Basic Clinical Pharmacokinetics

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sorption characteristics of the administered chemical form (e.g., salt, ester), the dosage form (e.g., tablet, capsule), the route of administration, the stability of the active ingredient in the gastrointestinal tract, and, the extent of drug metabolism before reaching the systemic circulation. Drugs can be metabolized by gastrointestinal bacteria, by the gastrointestinal mucosa, and by the liver before reaching the systemic circulation.

To calculate the amount of drug absorbed, the administered dose should be multiplied by a bioavailability factor, which is usually represented by the letter "F." For example, the bioavailability of digoxin (Lanoxin) is estimated to be 0.7 for orally administered tablets.[1,2] This means that if 250 μg (0.25 mg) of digoxin is given orally, the effective or absorbed dose can be calculated by multiplying the administered dose by F:

$$\text{Amount of Drug Absorbed or Reaching Systemic Circulation} = (F)(\text{Dose}) \qquad \text{Eq. 1}$$

$$= (0.7)(250\ \mu g)$$
$$= 175\ \mu g$$

It should be emphasized that this factor does not take into consideration the *rate* of drug absorption; it only estimates the *extent* of absorption. Although the rate of absorption can be important when rapid onset of pharmacological effects is required, it is not usually important when a drug is administered chronically. The rate of absorption is important only when it is so slow that it limits the absolute bioavailability of the drug, or when it is so rapid that too much drug is absorbed. The former occasionally occurs with some sustained-release preparations.[3,4]

Dosage Form

As noted earlier, bioavailability can vary among different formulations and dosage forms of a drug. For example, digoxin elixir has a bio-

dosage form of the same drug.

$$\text{Dose of New Dosage Form} = \frac{\text{Amount of Drug Absorbed From Current Dosage Form}}{\text{F of New Dosage Form}} \qquad \text{Eq. 2}$$

For example, if a patient who has been receiving digoxin 250 μg (0.25 mg) in the tablet dosage form, needs to receive digoxin elixir instead, an equivalent dose of the elixir would be calculated as follows:

$$\text{Dose of Elixir} = \frac{175\ \mu g}{0.77}$$
$$= 227\ \mu g$$

If the soft gelatin capsules of digoxin were to be administered, the bioavailability or F of the new dosage form would have been 1.0 and the equivalent dose would have been 175 μg.

The bioavailability of parenterally-administered drugs usually is considered to be 1.0. Drugs which are administered as inactive precursors that must then be converted to an active product are an exception to this rule. If some of the inactive precursor is excreted or eliminated from the body *before* it can be converted to the active compound, the bioavailability will be <1.0. For example, parenteral chloramphenicol is given as the succinate ester, and this chloramphenicol ester must be hydrolyzed to the active compound. The bioavailability of the parenterally-administered chloramphenicol succinate ranges from 55% to 95%, because from 5% to 45% of the chloramphenicol ester is eliminated renally before it can be converted to the active compound.[7]

follows:

$$\text{Amount of Drug Absorbed or Amount Reaching the Systemic Circulation} = (S)(F)(\text{Dose}) \qquad \text{Eq. 3}$$

The "S" factor should be included in all bioavailability equations as a constant reminder of its importance in assessing bioavailability of the active drug form. When a drug is administered in its parent or active form, the "S" for that drug is 1.0.

Equation 2 can now be expanded to consider the salt factor as well as the bioavailability when calculating the dose of a new dosage form:

$$\text{Dose of New Dosage Form} = \frac{\text{Amount of Drug Absorbed From Current Dosage Form}}{(S)\,(F) \text{ of New Dosage Form}} \qquad \text{Eq. 4}$$

Aminophylline is an excellent example of this principle. (See Figure 1.) Aminophylline is the ethylenediamine salt of the pharmacologically active moiety, theophylline. Eighty to eighty-five percent (by weight) of this salt is theophylline, so that the "S" for aminophylline is approximately 0.8. Uncoated aminophylline tablets are considered to be completely (100%) bioavailable; the bioavailability factor (F) for this dosage form is, therefore, 1.0. It is important to consider the salt form in determining the amount of theophylline absorbed from an aminophylline tab

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