SUPPORTING INFO

## Title

# Dual-pore protocells with multitasking capacities for simultaneous delivery of therapeutic enzymes and drugs in macrophage depletion therapy

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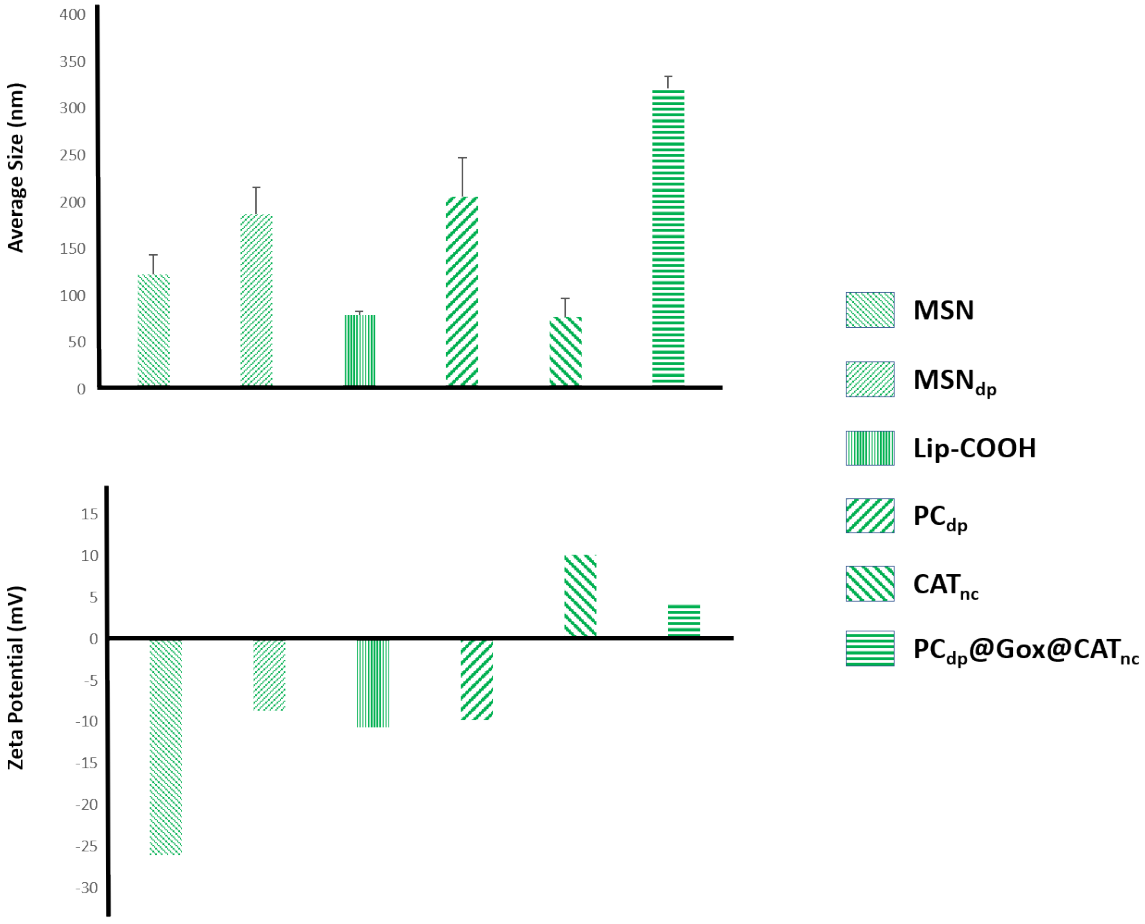


**Figure S1.** Hydrodynamic size measurements by Dynamic Light Scattering (DLS) and Zeta potential.

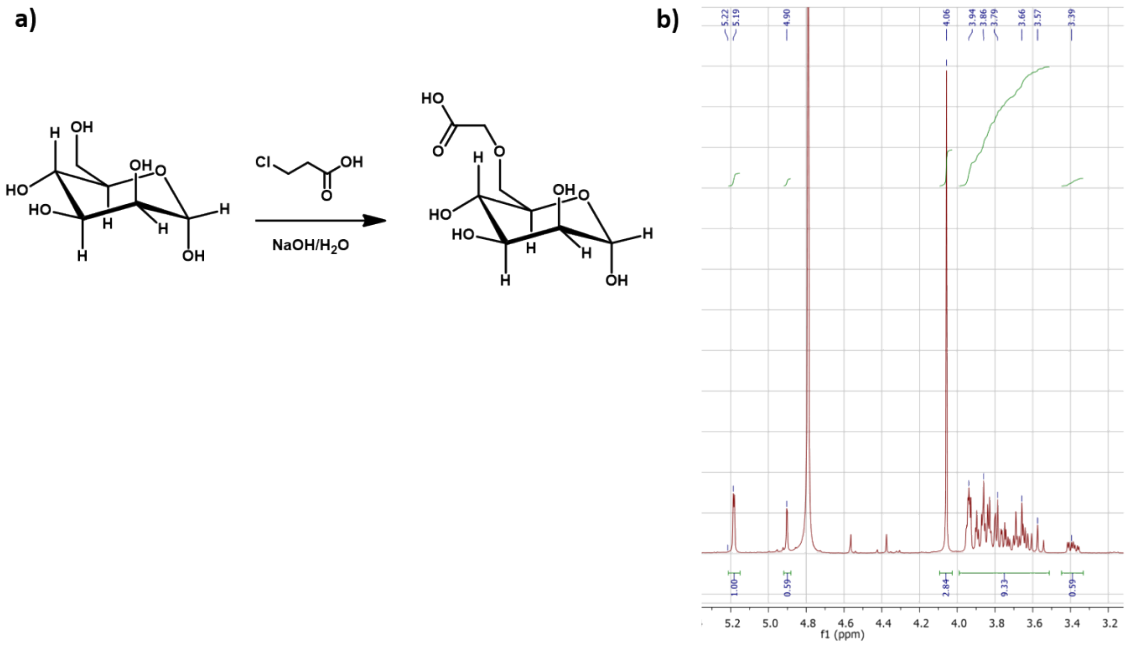


**Figure S2**. a) Synthetic scheme of carboxy-Man. a) $^{1}$H-NMR spectra of carboxy-Man.

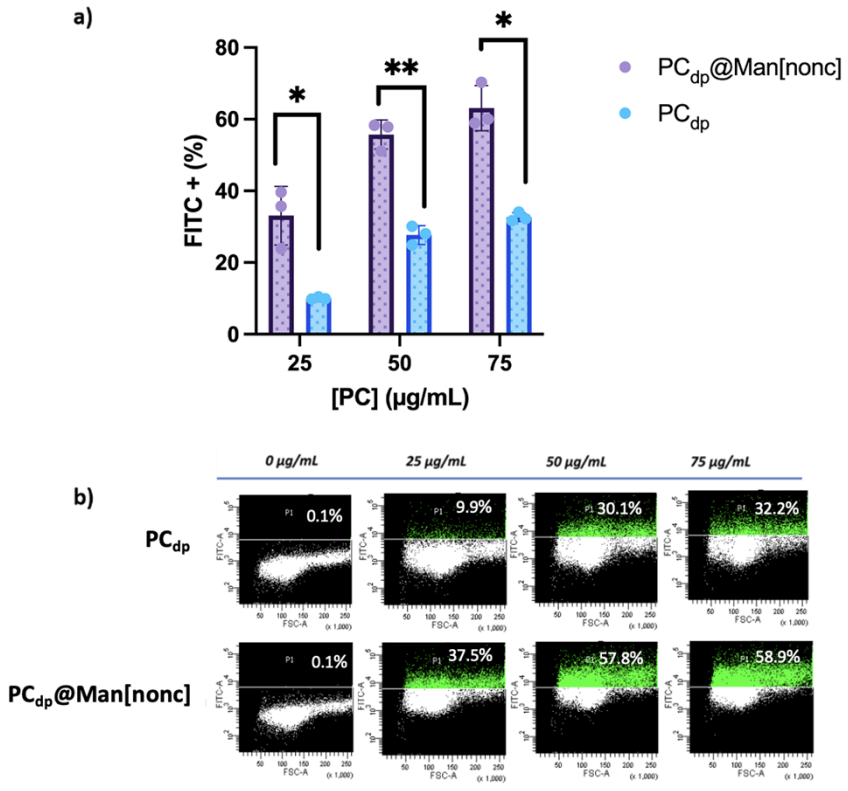


**Figure S3**. a) In vitro protocell uptake evaluation in RAW 264.7 cells treated with $PC_{dp}$ and non carboxylated manose modified protocells ($PC_{dp}$@Man[nonc]) at different dosages. All experiments were performed in triplicate and Student t-tests were carried out with *= $p < 0.05$, **= $p < 0.01$. b) Flow cytometry of RAW 264.7 cells treated

$$Loading\ Efficiency = \frac{Mass\ of\ cargo\ in\ nanoparticle}{Mass\ of\ cargo\ used\ in\ formulation} x100$$

$$Loading\ Capacity = \frac{Mass\ of\ cargo\ in\ nanoparticle}{Mass\ of\ nanoparticle} x100$$

**Figure S4**. Loading efficiency (LE) and loading capacity (LC) equations.

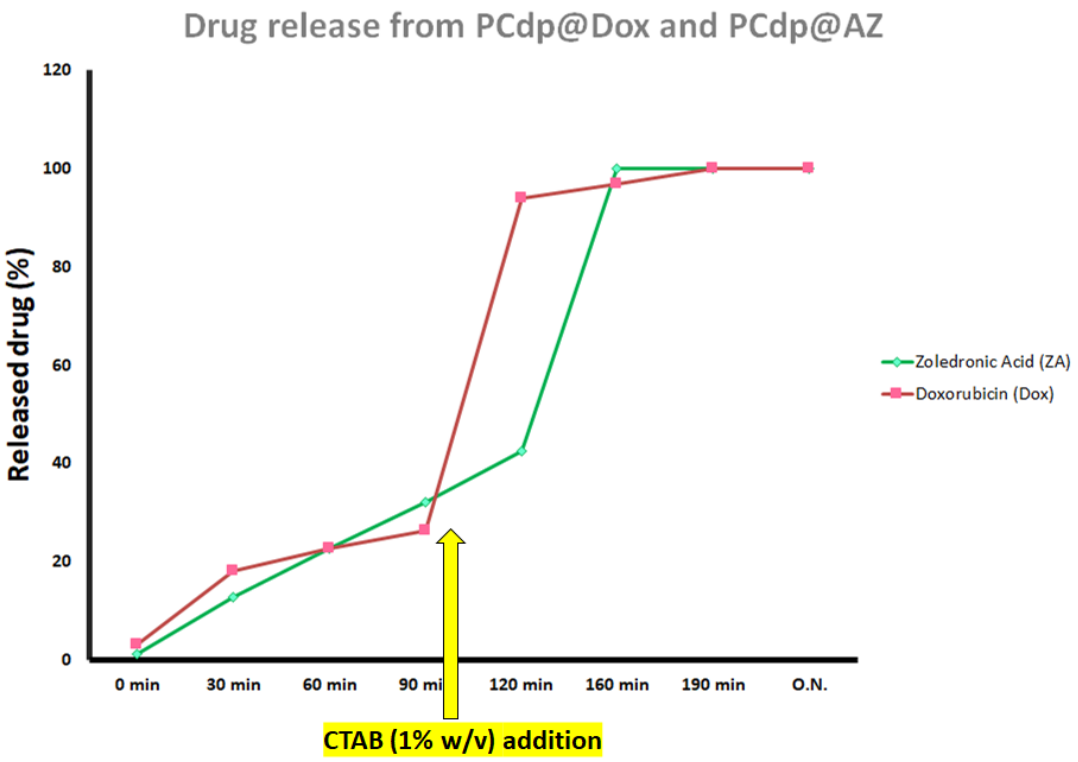


**Figure S5**. ZA and Dox release pattern of $PC_{dp}$@AZ and $PC_{dp}$@DOX suspended in PBS and treated with CTAB.

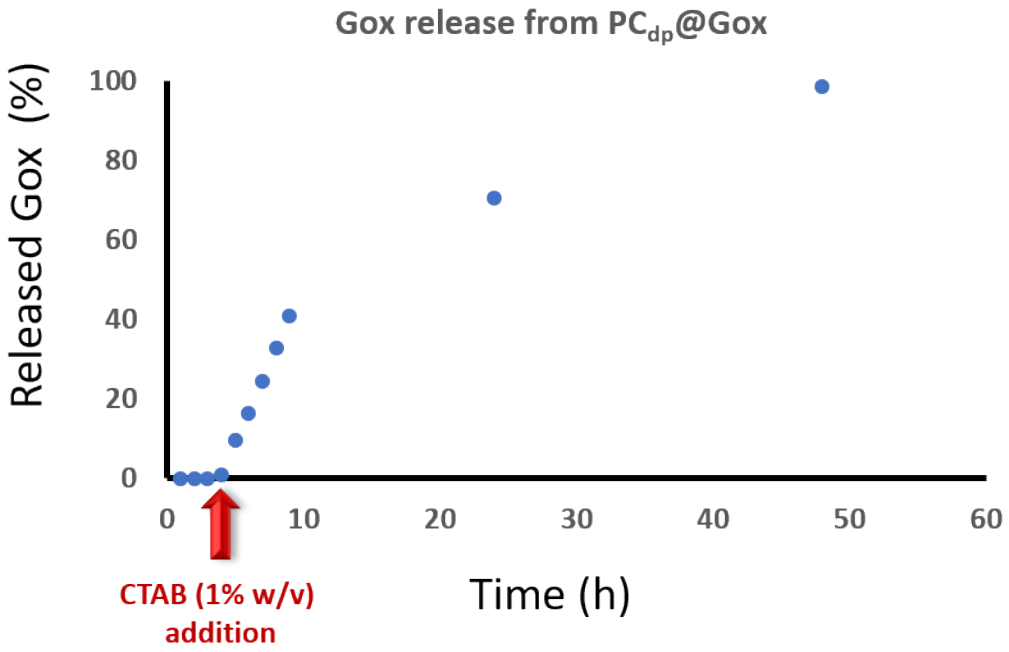


**Figure S6**. Gox release pattern of $PC_{dp}$@Gox suspended in PBS and treated with CTAB.

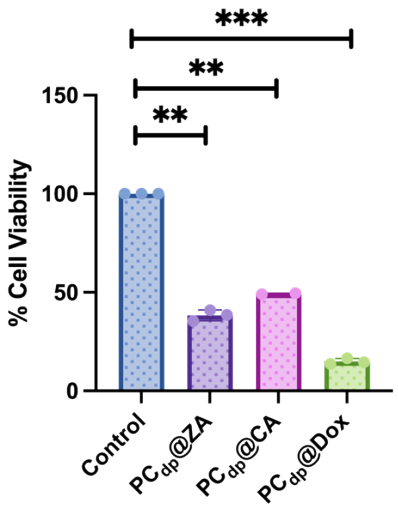


**Figure S7**. Cell viability evaluation of RAW 264.7 cells incubated with 150 µg/mL of protocells loaded with zoledronic acid ($PC_{dp}$@ZA), chlorogenic acid ($PC_{dp}$@CA) and doxorubicin ($PC_{dp}$@Dox). All experiments were performed in triplicate, and Student t-tests were carried out with ** = $p < 0.01$; *** = $p < 0.001$.

**Videos S1** and **S2** show protocell uptake by macrophages under flow conditions.