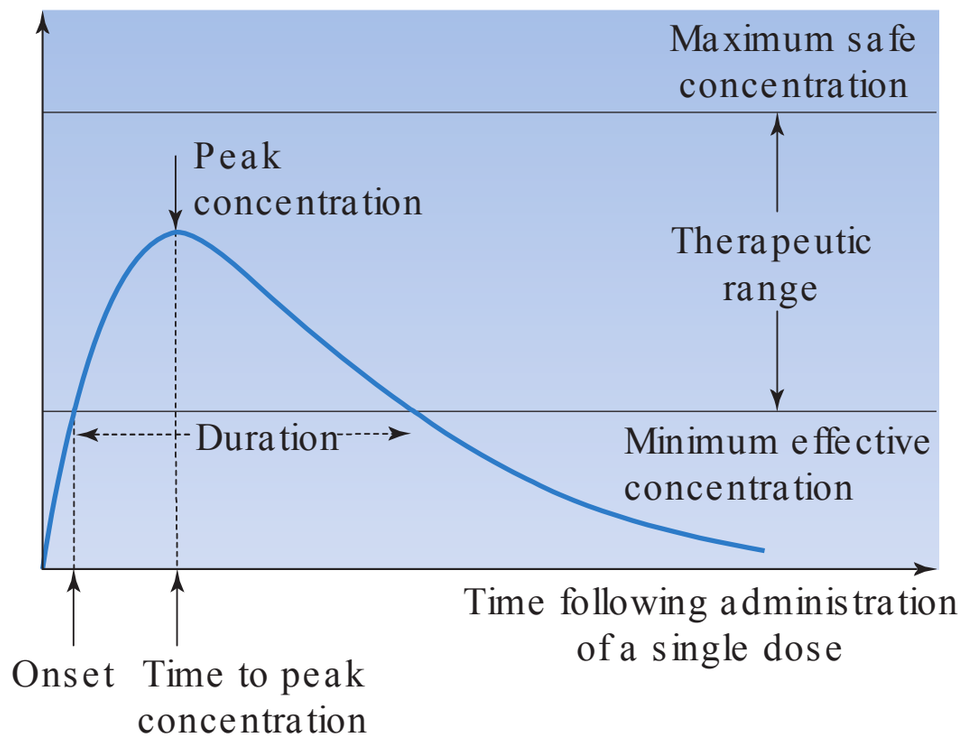

Fig. 21.9 • Relationship between the plasma concentration-time curve obtained following a single extravascular dose of a drug and parameters associated with the therapeutic or pharmacological response.

of the curve. It should be appreciated, however, that elimination of a drug begins as soon as it appears in the plasma.

Several parameters based on the plasma concentration-time curve that are important in bioavailability studies are shown in Figure 21.9, and are discussed below.

Minimum effective (or therapeutic) plasma concentration. It is generally assumed that some minimum concentration of drug in the plasma must be reached before the desired therapeutic or pharmacological effect is achieved. This is called the *minimum effective* (or *minimum therapeutic*) *plasma concentration*. Its value not only varies from drug to drug but also from individual to individual and with the type and severity of the disease state. In Figure 21.9 the minimum effective concentration is indicated by the lower line.

Maximum safe concentration. The concentration of drug in the plasma above which side-effects or toxic effects occur is known as the *maximum safe concentration*.

Therapeutic range or window. A range of plasma drug concentrations is also assumed to exist over which the desired response is obtained, yet toxic effects are avoided. This range is called the *therapeutic range* or *therapeutic window*. The intention in clinical practice is to maintain plasma drug concentrations within this range.

Onset. The *onset* may be defined as the time required to achieve the minimum effective plasma concentration following administration of the dosage form.

Duration. The *duration* of the therapeutic effect of the drug is the period during which the concentration of drug in the plasma exceeds the minimum effective plasma concentration.

Peak concentration. The *peak concentration* represents the highest concentration of the drug achieved in the plasma, often referred to as the C_{max}.

Time to peak concentration. This is the period of time required to achieve the peak plasma concentration of drug after the administration of a single dose. This parameter is related to the rate of absorption of the drug and can be used to assess that rate. It is often referred to as the T_{max}.

Area under the plasma concentration-time curve. This is related to the total amount of drug absorbed into the systemic circulation following the administration of a single dose, and is often known as the AUC.

Use of plasma concentration-time curves in bioavailability studies

In order to illustrate the usefulness of plasma concentration-time curves in bioavailability studies in the assessment of the rate and extent of absorption, the administration of single equal doses of three different formulations, A, B and C of the same drug to the same healthy individual by the same route of administration on three separate occasions can be considered. The assumption is made that sufficient time is allowed to elapse between the administration of each formulation such that the systemic circulation contained no residual concentration of drug and no residual effects from any previous administrations. It is also assumed that the kinetics and pattern of distribution of the drug, its binding phenomena, the kinetics of elimination and the experimental conditions under which each plasma concentration-time profile is obtained are the same on each occasion. The plasma concentration-time profiles for the three formulations are shown in Figure 21.10. The differences between the three curves are attributed solely to differences in the rate and/or extent of absorption of the drug from each formulation.

The three plasma profiles in Figure 21.10 show that each of the three formulations (A, B and C) of the same dose of the same drug results in different peak plasma concentrations. The area under the