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The pH of Topical Creams can Change Rapidly Following Application on the Skin In Vivo

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PURPOSE

The pH of a semisolid dosage form may be associated with multiple failure modes for the corresponding drug product. For example, pH may influence the ionization state, polymorphic form, stability, or solubility of the drug. Similarly, pH may influence the ratio of dissolved to undissolved drug, its distribution in the microstructure of the dosage form, the rheology, dose application, spreadability, product transfer, cosmetic acceptability, and comfort of the drug product when applied to sensitive, damaged or diseased skin. Therefore, an important consideration related to pH is the buffering capacity of the dosage form to maintain its pH in clinical use. The influence of the skin, in vivo, on the pH of topically applied dosage forms is not well understood, and the goal of this study was to evaluate the potential influence of dose application on skin, in vivo, on the change in pH of several commercially marketed and custom-manufactured creams and one gel across a range of pH.

METHOD

The native pH of the creams and the gel was first measured using an InLab Micro ® probe with special considerations for the nature of the material. A dose of 500 mg of each product was applied in a thin film on the volar forearm of five human subjects (n=5). After 1 h, the pH of the formulation was measured in vivo using a surface probe. The formulation was then recovered from the skin surface and measured using the InLab Micro® probe and the procedure that was initially utilized to characterize its native pH. Mechanistic studies were performed to investigate the relative contribution of atmospheric vs. physiological (skin) factors on the observed change in cream or gel pH following topical application on the skin in vivo. For example, the change in pH of the formulations was determined following application as a thin film on a glass slide at 32°C for 1h, during which it was exposed to atmospheric conditions, as well as other control conditions (not shown). The measurements of pH change under such control conditions were used to ascertain the independent contribution of skin and associated physiological factors on the change in formulation pH.

RESULTS

Figure 1

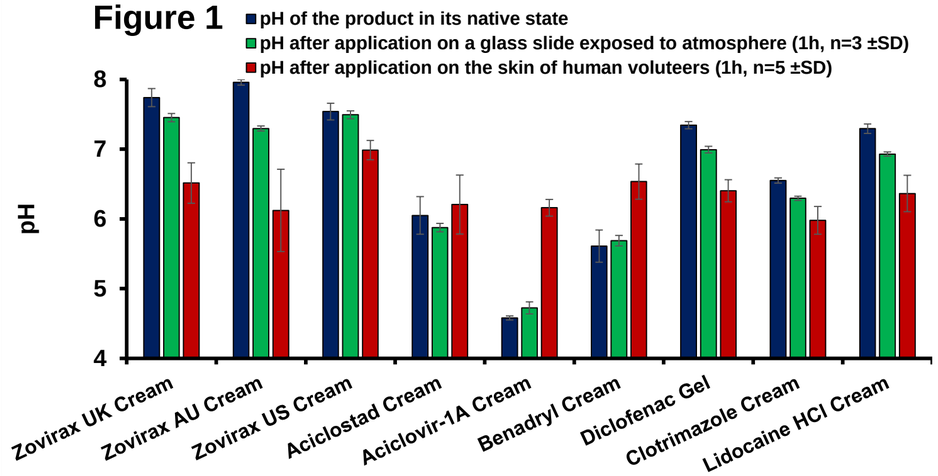

Fig. 1) Cream and gel formulations included in the study were characterized to have a native pH in the range of 4.58 ± 0.03 to 7.96 ± 0.04. The pH of the formulations changed significantly ($p<0.05$) within 1 h after application on the skin when the native pH was either less than 5 or more than 7. For formulations with a native pH in the range of 6 ± 1, their pH did not change significantly following topical application (t test., $p<0.05$). The average pH of all the products 1h after skin application was 6.36 ± 0.32.

Figure 2

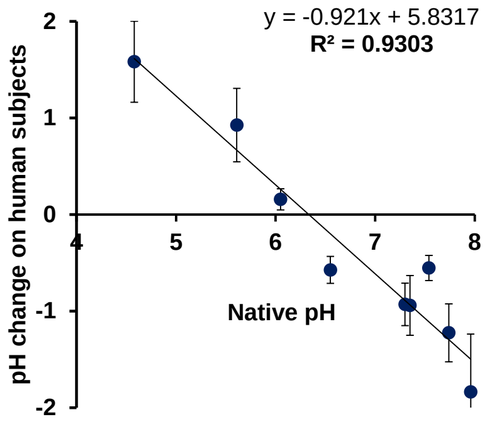

Fig. 2) Linear relationship of native pH to change in pH 1h following application to the skin, with an intercept at pH 6.33. The direction and magnitude of pH change was typically proportional to how far above or below pH 6.3 the native pH of the product was. (n=5 ±SD)

CONCLUSION

The results of this study illustrated that the pH of topically applied formulations can change rapidly after application on the skin in vivo. The mechanistic studies revealed that the change in pH following topical application in vivo appeared to be predominantly attributable to physiological factors associated with the skin, and that atmospheric conditions did not appear to contribute meaningfully to this effect. It is hypothesized that the change in the native pH of the formulations was due to a dominating buffering ability of the skin to maintain its native pH, relative to the buffering ability of the creams to maintain their native pH.

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