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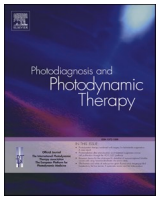

Synthesis and characterization of photosensitive gelatin-based hydrogels for photodynamic therapy in HeLa-CCL2 cell line

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ABSTRACT

Background: Hydrogel systems are increasingly gaining visibility involving biomedicine, tissue engineering, environmental treatments, and drug delivery systems. These systems have a three-dimensional network composition and high-water absorption capacity, are biocompatible, allowing them to become an option as photosensitizer carriers (PS) for applications in Photodynamic Therapy (PDT) protocols.

Methods: A nanohydrogel system (NAHI), encapsulated with chloroaluminium phthalocyanine (ClAlPc) was synthesized for drug delivery.. NAHI was synthesized using gelatin as based polymer by the chemical cross-linking technique. The drug was encapsulated by immersing the hydrogel in a 1.0 $mg.mL^{-1}$ ClAlPc solution. The external morphology of NAHI was examined by scanning electron microscopy (SEM). The degree of swelling of the synthesized system was evaluated to determine the water absorption potential. The produced nano-hydrogel system was characterized by photochemical, photophysical and photobiologial studies.

Results: The images from the SEM analysis showed the presence of three-dimensional networks in the formulation. The swelling test demonstrated that the nanohydrogel freeze-drying process increases its water holding capacity. All spectroscopic results showed excellent photophysical parameters of the drug studied when served in the NAHI system. The incorporation efficiency was 70%. The results of trypan blue exclusion test have shown significant reduction ($p < 0.05$) in the cell viability for all groups treated with PDT, in all concentrations tested. In HeLa cells, PDT mediated by 0,5 $mg.mL^{-1}$ ClAlPc encapsulated in NAHI showed a decrease in survival close to 95%. In the internalization cell study was possible to observe the internalization of phthalocyanine after one hour of incubation, at 37 °C, with the the accumulation of PS in the cytoplasm and inside the nucleus at both concentrations tested.

Conclusions: Given the peculiar performance of the selected system, the resulting nanohydrogel is a versatile platform and display potential applications as controlled delivery systems of photosensitizer for photodynamic therapy application.

1. Introduction

Photodynamic therapy (PDT) is a minimally invasive technique that can ablate tumors and other targets.. It has appeal in oncology because the use of chemotherapy, ionising radiation, or surgery does not preclude the use of PDT, and all these approaches can still be used in a patient who has received PDT [1–3].

PDT is based on the dynamic interaction between a photosensitizer drug (PS), light with a specific wavelength (generally in the red spectral region, ≥ 600 nm), and molecular oxygen, promoting the selective destruction of the target tissue by a non-free radical oxidative process for generation of singlet oxygen ($^1O_2$), for example [4–6].

Phthalocyanines are synthetic PSs comprising four indole units interconnected by nitrogen atoms. These PSs are promising in PDT treatment due to their high molar absorption coefficient between 650 and 700 nm (around 10^5 L mol^{-1} cm^{-1}), visible light with significant skin penetration [7,8]. The addition of the central metal in the tetrapyrrolic macrocycle leads to metallated phthalocyanine, among them is the chloroaluminium phthalocyanine (ClAlPc). This phthalocyanine is favorable for PDT, as it makes the excited triplet PS state sufficiently

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