

implants, a second surgery is essential once the drug supply has been exhausted (Kapoor et al. 2012).

Of the many controlled drug release technologies, *in situ* forming (ISF) implant systems have risen in their popularity for a range of biomedical applications such as tissue repair, cell encapsulation, microfluidics, bioengineering and drug delivery (Lendlein and Shastri 2010). The widespread interest in ISF systems can be attributed to a range of advantages which include site-specific action due to localized delivery, easy and less invasive application, extended delivery times, reduction in side effects associated with systemic delivery and also improved patient compliance and comfort (Hatefi and Amsden 2002; Chitkara et al. 2006). Depending upon their mechanism of implant formation, the ISF systems can be categorised into different types such as phase separation systems (e.g., thermoresponsive, solvent exchange and pH), crosslinked systems (e.g., photo-initiated, chemical and physical) and solidifying organogels (e.g., solubility change) (Abashzadeh et al. 2011; Gil and Hudson 2004). The most commonly used ISF systems are the thermoresponsive, pH, ions, photocrosslinked and solvent induced phase inversion (SPI) hydrogel implants. Importantly, administration by this method allows the injection of a relatively low viscosity material into the body which then solidifies to form a semi-solid depot that controls the drug delivery to provide long-term therapeutic action (Chitkara et al. 2006).

The Southern Research Institute carried some of the earliest work in the 1980s, which focused on the development of injectable depot systems for the treatment of periodontal disease with chemotherapeutics. The polymeric system allowed localised delivery of chemotherapeutic drugs, such as antimicrobials, directly into the infected gingival tissue instead of into the periodontal pocket between the infected tissue and tooth. The patents note the potential use of microspheres, microcapsules, nanoparticles, liposomes, fibres, spheres, films or rods made preferentially from biodegradable polymers, as removal would not be required after the chemotherapeutic agent was exhausted. The advantage cited for these systems is that the local delivery into the gingival tissue overcame the loss of active agent from the periodontal pocket due to the outward flow of the crevicular fluid. The liquid systems also allowed relatively simple administration to the required site and retention by the gingival tissue ensuring effective concentrations of the antimicrobial to kill the bacteria involved in periodontitis (Dunn et al. 1990; Dunn et al. 1997).

There are numerous methods by which implants may form *in situ*. This process a free flowing system solidify once introduced into the physiological environment. Depending upon their mechanism of implant formation the ISF can be categorised into different types such as phase separation systems.

The *in situ* formation of polymeric drug delivery systems can be attributed to a single or combination of different stimuli (Abashzadeh et al. 2011). Stimuli-sensitive polymers are often referred to as 'smart' polymers as their properties and characteristics are modified once they are exposed to stimuli. The ability of stimuli sensitive gels to swell or shrink is dependant on change of environmental conditions. A large number of possible stimuli and polymers have been investigated to determine their suitability and feasibility in relation to drug delivery and release. Both physical and chemical triggers have been applied to induce changes in systems. Chemical stimuli include ions, pH