

concentration of the polymers (Baloglu et al. 2011). Chen et al. reported the mechanical properties enhancing effect of natural borneol/(2-hydroxypropyl)- β -cyclodextrin (NB/HP- β -CD) on the thermosensitive composite hydrogel which might be due to the changes in the micelle packing and poloxamer entanglements of the composite hydrogel (Chen et al. 2013). TPA can also be utilized to determine the syringeability (ease of withdrawal of a product from a container) and injectability (injection into the intended administration site) of the *in situ* gelling systems (Madan et al. 2009; Cilurzo et al. 2011).

Most thermosensitive hydrogels are also used for the development of mucoadhesive systems to deliver to specific mucosal surface such as nasal (Balakrishnan et al. 2015), rectal (Yuan et al. 2012), vaginal (Sinem Yaprak et al. 2012), periodontal (Jones et al. 1997; Singh et al. 2014) and ocular (Edsman et al. 1998). Mucoadhesion is defined as the force, with which the formulation binds to the mucous membrane at body temperature. To achieve mucoadhesive characteristics the formulation should show a prolonged residence time and minimum drainage from the application site. The mucoadhesive strength of the hydrogel can also be determined by TPA by operating in a tension mode. Mucoadhesion is then measured by determining the area under the curve (AUC) from force-distance plot (Baloglu et al. 2011; Hurler et al. 2012).

Applications of Thermosensitive Hydrogels

Drug delivery

Along with the growing understanding of disease principle and development of new therapies, more and more attentions have been given to the efficient delivery of drugs so that therapeutic concentration could be attained at the desired location for specific duration. Thermosensitive hydrogels exhibit excellent properties for drug delivery as their ability of sol-to-gel transition at body temperature can be used as the trigger for efficient drug encapsulation within the hydrogel matrix. Initially hydrogels were used to deliver hydrophilic, small-molecule drugs due to their high affinity to water molecules. However, various approaches to modify the chemical/physical properties of hydrogels have been investigated to expand the range of drugs that could be loaded within hydrogels matrix. The hydrophobic and macromolecule drugs can be loaded by adopting one of the following three approaches. Firstly, hydrophobic domains can be created within the hydrogel networks by co-polymerizing with hydrophobic monomers (Yin et al. 2002). Secondly, hydrogels grafted with hydrophobic side chains could self-assemble to form hydrophobic domains during gelation that could incorporate hydrophobic drugs (Legros et al. 2008). Thirdly, cyclodextrin can be used to maintain the hydrophilic surface and hydrophobic core of hydrogels, which enables both water affinity of hydrogels and the payload and controlled release of hydrophobic drugs (Siemoneit et al. 2006).

The drug release from thermosensitive hydrogels can be affected by several parameters, including pore size, degradability of hydrogel, drug hydrophobicity, drug concentration and the presence of specific interactions between hydrogels and drugs (Jeong et al. 2000). Typically, the drug release mechanism from hydrogel is diffusion-controlled at an initial stage followed by a combination of diffusion and gel degradation