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mibellebiochemistry



Delentigo™

The age spot solution



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Erasing Age Spots and Equalizing the Skin Tone

Delentigo™ targets and lightens age spots by combining two active substances incorporated into separate liposomes:

- An extract of Swiss garden cress sprouts which is rich in sulforaphane, a powerful antioxidant phytonutrient
- Genistein, the biologically active form of the most abundant soy isoflavone.

Age spots appear on UV-exposed areas of the body mainly after 50. They are characterized by an increased production of two pigments: melanin and lipofuscin.

Delentigo™ prevents and regulates the formation of both pigments. It also inhibits the accumulation of lipofuscin in the skin by activating the proteasome, the cell's own cleaning system which degrades oxidized proteins.

Classical whitening actives don't work specifically on age spots. They tend to lighten the skin all over, that is to say both age spots and normally pigmented areas. If not applied only to the spot, the fading effect is not perceptible because the difference of pigmentation between the spot and the normally pigmented surrounding areas remains the same.

Clinical studies performed on Caucasian skin types showed that Delentigo™:

- visibly lightens age spots
- equalizes the skin tone by fading age spots more than the surrounding, normally pigmented skin.

Delentigo™ can therefore be applied all over the face in contrast to classical whitening actives which have to be applied only to the spots.

Claim Ideas for Delentigo™

- Creates an even skin tone
- Visibly reduces age spots
- Prevents photo-aging and dark spots

Applications

- Anti-aging products with correction of age spots
- Targeted treatment for dark spots
- Lightening formulations for discoloration
- Hand care products

Formulating with Delentigo™

- Recommended use level: 2–6 %
- Incorporation: For cold processes, dissolve Delentigo™ into the aqueous phase. In cold / hot processes, add during the cooling phase below 40°C.
- Thermostability: Temperatures of up to 60°C for a short time do not affect the stability of Delentigo™.

INCI / CTFA-Declaration

Lepidium Sativum Sprout Extract (and) Lecithin (and) Soy Isoflavones (and) Polysorbate 80 (and) Alcohol (and) Glycerin (and) Phenoxyethanol (and) Aqua / Water

Delentigo™

The efficient and targeted solution for age spots

Aging Leads to Irregular Pigmentation

- More than 90% of Caucasian subjects aged over 50 are affected by pigment spots.
- New studies showed that irregular pigmentation added up to 10 years on to the perceived age. It also plays a large role in the perception of women's health.

Age spots are, for this reason, a major skin concern along with wrinkles and sagging.

These hyperpigmentations called senile lentigo are typically found on UV-exposed areas of the body. They can range in size from one millimeter up to a few centimeters in diameter and vary in color from light brown to black.

Compared to the surrounding, normally pigmented skin, age spot areas are characterized by:

- an increased number of melanocytes and an increased production of melanin
- the overproduction of a second pigment, lipofuscin, a complex made of oxidized proteins and lipids, which accumulates with age.

Overproduction of Melanin in Age Spots

In keratinocytes, free radicals and reactive oxygen species (ROS) generated by UV light lead to the production of:

- α -MSH, a hormone which induces skin pigmentation by activating the melanocyte.
- Endothelin-1 (ET-1) and stem cell factor (SCF), two signaling molecules which stimulate melanocyte development, melanin production and dendrite formation. They are found in higher concentrations in age spots, explaining the higher melanin content compared to the surrounding, normally pigmented skin.

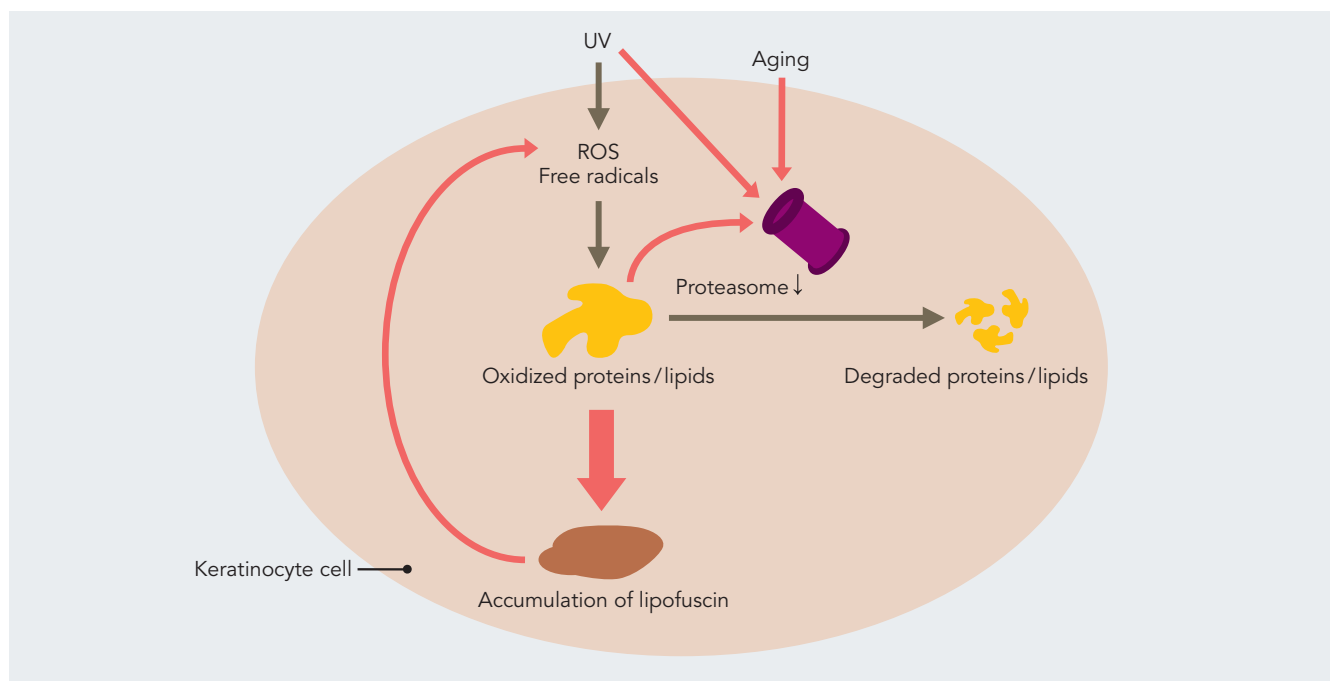
Accumulation of Lipofuscin in Age Spots

Lipofuscin accumulates during aging because:

- of increased oxidative stress factors
- proteasome activity declines with age. Proteasome is the cell's own cleaning and recycling system which degrades damaged and oxidized proteins. Besides, UV radiation impairs its functioning leading to the accumulation of oxidized and damaged proteins which, in turn, act as endogenous inhibitors of the proteasome.

Moreover the accumulation of lipofuscin leads to the release of ROS and free radicals, thus creating a vicious circle.

Formation and Effect of Lipofuscin



Delentigo™

Combination of cress and soya to minimize age spots

Garden Cress Sprouts Prevent both Melanin and Lipofuscin Formation

Garden cress sprouts are rich in sulforaphane, a phytonutrient able to neutralize reactive oxidants.

- Sulforaphane is actually a “second generation” antioxidant. Direct antioxidants such as the vitamins C and E need to be regenerated by other antioxidants once they have neutralized an oxidant. Indirect antioxidants (also called “second generation” antioxidants) are enzymes able to synthesize or regenerate antioxidants. Sulforaphane neutralizes free radicals and ROS that represent the first UV-induced triggers for formation of lipofuscin and melanin*.
- Besides, garden cress sprouts stimulate the proteasome activity and thus prevent the formation of lipofuscin*.
- Finally, garden cress sprouts inhibit the α -MSH-induced melanin synthesis*.

Genistein Inhibits the Formation of Age Spots

Genistein, the most abundant isoflavone in soy, is a natural inhibitor of the tyrosine kinase, an enzyme involved in several signaling cascades.

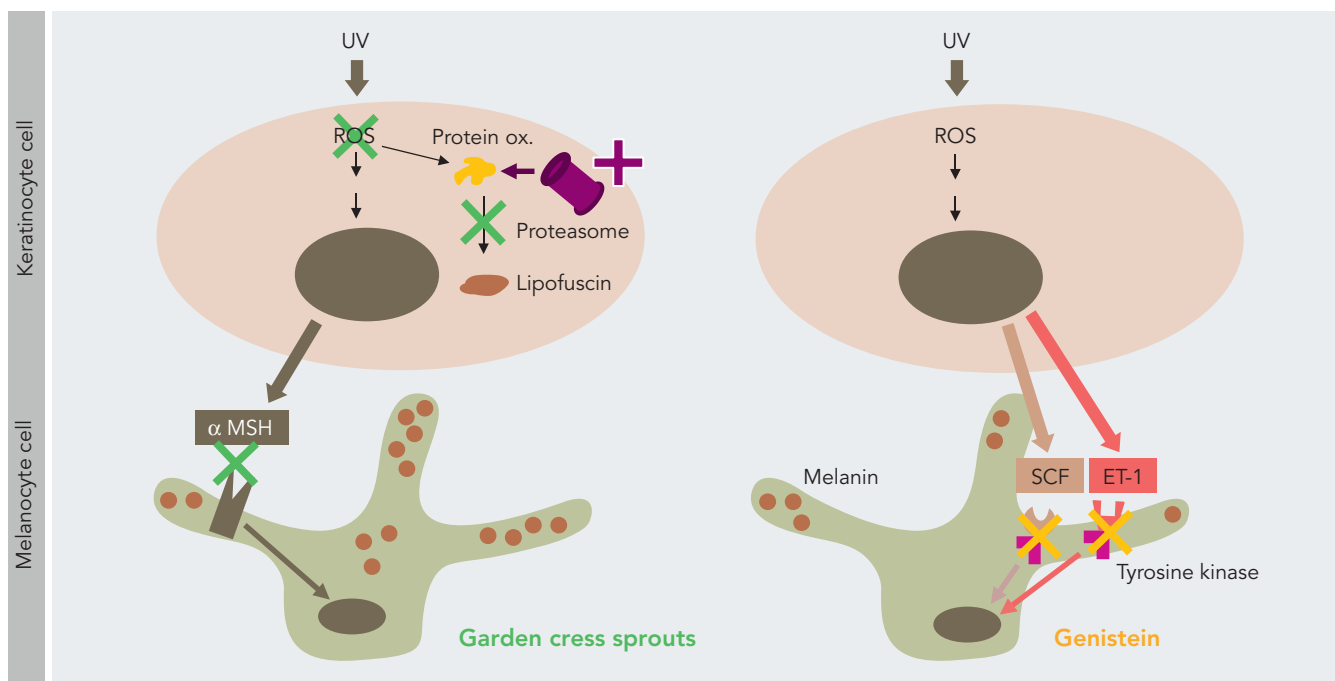
Tyrosine kinase, located at the intracellular side of the ET-1 and SCF's receptors, is important for the transmission of the receptor signal.

By inhibiting the tyrosine kinase, genistein blocks the signaling of ET-1 and SCF and thus prevents the formation of age spots as well as making them less visible.

Besides, genistein has antioxidant and anti-inflammatory activities.

*These activities have been demonstrated in vitro.

Mechanism of Delentigo™



Delentigo™

Study results



Prevention of Lipofuscin Formation by Stimulation of the Proteasome

In a cell-based screening assay using normal human dermal fibroblasts, the cress sprout extract (CSE) was shown to stimulate the proteasome system.

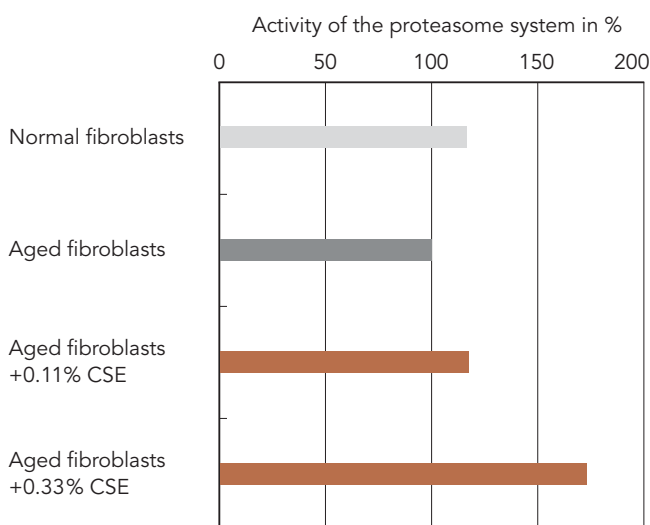
Activity of the proteasome was evaluated by means of Proteasome-Glo™ Assay (Promega) using a substrate whose degradation by the proteasome results in a luminescent signal. The emission of light which is measured with a luminometer, is proportional to proteasome activity.

Four hours after incubation, results showed that:

- with 0.11 % of the cress sprout extract, aged fibroblasts recover a proteasome activity equivalent to that of young fibroblasts.
- with 0.33 % of the cress sprout extract, the proteasome activity was found to be 70 % increased.

By stimulating the proteasome activity, the cress sprout extract can prevent and reduce the accumulation of oxidized proteins and thus inhibit lipofuscin formation.

Stimulation of the Proteasome Activity



Selective Depigmenting Effect

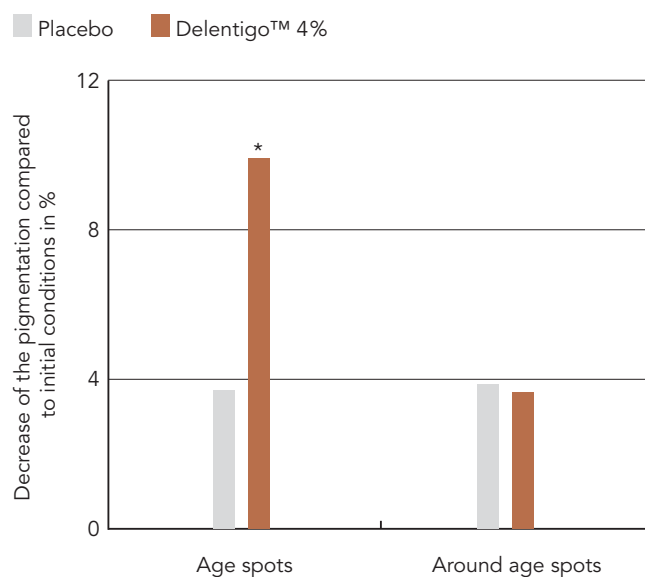
In a study with 10 Caucasian volunteers performed during winter, Delentigo™ was found to significantly lighten age spots without fading the surrounding, normally pigmented skin.

A cream containing 4 % Delentigo™ was applied twice daily to one hand of 10 women from 47 to 77 for 4 weeks. The other hand was treated with the placebo. On each hand, 3 age spots having a size ranging from 6 to 10 mm as well as 3 surrounding spotless skin areas were defined. Melanin pigmentation was measured using the Skin Pigmentation Analyzer® specifically designed for very small surfaces.

Delentigo™ was shown to significantly and selectively fade the age spots compared to the placebo:

- After 1 month of treatment, the melanin pigmentation was reduced by 6.2 % on the age spots.
- The melanin index of the normally pigmented skin was not modified.

Targeted Lightening of Age Spots



* p<0.05 versus initial conditions and placebo



A More Even Skin Tone

In a study with 12 Caucasian volunteers performed after summer, Delentigo™ was found to significantly even the skin tone.

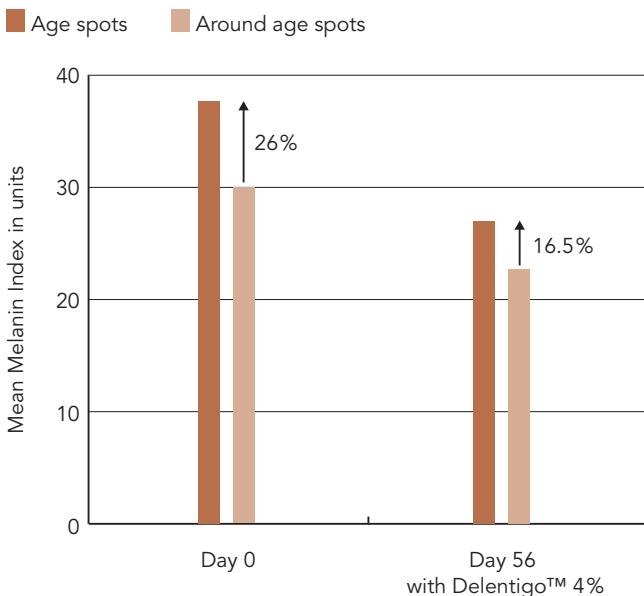
A cream containing 4% Delentigo™ was applied twice daily to one hand of 12 women from 40 to 66 for 8 weeks. On the treated hand, 4 age spots, having a size greater than 3 mm, were selected to be measured and followed up during the study. Spotless skin areas located next to the measured spots were also defined.

Melanin pigmentation was measured using the Skin Pigmentation Analyzer®. Besides, macrophotographs were taken using Visioface Quick.

After 2 months of treatment, Delentigo™ was shown to significantly equalize the skin pigmentation:

- Its lightening effect is stronger on age spots than on normally pigmented skin.
- The difference between the pigmentation of age spots and of the normally pigmented skin is reduced by about 50% compared to initial conditions. This leads to a more even skin tone.

Homogenization of the Skin Pigmentation



Visible Reduction of Age Spots



Before (Day 0)



After (Day 56) Delentigo™ 4%

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Marketing Benefits

- Targeted lightening effect
- Time-released activity thanks to the advanced vector system

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