CLINICAL EFFICACY AND SAFETY OF 25% L-ASCORBIC ACID (C'ensil™) FOR MELASMA

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Introduction

- Melasma

- Acquired hypermelanosis of the face

- Clinical pattern

; centrofacial, malar, mandibular

- Trigger factors

; UV exposure, pregnancy, hormones, oral contraceptives, genetic influence, thyroid abnormalities

Introduction

- Peeling agents
  - Remove various amount of epidermis and dermis together with melanin
  - trichloroacetic acid(TCA), alpha hydroxyacids(AHAs), gylcolic acid

- Melanocytotoxic agents
  - Reduce the conversion of L-dopa to melanin by inhibiting tyrosinase
  - hydroquinone, catechols, butylated hydroxyanisole

- Antioxidants
  - Protect the skin against damage from free radicals induced by UV radiation
  - L- ascorbic acid, α-tocopherol

Introduction

- Vitamin C

- Nonenzymatic biologic antioxidant

; neutralizing free radicals generated in aqueous compartment of the cell

; primary replenisher of Vit. E , inhibitor of lipid peroxidation, association in protecting lipid structure

; cannot scavenge lipophilic radicals within the memb.

- Depigmenting effect

; suppression of melanocyte proliferation factors

→ ROS: stimulation of mediators (IL-1α, α-MSH, PGE_2) involved in pigmentation

→ suppress secretion of IL-1α, PGE_2

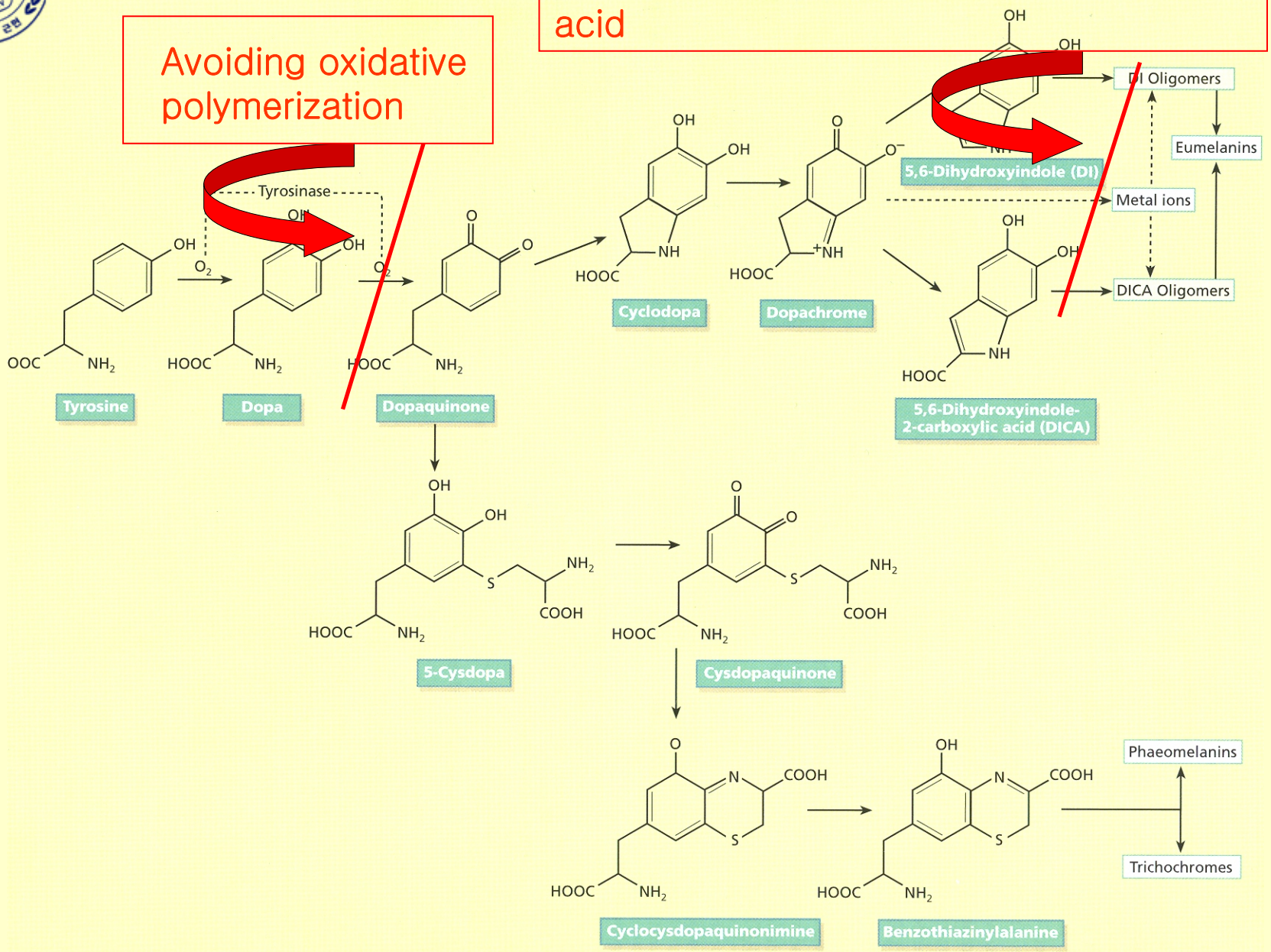
; interacting with *o*-quinones

→ reducing dopaquinone to dopa

; inhibiting the peroxidase-catalyzed melanogenic reaction*(Behrooz et al. 2002)*

Blocking 5,6-dihydroxyindole-2-carboxyl acid

Avoiding oxidative polymerization



Introduction

- Vitamin C

- Regulation of collagen production, biosynthesis (*Darr et al. 1996*)

; participation in hydroxylation of lysine, proline

→ promote formation of triple heilcal conformation of mature collagen

; increase mRNA of collagen type I, III

; increase tissue inhibition of matrix metalloproteinase mRNA

- Anti-inflammatory effect *(Carcamo et al. 2001)*

; inhibition of TNF-α, NF-κB, IL-1,IL-6

Introduction

- Penetration of Vit.C into the skin

- Hydrophilic characteristics

; poor penetration into lipophilic stratum corneum

- Instability in formulation

- *Pinnell et al(2001).*

; L-ascorbic acid in acidic formulation (pH < 3.5)

→ critical for percutaneous absortion of L-ascorbic acid

→ maximal L- ascorbic acid skin concentration; 20%

; induce irritation d/t acidic condition

- Ascorbic acid derivatives

- magnesium ascorbyl phosphate (MAP), ascorbly-6-palmitate

- Stable in aqueous solution

- After penetration, ascorbic acid derivatives convert to L- ascorbic acid

; remain on extracellular surface in derivatives form, less converted to L-ascorbic acid

C'ensil™

- **Stability & Penetration**

; L-ascorbic acid→ quickly oxidized, decomposes in aqueous solution

; solvent→ Amphiphilic Transdermal Delivery System

→ *N-Methyl-2-pyrrolidone*, *Dimethyl isocorbide*

1) N-Methyl-2-pyrrolidone

: chemical penetration enhancer, modify drug parameters for penetration, stabilize ascorbic acid in aqueous solution

→ *hydrophilic character*

2) Dimethyl isocorbide

: chemical penetration enhancer, reduce water content of stratum corneum, displace water in stratum corneum

→ *lipophilic character*

- **Concentration**; 25% L-ascorbic acid

; *N-Methyl-2-pyrrolidone*→ stabilize L- ascorbic acid, can increase skin concentration

Objectives

- To evaluate the efficacy of 25% L-ascorbic acid serum (C'ensil™) in the depigmentation of melasma

Method & Material

- **Patient selection**
  - 40 female patients with mild to severe melasma on face
  - 26~55 years (mean 37yr)
  - 27 patients; Fitzpetric type III, 13 patients; IV
  - Type of melasma
    ; by Wood light exam.
    ; 8 with epidermal type, 7 dermal type, 13 mixed type
  - Application of study cream
    ; twice- daily-full face application for 16 weeks (2006 June to September)

Method & Material

- **Evaluation of efficacy**

- Clinical photograph every 4 weeks
- To evaluate severity of melasma, calculate MASI score every 4 weeks
- To evaluate lightening effect, check mexameter reading every 4 weeks
- To evaluate skin condition, check TEWL, sebumeter reading every 4 weeks
- To evaluate the effect of melasma on patient's life of quality check MELASQOL at base and 16 weeks

Method & Material

- **Evaluation of efficacy**

1. MASI (Melasma Area and Severity Index) score

- area of involvement, darkness and homogeneity of melasma

1) Area of involvement(A)

2) Darkness(D), Homogeneity(H)

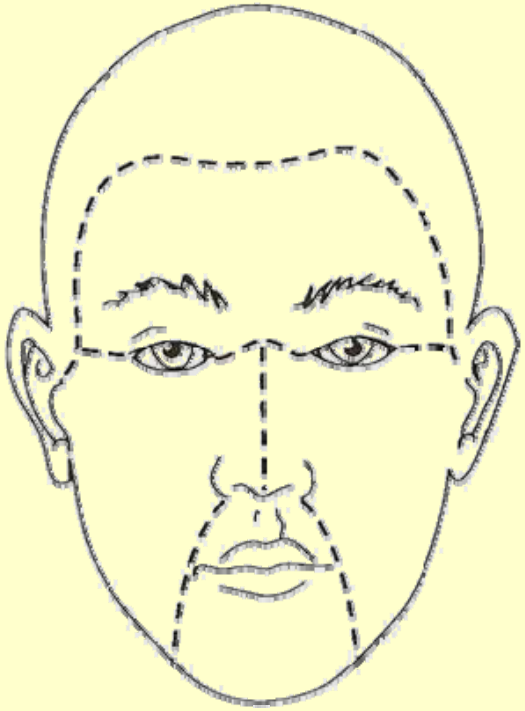
; parameter for scale

→ 0: absent, 1: slight, 2: mild, 3: marked, 4: maximum

MASI : area of involvement

Forehead R Malar L Malar Chin

MASI = 0.3A (D+H) + 0.3A(D+H) + 0.3A(D+H) + 0.1A(D+H)



; 4 area on the face

→ forehead(f:30%), right malar(rm:30%), left malar(lm:30%), chin(c:10%)

; involvement

→ 0: no involvement, 1: 1-9%, 2:10-29%, 3:30-49%, 4:50-69%, 5:70-89%, 6:90-100%

Method & Material

- **Evaluation of efficacy**

1.Mexameter, MX 18 probe

- provide a reproducible, objective estimate of the content of melanin (M value) and hemoglobin (erythema, E value)
- 3~4 melasma lesion, 5 non-affected facial area
- one area of inner surface of forearm (for control)
  : to evaluate the effect of tanning from sun exposure
- evaluate M value at 4, 8, 12, 16 weeks

2.TEWL (Trans-epidermal water loss), TM 300 probe

- important parameter for evaluating the function of epidermal barrier
- indicate the rate of migrating water from viable tissue through the layer of stratum corneum to the external environment
- two treated areas of face (forehead, Lt. cheek)
- at 4, 8, 12, 16 weeks

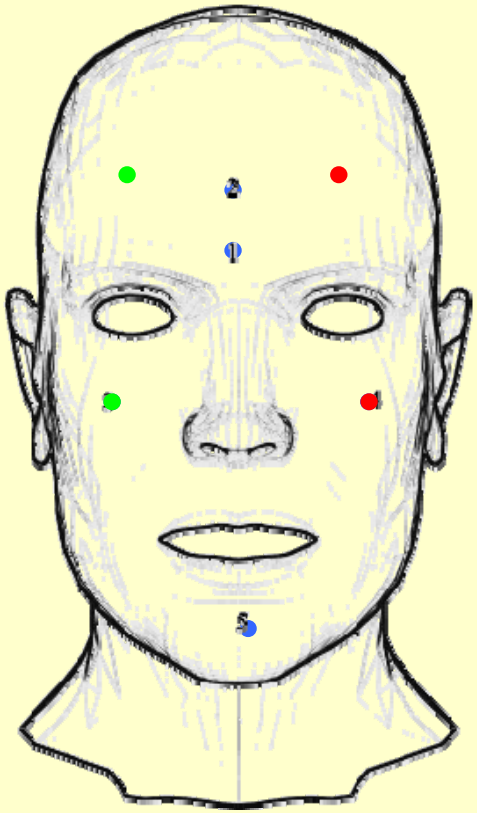
Method & Material

- **Evaluation of efficacy**

3. Sebumeter, SM 815 probe

- determining skin surface sebum
- direct measurement of the sebum secretion on skin
- two treated areas of face (forehead, Rt. cheek)
- at 4, 8, 12, 16 weeks

Evaluation of efficacy



• Mexameter

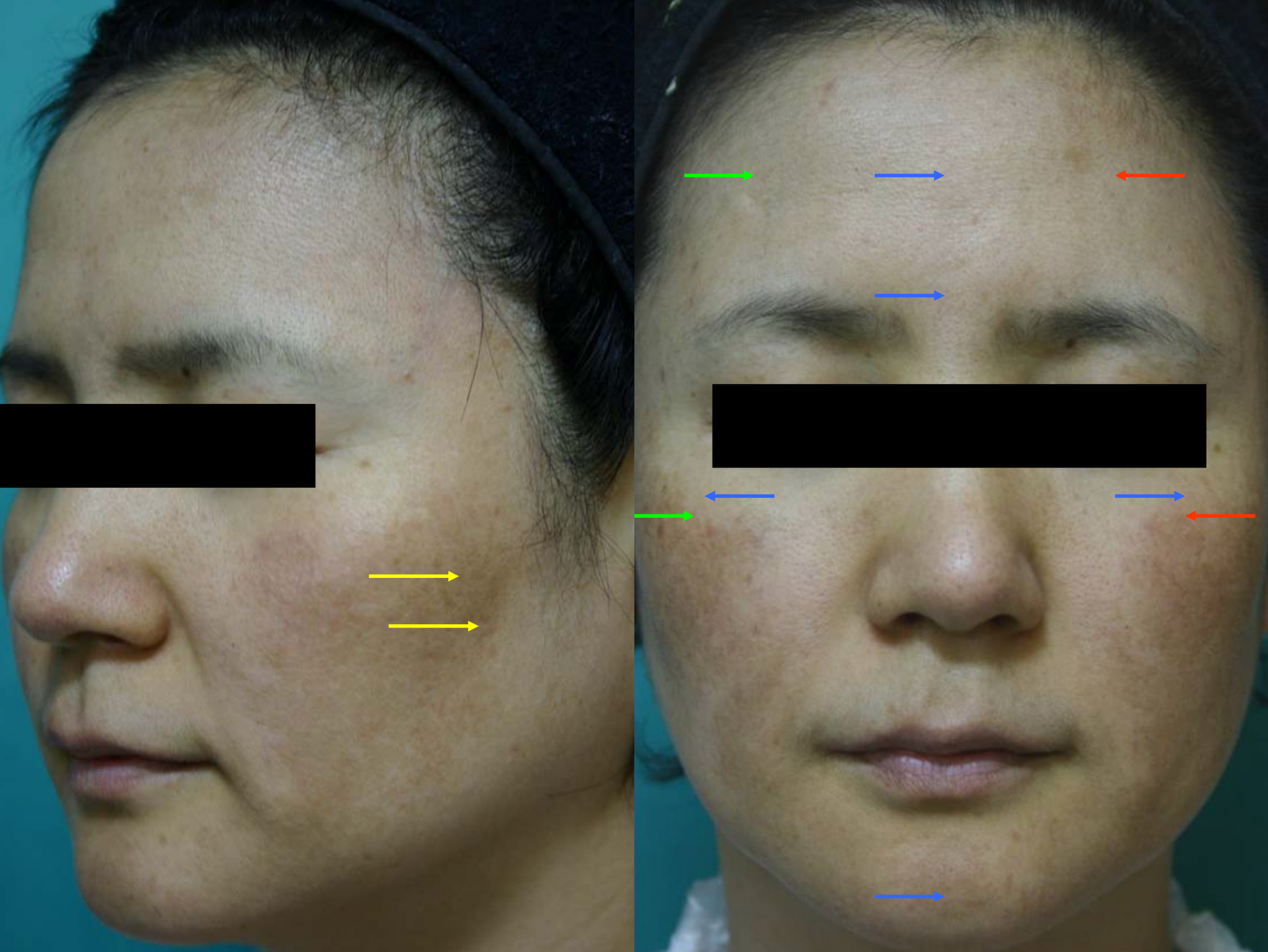
1) Glabella
2) Center of forehead
3) Rt.zygomatic prominence (Rt.zygoma)
4) Lt. zygomatic prominence
5) Chin

• Tewameter

1) Junction of mid. sagittal eyebrow line and horizontal line of center of forehead
2) Lt. zygomatic prominence

• Sebumeter

1) Junction of mid. sagittal eyebrow line and horizontal line of center of forehead
2) Rt. zygomatic prominence



Method & Material

- **MEALSQOL**

- 10 questions
  ; effect of melasma on various aspect of the affected patient's life on a scale
  ; scale ranging 1-7, overall ranging 7-70

- higher score indicating worse melasma- related health-related quality of life

MELASQOL

Melasma Quality-of-Life Scale

On a scale of 1 (not bothered at all) to 7 (bothered all the time), the patient rates how she feels about:

1. The appearance of your skin condition
2. Frustration about your skin condition
3. Embarrassment about your skin condition
4. Feeling depressed about your skin condition
5. The effects of your skin condition on your interaction with other people (eg, interaction with family, friends, close relationship)
6. The effects of your skin condition on your desire to be with people
7. Your skin condition making it hard to show affection
8. Skin discoloration making your feel unattractive to others
9. Skin discoloration making you feel less vital or productive
10. Skin discoloration affecting your sense of freedom

Result

- 39 of 40 patients; completed entire 16-week protocol

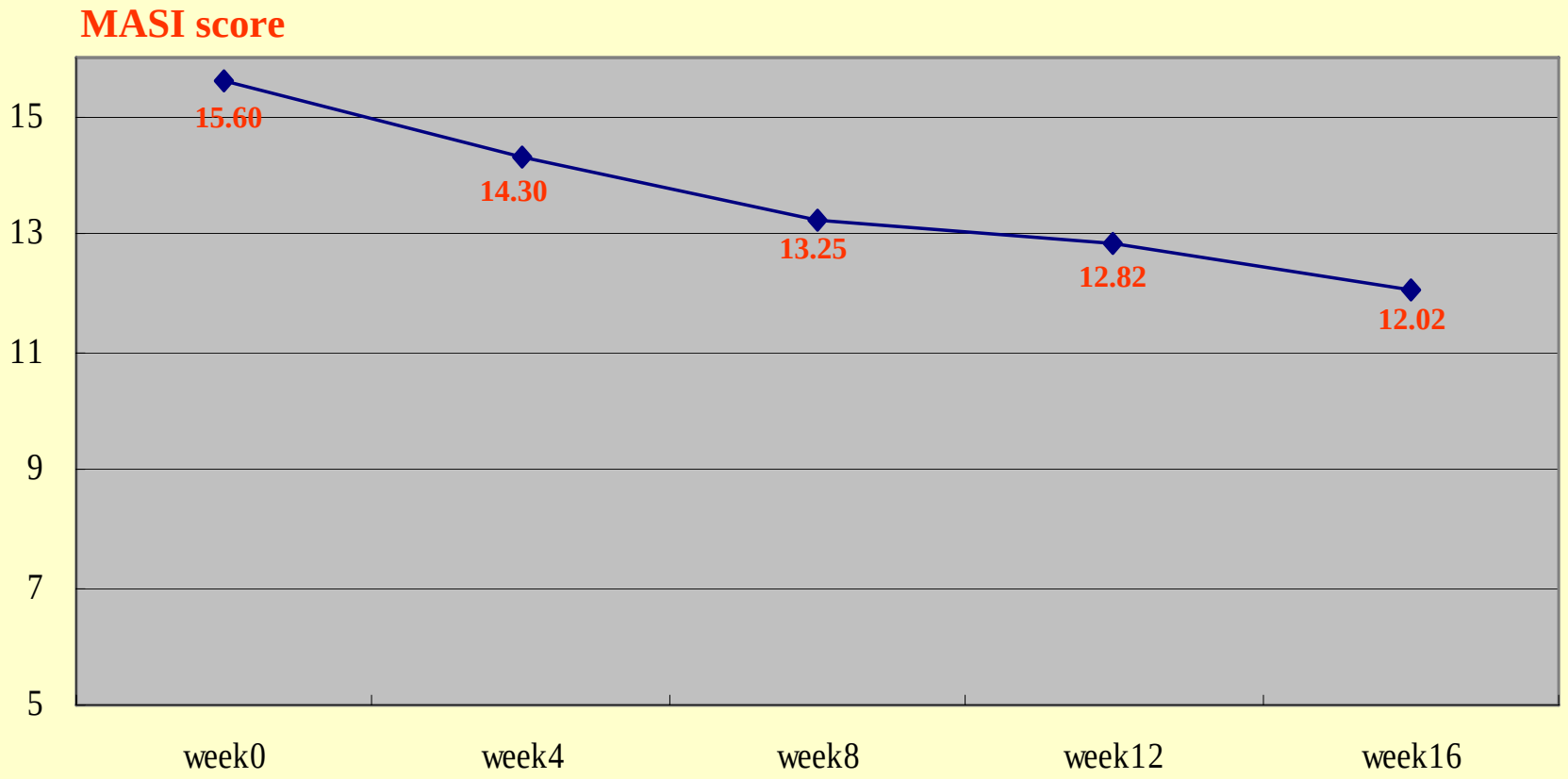
	baseline	4 week	8 week	12 week	16 week
MX (non-affected)	189.95	189.43	188.53	187.22	182.75
MX (melasma)	215.01	207.81	209.28	204.84	198.75
MX (control)	140.25	142.08	144.05	143.62	143.33
Sebumeter	13.26	9.11	8.81	10.27	10.17
TEWL	9.15	10.90	10.30	9.91	9.88
MASI	15.60	14.30	13.25	12.82	12.03
MELASQOL	39.85				36.23


Baseline
16 week


We reserve many other photos, due to the right of likeness of other patients.
Baseline
16 week

Result

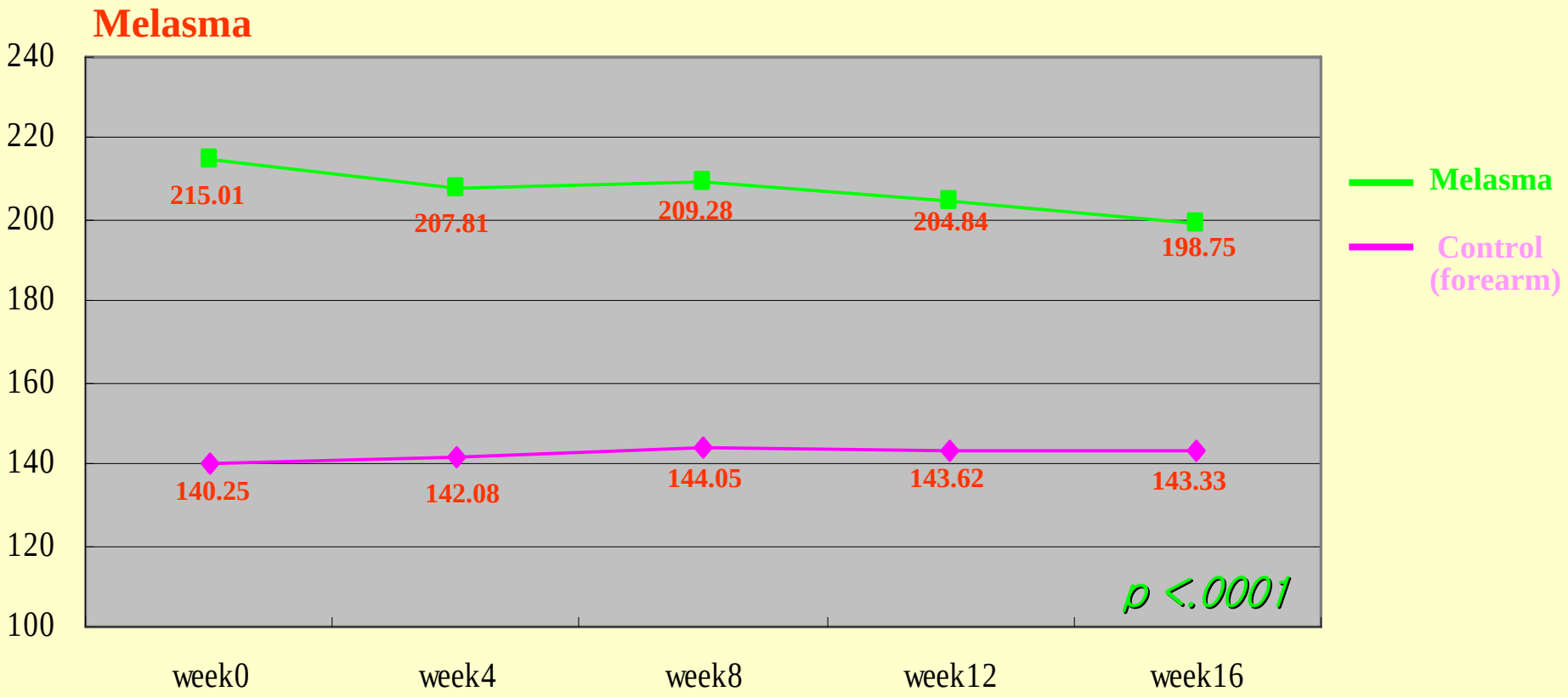
1. MASI (Melasma Area and Severity Index) score



$p < .0001$

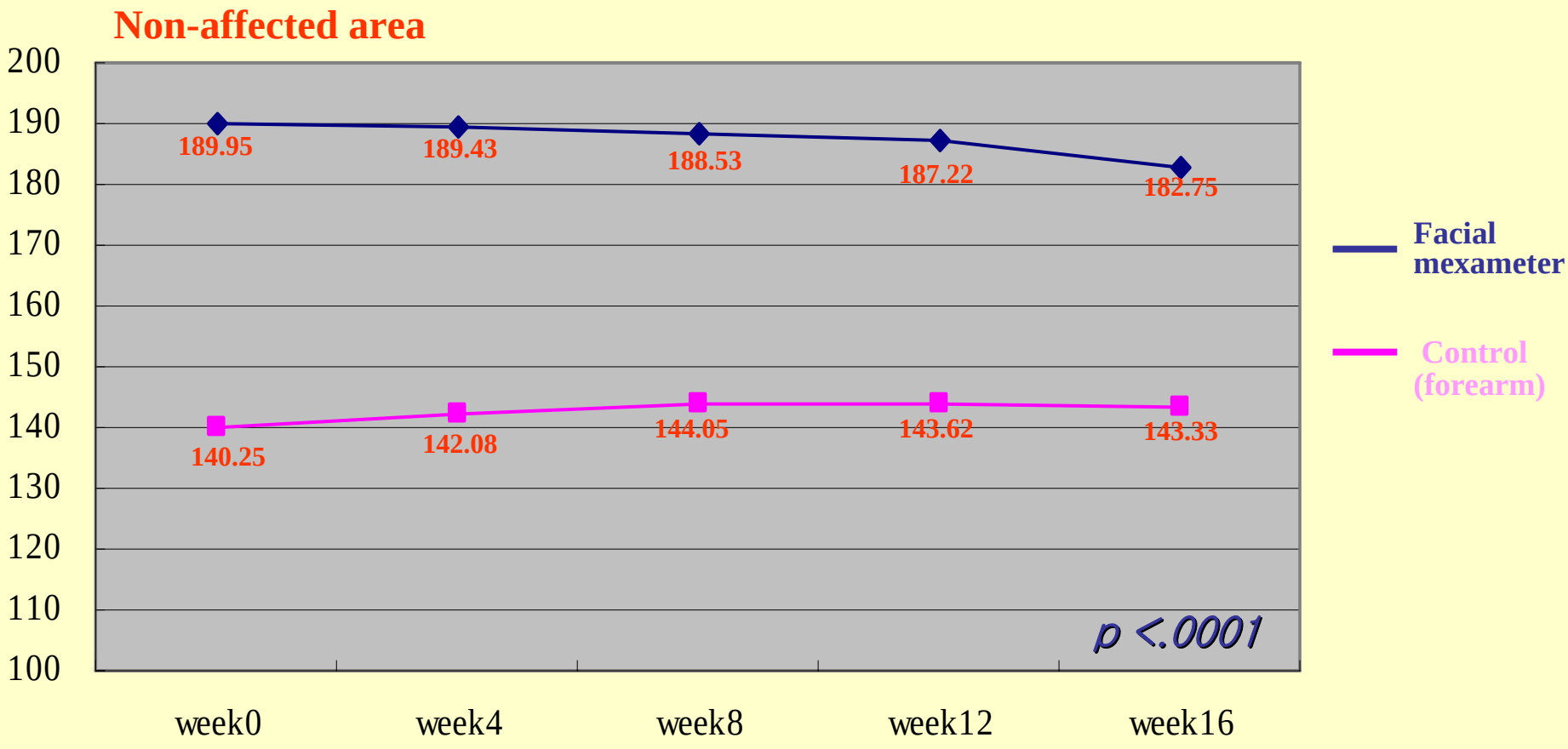
Result

2. Mexameter



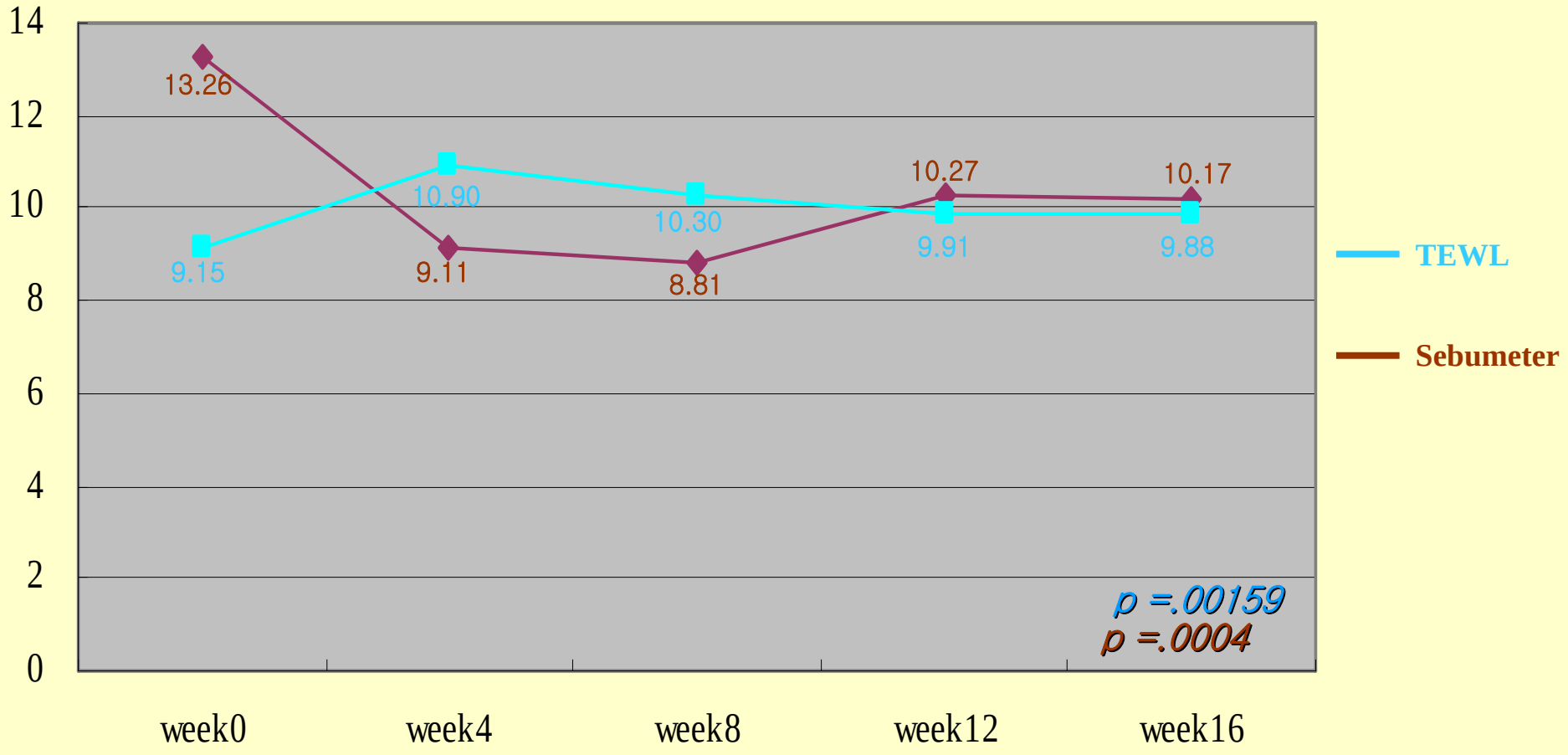
Result

2. Mexameter



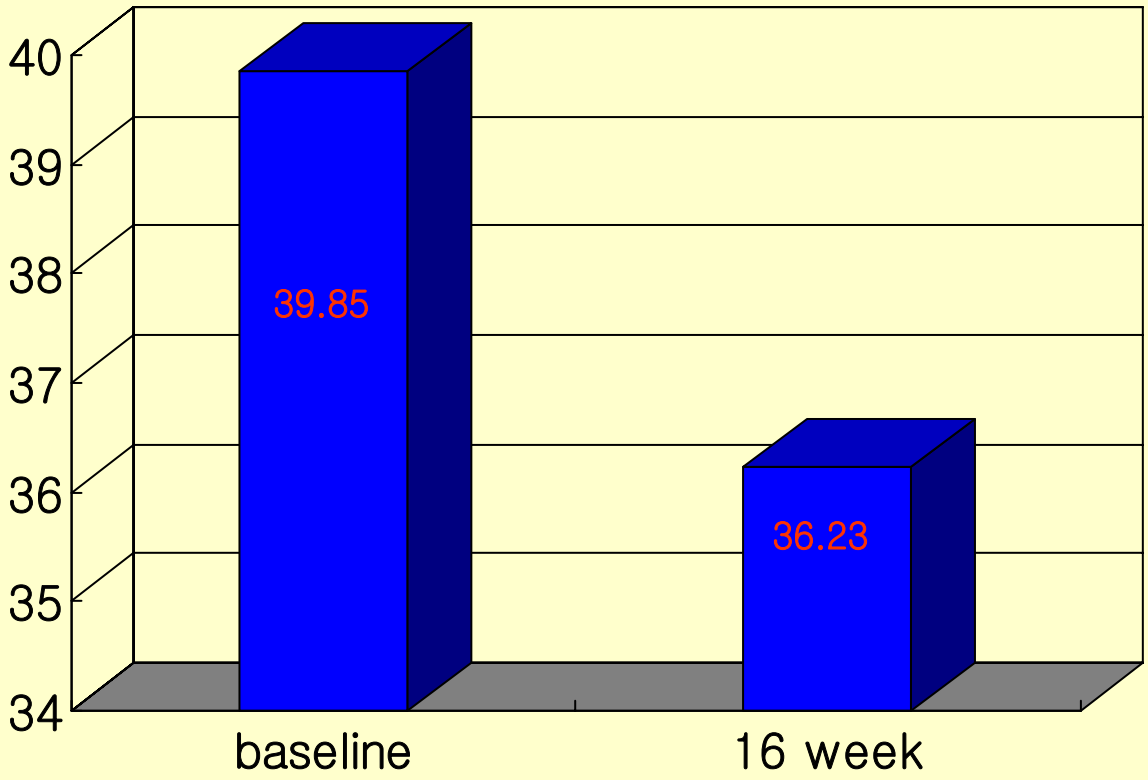
Result

4. TEWL & Sebumeter



Result

6. MELASQOL



Conclusion

- **Statistically significant differences showed a greater reduction in mexameter of melasma, non-affected area and MASI score at each study visit.**

→ *25% L-ascorbic acid revealed therapeutic efficacy for treating melasma and lightening of skin.*

- **Mexameter readings from the inner surface of forearm showed no significant change through the course of the study.**

→ *tanning from sun exposure was not significant factor*

Conclusion

- **Statistically significant differences showed a greater reduction in sebum secretion at each study visit.**

  → *25% L-ascorbic acid can produce therapeutic efficacy for reducing secretion of sebum.*

- **Statistically significant differences showed a increase trans-epidermal water loss at the 1st visit.**

  → *25% L- ascorbic acid induced disruption of stratum corneum for initial period of treatment.*

Conclusion

- 25% L-ascorbic acid serum (C'ensil^{TM})

- New, promising therapeutic agent for melasma
- Beneficial effect on lightening of skin preventing UV-induced tanning
- Beneficial effect on reducing sebum production

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