Data Article

Data on the determination of human epidermis integrity in skin permeation experiments by electrical resistance

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A B S T R A C T

The data presented in this article are related to the research article entitled “Design of in vitro skin permeation studies according to the EMA Guideline on quality of transdermal patches” (https://doi.org/10.1016/j.ejps.2018.09.014) [1].

In vitro permeation studies are generally carried out by Franz’s diffusion cell method using human epidermis as a membrane (Franz, 1975) [2]. The evaluation of membrane integrity is mandatory to assure the quality of the experiments. However, the methods used for this determination are different and the results are strictly dependent on the operative conditions. The article reports the electrical resistance values of human epidermis samples and in vitro skin permeability data of caffeine and benzoic acid. The data are used to establish a cut-off suitable for checking the skin integrity. This information may be useful to enable critical or extended analyses in order to contribute to the development of a compendial method.

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The determination of membrane electrical resistance (R) is an easy and fast method to verify the integrity of human epidermis samples used in in vitro permeation tests [1,3].

The resistance values (R₀) of epidermis samples obtained from three human donors ranged from 25.3 to 56.0 kΩ cm², immediately after being mounted on Franz’s diffusion cells. As shown in Fig. 1, when purified water was added in the donor compartment a slight decrease of R-values was observed after 24 h (R₂₄ = 35.6 ± 3.4 kΩ cm²), due to the membrane hydration. On the other side, the exposure of epidermis to solutions of sodium dodecyl sulfate (SDS) determined the reduction of R-value, which is dependent on the surfactant concentration and the exposure time. Indeed, the R-value of human epidermis exposed to 0.5 % w/v SDS solution drastically dropped off to 6.9 ± 4.3 kΩ cm² (R₂₄/R₀ < 0.1) and to 0.8 ± 0.2 kΩ cm² (R₂₄/R₀ < 0.01, Fig. 1) after 6 h and after 24 h, respectively. The 0.1% w/v SDS halved the electrical resistance to 17.8 ± 5.3 kΩ cm² after 24 h. Instead, the R₂₄-values after the treatment with a 0.05% w/v SDS solution (31.5 ± 7.1 kΩ cm²) were not statistically different from the untreated epidermis samples. Furthermore, a direct correlation between the surfactant concentration and R-values was observed (R²: 0.81). Considering that it is well-known that SDS (≥ 0.1 % w/v) alters the integrity of human epidermis by disrupting the inner structure of the stratum corneum [4], these preliminary results suggested that 20–25 kΩ cm² can be used as cut-off for excluding damaged membranes. To confirm this cut-off, the impact of R-value on the permeation of 1 % w/v caffeine or 0.3 % w/v benzoic acid solutions through human epidermis was investigated. The R-values of the...
epidermis samples and the calculated permeation fluxes \((J)\) of benzoic acid and caffeine are reported in Table 1 and Table 2, respectively. These model drugs were selected for their different physicochemical properties: the caffeine is a model of hydrophilic drugs, whereas benzoic acid a model of lipophilic drugs. In both cases, \(J\)-values increased for low \(R\)-values. In particular, using the Dixon’s \(Q\) test \((Q = 95\%)\), the \(J\)-values of benzoic acid can be considered outliers when the \(R\)-values are lower than 15 kΩ cm\(^2\). Due to the well-known high inter-donor variability of caffeine, the same statistical approach cannot be applied to caffeine dataset since Dixon’s \(Q\) test excluded as outliers the data that had to be accepted on the bases of literature \([5,6]\). Nevertheless, the caffeine \(J\) through the epidermis samples with an \(R\)-value lower than 20 kΩ cm\(^2\) resulted almost 100-fold higher than those obtained with epidermis samples having an electrical resistance equal or higher than 25 kΩ cm\(^2\).

On the bases of the actual dataset, all epidermis samples with an electrical resistance (measured with Agilent 4263B LCR Meter and setting the voltage at 100 mV and frequency at 100 Hz) lower than 25 kΩ cm\(^2\) have to be discarded.

| Donor ID | \(R\) (kΩ cm\(^2\)) | \(J_{benz}\) (µg/cm\(^2\) h) |
|----------|------------------|---------------------|
| 1        | 20.16            | 52.86               |
| 1        | 19.59            | 72.56               |
| 2        | 22.81            | 62.44               |
| 2        | 47.07            | 50.78               |
| 3        | 5.98             | **151.57**          |
| 4        | 23.02            | 65.93               |
| 5        | 22.81            | 58.30               |
| 5        | 17.68            | 64.72               |
| 6        | 32.23            | 42.90               |
| 6        | 33.98            | 38.89               |
| 7        | **10.94**        | **154.18**          |
| 7        | 19.59            | 43.43               |
| 7        | **12.53**        | **145.25**          |
| 9        | 31.42            | 57.77               |
| 11       | 44.09            | 46.57               |
| 11       | 23.02            | 54.77               |
| 12       | 31.42            | 66.34               |

Fig. 1. \(R_24/R_0\) calculated after 24-h incubation of human epidermis with SDS solution (0.05 % - 0.5 % w/v) and purified water as control (mean ± dv.st; \(n = 3\)). * \(p\)-value < 0.05 in comparison to control.
2. Experimental design, materials, and methods

2.1. Electrical resistance measurement after SDS exposure

The human epidermis samples were prepared following an internal standard procedure, as described by Casiraghi et al. [7]. The human epidermis samples were mounted on Franz’s diffusion cells [2], whose receptor compartments were filled with 0.9 % w/v saline solution. At the beginning of the experiment $R$-value ($R_0$) was measured by the instrument Agilent 4263B LCR Meter (Microlease, Italy), setting the voltage at 100 mV and the frequency at 100 Hz. The analyses were carried out filling the donor compartment with 0.5 mL 0.9 % w/v saline solution. Then, the donor solution was withdrawn and replaced with 0.5 mL of SDS solution at different concentrations, namely 0.05 %, 0.1 % and 0.5 % w/v. The temperature of epidermis surface was kept at 32 ± 1 °C throughout the experiment. At different time, each donor compartment was washed twice with 0.9 % w/v saline solutions and the $R$-value ($R_i$) was measured and compared to the initial values ($R_0$). Purified water was used as a reference.

2.2. In vitro permeation of benzoic acid and caffeine through human epidermis

Thirty-four human epidermis samples obtained from different donors (Donor ID: 1–12) were mounted on Franz’s diffusion cells, whose receptor compartments were filled with 0.9 % w/v saline solution. At the beginning of the experiment $R$-value ($R_0$) was measured by the instrument Agilent 4263B LCR Meter (Microlease, Italy), according to the experimental conditions reported above. Then, 0.5 mL of 1 % caffeine or 0.3 % benzoic acid solutions were added in the donor compartment. The in vitro permeation studies were performed using the same experimental protocol reported elsewhere [7]. The results were expressed as the average of parallel experiments performed in triplicate. The maximum flux ($J$) was determined as the slope of the linear portion of the plot of the cumulative amount permeated through the skin per unit area versus time.

### Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2018.10.098.

| Donor ID | $R$ (kΩcm$^2$) | $J_{caff}$ (µg/cm$^2$ h) |
|----------|----------------|--------------------------|
| 1        | 10.24          | 20.11                    |
| 2        | 19.53          | 24.13                    |
| 3        | 29.14          | 1.35                     |
| 3        | 36.30          | 0.83                     |
| 3        | 40.99          | 0.23                     |
| 4        | 34.85          | 0.22                     |
| 4        | 29.68          | 0.35                     |
| 5        | 12.78          | 10.43                    |
| 5        | 19.53          | 18.42                    |
| 8        | 33.68          | 0.83                     |
| 8        | 36.25          | 1.45                     |
| 9        | 25.36          | 0.40                     |
| 10       | 28.87          | 0.40                     |
| 10       | 56.55          | 0.55                     |
| 11       | 38.22          | 0.85                     |
| 12       | 33.39          | 0.53                     |
| 12       | 47.51          | 0.50                     |
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