Import and distribution for Serbia: Farmadria DOO
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EFFICACY TEST

Product Name	Tranexamic Acid
Product Code	AL00072
INCI Name	Tranexamic Acid
CAS Number	1197-18-8

Safety— Tranexamic Acid (up to 20% in water, MB Research Labs, USA)

Bovine Corneal Opacity and Permeability Test (BCOP, OECD 437)

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; No category can be assigned regarding the UN GHS Category

Safety— Summary of toxicological information

Test Items	Test methods / Guidelines	Test Result
Cytotoxicity Test	SN/T 2328-2009, MTT method	No toxicity at < 10.8 mg/mL
In vitro skin irritation - EpiSkin (Recombinant humanepidermal model)	OECD 439	Not irritating
In vivo skin irritation - Human patch test	Single occlusive patch test	Not irritating
In vitro eye irritation - BCOP (Bovine corneal opacityand permeability test)	OECD 437	IVIS: 0.95, mild irritant
In vitro skin sensitization - KeratinoSens test	OECD 442D	Not sensitizing
In vitro skin sensitization - DPRA test	OECD 442C	Not sensitizing
In vitro skin sensitization - DEREK prediction	QSAR	Not sensitizing
Germ cell mutagenicity - AMES (Bacterial Reverse Mutation Assay)	OECD 471	Not mutagenic

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Safety—Chemical Test & Microbial Test

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

Test requested:

1) Chemical Test: Arsenic, Antimony, Cadmium, Chromium, Cobalt, Lead, Mercury, Nickel, Platinum

2) Microbial Test: Staphylococcus aureus, Canadida albicans, bile-tolerant Gram-negative bacteria

Test methods:

1-1) Arsenic, Antimony, Cadmium, Chromium, Cobalt, Lead, Mercury, Nickel: analysis was performed by ICP-MS/ICP-OES

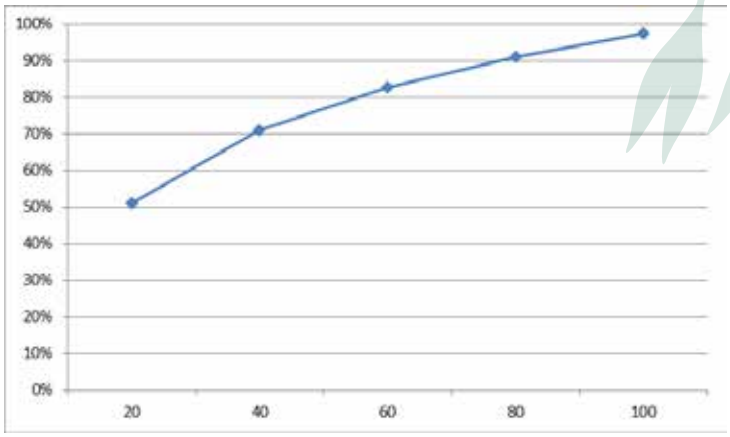
1-2) Platinum: with reference to US EPA 3052: 1996, analysis was performed by ICP-OES

2) European Pharmacopoeia 8.02.6.13A

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

In-Vitro test—Inhibiting Effect of Tranexamic Acid on Tyrosinase Activity

Sample	EC50 (mg/ml)
Tranexamic Acid	3.832



The concentration of Tranexamic acid (mg/ml)

Inhibiting effect on Tranexamic Acid on Tyrosinase Activity
(single phenol enzyme activity)

Conclusion: Through determination of tyrosinase activity inhibition, the result shows that EC50 value of Tranexamic acid is 3.832mg/ml.

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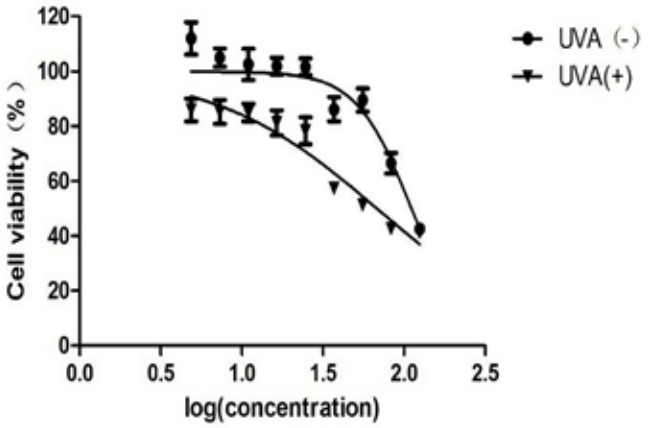
In-Vitro test—Phototoxicity Test of Tranexamic Acid



Cell survival at the same concentration of Tranexamic Acid UVA(-) and UVA(+)

Cell line:
Mouse embryonic fibroblast (NIH/3T3)

Test parameters:
Cell survival of Tranexamic acid UVA(-) and UVA(+)

Conclusion: The IC50 values of SpecWhite® TA were 110.9 mg/mL (UVA-) and 68.01 mg/mL (UVA+), and the PIF was 1.63. In accordance with OECD 432, the phototoxicity of Tranexamic Acid with a PIF＜ 2, predict "No phototoxicity".

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

Product:	2.5% and 0.5% TA Whitening Gel
Subjects:	2.5%: 15 females, 0.5%: 15 females
Age range:	27 - 53 years old
Test Site:	Face
Period:	8 weeks
Test Parameters:	Determination of skin color difference is expressed in △L and△E; △L (skin brightness value); △E (comprehensive valueof skin (including brightness, glossiness, smoothness, etc.))
Temperature:	20℃- 25℃
Humidity:	40% - 60%
Frequency:	Twice a day after cleaning face in the morning and evening
Design of Study:	Aim to assess the lightening effect of the test cosmetic product after 14days, 28 days and 56 days application in the female subjects

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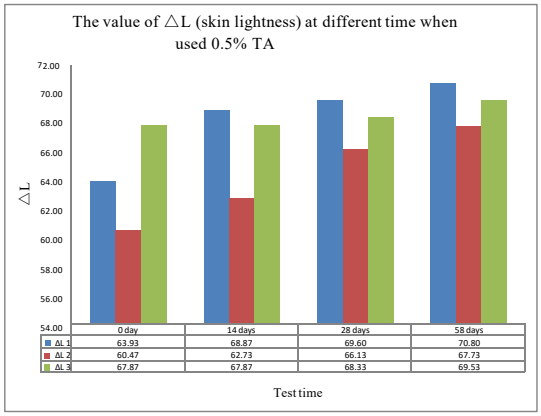
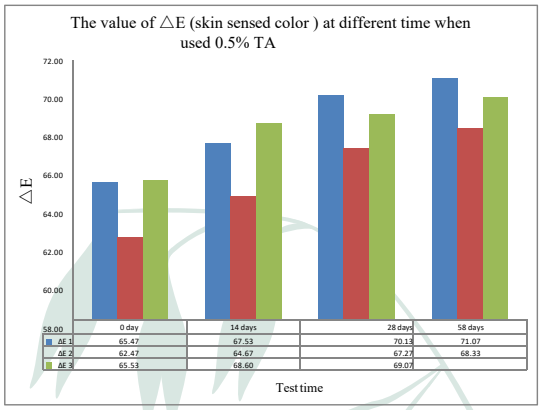
The △L and △E improved when using 0.5% TA whitening gel, comparing with the untreated

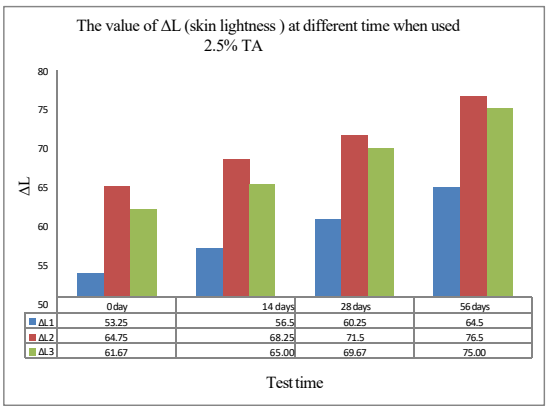


Comparing with the untreated, skin lightness improved significantly, which increased by 3.74% after 14 days, 6.13% after 28 days, 8.21% after 56 days by treating with 0.5% TA whitening gel, respectively.

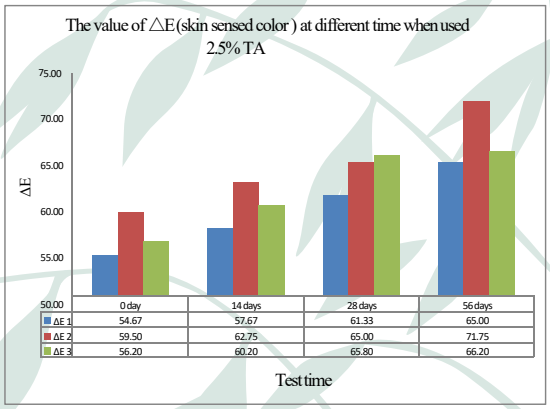


Comparing with the untreated, skin sensed color improved significantly, which improved by 3.74% after 14 days, 6.68% after 28 days, 8.23% after 56 days by treating with 0.5% TA whitening gel, respectively.

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



Comparing with the untreated, skin lightness improved significantly, which improved by 7.83% after 14 days, 12.11% after 28 days, 20.22% after 56 days by treating with 2.5% TA whitening gel, respectively



Comparing with the untreated, skin sensed color improved significantly, which improved by 6.02% after 14 days, 12.77% after 28 days, 19.12 % after 56 days by treating with 2.5% TA whitening gel, respectively.

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EFFICACY TEST

In-ViVo test—Skin Lightening & Whitening Results

Lightening & Whitening Pictures (0.5% TA whitening gel subject)

Fig. 1 0 day

Fig. 2 14 day

Fig. 3 28 day

Fig. 4 56 day

In-ViVo test—Anti-Spot Results

Anti-Spot pictures (0.5% TA whitening gel subject)

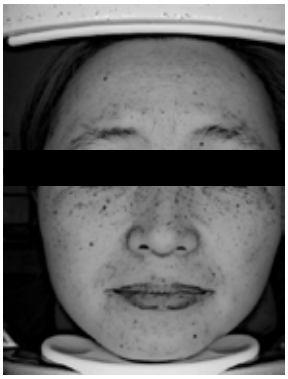

Fig. 1 0 day

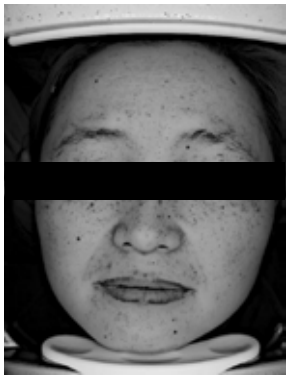

Fig. 2 14 day

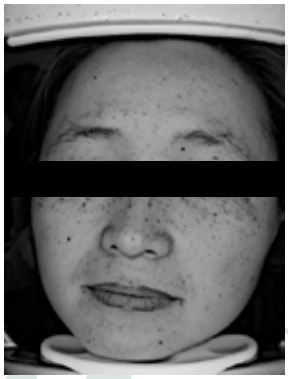

Fig. 3 28 day

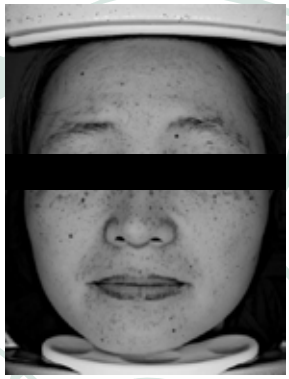

Fig. 4 56 day

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% TA whitening gel.

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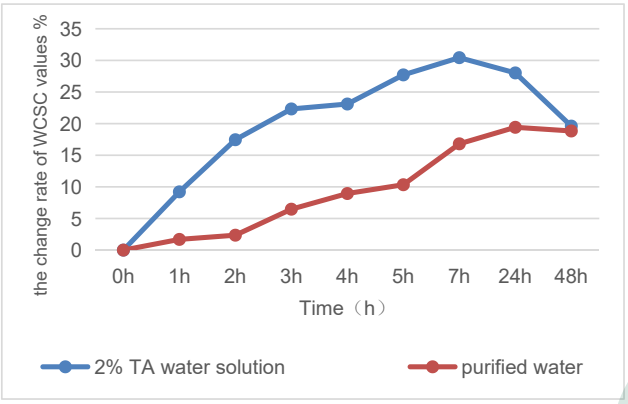
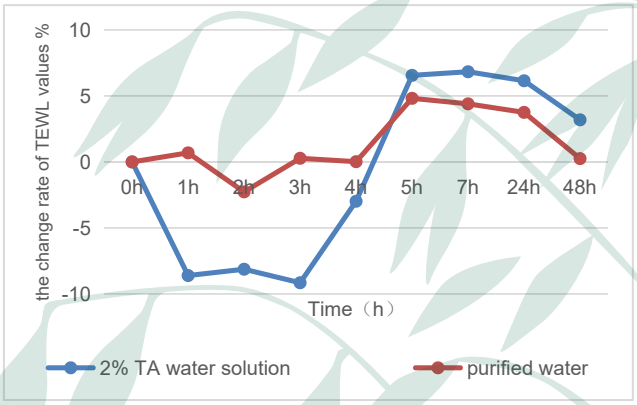
In-ViVo test—Moisturizing

Product:	2% TA water solution, purified water
Subjects:	10 females, 2 males
Test Site:	Inside of arms
Test Period:	0h, 1h, 2h, 3h, 4h, 5h, 7h, 24h, 48h
Test Parameters:	TEWL: Transepidermal water loss, WCSC: Water content in stratum corneum
Test Instrument:	MoistureMeter SC, VapoMeter SWL5
Temperature:	20 - 25℃
Humidity:	40 - 60%
Usage:	Apply quantified (0.1g±0.01g) samples at the labeled site
Design of Study:	Aim to assess the moisturizing ability of TA in 48h





Conclusions: According to the experimental results, water content in stratum corneum showed a trend of increasing, and transepidermal water loss showed a trend of decreasing first and then increasing after using TA. TA can increase water content within 48h, and reduce water loss within 4h, indicating that TA has good moisturizing ability.