

A new composition of polyetheramine-based cationic hydrogel particle: reduced charge density and cytotoxicity

Shuangcheng Tang^a, Lu Huang^a, Joe Daniels-Mulholland^b, Wei He^{a,b}

^a Department of Materials Science and Engineering, University of Tennessee, Knoxville

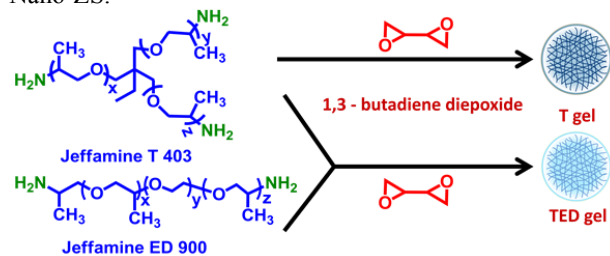
^b Department of Mechanical, Aerospace and Biomedical Engineering, University of Tennessee, Knoxville

Statement of Purpose

Cationic hydrogel particle is considered a promising therapeutic carrier for biomedical applications. Previously, polyetheramine-based hydrogel particles were reported as an alternative choice to the vinyllic based.¹ Using a non-catalytic approach, particles were fabricated with multiple-responsiveness toward temperature, pH and oxidation. However, the particles were biocompatible at relatively low concentrations (<10 $\mu\text{g/mL}$). It is hypothesized that the cytotoxicity depends on the positive charge density. Here, in order to improve the biocompatibility, we modified the composition of the polyetheramine-based hydrogel particles to attenuate the density of amine groups.

Materials and Methods

The TED gel particles were synthesized following the method preparing T gel particles.¹ In addition to Jeffamine T 403, 1,3-butadiene diepoxide, and water, a new monomer Jeffamine ED 900 was added at a molar ratio of 4:3 (Jeffamine T 403: Jeffamine ED 900). Characteristics of the hydrogel particles, including size and zeta potential, as well as temperature responsiveness, were studied by dynamic light scattering using a Zetasizer Nano-ZS.



Cytotoxicity of the gel particles against RAW 264.7 macrophages was examined at different concentrations using a WST-1 assay. Normalized cell viability was obtained by comparing the absorbance of treated cells to that of the untreated positive control.

Results and Discussion

A commercially available monomer, the Jeffamine ED 900 was introduced into the polyetheramine-based gel system. With about 12 ethylene oxide (EO) repeating units, the aforementioned monomer considerably extended the distance between neighboring amine groups and therefore reduced the charge density. Under the typical reaction condition, the obtained TED gel particles showed an average diameter of 240 nm at 25 $^{\circ}\text{C}$, less than the 270 nm of the T gel particles (Fig. 1a). The zeta potential of the TED gel particles was 45 mV, 20 mV

lower than that of the T gel (Fig. 1b). Furthermore, the temperature responsiveness of both particles was compared (Fig. 1c). Similar to the T gel particles, the TED gels were also responsive to temperature. However, the extent of volume change as a function of temperature was slightly less for the TED gels than for the T gels. Upon cooling from 45 $^{\circ}\text{C}$ to 0 $^{\circ}\text{C}$, the volume of TED gel particles showed a 3.5-fold increase, in contrast to the 3.7-fold change observed for T gels. The decrease of swelling ratio can be attributed to the higher solubility of the additional EO structure than that of propylene oxide (PO) units. At 45 $^{\circ}\text{C}$, the EO units in TED gel are less likely to be dehydrated, resulting in less volume change. The cytotoxicity was examined by quantification of cell viability. The medium lethal dose (LD 50) of the TED gel particles was 100 $\mu\text{g/mL}$, about 10 times to that of the T gel particles. The higher biocompatibility of TED gels was likely due to its lower charge density than T gel particles.

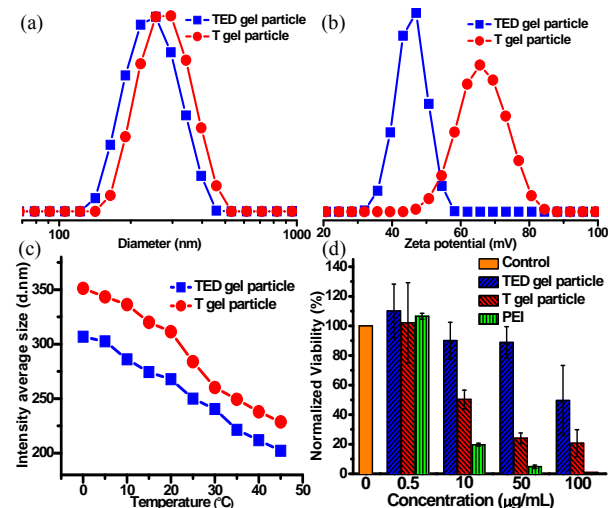


Figure 1. (a) Particle sizes distributions, (b) zeta potential distributions, and (c) temperature responsiveness of TED gel and T gel particles. (d) cell viability at different gel particle concentrations. Polyethylenimine (PEI) was also included for comparison (M_w 25,000).

Conclusion

The incorporation of a new comonomer to the original T gel formulation resulted in TED gel particles with slightly smaller size and much lower charge density. In addition, a reduction in cytotoxicity was observed, which will benefit the biomedical applications of these hydrogel particles.

Acknowledgements

Financial support from NSF (Award No. DMR-1055208) is greatly appreciated. JDM is grateful to partial support from the Center for Materials Processing at the University of Tennessee.

Reference 1. Tang, S.; Shi, Z.; Cao, Y.; He, W., *Journal of Materials Chemistry B* 2013, 1, (11), 1628-1634.