within the polymer network. Crosslinking can be categorized as physical or chemical depending on the interaction binding the polymer chains. Chemical cross-linking is defined as permanent and exists through covalent bonds; addition of a cross-linking agent is required. This form of cross-linking offers a high mechanical strength. The concentration of cross-linking can be easily adapted and is the key in modifying swelling and release of solutes from hydrogels. The density of cross-linking and distance between the cross-links directly impacts swelling capacity of the hydrogel. The mesh size of the structure created is indicative of the size of drug molecules that may be physically incorporated (Siepmann and Peppas 2011; Hoare and Kohane 2008). Notably, the cross-linking feature prevents dissolution of the polymer when exposed to solvent and enables the hydrogel to maintain the physical dimensions. Adapting the chemical properties of the cross-linker enables the production of hydrogels that offer a wide range of physical properties. For example, selecting a larger carbon chain length creates further distance between the cross-links thereby modifying swelling capacity and drug diffusion. Varying side-group moieties from the main carbon chain will also influence the fundamental characteristics, for example hydrophobic moieties may reduce swelling of the polymer or dictate the type of drug molecule incorporated. Increasing the concentration of cross-linking agent will increase the rigidity of the hydrogel structure and subsequently reducing the swelling capacity. Physical cross-linking is reversible and generally occurs through tangling of polymer chains and intermolecular ionic or hydrogen-bonding interactions (Ahmed 2015; Hoare and Kohane 2008; Berger et al. 2004). Physical cross-linking is equally valuable, for example, formulations involving HPMC-based tablets. These are created via a process of powder compaction, which consequently induces this physical cross-linking. Tablets can be moulded into specific shapes and maintain a high drug concentration whilst remaining structurally stable. Upon uptake of solvent the tablets will erode and disintegrate influencing the release of drug (Colombo et al. 1996; Gazzaniga et al. 2008).

Mathematical Modelling of Drug Release from Hydrogels

Understanding the kinetics involved in drug release from a hydrogel network can be complex, yet necessary in order to establish a relationship between drug diffusion and time. There is a range of mathematical equations in existence as a means of modelling release kinetics of drugs from respective polymeric carriers. The relevance/acceptance of the models does not suggest that these are entirely definitive of the release process and in many cases are theoretical simplifications of real systems. The accuracy of each model increases with increased model complexity. Existing models are expressed as mechanistic or empirical/semi-empirical models. The former are based on physical concepts such as diffusion, dissolution, swelling, degradation and precipitation thereby affording greater understanding of the drug release mechanism (Narasimhan 2001; Frenning et al. 2003; Frenning and Strømme 2003; Zhou and Wu 2003). The latter are considered to be descriptive and preclude many physical, chemical and biological factors affecting the release process, such as ionisation, varying temperature or pH (Singhvi and Singh 2011; Costa and Sousa Lobo 2001; Siepmann and Siepmann 2008).