

FAQs **PermeaPad**[®]

1. What is considered a good permeability coefficient?

The permeation coefficients are in the same order of magnitude as for PAMPA.

2. Is there an extraction method to use on the PermeaPad to calculate the amount of active that remains in the membrane?

You can split the barrier and dissolve/ extract with methanol or ethanol.

After your investigation you can dissolve/extract the active with ethanol or methanol by splitting the barrier to calculate the amount of active that remains in the membrane.

3. Do I have to separate the membranes before we use them?

Please do not separate membranes. The PermeaPad[®] Barrier consist of two cellulose membranes and in between there is the lipid layer. The biomimetic barrier (PermeaPad[®] Barrier) is ready to use.

4. How many times can we reuse the membranes?

- a. The PermeaPad[®] Barrier can be used once. After your investigation you can dissolve/extract the active with ethanol or methanol by splitting the barrier to calculate the amount of active that remains in the membrane.
- b. You put the used membrane in a little flask or something else (Flacon tube) and dissolve it with a known amount of the alcohol.

5. How can we check membranes' integrity?

At the following link, you can download a review (free access) describing integrity testing. It is described in chapter 4.1 Robustness.

Link: <https://www.sciencedirect.com/science/article/pii/S0928098718301751>

6. How is the PermeaPad[®] Barrier set-up?

The PermeaPad[®] Barrier consist of two cellulose membranes and in between there is the lipid layer. The biomimetic barrier (PermeaPad[®] Barrier) is ready to use.

7. What do I have to consider during the experiment Set-up?

1. The donor compartment should not use too low a concentration
2. The long intervals between the Measurement have to be adhered to achieve a high permeation
3. The analytics should be sensitive enough
4. Because of the blistering, the filling of chambers with water should always be from below. Air bubbles can minimize the active area of the membrane. This also leads to a slowed permeation

8. Should the membrane be rinsed with PBS before placing it between the horizontal cell?

No, please do not rinse the Membrane before use.

FAQs **PermeaPad**[®]

9. Which type of passive permeation your system can mimic? Which route of administration? Is it buccal, transdermal, or something else?

The PermeaPad[®] Barrier consist of two cellulose membranes and in between there is the lipid layer. It can be used to mimic the buccal or intestinal tract absorption.

Therefore, please find attached some publications.

10. What are the differences between PermeaPad[®] Plate and Barrier? And for which kind of application they were thought about?

The PermeaPad[®] Barrier is just the biomimetic membrane itself. You can get it in round disks with a diameter of 25 mm or 35 mm. Those can you place in franz-cells or side-by-side diffusion cells. Their applications are for samples with greater volumes and when you do not have a lot of samples. The PermeaPad[®] Plate is a 96-well Plate which has integrated the biomimetic membrane. It consists of a bottom plate, insert-plate (with biomimetic membrane) and a cover (see attached picture). This plate is ready to use and it is used for high-throughput screening. You can handle it with a pipette robot as well.

11. Is the permeation direction independent?

Yes, the permeation is direction independent.

You can put your sample (donor) either in the upper chamber or in the bottom chamber.

If you use the PermeaPad[®] Plate and the bottom plate is your acceptor chamber (depending on your experimental setup) then You can seal it and place the bottom plate (without insert-plate and cover) in your HPLC.

12. Can the bottom plate of the PermeaPad[®] Plate be placed in an HPLC analyzer?

Yes, the bottom plate of the PermeaPad[®] Plate can be placed in standard drawers / fixtures of 96-well plates from HPLC equipment. For this, the insert plate must be removed.

13. Can the bottom plate of the PermeaPad[®] Plate be covered with a sealing foil against evaporation? Application: HPLC

Yes, the bottom plate of the PermeaPad[®] Plate can be sealed with it.

14. What are the differences between the preparation from plate to barrier?

For the PermeaPad[®] Barrier you just need to prepare your samples (donor) and your acceptor solution and then you clamp the PermeaPad[®] Barrier in your permeation cells like franz-cells or side-by-side diffusion cells.

For the PermeaPad[®] Plate you just need to prepare your samples (donor) and your acceptor solution and pipet them into the wells.

FAQs PermeaPad®

15. Can the shape of the membrane change when in contact with water?

Yes, contact with water causes the membrane to bulge. As a result, the handling of the membrane can be difficult.

16. Can the two membranes of the PermeaPad® Barrier separate from each other?

If the PermeaPad® Barrier after your experiment, is swollen in water, you can separate the two membranes from each other. When dry and with considerate handling, the membranes should not separate from each other.

17. Is there any restriction in this preparation of the samples? Any substance or reagent that could destroy the plate or barrier?

The biomimetic membrane is resistive against a lot of substances. Here you can find the so far tested/ published substance:

[1] 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
<https://www.sciencedirect.com/science/article/pii/S0378517315300478>

[2] M. di Cagno et al. (2015): New biomimetic barrier Permeapad™ for efficient investigation of passive permeability of drugs. European Journal of Pharmaceutical Sciences 73: 29-34
<https://www.sciencedirect.com/science/article/pii/S0928098715001190>

[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
<https://www.sciencedirect.com/science/article/pii/S092809871630330X>

[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.
<https://www.sciencedirect.com/science/article/abs/pii/S0939641117301534>

18. Are the PermeaPad® Plate or the PermeaPad® Barrier Disposable?

Yes, both products are disposable.

19. Are there possibilities to API adhere in the membrane?

Yes, there is a possibility that API adhere in the membrane. If you use the PermeaPad® Barrier you can dissolve the lipid layer in methanol or ethanol after your test by placing it in vial or something similar. Afterwards you can analyze it in the HPLC as well.

FAQs PermeaPad®

20. Which should be your recommendation for blanked solution in order to check the integrity of the membrane from PermeaPad® Plate and PermeaPad® Barrier?

We recommend calcein as a blank solution for PermeaPad® Plate and PermeaPad® Barrier because they have the same membrane.

Read more about the robustness:

<https://www.sciencedirect.com/science/article/pii/S0928098718301751>

21. What is the focus of the PermeaPad® Plate and PermeaPad® Barrier?

The PermeaPad® Plate and PermeaPad® Barrier focus primarily on pharmacological research and are used in preclinical research.

22. There is a difference between the solubility test and the dissolution test. What differences are there?

- a. The term solubility has to differentiate between true (molecular) solubility and apparent solubility.

By strictly physical definition solubility is the solubility of a substance in a given pure solvent. For NCEs, this depends not only on the temperature but also on the pH or pka (in the case of dissociating substances) and thus also on the salt form (hydrochloride vs base) and on the crystal modification (solid state).

By the term "apparent solubility" more commonly used in the pharmaceutical field is meant both the above-mentioned true solubility plus all states of the substance which also contribute to the solubility, such as complexes (cyclodextrin) or micelles (surfactants). Since these states are u.a. can be influenced by formulation components, the apparent solubility is also often determined for formulations.

- b. With the term dissolution rate, the pharmacist usually means the dissolution / release rate from a formulation. But one can also determine the dissolution rate of the pure NCE, which mostly depends strongly on the particle size. To eliminate the influence of the particle size, one can determine the "intrinsic dissolution rate" of the pure NCE.

23. Can any request be made in any analysis?

Yes, each well has a separate access for measurement technology.

24. Is the PermeaPad Plate suitable for use in High Throughput Screening?

Yes, the PermeaPad® Plate was specially developed for use in High Throughput Screening and validated by various system providers.

25. How long can the PermeaPad Plate be stored?

We specify a storage period of 1 year, a use after longer-term storage should be easily possible

FAQs **PermeaPad**[®]

26. Is the PermeaPad[®] Plate suitable for a multiplate reader?

No, PermeaPad[®] Plate is not suitable for a multiplate reader because the bottom of the multiwell plate was not designed for transmittance measurement.

27. How do I recognize a damaged barrier?

You recognize a damaged barrier because of:

- cracks or air pockets between the two membranes.
- the membranes are shifted against each other

28. In which vessel can I use the PermeaPad[®] Barrier?

It can be used for example in a Franz cell or a side-by-side diffusion cell. You can also create alternative structures.

29. How around does the PermeaPad[®] Barrier have to be used?

The PermeaPad[®] Barrier has no preferential direction. How it is used, it does not matter.

30. Can the PermeaPad[®] products also simulate active transport?

No, PermeaPad[®] products can not simulate active transport. The PermeaPad[®] Barrier is a biomimetic membrane used to study passive mass transport.

31. How should the PermeaPad[®] products be stored?

Storage of PermeaPad[®] products:

- Store dry and dark at 25 ° C
- Protect from extreme temperatures
- Protect from dust and sunshin