delivery systems are being designed, it is important to consider factors that will affect their behaviour and, in particular, their transit times through certain regions of the gastrointestinal tract.

In general, most dosage forms, when taken in an upright position, transit through the oesophagus quickly, usually in less than 15 seconds. Transit through the oesophagus is dependent upon both the dosage form and posture.

Tablets/capsules taken in the supine (lying down) position, especially if taken without water, are liable to lodge in the oesophagus. Adhesion to the oesophageal wall can occur as a result of partial dehydration at the site of contact and the formation of a gel between the formulation and the oesophagus. The chances of adhesion will depend on the shape, size and type of formulation. Transit of liquids, for example, has always been observed to be rapid, and in general faster than that of solids. A delay in reaching the stomach may well delay a drug's onset of action or cause damage or irritation to the oesophageal wall, e.g. potassium chloride tablets.

Gastric emptying

The time a dosage form takes to traverse the stomach is usually termed the *gastric residence time, gastric emptying time* or *gastric emptying rate*.

Gastric emptying of pharmaceuticals is highly variable and is dependent on the dosage form and the fed/fasted state of the stomach. Normal gastric residence times usually range between 5 minutes and 2 hours, although much longer times (over 12 hours) have been recorded, particularly for large single dosage units.

In the fasted state, the electrical activity in the stomach – the interdigestive myoelectric cycle or migrating myoelectric complex (MMC), as it is known – governs its activity and hence the transit of dosage forms. It is characterized by a repeating cycle of four phases. Phase I is a relatively inactive period of 40–60 minutes with only rare contractions occurring. Increasing numbers of contractions occur in phase II, which has a similar duration to phase I. Phase III is characterized by powerful peristaltic contractions which open the pylorus at the base and clear the stomach of any residual material. This is sometimes called the *housekeeper wave*. Phase IV is a short transitional period between the powerful activity of phase III and the inactivity of phase I.

The cycle repeats itself every 2 hours until a meal is ingested and the fed state or motility is initiated. In this state, two distinct patterns of activity have been observed. The proximal stomach relaxes to receive food and gradual contractions of this region move the contents distally. Peristalsis – contractions of the distal stomach – serves to mix and break down food particles and move them towards the pyloric sphincter. The pyloric sphincter allows liquids and small food particles to empty while other material is retropulsed into the antrum of the stomach and is caught up by the next peristaltic wave for further size reduction before emptying.

Thus, in the fed state, liquids, pellets and disintegrated tablets will tend to empty with food, yet large sustained-or controlled-release dosage forms can be retained in the stomach for long periods of time. In the fasted state, the stomach is less discriminatory between dosage form types, with emptying appearing to be an exponential process and being related to the point in the MMC at which the formulation is ingested.

Many factors influence gastric emptying, as well as the type of dosage form and the presence of food. These include posture, the composition of the food and the effect of drugs and disease state. In general, food, particularly fatty foods, delays gastric emptying and hence the absorption of drugs. Therefore, a drug is likely to reach the small intestine most rapidly if it is administered with water to a patient whose stomach is empty.

Small intestinal transit

There are two main types of intestinal movement – propulsive and mixing. The propulsive movements primarily determine the intestinal transit rate and hence the residence time of the drug or dosage form in the small intestine. As this is the main site of absorption in the gastrointestinal tract for most drugs, the small intestinal transit time (that is, the time of transit between the stomach and the caecum) is an important factor with respect to drug bioavailability.

Small intestinal transit is normally considered to be between 3 to 4 hours although both faster and slower transit have been measured. In contrast to the stomach, the small intestine does not discriminate between solids and liquids, and hence between dosage forms, or between the fed and the fasted state.