

Integrated Packages: Oral Exposure

XenoGesis has developed a series of ADME packages which are designed to help clients answer key questions on how their drug discovery compounds behave in key areas such as absorption, clearance, distribution and oral bioavailability. The packages build sequentially to predict oral exposure in pre-clinical species and ultimately the likely efficacious pharmacokinetics and dose in man.

They are designed to be part of a robust iterative screening cascade during drug discovery ultimately leading to better informed decisions with an understanding of drug exposure with respect to efficacy and safety.

To find out more, contact a member of the XenoGesis team.
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This package has been designed to predict the oral exposure of a molecule. It will evaluate the fraction of dose that is likely to be absorbed, how much it is distributed, what the predicted hepatic clearance and its half-life is. It also builds in the predicted plasma concentration time of a single PO dose and oral bioavailability, C_{max} and T_{max} at this dose level.

Description of Service

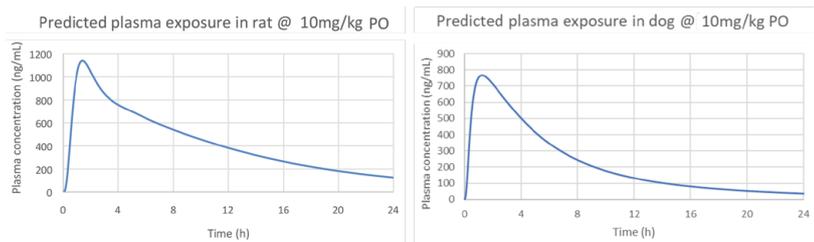
Prediction of plasma exposure following oral dosing using GastroPlus™

Data collected

- Caco-2 permeability
- Solubility in buffer and biorelevant media (thermodynamic - ideally PBS @ pH6.5, FeSSIF, FaSSIF and SGF)
- $\text{LogD}_{7.4}$
- pKa
- Blood:plasma ratio, Hepatocyte C_{Lint} , PPB (for each species)

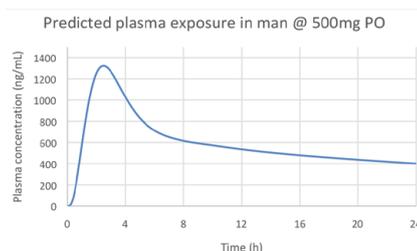
Report format

A written report will be generated with predicted hepatic clearance, volume of distribution, half-life and simulated concentration-time profile from 1mg/kg IV bolus dose for each species. Additionally, the report will include the predicted plasma concentration-time profile from single PO dose and oral bioavailability, C_{max} and T_{max} at the PO dose level.



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|---------------------|------|
| C_{max} (ng/mL) | 1100 |
| T_{max} (h) | 1.4 |
| Bioavailability (%) | 84 |

| | |
|---------------------|-----|
| C_{max} (ng/mL) | 770 |
| T_{max} (h) | 1.3 |
| Bioavailability (%) | 52 |



| | |
|---------------------|------|
| C_{max} (ng/mL) | 1300 |
| T_{max} (h) | 2.5 |
| Bioavailability (%) | 84 |

XenoGesis Ltd is an independent laboratory-based contract research organisation specialising in pre-clinical drug metabolism & pharmacokinetics (DMPK), quantitative bioanalysis, pharmacology and expert interpretation.

XenoGesis has state-of-the-art *in vitro*, *in vivo* and bioanalytical capabilities. With its expert pharmacokinetic/pharmacodynamic (PK/PD) interpretation and consultancy services, XenoGesis provides bespoke, iterative, data-driven feedback to clients with next step recommendations.