At present, these therapeutic agents are principally formulated into parenteral and respiratory dosage forms although other routes of administration are being considered and researched. Delivery of these biotechnologically-based drug substances via these routes of administration imposes additional constraints upon the selection of appropriate formulation excipients.

It is therefore apparent that before a drug substance can be successfully formulated into a dosage form, many factors must be considered. These can be broadly grouped into three categories:

1. biopharmaceutical considerations, including factors affecting the absorption of the drug substance from different administration routes
2. drug factors, such as the physical and chemical properties of the drug substance
3. therapeutic considerations, including consideration of the clinical indication to be treated and patient factors.

High-quality and efficacious medicines will be formulated and prepared only when all these factors are considered and related to each other. This is the underlying principle of dosage form design.

Biopharmaceutical aspects of dosage form design

Biopharmaceutics can be regarded as the study of the relationship between the physical, chemical and biological sciences applied to drugs, dosage forms and drug action. Clearly, understanding the principles of this subject is important in dosage form design, particularly with regard to drug absorption, as well as drug distribution, metabolism and excretion. In general, a drug substance must be in solution before it can be absorbed via absorbing membranes and epithelia of the skin, gastrointestinal tract and lungs into body fluids. Drugs are absorbed in two general ways: by passive diffusion and by carrier mediated transport mechanisms. In passive diffusion, which is thought to control the absorption of many drugs, the process is driven by the concentration gradient existing across the cellular barrier, with drug molecules passing from regions of high to low concentration. Lipid solubility and degree of ionization of the drug at the absorbing site influence the rate of diffusion. Recent research into carrier mediated transport mechanisms has provided much information and knowledge, providing guidance in some cases for the design of new drug molecules. Several specialized transport mechanisms are postulated, including active and facilitated transport. Once absorbed, the drug can exert a therapeutic effect either locally or at a site of action remote from the site of administration. In the latter case, the drug has to be transported in body fluids (as shown in Fig. 1.1).

When the dosage form is designed to deliver drugs via the buccal, respiratory, rectal, intramuscular or subcutaneous routes, the drug passes directly into the circulation blood from absorbing tissues, whilst the intravenous route provides the most direct route of all. When delivered by the oral route, onset of drug action will be delayed because of required transit time in the gastrointestinal tract prior to absorption, the absorption process and factors associated with hepatoenteric blood circulation. The physical form of the oral dosage form will also influence absorption rate and onset of action, with solutions acting faster than suspensions, which in turn generally act faster than capsules and tablets. Dosage forms can thus be listed in order of time of onset of therapeutic effect (see Table 1.2). However, all drugs irrespective of their delivery route remain foreign substances to the human body and distribution, metabolic and elimination processes commence immediately following drug absorption until the drug is eliminated from the body via the urine, faeces, saliva, skin or lungs in unchanged or metabolized form.

Table 1.2 Variation in time of onset of action for different dosage forms

Time of onset of action	Dosage forms
Seconds	Intravenous injections
Minutes	Intramuscular and subcutaneous injections, buccal tablets, aerosols, gases
Minutes to hours	Short-term depot injections, solutions, suspensions, powders, granules, capsules, tablets, modified-release tablets
Several hours	Enteric-coated formulations
Days to weeks	Depot injections, implants
Varies	Topical preparations