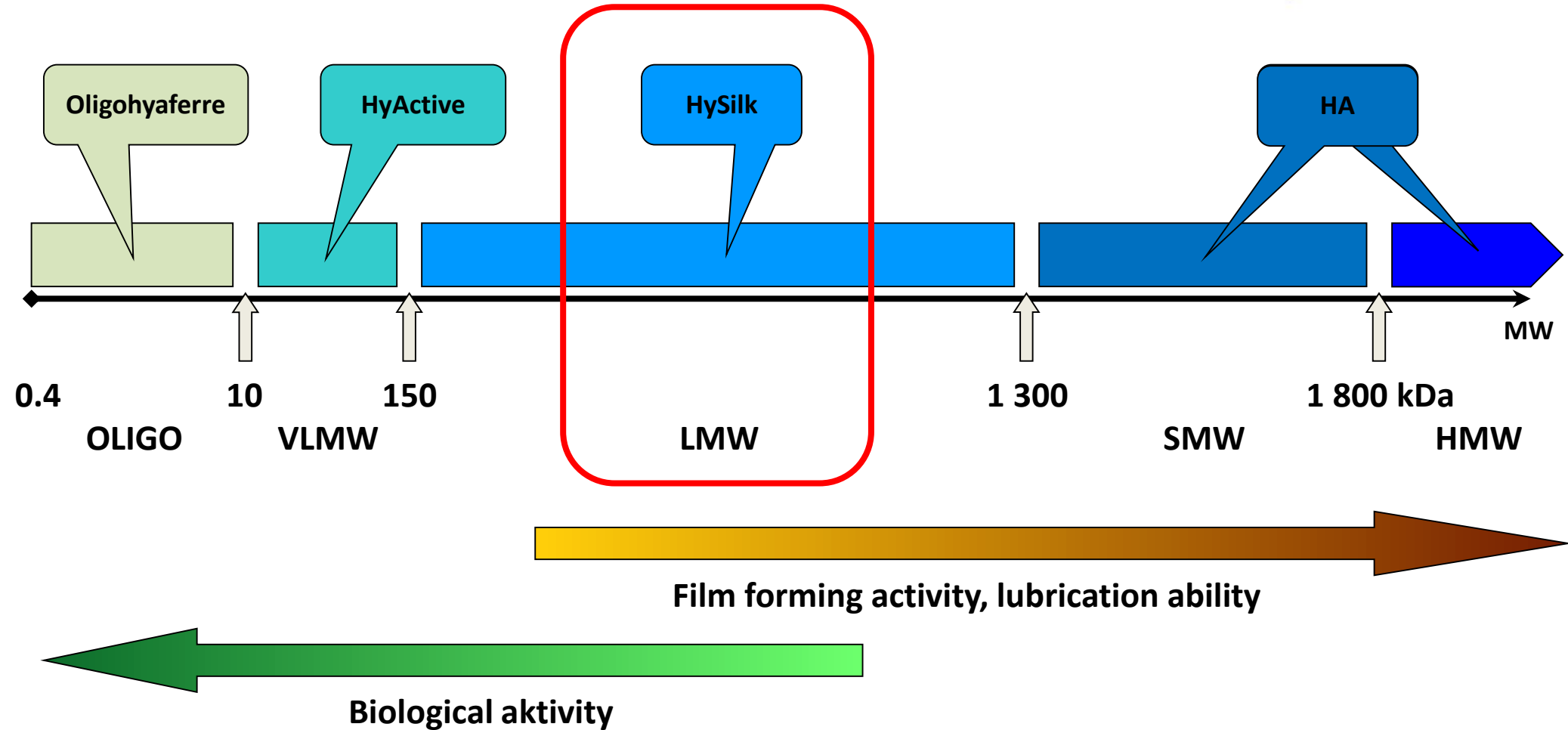


HySilk

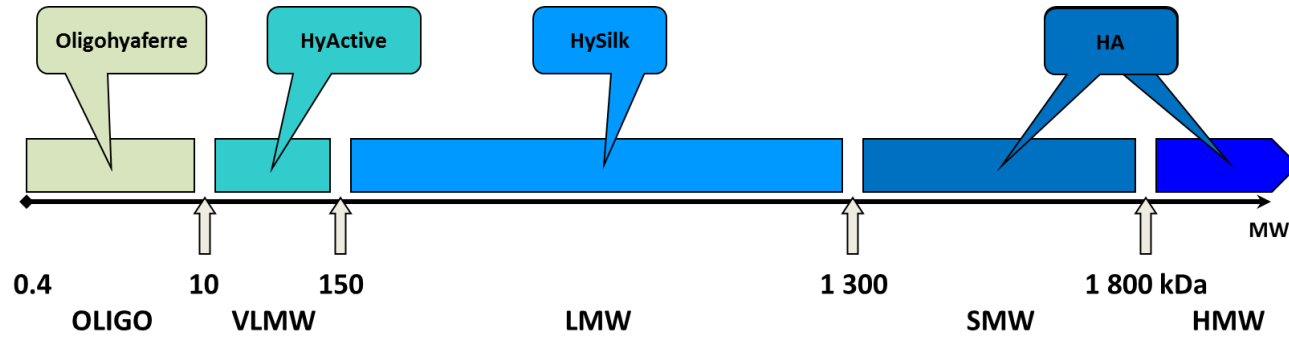
Low molecular weight hyaluronic acid

Overview of various MW of HA

MW of hyaluronan and its action

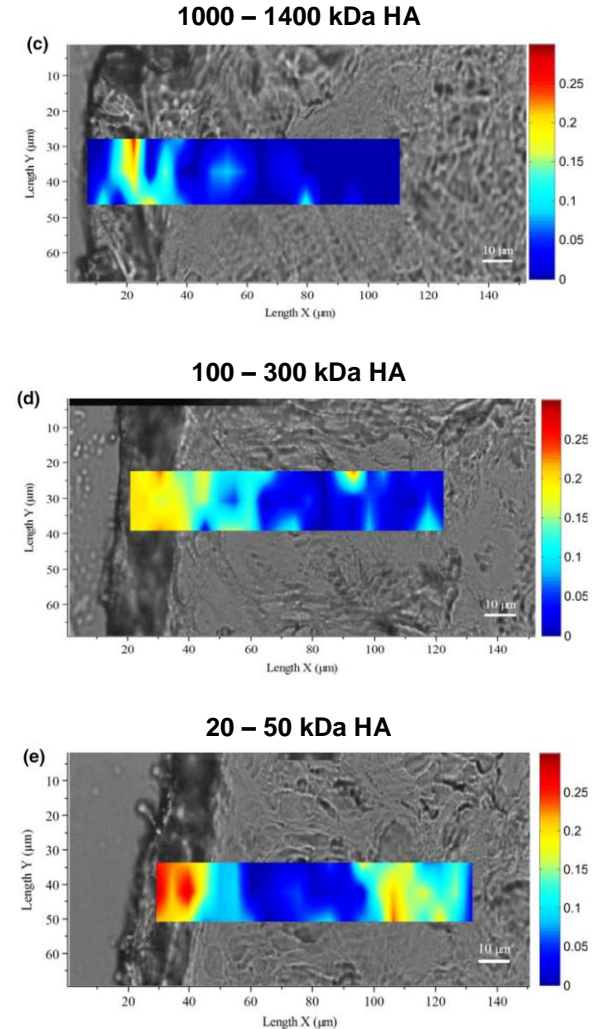


Penetration of different MW of hyaluronan



Essendoubi et al. Human skin penetration of hyaluronic acid of different molecular weights as probed by Raman spectroscopy. *Skin Res Technol.* 2015 Apr 16. doi: 10.1111/srt.12228.

PENETRATION OF HA OF VARIOUS MW by Raman spectroscopy

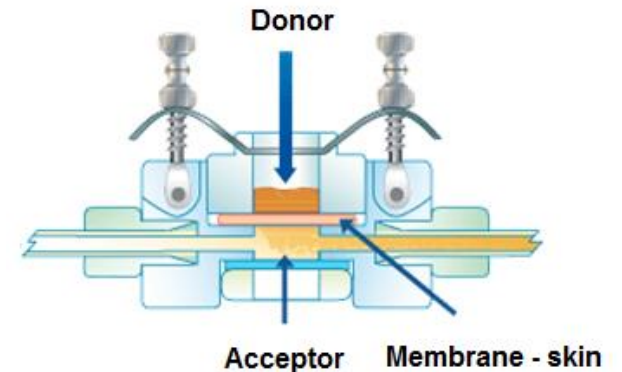
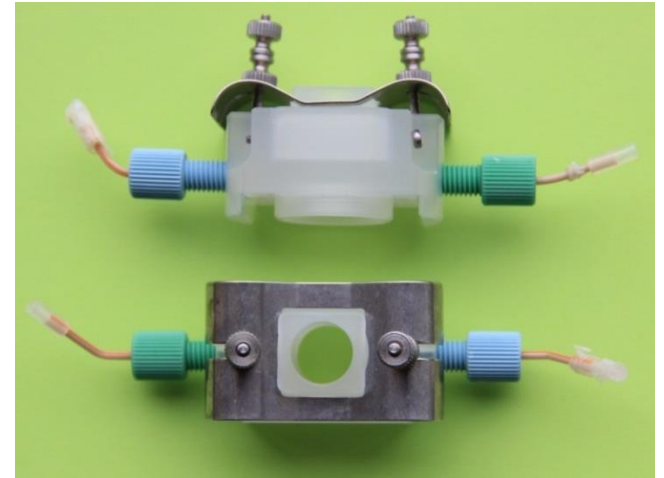


Penetration of different MW of hyaluronan (CONTIPRO PRELIMINARY DATA)



Experimental details

- HA of different MW in PBS
- Labelling-free method
- 20 hours, 37°C
- Franz diffusion cells
- Porcine auricular skin – **epidermis only**
- Quantification of HA by HPLC-MS in acceptor
(= penetration to dermis)



Penetration of different MW of hyaluronan (CONTIPRO PRELIMINARY DATA)



Product	HA in PBS	Acceptor concentration ($\mu\text{g}/\text{mL}$) = Penetration to dermis
HyActive	15 kDa	114 ± 32
HyActive	42 kDa	125 ± 27
HyActive	76 kDa	40 ± 21
HyActive	110 kDa	9 ± 6
HySilk	216 kDa	5 ± 1
	Control (PBS)	0.01 ± 0.01



MW of hyaluronan and its action



Low MW HA



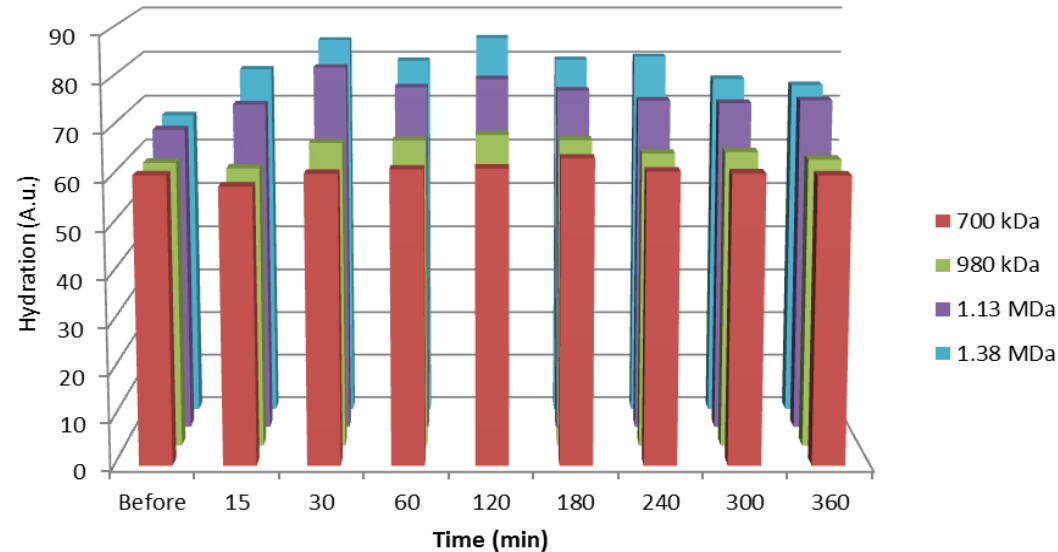
Biological activity



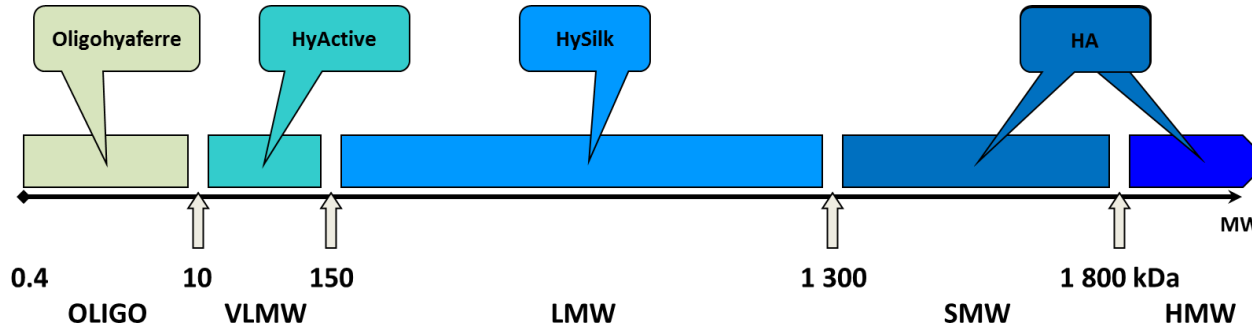
Film forming activity, lubrication ability

High MW HA

IMMEDIATE HYDRATION



MW of hyaluronan and its action



OligoHyaferre	HyActive	HySilk	SMW/HMW HA
Wrinkles	Wrinkles	Sebum reduction	Hydration
Elasticity	Texture	Hydration	Skin barrier
Hydration	Hydration	Texture	
<ul style="list-style-type: none"> Stimulates body's own HA synthesis Protects from ECM degradation Supports angiogenesis Nourishes skin Immunomodulator Keeps hydrating properties of HA 	<ul style="list-style-type: none"> Stimulates cell proliferation Support desquamation Reduces skin pores Stabilizes ECM Stimulates synthesis of ECM Keeps hydrating properties of HA 	<ul style="list-style-type: none"> Stimulates production of stratum corn. lipids and protects them Reduces sebum production Keeps hydrating properties of HA 	<ul style="list-style-type: none"> Film forming HA

HySilk

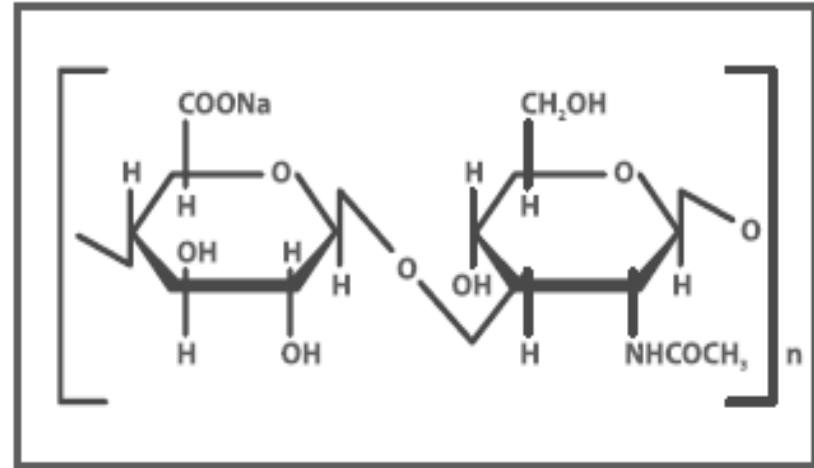
(LMW HA 150 - 1300 MDa)

HySilk

- LMW HA
- 150 – 1300 kDa
- Faster soluble in water
- Better penetration into skin
- High biological activity

Biological activity:

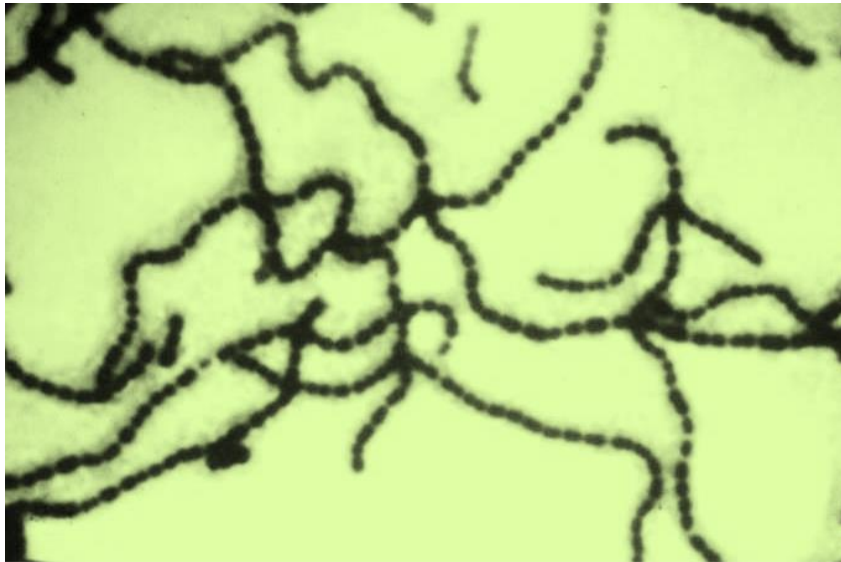
- Decreases **sebum** production
- Improves skin **texture**
- Increases **hydration**



HySilk - production



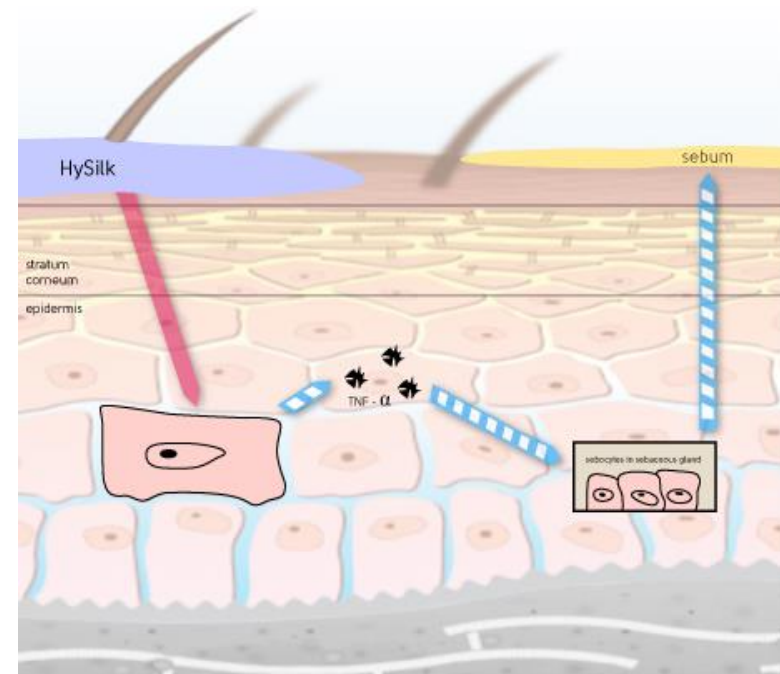
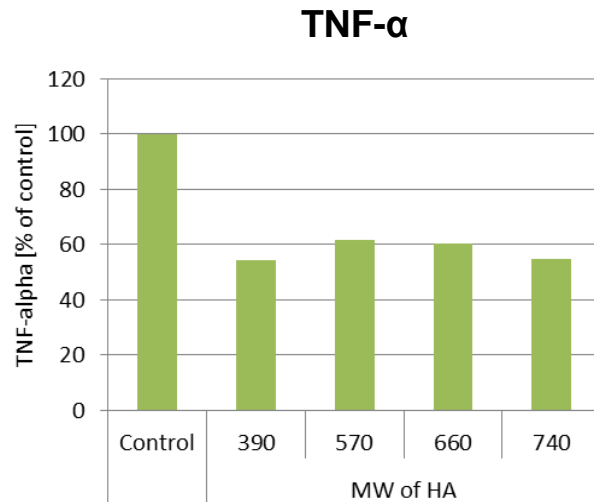
- Hydrolytical cleavage of high molecular weight hyaluronic acid
- Biotechnological production
- Fermentation of a non-haemolytic microbial strain *Streptococcus equi*



HySilk - oiliness

Down-regulation of **TNF- α**

- 0,05 % HySilk
- pro-inflammatory signalling molecule, increases sebum production
- Keratinocytes (NHEK) irradiated with UVB
- ELISA

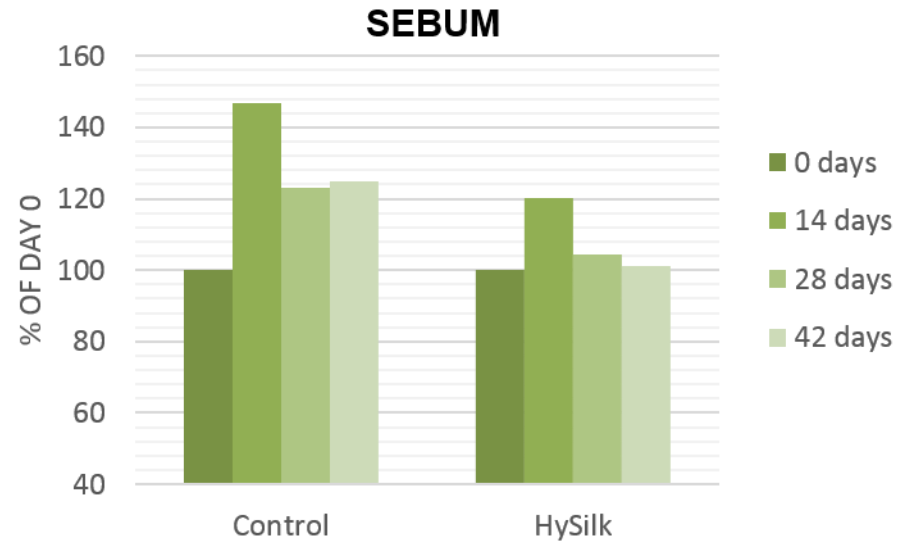


HySilk - oiliness



Reduces **oiliness**

- 0,2 % HySilk (320 kDa)
- 6 weeks
- n=20
- Sebumeter

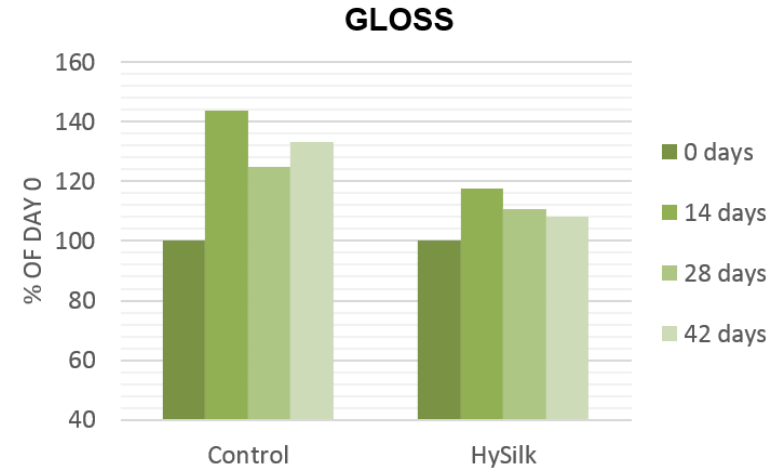
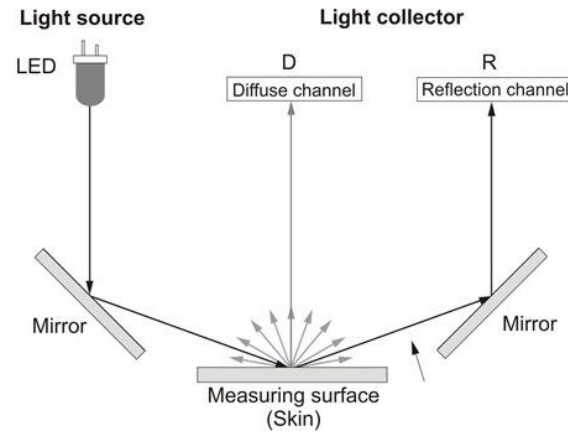


HySilk - oiliness



Reduces **oiliness**

- 0,2 % HySilk (320 kDa)
- 6 weeks
- n=20
- Glossometer

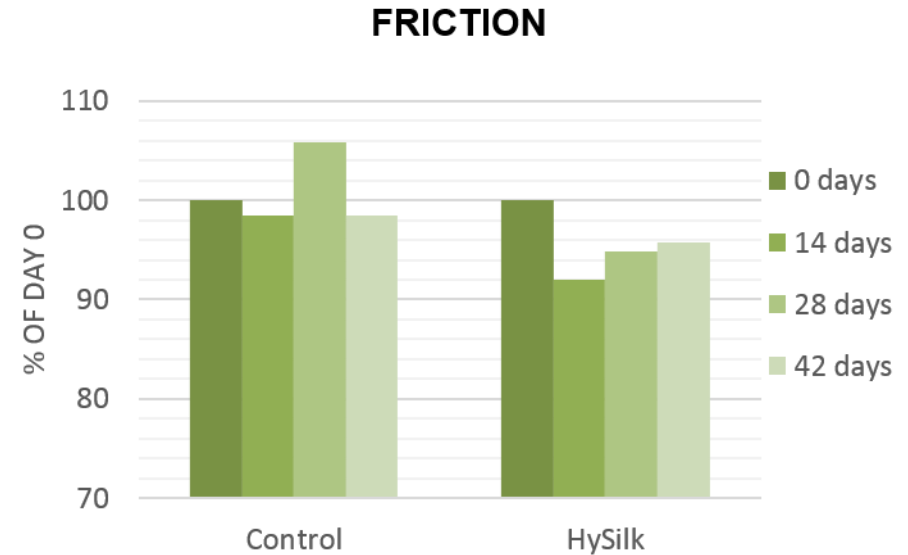
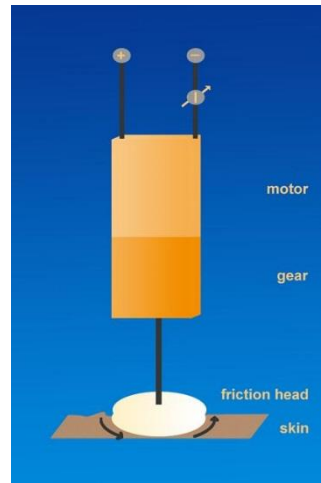


HySilk – skin texture



Reduces roughness

- 0,2 % HySilk (320 kDa)
- 6 weeks
- n=20
- Frictiometer



HySilk - skin barrier and hydration

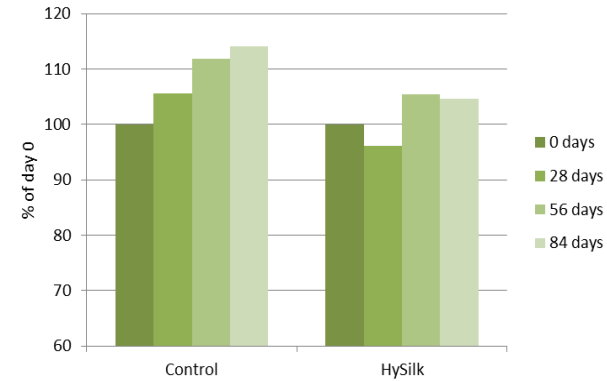


In vivo study:

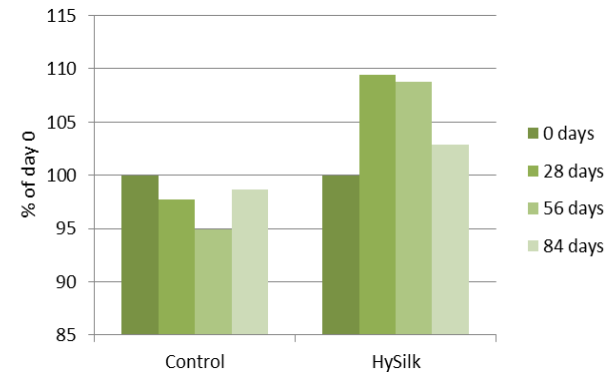
- 84 days
- 0.005 % HySilk
- 310 kDa
- n=8
- Tewameter
- Corneometer



TEWL



HYDRATION



HySilk – skin barrier and hydration

BIOLOGICALLY – NOT ONLY PHYSICALLY AS HMW HA

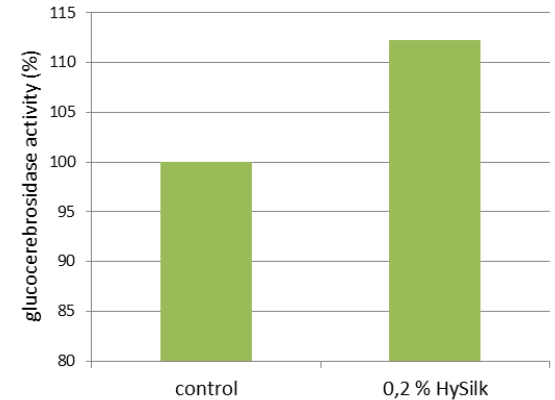
Increase in **β -glucocerebrosidase** activity

- important enzyme for production of stratum corneum lipids for **skin barrier** improvement
- Releases ceramides from their glucosyl precursors
- *In vivo*, forearm, 28 days, 11 volunteers, tape stripping
- Fluorescence assay

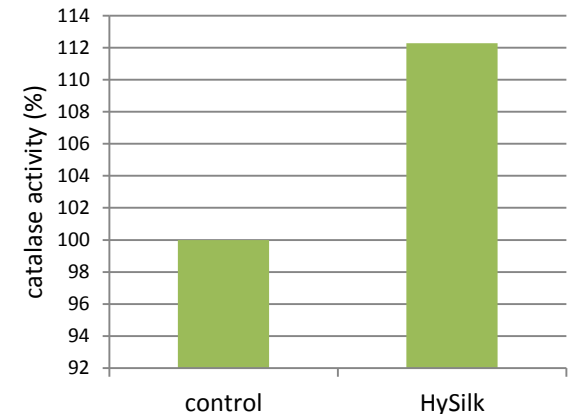
Increase in **catalase** activity

- Neutralizes **free radicals**
- Decreased damage of lipids and proteins
- *In vivo*, forearm, 20 days, 9 volunteers, tape stripping
- Colorimetric assay

β -GLUCOCEREBROSIDASE



CATALASE



HySilk – skin thickness

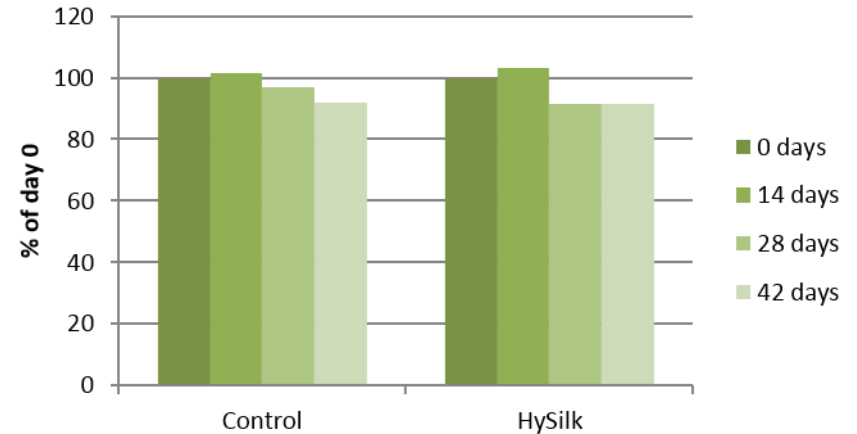


No effect on skin thickness in contrast to HyActive

- 0,2 % HySilk (320 kDa)
- 6 weeks
- n=20, external wrist
- In vivo reflectance confocal microscopy



SKIN THICKNESS



HySilk – conclusion



- **Low MW hyaluronic acid**
- Reduces skin **oiliness**
 - Reduces TNF- α
- Improves skin **texture**
- Improves **skin barrier** function and **hydration**
 - Hydrophilic molecule
 - Up-regulates β -glucocerebrosidase (improves stratum corneum lipids)
 - Up-regulates catalase (reduces lipid/protein damage by free radicals)

HySilk – technical data



INCI name: Sodium Hyaluronate

Samples: 1g of powder

Minimal ordering quantity: 1000 g

(If ordering smaller quantities, the price can be increased by the handling fees)

Recommended concentration in final products:

wide spectrum of formulations

0.01 – 0.25 % of powder

- **Appearance:** white powder or granules
- **Supplied form:** powder
1% solution (phenonip)
1% solution (phenoxyethanol)
- **Source:** fermentation of a non-haeolytic microbial strain *Streptococcus equi*.
- **Shelf-life:** 24 months
- **Compatibility and processing:** incompatible with cationic substances, e.g quaternary polymers and proteins. Recommended temperature for heating is 45–50 °C. It is also possible to heat the solution to higher temperatures like 70 °C for short time. Decreasing of molecular weight can occur. Extreme heating at the temperatures higher than 70 °C for long time can cause changes in molecular weight.
- **Solubility:** Fully soluble in water. Speed of dissolving depends on molecular weight. It is also soluble in a mixture of ethylalcohol, isopropylalcohol propylene glycol and butylen glycol with water up to ratio 1:1. Insoluble in solvents which are non-miscible with water.