up to 2 to 3 yr to degrade (Middleton and Tipton 2000). Its use for extremely prolonged release implants is therefore ideal. This polymer is widely accepted as being non-toxic and so biocompatibility is no issue (Gunatillake and Adhikari 2003). Recently, Zhang et al. 2015 studied the feasibility of using (ε-caprolactone-co-DL-lactide) as a biodegradable polymer for ISP system. The investigations proved that sustained *in situ* testosterone undeconate delivery could be obtained from (ε-caprolactone-co-DL-lactide). In addition, Ueda et al. 2007 investigated the use of the linear, polyester polymer poly(propylene-fumarate) (PPF) (an alternative to poly-α-hydroxyacid family) in SPI systems. PPF was used to study *in vitro* release of fluocinolone acetonide (FA) intended for ocular drug delivery applications. A release period of up to 62 wk was observed for the implants with an overall conclusion being drawn that PPF shows promise as a biocompatible polymer for use in SPI in ocular drug delivery (Ueda et al. 2007).

However, PLGA, PLA, and PLA-PEG causes accumulation of acidic degradation products generated during the hydrolysis and show a non-linear release profiles, which is especially challenging for delivery of hydrophilic macromolecules (i.e., peptides and proteins). To overcome this issues a collaborative research between Philipps-University of Marburg and Novartis Pharma AG led to the use of poly(ethylene carbonate) (PEC) polymer in SPI systems. PEC degrades through surface erosion, providing linear release profile. PEC containing SPI system has shown selective reduction in burst release of bovine serum albumin, which was depended upon solvent type chosen (Liu et al. 2010).

A biodegradable copolymer based on ε-caprolactone (CL) and D,L-lactide (LA), i.e. ([poly(ε-caprolactone)-random-poly(D,L-lactide)]-*block*-poly(ethyleneglycol)-*block*-[poly(ε-caprolactone)-random-poly(D,L-lactide)]), known as PLEC, was investigated as SPI-based implants. Introduction of PEG in this copolymer was to overcome the low hydrophilicity of LA and CL copolymers. Combining PLEC with tetrahydrofurfuryl alcohol (GF), a biocompatible solvent that has been used to deliver drugs such as phenytoin and diazepam as well as proteins by injection (Cornacchione et al. 2012; Renette et al. 2012), results in a SPI depot. This group concluded that this material was a successful candidate for further investigations relating to the development of ISF (Nasongkla et al. 2012).

Effect of solvent on SPI hydrogels

In order for an *in situ* forming polymer system to be feasible, the selected polymers must possess a good solubility in the solvent, with biocompatibility being a very important characteristic. A SPI hydrogel system uses solvents that are water miscible, biocompatible and organic in nature. Importantly, solvents should efficiently dissolve the polymer, be miscible with water and bodily fluids. Polarity of the solvent should be such that at least 10% should be soluble in water (Dunn et al. 2004) (Table 2). Solvent viscosity also plays an important role in SPI implant formation. For example, highly viscous solvents, combined with around 30% of polymer as well as drug, could pose difficulty when injecting via conventional needles. Therefore overall viscosity should be within the range that is syringeable. Formulations with a rate index of below one are those, which exhibit shear-thinning behaviour. This would therefore be beneficial as the application of force to inject the polymer formulation would exert a shear stress