

PCIA

JINHAN EXHIBITION CENTRE  
GUANGZHOU, CHINA

13-15 MARCH 2007

Personal Care Ingredients Asia



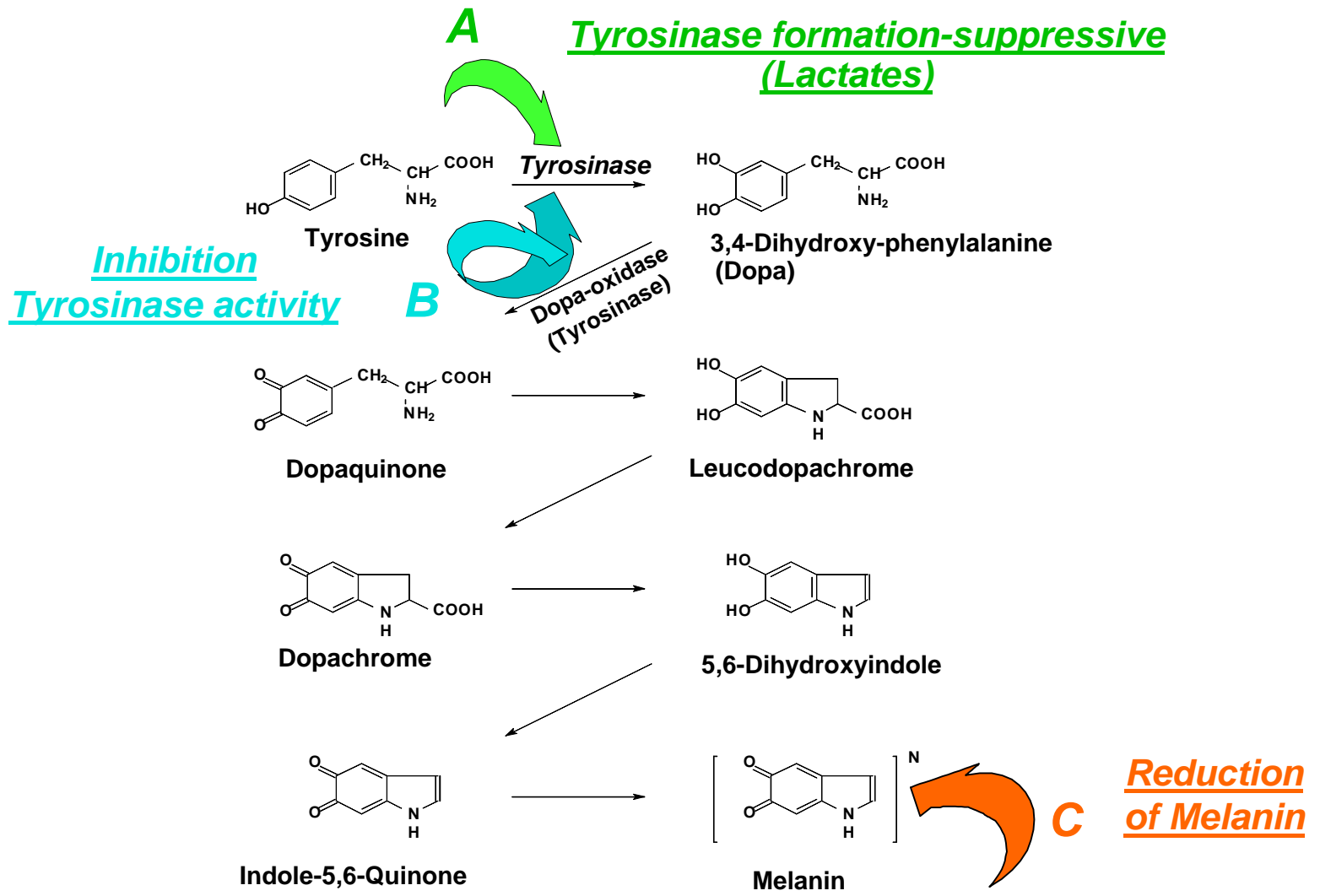
# L(+) Lactates for Skin Whitening



# **Content – L(+) Lactates for Skin Whitening**

- 1. Mechanism of skin-whitening**
- 2. Whitening – the start**
- 3. In vitro data**
- 4. In vivo data – Vitamin C + Lactates**
- 5. More whitening research**
- 6. Costs / Concentrations**
- 7. pH effect / AHA**
- 8. Conclusions**
- 9. Discussion**

# Mechanisms of whitening



## Types of whitening action

- Denaturation and death of pigment cells (C)
- Tyrosinase inhibiting action (B)
- Suppressing the formation of Tyrosinase (A)

## 1. Mechanism of skin-whitening

# Whitening ingredients – overview

	Tyrosinase suppressive action (A)	Tyrosinase inhibiting action (B)	Reduction of melanin (C)
Ascorbic acid (Vit-C) derivatives		√	
Kojic Acid		√	
Arbutin		√	
Licorice		√	
Nicotinamide (Vitamin B3)		√	
Mulberry extract		√	
Vegetable/Herb extracts		√	
Lactates	√		
Hydroquinone			√

## Whitening of lactates – the start

**Tyrosinase inhibitory/suppressive action of organic acids  
(in vitro) ( + = activity, – = no activity)**

Organic acids/salts	Tyrosinase inhibitory activity	Melanogenesis suppressive activity	Tyrosinase formation suppressive activity
Lactic acid/Sodium Lactate	–	+	+
Asparaginic acid	–	–	–
Glutaminic acid	–	–	–
Citric acid	–	–	–
Fumaric acid	–	–	–
Malic acid	–	–	–
Ascorbic acid (Vit. C)	+	+	–

## Whitening of lactates – the start

### L (+) Lactic acid and lactates – in vivo whitening experiment

Percentage of test-objects with significant whitening results

	Lactate concentration (w%)			
	2%	5%	8%	20%
Sodium Lactate	35%	80%	95%	100%
Ammonium Lactate	35%	75%	-	100%
Magnesium Lactate	30%	75%	90%	100%

- Conditions:
- 20 test-subjects
  - pH=5.5
  - measurement after 24 days
  - applying cream 3 times daily

## In Vitro Data – Melanoderm

### Objective:

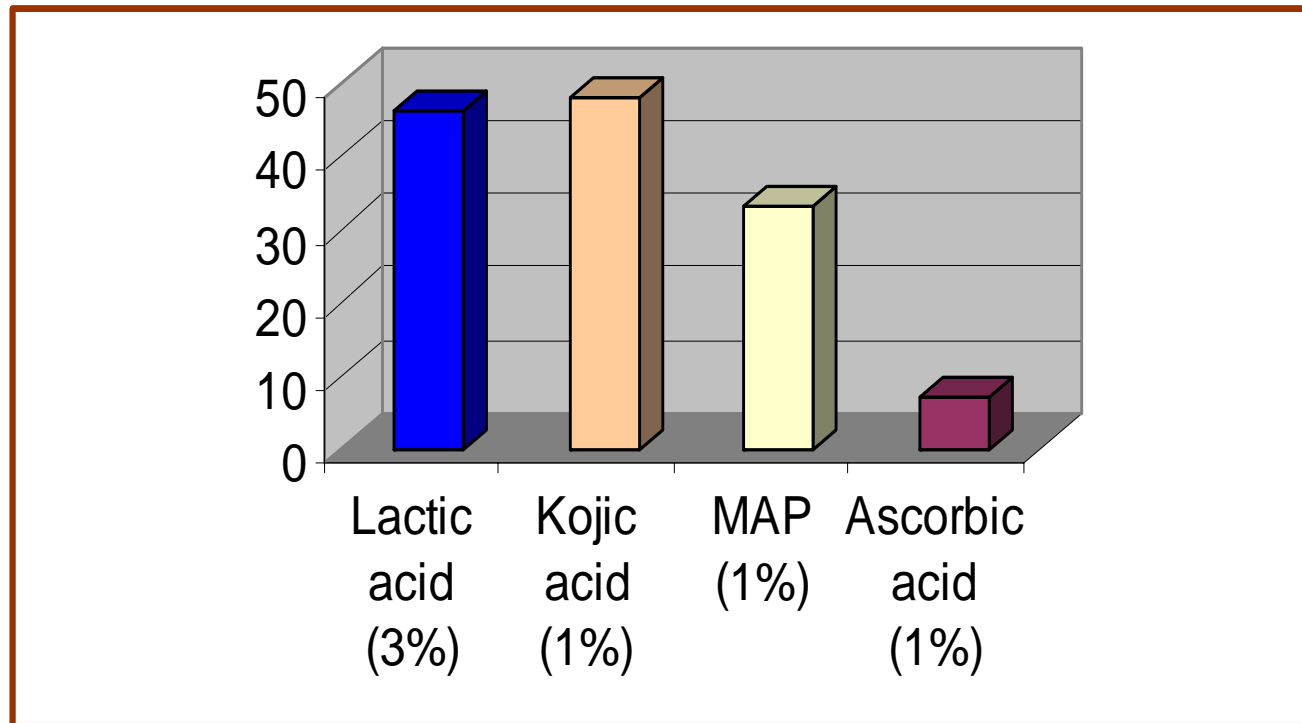
- To assess effect of whitening agents on tyrosinase suppression/inhibition (in vitro measurement; Melanoderm)

### Conditions:

- Whitening ingredients tested: Lactic acid(3%), Kojic acid(1%), Ascorbic acid (1%) and MAP (1%)
- Melanoderm: in vitro model of human epidermis. Model can be used to evaluate efficacy, stability and toxicity of whitening agents.

## In Vitro Data – Melanoderm

### Effect of whitening agents on tyrosinase inhibition/suppression



- Ascorbic acid only reveals modest results (oxidation?)
- Lactic acid and kojic acid reduce resp. 46% and 48%

## In vivo research – Vitamin C + Lactates

### Objective:

- To determine whether L(+) Lactic acid by itself or supplemented with ascorbic acid can whiten the skin
- To assess if synergistic effects between A and B type whitening ingredients could possibly take place.

### Conditions:

- 70 test subjects, Caucasian females ages 25-70 (rated 3 or 4 via Fitzpatrick Scale)
- 3 formulations, applying twice a day
- Objective (Minolta Chroma meter) and subjective (clinical grading; 1-100 scale) whitening measurement
- Duration whitening test 12 weeks (t=0, 4, 8, 12 weeks)

## Methodology – Test subjects

- Caucasian skin type 3 to 4 on Fitzpatrick scale

### Fitzpatrick scale

*Skin type: Sun burning and Tanning*

1. Always burns easily; never tans
2. Always burns easily; tans minimally
3. Burns moderately; tans gradually
4. Burns minimally; always tans well
5. Rarely burns; tans profusely
6. Never burns; deeply pigmented.

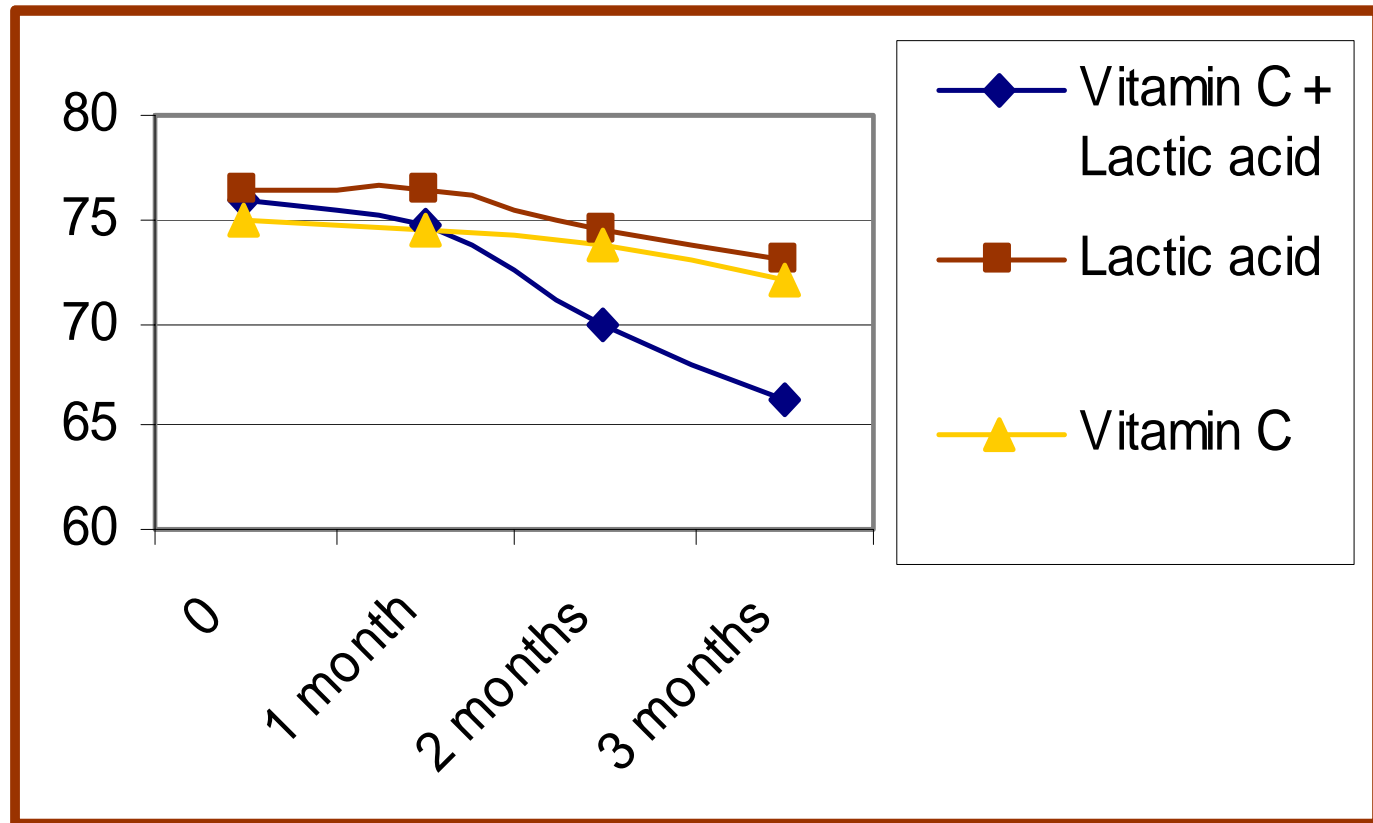
## Formulations

- 1.) Vitamin C (1%)
- 2.) Lactic acid (8.8%)
- 3.) Vitamin C (1%) + Lactic acid (8.8%)

### Conditions:

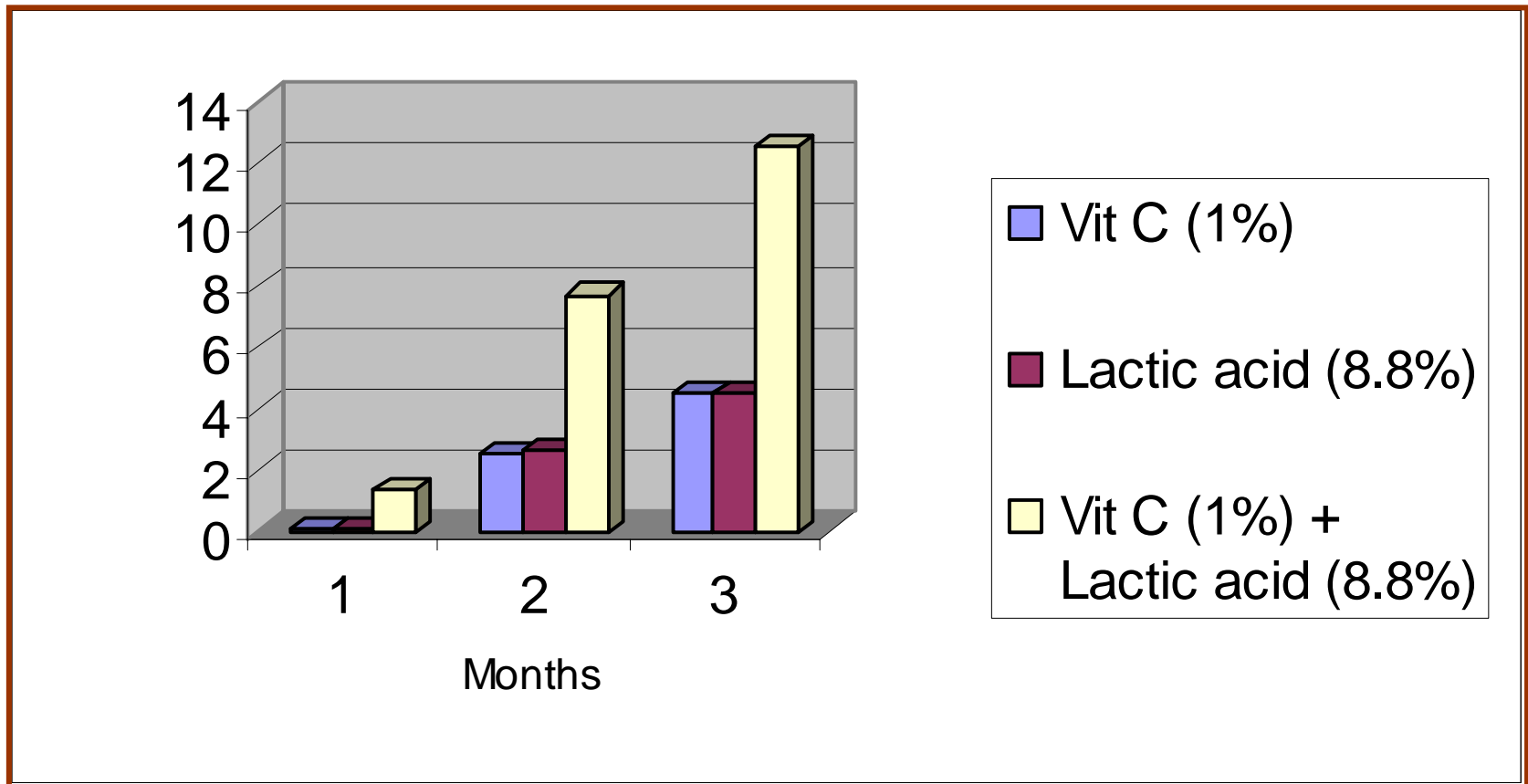
- pH 5, mild formulations, but *not* stable
- New formulations freshly prepared every 2 weeks
- 3 formulations, applying twice a day

## Measurement by Clinical grading



- Vitamin C + Lactic acid significant whitening after 3 months

## Measurement by Clinical grading



- Synergistic whitening effects achieved when Vitamin C is combined with Lactates in one formulation

## More Clinical Research

### Objective:

- To assess and compare the performance/ effectiveness of frequently used whitening ingredients in vivo.

### Conditions:

- Vehicle controlled double blind not randomized clinical trial
- 7 formulations, applying twice a day
- 30 test subjects; female, Asian skin type, 18-45 yr. old
- Objective (Mexameter) and subjective (4 point scale) whitening measurement
- Duration whitening test 12 weeks (t=0, 4, 6, 8, 12 weeks)

# Formulations

	Products	Concentration
A	Control/Placebo	0%
B	Sodium Lactate 60%	15%
C	Arbutin	1%
D	Licorice	0.3%
E	Kojic acid	1%
F	Sodium Lactate 60% + Arbutin	15% + 1%
G	Sodium Lactate 60% + Licorice	15% + 0.3%
H	Sodium Lactate 60% + Kojic	15% + 1%

- Mild, stable and “commercial” formulations; pH=5
- All formulations equal except for whitening ingredient
- F,G, H included to asses possible synergistic effects

## Methodology

### Objective measurement

- Mexameter (M16), Courage and Khasaka, Germany (Melanin Index)
- Scale 400-700, dark-skins range 450-550
- Duration whitening test 12 weeks (t=0, 4, 6, 8, 12 weeks)

### **“Photo-types” and ranges Mexameter**

- I: Celtic type (very fair skin, red hairs, freckles) 400-470
- II: Caucasian white (fair skin, blond, blue eyes): 410-490
- III: Mixed type (blond-brown hair, brown eyes): 420-510
- IV: Mediterranean type (dark hair, brown eyes): 420-520
- V: Dark skin: 450-550
- VI: Black Skin: 520-700

## Methodology

### Subjective Measurement

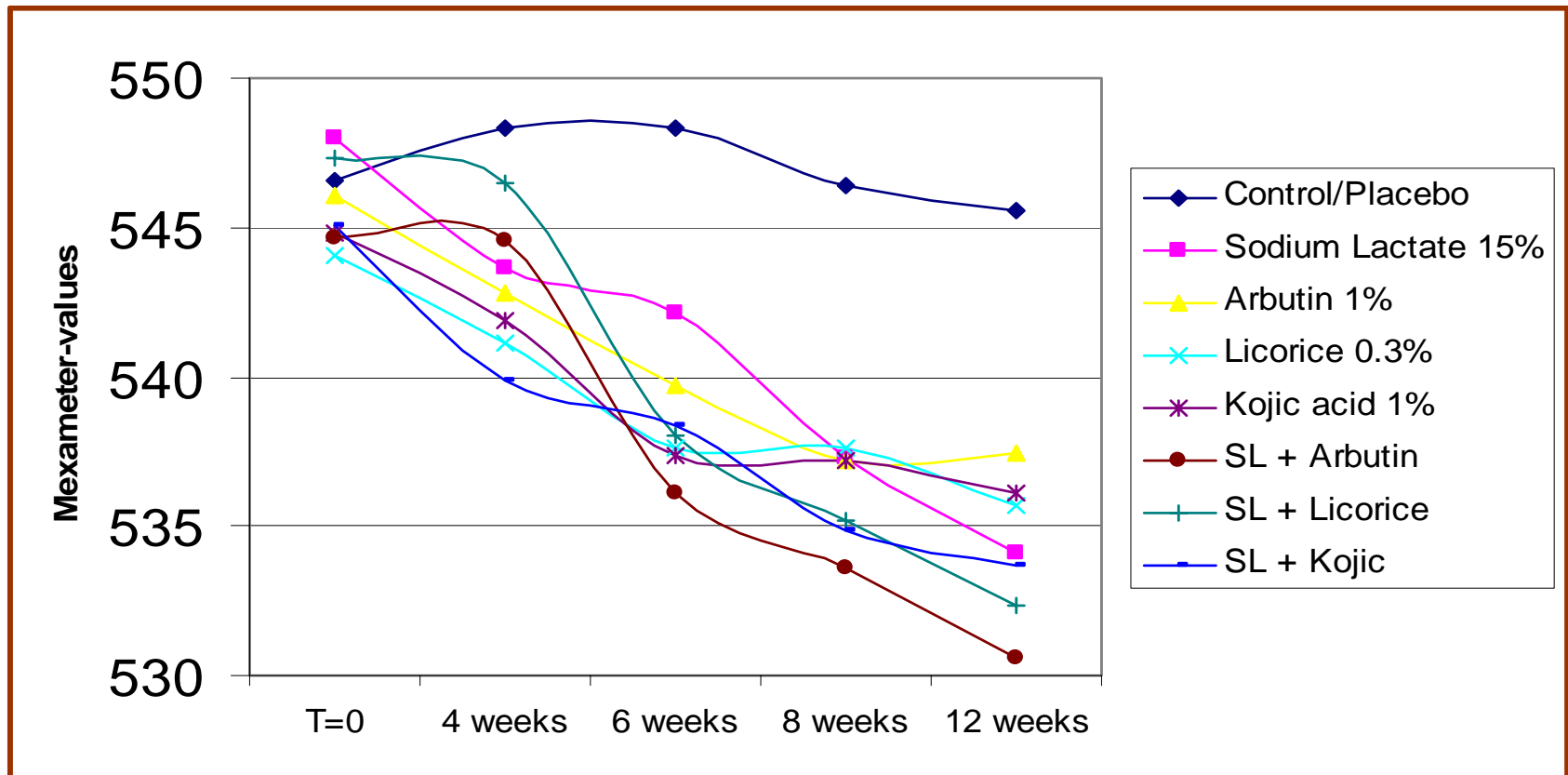
- On a 4-point scale.
- Assessment by dermatologist and panelist themselves

#### **Subjective measurements predominantly used:**

- Clinical grading: using color cards, comparison with skin color; expensive, 0-100 point scale, trained staff needed but very reliable
- 4-point scales: scaling of skin-color on 4 point scale, cheap, to be used in combination with objective measurement.

# Objective measurement

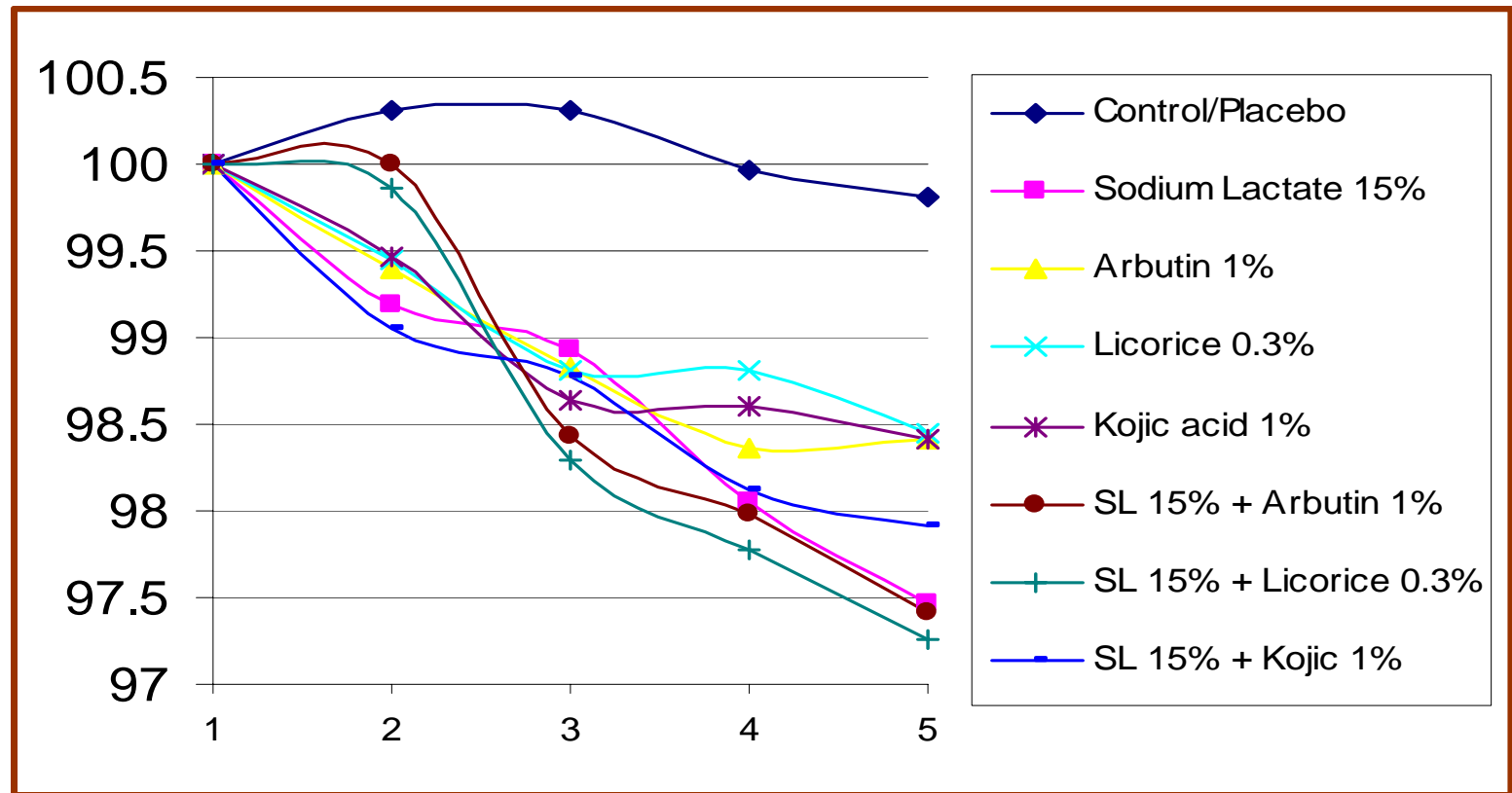
Whitening effect in time (3 months)



- Significant whitening effect for all treatments after 6 weeks

# Objective measurement; T=0 is index 100

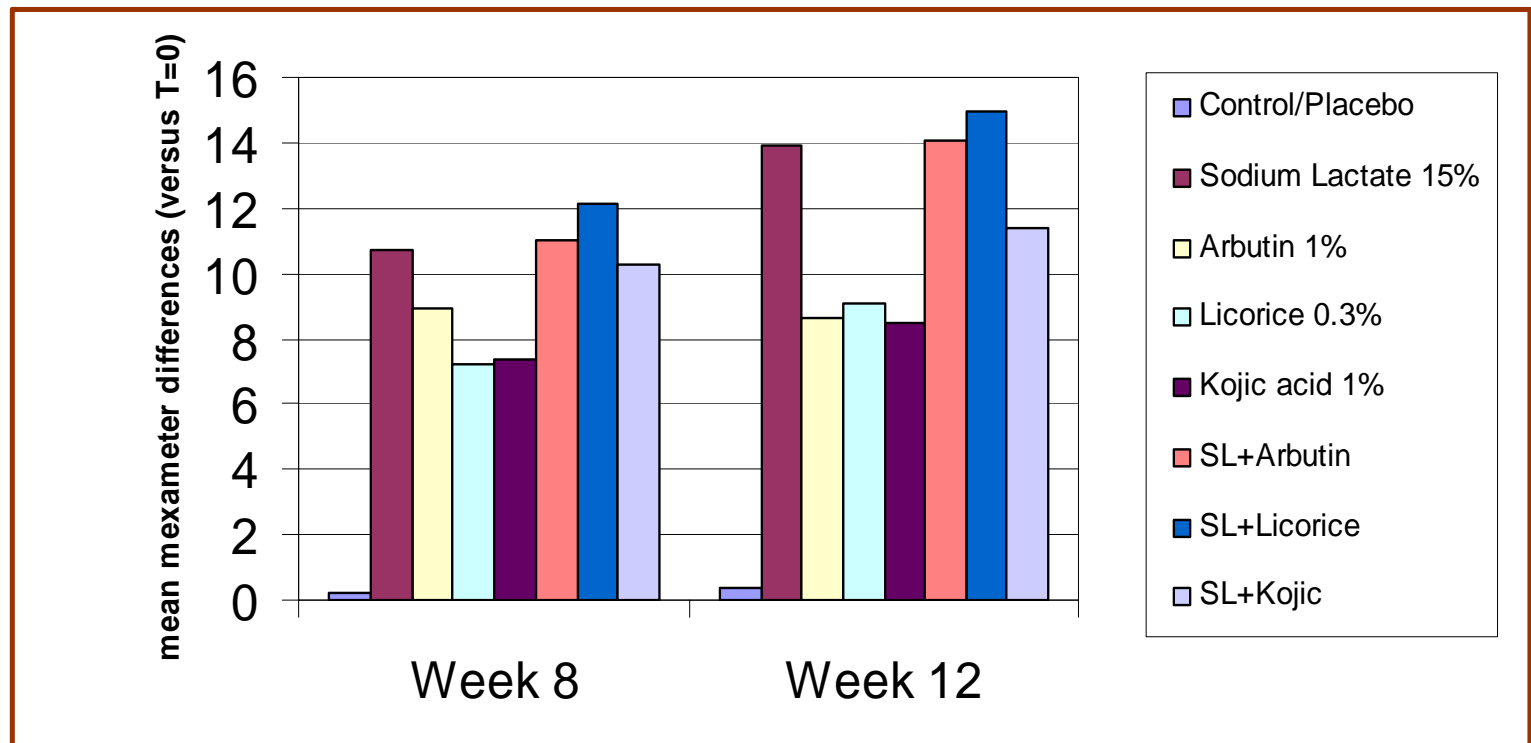
## Whitening effect in time (3 months)



- Form. without Sodium Lactate show stabilizing after week 6

## Objective measurement

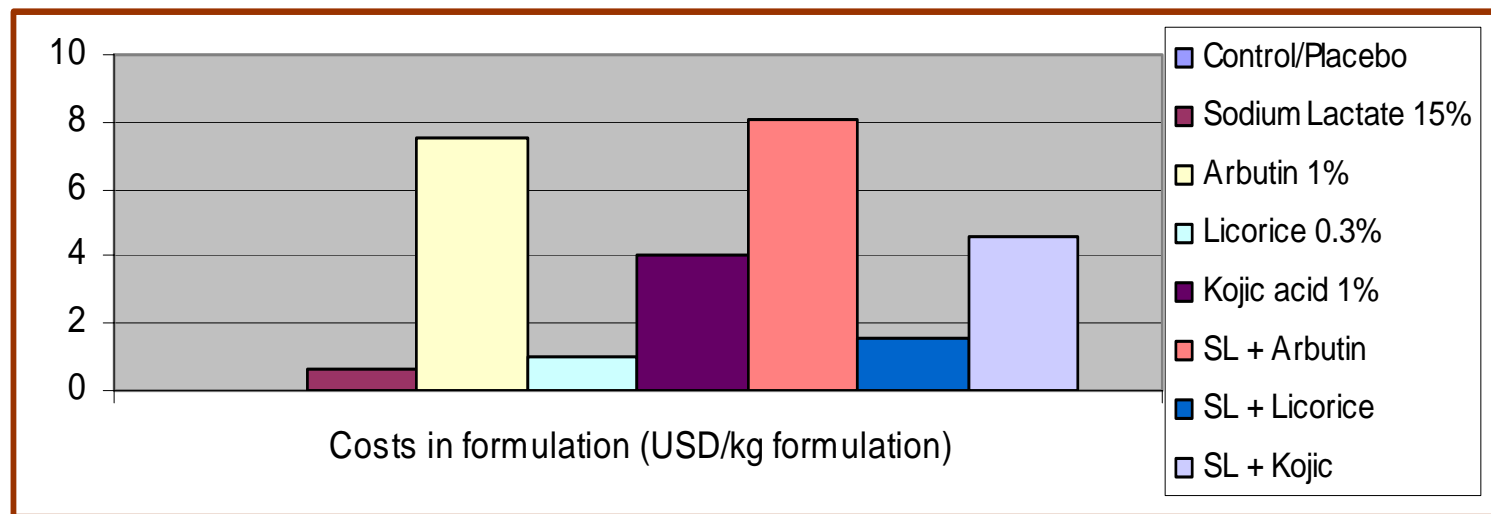
Differences in mexameter readings between T=0 and wk 8 resp. 12



- 5 points difference on mexameter scales is significant
- Sodium Lactate, SL+Kojic and SL+Licorice best performing

# Cost comparison formulations

Products	Price
Sodium Lactate 60%	4 US\$/kg
Arbutin	750 US\$/kg
Licorice	325 US\$/kg
Kojic acid	400 US\$/kg

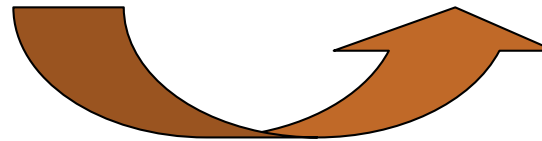


- Sodium Lactate cheapest and most effective whitening ingredient

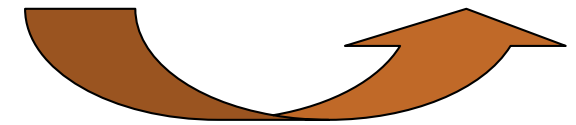
## 6. Summary on concentrations needed

Whitening effect is related to the lactate ion

Nr	Product	Product 100%	Lactate ion
4	8.8% Lactic acid 90%	8% Lactic acid (100%)	7.9%
5	15% Sodium Lactate 60%	9% Sodium lactate (100%)	7.2%



Correction for concentration



Correction for  $M_w$  (H=1; Na=23; L=98)

▪ **Conclusion: At least 7% Lactate ion should be added**

Equivalent to:

- 15% Sodium Lactate 60%** (= 7.2% Lactate)
- 8% Lactic acid 90%** (= 7.1% Lactate)
- 12% Calcium Lactate** (= 7.0% Lactate)

Calcium lactate:  $M_w=308$  g/mole,  $5H_2O=90$  g/mole,  $Ca^{2+}=40$  g/mole, Lactate = 178 g/mole

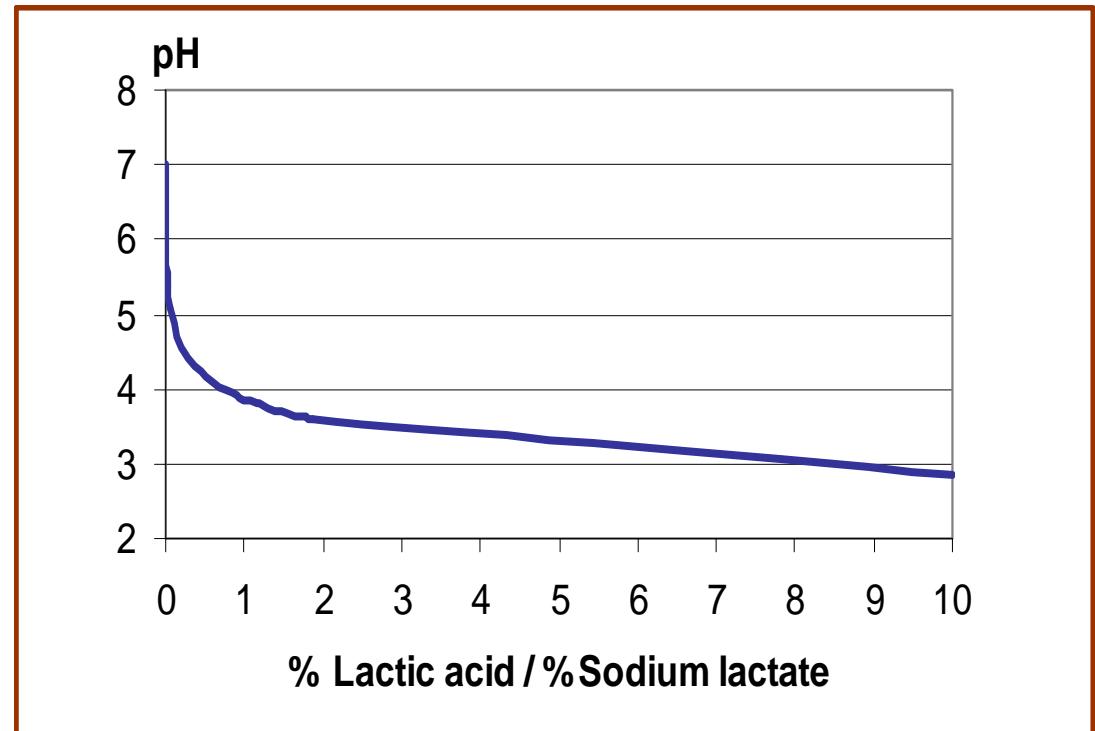
## Lactates and pH

- Experiments carried out at relatively neutral pH (5)
- At pH 5, hardly any Lactic acid is available in final formulation

pH=5 in formula:

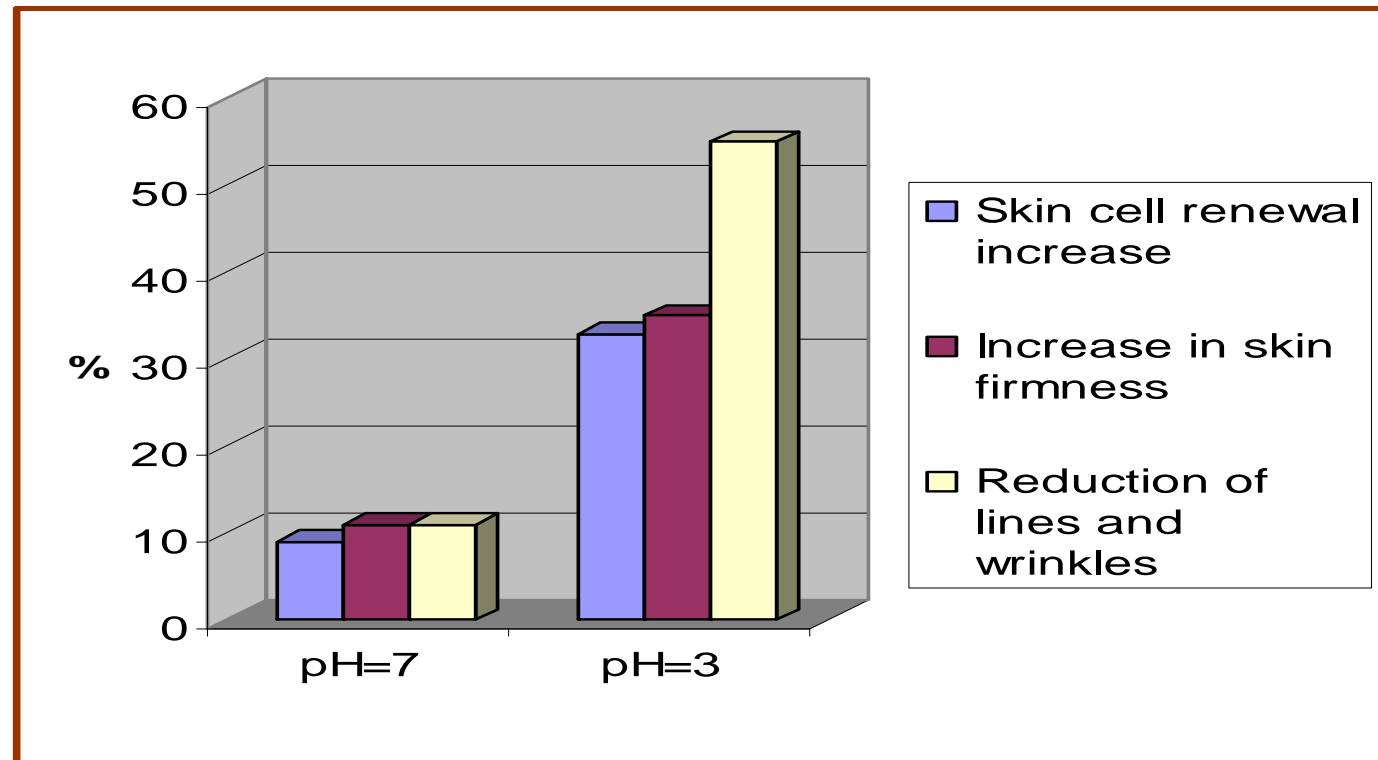
100 Sodium Lactate

6 Lactic acid



## pH-effect / AHA

*Rejuvenating benefits of Lactates; improvement in % after 8 weeks treatment*



- Exfoliating effect of Lactates increases at lower pH levels
- Exfoliating effect Lactates could enhance pace of whitening

## Conclusions L (+) Lactates in whitening

- **L(+)** Lactates are safe and effective and low cost whitening ingredients
- Formulated at lower pH incorporates additional peeling/exfoliating properties
- Additional moisturizing properties added to the whitening formulation
- Possibility to add properties such as ceramide increase and mineral enrichment

## Intended Future Clinical Research

- **Determine whitening capability/performance of Lactate salts (Zn-L, Ca-L vs. Na-L)**
- **Study the synergistic effects (if any) with other popular whitening active ingredients like Nicotin amide, Ascorbic acid, vegetable extracts like Brassica rapa juice extract**

## Safety concerns Hydroquinone / Kojic acid

- **Hydroquinone is suspected to be carcinogenic**
- **FDA ruling due for 30 December 2006 on imposing a ban on Hydroquinone**
- **Japanese dermatologists suspect Kojic acid may be carcinogenic (?)**
- **Japanese and Korean government ordered to stop using Kojic acid until investigations end**
- **Switzerland has banned Kojic acid**