Drug Partitioning in DMAEMA Containing Poly(HEMA)-based Hydrogels using Coomassie Brilliant Blue

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Statement of Purpose: Knowledge of the equilibrium partitioning capabilities of hydrogels would help in better understanding of the potential for loading and release of drugs with similar molecular structure. The primary objective of this work was to investigate the drug loading potential of novel, biomimetic p(HEMA)-based hydrogels by determination of the partitioning coefficient using zwitterionic Coomassie Brilliant Blue (CBB) as a drug surrogate. Such hydrogels are useful as coatings on implantable biosensors to mitigate the foreign body response and the release of an anti-inflammatory drug is one such enhancement strategy. The inclusion of a pH-dependent ionizable co-monomer was used to confer a pH dependence to the ionic character of the hydrogel and its influence on the partition coefficient investigated.

Methods: Poly(2-hydroxyethyl methacrylate)-based hydrogels possessing ionizable 2-(dimethylamino)ethyl methacrylate (DMAEMA) and cross-linked with varying concentrations (1, 3, 5, 7, 9 and 12 mol%) tetra(ethylene glycol) diacrylate (TEGDA) were synthesized and studied for their partitioning of zwitterionic CBB, a drug surrogate. Total hydration as determined by gravimetry and bound water content as determined by differential scanning calorimetry were correlated with the partition coefficient.

Results: Using UV-Vis spectroscopy, the partition coefficient of CBB within the various hydrogel/buffer systems was found to average 6.687±0.003 (for 95% confidence interval) but to rise monotonically from 6.712 (3 mole %) to 7.002 (12 mole %) as a function of TEGDA mol% or cross-link density. The absence of cationic DMAEMA was found to reduce the partition coefficient of CBB from and average value of 6.5 to 4.1 (Figure 1). Both formulations, with and without DMAEMA, showed only a modest dependence on pH over the physiologically relevant range, pH 5 – pH 9. There was no dramatic change in partition coefficient on either side of the known pKa of DMAEMA of 7.5 as expected.

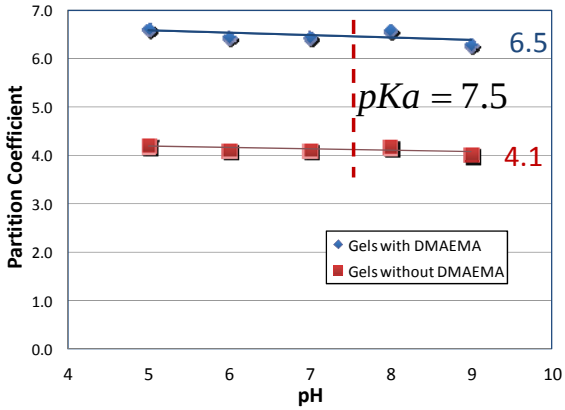

Figure 1. Partition coefficient of CBB for a hydrogel of 3 mol% TEGDA with or without DMAEMA obtained in a CBB/HEPES solution of 6.0 wt% at 37 °C.

Conclusions: The partition coefficient for the primary hydrogel formula was found to be 6.687±0.003 (95% confidence interval). The presence of DMAEMA resulted in a 1.44 fold increase in CBB loading confirming complex formation. The absence of DMAEMA nonetheless still resulted in considerable partitioning of CBB into the hydrogel suggesting that the affinity between CBB and DMAEMA may not be the only relationship controlling the change in partition coefficient.

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