Reviving the Skin from Within: Mechanistic Insights into a Well-Tolerated Dermal Filler - CPM-HA20G

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INTRODUCATION

Dermal fillers composed of hyaluronic acid (HA) combined with glycerol have been clinically shown[1,2] to enhance skin hydration and quality; the precise mechanisms underlying their efficacy have yet to be fully elucidated.

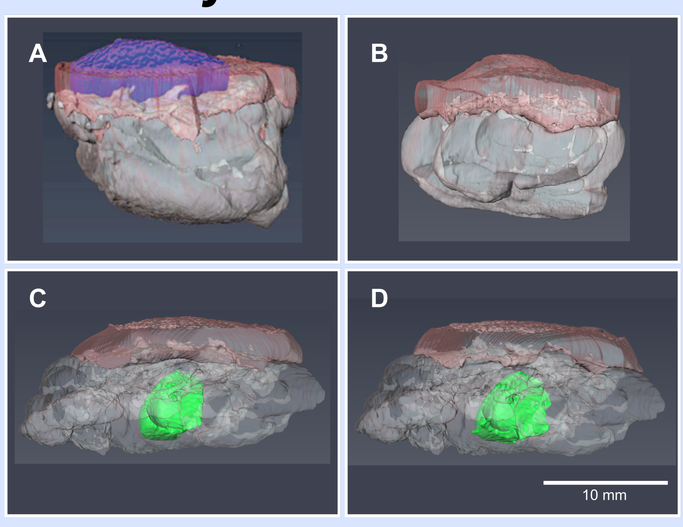
Here, we investigated the dual hydration mechanisms (Inner & Inside-Out Hydration), cell protection and tolerability, and tissue compatibility of the cohesive polydensified matrix (CPM) filler containing HA and glycerol (CPM-HA20G), focusing on glycerol's unique role.

METHODS

Primary normal human epidermal keratinocytes, *ex vivo* human skin models, and an *in vivo* study were conducted with CPM-HA20G (Belotero® Revive, Anteis S.A., Plan-les-Ouates, Switzerland, a company of the Merz Aesthetics® group) and its ingredient, glycerol. CMP-HA20G and the single humectant glycerol were compared to a sorbitol containing cross-linked HA dermal filler (HA12.5S) or the different humectants mannitol and sorbitol. Protein analysis, cell-based assays, 3D micro-computed tomography (µCT), corneometry, and histology were performed to assess hydration dynamics, glycerol uptake, cellular stress levels, oxidative stress protection (UVB and H_2O_2 induced), tissue integration, and inflammation.

RESULTS

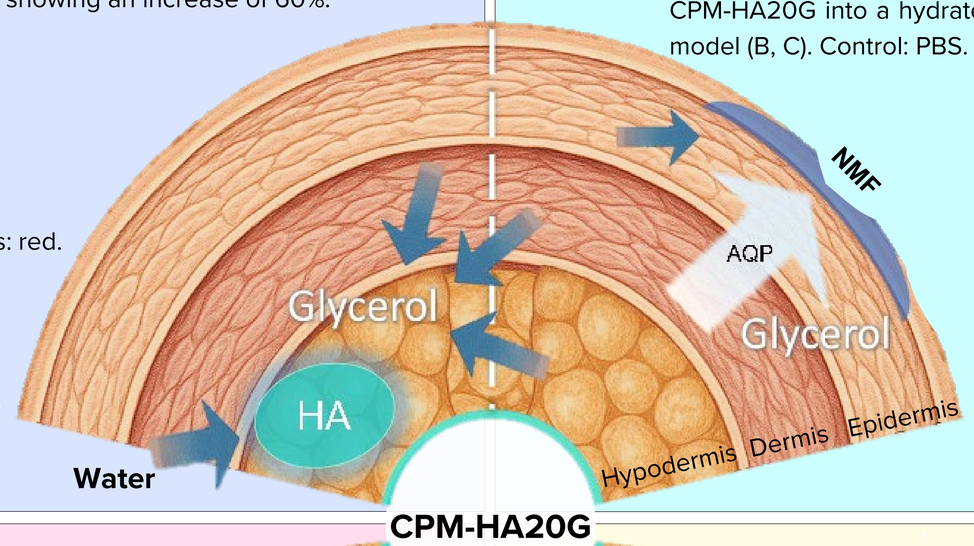
Inner Hydration



Hydrated injection site: blue (intradermal injection) or green (subcutaneous injection); Hypodermis: gray; Epidermis/Dermis: red. Scale: 10 mm.

Figure 1: Tissue hydration at the injection site. (A) 3D computer tomography analysis measurements after intradermal injection of dermal filler in a hydrated human skin model and (B) under dehydrated conditions. Hydrated subcutaneous bolus injection after 10 min (C) and (D) 120 min showing an increase of 60%.

Hyaluronic acid and glycerol act as natural humectants, hydrating the skin from within and providing the tissue with immediate inner hydration.



Inside-Out Hydration

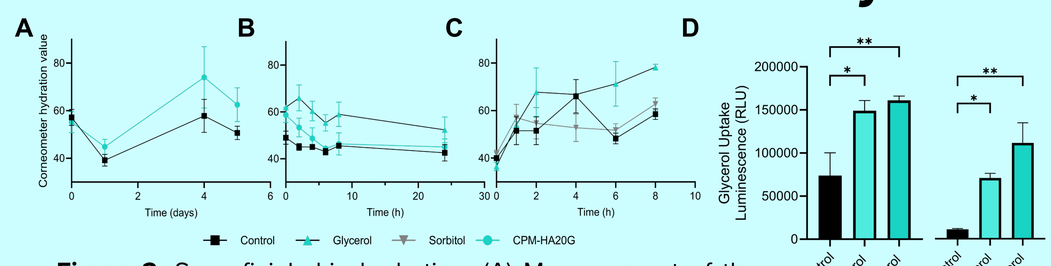
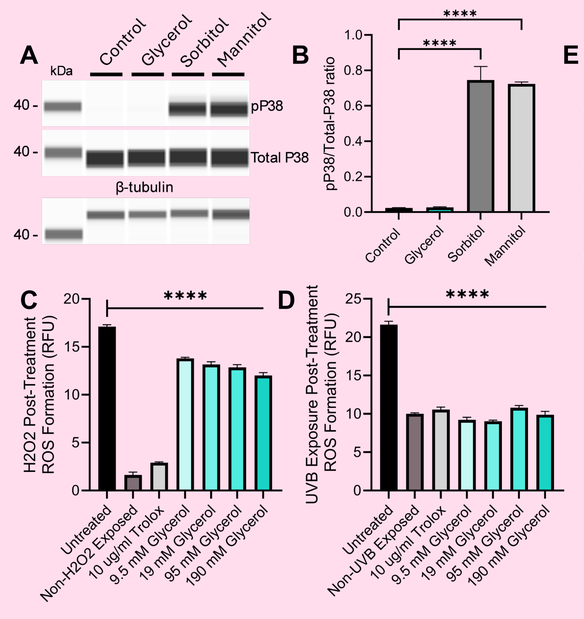


Figure 2: Superficial skin hydration. (A) Measurement of the superficial hydration effect of a 100 µL bolus injection of CPM-HA20G into a hydrated skin model (A), dehydrated skin model (B, C). Control: PBS.

Glycerol uptake via water-glycerol permeable aquaporin (AQP) channels into normal human keratinocytes in vitro after treatment with 95 or 190 mM of with 95 or 190 mM of glycerol for 2, and 72 h using a bioluminescent assay (D). Significance denoted as: * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; **** = $p < 0.0001$.

CPM-HA20G delivers Inside-Out Hydration, as glycerol can be uptaken in NHEKs and transported via terminal differentiation to the skin surface to act as a Natural Moisturizing Factor (NMF).

Cell Protection & Tolerability



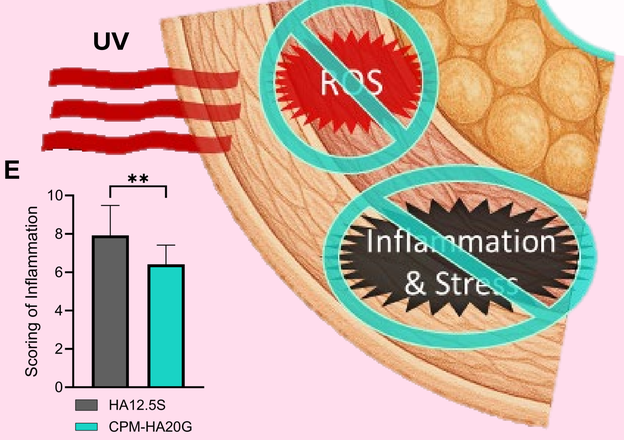
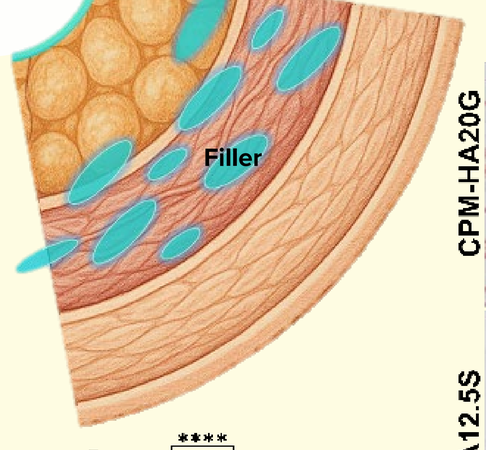
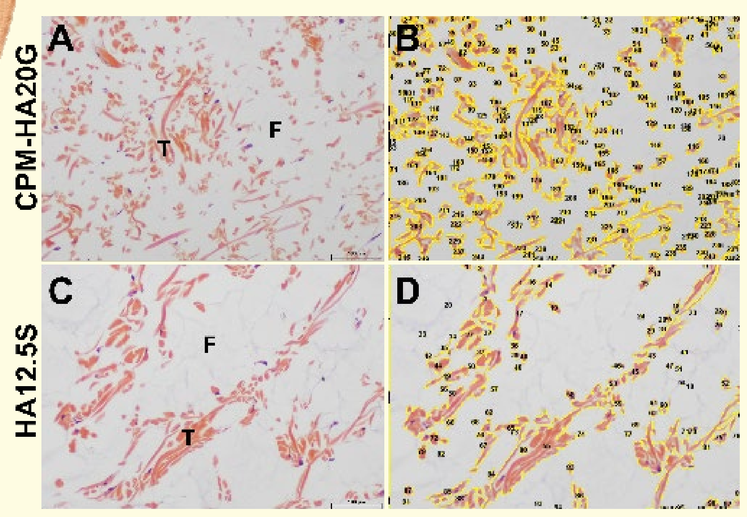


Figure 3: Reduced cellular stress response with glycerol compared with sorbitol, and mannitol (190 mM) (Western blot analysis A, Quantification B). ROS formation after exposure to H2O2 (C) and UVB (D) is reduced by Glycerol. Histopathological comparison of CPM-HA20G and HA12.5S for Inflammation (E). Significance denoted as: ** = $p < 0.01$; **** = $p < 0.0001$.

Glycerol provides protective functions against induced ROS formation and is well-tolerated by the skin, as it does not upregulate cell stress responses in-vitro or Inflammation in-vivo.

Tissue Integration





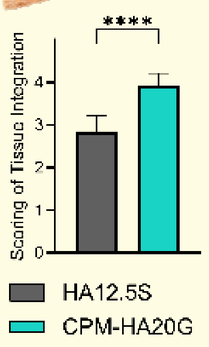


Figure 4: SHE staining of histological sections immediately after CPM-HA20G (A) and HA12.5S (C) injection. (B+D) Respective tissue segment quantification. Semiquantitative analysis of tissue integration after two weeks (E). Significance denoted as: ** = $p < 0.01$; **** = $p < 0.0001$. F= filler (grey); T= tissue(red); Scale = 100 µm.

Tissue integration of CPM-HA20G scores higher compared to similar HA-Filler.

CONCLUSIONS

- **CPM-HA20G achieves rapid hydration via a dual hydration mechanism and is well tolerable with good tissue integration.**
- **Glycerol was found to play a unique role in enhancing hydration without inducing stress responses, providing antioxidative capacity and cell protection.**
- **The results of this study confirm the positive effects observed in clinical studies[1,2] and provide a mechanistic basis for the efficacy of the dermal filler, CPM-HA20G.**

Reference:
[1]Hertz-Kleptow D, Hanschmann A, Hofmann M, et al. Facial skin revitalization with CPM-HA20G: an effective and safe early intervention treatment. CCID. 2019;Volume 12:563-572. doi:10.2147/CCID.S209256
[2]Park JY, Youn C, Lee C, et al. Facial Skin Quality Improvement After Treatment With CPM-HA20G : Clinical Experience in Korea. J Cosmet Dermatol. 2025;24(1):e16795. doi:10.1111/jocd.16795

COI Disclosure: KM, CH, SHJ, CW, DS, TH are employees of Merz Ax. SS, JYP, TSL, LAP are consultants for Merz Ax.