

*Fruits Extract Complex for Acne-care*

# VeryBerry™ ACNEcare



**Kiwi**  
*Actinidia chinensis*



**Strawberry**  
*Fragaria chiloensis*



**Yuzu**  
*Citrus junos*



**Unshiu-orange**  
*Citrus unshiu*



**Mangosteen**  
*Garcinia mangostana*



**Grape**  
*Vitis vinifera*

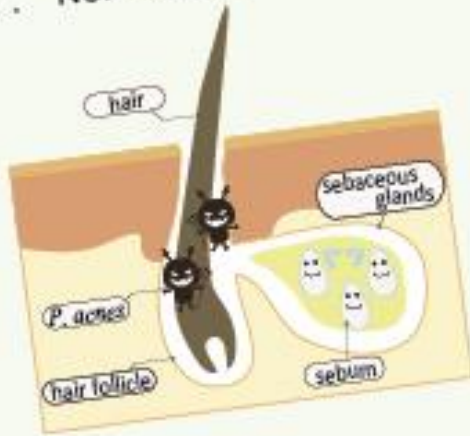


**Licorice**  
*Glycyrrhiza uralensis*

ORYZA OIL & FAT CHEMICAL CO., LTD.

# Introduction (How Acne Worsens)

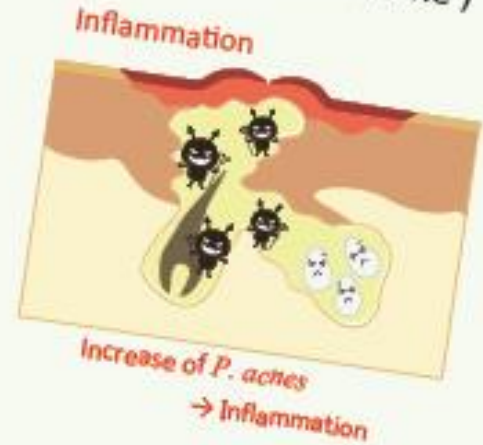
I. Normal skin



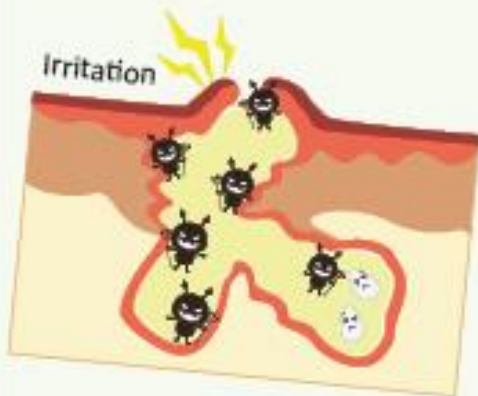
II. Comedo ( White Acne )



III. Papule ( Red Acne )



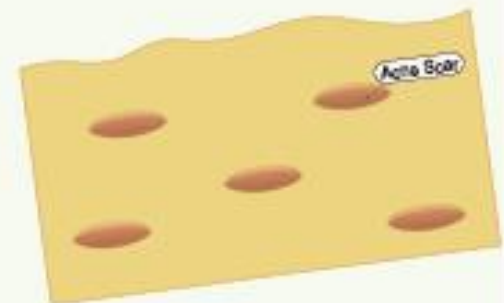
IV. Aggravation by irritation



V. Pustule ( Yellow Acne )



VI. Acne Scar



# Introduction (Kind of the Acne)

## Stage II (White Acne ; Comede)

The opening of a pore becomes thick and narrow due to declined turnover function. Sebum clogs the opening and acne is formed.

## Stage III (Red Acne ; Papule)

Sebum accumulates inside the pore, *P. acnes* and other bacteria consuming sebum grow rapidly, and inflammation occurs.

## Stage V (Yellow Acne ; Pustule)

Inflammation keeps occurring because of increased *P. acnes* and lipase generated by them. Various types of irritations worsen inflammation, generating suppuration.



Stage II

White Acne



Stage III

Red Acne



Stage V

Yellow Acne

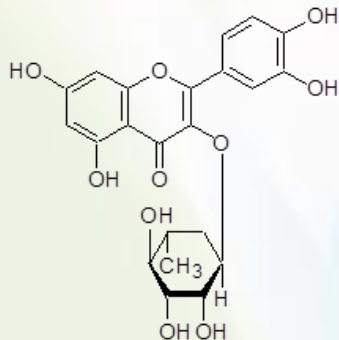
# Introduction of Fruit Extracts (1)



**Kiwi**

*Actinidia chinensis*

Kiwi Seed Extract rich in polyphenol (quercitrin etc.). This extract has an inhibitory effect of Dihydrotestosterone production, which is cause of generation of acne, and an inhibitory effect of lipase originated from the *Propionobacterium acnes*.



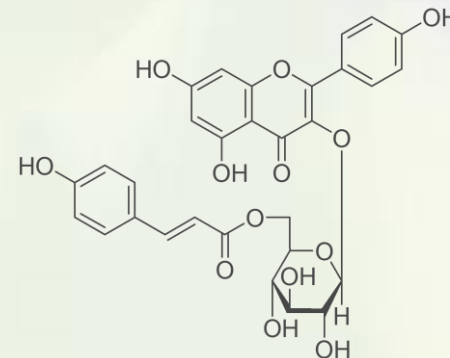
*Quercitrin*



**Strawberry**

*Fragaria chiloensis*

Strawberry is rich in vitamin C, polyphenols including anthocyanin, flavonoid, phenylpropanoid and ellagitannin. we discovered superior moisturizing effect by those functional components.



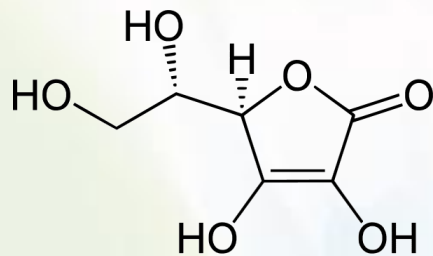
*Tiliroside*

# Introduction of Fruit Extracts (2)



**Yuzu**  
*Citrus junos*

Yuzu is believed to be effective to recover from fatigue, release pain, and enhance beauty because of its high content of organic acids including citric acid and tartaric acid as well as vitamin C.

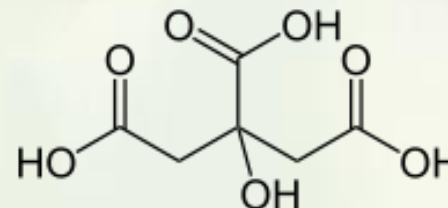


*Vitamin C*



**Unshiu-orange**  
*Citrus unshiu*

Unshiu-Orange Peel is rich in carotenoids, ( $\beta$ -cryptoxanthin,  $\beta$ -carotene), coumarins (auraptene, etc), limonoids (limonins, etc), flavonoids (tangeretin, nobiletin, hesperidin), and organic acid like citric acid.



*Citric acid*

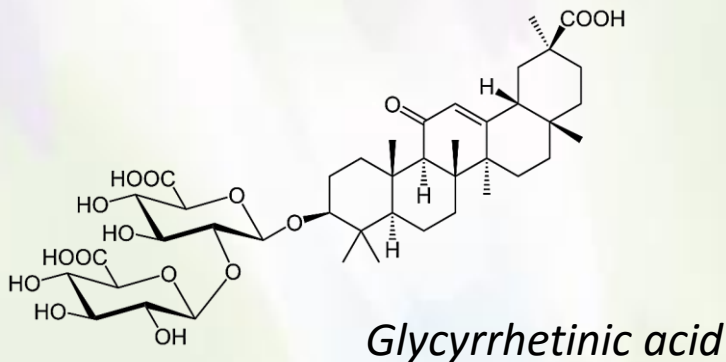
# Introduction of Fruit Extracts (3)



**Licorice**

*Glycyrrhiza uralensis*

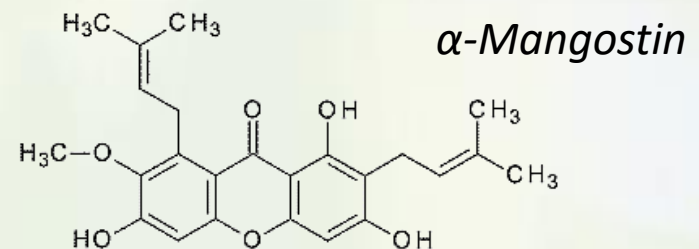
It is an important raw material for cosmetic products and quasi-drugs because it is believed to perform anti-allergic, anti-inflammatory, and skin-lightening effects.



**Mangosteen**

*Garcinia mangostana*

Its rind contains a high concentration of xanthenes, a type of polyphenol. It has been proven that xanthenes are very strong antioxidants with higher effects than other polyphenols and well-known antioxidants such as vitamin C and vitamin E.

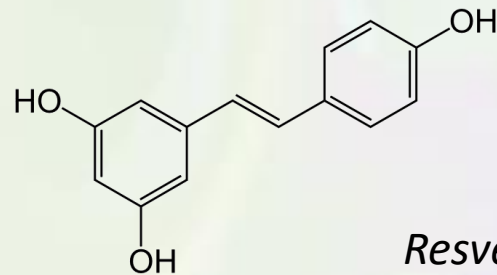


# Introduction of Fruit Extracts (4)



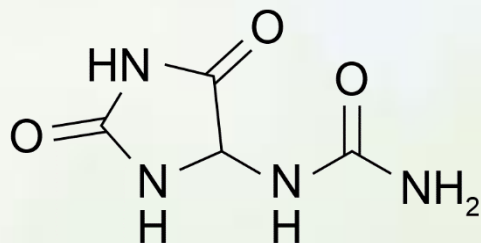
**Grape**  
*Vitis vinifera*

The purple color of grape skin is caused by anthocyanin polyphenol that is similar to a component in blueberries considered to be good for the eyes. Grapes also contain resveratrol which is currently attracting people's attention as a unique component of grapes.



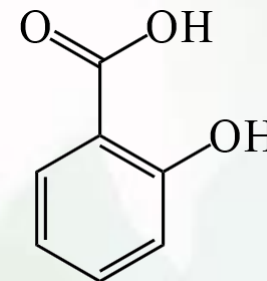
*Resveratrol*

# Introduction of Fruit Extracts (5)



**ALLANTOIN**

Allantoin is extremely effective to treat allergies and rough skin. It prevents rough skin and promotes skin regeneration by treating wounds and increasing cells. It is used for anti-aging and acne care because it has effects to remove old skin tissues and hardened corneum smoothly.



**SALICYLIC ACID**

Salicylic acid is used for acne care for roughly two purposes and effects. First, it softens corneum. Secondly, it prevents growth of germs. The skin can be kept in a condition where *P. acnes* cannot grow very well after it is washed and moisturized. Salicylic acid also has an anti-inflammatory effect to reduce inflammation by suppressing the activity of prostaglandin.



# Efficacy Evaluation of each Extracts

Effect	Extracts & Synthetic products
Inhibitory effect 5 $\alpha$ -reductase and lipase	KIWI
Anti-inflammatory	GRAPE, MANGOSTEEN, LICORICE, SALICYLIC ACID, ALLANTOIN
Antibacterial	GRAPE, MANGOSTEEN, SALICYLIC ACID
Peeling effect	YUZU, ORANGE, ALLANTOIN
Moisturizing effect	STRAWBERRY, ORANGE

# Efficacy Evaluation of each Extracts

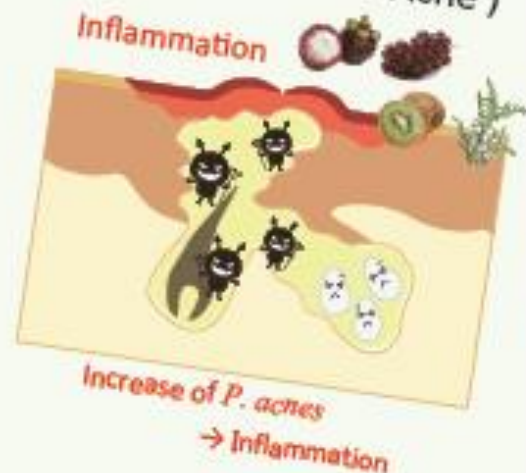
I. Normal skin



II. Comedo ( White Acne )



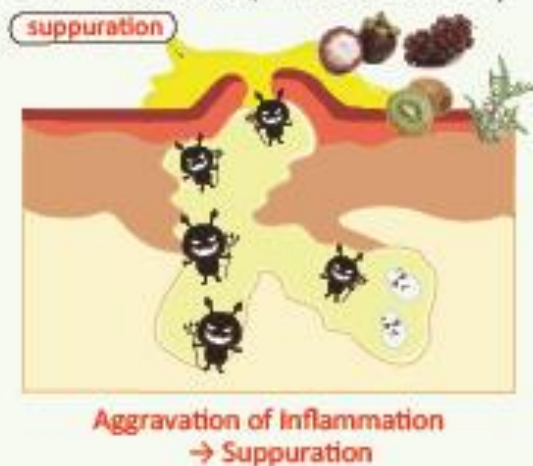
III. Papule ( Red Acne )



IV. Aggravation by irritation



V. Pustule ( Yellow Acne )

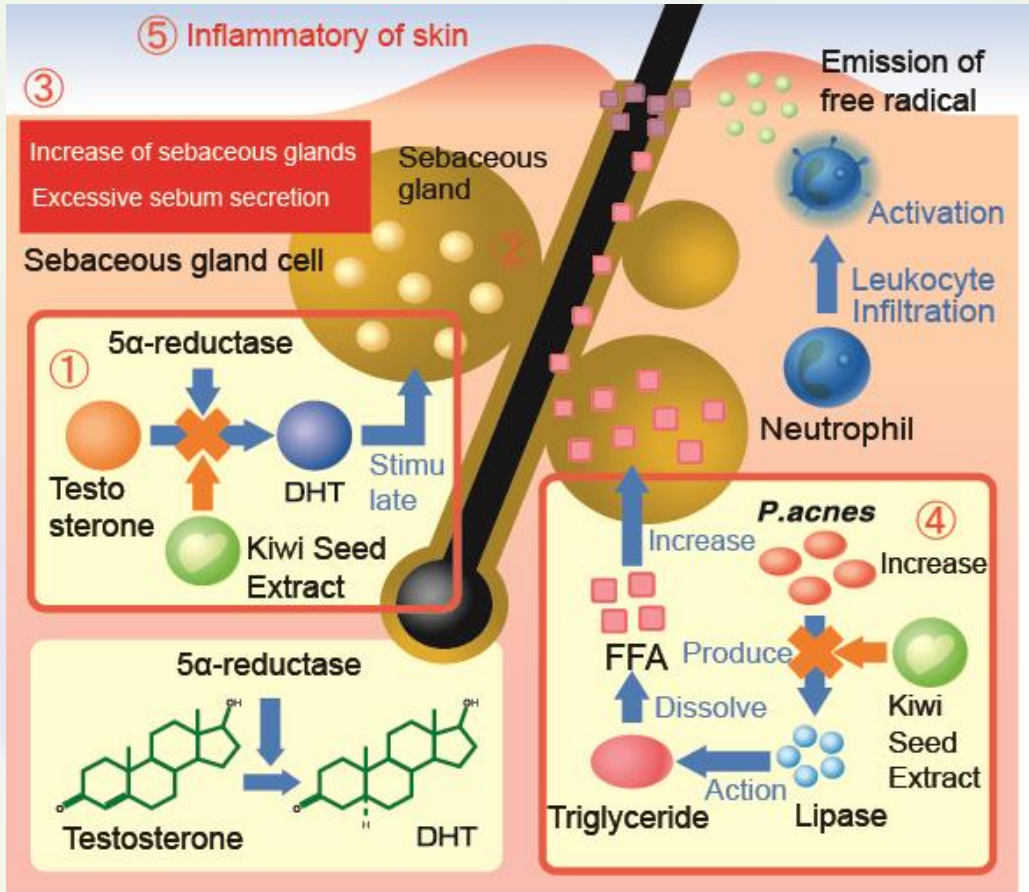


VI. Acne Scar



# Kiwi Seed Extract

## ◆ Pathophysiology of Acne



① Enhancement of male hormone

② Abnormal secretion of sebum

③ Increase of sebaceous glands

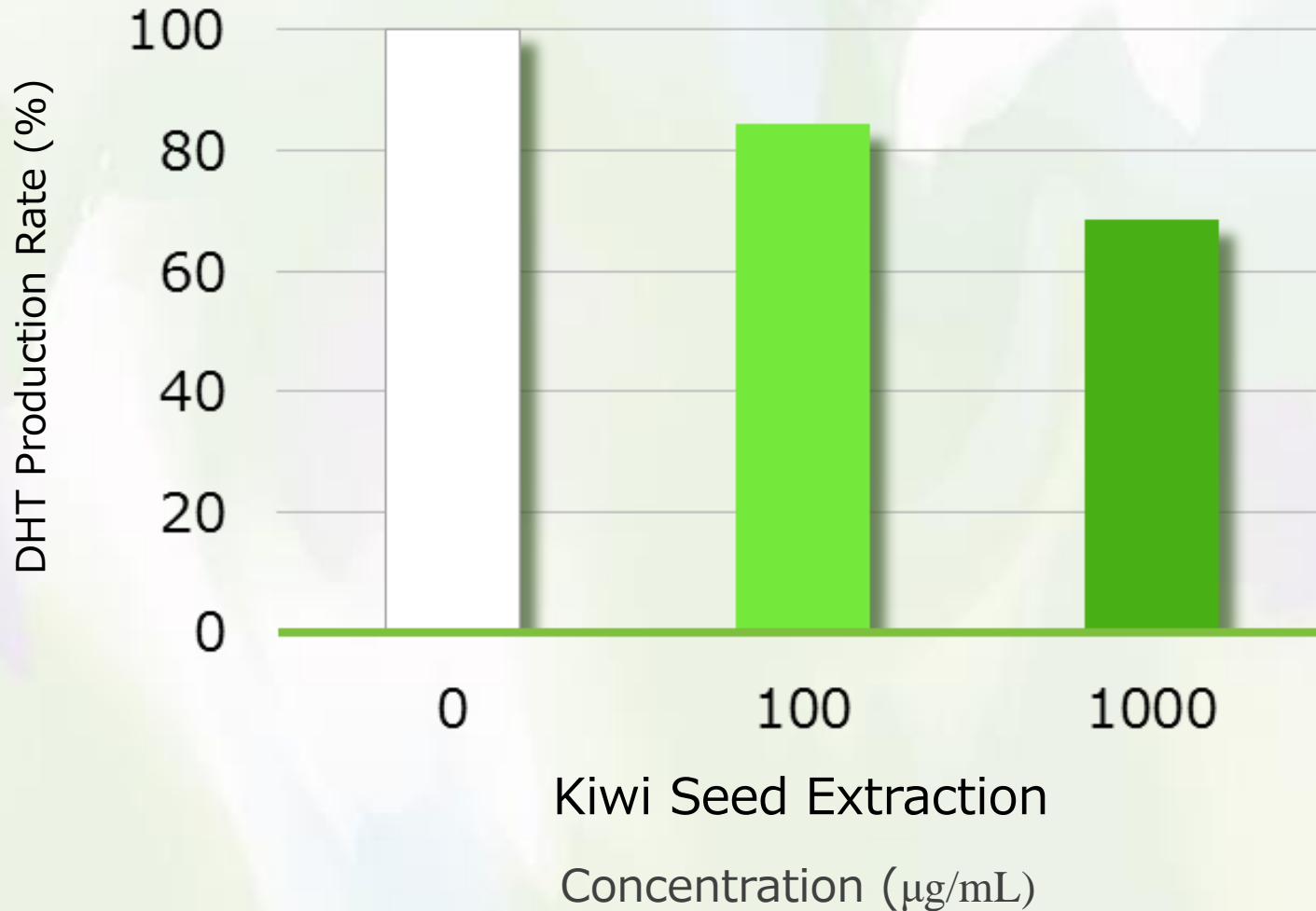
④ Growth of *P. acnes*

⑤ Inflammation of caused by acne

□ : Efficacy point of Kiwi Seed Extract

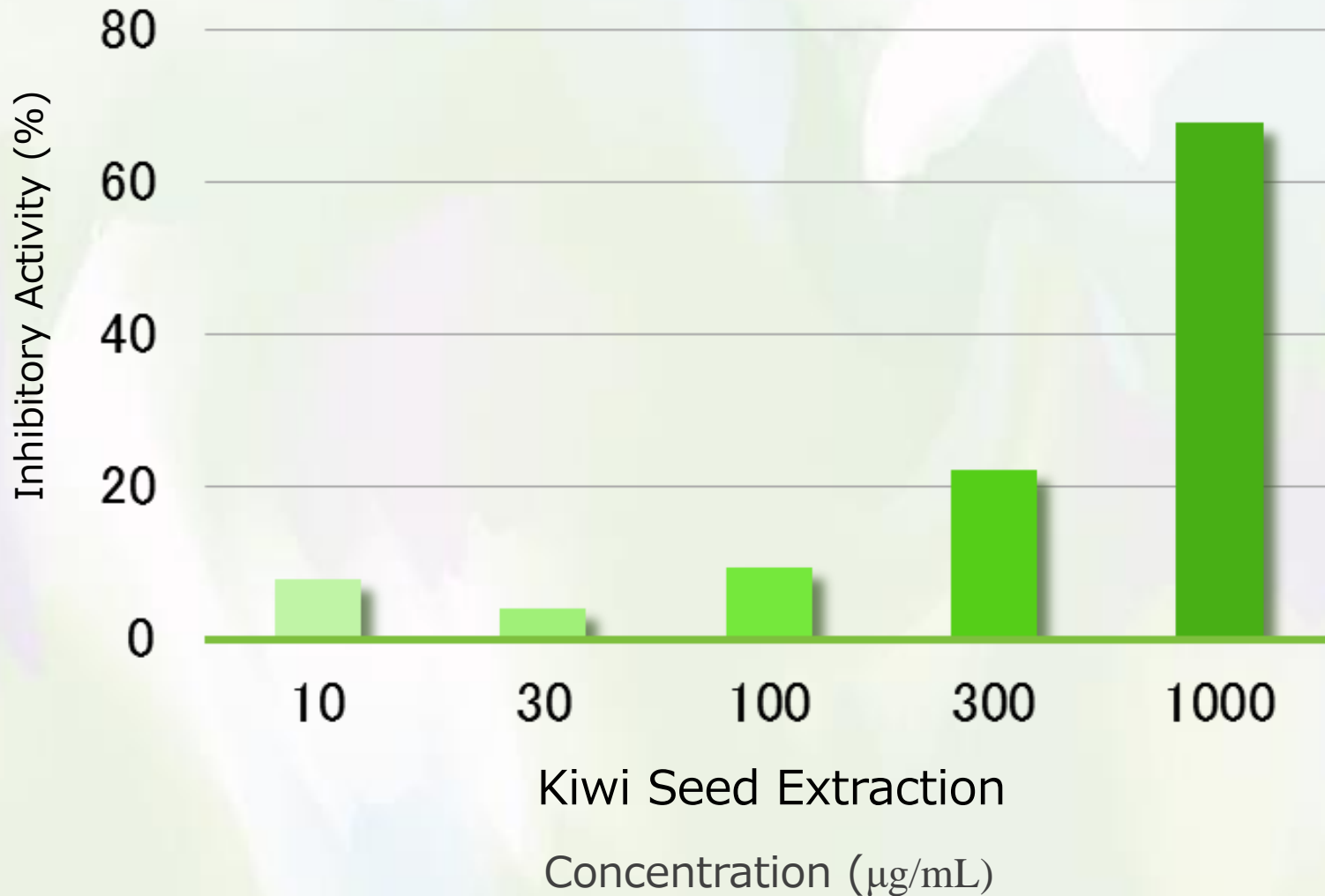
# Kiwi Seed Extract

## ◆ Inhibition of 5 $\alpha$ -reductase (*in vitro*)



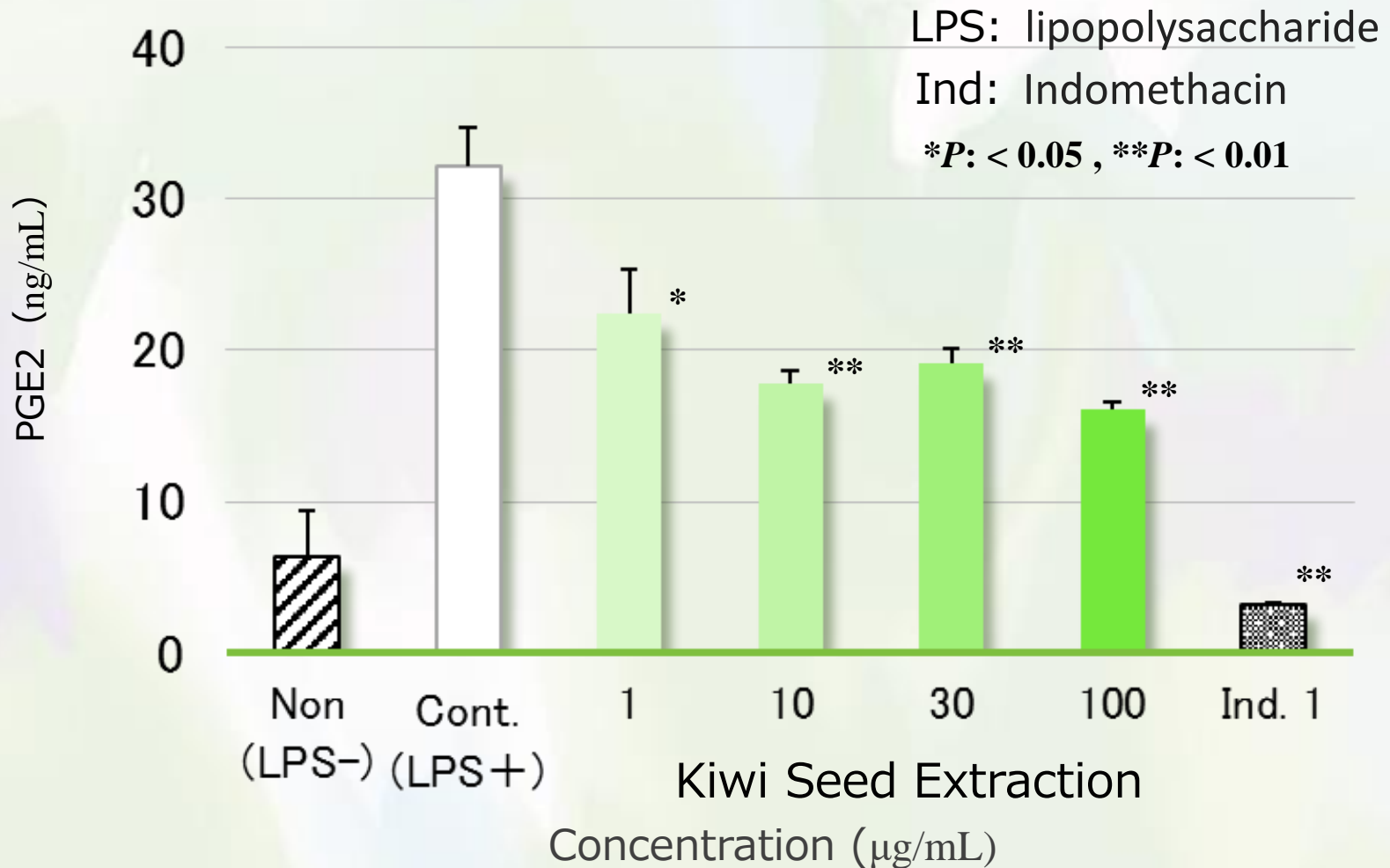
# Kiwi Seed Extract

- ◆ Inhibitory Effect of Lipase obtained from *P. acnes* (*in vitro*)



# Kiwi Seed Extract

- ◆ Inhibitory Effect of Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) Production (Anti-inflammatory Effect)



# Kiwi Seed Extract

## ◆ Improvement Effect of Acne (Monitor Test)

Test sample : Kiwi Seed Extract-LC

Test period : 2 weeks

Subjects : 9 people



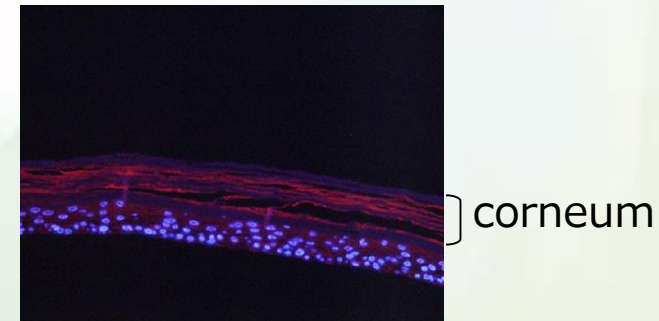
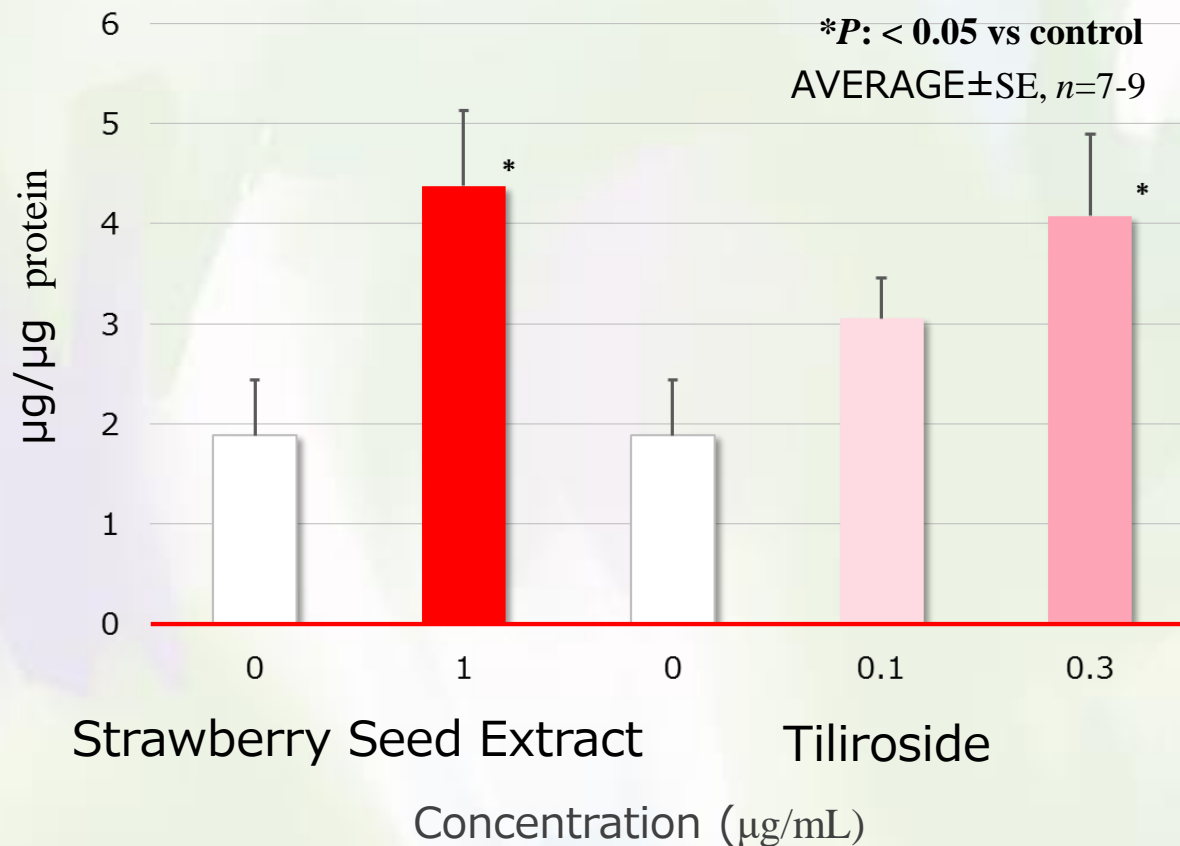
Start



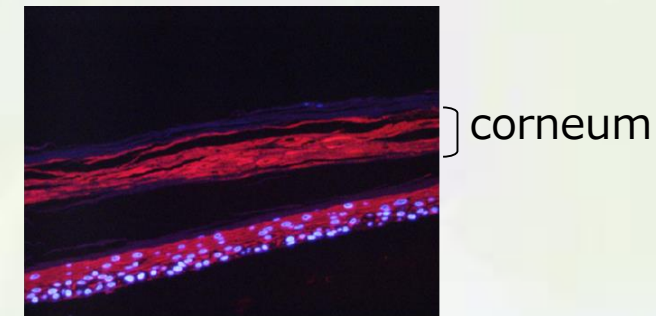
After 2 weeks

# Strawberry Fruit Extract

## ◆ Promotion Effect of Ceramide II Increase



Control

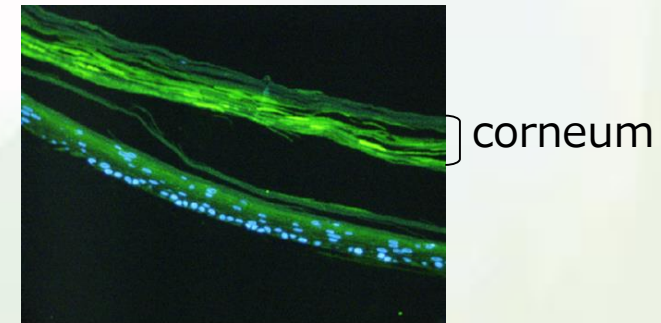
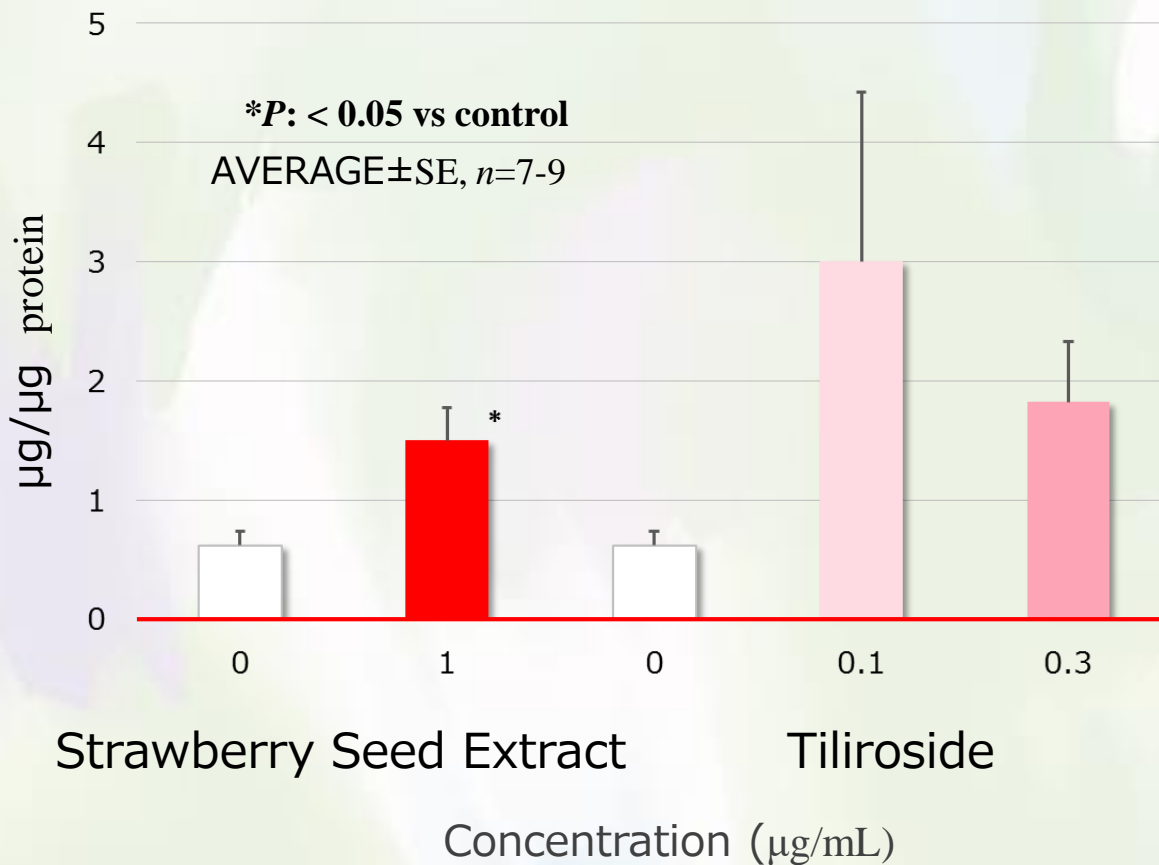


**Strawberry Seed Extract**  
(1 µg/mL)

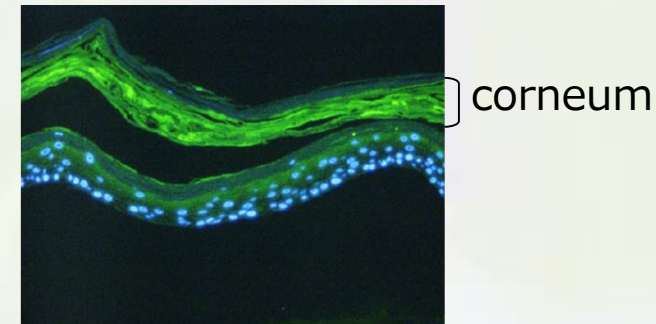


# Strawberry Fruit Extract

## ◆ Promotion Effect of Ceramide V Increase



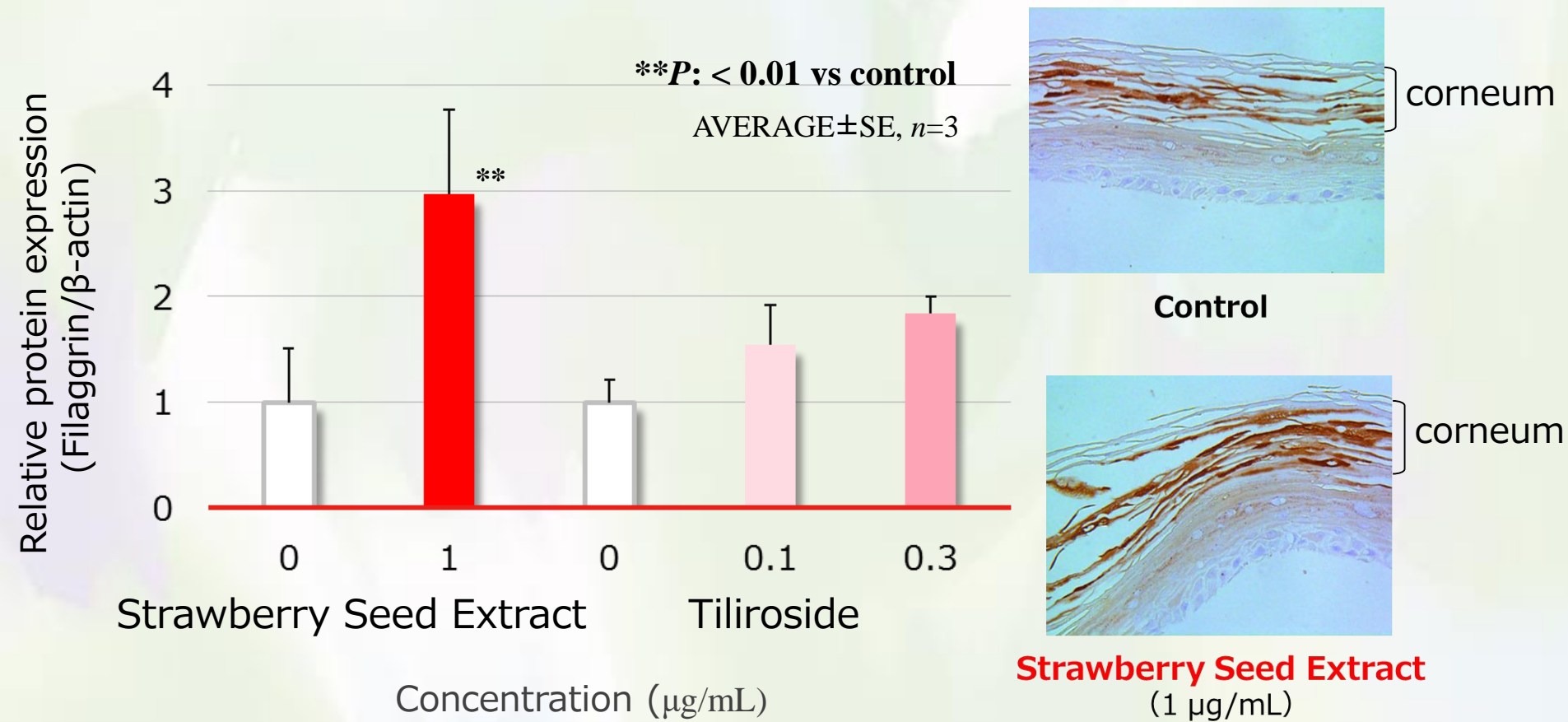
Control



**Strawberry Seed Extract**  
(1 µg/mL)

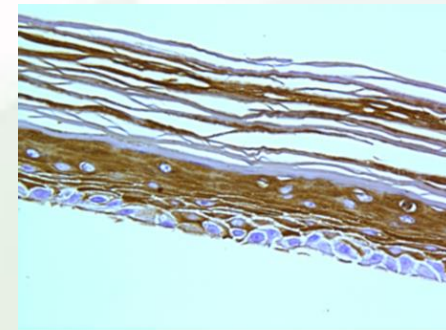
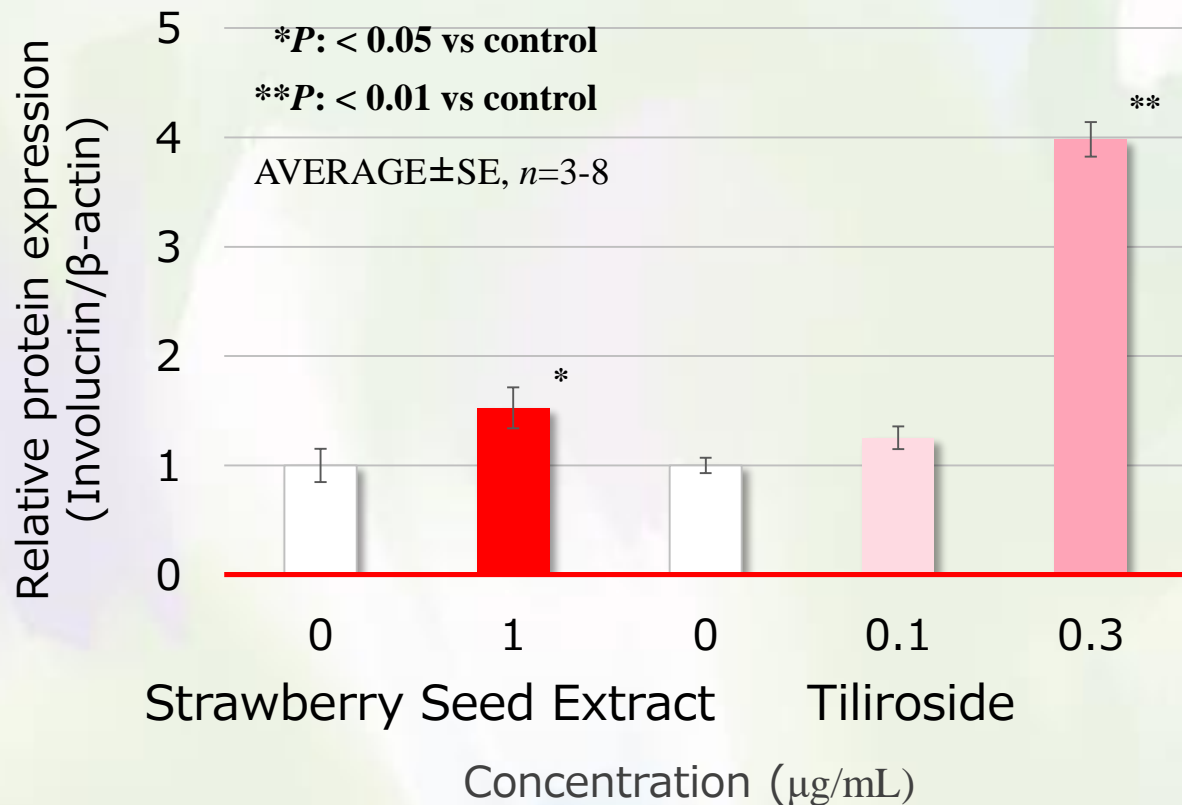
# Strawberry Fruit Extract

- ◆ Promotion Effect of Genes Expression Related to Skin Barrier Function (filaggrin)



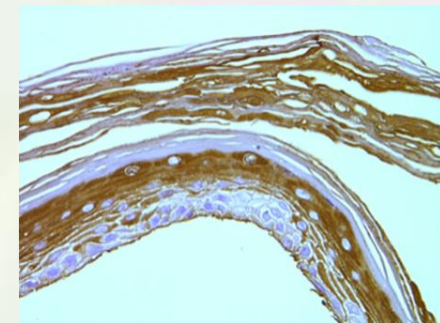
# Strawberry Fruit Extract

- ◆ Promotion Effect of Genes Expression Related to Skin Barrier Function (involucrin)



corneum

Control

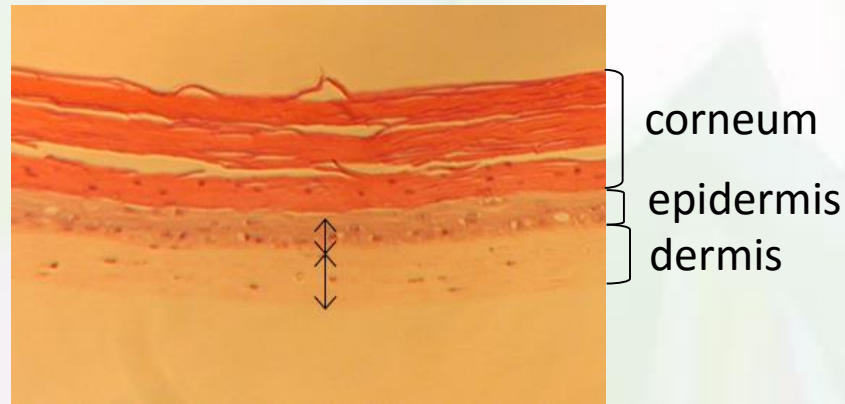


corneum

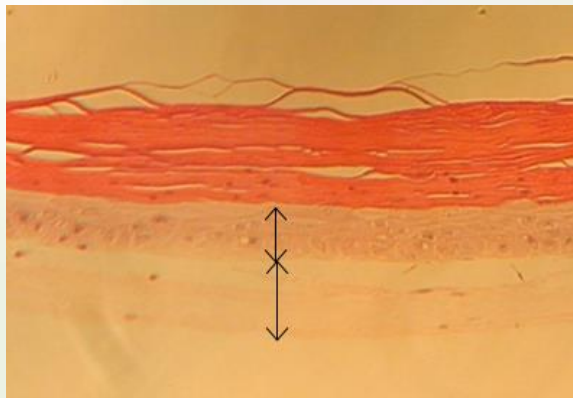
**Strawberry Seed Extract**  
(1  $\mu\text{g/mL}$ )

# Yuzu Seed Extract

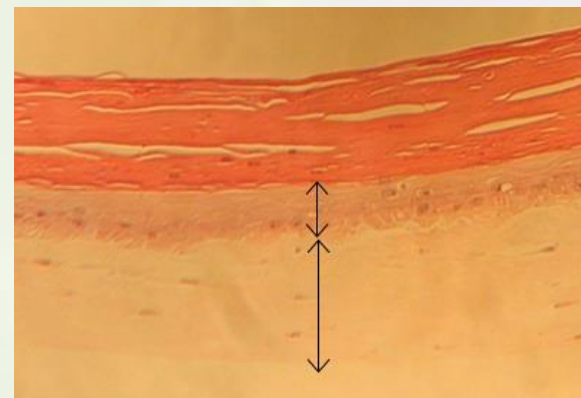
## ◆ Promotion Effect of Skin Turn-over



**Control**



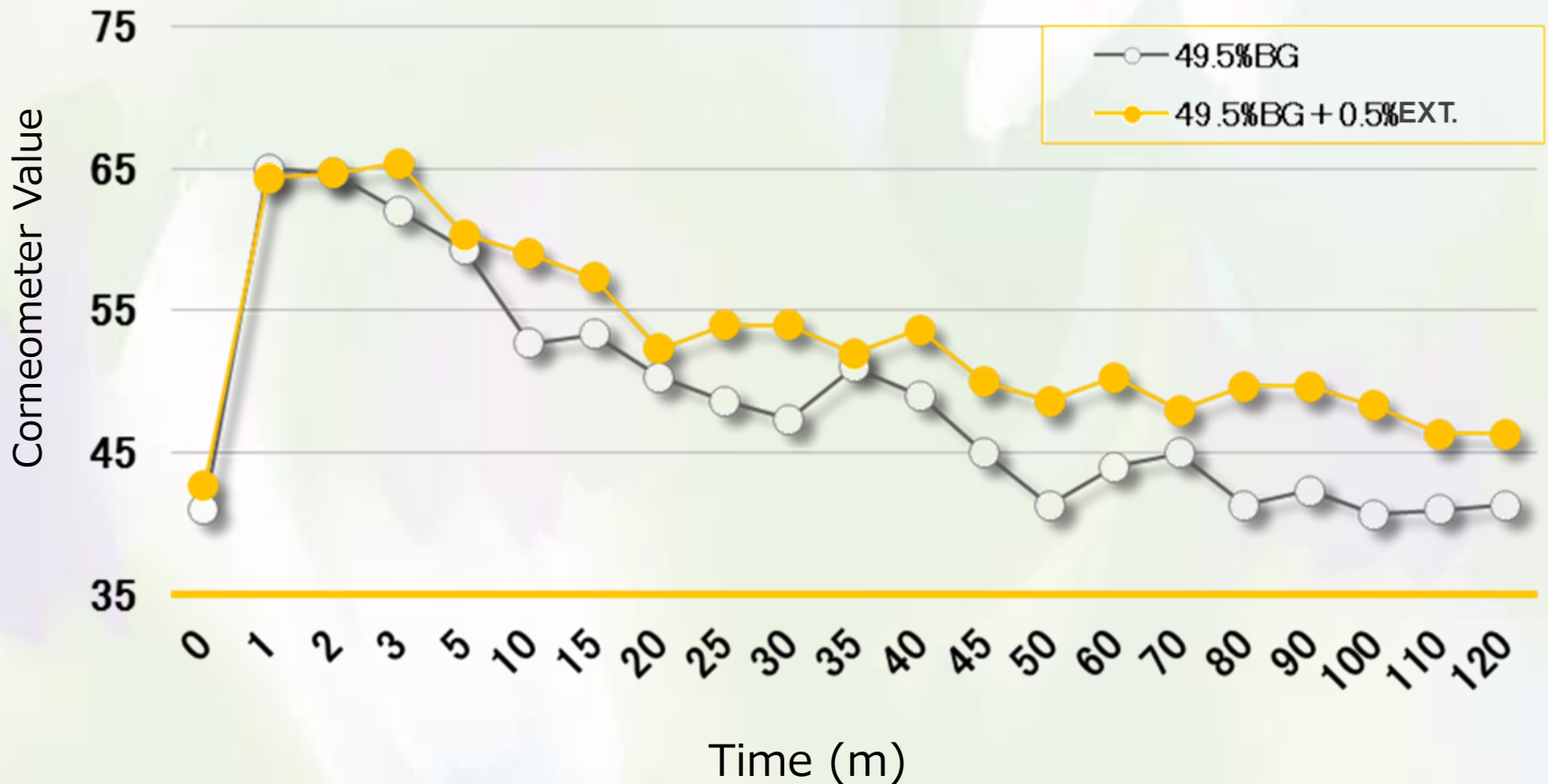
**Yuzu Seed Extract (10µg/mL)**



**Yuzu Seed Extract (100µg/mL)**

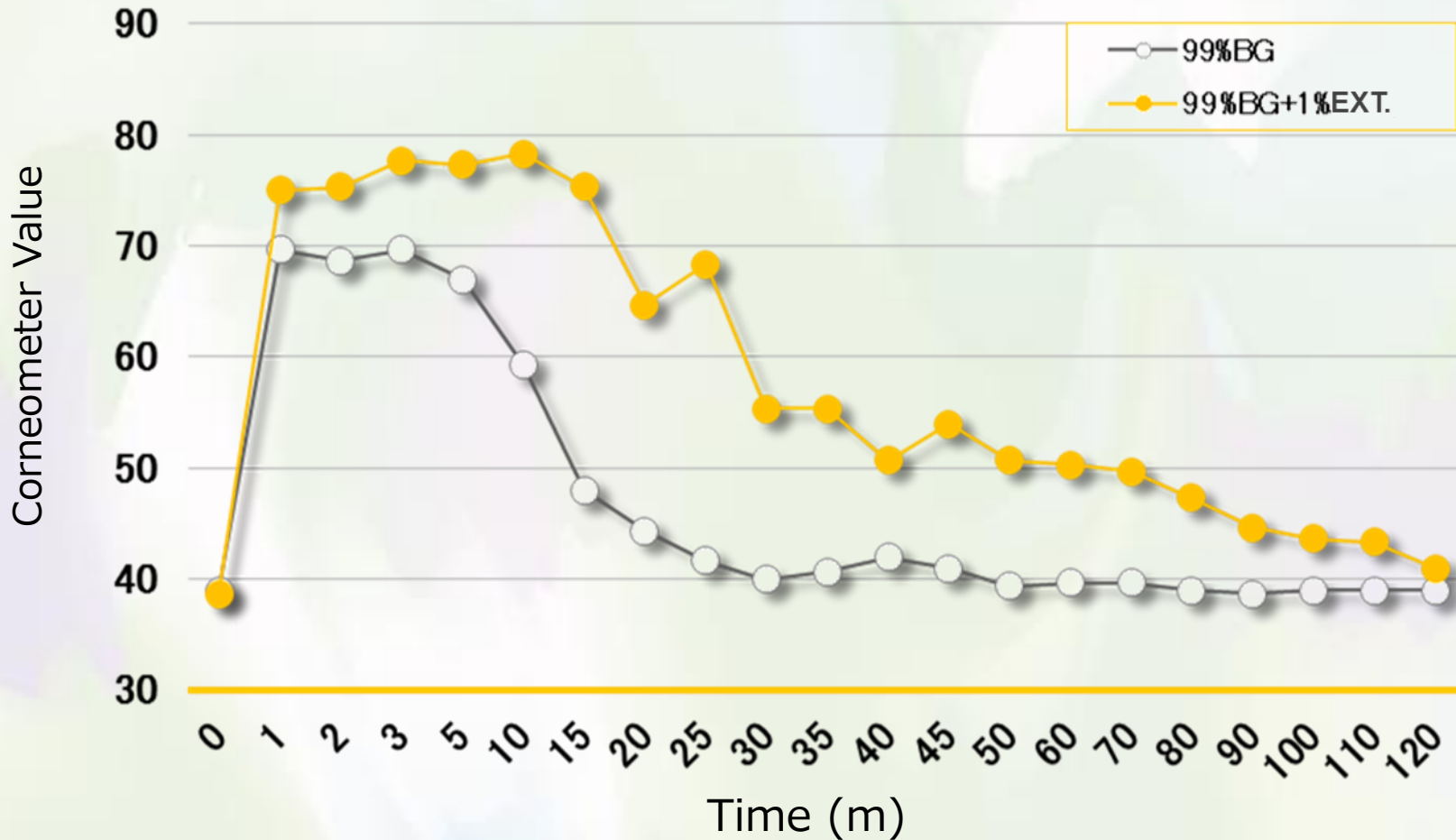
# Citrus Unshiu Peel Extract

## ◆ Moisturizing Effect I (Monitor Test)



# Citrus Unshiu Peel Extract

## ◆ Moisturizing Effect II (Monitor Test)



# Citrus Unshiu Peel Extract

- ◆ Promotion Effect of Skin Turn-over (Monitor Test)

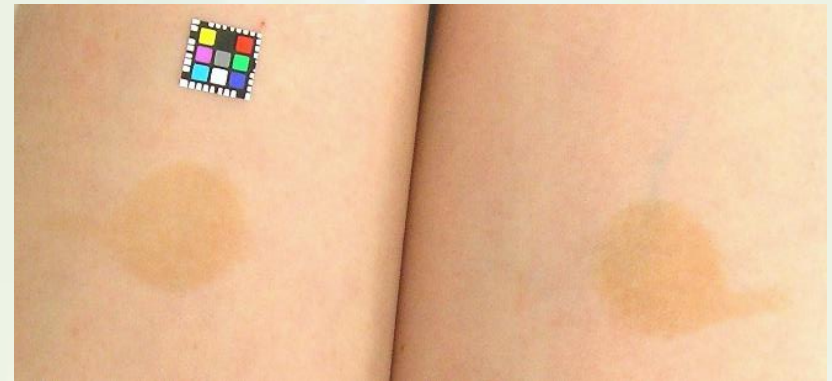
Test sample : CosmeHerbest™ ORANGE

Test period : 5 days

**Start**



**5 days**



**Citrus Unshiu Extract**

**Control**

**Citrus Unshiu Extract**

**Control**

# Mangosteen Peel Extract

- ◆ Determination of Minimum Inhibitory Concentration of  $\alpha$ -mangostin (AM) for *P. acnes*

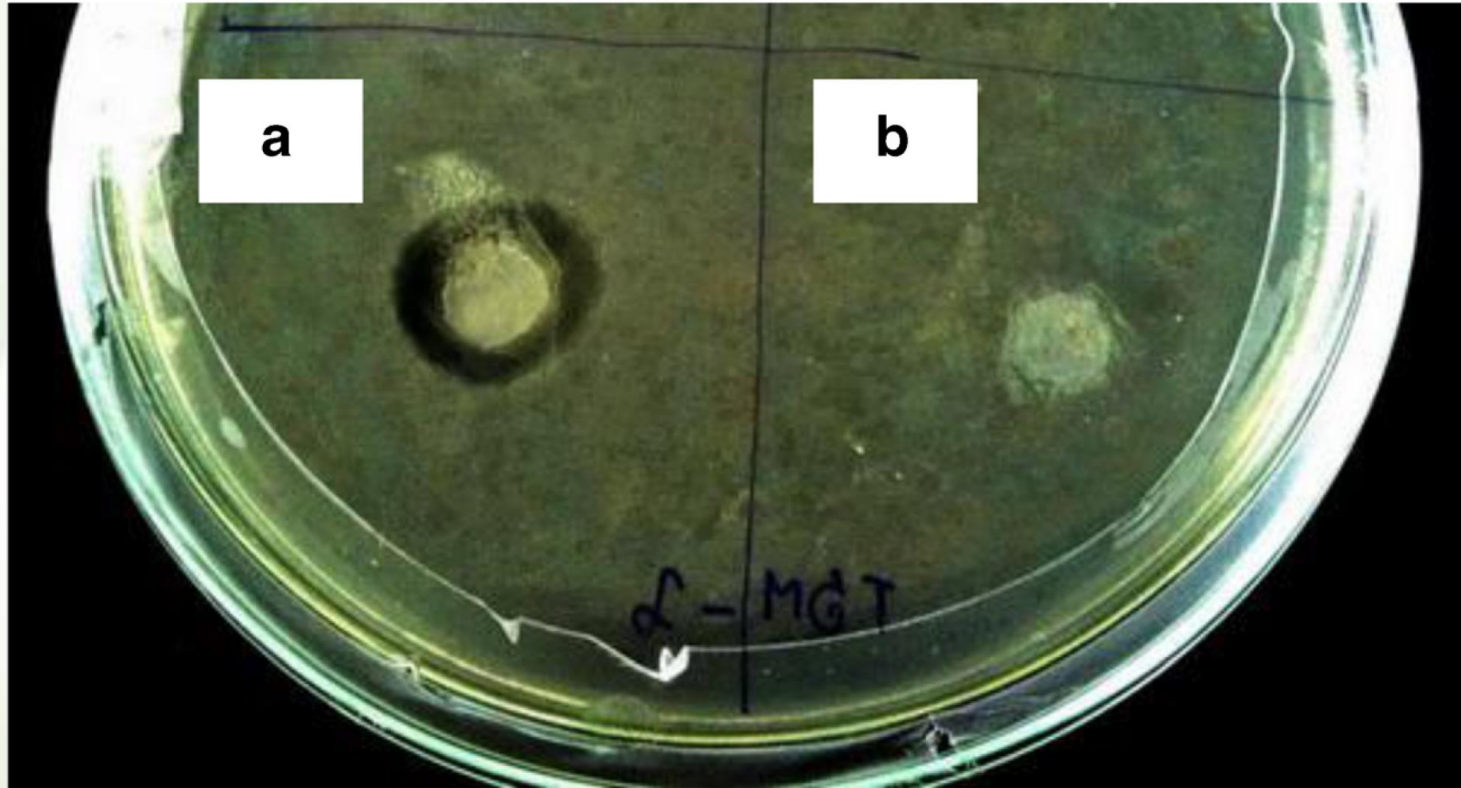
Test Solutions	<i>P. acnes</i> growth
0.5 $\mu\text{g/mL}$ AM	+
1.0 $\mu\text{g/mL}$ AM	-
2.0 $\mu\text{g/mL}$ AM	-
4.0 $\mu\text{g/mL}$ AM	-
8.0 $\mu\text{g/mL}$ AM	-
16.0 $\mu\text{g/mL}$ AM	-
32.0 $\mu\text{g/mL}$ AM	-
DMSO (negative control)	+
Brain-heart infusion broth (negative control)	+
Amoxicillin (positive control)	-

+ growth, - no growth



# Mangosteen Peel Extract

- ◆ Inhibitory Effect of *P. acnes*



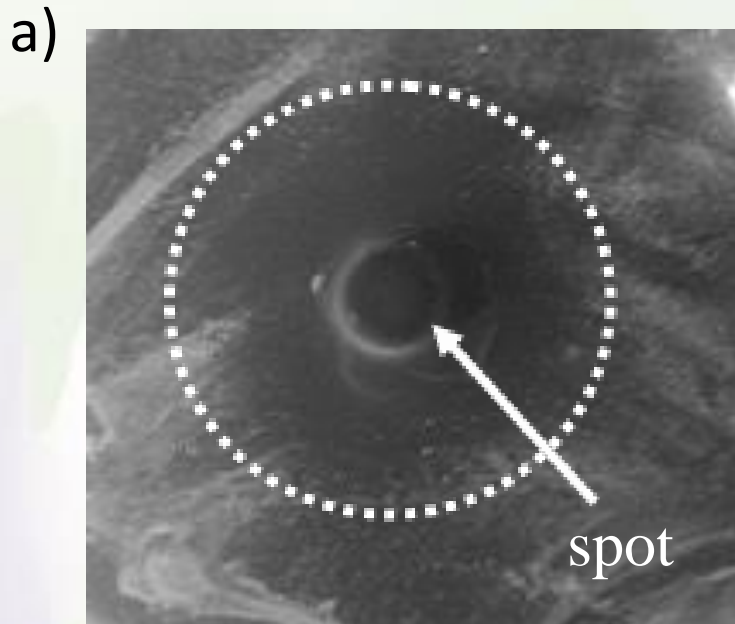
a : Alpha-Mangostin

b : control

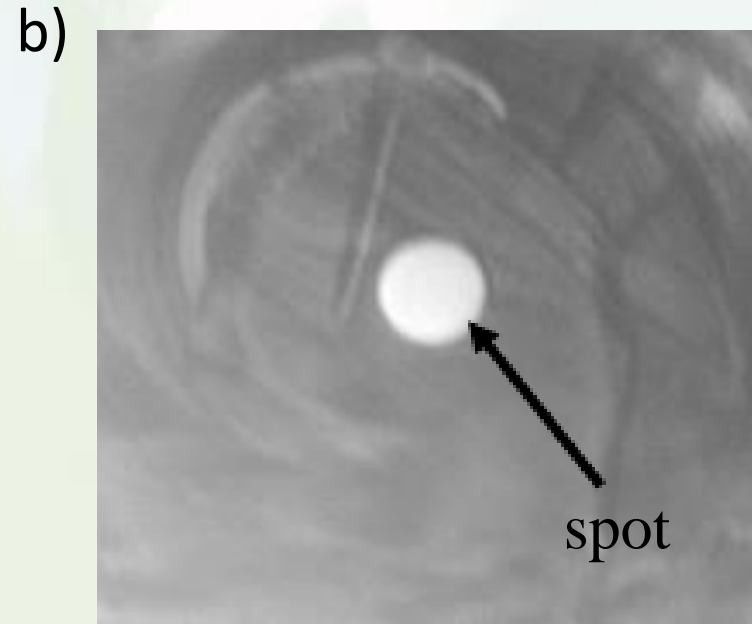
Inhibition zone

# Grape Leaf/Seed/Skin Extract

## ◆ Inhibitory Effect of *P. acnes*



a : Resveratrol

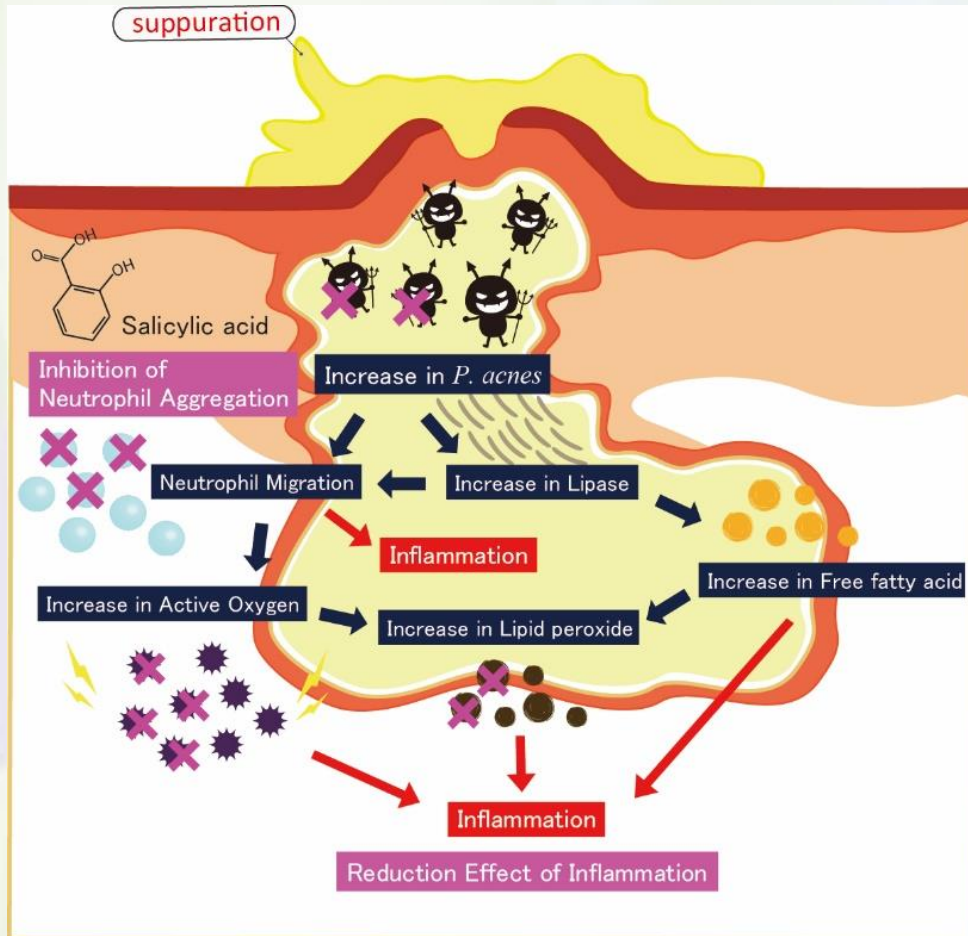


b : control

Inhibition zone

# Salicylic Acid

## ◆ Cause of Inflammation



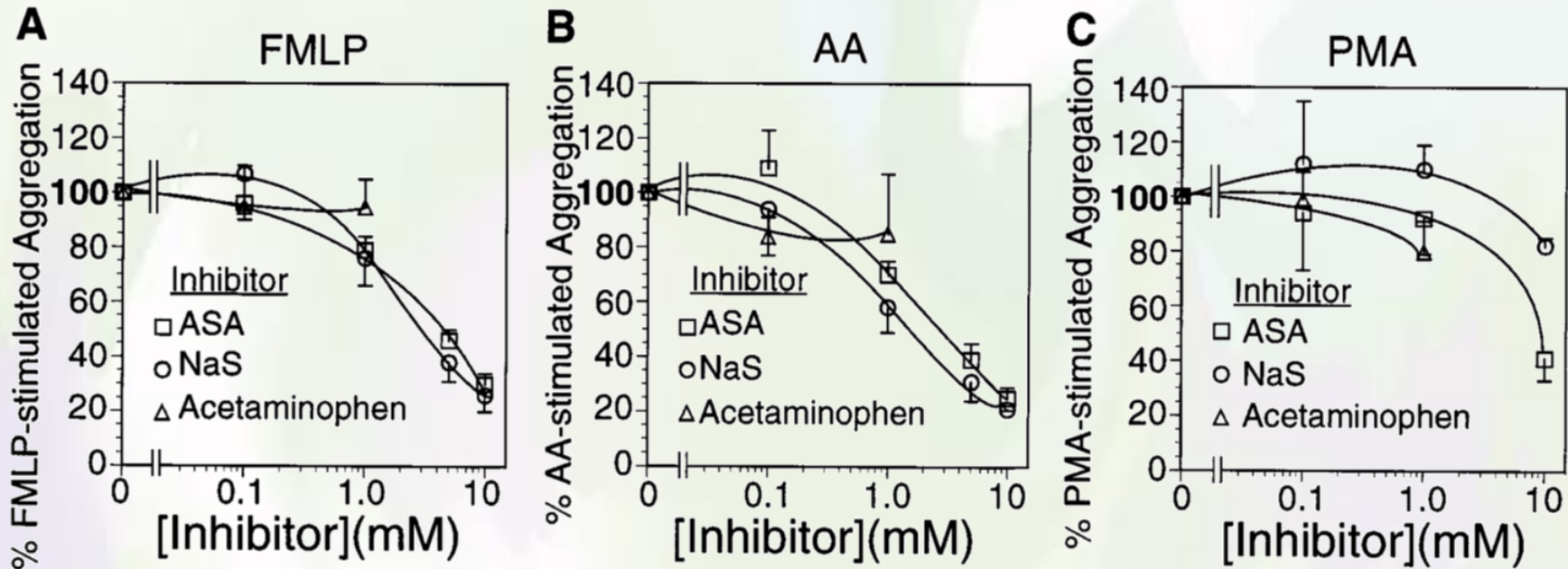
When pores are clogged and sebum accumulates inside, *P. acnes* grows inside them.

1. Inflammation caused by free fatty acids
2. Inflammation caused by neutrophil migration
3. Inflammation caused by lipid peroxide

# Salicylic Acid

## ◆ Palliation Effect of Inflammation

FMLP : *formylmethionyl-leucyl-phenylalanine*, AA : Arachidonic acid, PMA : Phorbol myristate acetate



Neutrophils were incubated for 10 min in the absence or presence of ASA (□), NaS (○), or acetaminophen (△), followed by stimulation with FMLP ;**A**, AA ;**B**, or PMA ;**C** for 2 min and measurement of aggregation. Results are expressed as percent of stimulated aggregation in the absence of inhibitor and are the means  $\pm$  6 SEM of three experiments.

# Anti-acne Study

## Anti-acne Effect on VeryBerry™ ACNEcare



**Kiwi**  
*Actinidia chinensis*



**Strawberry**  
*Fragaria chiloensis*



**Yuzu**  
*Citrus junos*



**Unshiu-orange**  
*Citrus unshiu*



**Mangosteen**  
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**Grape**  
*Vitis vinifera*

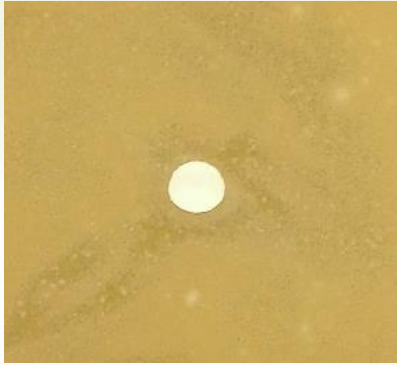
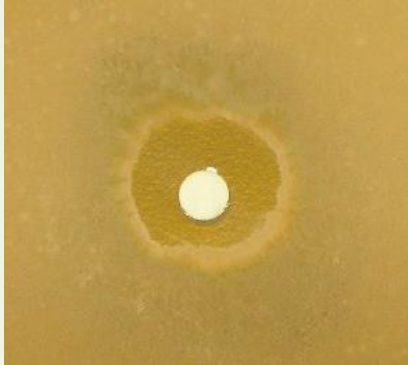
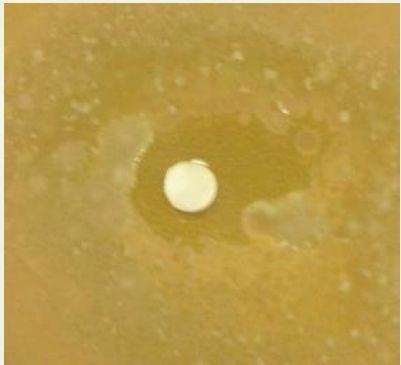


**Licorice**  
*Glycyrrhiza uralensis*

● Inhibition of *P. acnes*

# Inhibitory Effect of *P. acne* (*in vitro*)

## ◆ Inhibition of *P. acnes* on VeryBerry™ ACNEcare

	Water	50% Resorcinol	VeryBerry™ ACNEcare
Diameter of inhibition circle	0 cm	2.1 cm	1.7 cm
Photograph of inhibition circle			

# *in vivo* Study (Monitor Test)

## Anti-acne Effect on VeryBerry™ ACNEcare



**Kiwi**  
*Actinidia chinensis*



**Strawberry**  
*Fragaria chiloensis*



**Yuzu**  
*Citrus junos*



**Unshiu-orange**  
*Citrus unshiu*



**Mangosteen**  
*Garcinia mangostana*



**Grape**  
*Vitis vinifera*



**Licorice**  
*Glycyrrhiza uralensis*

● **Improvement Effect of Acne**

# Improvement Effect of Acne (*in vivo*)

## ◆ Improvement of Acne on VeryBerry™ ACNEcare

A monitor test was conducted in order to check the ability of VeryBerry™ ACNEcare for the improvement effect against *P. acnes*.

### **Test sample**

Carbomer gel incorporated 3% of VeryBerry™ ACNEcare diluted with 30% Propanediol water solution

### **Test subjects**

2 male and 3 female


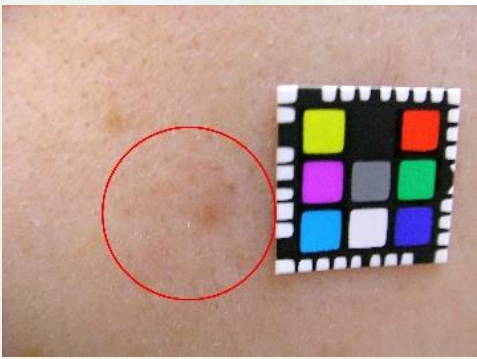


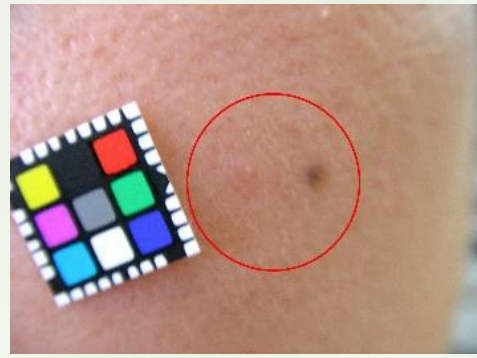
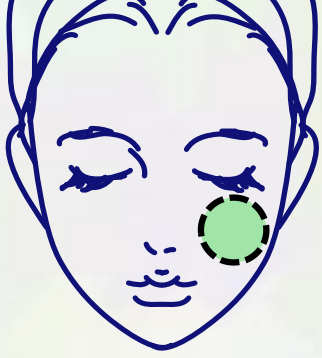
### **Test period**

Their acne conditions were visually checked 2 weeks after the acne formation. (When acne was completely healed within two weeks, the test was finished at that point.)



# Improvement Effect of Acne (*in vivo*)

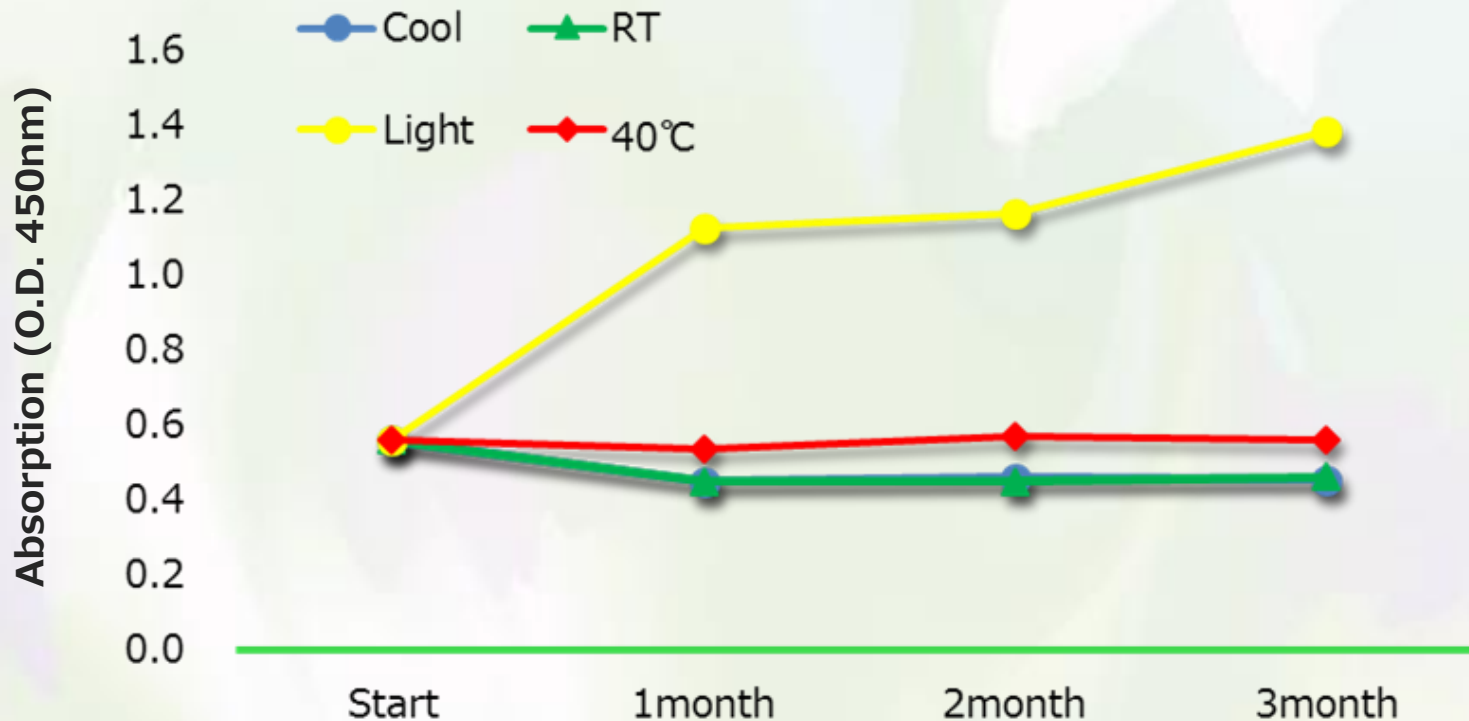
## ◆ Results

	START	After 2 weeks	Application part
No.1 M.M (23) F			
No.2 Y.Y (23) F			

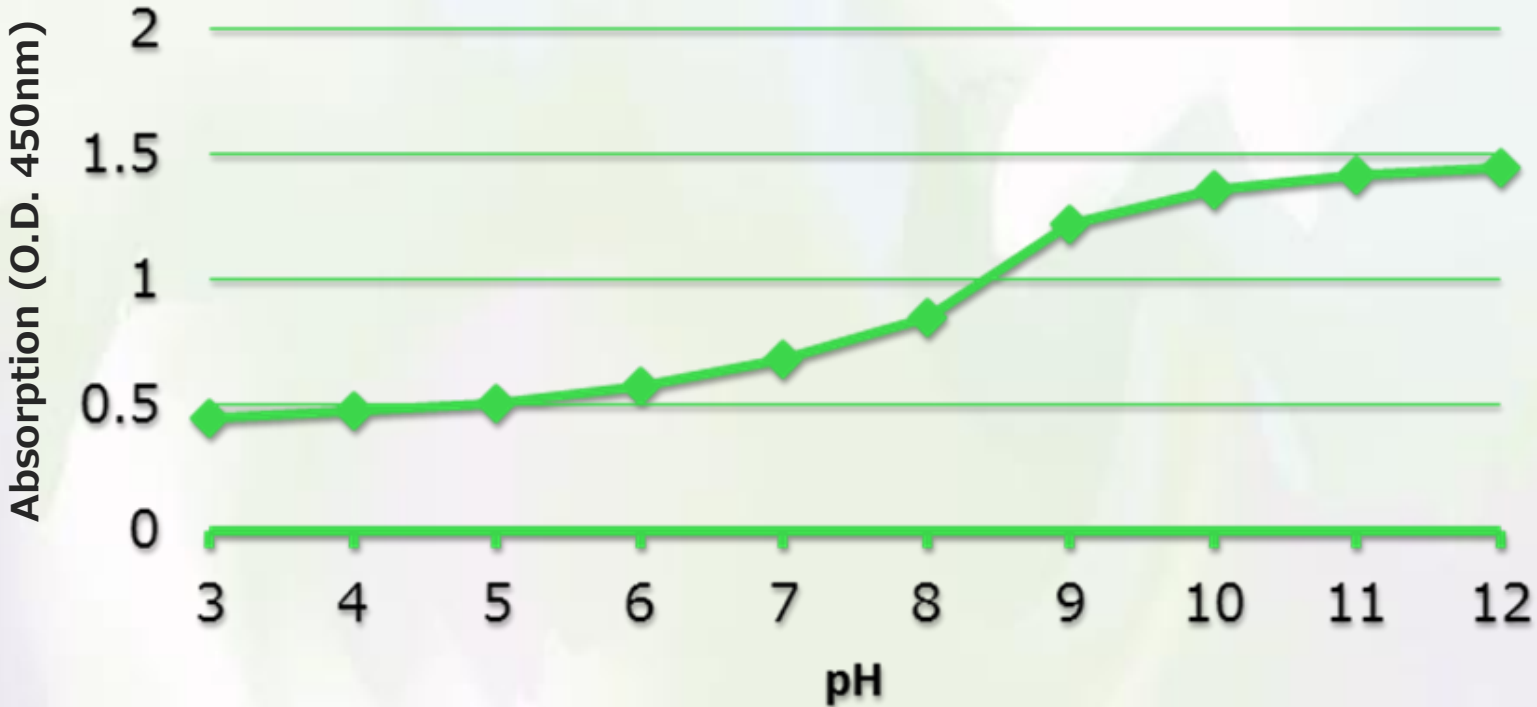
As shown in photo, improvement in acne conditions was observed. Acne conditions were improved or there was a tendency for improvement on four test subjects among the five. Judging from the results comprehensively, VeryBerry™ ACNEcare is expected to demonstrate an effect to improve acne conditions.

# Stability Test (Long-term Stability Test)

4°C : Cool, room temperature : RT, window side : Light



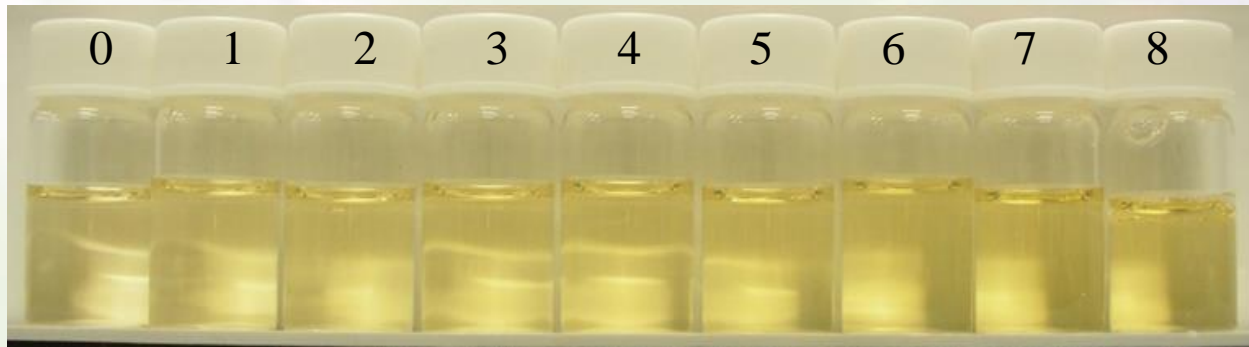
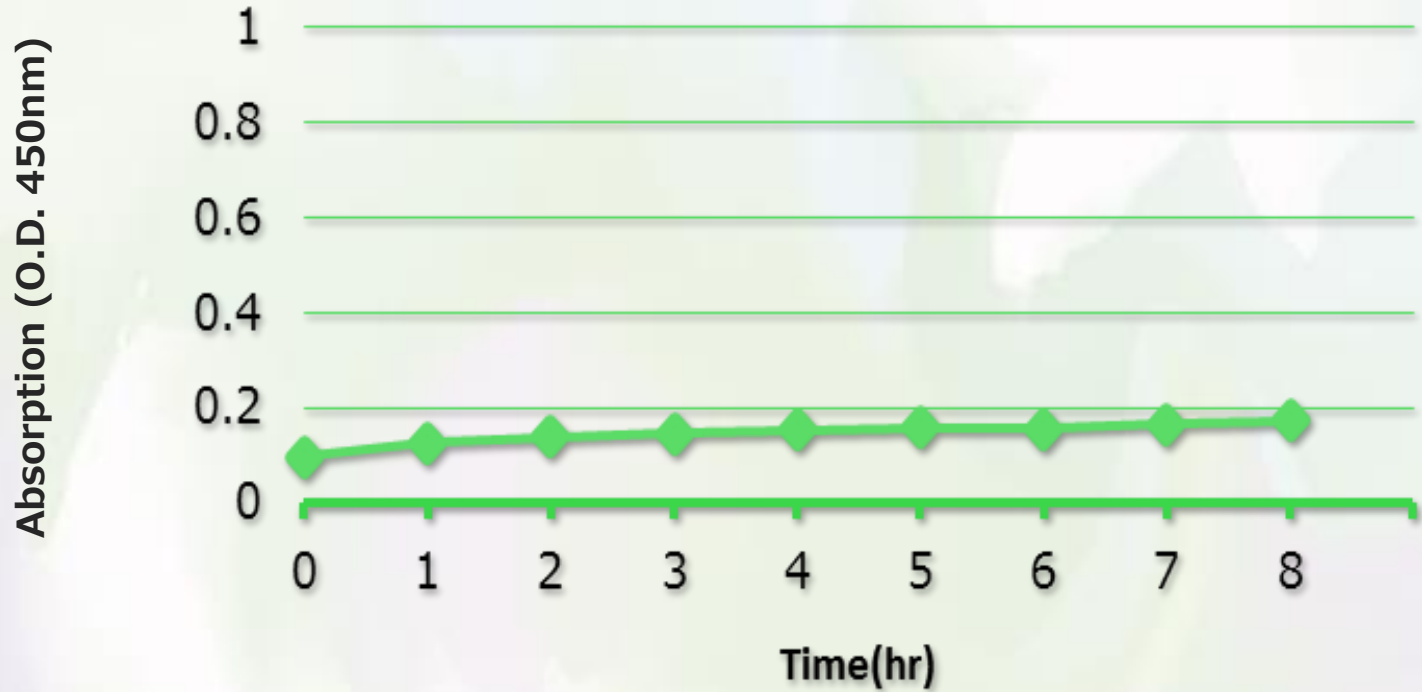
# Stability Test (pH Stability Test)



3 4 5 6 7 8 9 10 11 12

# Stability Test (Thermal Stability Test)

Condition: 10% VeryBerry™ ACNEcare Solution, 90°C, 8 hours



# Toxicological Safety Study

**Trade Name :** VeryBerry™ ACNEcare

Test Subject	Result	Test Method
Acute Oral Toxicity Test	Not Performed	
Primary Skin Irritation Test	No Irritation	EpiSkin™ method
Accumulated Skin Irritancy Test	Proceeding	RIPT method (50 people)
Sensitization Test	Proceeding	RIPT method (50 people)
Photo Toxicity Test	Not Performed	
Photo Sensitization Test	Not Performed	
Eye Irritation Test	No Irritation	SkinEthic™ HCE method
Mutagenicity Test	Negative	AmesTest (TA98, TA100, TA1535, TA1537, WP2uvrA)
Human Patch Test	Judgement for 24hours – (11), ± (1)	48hrs Closed Patch Test

# Product specification

Commodity	: Specification	Remarks
<b>Trade Name</b>	VeryBerry™ ACNEcare	
<b>Appearance</b>		
· Color	: Reddish yellow to dark reddish brown liquid	
· Odor	: Slightly characteristic odor	
<b>Identification</b>		
· Anthocyanin	: Positive	
· Flavonoid	: Positive	
· Saponin	: Positive	
· Polyphenol compounds	: Positive	
· Sugar	: Positive	
· Xanthone compounds	: Positive	
· Salicylic acid	: Positive	
· Allantoin	: Positive	
· Dipotassium Glycyrrhizinate	: Positive	
<b>pH (1→10)</b>	: 4.0 to 6.0	
<b>Purity Test</b>		
1) Heavy Metals	: 20 ppm max.	
2) Arsenic	: 2 ppm max.	
<b>Microbiological Exam.</b>		
1) Bacterial Count	: $1 \times 10^2$ /g max.	Hygiene Test
2) Mold, Yeast	: $1 \times 10^2$ /g max.	Hygiene Test
3) Coliform	: Negative	Hygiene Test

# Regulatory Status

INCI Name	化粧品国際中文標準名	CAS No.	EC No.
Water	水	7732-18-5	231-791-2
Propanediol	1,3-丙二醇	504-63-2	207-997-3
Salicylic Acid	水杨酸	69-72-7	200-712-3
Sodium Hydroxide	氢氧化钠	1310-73-2	215-185-5
Dipotassium Glycyrrhizate	甘草酸二钾	68797-35-3	272-296-1
Citrus Unshiu Peel Extract	温州蜜柑 (Citrus Unshiu) 果皮提取物	94266-47-4	304-454-3
Citrus Junos Seed Extract	香橙 (Citrus Junos) 籽提取物	94266-47-4	304-454-3
Allantoin	尿囊素	97-59-6	202-592-8
Actinidia Chinensis (Kiwi) Seed Extract	中华猕猴桃 (Actinidia Chinensis) 籽提取物	92456-63-8	310-127-6
Fragaria Chiloensis (Strawberry) Fruit Extract	草莓 (Fragaria Chiloensis) 果提取物	95193-64-9	305-877-6
Vitis Vinifera (Grape) Leaf Extract	葡萄 (Vitis Vinifera) 叶提取物	84929-27-1	284-511-6
Vitis Vinifera (Grape) Seed Extract	葡萄 (Vitis Vinifera) 籽提取物	84929-27-1	284-511-6
Vitis Vinifera (Grape) Skin Extract	葡萄 (Vitis Vinifera) 皮提取物	84929-27-1	284-511-6
Garcinia Mangostana Peel Extract	倒捻子 (Garcinia Mangostana) 果皮提取物	90045-25-3	289-884-9

# Packing Style



## **Packaging Style**

1kg PE Bottle, 5kg PE Cubic container / Outer: Carton box



## **Storage Condition**

Avoid high temperature and sun light, and ventilated area in closed original container.



**Thank you very much!**



ORYZA OIL & FAT CHEMICAL CO., LTD.