431n Development of Thermally Responsive Graft Copolymers for High Temperature-Activated Drug Delivery

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Thermosensitive hydrogels based on poly (2-hydroxyethyl methacrylate – g – N- isopropyl acrylamide), P(HEMA –g – NIPAAm) were synthesized to control the release of imbedded drugs. Utilizing PNIPAAm's lower critical solution temperature (LCST) of approximately 32o C, the release rate can be modulated by changing thermal conditions.

The LCST of PNIPAAM was tuned by making copolymer grafts with hydrophobic butyl methacrylate (BMA) and hydrophylic methacrylic acid (MAA) comonomers. Low molecular weight (~ 3000) polymers of NIPAAm were synthesized and grafted onto a HEMA backbone to control the mesh size for drug diffusion with variations in temperature.Theophylline and inulin release profiles were studied using PHEMA and P(HEMA –g – NIPAAm) at three different temperatures (17°, 22° and 37°C) with drug diffusion coefficients determined as a function of graft composition, graft length, graft density, temperature and drug type. The graft length was determined using gel permeation chromatography. The molecular weights between crosslinks and mesh sizes of both plain PHEMA and grafted PHEMA were calculated using Flory-Rehner and rubber-elasticity theories. The Biocompatibility of the polymers was studied using Drosophila Melanogaster cells to determine the relative toxicity as compared to sodium azide.