The influence of PEG molecular weight on apparent hydrogel microsphere size as measured by the Coulter Principle

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Statement of Purpose: Many researchers are currently investigating hydrogel microparticles for use in biomedical applications. Often, these investigations use the Coulter principle to evaluate the size distribution of their microparticles.[1-3] Since this method uses the displacement of electrolyte to determine particle size, the electrolyte contained within the swelled hydrogel microparticles results in an underestimate of actual particle diameters. Using polyethylene glycol diacrylate (PEGDA) hydrogel microspheres, we attempted to determine a relation between polymer molecular weight and apparent Coulter diameter that would provide a correction for the underestimated diameters provided.

Methods: Five polymer precursor solutions were created using different molecular weight PEGDA: 5 kDa, 10 kDa, 10+20 kDa (a 1:1 mix of 10 kDa and 20 kDa PEGDA), and 20 kDa. Each solution was prepared by combining 10 % (w/v),PEGDA ,and 1.5% (v/v) triethanolamine in HBS with 37 mM 1-vinyl-2-pyrrolidinone and 1.0 mM eosin Y. Mineral oil was combined with 3 µl/ml 2,2-dimethoy-2-phenyl acetophenonein 1-vinyl-2-pyrrolidinone (300 mg/ml). Microspheres were formed by adding the prepolymer solution to the oil solution and vortexing under white light to photo-polymerize the induced emulsion. Resulting microspheres were then extracted from the oil via centrifugation at 1300rpm for 5 min. Microspheres were then filtered to concentrate the sizes in the 100 – 250 µm range. Filtered microspheres were imaged and processed through imageJ to produce a distribution of the size count. Following imaging, samples were evaluated with a Beckman Coulter Multisizer III particle analyzer The results from both the microscope and the Coulter Counter were compared according to the Flory Rehner relation:

$$p = V_d/(1+V_d)$$

where V_d is the volume ratio of water absorbed into the gel phase in the equilibrium swollen state and p is percentage porosity.[4] We determined hydrogel percentage porosity and then used the relation determined by Horák et al. to determine microsphere diameters:

$$d_c/d_o = (1-\alpha p)^{1/3}$$

where d_c is the apparent Coulter diameter, d_o is the observed diameter and α is the percent filling of pores in a solid microparticle.[5] In order to determine V_d, we measured the weights of 100 µm thick by 1 cm diameter hydrogel disks after gellation, swelling, and lyophilization for each PEGDA molecular weight.

Results: Diameters measured by the Multisizer were consistently smaller than those determined by ImageJ analysis for every molecular weight PEGDA (Fig. 1). Values for α and f were determined (Table) and used to correct the apparent Coulter diameters (Figure).

Table. Parameters for PEGDA molecular weights except 3.4 kDa, which yielded too few microspheres for analysis.

PEGDA MW	α	f
5 kDa	1.46	0.559486498
10 kDa	1.415	0.536918686
10&20 kDa	1.365	0.537198322
20 kDa	1.3	0.537737352

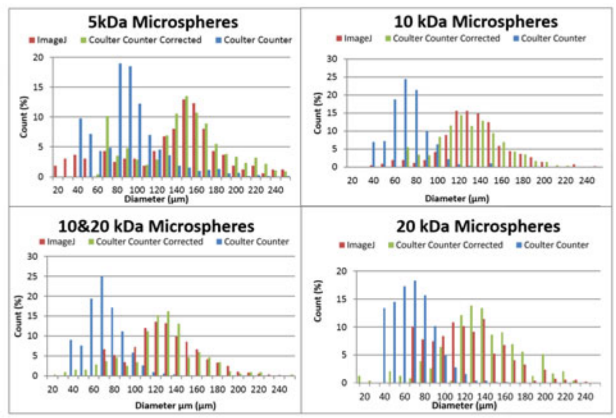

Figure. Measured, apparent and corrected distributions for various PEGDA molecular weights.

Conclusions: The results indicate that when using the Coulter principle to measure hydrogel microparticles, it is important to account for the effects of hydrogel swelling in electrolyte, which results in an apparent transparency to devices that use the Coulter principle. In future studies, we will attempt to determine parameter values for 3.4 kDa PEGDA microparticles.

References:

1. Dormer NH et al. Ann Biomed Eng. 2010 Jun; 38(6):2167-82. doi: 10.1007/s10439-010-0028-0.
2. Shin S et al. Biomaterials. 2010 May; 31(15):4353-9. doi: 10.1016/j.biomaterials.2010.02.013.
3. Avilés, MO et al. 2010. Biomaterials, 31(6):1140-1147. doi: 10.1016/j.biomaterials.2009.10.035
4. Padmavathi N., Chatterji P., Macromolecules. 1996;29;1976-1979
5. Horák D et al. Powder Technology 31.2 (1982):263-67.

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