

Effect of SDS concentration in the Coupling Medium on Ultrasound-Induced Changes in Skin Barrier

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Low-frequency ultrasound (US) has been shown to increase drug permeation into the skin. Sodium dodecyl sulphate (SDS) is often included in the coupling medium at 1 %w/v. We have shown a highly irregular relationship between the surfactant concentration and protein flux through skin in in vitro experiments (Table 1; Dahlan et al, 2005). The in vitro data suggested that lower SDS concentrations might induce similar protein permeation into the skin; lower SDS levels are expected to cause less skin irritancy. We, therefore, studied the effects of SDS concentration on US-induced changes in skin barrier properties in vivo, in mice and rats.

Pulses of ultrasound (20 kHz) were applied to the shaved abdominal skin of anesthetized animals via a coupling medium containing different concentrations of SDS (0, 0.001, 0.01, 0.1, 0.5(mice only) and 1 %w/v) for a total sonication time of 60s. US protocol for mice was 7.5 mm probe distance from skin, 20 ml coupling medium, 0.2s ON, 0.8s OFF and 20% amplitude while US protocol for rats was 5 mm probe distance, 20 ml, 0.5s ON, 0.5s OFF and 30% amplitude. Mice received a milder US treatment to avoid damage to their thinner skin. After US application, trans-epidermal water loss (TEWL, an indicator of changes in skin barrier properties;) were measured at 5, 15, 30, 45 and 60 min. High TEWL values are related to high water loss i.e. reduction in stratum corneum barrier.

In mice, the application of US in the presence of SDS at concentration below 0.5%w/v consistently showed low TEWL readings which were statistically the same as baseline i.e. readings before US application, indicating a good state of the skin barrier at all times. At higher SDS concentrations (0.5 and 1 %w/v), TEWL measurements increased significantly with 1 %w/v SDS giving the highest TEWL readings (at 60 min post-sonication TEWL was 5.3 times higher than baseline). Higher TEWL values with higher SDS concentration could not necessarily be predicted as the extent of cavitation (i.e. formation and collapse of gaseous bubbles which is expected to damage the skin) is inversely related to surface tension of the coupling medium. Therefore, similar TEWL values for high and low SDS concentration could have been expected.

Interestingly in rats, TEWL measurements of all treatment groups were (2.5 times greater than baseline, but were similar to one another at all times. No obvious relationship was seen between presence and absence of SDS and its concentration and TEWL. Surprisingly, lower SDS concentrations caused similar skin damage to higher SDS concentrations. It is possible that the harsher US conditions override any synergistic effects between US and SDS. It is not possible to compare the mice and the rat data as the US protocol was optimized for each species.

We can, therefore, conclude that in mice, 0.5 %w/v SDS might be sufficient for our subsequent in vivo experiments, while in rats lower SDS concentrations might be sufficient.

Table 1 Protein sonophoresis through rat skin.
(Data represents Mean±SD, n=5)

SDS concentration (%w/v) in coupling medium	Radiolabelled protein permeated (cpm)
0	85770±3054
0.001	83250±2085
0.004	83020±1509
0.01	43980±1349
0.04	29111±1579
0.1	41910±3502
1	74841±3502

Mitragotri, S. et al (2000) *J. Pharm. Sci.* **89**: 892-900
Dahlan, A. et al (2005) *J. Pharm. Pharmacol.* **57**: S92