

Supplementary material.

Oral supplementation with a new hyaluronic acid matrix ingredient, improves skin brightness, hydration, smoothness and roughness: Results from a randomized double-blinded, placebo-controlled study

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Table S1: Changes in skin barrier function and skin properties after the follow-up

Parameters	Area	Change in placebo group (n=24)	Change in HAm group (n=26)	p ¹	p ²	p ³
Hydration (AU), V2	Periocular Area	2.1 ± 15.0	5.7 ± 13.5*	0.337 (t)	0.033 (t)	0.3850 (t)
Hydration (AU), V3		2.2 ± 10.3	5.3 ± 12.1*	0.309 (t)	0.033 (t)	0.3264 (t)
Hydration (AU), V2	Cheek	10.2 ± 13.4**	10.8 ± 15.5**	0.002 (t)	0.002 (t)	0.8875 (t)
Hydration (AU), V3		9.7 ± 14.8**	10.6 ± 15.6**	0.004 (t)	0.002 (t)	0.8498 (t)
Elasticity R2 (%), V2	Periocular Area	-0.7 ± 18.1	-5.6 ± 19.6	0.858 (t)	0.156 (t)	0.3589 (t)
Elasticity R2 (%), V3		-1.8 ± 20.2	-5.4 ± 22.4	0.245 (w)	0.232 (t)	0.4664 (u)
Elasticity R2 (%), V2	Cheek	-8.0 ± 13.7**	-10.4 ± 20.9**	0.008 (t)	0.004 (w)	0.8082 (u)
Elasticity R2 (%), V3		-6.3 ± 15.7	-10.8 ± 16.4**	0.060 (t)	0.003 (t)	0.3347 (t)
Hardness (Shore 0), V2	Periocular Area	-1.8 ± 3.2*	-2.0 ± 5.2	0.011 (t)	0.089 (w)	0.5407 (u)
Hardness (Shore 0), V3		-3.2 ± 4.2**	-3.5 ± 5.5**	0.001 (t)	0.001 (w)	0.9458 (u)
pH, V2	Periocular Area	-0.3 ± 0.6*	-0.1 ± 0.6	0.018 (t)	0.397 (t)	0.2577 (t)
pH, V3		-0.5 ± 0.5****	-0.2 ± 0.5	<0.0001 (t)	0.113 (t)	0.0298 # (t)
Temperature (°C), V2	Periocular Area	-0.9 ± 2.0*	-0.8 ± 1.3**	0.038 (t)	0.003 (t)	0.8899 (w)
Temperature (°C), V3		-0.3 ± 1.5	-0.8 ± 1.1**	0.321 (t)	0.001 (t)	0.2399 (t)
Total Antioxidant Capacity (μC), V2	Periocular Area	-1.2 ± 3.4	-0.7 ± 3.8*	0.190 (w)	0.0368 (t)	0.4844 (u)
Total Antioxidant Capacity (μC), V3		-2.0 ± 2.9**	-2.4 ± 4.2**	0.002 (t)	0.009 (t)	0.7312 (t)
Erythema Index (AU), V2	Periocular Area	-11.3 ± 52.4	-23.3 ± 56.0*	0.3000 (t)	0.044 (t)	0.4381 (t)
Erythema Index (AU), V3		-6.7 ± 44.1	0.3 ± 63.4	0.2379 (w)	0.595 (w)	0.9458 (u)
Melanin Index (AU), V2	Periocular Area	0.0 ± 13.8	-5.5 ± 29.4	0.991 (t)	0.553 (w)	0.7049 (t)

Parameters	Area	Change in placebo group (n=24)	Change in HAm group (n=26)	p ¹	p ²	p ³
Melanin Index (AU), V3		-8.3 ± 19.9	-4.0 ± 34.2	0.052 (t)	0.419 (w)	0.7194 (t)
Deformability, V2 (mm)	Periocular Area	-0.1 ± 0.4	-0.1 ± 0.4	0.450 (t)	0.155 (t)	0.7261 (t)
Deformability (mm), V3		-0.4 ± 0.5***	-0.6 ± 0.4*****	0.0002 (t)	<0.0001 (t)	0.1661 (t)
Friction (AU), V2	Periocular Area	-11.9 ± 62.8	11.0 ± 72.5	0.363 (t)	0.447 (t)	0.2408 (t)
Friction (AU), V3		50.9 ± 138.4	40.1 ± 123.8	0.1753 (w)	0.364 (w)	0.7267 (u)
Brightness/Glow (AU), V2	Periocular Area	0.2 ± 1.6	0.8 ± 1.6*	0.523 (w)	0.017 (t)	0.1803 (u)
Brightness/Glow (AU), V3		0.6 ± 1.6	1.3 ± 1.8**	0.057 (t)	0.001 (t)	0.1830 (t)
Wrinkles (SE _w) - V2	Periocular Area	16.5 ± 47.8	-12.4 ± 51.0	0.104 (t)	0.226 (t)	0.044 [#] (t)
Wrinkles (SE _w) - V3		12.7 ± 45.7	-3.3 ± 68.6	0.185 (t)	0.806 (t)	0.3386 (t)
Wrinkles (SE _w) - V2	Cheek	12.5 ± 61.1	26.0 ± 35.0***	0.327 (t)	0.0009 (t)	0.3499 (w)
Wrinkles (SE _w) - V3		7.5 ± 55.4	17.2 ± 58.8	0.512 (t)	0.149 (t)	0.5548 (t)
Roughness (SE _r) - V2	Periocular Area	0.4 ± 2.3	0.3 ± 2.4	0.667 (w)	0.591 (t)	0.8082 (u)
Roughness (SE _r) - V3		0.2 ± 1.9	0.2 ± 1.7	0.5316 (t)	0.5467 (t)	0.9419 (t)
Roughness (SE _r) - V2	Cheek	-0.2 ± 1.3	0.7 ± 1.8	0.487 (t)	0.055 (w)	0.057 (u)
Roughness (SE _r) - V3		-0.3 ± 1.4	0.8 ± 1.5*	0.5980 (w)	0.0129 (t)	0.029 [#] (u)
Scaliness (SE _{sc}) - V2	Periocular Area	-0.3 ± 1.3	-0.6 ± 1.5*	0.3949 (w)	0.010 (w)	0.260 (u)
Scaliness (SE _{sc}) - V3		-0.3 ± 1.7	-0.8 ± 1.5**	0.203 (w)	0.009 (w)	0.5216 (u)
Scaliness (SE _{sc}) - V2	Cheek	0.1 ± 1.4	-0.1 ± 0.8	0.3641 (w)	0.5606 (t)	0.4203 (u)
Scaliness (SE _{sc}) - V3		-0.1 ± 1.0	-0.2 ± 0.9	0.8368 (w)	0.0750 (w)	0.1399 (u)
Smoothness (SE _{sm}) - V2	Periocular Area	34.1 ± 131.9	-71.1 ± 149.3*	0.2182 (t)	0.023 (t)	0.011 [#] (t)

Parameters	Area	Change in placebo group (n=24)	Change in HAm group (n=26)	P ¹	P ²	P ³
Smoothness (SE _{sm}) - V3		21.2 ± 191.7	-34.0 ± 189.8	0.5927 (t)	0.370 (t)	0.3115 (t)
Smoothness (SE _{sm}) - V2	Cheek	29.5 ± 130.7	46.3 ± 102.1*	0.279 (t)	0.029 (t)	0.6142 (t)
Smoothness (SE _{sm}) - V3		27.4 ± 141.8	20.1 ± 132.4	0.3528 (t)	0.446 (t)	0.8508 (t)

Abbreviations: Hyaluronic Acid Matrix (HAm); Stratum Corneum Hydration (SCH); Arbitrary Units (AU).

Data are expressed as absolute change (mean ± standard error). V2= changes V2 vs V1. V3=changes V3 vs V1.

P¹ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in placebo group.

P² value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in HAm group.

P³ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) test for independent samples to compare the change between placebo and HAm group.

*=p <0.05, **=p<0.01, ***=p<0.001 and ****= p<0.0001 vs basal; # =p<0.05 vs placebo

Table S2: Changes in skin according to age participants > 55 years old

Parameters	Area	Change in placebo group (n=17)	Change in HAM group (n=11)	P ¹	P ²	P ³
Hydration (AU), V2	Periocular Area	-0.8 ± 3.9	8.0 ± 4.9	0.7556 (t)	0.4603 (t)	0.1612 (t)
Hydration (AU), V3		1.1 ± 2.8	2.0 ± 2.6	0.7094 (t)	0.4603(t)	0.8218 (t)
Hydration (AU), V2	Cheek	8.9 ± 3.4*	14.9 ± 4.3**	0.0208 (t)	0.0063 (t)	0.2809 (t)
Hydration (AU), V3		10.4 ± 3.3**	8.4 ± 5.0	0.0067(t)	0.1251 (t)	0.7321 (t)
Elasticity R2 (%), V2	Periocular Area	1.8 ± 4.1	-1.5 ± 4.8	0.6722 (t)	0.7676 (t)	0.6185 (t)
Elasticity R2 (%), V3		-0.8 ± 5.7	-8.3 ± 3.9	0.4714 (w)	0.0575 (t)	0.3711 (u)
Elasticity R2 (%), V2	Cheek	-9.1 ± 3.1*	-12.5 ± 6.6*	0.0103 (t)	0.0449 (w)	0.9812 (u)
Elasticity R2 (%), V3		-6.7 ± 3.9	-9.6 ± 3.3*	0.1039 (t)	0.0163 (t)	0.6017 (t)
Hardness (Shore 0), V2	Periocular Area	-2.1 ± 0.8*	-2.7 ± 2.1	0.0141 (t)	0.3203 (w)	0.5253 (u)
Hardness (Shore 0), V3		-3.0 ± 1.1*	-4.1 ± 2.2	0.0176 (t)	0.0830 (w)	0.9064 (u)
pH, V2	Periocular Area	-0.3 ± 0.1	0.0 ± 0.2	0.0841 (t)	0.9777 (t)	0.2766 (t)
pH, V3		-0.4 ± 0.1**	0.0 ± 0.2	0.0037 (t)	0.9830 (t)	0.0456# (t)
Temperature (°C), V2	Periocular Area	-1.1 ± 0.5*	-1.1 ± 0.3**	0.0438 (t)	0.0066 (t)	0.9075 (t)
Temperature (°C), V3		-0.1 ± 0.4	-1.1 ± 0.4**	0.883(t)	0.009 (t)	0.0562 (t)
Total Antioxidant Capacity (μC), V2	Periocular Area	-1.0 ± 0.8	-1.7 ± 1.2	0.2019 (t)	0.1877 (t)	0.6041 (t)
Total Antioxidant Capacity (μC), V3		-1.9 ± 0.7*	-3.9 ± 0.9**	0.0125 (t)	0.0018 (t)	0.0915 (t)
Erythema Index (AU), V2	Periocular Area	-10.0 ± 11.7	-19.5 ± 14.1	0.4035 (t)	0.1973 (t)	0.6111 (t)
Erythema Index (AU), V3		0.0 ± 11.8	11.7 ± 19.0	0.7467 (w)	0.5515 (t)	0.7419 (u)
Melanin Index (AU), V2	Periocular Area	3.6 ± 3.2	3.5 ± 7.4	0.2854 (t)	0.6485 (t)	0.9949 (t)
Melanin Index (AU), V3		-5.3 ± 4.1	8.2 ± 10.1	0.2137 (t)	0.4369 (t)	0.2380 (t)
Deformability, V2 (mm)	Periocular Area	-0.1 ± 0.1	0.0 ± 0.1	0.5528 (t)	0.9796 (t)	0.7003 (t)
Deformability (mm), V3		-0.4 ± 0.1**	-0.8 ± 0.1*****	0.0057 (t)	<0.0001 (t)	0.0393 # (t)
Friction (AU), V2	Periocular Area	4.0 ± 11.9	38.3 ± 21.5	0.7405 (t)	0.1051 (t)	0.1421 (t)
Friction (AU), V3		62.3 ± 36.1	55.6 ± 43.6	0.1594 (w)	0.3652 (w)	0.8141 (u)
Brightness/Glow (AU), V2	Periocular Area	0.1 ± 0.4	0.6 ± 0.5	0.8831 (w)	0.2252 (t)	0.4098 (u)
Brightness/Glow (AU), V3		0.6 ± 0.4	1.7 ± 0.7*	0.1782 (t)	0.0308 (t)	0.1624 (t)

Parameters	Area	Change in placebo group (n=17)	Change in HAm group (n=11)	P ¹	P ²	P ³
Wrinkles (SE_w) - V2	Periocular Area	16.6 ± 11.2	-22.2 ± 16.9	0.1568 (t)	0.6377 (w)	0.1448 (u)
Wrinkles (SE_w) - V3		10.0 ± 12.1	-12.8 ± 20.1	0.4185 (t)	0.5387 (t)	0.3092 (t)
Wrinkles (SE_w) - V2	Cheek	6.0 ± 16.6	17.5 ± 11.4	0.7237 (t)	0.1568 (t)	0.6162 (t)
Wrinkles (SE_w) - V3		15.2 ± 15.1	6.0 ± 18.2	0.3281(t)	0.7475 (t)	0.7024 (t)
Roughness (SE_r) - V2	Periocular Area	-0.3 ± 0.4	0.2 ± 0.9	0.4938 (t)	0.7646 (w)	0.9250 (u)
Roughness (SE_r) - V3		-0.2 ± 0.5	0.2 ± 0.5	0.7102 (t)	0.7439 (t)	0.6291 (t)
Roughness (SE_r) - V2	Cheek	-0.3 ± 0.3	0.9 ± 0.4*	0.2644 (t)	0.050 (t)	0.0174 [#] (t)
Roughness (SE_r) - V3		-0.3 ± 0.4	1.1 ± 0.5*	0.8176 (w)	0.0601 (t)	0.0431 [#] (u)
Scaliness (SE_{sc}) - V2	Periocular Area	-0.2 ± 0.3	-1.0 ± 0.6	0.7909 (w)	0.1093 (t)	0.1263 (u)
Scaliness (SE_{sc}) - V3		-0.5 ± 0.3	-1.4 ± 0.6*	0.1749 (t)	0.0364 (t)	0.1725 (u)
Scaliness (SE_{sc}) - V2	Cheek	0.2 ± 0.1	-0.3 ± 0.3	0.1900 (t)	0.3638 (t)	0.1786 (w)
Scaliness (SE_{sc}) - V3		0.2 ± 0.1	-0.4 ± 0.2	0.1355 (w)	0.4219 (w)	0.1148 (u)
Smoothness (SE_{sm}) - V2	Periocular Area	51.8 ± 29.8	-88.3 ± 62.6	0.1010 (t)	0.1889 (t)	0.0330 [#] (t)
Smoothness (SE_{sm}) - V3		34.5 ± 53.5	-79.4 ± 62.8	0.5274 (t)	0.2348 (t)	0.1841 (t)
Smoothness (SE_{sm}) - V2	Cheek	28.6 ± 28.4	15.8 ± 35.3	0.3674 (t)	0.6636 (t)	0.7910 (t)
Smoothness (SE_{sm}) - V3		66.8 ± 30.2*	-25.2 ± 37.6	0.0384 (t)	0.5176 (t)	0.0643 (t)

Abbreviations: Hyaluronic Acid Matrix (HAm); Arbitrary Units (AU).

Data are expressed as absolute change (mean ± standard error). V2= changes V2 vs V1. V3=changes V3 vs V1.

P¹ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in placebo group.

P² value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in HAm group.

P³ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) test for independent samples to compare the change between placebo and HAm group.

*=p <0.05, **=p<0.01, ***=p<0.001 and ****= p<0.0001 vs basal; # =p<0.05 vs placebo

Table S3: Changes in skin according to age participants ≤ 55 years old

Parameters	Area	Change in placebo group (n=7)	Change in HAM group (n=15)	p ¹	p ²	p ³
Hydration (AU), V2	Periocular Area	8.9 $\pm$ 4.7	4.0 $\pm$ 2.9*	0.0734 (t)	0.0472 (t)	0.3737 (t)
Hydration (AU), V3		4.9 $\pm$ 2.3	7.8 $\pm$ 3.6*	0.0734 (w)	0.0472 (t)	0.5018 (w)
Hydration (AU), V2	Cheek	13.1 $\pm$ 5.0	7.7 $\pm$ 4.2	0.0781 (w)	0.0850 (t)	0.2903 (u)
Hydration (AU), V3		8.2 $\pm$ 6.9	12.2 $\pm$ 3.9**	0.2802 (t)	0.0078 (t)	0.5957 (t)
Elasticity R2 (%), V2	Periocular Area	-6.6 $\pm$ 7.9	-8.7 $\pm$ 5.7	0.4381 (t)	0.1474 (t)	0.8344 (t)
Elasticity R2 (%), V3		-4.0 $\pm$ 3.6	-3.3 $\pm$ 7.2	0.3032 (w)	0.6554 (t)	0.9279 (w)
Elasticity R2 (%), V2	Cheek	-5.4 $\pm$ 6.1	-8.9 $\pm$ 5.4	0.4059 (t)	0.1225 (t)	0.7052 (t)
Elasticity R2 (%), V3		-5.4 $\pm$ 6.0	-11.6 $\pm$ 5.1*	0.4027 (t)	0.0399 (t)	0.4806 (t)
Hardness (Shore 0), V2	Periocular Area	-1.0 $\pm$ 1.3	-1.5 $\pm$ 1.0	0.4537 (t)	0.1511 (t)	0.7677 (t)
Hardness (Shore 0), V3		-3.6 $\pm$ 1.1*	-3.1 $\pm$ 1.0**	0.0210 (t)	0.0086 (t)	0.7723 (t)
pH, V2	Periocular Area	-0.4 $\pm$ 0.2	-0.2 $\pm$ 0.2	0.1247 (t)	0.2973 (t)	0.4641 (t)
pH, V3		-0.6 $\pm$ 0.2**	-0.3 $\pm$ 0.1*	0.0051 (t)	0.0279(t)	0.1374 (t)
Temperature (°C), V2	Periocular Area	-0.5 $\pm$ 0.8	-0.6 $\pm$ 0.4	0.5485 (t)	0.1127 (t)	0.8942 (t)
Temperature (°C), V3		-0.9 $\pm$ 0.5	-0.5 $\pm$ 0.2	0.1201 (t)	0.0723 (t)	0.3543 (t)
Total Antioxidant Capacity (µC), V2	Periocular Area	-1.5 $\pm$ 1.6	0.1 $\pm$ 0.9	0.3660 (t)	0.9130 (t)	0.3442 (t)
Total Antioxidant Capacity (µC), V3		-2.3 $\pm$ 1.2	-1.3 $\pm$ 1.2	0.1145 (t)	0.5081 (w)	0.2592 (u)
Erythema Index (AU), V2	Periocular Area	-14.5 $\pm$ 24.8	-26.1 $\pm$ 16.3	0.5799 (t)	0.1318 (t)	0.6951 (t)
Erythema Index (AU), V3		-22.8 $\pm$ 10.1	-8.1 $\pm$ 16.7	0.0650 (t)	0.6332 (t)	04591 (w)
Melanin Index (AU), V2	Periocular Area	-8.5 $\pm$ 4.5	-12.1 $\pm$ 8.1	0.1079 (t)	0.4974 (w)	0.4809 (u)
Melanin Index (AU), V3		-15.7 $\pm$ 9.8	-12.9 $\pm$ 8.5	0.1589 (t)	0.1511 (t)	0.8444 (t)
Deformability, V2 (mm)	Periocular Area	-0.1 $\pm$ 0.2	-0.2 $\pm$ 0.1	0.6793 (t)	0.0737 (t)	0.5218 (t)
Deformability (mm), V3		-0.5 $\pm$ 0.2*	-0.5 $\pm$ 0.1**	0.0127 (t)	0.0017 (t)	0.8758 (t)
Friction (AU), V2	Periocular Area	-50.5 $\pm$ 29.9	-9.1 $\pm$ 17.8	0.1428 (t)	0.6176 (t)	0.2239 (t)
Friction (AU), V3		23.3 $\pm$ 43.1	28.7 $\pm$ 28.5	0.6081 (w)	0.7615 (w)	0.8879 (u)
Brightness/Glow (AU), V2	Periocular Area	0.5 $\pm$ 0.5	1.0 $\pm$ 0.4*	0.3440 (t)	0.0494 (w)	0.3237 (u)
Brightness/Glow (AU), V3		0.7 $\pm$ 0.3	1.0 $\pm$ 0.3*	0.0898 (t)	0.0115 (t)	0.6518 (t)
Wrinkles (SE _w) - V2	Periocular Area	16.3 $\pm$ 20.9	-5.3 $\pm$ 12.3	0.4665 (t)	0.6756 (t)	0.3593 (t)
Wrinkles (SE _w) -V3		19.4 $\pm$ 13.9	3.6 $\pm$ 18.4	0.2137 (t)	0.8479 (t)	0.5908 (t)

Parameters	Area	Change in placebo group (n=7)	Change in HAM group (n=15)	P ¹	P ²	P ³
Wrinkles (SE _w) - V2	Cheek	28.3 ± 14.1	32.2 ± 8.4**	0.0909 (t)	0.0018 (t)	0.8170 (t)
Wrinkles (SE _w) - V3		-11.0 ± 11.6	25.4 ± 15.1	0.3769 (t)	0.1151 (t)	0.1397 (t)
Roughness (SE _r) - V2	Periocular Area	2.0 ± 1.1	0.3 ± 0.5	0.1271 (t)	0.5687 (t)	0.1181 (t)
Roughness (SE _r) - V3		1.3 ± 0.3**	0.2 ± 0.4	0.0034 (t)	0.8469 (w)	0.0345 [#] (t)
Roughness (SE _r) - V2	Cheek	0.2 ± 0.6	0.6 ± 0.5	0.8158 (t)	0.3894 (w)	0.3976 (u)
Roughness (SE _r) - V3		-0.2 ± 0.2	0.5 ± 0.3	0.3810 (t)	0.1261 (t)	0.0759 (u)
Scaliness (SE _{sc}) - V2	Periocular Area	-0.5 ± 0.5	-0.2 ± 0.2	0.3850 (t)	0.0699 (w)	0.6217 (u)
Scaliness (SE _{sc}) - V3		0.3 ± 0.9	-0.3 ± 0.2	0.4375 (w)	0.1765 (t)	0.6723 (u)
Scaliness (SE _{sc}) - V2	Cheek	-0.1 ± 1.0	0.0 ± 0.2	0.9588 (t)	0.8881 (t)	0.9381 (w)
Scaliness (SE _{sc}) - V3		-0.8 ± 0.6	-0.1 ± 0.3	0.2188 (w)	0.1937 (w)	0.8601 (u)
Smoothness (SE _{sm}) - V2	Periocular Area	-9.0 ± 57.9	-58.5 ± 23.8*	0.8818 (t)	0.0286 (t)	0.3556 (t)
Smoothness (SE _{sm}) - V3		-11.1 ± 53.5	-0.7 ± 62.8	0.7745 (t)	0.9882 (t)	0.8853 (t)
Smoothness (SE _{sm}) - V2	Cheek	31.7 ± 56.5	68.6 ± 22.4**	0.5947 (t)	0.0085 (t)	0.4701 (t)
Smoothness (SE _{sm}) - V3		-68.2 ± 30.2	53.4 ± 37.6	0.2712 (t)	0.1395 (t)	0.0672 (t)

Abbreviations: Hyaluronic Acid Matrix (HAM); Arbitrary Units (AU).

Data are expressed as absolute change (mean ± standard error). V2= changes V2 vs V1. V3=changes V3 vs V1.

P¹ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in placebo group.

P² value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) for dependent samples to compare changes in each visit in HAM group.

P³ value after using Student T test (t), Wilcoxon test (w) or Mann-Whitney U test (u) test for independent samples to compare the change between placebo and HAM group.

*=p <0.05, **=p<0.01, ***=p<0.001 and ****= p<0.0001 vs basal; # =p<0.05 vs placebo