

# NOVEL PHOTOSENSITIZERS FOR THE DEVELOPMENT OF CHEMICALLY CROSSLINKED HYDROGEL NETWORKS AND THEIR APPLICATION IN PHOTODYNAMIC THERAPY

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Phthalocyanines are macrocyclic, aromatic compounds, which have been widely studied for their use as photosensitizers, presenting strong absorption in the 670–850 nm wavelength range and high ROS generation ability. However, their low water solubility is a limiting factor for their direct administration to the patient. Therefore, the development of novel carriers as drug delivery systems, such as hydrogels, which are hydrophilic polymer networks with three-dimensional configuration, capable of absorbing large amounts of water, is of high interest<sup>1</sup>.

The aim of the present work was the synthesis of novel chitosan-based hydrogels, using chemically modified phthalocyanines as crosslinkers. The structurally modified phthalocyanines were synthesized via a two-step reaction, followed by the preparation of the hydrogels via a Schiff-base reaction. The porosity, swelling behavior and *in vitro* release studies of/from the modified phthalocyanine-chitosan hydrogels in aqueous solutions with specific pH values, were determined. In addition, the new systems were structurally characterized by FT-IR spectroscopy and X-Ray diffraction. The optical properties of the novel hydrogels as well as their ability to produce ROS were also examined.

A slow *in vitro* release of phthalocyanine was observed in all the tested pH, presenting higher release rate under acidic conditions (pH 5.0) compared to the physiological pH, owing to the acid-labile imine bonds. The swelling study revealed that as the pH of the swelling medium decreased, the swelling ratio increased, which may be attributed to the protonated amino groups of chitosan. In addition, the experimental data obtained from the swelling study were adjusted to Schott's pseudo-second-order kinetics model. The study of the ability to produce ROS showed that the hydrogels improve the action of the photosensitizers. The photodynamic therapy efficacy of the phthalocyanine and the corresponding hydrogel against squamous carcinoma A431 cell line was also examined. The samples exhibited significant phototoxic activity under irradiation with different fluence rates at the concentration of 5 µg/mL, rendering them as promising theranostic systems.

## References

1. F. Bayat, A. R. Karimi, *Int. J. Biol. Macromol.* 2019, 129, 927-935.