Table 2. Properties of commonly used solvents in the preparation of SPI formulations. Information obtained from Sigma-Aldrich.

Solvent	Type	Physical characteristics	Water solubility	Melting Point (°C)	Boiling Point (°C)
NMP	HP	Colourless liquid	Completely miscible	–24	202
DMSO (Dimethyl sulfoxide)	HP	Colourless liquid	Completely miscible	16–19	189
Triacetin	HO	Colourless liquid	61.2 g/L at 20°C	3	258–260
Ethyl benzoate	HO	Colourless liquid	Limited solubility	–34	212
Benzyl benzoate (BB)	HO	Colourless liquid	15.4 mg/L at 20°C	17–20	323–324
Benzyl alcohol (BA)	HP	Colourless liquid	33 g/L at 20°C	–16–13	203–205
PEG500DME	HP	Light brown liquid	Completely miscible	–23	>250

HP: Hydrophilic; HO: Hydrophobic

and therefore cause thinning of the material (Kapoor et al. 2012). Solvent strength and its affinity for water direct the nature of phase inversion and implant formation. For example, solvent that have a high water affinity exhibit fast hydrogel forming phase inversion **(**fPI) such as NMP (Bakhshi et al. 2006; Malik et al. 2010; Wang et al. 2012) and DMSO (Kranz and Bodmeier 2007; 2008; Wang et al. 2012). Hydrophobic solvents exhibit slow forming phase inversion (sPI) such as triacetin (Brodbeck et al. 1999; Kranz and Bodmeier 2007; Malik et al. 2010) and ethylbenzoate (McHugh 2005; Brodbeck et al. 1999), this is further discussed in Section 4. Solvents that possess a water solubility of below 7% w/w have been shown to result in slower drug release due to a reduction in water uptake (Brodbeck et al. 2000). Solvents with high water miscibility exhibit higher rate of drug release relative to low water miscible solvents following order NMP > 2-pyrrolidone > triacetin > benzyl benzoate (Camargo et al. 2013).

A number of other solvents have also been detailed in the literature such as glycofurol (Eliaz and Kost 2000; Eliaz et al. 2000) and tetrahydrofuran (Hatefi and Amsden 2002) but studies on these solvent are limited. The mixture of BA and BB can also be used to obtain desired release profile (Kang and Singh 2005; Dong et al. 2011). However, SPI systems most commonly use DMSO and NMP solvents preferentially due to their pharmaceutical precedence over other solvents (Dunn et al. 1997). Schoenhammer et al. 2009a,b have described the use of poly(ethylene glycol) 500 dimethylether (PEG500DME) and also poly(ethylene glycol) dialkylether (PEG-DAE) as novel solvents for use in SPI systems. PEG500DME shown to stabilize the PLGA containing SPI systems and resulted in rapid phase inversion as the solvent has a high affinity for water (Schoenhammer et al. 2009a). The use of PEG-DAE also showed stability of injectable SPI systems for up to two months (Schoenhammer et al.