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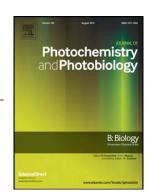
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ACCEPTED MANUSCRIPT

Uptake and photo-toxicity of Foscan®, Foslip® and Fospeg® in multicellular tumor spheroids

Elisa Gaio^a, Dietrich Scheglmann^b, Elena Reddi^{a*}, Francesca Moret^{a*}

^aDepartment of Biology, University of Padova, Via Ugo Bassi 58/B, 35121 Padova, Italy

^bBiolitec Research GmbH, Otto-Schott-Strasse 15, 07745 Jena, Germany

*Corresponding authors at: Department of Biology, University of Padova, Via Ugo Bassi 58/B, 35121 Padova, Italy

e-mail addresses: Elisa Gaio, elisa.gaio@studenti.unipd.it; Dietrich Scheglmann, Dietrich.Scheglmann@biolitec.com; Elena Reddi, elena.reddi@unipd.it; Francesca Moret, francesca.moret@unipd.it

Abstract

In cancer photodynamic therapy (PDT), an efficient and homogeneous intratumoral accumulation of the photosensitizer (PS) is required to induce cell damages in the entire tumor mass after light activation. Thus, in this study we investigated penetration ability and photodynamic efficiency of *meta*-tetra(hydroxyphenyl)chlorin (*m*-THPC) in standard formulation (Foscan®) and in its non PEGylated and PEGylated liposomal formulations, Foslip® and Fospeg®, in HeLa multicellular spheroids, as *in vitro* avascular models of solid tumors. Confocal microscopy studies demonstrated that *m*-THPC fluorescence was confined in the external cell layers of spheroids with a slightly higher accumulation of Foslip® and Fospeg® with respect to Foscan®. Irradiation with red light, following 24 h incubation of spheroids with the *m*-THPC formulations, caused however photodamages also in cells located in the central part of spheroids, as documented by transmission

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