

Photodynamic Hydrogel Based on Carbomer-TMPyP Complex: *In vitro* Release and *Pseudomonas aeruginosa* Photoinactivation †

Luciana Campagno ^{1,*}, Ana Apas ¹, Franco Ambrosioni ¹, Alvaro Jimenez-Kairuz ¹, Fabiana Alovero ^{1,*}

¹ Departamento de Ciencias Farmacéuticas, FCQ-Universidad Nacional de Córdoba and UNITEFA-CONICET. Córdoba, Argentina; luciana.paula.campagno@unc.edu.ar (L.C.); aapas@unc.edu.ar (AA); franexee@gmail.com (FA); ajimenez-kairuz@unc.edu.ar (A.J.K.); fabiana.alovero@unc.edu.ar (F.A.)

* Correspondence: luciana.paula.campagno@unc.edu.ar (L.C.); fabiana.alovero@unc.edu.ar (F.A.);

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Abstract: Photodynamic antimicrobial chemotherapy is a proposed alternative for localized infections in the era of antibiotic resistance. Although topical administration of a photosensitizer followed by irradiation is a viable application due to the accessibility of the target site, the design of effective and safe delivery systems for the photosensitizer is necessary. Previously, we designed hydrogels based on ionic complexes between Carbomer-974P and TMPyP, a commercially available cationic porphyrin. These hydrogels exhibited a slight delay in the photoinactivation of *P.aeruginosa* compared to TMPyP solution. Here we study the *in vitro* release kinetics from a hydrogel using Franz-type cells and the interaction/association kinetics of TMPyP with *P.aeruginosa* by fluorescence microscopy. Release profiles better-fit zero-order kinetics ($R^2=0.993$). The release rate from the hydrogel was 6.5 times slower than TMPyP solution. Hydrogel-treated cultures exhibited delayed appearance of fluorescent bacteria. Then, the hydrogel behaves as a reservoir of TMPyP from which it is slowly released by the dissociation of ionic pairs. Controlled release of TMPyP would modify its bacterial internalization/association kinetics, requiring prolongation of contact and irradiation period to achieve *P.aeruginosa* eradication. These results, together with the known bioadhesive and rheological properties of carbomer hydrogels, allow us to consider them a promising platform for designing topical TMPyP delivery systems.

Keywords: TMPyP; hydrogels; *Pseudomonas aeruginosa*; Franz-type cells; CLSM; Topical controlled release.

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Conflicts of Interest

The authors declare no conflict of interest.