

# Pre-clinical and clinical efficacy of a dermo-cosmetic skin lightening cream in women suffering from melasma

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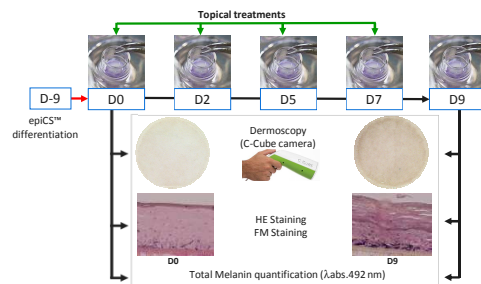
## Introduction

Melanin is a bio-pigment, synthesized within melanocytes. These cells localize in the basal layer of the epidermis. They transfer melanin to surrounding keratinocytes. The quantity, type and distribution of melanin in keratinocytes are one determinant of human skin color. Although melanin plays a critical role to protect skin from solar UV radiation, excess melanin synthesis can lead to hyper-pigmentation disorders such as melasma. Therefore, development of whitening products is of great interest to improve clinical and cosmetic concerns.

The aim of this study was to evaluate the efficacy of a skin lightening cream containing azelaic acid (12%) and glycolic acid (3%) with different approaches: *in vitro* with a pigmented reconstructed epidermis, *in vitro* with human skin explants and a clinical intra individual study. The dermatological safety of the product and the quality of life impact on subjects were also evaluated.

## Evaluation on Epidermis with Melanocytes

### Materials & Methods :



- Human Epidermis Equivalent with Melanocytes (epiCS™ 0.6 cm<sup>2</sup>, CellSystems™).
- Cream applied topically 4 times (D0, D2, D5 and D7)

### Results :

CIE L*a*b*	Day 0	D9 Placebo	D9 Kojic acid 1%	D9 Cream
L* (Lightness of the color)	85.2 +/- 0.04	81.15 +/- 0.86	83.57 +/- 0.65	86.53 +/- 0.42
a* (Chroma from green to red)	-0.99 +/- 0.19	1.73 +/- 0.07	0.69 +/- 0.17	-0.20 +/- 0.31
b* (Chroma from blue to yellow)	8.44 +/- 0.31	12.39 +/- 0.19	11.73 +/- 0.32	9.83 +/- 0.37
ITA* (Intensity of pigmentation)	76.52 +/- 0.47	68.30 +/- 0.49	70.74 +/- 0.80	74.52 +/- 0.47

ITA\* = arctan [(L\*50)/b\*] (180/π)

- Between Day 0 and Day 9 :**
- increase of pigmentation, decrease of luminance L\* and decrease of ITA.
- After treatment with kojic acid 1% :**
- decrease of pigmentation, increase of luminance L\* and increase of ITA.
- After treatment with the cream (D9) :**
- decrease of pigmentation, increase of luminance L\* and increase of ITA.

### Results :

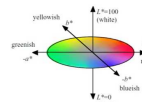
	Day 0	D9 Placebo	D9 Kojic acid 1%	D9 Cream
Hematoxylin Eosin (H/E) staining				
Fontana-Masson (F/M) staining				
Total melanin quantification (mg/ml)	0.010 +/- 0.006	0.0177 +/- 0.0009	0.0155 +/- 0.0009	0.014 +/- 0.002
% inhibition (compared to D9 placebo)	-	-	-12%	-20%

- Between Day 0 and Day 9 :**
- increase of Fontana-Masson staining and increase of total melanin.
- After treatment with kojic acid 1% :**
- decrease of Fontana-Masson staining and decrease of total melanin (-12%).
- After treatment with the cream (D9) :**
- decrease of Fontana-Masson staining and decrease of total melanin (-20%).

CIE L\*a\*b\*: color space describes colors visible to the human eye, was created to serve as a reference (device-independent model):

- L\*: Lightness (Luminance or Brightness), the lower L\*, the lighter the skin.
- a\*: Chroma from green to red.
- b\*: Chroma from blue to yellow.

With L\* and b\* values of a color, it is possible to calculate ITA\* (individual topology angle), a system developed for determining skin color. The lighter the skin, the higher the ITA\*.



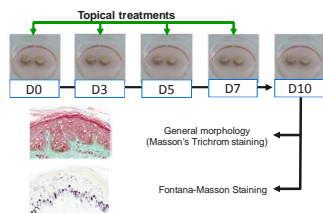
### Conclusion :

Goog correlation between F-M staining, total melanin quantification, Luminance L\* and ITA° angle.

## Evaluation on human skin explants

### Materials & Methods :

- Human skin explants (a 55 year old woman, phototype IV)
- Cream applied 4 times (D0, D2, D5 and D7)



### Results :

After 10 days treatment with the cream, the surface positive to melanin decreased by -22%.



## Clinical Evaluation in facial melasma

### Methods : Evaluations

The aim of this intra individual comparative study was to assess the clinical and instrumental efficacy of a skin lightening cream containing azelaic acid (12%) and glycolic acid (3%) in facial hyperpigmentation during 16 weeks :

- 31 volunteers included
- 16 weeks duration, visits at baseline, weeks 4, 8, 12 and 16
- Twice daily application
- Use of sunscreens recommended (real use situation)

#### CLINICAL

- Modified MASI
- Tolerance grading:
  - 0 = Low
  - 1 = Moderate
  - 2 = Good
  - 3 = Very Good

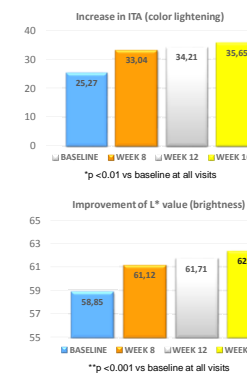
#### INSTRUMENTAL

- Chromameter
- Standard photography: Blinded Melasma severity grading (1-4)

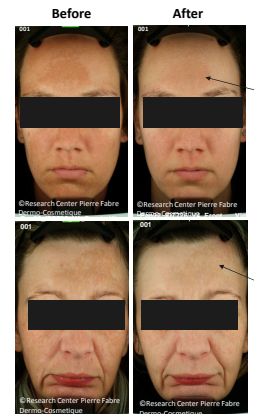
#### SUBJECTS

- QoL (MelasQoL)
- Cosmetic acceptability
- Efficacy assessment

### Results :



### Results :



### Conclusion :

- Improvement in ITA = color lightening;
- Improvement of brightening on facial pigmented lesions (mean, N=31)

## Conclusion

Altogether our data suggest that *in vitro* models could be used at a preclinical level to predict the pigmentation read-out of the clinical efficacy.

- Efficacy of the cream (azelaic acid 12% + glycolic acid 3%) on :
  - ✓ epidermis with melanocytes : total pigmentation, L\* and ITA angle.
  - ✓ human skin explants : FM staining and quantification.
- Clinical study: Progressive and significant improvement over 16 weeks of all parameters evaluated: skin brightening and lightening, reduction in % of affected area and improvement of Quality of Life. We have shown that this **skin lightening cream** containing azelaic acid (12%) and glycolic acid (3%) had a **significant whitening effect** *in vitro* and *in vivo* and can be used to **improve melasma**.



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