PermeaPad® GIT Barrier

EN

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Notes for the manual

Safety equipment
Notes with this symbol indicate that your personal protective equipment is to be worn

Manual
Notes with this symbol indicate that you have to carefully read the manual before use.

Information
Notes with this symbol indicate additional information.

Not for reuse
This is a disposable product. It is not allowed to use it more than once.

Usable until
The note with date indicates the best before date.

Batch and serial number
The letters and numbers following the symbol indicate the batch and serial number of the product.

Temperature limitation
The symbol indicates a temperature limit.

Qualification of Staff

The use of the product is restricted to technically trained staff. Additionally the manual must be read and fully understood

Legal Notice

Design changes in the interest of ongoing product improvement and changes in shape and color reserved. The scope of delivery may differ from product images. This document has been prepared with due care. PHABIOC GmbH assumes no liability for any errors or omissions. The determination of valid measurement results, conclusions and measures derived therefrom are solely the responsibility of the user. PHABIOC GmbH does not guarantee the correctness of the measured values or measurement results. Furthermore, PHABIOC GmbH assumes no liability for errors or damage resulting from the use of the measured values.

Security

Retain all safety instructions and instructions in order to consult them in the future.
This product may be used by children 14 years old or older, as well as by people with reduced physical, sensory or mental abilities or by people lacking experience and knowledge, if they have been supervised or instructed in the safe use of the device and understand the resulting hazards. Children are not allowed to play with the product.

- Do not use explosive substances with the product.
- Do not use strong chemicals with the product.
- Do not use the product after a fall. The product could have been damaged by the fall.
- The product is not a toy. Keep children and animals away.
- Protect the product from permanent direct sunlight.
- Do not open the product with a tool.
- Use the product only if adequate safety precautions have been taken at the workplace. Otherwise, do not use the product.

Observe the storage and operating instructions. If you store or transport the product improperly, the product may be damaged. Observe the information on handling (Chapter User Guidelines) and on storage of the product.

Do not reuse this product. Results of a used barrier are not reproducible after the product has been used for the first time and has made contact with the medium.

Wear protective equipment such as gloves, eye protection and protective clothing. Depending on which other products, substances or chemicals you use, further protective measures may be necessary. Pay particular attention to the respective safety data sheets for chemicals before using them.

Abstract

This developed biomimetic GIT Barrier enables an innovative approach for *in vitro* permeability assays*. Measurements with the GIT Barrier are easy, fast and reproducible. The simulation of passive mass transport can be performed by applying the PermeaPad® GIT Barrier in a conventional Franz-Cell, side-by-side diffusion cell or other set-up thereby measuring the permeability of a drug. Due to its unique and innovative structure the GIT Barrier is very robust, resistant and has a long shelf-life. As a consequence of these properties measurements are possible within a large pH range. Specific experimental conditions can be selected according to the substance studied.

* For research use only. Not for use in diagnostic procedures.

Technical Data

See data sheet PermeaPad® GIT Barrier:

https://phabioc.com/en/media/

Delivery Scope

The PermeaPad® GIT Barrier.

Storage

- dry and dark at 25°C
- protected from extreme temperatures
- protected from dust and sun
- in horizontal orientation
- store in the packaging until use

Please Note

If you store or transport the product improperly, the product may be damaged. Observe the information on handling (see User Guidelines) and storage of the product.

Permeability studies using PermeaPad® GIT Barrier in a Franz-cell set-up

AIM

Investigate the permeation of caffeine across the artificial, biomimetic GIT Barrier, PermeaPad® GIT Barrier.

MATERIALS AND CHEMICALS

Chemicals:

- Caffeine (CAS nr. 58-08-2)
- Purified water
- PBS

Materials:

- Ultrasonic bath
- Magnetic stirrer and stir bar
- Franz-cell permeation set-up with e.g. 5-7 mL chamber volume including temperature control.
- PermeaPad® GIT Barrier, 3 pieces
- Vacuum pipette
- Volumetric flasks (e.g. 10 ml)
- Beaker
- Micropipette (1-5 mL)
- Syringe + Cannula
- Container for samples (depending on quantification method)

Explanation Video:

How to prepare a Franz Cell – using PermeaPad® GIT Barrier - YouTube

➔ https://youtu.be/BDoHqrnSFPg

METHOD

Day 1 (Preparation of donor solutions and stock for calibration):

For the donor solution, prepare a 5 mM caffeine solution in purified water. For this, weigh in 8-10 mg caffeine in a 10 mL volumetric flask. Add 90% of the total volume of purified water and sonicate for approximately 30 min. Make up to final volume (i.e. 10 mL). Add a magnetic stir bar and stir to ensure complete dissolution. If particles still are visible, sonicate the donor solution for an additional 30 min before the permeation experiment. Repeat this procedure to prepare a stock of caffeine in purified water for preparation of a calibration curve. For the standard stock use at least 1 mg more than for the donor solution.

Day 1 (Permeation experiment):

To conduct the permeation experiment, fill the acceptor compartment with PBS (~5 mL; depending on cell size the volume may vary) and slightly overfill it to avoid air bubble formation after you put on the membrane. Adjust the volume to the calibration mark and put in the magnetic stir bar via the sampling neck. Place the PermeaPad® GIT Barrier on top of the Franz cell with the vacuum pipette. After that place the flat flange joint on top of the GIT Barrier and then place the donor chamber on top of it. Mount the cell clamp and connect the cell to the temperature control. Set the water bath to 25 °C (the correct temperature is very important). Assemble two more Franz-cells to get 3 replicates.

To start the experiment, add 5mM caffeine solution to the designated donor compartments (depending on cell size the volume may vary) and start the stirring (500 rpm). To facilitate the sampling procedure and to ensure the replicates are following the same time profile, fill the donor compartments with 1 min between each cell.

Take max. 500µL (volume may depend on quantification method) samples every 30 min from all cells for at least 3.5h. Refill the withdrawn solution with the same volume of fresh PBS after each sampling. At the end of the experiment also take a sample from the donor solution. Also take a sample from the 'left over' donor solution.

Quantification (Day 1/2):

Depending on the sensitivity of the instrument, the samples can be analyzed be UV spectroscopy, HPLC-UV, LC-MS/MS, etc.. For quantification of caffeine, prepare standards for a calibration curve by dilution from the standard stock. The concentration range should be approximately 0.2-100 µg/ml.

Conduct the quantification of both acceptor and donor samples according to a suitable method.

ANALYSIS

To determine the apparent permeability (P_{app}) of caffeine, plot the cumulative amount of caffeine (Q; in µg) permeated across the PermeaPad® GIT Barrier per area (A, in cm^2) against time (t; in sec). The linear part of this graph corresponds to steady state flux (*J*; in $\mu g/cm^2 \times s$):

$$J = \frac{dQ}{A \cdot dt}$$

To calculate the P_{app} (in cm/s), the steady state flux is normalized by the donor start concentration (C_0; in $\mu g/cm^3$; 1 cm^3 = 1 ml):

$$P_{app} = \frac{J}{C_0}$$

CONCLUSION

The PermeaPad® GIT Barrier is regarded to have the correct permeation properties when the P_{app} is 2×10^{-5} cm/s (± 5%). However, when an alternative permeation set-up was used (i.e. different cell volumes and/or a side by side cell set-up) the P_{app} may eventually vary to a higher degree due to the different stirring conditions, geometry and/or local temperature differences.

Additional Application Details [1-4]:

- Valid experiments require separation between donor and acceptor compartments and the absence of leakage. Use packings if appropriate.
- The membrane (PermeaPad® GIT Barrier) should not be pierced or torn off, e.g. with a pipette tip.
- The PermeaPad® GIT Barrier is functionally stable in a wide pH range and in the presence of co-solvents, surfactants and biomimetic media:
    - The PermeaPad® GIT Barrier is stable in the pH range of 1-10.
    - The PermeaPad® GIT Barrier is compatible with pH-gradient permeation set-ups:
        - Example: Donor compartment (pH=1) to the acceptor compartment (pH_{start}=7.3, pH_{end}=7.0) after 5 hours of trial.
    - Published co-solvents:
        - Ethylalcohol (up to 40%)
        - DMSO (up to 20%)
        - PEG400 (up to 10%)
    - Published surfactants:
        - Brji 97 (up to 5%)
        - Macrogolglycerol Ricinoleate; Cremophor® EL (up to 5%)
        - Polysorbate 60 (up to 4%)
        - Polysorbate 80 (up to 5%)
        - Natriumdodecylsulfat (up to 5%)
        - Triton-X (up to 1%)
    - Published biomimetic media:
        - FaSSIF
        - FeSSIF
        - FaSSGF
        - Pancreatic extract

References

[1] M. di Cagno et al. (2015): New biomimetic GIT Barrier Permeapad™ for efficient investigation of passive permeability of drugs. European Journal of Pharmaceutical Sciences 73: 29-34

[2] H. A. Bibi et al. (2015): Permeapad™ for investigation of passive drug permeability: The effect of surfactants, co-solvents and simulated intestinal fluids (FaSSIF and FeSSIF). International Journal of Pharmaceutics 493: 192-197

[3] H. A. Bibi et al. (2016): Use of Permeapad® for prediction of buccal absorption: A comparison to in vitro, ex vivo and in vivo method. European Journal of Pharmaceutical Sciences 93: 399-404

[4] H. A. Bibi et al. (2017): Simultaneous lipolysis/permeation in vitro model, for the estimation of bioavailability of lipid based drug delivery systems. European Journal of Pharmaceutics and Biopharmaceutics 117: 300-307.

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