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Glycerin inclusion levels for skin hydration: a data-driven approach

554

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Conclusions:

Retrospective analysis of 134 products containing various levels of Glycerin, revealed that in the context of clinical studies that would be performed on 20 volunteers:

- A single application of an emulsion, gel or solution containing at least 3 % of glycerin guarantee a significant increase of skin hydration in vivo, 2 and 8 hours after application.
- A single application of an emulsion, gel or solution containing at least 6.5 % of glycerin guarantee a significant increase of skin hydration in vivo, 24h after application.
- A simple linear mixed model (LMM) predicting hydration can be established, mostly relying on discrete inclusion levels of glycerin.
- Explanatory power of the LMM is substantial, conditional R^2 = 0.698 (full model) and marginal R^2= 0.676 (fixed effects alone).

Introduction:

Properties of glycerol and glycerin:

- Glycerin's hydration boosting effect has been evidenced by several instrumental methods in vivo relying on distinctelectrical principles: conductance (Skicon®), impedance (Nova DPM®) and capacitance (Corneometer®)[1].
- Glycerol greatly accumulates in the skin and creates a 'reservoir' in the depth of SC without disrupting the lamellar structure of the lipid bilayers. It increases both intracellular and extracellular space among corneocytes, improving the water holding capabilities of the SC [2].
- Corneodesmolytic-degradation of the corneodesmosomes is greatly enhanced by the inclusion of glycerin, thus facilitating desquamation [3].

Objectives:

- To establish the minimum inclusion levels of glycerin for a significant increase in skin hydration at 2, 8 and 24 hours in clinical settings.
- To predict percentage increase of skin hydration in vivo according to levels of glycerin.

Results:

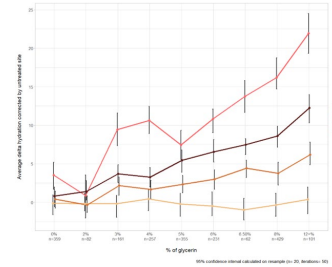

Figure 1: Mean capacitance changes (a.u.) at T0, 2h, 8h and 24h based on % of glycerin in products. The error bars correspond to a pessimistic 95% confidence interval (CI) calculated on 50 resampling of the data with 20 random hydration measures for a given % of glycerin as to simulate an hydration study. "n" represents the number of hydration measures in the study treated with products containing a given % of glycerin.

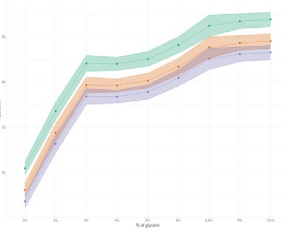

Figure 2: Impact of percentage of glycerin and time fixed effects on hydration according to the LMM. The ribbons around each line/dot represent the standard error. Hydration at 24h is in purple, 8h in orange and 2h in green. The uncertainty of the random effects from the full LMM are not taken into consideration here..

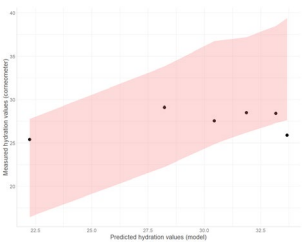

Figure 3: Average hydration values predicted by the LMM compared with average experimental hydration values for a study containing 6 products, acting as a test set. The ribbons around each line/dot represent the prediction intervals (uncertainty) of the LMM calculated by the merTools package in R.

- Increase in hydration at 2; 8 and even 24h was observed as the % of glycerin increases, meaning that a causal relationship between glycerin levels and hydration was plausible.
- 3% glycerin led to a strong increase hydration after 2h and 8h compared to baseline (0h) and corrected to the untreated site.
- This increase was less clear at 24h, until 6.5% glycerin levels.

- Sharp increase of hydration for products with 3% glycerin according to fixed effects (percentage of glycerin and time) predicted by LMM.
- Hydration forms a plateau for glycerin levels above 3 until around 6% of glycerin.
- Second hydration plateau from 6.5 to 12+% glycerin.

- Predicted hydration by the LMM for 6 products
- The generated prediction intervals are satisfactory.
- Only one out of six products had an average experimental hydration value out of bounds with an actual experimental hydration of 25.88 on average vs a predicted lower bound of 27.61. It is likely to stem from the powder content of this product, which may prevent an ideal contact between the probe and the skin.

Materials & Methods:

The data set contained Corneometer® data of women and men panellists who took part to various studies . The design of experiment was an in vivo open study, with randomized and controlled (32mg/cm^2) product application performed by a trained investigator on forearms, after baseline Corneometer® measurements. The Corneometer® raw data of 134 products were compiled with formulation types consisting of emulsions (e.g. creams, lotions) watery gels and solutions (e.g. toners).

Software used

All statistical models were established using R (version 4.1.2) and RStudio (2021.09.1+372 "Ghost Orchid" Release) for Windows 10, together with the lme4 package (version 1.1-29) for linear mixed-effect models, ggplot2 package (version 3.3.5) for plots, merTools (version 0.5.2) for predicting hydration values of products outside the dataset based on model's uncertainty, sjPlot (version 2.8.10) for generation of summary table of fixed and random effects and MuMIn package (version 1.46.0) for pseudo-R-squared calculations.

Modelling

The LMM used in this work is:
hydration ~ glycerin + water + time point * baseline + (1|study/panellist)

The response variable (the effect we try to predict) is hydration (continuous), the fixed effects are glycerin (categorical, 9 levels), water (continuous), timepoint (categorical, 3 levels) and baseline, which corresponds to hydration at the site before treatment (continuous). The random effects controlling for non-independence of the data are(1|study/panellist) which represents the nested structure of our data such as panellist ⊂ study. study has 31 levels and panellist, 606. The glycerin variable was discretized due to its pseudo-discrete distribution. The model has been built using Restricted Maximum Likelihood (REML), an improvement over maximum likelihood estimation for mixed-effects modeling. For our LMM to be valid, assumptions of linearity of predictors, homoscedasticity of residuals and their normal distribution were checked and deemed to be met.

References:

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