РАЗДЕЛ III

БИОФИЗИКА

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FUNCTIONAL PROPERTIES OF SPIN TRAPPING AGENTS FOR ENHANCED DETECTION OF SINGLET OXYGEN IN PHOTODYNAMIC THERAPY APPLICATIONS

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Abstract

Photodynamic therapy (PDT) utilizes photosensitizers (PSs) generating singlet oxygen ($^1O_2$) upon light activation to eliminate cancer cells. Accurate PS $^1O_2$ generation capacity assessment is essential for novel PSs. This study presents novel $^1O_2$ spin traps with enhanced efficiency at physiological pH, where the others are ineffective, enabling measurements in biologically relevant environments.

PDT is a clinically promising cancer treatment that relies on PS reacting with triplet oxygen and generating reactive oxygen species (ROS) upon light activation, leading to targeted cell death [1, 2]. Among ROS, $^1O_2$ is recognized as the primary cytotoxic agent responsible for therapeutic efficacy in tumors with a regular oxygen supply. The advancement of PDT technology critically depends on identifying and characterizing new PSs with high ROS generation efficiency.

Accurate evaluation of $^1O_2$ production is essential for the development and optimization of PSs. The spin trapping (ST) technique combined with electron paramagnetic resonance (EPR) spectroscopy is a powerful approach for detecting ROS. In this method, a diamagnetic ST reacts with ROS to form a stable paramagnetic radical detectable by EPR, enabling quantitative and selective measurement of ROS. However, most contemporary $^1O_2$ STs often exhibit an undesired pH increase, which can induce side reactions [3], including radical degradation and aggregation of PS molecules like cationic porphyrins. Additionally, the strong alkalinity of these compounds obstructs $^1O_2$ capturing at physiological conditions. These issues hinder the reliable assessment of PS performance in biologically relevant environments.

This study presents the evaluation of both established and novel STs. The novel STs feature a trimethylammonium substituent at the 4-position of the piperidine ring, designed for enhanced solubility and efficiency at physiological pH. Their pKa values were measured via NMR. Then, using the model PS meso-5,10,15,20-tetrakis(N-methylpyridyl-4′) porphyrin, the steady-state photolysis experiments at different pH levels were conducted to determine their efficiency. Control experiments with sodium azide confirmed the high selectivity of these STs for $^1O_2$. The improved functional properties of these STs enable more precise and reliable ROS measurement, facilitating the screening and development of effective PS for PDT.

Our findings contribute to the technological advancement of PDT by providing robust tools for singlet detection under physiological conditions, supporting the engineering of next-generation PSs with optimized therapeutic performance.

References

1. Falk-Mahapatra R., Gollnick S.O. Photodynamic therapy and immunity: an update // J. Photochem. Photobiol. 2020. Vol. 96, No. 3. P. 550–559.

2. Kaeser P. S., Regehr W. G. Molecular mechanisms for synchronous, asynchronous, and spontaneous neurotransmitter release // Annu. Rev. Physiol. 2014. Vol. 76. P. 333–363.

3. Victória H. F. V. et al. Detection of singlet oxygen by EPR: The instability of the nitroxyl radicals // Free Radic. Biol. Med. 2022. Vol. 180. P. 143–152.