Clinical Trial Results of Novel Topical Skin Brightener & Brightening Microneedling Solution

Cellese conducted a clinical study of AnteAGE MD® Brightener & Brightening Microneedling Solution. Both contain ingredients that affect multiple physiologic pathways to reduce the appearance of undesired cutaneous pigmentation. Study results proved their efficacy in improving the appearance of pigmentation of facial skin.

Abstract:

Two products containing ingredients that affect multiple pathways involved in melanogenesis, keratinocyte melanin uptake and cellular exfoliation were evaluated in a randomized clinical trial of thirty-one participants of both genders from 30 to 70 years of age. Skin types were Fitzpatrick I to V. Subjects were divided into a group that used only the topical Brightener product at home, and a group that in addition also received professional microneedling sessions with Brightener Microneedling Solution.

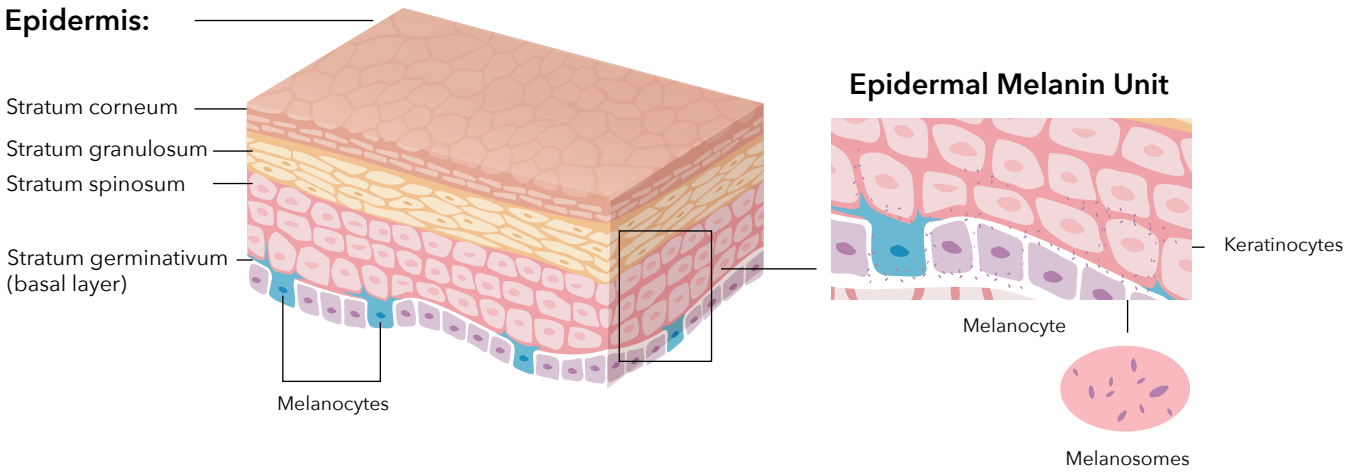
Eligible participants had complaints of conspicuous dark spots or discoloration of the face. Fifteen participants were assigned to the Homecare Group, for which they received AnteAGE MD® Brightener alone. Product was given on day 1 of the study and participants were asked to use it once daily for 60 days. Sixteen participants were assigned to the Microneedling Group. In addition to AnteAGE MD® Brightener for once-daily use, at day one and monthly for two additional months subjects received professional microneedling sessions with AnteAGE MD® Brightening Microneedling Solution.

Subjects consented to high resolution photographs and completed subjective questionnaires at the beginning and end of the study. Using beginning and end-of-study photographic documentation, a licensed skincare professional assessed visible changes in participants' facial skin. Changes were on a cumulative average percentage basis including tone, dark spots, age spots, evenness of color, radiance, blotchiness, redness and hyperpigmentation. Results for both groups were highly positive in all areas.

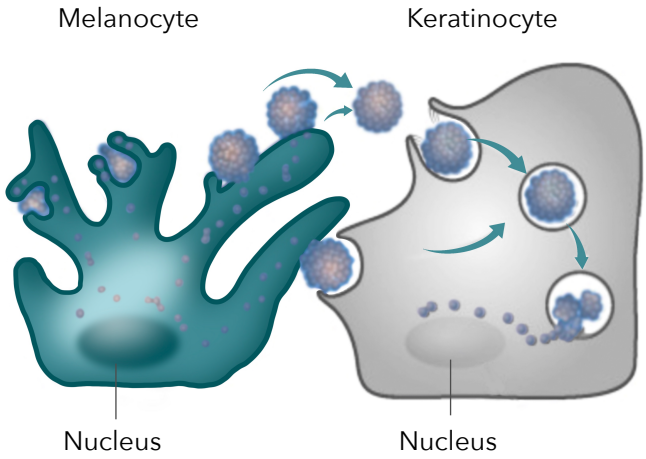
Introduction:

Melanin is an evolutionary protective pigment whose skin function is as a barrier against ultraviolet (UV) solar radiation. All races have similar numbers of melanin producing cells located within the stratum basalis of the epidermis. Skin color differences result from the pigment content and characteristics of the melanosomes produced by the melanocytes.

Caucasian skin has the smallest amount of pigment and smallest melanosomes; darkly pigmented skin has larger, wider and denser melanosomes. Inflammation from any source, including damage from UV radiation, is a potent stimulus for increased melanin production. Darker Fitzpatrick skin types are more prone to develop aesthetically displeasing hyperpigmentation.



Melanosomes produced by melanocytes are expelled and subsumed into nearby keratinocytes. The melanin-laden keratinocytes slowly migrate to the skin surface where they are eventually sloughed off, a process that takes four to six weeks.



Products to reduce undesired pigmentation are sought by many people. Hypermelanosis in the form of melasma, café au lait spots, solar lentiginosis, and post-inflammatory hyper-pigmentation are common concerns although some individuals seek general overall skin lightening.

Melanogenesis takes place within the melanosomes, catalyzed by the enzyme tyrosinase. Inhibitors of this enzyme have long been mainstay ingredients in depigmenting products. This approach, however, addresses only one of several processes in melanin production, deposition and removal.

The novel products tested contain ingredients that address seven pathways, or Mechanisms of Action (MOA's), that affect pigmentation – before, during and after melanogenesis.

The study products contain ingredients that:

1. Inhibit tyrosinase activity and co-factors
2. Promote tyrosinase degradation
3. Down regulate gene expression that promotes melanogenesis
4. Inhibit the pro-melanogenetic effects of UV
5. Inhibit melanosome transfer from melanocyte to keratinocyte
6. Increase exfoliation of pigmented keratinocytes
7. Counter the inflammation stimulus of UV and other stresses

Method:

Thirty-one participants of both genders from 30 to 70 years of age with Fitzpatrick skin types I to V were randomly divided into two groups. All participants had complaints of conspicuous dark spots or discoloration of the face. The Homecare Group (15 subjects) used the topical Brightener product at home once daily for 60 days. The Microneedling Group (16 subjects) used topical Brightener once daily for 90 days and in addition received professional microneedling with Brightener Microneedling Solution on three occasions – on study day one and twice more at monthly intervals.

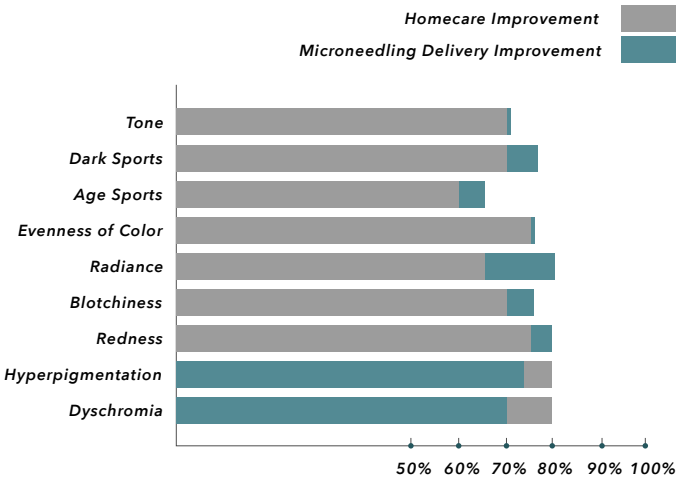
Microneedling was performed by a licensed professional at 1.0 mm depth using an electrically powered oscillating pen device after 20 – 30 minutes of topical anesthetic pre-treatment (benzocaine lidocaine, tetracaine) and disinfection with 70% isopropyl alcohol. During and immediately following microneedling, two milliliters of Brightening Microneedling Solution was applied with a roller-ball applicator in multiple coats to all treated areas.

Subjects consented to high resolution photographs with The Observ® Skin Diagnostic Device which uses skin fluorescence and polarized light to reveal surface and deeper skin detail. Participants completed subjective questionnaires at the beginning and end of the study. Using beginning and end-of-study photographic documentation, a licensed skincare professional assessed visible changes in participants' facial skin. The zero to five scoring system below was used for questionnaire and photos evaluation:

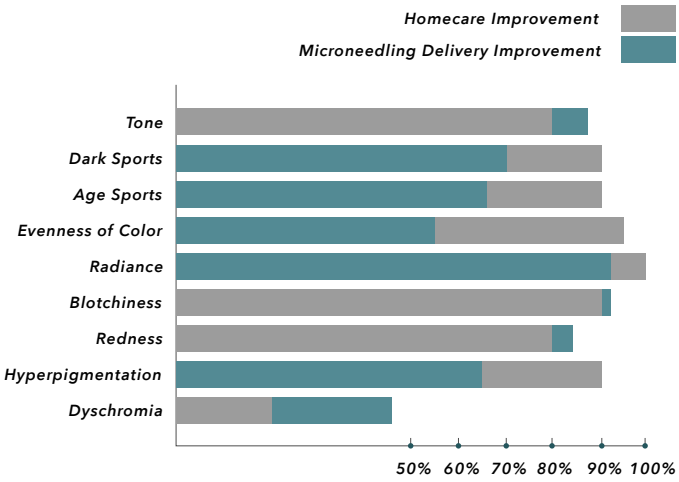
1	AnteAGE® made the problem worse
2	No improvement with AnteAGE®
3	Minor improvement with AnteAGE®
4	Moderate improvement with AnteAGE®
5	Considerable improvement with AnteAGE®
6	Remarkable improvement with AnteAGE®

Results:

The tabular results below reflect the percentage cumulative improvement reported by participants comparing their start-of-study questionnaire score to their end-of-study scores.



The tabular results below reflect the percentage cumulative improvement reported by a skincare professional comparing start-of-study Observ® photos to end-of-study photos.



There were no adverse events reported during the study.

Active Ingredients:

Brightener Ingredients	Mechanism of Action
Alpha-Bisabolol	Inhibition of the cAMP response element (CRE) which regulates alpha-Melanocyte Stimulating Hormone (a-MSH) activity.
Bone Marrow Stem Cell Conditioned Media	Physiologically balanced bio-signals reduce inflammation to promote even skin tone and healthy levels of pigmentation.
Camellia Sinensis Leaf Extract	Catechins from green tea have recognized anti-inflammatory and anti-melanogenic effects in skin.
Epidermal Growth Factor (EGF)	Promotes cellular growth and accelerated wound healing which reduces overall inflammatory stimulus of melanocyte activity.
Galangin	Flavonoid from ginger family which inhibits tyrosinase activity.
Licorice Root Extract	Isoflavonoids have recognized inhibitory effect on tyrosinase activity, inflammation, melanosome transfer and antioxidant potency.
Morus Alba Leaf Extract	Mulberry leaf constituents inhibit melanin biosynthesis, provide superoxide scavenging activity and protect against cellular oxidation.
N-Acetyl Glucosamine (NAG)	NAG reduces melanogenesis, is potentiated when combined with niacinamide, has antioxidant potency and promotes exfoliation.
Niacinamide (Vit B3)	Reduces melanosome transfer, decreases inflammation.
Oligopeptide-51	Bioengineered peptide inhibits tyrosinase activity via TRP-1 and TRP-2 expression and promotes cellular regeneration.
Phytol	Diterpene that stimulates keratinocyte proliferation, upregulates PPAR activity and stimulates retinoid-x receptors.y.
Tetrahexyldecyl Ascorbate	Potent antioxidant which stimulates collagen production and reduces pigmentation by inhibiting melanogenesis.
Tranexamic Acid	Inhibits tyrosinase activity, reduces Prostaglandin E2, inhibits UV induced melanocyte stimulation and melanosome transfer.
Transforming Growth Factor Beta 3 (TGF-ß3)	Regulates epidermal and dermal cells during healing and downward modulation of inflammation.

Brightener Microneedling Solution Ingredients	Mechanism of Action
Bone Marrow Stem Cell Conditioned Media	Physiologically balanced bio-signals reduce inflammation to promote even skin tone and healthy levels of pigmentation.
IL-10 (sh-Polypeptide-6)	Interleukin 10 is a potent anti-inflammatory cytokine.

Active Ingredients:

Nonapeptide-1	A peptide, derived from melanocyte stimulating hormone (MSH), prevents the activity of tyrosinase in melanocytes.
N-Acetyl Glucosamine	NAG reduces melanogenesis, is potentiated when combined with niacinamide, has antioxidant potency and promotes exfoliation.
TGF-b3 (sh-Polypeptide-5)	An anti-inflammatory cytokine that modulates inflammatory responses through a variety of mechanisms.
Tetrapeptide-30	Synthetic peptide of four amino acids with anti-inflammatory, tyrosinase inhibiting, and melanin transfer preventing effects.
Tranexamic Acid	Inhibits tyrosinase activity, reduces Prostaglandin E2, inhibits UV induced melanocyte stimulation and melanosome transfer.

Discussion:

The products tested in this study represent a new concept in improving the appearance of skin pigment abnormalities. Unlike traditional products containing hydroquinone or other tyrosinase inhibitors, active ingredients in Brightener address seven pigment pathways: melanocyte stimulation and control, melanin synthesis and production, melanin uptake and dispersal, and cellular exfoliation. Brightener Microneedling Solution combines the natural anti-inflammatory benefits of Bone Marrow Stem Cell Conditioned Media, potentiated by IL-10, along with a synthetic peptide that inhibits tyrosinase and a monosaccharide amide that reduces free radicals as it also promotes exfoliation.

A randomized study of thirty-one participants aged 30 to 70 years of age of both genders with Fitzpatrick skin types I to V confirmed that Brightener and Brightener Microneedling Solution produce significant and safe brightening and improved appearance of undesired facial pigmentation, regardless of etiology.

References:

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