SYNTHESIS OF NEW BODIPYS FOR PHOTODYNAMIC THERAPY ON HUMAN LUNG CANCER CELL LINE H1299

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INTRODUCTION

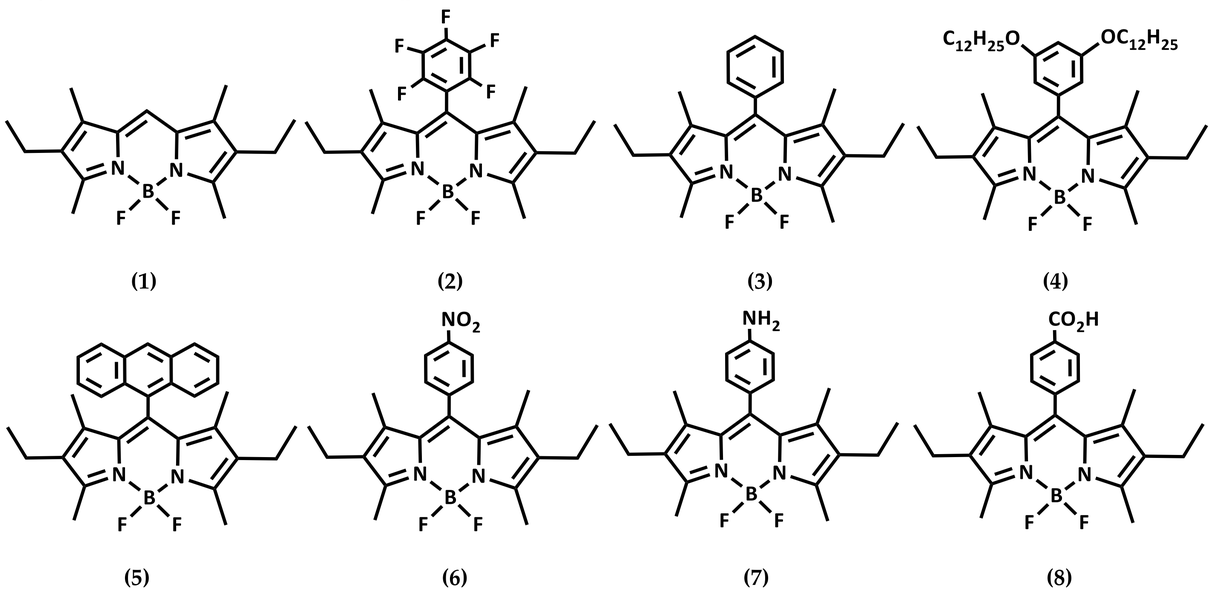
Despite the existence of several therapeutic options, lung cancer remains the leading cause of cancer death and the most diagnosed worldwide for men and women. Therefore, the need for new and more effective therapies with fewer side effects is a concern. Photodynamic Therapy (PDT) relies on the administration of a photosensitizer that is subsequently activated by light of appropriate wavelength and reacts with oxygen. As a result, reactive oxygen species (ROS) are produced leading to cell death. The use of PDT in the treatment of cancer is still limited, due to the low number of approved drugs. In light with this, as an alternative class of the porphyrin-based photosensitizers, boron−dipyrromethenes (BODIPY) have been studied by us as potential PDT drugs.

OBJECTIVES

This work aims to develop new photosensitizers for PDT. Eight compounds of the family of the boron−dipyrromethenes (BODIPY) have been synthesized and evaluated on the human lung cancer cell line H1299.

MATERIALS AND METHODS

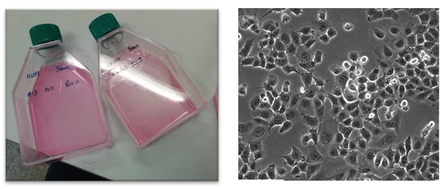
Synthesis of BODIPY compounds



BODIPY's were prepared through the condensation of the correspondent aldehyde with two mono a-free pyrroles, leading to the formation of a dipyrromethane which was oxidized to dipyrromethene by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and, finally, complexed with boron by addition of $BF_3.Et_2O$ in the presence of triethylamine.

Cell Studies

Cell line was purchased from the American Type Culture Collection. Cell culture flasks were kept on a humidified atmosphere with 95% air and 5% CO_2, at a temperature of 37 ° C in a HeraCell incubator.
Cells were seeded at a density of 100.0000 cells/mL. Cells were incubated with two concentrations of each compound 10 and 50 µM.



Then the cells were irradiated with 10 Joules for photodynamic therapy.

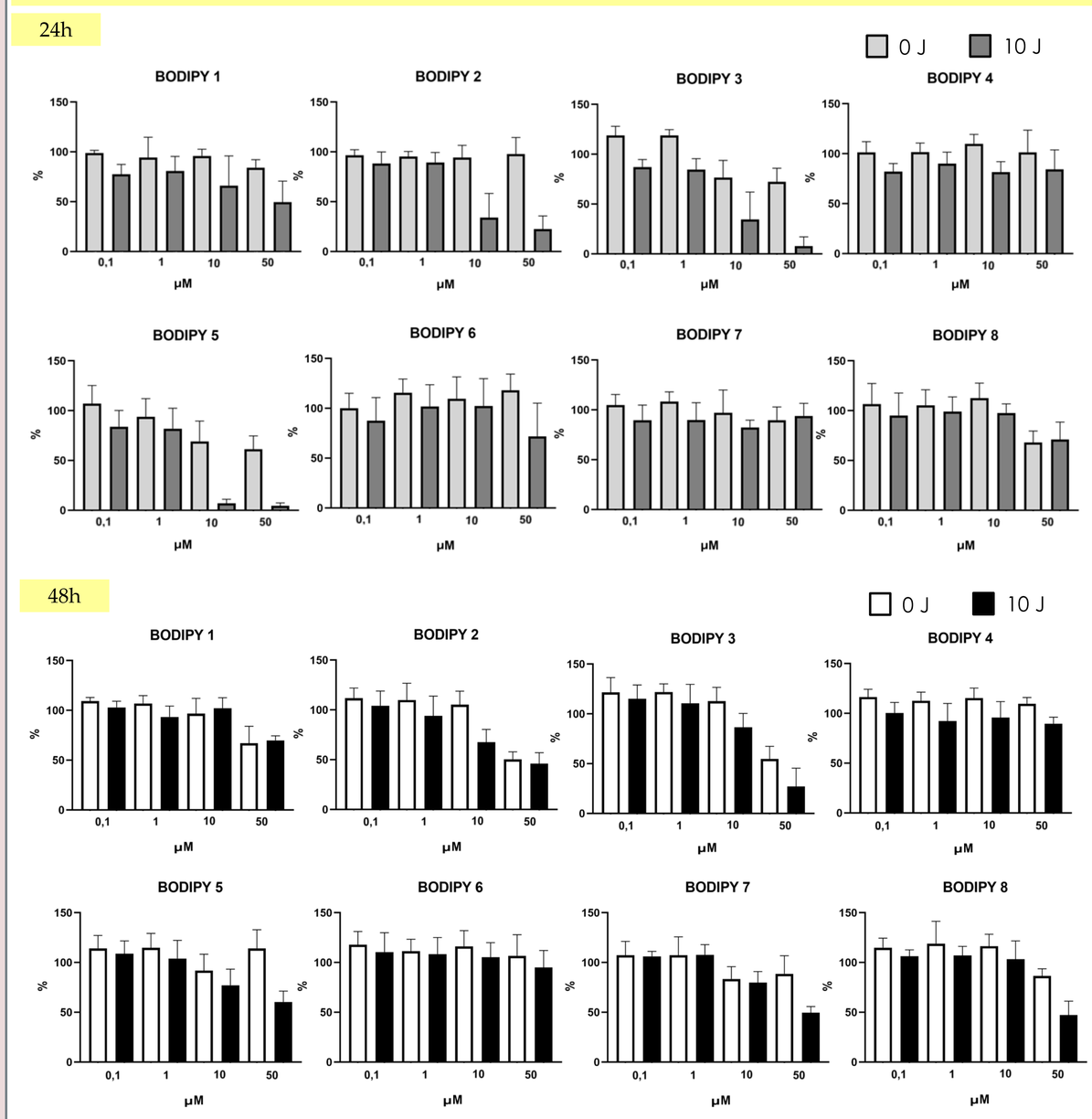
Metabolic activity and protein synthesis were measured by colorimetric cytotoxicity assays were run to determine the compounds activity, at regular periods under the same conditions.

The **MTT assay** is meant to assessing cell metabolic activity. The MTT (dimethylthiazol-diphenyltetrazolium bromide) assay is based on mitochondrial uptake and succinate dehydrogenase reduction of the soluble, yellow, MTT tetrazolium salt to the insoluble blue MTT formazan.

The **SRB assay** is meant to evaluate cell density determination, based on the measurement of cellular protein content. The sulforhodamine B (SRB) assay is based on the ability of the SRB dye to bind basic amino acid residues on proteins.

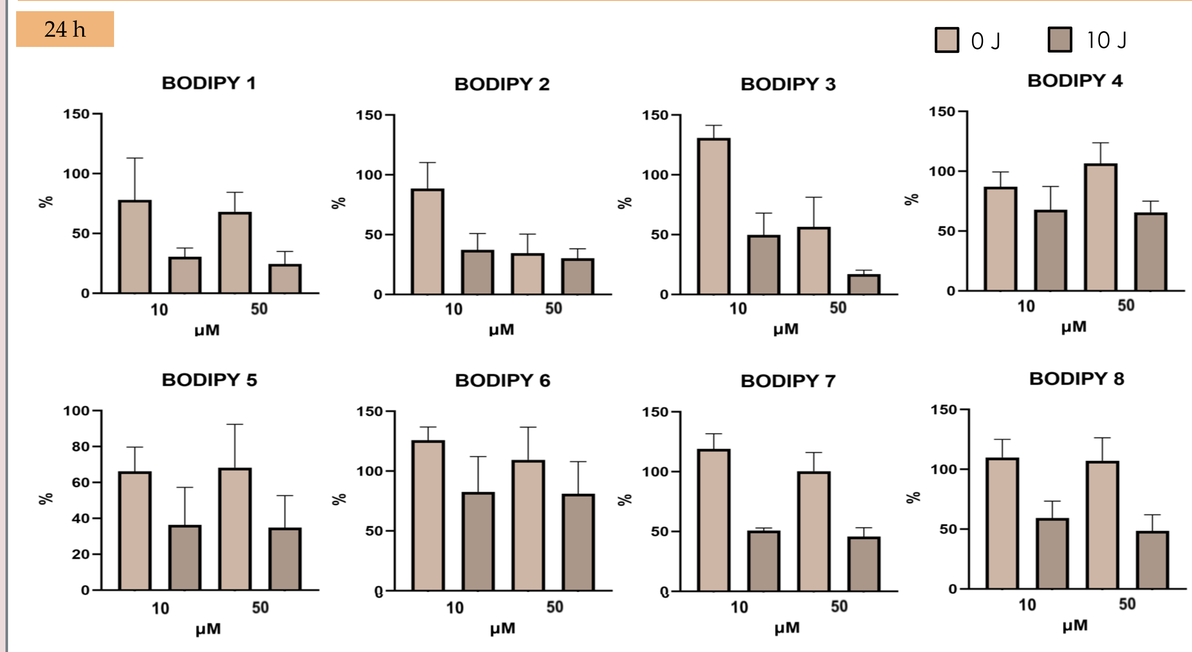
RESULTS AND DISCUSSION

MTT assay



Generally, the cell response was dependent on the BODIPYs concentration and time. BODIPY 2, 3 and 5 based PDT led to a significant loss of viability in both times.

SRB assay



Furthermore, BODIPYs 2 and 3 were cytotoxic *per se*, as shown by experiments where irradiation step was omitted. Although BODIPYs 1, 4, 6, 7 and 8 have not revealed a significant reduction in metabolism of cells, they promoted a decrease of protein content. So, it would be interesting to explore the reasons for these results.

CONCLUSIONS

- ✓ Our results show that the newly synthesized compounds have some potential for Photodynamic Therapy.
- ✓ The response of photodynamic treatment is dependent not only on the concentration of the photosensitizer but also on the incubation time. There is a significant decrease in protein content after treatment.
- ✓ BODIPYs 2 and 5 are the most interesting photosensitizers.

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