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## Nanoformulation of Pheophorbide-a for Photodynamic Therapy in a Human Lung Cancer Spheroid Model

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Pheophorbide a (PPBa) is a natural compound derived from chlorophyll, and its photophysical and photochemical properties makes it useful as a photosensitizer for photodynamic therapy (PDT). However, PPBa stability in biological environments and its bioavailability are crucial for effective therapy. Nanoparticle formulation of PPBa can improve its solubility and stability. The aim of this study is to make use of liposomal nanocomplex of PPBa as photosensitizer in PDT (at 15 J/cm<sup>2</sup> fluency) on A549 spheroid cells. Thin-film hydration method was used for synthesis of NPs. Characterization of Lipo@PPBa were carried out using UV-Vis spectroscopy, TEM, SEM, FTIR and DLS. Moreover, cytotoxicity of NPs was evaluated at various concentrations via MTT assay. The IC<sub>50</sub> dose was calculated for the evaluation of phototoxic effects under 660 nm laser irradiation at 15 J/cm<sup>2</sup>. UV-Vis spectroscopy showed a specific peak at 220 nm for lipids and two peaks for PPBa at 400 nm and 670 nm, respectively. TEM and SEM images illustrated that the size and shape of NPs were 45 nm and wavy crest, respectively. DLS data showed that the NPs have positive surface charge with zeta potential of 25 mV. MTT assay indicated that IC<sub>50</sub> of Lipo@PPBa nanocomplex in PDT was 1 µM, which reduced the cell viability to 48%. In conclusion, Lipo@PPBa showed significant phototoxic effects on A549 spheroid cells. However, more investigations on targeted therapy using Lipo@PPBa is recommended.

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