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Dual pH-Temperature Sensitive PolyVivo Poly(dimethylaminoethyl methacrylate-co-methoxy polyethylene glycol) (P(DMAEMA-co-mPEG)) (AO19)

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This document describes testing of the dual-sensitive properties of PolyVivo product AO19 (P(DMAEMA-co-mPEG)) in response to changes in temperature and pH.

Background

The chemical structure for P(DMAEMA-co-mPEG) is shown in Figure 1. Due to the presence of the tertiary amine on the end of the dimethylaminoethyl methacrylate group, the polymer as a whole has the potential to ionize at low pH. This property lends itself to sensitivity towards pH. The polymer itself is a known thermogel, with temperature sensitivity owing both to the DMAEMA units and the PEG units present along the backbone. Dual pH-temperature sensitivity was established as follows.

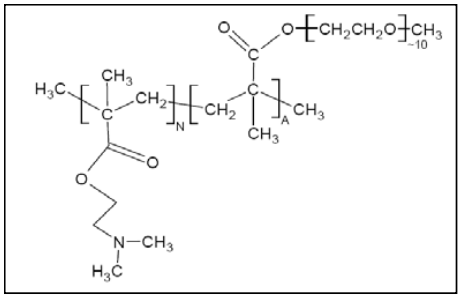

Figure 1. P(DMAEMA-co-mPEG) chemical structure

Testing

A series of solutions with varying pH values were generated:

- 0.1 M sodium bicarbonate ($NaHCO_3$; pH 8.28)
- Phosphate buffered saline (PBS; pH 7.30)
- 0.1 M acetic acid (pH 3.30)

A sample of AO19 was dissolved in each of these solutions at a concentration of 20% (w/v). The dissolution took place over the course of three days and at approximately 4°C.

After cold dissolution, the samples were allowed to warm to room temperature and observed to see whether the appearances of the three different pH solutions varied. The solutions were photographed to record their appearances (Figure 2). It was noted that at room temperature, the three solutions were liquid and clear.

Next, the three samples were heated to 37°C in a shaking incubator and again observed for changes in appearance. The heated solutions were photographed to record their appearances (Figure 3). It was noted that the solutions with pH 7.3 and 8.3 transitioned to an opaque white color, while the solution at pH 3.3 remained clear.

Results

Figures 2 and 3 show the results of this test.

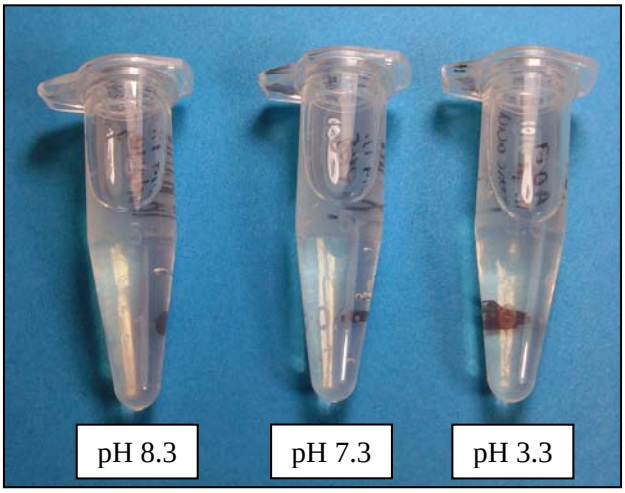

Figure 2. Room temperature, left to right: AO19 dissolved in $NaHCO_3$ (pH 8.3), PBS (pH 7.3), acetic acid (pH 3.3)

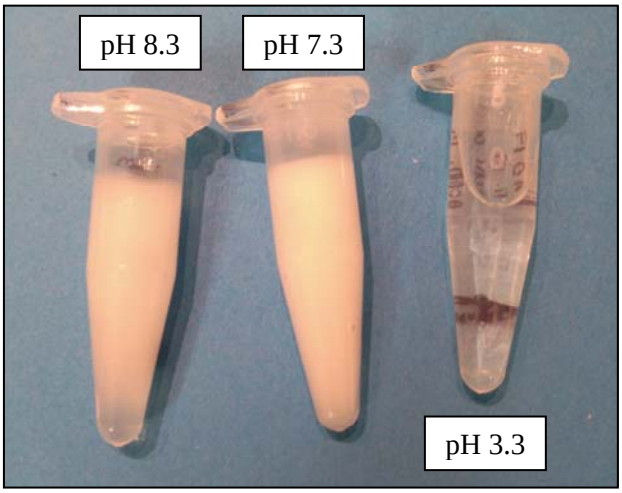

Figure 3. At 37°C, left to right: AO19 dissolved in $NaHCO_3$ (pH 8.3), PBS (pH 7.3), acetic acid (pH 3.3)

Conclusion

The testing described here indicates that the product PolyVivo AO19 (P(DMAEMA-co-mPEG)) has sensitivity towards both temperature and pH of the solution in which it is incubated. This sensitivity is the reverse of another dual sensitive polymer, PolyVivo AO14 (P(NIPAM-co-AA), which exhibits reduced thermogelation at high pH due to poly(acrylic acid) residues. In the case of AO19, the presence of ionizable DMAEMA units allows for the material to exhibit reduced gelation at low pH values. This property may be useful for drug delivery therapies, as certain portions of the body have low pH, as does the cancer cell microenvironment[1]. This property may also be useful for applications towards pH sensors and microsensors[2].

References

1. Stubbs, Marion, Paul MJ McSheehy, John R. Griffiths, and C. Lindsay Bashford. "Causes and consequences of tumour acidity and implications for treatment." *Molecular Medicine Today* 6, no. 1 (2000): 15-19.

2. Richter, Andreas, Georgi Paschew, Stephan Klatt, Jens Lienig, Karl-Friedrich Arndt, and Hans-Jürgen P. Adler. "Review on hydrogel-based pH sensors and microsensors." *Sensors* 8, no. 1 (2008): 561-581.