Solubility

Using small-molecule as hydrophilic drugs having high solubility's in both the hydrophilic hydrogel matrix and the aqueous solvent, it is relatively simple to load a high quantity of drug into a hydrogel by simple partitioning from a concentrated aqueous drug solution. However, this process is relatively inefficient in the case of large macromolecule drugs (e.g., proteins, nucleic acids, etc.), which have diffusive limitations to their partitioning into a hydrogel phase, or hydrophobic drugs, which are sparingly soluble in both the aqueous and the hydrogel phases. Macromolecular drug uptake is typically restricted by the diffusion of the macromolecular drug payload through the hydrogel network and thus can be addressed at least partially by engineering the pore size of hydrogels.

The problem with hydrophobic drugs is in many respects a more difficult problem given the inherent incompatibility of the hydrophilic hydrogel network and the hydrophobic drug. Thus, the problem of hydrophobic drug use is twofold: how to load the hydrophobic drug into the gel matrix and, once present, how to effectively release the drug into the aqueous gel environment. A variety of strategies have been used to improve hydrophobic drug loading into hydrogels. One simple approach is to form a solid molecular dispersion of a poorly soluble drug, exploiting the enhanced solubility of many hydrophobic compounds in the amorphous state rather than the crystalline state (Zahedi and Lee 2007). By this strategy, drugs are loaded into hydrogels in an appropriate solvent and bind strongly to the polymer chains in the hydrogel via hydrogen bonding interactions, preventing drug recrystallization when the hydrogels are exposed to water and enhancing release of the hydrophobic drug. However, drug recrystallization typically occurs over time, limiting the commercial use of solid molecular dispersions. Instead a variety of strategies for introducing hydrophobic domains directly into otherwise hydrophilic hydrogel networks have permitted significant improvements in the loading of hydrophobic drugs. These strategies foresee random copolymerization of a hydrophobic monomer, grafting of hydrophobic side chains, incorporation of cyclodextrin (Dupinder and Seema 2013).

Furthermore an electrochemistry method for inducing a greater loading of drugs with low affinity to the hydrophilic gel, such as large hydrophobic molecules or macromolecules consists of exploiting the presence of charges on the skeleton of the drug. In this case the gel while being hydrophilic must be non-ionic. The non-ionic hydrogel is pasted on the electrode carrying a charge opposite to that of drug. The electrode is then immersed in the solution and submitted to electrical stimulus (Fantozzi et al. 2010). The drug is convinced to enter into the hydrogel in a substantial amount. By changing the polarity of the electrode a substantial delivery of the drug can be also obtained. The Guar Gum hydrogel, a polysaccharide non ionic hydrogel was used as a drug scaffold that remains inert to the current flow and permits the migration of the ionic drug, bleomycin. However all of these classes of drugs are becoming increasingly important clinically as a result of improved understanding of the molecular basis of disease and the more frequent application of molecular design approaches.