Bodipy photosensitizer linked hybrid nanomaterials for photodynamic therapy

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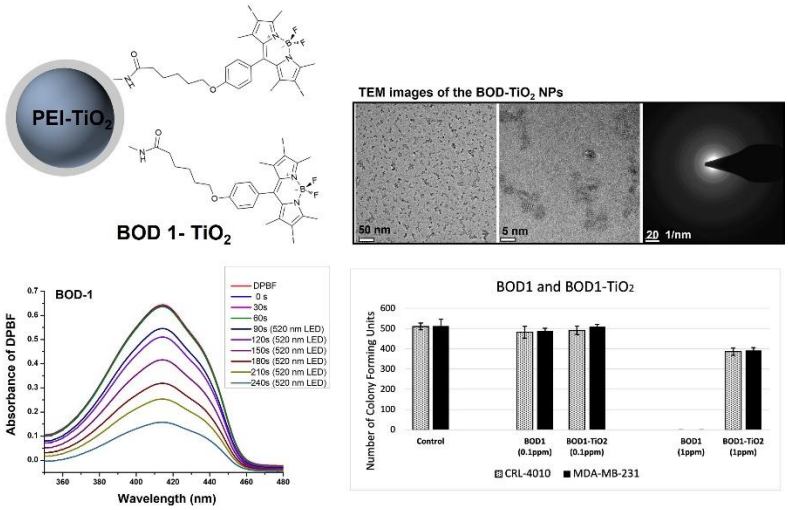
Presenting Author' Biography

Seda Demirel Topel has received her PhD degree in Organic Chemistry (2013, Akdeniz University, Turkey). In the first years of her PhD, she joined the Natural Products group as a researcher at Lund University, Sweden, then continued her PhD studies at National Nanotechnology Research Center (UNAM), Bilkent University, Turkey in the field of organic-hybrid nanoparticles for photodynamic therapy (2010-2013). Then she continued her studies as a post-Doc fellow at the Department of Molecular Sciences, SLU, Sweden in 2013-2014. Currently, she is working as Assist. Prof. at the Department of Electrical &Electronics Engineering at Antalya Bilim University, since 2017. Her research interests include the synthesis and characterization of various types of nanoparticles such as silicon dioxide, titanium dioxide, superparamagnetic iron oxide and upconversion nanoparticles and their hybrid forms with organic ligands for biological applications such as theranostics, bio-imaging and controlled drug delivery.

Graphical Abstract



Abstract

Photodynamic therapy (PDT) is an alternative clinically approved treatment method to obliterate the cancerous lesion by producing reactive oxygen species (ROS) via activated a photosensitiser (PS) molecule at a certain wavelength[1]. In recent years, Bodipy (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) as a photosensitizer molecule has been extensively investigated in PDT[2,3]. However, the use of many Bodipy PS in PDT has been limited due to their insolubility in aqueous solution. Therefore, nanotechnology offer tremendous solutions to build up nano-carrier systems for insoluble molecules. We have herein developed a stable formulation of hybrid Bodipy PS via conjugation of TiO_2 nanoparticles to the Bodipy PS. In this study, a heavy metal substituted Bodipy PS molecule has been synthesized and linked to polyethyleneimine (PEI) functionalized TiO_2 nanoparticles to increase the stability and biocompatibility of the photosensitizer in physiological conditions (pH:7.4) as a potential photodynamic therapy agent. PEI-TiO_2 nanoparticles have been prepared by a hydrothermal method which yields anatase phase crystals with an average diameter of 5 nm. Singlet oxygen studies reveal that the pure Bodipy derivative (BOD 1) has been resulted to 85% decrease in the absorbance of trap molecule, DPBF (diphenyl benzoisofuran), in 180 seconds under 532 nm LED light. Furthermore, the cytotoxicity for the hybrid photosensitizer has been tested against CRL-4010 and MDA-MB-231 cancer cell lines under UV light exposure at a certain time. BOD1-TiO_2 nanoparticles have been found to be effective on both cell lines. IC_{50} value has been calculated as 0.16 ppm and 0.23 ppm for pure BOD 1 on CRL-4010 and MDA-MB-231 cells, respectively, after 5 minutes LED light irradiation. However, IC_{50} values have been raised to 115.60 and 99.53 ppm on CRL-4010 and MDA-MB-231 cell lines, respectively, when BOD1 was functionalized with PEI-TiO_2 nanoparticles. Colony forming experiments show that BOD1 at a concentration of 1 ppm in DMSO has been completely inhibited the colony formation for both cancel cell lines. When BOD1 conjugated to TiO_2 nanoparticles, it has been revealed that it has not superior effect like bare BOD1 on colony formation, however exhibited approximately 20 % inhibition for both cancer cells due to the low conjugation effect of BOD1 to TiO_2 nanoparticle. Nevertheless, the resultant BOD1-TiO_2 hybrid formulation has been exhibited a stable dispersion in physiological solution to apply as a singlet oxygen generator for PDT.

Keywords: photodynamic therapy; TiO_2; Bodipy; CRL-4010 cells; MDA-MB-231cells

Acknowledgements

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