Thermoresponsive and Degradable Poly(oligoethylene glycol methyl ether methacrylate) (POEGMA) Nanogels for Targeted Drug Model Release

Mazrina Mazlan[1,2], Tom O. McDonald[1,2],

[1]Department of Chemistry, The University of Manchester, Oxford Road, Manchester, M13 9PL

[2]Department of Materials, Henry Royce Institute, The University of Manchester, Oxford Road, Manchester, M13 9PL

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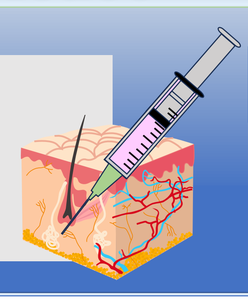
References



Reducing Dependence on Oral Medication

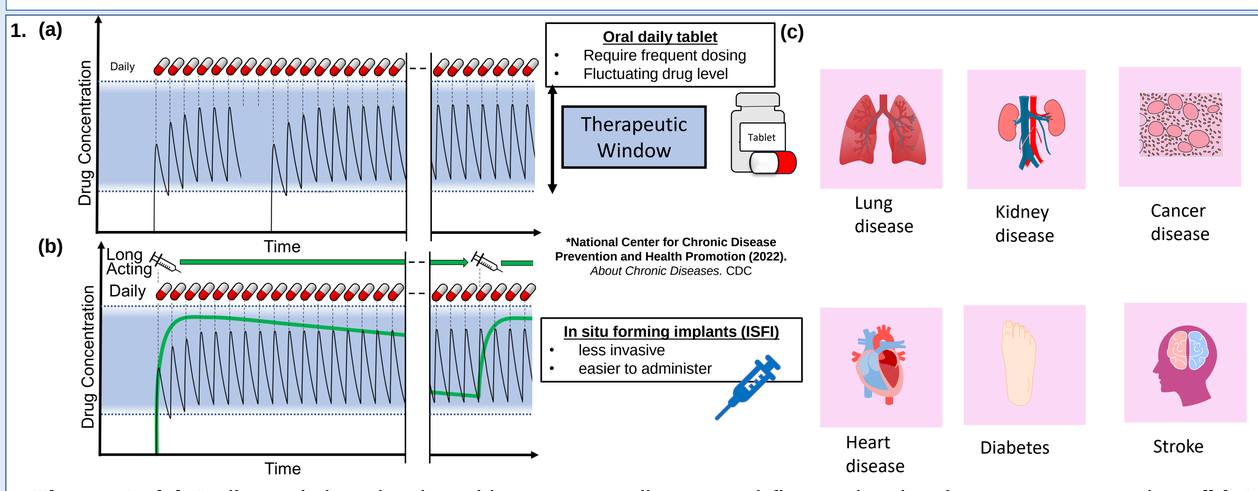


Figure 1. (a) Daily oral drug intake with poor compliance and fluctuation in plasma concentration. **(b)** *In situ* forming implant provides steady drug levels **(c)** Chronic diseases that require long-term medication

Introduction to POEGMA Nanogels

📌Poly(N-isopropylacrylamide) (PNIPAM) is a widely studied thermoresponsive polymer.
Potential of toxicity of its acrylamide monomer residual limits its potential in biomedical applications.
🌿An attractive alternative to PNIPAM is poly(oligoethylene glycol methyl ether methacrylate) (POEGMA) , due to the lower toxicity issues of the methacrylate monomers (Alejo et al., 2018; Yin et al., 2020).
🔥POEGMA's thermoresponsive behaviour can be tuned by tailoring mass fraction of 2-(2-methoxyethoxy) ethyl methacrylate (MEO_2MA), side chain length ≈ 2 ethylene glycol units) to oligo (ethylene glycol) methacrylate (OEGMA), side chain length ≈ 4–9 ethylene glycol units, typically tunable within the 15–60 °C range.
🩹Degradable nanogels can be synthesised using N,N'-bis(acryloyl)cystamine (BAC) as the crosslinker, suitable for controlled drug delivery.

Mechanism of POEGMA Nanogels Behaviour

⇨ Polymerisation of MEO_2MA and OEGMA nanogels using N,N'-bis(acryloyl)cystamine (BAC) via dispersion polymerisation (Johnson *et al.* 2021).The mechanism of synthesis can be seen in figure 2.

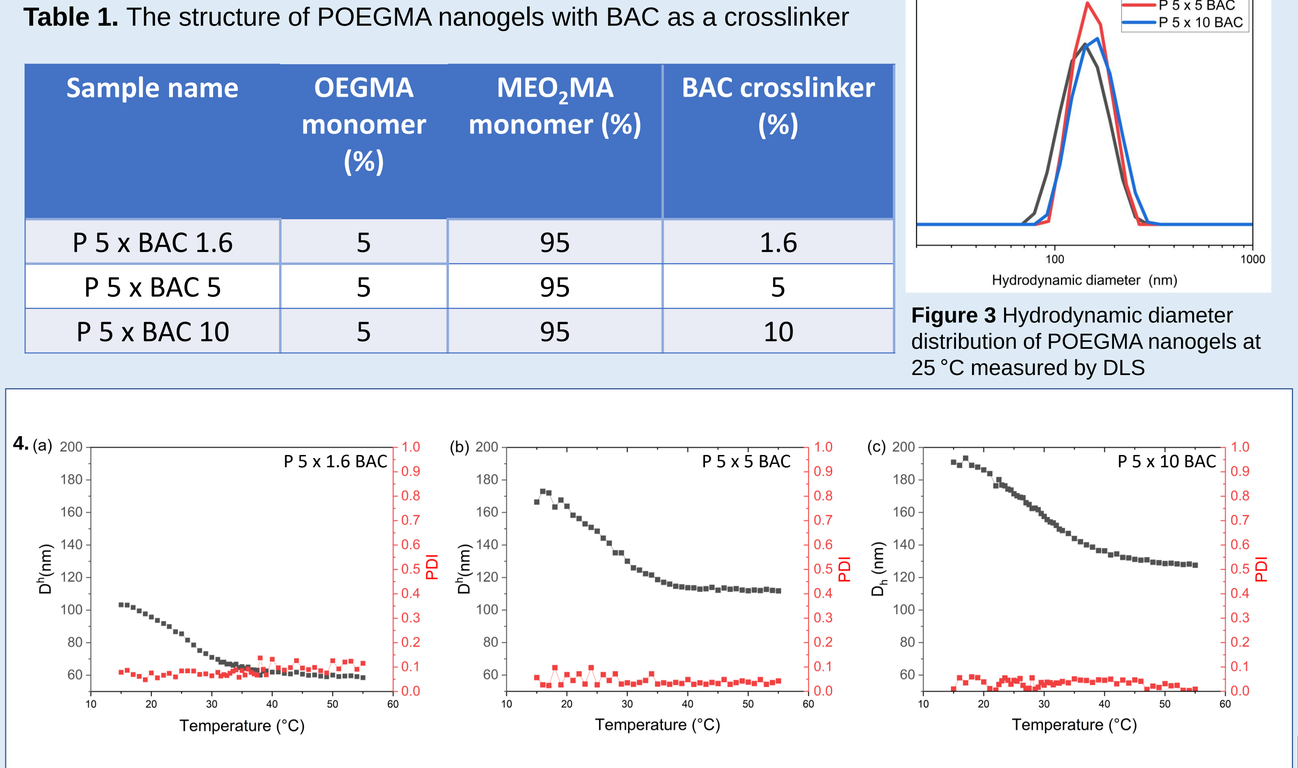


Figure 2. (a) The structure of degradable POEGMA with BAC as a crosslinker
(b) Thermoresponsive behaviour in (a) water (b) salt

Composition of POEGMA Nanogels

⇨The composition of POEGMA nanogels are listed as in table 1:

Table 1. The structure of POEGMA nanogels with BAC as a crosslinker

Sample name	OEGMA monomer (%)	MEO_2MA monomer (%)	BAC crosslinker (%)
P 5 x BAC 1.6	5	95	1.6
P 5 x BAC 5	5	95	5
P 5 x BAC 10	5	95	10

Figure 3 Hydrodynamic diameter distribution of POEGMA nanogels at 25 °C measured by DLS

Figure 4 Thermoresponsive behaviour in water **(a)** 1.6 % **(b)** 5% and **(c)**10% crosslinker

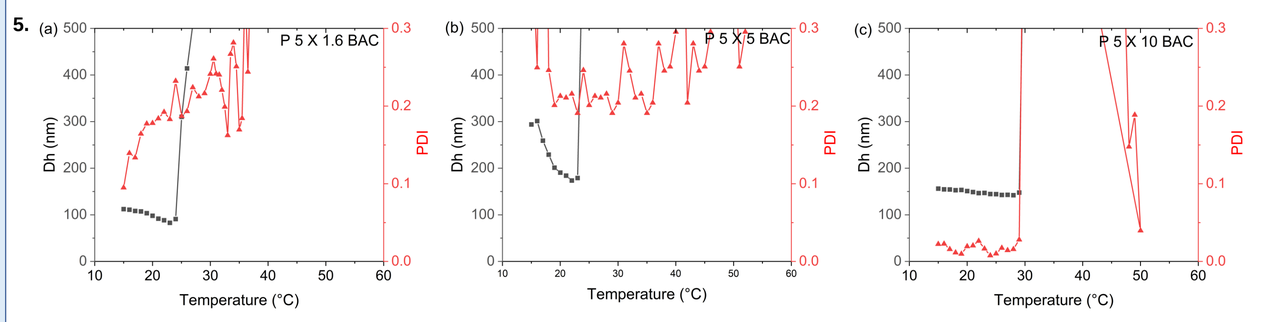


Figure 5 Thermoresponsive behaviour in PBS **(a)** 1.6 % **(b)** 5% and **(c)**10% crosslinker

^{1}HNMR structure and Zeta Potential of POEGMA Nanogels

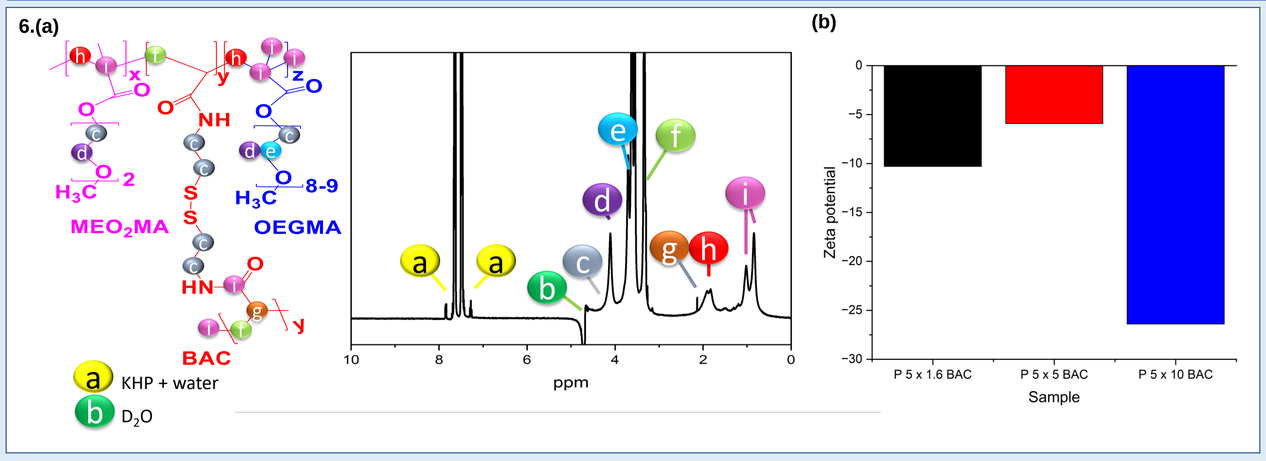
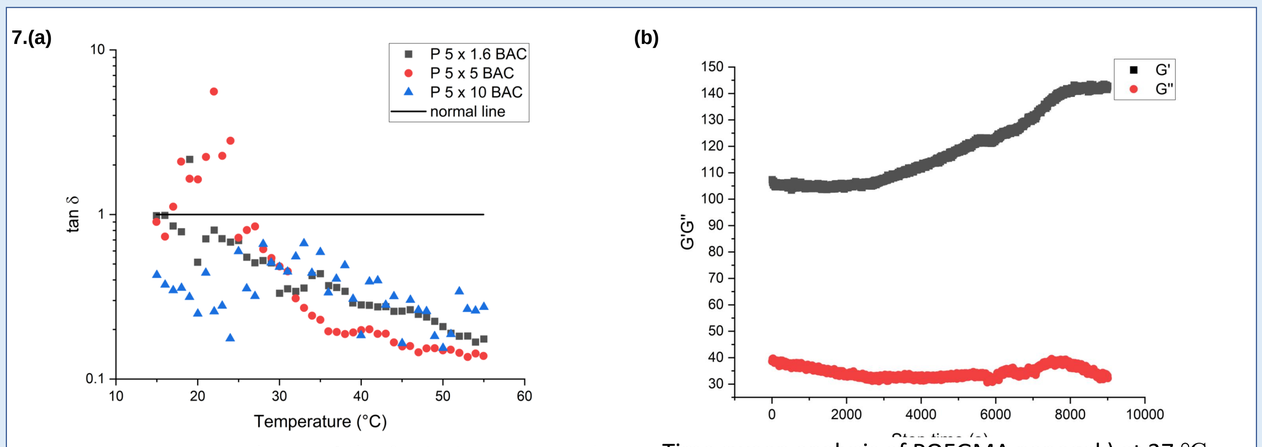


Figure 6.(a) ^{1}HNMR structure and **(b)** zeta potential of POEGMA samples

Rheology of POEGMA Nanogels



Temperature sweep (15–55 °C) of POEGMA nanogels showed a transition from a swollen, viscous state (tan δ > 1) to a compact, elastic network (tan δ < 0.2), indicating thermoresponsive volume phase transition.

Time sweep analysis of POEGMA nanogel) at 37 ℃ P 5 X 5 BAC showed stable mechanical properties, with G′ ranging from 105–107 MPa and G″ from 38.2–39.7 MPa, indicating good structural integrity over time.

Figure 7. (a) Temperature sweep and **(b)** time sweep of POEGMA samples

POEGMA for In Situ Forming Depo Application

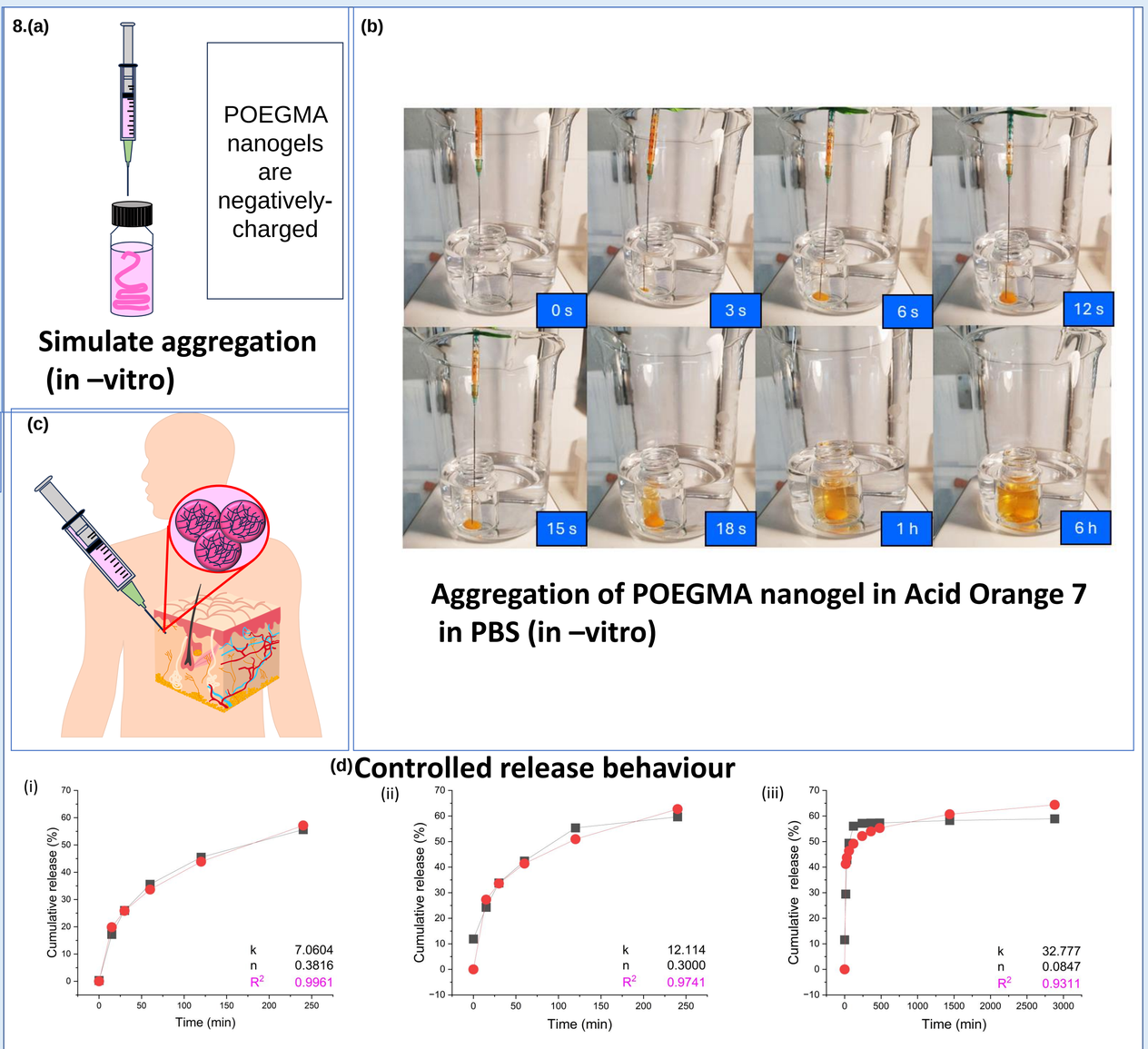


Figure 8. P 5 x 1.6 BAC sample undergo aggregation **(a)** in-vitro **(b)** Aggregation in Acid Orange 7 **(c)** simulate aggregation in-vivo and **(d)** Controlled release of differently charged dyes from P 5 x 1.6 BAC nanogel analysed using the Korsmeyer–Peppas model (i) Acid Orange 7 (negatively charge) , (ii) Rhodamine B positively charge and (iii) Bromophenol Blue (neutral)

Conclusion

Size : POEGMA nanogels measured **142–164nm** with **monomodal, narrow distribution**.

Crosslinker effect : Varying BAC concentrations had **no significant impact** on nanogel size.

Rheology: Time sweep analysis showed **stable G′ and G″**, indicating **good mechanical** integrity over time

Application

Drug release : Release of differently charged dyes from POEGMA was well fitted to the Korsmeyer-Peppas Model

Conclusion: Results support the potential of POEGMA nanogels for sustained drug delivery.