Bacteria, which are mainly localized within the colonic region of the gastrointestinal tract, secrete enzymes that are capable of a range of reactions. These enzymes have been utilized when designing drugs or dosage forms to target the colon. Sulfasalazine, for example, is a prodrug of 5-aminosalicylic acid linked via an azo bond to sulfapyridine. The sulfapyridine moiety makes the drug too large and hydrophilic to be absorbed in the upper gastrointestinal tract, and thus permits its transport intact to the colonic region. Here the bacterial enzymes reduce the azo bond in the molecule and release the active drug, 5-aminosalycylic acid, for local action in colonic diseases such as inflammatory bowel disease.

Influence of food in the gastrointestinal tract

The presence of food in the gastrointestinal tract can influence the rate and extent of absorption, either directly or indirectly via a range of mechanisms.

Complexation of drugs with components in the diet. Drugs are capable of binding to components within the diet. In general this only becomes an issue (with respect to bioavailability) where an irreversible or an insoluble complex is formed. In such cases the fraction of the administered dose that becomes complexed is unavailable for absorption. Tetracycline, for example, forms non-absorbable complexes with calcium and iron, and thus patients are advised not to take products containing calcium or iron, such as milk, iron preparations or indigestion remedies, at the same time of day as the tetracycline. However, if the complex formed is water soluble and readily dissociates to liberate the 'free' drug then there may be little effect on drug absorption.

Alteration of pH. In general, food tends to increase stomach pH by acting as a buffer. This is liable to decrease the rate of dissolution and subsequent absorption of a weakly basic drug and increase that of a weakly acidic one.

Alteration of gastric emptying. As already mentioned, some foods, particularly those containing a high proportion of fat, and some drugs tend to reduce gastric emptying and thus delay the onset of action of certain drugs. Food slows the rate of absorption, due to delayed gastric emptying, of the antiretroviral nucleoside analogues lamivudine and zidovudine; however this is not considered to be clinically significant.

Stimulation of gastrointestinal secretions. Gastrointestinal secretions (e.g. pepsin) produced in response to food may result in the degradation of drugs that are susceptible to enzymatic metabolism and hence in a reduction in their bioavailability. The ingestion of food, particularly fats, stimulates the secretion of bile. Bile salts are surface-active agents and can increase the dissolution of poorly soluble drugs, thereby enhancing their absorption. However, bile salts have been shown to form insoluble and hence non-absorbable complexes with some drugs such as neomycin, kanamycin and nystatin.

Competition between food components and drugs for specialized absorption mechanisms. In the case of those drugs that have a chemical structure similar to nutrients required by the body for which specialized absorption mechanisms exist, there is a possibility of competitive inhibition of drug absorption.

Increased viscosity of gastrointestinal contents. The presence of food in the gastrointestinal tract provides a viscous environment which may result in a reduction in the rate of drug dissolution. In addition, the rate of diffusion of a drug in solution from the lumen to the absorbing membrane lining the gastrointestinal tract may be reduced by an increase in viscosity. Both of these effects tend to decrease the bioavailability of a drug.

Food-induced changes in presystemic metabolism. Certain foods may increase the bioavailability of drugs that are susceptible to presystemic intestinal metabolism by interacting with the metabolic process. Grapefruit juice, for example, is capable of inhibiting the intestinal cytochrome P450 (CYP3A family) and thus, when taken with drugs that are susceptible to CYP3A metabolism, is likely to result in their increased bioavailability. Clinically relevant interactions exist between grapefruit juice and the antihistamine terfenadine, the immunosuppressant ciclosporin, the protease inhibitor saquinavir and the calcium channel blocker verapamil.

Food-induced changes in blood flow. Blood flow to the gastrointestinal tract and liver increases shortly after a meal, thereby increasing the rate at which drugs are presented to the liver. The metabolism of some drugs (e.g. propranolol) is sensitive to their rate of presentation to the liver; the faster the rate of presentation, the larger the fraction of drug that escapes first-pass metabolism. This is because the enzyme systems responsible for their metabolism become saturated by the increased rate