



PAMPA Platform

Parallel Artificial Membrane Permeability Assay

Pion's PAMPA is an *in vitro*, high-throughput screening assay highly correlated to biological membrane permeability

Pion PAMPA is used in discovery and pre-formulation for screening excipients, solvents, and APIs to rank order formulations and drug candidates on the basis of permeability. Each PAMPA well uses artificial lipid membranes that mimic drug uptake in the gastrointestinal tract (GIT) or across the blood-brain barrier (BBB) to provide robust, reliable, biorelevant results. Measuring concentration on both sides of a bio-mimetic membrane in our STIRWELL™ 96-well plate format improves the assessment of the absorption potential and provides more realistic IVVC predictions. (Fig. 1).



***In Vivo* Correlation**



Complete Solution



High Throughput



Reproducible Results



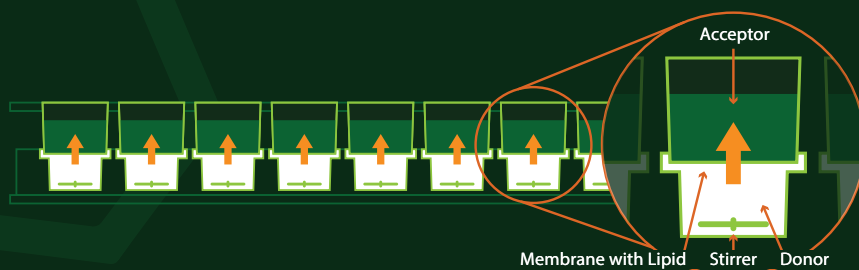
Easy Data Interpretation

Compound Selection with Confidence

PAMPA enables efficient evaluation of the passive permeability of APIs and the absorption potential of simple or complex formulations. By effectively mimicking many of the properties of biological membranes it can minimize reliance on expensive *in vivo/in situ* studies, reducing the time and cost for selecting drug candidates. Pion's Double-Sink™ PAMPA assay also allows formulators to simultaneously study how excipients impact the solubility and permeability of APIs, to accelerate formulation screening activities.

Figure 1. PAMPA STIRWELL Sandwich™

Combined, the pH differential between the donor and acceptor compartments and the scavenger in the sink buffers are key to Pion's unmatched biorelevant results.



Double-Sink Method

In vivo pH is mimicked by both the donor PRISMA HT buffer, and the Acceptor Sink / Brain Sink Buffers. The Sink Buffers also contain a scavenger so that the compound that permeates the membrane does not limit further absorption.

The Pion PAMPA Advantage



Complete Solution

The complete PAMPA system includes our 96 well STIRWELL plates, the Gut-Box™ stirring system and PAMPA Explorer™ software.



High Throughput

The STIRWELL plates in Pion's PAMPA sandwich kits contain a pre-loaded stir bar in each well, providing dynamic stirring for each assay, allowing for high-throughput screening of multiple compounds simultaneously.



Reproducible Results

While orbital shakers can lead to edge effects in the assay plates, GutBox provides consistent agitation across the whole plate, allowing for more reproducible data.



In Vivo Correlation

Gut-Box controls stirring speed to match the hydrodynamics of the intestinal tract or the blood brain barrier. The adjustable stirring allows you to mimic the ABL (aqueous boundary layer), allowing for higher accuracy and reducing assay time.[1] While other permeability assays have only been validated against *in-vitro* cell models, Pion GIT PAMPA and BBB PAMPA, have been validated to correlate with the human jejunum and rat BBB permeability.[1,2,]



Easy Data Interpretation

PAMPA Explorer software for easy data interpretation. SW includes a plate-reader data wizard, results visualization, and reporting. Data output is the complete mass balance including membrane retention.

The Gut-Box

The Gut-Box (Fig. 2) was designed by Pion to complement our PAMPA Systems, resulting in the most comprehensive turn-key assays in the market for predicting *in vivo* permeability. Mount any 96 well plate (loaded with stirrers) on top of the Gut-Box and choose your stirring speed. The Gut-Box stirring mimics the hydrodynamics for various bio-mimetic models. It extends the permeability response for an additional order of magnitude, allowing more accurate biological membrane permeability predictions.



Figure 2.
PAMPA Gut-Box

Product Configurations

PAMPA kits (Fig. 3) include 96-well STIRWELL Plates and are configured to measure either GIT or BBB permeability.



Figure 3.
PAMPA Kits

GIT PAMPA KIT	BBB PAMPA KIT
STIRWELL PAMPA Sandwich	
Gastro-intestinal tract Lipid	Blood-brain barrier Lipid
PRISMA HT buffer pH adjusted to intestinal conditions	PRISMA HT buffer pH adjusted to pH 7.4
Acceptor Sink Buffer (ASB)	Brain Sink Buffer (BSB)
Support Plates	
Reservoir	
Ampoule Breaker	
PAMPA Explorer Software license	

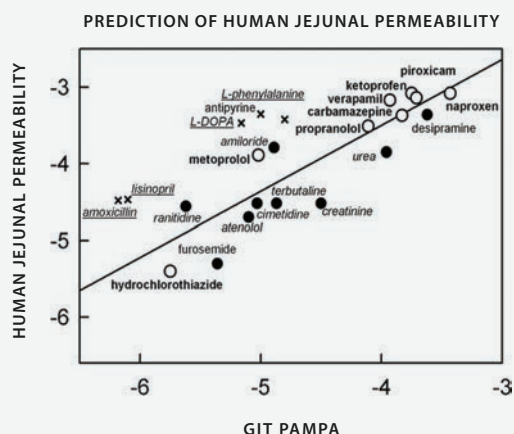


Figure 4. GIT PAMPA vs. Human Jejunal Permeability

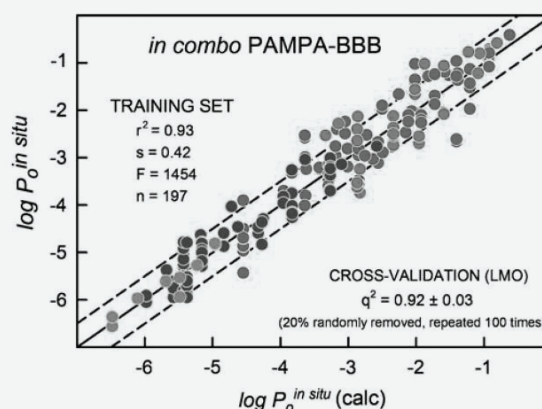


Figure 5. BBB PAMPA vs. Rodent Brain Perfusion

GASTRO-INTESTINAL TRACT (GIT) PAMPA

GIT PAMPA vs. Human Jejunal Permeability

The GIT PAMPA (Double-Sink) model was developed and optimized by Pion and then validated against human jejunal permeability data, generated by Uppsala University, for a diverse dataset of 17 compounds (Fig. 4).

BLOOD-BRAIN BARRIER (BBB) PAMPA

BBB PAMPA vs. Rodent Brain Perfusion

Nearly 200 CNS compounds were used for building the BBB PAMPA model. The developed model can predict rodent brain perfusion uptake rate better than more expensive cell-based assays (Fig. 5).



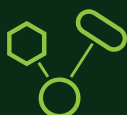
WHY USE PION PAMPA

We are the PAMPA Pioneers

Did you know that Pion was the very first company to commercialize a PAMPA offering in 1998, and we are the true pioneers in PAMPA development and theory? The Pion PAMPA product has proven correlation to human permeability. The legacy of Pion's PAMPA technology is widely referenced in scientific publications and in the industry book: *Absorption and Drug Development, Solubility, Permeability and Charge State*, Avdeef, Alex. Hoboken, New Jersey, Wiley and Sons, 2012.

Drug Candidate Screening:

PAMPA with Gut-Box is a high-throughput early-stage screening assay for accurate rank ordering compounds by their permeability characteristics. Since permeability is a critical component of *in vivo* drug absorption, PAMPA is considered a valuable tier 1 ADME assay. [4]



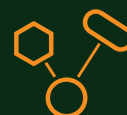
Optimizing Chemical Structures:

Researchers use PAMPA results to make informed decisions on structural modifications to the molecule that may enhance permeability and subsequent bioavailability.



Excipient Selection:

PAMPA has been shown to be a quick, and accurate method to assess the effect of excipients on the permeability of sparingly soluble drug candidates.



PION ANALYTICAL SERVICES

Don't have the time or equipment to do your own assays? Send them to us!

Pion Analytical Services offers Parallel Artificial Membrane Permeability Assay (PAMPA) testing to determine passive membrane permeability. We are the experts you can trust with your analysis.

REFERENCES

- [1] "Avdeef et. al. PAMPA - Critical Factors for better Predictions of Absorption. *Journal of Pharmaceutical Sciences*, 2007; 96, (11): 2893-909."
- [2] "Tsinman et. al. Physicochemical Selectivity of the BBB Microenvironment Governing Passive Diffusion—Matching with a Porcine Brain Lipid Extract Artificial Membrane Permeability Model. *Pharmaceutical Research*, 2011; 28:337–363."
- [3] "Kato et.al. Development and validation of PAMPA-BBB QSAR model to predict brain penetration potential of novel drug candidates. *Frontiers in Pharmacology*; 2023, 14, 1291246."
- [4] "Williams et al. Using *in vitro* ADME data for lead compound selection: An emphasis on PAMPA pH 5 permeability and oral bioavailability. *Bioorganic and Medicinal Chemistry* 2022, 56, 116588."