Photodynamic Therapy Based on Protoporphyrin IX-loaded Boron Nitride Nanotubes as Photosensitizing Solutions to Induce Apoptosis in A375 Cells

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Due to the lack of minimally invasive and selective treatments for melanoma, the effectiveness of photodynamic therapy (PDT) based on boron nitride nanotubes (BNNT) loaded with Protoporphyrin IX (PpIX) was evaluated to increase intracellular accumulation of the photosensitizer and induce apoptosis in A375 cells. PpIX, a porphyrinoid derivative precursor to the 5-ALA metabolism, induces cell death in neoplastic cells. Therefore, it was established that if BNNT retain their ability to load drugs and PpIX is activated through irradiation, the photosensitizer will accumulate intracellularly, and PDT will induce apoptosis in A375 cells. In this in-vitro study, A375 cells were treated with PDT based on PpIX and BNNT+PpIX at 20%. PDT showed effectiveness in reducing cell viability in an MTT assay, while cells treated with the compounds without irradiation showed higher viability. The interaction of PpIX with BNNT facilitated intracellular localization, with ~60-70% colocalization in the cells, mostly in the mitochondrial region. Singlet oxygen ($^1O2$), generated by the activation of PpIX under irradiation (QYs = 26%), induced apoptosis, as evidenced by Annexin V (+) cytometric detection and the absence of PI (-), with no significant signs of necrosis. This means that specifically, the integration of nanotubes in the treatment caused the photosensitizer to accumulate successfully in the mitochondrial region, which triggered the activation of the apoptotic pathway, so the hypothesis was accepted. A T-test found a statistically significant difference between both PDT treatments compared to treatments without irradiation (p value= 0.001/ confidence interval 99.9% and p value= 0.01/ confidence interval 99%).

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