GROUP
斯 拜 科

Good Quality Comes
From Qualified Materials

ACID
SOLUTION

Lough off dead surface layers, can indeed reveal softer, healthier-looking skin. Restore radiance to dull and tired skin. Make skin soft and smooth with youthful gloss.

Spec Chem Group (Sep 2020)

MAKE YOUR SKIN FRUITY & GLOSS

Spec Chem's Acid Portfolio

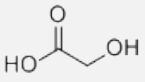
1	SpecWhite® KA	Kojic Acid	Amino Acid & Peptide Derivative and Analogue Heterocyclic compound & its esters
2	SpecWhite® KAD	Kojic dipalmitate	Amino Acid & Peptide Derivative and Analogue Heterocyclic compound & its esters
3	SpecWhite® TA	Tranexamic Acid	Amino Acid & Peptide Derivative & Analogue
	SpecWhite® 05	Oxothiazolidinecarboxylic Acid	Amino Acid & Peptide Derivative & Analogue Prodrug of Glutathione
4	SpecWhite® FA	Ferulic Acid	Hydroxycinnamic acids (hydroxycinnamates)
5	SpecWhite® NFA*	Ferulic Acid	Crude rice bran, Plant-derived Extract Hydroxycinnamic acids (hydroxycinnamates)
6	SpecWhite®DL-MA	Mandelic Acid	α-/Alpha-Hydroxy Acid (AHA)
7	SpecKare® ALA	Azelaic Acid	Dicarboxylic Acid
8	SpecKare® LBA	Lactobionic Acid	α-/Alpha-Hydroxy Acid (AHA) polyhydroxy acid PHA,Gluconolactone
9	SpecWhite® PLGA70	Glycolic Acid	α-/Alpha-Hydroxy Acid (AHA)
10	SpecWhite® PLGA99	Glycolic Acid	α-/Alpha-Hydroxy Acid (AHA)
11	SpecWhite® SLA	Salicylic Acid	β-/Beta-Hydroxy Acid (BHA)
12	SpecWhite® SLA（natural）	Salicylic Acid	β-/Beta-Hydroxy Acid (BHA)
13	SpecWhite® NSLA	Sodium Salicylate	β-/Beta-Hydroxy Acid (BHA), Slat
14	SpecKare® CSA	Capryloyl Salicylic Acid	β-/Beta-Hydroxy Acid (BHA),Ester
15	SpecKare® BSA	Betaine Salicylate	BHA derivatives
16	SpecWhite®4MSP	Potassium Methoxysalicylate	BHA derivatives
17	SpecKare® GlyAA*	Glycyrrhizic Acid	Plant-derived Extract ≤0.1%
18	SpecWhite® GA*	Glycyrrhetinic Acid	Plant-derived Extract ≤2.0%
19	SpecWhite® SG	Glycyrrhetinyl Stearate	Glycyrrhetinic Acid Ester ≤1.0%

***Not Plant Extracts, but rather Specific Chemical species that may be isolated from the licorice plant, Plant-derived Extract**

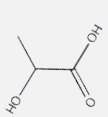
Contents

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

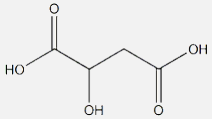
The Classical AHA with smallest molecular



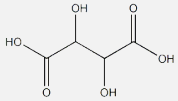
SpecWhite® PLGA70/90
Glycolic Acid



Lactic acid

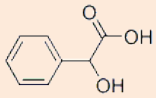


Malic acid



Tartaric acid

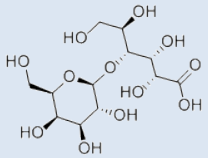
Academically speaking, **Fruit Acid** is the **"Alpha Hydroxyl Acid",** including: lactic acid and citric acid and above acids (**glycolic acid and mandelic acid** etc.)



SpecWhite® DL-MA
Mandelic Acid

The 2nd Generation of AHA

Slowly, Mild & Safe…



SpecKare® LBA
Lactobionic Acid

The 3th Generation of AHA

Multifunctional, Mild & value-added…

Gluconolactone, Aldobionic acid

Polyhydroxy acid (PHA)

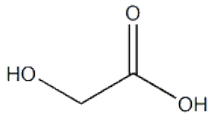
01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Brief Introduction of glycolic acid (PLGA)

glycolic acid (hydroacetic acid or hydroxyacetic acid); with chemical formula C2H4O3 (also written as HOCH2CO2H), is ***the smallest α-hydroxy acid (AHA).***

This colorless, odorless, and hygroscopic crystalline solid is highly soluble in water. It is used in various skin-care products.

GA is slightly stronger than acetic acid due to ***the electron-withdrawing power*** of ***the terminal hydroxyl group***. The carboxylate group can coordinate to metal ions forming coordination complexes. Of particular note are the complexes with Pb2+ and Cu2+ which are significantly stronger than complexes with other carboxylic acids. This indicates that the hydroxyl group is involved in complex formation, possibly with the loss of its proton.



The Structure of glycolic acid
Mw=76Da

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Application of glycolic acid (PLGA)

- Used in food processing as a flavoring agent and as a preservative
- Used in the pharmaceutical industry as a skin care agent
- Used in adhesives and plastics,
- Glycolic acid is often included in emulsion polymers, solvents and additives for ink and paint in order to improve flow properties and impart gloss
- It is used in surface treatment products that increase the coefficient of friction on tile flooring. It is the active ingredient in the household cleaning liquid Pine-Sol.

Skin Care

Due to ***its capability to penetrate skin***, glycolic acid finds applications in skin care products, most often as a chemical peel. Physician-strength peels can have a pH as low ***as 0.6 (strong enough to completely keratolyze the epidermis),*** while acidities for home peels can be as low as 2.5. Once applied, glycolic acid reacts with the upper layer of the epidermis, ***weakening the binding properties of the lipids that hold the dead skin cells together. This allows the stratum corneum to be exfoliated, exposing live skin cells***.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

SpecWhite® PLGA 99 Information :

Item No.:	110021-1
Product name:	SpecWhite® PLGA 99
INCI name:	glycolic acid
Chemical/IUPAC Name:	Acetic acid, hydroxy-
CAS No.:	79-14-1
EC No.:	201-180-5
Dosage:	0.5-10.0% (daily use), 10.0-30.0% (special use) 30-70% (other use)
Package:	Customization
Storage:	Keep in a tightly closed container, stored in a cool, dry, ventilated area.
Shelf life:	1 years

Molecular Weight: 76.05 g/mol

Items	Specification
Appearance	White crystals
Total acids	≥99%
Heavy metal content	≤10ppm
Iron	≤10ppm
Chloride	≤10ppm
Residue on ignition	<0.05%
Ash	<0.10%

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

SpecWhite® PLGA 70 Information :

Item No.:	110021-2
Product name:	SpecWhite® PLGA 70
INCI name:	glycolic acid
Chemical/IUPAC Name:	Acetic acid, hydroxy-
CAS No.:	79-14-1
EC No.:	201-180-5
Dosage:	1.0-14.0% (daily use), 14.0-40.0% (special use) 40-100% (other use)
Package:	Customization
Storage:	Keep in a tightly closed container, stored in a cool, dry, ventilated area.
Shelf life:	1 years

Items	Specification
Appearance	Light yellow liquid
Color(Pt-Co)	≥ 30
Total acids	≥ 70%
Heavy metal content	≤ 10ppm
Iron	≤ 10ppm
Chloride	≤ 10ppm

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Commercial Products with Glycolic Acid

L'Oreal Paris (2019)

Revitalift Derm Intensives 10% Pure Glycolic Acid Serum
NEW Resurfacing 10% Pure Glycolic Acid Daily Serum
visibly evens tone, reduces dark spots & wrinkles.

Paula's Choice

Resist Weekly Resurfacing Treatment 10%

Aha 2019

Paula's Choice Resist Weekly Resurfacing Treatment with 10% AHA is a potent Glycolic Acid treatment that reveals younger-looking, more radiant skin overnight.

Eucerin

Dermopurifyer Skin

Renewal Treatment (2019)

The innovation: 10% Hydroxy Complex - highly effective combination of peeling agents Glycolic-, Salicylic- and Polyhydroxy acid - helps to resurface the skin, unclogs pores and removes dead skin cells.

The Ordinary

Aha 30% + Bha 2% Peeling

Solution (2018)

A 10-minute exfoliating facial with 30% Alpha Hydroxy Acids (Glycolic/Lactic/Tartaric/Citric), 2% Beta Hydroxy Acid (Salicylic Acid), Hyaluronic Acid Crosspolymer, Vitamin B5, Black Carrot and Tasmanian Pepperberry.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

DCL

Aha Resurfacing Lotion 20 Intensive Exfoliating Treatment

Address severe sun damage and very dry, rough skin with the AHA Resurfacing Lotion 20 from DCL. Formulated with a potent concentration of 20% Glycolic Acid.

Dermasence

MelaBlok 2019

Glycolic Acid 10.0%,

Lightens skin and fading dark spots.

Topix

Glycolix Elite Facial Cream 20% (2019)
Contains 20% Glycolic Acid. Glycolic Acid helps to gently slough, or exfoliate, the dead cell layer which manifests fine lines and uneven skin tones.

Geek & Gorgeous

Smooth Out 12% AHA (Glycolic Acid+Lactic Acid) + Cactus Exfoliating Liquid

12% AHA + Cactus Exfoliating Liquid, which instantly softens and brightens the skin and smooths wrinkles over the long term and gives the skin a youthful and healthy appearance.

Creamy

Creme 10% AHA (Glycolic Acid)

Ácido Glicólico + Niacinamida （2020）

Creamy Glycolic is a deep moisturizer that helps to smooth the skin, improving color, texture and reducing pores.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Efficacy Test of PLGA (Glycolic Acid)-Clinical trail-Anti-acne Properties of Glycolic acid (10%) -120 patients

Acne is characterized by hyperseborrhea, follicular hyperkeratosis, and growth of propionibacteria. Alpha hydroxy acids depending on the pH of the finished product exhibit comedolytic as well as antimicrobial properties.

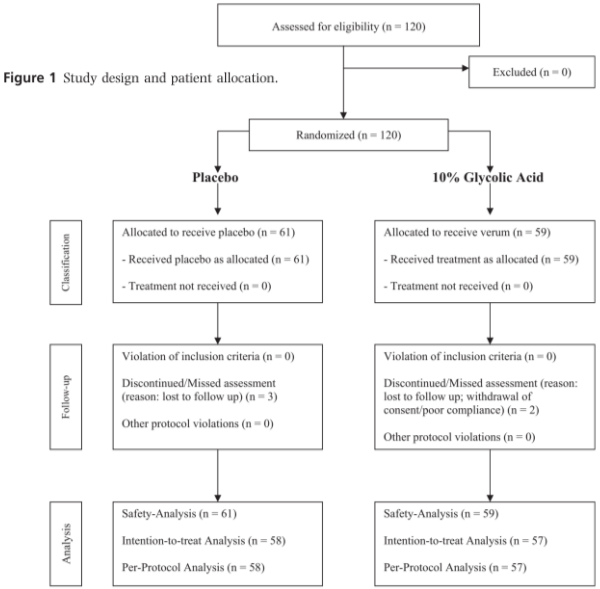


Figure 1 Study design and patient allocation.

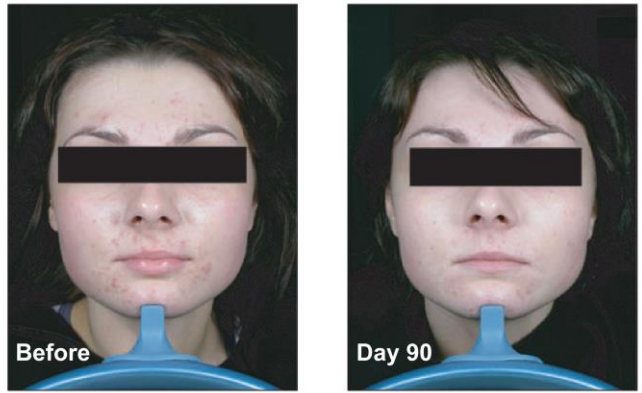


Figure 2 Clinical images before (Leeds score 0.75) and 90 days (Leeds score 0.25) after application of a 10% glycol containing oil-in-water emulsion.

Acne improved significantly in the verum group up to day 90. Already at day 45, there was a statistical significant (5% level) difference against placebo.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Efficacy Test of PLGA (Glycolic Acid) & DL-MA (Mandelic Acid)—Clinical trail-Anti-acne Properties of PLGA (10%) -120 patients

Acne is characterized by hyperseborrhea, follicular hyperkeratosis, and growth of propionibacteria. Alpha hydroxy acids depending on the pH of the finished product exhibit comedolytic as well as antimicrobial properties.

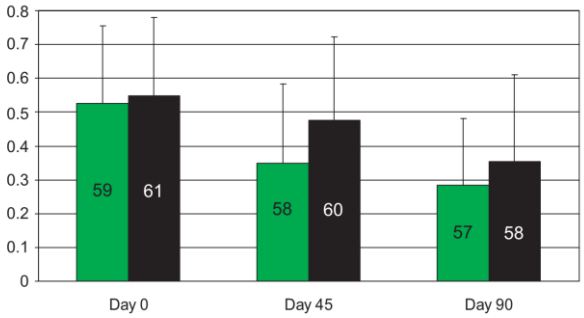


Figure 3 Overall Leeds score over time for the 10% glycolic acid containing oil-in-water emulsion (green) and for placebo (black) (oil-in-water emulsion without glycolic acid) (mean ± SD; numbers in the bars denote the patients available for assessment at that time).

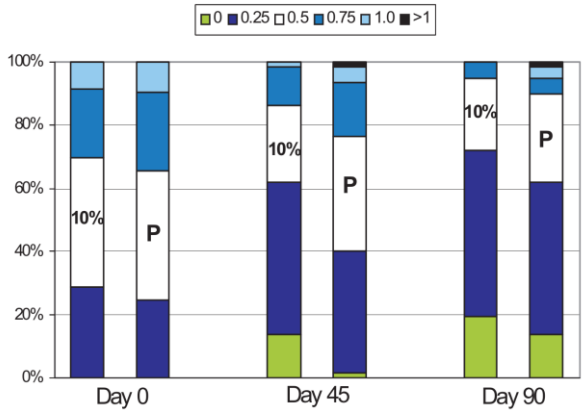


Figure 4 Individual Leeds score over time.

The 10% glycolic acid containing oil-in-water emulsion improved mild acne applied as monotherapy in this study significantly, already after 45 days of treatment.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Application Guide of Glycolic Acid-Combination of PLGA and sunscreens to prevent UV sensitivity

In an initial study, 4 subjects were treated daily with 2 formulations containing AHA with sunscreens and exposed after the last application to 1 MED. Twenty hours after the exposure,
shave biopsies were taken to assess presence of SBCs. Both products had a sun protection factor (SPF) of 2.9 and an AHA content in the range of 4-8% (glycolic acid). No evidence of SBCs formation versus untreated controls was observed (Table II) .

In a second study, subjects were treated daily with a known amount of moisturizer for 22 days,
then they were exposed to 1 MED after the last moisturizer application. SBCs were measured
from shave biopsies taken 20 hours after the exposure. All moisturizer products that had sunscreen protection in the range 2.9-3.5 and AHA in the range of 2-8% (lactic acid and glycolic acid) showed no evidence of SBCs formation compared with untreated controls (Table III).

Table II: sun burn cells (SBC) formation in human skin treated with two lotion products after an UV exposure of 1 minimal erythema dose (MED)

Lotion product (AHA content)	Panelists	Study duration	SBCs	UV Exposure (daily)	SPF
Untreated control	4	4 days	1.06	1 MED	
Test product A 4% Glycolic acid 1.5% EHMC *	4	4 days	0.024	1 MED	2.9
Test product B 8% Glycolic acid 1.5% EHMC *	4	4 days	0.044	1 MED	2.9

* EHMC : ethylhexyl methoxycinnamate

Table III: sun burn cells (SBC) formation in human skin treated with several lotion products after an UV exposure of 1 minimal erythema dose (MED)

Lotion product (AHA content)	Panellist	Study duration	SBCs	UV Exposure (daily)	SPF
Untreated control(mean)	15	22 days	0.277	1 MED	
Test product B 8% Glycolic acid 1.5% EHMC *	5	22 days	0.088	1 MED	2.9
Test product C 1% Lactic acid 1% Glycolic acid 2.0% EHMC *	5	22 days	0.044	1 MED	3.1
Test product D 1% Lactic acid 1% Glycolic acid 2.5% Benzophenone-4	5	22 days	0.040	1 MED	2.4
Test product E 6% Lactic acid 1.9% EHMC *	5	22 days	0.028	1 MED	3.3
Test product F 6% Lactic acid 1.9% EHMC *	5	22 days	0.036	1 MED	3.5

* EHMC : ethylhexyl methoxycinnamate

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Concentration of Glycolic Acid (GA) use by FDA Product Category

Ingredient	FDA Code†	Product Category	Maximum Concentration of Use
Glycolic Acid	03D	Eye lotion	0.035-0.49%
Glycolic Acid	05A	Hair conditioners	3.5-4.5%
Glycolic Acid	05B	Hair sprays aerosol pump spray	 0.0005% 0.05%
Glycolic Acid	05E	Rinses (noncoloring)	0.0062%
Glycolic Acid	05F	Shampoos (noncoloring)	0.04-0.5%
Glycolic Acid	05G	Tonics, dressings and other hair grooming aids	0.6%
Glycolic Acid	06B	Hair tints	4%
Glycolic Acid	06H	Other hair coloring preparations	0.0008%
Glycolic Acid	07C	Foundations	0.012-4%
Glycolic Acid	08C	Nail creams and lotions	4.1%
Glycolic Acid	10A	Bath soaps and detergents	0.06%
Glycolic Acid	12A	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.14-50%
Glycolic Acid	12B	Depilatories	3.7%
Glycolic Acid	12C	Face and neck products not spray	 0.035-50%
Glycolic Acid	12D	Body and hand products not spray	 0.35-10%
Glycolic Acid	12F	Moisturizing products foot cream	 2.1%
Glycolic Acid	12G	Night products not spray	 4-4.1%
Glycolic Acid	12H	Paste masks and mud packs	0.099-6.1%
Glycolic Acid	12I	Skin fresheners	0.12%
Glycolic Acid	12J	Other skin care preparations	4.1%

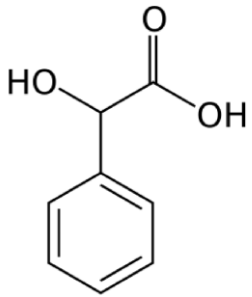
The CIR Expert Panel concludes that GA is safe for use in cosmetic products at concentrations ≤10%, at final formulation pH≥3.5, when formualted to avoid increasing sun sensitivity or when directions for use include the daily use of sun protection. GA is safe for use in salon products at concentrations ≤30%, at final formualtion pH≥3.0, in products designed for brief, discontinuous use followed by through rinsing from skin, when applied by trained professionals, and when application is accompanied by directions for the daily use of sun protection.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Brief Introduction of Mandelic Acid (MA)

Mandelic acid is an aromatic alpha hydroxy acid with the molecular formula C6H5CH(OH)CO2H. It is a white crystalline solid that is soluble in water and polar organic solvents.

- The molecular weight of mandelic acid is about 152.1 daltons *which* ***is larger than other alpha hydroxy acids*** (glycolic acid is 76.0 daltons, for example). This larger size allows mandelic acid to **penetrate the skin more slowly** which in turn makes it ***very gentle*** and suitable for all skin types including the most ***sensitive skin***.
- It is a ***useful precursor*** to various drugs. Mandelic acid has a long history of use in the ***medical community*** as an antibacterial, particularly in the treatment of urinary tract infections. The drugs ***cyclandelate*** (*Vasodilator which has spasmolytic effect on vascular smooth muscle*) and *homatropine* (*Synthesize anticholine, block acetylcholine, used for ophthalmic examination and optometry*) are esters of mandelic acid.

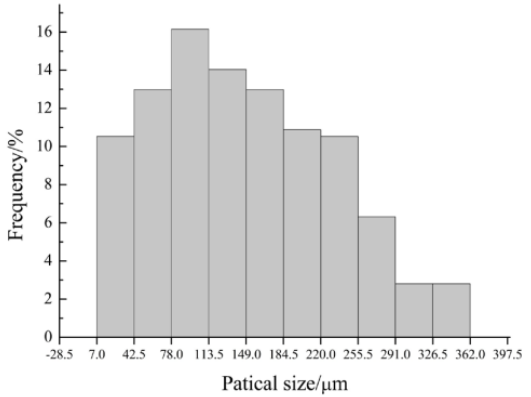


The Structure of Mandelic Acid
Mw=152Da

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

The features of SpecWhite® DL-MA :

- ✓ More gentle, especially designed AHA for sensitive skin type
- ✓ With larger molecular size, No excessive percutaneous absorption, no more irritation
- ✓ Gentle Lift off dead skin cells & Even
- ✓ Excellent Skin Brightening Properties & Lightening PIH (Post inflammatory hyperpigmentation)
- ✓ Excellent inhibiting effect on tyrosinase activity
- ✓ With Strong reducing capability, compared with other organic acids
- ✓ Complexion Solution to Acne & Comedone Prone Skin
- ✓ Antibacterial properties, as a urinary antiseptic& anti-acne agent
- ✓ Can improve in acne, skin texture, wrinkles, lentigenes, and melasma
- ✓ Third-party approved its safety, skin & eye non-irritation, non-sensitisation.



The Particle Size of SpecWhite®DL-MA is normally distributed

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Product Information of SpecWhite® DL-MA :

Item No.:	110010
Product name:	SpecWhite® DL-MA
INCI name:	Mandelic Acid
Chemical/IUPAC Name:	Benzeneacetic acid, .alpha.-hydroxy-
CAS No.:	90-64-2
EC No.:	202-007-6
Dosage:	0.5-4.0% (daily use), 4.0-15.0% (special use)
	25% (Max Level, Already Approved)
Package:	25kg/barrel
Storage:	Store at cool and dry, dark place, tightly closed.
Shelf life:	2 years
Application:	Antimicrobial

Analysis	Specification
Appearance	White crystal powder
Assay(on dry basis)	99.0% Min
Melting point	118℃-121℃
Moisture	0.5% Max

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Eye Irritation—OECD TG 437《Bovine Corneal Opacity and Permeability Test Method》——*The third-party data*

Name of Sample	SpecWhite® DL-MA (DL-mandelic acid)
Test Type	Commission Test
Applicant	Spec-chem industry inc
Address	No.10 Wanshou Road PuKou Economic Development Zone(ShiLin Industrial Park),Nanjing,Postal 211800,P.R. of China
Sample Source	Deliver form applicant
Sample Quantity	1 package
Specification & Batch	50g
State and Characteristic	White powder
Received Date	11th May, 2018
Completion Date	25th, May 2018
Item Tested	Eye Irritation
Test Method	OECD TG 437《Bovine Corneal Opacity and Permeability Test Method》(2017)

Group	Corrected mean opacity	Corrected mean OD_{490} value	IVS	Prediction（UN GHS）
NC	−0. 190±0. 110	0. 049±0. 001	------	------
PC	24. 692±1. 060	0. 822±0. 275	37. 017±3. 775	No prediction can be made
TA	1. 639±0. 478	0. 055±0. 022	2. 460±0. 793	No Category

Positive Control (PC): ethanol; Negative Control (NC): ultrapure water; Test Article (TA): Diluted into 0.5% with ultrapure water; MEM medium: MEM medium with and without phenol red contain 1% new born calf serum; HBSS: Hank's Buffered Salt Solution with antibiotics; Sodium fluorescein solution： 4mg/mL in DPBS（ with Ca2+ and Mg2+）

Conclusion：According to the OECD TG 437-2017, under the condition of this test, the TA "SpecWhite® DL-MA (Mandelic Acid)" is predicted as No Category（UN GHS）.

SpecWhite® DL-MA (Mandelic Acid)—No eye irritation!

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Eye Irritation—Chorioallantoic Membrane Vascular Assay (CAMVA)——*The third-party data*

Name of Sample	SpecWhite® DL-MA (DL-mandelic acid)
Test Type	Commission Test
Applicant	Spec-chem industry inc
Address	No.10 Wanshou Road PuKou Economic Development Zone(ShiLin Industrial Park),Nanjing,Postal 211800,P.R. of China
Sample Source	Deliver from applicant
Sample Quantity	1 package
Specification & Batch	50g
State and Characteristic	White powder
Received Date	11th May, 2018
Completion Date	23rd, August 2018
Item Tested	Eye Irritation
Test Method	Chorioallantoic Membrane Vascular Assay （CAMVA）

If any vascular effect was observed, the egg was considered positive. Recording of positive or negative responses will be all that is required for determining an RC_{50} value.

RC_{50}	Prediction
> 3.0%	no irritation
>1.0%, ≤3.0%	medium irritation
<1.0%	severe irritation

Conclusion: According to the criteria of CAMVA, under the condition of this test, the testing article " SpecWhite® DL-MA (Mandelic Acid)" RC_{50}=13.09% & 95% CI:8.51%-20.22% is no eye irritation potential.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Skin Irritation— Human Patch Test——***The third-party data (Intertek)***

Testing Sample: Aqueous solution of 5.0% **SpecWhite® DL-MA**

Negative Control: Distilled Water

Test Method:

A suitable patch test chamber was chosen, the specimen (0.020-0.025g) was putted into the chamber and fixed onto the subjects' back by special adhesive tape.

Af6ter 24h patch was removed, dermatologist observed the reaction at 0.5h, 24h, 48h after the patch removed and recorded the result according to the "Skin adverse reaction grading standard" in STSC

Test results

Group	Observing time	Number of subjects	Number of subjects have adverse reaction					
			0	1	2	3	4	Sum (1-4)
Testing sample	0.5h	33	32	1	0	0	0	1
	24h	33	31	2	0	0	0	2
	48h	33	32	1	0	0	0	1
Negative control	0.5h	33	33	0	0	0	0	0
	24h	33	33	0	0	0	0	0
	48h	33	33	0	0	0	0	0

SpecWhite® DL-MA shows

Non obvious skin irritation

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Ames Test—Carcinogenicity——***The third-party data***

Test substance: SpecWhite® DL-MA(DL-Mandelic acid)

Quantity: 20g/package×1

Batch No.: 20171010

Physical appearance: White powder

Study sponsor: Spec-chem Industry Inc.

Method: Salmonella Typhimurium/Reverse Mutation Assay

Strain: TA 97a, TA98, TA100 and TA102

Reference: Hygienic standard for cosmetics(2015),ministry of health of the peoples republic of China

Result:

Table 1 Mean of the reverting colonies from Ames test of SpecWhite® DL-MA(DL-Mandelic acid)

	Dosage	TA97		TA98		TA100		TA102	
	(ug/plate)	+S_9	–S_9	+S_9	–S_9	+S_9	–S_9	+S_9	–S_9
Sample	625	124±11	107±6	29±3	39±4	106±7	134±8	312±14	286±8
	1250	137±5	105±8	32±4	34±5	109±12	140±5	293±24	300±15
	2500	140±5	115±9	29±4	41±2	109±4	151±25	298±13	301±5
	5000	153±9	122±10	31±2	34±5	107±6	137±3	305±7	308±8
		130±10	105±7	31±2	35±1	117±10	133±12	284±14	287±7
Sterile water	0.1ml	132±8	98±11	30±2	36±3	114±8	149±4	309±7	290±10
Dexon	50		881±112		671±94				783±58
2-AF	10	888±12		958±49		885±37			
NaN_3	1.5						778±114		
1,8-DHAQ	50							732±67	

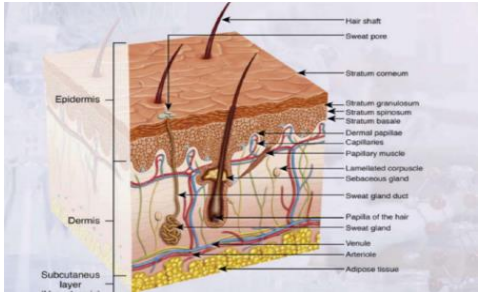
Test result: No positive result was found with all the test strains in the presense and absence of metabolic activation system.

SpecWhite® DL-MA shows No Carcinogenicity.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

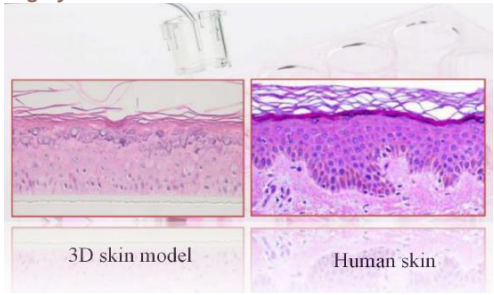
Skin model—OECD TG 439《In vitro skin irritation:Reconstructed Human Epidermis (RHE) Test Method》(2015):

Cosmetics and skin interactionsa



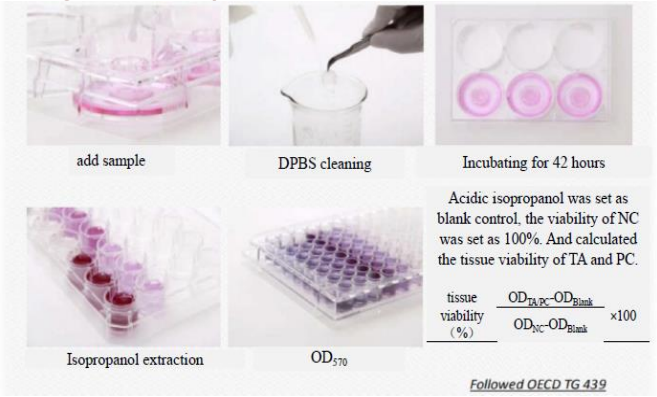
Acute skin irritation is a local, reversible inflammatory response resulting from normal skin contact with irritating drugs. The mechanism of skin irritation occurs because the test substance contacts the skin by expanding, infiltrating or destroying the epidermal barrier, and then acting on the stratum corneum cells to produce a toxic effect.

Highly Similar



The method employs a three dimensional human skin model with a functional epidermal stratum corneum structure, which is evaluated by the percentage of the stimulating or corrosive threshold dose level defined by the test substance after the skin is exposed and the cell viability is decreased by measurement. The irritant strength of the test substance.

Testing Process of Episkin Model



Result of skin irritation in vitro on Episkin skin model

Group	Mean tissue relative viability (%)	UN GHS Prediction
NC	100.00±1.65	---
PC	5.61±2.19	Category 1/2
TA	86.25±5.50	No Category

Conclusion: (according to OECD TG 439 chemicals in vitro skin irritation) reconstructed human epidermis test method, under the testing conditions, the tissue viability of the sample "**SpecWhite® DL-MA**" **is 86.25% (viability >50%)** and it is considered as no skin irritation.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Skin Sensitisation (in vitro) ——H-CLAT (Human Cell Line Activation Test)—*The third-party data*

Name of Sample	SpecWhite® DL-MA (DL-mandelic acid)
Test Type	Commission Test
Applicant	Spec-chem industry inc
Address	No.10 Wanshou Road PuKou Economic Development Zone(ShiLin Industrial Park),Nanjing,Postal 211800,P.R. of China
Sample Source	Deliver form applicant
Sample Quantity	1 package
Specification & Batch	50g
State and Characteristic	White powder
Received Date	11th May, 2018
Completion Date	15th, July 2018
Item Tested	Skin sensitisation
Test Method	OECD TG442E（2018）In Vitro Skin Sensitisation Assays Addressing The Key Event On Activation Of Dendritic Cells On The Adverse Outcome Pathway For Skin Sensitisation -Annex I: In Vitro Skin Sensitisation: Human Cell Line Activation Test (H-CLAT)

Prediction model According to OECD TG442E-ANNEX I (2018), if the RFI of CD86 is equal to or greater than 150% at any dose (>50% of cell viability) AND/OR the RFI of CD54 is equal to or greater than 200% at any dose (>50% of cell viability), the test article is considered as positive.

Table 2 The RFI of CD86 and CD54 at different concentration

Con.（μg/mL）	Mean RFI $_{CD86}$（%）	Mean RFI $_{CD54}$（%）
2790.82	87	105
3348.98	88	111
4018.78	79	124
4822.53	58	171
5787.04	82	144

Conclusion: According OECD TG442E-ANNEX I (2018), under the condition of this test, the result of TA **"SpecWhite® DL-MA (Mandelic Acid)"** with mean RFI CD86<200 and mean RFI CD54<150 is predicted as negative.

SpecWhite® DL-MA has no skin sensitisation !

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Commercial Products with Glycolic Acid

For Beloved One (2020)

7% Mandelic Acid + Azelaic Acid Gentle

Renewing Brightening Peel

7% Mandelic Acid + Azelaic Acid This renewal serum is formulated with 7% mandelic acid to gently exfoliate dead skin, refine rough skin texture, and improve skin elasticity and firmness.

The Ordinary

Mandelic Acid 10% + Ha

Mandelic Acid 10% + HA offers superficial dermal peeling that is gentler than other alpha hydroxy acids. The molecular weight of mandelic acid is 152.1 daltons which is larger than other alpha hydroxy acids (glycolic acid is 76.0 daltons, for example). This larger size allows mandelic acid to penetrate the skin more slowly which in turn makes it very gentle and suitable for all skin types including the most sensitive skin.

Garden of Wisdom

Mandelic Acid 10% Serum

Mandelic acid is an alpha hydroxy acid which gently exfoliates dead skin cells from skin's surface. Because of its larger molecular size, Mandelic acid penetrates slowly into the dermal layer.

BY WISHTREND

Mandelic Acid 5% Skin Prep Water

A hydrating and non-irritating exfoliant that can be used daily. Formulated with Mandelic Acid, it acts as an exfoliating treatment that improves the skin tone and texture while boosting the effectiveness of other products.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Commercial Products with Glycolic Acid

philosophers
— REWARDS —

Refreshing & Refining moisturizer
renewed hope in a jar

$37.00
size| 4 oz.

$39.00
size| 2 oz.

aqua/water/eau, cyclopentasiloxane, stearic acid, glycerin, butylene glycol, c12-15 alkyl benzoate, glycolic acid, dimethicone, polyacrylamide, cetearyl alcohol, phenoxyethanol, sodium hydroxide, c13-14 isoparaffin, dimethicone crosspolymer, ceteareth-20, ammonium acryloyldimethyltaurate/vp copolymer, polysilicone-11, acrylates/c10-30 alkyl acrylate crosspolymer, laureth-7, citric acid, chlorphenesin, **mandelic acid**, tocopheryl acetate, synthetic fluorphlogopite, ethlhexyl palmitate, propanediol, parfum/fragrance, disodium edta, adenosine, evodia rutaecarpa fruit extract, limonene, faex/yeast extract/extrait de levure, magnesium stearate, opuntia coccinellifera flower extract, silica dimethyl silylate, caprylyl glycol, bht, ethylhexylglycerin, hyaluronic acid, silanetriol, sodium hyaluronate, sorbic acid, hexylene glycol, bismuth oxychloride (ci 77163). octinxiate (6.99%), avibenzone (2.7%), octocrylene (2%)

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Whitening Property of SpecWhite® DL-MA—Inhibiting effect on tyrosinase activity

The concentration of the pure compound was measured which caused a 50 % inhibition of tyrosinase activity (EC50).

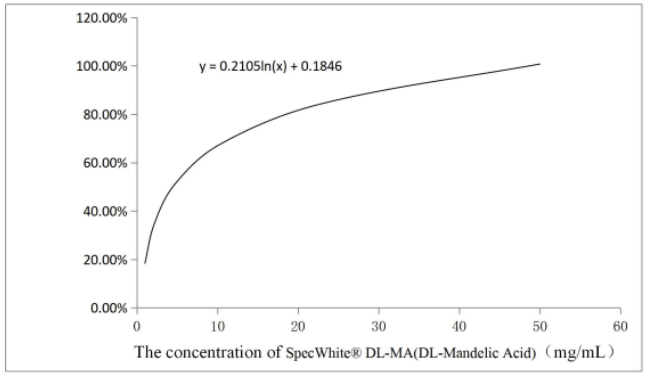


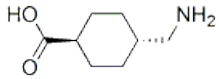
Figure 1 SpecWhite® DL-MA(DL-Mandelic Acid) on the Inhibition of Tyrosinase Activity

(single phenol enzyme activity)

Summary:

- Through determination of tyrosinase activity inhibition, the result shows that SpecWhite® DL-MA (Mandelic Acid)EC50 value is 0.274 mg/mL, very effective inhibiting capability!
- SpecWhite® DL-MA is benificial to reduce skin's melanin production, suitable for skin whitening & lightening application.

SpecWhite® TA



01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Antibacterial Property of Mandelic acid—urinary tract infections

- In some hospitals a 1.0% solution (pH=2.4) of Mandelic acid (MA) is used as bladder irrigation fluid to prevent Urinary tract infections associated with indwelling urethral catheterization.
- Some exoeriments on the bactericidal activity of MA when used in cases of indwelling catheter or of urinary tract infection.
- Formula: 60.4g citric acid, 0.9g calcium carbonate, 0.1 EDTA (Na-salt), 6g gluconolactone, 27.2g magnesium carbonate hydroxide in distilled water (ad 1000mL).

Table 1. Effect on pH on bacterial growth[1] in the presence of 0.5 and 1 % mandelic acid.

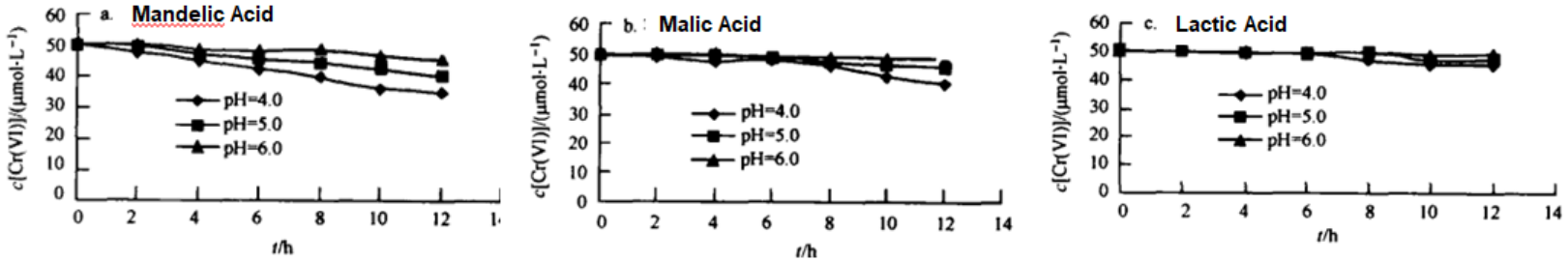
	pH 4.0				pH 4.5				pH 5.0					pH 5.5					pH 6.0				
	1	2	3	4[2]	1	2	3	4	1	2	3	4	5	6	7	8	9	5	6	7	8	9
0.5 % Mandelic acid																						
Escherichia coli	−	−	−	−[3]	−	−	−	−	+	+	+	+	−	+	+	−	+	−	+	+	−	+
Klebsiella pneumoniae	−	−	−	−	−	−	−	−	+	+	+	+	−	+	+	−	−	−	+	+	−	+
Proteus mirabilis	−	−	−	−	−	−	−	−	+	+	+	+	−	+	+	−	−	−	+	+	−	+
Enterococcus spp.	−	−	−	−	−	−	−	−	+	+	+	+	−	+	+	−	−	−	+	+	+	+
1 % Mandelic acid																						
Escherichia coli	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	+	−	−	−	+
Klebsiella pneumoniae	−	−	−	−	−	−	−	−	+	+	+	−	−	−	−	−	−	−	−	−	−	+
Proteus mirabilis	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	−	+
Enterococcus spp.	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	+	−	−	−	+

Summary:

When pH=4.0 & 4.5, both 1.0% and 0.5% Mandelic Acid show excellent anti-bacterial activity, applied in rinary tract infections. No growth of testing bacteria were observed.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Reducing Capacity (Antioxidant) of Mandelic Acid (MA) VS Malic Acid VS Lactic Acid



Effect of pH on the reduction of 50μmol·L⁻¹ Chromium:Cr (VI) by different organic acids at 25 ℃. a:mandelic acid, b:malic acid, c:lactic acid

Summary:

- Among testing organic acids, **a: Mandelic Acid (MA)** has **the strongest reducing capacity**, compared with b: Malic Acid and c:Lactic Acid. ***(mandelic acid > malic acid > lactic acid)***
- The reducing capacity of mandelic acid **depends on the pH**, the lower pH is, the better reducing capacity is.
- Can be used in industrial wastewater treatment.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

In vivo—Evaluation of Mandelic acid on improvement in acne, skin texture, wrinkles, lentigenes, and melasma

Chemical peels were performed with 30% and 50% mandelic acid (MA).

- A 2% mandelic acid wash was used to cleanse the skin, followed by the application of mandelic acid using gauze applicators. As the product was applied, the skin was gently rubbed. Exposure times were usually limited to 5 minutes; however, longer applications also appeared to be safe. Peels were performed at weekly or biweekly intervals. After the peel, the skin was cleansed with water, and a mild topical steroid (desonide 0.05% lotion) was applied in a single application.
- For 2 to 4 weeks before and after laser resurfacing, patients were treated with mandelic acid products and a semi-permeable ointment designed to aid healing after laser surgery. Patients were evaluated for the following: time to reepithelialization, incidence of gram-negative infections, duration of postresurfacing erythema, postinflammatory pigmentation, milia, and other postoperative complications.

Fig. 1: Melasma in 45-year-old female (left) with hyperpigmentation caused by glycolic acid plus hydroquinone, and same patient (right) 9 months after use of mandelic acid BID.

Fig. 2: Melasma and lentigenes in 48-year-old female (left), and same patient one month after use of mandelic acid (dark lesion under left eye removed with liquid nitrogen).

Fig. 3: 29-year-old female with 11-year case of melasma (left), and same patient after one month of mandelic acid BID (right).

*** The most notable result of using mandelic acid after laser peels was the lack of postoperative gram-negative infections, besides MA helps to remove dead-skin fragments.**

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Efficacy Test of PLGA (Glycolic Acid) & DL-MA (Mandelic Acid)

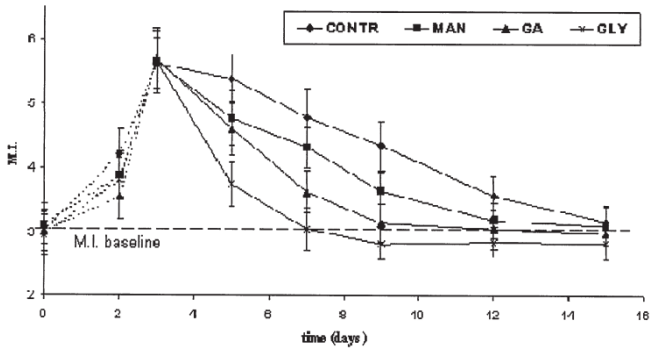


*Figure 1. Trends of the melanin index (M.I.) vs time (days) for subjects recruited in the CONTR (no topical treatment), 10% **GLY (glycolic acid, PLGA)**, 10% MAN (mandelic acid), and 10% GA (grape acids) groups.*

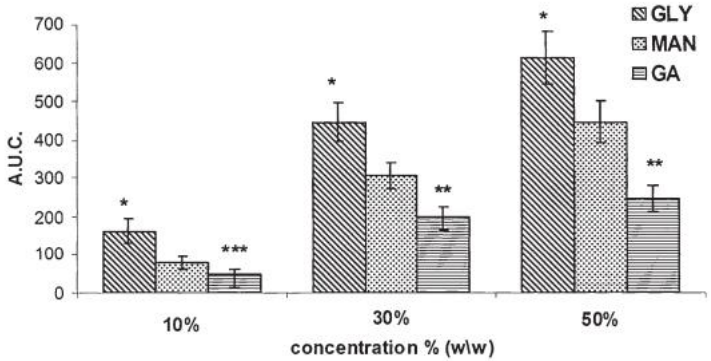


*Figure 2. Mean area under curve (AUC) values (± SD) obtained by applying GLY (glycolic acid), MAN (mandelic acid), and GA (grape acids) formulations at three different concentrations (10%, 30% and 50% w/w) to skin sites of subjects admitted into the study. AUC values were directly related to the degree of skin erythema induced by topical application of the formulations. *p < 0.05 (signifi cantly different) vs MAN and GA; **p < 0.05 (signifi cantly different) vs MAN; ***p > 0.05 (no signifi cantly different) vs MAN.*

- **PLGA induced the faster skin exfoliation compare with other AHAs (Mandelic acid, Grape acid), Thus glycolic acid is suitable for quick-acting formulation.**
- **Mandelic Acid can induce a relatively slower and safe peeling action compared with glycolic acid, less erythema and photosensitizing effect.**

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Anti-acne Effect of Mandelic Acid VS Glycolic Acid

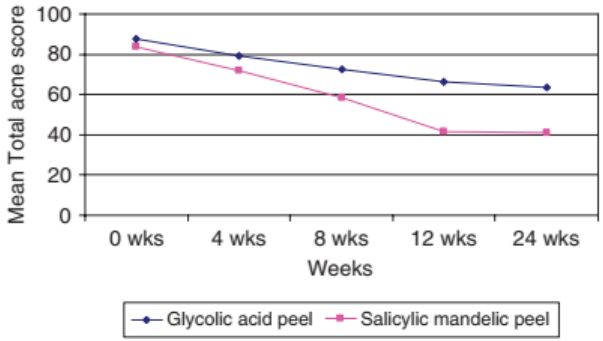


Figure 2. Comparison of effects of glycolic acid peels and salicylic–mandelic acid peels on total acne score.

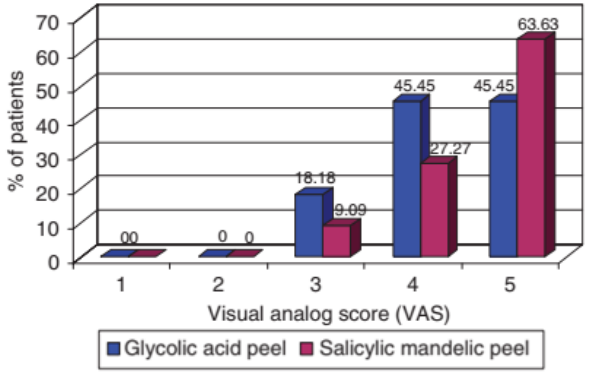


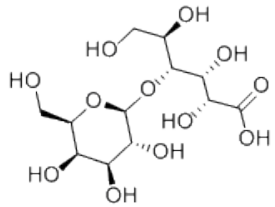
Figure 3. Comparison of visual analog scale with glycolic acid peels and salicylic–mandelic acid peels (patients at 24 weeks).

RESULTS: Both the agents were effective, but SMPs (salicylic–mandelic acid combination peels) had a higher efficacy for most active acne lesions ($p<.001$) and hyperpigmentation ($p<.001$). Side effects were also lesser with SMPs.

CONCLUSION: Both the agents were effective and safe in Indian patients, with SMPs being better for active acne and post-acne hyperpigmentation.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

The Overview of LBA



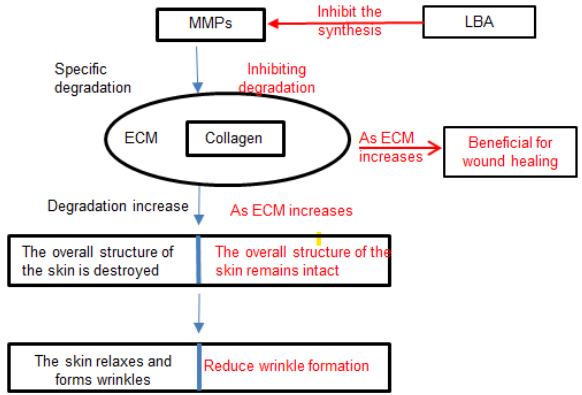
The Structure of lactobionic acid
Mw=358Da

The molecular constituents of lactobionic acid:

- **Gluconic acid** has been shown to provide significant anti-aging effects when incorporated into formulations as gluconolactone.
- **Galactose** is a chemically neutral sugar found in the body that is utilized by skin during glycosaminoglycan and collagen syntheses, and cell migration.

Lactobionic acid is a polyhydroxy bionic acid with numerous skin care benefits. It is a potent moisturizer and antioxidant, and is nonirritating to skin. Make it an ideal choice for skin care, its benefits include:

- ✓ improvements in skin texture, clarity and roughness
- ✓ Increased skin firmness and elasticity
- ✓ Increased skin thickness/plumping
- ✓ Improvements in skin texture, suppleness, degree of hydration and elasticity
- ✓ Enhance wound healing
- ✓ No irritation, the 3th AHAs, milder & safer choice



01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

SpecKare® LBA Information

Item No.: 110034

Product name: SpecKare® LBA

INCI name: LACTOBIONIC ACID

CAS No.: 96-82-2

EC No.: 202-538-3

Dosage: 0.5-2.0%, 2.0-10.0%, 10-25%

Package: 1kg or customized

Storage: Store in cool place. Keep container tightly closed in a dry and well-ventilated place.

Shelf life: 2 years .

Application: Serum/Cream/Lotion/Essence etc.

Preservative Free:

Items	Specification		
Appearance	White or almost white crystalline powder		
Identification	-By IR: Positive-By TLC: Positive		
Specific optical rotation	+23°~+29°		
Solubility	Freely soluble in water, slightly soluble in glacial acetic acid, anhydrous ethanol and in methanol		
Appearance of solution	The solution is clear & not more intensely coloured than reference solution		
PH	1.0-3.0		
Calcium	≤500ppm	Silicates	≤200ppm
Chloride	≤500ppm	Iron	≤100ppm
Sulfate	≤500ppm	Heavy Metals	≤10ppm
Reducing sugars	≤0.2%		
Water Content	≤5.0%		
Assay	98.0%-102.0%		
Total Ash	≤0.1%		
Endotoxin Level	10EU/g		
Salmonella	Negative		
E.coli	Negative		
Pseudomonas	Negative		

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Commercial Products with LBA

HomeFacialPro (HFP)
Lactobionic Acid Series

Estee Lauder
Lactobionic Acid Series

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

In Vivo Test-Melanin Index(MI), Erythema Index(EI), Electrical Capacitance(EC) ＆Transepidermal Water Loss(TEWL)

Test product：	E-LBA-active （alkylpolyglucoside-based emulsion with lactobionic acid）
Device Model:	Tewameter®TM 210 ,capacitance-based Corneometer® CM 825＆Mexameter® MX 18.(CK)
Subjects：	25 volunteers with moderately dry skin
Average age：	mean age 31.4 ± 7.9 years old
Test Site：	The flexor sides of their forearms were treated with E-LBA (active) on the left and E (placebo) on the right arm using a carton template with two empty spaces of 9 cm^2. One rectangle was left as an untreated control (UC) on each arm (UC-left and UC-right).
Test Period：	0d, 2 weeks, 4 weeks
Evaluation Parameters:	TEWL(g/m^2h)； EC (Hydration); MI ＆EI (evaluate the skin color)
Temperature：	20℃- 25℃
Humidity：	40% - 60%
Application Frequency：	Subjects were asked to apply color-coded samples twice daily. Measurements were taken at baseline, and after 2 and 4 weeks of the treatment in the morning, before the first daily application.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

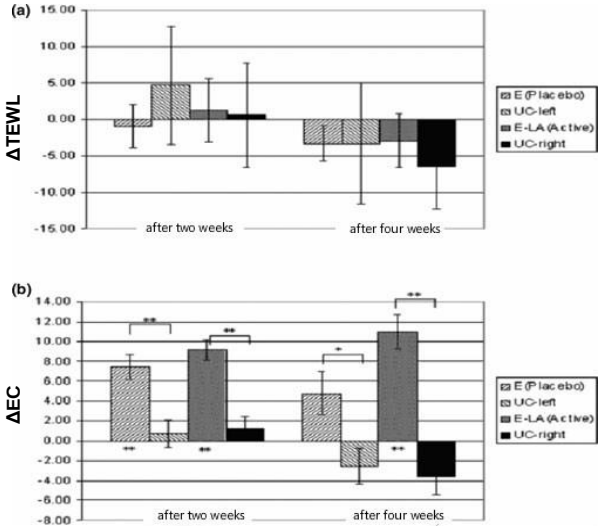


Fig1.The effect of topical application of the sample E-placebo (alkylpolyglucoside-based emulsion without LBA) and E-LBA-active (alkylpolyglucoside-based emulsion with LBA) on (a) TEWL, (b) EC and untreated controls (UC).

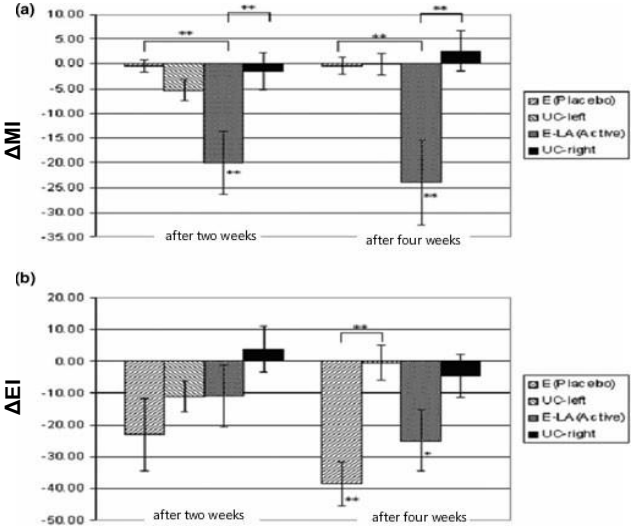


Fig2. The effect of topical application of the sample E-placebo (alkylpolyglucoside-based emulsion without LBA) and E-LBA-active (alkylpolyglucoside- based emulsion with LBA) on (a) MI, (b) EI and untreated controls (UC).

- No significant changes in TEWL values, indicating no damage of the skin barrier function.(Fig.1a).
- The application of both samples (E-LBA and E) resulted in a significant improvement of skin moisture (increase of EC,Fig.1b), compared with both UC and baseline.
- The obtained MI values (Fig. 2a) clearly demonstrate that there was a significant lightening of the skin sites treated with E-LBA sample, after only 2 weeks.
- EI was significantly decreased after the application of E (placebo) sample (Fig. 2b).EI was also decreased after the application of E-LBA sample, indicating a lack of skin irritation.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

In Vivo tests—Anti-aging

Test product： A topical cream formulation containing 8% lactobionic acid

Subjects： 31women,Fitzpatrick types II and III (29 Caucasian, 2 Asian)

Average age： 39-60 years old.

Test Period： 0d, 6 weeks, 12 weeks

Application Frequency： lactobionic acid, 8% cream, pH 3.8 was applied twice daily to the face and 3 times daily to one forearm; one forearm remained untreated as a control for forearm measurements.

Clinical Evaluations：

– Clinical Grading (weeks 0, 6, 12)： scores were collected visually by a trained evaluator using a 0 to 10 scale with 0.25 point increments for the following parameters:

Parameter	Site for Grading	Low Extreme of Scale	High Extreme of Scale
Fine Lines	Eye area	0 = None	10 = Severe
Coarse Wrinkles	Eye area	0 = None	10 = Severe
Pore Size	Cheek	0 = Invisible	10 = Very Large
Laxity	Cheek	0 = Firm, unpliable	10 = Loose, pliable
Roughness	Cheek	0 = Soft, smooth	10 = Rough, coarse
Sallowness	Face	0 = Light, non-yellow	10 = Dark, matte
Clarity	Face	0 = Dull, matte	10 = Clear, radiant
Mottled Pigmentation	Face	0 = Even tone	10 = Mottled, uneven tone

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

-Pinch Recoil (weeks 0, 6, 12)：	Measurements were taken of the under eye area to assess skin elasticity by pinching the skin and recording time with a stopwatch (in hundredths of a second) to full recovery of the skin. The measurements were performed in triplicate, and the average score was reported. Pinch recoil is a recognized indicator of skin resiliency and firmness.
-Total Skin Thickness (plumping) Measurements (weeks 0, 12)：	Were collected on the outer forearms, using a hinged pinching device and digital calipers as previously described. Duplicate measurements representing a two-fold thickness of skin were taken and averaged at baseline and endpoint for both the treated and untreated control arms.
-Irritation/Safety Grading (weeks 0, 6, 12)：	Global evaluation of objective irritation and safety was conducted for dryness, erythema and edema and subjective irritation scores were collected for burning, stinging, itching, tightness and tingling. Scale: 0–3 (none, mild, moderate, severe).
-Digital Photography (weeks 0, 12)	Was collected using standardized lighting and positioning.
-Self-Assessment (weeks 0, 6, 12)	Was collected via questionnaires.
-3-millimeter Punch Biopsies	Were collected at endpoint on the forearms of several study participants. Biopsies were stored in 10% formalin and subsequently processed for histological assessments.

01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Clinical Photographs

Improvements to skin laxity and texture at 12 weeks

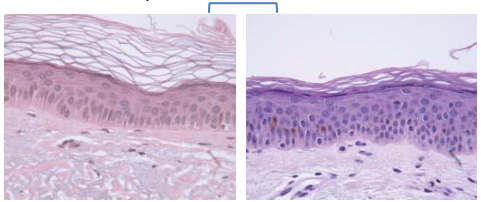
Diminished periocular fine lines and improved eyelid texture at 12 weeks

Diminished periocular fine lines and smoother texture at 12 weeks

Histology Results

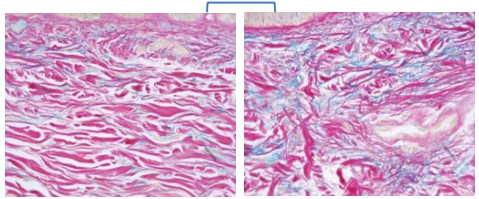
Increased viable epidermal thickness and a more compact stratum corneum.

Epidermal Structure: 400X



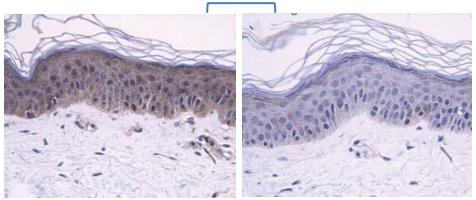
Increased density of dermal colloidal iron staining (blue color) representing glycosaminoglycans/acid mucopolysaccharides(GAGs)

GAGs: 400X



Decreased density of MMP9 staining (brown color) within keratinocytes

MMP9: 400X



Left: Untreated control; Right:Lactobionic acid 8%

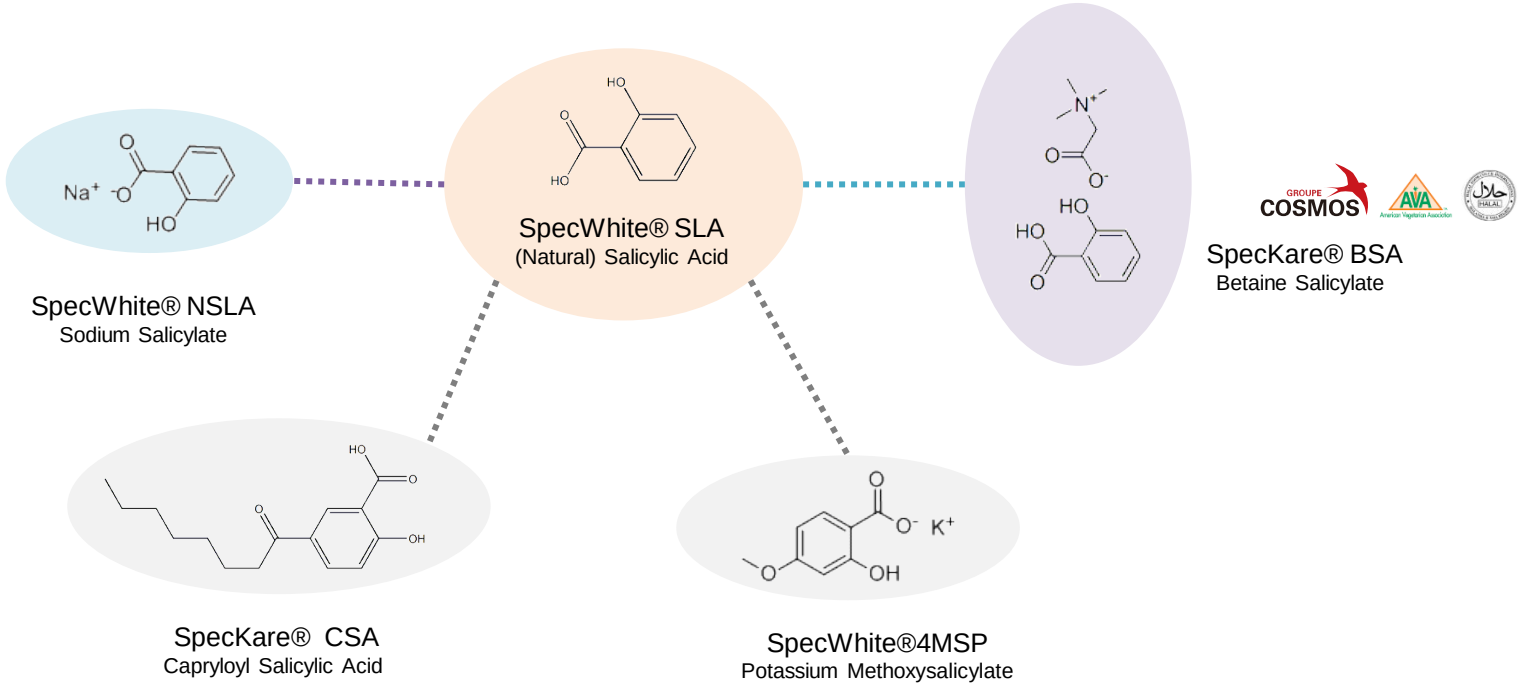
01 Introduction of α-/Alpha-Hydroxy Acid (AHA)

Guide for Selection

	Exfoliating Speed	Reducing Capacity	Moisture-retlining Capacity	Skin-lightening Capacity	Anti-aging Capacity	Mildness
SpecWhite® PLGA70/90 Glycolic Acid	★★★★★	★★★★☆	★☆☆☆☆	★★★☆☆	★★☆☆☆	★★☆☆☆
SpecWhite® DL-MA Mandelic Acid	★★★☆☆	★★★★★	★★☆☆☆	★★★☆☆	★★★☆☆	★★★★☆
SpecKare® LBA Lactobionic Acid	★★☆☆☆	★★☆☆☆	★★★★★	★★☆☆☆	★★★★★	★★★★★

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

β-/Beta-Hydroxy Acids (BHA) & Derivatives



02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

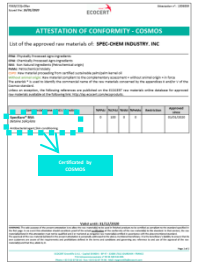
Product Information of SpecKare® BSA：

Item No.:	120017
Trade name:	SpecKare® BSA
INCI name:	Betaine Salicylate
CAS No.:	17671-53-3
Use Level:	0.1-6.0%
Application:	Anti-acne, Keratolytic, Moisturizer, Smoothen skin, Antimicrobial, Hair Care & others
Storage:	Store at cool and dry place, tightly closed.
Shelf life:	2 years
Package:	1kg, 25kg

Items	Specification
Appearance	White powder
Odor	Characteristic
Assay(wt%)	＞98
pH(1% Aqua)	2.0-5.0
Residue on Ignition(wt%)	＜0.15
Heavy metal(ppm)	＜10
Total Plate Count (CFU/g)	＜1000
Yeast＆ Mold(CFU/g)	＜100
E.Coli(CFU/g)	Negative
Pseudomonas aeruginosa	Negative
Staphylococcus aureus	Negative


ATTESTATION OF CONFORMITY
RAW MATERIALS
COSMOS

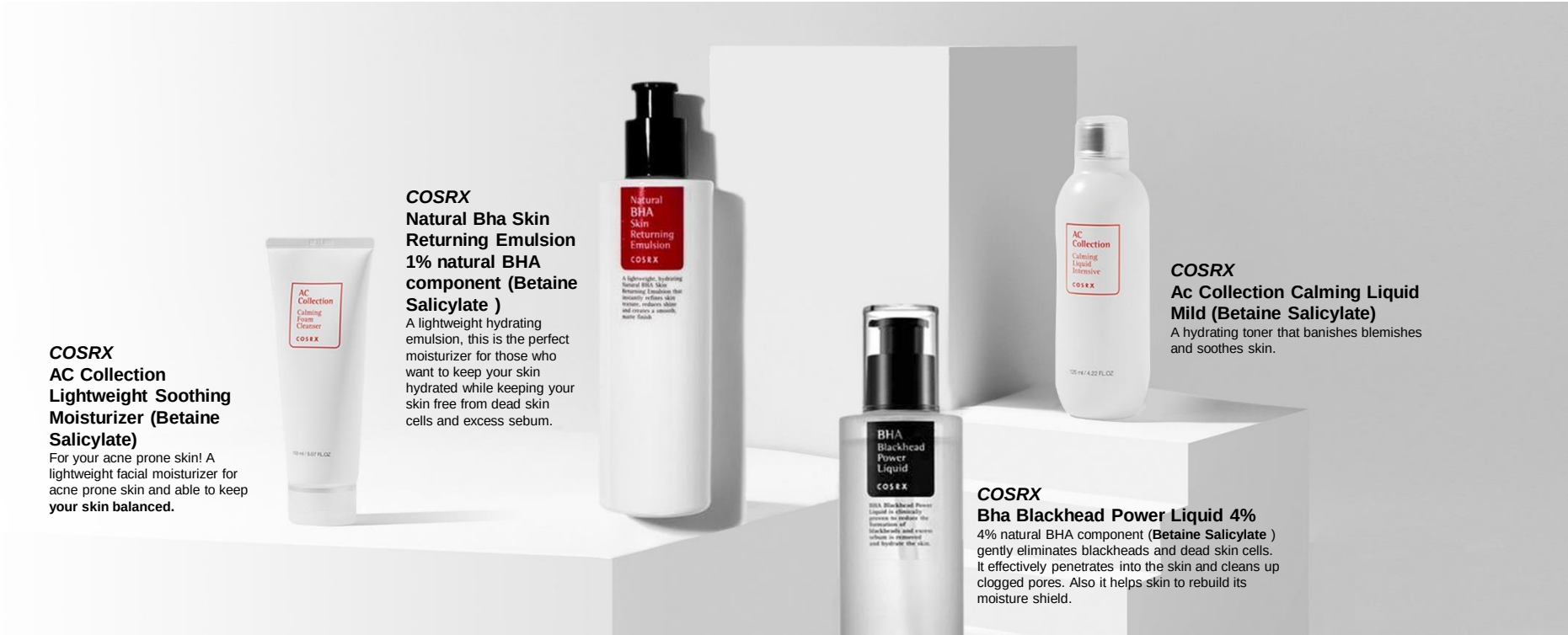
SPEC-CHEM INDUSTRY, INC


ATTESTATION OF CONFORMITY - COSMOS

List of the approved raw materials of: SPEC-CHEM INDUSTRY, INC

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

Commercial Products with BSA



COSRX
AC Collection Lightweight Soothing Moisturizer (Betaine Salicylate)
For your acne prone skin! A lightweight facial moisturizer for acne prone skin and able to keep **your skin balanced.**

COSRX
Natural Bha Skin Returning Emulsion 1% natural BHA component (Betaine Salicylate)
A lightweight hydrating emulsion, this is the perfect moisturizer for those who want to keep your skin hydrated while keeping your skin free from dead skin cells and excess sebum.

COSRX
Bha Blackhead Power Liquid 4%
4% natural BHA component (**Betaine Salicylate**) gently eliminates blackheads and dead skin cells. It effectively penetrates into the skin and cleans up clogged pores. Also it helps skin to rebuild its moisture shield.

COSRX
Ac Collection Calming Liquid Mild (Betaine Salicylate)
A hydrating toner that banishes blemishes and soothes skin.

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

Commercial Products with BSA

Hanskin
Pore Cleansing Oil [Bha, Betaine Salicylate, 100ppm]

Dr Ceuracle
Tea Tree Purifine 70 Toner, Betaine Salicylate
A hydrating toner formulated with soothing 70% tea tree extract and betaine salicylate (BHA), which exfoliates dead skin cells and helps minimize breakouts for more even-toned, radiant complexion.

Neutralyze
Exfoliating Pads (Betaine Salicylate)

Perricone MD
Exfoliating Pore Refiner(Betaine Salicylate)
Gently exfoliates and clarifies, helping to prevent noticeable pores while refining rough skin.

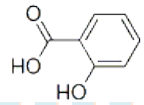
Dr. Jart+
Dermask Ultra Jet Peeling Solution: Peeling Essence
See fresh, smooth, clear skin with this innovative bubbling mask that exfoliates skin's surface and evens out the appearance of skin tone

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

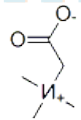
(Salicylic Acid) Irritant-*SCCS/1601/18*:

1. As preservative in all cosmetics ≤ 0.5% (acid)
2. Not Applicable to any oral product (Lipsticks is exception)
3. Cause serious damage to the eye
4. Rinse-off products ≤ 2.0% (≤ 3.0 rinse-off hair products)
5. Body lotion, eye shadow, mascara,eyeliner, lipstick & roll on deodorant ≤ 0.5%
6. Not to be used for children <3 years old (shampoo is exception)

Salicylates (Calcium Salicylate, Magnesium Salicylate, MEA-Salicylate, Potassium Salicylate, Sodium Salicylate, and TEA-Salicylate; Capryloyl Salicylic Acid, C12-15 Alkyl Salicylate, Isocetyl Salicylate, Isodecyl Salicylate, Methyl Salicylate, Myristyl Salicylate, Ethylhexyl Salicylate; and Tridecyl Salicylate, and the esters Butyloctyl Salicylate and Hexyldodecyl Salicylate)



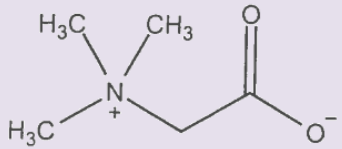
Salicylic Acid (Figure 1), an aromatic monohydroxybenzoic acid (specifically, 2-hydroxybenzoic acid) is a colorless, crystalline organic acid that can be derived from salicin (a β-glucoside in willow bark).
→foliant, smoothing agent, anti-microbial, anti-acne, keratolytic agent



Betaine, is a naturally occurring N-trimethylated amino acid, also called trimethylglycine, and can be isolated from sugar beets. It is a common component in the human diet.
→hair conditioning agents, humectants, moisturizers, skin conditioning agents

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

Why Choose Betaine as another component?



Betaine

- Natural Origin: be extracted from sugar beets.
- According to 2013 VCPR (FDA Voluntary Cosmetic Registration Program) betaine has the most reported uses in cosmetics and personal care products, with a total of 459, the majority of the uses are in leave-on skin care preparations
- In the Council's(Personal Care Products Council) use concentration survey, betaine had a maximum use concentration range of 0.0001%-8.7%.
- Betaine is used in hair spray at up to 3% and in moncoloring powders at up to 0.0001%, would not be respirable (ie not enter the lungs)
- (Alkyl) Betaine are not restricted from use in any way under the rules governing cosmetic products in the EU.

SpecKare®BSA (Betaine salycilate) is the product formed by natural betaine with natural salycilic acid !

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

- SpecKare®BSA (Betaine salycilate) combines famous exfoliant & anti-acne agent, salicylic acid and gentle moisturizer, betaine.
- It counts as a mild exfoliant and natural moisturizer, skin smoothing agent, antimicrobial agent and keratolytic agent.
- In K-Beauty products, as due to regulations, pure salicylic acid can be used only in tiny amounts in South-Korean formulations. A generally accepted ballpark number is that betaine salicylate is twice as gentle as salicylic acid, i.e. a 4% betaine salicylate product is similar to a 2% salicylic acid one.

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

Anti-acne Property

MIC(minimum inhibitory concentration) of SpecKare®BSA on

Propionibacterium acnes(ATCC11827)

According to double dilution method, (flat amount of bacteria is 104 ~ 105CFU/, plate) in 36 ℃ under anaerobic conditions for 48 hours, then observe the growth of dish colony

Teststrains / Sample name	Propionibacterium acnes(ATCC11827)
SpecKare™BSA	2.5%

SpecKare®BSA can mildly and effectively eliminates pimples at the root, to give you smooth, clear skin. Especially for oily problematic skin. Shrinks the pores and cleanses them in depth.

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

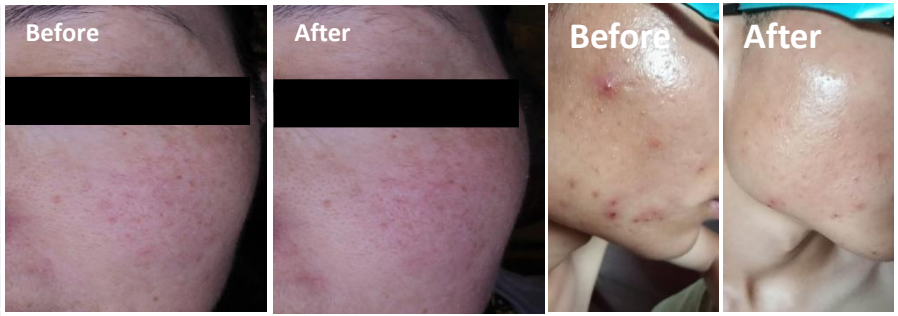
In vivo-Clinical Anti-acne Test (SpecKare®BSA 2.0 w/w%)

Subjects：	Volunteers with acne
Sex:	Females or males
Age range:	18 - 55years old;
Test Site：	Face
Application Frequency：	Twice a day after cleaning face in the morning and evening.
Test Period：	4 weeks (2018.05.21 - 2018.06.19).
Test Parameters：	Determinate the skin wrinkle with VisioFace 1000D or camera, Take photos.

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

In vivo-Clinical Anti-acne Test (Results-SpecKare®BSA 2.0 w/w%)

	Product Name	INCI Name	Dosage(%)
A	SpecKare™ BSA	Betaine Salicylate	2
	Water	Aqua	To 100
	NaOH(20%)	Sodium hydroxide	1.5
B	Butanediol	1,3-Butanediol	10
	SpecKare™ NK2	Dipotassium Glycyrrhizinate	0.2
	SpecKare™ QP	Quaternized Panthenol	0.5
	SpecPure™ AVP2	Aloe Vera gel powder (Freeze)（ 200:1）	1
	SpecKare™ HAL	Sodium Hyaluronate(1%Liquid)	1
	EDTA-2Na	Disodium EDTA	0.05
	SpecKare™ TRHL	Trehalose	3
	SpecKare™ NMF50	Betaine	2
	SpecWhite® GA100	Glycyrrhiza Glabra,Dipotassium Glycyrrhizinate,Aloe Vera leaf extract,Gamellia sinensis o.ktze,Cortex mori extract	5
	ParbFree® IPMP100	o-Cymen-5-ol	0.7
	EGF Plus	sh-oligopeptide-1（liquid）	0.3



Summary: Acne and redness of volunteers have been effectively reduced, skin become moisturizing, smooth and bright, while without irritation.

Procedure: 1.Mix phase A while stirring at room temperature to dissolve completely. 2.Add phase B into A while stirring at room temperature to dissolve completely.

Properties: Appearance: Lightly yellowish clear liquid; pH:4.7; Stability: 45℃, -18℃, one month

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

Use Guidance

Solvent: Alcohol(95%)

Solvent: Propylene glycol

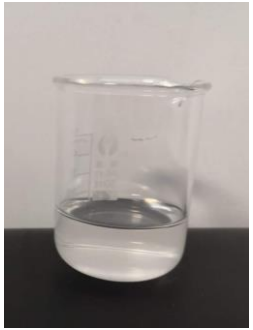
Solvent:Butylene Glycol

Solvent:Glycerin

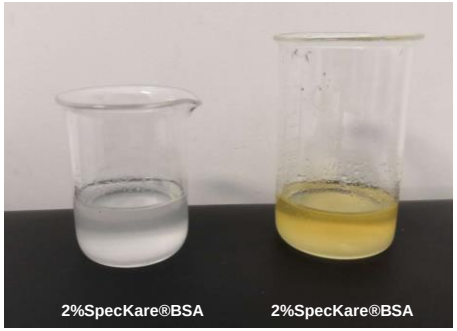
➢4%SpecKare®BSA completely soluble in alcohol, propylene glycol, butylene glycol.

➢2%SpecKare®BSA not completely dissolved in glycerin.

2%SpecKare®BSA
Aqueous solution, non-soluble
Initial pH 2.8



2%SpecKare®BSA
Aqueous solution, soluble
pH≥4.3



Solvent: White oil SpecKare® BTS Oil (Camellia Sinensis Seed Oil)

➢2%SpecKare®BSA insoluble in water, When using NaOH to adjust the pH to 4.3 , it is completely dissolved.

➢2%SpecKare®BSA insoluble in white oil and SpecKare® BTS Oil (Camellia Sinensis Seed Oil).

02 Introduction of β-/Beta-Hydroxy Acids (BHA) & Derivatives

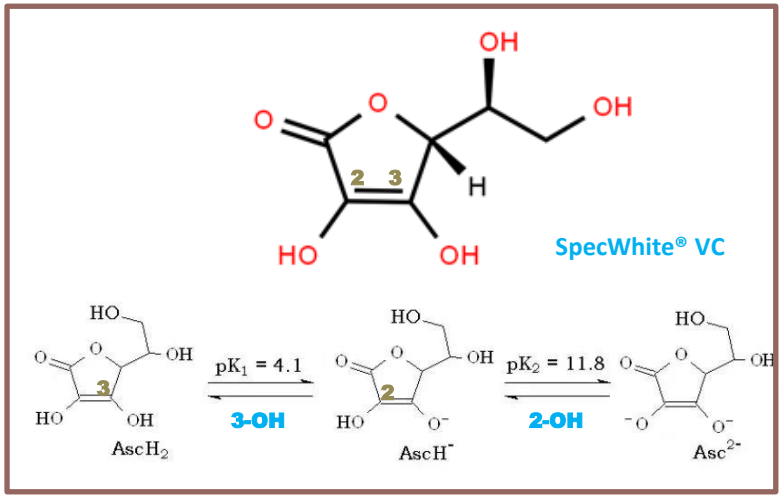
α-hydroxy Acid (AHA) VS β-hydroxy Acid (BHA)

	Exfoliating Speed	Anti-wrinkle Capacity	Anti-clog & bump Capacity	Moisture-retlining Capacity	Oil-control Capacity	Skin Type
AHA	★★★★★	★★★★☆	★★★☆☆	★★★☆☆	★★☆☆☆	Dry to Neutral Type
BHA	★★☆☆☆	★☆☆☆☆	★★★★★	★★☆☆☆	★★★★☆	Neutral to Oily Type

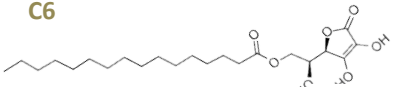
- AHAs usually work on skin's surface, generally preferred for normal to dry, sun-damaged skin due to their ability to enhance natural moisturizing factors within skin, reducing the visible signs of sun damage, including crepe-y skin and wrinkles.
- BHA usually work on skin's surface and deep inside the pore, more oil soluble than AHA, often preferred for normal to oily skin prone to bumps, clogs, blemishes and enlarged pores. BHA also has natural skin-calming properties, gentle for skin that's sensitive or prone to redness or rosacea, suitable for bumpy skin disposed to millia.

03 Introduction of Tyrosinase Inhibitor

Ascorbic Acid and Its Derivatives

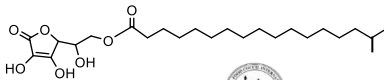


C6



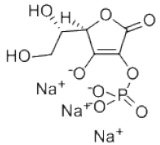
SpecWhite® AP

C6



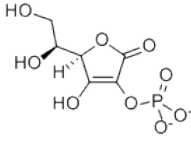
SpecWhite®AI

C2



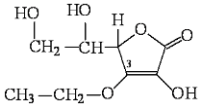
SpecWhite® SAP

C2



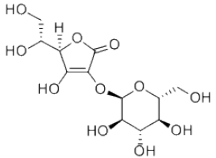
SpecWhite® MAP

C3



SpecWhite® VCE
Global Top 5

C2



SpecWhite® 02

03 Introduction of Tyrosinase Inhibitor

Guide for Selection

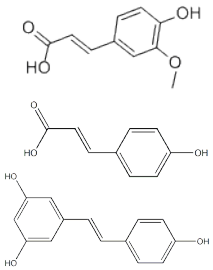
SpecWhite® VC REACH Registrated	Ascorbic Acid	Water Soluble	3.5-4.0, Anhydrous
SpecWhite® 02 COSMOS Approved	Ascorbyl Glucoside	Water Soluble	5.5-7.0 (6.5) Citric Acid/ sodium citrate Buffer Chelating Agent
SpecWhite® VCE	3-0-Ethyl Ascorbic Acid	Water Soluble, Polyols Soluble	4.0-6.5 Sodium Metabisulfite Chelating Agent
SpecWhite® MAP	Magnesium Ascorbyl Phosphate	Water Soluble	7.0-9.5 Phosphate Buffer Chelating Agent
SpecWhite® SAP	Sodium Ascorbyl Phosphate	Water Soluble	7.0-9.5 Phosphate Buffer Chelating Agent
SpecWhite® AP	Ascorbyl Palmitate	Lipid Soluble, Polyols Soluble +Solubilizer	No much pH limitation, Antioxidant
SpecWhite® AI	Ascorbyl Isostearate	Lipid Soluble, Polyols Soluble +Solubilizer	No much pH limitation, Antioxidant
SpecWhite® ATP	Ascorbyl Tetraisopalmitate	Lipid Soluble, Polyols Soluble +Solubilizer	No much pH limitation, Antioxidant

03 Introduction of Tyrosinase Inhibitor

Competitive Substances

L-tyrosine (precursor of melanin) Derivatives

- Competitively binds to enzymes
- Reducing ability
- Acid properties, smooth, anti-aging



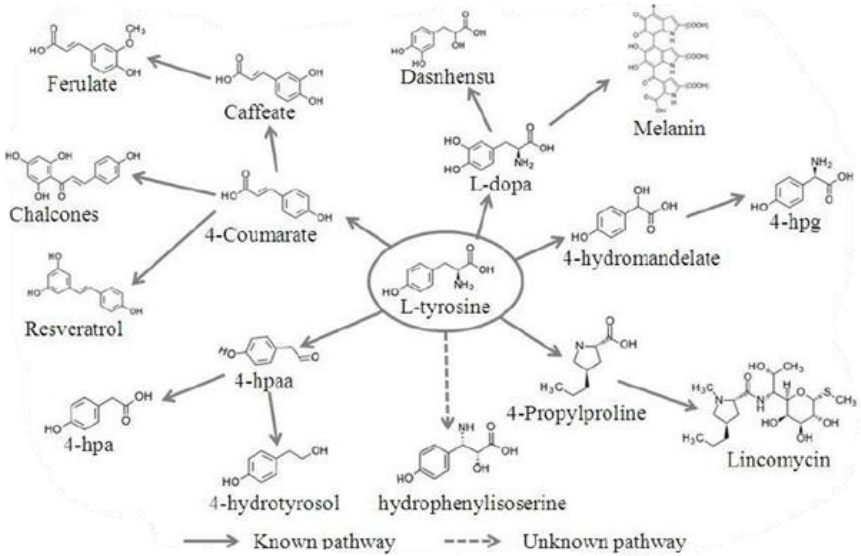
SpecWhite® NFA (Natural) (Ferulic Acid)

SpecWhite® FA (Ferulic Acid)

SpecKare® p-CA (4-Hydroxycinnamic Acid)

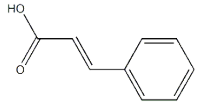
SpecKare® Resveratrol

SpecKare® Resveratrol (Natural)

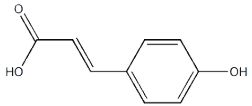


03 Introduction of Tyrosinase Inhibitor

Hydroxycinnamic acids (hydroxycinnamates)

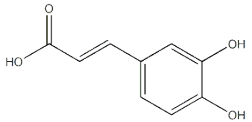


Structure of (trans-) Cinnamic Acid

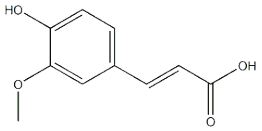


Structure of p-Coumaric Acid

SpecKare® p-CA

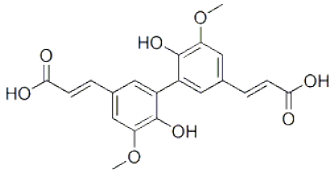


Structure of Caffeic Acid

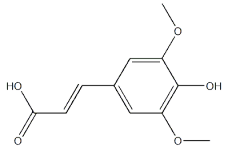


Structure of Ferulic Acid

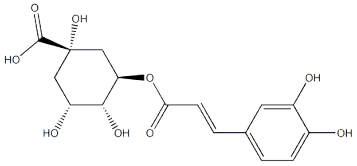
SpecWhite® FA & SpecWhite® NFA



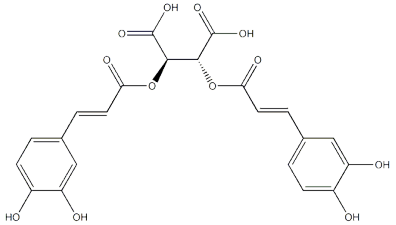
Structure of Diferulic Acid



Structure of Sinapinic Acid



Structure of Chlorogenic Acid



Structure of Cichoric acid

A class of aromatic acids or phenylpropanoids having a C6–C3 skeleton. These compounds are hydroxy derivatives of cinnamic acid. Above phytochemicals can be found in natural plant and food.

03 Introduction of Tyrosinase Inhibitor

Item No.:	110011
Trade Name:	**SpecWhite® FA**
INCI Name:	Ferulic Acid
CAS No.:	1135-24-6
Use Level:	Daily care 0.1-0.5%, special care 0.5-3%
Storage:	Store in cool place. Keep container tightly closed in a dry and well-ventilated place.
Shelf life:	2 years
Package:	1kg, 5kg

Items	Specification
Appearance	Slight yellow powder
Assay	≥99%
Loss on drying	Not more than 0.5%
Heavy Metal	<10ppm
Arsenic	Not more than 3ppm
Melting point	170℃-175℃
Sulfated ash	Not more than 0.1%
Chloride	Not more than 90ppm
Sulfate	Not more than 100ppm

03 Introduction of Tyrosinase Inhibitor

(From Natural Source)

Item No.:	110011-1
Trade Name:	**SpecWhite® NFA**
INCI Name:	Ferulic Acid
CAS No.:	1135-24-6
Use Level:	Daily care 0.1-0.5%, special care 0.5-3%
Storage:	Store in cool place. Keep container tightly closed in a dry and well-ventilated place.
Shelf life:	2 years
Package:	1kg, 5kg

Items	Specification
Appearance	White or off- White powder
Assay	≥98%
Loss on drying	Not more than 1%
Heavy Metal	<10ppm
Smell	Rice bran oil-specific, no peculiar smell
Melting point	169℃-174℃
Sulfated ash	Not more than 5%
Total Plate Count	<1000CFU/gm
Yeast & Mold	<100CFU/gm
Salmonella	Negative
E.Coli	Negative

03 Introduction of Tyrosinase Inhibitor

Commercial Products with FA+VC

SkinCeuticals

Serum 10 Aox+

A daytime introductory vitamin C serum for sensitive skin that offers environmental protection and improves the appearance of aging (2018) **Ascorbic Acid 10.0%+ Ferulic Acid 0.2%,**

SkinCeuticals

C E Ferulic

A daytime antioxidant serum delivers advanced environmental protection, while reducing the appearance of fine lines and wrinkles. (2016) **Ascorbic Acid 15.0%+Ferulic Acid 0.5%**

Ausceuticals

20% Vitamin C Serum (Reformulated)

Combining the highest beneficial concentration of **Vitamin C, E, Ferulic Acid, Glutathione** and Hyaluronic acid, Ausceuticals brings you a potent antioxidant serum that goes on smooth and works deep down below the skin's surface. A pH of 2.9 ensures the perfect conditions for absorption.

SkinCeuticals

Serum 20 AOX+

A daytime antioxidant serum that provides environmental protection with the maximum concentration of pure vitamin C proven effective on skin, while improving the appearance of wrinkles (2018) **Ascorbic Acid 20.0%+Ferulic Acid 0.2%**

The Ordinary

Resveratrol 3% + Ferulic Acid 3%

This formula combines very high concentrations of two of the most powerful and important antioxidants in skincare: Resveratrol and Ferulic Acid.

03 Introduction of Tyrosinase Inhibitor

Commercial Products with FA+VC

Liz K

First C Serum

This treatment is formulated with 13% pure Vitamin C (Absorbic Acid) to help brighten and even out skin tone, fight premature aging, and soothe skin.

Ingredients overview

Water, Butylene Glycol, **Ascorbic Acid**, Alcohol, Propanediol, Propylene Carbonate, Diethoxyethyl Succinate, Arbutin, Portulaca Oleracea Extract, Viscum Album (Mistletoe) Extract, **Ferulic Acid**, Pinus Pinaster Bark Extract, Rosa Canina Fruit Extract, Camellia Sinensis Leaf Extract, Glycyrrhiza Uralensis (Licorice) Extract, Cinnamomum Cassia Bark Extract, Aronia Arbutifolia Extract, Euterpe Oleracea Fruit Extract, Sparassis Crispa Extract, Hericium Erinaceum (Mushroom) Extract, Phellinus Linteus Extract, Lentinus Edodes Extract, Ganoderma Lucidum (Mushroom) Extract, Cordyceps Sinensis Extract, Phaseolus Radiatus Seed Extract, Tagetes Erecta Flower Extract, Cudrania Tricuspidata Bark Extract, Vaccinium Myrtillus Fruit Extract, Cudrania Tricuspidata Fruit Extract, Hippophae Rhamnoides Fruit Extract, Rubus Coreanus Fruit Extract, Superoxide Dismutase, Thioctic Acid, Xanthophylls, Melatonin, Caffeic Acid, **Glutathione**, Nicotinoyl Sh-Pentapeptide-19, Caffeine, Ubiquinone, Hydroxycinnamic Acid, Dipropylene Glycol, Levan, Tremella Fuciformis (Mushroom) Extract, Acetyl Cysteine, Polysorbate 60, Allantoin, Panthenol, Octyldodeceth-25, Decyltetradeceth-25, Octyldodeceth-16, Boerhavia Diffusa Root Extract, Propyl Gallate, Tocopherol, Pentylene Glycol, Adenosine, Polyacrylate Crosspolymer-6, Bis-Peg-18 Methyl Ether Dimethyl Silane, Tromethamine, Ethylhexyl Methoxycrylene, Ammonium Acryloyldimethyltaurate/Vp Copolymer, 1,2-Hexanediol, Carnitine, Arginine, Glycine, Sodium Hyaluronate, Tetrasodium Edta, Sodium Carbonate, Pvp, Fullerenes, Sh-Oligopeptide-1, Peg-240/Hdi Copolymer Bis-Decyltetradeceth-20 Ether, Ethylhexyl Salicylate, Sodium Metabisulfite, Lecithin, Sodium Phosphate, Fragrance

03 Introduction of Tyrosinase Inhibitor

Features of SpecWhite® FA

- ✓ Natural antioxidant agent, effective removal of free radicals
- ✓ Boost the antioxidant effect of Vitamin C & E
- ✓ Photoprotective agent, reducing the damage caused by UV
- ✓ Increase firmness and replenishes lipids to reduce wrinkles
- ✓ Be useful for protection against photoaging and skin cancer
- ✓ Sunscreen effect, work not only at the skin's surface but also inside skin
- ✓ Existing in List of China *(2015)* & International *(2010)* Cosmetic Ingredients Inventory

03 Introduction of Tyrosinase Inhibitor

Mechanism

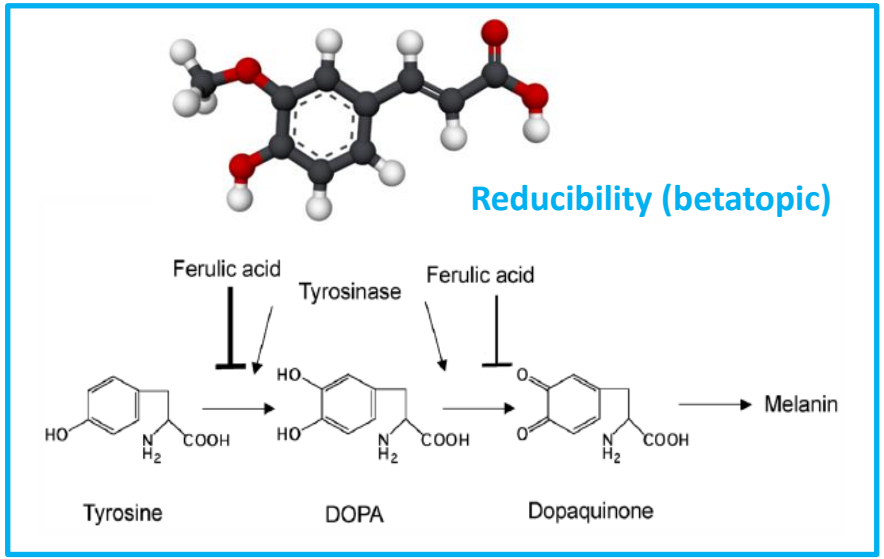
Ferulic acid is a hydroxycinnamic acid (E)-3-(4-hydroxy 3-methoxy-phenyl)prop-2-enoic acid) that inhibits nitrosamine formation, and has also been shown to exert anti-oxidant, anti-inflammatory and antitumor effects in vivo.

In the application of cosmetics, ferulic acid has three main functions for whitening and lightening：

1. Strong antioxidant activity.

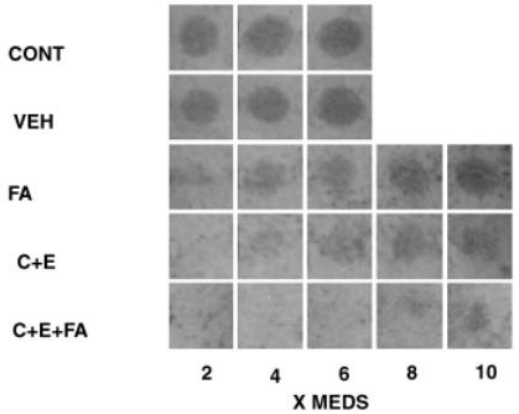
2. Inhibition of tyrosinase activity-Its structure is similar to that of tyrosine and levodopa.

3. It prevents UVB damage-The structure of ferulic acid contains a pair of conjugated double bonds. It is highly absorbent to UV at 290-350nm.



03 Introduction of Tyrosinase Inhibitor

Photoprotection to solar-simulated radiation (provided by daily topical applications of the solution for 4 consecutive days)



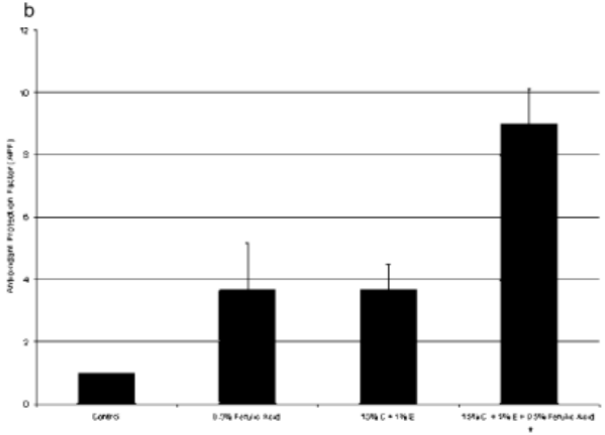


Figure 1. Photoprotection by topical antioxidant formulations. Skin was pretreated with vehicle, 0.5% ferulic acid, 15% vitamin C and 1% vitamin E, 15% vitamin C and 1% vitamin E. and 0.5% ferulic acid and irradiated with solar-simulated radiation 2 x to 10 x minimal erythema dose (MED) at 2 x MED intervals. Evaluation was carried out 1 d later. (a) Visual erythema of photoprotection provided by antioxidant solutions.

- **Both 0.5% ferulic acid alone and 15% L-ascorbic acid + 1% a-tocopherol together provided about 4-fold protection (Fig 1a, b).**
- **Similar photoprotection has been previously reported for 15% L-ascorbic acid + 1% a-tocopherol.**
- **The combination of 15% L-ascorbic acid, 1% atocopherol, 0.5% ferulic acid provided approximately 8-fold protection and was statistically different than ferulic acid alone or the combination of vitamins C and E**

03 Introduction of Tyrosinase Inhibitor

Photoprotection to solar-simulated radiation (provided by daily topical applications of the solution for 4 consecutive days)

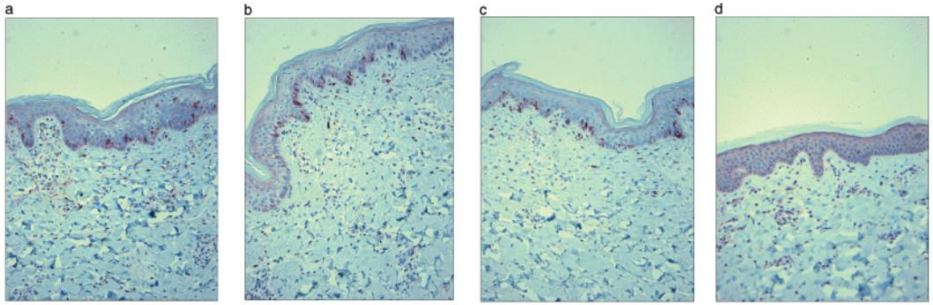


Figure 3 Immunochemistry of activated caspase-3 after solar-simulated irradiation. Skin was pretreated with 0.5% ferulic acid, 15% vitamin C and 1% vitamin E, or 15% vitamin C and 1% vitamin E, and 0.5% ferulic acid and exposed to 4 minimal erythema dose. After 24 h formalin-fixed tissues were stained with antibodies to activated caspase-3. (a) Vehicle-treated irradiated skin; (b) 0.5% ferulic acid-treated irradiated skin. (c): 15% vitamin C and 1% vitamin E-treated irradiated skin; (d) 15% vitamin C and 1% vitamin E, and 0.5% ferulic acid-treated irradiated skin.

Figure 3 shows immunohistochemistry of activation of caspase-3 by 4x MED of solar-simulated light. Activation occurs in both epidermis and dermis (Fig 3a–c); in epidermis, activation is particularly strong in the basal layer. Ferulic acid alone (3b) and vitamins C þ E (3c) provide partial protection but vitamins C, E, and ferulic acid (3d) provides virtually complete protection.

In order to determine whether the addition of ferulic acid augmented this protection, we investigated the relative dose–response protection of these formulations (Fig 4). After 8 MED, ferulic acidtreated skin was about one third positive (Fig 4b) and vitamin C þ E-treated skin was about 15% positive and fluorescence was less intense (Fig 4c). Skin treated with vitamins C, E, and ferulic acid was completely negative (Fig 4d)

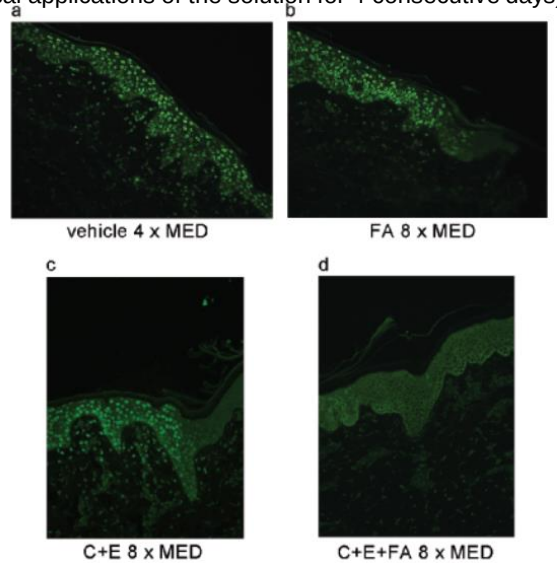


Figure 4 Immunochemistry of thymine dimers after solar-simulated irradiation. Skin was pretreated with vehicle, 0.5% ferulic acid, 15% vitamin C and 1% vitamin E, or 15% vitamin C and 1% vitamin E, and 0.5% ferulic acid and exposed to 4 x or 8 x minimal erythema dose (MED). After 24 h formalin-fixed tissues were stained with antibodies to thymine dimers. (a) Vehicle-treated skin after 4 x MED; (b) 0.5% ferulic acid-treated skin after 8 x MED; (c) 15% C and 1% vitamin E-treated skin after 8 x MED; (d) 15% vitamin C and 1% vitamin E, and 0.5% ferulic acid-treated skin after 8 x MED.

03 Introduction of Tyrosinase Inhibitor

Skin brightening-Ferulic acid can effectively inhibit the production of melanin in B16 cells

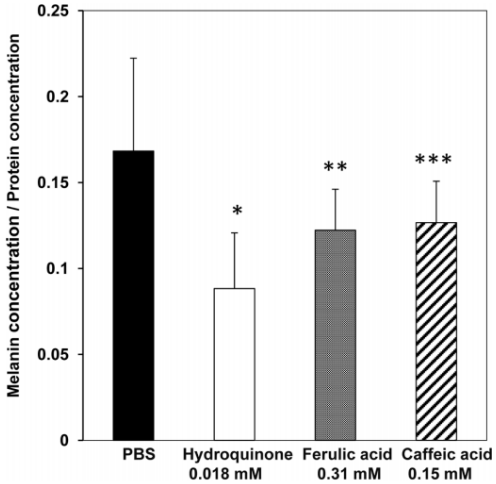


Fig. 2. Ferulic Acid and Caffeic Acid Decreased Melanin Production in B16 Melanoma Cells, as Determined by Examining the Color of the Cell Pellet

Table 1. IC_{50} Values for Toxicity of Ferulic Acid and Caffeic Acid on Melanoma Cell

Sample	IC_{50} (mM)	Concentration of no toxicity (mM)
Ferulic acid	N.I. (0.041 to 1.287)	>1.287
Caffeic acid	0.348 (0.045 to 1.39)	0.173
Hydroquinone	0.053 (0.018 to 1.135)	0.018

N.I.: no toxicity.

Table 2. Effect of Ferulic Acid or Caffeic Acid on Inhibition of DOPA Synthesis from Tyrosine

Sample	Final concentration (μM)	Inhibition ratio (%)
Ferulic acid	51.5	98.2±0.7*
	25.8	42.3±10.4
Caffeic acid	55.5	15.7±3.5
Hydroquinone	0.5	45.1±5.5*

*$p<0.0001$ compared with negative control.

*The change in color was compared with the positive control (hydroquinone) and negative control (PBS). Melanin content was measured at 405 nm. Data are pre sented as the meantstandard deviation (S.D.). The results were analyzed using the Dunn-Bonferroni post-hoc method (n=5). *p<0.0001 compared with the negative control. *p<0.02 compared with the negative control. p<0.03 compared with the negative control.*

03 Introduction of Tyrosinase Inhibitor

Ferulic acid can reduce the inflammation caused by UV irradiation by inhibiting the phosphorylation of Casein kinase 2

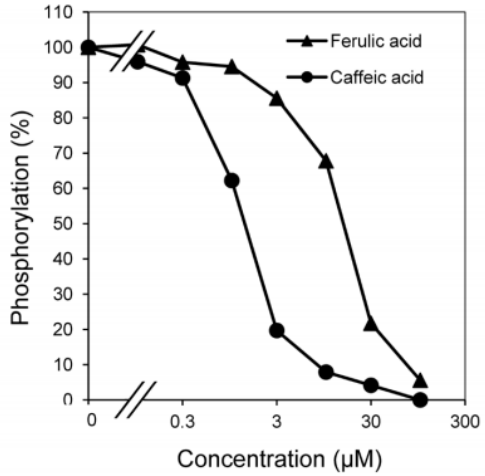
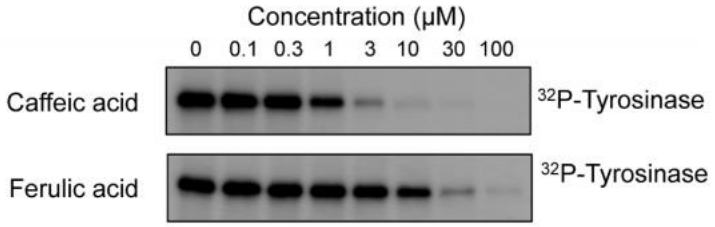


Fig. 3. Inhibitory Effects of Ferulic Acid and Caffeic Acid on the Phosphorylation of Tyrosinase by CK2 in Vitro



Mixtures of recombinant human tvrosinase, CK2 and [p-3P ATP in the presence or absence of ferulic acid or caffeic acid used to check the phosphorylation of tyrosinase by CK2. 3p-Labeled tyrosinase in the reaction mixtures was detected by autoradiography after SDS-PAGE.

03 Introduction of Tyrosinase Inhibitor

Formulation Example: Anhydrous Whitening & Anti-spot Essence

	Product Name	Supplier/ INCI Name	w/w%	Function
A	SpecWhite® VCE	Spec Chem/ 3-o-Ethyl Ascorbic Acid	10	Whitening & Anti-spot Agent
	Butylene Glycol		10	Humectant
	Dipropylene Glycol		5	
	SpecWhite® FA	Spec Chem/ Ferulic Acid	0.5	Whitening & Anti-spot Agent
	Glycerin		69	Humectant
	PrzvFree® CE85	Spec Chem/ Caprylyl Glycol & Ethylhexylglycerin	0.5	Preservative

Procedure:

Mix part A while stirring until completely dissolved.

Properties:

Appearance: slightly yellow liquid

Stability: 1 month @45 ℃ , 1 month@- 18 ℃

Features: This potent Anhydrous Essence with 10% Specwhite® VCE can even out skin tone and go on smooth and works deeps down below the skin surface, restoring youthful skin! By synergistically combining with Specwhite® FA, It also helps soften skin and fade sunspots, and prevents the formation of new free radicals in the skin from the damage.

03 Introduction of Tyrosinase Inhibitor

Tips

Solubility:

1. Soluble in 1,3-propylene glycol, butanediol, dipropylene glycol.
2. In water system: 0.5% SpecWhite® FA + 10% dipropylene glycol + water (pre-dissolve FA in dipropylene glycol and then add it to water)

Dosage: Daily care 0.1-1.0%, special care 1.0-4.0% or more

pH: 3-7

Usage: It is recommended to mix with 1,3-propylene glycol, Butylene Glycol, Isopentyldiol, Glycol (or other solvent) and heat to 60 ℃ before adding to the system.

New Claims（Ectogenic to Endogenic）:

- Recent studies substantiating the shortcomings of sunscreen protection support the need for a different approach to photoprotection. Sun protection factor is measured at 2 mg per cm^2, yet in actual use, sunscreen application is only 0.4–0.5 mg per cm2 (Wulf et al, 1997; Autier et al, 2001).
- Since SPF is an exponential measurement, at reduced levels, relative photoprotection of any sunscreen is no more than 3–4-fold. In addition, SPF is a measurement of UVB only and reveals nothing about UVA photoprotection, protection necessary to protect against oxidative stress.
- Indeed a recent study of three high SPF broad-screen sunscreens revealed that at 2 mg per cm2 application, UVA induced free radical formation was reduced only 55% with even worse protection when application levels were decreased (Haywood et al, 2003). Sunscreens are designed to be shields for the skin, protecting the skin by absorbing harmful UV radiation.
- Since they work at the surface of the skin, they are easily removed by washing or rubbing. Antioxidants, in contrast, are designed to work not only at the skin's surface but also inside skin.

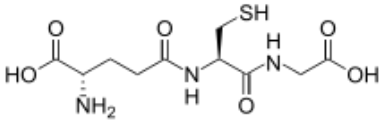
Spec Chem's Anti-photoaging Solution

1	SpecWhite® TA	Tranexamic Acid	凝血酸
2	SpecWhite® FA	Ferulic Acid	阿魏酸
3	SpecWhite® NFA	Ferulic Acid	阿魏酸
4	SpecKare® Resveratrol	Resveratrol	白藜芦醇
5	SpecKare® Resveratrol（Natural）	Resveratrol	白藜芦醇
6	SpecPure® Aqua GBE	Ginkgo Biloba Leaf Extract	银杏（GINKGO BILOBA）叶提取物
7	SpecWhite® G02 (water-soluble)	Glycyrrhiza Glabra (Licorice) Root Extract	光果甘草（GLYCYRRHIZA GLABRA）根提取物
8	SpecWhite® G20	Glycyrrhiza Glabra (Licorice) Root Extract	光果甘草（GLYCYRRHIZA GLABRA）根提取物
9	SpecWhite® G40	Glycyrrhiza Glabra (Licorice) Root Extract	光果甘草（GLYCYRRHIZA GLABRA）根提取物
10	SpecWhite® G90	Glycyrrhiza Glabra (Licorice) Root Extract	光果甘草（GLYCYRRHIZA GLABRA）根提取物

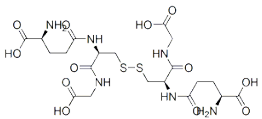
Spec Chem's Anti-photoaging Solution

11	SpecWhite® GA100	Glycyrrgiza Glabra (Licorice) Root Extract Dipotassium Glycyrrhizate Aloe Yohjyu Mastu Ekisu Camelllia Sinensis Extract Morus Alba Root Bark Extract Butylene Glycol Water	光果甘草（GLYCYRRHIZA GLABRA）根提取物 甘草酸二钾 芦荟提取物 茶（CAMELLIA SINENSIS）提取物 桑（MORUS ALBA）根皮提取物 丁二醇 水
12	SpecWhite®GA100	Glycyrrhiza Glabra Root Extract Dipotassium Glycyrrhizate Aloe Vera leaf extract Gamellia sinensis o.ktze Extract Cortex mori extract Butylene Glycol, Aqua.	光果甘草根提取物 甘草酸二钾 芦荟叶提取物 绿茶提取物 桑白皮提取物 丁二醇 水
13	SpecAWK® Plus	Panax Notoginseng Root Extract Gastrodia Elata Root Extract Poria Cocos Sclerotium Extract Glycyrrhiza Uralensis (Licorice) Root Extract Panax Ginseng Root Extract CARTHAMUS TINCTORIUS (SAFFLOWER) FLOWER EXTRACT Scutellaria Baicalensis Root Extract LYCIUM CHINENSE FRUIT EXTRACT Salvia Miltiorrhiza Extract Paeonia Suffruticosa Root Extract Propanediol (Corn Derived)	三七（PANAX NOTOGINSENG）根提取物 天麻（GASTRODIA ELATA）根提取物 茯苓（PORIA COCOS）菌核提取物 甘草（GLYCYRRHIZA URALENSIS）根提取物 人参（PANAX GINSENG）根提取物 红花（CARTHAMUS TINCTORIUS）花提取物 黄芩（SCUTELLARIA BAICALENSIS）根提取物 枸杞（LYCIUM CHINENSE）果提取物 丹参（SALVIA MILTIORRHIZA）提取物 牡丹（PAEONIA SUFFRUTICOSA）根提取物 1，3-丙二醇（玉米来源）

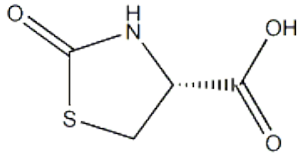
04 Amino Acid & Peptide Derivative and Analogue



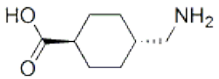
SpecKare® GSH
Glutathione



SpecKare®GSSG
(oxidized Oxidized Glutathione)



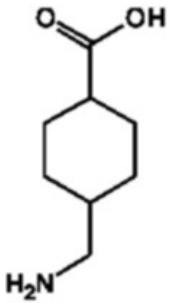
SpecWhite® 05
Oxothiazolidinecarboxylic Acid



SpecWhite® TA
Tranexamic Acid

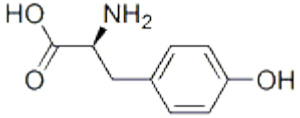
04 Amino Acid & Peptide Derivative and Analogue

Tranexamic acid also is known as a pharmaceutical agent. Already in 2011, it has been entered on the “Model List of Essential Medicines” (EML) of the World Health Organisation (WHO) - in particular for the treatment of trauma after traffic accidents or in the case of haemorrhagic risks and even fatal haemorrhage. Tranexamic acid (= International Nonproprietary Name, INN), from the chemical viewpoint, is an amino acid, and more precisely, we are speaking of trans-4-(aminomethyl) cyclohexanecarboxylic acid.



Structure of tranexamic acid

A chance discovery for dermatology： In dermatology the effects of tranexamic acid have been known for a long time, namely in the context of pigment disorders. The first report on the treatment of melasmas with tranexamic acid dates back to 1979 and comes from an accidental observation after the oral administration of tranexamic acid. In the particular case, the intensity of a melasma was significantly reduced within a period of two to three weeks.



Structure of Tyrosine

1)18th Meeting of the WHO Expert Committee; 2)Sadako N, Treatment of melasma with tranexamic acid, The Clin Rep 1979; 13: 3129-31

04 Amino Acid & Peptide Derivative and Analogue

Melasmas or hyperpigmentations form in a variety of ways.

They are triggered by miscellaneous endogenic and exogenous influences such as:

1. UV radiation of the sunlight
2. photosensitization, or in other words, the reduced sensitivity threshold of the skin to light caused by essential oils for instance
3. hormonal influences, as for example during pregnancy
4. inflammation mediators such as prostaglandins and cytokines (post-inflammatory hyperpigmentation)
5. AGE (Advanced Glycation Endproducts), or in other words, products that form in the body due to the reaction of proteins or lipids with carbohydrates; they are held responsible for a variety of health implications
6. other deposits of endogenous metabolic products

04 Amino Acid & Peptide Derivative and Analogue

Mechanism of action of tranexamic acid (TXA) in Melasma

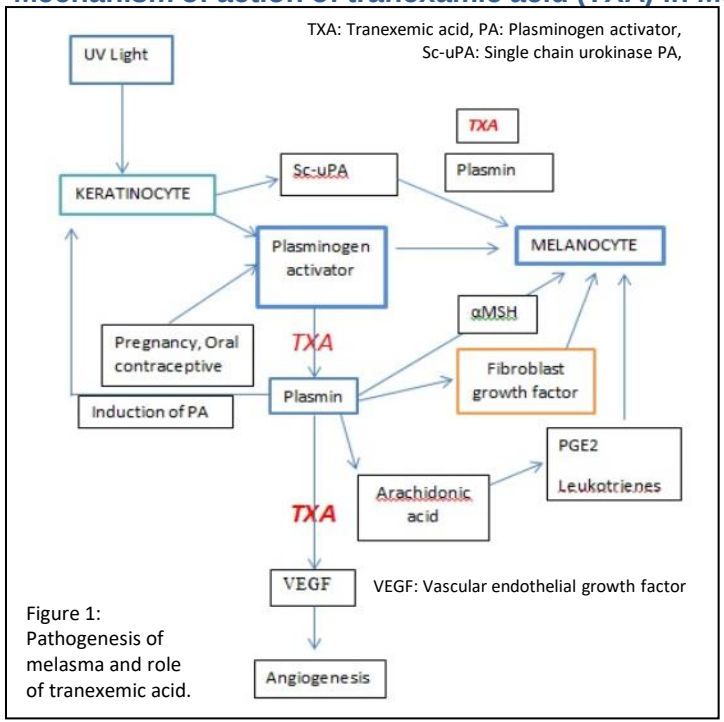


Figure 1: Pathogenesis of melasma and role of tranexemic acid.

- TXA prevents UV-induced pigmentation by interfering with the structure of plasminogen and preventing the binding of plasminogen to the lysine-binding sites of keratinocytes.
- The consequences of such event are less free arachidonic acid leading to a reduced ability to produce prostaglandins and thus decreased melanocyte tyrosinase activity and melanogenesis.
- Also, action of TXA on angiogenesis via plasmin could also play a contributory role in its action on melasma.
- Blocking of the Sc-uPA pathway may be another mechanism through which TXA reduces hyperpigmentation.
- TXA is found to be similar to tyrosine in the part of its structure, which can competitively inhibit the activity of tyrosinase.

3) Poojary S, Minni K (2015) Tranexamic Acid in Melasma: A Review. Pigmentary Disorders 2: 228.

04 Amino Acid & Peptide Derivative and Analogue

Commercial Products

Shiseido

Aqualabel Balance Care Lotion Moist

Brightening and hydrating lotion with Tranexamic Acid and Dipotassium Glycyrrhizate to lighten pigmentation.

Shiseido

White Lucent Luminizing Infuser

A beautifully bright complexion can be yours with this essence-rich brightening softener.

Shiseido

Aqualabel Balance Care Milk

Aqualabel Balance Care Milk is a light, moisturising milk with pigmentation lightening ingredients.

Medicube

Red Erasing Camu Camu Serum

Helps to soothe the skin redness and it's safe to use since it contains Centella Asiatica and Portulaca extract. With Vitamin C that helps dark melanin pigmentation in becoming light again.

The Inkey List

The Tranexamic Acid Night Treatment

An overnight treatment that helps target the appearance of hyperpigmentation and dark spots for a more even skin tone.

04 Amino Acid & Peptide Derivative and Analogue

Commercial Products

DMSR Complexion
Skin Care
Liposomes

SHISEIDO
MELANOREDUC
E CR

CLE DE PEAU
BEAUTE
BRIGHTENING
SERUM SUPREME

IPSA THE TIME
RESET AQUA

04 Amino Acid & Peptide Derivative and Analogue

Product Name: SpecWhite® TA

INCI Name: Tranexamic acid

CAS No.: 1197-18-8

Dosage: Daily Care: 0.5-2%

Usage: Add at the last step, temperature below 40℃

Package: 1KG/25KG

Storage: Store in cool place. Keep container tightly closed in a dry and well-ventilated place.

Shelf life: 3 years

Application: Water/Lotion/Emulsion/Serum/Cream

Preservative Free:

Items	Specification
Characteristics	A white crystalline powder, freely soluble in water and in glacial acetic acid, practically insoluble in alcohol and in acetone
Identification	IR
Loss on drying	Not more than 0.5%
pH	7.0-8.0
Related substance	Impurity A: ≤ 0.1%
	Impurity B: ≤ 0.2%
	Any other impurity: ≤ 0.1%
	All other Impurities: ≤ 0.2%
Chlorides	≤140ppm
Heavy metals	≤ 10ppm
Assay	99.0-101.0%
Sulphated ash	≤ 0.1%
Conclusion	Conform with BP2009

04 Amino Acid & Peptide Derivative and Analogue

Features of Specwhite® TA :Spot Removing & Lightening

- **Compliance with Japanese Pharmacopoeia 4th**
- **Mild to skin and mucous membrane (CAMVA & BCOP)**
- **Strict Quality control on heavy metals and microorganism**
- **Verified by clinical test,** Tranexamic acid is suitable to all kinds of skin for removing pigmentation, lightening skin and reducing spots, such as:
  - Pigmentation after sun exposure
  - Dark spots (melasma, freckles and senile lentigo and etc.)
  - Sensitive skin, acne and inflammation
  - Postoperative care after laser, pulsed light treatment

04 Amino Acid & Peptide Derivative and Analogue

Safety—Japanese Pharmacopoeia(the 4th) by JFRL accredited by the Japanese Government

JFRL

Japan Food Research Laboratories
Accredited by the Japanese Government
52-1 Motoyoyogi-cho, Shibuya-ku, Tokyo 151-0062, Japan

CERTIFICATE OF ANALYSIS

Client: SPEC-CHEM INDUSTRY INC.
No. 10 Wanshou Road PuKou Economic Development Zone (ShiLin Industrial Park), Nanjing, Postal 211800, P.R. of China

Sample name: SpecWhite TA (Tranexamic acid)

Received date: November 21, 2017

This is to certify that the following result(s) have been obtained from our analysis on the above-mentioned sample(s) submitted by the client.

Test Result(s)

Test Item	Result	QL	N	M
Tranexamic Acid	-----	------	1	
Identification	Conformable	------		
pH	Conformable (7.4)	------		
Purity	-----	------		
Clarity and color of solution	Conformable	------		
Chloride	Conformable	------		
Heavy metals	Conformable	------		
Arsenic	Conformable	------		
Related substances	Conformable	------		
Loss on drying	Conformable (0.1 %)	------		
Residue on ignition	Conformable (Not more than 0.05 %)	------		
Assay (content)	Conformable (99.8 %)	------		
Description (not indicating standards for conformity)	-----	------		
Color and Physical form	White crystalline powder	------		
Solubility	-----	------		
Water	Freely soluble	------		
Ethanol (99.5)	Practically insoluble	------		

QL: Quantitation limit N: Notes M: Method

Notes

1:The Japanese Pharmacopoeia, Seventeenth Edition.

04 Amino Acid & Peptide Derivative and Analogue

Safety— Specwhite® TA (up to 20% in water, MB Research Labs, USA)

Chorioallantoic Membrane Vascular Assay (CAMVA)

CONCENTRATION: 0.5%	EGG NUMBER									
OBSERVATIONS	31	32	33	34	35	36	37	38	39	40
Normal	X	X	X	X	X	X	X	X	X	X

CONCENTRATION: 1%	EGG NUMBER									
OBSERVATIONS	11	12	13	14	15	16	17	18	19	20
Normal	X	X	X	X	X	X		X	X	X
Capillary injection							X			

- **The RC50 and 95% confidence limits are: 4.4%(2.2%,9.0%)**

Bovine Corneal Opacity and Permeability Test (BCOP)

Cornea No.	Corrected Opacity Scores								Corrected O.D.
	10 Minute Scores				2 Hour Scores				
1	C1	2	C2	2	C1	1	C2	1	-0.006
2	C1	1	C2	2	C1	0	C2	1	-0.012
3	C1	0	C2	1	C1	0	C2	0	-0.004
4	C1	4	C2	4	C1	2	C2	3	-0.015
5	C1	5	C2	4	C1	1	C2	2	-0.011
Corrected Mean Optical Density =									-0.010
2 Hour Corrected Mean Opacity Score[2] =									1.1

Calculated *In Vitro* Irritancy Score
1.1 + 15 (-0.010)
1.1 + -0.15
0.95

- **The calculated In Vitro Irritancy Score of Tranexamic acid (ViaDerm TXA / SpecWhite TA) 20% in Water is 0.95; therefore, the test article is considered a mild irritant according to Gautheron et al. No category can be assigned regarding the UN GHS Category, as per the OECD Test Guideline No. 437.**

04 Amino Acid & Peptide Derivative and Analogue

Safety—Chemical Test (heavy metal) & Microbial Test

1) Chemical Test: Arsenic, Antimony, Cadmium, Chromium, Cobalt, Lead, Mercury, Nickel, Platinum
2) Microbial Test: Staphylococcus aureus, Canadida albicans, bile-tolerant Gram-negative bacteria

SAMPLE DESCRIPTION: Sample in bag

TEST RESULT(S):

Test Item(s)	Unit(s)	Test Method(s)	Test Result(s)	Method Detection Limit
Arsenic	mg/kg	1-1)	Not detected	0.2
Antimony	mg/kg		Not detected	0.2
Cadmium	mg/kg		Not detected	0.2
Chromium	mg/kg		Not detected	0.2
Cobalt	mg/kg		Not detected	0.2
Lead	mg/kg		Not detected	0.2
Mercury	mg/kg		Not detected	0.2
Nickel	mg/kg		Not detected	0.2
Platinum	mg/kg	1-2)	Not detected	10

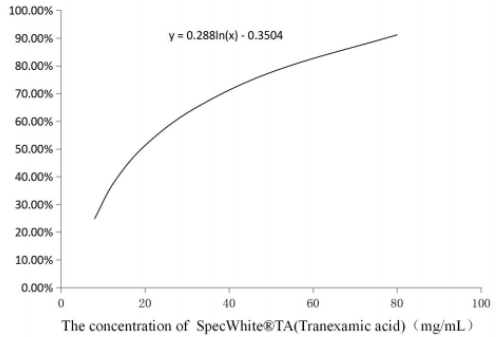
Test items	Test methods	Test results
Staphylococcus aureus /g	2)	Not detected
Bile-tolerant Gram-negative bacteria /g		Not detected
Candida albicans /g		Not detected

Chemical Test (Arsenic, Antimony, Cadmium, Chromium, Cobalt, Lead, Mercury, Nickel, Platinum) & Microbial Test (Staphylococcus aureus, Canadida albicans, bile-tolerant Gram-negative bacteria) are not detected.

04 Amino Acid & Peptide Derivative and Analogue

In-Vitro test–Inhibiting Effect of Specwhite® TA on Tyrosinase Activity

Sample	EC50（mg/ml）
SpecWhite®TA (Tranexamic acid)	3.832



Inhibiting effect on SpecWhite®TA on Tyrosinase Activity (single phenol enzyme activity)

Conclusion

Through determination of tyrosinase activity inhibition, the result shows that SpecWhite®TA (Tranexamic acid) EC50 value is 3.832mg/ml。

04 Amino Acid & Peptide Derivative and Analogue

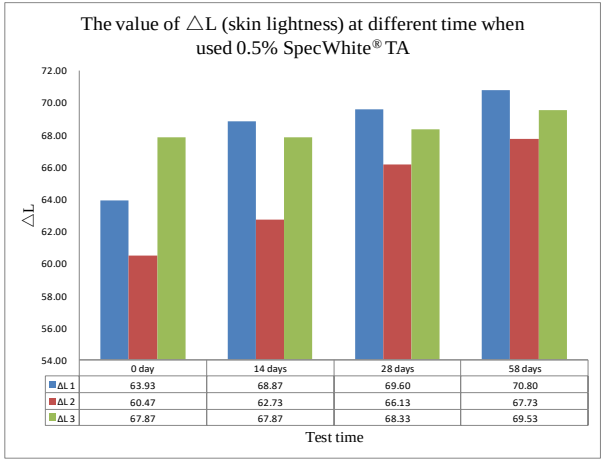
In-ViVo test—Skin Lightening & Whitening & Anti-spot

Product:	2.5% SpecWhite® TA and 0.5% SpecWhite® TA
Subjects：	2.5%:15 female, 0.5%:15 female
Age range:	27 - 53years old
Test Site：	Face
Period:	8 weeks
Test Parameters：	Determination of skin color difference is expressed in△L and△E; △L(Difference in lightness between in two spots, each certain value-reference site); △E（a parameter to classify the sensed color difference, each certain value -reference site).
Temperature:	20℃- 25℃;
Humidity:	40% - 60%
Application Frequency：	Twice a day after cleaning face in the morning & evening
Design of Study:	Aim to assess the lightening effect of the test cosmetic product after 14 days,28 days and 56days application in the female subject.

Amino Acid & Peptide Derivative and Analogue

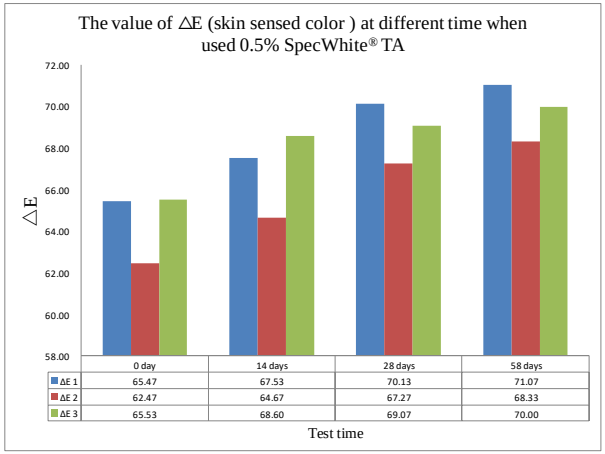
In-ViVo test—Skin Lightening & Whitening Results

The △L and △E improved when using 0.5% SpecWhite® TA, comparing with the untreated



	0 day	14 days	28 days	58 days
ΔL 1	63.93	68.87	69.60	70.80
ΔL 2	60.47	62.73	66.13	67.73
ΔL 3	67.87	67.87	68.33	69.53

Comparing with the untreated, skin lightness improved significantly, skin lightness increased by 3.74% after 14days, 6.13% after 28days, 8.21%after 56days by treating with 0.5% SpecWhite® TA;



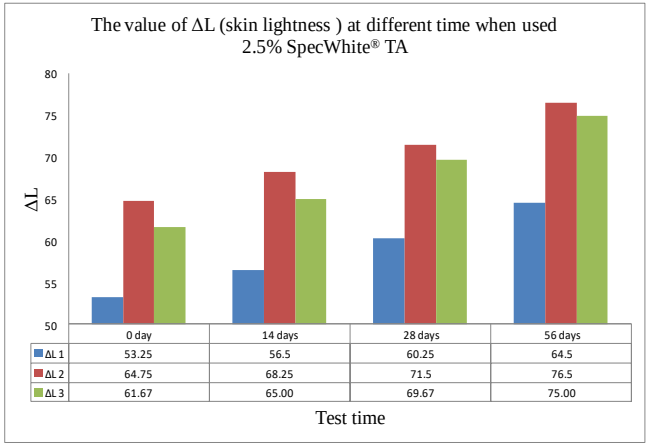
	0 day	14 days	28 days	58 days
ΔE 1	65.47	67.53	70.13	71.07
ΔE 2	62.47	64.67	67.27	68.33
ΔE 3	65.53	68.60	69.07	70.00

Comparing with the untreated, skin sensed color improved significantly, skin whiteness improved by 3.74% after 14days, 6.68% after 28days, 8.23% after 56 days by treating with 0.5% SpecWhite® TA;

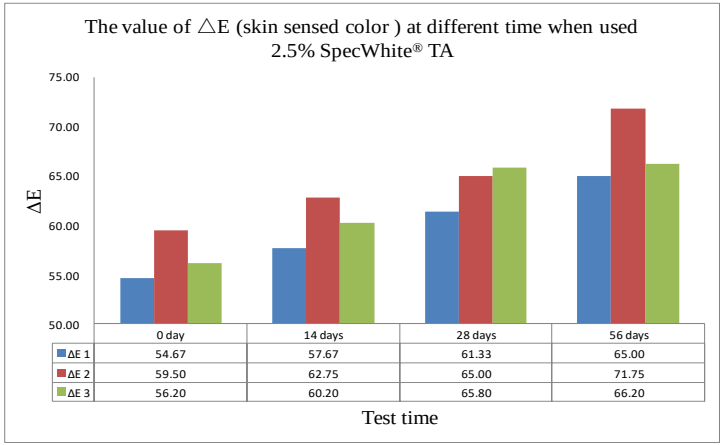
Amino Acid & Peptide Derivative and Analogue

In-ViVo test—Skin Lightening & Whitening Results

The △L and △E improved when using 2.5% SpecWhite® TA, comparing with the untreated



Comparing with the untreated, skin lightness improved significantly. Skin lightness improved by 7.83% after14 days,12.11% after 28 days, 20.22% after 56 days by treating with 2.5% SpecWhite® TA .



Comparing with the untreated, skin sensed color improved significantly, skin whiteness improve 6.02% after 14days, 12.77% after 28days, 19.12 % after 56 days by treating with 2.5% SpecWhite® TA.

04 Amino Acid & Peptide Derivative and Analogue

In-ViVo test—Skin Lightening & Whitening Results

Lightening & Whitening Pictures (0.5% SpecWhite® TA subject)

Fig. 1 0 day

Fig. 2 14 day

Fig. 3 28 day

Fig. 4 56 day

04 Amino Acid & Peptide Derivative and Analogue

In-ViVo test—Anti-Spot Results

Anti-Spot pictures (0.5% SpecWhite® TA subject)

Fig. 1 0 day

Fig. 2 14 days

Fig. 3 28 days

Fig. 4 56 days

Comparing with the untreated, spot amount & spot area & spot area ratio declined significantly after 14 days. Spot amount declined by 4.17% after 14 days, 8.37% after 28 days,12.50% after 56 days. Spot area decline 12.04% after 14 days,18.52% after 28 days, 25.73% after 56 days. Spot area ratio decline 10.81% after 14days,18.92% after 28 days,29.73% after 56 days when treating with 0.5% SpecWhite® TA.

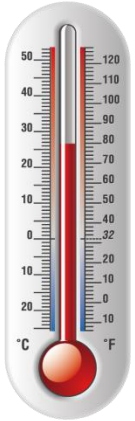
Amino Acid & Peptide Derivative and Analogue

Stability-Effect of Temperature on TA(HPLC)

Prepare 2.5% TA solution with purified water. Put the 2.5% TA solution at 25 ℃ and 50 ℃ respectively for 10 days.

Results: There was no significant change in the appearance and odor, and the content were compared as follows

Condition		Peak Area	Relative Amount
2.5% TA @pH=6.7	25℃	446044	100%
2.5% TA @pH=6.7	50℃	447776	100%
Reference substance	Initial	424984	100%



Amino Acid & Peptide Derivative and Analogue

Stability-Effect of pH on TA(HPLC)

Prepare 2.5% TA solution with purified water. Adjust the pH to 3.0, 4.0, 5.0, 6.0, 6.5, 8.0 respectively for testing.

Results: There was no significant change in the appearance and odor during pH 4.0-6.5, and the content were compared as follows.

pH of Sample	Peak Area	Relative Amount %
PH4.0	943456	100%
PH5.0	925557	100%
PH6.0	948076	100%
PH6.5	946341	100%
PH8.0	840593	89.2%

SepcWhite® TA has a very wide application pH range: 4.0-6.5, and will not be affected by increasing pH during this range.

04 Amino Acid & Peptide Derivative and Analogue

Formulation Example 1: Whitening & Lightening & Spot-removing Gel (0.5% SpecWhite® TA)

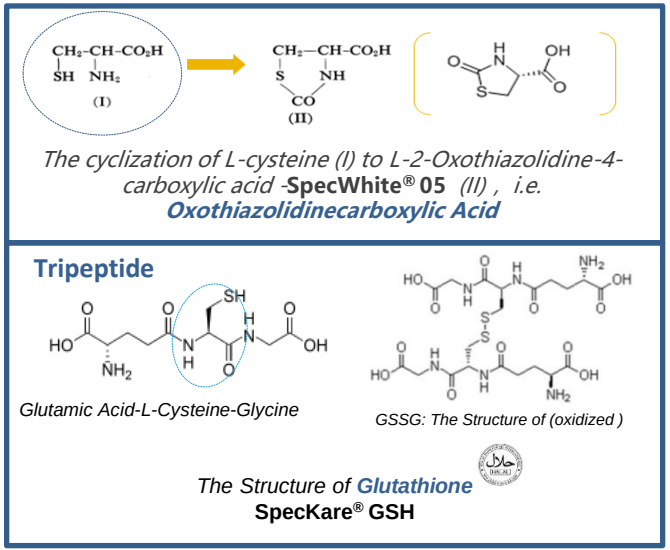
	Product Name	INCI Name	Dosage(%)	Supplier
A	EMT-10	Hydroxyethylacrylate / Sodium Acryloyldimethyl Taurate Copolymer	1.2	
	CC	Carbonicacid,dioctylester	2.0	
	EH	Ethylhexyl Ethylhexanoate	2.0	
	CDM3526	C26-28 Alkyl Dimethicone	0.2	
B	Glycerin	Glycerin	8.0	
	SpecThem™ XTG200	Xanthan Gum	0.18	SC
	SpecThem™ SCB21	Carbomer	0.15	SC
	SpecKare™ ALLA	Allantion	0.1	SC
	H-200	Glycerin (and) Glyceryl Polyacrylate	6.0	
	Water	Aqua	To 100	
	SpecKare™ HAL	Sodium Hyaluronate(1%Liquid)	5.0	SC
	SpecKare™ NMF50	Betaine	2.0	SC
C	TEA	Tris(2-Hydroxyethyl)Amine	0.13	
	ParbFree® PCG	Caprylyl Glycol（and）Phenoxyethanol	0.8	SC
	Fragance		0.02	
	SpecWhite® TA	Tranexamic acid	0.5	SC

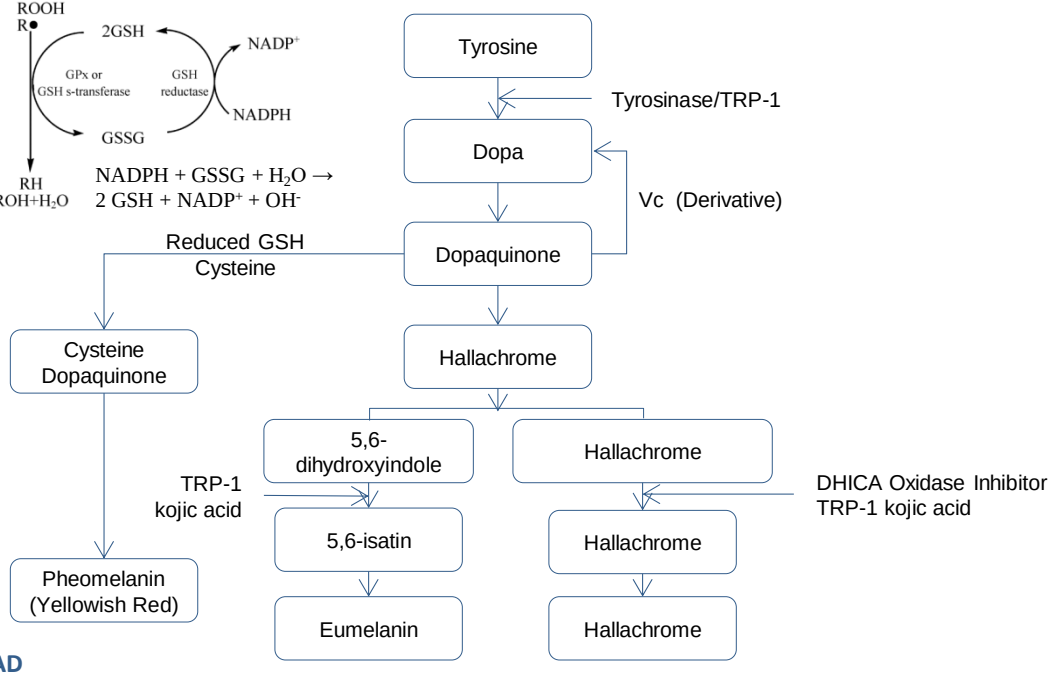
04 Amino Acid & Peptide Derivative and Analogue

Formulation Example 2: Whitening & Lightening & Spot-removing Gel (2.5% SpecWhite® TA)

	Product Name	INCI Name	Dosage(%)	Supplier
A	EMT-10	Hydroxyethylacrylate / Sodium Acryloyldimethyl Taurate Copolymer	1.2	
	CC	Carbonicacid,dioctylester	2.0	
	EH	Ethylhexyl Ethylhexanoate	2.0	
	CDM3526	C26-28 Alkyl Dimethicone	0.2	
B	Glycerin	Glycerin	8.0	
	SpecThem™ XTG200	Xanthan Gum	0.18	SC
	SpecThem™ SCB21	Carbomer	0.15	SC
	H-200	Glycerin (and) Glyceryl Polyacrylate	6.0	
	Water	Aqua	To 100	
	SpecKare™ HAL	Sodium Hyaluronate(1%Liquid)	5.0	SC
	SpecKare™ NMF50	Betaine	2.0	SC
C	TEA	Tris(2-Hydroxyethyl)Amine	0.13	
	ParbFree® PCG	Caprylyl Glycol（and）Phenoxyethanol	0.8	SC
	Fragance		0.02	
	SpecWhite® TA	**Tranexamic acid**	**2.5**	**SC**

04 Amino Acid & Peptide Derivative and Analogue





Other Peptdies: **SpecPed® LCS/T30P/DE12P/H2P/N1P**

Nice Pink Colore: **SpecWhite® KA (fermented)/SpecWhite® KAD**

04 Amino Acid & Peptide Derivative and Analogue

Product Name: SpecKare® GSH （HALAL Certificated）
INCI Name: Glutathione
CAS No.: 70-18-8
EC No.: 200-725-4
Dosage: 0.5-5.0%
Usage: Very stable, Can be added before or after emulsion.
Package: Customization
Storage: Keep in dark and cool place
Shelf life: 2 years
Application: Lotion/Emulsion/Serum/Cream etc.
Preservative Free:

Items	Specification
Appearance	White Crystalline powder
Content	More than 98%
Identification A. Specific optical rotation B. IR	[α]D20 : -15.5 º ~ -17.5 º Comply with the reference
Appearance of solution	Clear and Colorless
Solubility	Freely soluble in water, very slightly soluble in ethanol

04 Amino Acid & Peptide Derivative and Analogue

The Features of SpecKare® GSH:

- ✓ Natural Origin by Biological Fermentation
- ✓ Proved Safety by invitro & invivo test
- ✓ Protect mitochondria from oxidative damage, a powerful antioxidant agent
- ✓ Lighten & whiten skin
- ✓ Boost antioxidant effect of VC & VE
- ✓ Fighting inflammation
- ✓ Stimulate detoxification system
- ✓ Water-soluble, easy to use with more formulation flexibility

Suggested Application:

- ✓ Urban skin problems (Stress, Pollution, Glycosylation)-Wake up & immediate repair skin and let it glow again
- ✓ Dull Skin-Lightening & Whitening skin
- ✓ Aging Skin-Scavenging free radical, Keep youthful & Lock time

04 Amino Acid & Peptide Derivative and Analogue

3.1 Mutagenicity-Jiangsu Provincial Center for Diseases Control and Prevention

An "Ames test" of SpecKare® GSH was performed on Salmonella Typhimurium/Reverse Mutation Assay on Strain: TA 97a,TA98,TA100 and TA102 With Hygienic standard for cosmetics(2015),ministry of health of the peoples republic of China method.

Method: Standard plate incorporation method

Add 0.1 ml test strain and 0.1 ml sample and 0.5ml S9 to top medium, mix then add to minimum Nutritionla Medium, 3 replicated per concentration, 4does.

Vehicle control is sterile water, 4 positive control is dexon, NaN3, 2-AF, 1,8-DHAQ is dissolved by sterile water and DMSO respectively, plates were inverted and incubated at 37 for 48h, record.

Result: No positive result were found with all the test strains in the presense and absence of metabolic activation system.

Result:

Table 1 Mean of the reverting colonies from Ames test of SpecKare™ GSH(L-Glutathione Reduced)

Dosage(ug/plate) Sample	TA97		TA98		TA100		TA102	
	+S9	–S9	+S9	–S9	+S9	–S9	+S9	–S9
625	123±9	128±8	33±5	30±1	99±10	123±9	274±18	278±12
1250	126±11	129±4	32±3	30±1	104±9	124±11	287±20	288±6
2500	118±20	126±16	36±5	37±5	90±5	147±14	284±17	287±19
5000	119±6	129±3	33±4	38±3	98±15	135±5	294±8	313±18
	140±2	114±10	31±2	32±4	117±8	124±10	313±12	276±9
Sterile water0.1ml	128±4	117±15	33±2	32±3	118±6	126±5	331±6	293±15
Dexon 50		1134±106		1279±271				817±118
2-AF 10	1124±117		1163±44		1102±66			
NaN_3 1.5						1223±58		
1,8-DHAQ 50							830±72	

3.2 Human skin irritation (Result: None of 30 subjects has adverse reaction after patching test)

SpecKare® GSH was diluted into 10% with distilled water on 30 volunteers [30 in total (4males, 26 females), aged from 18 to 60], and (0.020g-0.025g) was putted into the chamber and fixed onto the subjects' back by special adhesive tape. After 24h the patches were removed, dermatologist observed the irritation reaction at 0.5h, 24h, 48h after the patch removed and recorded the result according to the "skin adverse reaction grading standard" in STSC.

Method: *Safety and Technical Standards for Cosmetics, Version 2015*

Negative control: Distilled water.

Level	Score	Reaction
–	0	Negative reaction
±	1	Equivocal / uncertain reaction; Only a mild erythema
+	2	Weak positive reaction (erythema reaction); erythema, infiltration, edema, pimples
++	3	Strong positive reaction (herpes reaction); erythema, infiltration, edema, rash, herpes; reaction can exceed the test area
+++	4	Extreme positive reaction (fusion of herpes reaction); obvious erythema, severe infiltration, edema, fusion of herpes; reaction beyond the pilot area

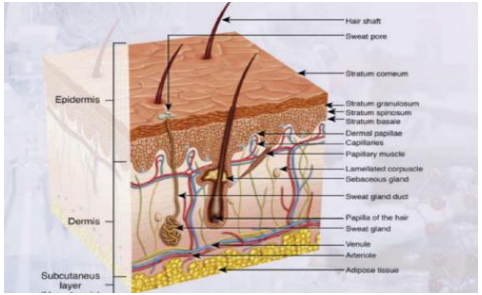
Test results

Group	Observing time	Number of subjects	Number of subjects have adverse reaction					
			0	1	2	3	4	Sum (1-4)
Testing sample	0.5h	30	30	0	0	0	0	0
	24h	30	30	0	0	0	0	0
	48h	30	30	0	0	0	0	0
Negative control	0.5h	30	30	0	0	0	0	0
	24h	30	30	0	0	0	0	0
	48h	30	30	0	0	0	0	0

04 Amino Acid & Peptide Derivative and Analogue

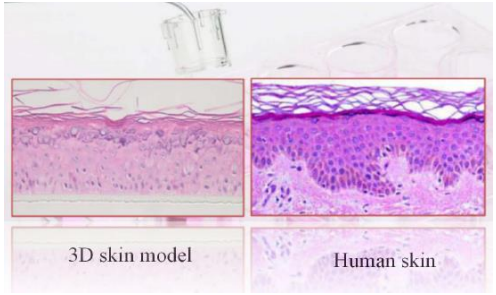
3.3 Skin irritation test-By 3D Reconstructed Human Epidermis (Episkin)-(OECD 439-CALT-BIO: Testing the skin stimulation of the sample

Cosmetics and skin interactionsa



Acute skin irritation is a local, reversible inflammatory response resulting from normal skin contact with irritating drugs. The mechanism of skin irritation occurs because the test substance contacts the skin by expanding, infiltrating or destroying the epidermal barrier, and then acting on the stratum corneum cells to produce a toxic effect.

Highly Similar



The method employs a three dimensional human skin model with a functional epidermal stratum corneum structure, which is evaluated by the percentage of the stimulating or corrosive threshold dose level defined by the test substance after the skin is exposed and the cell viability is decreased by measurement. The irritant strength of the test substance.

Testing Process of Episkin Model

Result of skin irritation in vitro on Episkin skin model

Group	Positive control (5% SDS)	Negative control (pure water)	10% SpecKare ® GSH
Mean OD±SD	0.031±0.00	0.741±0.01	0.621±0.01
Viability (%)	4.00±0.58	100	83.8±0.01

Conclusion: (according to OECD TG 439 chemicals in vitro skin irritation) reconstructed human epidermis test method， under the testing conditions, the tissue viability of the sample " 10% SpecKare ® GSH " is 83.8% (viability >50%) and it is considered as no skin irritation.

Amino Acid & Peptide Derivative and Analogue

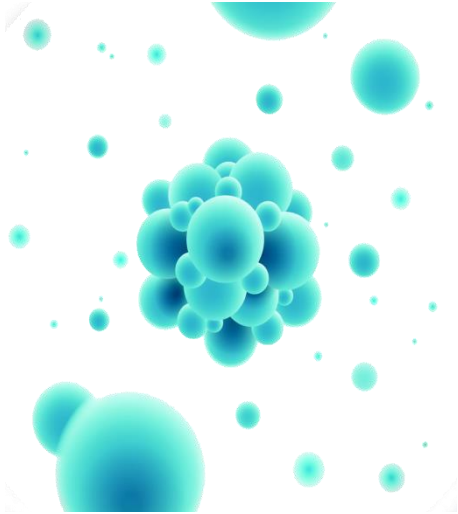
3.4 h-CLAT Skin sensitization (Cytotoxicity CD54/CD86 Testing)-(OECD 442E 2017)

Cytotoxicity Result: Result of GSH in vitro cytotoxicity (Mean±SD)

	Blank Control	Solvent Control	0.5%	0.1%	0.005%
Viab (%)	-	95.58±0.76	95.65±1.12	96.49±0.42	95.58±0.76

CD54/CD86 prediction result: h-CLAT result of GSH (Mean±SD)

	0.5%	0.1%	0.005%
RFI CD54	101.47±2.6	101.84±6.76	138.79±3.90
RFI CD86	88.53±1.66	122.21±8.53	106.18±6.24



Conclusion: **According to OECD 442E, mean cell viability of 0.5%, 0.1%, 0.005% substance- SpecKare® GSH are 95.65%, 96.49%, 95.58%, the cell viability of 0.5% and less than 0.5% concentration substance are above 50%. Mean RFI CD54 is less than 200. Mean RFI CD86 is less than 150. The Substance- SpecKare® GSH is non-skin sensitizer for dendritic cells.**

Amino Acid & Peptide Derivative and Analogue

3.5.1 Eye irritation (in vitro)-1% SpecKare® GSH-CAWVA (EURL ECVAM DB-ALM)

Score	Vascular response	Code	Description
0	Normal	N	No response was observed, and CAM was normal
1	Ghost Vessels	G	The vessel was white without blood flow and vessel tube was clear.
2	Capillary Injection	C	Capillary Injection or blood flow of small vessel on CAM was increased
3	Minimal Hemorrhaging	MH	Less than 25% of the area was covered by fine bleeding points in the ring
4	Slight Hemorrhaging	SL	25-50% of the area was covered by bleeding points in the ring
5	Moderate Hemorrhaging	Mod	A mass or 50-75% of the area was covered by bleeding points in the ring
6	Severe Hemorrhaging	SH	More than 75% of the area was covered by bleeding points in the ring; dark brown crusts may occur.

The results of screening tests and formal experiments are shown in the table below.

Form 1 Screening test

Number	1	2	3	4	5	6	7	8	9
Concentration（%）	1	1	1	0.5	0.5	0.5	0.1	0.1	0.1
Response	N	MH	N	N	N	N	N	N	N

Form 2 Formal test

Concentration（1%）											
Number	1	2	3	4	5	6	7	8	9	10	Positive
Response	N	N	N	MH	N	MH	N	N	G	N	3/10
Concentration（0.5%）											
Number	1	2	3	4	5	6	7	8	9	10	Positive
Response	N	N	N	G	N	N	N	N	N	N	1/10
Concentration（0.1%）											
Number	1	2	3	4	5	6	7	8	9	10	Positive
Response	N	MH	N	N	N	N	N	N	N	N	1/10

Conclusion: according to the criteria of CAMVA, under the experimental conditions, the sample “1% SpecKare® GSH” has no eye irritation!

3.5.2 Eye/Ocular irritation (in vitro)-0.5% SpecKare® GSH-nonirritating (OECD 437 2013)

BOCP: Bovine cornea opacity and permeability test

IVS	Prediction
≤3	No Category
> 3，≤55	No prediction can be made
>55	Category 1

The results of opacity, permeability (OD values) and calculated IVS are showed as table 1.

Table 1. The results of in vitro score

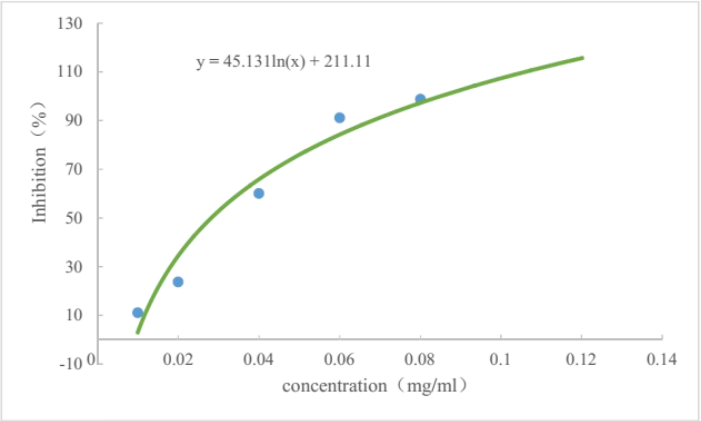
Corrected Opacity (mean±SD)	Corrected OD (mean±SD)	IVS (mean±SD)
-0.2969±0.4306	0.0098±0.0164	-0.1494±0.6630

Conclusion: according to the OECD 437 (2013) Standard for "Bovine cornea opacity and permeability test method for identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage", under the conditions of this study, the IVS of the test article is-0.1494, which calssified as No Category. The sample "5% L-Glutathione Reduced" is non eye irritants.

Amino Acid & Peptide Derivative and Analogue

3.5 Inhibiting Effect of SpecKare® GSH on Tyrosinase Activity-Skin Whitening

sample	concentration	Oxidation rate（%）
Vc	0.2 mg/ml	95.2%
SpecKare™ GSH	0.08 mg/ml	98.6%
SpecKare™ GSH	0.06 mg/ml	90.1%
SpecKare™ GSH	0.04 mg/ml	60.1%
SpecKare™ GSH	0.02 mg/ml	23.9%
SpecKare™ GSH	0.01 mg/ml	11.3%



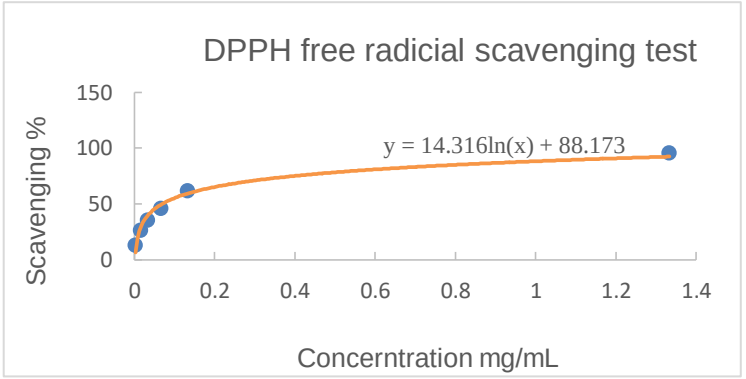
Summary:

1) according to above results, SpecKare® GSH has better inhibiting effect than Vc, the inhibiting rate of Vc (at 0.2 mg/ml) on mushroom tyrosinase enzyme activity is 95.2%, while the inhibiting rate of SpecKare® GSH (at 0.08 mg/ml) on tyrosinase enzyme activity can reach 98.6%.
2) according to the dose-response curve calculation, IC50 value of SpecKare® GSH is 0.028 mg/ml.

Amino Acid & Peptide Derivative and Analogue

3.5 Antioxidant Effect of SpecKare® GSH-Scavenging Free Radical DPPH

Sample	Concentration (mg/mL)	Scavenging effect (%)
SpecKare® GSH	0.0033	12.6
SpecKare® GSH	0.017	26.1
SpecKare® GSH	0.033	35.4
SpecKare® GSH	0.067	45.7
SpecKare® GSH	0.13	61.6
SpecKare® GSH	1.3	95.3



Summary:

1) according to Brand-Williams (1995) method, SpecKare® GSH can reduce DPPH up to 95.3% when at 1.3mg/mL.
2) according to the dose-response curve calculation, EC50 value of SpecKare® GSH is 0.0695 mg/ml.

04 Amino Acid & Peptide Derivative and Analogue

Formulation Example 1: Whitening Essence

	Product Name	Supplier/ INCI Name	w/w%	Function
A	Steareth -20		0.2	Emulsifier
	SpecSufc® M68	Spec Chem/ Cetearyl Glucoside & Cetearyl Alcohol	0.05	Emulsifier
	SpecThem® GMS	Spec Chem/ Glyceryl Stearate	0.05	Emulsifier
	Dimethicone		1	Tactile Enhancers
	Squalane		1	Soft agent
	SpecKare® VEA	Spec Chem/ Tocopheryl Acetate	0.1	Antioxidant
	Hydroxyethyl acrylate / sodium acryloyldimethyl taurate copolymer		0.5	Stabilizer
B	SpecThem® SCB21	Spec Chem/ Acrylates/c10-30 alkyl acrylate crosspolymer	0.1	Stabilizer
	Butylene Glycol		3	Humectant
	Glycereth-26		2	Humectant
	Water		To 100	
	Cyclodextrin		0.1	Stabilizer
	SpecKare® NMF50	Spec Chem/ Betaine	2	Humectant
	SpecKare® TRHL	Spec Chem/ Trehalose	2	Humectant
	Disodium EDTA		0.05	Chelating Agent
	SpecKare® ALLA	Spec Chem/ Allantoin	0.05	Conditioning Agent

(To be continued)

Procedure:

1.Mix part A and heat to 80℃, stirring until completely dissolved;
2.Mix part B components and stir well;
3.Mix A and B, homogenize for 5min;
4.Disperse the part C and cool the base below 60℃, then add part C;
5. Cool the base below 45℃, add part D, stirring until room temperature.

Properties:

Appearance: Light yellow liquid
pH: 5.61 (1:10 aqueous solution)
Viscosity: 980(25 ℃, 4 #, 30 rpm,mpa.s)
Stability: 1 month 45 ℃ , 1 month - 18 ℃

Features:

Whiten skin, absorb quickly, smooth texture.

04 Amino Acid & Peptide Derivative and Analogue

Formulation Example 1: Whitening Essence

	Product Name	Supplier/ INCI Name	w/w%	Function
C	SpecKare® ARG	Spec Chem/ Arginine	0.1	Skin conditioning
	SpecKare® HAL(1% Liquid)	Spec Chem/ Sodium Hyaluronate	2	Humectant
	ParbFree® PE91	Spec Chem/ Phenoxyethanol & Ethylhexylglycerin	0.8	Preservative
D	SpecKare® VCE（P&C)	Spec Chem/ Ascorbyl Glucoside	2	Whitening Agent
	SpecKare® GSH	Spec Chem/ Glutathione	0.1	Antioxidant Agent
	Fragrance		0.1	

Procedure:

1.Mix part A and heat to 80℃, stirring until completely dissolved;
2.Mix part B components and stir well;
3.Mix A and B, homogenize for 5min;
4.Disperse the part C and cool the base below 60℃, then add part C;
5. Cool the base below 45℃, add part D, stirring until room temperature.

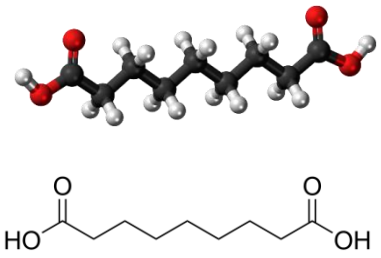
Properties:

Appearance： Light yellow liquid
pH： 5.61 (1:10 aqueous solution)
Viscosity： 980(25 ℃, 4 #, 30 rpm,mpa.s)
Stability: 1 month 45 ℃ , 1 month - 18 ℃

Features:

Whiten skin, absorb quickly, smooth texture.

05 Introduction of Dicarboxylic Acid



The Structure of Azelaic Acid
(with 7 Carbon Separation,
with C9 in total)

- Azelaic Acid belongs to the dicarboxylic acids which mostly function in cosmetics as pH Adjuster & Fragrance.
- Azelaic Acid is terminally finctionalized straight alky chains cgaracterized by a separation between the carboxylic acid functional group of 7.
- It is previously called Azelaic Acid because its English name is similar to that of azalea (rhododendron), but the two are not related.
- Azelaic Acid first detected in rancid fats and is a naturally occurring dicarboxylic acid that can be found in dietary sources, such as whole grains.
- USA Cosmetic Ingredient Review Expert Panel concluded that Azelaic Acid is safe in the present practices of use and concentration since 2012.

05 Introduction of Dicarboxylic Acid

Commercial Products:

BioDerma *Pigmentbio Daily Care SPF 50+*

Effectively protects skin cells, high-power index sun protection, can delay the signs of aging caused by sunlight.

Paula's Choice *10% Azelaic Acid Booster*

Regulate skin condition, remove acne-causing substance, improve spot problem.

Unia Acne-Derma 20% Azelaic Acid Cream

20% Azelaic acid cream that has Anti-acne and skin brightening properties.

Dr Dennis Gross Clinical Grade Ipl Dark Spot Correcting Serum

The Ordinary *Azelaic Acid Suspension 10%*

High concentration of azelaic acid can eliminate the bacteria on the skin surface and hair follicles, inhibit the excessive secretion of oil, inhibit reactive oxygen radicals, anti-inflammatory, and prevent hair follicle keratinization caused by mouth closure, black heads, acne.

Bayer Skinoren

20% Azelaic Acid treatment.

05 Introduction of Dicarboxylic Acid

Product Information of SpecKare® ALA:

Trade Name:	SpecKare® ALA
INCI name:	Azelaic acid
CAS No.:	123-99-9
Dosage:	1%-10%（Cosmetics）
	10-20% (Drug and etc.)
Suggested pH：	4.5-5.5
Storage:	Cool and dry place, protect from light
	2-8℃ for long time storage
Shelf life:	3years
Package:	1kg\10kg or Customizable

Items	Specification
Description	White to slightly yellow monocline rhombus crystalline, needle crystalline powder
Identification	Positive
Clarity and colour of solution	5ml 1% 1N NaOH solution is colorless and clear
Chlorides	≤0.005%
Sulfates	≤0.025%
Heavy metals	≤0.001%
Fe	≤0.002%
Melting Point	104℃ - 109℃
Water	≤0.5%
Assay	≥99.0%
Particle size	98% < 50μm, min 30% < 30μm

05 Introduction of Dicarboxylic Acid

The Features of SpecKare® ALA

- ✓ Works against acne-causing Propionibacterium acnes (P. acnes), an awesome choice for acne-prone skin.
- ✓ Works on the cells that line hair follicles by changing the way they mature and proliferate, which decreases follicular 'plugging' & helps prevent blackheads, whiteheads.
- ✓ Has anti-keratinizing effect on normal skin & reduce the synthesis of filamentous keratin & prevents excessive keratinization of hair follicles.
- ✓ Inhibits the production of reactive oxygen free radicals and exerts anti-inflammatory effects.
- ✓ Inhibit tyrosinase activity and pigment synthesis in abnormal pigment cells & inhibits DNA synthesis and mitochondrial enzyme activity in abnormal pigment cells
- ✓ Help reducing malignant cell proliferation activity & prevent malignant melanoma from developing in malignant freckles.
- ✓ Especially effective for post-inflammatory hyperpigmentation (that often comes with acne) and melasma (Not for lightening age spots that are called solar lentigines)
- ✓ It is a prescription drug in the US but can be freely purchased in the EU in an up to 10% concentration

05 Introduction of Dicarboxylic Acid

Acne Treatment

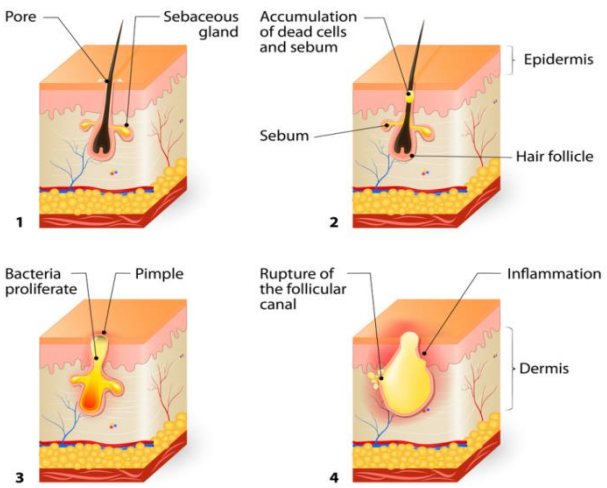


Diagram of acne formation

The physiological and pathological mechanisms of acne appear to depend on four major factors, namely :

(1) sebum production and excretion,

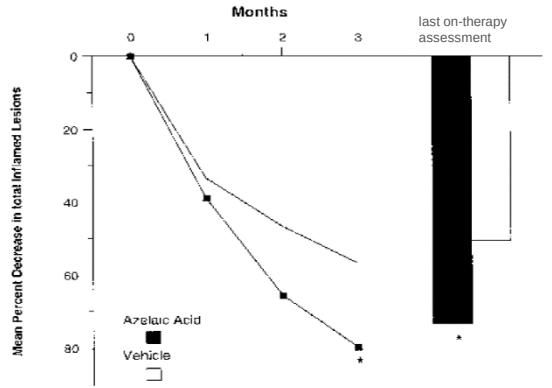
(2) keratinization of follicular pathways,

(3) microbial colonization of pilosebaceous units per follicle,

(4) inflammatory responses in the surrounding areas of hair follicles.

- ✓ Azelaic acid is effective against acne because of its ability to combat all of these activity.
- ✓ Azelaic acid is a competitive inhibitor of mitochondrial oxydoreductases and 5-a-reductase.
- ✓ Azelaic acid also has antibacterial properties against aerobic and anaerobic bacteria, including propionibacterium acnes.
- ✓ Azelaic acid is an antikeratinizing agent, which can inhibit the proliferation of keratinocytes and modulatiog the differentiation of epidermal cells.

05 Introduction of Dicarboxylic Acid



Reduction in total inflammatory lesion counts. Significantly greater reductions with azelaic acid cream were observed at month 3 (p=0.012) and, overall, for the last on-therapy assessment (p=0.011).*
(mean count at baseline=22.9; last on-therapy count=6.6) was found in the azelaic acid group, compared with 46.5% (mean count at baseline=23.4; last on-therapy count=12.8) in the vehicle group. Significant treatment differences were observed after 2 months (p=0.023) and 3 months (p=0.016) of treatment and for the reductions at the last on-therapy assessment (p=0.013).
The mean reduction in pustules achieved for the last ontherapy visit was 81.9% (mean count at baseline=7.9; last ontherapy Count=1.7) in the azelaic acid group, compared with 70.1% (mean count at baseline=8.2; last on-therapy Count=2.5) in the vehicle group. No significant treatment differences were found for the reduction in pustules.

Treatment of Papulo-pustular Rosacea

Result:

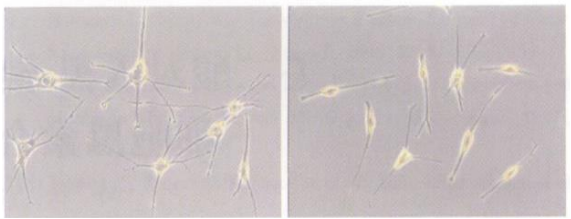
Azelaic acid cream produced significantly greater reductions than vehicle in total inflammatory lesion count. From baseline to the last on-therapy assessment, the mean decrease in the sum of papules and pustules was 73.4% in the azelaic acid group (mean count at baseline~30.8; last on-therapy count=8.3) compared with 50.6% (mean count at baseline=31.7; last on-therapy count=15.3) in the vehicle group(p=0.011). Treatment difference was also noted in the completed patients at the month 3 examination (p=0.012).

With regard to the single type of inflammatory lesions between-group differences were evident for papules but not for pustules. A mean overall decrease in papules of 71.5%

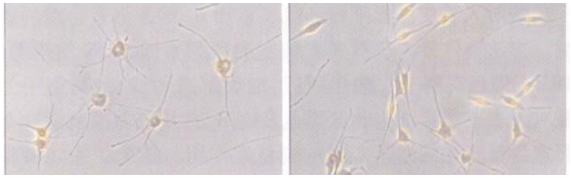
Reference: Acta Derm Venereol 1999; 79: 456–459

05 Introduction of Dicarboxylic Acid

TRP 1 staining



A. blank control group　　B. 0.5 mmol/L azelaic acid



A. blank control group　　B. 0.5 mmol/L azelaic acid

A and B are the control group and the drug group before staining, C and D are the control group and the drug group after TRP-1 staining; A and C can be seen that the dendritic cells of normal cells are mostly 3-5 poles, more After reaching 10 poles, 72 hours after B and D azelaic acid treatment, the cell dendrites were mostly reduced to 2 poles.

Skin Lightneing & Whitening

Result:

Compared with before staining, brown particles were deposited around the cell body after staining, but no obvious brown particles were seen in the dendrites.

After 72 hours of azelaic acid treatment of human epidermal MC, dendritic cells were reduced. Normal epidermal MC dendrites were mostly 3-5 poles, and as many as 10 poles.

After drug action, it can be seen that the dendrites of the cells are mostly reduced to 1-2 poles. In mouse melanoma B_{16} cells, 72 hours after azelaic acid treatment, there was no visible morphological change.

Reference: 2006. Effects of Azelaic acid onmelanin synthesis of humanmelanocyte and mouse B16melanoma cells in vitro

05 Introduction of Dicarboxylic Acid

Effects of Azelaic Acid on tyrosinase activity and melanin synthesis in human epidermal MC and mouse melanoma B_{16} cells

Effect of factors (mmol/L)	Tyrosinase activity		Melanin content	
	B_{16}	MC	B_{16}	MC
0.1	90.48±5.01*	88.57±4.51**	92.56±3.65*	90.02±3.01**
0.5	54.74±8.33▲*	76.39±4.37▲**	87.59±2.36▲**	82.12±2.45▲**
1.0	76.26±7.31**	47.47±5.81**	68.61±3.73**	71.42±2.51
5.0	65.21±5.39**	ND	59.30±4.01**	ND
0.5★	93.60±2.79	85.01±4.72	92.80±4.21	88.11±2.13

*Tyrosinase activity and melanin content were expressed as percentage of A value in the control group. The corresponding value of the blank control group was set as 100%, and the comparison between each group and the blank control group was *P <0. 05, **P <0. 01. ★ the concentration is the concentration of hydroquinone, in units of μmol/L. Compared with hydroquinone, ▲P <0. 05. ND stands for unmeasured.*

Skin Lightening & Whitening

Result:

Azelaic acid has been shown to inhibit tyrosinase activity and melanin synthesis in mouse melanoma B_{16} cells and human epidermal MC in a concentration dependent manner.

Compared with the blank control group, 0.1 mmol/L azelaic acid showed inhibition of tyrosinase activity and melanin synthesis in human epidermal melanocytes (P<0.01), and the same concentration of azelaic acid also inhibited tyrosinase activity and melanin synthesis in B_{16} Cells (P<0.05).

Compared with 0.5 μmol/L hydroquinone in positive control, the effect of 0.5 mmol/L azelaic acid was significantly higher than that of hydroquinone (P<0.05).

Reference: 《Effects of Azelaic acid onmelanin synthesis of humanmelanocyte and mouse B16melanoma cells in vitro》

05 Introduction of Dicarboxylic Acid

Application guide of SpecKare® ALA：

Dosage： 1-10% (Cosmetics) & 10-20% (Drug and etc.)

Suggested pH： 4.0-6.5

Application：

Acne treatment; reduce spot; whitening ; treatment of Papulo-pustular Rosacea.

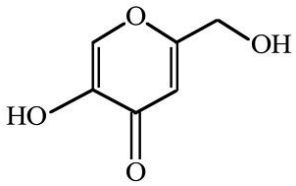
Usage:

It is recommended to add ethoxy diethylene glycol to facilitate solution. SpecKare® ALA can be incorporated to the formulation in the final stage of the manufacturing process, when the temperature is below 45℃, and also can be add into butylene glycol while heating to 80 ℃ (<90℃ is acceptable) until dissolved.

Other (Noncosmetic) Applications:

- Direct or indirect food additives
- Manufacture of Polymer
- Synthesize cyclic ketones, like macrocyclic musk compounds

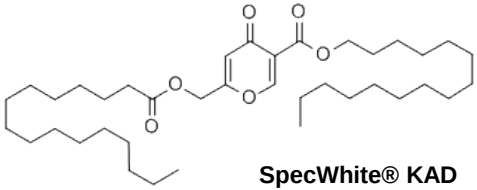
06 Introduction of Heterocyclic compound & its esters



SpecWhite® KA
Kojic Acid

The structure of kojic acid structure

- Kojic acid was discovered in 1907 through isolation from the mycelia of Aspergillus oryzae grown on steamed rice (the term koji means steamed rice in Japanese).
- Kojic acid is classified in the group of organic acids, which is obtained from different types of fungi during aerobic fermentation process.
- The hydroxyl group in the carbon 5 position from the γ-pyrene ring gives a weak acidic property to the KA molecule, which leads to the formation of salt by some metals such as sodium, zinc, copper, calcium, nickel, and cadmium.



SpecWhite® KAD
Kojic dipalmitate

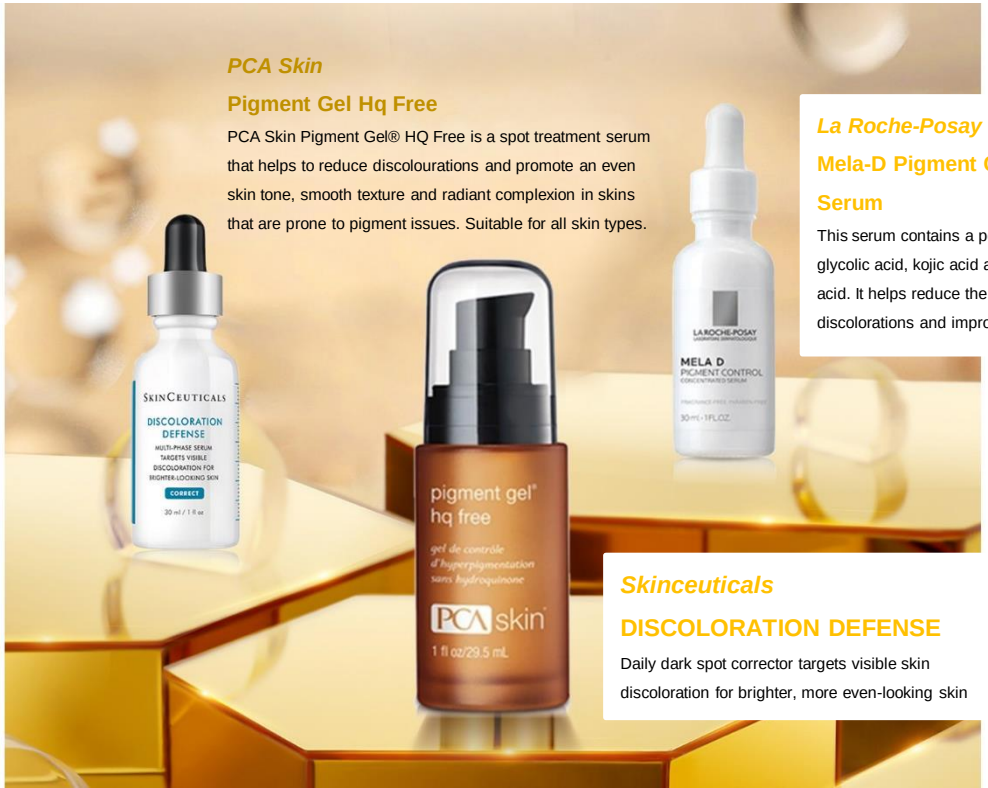
06 Introduction of Heterocyclic compound & its esters

Commercial Products:

Skinceuticals

PHYTO CORRECTIVE GEL

A hydrating, soothing gel serum with botanical ingredients ideal to calm and hydrate skin while improving visual redness



PCA Skin

Pigment Gel Hq Free

PCA Skin Pigment Gel® HQ Free is a spot treatment serum that helps to reduce discolourations and promote an even skin tone, smooth texture and radiant complexion in skins that are prone to pigment issues. Suitable for all skin types.

La Roche-Posay

Mela-D Pigment Control Glycolic Acid Serum

This serum contains a potent triple-acid complex with 10% glycolic acid, kojic acid and micro-exfoliating lipo-hydroxy acid. It helps reduce the look of dark spots and discolorations and improve skin radiance.

Skinceuticals

DISCOLORATION DEFENSE

Daily dark spot corrector targets visible skin discoloration for brighter, more even-looking skin

06 Introduction of Heterocyclic compound & its esters

Product name: SpecWhite®KA
INCI name: Kojic acid
CAS No.: 501-30-4
EC No.: 207-922-4
Dosage: 0.5-2.0 (daily use); 2.0-4.0% (lightening etc.)
Package: Customization
Storage: Ventilation, dry warehouse stored at room temperature
Shelf life: 2 years (unopened) .
Application: Creams, Lotions, Sprays and other skin products

Items	Specification
Appearance	White or off white crystals
Purity (%)	99.0min
Melting point (℃)	152-156
Loss on drying (%)	Not more than 1.0
Residue on ignition (%)	Not more than 0.2
Heavy metals (pb) (ppm)	Not more than 3
Arsenic (ppm)	Not more than 1
Iron (ppm)	Not more than 10
Chloride (ppm)	Not more than 100

06 Introduction of Heterocyclic compound & its esters

SpecWhite®KA-(Eco-cert) Natural certificated

F363(GC)v07en
Issued the: 16/01/2019

ECOCERT

Attestation n°: 856886

ATTESTATION OF CONFORMITY
- RAW MATERIALS -
ECOCERT COSMETICS

This attestation has been granted by ECOCERT Greenlife to the company:

SPEC-CHEM INDUSTRY. INC

10 WanShou Road (Shi Lin Industrial Park)
NANJING
CHINA

whose non-organic raw materials (listed hereafter) have been assessed as compliant to the current version of the ECOCERT standard:

NATURAL AND ORGANIC COSMETICS

This attestation of conformity has been issued on the basis of the terms and conditions for the verification of raw materials according to the ECOCERT standard defining Natural and Organic Cosmetics available on the ECOCERT website: http://www.ecocert.com and the conformity has been established according to the requirements related to the raw materials contained in this standard.

Issued in : L'Isle Jourdain,
the: 16/01/2019,

by: Matthieu Boufflartigue
Raw materials service manager

Valid until: 31/12/2019

Page 1 of 2

F363(GC)v07en
Issued the: 16/01/2019

ECOCERT

Attestation n°: 856886

ATTESTATION OF CONFORMITY - ECOCERT COSMETICS

List of the approved raw materials of: **SPEC-CHEM INDUSTRY. INC**

Nat : Natural or from natural origin
Veg: Physically processed vegetal ingredients
Synth : Synthetic (petrochemical)

Unless an exception, the following references are published on the ECOCERT raw materials online database for approved raw materials available at the following link: http://ap.ecocert.com/ecoproduits

Commercial name / INCI / Function	%Nat	%Veg	%Synth	Restriction	Approved since
SpecWhite KA *Kojic Acid* Whitening agent	100	0	0		01/01/2019

Valid until: 31/12/2019

WARNING: The sole purpose of the present attestation is to allow the raw material(s) to be used in finished products to be certified as compliant to the standard specified in the first page. In no event this attestation should constitute proof of the actual certification of the conformity of the raw material(s) to this standard. In that context, the raw material(s) listed in this attestation must not be qualified and / or marketed as «organic» raw material(s) certified in accordance with the above mentioned standard.
The approval of the raw material(s) listed in the present attestation is personally addressed to the above-mentioned beneficiary. It is the beneficiary's liability to ensure that its own customers are aware of the requirements and prohibitions defined in the terms and conditions and governing any reference to and use of the approval of the raw material(s) and that they abide by it.

Page 2 of 2

Regulations:

Regulated of chemicals on:

- ✓ IECSC--Inventory of Existing Chemical Substances in China
- ✓ EINECS—European Inventory of Existing Commercial Chemical Substances
- ✓ PICCS—Philippine Inventory of Chemicals and Chemical Substances
- ✓ NZIoC—New Zealand Inventory of Chemicals
- ✓ TCSI—Taiwan Chemical Substance Inventory
- ✓ ECL—Korean Existing Chemicals List

Regulated of cosmetics on:

- ✓ CTFA-International Cosmetic Ingredient Dictionary and Handbook
- ✓ IECIC-Inventory of Existing Cosmetic Ingredients in China
- ✓ Cosing-European Commission database for information on cosmetic substances and ingredients

06 Introduction of Heterocyclic compound & its esters

Safety of Kojic acid (All Data from the Third Party, We-Spec Chem Hasn't Conducted Any Animal Test)

- In acute mouse studies with kojic acid, oral, subcutaneous,and intraperitoneal LD50 values were 5.1, 2.7, and 2.6 g/kg body weight, respectively.
- In rats, the LD50 values were greater than 2 g/kg body weight in oral and dermal studies, and 2.6 and 2.4 g/kg body weight in subcutaneous and intraperitoneal studies, respectively.
- The subchronic oral toxicity study in male rats concluded with a NOEL for kojic acid of 125 mg/kg per d.
- Kojic acid was not an ocular irritant but was a mild dermal irritant in rabbits.
- In guinea pigs, this ingredient was not a der_x 0002_mal sensitizer but did produce slight skin reactions with UV light exposure in acidic conditions in human repeat insult patch tests, 1% and 2% kojic acid was not sensitizing.
- Several studies of kojic acid, with doses tested up to 900 mg/kg per d in rodents, found the substance was not a reproductive or developmental toxicant.
- In vivo mammalian tests of kojic acid were negative for genotoxicity. Kojic acid was a weak photo-mutagen in a photo-reverse mutation assay and a chromosomal aberration study with light irradiation.
- International Agency for Research on Cancer has concluded that kojic acid is a group 3 carcinogen—not classifiable to human carcinogenicity.

Kojic acid was not a toxicant in acute, chronic, reproductive, and genotoxicity studies.

《USA: Final Report of the Safety Assessment of Kojic Acid as Used in Cosmetics》

06 Introduction of Heterocyclic compound & its esters

Features of SpecWhite®KA

- ✓ Tyrosinase inhibitor & Skin lightening agent
- ✓ Ultra violet filter & Radical scavenging activity
- ✓ Helps collagen production
- ✓ Treats skin disorders such as melasma and other related diseases
- ✓ Acts as an antibiotic against human tubercle bacilli, gram-negative and gram-positive microorganisms.
- ✓ Excellent antibacterial activity

Solubility

Soluble in water,ethanol, acetone;sparingly soluble in ether, ethyl acetate, chloroform, pyridine; insoluble in benzene.

Dosage

0.1-1% in daily skin care products. 1- 4% in Specific purpose products.

Usage

- ✓ It can be incorporated to the formulation in the final stage of the manufacturing process, when the temperature is below 45℃
- ✓ Please kindly to avoid using it with metal ions, and adding chelating agents to the f ormulation may be better.
- ✓ The recommended pH for the formulation containing KA is bout 5-6.

06 Introduction of Heterocyclic compound & its esters

Inhibitory effect on tyrosinase activity:

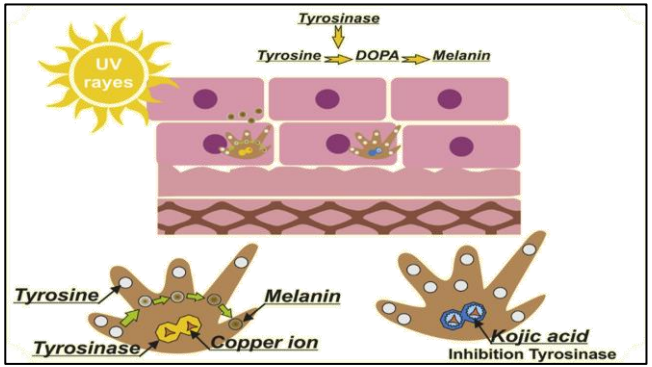


Fig. 1 Tyrosinase inhibitory mechanism of KA in melanin biosynthesis for creating melanin by KA.

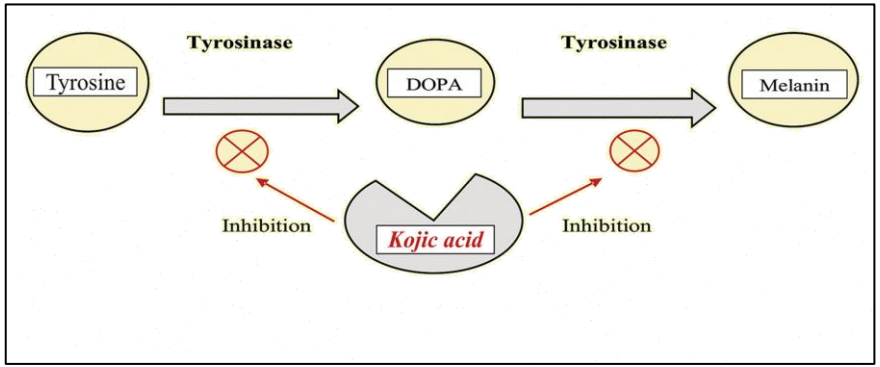


Fig. 2 Inhibiting the activities of tyrosinase by KA

- Tyrosinase contain copper ion in the active site. When exposed to UV rays, the copper ion commands the tyrosinase to become more active.
- KA captures the copperion, preventing that from activating the tyrosinase. By inhibiting the activities of tyrosinase, KA can also prevent creating melanin.

《Kojic acid applications in cosmetic and pharmaceutical preparations》

06 Introduction of Heterocyclic compound & its esters

(in vitro) Inhibitory effect on tyrosinase activity:

Report No.:	SC-201911A
Sample name:	**SpecWhite®KA**
Batch number:	20180808
Sample Description:	White crystal
Test date:	2019.10.29
Test objective:	Test tyrosinase activity inhibition of raw materials
Test Materials:	Tyrosinase, L-dopa, phosphate buffer saline, Vc, Microplate Reader
Test Procedure:	Anti-tyrosinase activity was performed in 96 well microplate. The samples were dissolved with solution buffer in different concentration. The sample was mixed with 80 μL of the phosphate buffer (pH 6.8) and 40 μL of L-tyrosine (5 mmol/L). And the mixed solution was incubated at 37℃ for 10 min. Then 40 μL of mushroom tyrosinase solution (150 U/mL) was added and incubated at 37℃ for 5-10 min. After incubation, the visible absorption was measured at 490 nm. Tyrosinase inhibition (T) was calculated as in Equation (1). T (%) = [1- (A - B) /(C - D)]*100 …….. (1) Where A is the absorbance value of test sample, B is the absorbance value of blank sample, C is the absorbance value of control and D is the absorbance value of blank control.

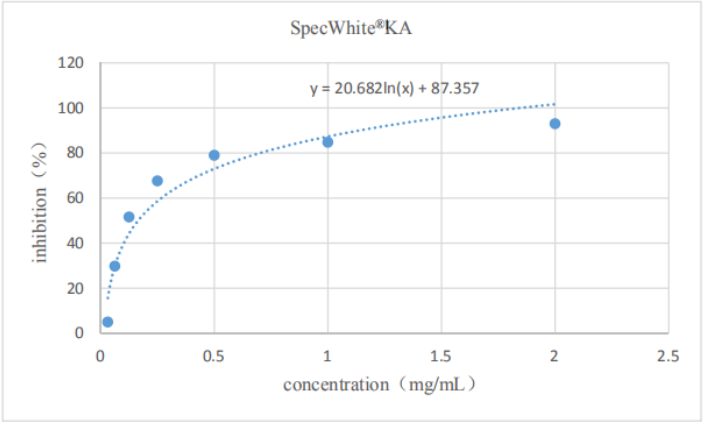


Figure 1 sample on the inhibition of tyrosinase activity

Sumarry: SpecWhite®KA has a strong inhibitory effect on tyrosinase activity.The inhibition rate of 2.0 mg/mL SpecWhite®KA on tyrosinase enzyme activity can reach 93.0%, and the IC50 value of SpecWhite®KA is calculated to 0.16 mg/mL according to the dose-response curve.

06 Introduction of Heterocyclic compound & its esters

In Vivo Test-Improves melasma

Test Purpose: This study was undertaken to see if the addition of kojic acid to the existing regime (2% hydroquinone and 10% glycolic acid) will further improve the lightening of melasma.

Test Sample: Two sets of treatment gels were used—one containing 2% hydroquinone and 10% glycolic acid and the other containing 2% kojic acid in the same formulation (ie., 2% hydroquinone and 10% glycolic acid).

Subjects: 40 Chinese women with epidermal melasma (confirmed by Wood's light)

Age range: 32-58 years old

Test Site: Face

Application Method: Each patient had use the gels twice a day, one on each side of the face.The side receiving the kojic acid was randomized. The patient had to use a physical sunblock containing titanium dioxide SPF 15 over the gels daily

Test Period: 12 weeks

Efficacy evaluation method: Clinical evaluation, photographs, and self-assessment questionnaires

《Treatment of Melasma Using Kojic Acid in a Gel Containing Hydroquinone and Glycolic Acid》

06 Introduction of Heterocyclic compound & its esters

In Vivo Test Results-Improves melasma

Table 1. Patients Showing Improvements in Melasma During the Study on the Sides with or without Kojic Acid

	With kojic acid			Without kojic acid		
Improvement in melasma	*4 weeks*	*8 weeks*	*12 weeks*	*4 weeks*	*8 weeks*	*12 weeks*
0	1	0	0	1	0	0
0–25%	18	7	2	19	10	1
25–50%	16	22	14	19	20	20
50–75%	5	8	15	1	10	14
75–99%	0	3	7	0	0	5
Clear	0	0	2	0	0	0
Total	40	40	40	40	40	40

Improvement was assessed as 0–25%,25–50%, 50–75%, more than 75%, and clear, and given scores of +1, +2, +3, +4, and +5, respectively.
All had malar melasma with 3 having melasma on the forehead and chin as well. They had their melasma for 2 to 10 years, the majority having had the condition for more than 5 years. All had previous treatments with hydroquinone but not kojic acid or glycolic acid. All had stopped treatments at least 4 weeks prior to the study. Sunlight aggravated melasma in all patients; 21 out of 40 (52.5%) had a family history of melasma.

- At theend of the study, all patients showed improvement in their melasma, regardless of whether kojic acid was used or not.
- The overall reduction in melasma varied from 25% to 100% or from a score of +1 to +5.
- Only two patients had complete clearance of their melasma, and this was on the side where kojic acid was used.

《Treatment of Melasma Using Kojic Acid in a Gel Containing Hydroquinone and Glycolic Acid》

06 Introduction of Heterocyclic compound & its esters

In Vivo Test Results--- Improves melasma

Table 2. Patients Showing More than 50% Improvement in Melasma at the End of the Study (12 Weeks)

Improvement in melasma	*With kojic acid*	*Without kojic acid*
Less than 50%	16 (40.0%)	21 (52.5%)
More than 50%	24 (60.0%)	19 (47.5%)
Total	40 (100.0%)	40 (100.0%)

Results: More than half of the melasma was cleared in 24 out of 40 (60%) patients using kojic acid in 2% hydroquinone and 10% glycolic acid gel compared with 19 out of 40 (47.5%) patients using the same gel (2% hydroquinone and 10% glycolic acid) without kojic acid.

Kojic acid helps improve refractory melasma.

《Treatment of Melasma Using Kojic Acid in a Gel Containing Hydroquinone and Glycolic Acid》

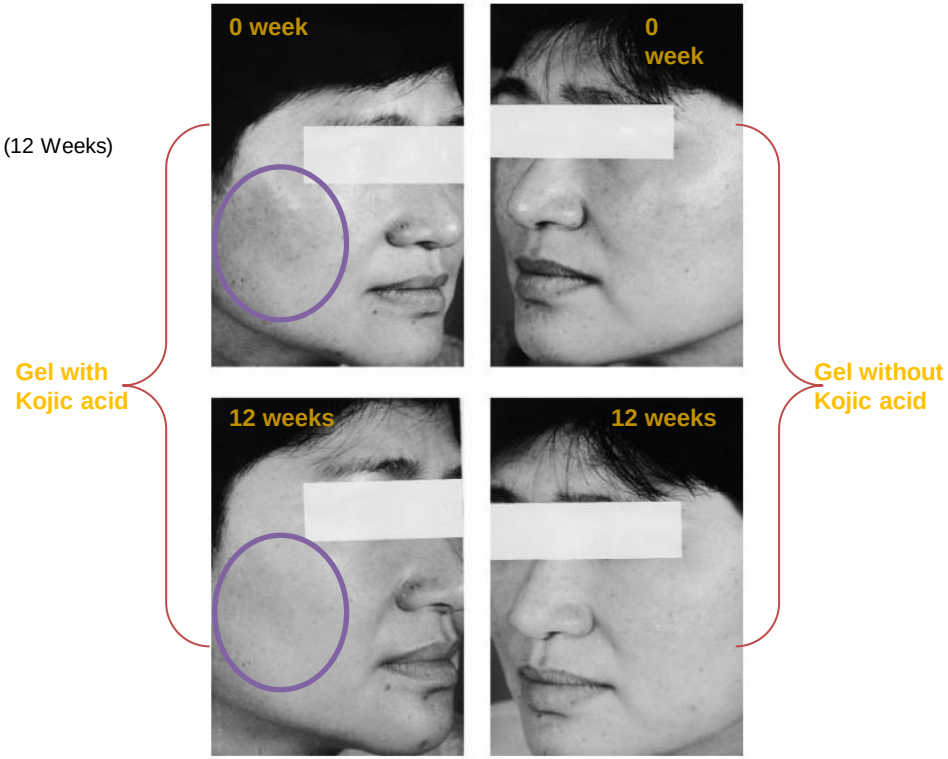


Figure.1 Photos of typical subjects

06 Introduction of Heterocyclic compound & its esters

In Vivo Test Results--- Improves melasma

Table 3. Improvement in Melasma Comparing the Side with Kojic Acid and the Side without Kojic Acid

Improvement	*With kojic acid*	*Without kojic acid*
More effective	17 (42.5%)	5 (12.5%)
No difference	18 (45.0%)	18 (45.0%)
Less effective	5 (12.5%)	17 (42.5%)
Total	40 (100.0%)	40 (100.0%)

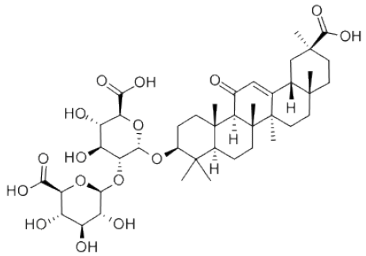
Table 4. Improvement in Melasma as Assessed by Doctor and by Patients

	With kojic acid		*Without kojic acid*	
	Better	*Same*	*Better*	*Total*
Doctor	17 (42.5%)	18 (45.0%)	5 (20.0%)	40
Patient	18 (45.0%)	19 (47.5%)	3 (17.5%)	40

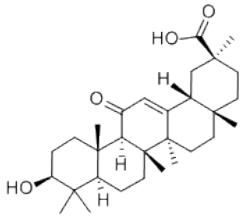
- Seventeen out of 40 (42.5%) patients had a more dramatic reduction in melasma on the side receiving kojic acid (in 2% hydroquinone and 10% glycolic acid and gel).
- Both concurred that kojic acid did not worsen the melasma. Instead, addition of kojic acid either improved the melasma further or made no difference in the final result.

《Treatment of Melasma Using Kojic Acid in a Gel Containing Hydroquinone and Glycolic Acid》

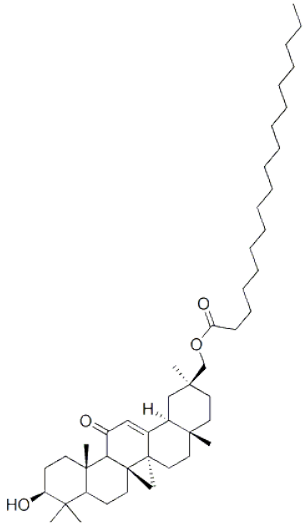
07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters



SpecKare® GlyAA
Glycyrrhizic Acid



SpecWhite® GA
Glycyrrhetinic Acid



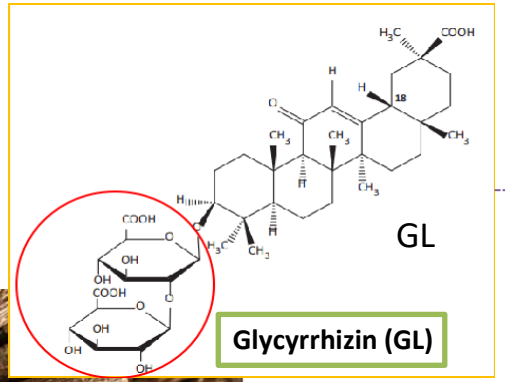
SpecWhite® SG
Glycyrrhetinyl Stearate

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

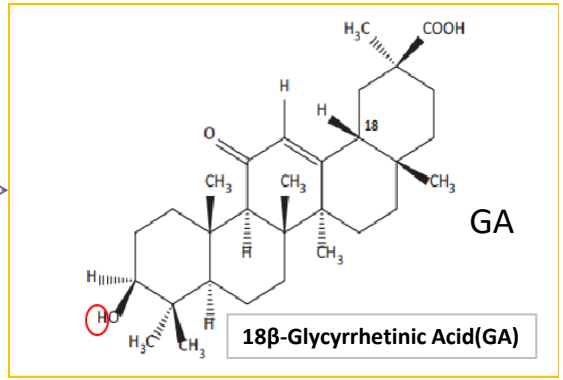
Glycyrrhetinic acid (GA)

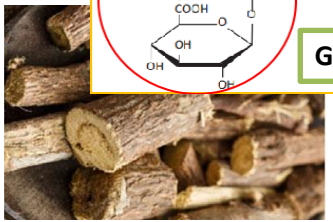
Glycyrrhizic acid (GL or glycyrrhizin), a triterpenoid saponin glycoside, is the major water-soluble constituent of licorice root, while **18β-glycyrrhetinic acid (GA or glycyrrhetic acid)** is the key metabolite of glycyrrhizic acid .

During metabolism in the plant by glucuronidase, or by intestinal bacteria after oral ingestion, glycyrrhizin is hydrolyzed into two pentacyclic triterpenoids, which are stereoisomers: 18α- and 18β-glycyrrhetinic acids.



hydrolysis





Glycyrrhiza Glabra (Licorice) root

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Commercial Products:

Clinique

Even Better Brighter Moisture Mask

A skin-brightening intensely moisturizing facial mask. Restores radiance and luminosity to dull skin, provides gentle exfoliation for brighter, more even-toned skin, hydrates and helps strengthen skin's moisture barrier.

Tom Ford

Face Protect Broad Spectrum Spf 50

The essential base for healthy-looking summer skin year-round. The SPF skin protector is the first defense against the harmful effects of the sun. fortified with powerful anti-oxidants and soothing anti-irritants, the lightweight and fast-absorbing formula primes and calms the look of skin, smoothing it for effortless makeup application. Easily blends into skin, leaving it looking brighter and more luminous.

Estee Lauder

Daywear Antioxidant 72H-Hydration Sorbet Creme SPF 15

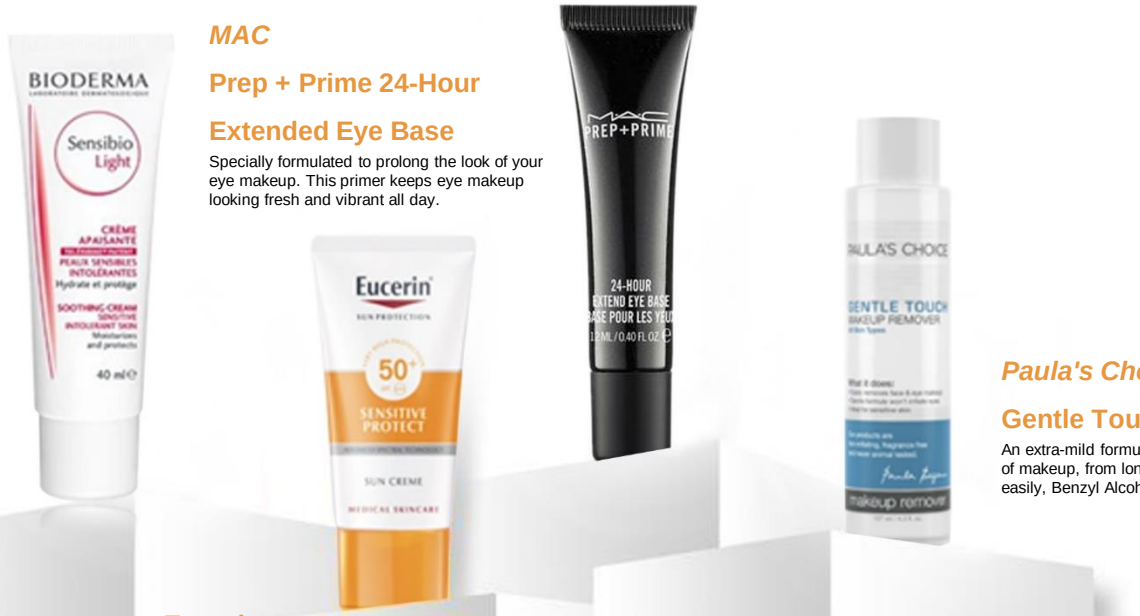
La Mer

Genaissance De La Mer The Serum Essence

This advanced broth infuses skin with the life-generating energies of the sea, helping it visibly renew from within. In moments, genesis begins. Day after day, skin is infused with a new look of life. Contours appear lifted and firmed, pores are refined and skin becomes plumper, suppler and more translucent.

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Commercial Products:



Bioderma

Sensibio Light Soothing Cream

A daily moisturising and protecting treatment for sensitive skin that increases the tolerance threshold.

MAC

Prep + Prime 24-Hour Extended Eye Base

Specially formulated to prolong the look of your eye makeup. This primer keeps eye makeup looking fresh and vibrant all day.

Eucerin

Sun Creme Sensitive Protect Spf 50+

A sun creme for the face that combines very high UV protection with cell and DNA protection. This easily-absorbed creme is ideal for normal and dry skin.

Paula's Choice

Gentle Touch Makeup Remover

An extra-mild formula that effortlessly dissolves all types of makeup, from long-wearing to waterproof, quickly and easily, Benzyl Alcohol

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Product Information:

Trade Name:	SpecWhite®GA
Product No.:	110037
INCI name:	Glycyrrhetinic Acid
CAS No.:	471-53-4
EC No.:	207-444-6
Use Level:	0.05-2%
Storage:	Store in cool place. Keep container tightly closed in a dry and well-ventilated place.
Shelf life:	2 years.
Package:	Customization

Items	Specification
Appearance	White crystal powder
Assay (Potentiometry)	98.0-101.0%
Infrared absorption	Complies
TLC	Complies
Color reaction	Complies
Loss on drying	≤0.5%
Sulphated ash	≤0.2%
Specific Rotation	+145° to +154°(dried substance)
Residual ethanol	≤0.5%
Related substances	Total:≤2.0%
	Any inpurity:≤0.7%
Heavy metals	≤20ppm

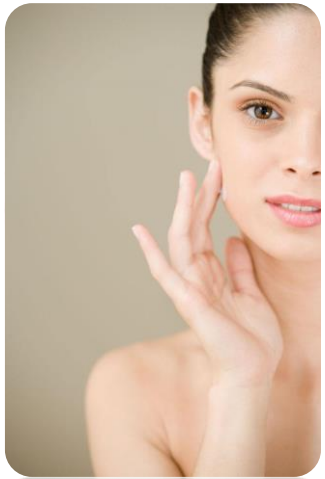
07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Safety of Glycyrrhetinic acid (All Data from the Third Party, We-Spec Chem Hasn't Conducted Any Animal Test)

- In rats given radioactive Glycyrrhetinic Acid orally, 86% of the radioactivity was recovered in 1 to 3 days with 83% in the feces, 1% in the urine and 4% remained in the liver. In rats given radioactive Glycyrrhetinic Acid subdermally, 74% of the radioactivity was recovered with 73% in the feces and 1% in the urine.
- The acute intraperitoneal LD50 for Glycyrrhetinic Acid in mice was 308 mg/kg and the oral LD50 was >610 mg/kg. The oral LD50 in rats was reported to be 610 mg/kg.
- Glycyrrhetinic Acid at 100 mg/ml was not irritating to shaved rabbit skin.
- Glycyrrhetinic Acid at concentrations up to 6% was not an irritant or a sensitizer.

USA CIR 2007《Final Report on the Safety Assessment of GlycyrrhetinicAcid, Potassium Glycyrrhetinate, Disodium Succinoyl Glycyrrhetinate, Glyceryl Glycyrrhetinate, Glycyrrhetinyl Stearate, Stearyl Glycyrrhetinate, Glycyrrhizic Acid, Ammonium Glycyrrhizate, Dipotassium Glycyrrhizate, Disodium Glycyrrhizate, Trisodium Glycyrrhizate, Methyl Glycyrrhizate, and Potassium Glycyrrhizinate》

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters



The Features of SpecWhite® GA

- ✓ Inhibits the growth of B16 melanoma cells,natural skin whitening agent
- ✓ Affects glucocorticoid receptor signaling to inhibit inflammation.
- ✓ Inhibits Methicillin-Resistant Staphylococcus aureus (MRSA) survival, natural antibacterial agent
- ✓ Excellent antiseptic & anti-infective property, can reduce the size of the abscess
- ✓ Regulate the skin's immune function, enhance skin's disease resistance
- ✓ Plays a key role against radiation-induced skin damage

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Glycyrrhetinic Acid (GA) inhibits the growth of B16 melanoma cells.

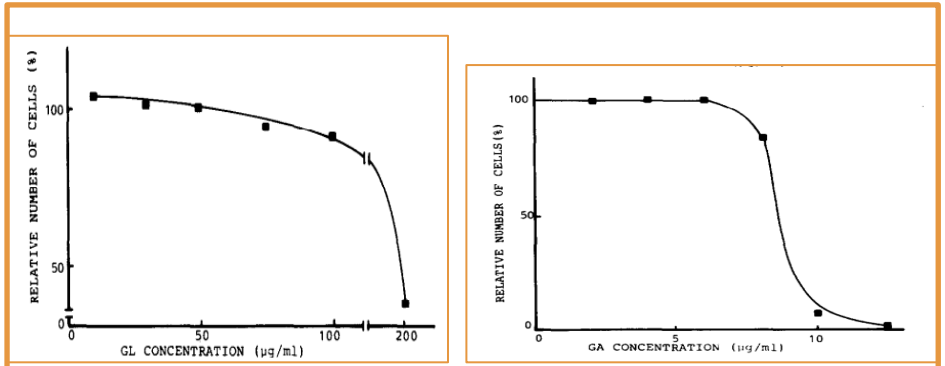


Fig. 1. Effects of GL and GA on growth of B16 melanoma cells. Twenty four hours after plating, GL or GA at various concentrations was added individually to separate dishes. At the termination of the experiments on day 4, the cells were detached with 0.01% trypsin solution in phosphate buffered saline and counted with an electronic counter. Each point represents an average ofJive experiments; bars, S.E.

Summary:

- **Glycyrrhetinic Acid(GA)** inhibited the growth of B16 melanoma cells in a dose-dependent manner and caused complete inhibition at concentrations over 10 μg/ml.
- while **Glycyrrhizin (GL)** did not inhibit cell growth even at concentrations over 100μg/ml.

《Effects of Glycyrrhizin and Glycyrrhetinic Acid on Growth and Melanogenesis in Cultured B16 Melanoma Cells》

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Glycyrrhetinic Acid (GA) inhibits the growth of B16 melanoma cells.

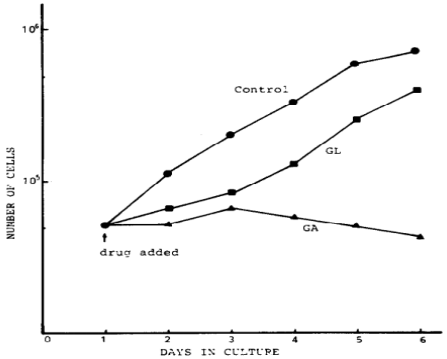


Fig. 2. Growth curves of melanoma cells treated with GL or GA. Cells 5 X lo^4 were cultured with either no additions (●), 200 μg/ml GL (•) or 12.5 μg/ml GA (▲). At the indicated times cells were harvested from the culture flasks and counted with an electronic particle counter.

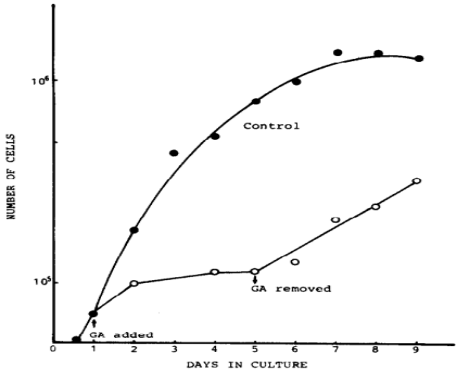


Fig. 3. Reversibility of GA inhibition on the growth of B16 melanoma cells in culture. Cells (5 X 10^4) were plated in Falcon dishes (35 mm), 12 h after plating, GA (12.5 μg/ml) was added to culture. At the indicated day, GA was removed. The number of cells in the control and GA-treated cultures was determined.

《Effects of Glycyrrhizin and Glycyrrhetinic Acid on Growth and Melanogenesis in Cultured B16 Melanoma Cells》

Summary:

- The growth of B16 melanoma cells cultured in a medium containing 12.5 μg/ml of GA was completely inhibited even after 1 day in culture.(Fig. 2)
- When GA was removed after 4 days of treatment, growth did not begin for a period of 24 h. A slight increase in growth was observed at 2 days after removal of GA, but the growth rate did not recover completely during the period of observation (4 days after removal of GA). (Fig. 3)
- **GA can effectively inhibits the growth of B16 melanoma cells!**

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

18 β-Glycyrrhetinic Acid inhibit LPS-induced expression of inflammatory cytokines.

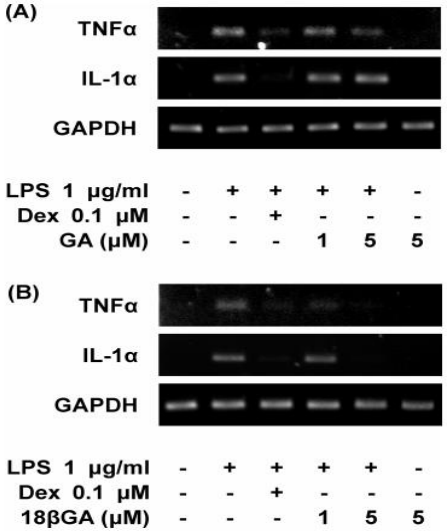


Figure 1. Effects of GA and 18βGA on LPS-induced expression of inflammatory cytokine genes. Cells were coincubated with 1 μM and 5 μM GA (A) or 18βGA (B) and 1 μg/mL LPS for 6 h. Dexamethasone (Dex, 0.1 μM) treatment was used as positive control

Summary:

- Dexamethasone (Dex) treatment, which served as the positive control, markedly reduces TNFR and IL-1R expression.
- At concentrations of 1 and 5 μm, **GA (Glycyrrhizic Acid)** could decrease TNFR expression in a dose-dependent mannar, but **18β-GA (18β-Glycyrrhetinic Acid)** reduced TNFR and IL-1R expression in a dose dependent manner (Figure 1A,B)
- These results indicate that GA and 18βGA inhibit LPS-induced expression of inflammatory cytokines.
- **Both GA & 18β-GA have anti-inflammatory effect and 18β-GA (SpecWhite®GA belongs to this type) performs better.**

《Glycyrrhizic Acid and 18β-Glycyrrhetinic Acid Inhibit Inflammation via PI3K/Akt/GSK3β Signaling and Glucocorticoid Receptor Activation》

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

18β-Glycyrrhetinic Acid affects glucocorticoid receptor signaling to inhibit inflammation.

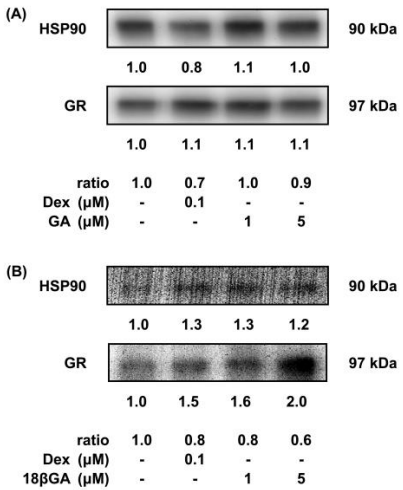


Figure 2.Effects of GA and 18ßGA on GR activation. Cells were incubated with GA (A) or 18ßGA (B) for 1 h in DMEM medium containing 10% FBS. After treatment, cell lysate was incubated with anti-GR antibody to isolate intracellular GR-HSP90 complexes. After purification, samples containing GR-HSP90 were subjected to Western blot analysis for GR and HSP90 content.

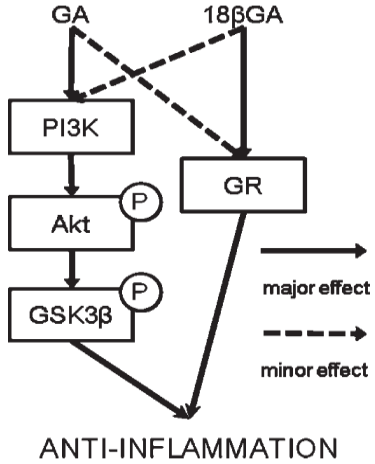


Figure 3. Potential anti-inflammatory mechanisms of GA and 18βGA

Summary:

- Dissociation of glucocorticoid receptor(GR) and HSP90 was used as a readout of GR activation.GR negatively interacts with NF-κB and AP1, two well-characterized inducers of pro-inflammatory cytokine expression.
- Following coincubation with GA (1 and 5 μm) for 1 h, the ratio of HSP90/GR does not change compared to controls. Alternatively, 18β-GA treatment decreases the HSP90/GR ratio at the same concentrations.
- The results suggest that **18β-GA** promotes GR-HSP90 dissociation more efficiently **than GA.**
- **Both GA & 18β-GA have anti-inflammatory effect and 18β-GA (SpecWhite®GA belongs to this type) performs better.**

《Glycyrrhizic Acid and 18ß-Glycyrrhetinic Acid Inhibit Inflammation via PI3K/Akt/GSK3ß Signaling and Glucocorticoid Receptor Activation》

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

18β-glycyrrhetinic acid (GRA/18β-GA) attenuates survival of Methicillin-resistant S. aureus(MRSA) in vitro.

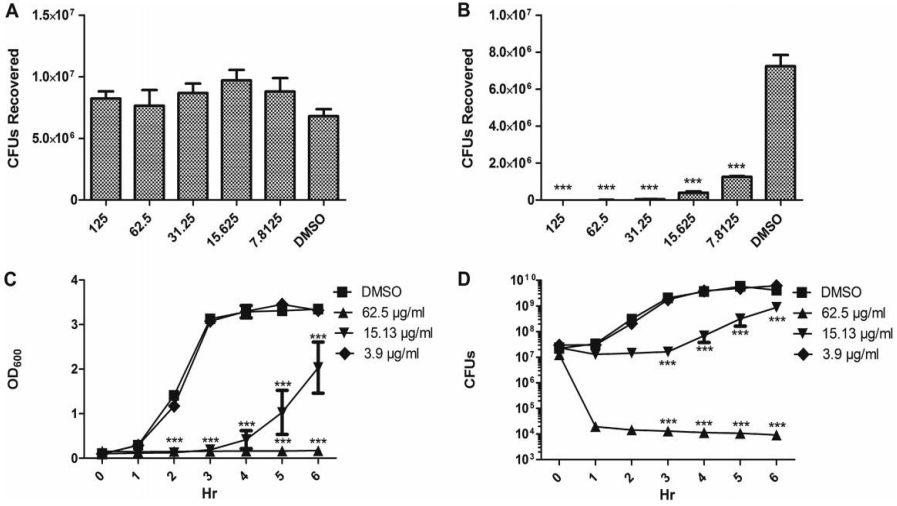


*FIG 1 GRA inhibits MRSA growth in a dose-dependent manner. MRSA strain LAC was grown to mid-exponential phase and resuspended in TSB (2 ×10^{5}CFU) and incubated with varied concentrations of GA or GRA. CFU recovered following incubation for 1 h with varied concentrations of GA (A) or GRA (B). (C and D) OD600 (C) and CFU (D) values recovered at each hour following incubation of 2 ×10^7 CFU LAC with varied concentrations of GRA over a 6-h time course.***, P<0.001, as determined by one-way ANOVA with Tukey's posttest (A and B) or two-way ANOVA with Bonferroni comparison (C and D) compared to bacteria grown in DMSO (data are from three separate experiments).*

Summary:

- Following incubation with **glycyrrhizic acid(GA),** growth exceeded initial inoculum at all concentrations (Fig. 1A).
- However, following incubation with **18β-glycyrrhetinic acid(GRA),** there was a significant decrease in the numbers of CFU recovered from all concentrations tested, compared to the numbers of CFU recovered following incubation with DMSO(Fig. 1B).
- GRA/18β-GA demonstrated concentration-dependent inhibition of growth.
- **18β-GA shows anti-bacterial property.**

《18β-Glycyrrhetinic Acid Inhibits Methicillin-Resistant Staphylococcus aureus Survival and Attenuates Virulence Gene Expression》

07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

18β-glycyrrhetinic acid(GRA/18β-GA) reduces severity of MRSA skin infection-antiseptic

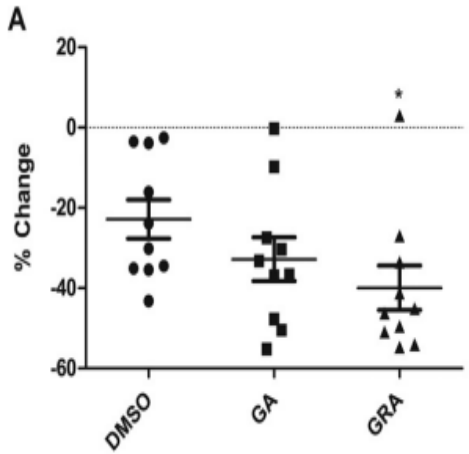


FIG 2 GRA attenuates MRSA severity during skin infection. Mice (n=10) were inoculated subcutaneously with 2 ×10^7 CFU of LAC. (A) Percent reduction in abscess size following daily treatment with DMSO, GRA (600μg/ml), or GA (600μg/ml) from day 3 to day 7. Percent change in size was calculated over a 4-day period (day 3 through day 7) using the formula % change = (size on day 7- size on day 3)/size on day 3× 100 (, P <0.05 as determined by ANOVA and Tukey's posttest when comparing DMSO- and GRA-treated mice).*

Summary:

- Treatment with **GRA/18β-GA reduced the size of the abscess over time** versus DMSO treatment.
- From day 3 to day 7, GRA treatment **significantly reduced the size of the abscesses** by 39.97% ± 5.53% compared to DMSO treatment.

《18β-Glycyrrhetinic Acid Inhibits Methicillin-Resistant Staphylococcus aureus Survival and Attenuates Virulence Gene Expression》

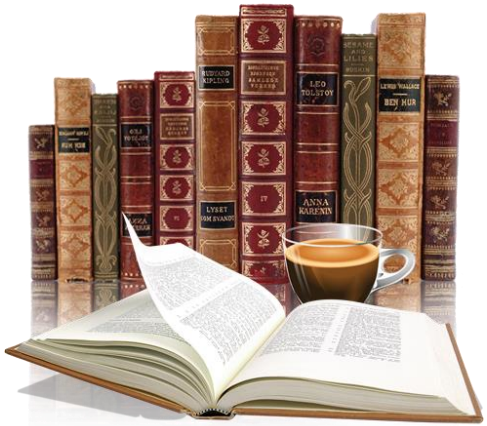
07 Introduction of Glyceyrrhetinic/Glycyrrhizic Acid & its esters

Application guide：

Compatibility	It is recommended to dissolve in propylene glycol, pentanediol and other alcohols before adding to the formula. Not recommended for mixing with alkaline substances
Dosage	0.05-2%
Usage	It can be incorporated to the formulation in the final stage of the manufacturing process, when the temperature is below 45℃

References:

1. *Tasic-Kostov et al., 2010*
2. *Ferulic Acid Stabilizes a Solution of Vitamins C and E and Doubles its Photoprotection of Skin Fu-Hsiung Lin, Jing-Yi Lin,w Ravindra D. Gupta, Joshua A. Tournas, James A. Burch, M. AngelicaSelim, Nancy A. Monteiro-Riviere,z James M. Grichnik, Jan Zielinski,y and Sheldon R. Pinnell*
3. *Biochemical Characterization of Ferulic Acid and Caffeic Acid Which Effectively Inhibit Melanin Synthesis via Different Mechanisms in B16 Melanoma Cells Hiroko Maruyama,*,a Fumitaka Kawakami,b Thet-Thet Lwin,c Motoki Imai,a and Fazel Shamsad*



Thank you for your attention!

Spec-Chem Group

www.specchemind.com

sc@specchemind.com

+86 25 84523390/84523391