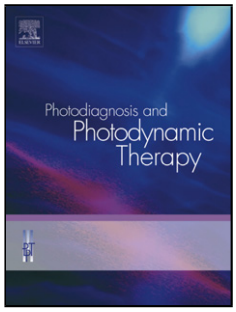

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Dose-dependent Photochemical/Photothermal Toxicity of Indocyanine Green-Based Therapy on Three Different Cancer Cell Lines

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Highlights

- The features of indocyanine green-based photodynamic therapy were researched.
- The action mechanism, singlet oxygen production and cellular uptake of indocyanine green were investigated.
- The dose-dependent cytotoxicity on three cell lines were compared.
- The consequences of aggregation problem and possible reasons for the sensitivity difference between cell lines were discussed.

Abstract. The Food and Drug Administration-approved Indocyanine Green can be used as a photosensitizer to kill cancer cells selectively. Although indocyanine green is advantageous as a photosensitizer in terms of strong absorption in the near-infrared region, indocyanine green-based cancer treatment is still not approved as a clinical method. Some reasons for this are aggregation at high concentrations, rapid clearance of the photosensitizer from the body, low singlet oxygen quantum yield, and the uncertainty concerning its action mechanism. This *in vitro* study focuses on two of these points: "what is the cell inhibition mechanism of indocyanine green-based therapy?" and "how the dose-dependent aggregation problem of indocyanine green alters its cell inhibition efficiency?" The following experiments were conducted to provide insight into these points.
Nontoxic doses of indocyanine green and near-infrared laser were determined. The aggregation behavior of indocyanine green was verified through experiments. The singlet oxygen quantum yield of indocyanine green at different concentrations were calculated. Various indocyanine green and energy densities of near-infrared light were applied to prostate cancer, neuroblastoma, and colon cancer cells. An MTT assay was performed at the end of the first, second, and third days following the treatments to determine the cell viability. Temperature changes in the medium during laser exposure were recorded. ROS generation following the treatment was verified by using a Total Reactive Oxygen Species detection kit. An apoptosis detection test was performed to establish the cell death mechanism and, finally, the cellular uptakes of the three different cells were measured. According to the results, indocyanine green-based therapy causes cell viability decrease for three cancer cell lines by means of excessive reactive oxygen species production. Different cells have different sensitivities to the therapy possibly because of the differentiation level and structural differences. The singlet oxygen generation of indocyanine green decreases at high concentrations because of aggregation. Nevertheless, better cancer cell killing effect