Tytuł projektu

Nowe kompozyty biopolimerowe zawierające fotoaktywne związki typu BIODIPY jako potencjalne leki do PDT

Project title

Novel biopolymer composites containing photoactive BODIPY compounds as a potential drugs for PDT

Dyscyplina /Area of science

Nauki chemiczne

PROJECT DESCRIPTION

Project goals

In the first stage, the photostability and the ability of the new BODIPY systems to generate singlet oxygen under the influence of visible irradiation will be examined. Compounds that will be selected as prognostic for therapy will be used to obtain composites with biopolymers such as proteins and polysaccharides. Biopolymers will be selected to enrich the system with elements that allow the immune mechanism to be activated mainly in therapy. The photostability and photoactivity of the obtained composites will be examined as new drug forms. The obtained composites will then be enriched with the addition of magnetic nanoparticles, which are known to have the ability to selectively accumulate in the tumor tissue due to the presence of iron. One of the elements of the project due to the new photosensitizer structures will also be to propose new photodegradation mechanisms for these compounds based on available analytical techniques: ATR-FT IR, HPLC, LC-MS. In addition, the results obtained for photodegradation will be supported by the results theoretically made using calculation methods.

Outline

Photodynamic therapy (PDT) is a binary anticancer technique combining elements of chemo and radiotherapy. It is a very promising method of cancer treatment using free radicals for selective reduction of cancerous tissue. This therapy demands present of three basic elements: 1) photosensitizer, responsible for sensitivity of diseased tissue, 2) source of light causing mobilization of photosensitizer and 3) oxygen dissolved in tissue being treated. There are two mechanisms of PDT action: vascular and immunological. Vascular targeting therapy has been shown to produce reactive oxygen species intravascularly (singlet oxygen). The main aim of this mechanism is maximal cell killing by inducing tumor vascular shutdown. It is also believed that PDT induced immune modulation, either immune stimulating, mediated by natural killer (NF) cell and macrophages, or immune suppressing (immunological mechanism).

Currently, a lot of photoactive compounds are known that could be used in PDT, but only about twelve are used clinically. We are constantly looking for new photoactive substances that will ensure selective destruction of cancer cells with the best possible pharmacotherapy economics (quality of life of the patient, number of subsequent irradiations and low dose of the therapeutic compound).

Work plan

- Synthesis and characterization of novel BODIPY compounds.
- Test of photostability of the compounds obtained under the influence of UV and visible irradiation and proposing of a mechanism for BODIPY photodegradation.
- Determination of the ability to singlet oxygen generation for the obtained compounds.
- Obtaining a series of composites containing selected BODIPY compounds and biopolymers and examining their photostability and photoactivity in the context of PDT therapy.
- Enrichment of selected BODIPY composites - a biopolymer in the addition of magnetic nanoparticles. Investigating their photostability and photoactivity.
- Comparison of results obtained experimentally with the results of theoretical calculations.

Literature

[1] A. Loudet and K. Burgess, "BODIPY Dyes and Their Derivatives: Syntheses and Spectroscopic Properties," *Chem. Rev.*, vol. 107, no. 11, pp. 4891–4932, 2007.

[2] Z. Wang, Y. Xie, K. Xu, J. Zhao, and K. D. Glusac, "Diiodobodipy-styrylbodipy Dyads: Preparation and Study of the Intersystem Crossing and Fluorescence Resonance Energy Transfer," *J. Phys. Chem. A*, vol. 119, no. 26, pp. 6791–6806, 2015.

[3] J. H. Gibbs *et al.*, "Spectroscopic, computational modeling and cytotoxicity of a series of meso-phenyl and meso-thienyl-BODIPYs," *Bioorganic Med. Chem.*, vol. 21, no. 18, pp. 5770–5781, 2013.

[4] Y. Ito, Ed., *Photochemistry for Biomedical Applications*. Singapore: Springer Singapore, 2018.

[5] K. Ziems, S. Gräfe, and S. Kupfer, "Photo-Induced Charge Separation vs. Degradation of a BODIPY-Based Photosensitizer Assessed by TDDFT and RASPT2," *Catalysts*, vol. 8, no. 11, p. 520, 2018.

[6] M. J. Ortiz *et al.*, "Synthesis and functionalization of new polyhalogenated BODIPY dyes. Study of their photophysical properties and singlet oxygen generation," *Tetrahedron*, vol. 68, no. 4, pp. 1153–1162, 2012.

[7] W. Wu, H. Guo, W. Wu, S. Ji, and J. Zhao, "Organic Triplet Sensitizer Library Derived from a Single Chromophore (BODIPY) with Long-Lived Triplet Excited State for Triplet–Triplet Annihilation Based Upconversion," *J. Org. Chem.*, vol. 76, no. 17, pp. 7056–7064, Sep. 2011.

[8] P. P. Goswami *et al.*, "BODIPY-Derived Photoremovable Protecting Groups Unmasked with Green Light," *J. Am. Chem. Soc.*, vol. 137, no. 11, pp. 3783–3786, Mar. 2015.

Required initial knowledge and skills of the PhD candidate

- ➔ Knowledge about basic chemistry, polymer chemistry and photochemistry
- ➔ Analytical thinking
- ➔ Eager to learn
- ➔ Interest in interdisciplinary issues (from the borderline of chemistry and medicine)
- ➔ Permanent self-education
- ➔ Eager to work hard

Zgłaszający projekt/ Author of the project

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Proponowani promotorzy i mentorzy/prospective supervisors

1) promotor główny/ main supervisior

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2) promotor pomocniczy / co-supervisor

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