



Physiological Variability and Its Influence on Oral Drug Bioavailability: An Emerging Perspective

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Opinion

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Abstract

Oral drug administration remains one of the most widely used routes for delivering therapeutic agents because of its convenience, patient acceptability, and cost-effectiveness. However, the bioavailability of orally administered drugs can vary considerably among individuals and within the same individual over time. This variability is strongly influenced by physiological differences within the gastrointestinal tract, including gastric pH, gastric emptying, intestinal transit, gastrointestinal fluid composition, bile secretion, enzymatic activity, transporter expression, and intestinal blood flow. Age, food intake, disease conditions, concomitant medications, hydration status, and other biological factors may further modify gastrointestinal physiology and consequently affect drug absorption. Such physiological variability can alter both the rate and extent of systemic drug exposure, resulting in differences in pharmacokinetic parameters such as area under the curve (AUC) and maximum plasma concentration (C_{max}).

Keywords: Oral Drug Bioavailability; Physiological Variability; Drug Absorption; Gastrointestinal Physiology; Gastric Emptying; Intestinal Transit; Gastric pH; Food Effect; Drug Transporters; PBPK Modeling; Pharmacokinetics; Personalized Medicine

Abbreviations

Area Under the Curve (AUC); Maximum Plasma Concentration (C_{max}); Physiologically Based Pharmacokinetic (PBPK); Gastrointestinal (GI); Oral Bioavailability (F); Pharmacokinetics (PK).

Introduction

Oral administration is a preferred route of drug delivery for many therapeutic agents because it is convenient, non-invasive, and generally associated with high patient compliance. However, the administration of the same dose does not necessarily result in identical systemic drug exposure in every individual. The fraction of an orally administered drug that reaches systemic circulation depends on a

sequence of processes occurring within the gastrointestinal tract, including disintegration, dissolution, gastrointestinal transit, membrane permeation, intestinal metabolism, and transport. Variability in any of these processes may influence the final bioavailability of a drug [1].

Physiological characteristics of the gastrointestinal tract can differ substantially between individuals and may also fluctuate within the same individual. Gastric pH, gastric emptying rate, intestinal motility, bile secretion, gastrointestinal fluid volume, and intestinal transit time are examples of physiological factors that can influence drug absorption. These parameters may be modified by food intake, age, disease, concomitant medications, and other biological conditions.

The relationship between physiological variability and oral drug bioavailability has therefore become increasingly important in pharmaceutical research. While traditional pharmacokinetic assessments generally focus on measurable parameters such as AUC and C_{max}, understanding the physiological mechanisms responsible for differences in drug exposure can provide valuable information for formulation development and clinical dosing.

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