

# IN VITRO AND EX VIVO EVALUATION OF BARRIER AND HYDRATION BENEFITS OF A UREA DERIVATIVE

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## 1 INTRODUCTION

**Introduction:** Urea is an essential component of skin's natural moisturizing factor (NMF) and is used as a moisturizer, barrier strengthener, and keratolytic agent.<sup>1</sup> While proven effective in topical formulations, urea is difficult to stabilize at skin-balanced pH. This study evaluated the efficacy of a urea derivative, hydroxyethyl urea (HEU), for relevance in skincare formulations for patients with xerosis.

## 2 MATERIALS AND METHODS

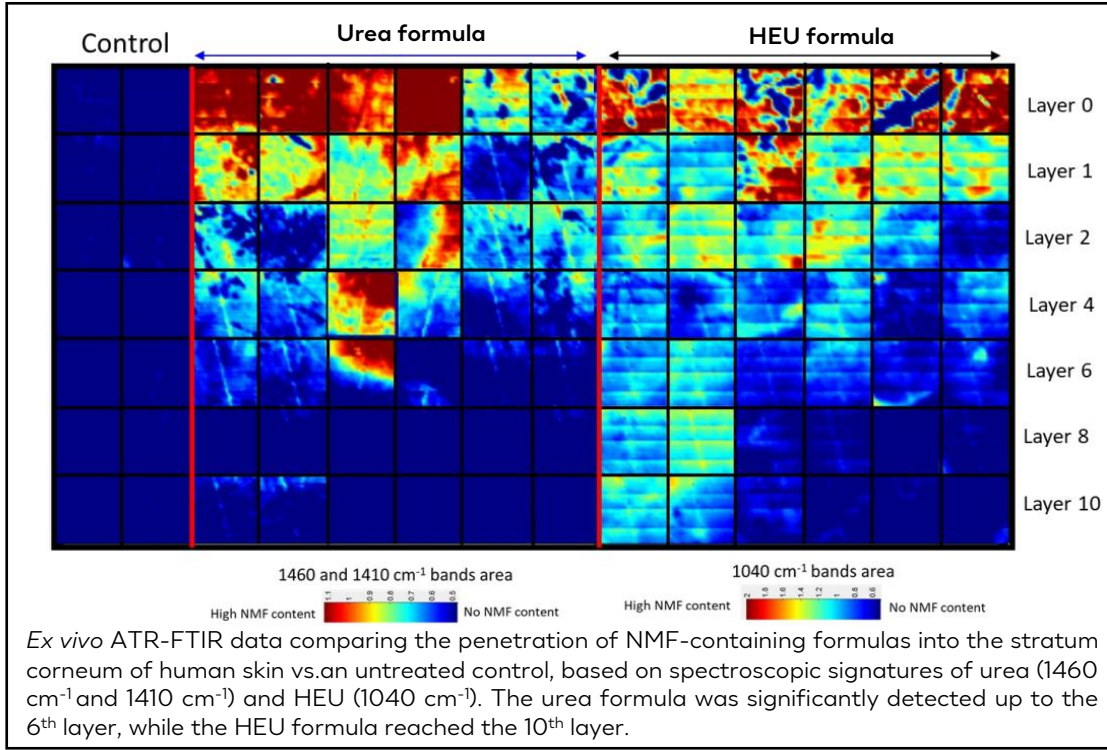
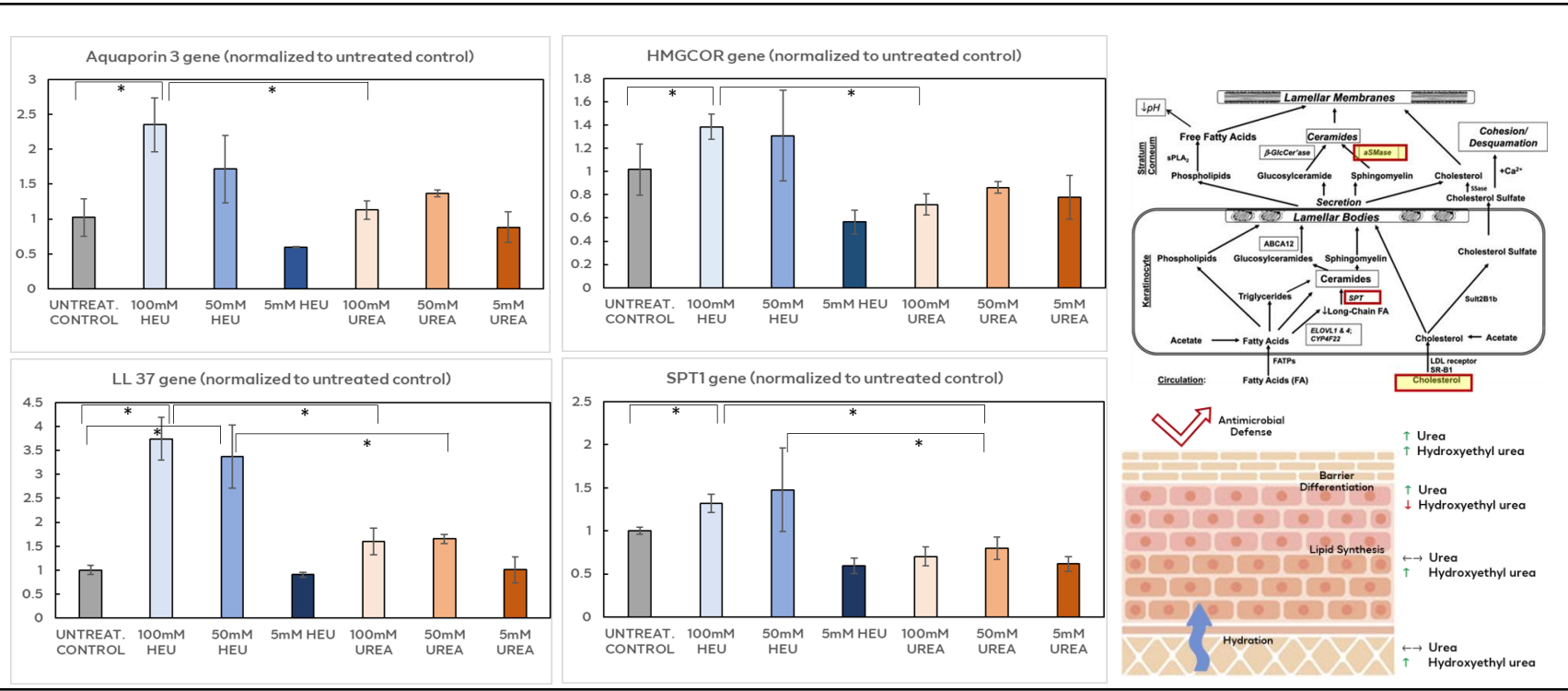
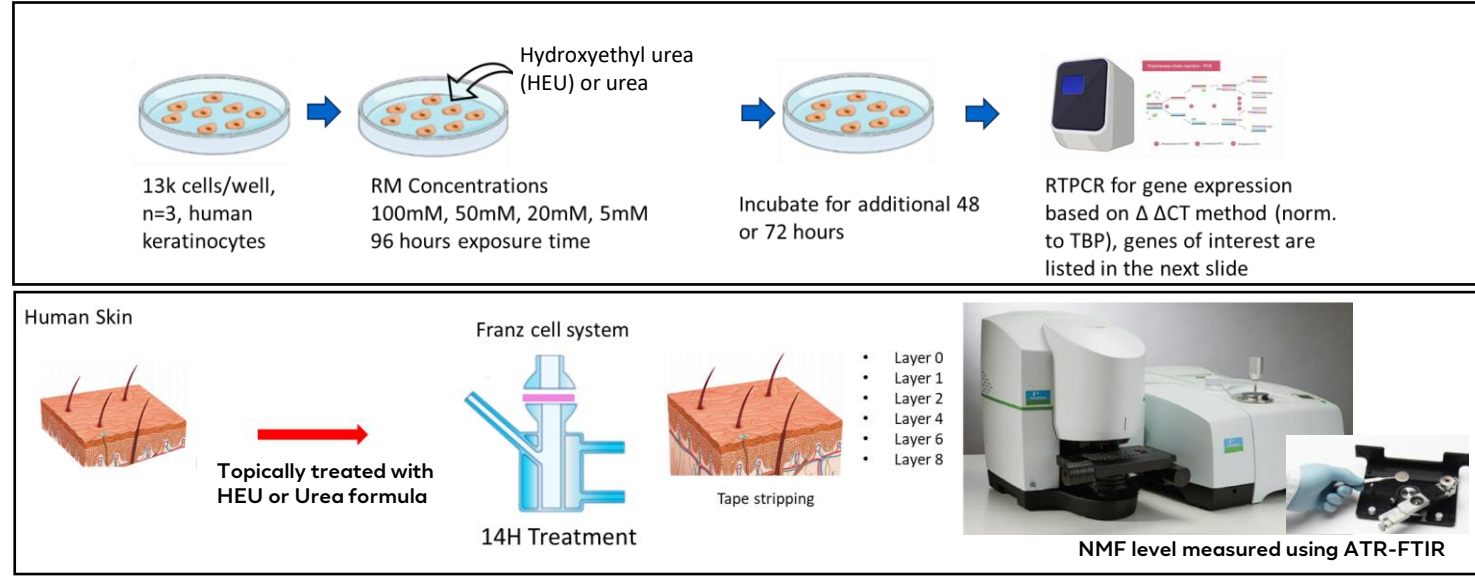
### Effects of HEU to modulate keratinocyte gene expressions

To assess the effects of HEU on modulating genes related to hydration (Aquaporin-3), anti-microbial defense (LL37) and lipid biosynthesis (HMGCoR and SPT1), human keratinocytes were exposed to varying concentration of urea and HEU for 3 days. The cells were then harvested, and the gene expression was measured using RTPCR.

### Effects of HEU to enhance NMF level in the stratum corneum

To further assess effects on NMF levels, human *ex vivo* skin was placed in a Franz diffusion cell and equivalent concentrations of HEU formula vs. urea formula were applied onto the skin surface. After 14 hours, ATR-FTIR spectroscopy was used to evaluate the NMF concentration through different stratum corneum depths.

## 3 RESULTS AND DISCUSSION



**KEY FINDINGS**

- HEU significantly upregulates Aquaporin-3, LL37 and HMGCoR and SPT1 genes compared to the untreated control and urea treatment in the keratinocytes.
  - Aquaporin-3 is an essential membrane transporter of water and glycerol in the epidermis<sup>2</sup>, LL37 (Cathelicidin antimicrobial peptide) is part of the antimicrobial peptide family that plays an important role for cutaneous immunity<sup>3</sup>, HMGCoR is the rate-limiting enzyme for cholesterol biosynthesis<sup>4</sup> and SPT1 is the rate-limiting enzyme in the synthesis of ceramide and sphingomyelin<sup>5</sup>.
- While both formulations increase NMF content as measured using ATR-FTIR, the HEU formula was able to increase the level of NMF in deeper layers of the stratum corneum compared to the urea formula.

## 4 CONCLUSION

Using two model systems, HEU demonstrated an upregulation in skin hydration and barrier related genes and increased NMF levels within the skin when compared to urea, suggesting that HEU may be a useful alternative for urea topical skin care treatments.

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