

at later stages. As reported by Jeong et al. hydrophilic drug has greater tendency to be partitioned into the hydrophilic domain of thermosensitive hydrogels, while the hydrophobic drug tends to be partitioned into the hydrophobic core of the hydrogel. This property results in faster release rate of hydrophilic drugs compared with that of hydrophobic drugs. To reduce the release rate of drugs from hydrogels, there are several approaches to be applied, such as enhancing the physical and chemical interactions between loaded drug and the hydrogel matrix, modifying the microstructure of the hydrogel (including interpenetrating polymer networks (IPNs)), surface diffusion control and composite hydrogels (Hoare and Kohane 2008). The drug release kinetics, can also be tailored by adjusting gelation temperature, altering mechanical properties and incorporating additives (Li and Guan 2011).

Several advantages of thermosensitive hydrogels such as biocompatibility, biodegradability and non-toxic nature contribute to their wide application in drug delivery. Multiple routes of administration have been investigated for drugs loaded within thermosensitive hydrogels: ocular delivery (Gao et al. 2010), periodontal delivery (Ji et al. 2010), nasal delivery (Wu et al. 2007) and transdermal delivery (Muzzarelli and Muzzarelli 2005). For ocular administration, Hao et al. (2014) fabricated a poloxamers based composite thermosensitive hydrogel containing drug loaded solid lipid nanoparticles to achieve a sustained release of Resina Draconis. Also, Gao et al. (2010) investigated that the ocular delivery of dexamethasone acetate (DXA) via PLGA-PEG-PLGA thermosensitive hydrogel matrix has promising potential for the treatment of eye diseases. β -GP chitosan-based thermosensitive hydrogel loaded with 0.1% chlorhexidine (Chx) was applied for periodontal therapy where over 18 h release of Chx was observed which efficaciously inhibited primary periodontal pathogens (Ji et al. 2010). Thermosensitive hydrogels could also offer sustained release of the anti-cancer drugs at specific targets (Li and Guan 2011). PEG-based thermosensitive hydrogels (PLGA-PEG-PLGA triblock copolymers) have been reported as carriers for anticancer drug, such as ricin and paclitaxel, and was able to provide sustained release for 18 and 50 days respectively (Zentner et al. 2001; Chang et al. 2011; Alexander et al. 2013). In addition, thermosensitive hydrogels are also applied for insulin therapy (Kwon and Kim 2003), growth factor delivery (Mattioli-Belmonte et al. 1999) and enzyme immobilisation (Shiroya et al. 1995). Chitosan-based thermosensitive hydrogels have also sparked great interest in local tumor therapy (Bhattarai et al. 2010). The drug delivery manners are particularly important for cancer treatment as most of anticancer drugs are nonspecific and have shown toxicity to normal cells thereby causing serious side effects. Chitosan-based thermosensitive hydrogel is one of the most important natural hydrogels in drug delivery application. An injectable thermosensitive chitosan- β -GP based hydrogel was prepared to deliver the antineoplastic drug paclitaxel and exhibited excellent efficacy in a site-directed, controlled-release of paclitaxel (Ruel-Gariépy et al. 2004).

The chitosan- β -GP system has been reported to deliver bone morphogenetic protein (BMP) *in vivo* and normal cartilage formation was observed for over 3 weeks (Chenite et al. 2000). However, some limitations of chitosan- β -GP system have restrained their applications. One of the limitations is its fast release rate of proteins and low molecular weight drugs (Gordon et al. 2010), whereas, this problem could be solved by encapsulating the drug with liposome and then incorporating it in chitosan-