

## **Synovea<sup>®</sup> HR:** The New Gold Standard in Skin Lightening & Even Toning

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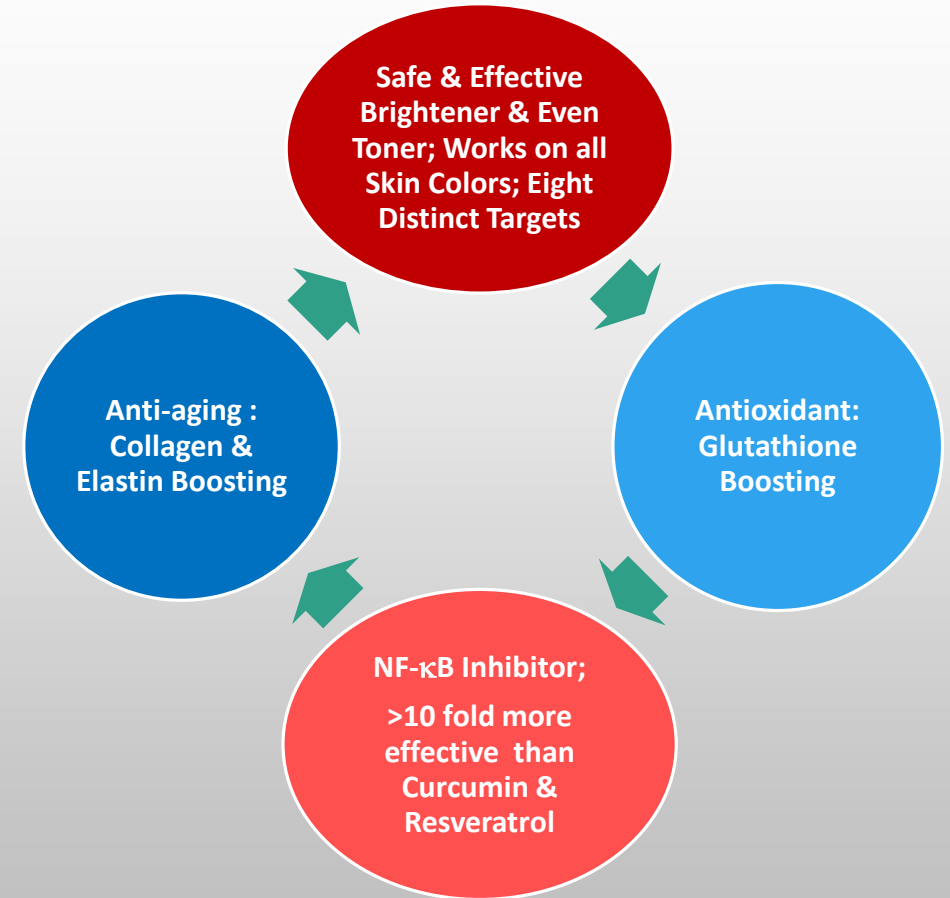
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# Synovea® HR: Product Overview

Trade Name	Synovea® HR
Chemical name	4-Hexylresorcinol
CAS Number	136-77-6
INCI Name	Hexylresorcinol
Appearance	Solid
Purity	99% min (typically, 99.5 to 99.9%); Residual resorcinol 0.05% (typically, <0.01%)
Country of origin	India
Miscibility	>20% in a wide-range of hydrophobic emollient esters, solubilizers , HydraSynol™DOI, HydraSynol™ IDL & glycols; <b>Do not use Ethanol</b>
Use level & formulation pH	0.5 to 1%; pH <6.0
Patent status	Multiple allowed foreign patents
Regulatory	Globally approved



**Anti-microbial Activity – Requires less amount of preservatives**

Asyntra® SL (INCI: Caprylic/Capric Triglycerides and Hexylresorcinol and Ethyl Linoleate)

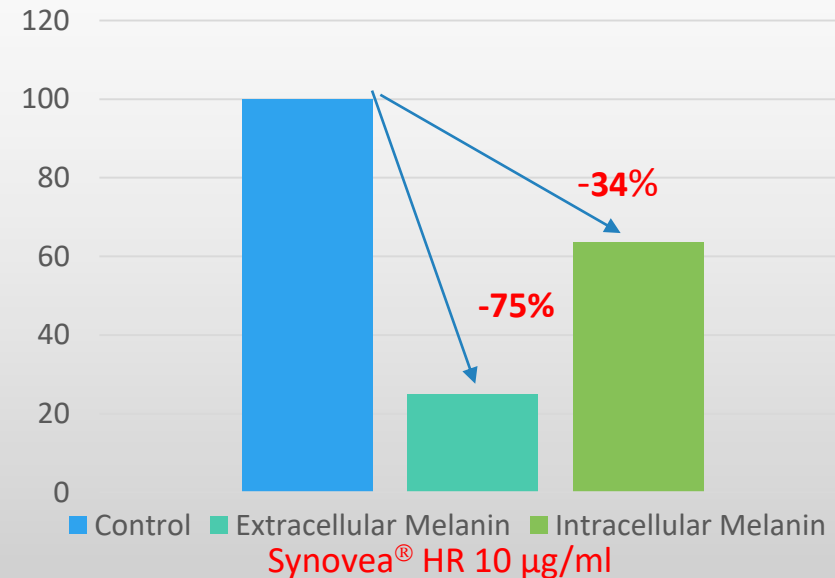
# In-vitro Melanin Inhibitory Activity of Synovea® HR

## Protocol

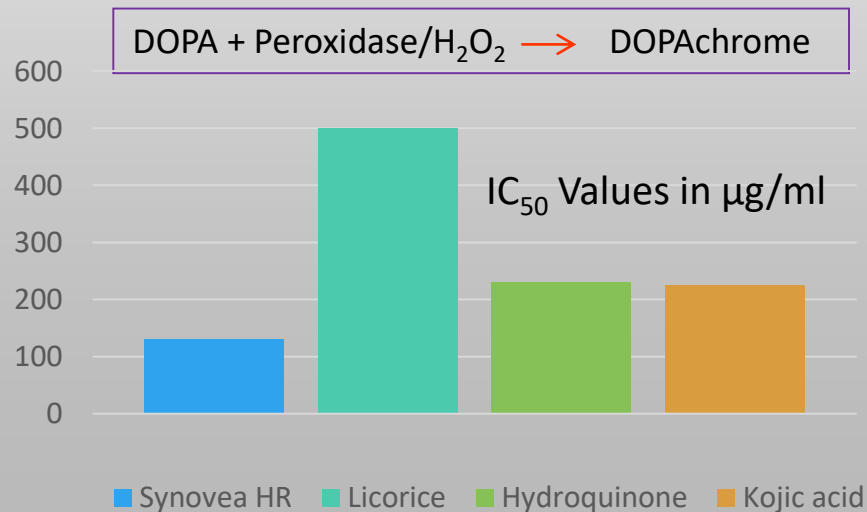
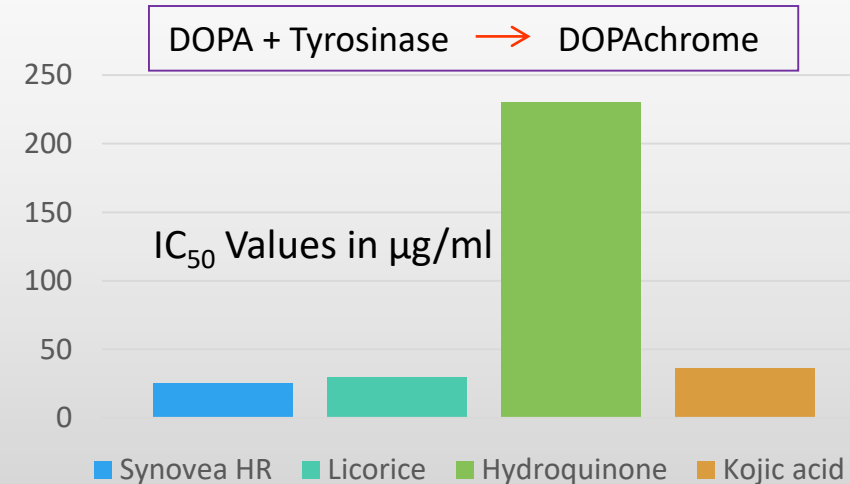
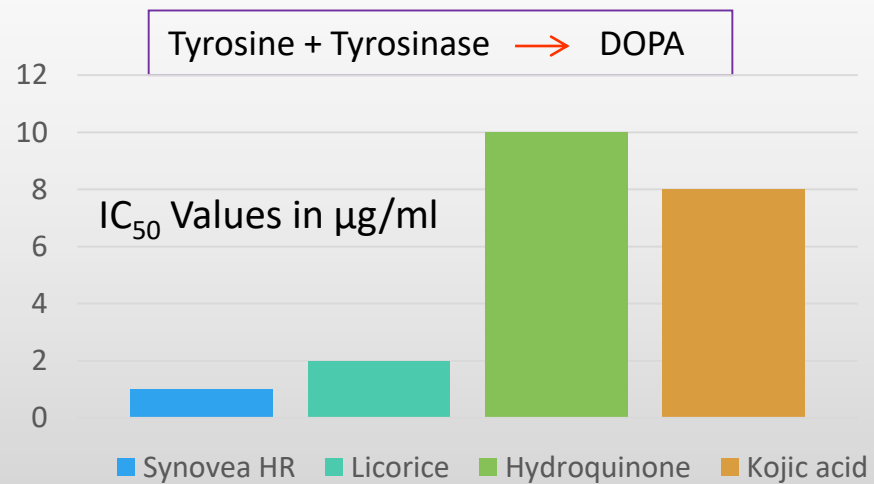
**Reference:** Ando H, Funasaka Y, Oka M, Ohashi A, Furumura M, Matsunaga J, Matsunaga N, Hearing VJ, Ichihashi M, *J Lipid Res*, 40:1312-1316, 1999

- B16 melanocyte cells in DMEM supplemented with 10% calf serum
- Incubated with Synovea® HR for 72 hrs
- Photographed cultures to show the effect in the extracellular melanin production: control vs product
- Counted cells and quantified melanin level by measuring absorbance at 490 nm

% Reduction in Melanin



# In-vitro Enzyme Inhibitory Activity: Synovea® HR vs. Key Skin Lighteners



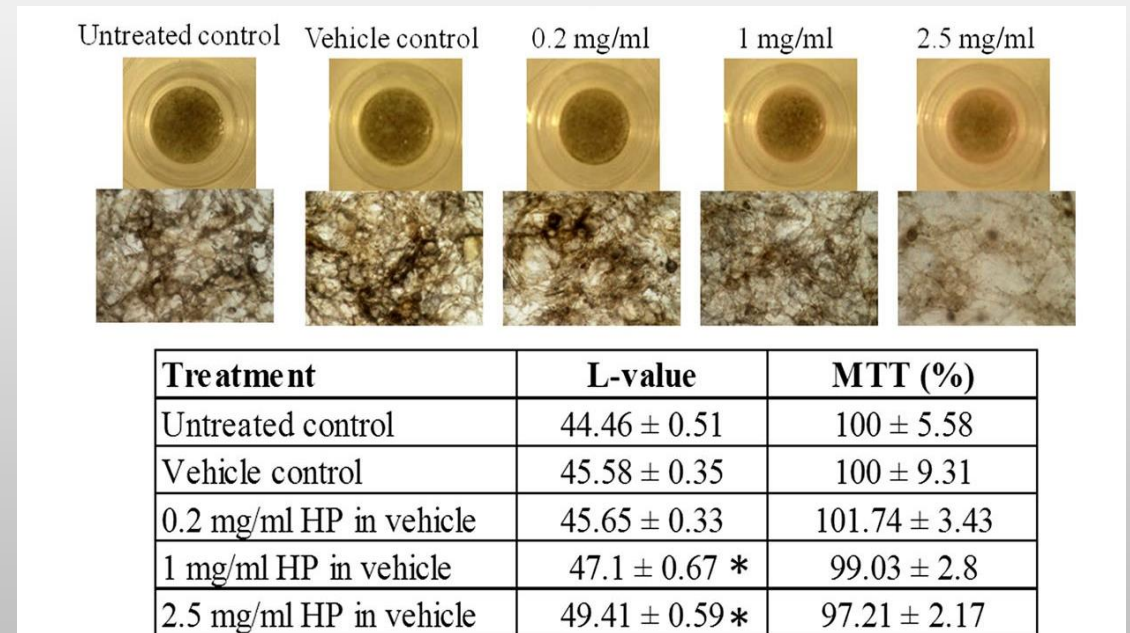
## Conclusion:

Synovea® HR has the most effective melanin inhibitory (in-vitro) activity over other well-known commercial products

# Hexylesorcinol Inhibits Melanogenesis in Pigmented Human Epidermal Equivalents

## PROTOCOL

- ❑ Pigmented human epidermal equivalents (melanoderm™) from Mattek corporation with melanocytes derived from black donor
- ❑ Treated with vehicle or Hexylresorcinol (5 µl / application) once daily in duplicate. Tissues were harvested on day 9
- ❑ Macroscopic and microscopic (4009) images taken with a digital camera. Tissues were then subjected to light measurement with a spectrophotometer, followed by MTT assay according to the manufacturer's protocol
- ❑ No cellular toxicity observed on melanocytes



HP = Hexylresorcinol; \* $p < 0.05$ )

**Data obtained from:** YK Won et al. Clinical efficacy and safety of 4-hexyl-1,3-phenylenediol for improving skin hyperpigmentation, Arch Dermatol Res, 306:455–465, 2014 (J&J Study)

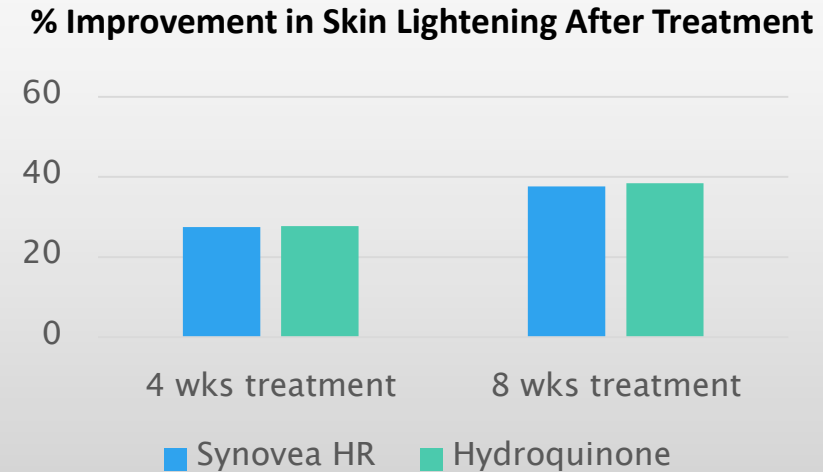
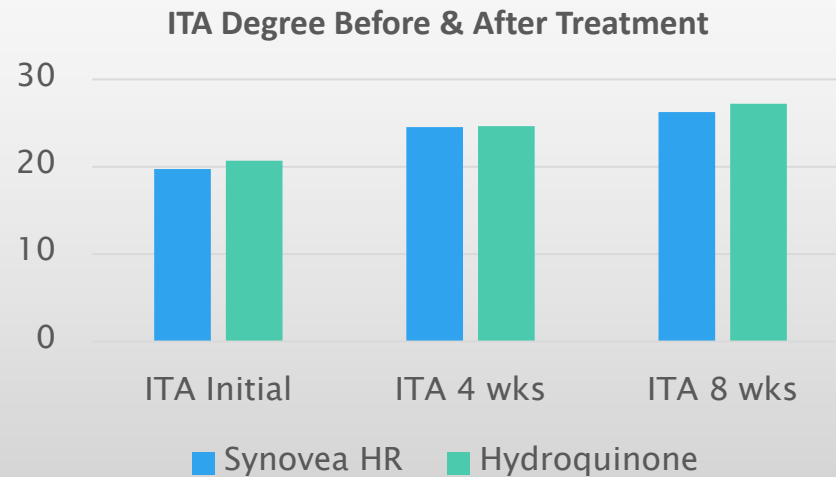
**Synovea<sup>®</sup> HR:**  
Human Clinical Studies: Normal & Hyper-pigmented Skin

# Skin Lightening Clinical Study: Synovea<sup>®</sup> HR vs. Hydroquinone

## PROTOCOL:

- ❑ **Human volunteers** – Asian, Caucasian, Hispanic & African-American
  - 13 subjects (ITA<sup>0</sup> ranging from 7 to 31)
- ❑ **Study duration** - 8 weeks (November 2006 to January 2007)
- ❑ **Test sites** - Left & right arms
- ❑ **Test substances** - 0.5% Synovea<sup>®</sup> HR in a lotion vs 2% Hydroquinone in a lotion
- ❑ **Application frequency** - Twice a day
- ❑ **Quantification of performance** - Represented using the individual typology angle (COLIPA SPF test method); Measured by chromametric measurement;  $\Delta E$  of ITA<sup>0</sup> was calculated by subtracting average ITA<sup>0</sup> of the treated site from that of the average baseline (first day of study)

# Skin Lightening Clinical Study: Synovea® HR vs. Hydroquinone



## Results

- ❑ Skin lightening effectiveness of 0.5% Synovea® HR compares well with 2% Hydroquinone
- ❑ **Synovea® HR requires 1/4<sup>th</sup> the amount** to have similar effect as Hydroquinone
- ❑ Highly significant statistically: p-value <0.05 ( 4 weeks); <0.005 (8 weeks)

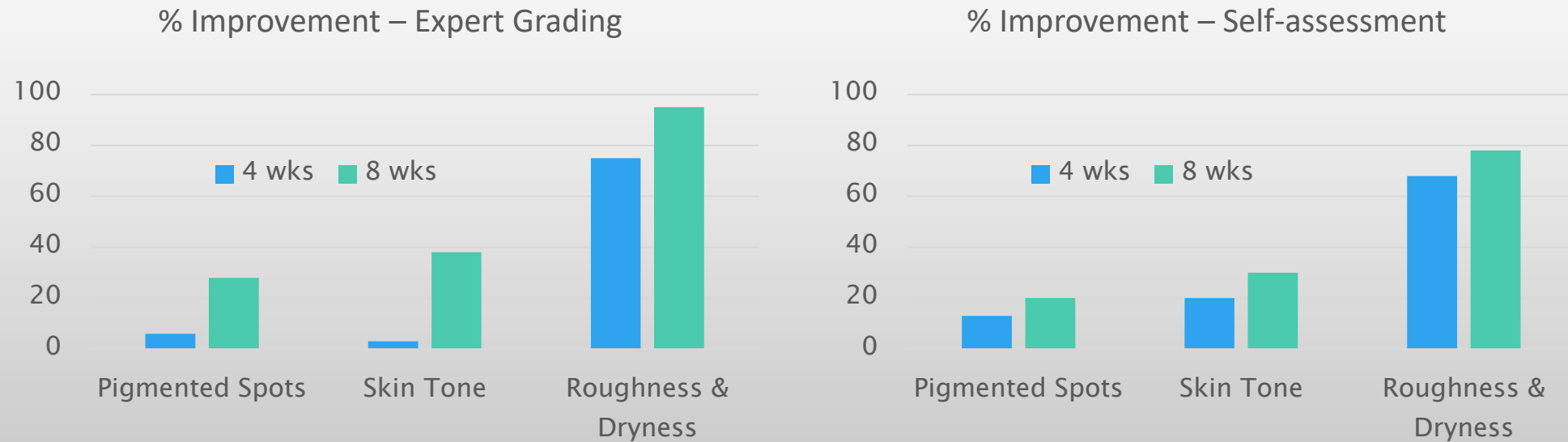


# Hyperpigmentation Control Study with Synovea® HR

## PROTOCOL:

- ❑ **Human volunteers** - 18; Caucasian (10), Asian(7) and Hispanic (1)
- ❑ **Study duration** - 8 weeks; May 2012 to July 2012
- ❑ **Study location** - Australia
- ❑ **Test sites** - Hand
- ❑ **Test substances** - 1% Synovea® HR lotion
- ❑ **Application frequency** - Twice a day entire hand(no sunscreen applied)
- ❑ **Quantification of performance** -
  - Comparative ITA<sup>0</sup> before & after treatment
  - Expert grading & Self-assessment (scale 0 to 4) – (1) Skin tone, (2) Reduction in hyperpigmentation spots (3) Roughness & dryness
  - Photography

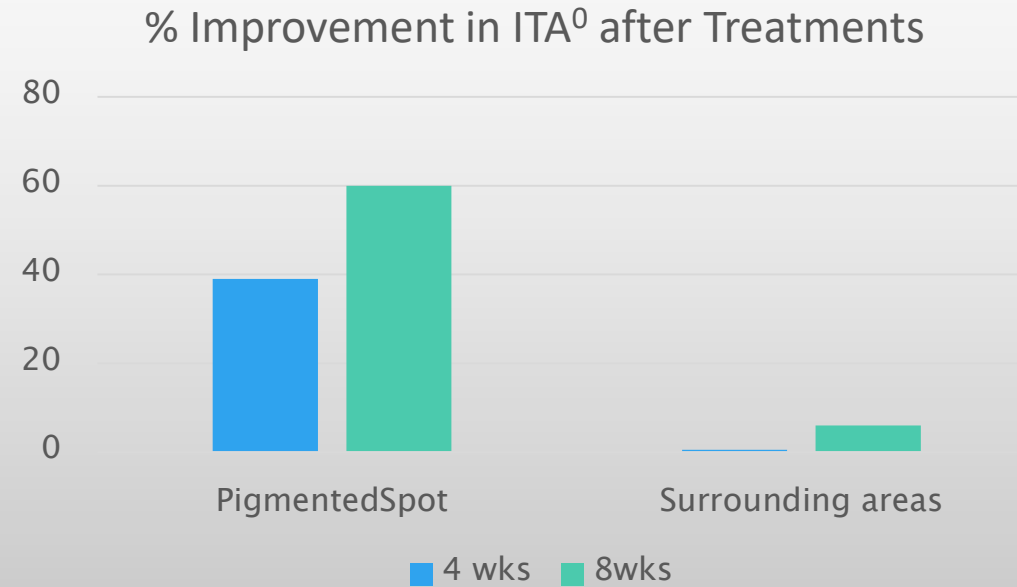
# Hyper-pigmentation Control Study with Synovea® HR



**Conclusion:**

Statistically significant (<0.05) improvement in skin appearance seen with 1% Synovea® HR lotion

# Hyper-pigmentation Control Study with Synovea® HR



**Conclusion:**

Significant even toning without affecting the surrounding areas with 1% Synovea® HR lotion

# Synovea® HR Reduces Hyper-pigmented Skin: African Subjects

## PROTOCOL:

- ❑ **Human volunteers** – African, 20 subjects aged 31 to 51 yrs.
- ❑ **Study duration** - 8 weeks
- ❑ **Study location** - France
- ❑ **Test sites** - Face
- ❑ **Test substances** – Cream A: 0.75% Synovea® HR + 2% Niacinamide and SPF 30 sunscreen lotion  
+ Cream B: 1% Synovea® HR + 3% Niacinamide
- ❑ **Application frequency** – Cream A during the day and Cream B during the night
- ❑ **Quantification of performance** -
  - Comparative ITA<sup>0</sup> before & after treatment
  - Subjective assessment by the volunteers
  - Photography

# Synovea<sup>®</sup> HR Reduces Hyper-pigmented Skin: African Subjects

## RESULTS:

- ❑ Comparison of ITA<sup>0</sup> at baseline and after 8 weeks product application showed
  - Reduction in 20% hyper-pigmented spots vs. 14% surrounding areas
- ❑ Significant improvement seen in clarity, complexion, hydration & reduction in pigmented spots, after 4 and 8 weeks of product application
- ❑ 95% volunteers expressed that their skin had “Healthy Glow”
- ❑ 89% volunteers would like to continue using the product irrespective of product pricing

# Clinical Study Results: Photographic Comparison between Baseline & After Treatment

**Volunteer # 9**



Baseline



After 8-week treatment

# Clinical Study Results: Photographic Comparison between Baseline & After Treatment

**Volunteer # 17**

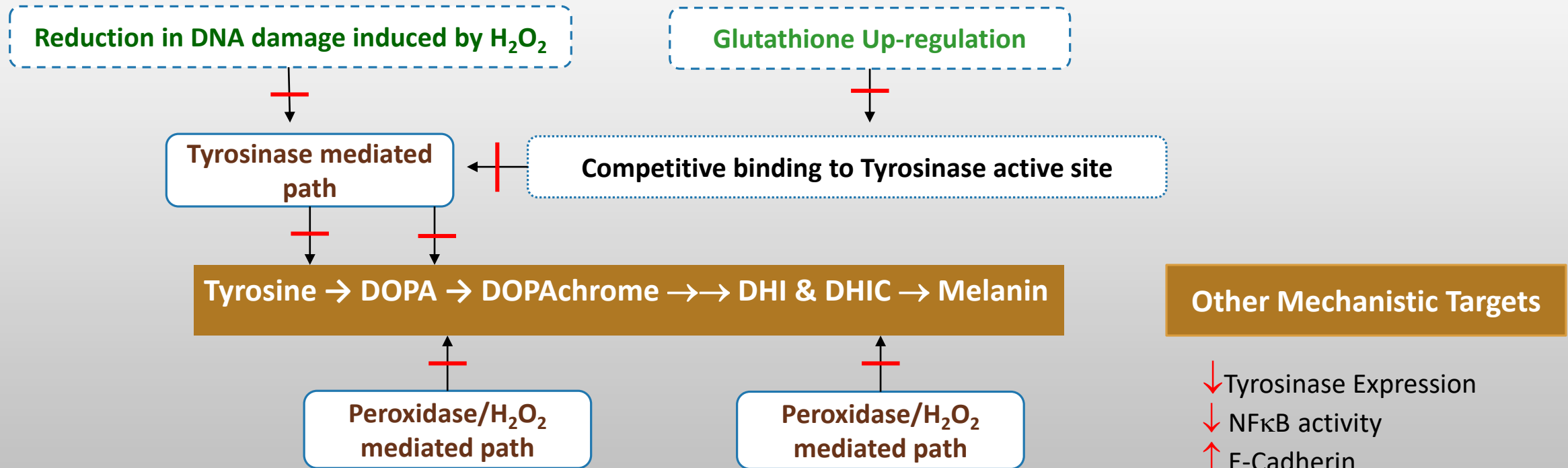


Baseline



After 8-week treatment

# Synovea<sup>®</sup> HR Inhibits Multiple Sites in the Melanogenesis Pathways





# Skin Protective Properties of Synovea® HR

## ❑ Cell Protection

- Up-regulating Glutathione, Glutathione peroxidase & Glutathione reductase (Free Radical Research, 37(5):509-514, 2003)

## ❑ DNA Protection

- Providing long-term protection of DNA degradation under UV light (Mikrobiologija, 75(5):662-669, 2006); 75(5):654-661, 2006)

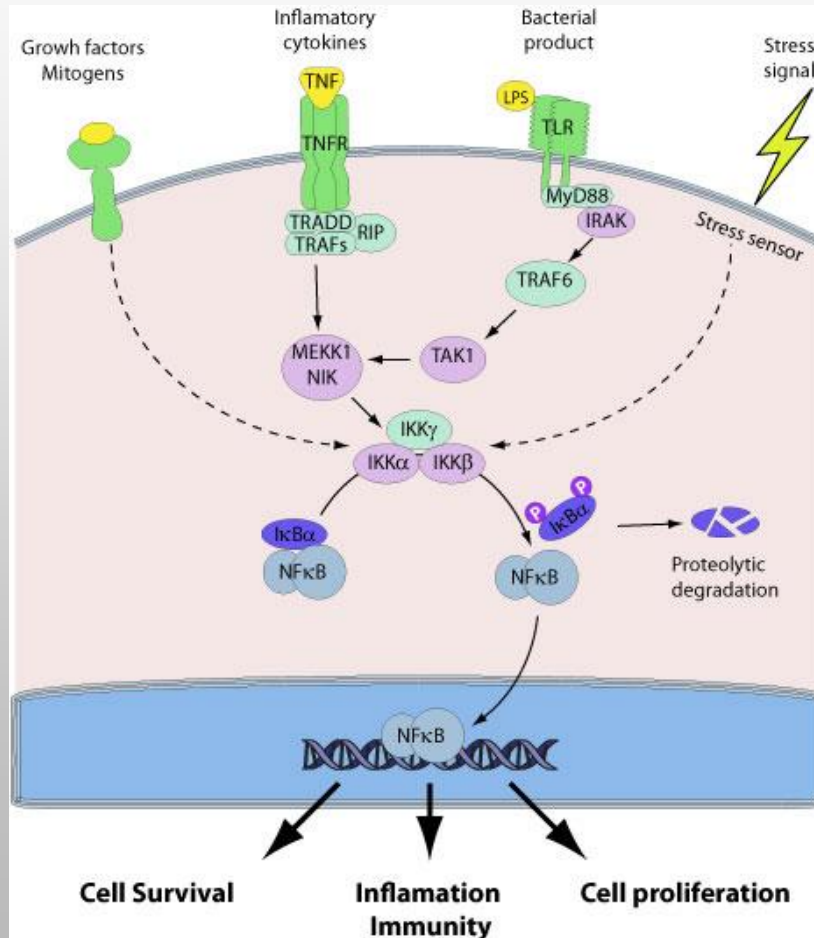
## ❑ DNA Repair

- Inhibiting DNA damage and improving DNA repair via NFκB pathway (Intertech, chapter 8, <http://dx.doi.org?10.5772?54341>, 2013)

## ❑ Protein Protection

- Protecting collagen and other proteins by reducing Glycation (J Agric Food Chem, 54(14):5120-5126, 2006)

# Synovea<sup>®</sup> HR: A Strong Inhibitor of Master Pro-inflammatory Transcription Factor NFκB



**Synovea<sup>®</sup> HR is 8 and 16-fold more effective than Resveratrol & Curcumin**  
Reference: Yang et al., Food Chemistry, 160:338-345, 2014

Compound	Amount Required to Inhibit NFκB Activity by >90%
Synovea <sup>®</sup> HR	6.25 μg/ml
Resveratrol	50 μg/ml
Curcumin	100 μg/ml

## What is NF-κB?

- NF-κB is a pleiotropic transcription factor which is present in almost all cell types
- NF-κB activation is a major mediator of inflammation in most diseases
- **Inhibition of NF-κB activation can suppresses inflammation**
- In unstimulated cells, NF-kappa-B dimers are sequestered in the cytoplasm via physical association with NF-kappa-B inhibitory proteins, called I-kappa-Bs.
- Upon activation, NF-kappa-B separates from I-kappa-B and migrates to the nucleus to activate gene transcription

# Key Publications

1. RK Chaudhuri, Hexylresorcinol: Providing skin benefits by modulating multiple molecular targets, In *cosmeceuticals and active cosmetics*, 3rd edition, Eds. Raja K Sivamani, Jared Jagdeo, Peter Elsner, Howard I Maibach, Francis & Taylor, Boca Raton, Chapter 7, pp 73-83, 2015
2. S Tucker-Samaras, M Kizoulis, S Kaur, M Southall, J Fantasia, 4\_hexyl-1,3-phenylenediol, An NF-κB inhibitor, improves photodamaged skin and clinical signs of ageing in double-blinded, randomized controlled trial, *Brit J Dermatol*, 173(1):218-227, 2015
3. YK Won, CJ Loy, M Randhawa, MD Southall, Clinical efficacy and safety of 4-hexyl-1,3-phenylenediol\* for improving skin hyperpigmentation, *Arch Dermatol Res*, 306(5):455-465, 2014
4. S Kaur, T Oddos, S Tucker-Samaras, MD Southall, Regulation of DNA repair process by the proinflammatory NFκB pathway, Intertech, Chapter 8, <http://dx.doi.org?10.5772?54341>, 2013
5. RK Chaudhuri, Effective skin lightening with skin protective properties, *Personal Care*, 39-44, 2010

\*note: 4-Hexyl-1,3-phenylenediol = Hexylresorcinol

## Concluding Remarks

- ❑ Safe & effective skin lightener/even toner
  - 80+ years history of human use; edible
  - Clinically proven to match hydroquinone performance with 1/4<sup>th</sup> of the dose.
  - Clinically proven to work for normal & hyper-pigmented skin & all ethnic groups
  
- ❑ Skin protection provided by
  - Protecting DNA damage & repairing damaged DNA by inhibiting NFκB
  - Stimulating glutathione to protect cells
  - Reducing glycation to protect protein
  - Reducing inflammation by inhibiting NFκB; Far superior to Resveratrol and Curcumine
  
- ❑ Antiaging benefits provided by
  - Stimulating collagen & elastin
  - Clinically proven to reduce multiple signs of aging