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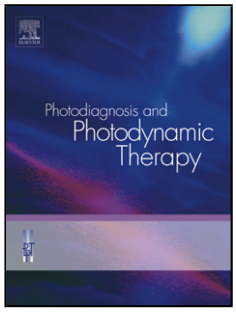

Title: Chlorin Nanoparticles for Tissue Diagnostics and Photodynamic Therapy

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Chlorin Nanoparticles for Tissue Diagnostics and Photodynamic Therapy

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Highlights:

- The chlorin Temoporfin, mTHPC, nanoparticles (NPs) are taken up by macrophages in inflamed tissue.
- The fluorescence of nanoparticles is quenched due to the crystalline structure. When molecules dissolve from the NPs, then they become fluorescent and photoactive.
- Inflamed and cancerous tissue can specifically be diagnosed and treated by PDT because macrophages are localized in high content in the tisuues.
- In macrophages, phototoxicity of NPs is stronger compared to sensitizer Foslip.
- Apoptosis seems to be the predominant cell death mechanism

Abstract:

Background: Organic crystalline nanoparticles (NPs) are not fluorescent due to the crystalline structure of the flat molecules organized in layers. In earlier experiments with Aluminum Phthalocyanine (AlPc)-derived NPs, the preferential uptake and dissolution by macrophages was demonstrated [3]. Therefore, inflamed tissue or cancer tissue with accumulated macrophages may exhibit specific fluorescence in contrast to healthy tissue which does not fluoresce. The present study addresses the photobiological effects of NP generated from Temoporfin (mTHPC), a clinically utilized photosensitizer belonging to the chlorin family.
Methods: *In-vitro* investigations addressing uptake, dissolution and phototoxicity of mTHPC NP vs. the liposomal mTHPC formulation Foslip were performed using J774A.1 macrophages and L929 fibroblasts. For total NP uptake analysis, the cells were lysed, the nanoparticles dissolved and the fluorescence quantified. The intracellular molecular dissolution was measured by flow cytometry. Fluorescence microscopy served for controlling intracellular localization of the dissolved fluorescing molecules. Reaction mechanisms after PDT (mitochondrial activity, apoptosis) were analyzed using fluorescent markers in cell-based assays and flow cytometry.
Results: Organic crystalline NP of different size were produced from mTHPC raw material. NP were internalized more efficiently in J774A.1 macrophages when compared to L929 fibroblasts, whereas uptake and fluorescence of Foslip was similar between the cell lines. NP dissolution correlated with internalization levels for larger particles in the range of 200-500 nm. Smaller particles (45 nm in diameter) were taken up at high levels in macrophages, but were not dissolved efficiently, resulting in comparatively low intracellular fluorescence. Whereas Foslip was predominantly localized in membranes, NP-mediated fluorescence also co-localized with