



ORYZA OIL & FAT CHEMICAL CO., LTD.

Fruits Extract Complex for Whitening

VeryBerry™ WHITE



Cowberry
Vaccinium vitis-idaea



Mango
Mangifera indica



Unshiu-orange
Citrus unshiu



Seabuckthorn
Hippophae rhamnoides



Litchi
Litchi chinensis

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1. Introduction

Human skin can be roughly classified into the epidermis and dermis. The epidermis guards the body and the dermis supports the skin with its collagen, elastin, and other components. These two layers are joined by the basement membrane, where cells that produce melanin pigments called “melanocytes” exist.

Inside the skin, an appropriate amount of melanin is produced in melanocytes and is discharged as the skin metabolizes to maintain the skin tone at a constant level. Melanin is produced to protect the skin and a large amount is produced when the skin tans. When melanin formation is no longer necessary, the production amount returns to its normal level, melanin content in the skin gradually lowers, and the skin recovers its original tone. However, when a large amount of melanin is produced in a local area or melanin cannot be discharged from the skin smoothly for some reason, the skin tone of the specific area becomes dark and dark spots develop. Current skin-lightening agents are developed to reduce dark spots by functions such as preventing the start of melanin formation, inhibiting melanin formation, promoting the discharge of melanin, or lightening the color of melanin. However, if melanin formation does not stop and melanin is continuously produced in a local area even after melanin is discharged, the area becomes a dark spot. Melanin formation starts when other cells in the skin sense UV-ray and send melanocytes a command to produce melanin, not because melanocytes sense UV-ray.

When the skin is exposed to UV-ray, some reactions occur in a step-by-step order to protect the body from UV-ray. The first reaction is darkening of melanin. Usually, melanin pigments are light brown and are found evenly in human skin, determining skin tone. When exposed to UV-ray, they turn into an oxidized form and darken. This can be considered skin’s defensive reaction because melanin absorbs UV-ray to prevent it from entering deeper areas of the skin. Because of this reaction, the skin becomes darker several hours after tanning. Since this is also a type of oxidation reaction, skin tone can recover relatively quickly by applying vitamin C or ingesting it in a large amount. A typical example of this reaction is that tanning makes freckles more outstanding.

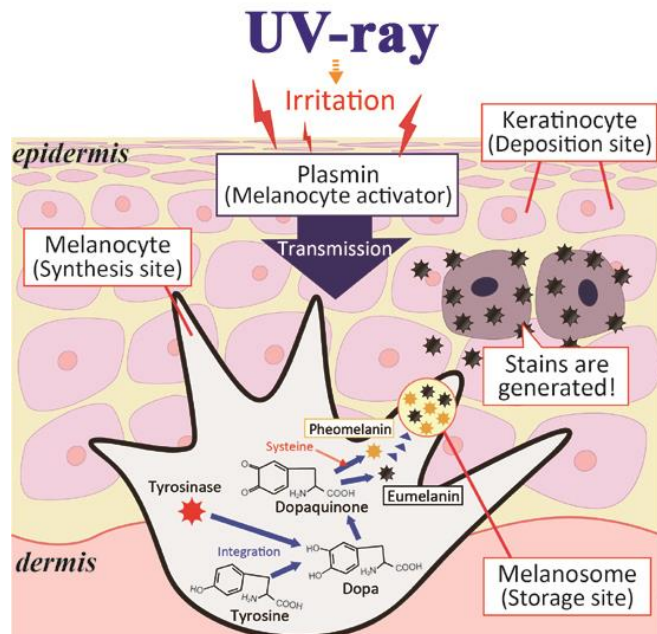


Fig.1: Mechanism of Melanin Production

2. Pathway and Points of Action of Skin-Lightening Agents

Liver spots, senile pigment freckles, and post-inflammatory pigmentation are typical dark spots appearing on the skin of people in their thirties and after. Liver spots are map-like brown spots appearing in areas from the lower eyelids to cheeks and they become worse by pregnancy, ingestion of birth control pills, and irritations from UV- ray and friction. When inflammation occurs on the skin due to UV-ray or any other factors, “stem cell growth factor (SCF)” and proinflammatory cytokine and other factors that cause inflammation temporarily promote the synthesis of melanin pigments in melanocytes. When this condition is sustained, post-inflammatory pigmentation occurs.¹⁾

These inflammatory conditions usually improve as time goes by. However, when DNA damage caused by repeated UV-ray exposure cannot be repaired and melanocytes in a specific area keep producing melanin pigments, “senile pigment freckles” or “solar lentigo” develop. When damage advances even more, a precancerous state called “solar keratosis” develops. Recently, it has been reported that “pre” melanin accumulated in the epidermis due to exposure to UV-ray becomes melanin. (Melanin pigments are produced outside melanocytes as well.) To prevent above, the following measures can be taken.

STEP 1 :	Cut off reactive oxygen caused by external stress such as UV-ray, dryness, and air pollutants in the epidermis.
STEP 2 :	Block chemical messengers such as endotheline, prostaglandin E ₂ , and histamine that are signals to stimulate keratinocytes to start melanin synthesis before transition to melanocytes.
STEP 3 :	Inhibit (Control) the production of melanin pigments in melanocytes.
STEP 4 :	Inhibit the transfer of melanin pigments from melanocytes to keratinocytes.
STEP 5 :	Promote the discharge of melanin accumulated in keratinocytes (promotion of turnover).

Skin-lightening cosmetic products currently available contain various ingredients to perform the actions above. Examples are: “chamomile extract” to control the action of endotheline; “tranexamic acid” to control the action of prostaglandin E₂; “hydroquinone,” “vitamin C derivative,” and “arbutin” to inhibit tyrosinase; “hydrolyzed prune extract” and “energy signal AMP” to inhibit melanin transfer; and “retinoic acid” and “AHA” to accelerate turnover.

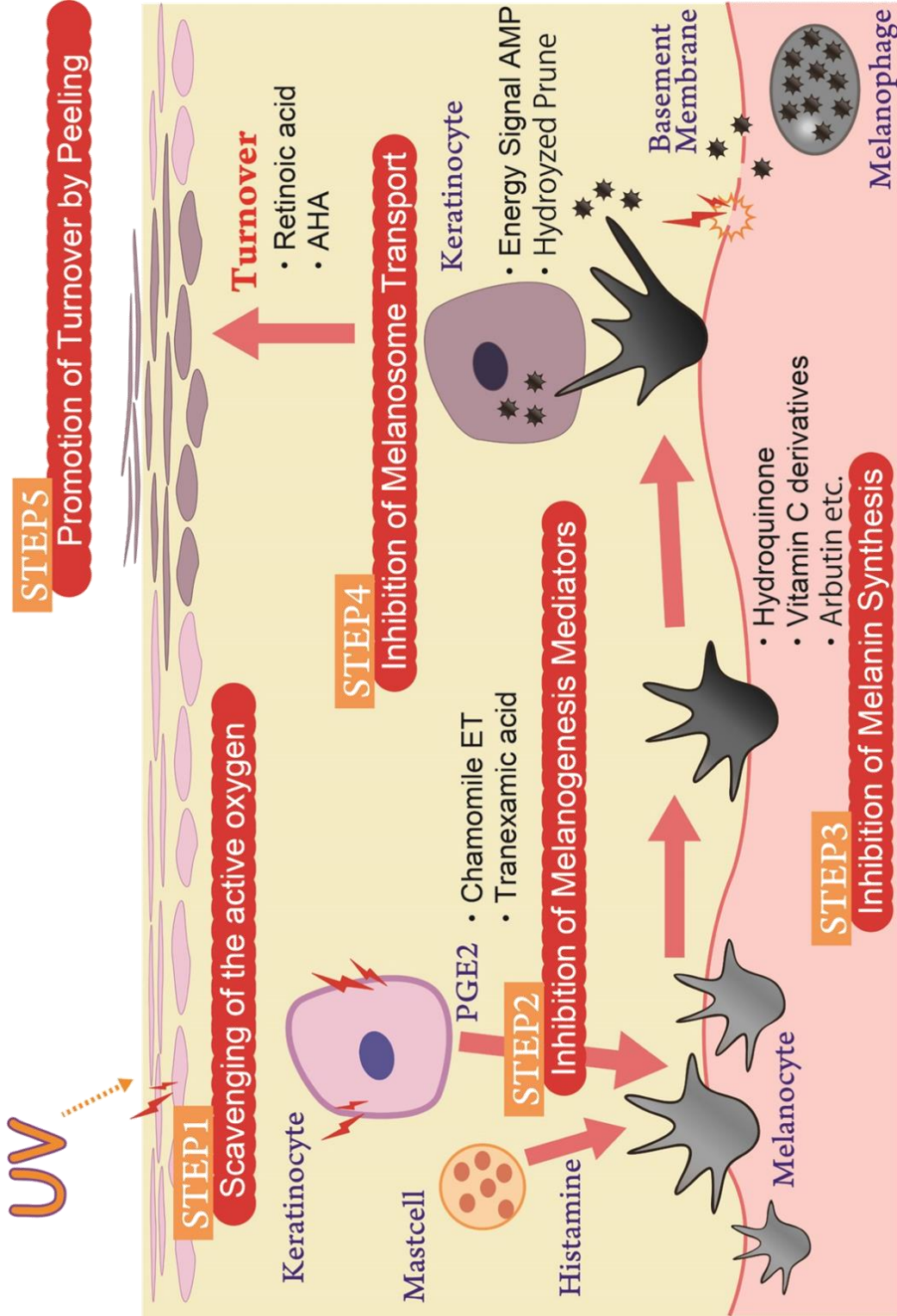


Fig.2: Mechanism of Various Whitening Agents on Commercial Products

3. Fruit Extracts and Active Component in VeryBerry™ WHITE

3-1 COWBERRY / *Vaccinium vitis-idaea*

Cowberry is a native plant of the forests of Lapland and Northern Eurasia. The fruits of Cowberry are nutritionally rich in vitamin C and other phytonutrients. Cowberries are collected in the wild in Finland and eaten raw, which preserves most of their nutrients. Besides, cowberries can be incorporated into juices, jam, syrup and other form of processed food. With respect to the functional effect of cowberry, it has been renowned for its rich phytochemical contents such as arbutin, anthocyanidin and procyanidin. Research studies on the functional effects of cowberry are increasing in recent years. With great honor, Oryza Oil & Fat Chemical Co., Ltd. together with Fingredients Ltd. successfully developed “LINGONBERRY Extract” standardized with arbutin featuring on healthy skin whitening. It is extracted from the fruits of wild cowberry without an organic solvent.



3-2 MANGO²⁾ / *Mangifera indica*

The mango tree is a tall evergreen belonging to the sumac family and its scientific name is *Mangifera indica*. It is native to South Asia where it has been cultivated as a fruiting tree. It has 10 to 20 cm long egg-shaped fruits. It becomes yellow when ripe and has a single seed. Mango fruits are juicy and tasty. They have a sweet-and-sour taste and unique smell. Mango is a typical tropical fruit. In Japan, it has become very popular because domestic production of mango increased around the year 2000 as well as imports from Mexico, Thailand, and Philippines. Despite these alluring characteristics, mango belongs to the sumac family. Its leaves do however contain a large amount of mangiferin, which is a type of xanthone. For this reason, mango is believed to have anti-inflammatory and antioxidant activities.



3-3 UNSHIU-ORANGE / *Citrus unshiu*

Unshiu mikan or Citrus unshiu Marc is commonly known as Satsuma, Satsuma Mandarin or Satsuma Orange in the Western society. Unshiu mikan is originated from Kagoshima (Satsuma). There are approximately 900 species of citrus in the world. Japanese oranges are unique to Japan and appeared 1,200 years ago. It was regarded as fruit for perpetual youth and longevity as described in Kojiki and Nihon Shoki. Japanese seedless orange was generated by mutation 400 years ago. The name Unshiu mikan originated from Unshiu area in China where it is famous for production of oranges. There are various type of Citrus Unshiu, e.g. “Kumamoto mikan”, “Ehime mikan”, “Arita mikan” and “Shizuoka mikan”.



3-4 LITCHI / *Litchi chinensis*

An origin of Litchi is the southern China, have been cultivated for over 3,000 years. As is observed in historical tales of Yang-kuei-fei, litchis were particularly treasured in ancient times when it was difficult to keep freshness, litchis are evergreen subtropical trees. The flowers are small and pale white–light yellow. The fruits are roundish stone fruits with a thin solid pericarp and a torus surface, and turn from vivid red to dark red when ripe. The seeds are short oval, and isolated and covered with a white flesh juicy aril. This aril is delicious. The aril is one of the five major fine fruits in tropical and subtropical zones and has been loved by people in China. Litchi trees, which are about 5-15 m tall, are widely cultivated as fruit trees. Litchis bloom in February-March and ripe in June-July. Litchi is generally eaten raw. Fresh fruits are used for fruit cocktails and salads, and canned ones are for dessert and flavoring of Chinese tempura. Litchis are sweet and have been treasured as a tonic in China or decocted as a cough medicine. The seeds were made into ointments and used for skin disease. The trees live long, and even 200-year-old trees bear fruits.



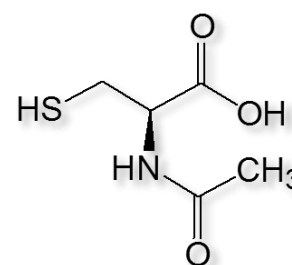
3-5 SEABUCKTHORN / *Hippophae ramnoides*

Seabuckthorn (*Hippophae Rhamnoides*) is fruit of a deciduous shrub from the *Elaeagnaceae* family. It is eaten by people in temperate to subarctic zones including Northern Europe, the central areas of the Eurasian Continent, and Canada. It is a vigorous plant that can grow in harsh environments with extreme temperature variation, dry weather, sandstorms, denudation of soil, or even in barren areas. The plant already existed approximately 70 million years ago and has survived for this long time because of its strong vital force. Seabuckthorn is called various names, for example sea-buckthorn (English), 沙棘 (shājí, Chinese), Ч а ц а р г а н а (Mongolian), oblepikha (Russian), and sanddorn (German).



3-6 N-Acetyl-L-Cysteine³⁾

N-acetylcysteine (NAC) is an extremely useful amino acid. NAC is used as a drug, a detox agent to discharge toxins from the body, and an anti-aging supplement in some countries. NAC is also known as an anti-aging amino acid. Our body has an antioxidant called glutathione which is one of most important antioxidants. NAC is believed to be a precursor substance of glutathione and can increase the glutathione content in the body. It is believed that reactive oxygen causes aging. When the body has a sufficient amount of glutathione and other antioxidants, they neutralize excessively-generated reactive oxygen and cancel its negative influence. They also have an activity to inhibit the activity of tyrosinase in the melanin synthesis pathway that influences skin tone, an action to guide tyrosinase to the pathway to synthesize pheomelanin which is yellow melanin, and an action to make dark spots and freckles less visible.



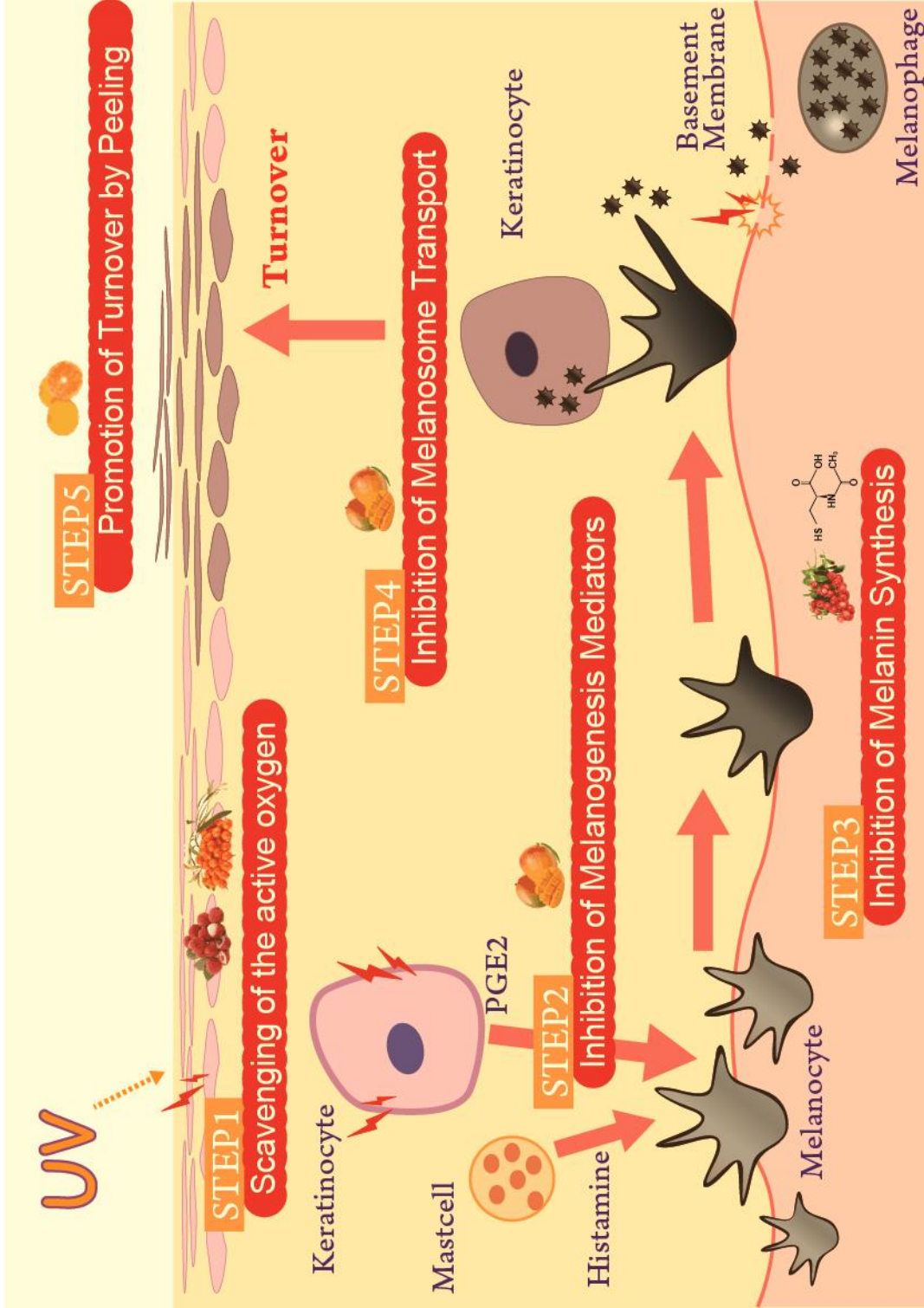


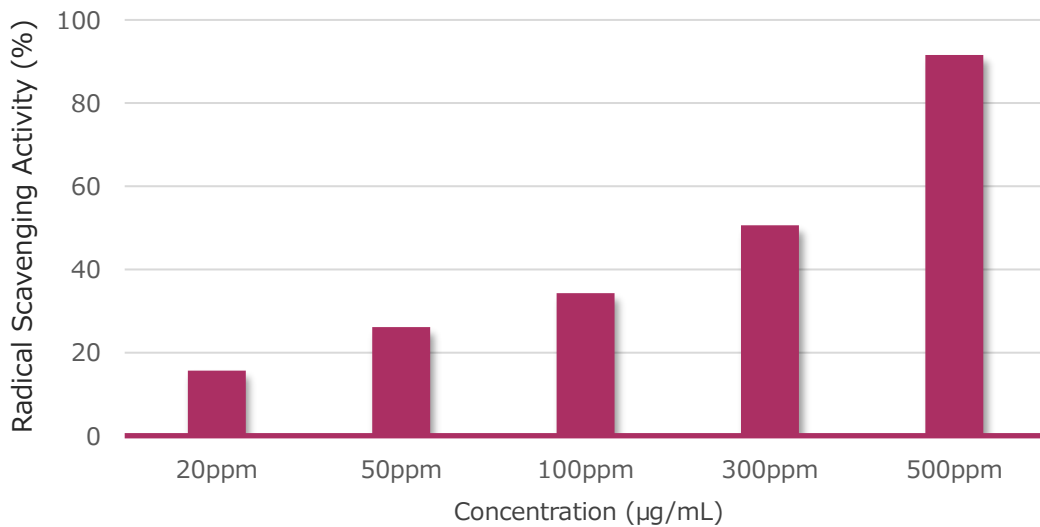
Fig.3: Whitening Mechanism of VeryBerry™ WHITE

4. Efficacy Evaluation of each Plant Extracts

4-1 STEP 1: Radical Scavenging Effect

4-1-1 SOD Like Activity / LITCHI Seed Extract

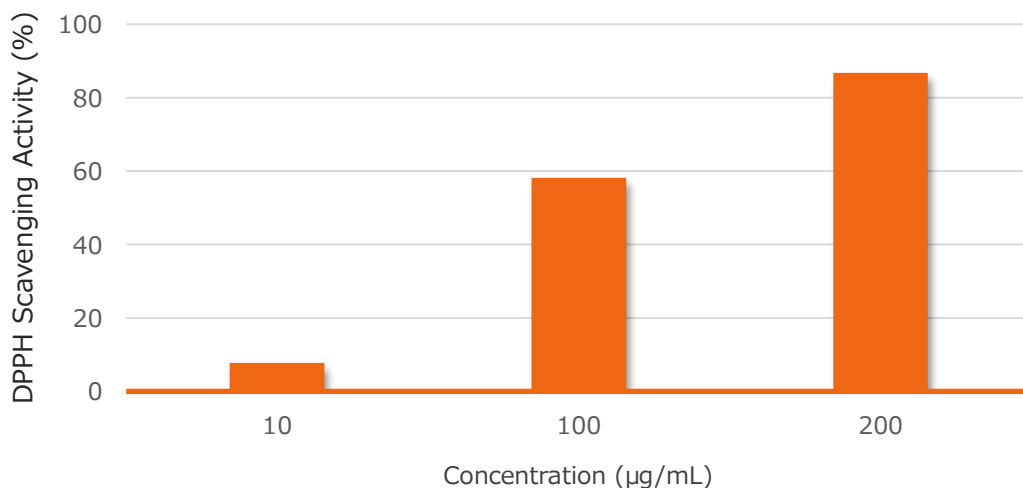
In the human body, the presence of active oxygen species (O_2^- radicals) causes cellular damage, which induces cancer and inflammation, and promotes aging. In particular, in the skin, active oxygen is considered to be a cause of spots, freckles, and wrinkles. LITCHI Seed Extract showed SOD-like activity (elimination of active oxygen) and eliminated radicals.



SOD like Activity on Litchi Seed Extract (Solid)

4-1-2 DPPH Scavenging Activity / SEABERRY Fruit Extract

Reactive oxygen combats using its oxidizing power in order to protect our body from the attack of bacteria and viruses that have entered the body. However, since it attacks normal cells as well as bad cells, excessive reactive oxygen negatively influences the body. This indicates that SEABERRY Fruit Extract has an action to protect living bodies against attacks of reactive oxygen caused by external irritation.

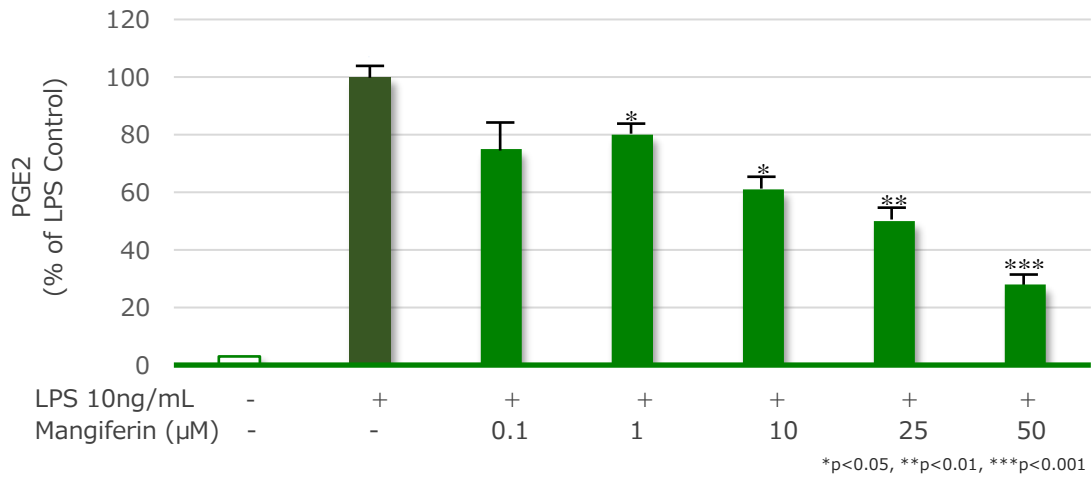


DPPH Scavenging Activity on Seaberry Fruit Extract

4-2 STEP 2: Inhibitory Effect of Chemical Mediators

4-2-1 Inhibitory Effect of Prostaglandin E₂ (PGE₂) Production / MANGO Leaf Extract

We have examined the variation of PGE₂ upon mangiferin, is the main component in Mango Leaf Extract, were 0.1 to 50µM added to PGE₂, which is produced by lipopolysaccharide. As a result, mangiferin is suppressed in a concentration-dependent manner PGE₂ production amount was understood.

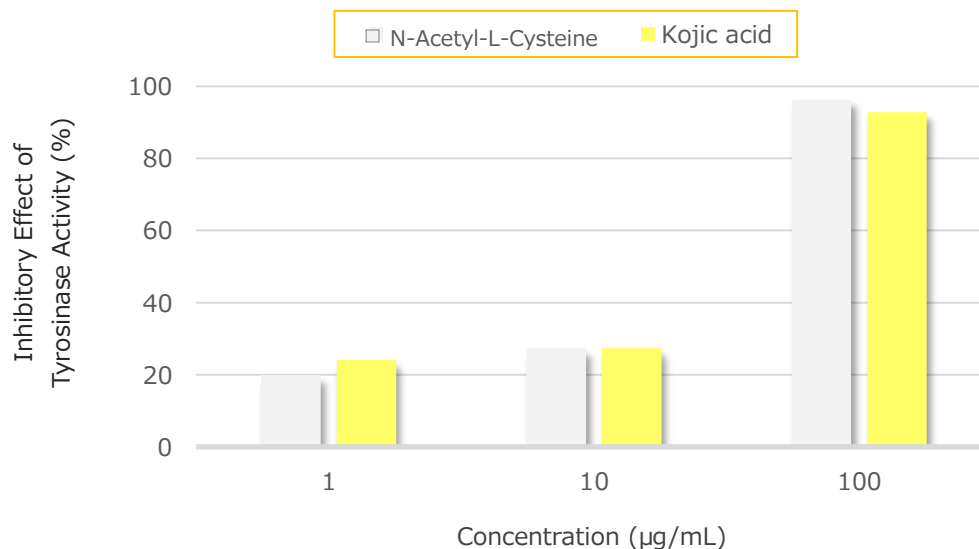


Inhibitory of LPS-induced PGE₂ production

Data: Archives of Biochemistry and Biophysics 477 (288), 253-258

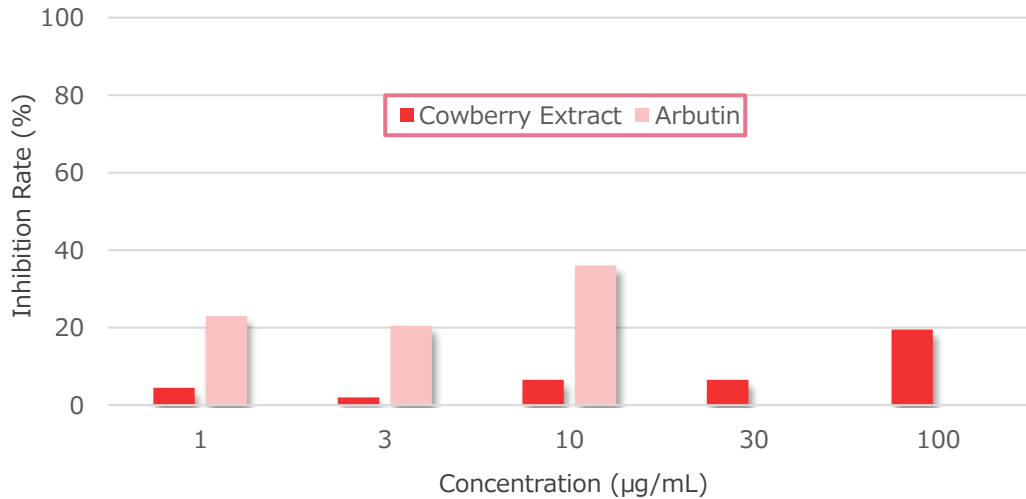
4-3 STEP 3-1: Inhibitory Effect of Tyrosinase Activity / N-Acetyl-L-Cysteine

We examined inhibitory effect of tyrosinase activity, after adding 1, 10, and 100µg / mL of N-Acetyl-L-Cysteine, is a glutathione precursor, into tyrosinase (Mushroom derived) solution, and reacted by adding L-DOPA solution. As a result, the N- acetyl -L- cysteine was confirmed to be suppressed in a concentration-dependent manner tyrosinase activity.



STEP 3-2: Inhibitory Effect of Melanin Production / Cowberry Fruit Extract

The effect of COWBERRY Fruit Extract on melanin production was experimented and compared with β -arbutin. Results showed that COWBERRY Fruit Extract demonstrated concentration dependent inhibition on melanin production.



Inhibitory of Melanin Production

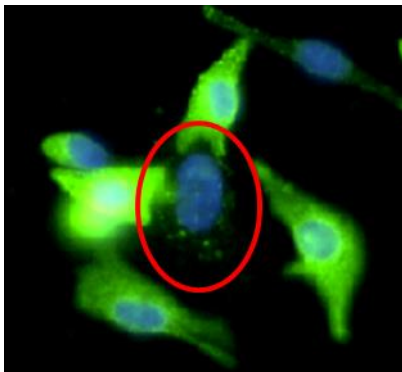
4-4 STEP 4 Inhibitory of Melanin Transfer to Keratinocytes / MANGO Leaf Extract

Melanin, produced in the melanocytes, will be the brown color by the auto-oxidation after delivering to keratinocytes. We conducted whether mango leaf extract shows an inhibitory effect of melanin transfer from melanocytes to keratinocytes. As a result, we confirmed that the mango leaf extract, has an inhibitory effect of melanin transfer to keratinocytes.

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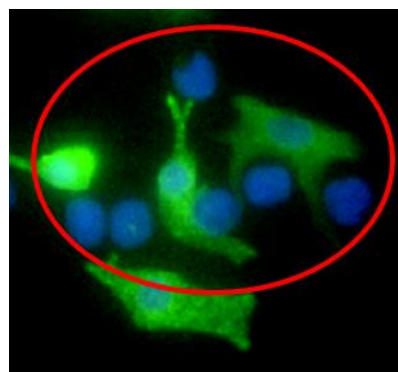
- Melanocytes normal human neonatal epidermal melanocytes NHEM (NB)
- Keratinocytes cervical immortalized normal keratinocytes cells NCE16

Control



Melanosomes (small green particles) are transferring from melanocytes to keratinocytes.

MANGO Leaf Extract



Migration of melanosomes is not observed.

4-5 STEP 5 Promotion Effect of Skin Turn-over / UNSHIU-ORANGE Peel Extract

The tanning agent were applied on the left and right forearm inside by patch test plaster for three hours. The skin color changed to brown color after 24hours and color photo was taken (Photo No. ①). Then, the control lotion was applied on right forearm twice a day, and the sample lotion was applied on the left forearm twice a day for five days (Photo No. ②). Determination was performed by the naked eye by comparing the left and right.

- Tanning agent / 10% DHA solution
(10% Dihydroxyacetone, mixture of ethanol: BG: water = 20: 30: 50)
- Control Lotion (30% Propanediol water solution)
- Sample Lotion (undiluted CosmeHerbest™ ORANGE, Lot. M-524)



Photo ①
24 hours after applying DHA for the confirmation of browning on both forearm

Applied the Sample Lotion



Applied the Control Lotion

Photo ②
5days after applying DHA + Control (Right forearm) and the Sample (Left forearm)

Fig.6: Promotion Effect of Turn-over on CosmeHerbest™ ORANGE

5. Whitening Effect on VeryBerry™ WHITE

5-1 Inhibitory Effect of Tyrosinase Activity

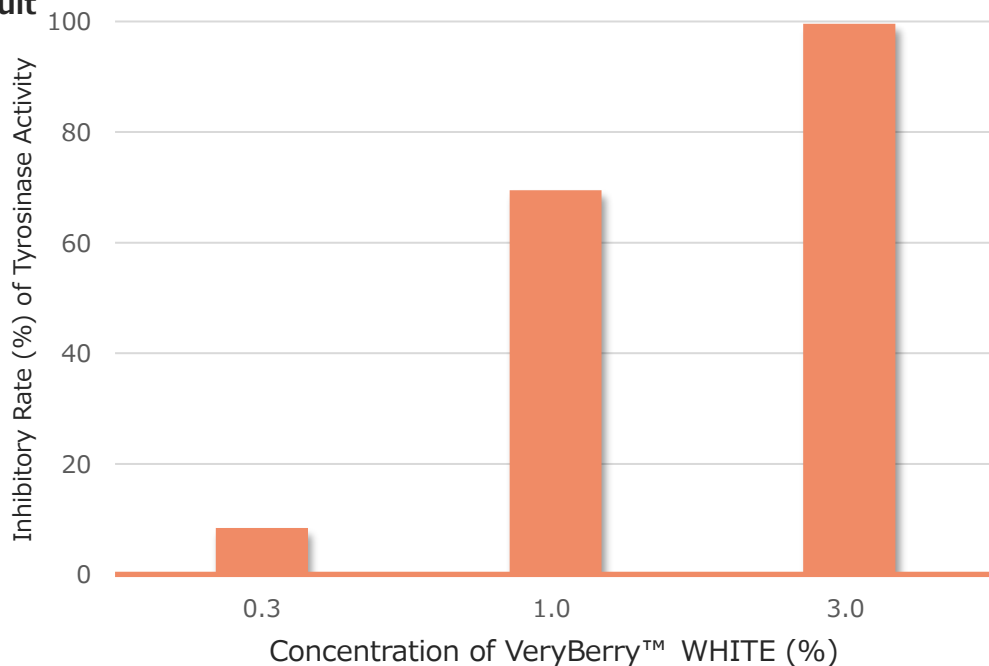
Test Method

70 μ L/well of the sample solutions, prepared for each concentration, were added to 70 μ L/well of tyrosinase solution, dissolved 0.1M phosphate buffer (pH7.0) 100 Unit/mL (from mushroom, Sigma Co.), and incubated for 5 minutes at 37 °C. After incubation, followed by measuring the absorbance at 490nm in a microplate reader, 70 μ L/well of L-DOPA solutions which is prepared 1 mg/mL of the L-DOPA dissolved in 0.1M phosphate buffer solution in advance, was added, and incubated at 37 °C 5 minutes. After incubation, we measured the absorbance at 490nm in a microplate reader. Incidentally, the same manner as the control, added water instead of the sample solution was measured and calculated the inhibitory ratio by comparison with the control.

Test Sample

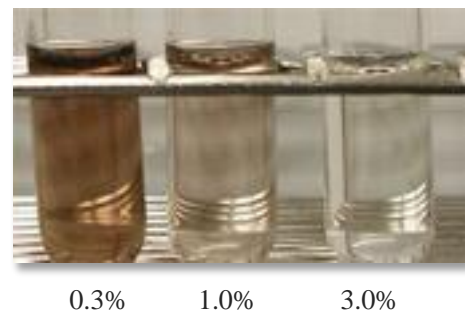
· VeryBerry™ WHITE Lot Number M-520

Test Result



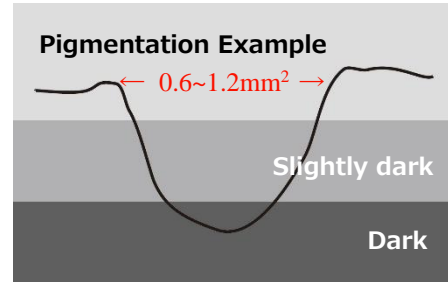
Consideration

We confirmed the inhibitory ratio of tyrosinase activity at 8.4% in a 0.3% dose, 69.5% in 1.0% dose and 99.6% in 3.0% dose of VeryBerry™ WHITE. It is expected whitening effect after using 1 to 2 months later formulated 3.0% dose of Very Berry WHITE in the finished cosmetic preparations.





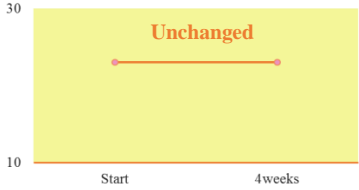


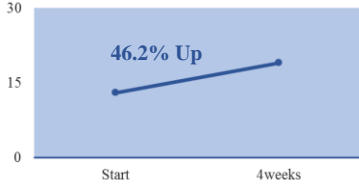


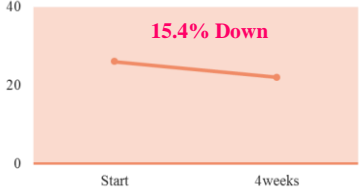


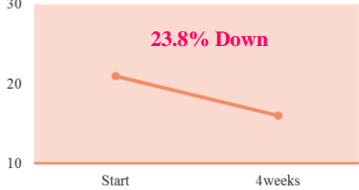


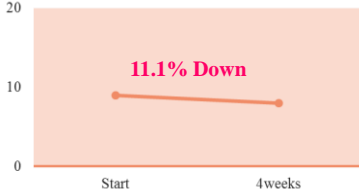


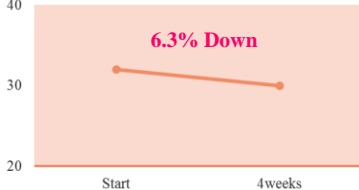


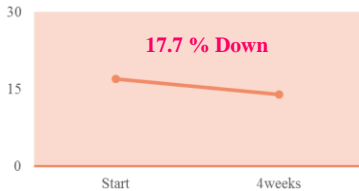


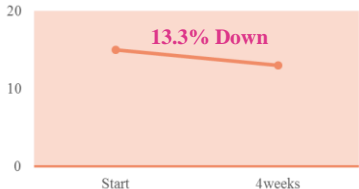
5-2 Improvement of Pigmentation on VeryBerry™ WHITE (in vivo Test)

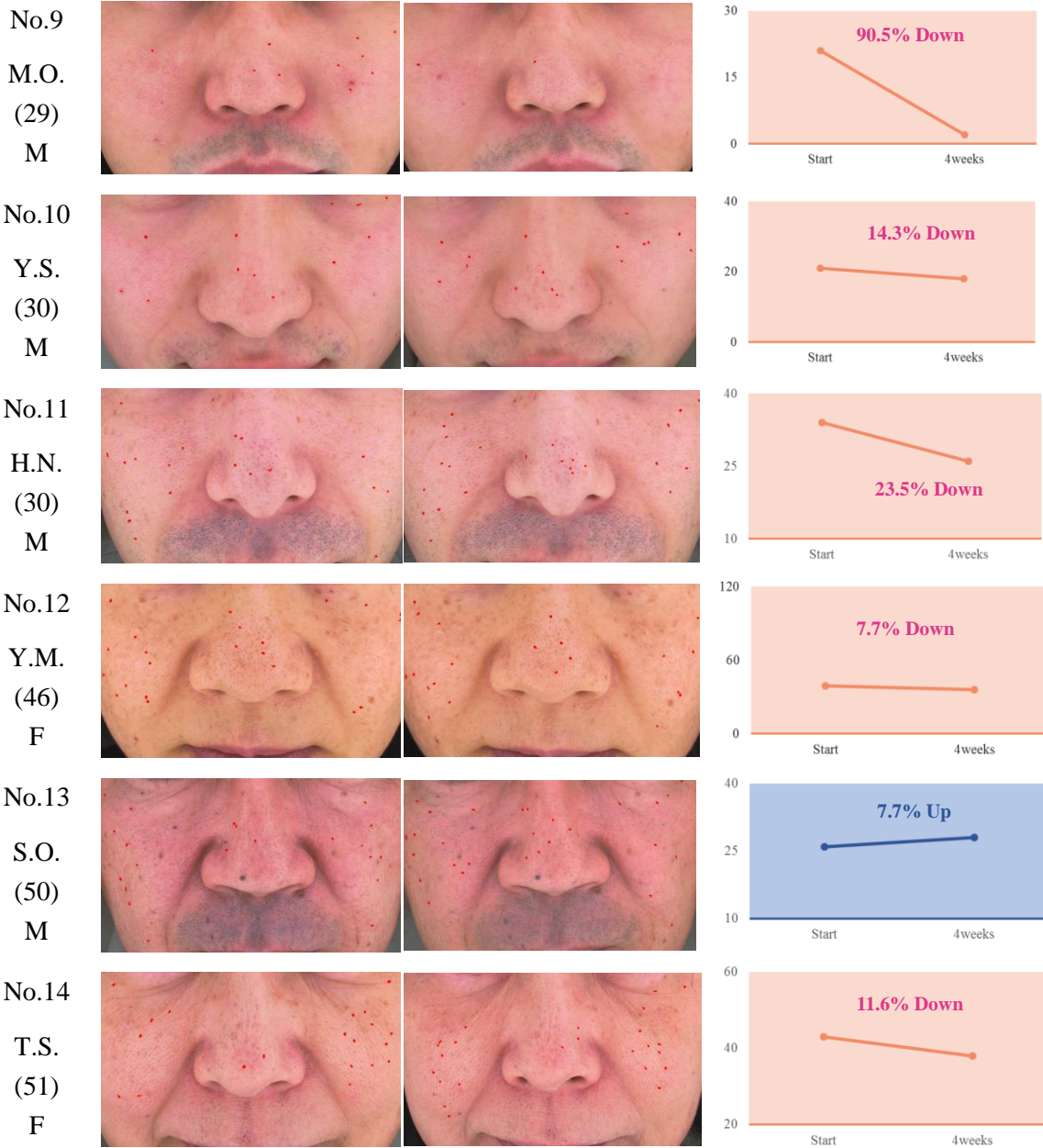
The effect to improve pigmentation areas was measured using the Robo Skin Analyzer. As shown in the photos below, pigmentation level is not very clear in color photos. Continuous areas with a size of 0.6 to 1.2 mm² can be detected as "slightly dark areas" and "dark areas" as compared to surrounding areas in monochrome photos are detected as "pigmentation areas".



Test Result

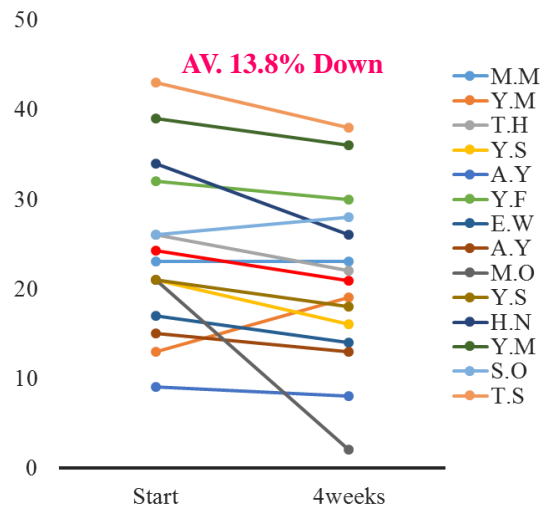
Subject	Age	Sex	Number of Pigmentation		Rate of Change (%)
			Start	4 weeks	Start as 100
M.M	23	♀	23	23	100.00
Y.M	24	♀	13	19	146.15
T.H	25	♂	26	22	84.62
Y.S	25	♂	21	16	76.19
A.Y	26	♀	9	8	88.89
Y.F	27	♂	32	30	93.75
E.W	27	♀	17	14	82.35
A.Y	29	♀	15	13	86.67
M.O	29	♂	21	2	9.52
Y.S	30	♂	21	18	85.71
H.N	30	♂	34	26	76.47
Y.M	46	♀	39	36	92.31
S.O	50	♂	26	28	107.69
T.S	51	♀	43	38	88.37
Ave.			24.3	20.9	86.18

	START	After 4 weeks	Improvement of Pigmentation
No.1 M.M. (23) F			 Unchanged
No.2 Y.M. (24) F			 46.2% Up
No.3 T.H. (25) M			 15.4% Down
No.4 Y.S. (25) M			 23.8% Down
No.5 A.Y. (26) F			 11.1% Down
No.6 Y.F. (27) M			 6.3% Down
No.7 E.W. (27) F			 17.7% Down
No.8 A.Y. (29) F			 13.3% Down



Consideration

When VeryBerry™ WHITE was applied for two months, pigmentation significantly reduced on 11 subjects out of 14. According to the result, VeryBerry™ WHITE is expected to have an effect to reduce pigmentation as well as visible pores.



5-3 Improvement of Stains on VeryBerry™ WHITE (*in vivo* Test)

The effect to reduce pigmentation areas was measured using the Robo Skin Analyzer just like the effect to reduce visible pores. As shown in the photos below, pigmentation level is not very clear in color photos. Continuous areas with a size of 1.2 mm² or larger of which margin can be detected as "slightly dark areas" and "dark areas" as compared to surrounding areas in monochrome photos are detected as "pigmentation areas." Pigmentation was evaluated in three levels by their tone and contrasting intensity. Relatively light pigmentation is classified to level 1 and shown in red, dark pigmentation is classified to level 3 and shown in blue, and pigmentation in between the two is classified to level 2 and shown in yellow.

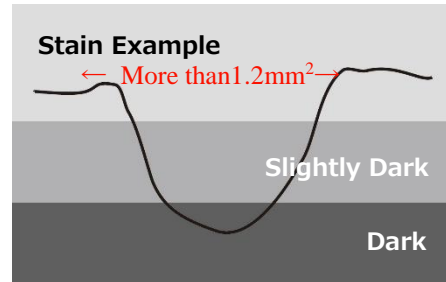




Image Example

Color photo (Nose)

Monochrome photo (Nose)

Evaluation of Stains


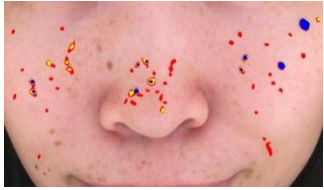
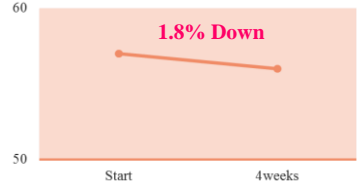


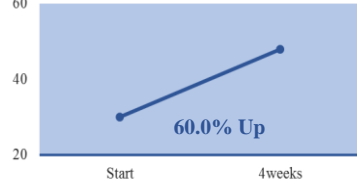


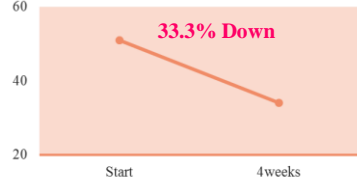


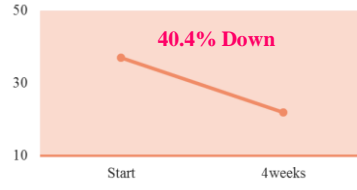


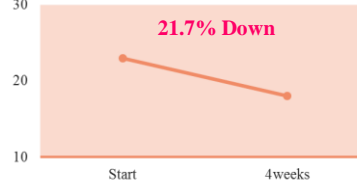


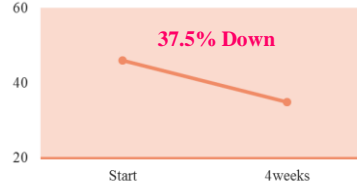


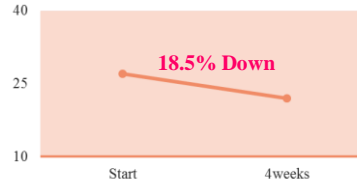


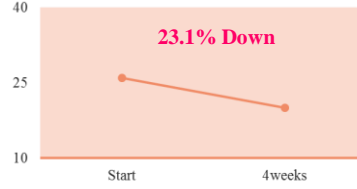
Level 1 →

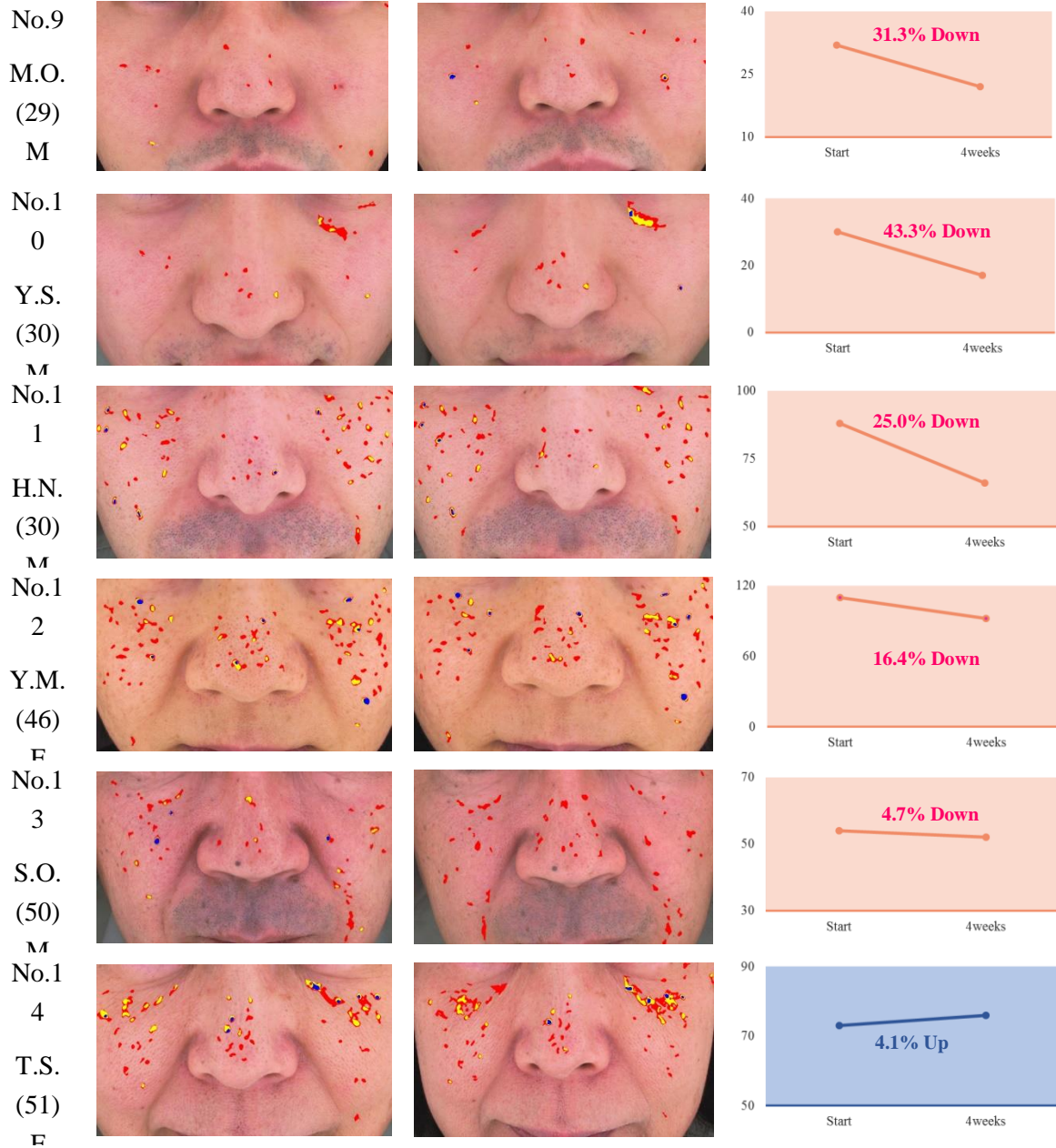
Level 2 →

Level 3 →

Test Result

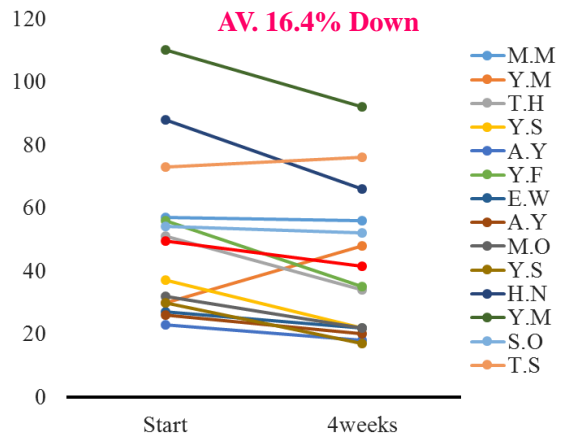
Subject	Age	Sex	Number of Stain		Rate of Change (%)
			Start	4 weeks	Start as 100
M.M	23	♀	57	56	98.25
Y.M	24	♀	30	48	160.00
T.H	25	♂	51	34	66.67
Y.S	25	♂	37	22	59.46
A.Y	26	♀	23	18	78.26
Y.F	27	♂	56	35	62.50
E.W	27	♀	27	22	81.48
A.Y	29	♀	26	20	76.92
M.O	29	♂	32	22	68.75
Y.S	30	♂	30	17	56.67
H.N	30	♂	88	66	75.00
Y.M	46	♀	110	92	83.64
S.O	50	♂	54	52	96.30
T.S	51	♀	73	76	104.11
Ave.			49.6	41.4	83.57

	START	After 8 weeks	Improvement of Stains
No.1 M.M. (23) F			 1.8% Down
No.2 Y.M. (24) F			 60.0% Up
No.3 T.H. (25) M			 33.3% Down
No.4 Y.S. (25) M			 40.4% Down
No.5 A.Y. (26) F			 21.7% Down
No.6 Y.F. (27) M			 37.5% Down
No.7 E.W. (27) F			 18.5% Down
No.8 A.Y. (29) F			 23.1% Down



Consideration

When VeryBerry™ WHITE was applied for two months, stains significantly reduced on 12 subjects out of 14. According to the result, VeryBerry™ WHITE is expected to have an effect to reduce pigmentation as well as visible pores.



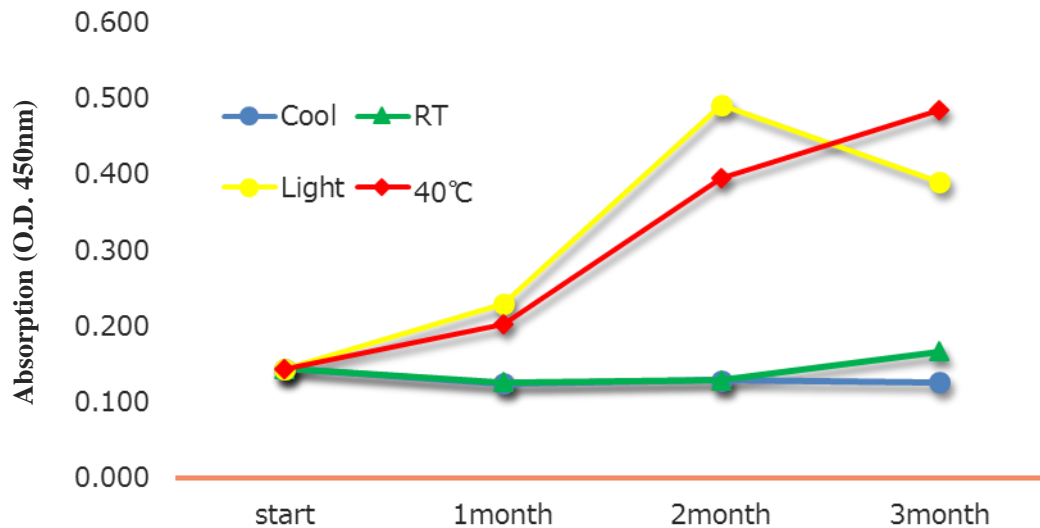
6. Stability Test

6-1 Long Term Stability

Store VeryBerry™ WHITE as it was, in a cool dark place at 4°C, room temperature, window side and at 40°C and observed color change and determined the absorbance at 450nm for 3 months.

Test Sample

VeryBerry™ WHITE (Undiluted; Lot No. M-520)



Test Result and Consideration

The test results have been rising absorbance at window side and at 40°C for 3 months after.

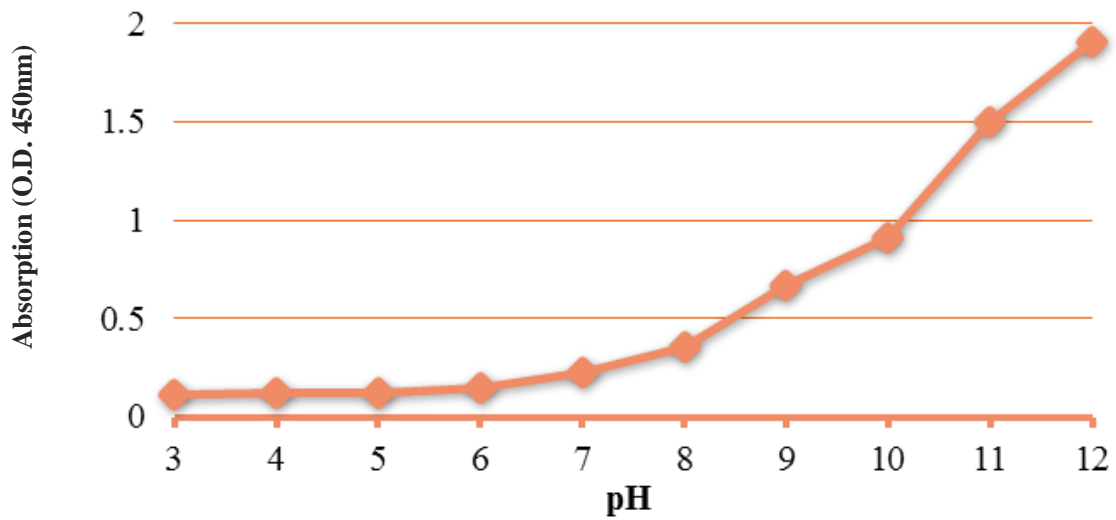
Please store the product in a cool (around 5 c/degree), dark, and ventilated area. Keep it away from high temperature and sunlight, and store it closed container.

6-2 pH Stability Test

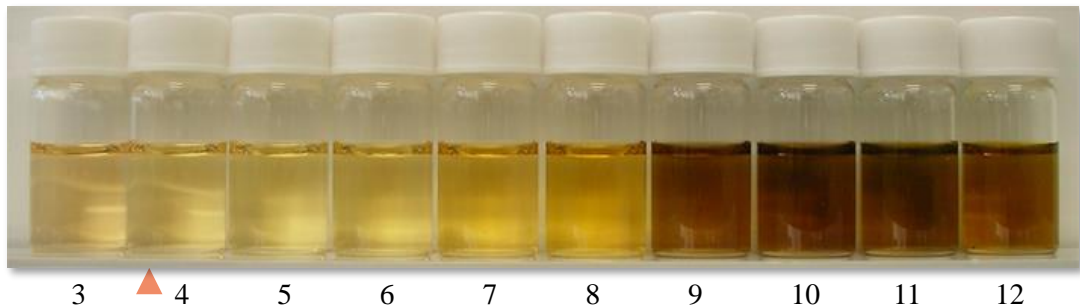
pH of VeryBerry™ WHITE was adjusted from 3 to 12 by hydrochloric acid and sodium hydroxide, observed the color change and determined the absorbance at 450nm.

Test Sample

VeryBerry™ WHITE (Undiluted; Lot No. B-501)



Test Result



Consideration

From acidic, weakly acidic, and until the neutral zone is a stable and pale yellow color was stable and unchanged the color tone, but the color tone rapidly brownish in the alkaline side. Please use it in the neutral zone from the acidic side.

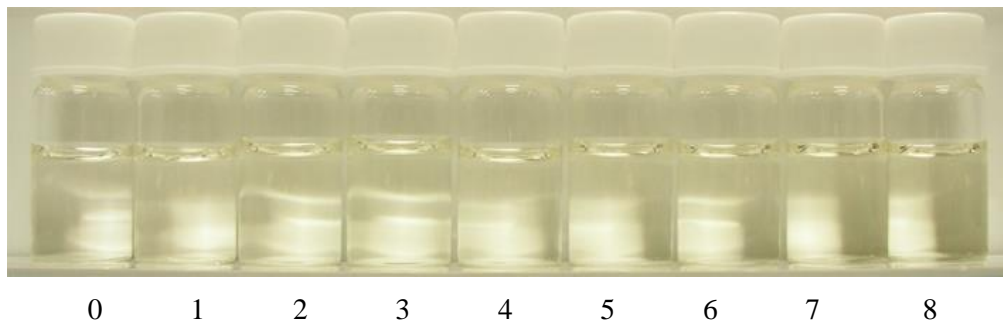
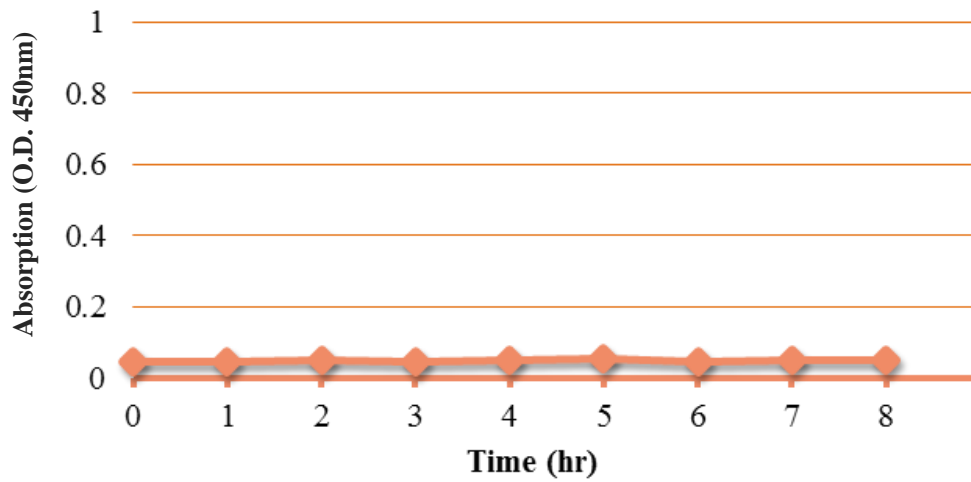
6-3 Thermal Stability Test

Adjust 10% concentration of VeryBerry™ WHITE with purified water and heat at 90°C for 8 hours and observed the color change and determined the absorbance at 450nm.

Test Sample

VeryBerry™ WHITE (10% water solution; Lot No. B-501)

Test Result



Consideration

10% aqueous solution of VeryBerry™ WHITE was heated for 8 hours at 90 °C, as shown in the photo, the color tone did not change, and it is considered that thermal stability on VeryBerry™ WHITE relatively stable when heated for 8 hours.

7. Compatibility Test

(○ : Clear, Δ : Turbid , × : Precipitate)

	(%)	Trade Name	INCI Name	Result	
		Manufacturer		1hr	24hr
Cation	3.0	QUARTAMIN 86W Kao Corporation	Steartrimonium Chloride / Water	○	×
Anion	10.0	SOYPON SLE Kawaken Fine Chemical Co., Ltd.	Sodium Lauroyl sarcosinate	○	○
	10.0	EMAL 20C Kao Corporation	Sodium Laureth Sulfate / Water	○	○
	10.0	AMISOFT CT-12S Ajinomoto Co., Inc.	Water / TEA-Cocoyl Glutamate	○	○
Nonion	10.0	PYROTER GPI-25 Nihon Emulsion Co., Ltd.	Glycereth-25 PCA Isostearate	○	○
	10.0	SALACOS PG-218 Nisshin Oilio Group Co., Ltd.	Polyglyceryl-10 Dioleate / Tocopherol	×	×
	10.0	RHEODOL 460V Kao Corporation	Sorbeth-60 Tetraoleate	○	○
	10.0	RHEODOL TW-0120V Kao Corporation	Polysorbate 80	○	○
Amphoteric	5.0	AMPHITOL 20AB Kao Corporation	Lauramidopropyl Betaine	○	○
	10.0	SOFTAZOLINE LSB 29% aq. Kawaken Fine Chemical Co., Ltd.	Lauramidopropyl Hydroxysulfate	○	○
Silicone	10.0	KF-96A-10CS Shin-Etsu Chemical Co., Ltd.	Dimethicone	×	×
	10.0	KF-96A-300CS Shin-Etsu Chemical Co., Ltd.	Dimethicone	×	×
	10.0	KF-995 Shin-Etsu Chemical Co., Ltd.	Cyclopentasiloxane	×	×
	10.0	Silwet L-7604 Momentive Performance Materials	PEG-8 Dimethicone	○	○
	10.0	Silwet L-7622 Momentive Performance Materials	PEG-8 Dimethicone	×	×

VeryBerry™ WHITE was adjusted to 10% concentration. Other products were adjusted to the concentration in the table with purified water, mixed VeryBerry™ WHITE and other ingredients, observe the compatibility at 1 hour and 24 hours after mixing.

8. Toxicological safety Test

Trade Name		VeryBerry™ WHITE	
Test Subject	Result	Test Method	
Acute Oral Toxicity Test	Not Performed		
Primary Skin Irritation Test	Not recognize any stimulus	EpiSkin™ method	
Accumulated Skin Irritancy Test	Not recognize any stimulus	RIPT method (50 people)	
Sensitization Test	Not recognize any sensitization	RIPT method (50 people)	
Photo Toxicity Test	Not Performed		
Photo Sensitization Test	Not Performed		
Eye Irritation Test	Not recognize any stimulus	SkinEthic™ HCE method	
Mutagenicity Test	Negative	AmesTest (TA98, TA100, TA1535, TA1537, WP2uvrA)	
Human Patch Test	Judgement for 24hours – (10)、± (2)	48hrs Closed Patch Test	

9. Recommended Planning and Guide Formulation

(Formulation Provided by Nihon Emulsion Co., Ltd.)

- Cleansing Form
- Whitening Serum
- Face Wash Cream
- Whitening Lotion
- Face Wash Soap
- Whitening Cream

9-1 Formulation 1 CLEANSING FOAM No.IFS-4478

No.	Trade Name	Manufacturer	%	INCI Name
1	ELDEW PS-306	Ajinomoto Co., Inc.	0.50	Phytosteryl/Behenyl/Octyldodecyl Lauroyl Glutamate
2	EMALEX EG-di-SE	Nihon Emulsion Co., Ltd.	4.00	Glycol Distearate
3	Lauric acid (NAA122)	NOF Corporation	1.00	Lauric acid
4	Myristic acid (NAA142)	NOF Corporation	3.00	Myristic acid
5	EMALEX SEG-07	Nihon Emulsion Co., Ltd.	4.00	Glyceryl Stearate, PEG-10 Stearate
6	PYROTER CPI-40	Nihon Emulsion Co., Ltd.	3.00	PEG-40 Hydrogenated Caster Oil, PCA Isostearate
7	Amisol LDE	Kawaken Fine Chemical	3.00	Lauramide DEA
8	Oryza Tocotrienol-90	Oryza Oil & Fat Chemical	qs	Tocotrienol, Tocopherol, Oryza Sativa (Rice) Bran Oil
9	Alanon ALE (30% AI)	Kawaken Fine Chemical	25.00	Sodium Lauroyl Methylaminopropionate, Water
10	Zemea Propanediol	DuPont	15.00	Propanediol
11	Purified Water		9.50	Water
12	VeryBerry™ WHITE	Oryza Oil & Fat Chemical	1.00	*1
13	CosmeHerbest NADESHIKO	Oryza Oil & Fat Chemical	1.00	Water, Propanediol, Dianthus Longicalyx Seed Extract
14	Amisoft LS-11F	Ajinomoto Co., Inc.	30.00	Sodium Lauroyl Glutamate
			100.00	

*1: Water, Propanediol, Acetyl Cystein, Vaccinium Vitis-Idaea Fruit Extract, Sodium Sulfite, Citrus Unshiu Peel Extract, Hippophae Rhamnoides Fruit Extract

Manufacturing Method

- 1) Stir and dissolve Ingredients No.1 to 8 at 60℃.
- 2) After dissolving 1), add and dissolve Ingredients No.9 to 14 at 70℃.
- 3) Stir slowly by paddle at 70℃ for 1 hour and remove bubble.
- 4) Cool while stirring by paddle until at 40℃ as the product.

9-2 Formulation 2 REVITAL CREAM No.MCC-476

No.	Trade Name	Manufacturer	%	INCI Name
1	Liquid Petrolatum (70")		8.00	Mineral Oil
2	AMITER MA-HD	Nihon Emulsion Co., Ltd.	4.00	Hexyldecyl Myristoyl Methylaminopropionate
3	KF-96A (10mm ² /s)	Shin-Etsu Chemical	4.00	Dimethicone
4	Behenyl Alcohol (BH-65)	Toho Chemical	2.00	Behenyl Alcohol
5	Kanette O	BASF	4.00	Cetearyl Alcohol
6	EMALEX PG-M-S	Nihon Emulsion Co., Ltd.	1.00	Propylene Glycol Stearate
7	EMALEX SEG-07	Nihon Emulsion Co., Ltd.	4.00	Glyceryl Stearate, PEG-10 Stearate
8	Butylparaben		0.10	Butylparaben
9	Amisoft HS-11P(F)	Ajinomoto Co., Inc.	0.30	Sodium Stearoyl Glutamate
10	Sorbitol Solution (70% AI)		5.00	Sorbitol, Water
11	Concentrated Glycerine		4.00	Glycerin
12	Methylparaben		0.30	Methylparaben
13	Keltrol T (1% soln.)	Sumitomo Dainippon Pharma	10.00	Xanthan Gum, Water
14	VeryBerry™ WHITE	Oryza Oil & Fat Chemical	1.00	*1
15	Purified Water		52.30	Water
			100.00	

*1: Water, Propanediol, Acetyl Cystein, Vaccinium Vitis-Idaea Fruit Extract, Sodium Sulfite, Citrus Unshiu Peel Extract, Hippophae Rhamnoides Fruit Extract

Manufacturing Method

- 1) Heat and dissolve Ingredients No.1 to 8 at 70°C .
- 2) Heat and dissolve Ingredients No.9 to 15 at 75°C .
- 3) While stirring 1) by homogenizer and emulsify adding 2) at 3,000r.p.m. for 5 minutes.
- 4) Change to paddle and cool while stirring until at 40°C as the product.

9-3 Formulation 3 SKIN LOTION No.3864F-8

No.	Trade Name	Manufacturer	%	INCI Name
1	EMALEX CC-168	Nihon Emulsion Co., Ltd.	1.90	Cetyl Ethylhexanoate
2	ELDEW PS-203	Ajinomoto Co., Inc.	0.10	Phytosteryl/Octyldodecyl Lauroyl Glutamate
3	AMITER LGOD-2(H)	Nihon Emulsion Co., Ltd.	0.30	Diocetyldodeceth-2 Lauroyl Glutamate
4	Pyroter CPI-30	Nihon Emulsion Co., Ltd.	0.50	PEG-30 Hydrogenated Casttor Oil PCA Isostearate
5	Oryza Tocotrienol-90	Oryza Oil & Fat Chemical	0.05	Tocotrienol, Tocopherol, Oryza Sativa (Rice) Bran Oil
6	Propylparaben		0.05	Propylparaben
7	Methylparaben		0.05	Methylparaben
8	EDTA-3Na		0.01	Trisodium EDTA
9	Magnesium Chloride		0.01	Magnesium Chloride
10	Calcium Chloride		0.01	Calcium Chloride
11	EMALEX SLP	Nihon Emulsion Co., Ltd.	0.05	Hydrogenated Lecithin
12	Amisoft CS-11F	Ajinomoto Co., Inc.	0.05	Sodium Cocoyl Glutamate
13	Keltrol T (1% soln)	Sumitomo Dainippon Pharma	5.00	Xanthan Gum, water
14	Carbomer 940 (1% soln)		20.00	Carbomer, Water
15	1,3-Butylene Glycol		10.00	Butylene Glycol
16	Concentrated Glycerin		10.00	Glycerin
17	Glycine		0.10	Glycine
18	Purified water		48.52	Water
19	L-Arginine		0.30	Arginine
20	Purified Water		2.00	Water
21	CosmeHerbest™ SAKURA	Oryza Oil & Fat Chemical	0.50	Water, Butylene Glycol, Prunus Lannensianna Flower Extract
22	VeryBerry™ WHITE	Oryza Oil & Fat Chemical	0.50	*1
			100.00	

*1: Water, Propanediol, Acetyl Cystein, Vaccinium Vitis-Idaea Fruit Extract, Sodium Sulfite, Citrus Unshiu Peel Extract, Hippophae Rhamnoides Fruit Extract

Manufacturing Method

- 1) Heat and stir Ingredients No. 1 to 6 at 75 °C . (A phase)
- 2) Heat and stir Ingredients No. 7 to 18 at 75 °C . (B phase)
- 3) Dissolve Ingredients No.19 and 20. (C phase)
- 4) Stir B phase by homogenizer, add A phase, then add C phase and emulsify at 3000rpm for 5 minutes.
- 5) Cool by water bath after emulsifying, add Ingredients No.21 and 22 at 45 °C , furthermore, cool until at 30 °C as the product.

9-4 Formulation 4 NATURAL PEARL ESSENCE No.PTR4-36A

No.	Trade Name	Manufacturer	%	INCI Name
1	Cetanol KS	HAI	1.00	Cetyl Alcohol
2	DC246		5.50	Cyclohexasiloxane
3	EMALEX GWIS-150	Nihon Emulsion Co., Ltd.	1.50	PEG-50 Glyceryl Isostearate
4	Stearyl Alcohol (8688)	Kao Chemical	0.50	Stearyl Alcohol
5	Stearic acid (NAA1850)	NOF Corporation	1.00	Stearic acid
6	Palmitic acid (NAA160)	NOF Corporation	2.50	Palmitic acid
7	Oryza Tocotrienol-90	Oryza Oil & Fat Chemical	0.10	Tocotrienol, Tocopherol, Oryza Sativa (Rice) Bran Oil
8	Fragrance		0.03	Fragrance
9	Propylparaben		0.10	Propylparaben
10	Ethanol		6.00	Alcohol
11	Methylparaben		0.10	Methylparaben
12	1,3-Butylene Glycol		5.00	Butylene Glycol
13	Glycerin		10.00	Glycerin
14	Natrosol 250HHR		0.45	Hydroxyethylcellulose
15	Carbomer 940		0.20	Carbomer
16	Nicotinamide		2.00	Niacinamide
17	Trimethylglycine		2.00	Betaine
18	Iron Oxide, Mix (Red)		0.02	Iron Oxide, Red, Butylene Glycol / 10:90
19	Water		55.78	Water
20	VeryBerry™ WHITE	Oryza Oil & Fat Chemical	3.00	*1
21	Ascorbyl PM		0.02	Magnesium Ascorbyl Phosphate
22	Potassium Hydroxide		0.20	Potassium Hydroxide, Water
23	EDTA-2Na (1% soln)		1.00	Disodium EDTA, Water
24	Water		2.00	Water
			100.00	

*1: Water, Propanediol, Acetyl Cystein, Vaccinium Vitis-Idaea Fruit Extract, Sodium Sulfite, Citrus Unshiu Peel Extract, Hippophae Rhamnoides Fruit Extract

Manufacturing Method

- 1) Heat and stir Ingredients No.1~10 at 45℃ until transparent.
- 2) After dissolving Ingredients No.11 and 12 at 50℃, then add Ingredients No.13 toNo.21 in order and prepare making dispersion.
- 3) Separately, dissolve Ingredients No.22 to 24 at 50℃ in advance.
- 4) Control 2) the temperature at 40℃, add gradually 1) and stir by homogenizer at 2500rpm for 10minutes, and neutralize at 40℃ in order to make pearl texture, after making pearl texture, and cool 20 to 30℃ as the products

* Pearl texture will be appear around 38℃ or keep the temperature at 40℃ to allow to stand for some time.

10. Product Specification

Commodity	Specification	Remarks
Trade Name	VeryBerry™ WHITE	
Appearance		
· Color	: Pale orange to pinkish orange liquid	
· Odor	: Slightly pungent odor	
Identification		
· Anthocyanin	: Positive	
· Flavonoid	: Positive	
· Saponin	: Positive	
· Polyphenol compounds	: Positive	
· Xanthone compounds	: Positive	
· N-Acetyl-L-Cysteine	: Positive	
pH (1→10)	: 3.0~4.5	
Purity Test		
1) Heavy Metals	: 20 ppm max.	
2) Arsenic	: 2 ppm max.	
Microbiological Examination		
1) Bacterial Count	: 1×10^2 CFU/g max.	Hygiene Test
2) Mold, Yeast	: 1×10^2 CFU/g max.	Hygiene Test
3) Coliform	: Negative	Hygiene Test

These standards and test method are referred to General Notices and General Tests, Processes and Apparatus of The Japanese Standards of Quasi-drug Ingredients, unless otherwise specified.

11. Labelling Name

INCI Name	化粧品国際中文標準名
Water	水
Propanediol	1,3-丙二醇
Acetyl Cystein	乙酰半胱氨酸
Vaccinium Vitis-Idaea Fruit Extract	越桔 (VACCINIUM VITIS-IDAEA) 果提取物
Sodium Sulfite	亚硫酸钠
Citrus Unshiu Peel Extract	温州蜜柑 (CITRUS UNSHIU) 果皮提取物
Hippophae Rhamnoides Fruit Extract	沙棘 (HIPPOPHAE RHAMNOIDES) 果提取物
Litchi Chinensis Seed Extract	荔枝 (LITCHI CHINENSIS) 籽提取物
Mangifera Indica Leaf Extract	芒果 (MANGIFERA INDICA) 叶提取物

12. Others

16-1 Packaging Style

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

16-2 Storage Condition

Avoid high temperature and sun light, store the product in a cool (around 5 °C), dark, and ventilated area in closed original container.

13. References

- 1) <http://www.mildix.com/column/3-skincarecosmetics/55-bihakukesyouhin.html>
- 2) <https://ja.wikipedia.org/wiki/%E3%83%9E%E3%83%B3%E3%82%B4%E3%83%BC>
- 3) <https://en.wikipedia.org/wiki/Acetylcysteine>

From product planning to OEM

Please feel free contact if you need more additional information or our assistance :

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striving for the development of the new functional cosmetic ingredients to promote health and general well-being.

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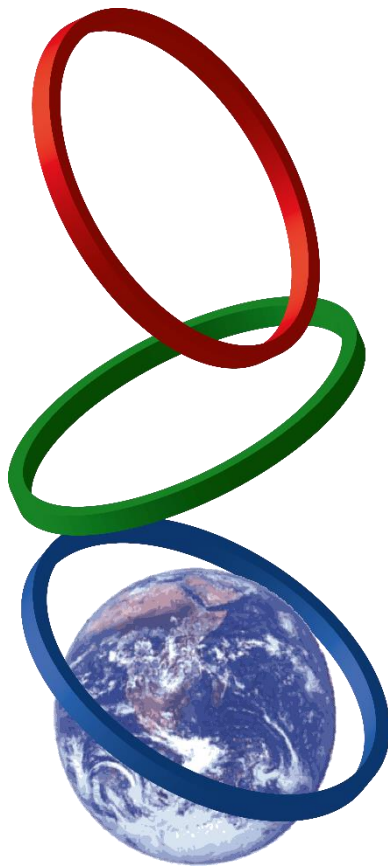
*The contents of this catalogue may be changed without prior notice.

*Correction : Updated Tokyo office address

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