

A large, white, 3D-rendered ribbon graphic that curves and loops across the left side of the image.

CrossLinked^{HA}

CrossLinkedHA for topical application

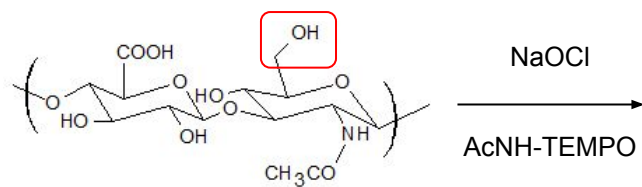
- Creates solid hydrogels in water solutions
- Often used as a dermal filler
- More types exist on the market
- Contipro's type is dedicated **for topical applications**



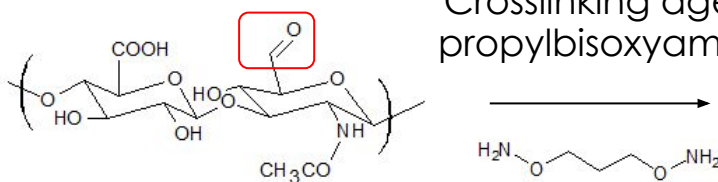
Benefits of topical application:

- Excellent water-holding capacities for the skin hydration
- Keeps active ingredients in its pores – continuous release into the skin
- Higher stability against hyaluronidases – stays longer on the skin

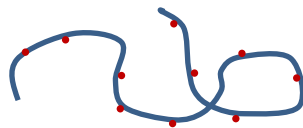
Patented Preparation



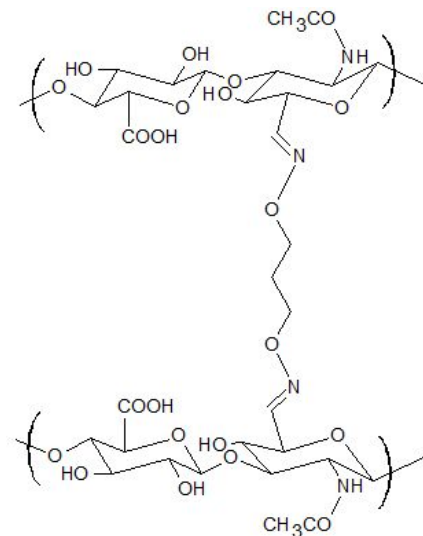
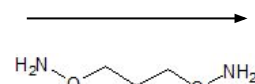
Sodium Hyaluronate
(300 kDa)



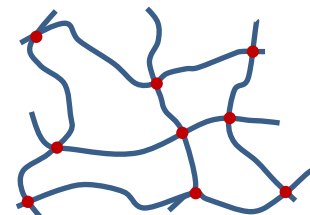
Oxidized Sodium Hyaluronate
(aldehyde)



Crosslinking agent
propylbisoxamine



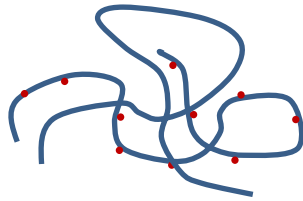
Sodium Hyaluronate Crosspolymer-3



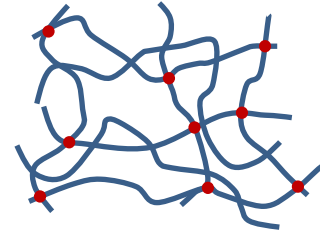
Final Form of CrossLinked^{HA}: Water Soluble Powder



- Additional HA is used during crosslinking
- HA integrates into crosslinked HA network
- HA softens the crosslinked gels and increases water solubility of final xerogel
- Various ratios were tested – 1 : 5 works the best



Crosslinking



Oxidized Sodium Hyaluronate
(300 kDa)

+

Sodium Hyaluronate
(300 kDa)

Sodium Hyaluronate
Crosspolymer

+

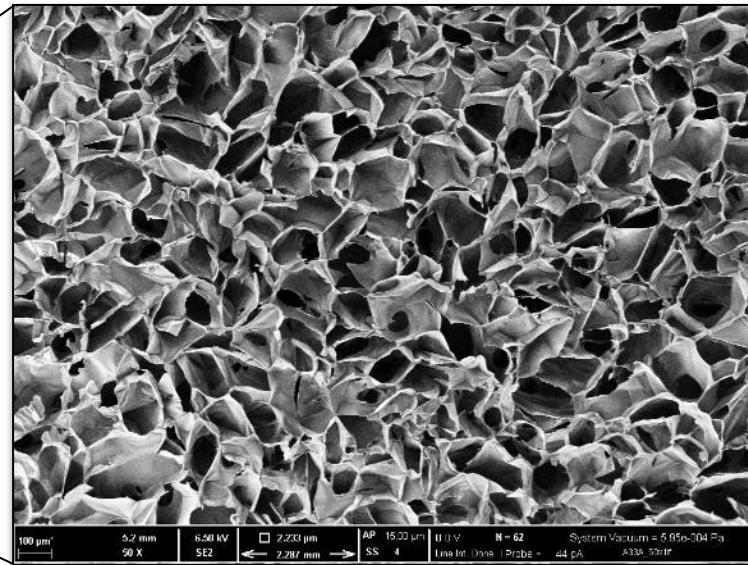
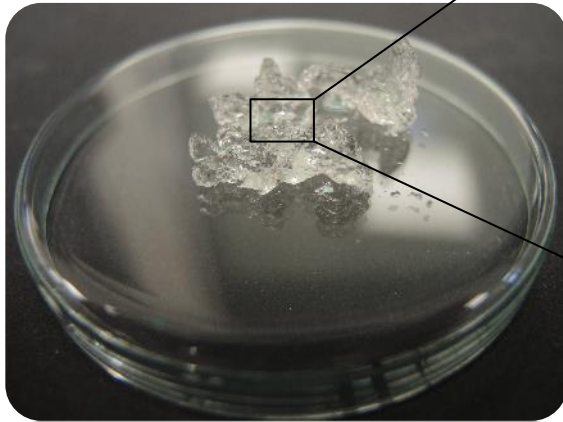
Integrated hyaluronan chains

=

Water soluble final powder

„Loading“ Abilities of CrossLinked^{HA}

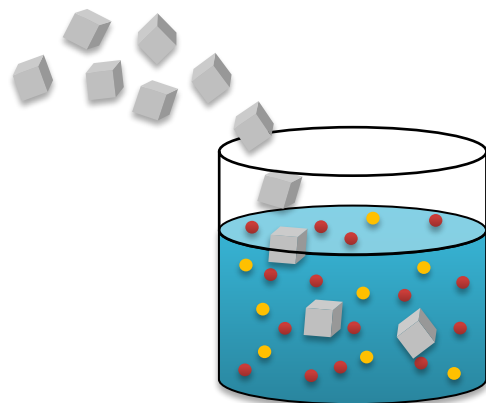
Hydrogels containing integrated HA have porous structure to keep water and active substances inside.



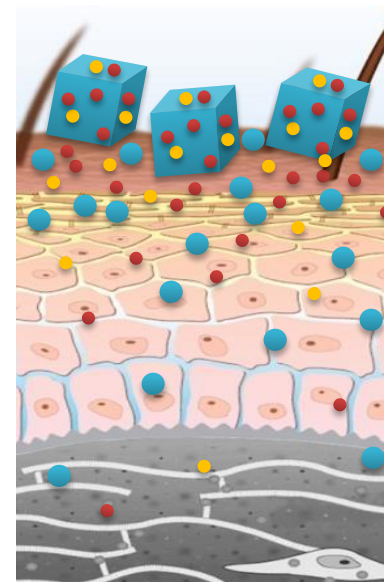
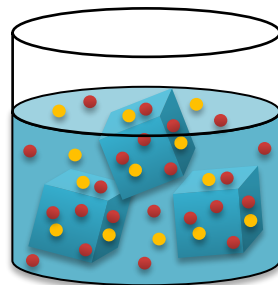
Picture from scanning electron microscope (CrossLinked^{HA} + HA gel before disintegration)

Release into the Skin

CrossLinked^{HA} xerogel



Hydrogel



In Vitro Results

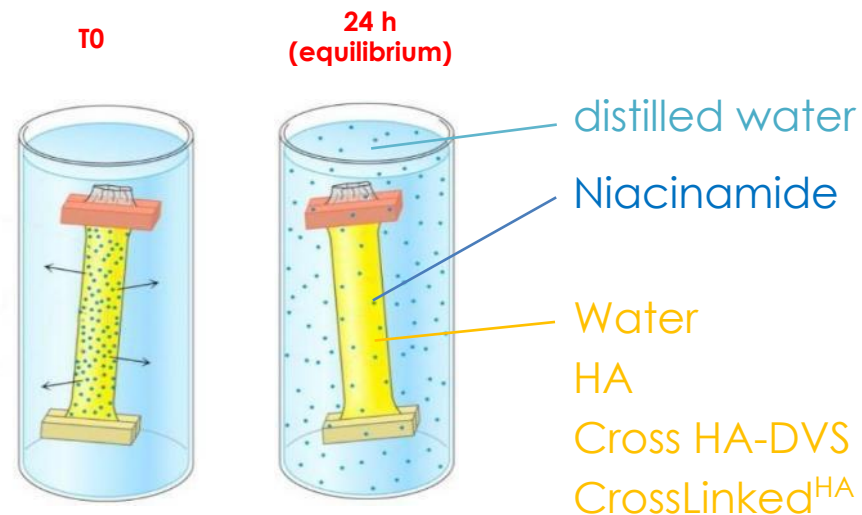
Release of Absorbed Actives

Niacinamide (vitamin B3, 0,05 %)

- Common cosmetic active ingredient
- Easy detection (yellow color, measurement of absorbance)

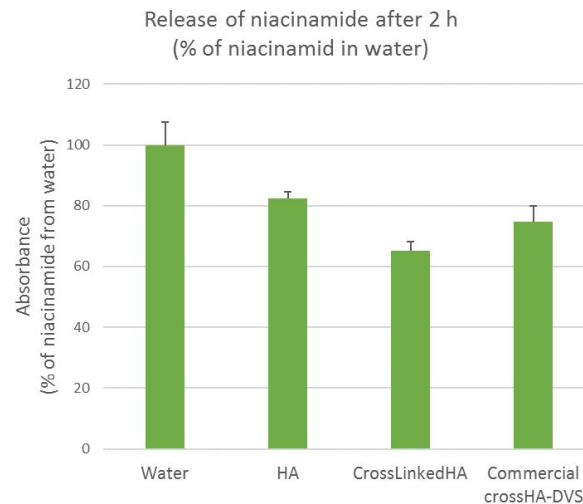
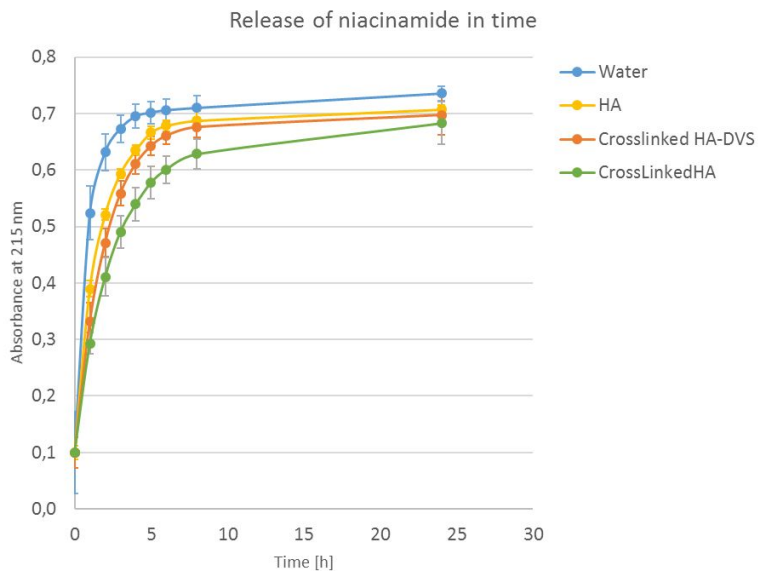
Dialysis

- Against water
- Tested environments:
 - Water
 - 0,5 % HA (300kDa)
 - 0,5 % crosslinked HA-DVS as a competitor (+ HA 1:5)
 - 0,5 % CrossLinked^{HA} (+ HA 1:5)

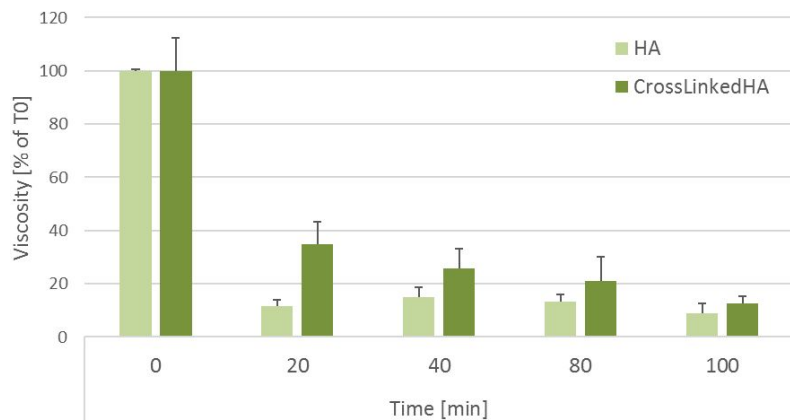


Release Rate

- Continuous, long-term delivery of actives into the skin
- More efficient utilization of actives by skin cells
- Less risk of irritation



Resistance against Hyaluronidases

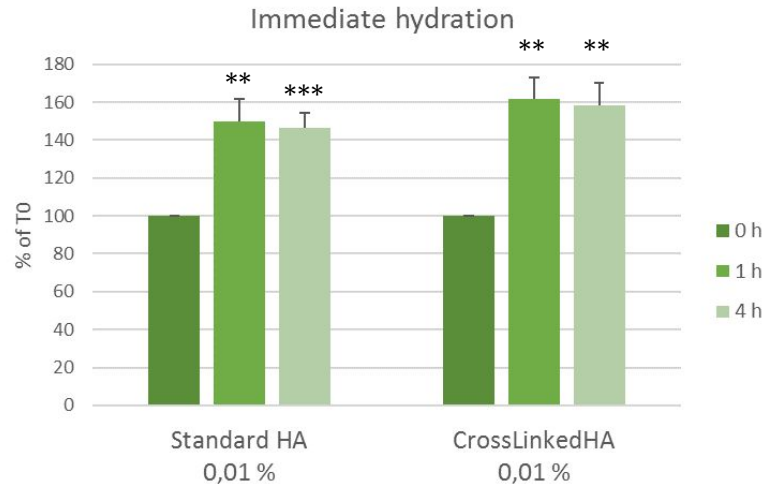


- Bovine testicular hyaluronidase (BTH)
- 2 % HA (300 kDa)
- 2 % CrossLinked^{HA}
- 37 °C
- Measurement of solution viscosity in time using a rheometer

**CrossLinked^{HA} is more stable than HA,
so it stays longer on the surface of the skin.**

In Vivo Results

Study 1 – Immediate Hydration

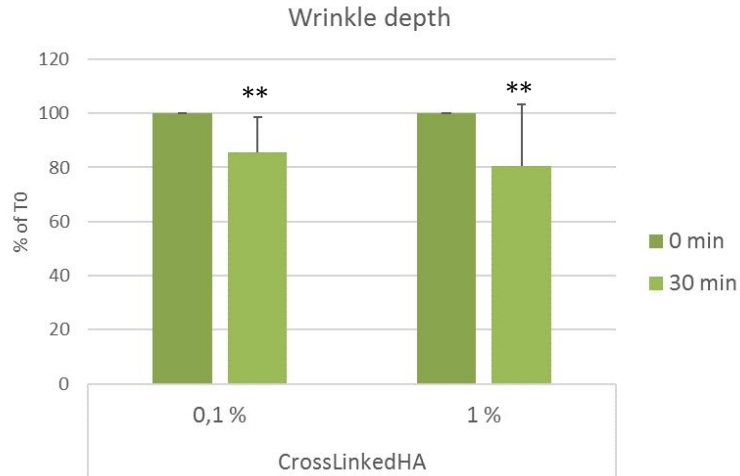


- 8 volunteers (6 women, 2 men)
- 26-37 years, average 31,3 years
- 0,01 % CrossLinked^{HA} in emulsion
- 0,01 % Standard HA 1,6 MDa in emulsion
- Split-face study
- 1 h, 4 h
- Corneometry (hydration)

CrossLinked^{HA} has immediate hydrating effect and exceptional hydrating properties (higher than HA).

Study 2 – Immediate Reduction of Wrinkles

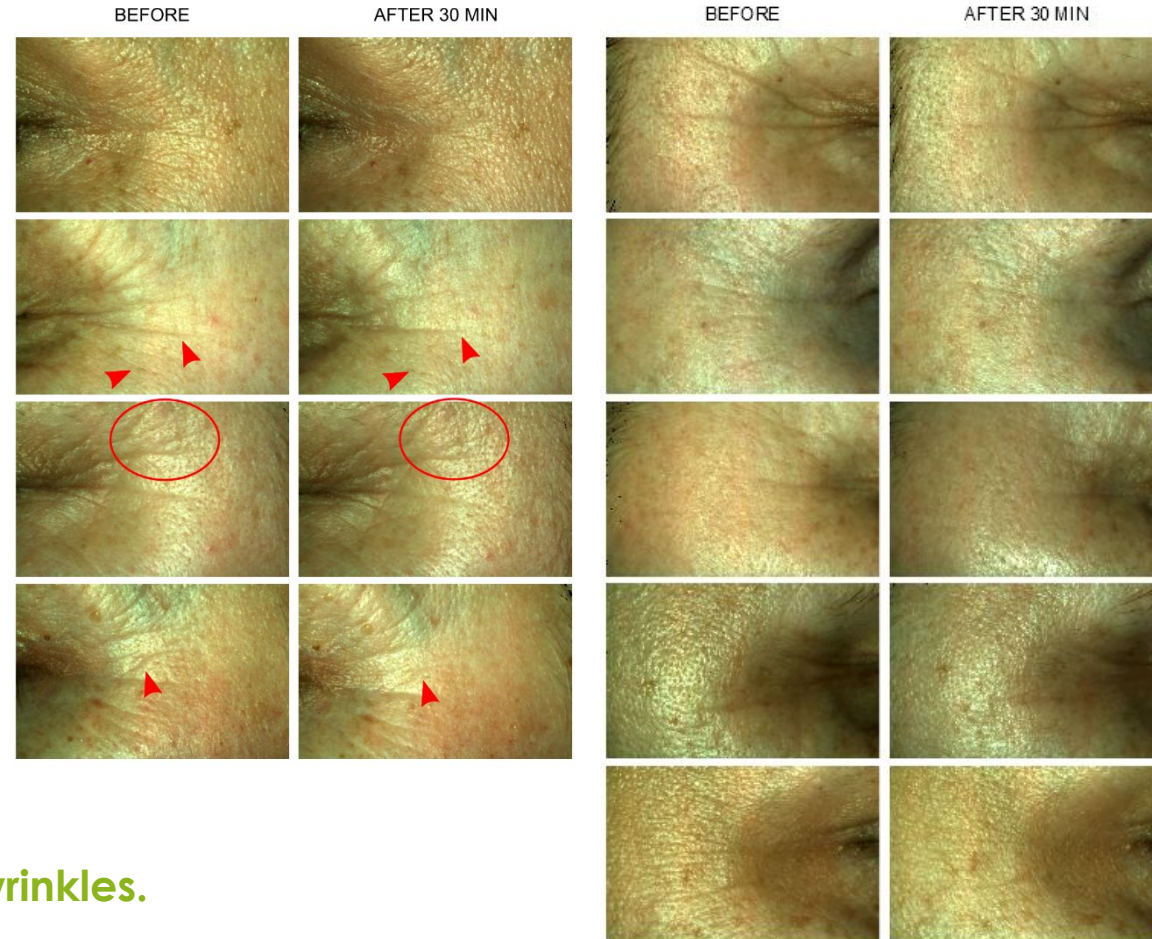
- 0,1 % and 1 % CrossLinked^{HA} serum (in water)
- 5 women with crow's feet wrinkles
- 37-55 years, 46,6 on average
- 30 min
- Primos 3D camera



CrossLinked^{HA}

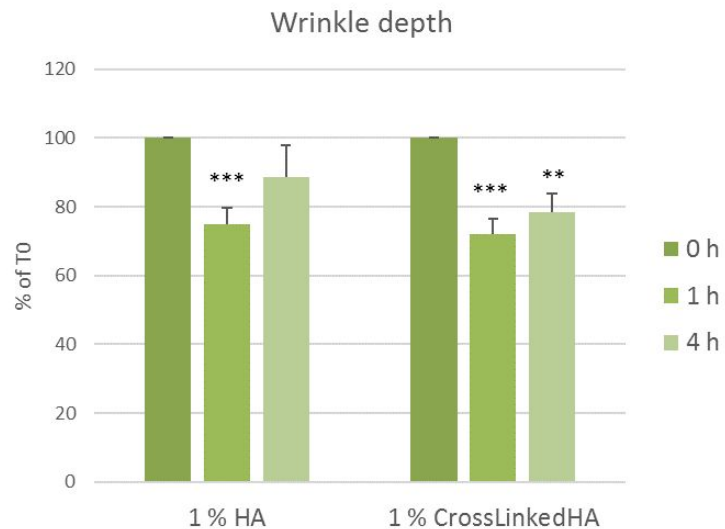
0,1 % - fine lines

1 % - deep wrinkles



CrossLinked^{HA} has immediate effect on wrinkles.

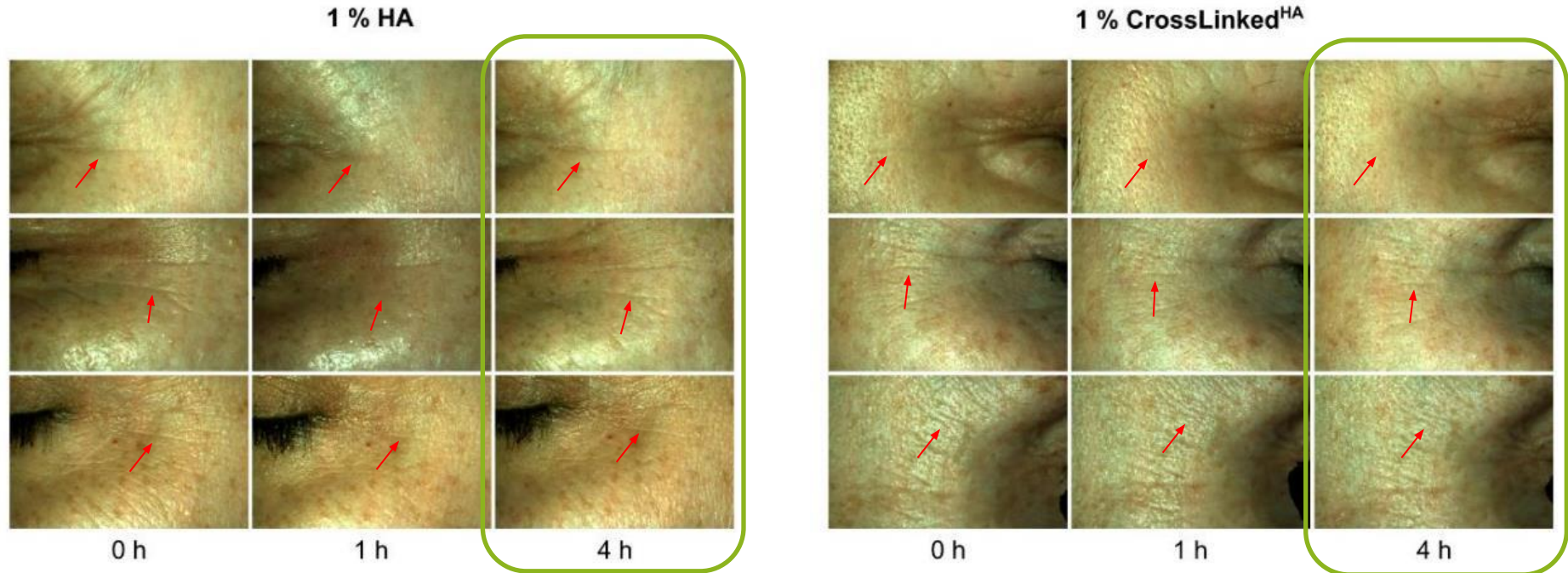
Study 3 – Comparison of Anti-wrinkle Effects with HA



- 1 % CrossLinked^{HA} serum (in water)
- 1 % standard HA 1,6 MDa (in water)
- Split-face study
- 1 h, 4 h
- 11 women with crow's feet wrinkles
- 36-50 years, 44,8 on average
- 30 min
- Pictures with Primos 3D camera

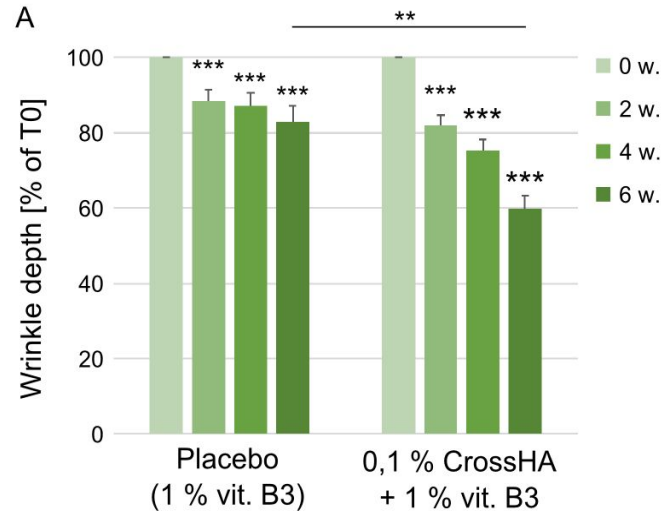
CrossLinked^{HA} effect on wrinkles lasts longer than the effect of HA.

Study 3 – Comparison with HA



CrossLinked^{HA} effect on wrinkles lasts longer than the effect of HA.

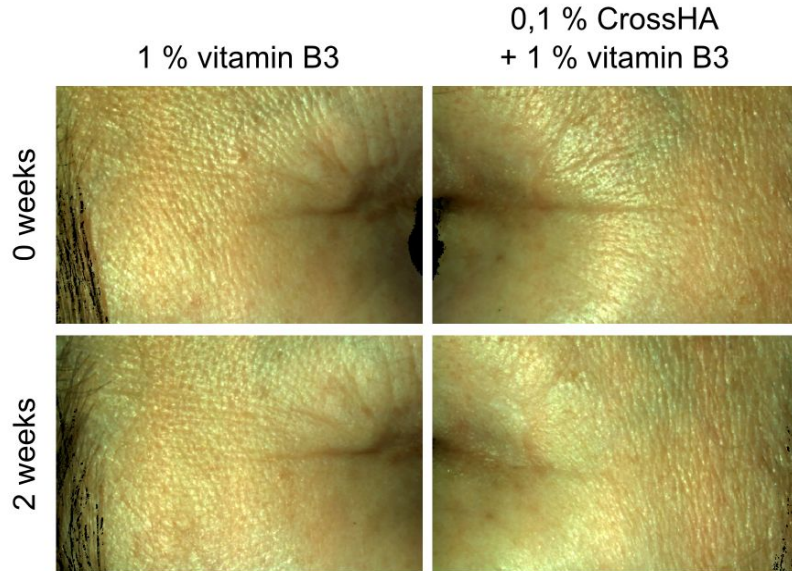
Study 4 – Long-term effect on wrinkles



- 0,1 % CrossLinked^{HA} + 1 % vit. B3
- Placebo: 1 % vit. B3
- Form: a cream
- 15 women (35-55 years, 43,5 on average)
- Split-face study
- 6 weeks
- Pictures with Primos 3D camera

CrossLinked^{HA} has a long-term anti-wrinkle effect

Study 4 – Long-term effect on wrinkles



- 0,1 % CrossLinked^{HA} + 1 % vit. B3
- Placebo: 1 % vit. B3
- Form: a cream
- 15 women (35-55 years, 43,5 on average)
- Split-face study
- 6 weeks
- Pictures with Primos 3D camera

CrossLinked^{HA} has a long-term anti-wrinkle effect

Study 4 – Long-term effect on wrinkles



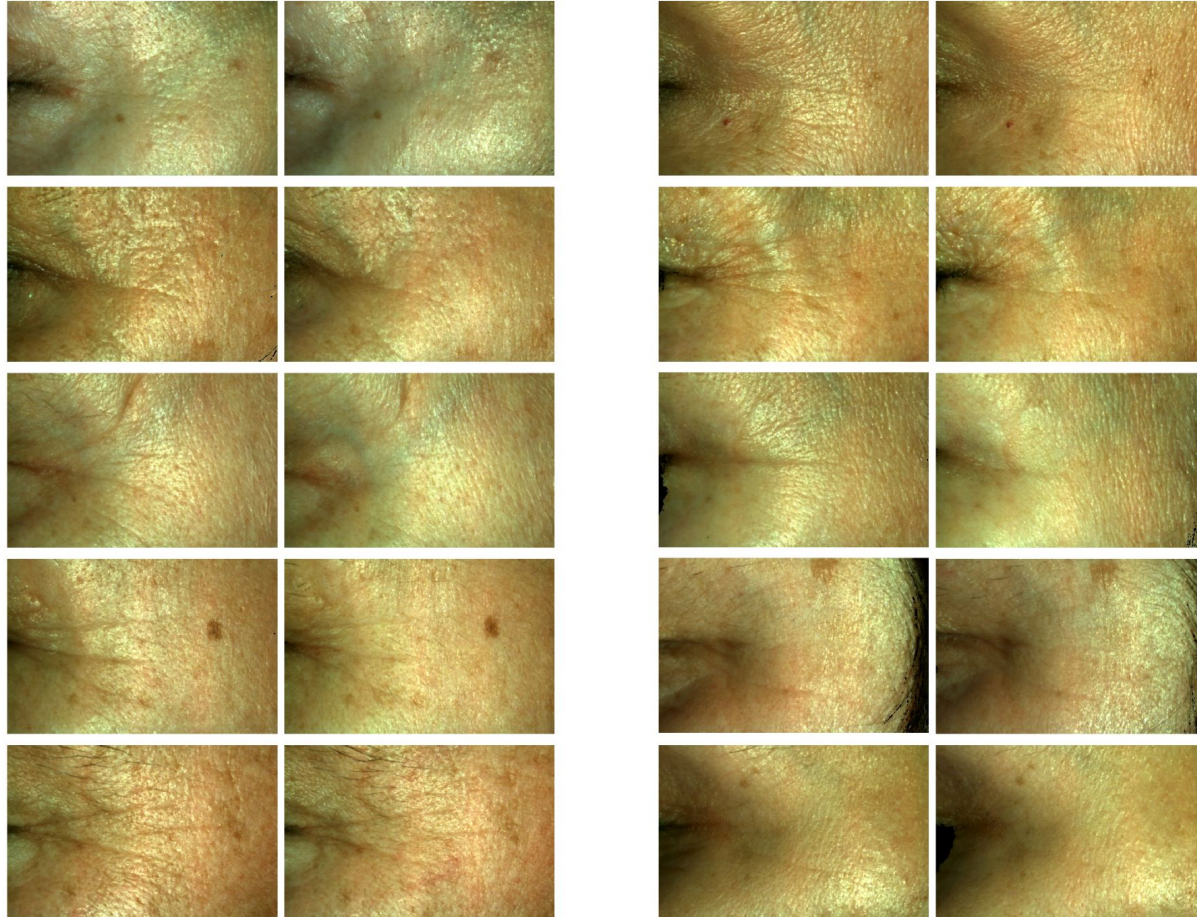
0,1 % CrossHA + 1 % vitamin B3

0 weeks

2 weeks

0 weeks

2 weeks



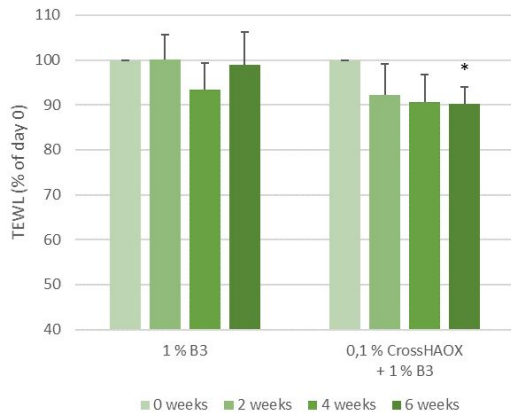
- 0,1 % CrossLinked^{HA} + 1 % vit. B3
- Placebo: 1 % vit. B3
- Form: a cream
- 15 women (35-55 years, 43,5 on average)
- Split-face study
- 6 weeks
- Pictures with Primos 3D camera

CrossLinked^{HA} has VISIBLE long-term anti-wrinkle effect even on deep mimic wrinkles

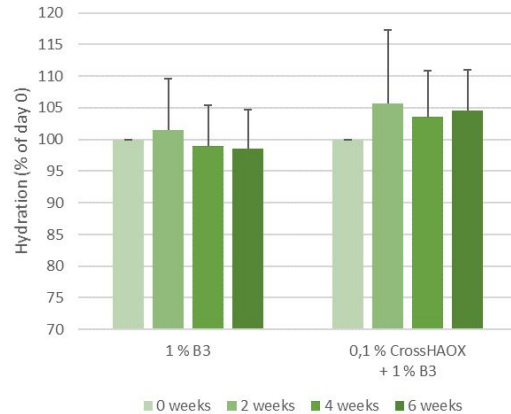
Study 4 – Long-term effect



TEWL



Hydration



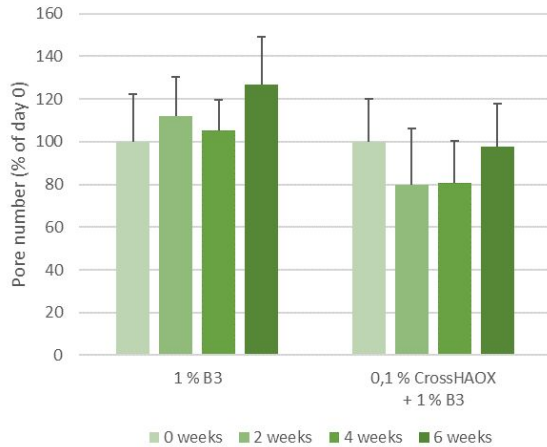
- 0,1 % CrossLinked^{HA} + 1 % vit. B3
- Placebo: 1 % vit. B3
- Form: a cream
- 15 women (35-55 years, 43,5 on average)
- Split-face study
- 6 weeks
- Tewameter, corneometer

CrossLinked^{HA} improves TEWL and hydration

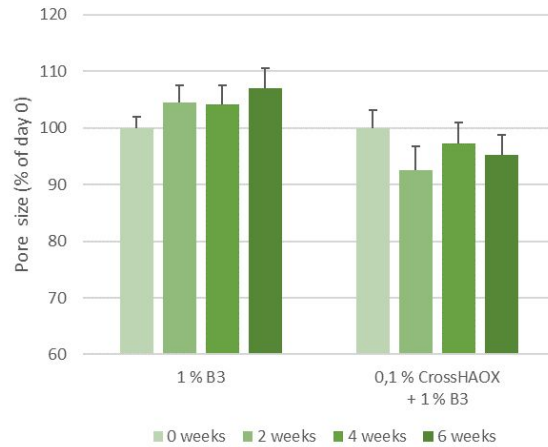
Study 4 – Long-term effect



Pore number



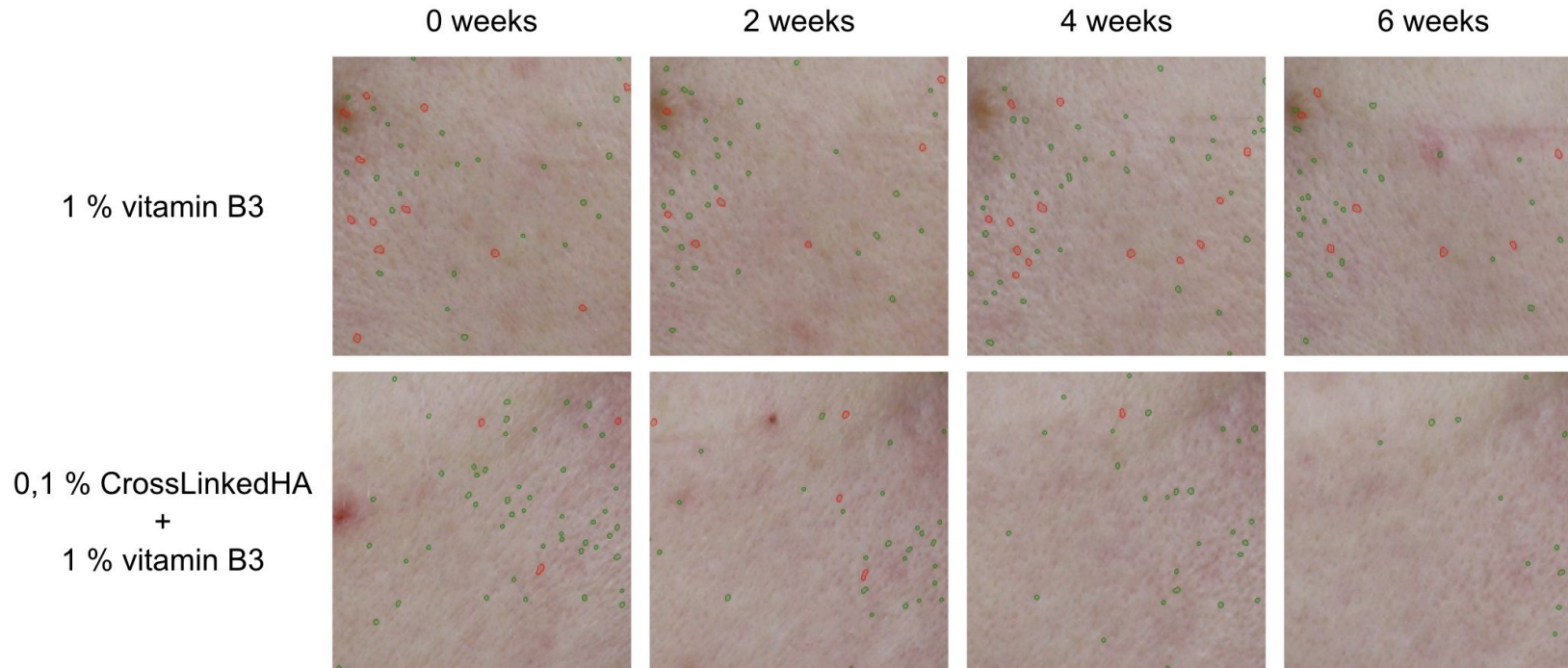
Pore size



- 0,1 % CrossLinked^{HA} + 1 % vit. B3
- Placebo: 1 % vit. B3
- Form: a cream
- 15 women (35-55 years, 43,5 on average)
- Split-face study
- 6 weeks
- Visioface

**CrossLinked^{HA} in combination with 1 % vit. B3
reduces number/size of the skin pores**

Study 4 – Long-term effect



**CrossLinked^{HA} in combination with 1 % vit. B3
reduces number/size of the skin pores**

Study 4 – Long-term effect



0,1 % CrossLinkedHA
+
1 % vitamin B3

1 % vitamin B3

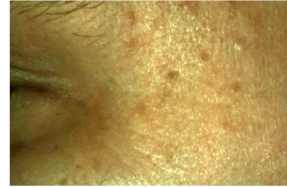
0 weeks



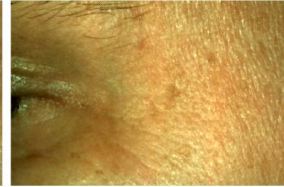
6 weeks



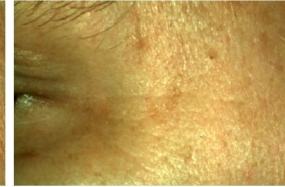
0 weeks



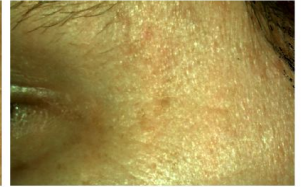
2 weeks



4 weeks



6 weeks



0 weeks



2 weeks



4 weeks



6 weeks



CrossLinked^{HA} effectively delivers vit. B3 into the skin and increases its lightening and anti-spots effects

(crossHA itself does not have an effect on the skin color and pigmented spots)



For more information, please
contact our sales department

jenikova@contipro.com