of fluid in order for drug release to occur. Less free liquid is available as the modified-release dosage form travels down the gut.

Fluid composition (beyond pH) is also important. The presence of ions, fats, enzymes and salts can all affect drug release mechanisms from modified-release dosage forms. For example, fats may slow down release from swelling matrix systems, meaning that required blood levels may not be achieved as quickly in their presence. Sugars can sometimes disrupt controlled-release gels.

Designing a modified-release formulation: factors to consider

There are several decisions that need to be taken when designing a modified-release formulation. Assuming it has been established that a drug is a suitable candidate for modified-release drug delivery, the following points should be considered:

Single-unit dosage form or multiple-unit dosage form

A modified-release formulation can be designed as a single-entity (usually a tablet) (Fig. 31.5b). Single-unit tablets are sometimes known as *monolithic* dosage forms. A single-unit dosage form is advantageous from a manufacturing standpoint, as it can often be manufactured using conventional techniques, such as compaction and film coating. There may be some biopharmaceutical disadvantages to tablet formulations however. For example, as they do not disintegrate in the stomach, the dosage form could become trapped in the stomach for a long time (with food). For drugs targeted to the small or large intestine, this could prevent them reaching their site of action. Multiple-unit systems (e.g. pellets or granules filled into a hard capsule shell, Fig. 31.5a) may have more reproducible gastric emptying and have a reduced risk of dose dumping. However these can be more difficult to manufacture (requiring extrusion spheronization or drug loading onto seed cores) and to scale-up.

Matrix formulation or coated formulation

The release of an active pharmaceutical ingredient can be modified by two main methods (Figure 31.6). Firstly, the release modifying ingredients can be

Fig. 31.5 • The use of multi-unit pellets in a capsule **(a)** or a single-unit tablet **(b)** for modifed-release drug delivery.

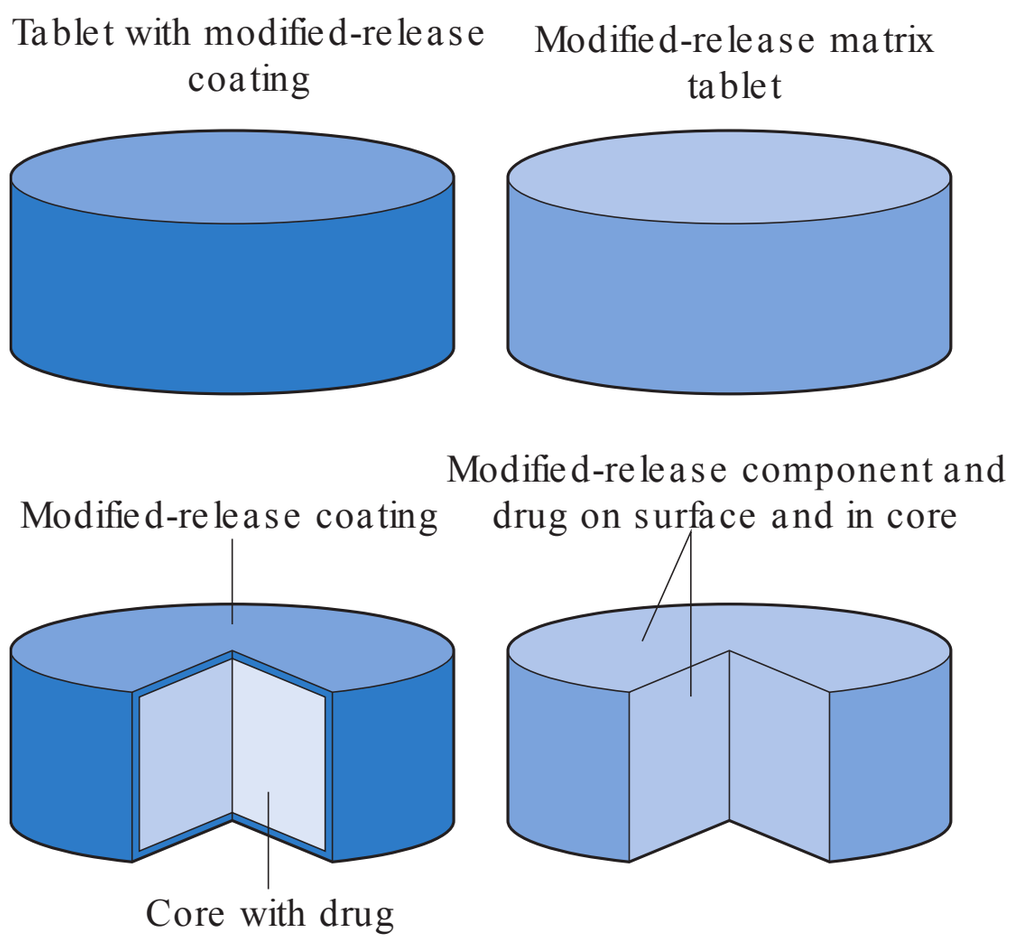

Fig. 31.6 • Coated and matrix tablets for modifed release.