APPLIED BIOPHARMACEUTICS & PHARMACOKINETICS

FIFTH EDITION

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PHYSIOLOGIC FACTORS RELATED TO DRUG ABSORPTION

The systemic absorption of a drug is dependent on (1) the physicochemical properties of the drug, (2) the nature of the drug product, and (3) the anatomy and physiology of the drug absorption site. All of these considerations are important in the manufacture and biopharmaceutic evaluation of drug products (Chapter 14). Proper drug product selection requires a thorough understanding of the physiologic and pathologic factors affecting drug absorption to assure therapeutic efficacy and to avoid potential drug–drug and drug–nutrient interactions. This chapter will focus on the anatomic and physiologic considerations for the systemic absorption of a drug.

ROUTE OF DRUG ADMINISTRATION

Drugs may be given by parenteral, enteral, inhalation, transdermal (percutaneous), or intranasal route for systemic absorption. Each route of drug administration has certain advantages and disadvantages. Some characteristics of the more common routes of drug administration are listed in Table 13.1. The systemic availability and onset of drug action are affected by blood flow to the administration site, the physicochemical characteristics of the drug and the drug product, and by any pathophysiologic condition at the absorption site.

Many drugs are not administered orally because of drug instability in the gastrointestinal tract or drug degradation by the digestive enzymes in the intestine. For example, erythropoietin and human growth hormone (somatrophin) are administered intramuscularly, and insulin is administered subcutaneously or intramuscularly, because of the potential for degradation of these drugs in the stomach or intestine. Biotechnology products (Chapter 18) are often too labile to be administered orally and therefore are usually given parenterally. Drug absorption after subcutaneous injection is slower than intravenous injection. Pathophysiologic

TABLE 13.1 Common Routes of Drug Administration

ROUTE	BIOAVAILABILITY	ADVANTAGES	DISADVANTAGES
Parenteral Routes			
Intravenous bolus (IV)	Complete (100%) systemic drug absorption. Rate of bioavailability considered instantaneous.	Drug is given for immediate effect.	Increased chance for adverse reaction. Possible anaphylaxis.
Intravenous infusion (IV inf)	Complete (100%) systemic drug absorption. Rate of drug absorption controlled by infusion rate.	Plasma drug levels more precisely controlled. May inject large fluid volumes. May use drugs with poor lipid solubility and/or irritating drugs.	Requires skill in insertion of infusion set. Tissue damage at site of injection (infiltration, necrosis, or sterile abscess).
Intramuscular injection (IM)	Rapid from aqueous solution. Slow absorption from nonaqueous (oil) solutions.	Easier to inject than intravenous injection. Larger volumes may be used compared to subcutaneous solutions.	Irritating drugs may be very painful. Different rates of absorption depending on muscle group injected and blood flow.
Subcutaneous injection (SC)	Prompt from aqueous solution. Slow absorption from repository formulations.	Generally, used for insulin injection.	Rate of drug absorption depends on blood flow and injection volume.
Enteral Routes			
Buccal or sublingual (SL)	Rapid absorption from lipid-soluble drugs.	No "first-pass" effects.	Some drugs may be swallowed. Not for most drugs or drugs with high doses.
Oral (PO)	Absorption may vary. Generally, slower absorption rate compared to IV bolus or IM injection.	Safest and easiest route of drug administration. May use immediate-release and modified-release drug products.	Some drugs may have erratic absorption, be unstable in the gastrointestinal tract, or be metabolized by liver prior to systemic absorption.
Rectal (PR)	Absorption may vary from suppository. More reliable absorption from enema (solution).	Useful when patient cannot swallow medication. Used for local and systemic effects.	Absorption may be erratic. Suppository may migrate to different position. Some patient discomfort.
Other Routes			
Transdermal	Slow absorption, rate may vary. Increased absorption with occlusive dressing.	Transdermal delivery system (patch) is easy to use. Used for lipid-soluble drugs with low dose and low MW.	Some irritation by patch or drug. Permeability of skin variable with condition, anatomic site, age, and gender. Type of cream or ointment base affects drug release and absorption.
Inhalation and intranasal	Rapid absorption. Total dose absorbed is variable.	May be used for local or systemic effects.	Particle size of drug determines anatomic placement in respiratory tract. May stimulate cough reflex. Some drug may be swallowed.

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