LED LIGHT SOURCES FOR PDT AND IN VITRO PHOTODYNAMIC STUDIES

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Introduction

The mortality rate from various oncological diseases remains consistently extremely high, even in spite of recent breakthrough discoveries in the field of cancer therapy. One of the most promising cancer treatments is photodynamic therapy (PDT) combined with fluorescence diagnostics (FD). Because of this photodynamic therapy is widely implemented in clinical practice. This contributes to the development of new devices for fluorescence diagnostics and PDT.
Theory

The photodynamic action (PDA) leads to photo-oxidative destruction of molecular structures that ensure the functioning of tumor cells and pathogens such as bacteria and viruses by reactive oxygen species (ROS). Photosensitizer (PS) molecules catalyze the generation of ROS upon excitation with light. Light transfers the energy necessary for this process to the medium containing the PS. However, only the part of the light energy is absorbed by PS molecules. The relative absorbed photodynamic dose (RAPD) [1] depends on the properties of PS (extinction, concentration in a sensitized medium, wavelength and shape of the spectral contour at this concentration) and properties of the medium (scattering and absorption by endogenous pigments, in particular, hemoglobin and water).

Light-emitting diodes (LED) are widely used as light sources for PDA [2]. These sources provide light with high intensity, and their light spectrum is narrow ($\Delta \lambda_{\text{LED}} = 20-30$ nm) in comparison with the spectral width of the absorption band of PS. Such light sources can generally be created with most wavelengths suitable for PS excitation (at least in the red and near infrared spectral ranges).

[1] Pogue et al., 1997
[2] Loschenov et al., 2013
The main approaches to using LED light sources for PDA

The main approaches to the use of LED for PDA are related to the spatial distribution of the exciting light energy, which should ensure its efficient use for PS excitation. An important task in photodynamic therapy of tumors is to achieve a high intensity of PDA in the deep layers of tumor nodes, which makes it necessary to provide high values of the light energy absorbed by the PS in these layers. The main losses of light energy in biotissue are caused by the absorption of endogenous pigments (hemoglobin and water), the total absorption of which is minimal in the range of 660-950 nm (so-called "spectral window of biotissue transparency").

The wavelength of exciting light is usually chosen near the spectral maximum of the PS absorption band, although in some cases light with longer wavelength can be used to increase the PDA depth. The sources of light based on LEDs can be used to irradiate tumor nodules of both small (less than 1 cm) sizes and superficial nodules of a large area, as well as for aims related to the study of new PS.

The second approach is used for photodynamic inactivation (PDI) of pathogens [1, 2]. PDI is carried out, as a rule, on surfaces of a sufficiently large area in thin layers of a sensitized biological medium (more than 0.5 cm). PDA in thin sensitized layers is also realized during in vitro screening studies of PS, which are carried out to assess the sensitivity of different biocells to PDT, to study its mechanisms and properties of PS.

[1] Strakhovskaya et al., 2020
[2] Sharshov et al., 2021
Spectral characteristics of PS and LEDs

Figure 1. Normalized spectra (1) of the absorption of photosensitizers (a - \( \text{H}_{18}\text{ClN}_{3}\text{S} \), b - \( \text{ZnPcChol}_{8} \), c - \( (3\text{-PyBrE})_{4}\text{BCBr}_{4} \)) and normalized light spectra (2) of LEDs for their excitation.
New LED devices for PDA

Figure 2. Powerful device based on a group of LEDs:
A) - device with a manipulator for adjusting the aiming at the irradiated area;
B) - device in the section showing the location of internal components: LEDs, radiators and coolers.
New LED devices for PDA

Figure 3. Profile the radiation power density of the device at different heights of the device above the detector:

A) The optical axes of the LED light beams with a light divergence about 48° are directed to the center of the spherical surface.

B) The LEDs located near the center of the in the mount had a low divergence of the light beam (about 23°), LEDs located at the periphery - of about 48°.
New LED devices for PDA

Figure 3. A series of compact devices with different wavelengths based on single powerful LED with an optical system projecting the chip image onto the irradiated foci have been created for the irradiation of small tumor foci. These devices provide irradiation of foci about $1 \times 1 \, \text{cm}^2$ with a power density of up to 180 mW/cm$^2$. 
Figure 4. Functional diagram of a device for in vitro PDA research: 1 - optical cell; 2 - sensitized layer containing biological micro-objects; 3 - sensitized layer surface; 4 - LED; 5 - optical two-lens system; 6, 7, 16 - transparent walls of optical cell; 8 - optical fiber bundle; 9 - optical fiber connected to the laser 11 output; 10 - fiber connected to the input of the spectra-analyzer LESA-01-BIOSPEC; 11 - laser for fluorescence excitation; 12 - spectra-analyzer LESA-01-BIOSPEC; 13 - optical fiber connected to the output of a broadband light source (for absorption studying) or to the output of an additional laser (for scattering studying); 14 - broadband light source; 15 - laser with wavelength outside the spectral range of the absorption band of a sensitized layer for scattering studying; 17 - optical fiber connected to the input of the dynamic light scattering spectrometer 18.
Conclusion

A number of LED sources have been created with high light power and power density for excitation of photosensitizers of different spectral ranges. They will be widely used as light sources for in vivo and in vitro photodynamic research and various PDT applications.

Acknowledgements
The research was funded by RFBR according to the project #20-04-60084, by RFBR and BNSF according to the bilateral project (RFBR #20-52-18008, BNSF #KP-06-Russia/9-2020).
Thank you for attention!