

ability of the hydrogel is used to regulate the cell attachment and detachment from the surface (Kumashiro et al. 2010; Reed et al. 2010; Varghese et al. 2010). The cells are mixed with the thermosensitive polymer at room temperature and then injected into the body. Upon injection the LCST of the polymer is exceeded at body temperature and the polymer solution transforms into a gel, encapsulating the cells within the 3D network scaffold (Ward and Georgiou 2010). The encapsulated cells grow within the hydrogel scaffold, proliferate and differentiate to restore the damaged tissue. A variety of naturally or synthetically derived thermosensitive hydrogels have been utilised for tissue engineering applications. Natural polymers such as collagen, chitosan, gelatin, alginates and agarose show excellent biocompatibility but often undergo rapid degradation upon contact with body fluids (Tan and Marra 2010).

Chitosan and its derivatives have been extensively investigated for tissue engineering due to their biocompatibility, biodegradability, low immunogenicity and cationic nature (Berger et al. 2004; Ganji et al. 2007). To develop an *in situ* injectable hydrogel, chitosan is usually combined with β -GP that enhances its solubility at physiological neutral pH and changes its gelation temperature to 37°C. This chitosan- β -GP composite has shown application in cartilage tissue engineering (Jin et al. 2009), due to chitosan structural resemblance with the glycosaminoglycans present in cartilage providing good cytocompatibility with cartilage tissues, the chondrocytes. Additionally β -GP also acts as an osteogenic supplement, promoting cartilage growth (Moreira et al. 2016). Chitosan- β -GP scaffolds have also been explored for nerve and bone tissue engineering (Tahrir et al. 2015). Chitosan have shown good nerve affinity and enhanced neurite growth with up-regulation of neurofilament-H mRNA (Yang et al. 2009). Neural stem cells differentiate either into astrocytes or as oligo-dendrocytes. Hence to achieve differentiation of neural cells into particular desired phenotypes, hydrogel chitosan- β -GP scaffolds have been surface modified with extracellular matrix (ECM) derived peptides to target specific nerve tissue regeneration and to enhance the efficiency of stem cell differentiation (Kuraitis et al. 2012; Hsu et al. 2013). This approach was utilized to target specific neurological disorders.

Another potential application of thermosensitive hydrogels is in bone tissue engineering. Bone tissues have very limited self-healing ability and therefore bone tissue repair remains a challenge. Moreover the most important requisite for bone tissue engineering application is that the scaffold should provide appropriate mechanical properties along with ECM properties to serve as temporary skeletal framework. To improve the mechanical properties of hydrogel a composite hydrogel of chitosan has been developed by incorporating collagen (Wang and Stegemann 2010). The incorporation of collagen provided the desired mechanical strength and the composite exhibited approximately three times higher stiffness compared to hydrogel without collagen. The composite was also able to retain 90% of cell viability. Dessi et al. reported development of novel composite hydrogels based on chitosan reinforced by β -tricalcium phosphate for bone tissue engineering application (Dessi et al. 2013). This hydrogel exhibited gel phase transition at body temperature and the presence of inorganic component provided a strong gel structure that mimicked natural bone tissue favouring enhanced cellular activity. PEG/PCL hydrogels, due to their extensively porous structure and biocompatibility have also been extensively investigated for bone tissue engineering (Fu et al. 2012; Ni et al. 2012; Ni et al. 2014).