

## Probing Cellular Uptake of Different Delivery Approaches for Porphyrinic Photosensitizers on HeLa cells

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Porphyritic photosensitizers are used in Photodynamic therapy (PDT) of cancer and other non-cancerous diseases. They are promising compounds because of their intrinsic phototoxicity, tumor accumulation and low dark toxicity. Porphyrin-polymer systems are used in order to prevent porphyrin aggregation and increase or maintain PDT efficacy. Previously, we have shown by <sup>1</sup>H NMR spectroscopy that the photosensitizer serine-chlorin e6 (SerCE) is disaggregated upon insertion into either the polymer polyvinylpyrrolidone (PVP) or into polymer micelles consisting of Kolliphor P188 (KP188) [1, 2].

The aim of the current study was to probe and compare the impact of the carrier systems, i.e. PVP and KP188, on the cellular uptake of two different porphyritic compounds, SerCE and chlorin e4(CE4), after treatment in the dark. Compared to SerCE, the serine-amide side chain is replaced by a methyl group in CE4 rendering the molecule more hydrophobic forming larger aggregates. Similar to SerCE, CE4 aggregates could be dissolved upon insertion into PVP or KP polymers. Uptake of both compounds into HeLa cells was tested using the ImageStream flow cytometer. The fluorescence data indicated that the cellular uptake was decreased in the presence of Kolliphor P188 compared to SerCE alone. Similarly, a slight decrease was observed when SerCE was combined with PVP. On the contrary, CE4 exhibited three times higher cellular uptake when combined with Kolliphor P188 and four times higher uptake when combined with PVP. The increased uptake of CE4 may be attributed to its hydrophobicity, allowing more efficient incorporation into Kolliphor P188 micelles and the PVP network. Even though successfully monomerized by the carrier systems, the more hydrophilic properties of SerCE most likely account for the lack of improved carrier-mediated cellular uptake. In conclusion, oligomer or higher aggregated species forming porphyritic compounds exhibit different cell uptake behavior when combined with polymeric carriers.

[1] M. Hädener, I. Gjuroski, J. Furrer, M. Vermathen, *J. Phys. Chem. B*, **2015**, 119, 12117-12128.

[2] I. Gjuroski, J. Furrer, M. Vermathen *Chimia*, **2015**, 69 (S 7-8), MC-151.