Skin PAMPA

Studying semi-solid formulations of diclofenac using Skin PAMPA

Introduction: Studying the permeation properties of formulations is crucial in all stages of dermal and transdermal formulation development. Most of the available methods suffer from being labor-intensive and having poor reproducibility. Skin PAMPA technology is a useful tool for the early stages of development as it is an easy-to-use, cost-effective, and standardized model with significantly lower variation compared to most of the available methods. This technical note provides an example of studying three commercially available diclofenac formulations using Skin PAMPA model.

Figure 1

Sample Application: Figure 1 shows the key steps of formulation application. In contrast to a standard Skin PAMPA setup, the standard bottom plate is not used. The plate shown in Figure 1 is the formulation plate that has been designed for semi-solid applications. Pipette 70 µL of semi-solid sample into each well (positive displacement pipette is recommended for this step) and place the top plate on top of this plate to form the sandwich. As figure 2 illustrates, a 1 mm thin layer of formulation will be formed on the bottom side of the membrane, which is about 10 times more than the finite dose.

Figure 2

Assay parameters:
- API: diclofenac
- Matrix: commercial gel
- Acceptor solvent: Prisma HT pH = 7.4 buffer
- Acceptor volume: 250 µL
- Incubation temperature: 32 °C
- Stirring in acceptor wells with Gut Box™
- Stirring speed: 100 µm* UWL thickness
  *stirring equipment is pre-calibrated and stirring speed can be set to match a desired unstirred water layer thickness
- Sampling: 4 timepoints (0.5 h, 1 h, 3 h, 6 h)
- Sample volume: 150 µL, refilled with fresh buffer
- Sample analysis: UV plate reader
Results and Discussion: Figure 3 illustrates the permeated amount vs. Time profile of three formulations. All three flux profiles have a linear slope after a short lag time. Having four timepoints provides a suitable amount of data to calculate flux and to determine lag time. Although human skin data are not available, the comparison of Form2 and Form3 is relevant as they are the products of the same manufacturer. Better permeation properties were expected in case of Form3 because it is the second generation of Form2. The comparison demonstrates higher flux for Form3, which is in good agreement with the proposed expectation.

Flux calculation: Flux can be calculated based on the graph shown in Figure 3. The linear part of the slope of time vs. cumulated permeated amount plot provide the flux data, while the intersection with the x-axis indicates the lag time. Flux divided by donor concentration provides the permeability data.

Conclusion and Outlook: This technical note describes an assay for semi-solid formulation testing using Skin PAMPA model. The standard application has been slightly modified to make it suitable for this application. The investigation of three commercially available gels has been demonstrated and flux and lag-time calculation has been completed. The described assay suggests that Skin PAMPA can be a useful tool for studying semi-solid formulations in the formulation development process.