do not require enzymatic treatment in their preparation, they may give a higher degree of in vivo correlation than hepatocytes or microsomes.

Assessment of bioavailability

The measurement of bioavailability gives the net result of the effect of the release of drug into solution in the physiological fuids at the site of absorption, its stability in those physiological fuids, its permeability and its presystemic metabolism on the rate and extent of drug absorption by following the concentration-time profile of drug in a suitable physiological fuid. The concentration-time profile also gives information on other pharmacokinetic parameters, such as the distribution and elimination of the drug. The most commonly used method of assessing the bioavailability of a drug involves the construction of a blood plasma concentration-time curve, but urine drug concentrations can also be used and are discussed below.

Plasma concentration-time curves

When a single dose of a drug is administered orally to a patient, serial blood samples are withdrawn and the plasma assayed for drug concentration at specific time points after administration. This enables a plasma concentration-time curve to be constructed. Figure 21.8 shows a typical plasma concentration-time curve following the oral administration of a tablet.

At zero time, when the drug is first administered, the concentration of drug in the plasma will be zero. As the tablet passes into the stomach and/or intestine it disintegrates, the drug dissolves and absorption occurs. Initially, the concentration of drug in the plasma rises as the rate of absorption exceeds the rate at which the drug is being removed by distribution and elimination. Concentrations continue to rise until a maximum (or peak) is attained. This represents the highest concentration of drug achieved following the administration of a single dose, often termed the C_{max} (or C_{pmax} in the specific case of maximum plasma concentration). It is reached when the rate of appearance of drug in the plasma is equal to its rate of removal by distribution and elimination.

The ascending portion of the plasma concentration-time curve is sometimes called the *absorption phase*. Here the rate of absorption outweighs the rate of removal of drug by distribution and elimination. Drug absorption does not usually stop abruptly at the time of peak concentration but may continue for some time into the descending portion of the curve. The early descending portion of the curve can thus reflect the net result of drug absorption, distribution, metabolism and elimination. In this phase, the rate of drug removal from the blood exceeds the absorption rate and therefore the concentration of the drug in the plasma declines.

Eventually drug absorption ceases when the bioavailable dose has been absorbed, and the concentration of drug in the plasma is now controlled only by its rate of elimination by metabolism and/or excretion. This is sometimes called the *elimination phase*

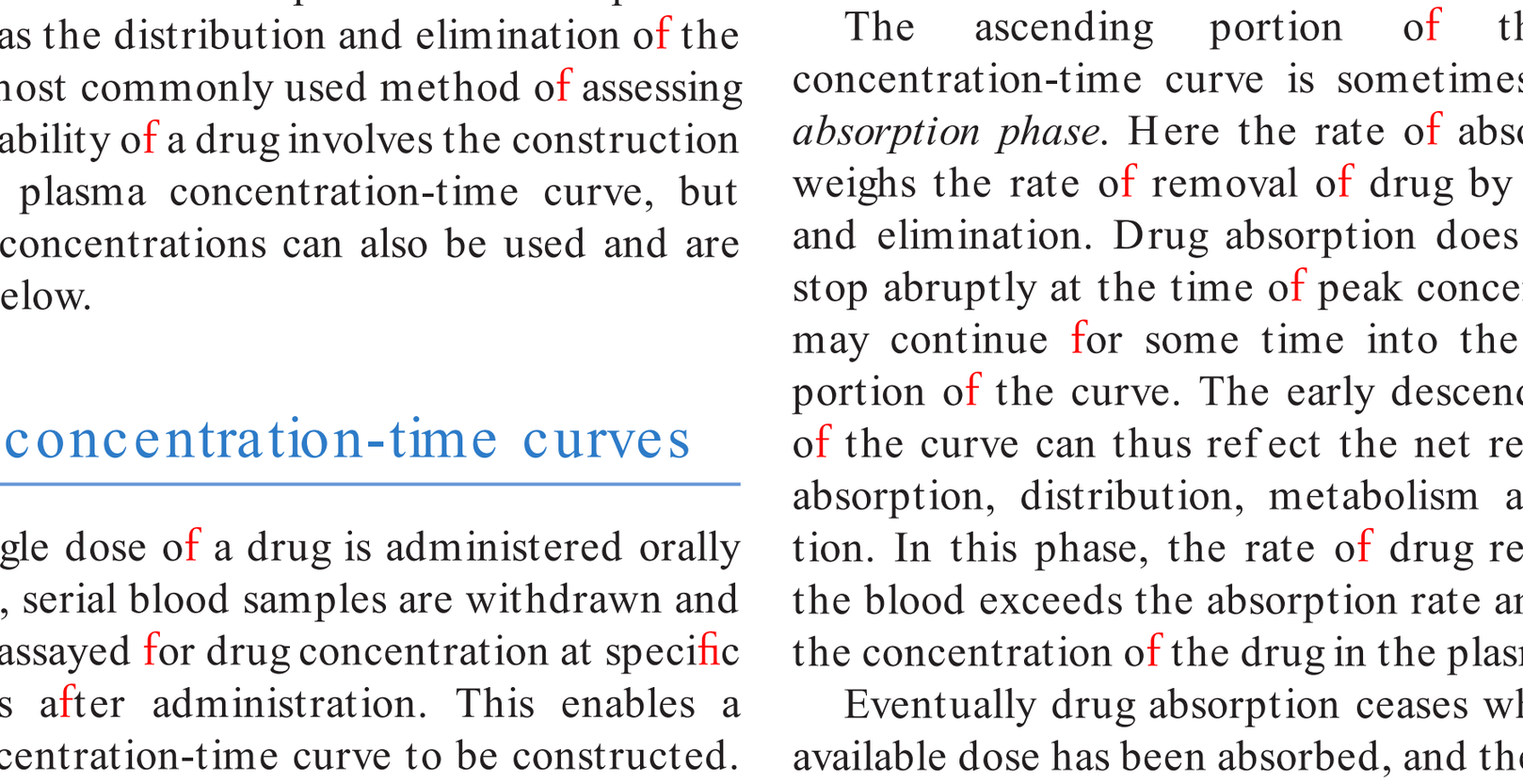

Fig. 21.8 • A typical blood plasma concentration-time curve obtained following the peroral administration of a single dose of a drug in a tablet.