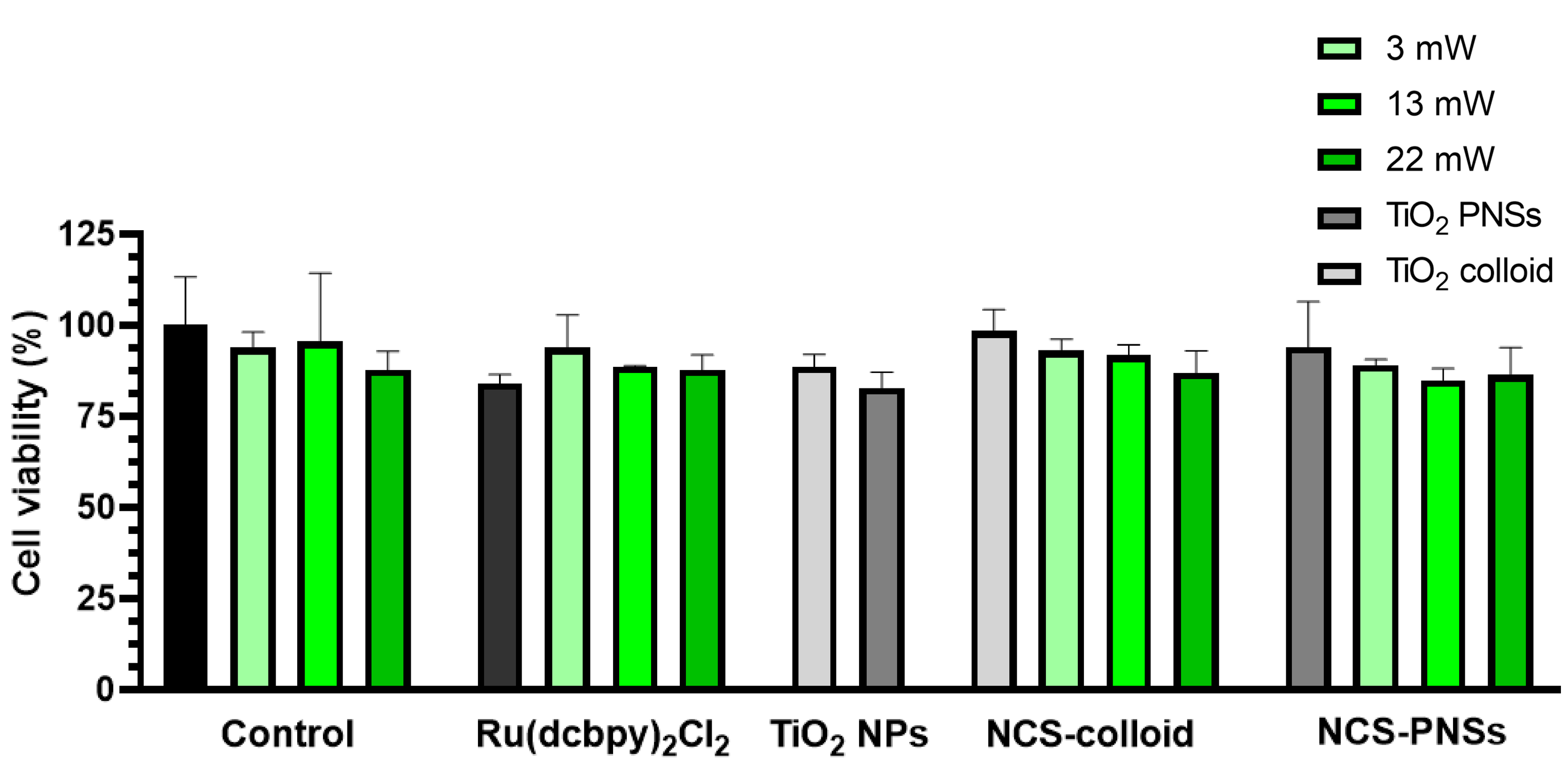

Fig. 4. Cytotoxicity of Ru(dcbpy)2Cl2, NCSs and TiO2 NPs on HeLa cell line. Results are expressed as % of control.

Despite the expectations, in the photocytotoxic profile on the HeLa cell line (Fig. 4.), none of the treatments (TiO2 NPs, Ru(dcbpy)2Cl2, and NCSs) alone or in combination with the visible light haven't shown significant cytotoxicity. Therefore, it seems that green light doesn't have any impact on HeLa cells. However, the treatment effect is more pronounced in the preliminary cytotoxicity investigation of the TiO2 PNSs on the amelanotic melanoma cells [4]. This suggests the diverse effect of NCS/light combination on different cancer cell lines and implies specificity.

CONCLUSION

The presented bandgap energies point towards the potential use of NCS in visible-light-driven cancer therapy. However, further research on different cell lines is required to evaluate the response of various cancer cell lines towards NCS/visible light treatment.

LITERATURE

[1] G. G. Genchi, Metal Oxides, 2021 (337-352)
[2] Nešić M., Žakula J., Stepić M. et al. J. Photochem. Photobiol. A Chem. 2017, 347, pp. 55–66.
[3] Matijević M., Nešić M., Stepić M. et al. Opt. and Quant. Elect, 2018, 50 (6)
[4] Matijević M., Petković M., Lopis I. E. et al. 56th International Conference on Medicinal Chemistry RICT, 2021, pp. 134-135.
[5] Kumar P., Joshi C., Labhsetwar N. et al. Nanoscale, 2015, 5, pp. 15258-15267

COHERENCE CENTER (CENTER FOR LIGHT-BASED RESEARCH AND TECHNOLOGIES)

„VINČA" INSTITUTE OF NUCLEAR SCIENCES NATIONAL INSTITUTE OF THE REPUBLIC OF SERBIA