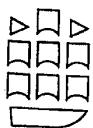


Pharmaceutics: The Science of Dosage Form Design

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Factors influencing bioavailability: factors influencing drug absorption from the gastrointestinal tract

DRUG ABSORPTION FROM THE GASTROINTESTINAL TRACT

Structure of the gastrointestinal tract

Mechanisms of drug transport across the gastrointestinal/blood barrier

Passive diffusion

Carrier-mediated transport

Active transport

Facilitated diffusion or transport

Ion-pair absorption

Convective absorption (pore transport)

Pinocytosis

PHYSIOLOGICAL FACTORS INFLUENCING DRUG ABSORPTION FROM THE GASTROINTESTINAL TRACT

Surface area of the gastrointestinal absorption sites

pH of gastrointestinal fluids

Gastric emptying rate

Intestinal motility

Drug stability in the gastrointestinal tract

Hepatic metabolism

Influence of food and diet

Alteration in the rate of gastric emptying

Stimulation of gastrointestinal secretions

*Competition between food components and drugs
for specialized absorption mechanisms*

*Complexation of drugs with components in the
diet*

Increased viscosity of gastrointestinal contents

Food-induced changes in blood flow to the liver

Miscellaneous physiological factors influencing gastrointestinal absorption

PHYSICOCHEMICAL FACTORS INFLUENCING DRUG ABSORPTION FROM THE GASTROINTESTINAL TRACT

Drug dissociation constant and lipid solubility

pH-partition hypothesis of drug absorption

Absorption of a weak acidic drug

Absorption of a weak basic drug

Limitations of the pH-partition hypothesis

Dissolution rate of drugs

*Absorption from solution or following rapid
dissolution of solid drug particles*

*Absorption following the slow dissolution of solid
drug particles*

*Factors influencing the dissolution rates of drugs
in the gastrointestinal tract*

Physiological conditions

Particle size

Crystal form

**Solubility of drug in the diffusion layer
(salt forms)**

Complexation

Adsorption

Chemical stability of drugs in the gastrointestinal fluids

DOSAGE FORM FACTORS INFLUENCING DRUG ABSORPTION FROM THE GASTROINTESTINAL TRACT

Influence of excipients

Diluents

Surfactants

Viscosity-enhancing agents

Influence of the type of dosage form

Aqueous solutions

Aqueous suspensions

Soft gelatin capsules

Hard gelatin capsules

Tablets

Uncoated tablets

Coated tablets

Enteric coated tablets

DRUG ABSORPTION FROM THE GASTROINTESTINAL TRACT

The various factors which can influence drug release from dosage forms and absorption into the systemic circulation will be considered in this chapter by reference to the peroral (i.e. gastrointestinal) route of administration. This route is chosen as the example, since the majority of drugs are administered orally and the vast majority of orally administered drugs are intended to be absorbed from the gastrointestinal tract. Thus, a

detailed consideration of the factors which can influence the absorption of drugs from this region is warranted.

In order that the reader may gain an insight into the numerous factors which can potentially influence the rate and extent of appearance of intact drug into the systemic circulation, a schematic illustration of the steps involved in the release and gastrointestinal absorption of a drug from a tablet is presented in Fig. 9.1. It is evident from this diagram that the rate and extent of appearance of intact drug into the systemic circulation depends

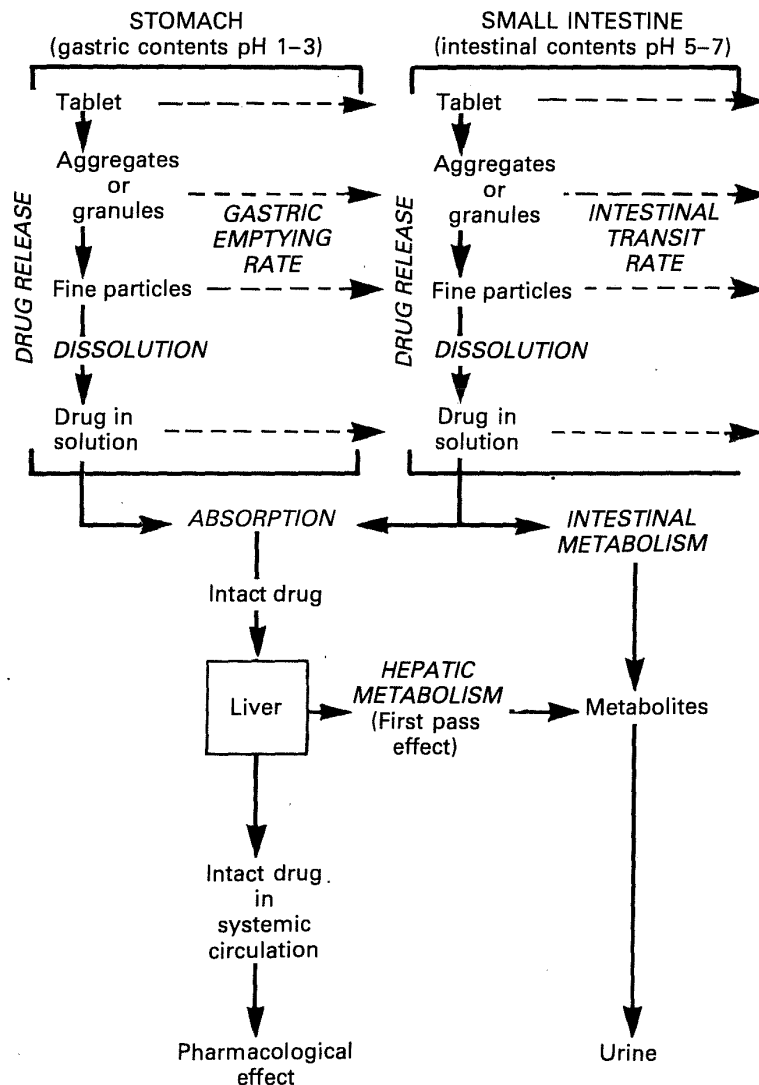


Fig. 9.1 Schematic illustration of steps involved in the appearance of intact drug in the systemic circulation following peroral administration of a tablet. Potential rate-limiting steps with respect to drug bioavailability are shown in italic capitals. (After Barr, 1972)

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