

means of overcoming degradation prior to reaching the desired site of administration (Lin and Metters 2006). Novel formulations involving polymer-drug conjugation utilize this mechanism of action. These are distinctively different from previous formulations discussed whereby new chemical entities are formed, defined by the covalent bonding between drug and polymer (Duncan 2006). The research is based on the premise that water-soluble polymers are well established as inert within the human body; incorporating specific functionalities within the structure can render the carriers as a recognizable entity to specific target sites within the body (Kopecek 2013). Polymers that have currently been researched with this focus include N-(2-hydroxypropyl) methacrylamide, polyglutamic acid (PGA), polyethyleneglycol (PEG), polysaccharides and hydroxypropyl methacrylamide (HPMA) (Pasut and Veronese 2007; Duncan 2006; Kopecek 2013; Khandare and Minko 2006; Harris and Chess 2003). These have been utilized as co-polymer-drug conjugates incorporating low molecular weight compounds that are either conjugated directly to the polymer structure or bonded to a spacer, which is attached to the structure. The drug then assumes the form of a pro-drug in that it remains inactive while travelling through the body until reaching the site of delivery. Formulations are under clinical trial involving several anticancer drugs particularly paclitaxel, doxorubicin and camptothecin (Li and Wallace 2008; Singer 2005; Duncan 2007; Pasut and Veronese 2007). There are many associated advantages of delivering treatments using the polymeric-based carriers; improvement in solubility of hydrophobic drug molecules can ultimately increase biocompatibility and reduce side effects due to a more site specific delivery (Duncan 2006; Kopecek 2013; Surapaneni et al. 2012; Pasut and Veronese 2007; Khandare and Minko 2006; Harris and Chess 2003). In addition, these carriers have proven to overcome multi-drug resistance by operating in opposite gradients from treatment of the independent drug. Research has investigated carriers composed of two polymers conjugated with two individual drugs but also a single polymer conjugating with one or two drugs, depending on the treatment or targeted delivery required (Kopecek 2013). Other applications of these systems have been researched for treatment of musculoskeletal conditions and inflammatory or infectious diseases. The macromolecular structures involved in the formulations inhibits administration via the traditional oral route due to poor bioavailability therefore parental administration is utilized (Duncan 2006). Combining the processes of polymer-drug conjugation and triggered release, the theory has been applied in relation to coatings of biomedical devices. McCoy et al. investigated release of the known antimicrobially active agent naladixic acid by conjugation with various esters for co-polymerization with the hydrophilic monomer HEMA, utilizing an environmental trigger to stimulate release and treat infection. The elevation in pH in the presence of urease releasing bacteria induced cleavage of the ester from the polymeric network with subsequent release of the naladixic acid (McCoy et al. 2016). In using water-soluble polymers as a carrier device, the previously discussed phenomena apply with regards to swelling and/or erosion of the device itself. Currently, modelling release kinetics of the mentioned formulations has not been defined. The nature of the formulations discussed demonstrates unique tailoring. Cleavage of the drug from the network structure would be the expected rate-limiting factor given the specific delivery of these applications. Specific bonding between drugs and polymers or spacers results in subsequent triggered release and can be associated with intracellular