

SpecWhite® DL-MA

(Mandelic Acid)

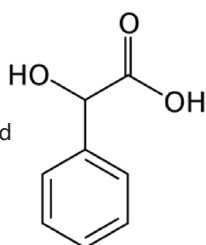
- Especially designed AHA for sensitive skin type
- Solution to Acne & Comedone Prone Skin
- Gentle Lift off dead skin cells & Even Complexion
- Excellent Skin Brightening Properties & Lightening PIH (Post inflammatory hyperpigmentation)
- Extraordinary reducing capacity

Brief Introduction of Mandelic Acid (MA)

Mandelic acid is an aromatic alpha hydroxy acid with the molecular formula $C_6H_5CH(OH)CO_2H$.

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

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°C-121°C
Moisture	0.5% Max

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 from applicant
Sample Quantity	1 package
Specification & Batch	50g
State and Characteristic	White powder
Received Date	11 th May, 2018
Completion Date	25 th , 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!

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	11 th May, 2018
Completion Date	23 rd , 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 RC₅₀ 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)" RC50=13.09% & 95% CI:8.51%-20.22% is no eye irritation potential.

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

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.
After 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

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)

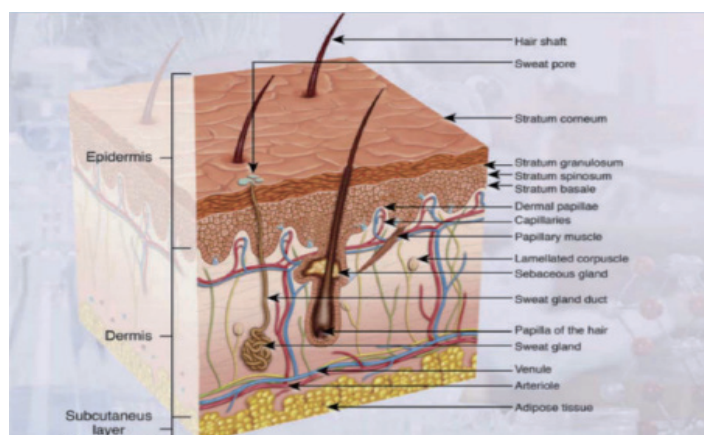
Sample	Dosage (ug/plate)	TA97		TA98		TA100		TA102	
		+S ₉	-S ₉	+S ₉	-S ₉	+S ₉	-S ₉	+S ₉	-S ₉
625	124±11	107±6	29±3	39±4	106±7	134±8	312±14	286±8	
1250	137±5	105±8	32±4	34±5	109±12	140±5	293±24	300±15	
2500	140±5	115±9	29±4	41±2	109±4	151±25	298±13	301±5	
5000	153±9	122±10	31±2	34±5	107±6	137±3	305±7	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		988±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 presence and absence of metabolic activation system.

SpecWhite® DL-MA shows No Carcinogenicity.

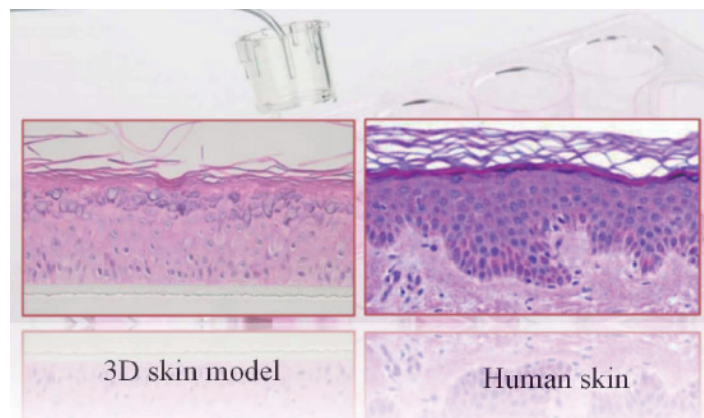
Skin model—OECD TG 439 «In vitro skin irritation: Reconstructed Human Epidermis (RHE) Test Method» (2015):

Cosmetics and skin interactionsa



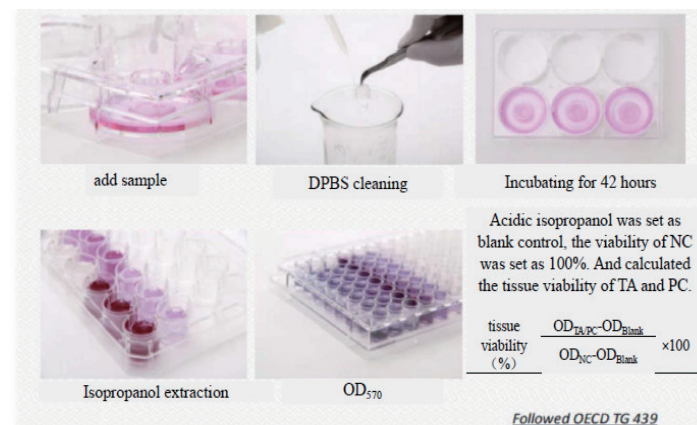
Acute skin irritation is a local, reversible inflammatory response resulting from normal skin contact with irritating drugs. The mechanism of skin irritation occurs because the test substance contacts the skin by expanding, infiltrating or destroying the epidermal barrier, and then acting on the stratum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

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	11 th May, 2018
Completion Date	15 th , 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

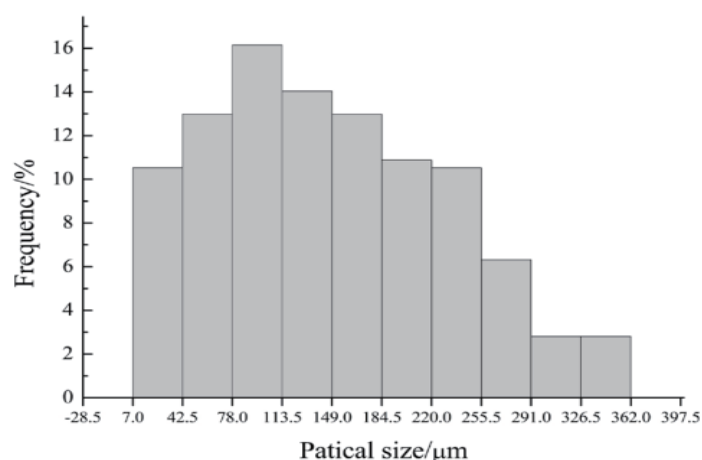
Con. (μg/mL)	Mean RFI _{CD86} (%)	Mean RFI _{CD54} (%)
2790.82	87	105
3348.98	88	111
4018.78	79	124
4822.53	58	171
5787.04	82	144

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 !

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

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 growth¹ 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																						
<i>Escherichia coli</i>	---	---	---	3	---	---	---	---	++++	++++	++++	+	+++	+++	+	+++	+	+++	+++	+	+++	+
<i>Klebsiella pneumoniae</i>	---	---	---	---	---	---	---	---	++++	++++	++++	+	+++	+++	+	+++	+	+++	+++	+	+++	+
<i>Proteus mirabilis</i>	---	---	---	---	---	---	---	---	++++	++++	++++	+	+++	+++	+	+++	+	+++	+++	+	+++	+
<i>Enterococcus spp.</i>	---	---	---	---	---	---	---	---	++++	++++	++++	+	+++	+++	+	+++	+	+++	+++	+	+++	+
1% Mandelic acid																						
<i>Escherichia coli</i>	---	---	---	---	---	---	---	---	+	---	---	---	---	---	---	---	---	+	---	---	++++	++++
<i>Klebsiella pneumoniae</i>	---	---	---	---	---	---	---	---	+++	+	---	---	---	---	---	---	---	+++	+	---	++++	++++
<i>Proteus mirabilis</i>	---	---	---	---	---	---	---	---	+	---	---	---	---	---	---	---	---	+	---	---	++++	++++
<i>Enterococcus spp.</i>	---	---	---	---	---	---	---	---	+	---	---	---	---	---	---	---	---	+	---	---	++++	++++

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.

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).

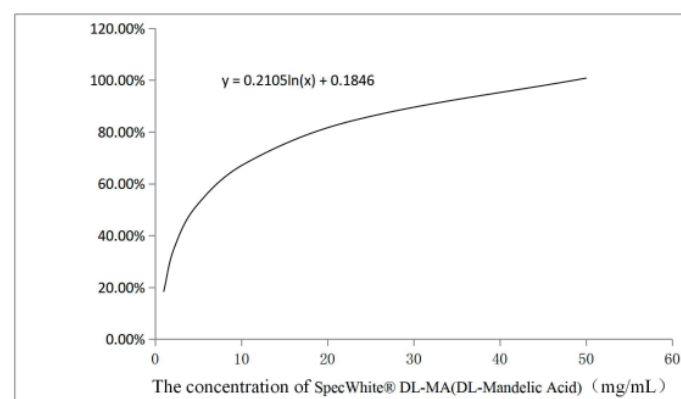


Figure 1 SpecWhite® DL-MA(DL-Mandelic Acid) on the Inhibition of Tyrosinase Activity

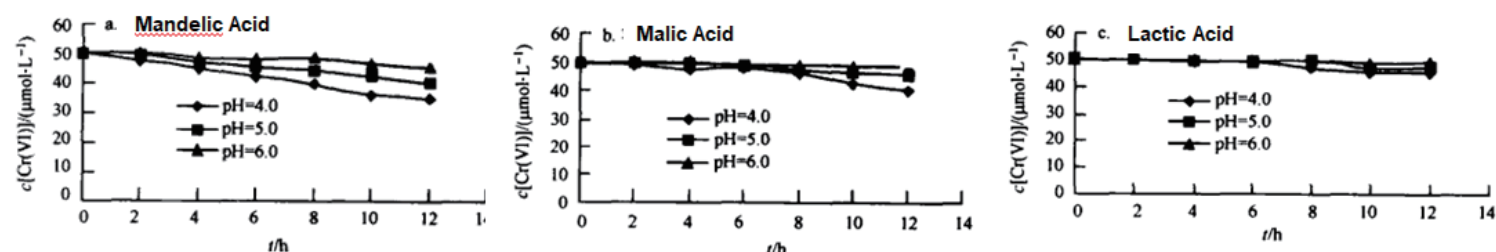
(single phenol enzyme activity)

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 beneficial to reduce skin' s melanin production, suitable for skin whitening & lightening application.



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



Effect of pH on the reduction of 50 μ mol·L⁻¹ Chromium:Cr (VI) by different organic acids at 25°C. 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.

Exfoliating Effect & Mildness of Mandelic Acid VS other acids

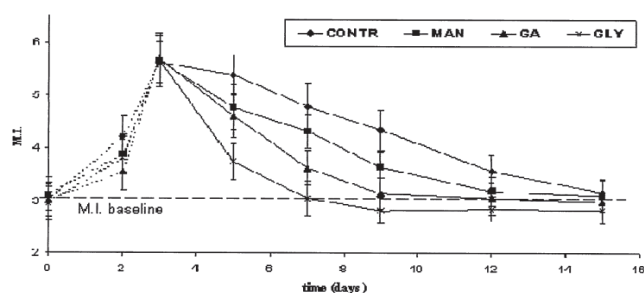


Figure 1. Trends of the melanin index (M.I.) vs time (days) for subjects recruited in the CONTR (no topical treatment), 10% GLY (glycolic acid), 10% MAN (mandelic acid), and 10% GA (grape acids) groups.

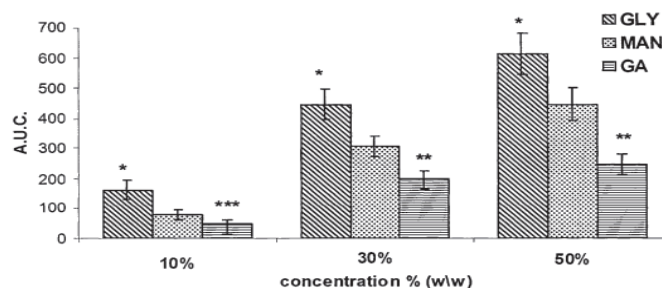


Figure 2. Mean area under curve (AUC) values (± SD) obtained by applying GLY (glycolic acid), MAN (mandelic acid), and GA (grape acids) formulations at three different concentrations (10%, 30% and 50% w/w) to skin sites of subjects admitted into the study. AUC values were directly related to the degree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

Glycolic Acid induced a faster skin exfoliation and more intense erythema and higher photosensitizing effect.
Mandelic acid & Grape acid can induce a relatively slower and safe peeling action compared with glycolic acid.

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.

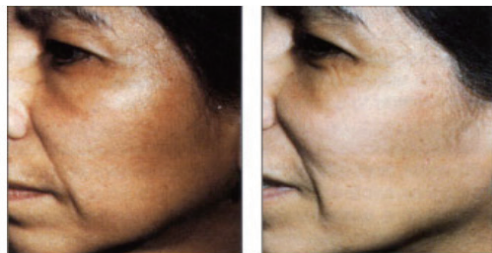


Fig. 1: Melasma in 45-year-old female (left) with hyperpigmentation caused by glycolic acid plus hydroquinone, and same patient (right) 9 months after use of mandelic acid BID.



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.**

Anti-acne Effect of Mandelic Acid VS Glycolic Acid

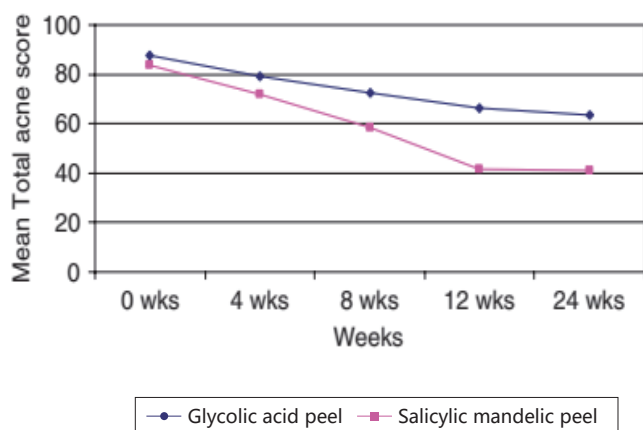


Figure2. Comparison of effects of effects of glycolic acid peel and salicylic-mandelic acid peels on total acne score.

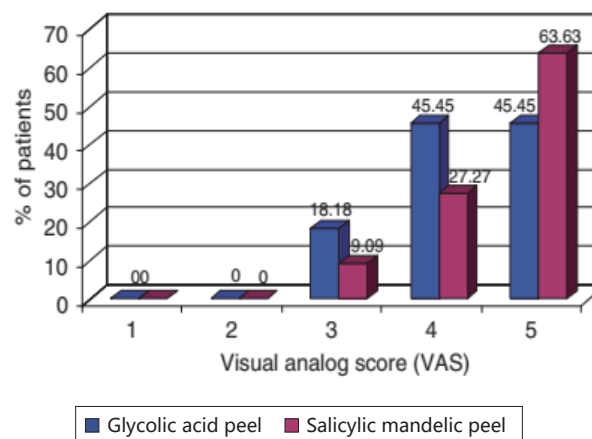


Figure3. Comparison of visual analog scale with glycolic acid peels and salicylic-mandelic acid peels (patients at 24 weeks).

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.

Formulation Example: Black Tea Scrub Cream (2% SpecWhite® DL-MA)

	Product Name	Supplier/ INCI Name	w/w%	Function
A	Glycerin		10	Humectant
	Hydroxypropyl Methylcellulose		0.5	Thickener
	SpecThem® XTG200	Spec Chem/ Xanthan Gum	0.2	Thickener
	Water		To 100	
B	SpecSufe® APG1214	Spec Chem/ Lauryl Glucoside	5	Nonionic Surfactant
C	Stearic Acid		4	Emulsifier
	SpecThem® GMS	Spec Chem/ Glyceryl Stearate	3	Emulsifier
	SpecThem® C1618	Spec Chem/ Cetearyl Alcohol	3	Hydrophilic Thickener
	SpecSufe® M68	Spec Chem/ Cetearyl Glucoside & Cetearyl Alcohol	2	Emulsifier
D	Citric Acid (20% liquid)		pH to 5.5-6.5	pH Adjuster
E	SpecKare® PQ -39	Spec Chem/ Polyquaternium-39	0.5	Film-forming agent
	Disodium EDTA		0.1	Chelating Agent
	SpecKare® DPA	Spec Chem/ Panthenol	0.5	Humectant
	ParbFree® PCG	Spec Chem/ Caprylyl Glycol & Phenoxyethanol	0.7	Preservative
	SpecPure® BTS Saponins	Spec Chem/ Camellia sinensis seed extract	2	Surfactant
	SpecWhite® DL-MA	Spec Chem/ Mandelic Acid	2	Exfoliator
	SpecPure® BML60	Spec Chem/ Bromelain	0.1	Exfoliator
	Prunus Amygdalus Dulcis (Sweet Almond) Shell Powder		1	Abrasive
	Fragrance		0.1	

Procedure:

1. Mix part A and heat to 80°C, stirring until completely dissolve, add part B;
2. Disperse the part C, then add part C, homogenize for 2 min;
3. Cool the base below 60°C, then add part D,
4. Cool the base below 45°C, then add part E, stirring until room temperature.

Properties:

Appearance:

Light brown cream

pH:

5.74 (1:10 aqueous solution)

Viscosity:

11520 (25°C, 4#, 30 rpm, mpa.s)

Stability:

1 month @45°C, 1 month @ - 18°C



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