Abstract

As modern life becomes increasingly fast-paced, the number of civilization-related diseases, including cancer, continues to rise. This situation drives the search for new solutions to treat diseases, but also to monitor biological processes occurring in living organisms. As a result, scientists are particularly interested in developing diagnostic methods that are fast, affordable, and non-invasive. The main aim of this doctoral research focused on the development of new markers that may find applications both in the labeling of biomolecules and drugs, as well as in medical diagnostics and bioimaging.

The first part of the research focused on the investigation of metal carbonyl markers, which can be easily detected using infrared (IR) spectroscopy. These compounds contain (di)bromomaleimide fragments which readily react with biomolecules possessing thiol groups. One of the protein modification strategies which was applied in this work involves the incorporation of a maleimide derivative into a disulfide bridge – a process known as rebridging. Metal carbonyl dithiomaleimide compounds undergo an interesting transformation during irradiation with visible light - they lose the metal carbonyl part and turn into non-substituted dithiomaleimide derivatives which emit fluorescence. Biological studies showed that the metal carbonyl compounds are toxic to cancer cells, while their organic analogues are not cytotoxic. Confocal microscopy studies suggest that compounds containing the metal carbonyl unit enter/ penetrate cells more easily than their purely organic analogues.

The synthetic methods developed in this work also enabled to obtain fluorescent markers containing a pyrene fluorophore and a cyclooctyne group capable of participating in so-called “click” reactions. These compounds show attractive photophysical properties both in solution and in the solid state, making them promising fluorescent probes. Due to the presence of the cyclooctyne fragment, these markers can undergo bioorthogonal reactions - highly selective chemical reactions that take place inside biological systems without disturbing them. This property was successfully used for the direct labeling of biomolecules, producing strongly fluorescent conjugates. Moreover, biological studies indicate that these compounds are non-toxic to both normal and cancer cells, and thus may represent a safe alternative to isotopic labels.

Finally, the study also included modifications of the maleimide ring using pyrene and its sulfur/thiol derivative. However, the resulting pyrene-substituted (di)thiomaleimide derivatives did not exhibit luminescent properties.