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Nanocarriers based on methyluracil derivatives for the redox-mediated delivery of photosensitizers to cancer cell

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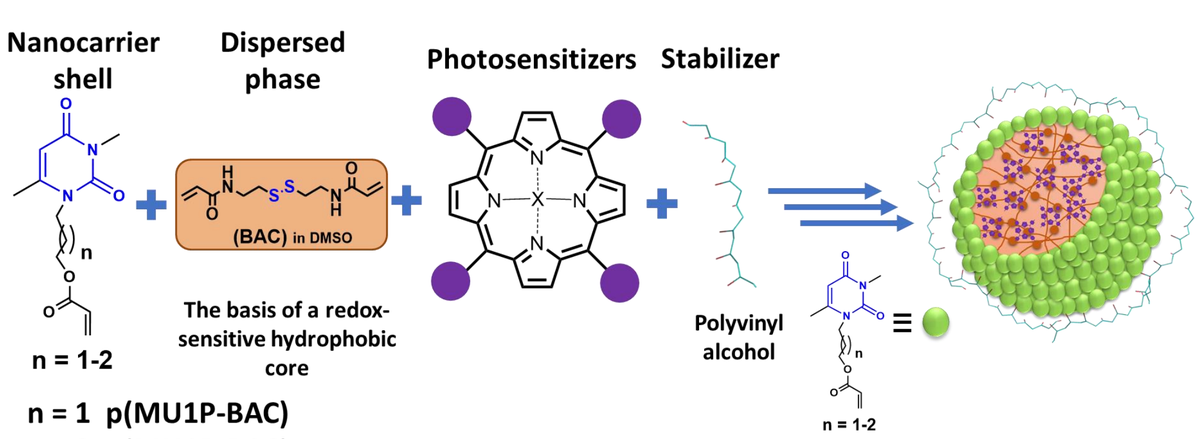
INTRODUCTION & AIM

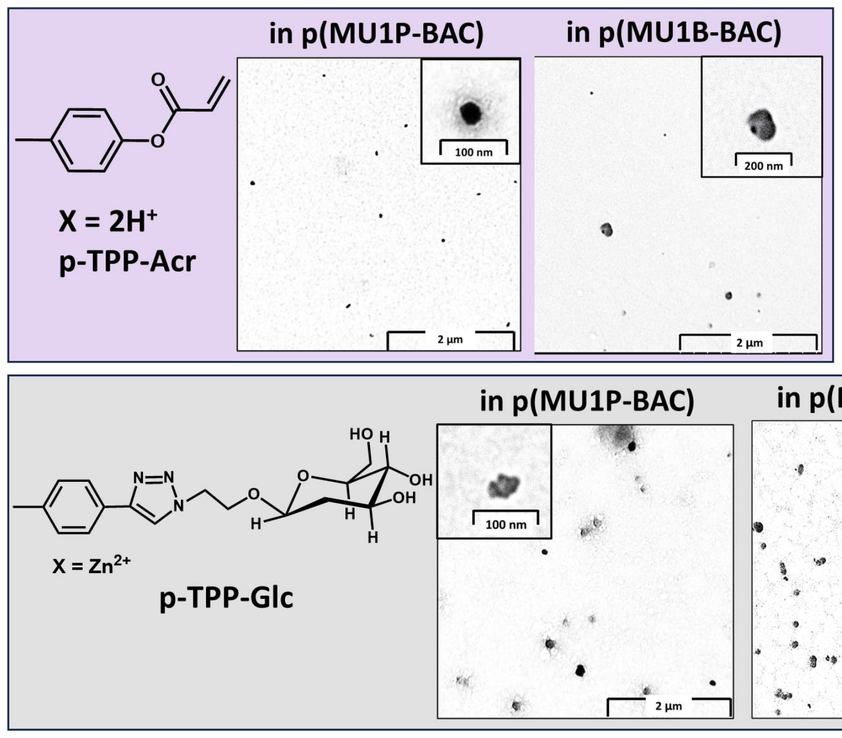
In recent decades, new methods of cancer treatment have been developed. One of these methods is photodynamic therapy (PDT), which is non-invasive and based on the generation of reactive oxygen species (ROS) when light interacts with photosensitizers (PS). Porphyrin-type PS show promise. However, they often have minimal solubility in water and reduced bioavailability under physiological conditions. To address this issue, nanocarriers have been created to deliver porphyrin-type PS more effectively, increasing the depth of penetration into cellular structures and enhancing the therapeutic effect of PDT.

RESULTS & DISCUSSION

Here we present nanocarriers obtained through the nanoemulsion polymerization between homologous methyluracil derivatives and *N,N'*-bis(acryloyl)cystamine. Methyluracil derivatives form the shells of the nanocarriers, while *N,N'*-bis(acryloyl)cystamine, dissolved in DMSO, acts as the dispersed phase to form a hydrophobic core. Two PS were encapsulated within the core of each carrier: a representative of glycoporphyrin or porphyrin with acrylate fragments, which was presumably covalently cross-linked with the acrylate groups of the initial compounds.



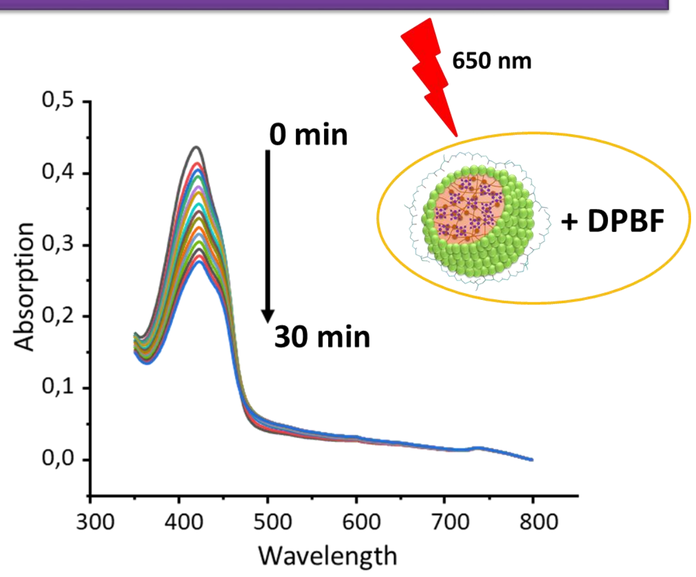
TEM images



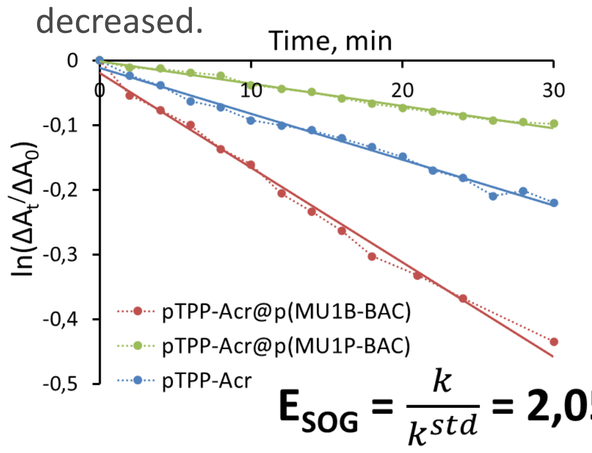
According to transmission electron microscopy data, carrier sizes ranged from 50 to 200 nanometers.

Registration of the formation of reactive oxygen species during irradiation

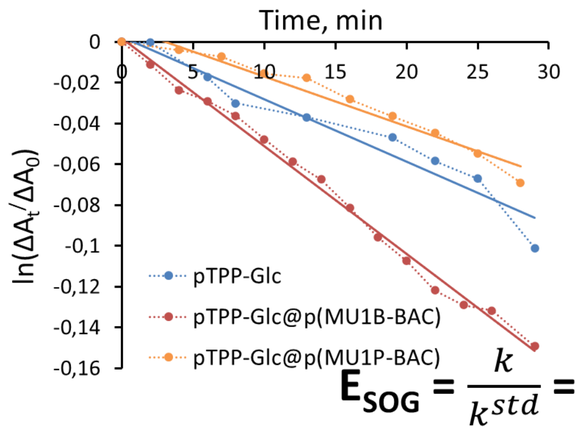
Registration of ROS formation was carried out using UV-Vis absorption spectroscopy and 1,3-diphenylisobenzofuran (DPBF), since the product of the photooxidation reaction (1,2-dibenzoyl benzene) does not absorb visible light. The studies were carried out with a solution with a PS and PS encapsulated in nanocarriers.



The DPBF photodegradation constants were calculated from the slope tangent of the graphs of $\ln(\Delta A_t/\Delta A_0)$ versus time, and the relative efficiency of singlet oxygen formation was estimated on the base of these constants. As a result, it was concluded that singlet oxygen is generated almost 2 times faster with carriers based on butylene acrylate methyluracil, however, with nanocarriers based on propylene acrylate methyluracil, the efficiency decreased.

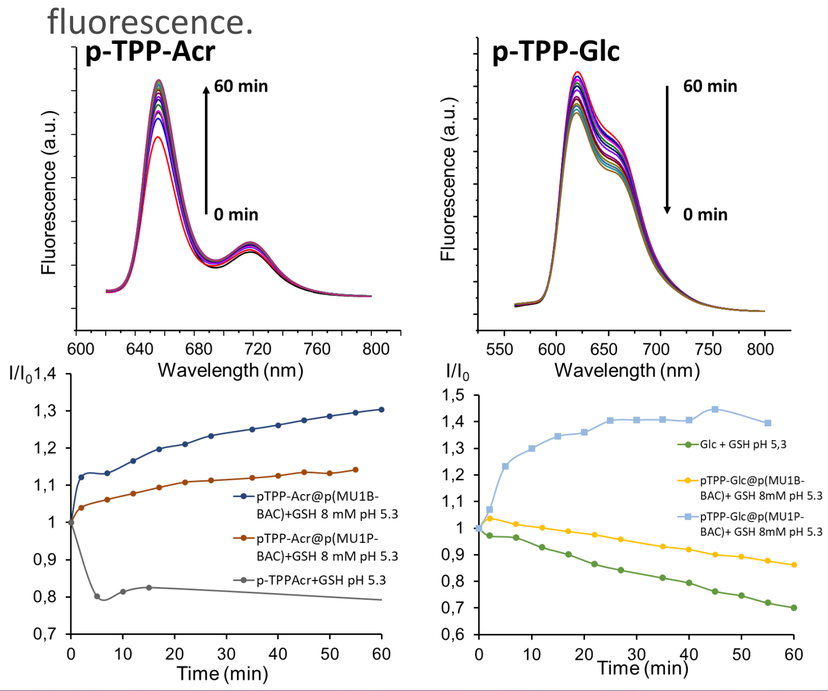


$E_{SOG} = \frac{k}{k^{std}} = 2{,}05$



$E_{SOG} = \frac{k}{k^{std}} = 1{,}7$

The sensitivity of the nanocarrier to the redox environment of cells was performed by adding glutathione (GSH) to nanocarriers with encapsulated PS. The concentration of the tripeptide corresponded to the concentration in cancer cells (8 mM). The reaction of the thiol-disulfide bond exchange within the core of the nanocarriers and the sulfhydryl group of glutathione results in the breakdown of the carrier, the release of PS, and an increase in fluorescence.



A multifaceted trend is evident in the behavior of glycoporphyrin, with both an increase and decrease in intensity, which is likely a result of a more intricate process involving the additional coordination and bonding of the sulfhydryl group of glutathione and zinc in the porphyrin.

CONCLUSION

New nanocarriers for the delivery of photosensitizers have been obtained. The capacity to generate singlet oxygen has been investigated, and it has been demonstrated that nanocarriers are susceptible in the reductive environment of cancerous cells.