with some other excipient materials) and compressed into a tablet. The polymer is usually in the form of a powder or granule, and tablets will be manufactured by direct compression or roller compaction (dry granulation processes). The resulting tablet has drug material interspersed between polymer particles. On exposure to fluid, the polymer material in the tablet starts to swell, producing a gel matrix. The gel can then allow drug release by dissolution of the gel and the drug trapped within it or erosion of the gel and release and dissolution of drug particles trapped within it.

The rate at which water can diffuse through the tablet – and later through the hydrated gel – affects the drug release rate. The rate of hydration is affected by the structure of the gel. Hydrophilic gels can be regarded as a network of interlinked/interspersed polymer stands. In the interstitial spaces between the strands is a continuous phase through which water and drug may diffuse. The interstices connect together to form a tortuous pathway through the gel. The tortuosity of this pathway is therefore critical for drug release. This can be affected by using polymers of different molecular weights or by using cross-linked gels, and so release rate can be modified by these factors. Increasing the polymer concentration can also make the 'pathways' fewer, and slows down drug release.

Polymers, such as hydroxypropyl methylcellulose or polyethylene oxide (which are commonly used for modified-release matrix systems), do not actually form true gels and are better described as forming very viscous solutions. Their structure is more dynamic than true gels (e.g. cross-linked alginic acid) as the chains can move relative to one another, so the interstitial continuum is not fixed. The mechanism of drug release is depicted in Figure 31.7. Diffusion-based release mechanisms usually follow zero-order or first-order kinetics (assuming sink conditions in the gastrointestinal tract and sufficient fluid) but additional erosion of the matrix due to gastrointestinal motility and hydrodynamics can complicate the true in vivo release rate. Often polymer type and concentration are used to control drug release, which can be tailored (faster and slower) as required (Fig. 31.8).

Hydrophilic matrix systems would generally be selected where a sustained drug release is required. They have the advantage of using standard safe excipients, use standard technologies, are well-established and can attain high drug loads. They do have the risk of 'food effects', whereby different blood profiles are attained in the fed and fasted states. This often results from the challenge of the gastrointestinal environment which is variable with respect to fluid, food and transit. These can be challenging factors for a hydrophilic matrix tablet.

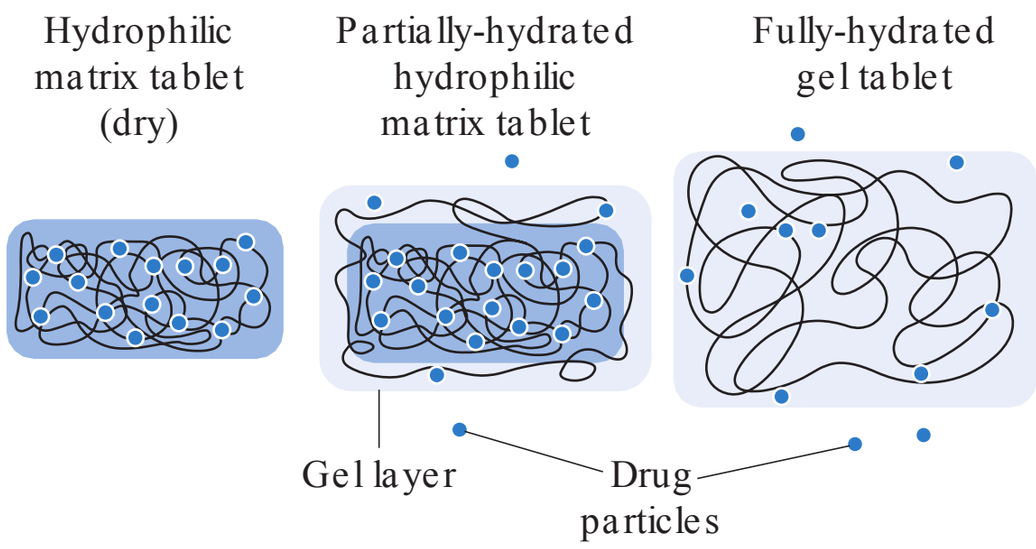

Fig. 31.7 • Process of drug release from a hydrophilic matrix. Water has to penetrate the dry matrix tablet, as the tablet becomes hydrated, drug can diffuse out.

Insoluble polymer matrix

These are far less commonly used than their water-soluble/swellable counterparts. They consist of an inert matrix system in which drug is embedded in an inert polymer. Their structure has been likened to that of a sponge. If drug molecules were interspersed throughout a sponge and water was applied, drug could leach out via the water filled channels (Fig. 31.9). In contrast to hydrophilic matrices, these systems stay intact throughout the gastrointestinal tract.

Drug release rate from insoluble polymer matrices is controlled by the pore size and number of pores, and tortuosity of the matrix. Pore-forming agents can be added to increase tortuosity and facilitate drug release. The release mechanism will also depend greatly on how the drug is dispersed within the system (dissolved, molecularly dissolved, or dispersed). The drug release does not follow zero-order kinetics; drug release decreases with time due to the increasing distance drug molecules have to travel to reach the surface of the device.

Like their hydrophilic counterparts, insoluble matrices represent a relatively simple concept which uses standard tabletting technology. However, they can also suffer some food effects, in particular related to rapid transit through the small intestine, or entrapment in the stomach in the fed state.