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Synergistic Effects of 4D Hyaluronic Acid and γ-Polyglutamic Acid in Hydration Enhancement and Anti-Aging: Immediate and Long-Term Efficacy.

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BACKGROUND

Hydration plays a fundamental role in maintaining skin health and delaying the visible signs of aging [1]. Formulations combining multi-dimensional hyaluronic acid (4D-HA) and y-polyglutamic acid (y-PGA) offer a promising approach to enhancing skin hydration and strengthening the epidermal barrier. This study evaluated the synergistic effects of 4D-HA and y-PGA in improving hydration, reducing transepidermal water loss (TEWL), and addressing key anti-aging parameters in a short-term single application, as well as a 4-week treatment.

METHODS

Formulations containing 2% 4D-HA, 2% y-PGA, and their combination were tested for hydration enhancement and TEWL reduction over 5 hours following a single application. Skin topography, including scaliness and fine lines, was analyzed 3 hours post-application. Additionally, a 4-week study was conducted with 24 female volunteers aged 22–58 to evaluate the anti-aging efficacy of a topical formulation containing the 4D-HA/y-PGA combination enriched with Laminaria ochroleuca extract, vitamin E, and shea butter. Parameters assessed included skin firmness, melanin content, and smoothness. Subjective analysis was performed based on survey data.

RESULTS

The combination of 4D-HA and y-PGA demonstrated synergistic effects in hydration enhancement, significantly outperforming the individual ingredients. The formulation also effectively reduced transepidermal water loss (TEWL) over a 5-hour period following a single application, providing prolonged and consistent results compared to the individual components. Skin topography analysis showed a significant reduction in scaliness and fine lines within 3 hours of a single application, highlighting immediate skin-smoothing benefits.

In the 4-week study, the enriched 4D-HA/y-PGA formulation containing Laminaria ochroleuca extract, vitamin E, and shea butter (no. 2672) evoked notable anti-aging effects. Skin firmness improved by 39% in the whole group and by 46%, with 90% of participants experiencing significant enhancements. A 12% reduction in melanin content was observed, indicating a brightening effect, while smoothness increased by 34% in 60% of volunteers, reflecting a visible reduction in fine lines and texture irregularities. These results underscore the potent efficacy of the formulation in addressing multiple signs of aging through improved hydration and barrier function.

Preliminary in vivo study



Figure 1. Instrumental measurement of skin moisturization taken 5 hours after a single application of the tested emulsion containing 2% of 4D-hyaluronic acid or Y-PGA and their combination. Emulsion showed synergy effect (4,6 accordind to Kull's equation*) measured for results obtained after 5 h. *score >1 indicates a synergy effect



Figure 2. Instrumental measurement of transepidermal water loss (TEWL) taken 5 hours after a single application of the tested emulsion containing 12% of 4D-hyaluronic acid or Y-PGA and their combination. Emulsion showed synergy effect (3,7 according to Kull's equation*) in all measured points.

D0



Figure 3. Instrumental measurement of skin topography (Visioscan, Scaliness) taken 3 hours after a single application of the tested emulsion containing 2% of 4D-hyaluronic acid and 2% Y-PGA, which showed synergy effect.



Figure 4. Instrumental measurement of fine wrinkles and unevenness (Visioscan, Volume) taken 3 hours after a single application of the tested emulsion containing 2% of 4Dhyaluronic acid and 2% Y-PGA, which showed synergy effect.

D28

In vivo study, formulation 2672

D28



Figure 5. Female subject (age 55). Instrumental analysis showed the reduction in number and volume of wrinkles (by 37% and 39%, respectively) after 4 weeks of product application.



Figure 6. Female subject (age 58). Instrumental analysis showed the reduction in number and volume of wrinkles (by 38% and 20%, respectively) after 4 weeks of product application.



Figure 7. Female subject (age 55). Instrumental analysis showed the reduction in number and volume of wrinkles (by 28% and 32%, respectively) after 4 weeks of product application.

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Figure 8. Female subject (age 50). Instrumental analysis showed the reduction in numbers and intensity of discolorations (by 30% and 17%, respectively) after 4 weeks of product application.

Instrumental evaluation of skin condition (n=10)		
Skin parameter	Results	
Ser- skin scaliness	Improvement (reduction in skin scaliness) by 48% in 60% of volunteers and for whole group by 16%	
Sesm – smoothness with moisturization	Improvement in skin smoothness with moisturization by 34% in 60% of volunteers	
Surface – level of skin smoothness	Improvement in skin smoothness by 12% in 70% of volunteers and for whole group by 5%	

Table 1. Instrumental evaluation of skin condition before and after 4 weeks test of product usage. Skin parameters measured: Ser, Sesm and Surface topography parametrs - Visioscan VC 20 plus. All measured skin parameters improved.



Figure 9. Instrumental evaluation of skin condition before and after 4 weeks test of product usage. Skin parameters measured: Skin parameters measured: firmness- Cutometer Dual MPA 580; melanin content, skin redness- Mexameter MX18. All measured skin parameters improved. All measured skin parameters improved.

CONCLUSIONS

Volunteers' self-assessment taken after 3 weeks of tested product usage (n= 23).		
Statement	% of volunteers	
Skin is soft to the touch	100%	
Skin is smoother	87%	
Product improves the skin's elasticity	78%	
Skin feels firmer	78%	
Skin is intensely moisturized and this effect is long-lasting	74%	

Table 2. Volunteers self-assessment taken after 4 weeks of tested product usage.

Self- assessment taken by volunteers confirmed, that tested night cream improved skin smoothness, elasticity and firmness. It also made soft to the touch. Moreover volunteers noticed improvement in skin moisturization and that efekt is long-lasting.

The results demonstrate the efficacy of combining 4D-HA and γ-PGA in enhancing hydration and skin barrier function, essential components of an anti-aging regimen. Synergistic effect of two potent moisturizers was an unexpected outcome leading to a notable, long-lasting hydration after a single application. The enriched formulation further underscores the role of proper hydration in improving skin firmness, reducing pigmentation, and enhancing smoothness. These findings support the integration of multi-dimensional hydration strategies into anti-aging treatments to strengthen the skin barrier and slow aging processes. Further studies are warranted to explore long-term benefits and potential applications in broader populations.

SIGNIFICANCE

This research advances the understanding of how targeted hydration strategies can impact skin aging. The demonstrated efficacy of the 4D-HA and y-PGA combination, especially when enriched with other active ingredients, offers a scientifically grounded approach to designing skincare formulations that promote hydration, barrier function, and anti-aging benefits. These findings support the integration of advanced hydrating agents into aesthetic medicine practices, bridging the gap between cosmetic skincare and therapeutic skin health interventions

References

1. Bukhari SNA et al. Hyaluronic acid, a promising skin rejuvenating biomedicine: A review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. Int J Biol Macromol. 2018