

Supplementary Information

Side chain variations radically alter the diffusion of poly(2-alkyl-2-oxazoline)s functionalised nanoparticles through a mucosal barrier

Edward D.H. Mansfield,^a Victor R. de la Rosa,^b Radoslaw M. Kowalczyk,^c Isabelle Grillo,^d
Richard Hoogenboom,^b Katy Sillence,^e Patrick Hole,^e Adrian C. Williams,^a
Vitaliy V. Khutoryanskiy^{a*}

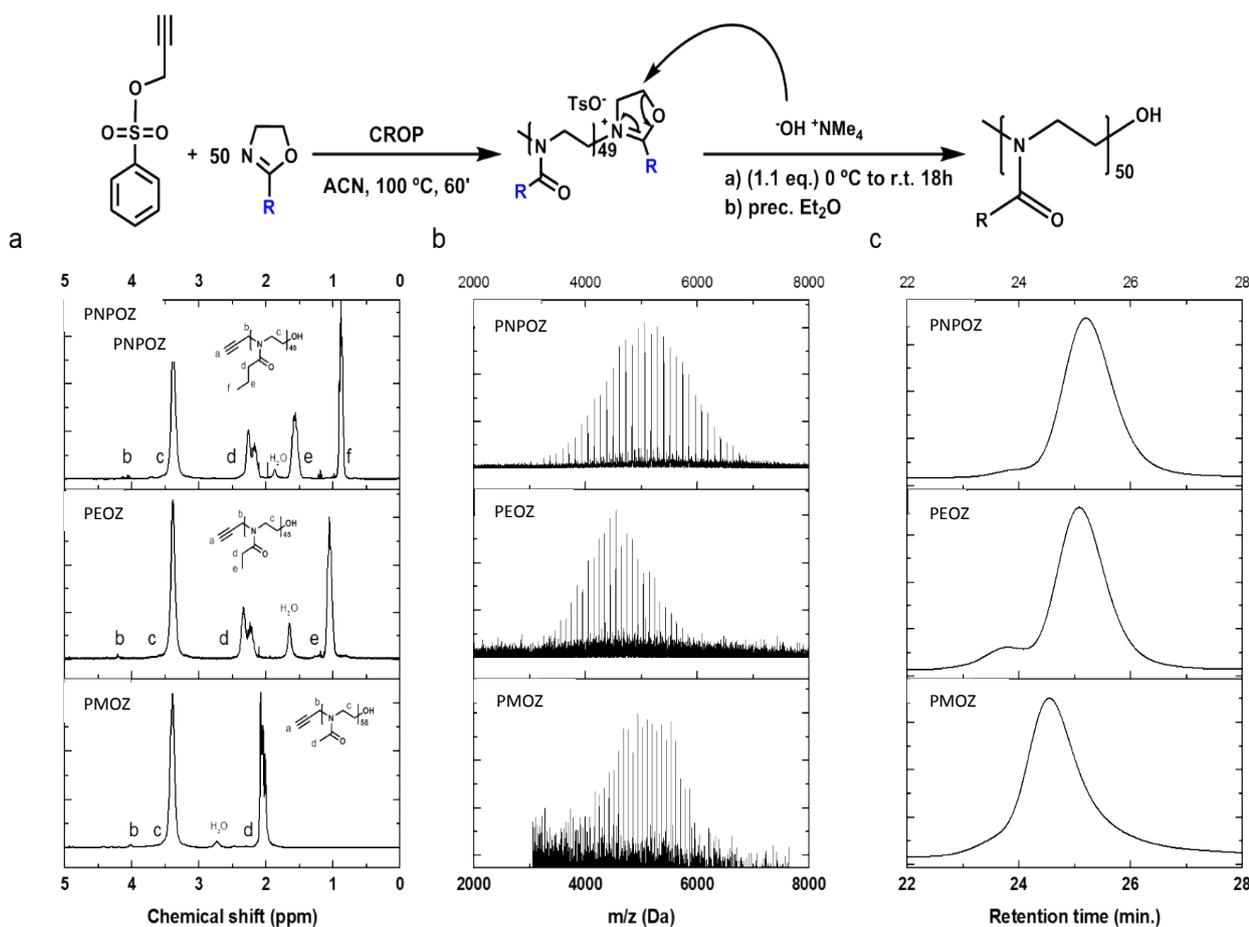


Figure S1. Top: Synthesis of propargyl-functionalised poly(2-alkyl-2-oxazoline)s. R = CH₃- (PMOZ), CH₃CH₂- (PEOZ), or CH₃CH₂CH₂- (PNPOZ). Bottom: a) ¹H-NMR spectra of propargyl-POZ polymers in CDCl₃ (300 MHz) and b) corresponding MALDI-TOF mass spectrum confirming the intended polymer structure. Major distribution: Na⁺ adduct. Secondary distribution: K⁺ adduct. c) Size exclusion elugrams for the three polymers. Albeit a high molecular weight shoulder is observed in all SEC traces, ascribed to chain coupling, well-defined polymers were obtained with dispersity values below 1.10. SEC eluent: N,N-dimethylacetamide containing 50 mM LiCl, calibrated against PMMA standards.

Polymer	Mn (SEC)	Mn (MALDI)	Đ (SEC)
PMOZ	10 800	5 000	1.09
PEOZ	9 000	4 500	1.08
PNPOZ	8 000	5 100	1.06

Table SII. Size exclusion chromatography data for the synthesised propargyl-functional poly(2-alkyl-2-oxazoline)s. The average molecular mass calculated by SEC is relative to PMMA standards and depends on the polymer hydrophilicity; therefore, the average molecular mass calculated by MALDI-ToF MS is also provided.

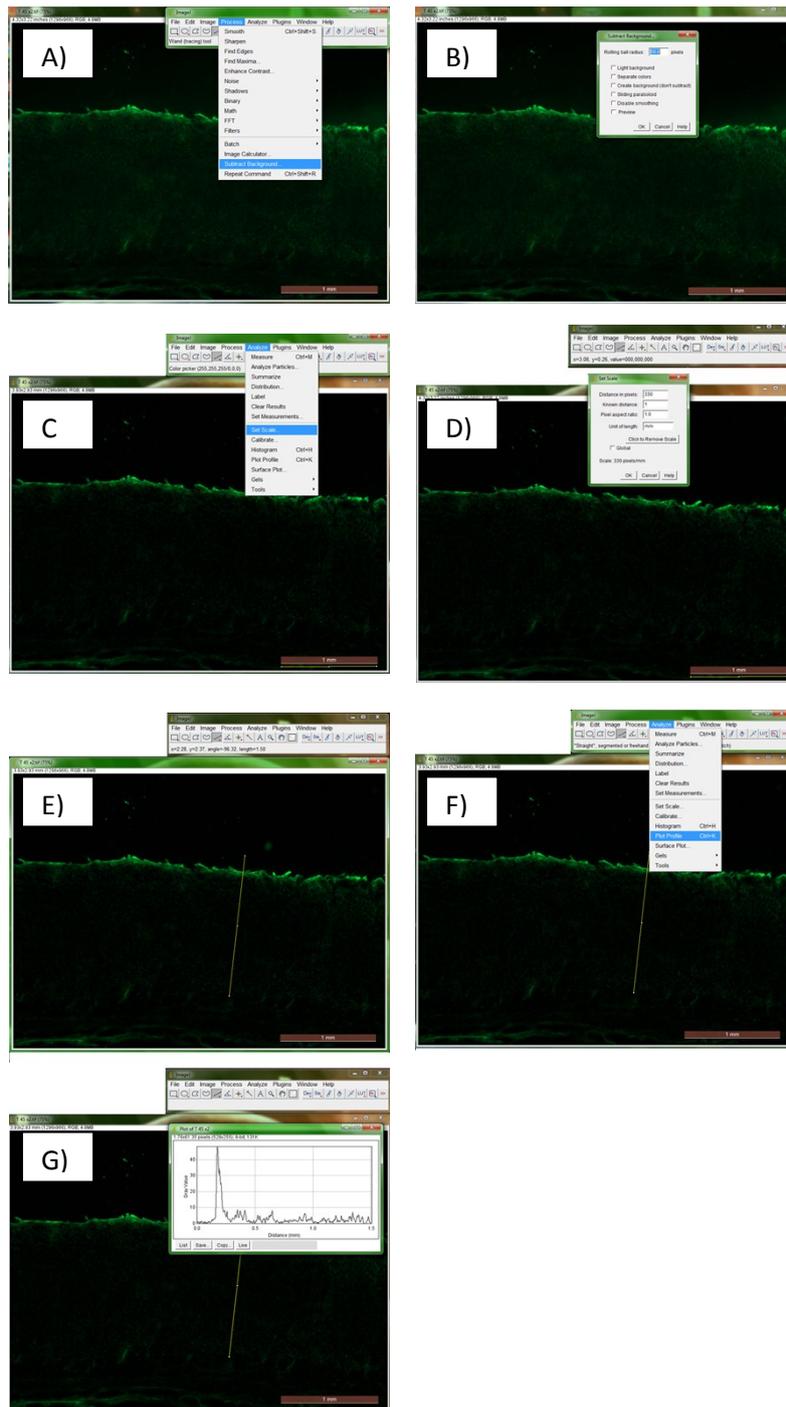


Figure SI.2. Representative description of ImageJ protocol. A and B) show subtraction of the background (process>subtract background). C and D) show how the scale was set. A line was drawn to the same length as the scale bar determined from the Leica software, followed by analysis>set scale. The units were changed to match that of the scale bar (default inches was changed to mm). E, F, and G) show the analysis. A line was drawn (1.5 mm in length) crossing the mucus barrier, followed by analyse>plot profile (ctrl+k). The determined plot (shown in G) was then saved into excel format. This was repeated for a further 4 lines per image, at random locations along the mucus barrier. In Excel, each plot profile was assessed individually, and the size of the initial peak was measured to determine the start point, and end point along the x-axis,

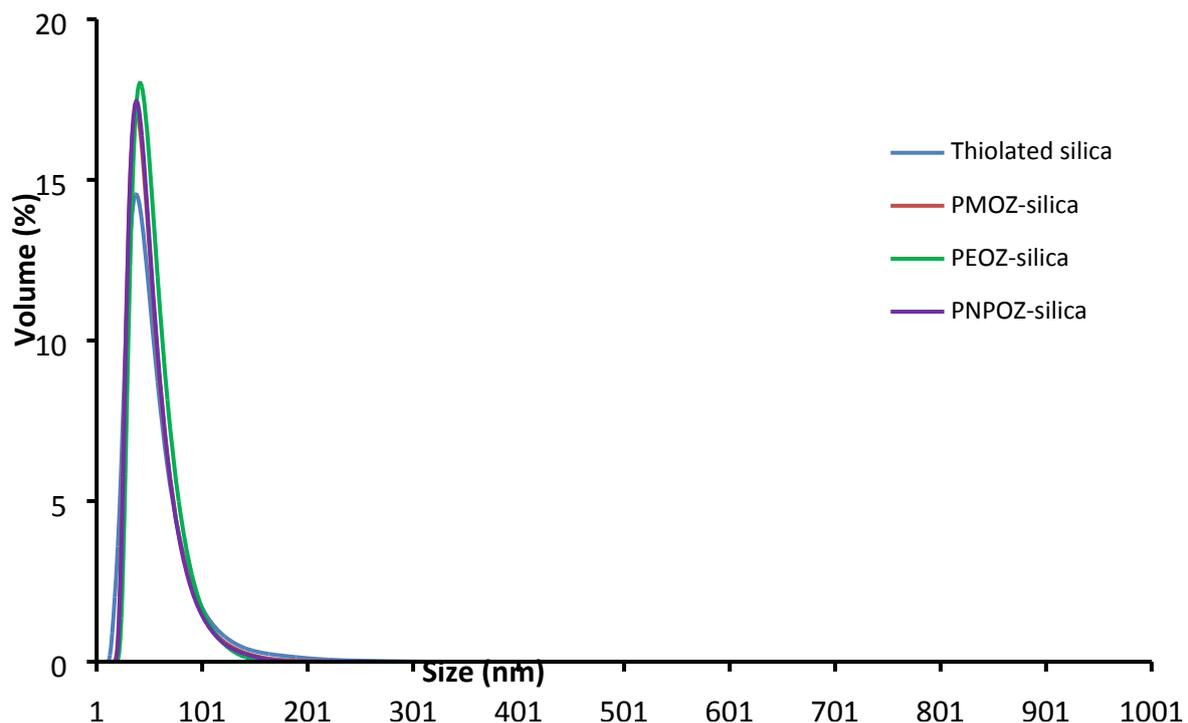


Figure SI.3 DLS size distributions for thiolated silica (blue), PMOZ-silica (red), PEOZ-silica (green), and PNPOZ-silica (purple).

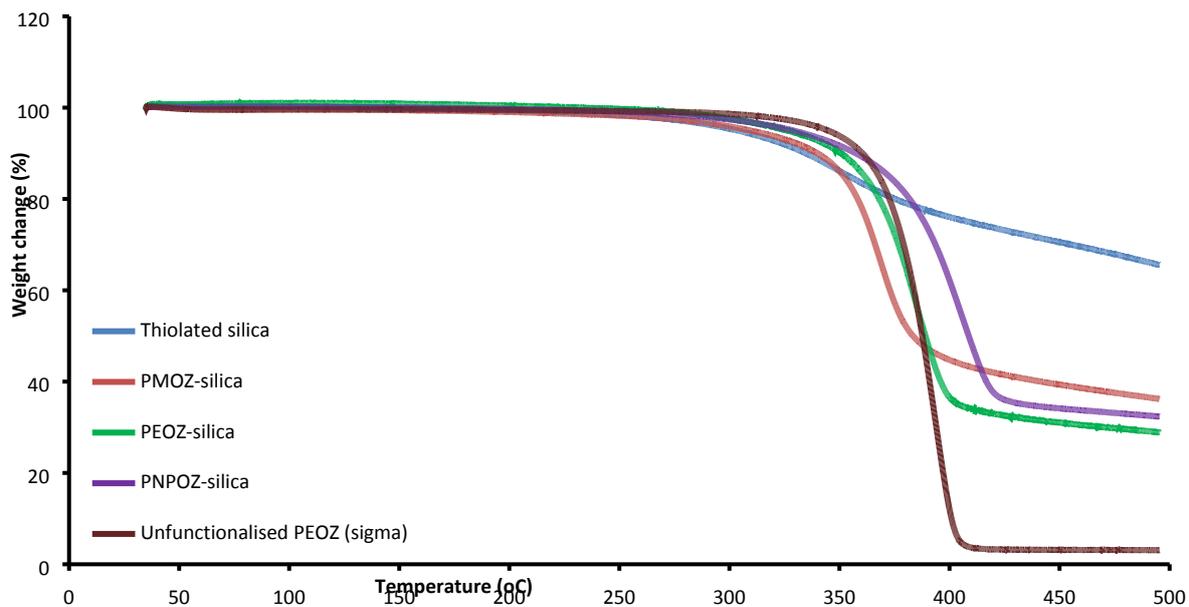
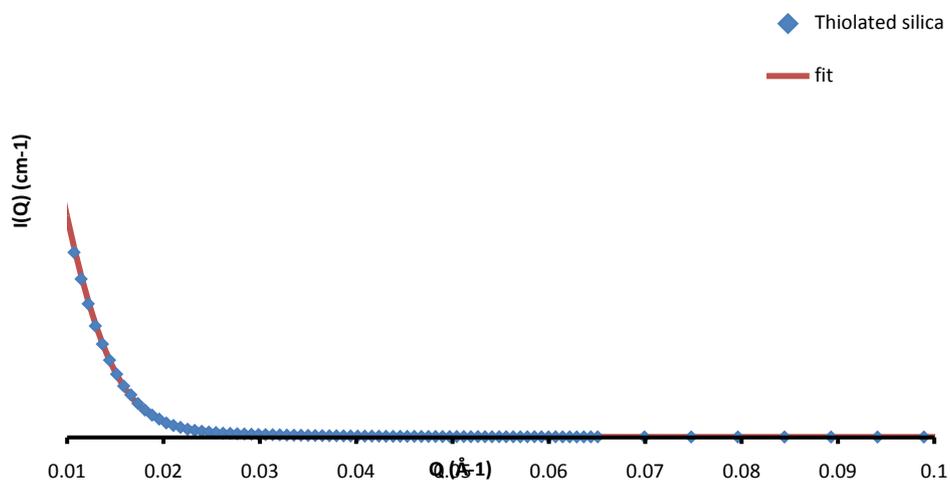


Figure SI.4 TGA curves showing the thermal decomposition of thiolated (blue), pMOZ functionalised silica (red), pEOZ functionalised silica (green), and pNPOZ functionalised silica (purple). The unfunctionalised polymer is shown brown.



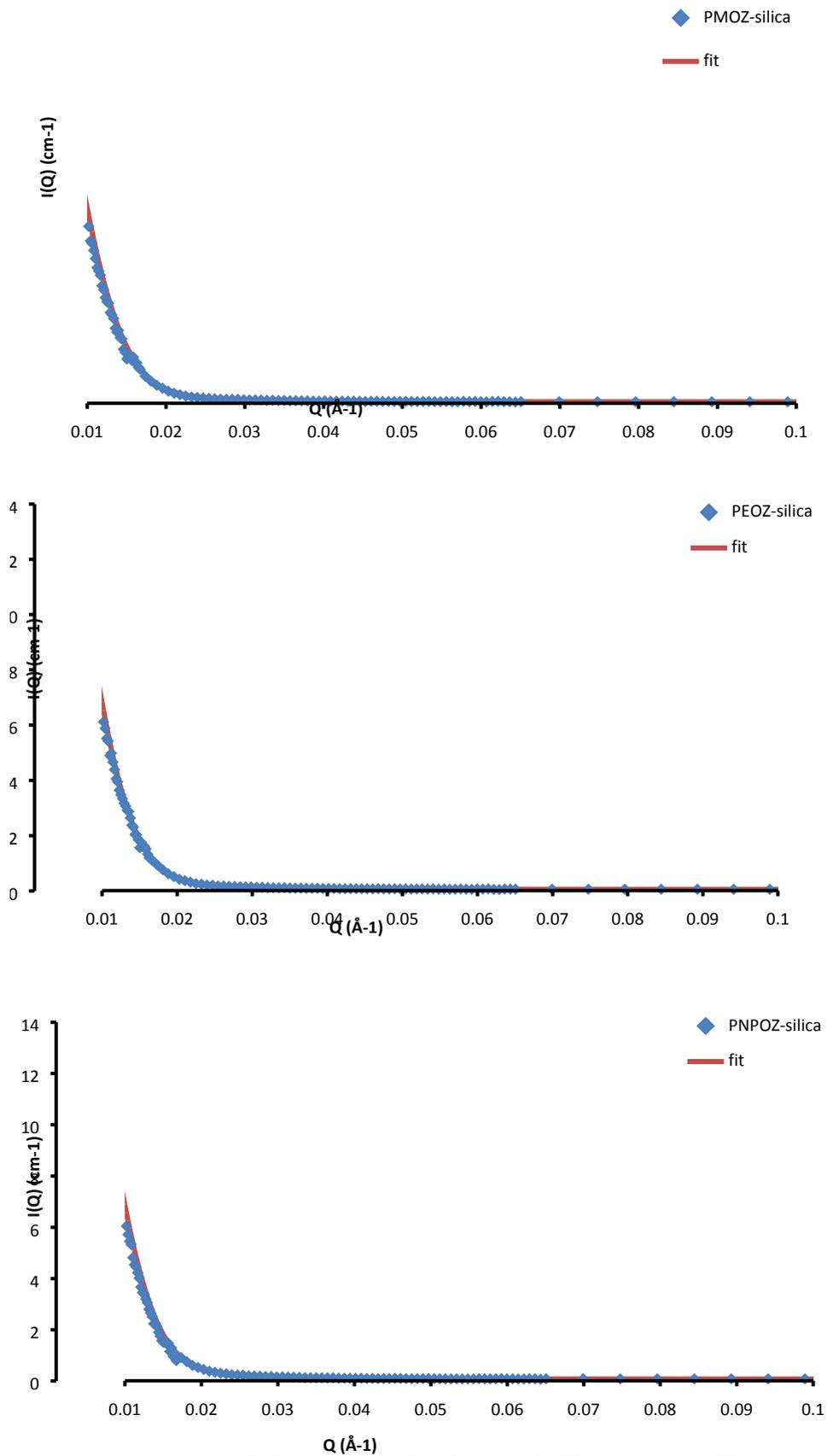


Figure SI.5 SANS fitting profiles for thiolated silica, PMOZ-silica, PEOZ-silica and PNPOZ-silica. All data were fitted to a spherical form factor with the addition of a shell model using the SASview programme.

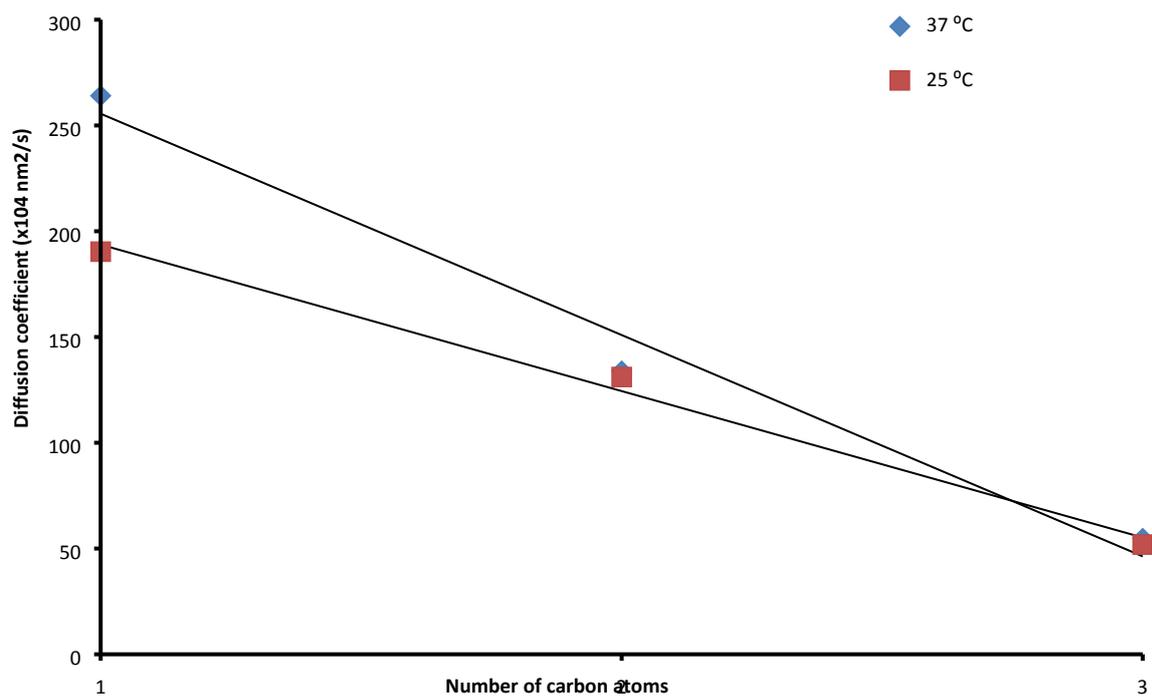


Figure SI.6 Diffusion coefficient of functionalised silica nanoparticles as a function of alkyl chain length, at both 25 and 37 °C.

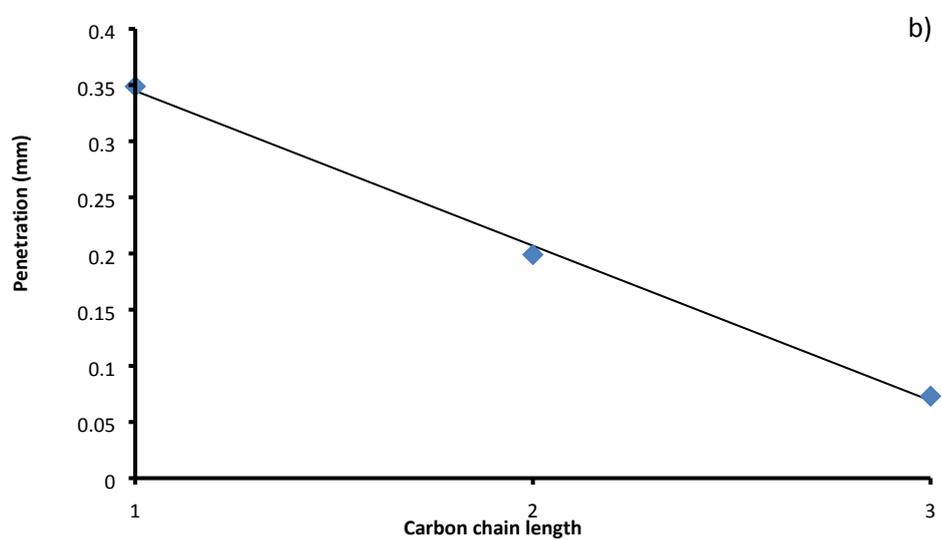
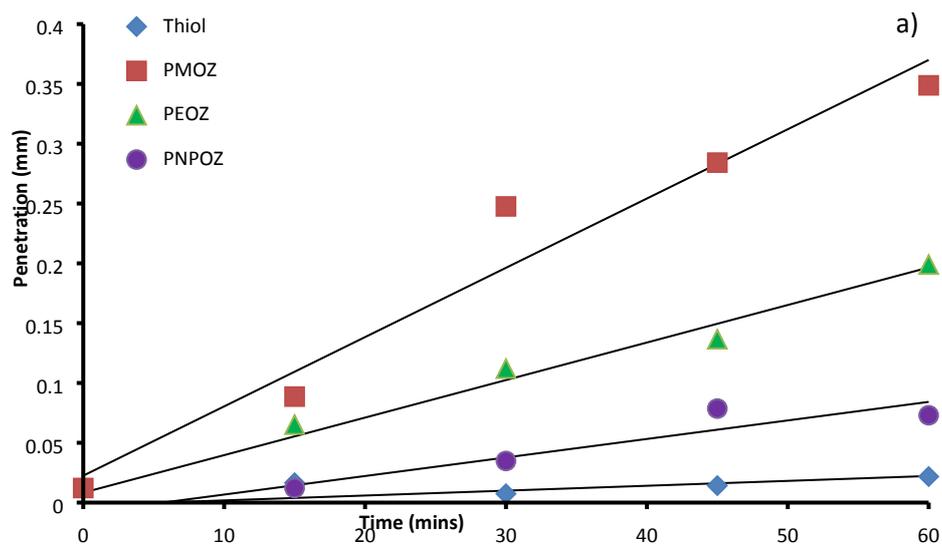


Figure SI.7 a) Penetration of functionalised and unfunctionalised nanoparticles into a gastric mucosa as a function of time. b) Penetration of functionalised nanoparticles into a gastric mucosa as a function of alkyl chain length.

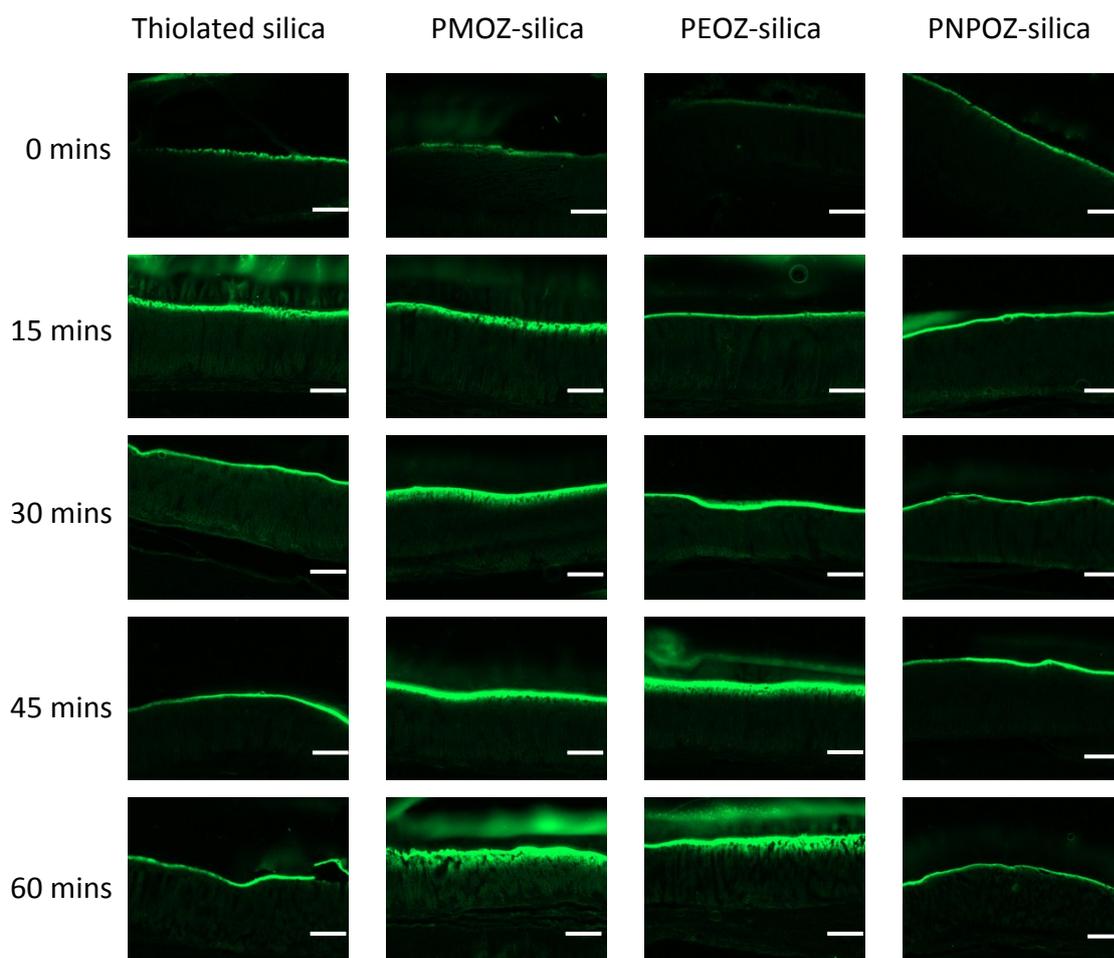


Figure SI.8 Exemplary images showing the penetration of fluorescently labelled functionalised and unfunctionalised silica through a gastric mucosa, at different time intervals. The scale-bar represents 1 mm in all cases.