**The effect of a humectant emollient cream containing 5% urea compared to a non-humectant emollient on the skin barrier in older people with dry skin**

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**Background:** Xerosis affects between 30 and 75% of older people. The development of xerotic skin conditions, such as atopic dermatitis, asteatotic eczema and winter xerosis, is associated with a skin barrier defect. This defect is characterised by reduced levels of natural moisturising factor (a collection of natural humectants including urea, pyrrolidone carboxylic acid [PCA], and lactate), abnormal intercellular lipid levels in the stratum corneum (SC), and elevated skin surface pH (linked to increased skin barrier breakdown). Emollients are widely used to treat xerosis, however there is limited mechanistic evidence of their effects on the skin barrier.

**Objective:** The aim was to compare the effect of a humectant emollient, containing 5% urea and lactate, to a non-humectant emollient on the properties of the skin barrier.

**Methods:** Two cohorts of 21 volunteers aged 60+ years with dry skin were recruited. The first applied 2 fingertip units twice daily of the humectant emollient to one forearm and no treatment to the other for 28-days. The second applied the humectant emollient to one forearm and the non-humectant emollient to the other observing the same treatment parameters. Treatment allocation was randomised. The biophysical and biological properties of the skin were determined approximately 20 hours after cessation of treatment. Local research ethics committee approval was granted.

**Results:** Compared to no treatment, the humectant emollient significantly: improved skin barrier function (decreased TEWL), SC integrity and skin hydration (capacitance); decreased skin surface pH 0.14 units and reduced SC protease activity by 43%. The humectant and non-humectant emollients had similar effects on TEWL and capacitance, however the humectant emollient was associated with significantly improved SC integrity (TEWL after 20 tape-strips was 24 vs. 35 g/m2/h), lower skin surface pH (5.00 vs. 5.23) and protease activity (1.24 vs. 1.61 nU/µg); elevated SC lactate levels (157% vs. 81%) and PCA (not present in either formulation) levels (143 vs 106%) compared to before treatment; and increased water (SC specific hydration) and NMF (carboxylate) content in the upper SC (172 vs 109%) assessed by *in vivo* ATR-FTIR.

**Conclusions:** In contrast to the non-humectant emollient, the humectant emollient significantly improved skin barrier condition, associated with elevated NMF levels (exogenously and endogenously, putatively via increased filaggrin expression), reduced skin surface pH and decreased protease activity. This highlights the significant difference in effects of emollients on the skin barrier, and their potential to treat xerotic skin conditions.