In-gel generated palladium nanostructures as bioorthogonal uncaging reactors

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In the quest for alleviating the severe side-effects of chemotherapy, a promising approach is through prodrugs; an inactivated form of the drug which is administered systemically but activated locally. Bioorthogonal chemistry has the potential to generate high doses of drug at the tumour site with minimal off-target exposure[1]. To harness the potential of bioorthogonal prodrugs, implantable heterogenous catalysts of polymers with immobilised metal nanoparticles are required. Polymers based on poly(2-hydroxyethyl methacrylate) with different levels of hydrophilicity were functionalized with either Pd nanocubes (~10 nm) or Pd nanosheets (<200 nm). Using a Pd-sensitive fluorogenic model compound, propargylated resorufin, the nanosheets showed higher catalytic activity than the nanocubes, as well as better metal retainment within the hydrogels. The more hydrophilic polymers showed improved diffusion, conversion and release, and better recyclability. Converted product was sequestered by the polymer and released with delay, establishing a potential route to sustained release. These heterogenous catalysts can facilitate the clinical translation of bioorthogonal prodrugs.

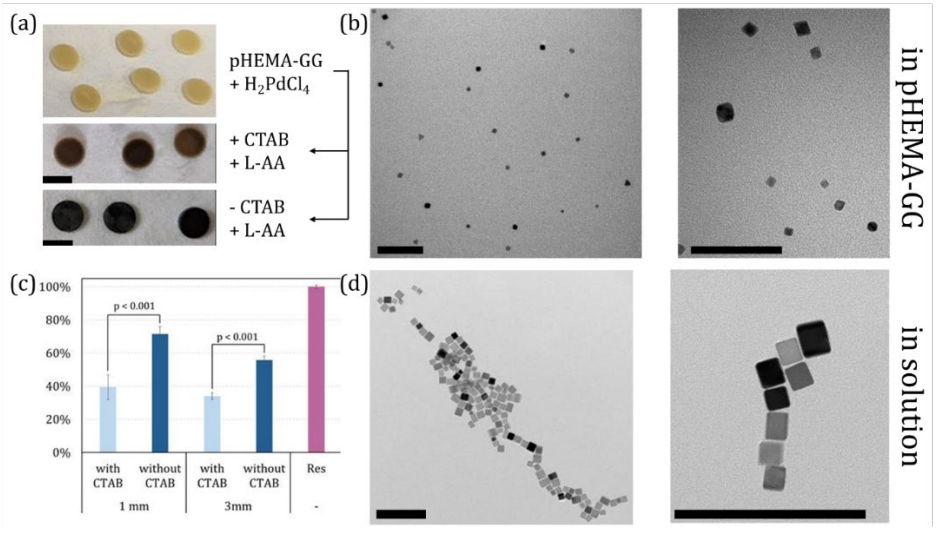

Figure 1: In situ preparation of Pd nanocubes (PdNC) inside pHEMA-GG hydrogels. (a) Pd precursor solution was left to diffuse into pHEMA-GG hydrogels, and reduced with L-AA with or without prior heating in CTAB solution. (b) TEM images of PdNC inside pHEMA-GG hydrogels. (c) Conversion of proresorufin by pHEMA-GG-PdNC discs for both methods, with CTAB (light blue) and without CTAB (dark blue). (d) TEM images of PdNC prepared in solution. Scale bars 6 mm (a) and 100 nm (b, d)

References:

[1] Bray, T.L.et al. *Chem Sci* **2018**, *9*, 7354–7361.