

Care
Creations™

Actiwhite™

The tailor-made whitener and
spot preventer to improve skin appearance

Beauty Creations
The Passion for Beauty

 **BASF**
The Chemical Company

Lightening the skin complexion and giving skin back its original glow are the major challenges for the cosmetic world, as they target all generation.

Reduction of the age spots consists of decreasing the melanin present in the skin, preventing its formation and diminishing its transport. Although many depigmentation ingredients act on melanin formation inhibition through tyrosinase, few of them combine rapidly visible *in vivo* effectiveness, compliance with Asian regulatory requirements and high-cutaneous tolerance.

Recognized depigmentation substances are either unstable in formulation, cytotoxic like hydroquinone, or even sensitizing such as kojic acid.

These disadvantages have given us the foundations for a new strategy of depigmentation ingredient development.

BASF Beauty Creations has chosen a new target involved in the biogenesis of **melanosome** and **melanins**: the **PMEL-17 gene**[□].

Our strategy has led to the development of Actiwhite™, which **inhibits the maturing of melanosomes** through reduction of the expression of gene PMEL-17 and **deactivates tyrosinase** *in vitro*.

[□] see glossary

Actiwhite™

Melanogenesis regulator

Actiwhite™ with a **good cutaneous tolerance**, is a water-dispersible white powder which is easy to formulate in all formulation types (4<pH<8).

Actiwhite™ is a **synergistic complex** of sucrose dilaurate and pea extract that is in line with the regulatory requirements of the Chinese and Japanese Quasi-Drug markets.

Actiwhite™ has been subject to two clinical studies demonstrating its **skin-lightening** effect and ability to correct **age spots**.

Properties

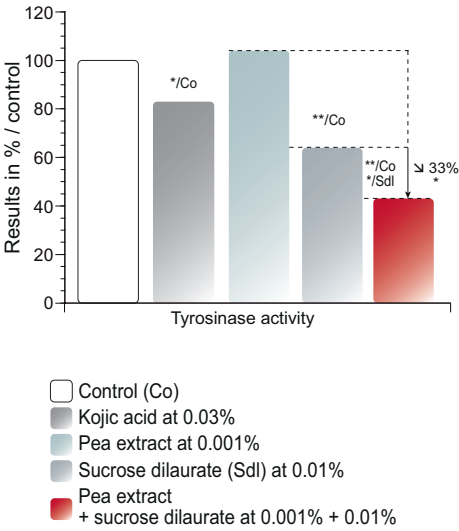
- Inhibitor of PMEL-17 gene expression, implicated on the melanosomal maturation.
- Inhibitor of tyrosinase activity.

Applications

- Brightening, anti-dark spots and body care.
- Radiance care: complexion perfecter.
- Express spots eraser for face and hands.
- Concentrated lightening care for neck and cleavage.

Synergy of Actiwhite™ components

The combination of the pea extract and sucrose dilaurate has a greater inhibiting effect compared to the same raw material tested individually.



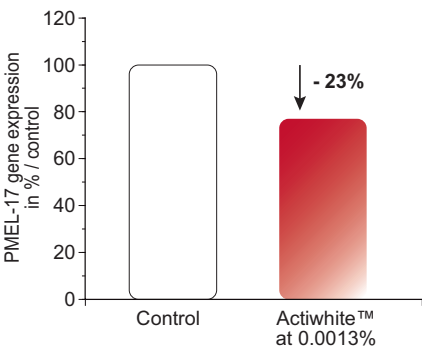
+ 33 % effectiveness in combination.

Mean of 1 assay in triplicate - Paired Student's t test - *: $p < 0.05$ - **: $p < 0.01$

In vitro study on B16 melanocytes.

Tyrosinase activity measurement by optical density.

Regulation of gene PMEL-17



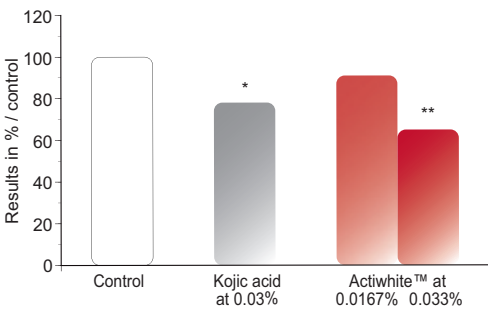
Decrease of **PMEL-17** gene expression.

Actiwhite™ has reduced the expression of gene PMEL-17, involved in both maturing melanosome and synthesising melanins.

In vitro study on human epidermal melanocytes.

A melanogenesis specific DNA chip was used and the variations in expression of the PMEL-17 gene were confirmed by qRT-PCR.

Tyrosinase inhibitor



Significant reduction of **tyrosinase activity**.

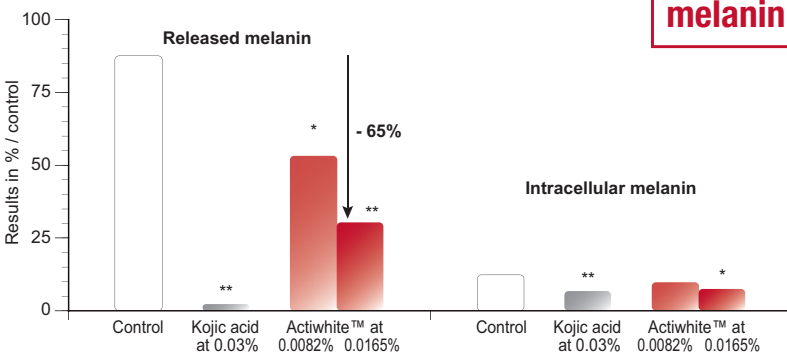
Mean of 4 assays in triplicate – Paired - Student's t test - *: $p < 0.05$ - **: $p < 0.01$

The anti-tyrosinase activity of Actiwhite™ is similar to kojic acid.

In vitro study on B16 melanocytes.

Tyrosinase activity measurement by optical density.

Melanogenesis reduction



Significant reduction of the released **melanin** quantity.

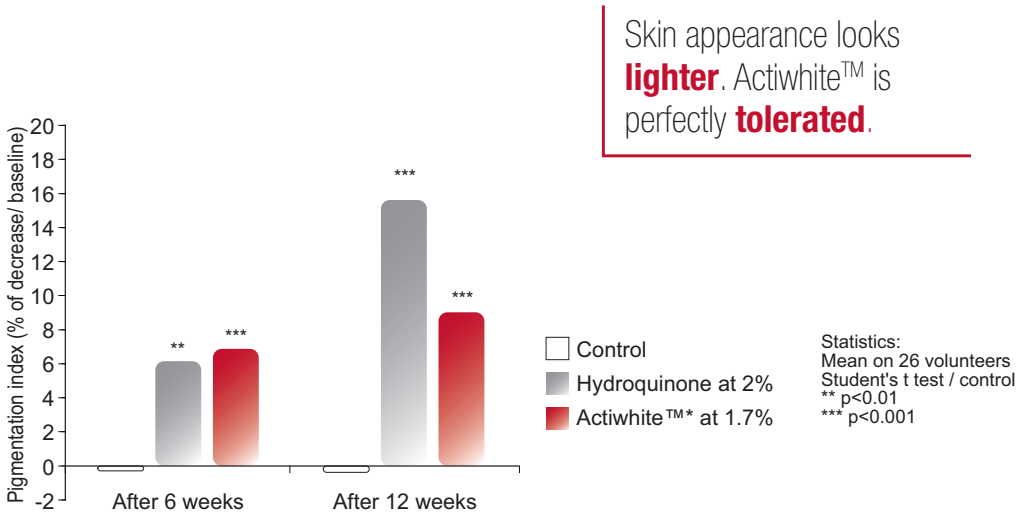
Mean of 5 assays in triplicate - Student's t test - *: $p < 0.05$ - **: $p < 0.01$

In vitro study on B16 melanocytes.

Measurement of the proportion of released and intracellular melanin by optical density.

Clinical evaluation of lightening efficacy

After 12 weeks...



Skin appearance looks **lighter**. Actiwhite™ is perfectly **tolerated**.

* This clinical study was conducted with sucrose dilaurate and pea extract at a dose equivalent to Actiwhite™ at 1.7%.

After 6 weeks of treatment, the lightening effect of Actiwhite™ is equivalent to the hydroquinone our reference substance which is tested under the same conditions. Actiwhite™ does not cause any cutaneous irritation.

After 12 weeks of treatment, our results with Actiwhite™ are still significant. The tolerance of Actiwhite™ is optimum.

***In vivo* study**

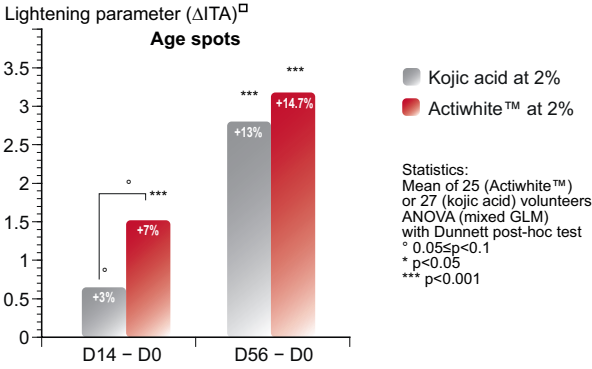
Randomized trial on 26 Asian female volunteers, aged between 18 to 45, with dark or very dark skin on the outside forearm.

Twice a day application of an emulsion containing 1.7% Actiwhite™ or 2% hydroquinone. Non treated area is used as control. Measurement of pigmentation index by Mexameter®.

Clinical study: anti-age spot effect

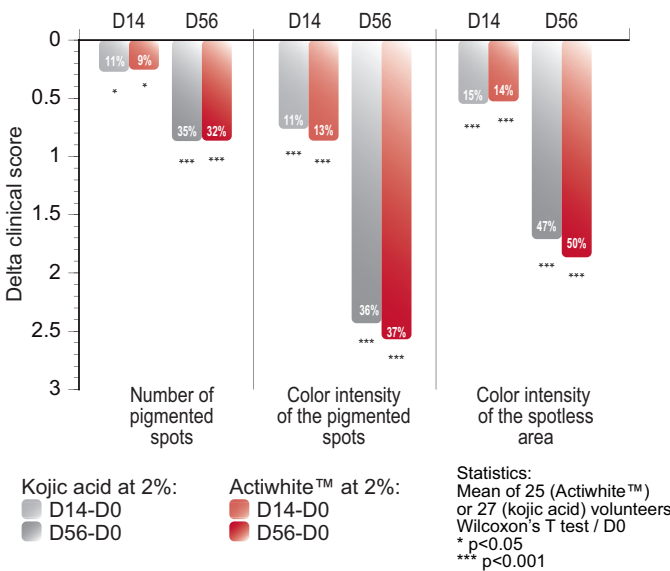


Colorimetric measurements



After 14 days, age spots are **significantly lighter**.

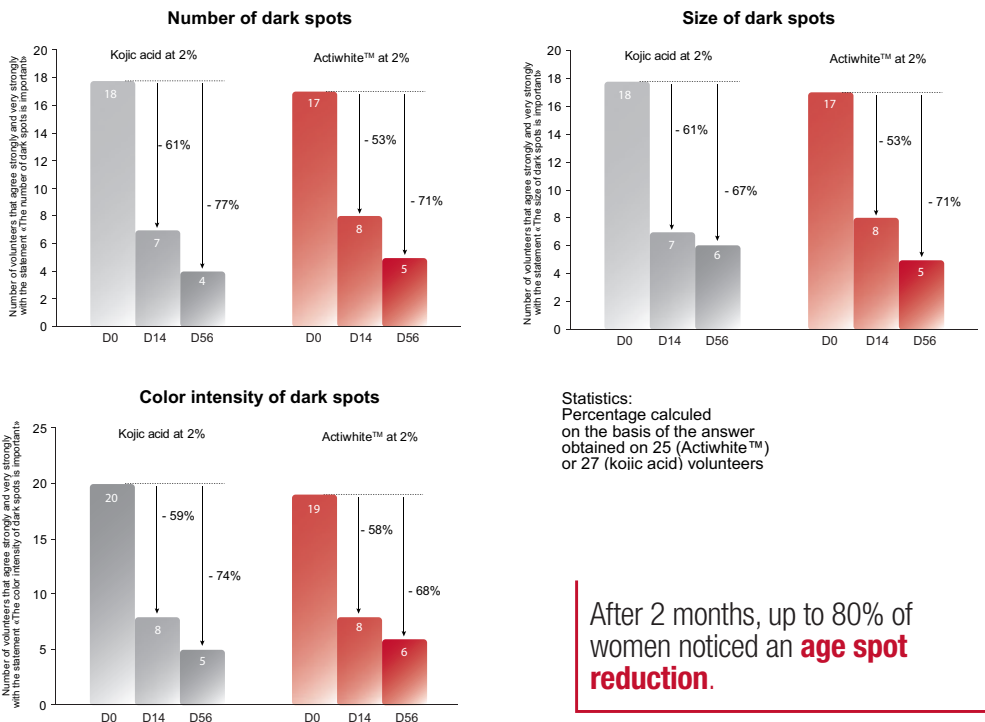
Evaluation by a dermatologist



After 56 days, the dermatologist evaluated that age spots are:

- **less numerous**,
- **less visible**,
- **smaller**.

Self-assessment



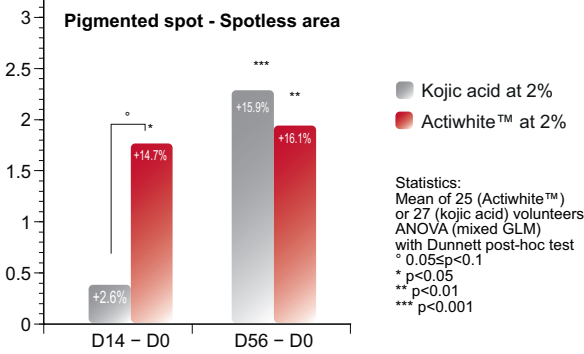
After 2 months, up to 80% of women noticed an **age spot reduction**.

Clinical study: skin complexion

new

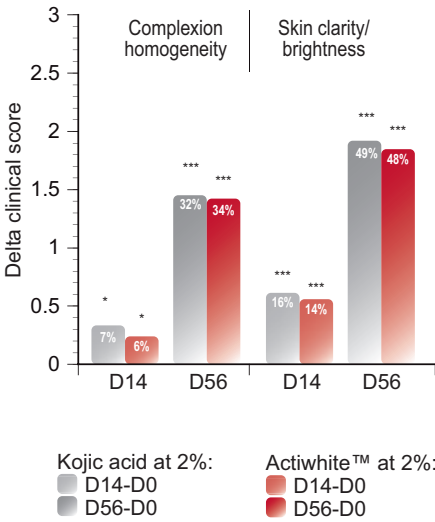
Colorimetric measurements

Lightening parameter (Δ ITA)[□]



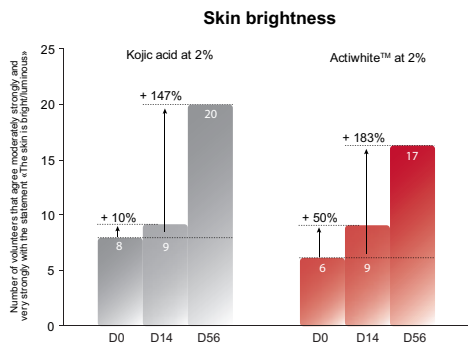
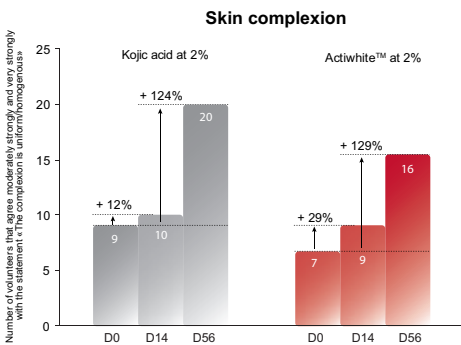
After 56 days, skin complexion is more **homogeneous**.

Evaluation by a dermatologist



After 14 days, the dermatologist evaluated that the skin is more **luminous** and has **uniform color**.

Self-assessment



Statistics:
Percentage calculated on the basis of the answer obtained on 25 (Actiwhite™) or 27 (kojic acid) volunteers

At 2%, the effects of Actiwhite™ and kojic acid are considered to be **comparable**.

After 14 days...

new

Visible effect confirmed by users.

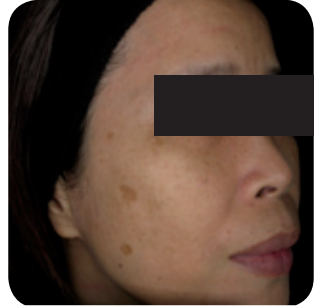
Visualization



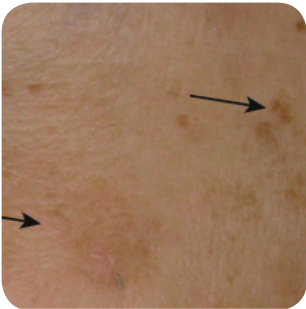
D0



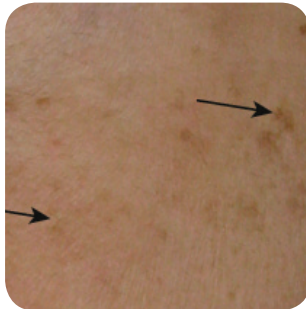
D14



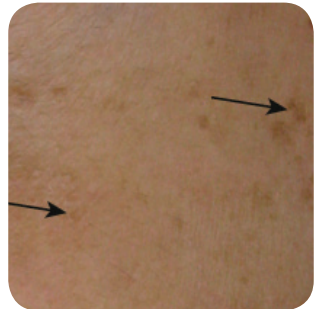
D56



D0



D14



D56

In vivo study

Randomized trial on 25 Asian female volunteers between 18 to 70 years old of having a phototype III and IV, all skin types. The specific requirement was the presence of well-defined pigmented spots on each side of the face associated to a spotless area.

Twice a day application for 8 weeks of an emulsion containing 2% Actiwhite™ or 2% kojic acid. Evaluation by colorimetric measurement ($\Delta\text{ITA}^{\square}$), dermatologist, self-assessment and macrophotograph of visibility, size and number of the age spot, skin complexion.

Summary datasheet

REFERENCE Actiwhite™ PW LS 9860

DESCRIPTION Synergistic complex of pea extract and sucrose dilaurate.

DOSE OF USE 2%

REGULATORY DATA

INCI (US) Maltodextrin , Sucrose Dilaurate , Sodium Cocoyl Glutamate , Pisum Sativum (Pea) Extract

CAS 9050-36-6, 25915-57-5, 68187-32-6, 90082-41-0

EINECS 232-940-4, 247-345-5, 269-087-2, 290-130-6

China All the raw materials comprising the INCI name Actiwhite™ are listed on the "International Cosmetic Ingredient Standard Chinese Name"(2007 version).

Japanese Cosmetic Denomination

Marutodekisutorin(556716), Jiraurinsansukurohsu(005227), Kokoirugurutaminsan Na(502046), Endouekisu(532281). Each of the Actiwhite™ ingredients complies with Japanese Standard of Quasi-Drug Ingredients (JSQI) or the corresponding monograph for quasi-drug additive use (Maltodextrin is covered in JP by Dextrin, 1422).

Preservative None

Natural label Raw material conform to Ecocert standards of Natural and Organic cosmetics.

PRELIMINARY SPECIFICATIONS

Organoleptic characteristics white powder, low odor

pH 4.5 - 6.5 (product at 2%)

Water content ≤ 5.0%

Total nitrogen 0.35 - 0.60%

Sucrose dilaurate 27.0 - 39.0%

Free sugar 55.0 - 65.0%

Microbiological control Upon request

FORMULATION

Solubility Dispersible in water.

Mode of incorporation Incorporated into the water phase at 80°C, or at room temperature for cold processing.

Recommended pH 4 - 8

PATENT APPLICATION EP1993508 (DE, FR, IT, GB, ES) and its equivalents in KR, JP, US

CUSTOMS CODE 38 24 90 97

STORAGE At ambient temperature (15-25°C), in its original packaging, protected from moisture and light.

SHELF LIFE 24 months



MANUFACTURER

BASF Beauty Care Solutions France SAS
3 rue de Seichamps - 54425 Pulnoy
(France)

Commercial sample of Actiwhite™ and examples of formulation (at 2% in a hydrogel and an emulsion).

GLOSSARY

qRT-PCR: "quantitative Reverse Transcriptase - Polymerase Chain Reaction" is a method of quantifying the expression of genes.

PMEL-17 gene: gene coding for the Premelanosomal protein Pmel-17 involved in melanosome biogenesis, the seat of melanin synthesis.

B16 melanocytes: melanocyte cellular line classically used to test melanin ratios.

Δ ITA (Individual Typological Angle): the skin color is defined according to its luminosity L and its ITA. It defines the degree of pigmentation of the skin of an individual. The higher the ITA, the lighter the skin.

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