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From Instant Hydration to Skin Longevity: Molecular Weight-Driven Effects of Poly-γ-glutamic Acid

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abstract

Hydration is fundamental to skin health, influencing barrier integrity, cellular function, and visible appearance. Poly-γ-glutamic acid (γ-PGA), a biopolymer known for its exceptional water-binding capacity, offers new opportunities to enhance hydration beyond what traditional hyaluronic acid can achieve. This article investigates two γ-PGA–based ingredients: AQUARICH®-MAX, a high–molecular-weight film-forming polymer that delivers immediate and long-lasting surface hydration, and AQUARICH®-OLIGO, a low-molecular-weight oligomer engineered for deep penetration and skin longevity benefits.

Introduction

The skin, the body's largest organ, serves as the primary protective interface between an individual and the environment. Its barrier functions are primarily attributed to the epidermis, the outermost layer of the skin, with the stratum corneum (SC) playing a key role in maintaining these functions [1]. These barrier functions are greatly weakened with loss of water in the skin, compromising both hydration and bioactivity, leading to accelerated skin ageing such as reduced firmness from disrupted collagen, or increased redness from inflammation [2]. Cosmetic products can help mend this through molecular weight-dependent penetration. The best example for this is hyaluronic acid: High molecular weight (HMW) hyaluronic acids stay on the surface to deliver hydration by binding water and forming films, while low molecular weight (LMW) variants penetrate deeper to prevent typical signs of skin ageing caused by loss of hydration [3].

Hyaluronic acid (HA) has long been the gold-standard humectant used to address moisture loss. However, topical hyaluronic acid (HA) presents certain challenges: its high molecular weight restricts penetration beyond the stratum corneum, and it exhibits a short residence time due to rapid diffusion or wash-off [5, 6]. These limitations drive the market need into more advanced biopolymers.

Poly-γ-glutamic acid (γ-PGA) is a naturally occurring, water-soluble polymer produced through fermentation by *Bacillus subtilis*. Known from the traditionally fermented soybean product, natto or cheonggukjang, it is built through γ-carboxyl linkages that create a flexible, highly anionic chain with exceptional water-binding capacity. This unique structure resists enzymatic degradation and enables γ-PGA to deliver strong moisturization, surface film formation, or deep penetration depending on molecular weight [7].

AQUARICH®-MAX and AQUARICH®-OLIGO represent two advanced γ-PGA technologies based on this molecular-weight–dependent behavior. AQUARICH®-MAX, due to its high molecular weight of approx. 2000 kDa, primarily acts on the skin surface, forming a flexible, moisture retentive film that delivers immediate and long-lasting hydration.

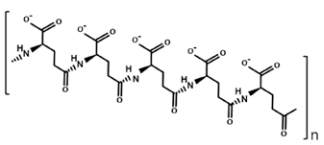
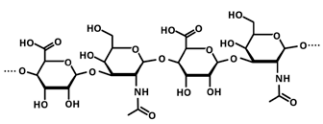
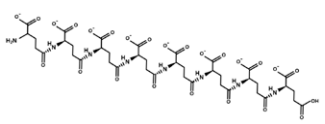
AQUARICH®-MAX	Hyaluronic Acid	AQUARICH®-OLIGO
		
On average 2000 kDa	Large polysaccharide available in different MW	On average 1 kDa
Very strong water binding capability (~70 H-acceptors and donors / kDa)	Strong water binding capability (~57 H-acceptors and donors / kDa)	Very strong water binding capability (~70 H-acceptors and donors / kDa)
High biologic activity (prebiotic)	Low biologic activity	High biologic activity (prebiotic)
High stability: cannot be degraded by hyaluronidase or regular peptidases	Low stability: will be degraded by hyaluronidase	High stability: cannot be degraded by hyaluronidase or regular peptidases

Table 1: Comparison of AQUARICH®-MAX, Hyaluronic acid and AQUARICH®-OLIGO.

In contrast, AQUARICH®-OLIGO penetrates deeper epidermal and dermal layers, supporting cellular hydration, improved skin tone, evenness, and structural integrity. Its biological activity contributes to reduced epidermal senescence, improved collagen and hyaluronic acid levels, and a balanced, calm complexion, making it a high-performance ingredient for skin longevity concepts **(Table 1)**.

Materials and Methods

Skin hydration was evaluated following a single application of the cosmetic formulation with 0.1% AQUARICH®-MAX, and 0.1% high-molecular weight (HMW) Hyaluronic Acid accordingly, to the forearm. Measurements were taken before product application and subsequently after 30 minutes, as well as after 1 and 2 days. This assessment was conducted on a Chinese panel.

To determine the increase in hyaluronic acid content, normal human dermal fibroblasts (NHDF) were cultured under standard conditions and incubated with 10 ng/ml TGF-β and 0.01%, 0.02% and 0.10 % AQUARICH®-MAX for 48 hours. The hyaluronic acid levels in the culture supernatants were quantified using an ELISA assay.

Skin penetration was assessed after topical application of the cosmetic formulations to the forearm of a European panel. Measurements were performed 30 minutes after application.

The reduction of visible and red spots was examined following twice-daily application of placebo, 0.1% AQUARICH®-OLIGO, and 0.1% of 50 kDa hyaluronic acid to the face over a 28-day period. Evaluations were carried out before treatment, and again after 14 and 28 days on a European panel.

Pore visibility was evaluated using the same application and concentration regimen as for the reduction of visible and red spots. The study involved twice-daily facial application over 28 days, with measurements taken at baseline, day 14, and day 28 on a European panel.

Improvements in dermal parameters were investigated through twice-daily facial application of the cosmetic formulation over 28 days. Assessments were performed before treatment and after 14 and 28 days on a European panel.

Results

AQUARICH®-MAX produced a rapid and marked increase in skin hydration after a single application. Thirty minutes post-application, hydration levels increased by 59.6% compared to baseline. This improvement was significantly higher than the responses observed with placebo or high-molecular-weight hyaluronic acid.

The hydration effect persisted over time, with a measurable effect still present after 24 and 48 hours, indicating a prolonged moisturization profile. The graph below **(Figure 1)** illustrates the strong and sustained improvement relative to placebo and HMW hyaluronic acid, reflecting the superior water-binding properties of AQUARICH®-MAX.

To further investigate whether this hydration performance is supported by biological activity at the cellular level, the effect of AQUARICH®-MAX on endogenous hyaluronic acid synthesis was evaluated *in-vitro*.

In-vitro testing using NHDF cells showed that AQUARICH®-MAX significantly stimulated endogenous hyaluronic acid production. At the highest tested concentration (0.1%), hyaluronic

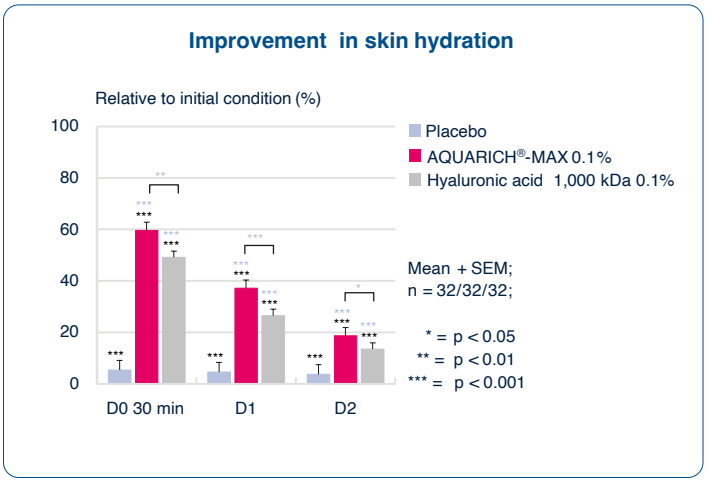


Fig. 1 Improvement in skin hydration of 0.1% AQUARICH®-MAX, 0.1% HMW Hyaluronic acid and placebo across the measurement points of the 48 hours experiment.

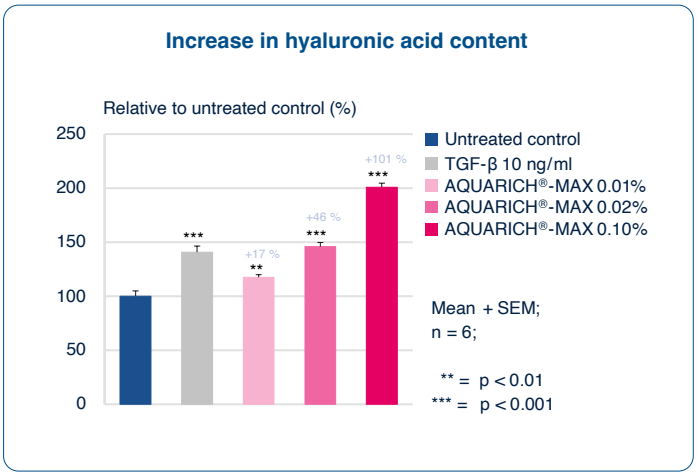


Fig. 2 Dose-dependent relationship of 0.01 %, 0.02 %, and 0.10 % AQUARICH®-MAX to 10 ng/ml TGF-β as positive control, relative to untreated control.

acid levels increased by up to 101% compared to the untreated control. This effect markedly exceeded the response induced by 10 ng/mL TGF-β. TGF-β served as the positive reference as it is a major factor of regulating fibroblast differentiation and was found to be capable to produce matrix bound HA [8]. The bar chart below **(Figure 2)** further shows a clear dose-dependent relationship of AQUARICH®-MAX.

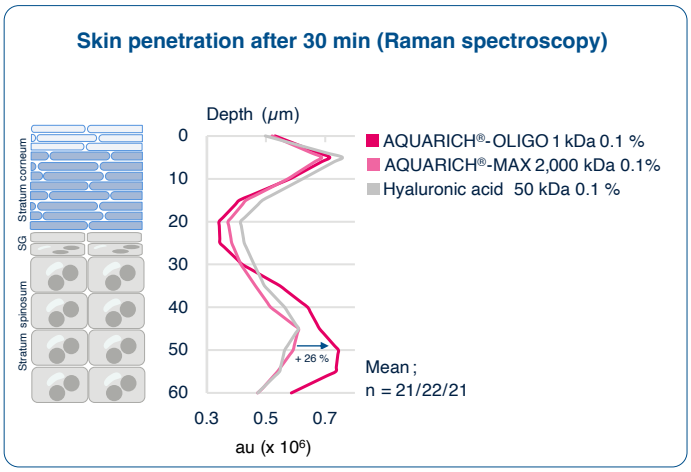


Fig. 3 Depth in skin surface (y-axis) against Raman signal intensity (au x 106).

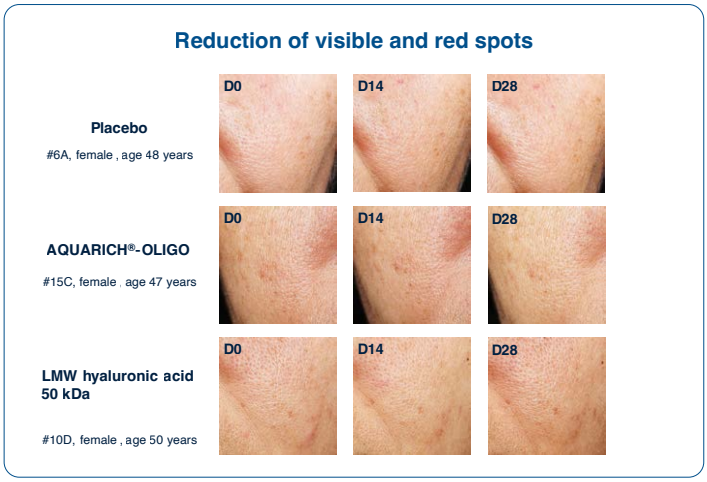


Fig. 4 Reduction of visible and red spots recorded on VISIA photography over the 28-day period.

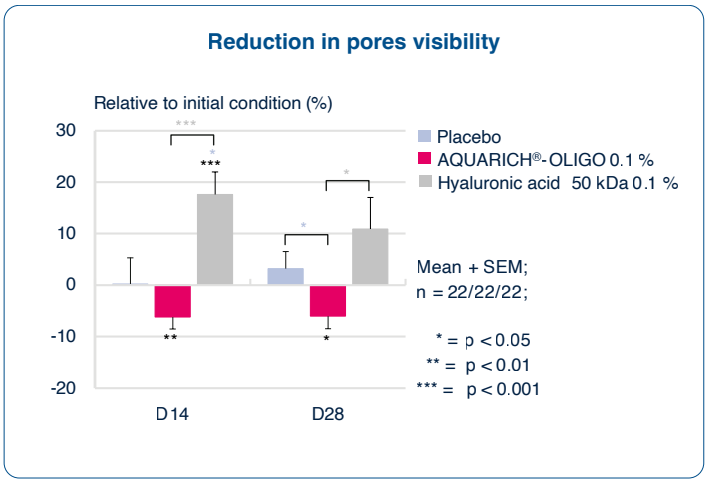


Fig. 5 Reduction of pores area visibility of 0.1 % AQUARICH®-OLIGO, 0.1% LMW hyaluronic acid and placebo at D14 and D28.

All three tested formulations, AQUARICH®-OLIGO, AQUARICH®-MAX, and 50 kDa hyaluronic acid, were tested for skin penetration through Raman spectroscopy at the same concentrations of 0.1 % **(Figure 3)**. High signal intensity was detected in the stratum corneum, which reflects a typical profile for high molecular weight cosmetic substances, confirming the surface moisturizer and film former abilities of AQUARICH®-MAX, AQUARICH®-OLIGO and Hyaluronic Acid.

Due to its low molecular weight, AQUARICH®-OLIGO demonstrated the greatest penetration depth, surpassing Hyaluronic acid by 26%. It penetrated to the stratum granulosum and exhibited the highest Raman signal intensity within the deeper epidermal layers of stratum spinosum after 30 minutes.

The penetration profile confirms that molecular size is a key determinant of epidermal distribution, with AQUARICH®-OLIGO outperforming both AQUARICH®-MAX and 50 kDa hyaluronic acid.

Based on its penetration profile, AQUARICH®-OLIGO was further assessed for its effectiveness in improving skin appearance and tone uniformity, reinforcing its positioning as a low molecular weight longevity ingredient.

Twice-daily facial application of AQUARICH®-OLIGO over 28 days resulted in a 4.5% reduction in visible spots and an 11.9% reduction in red spots compared to baseline. Neither placebo nor the hyaluronic acid produced a comparable effect. AQUARICH®-OLIGO demonstrated significant improvements in reducing visible spots compared to baseline, placebo, and hyaluronic acid. Additionally, it showed a significant reduction in the count of red spots when compared to baseline and placebo. Representative before/after images clearly show the skin-tone evening and reduction in localized redness **(Figure 4)**.

In addition to improvements in skin tone homogeneity, changes in skin surface morphology were investigated, with a focus on pore visibility.

AQUARICH®-OLIGO at a concentration of 0.1% significantly reduced pore visibility over the 28-day treatment period, with improvement evident as early as day 14. At both time points, AQUARICH®-OLIGO outperformed the placebo and the 50 kDa hyaluronic

acid reference, the latter showing a 17.6% increase in pore visibility at day 14 and remaining above baseline at day 28. Image analysis confirmed an approximate 6% reduction after 28 days compared to baseline, while placebo exhibited only minimal variation.

The bar chart **(Figure 5)** further illustrates these differences, highlighting the consistent reduction achieved by AQUARICH®-OLIGO at day 14 and day 28, in contrast to the persistent increase observed with the hyaluronic acid reference and the negligible changes with placebo.

Photographic documentation **(Figure 6)** supports these instrumental findings. AQUARICH®-OLIGO shows a visible refinement of skin surface structure from D0 to D28, with progressively less pronounced pore openings. In comparison, placebo images show minimal changes, whereas the hyaluronic acid reference displays increased prominence throughout the study period.

Finally, to evaluate whether these visual improvements are accompanied by structural changes within the dermis, subepidermal low echogenicity band (SLEB) thickness and dermal density were assessed using ultrasound imaging **(Figure 7)**.

After 28 days, AQUARICH®-OLIGO decreased the sub-epidermal low-echogenic band (SLEB) thickness by 12.5%, and overall dermal density increased by 25.7% relative to initial condition. Both parameters showed significant differences compared to the placebo group after the 28-day period. Ultrasound images illustrate the progressive increase in echogenicity within the dermis with AQUARICH®-OLIGO over the 28-day period.

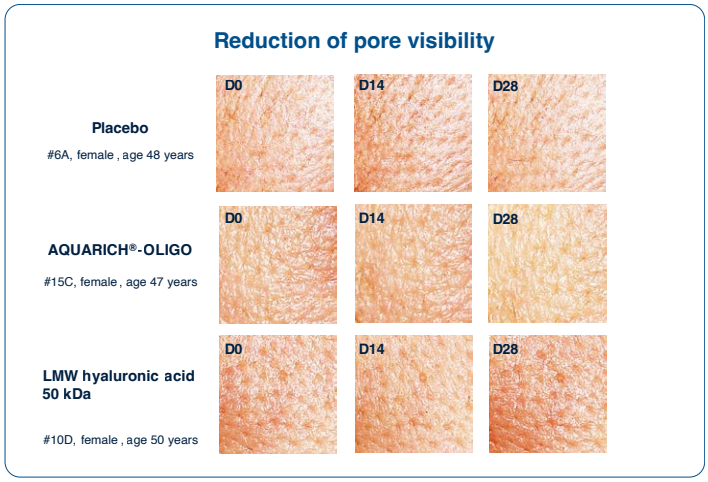


Fig. 6 Photographic documentation of pore visibility with 0.1% AQUARICH®-OLIGO, 0.1% LMW hyaluronic acid and placebo at D14 and D28.

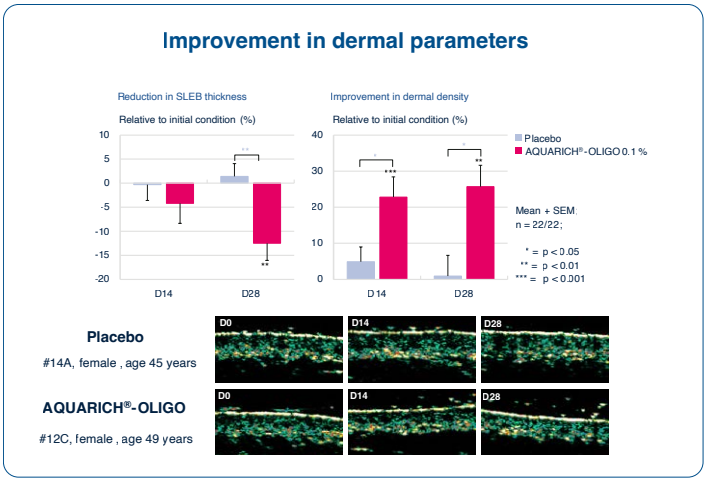


Fig. 7 Measurements of dermal collagen by means of ultrasonography of 0.1% AQUARICH®-OLIGO compared to placebo relative to initial condition as well as SLEB band of the tested formulations.

Discussion

The results demonstrate the multifunctional performance of AQUARICH®-MAX and AQUARICH®-OLIGO across complementary skin parameters. The rapid and long-lasting hydration observed after a single application of AQUARICH®-MAX highlights its strong water-binding and water-retention capacity. The effect exceeded that of high-molecular-weight hyaluronic acid, indicating an enhanced ability to support skin moisture. The prolonged hydration up to 48 hours suggests that high molecular weight γ-PGA interacts efficiently with the stratum corneum matrix, contributing to a more stable hydration profile.

The *in-vitro* experiments further support this assumption, as AQUARICH®-MAX significantly stimulated endogenous hyaluronic acid synthesis in dermal fibroblasts. The increase of up to 101% compared to untreated control, and the stronger effect relative to TGF-β underline its capacity to activate dermal pathways responsible for maintaining hydration. Together, the *in-vivo* and *in-vitro* results point toward a dual mechanism involving both immediate and long-lasting hydration on the skin surface and enhanced intrinsic moisturization through increased hyaluronic acid production.

The penetration study provides additional mechanistic insight. AQUARICH®-OLIGO, due to its low molecular weight, penetrated deeply into the epidermal layers, reaching the stratum granulosum most effectively compared to LMW hyaluronic acid and AQUARICH®-MAX. This deeper deposition aligns with the functional benefits observed *in-vivo*, particularly in the reduction of visible and red spots, pore visibility, and improvements in dermal parameters.

The reduction in pore visibility observed for AQUARICH®-OLIGO can be explained by differences in hydration depth and tissue response when compared to conventional hyaluronic

acid. Superficial hydration induced by hyaluronic acid primarily affects the stratum corneum, leading to epidermal swelling and surface-level plumping. This swelling increases the topography between pores and the surrounding tissue, causing pores to appear larger and more pronounced. This mechanism is consistent with the observed increase in pore visibility for the hyaluronic acid reference during the clinical study.

In contrast, AQUARICH®-OLIGO provides deeper hydration and supports collagen-related dermal processes, resulting in a more uniform hydration profile across epidermal and dermal layers. This deeper tissue hydration leads to dermal plumping and improved firmness, leveling the skin surface between pores rather than accentuating pore openings. As a result, pores appear smaller and less visible. The early and sustained reduction in pore visibility measured instrumentally, together with the photographic documentation, is consistent with this depth-dependent mechanism.

The improvements in dermal structure observed by ultrasound further support this interpretation. The reduction in SLEB thickness and the increase in dermal density indicate enhanced dermal organization, which contributes to improved mechanical support of the epidermis.

Taken together, the data positions AQUARICH®-MAX as a hydration-focused active delivering both immediate and long-lasting moisturization benefits. Its rapid increase in skin hydration, combined with sustained effects as well as stimulation of endogenous hyaluronic acid synthesis highlights its role that supports both surface water retention and intrinsic moisture regulation.

In contrast, AQUARICH®-OLIGO addresses skin quality and resilience through deeper epidermal penetration and progressive structural improvements. Its ability to penetrate viable skin layers is reflected in long-term benefits on skin tone uniformity, pore visibility, and dermal architecture. The observed improvements in dermal density and reduction of SLEB thickness further indicate support of skin structure over time.

Together, AQUARICH®-MAX and AQUARICH®-OLIGO form a complementary active concept that combines immediate hydration performance with long-term skin improvement, addressing both short-term sensory needs and long-term skin health in modern cosmetic formulations.

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