Variables Affecting Drug Entrapment

Drug loading is dependent on many variables, such as the molecular weight and charge density of both the drug and hydrogel, degree of cross-linking, nature of the solvent, and mixing conditions. Drug loading (D.L.) range per unit mass of a polymer can be estimated from the following simple relationship:

$$(Vs/Wp)xCo = D.L.limit$$

Where: Vs is the adsorbing solvent,Wp is the dried polymer weight, Co is the drug concentration in solution (Kim et al. 1992).

Cross-linking Degree

Generally as the cross-linking degree increases, the drug loading and release rate decreases due to the reduced effective diffusion coefficient in the post loading method. On the contrary in the *in situ* loading method, higher the concentration of cross-linking agent then higher will be the entrapment efficiency. The higher amount of glutaraldehyde appears to favor the cross-linking reaction, obtained with an increase in loading efficiency.

Interactions

Also the interaction between drug and polymer contributes to increasing loading efficiency (Chuang et al. 2000). Charge interactions between ionic polymers and charged drugs have frequently been employed to increase the strength of the interactions between the gel and a target drug and to improve drug entrapment. Phosphate-functionalized polymers are effective because of their multivalent anionic charge. Phosphate-containing soft contact lenses can bind the cationic drug naphazoline in quantities directly proportional to the phosphate content (Sato et al. 2005). Similarly, the uptake of cationic lysozyme into N-isopropylacrylamide-based hydrogels functionalized with polyoxyethyl phosphate-containing comonomer is significantly enhanced compared to non-functionalized PNIPAM hydrogels (Nakamae et al. 2004). Amino functional groups can similarly be applied to uptake anionic drugs. For example, copolymerization of 4-vinylpyridine or N-(3-aminopropyl) methacrylamide increased the loading of non steroidal anti-inflammatory drugs (NSAID) into a poly(hydroxyethylmethacrylate) hydrogel by more than one order of magnitude (Andrade-Vivero et al. 2007). Both anionic and cationic functional groups typically found in carbohydrate-based polymers can have significant effects on increasing the loading of a drug of opposite charge (Rodriguez et al. 2003). On the other hand, if hydrophobic interaction is a dominant force between the drug and the polymer, relatively hydrophobic polymers are more advantageous in increasing loading efficiency.