

Spot
Corrector



Whitening Active
Safe, Easy to Use and Color-**Stable**

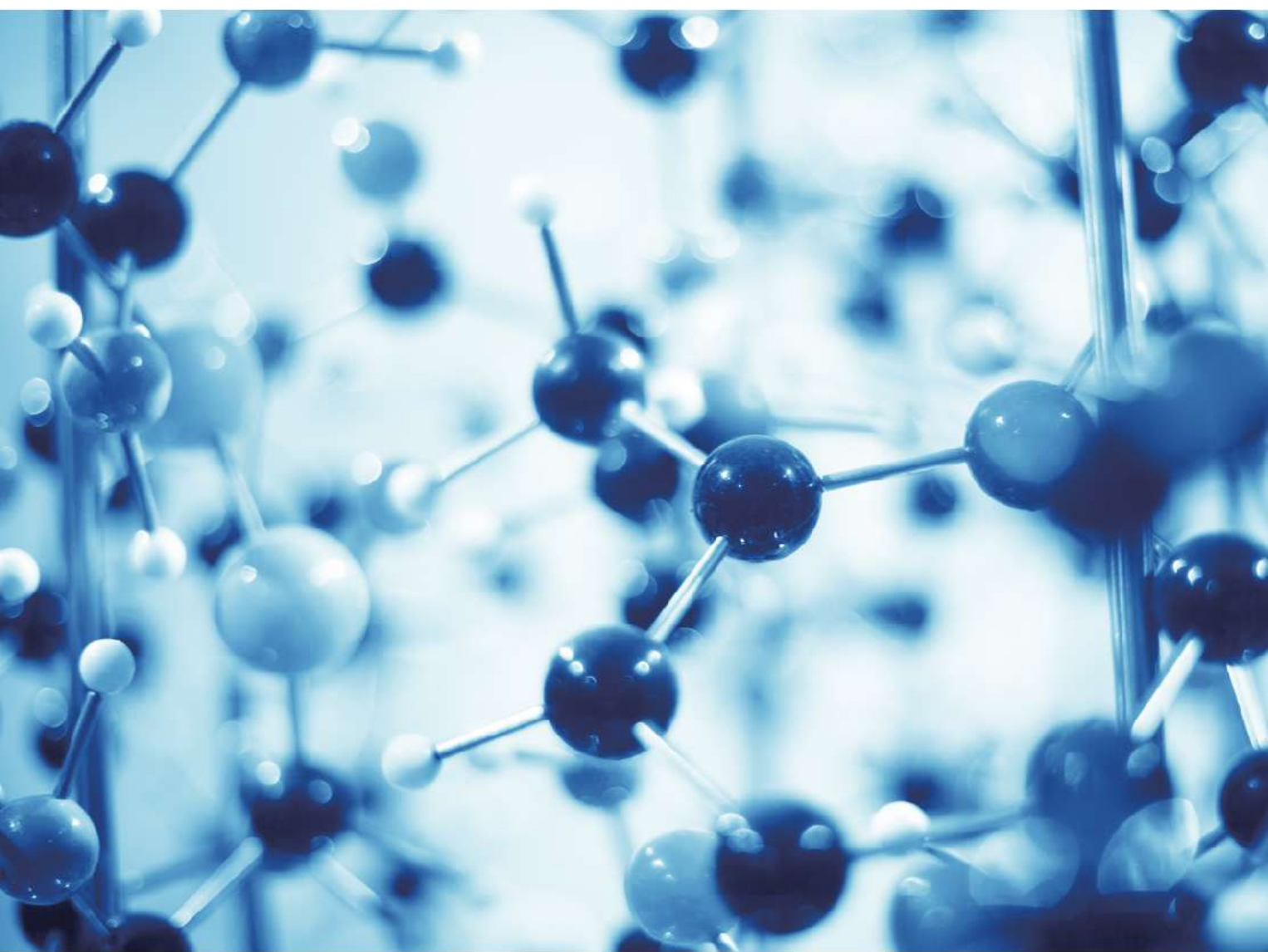
Advanced
Whitening Peptide

GenoWhiteTM

Acetyl Glycyl β -Alanine

March
2014





GenoWhite™ Advanced Whitening Peptide

A Powerful “Spot Corrector” with Excellent Safety and Stability Profile

Our Latest Patent Pending Innovation

Perfect skin tone has always been endlessly explored as an important beauty topic. The market shows a general demand for whitening products with the aim to lighten skin complexion and lessen pigmentation for a more radiant look. Asian culture highly praises lighter and even skin tone, which they associate with higher social status. Western culture, however, appreciates tanned skin as a representation of better lifestyle and vitality. No matter how the cultural preferences differ, people pursue a lighter, fairer skin tone and appearance as a more appealing look.

After five years of rigorous R&D process and validation, Corum is introducing its latest patent pending innovation: GenoWhite™, a small molecule peptide with fast dermal penetration feature. At a relatively low usage level, GenoWhite™ can already yield outstanding performance - melanin reduction, inhibition of melanin transport, and inhibition of all three melanin-generating enzymes, tyrosinase, tyrosinase-related protein 1 (TRP-1) and TRP-2. GenoWhite™ also functions genetically to diminish the melanin-promoting transcription factor microphthalmia associated transcription factor (MITF) by up to 30% of its basal level. Also, *ex-vivo* and *in-vivo* tests both indicate its significant effectiveness on age spot whitening in only 9 and 14 days, respectively.

Proven by a series of extensive studies, GenoWhite™ is an extremely potent, fast-acting “spot correcting” and whitening agent that is easy to formulate with.

Claim Ideas for GenoWhite™

- ◆ Lighten skin
- ◆ Reduce dark spots
- ◆ Improve skin clarity
- ◆ Even out skin tone
- ◆ Prevent pigmentation

Applications

- ◆ Skin whitening/ lightening
- ◆ Age spot corrector

Storage

- ◆ Protect from light, heat and moisture.

INCI Declaration

- ◆ Product name: GenoWhite™
- ◆ INCI (English): Acetyl Glycyl β-Alanine

Additional Information

- ◆ White powder
- ◆ Purity (HPLC): 99% min.
- ◆ Water soluble
- ◆ Superior stability
- ◆ Easy to use and suitable for all types of formulation
- ◆ Recommended concentration: 0.5 - 2%
- ◆ China REACH registration: In progress
- ◆ Patent-pending

New Innovation

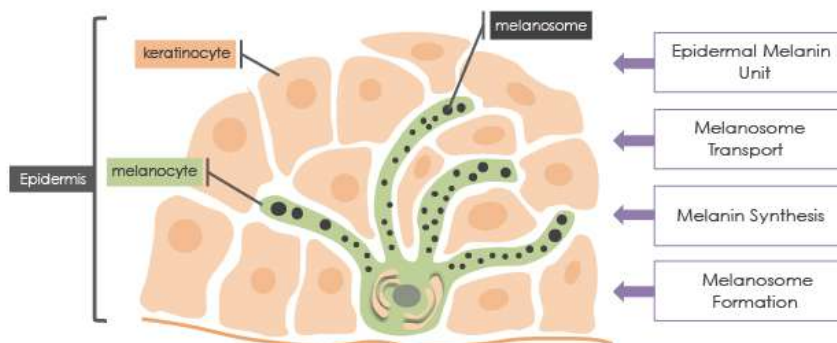
Potent Whitening Technology to Combat Skin Pigmentation

The Mechanism of Pigmentation

Melanogenesis is a complex process controlled by various factors, which are mainly determined by the activation of MITF, the key regulator responsible for the synthesis of three melanin-generating enzymes: TRP-1, TRP-2 and tyrosinase. Skin pigmentation includes three major processes - melanosome formation, melanin synthesis, and melanosome transport. Visible skin pigmentation depends primarily on the synthesis of melanin. Melanosomes are organelles of pigment cells, in which melanins are synthesized and stored. When melanosome matures, the ultimate step is to be transported from perinuclear region of melanocytes to its dendritic tip via intracellular cytoskeleton system. The synthesized melanin in fully mature melanosomes will be subsequently distributed to neighboring keratinocytes toward upper skin layer, resulting in dull and pigmented skin.

Several anchoring proteins have been identified as crucial molecules involved in the melanosome transport process. Rab27a, Myosin Va and melanophilin are three factors constituting a tripartite complex to mediate proper transfer of melanosomes. Aside from melanin transport, the cellular and molecular interactions between melanocytes and keratinocytes also play a very important role. Epidermal melanin unit, a proposed anatomical model, is a functional and structural complex in epidermis consisting of both cell types; there are 36 keratinocytes surrounding each melanocyte to form a specialized cell group. The cross-talk of the epidermal melanin unit is critically connected and controlled through paracrine released in between the cell group.

Mechanism of Pigmentation



Inhibition of MITF

MITF is a basic-helix-loop-helix leucine zipper transcription factor involved in melanocytes development, which acts as the master gene for melanocyte survival. It is also the key factor regulating the transcription of major melanogenic proteins, such as tyrosinase, TRP-1 and TRP-2. Under UV exposure, α -melanocyte stimulating hormone (α -MSH), an endogenous peptide hormone promoting melanin synthesis, is induced and further leads to MITF up-regulation.

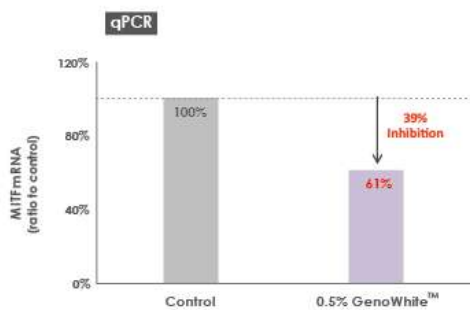
To investigate the transcription regulation of GenoWhite™ on MITF, its mRNA level was studied by quantitative real-time polymerase chain reaction (PCR), and the result shows an outstanding performance that up to 39% of MITF was inhibited.

Inhibition of Tyrosinase

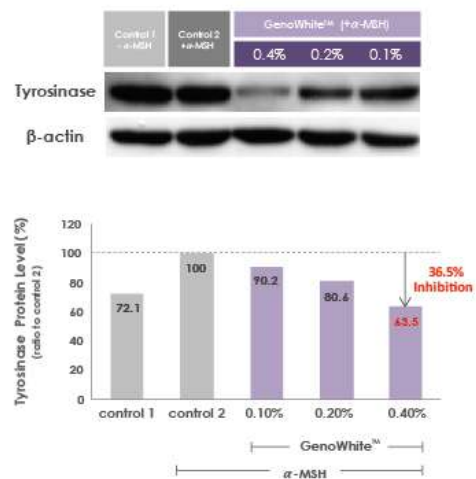
Tyrosinase is the key enzyme catalyzing the rate-limiting step during melanogenesis. In this study, the functional level of tyrosinase was evaluated using A375 human melanoma cell. GenoWhite™ at different concentrations (0.1%, 0.2% and 0.4%) were treated to the cells together with α -MSH, incubating for 3 days followed by Western blot analysis.

Results show a significant induction of tyrosinase level by α -MSH, but 0.4% GenoWhite™ can efficiently inhibit the protein level of tyrosinase up to 36.5%.

Inhibition of MITF



Inhibition of Tyrosinase



The Role of TRP-1/TRP-2

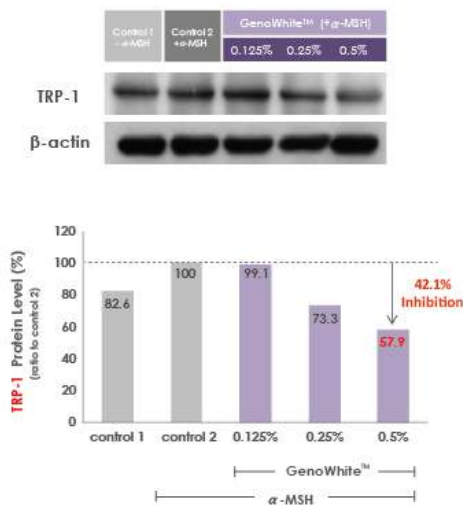
TRP-1 and TRP-2 are crucial catalysts during melanogenesis that function to modify the determination of melanin types, especially for eumelanin, the pigment found abundantly in hair and skin which primarily imparts black and darker colors. TRP-1, also known as DHICA oxidase, is the major enzyme catalyzing the oxidation and polymerization of DHICA monomers into eumelanin. TRP-2, known as DCT, on the other hand, serves as eumelanogenic enzyme to facilitate DHICA formation. TRP-2 is also known to stabilize tyrosinase activity that is essential to initiate the melanin synthesis.

Inhibition of TRP-1/TRP-2

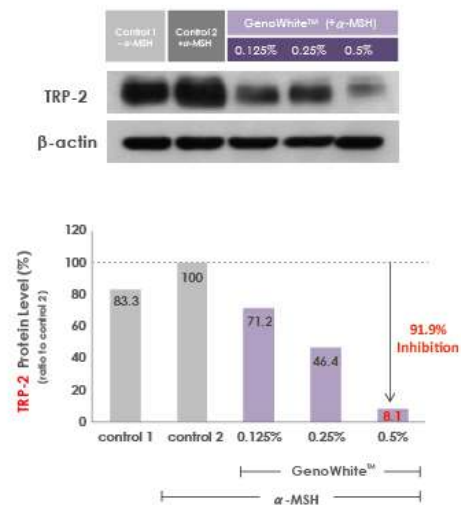
A study was carried out to evaluate the effect of GenoWhite™ on TRP-1 and TRP-2 levels. Cells were treated with 0.125%, 0.25% and 0.5% of GenoWhite™ together with α -MSH, respectively, and analyzed by Western blot.

Results show an excellent property of GenoWhite™ on inhibiting the protein level of both enzymes. When 0.5% of GenoWhite™ was applied, 42.1% of TRP-1 reduction was achieved. Under the same treatment, the performance is even better for TRP-2 as it showed that up to 91.9% of protein was inhibited by GenoWhite™.

Inhibition of TRP-1



Inhibition of TRP-2



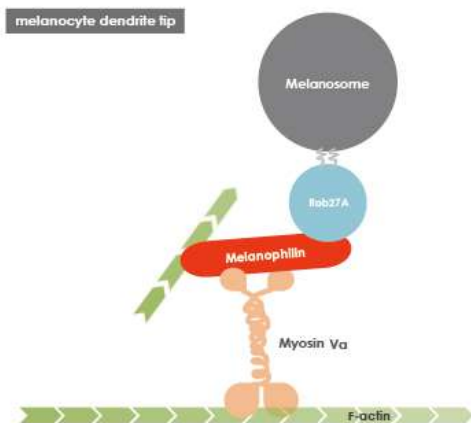
The Actin-Based Melanosome Transport System

The ultimate step of melanogenesis is to transport the melanosomes to keratinocytes through the protruded dendritic region of melanocytes. During pigment transportation, an intracellular transport system is required and involves three proteins, namely Rab27A, Myosin Va, and melanophilin. Rab27a mediates the binding of Myosin Va to melanosomes through another linker protein, melanophilin, which is the key regulator for the transport process, functioning as a Rab27a effector protein, a cargo recognition mediator for Myosin Va, and an anchorage for the actin cytoskeleton. The tripartite system is essential for successful transfer of melanosomes to achieve normal skin pigmentation.

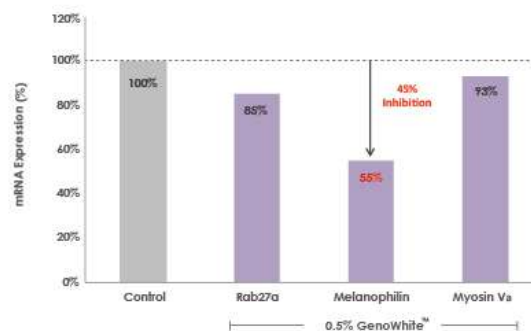
Down-Regulation of Melanophilin by GenoWhite™

B16 mouse melanoma cells were used to investigate the effect of GenoWhite™ on melanosome transport. 0.5% of GenoWhite™ was treated and the genetic expression of Rab27a, Myosin Va and melanophilin were studied by qPCR. Results show an outstanding performance of GenoWhite™ to achieve 45% of mRNA inhibition on melanophilin, the essential anchoring protein for melanosome transport.

The Melanosome Transport System



Inhibition of Melanosome Transport



GenoWhite™

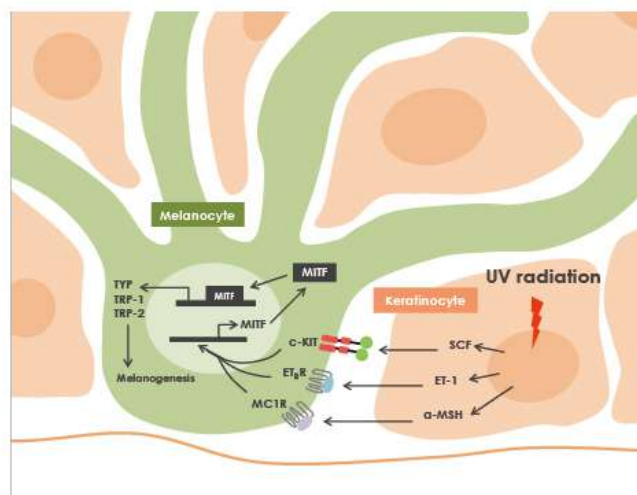
Efficacy Study

Epidermal Melanin Unit Cross-talk

The cross-talk between melanocytes and keratinocytes is very active and delicately controlled during UV exposure. Paracrines involved include stem cell factor (SCF) and endothelin-1 (ET-1), which are keratinocyte-derived factors mediating the proliferation and differentiation of melanocytes. SCF and ET-1 are cytokines that are remarkably up-regulated at both protein and gene levels in UVB-exposed skin epidermis, playing major roles in skin pigmentation. By working through its own receptor, ET_BR, the UV-induced ET-1 can enhance the transcription of MC1R, the receptor of α -MSH, to further promote melanin synthesis.

When SCF and ET-1 bind to their corresponding receptors c-KIT and ET_BR, melanogenesis is triggered by activation of MITF along with the generation of tyrosinase, TRP-1 and TRP-2. Each signaling cascade was reported to be associated with different phases of UVB-induced melanogenesis. By either blocking ligand/receptor interaction or inhibiting the synthesis of each component can indeed cause dysfunction of the pigmenting process, therefore limiting the skin pigmentation.

The Role of SCF and ET-1 in Pigmentation

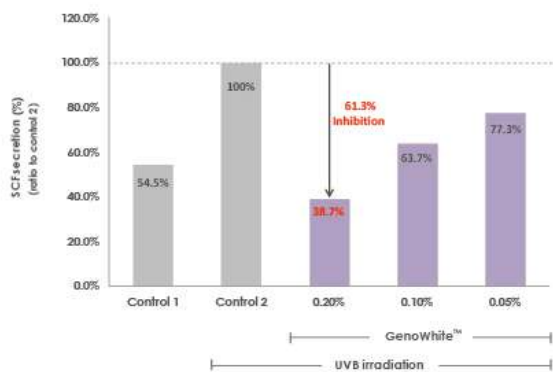


Down-Regulation of SCF and ET-1

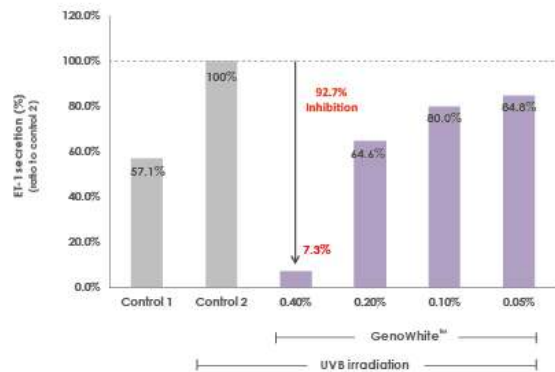
ELISA is a quantitative enzyme immunoassay technique to evaluate the activity of proteins. To investigate the effect of GenoWhite™ on keratinocyte-derived SCF and ET-1, monoclonal antibodies specific for each protein were pre-coated onto a microplate followed by the measurement of SCF and ET-1 through the intensity of color generated from the substrate solution interaction.

Normal Human Epidermal Keratinocytes (NHEK) were used as model system to study the effect of GenoWhite™. The results show that both SCF and ET-1 level were increased upon UVB irradiation. As a potent whitening agent, GenoWhite™ remarkably reduced SCF up to 61.3% when only 0.2% was applied. At the same treatment level, it also shows a great inhibition rate of 35.4% over ET-1. When the percentage was increased to 0.4%, up to 92.7% of ET-1 was inhibited, achieving an almost complete suppression over the melanogenic cytokine.

Inhibition of SCF



Inhibition of ET-1

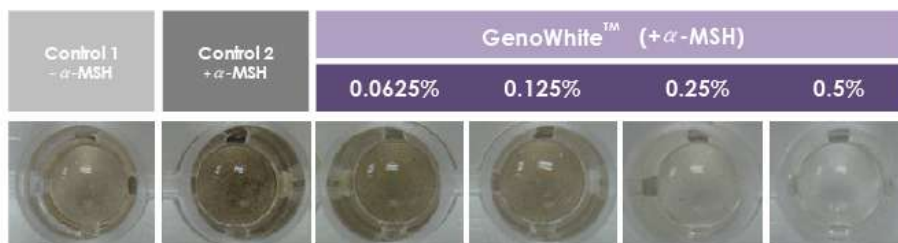


Inhibition of Melanin Synthesis

In an *in-vitro* study conducted on melanocytes, GenoWhite™ was shown to effectively inhibit melanin formation. B16 melanoma cells were cultured with α -MSH and the melanin content was determined by change in solution color. The cell viability was monitored in parallel to ensure there was no cytotoxic effect during the test.

The results indicate that GenoWhite™ efficiently reduced α -MSH-induced melanin formation in a dose-dependent manner. Also, the cell viability remains the same as before treatment.

Inhibition of Melanin Content



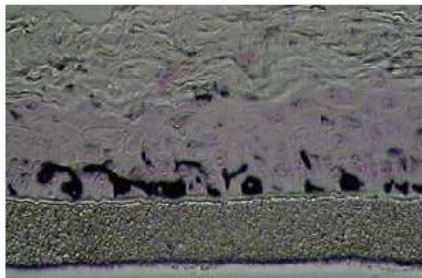
Melanin Assessment: Ex-Vivo Whitening Study

MelanoDerm™ is an ex-vivo tissue model of human epidermis, prepared from co-cultured human keratinocytes and melanocytes, used in a melanin assessment study. This melanin assay is designed to assess the potential of a test material to induce changes in tissue pigmentation.

The MelanoDerm™ tissue was incubated with 2% of GenoWhite™ in assay medium to investigate the melanin content. The results show that after only 9 days of incubation, the melanin content significantly decreased compared with the controlled tissue, indicating the excellent ability of GenoWhite™ to reduce skin pigmentation.

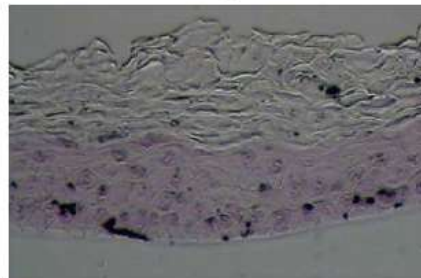
Inhibition of Melanin Production

Day 0



Untreated tissue

Day 9



2% GenoWhite™

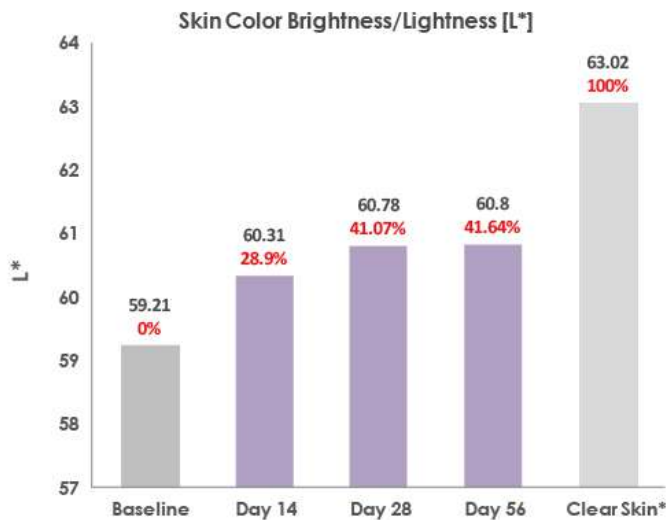
In-Vivo Age Spot Reducing Test-I

A study was conducted by AMA Laboratories, USA, in accordance to the chromametry principle to evaluate the effectiveness of GenoWhite™ to reduce hyperpigmentation on human face. Instrumental Color Determinations to corroborate visual analysis were performed using Minolta Chromometer to detect subtle changes in color by a three dimensional profile of hue, value and chroma, which are translated into color coordinates a*(green to red), b*(blue to yellow) and L*(light to dark). 10 female subjects were enrolled in the panel demographics.

Improvement on Skin Lightening

The results demonstrate that GenoWhite™ achieves profound increase in L* value which is associated with skin lightening. The mean results were considered statistically significant at each evaluation time point with 28.9%, 41.07% and 41.64% of L* value improvement observed after 14, 28 and 56 days of application, respectively.

Inhibition of Melanin Production



*Defined as the most natural, untanned skin tone of each individual.

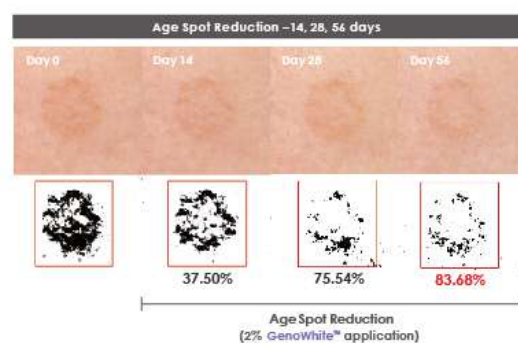
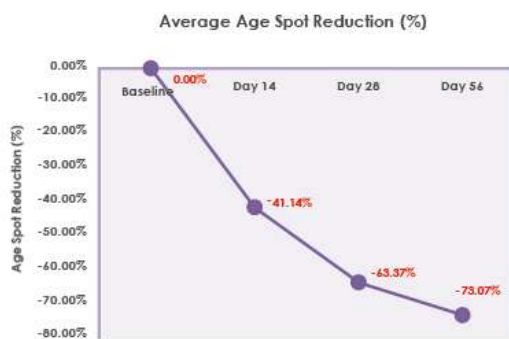
In-Vivo Age Spot Reducing Test-II

Particularly detailed, high resolution digital photographs were taken at baseline and again after 14, 28 and 56 days of GenoWhite™ application and comprehensively evaluated using Reverse Photo Engineering. Every stage of the progression from each treatment was photographically documented, providing both visual and computerized records of GenoWhite™ efficacy on five subjects' faces, age ranged from 38-49 with noticeable age spots.

Reduction of Age Spots

Data was obtained through matched scientific photography on a subset of five subjects. Image analysis software demonstrated that GenoWhite™ reduced the appearance of age spots up to 41.14%, 63.37% and 73.07% on day14, day28 and day56, accordingly. These results are considered statistically significant. GenoWhite™ is a highly effective "spot corrector" that works in just 14 days.

Age Spots Reduction



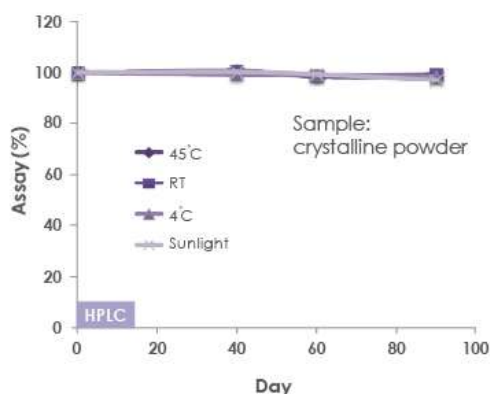
GenoWhite™

Stability Study

In addition to being highly effective, GenoWhite™ also shows superior stability. The purity of GenoWhite™ crystalline powder and transmittance of its aqueous solution were evaluated when retained in 45°C, room temperature (RT), 4°C, and under sunlight for 90 days.

Crystalline Powder: Purity

The purity of GenoWhite™ crystalline powder, evaluated by HPLC, remained consistent under the four different conditions.

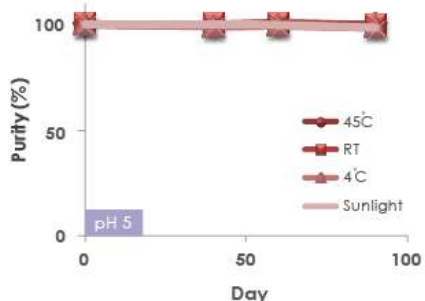
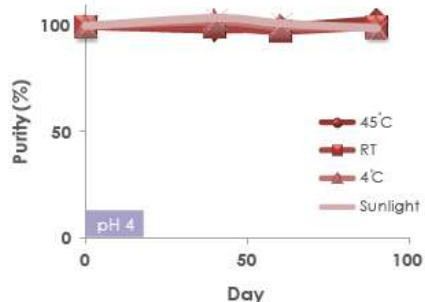
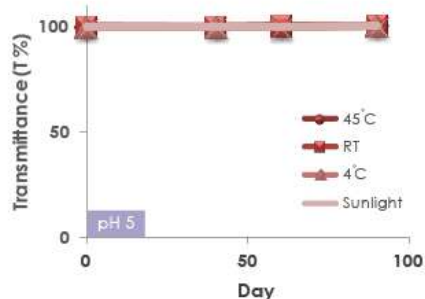
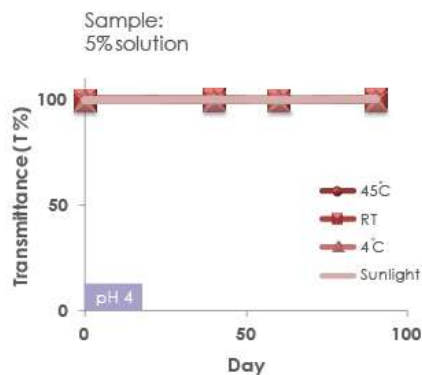


5% Aqueous Solution: Transmittance

The transmittance of 5% GenoWhite™ aqueous solution was evaluated. Results show that the sample color stayed transparent at 45°C, RT, 4°C, and under sunlight for 90 days, and even remained unchanged under different pH value at pH 4 and pH 5.

5% Aqueous Solution: Purity

The purity of 5% GenoWhite™ aqueous solution also remained consistent under 45°C, RT, 4°C, and sunlight for 90 days, at both pH 4 and pH 5.



GenoWhite™

Advanced Whitening Peptide

Claim Ideas for GenoWhite™

- Skin lightening/ Whitening
- Reduce dark spots
- Improve skin clarity
- Even out skin tone
- Prevent pigmentation

Applications

- Skin whitening/ lightening
- Spot corrector

Marketing Benefits

- Advanced whitening peptide
- New and Patented
- Non irritant, non-mutagenic and non-toxic
- Suitable for all types of formulation and easy to formulate



CORUM

6F, No. 360, Ruei Guang Rd., Neihu, Taipei, Taiwan
Tel: 886-2- 87516060 | Fax: 886-2- 87516363
sales@corum.com.tw | www.corum.com.tw