sample (Lin and Metters 2006; Siepmann and Peppas 2011). This coefficient can be calculated by a variety of equations determined by and accounting for the nature and geometry of the polymeric meshwork structure. Equation 4 can be applied to swellable polymers where it is necessary to account for diffusion through the structure in the most swollen state. Influential properties such as polymer volume fraction and mesh size are included.

Equation 4: Prediction of drug diffusion coefficient summarized by Lin and Metters (Lin and Metters 2006)

$$\frac{D_g}{D_0} = f(r_s . v_{2.s} . \zeta) \tag{4}$$

D_g and D_0 are the drug diffusion coefficients in the swollen hydrogel network and the pure solvent respectively, r_s is the size of the drug entrapped, $v_{2.s}$ is the polymer volume fraction in the swollen state and ζ is the mesh size of the network. The latter two components are established through calculation of network parameters of the hydrogel formulation (Ende and Peppas 1996). The size of the drug molecules involved is a necessary consideration: should this be larger than the mesh size itself, drug will remain entrapped within the structure. It is apparent through consideration of these calculations, that diffusion controlled drug release can be manipulated by the structure of the polymer network. The cross-link density will directly impact on the degree of swelling and consequently the path length for diffusion.

In relation to hydrogel formulations specifically, diffusion is not always solely dependent on time. To account for this variation Equation 5 was derived and is a highly useful tool in determining the mechanism by which release occurs from the polymer.

Equation 5: Peppas Power Law equation describing the mechanism of solute diffusion from a thin polymer slab

$$\frac{M_t}{M_\infty} = kt^n \tag{5}$$

M_t and M_∞ are the mass of drug released at times t and infinity respectively and k is an experimentally determined parameter corresponding to a constant that incorporates structural and geometric characteristics of the system. The release exponent, n, defines this mechanism by correlating the calculated value with those in Table 1. The constants, k and n, are uniquely determined for each drug-polymer system and will vary depending on the geometry of the device (Ritger and Peppas 1987a).

Swelling Controlled Drug Release

Diffusion-controlled release from a thin device of planar geometry results in a release exponent of 0.5. Should the rate-limiting step of drug release be determined by the uptake of solvent into the formulation, release is described as Case II, with a relative diffusional exponent value of 1 (Table 1). The rate of drug release will be influenced