Oral solid dose

Predicting food effects in oral drug delivery using PBPK modeling

Integrated pharmacokinetic and molecular modeling provided early insight into food-dependent absorption behavior.

Development challenge

Food effects can significantly influence the absorption of poorly soluble oral drugs. Understanding these effects early in development can inform formulation strategy and clinical study design.

Fenofibrate, a lipophilic prodrug, demonstrates increased absorption when administered in the fed state compared with the fasted state.

Combining PBPK and molecular modeling

To better understand this behavior, modeling tools within the OSD Predict™ framework were used to combine physiologically based pharmacokinetic (PBPK) modeling with molecular dynamics simulations.

The PBPK model simulated plasma concentrations of fenofibric acid following oral administration of fenofibrate in fasted and fed conditions. Molecular dynamics simulations were used to evaluate drug interactions with gastrointestinal media under both conditions.

Understanding dissolution mechanisms

The modeling framework provided insight into the dissolution behavior of the drug and its interaction with micellar structures present in fed-state media.

Simulation results indicated stronger interactions with fed-state media, supporting the formation of micelle-like aggregates that enhance solubilization and drug absorption.

Development outcome

The integrated model predicted an approximately 11% increase in Cmax in fed conditions, consistent with observed experimental data.

By combining molecular-level insights with pharmacokinetic modeling, this approach clarified the mechanisms behind food-dependent absorption and provided early guidance for formulation and clinical development strategies.

At a glance

Program focus

Understanding food-dependent absorption behavior for a poorly soluble oral drug.

Methods used

Integrated physiologically based pharmacokinetic (PBPK) modeling and molecular dynamics simulations.

Drug system evaluated

Fenofibrate (prodrug) and its active metabolite fenofibric acid under fed and fasted conditions.

Key technical finding

Molecular simulations showed stronger interactions with fed-state media, supporting micelle-like aggregate formation that enhances solubilization.

Development impact

The integrated model predicted an ~11% increase in Cmax under fed conditions, providing early insight into food-effect mechanisms during development.

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