The gastrointestinal tract is discussed in detail in this chapter and a detailed description of the physiology of some of the other more important routes of administration is given in the relevant chapters of Part 5 of this book. The oral route of delivery is by far the most popular, with over 80% of medicines being given by mouth, mainly because it is natural and convenient for the patient and because it is relatively easy to manufacture oral dosage forms. Oral dosage forms do not need to be sterilized, are compact, and can be produced cheaply in large quantities by automated machines. This chapter and the next will therefore be confined to discussing the biopharmaceutical factors (that is, physiological, dosage form and drug factors) that influence oral drug absorption.

Physiological factors influencing oral drug absorption

The gastrointestinal tract is complex. Figure 19.1 outlines some of the main structures involved in and key physiological parameters that affect oral drug absorption. In order to gain an insight into the numerous factors that can potentially influence the rate and extent of drug absorption into the systemic circulation, a schematic illustration of the steps involved in the release and absorption of a drug from a tablet dosage form is presented in Figure 19.2. It can be seen from this that the rate and extent of appearance of intact drug in the systemic circulation depend on a succession of kinetic processes.

The slowest step in this series, which is the rate-limiting step, controls the overall rate and extent of appearance of intact drug in the systemic circulation. The rate-limiting step will vary from drug to drug. For a drug which has a very poor aqueous solubility, the rate at which it dissolves in the gastrointestinal fluids is often the slowest step and the bioavailability of that drug is said to be *dissolution-rate limited*. In contrast, for a drug that has a high aqueous solubility, its dissolution will be rapid and the rate at which the drug crosses the gastrointestinal membrane may be the rate-limiting step termed *permeability limited*.

Other potential rate-limiting steps include the rate of drug release from the dosage form (this can be by design, in the case of controlled-release dosage forms), the rate at which the stomach empties the drug into the small intestine, the rate at which the drug is metabolized by enzymes in the intestinal mucosal cells during its passage through them into the mesenteric blood vessels, and the rate of

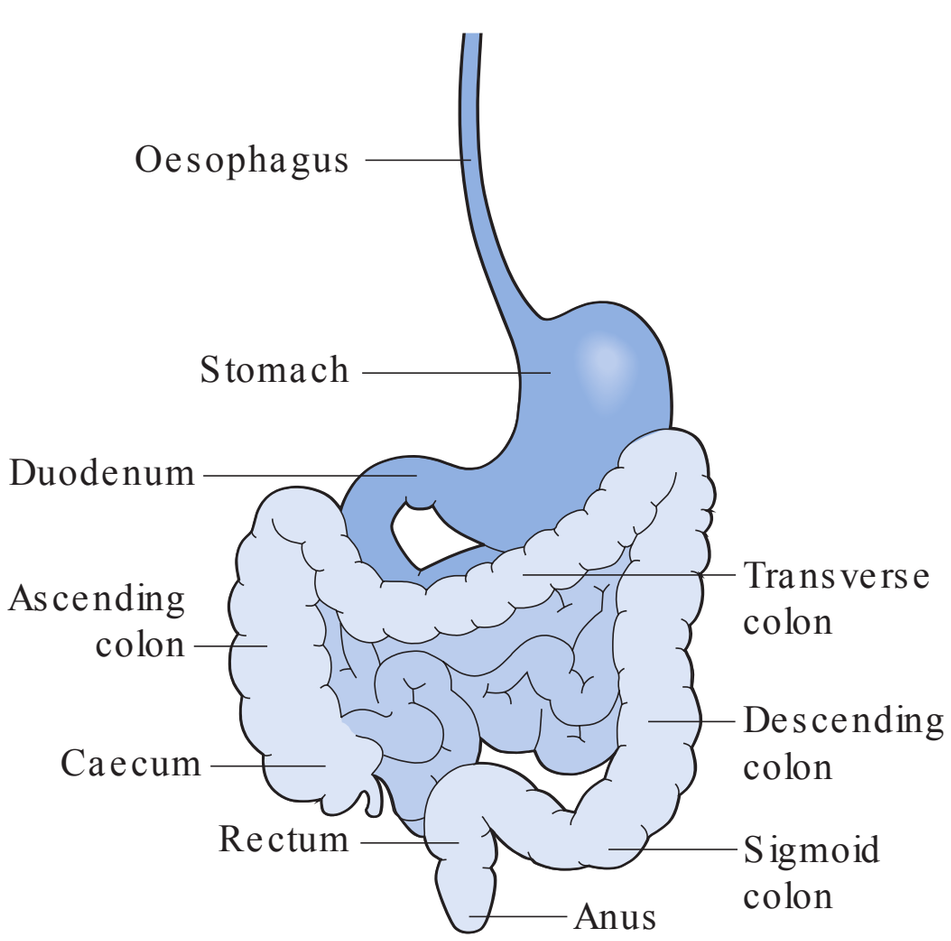

Fig. 19.1 • The gastrointestinal tract.

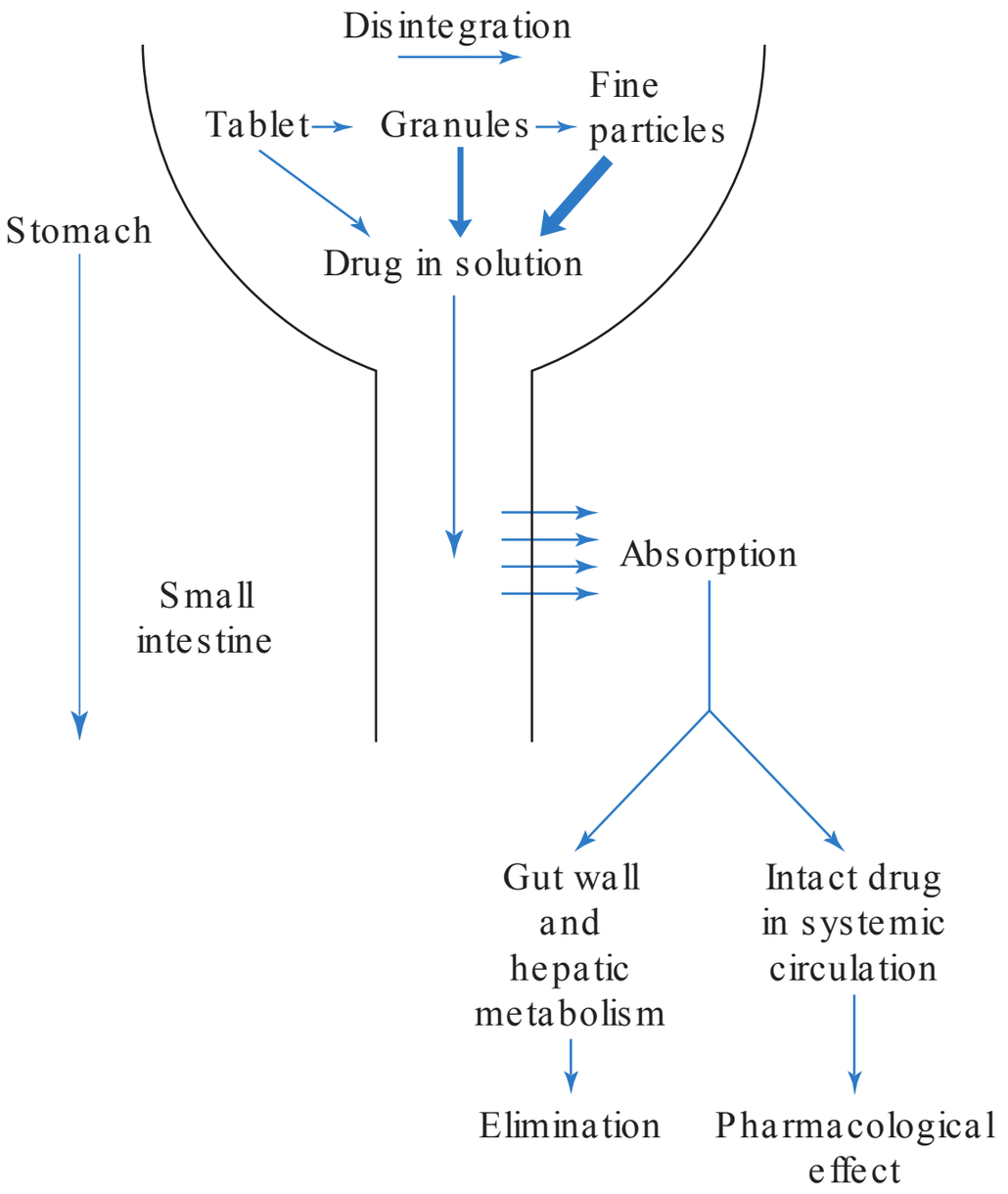

Fig. 19.2 • Steps involved prior to a pharmacological effect, after administration of a rapidly disintegrating tablet.