*Distributed By –*
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CONTIPRO

# HyWhite

## First Whitening Hyaluronic Acid

Approved by ECOCERT RAW MATERIAL

COSMOS APPROVED

# HyWhite – Sodium Linolenoyl Hyaluronate

- Natural derivative of a-linolenic acid  and hyaluronic acid
- COSMOS approved

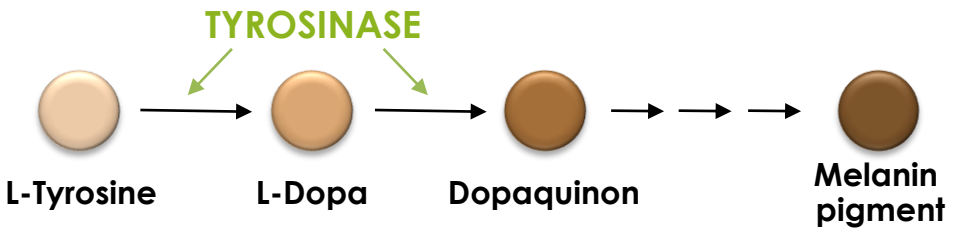
## a-Linolenic acid

- Omega 3-fatty acid (essential acid)
- Seeds oils: chia, linseed, canola, soybean, walnut
- Whitening effect *in vitro*, not *in vivo* in human skin
- Other effects: energy production, antioxidant, anti-inflammatory

## Hyaluronic acid

- Low molecular weight 5-10 kDa
- Penetrates deep into the skin and into skin cells
- Delivers a-linolenic acid to its target – tyrosinase in melanocytes
- Protects a-linolenic acid against degradation
- Many other beneficial effects

# Mechanism of Action



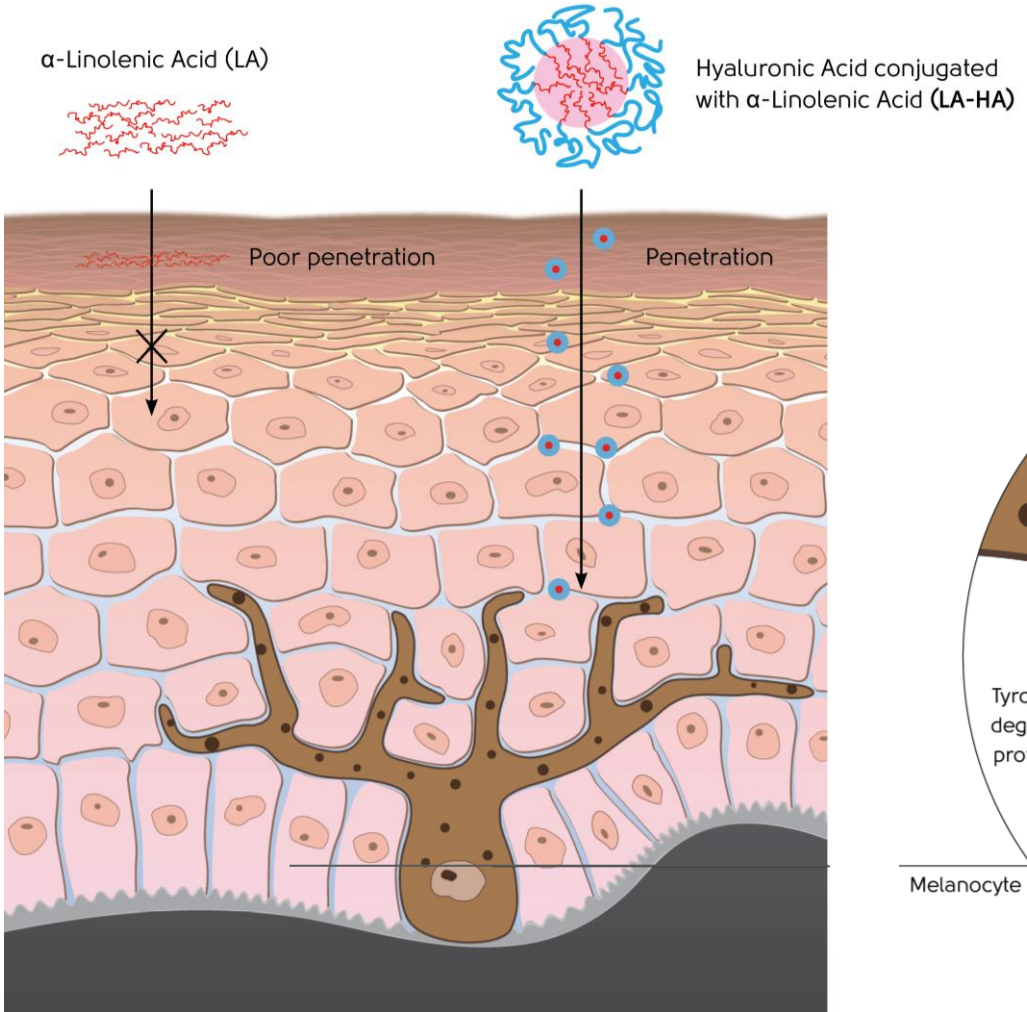

## a-Linolenic acid

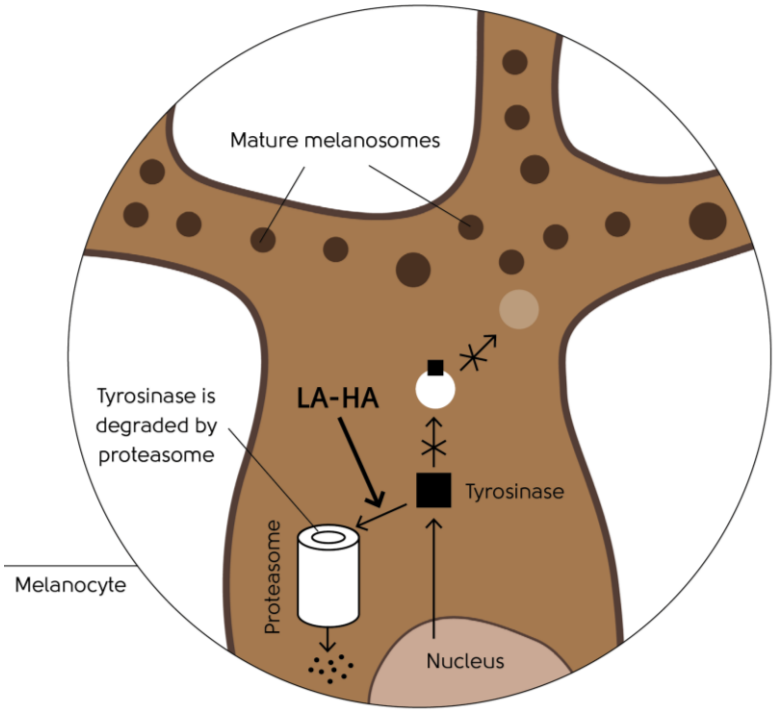
- Increases degradation of tyrosinase – a key enzyme in melanogenesis
- Proteasome activator – the degradation of tyrosinase occurs via proteasome
- Increases desquamation (faster removal of pigmented cells – whitening)

## Hyaluronic acid

- Effectively delivers a-linolenic acid to the target – tyrosinase in melanocytes
- Moisturizing effects support proper function of enzymes important for desquamation (faster removal of pigmented cells – whitening effect)

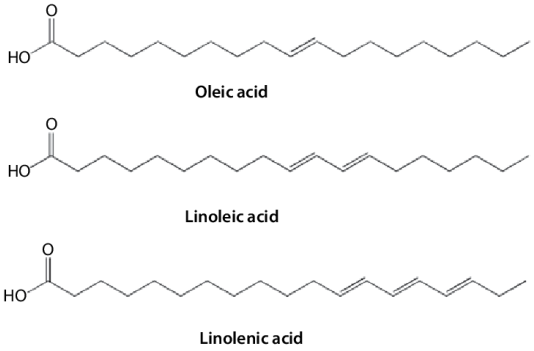
# Mechanism of Action



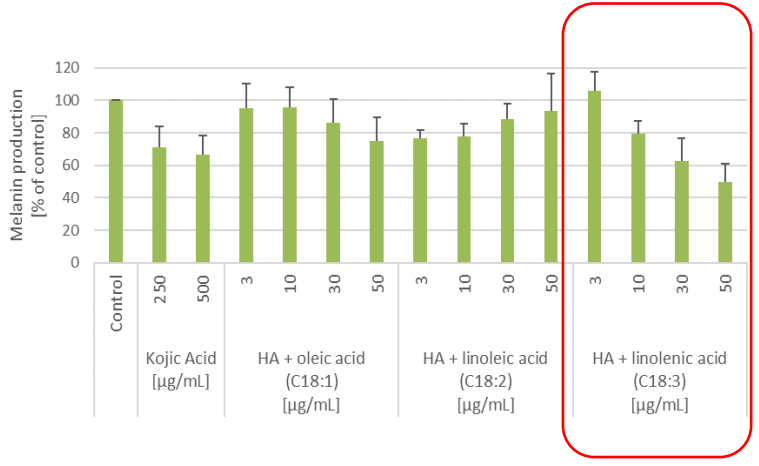
# *In Vitro* Results

# Why a-Linolenic Acid?




## Different derivatives with HA were tested:

- HA + oleic acid (1 unsaturated bond)
- HA + linoleic acid (2 unsat. bonds)
- HA + a-linolenic acid (3 unsat. bonds)



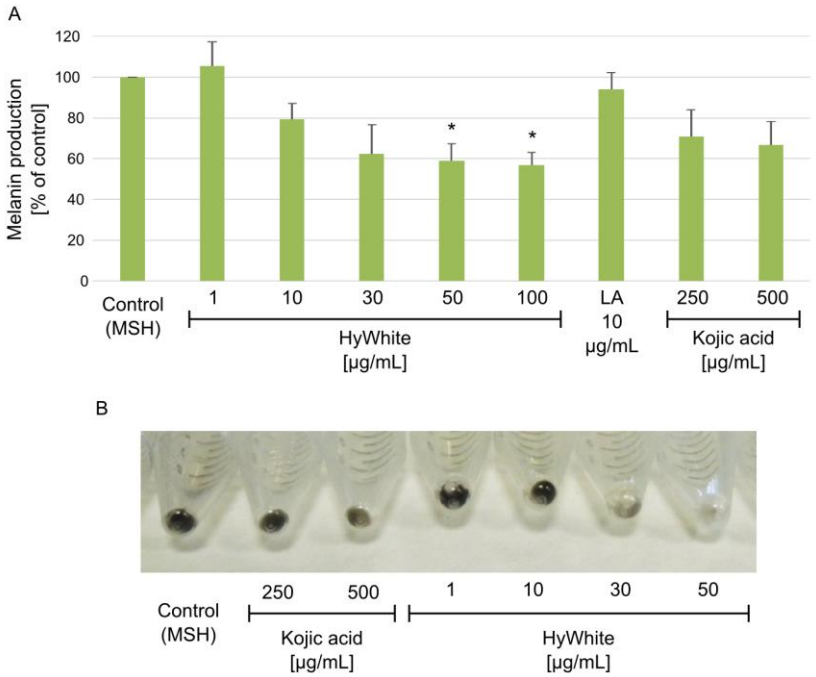

## Melanin production test:

- B16-F10 melanocytes
  + melanocyte-stimulating hormone
- 48 treatment with derivatives
- Spectrophotometrical analysis

## Derivative of HA with a-linolenic acid:

- **Was the most active**
- More active than kojic acid
- Active in very low concentrations (0,001%)

# Reduction of Melanin Production

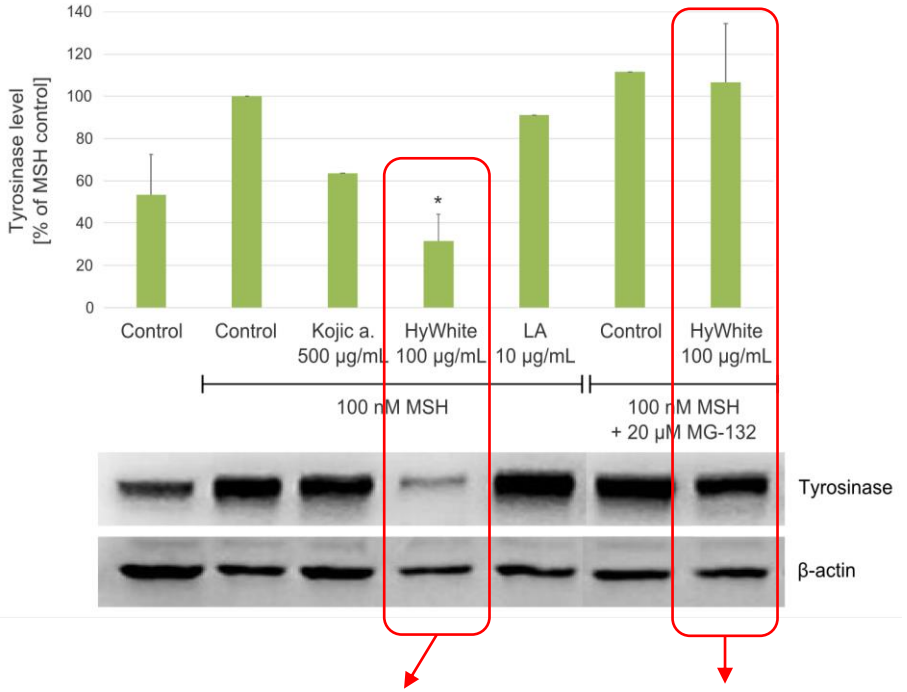



- B16-F10 melanocytes
- 48 treatment
- Spectrophotometrical analysis

**HyWhite is more effective than:**

- a-Linolenic acid (LA) itself
- Kojic acid

# Increase in Tyrosinase Degradation is Mediated by the Proteasome




HyWhite increases degradation of tyrosinase.

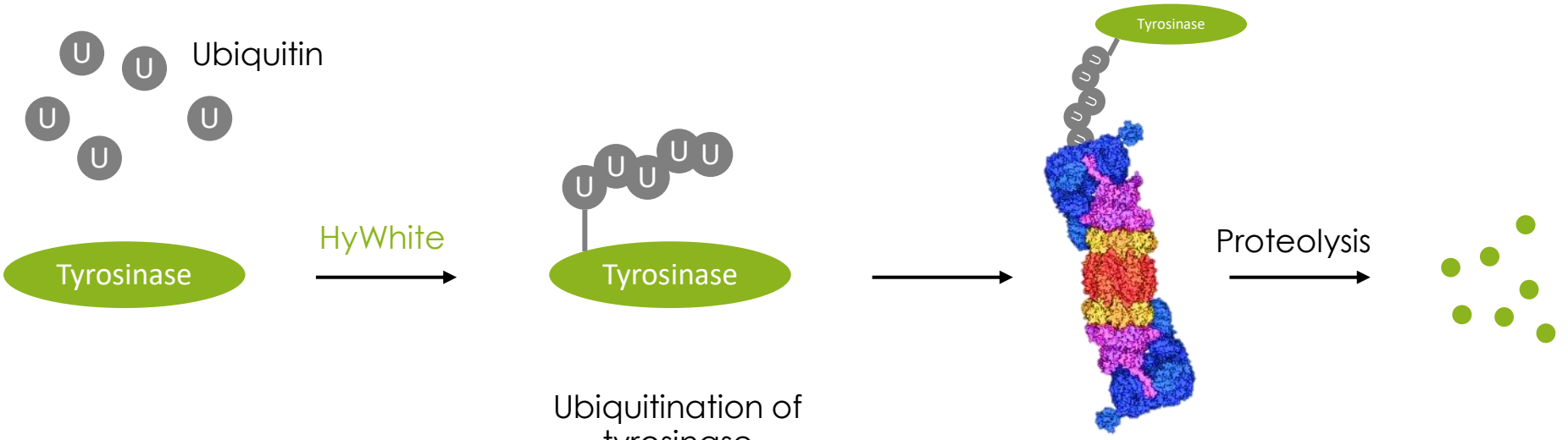
When proteasomes are inhibited by MG-132, tyrosinase is not degraded by HyWhite.

- B16-F10 melanocytes
- 48 h treatment
- MG-132 – proteasome inhibitor
- Western blotting analysis

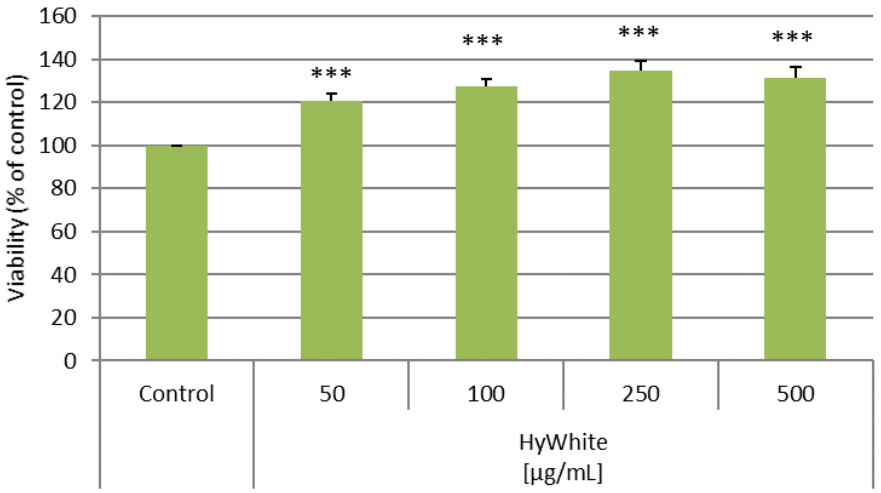
**Proved:**

- Increased degradation of tyrosinase induced by HyWhite is mediated by the proteasome.

# Increase in Tyrosinase Degradation is Mediated by the Proteasome



# Increase in Cell Viability




- 3T3 fibroblasts
- 24 h
- MTT cell viability assay

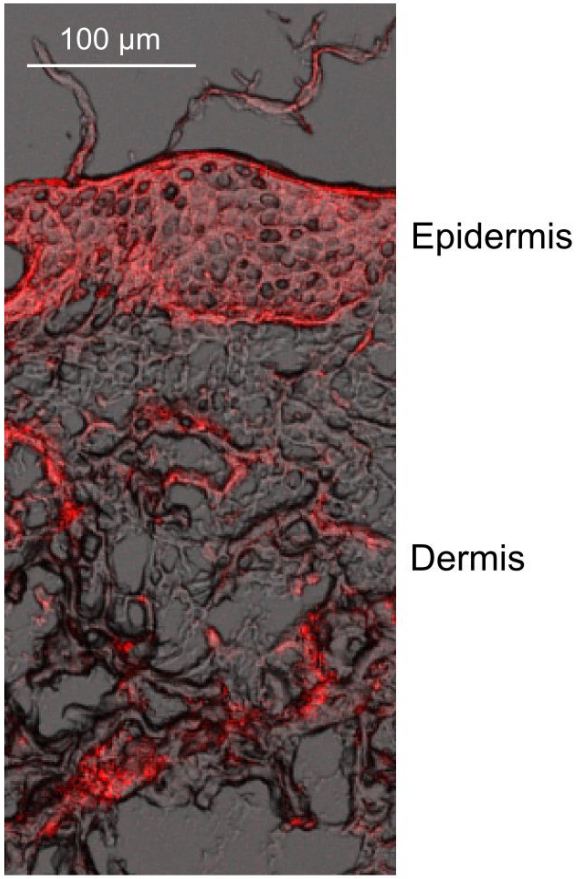
**HyWhite increases cell viability.**

Fatty acid serves as a source of energy for the cells.

# Penetration into the Skin

- HyWhite conjugated with Alexa Fluor 568 (red fluorescent dye), 0,5 mg/mL
- Porcine skin explants (inner auricles)
- Franz diffusion cells, 24 h at 37 °C
- Confocal microscopy

**HyWhite penetrates deep into the skin**



# *In Vivo* Results:
# External Study by Intertek

# Design of the Study

Volunteers:

- 35 Asian women 20-50 years
- With pigmentation disorders
- 8 weeks

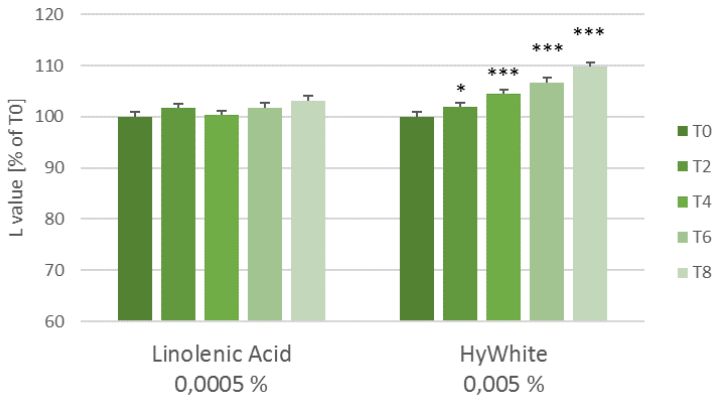
Split-face:

- 0,005 % HyWhite cream (DS = 10 %)
- 0,0005 % a-linolenic acid as a placebo cream

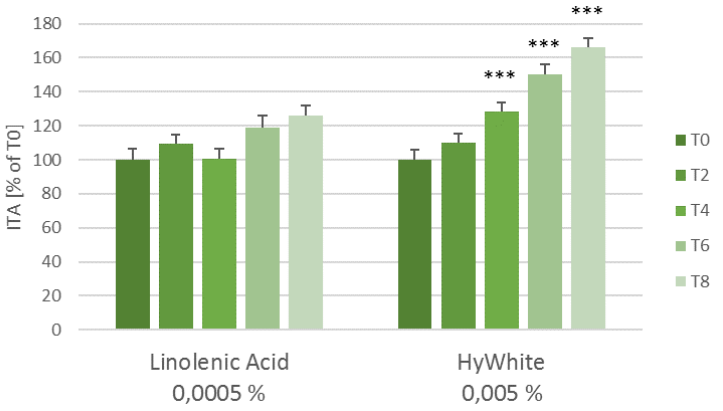
Measurement devices:

- Colorimeter (L-value, ITA)
- Mexameter (melanin)
- Visia-CR (high resolution camera, image analysis of pigmented spots and color uniformity)

# Luminiscence and Lightness



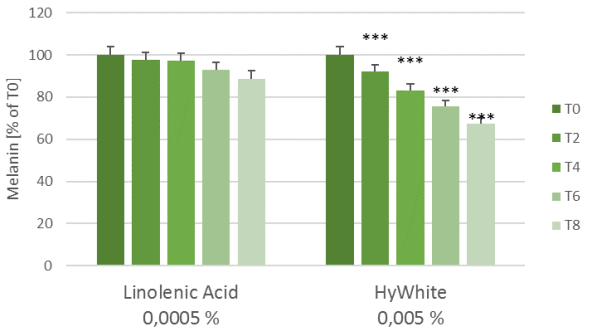

6,6 % increase
in luminescence (L value)




40,1 % improvement
in the skin lightness (ITA)

# Decrease of Melanin

Week 0 Week 2



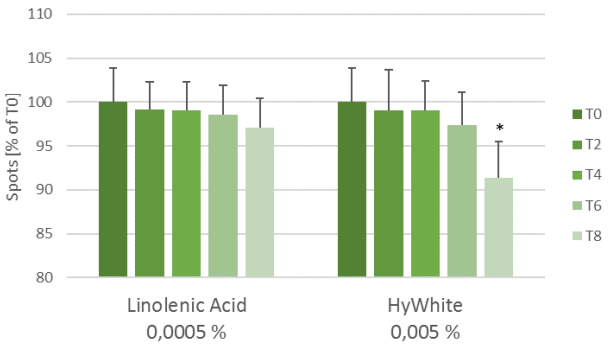

Week 0 Week 8

21,3 % decrease
of melanin content

# Decrease of Pigmented Spots

Week 0 Week 8

Week 0 Week 2



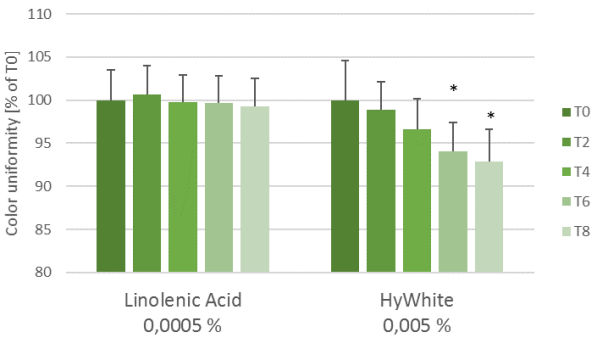

5,6 % decrease
of pigmented spots

Week 0 Week 2

# Improvement of Colour Uniformity

Week 0 Week 2

Week 0 Week 6




Week 0 Week 8

6,4 % improvement
of color uniformity

# *In Vivo* Results: Study by Contipro

# Design of the Study

Volunteers:

- 15 Caucasian women 37-56 years
- Darker skin (ITA < 40)
- 6 weeks

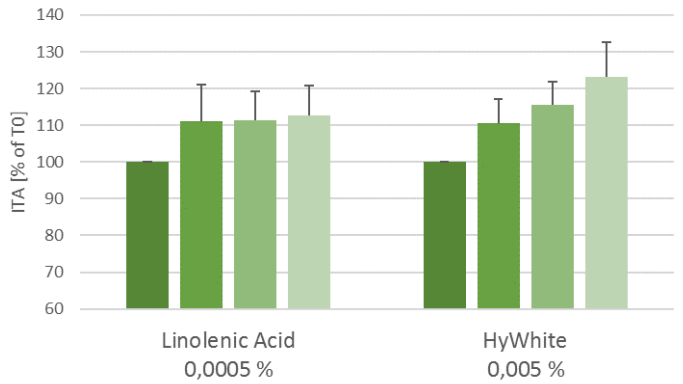
Split-face:

- 0,005 % HyWhite cream (DS = 10 %)
- 0,0005 % a-linolenic acid as a placebo cream

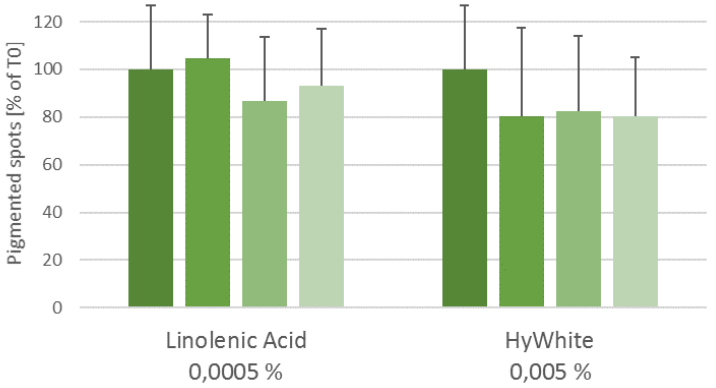
Measurement devices:

- Colorimeter (ITA)
- Visioface (pigmented spots)
- Vivascope (internal skin structure)

# Lightness and Pigmented Spots




10,6 % improvement
of the skin lightness (ITA)




24,0 % reduction
of pigmented spots (2 weeks)

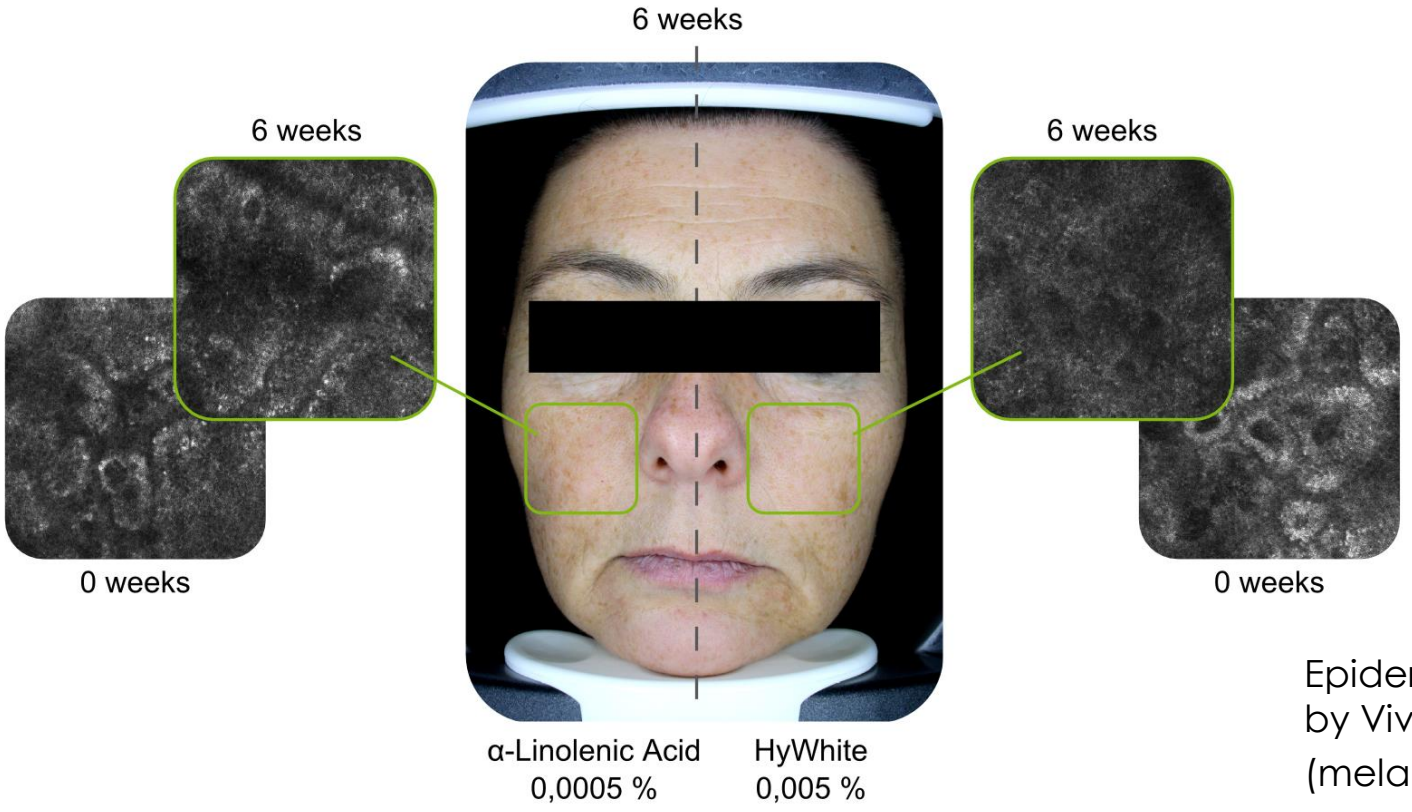
12,9 % reduction
of pigmented spots (6 weeks)

# Lightning and Spots Evidence

Week 0 Week 6

Week 0 Week 6

# Pigmented Cells Evidence

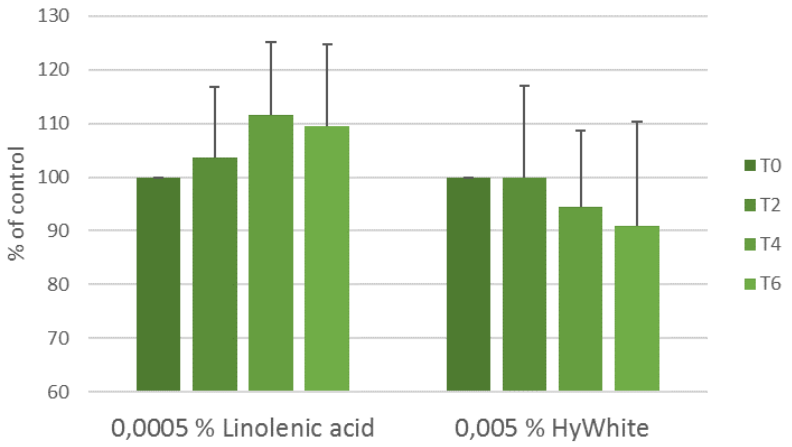



Epidermal basal cell layers showed by Vivascope

(melanin visible as white spots)

Number of pigmented cells decreased after HyWhite application

# Hyperpigmented Cells Evidence




18,6 % less number
of hyperpigmented cells

# Feedback from a customer

*„Just to share with you about the feedback on various dosage of HyWhite from customers:*

- *At 0.005% - rather poor feedback as the result is slow and not significant*
- *At 0.05% - dark spot/area from acne becomes paler and skin becomes whiter*
- *At 0.1% - noticeably whiter skin*
- *At 0.15% - noticeable whiter skin in a short time, pore and melasma reduction*
- *At 0.2% - Rapid whiter skin and considerably reduction of melasma (one customer shared with us that at this dosage of 0.2 % of HyWhite in comparison with 2 % of Alpha arbutin, the result of 0.2 % HyWhite is much more significantly whiter in a very short period of time with a good feeling of pore reduction)“*

# HyWhite: Conclusion

# HyWhite

**Sodium linolenoyl hyaluronate:**

- Derivative of a-linolenic acid and hyaluronic acid
- Amphiphilic molecule (both hydrophilic and lipophilic)
- Better penetration into the skin and skin cells
- Cosmos approved

**Mechanism of action:**

- Tyrosinase degradation by the proteasomes

**Highly effective in very low concentrations:**

- From 0,005%
- **1 g** is enough for **20 kg** of a whitening cream

**Whitening effects:**

- Skin whitening
- Reduction of pigmented spots
- Increased color homogeneity

- Does not depend on the type of the skin (Asian or Caucasian)

# HyWhite Technical Sheet

**INCI:** Sodium Hyaluronate and Linolenic Acid

**Certification:** Cosmos approved

**Samples:** 1 g

**Minimal ordering quantity:** 1 kg
(If ordering smaller quantities, the price may increase due to handling fees)

**Recommended concentration:** 0,005 – 0,01 %

**Appearance:** White to slightly yellow powder

**Supplied form:** powder

**Shelf-life:** 12 months

**Source:** HyWhite is produced by chemical modification of low molecular weight hyaluronic acid with a-linolenic acid. Hyaluronic acid is obtained by fermentation, a-linolenic acid is from a plant source.

**Compatibility and processing:** Sensitive to heat and high humidity; avoid prolonged heating (heating over 60 °C for 60 min can lead to a decreased degree of substitution and degradation by oxidation). Extreme pH (less than 4 or more than 10) leads to further decomposition. Incompatible with cationic substances, e.g. surfactants or polymers (polyquarternium-4, polyquarternium-10, etc.)

**Solubility:** Fully soluble in water; soluble in aqueous mixture of ethyl alcohol and isopropyl alcohol

# Contipro

- World leader in research and manufacturing of hyaluronic acid.
- Innovations in biotechnologies since 1990.
- Reliable partner of successful brands.