Harnessing core chain mobility in tuning small molecule release rates from polymer micelles

Ryan Carrazzone[1], Jeffrey Foster[2], and John Matson[1]

1. Virginia Polytechnic Institute and State University, Blacksburg, Virginia, United States
2. University of Birmingham, Birmingham, Birmingham, United Kingdom

Polymer micelles have been widely studied as drug delivery agents, but methods for precisely tuning their rates of drug release are limited. We sought to develop systems with tunable drug release rates through control of polymer chain mobility. To achieve this goal, we designed systems based on amphiphilic block copolymers (BCPs) of poly(ethylene glycol) and polymethacrylates or polyacrylates. We attached H_2S-releasing *S*-aroylthiooxime (SATO) groups to the constitutional units of the hydrophobic block. Upon self-assembly in water, SATO groups were sequestered within the hydrophobic micelle core. SATO groups release H_2S in response to reaction with thiols such as cysteine (Cys); thus, we hypothesized that controlling the rate of diffusion of triggering Cys molecules into the micelle core might impart control over the H_2S release rate. To investigate this hypothesis, we prepared a series of amphiphilic BCPs with varying amounts of a plasticizing co-monomer in the hydrophobic block. H_2S release rates from these micelles varied with glass transition temperature (T_g) of the core-forming block, with a difference of over 20-fold ($t_{1/2}$ = 0.18 – 4.2h) between the two extremes, signifying a relationship between release rate and core chain flexibility. To further investigate this idea, we prepared a series of amphiphilic BCPs which incorporated varying amounts of a crosslinker into the core-forming block. We observed a 2-fold decrease in H_2S release half-life, with increasing crosslinking percentages in the micelle core, supporting our hypothesis that influencing core mobility could tune the rate of H_2S release. We believe these methods for tuning drug release from polymer micelles may inform future designs of polymeric drug delivery systems.

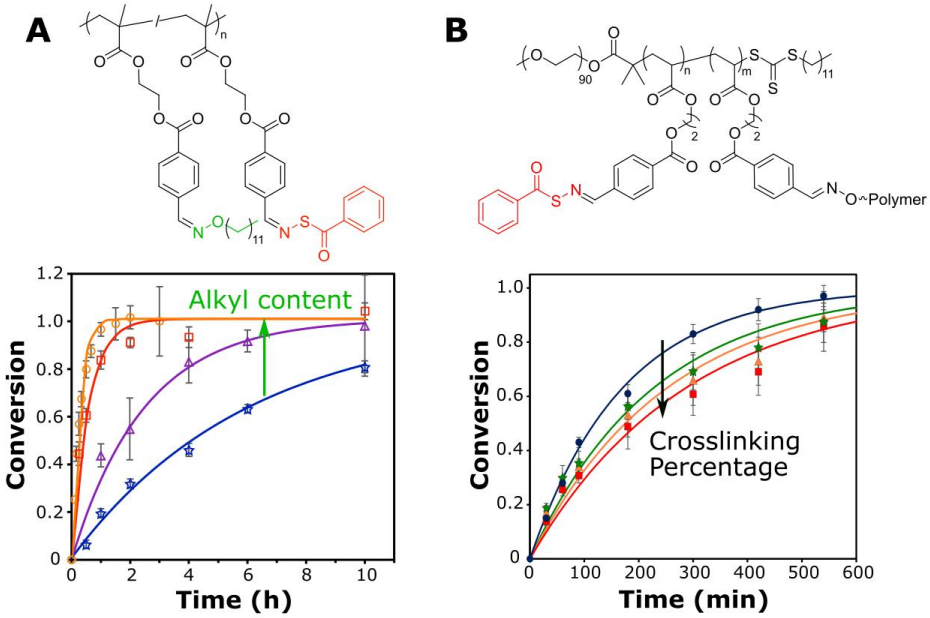

Figure 1. (A) Chemical structure of the core-forming block of amphiphilic BCPs incorporating SATO groups and plasticizing comonomer, and H_2S release curves relating to incorporation of comonomer. (B) Chemical structure of amphiphilic BCPs incorporating crosslinks into the core-forming block, and H_2S release curves relating to crosslinking percentage.