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# Development of Functional Cosmetic “ASTALIFT WHITE”

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## Abstract

We have developed “ASTALIFT WHITE”, which contains our unique dispersion “nano-AMA”, as a new skin care brand for women of all ages with skin problems such as dark spots and dullness. We focused on the brightening component “AMA”, which has anti-inflammatory effects. It contains three main components, “Asiatic acid”, “Madecassic acid” and “Asiaticoside”. However, they are slightly soluble both in water and oil, so we developed approximately 20 nm water-dispersions, which is expected to penetrate into the skin. A comparison of “nano-AMA” with normal “AMA” showed that it had up to double the inhibitory effect on melanin production in a 3D skin model. Furthermore, “nano-AMA” greatly suppressed the dendrites’ elongation of the melanocytes. We performed a clinical test for 8 weeks to evaluate the effects of the serum “ESSENCE INFILT” which is formulated with “nano-AMA”. We observed a significant decrease in the melanin index, which indicates the depth of blemishes, and most subjects perceived a brightening effect.

## 1. Introduction

At FUJIFILM we have developed unique and functional skin care products by applying photographic expertise. On March 1, 2013, we launched onto the market a new brightening\*<sup>1</sup> skin care brand, the ASTALIFT WHITE series (nonmedicinal products), for women of all ages who have skin problems such as blemishes and dullness of the skin (Fig. 1).

Dark spots, freckles and dullness of the skin are common problems for many women in their late 20s or over. The market size of the brightening cosmetics in Japan is approximately 150 billion yen. However, according to a survey\*<sup>2</sup>, nearly 70% of the users of those cosmetics are not satisfied with their effects (Fig. 2). Therefore, to respond to their needs, we have striven for the development of skin care products with high brightening effects.



Fig. 1 The new cosmetic brand “ASTALIFT WHITE”.

\*1 Preventing the production of melanins to suppress the outbreaks of dark spots and freckles

\*2 A survey conducted by FUJIFILM

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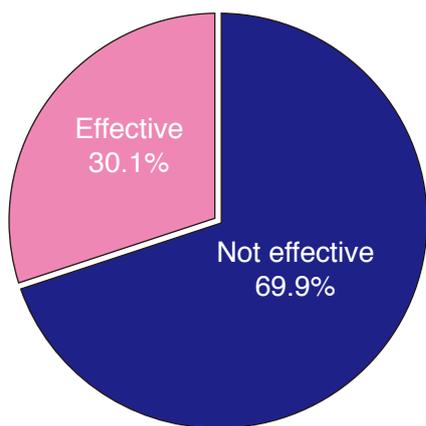


Fig. 2 Survey results on skin brightening effect of the cosmetic product.

## 2. Histological characteristics of dark spots

Histologically, dark spots are defined by elongated rete ridges deeply protruding into the dermis and forming buds, and a massive accumulation of melanin and an increased number of melanocytes in the basal layer of the buds.<sup>1)</sup> (Fig. 3) Therefore it is important to deliver brightening components to the deep skin layer in order to reduce dark spots.

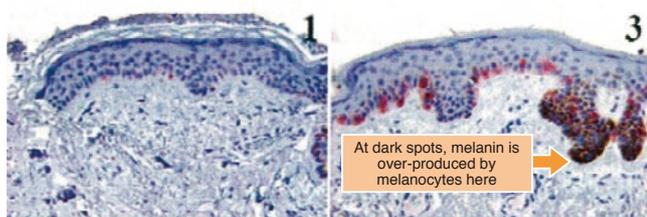


Fig. 3 Skin structure of normal region (1) and of spot (3)

## 3. Development of ASTALIFT WHITE

### 3.1 Nanoization of a brightening component, AMA, into a size of approx. 20 nm with our unique technology

#### Focusing on “AMA”

*Centella asiatica* is an Apiaceae herb that widely inhabits the subtropical zone (Fig. 4). From a legend that wild tigers cured wounds by rubbing themselves against it, the plant is also called *tiger's herb*. It is known to have excellent wound healing and anti-inflammatory effects and has thus often been used as a medicinal herb in folk remedies such as Ayurveda. Among the constituents of that *Centella asiatica* extract, we focused on a brightening component, AMA, which contains three ingredients with high anti-inflammatory effects: asiatic acid, madecassic acid and asiaticoside (Fig. 5).



Fig. 4 *Centella asiatica*.

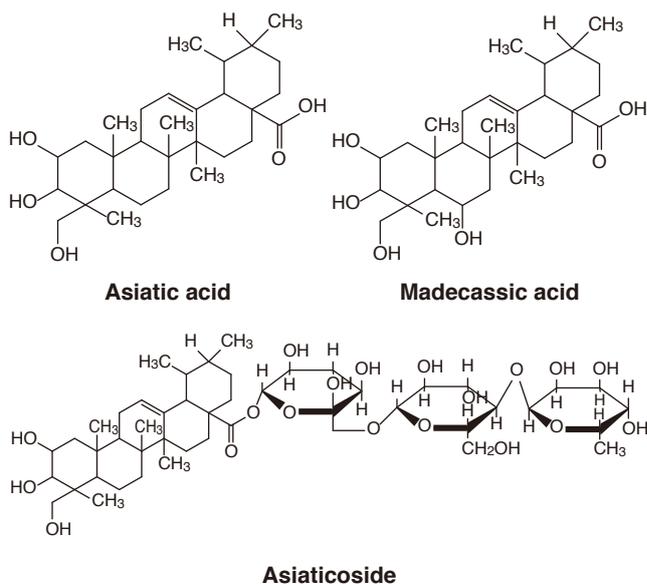


Fig. 5 The structures of Asiatic acid, Madecassic acid and Asiaticoside.

## Development of “nano-AMA”

AMA, which is a brightening compound of the above three ingredients, does not easily dissolve in either water or oil. In addition, because of the similarity of their structures, the ingredients easily aggregate to each other. Therefore, in order to deliver AMA to the deep skin, it is necessary to increase its permeability by nanoizing it. To solve those problems, combining them complexly with natural amphiphilic ingredients, we established nano unit technology that effectively arranges and stabilizes those ingredients, without causing aggregation, so they can exhibit their effects. With that technology, we succeeded in the development of nano-AMA with a size of approx. 20 nm that can be expected to infiltrate into the skin (Fig. 6). With a large particle diameter, non-nanoized AMA does not let light pass through; therefore, it looks turbid. On the other hand, the nano-AMA we developed is stabilized with a very small particle diameter and looks transparent, letting light pass through (Fig. 7).

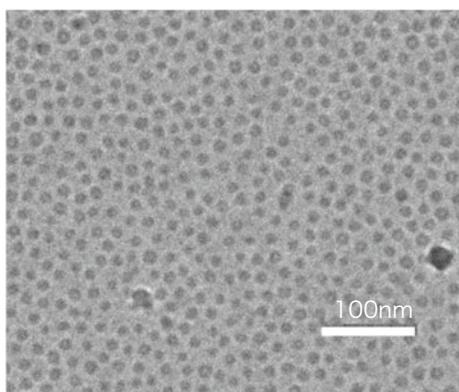


Fig. 6 Cryo-TEM image of nano-sized AMA dispersion of ice-embedded sample.



Fig. 7 “Micro-sized AMA” (left) and “nano-sized AMA dispersion” (right).

### 3.2 Confirmation of the effectiveness of the brightening component, AMA, with a skin equivalent

#### Inhibitory effect of nano-AMA on melanin production

To verify the effects of nano-AMA and non-nanoized, normal AMA on melanin-producing melanocyte cells, we conducted a test using a 3D skin equivalent containing melanocytes, with a similar structure to that of human skin (Fig. 8). The skin equivalent simulated the condition of melanocytes that exist in the deep skin.

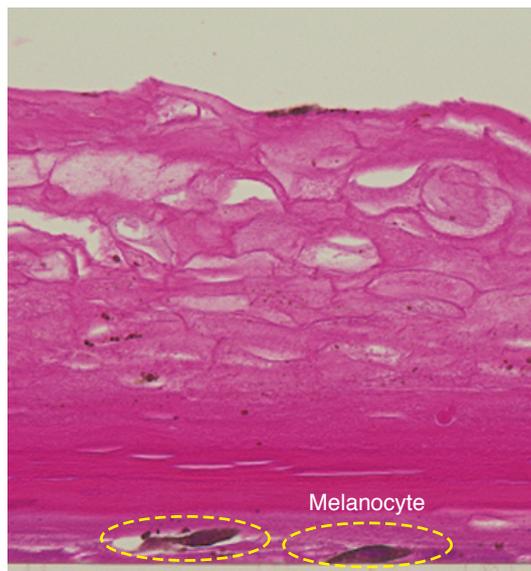


Fig. 8 3D-skin equivalent of human skin including melanocytes.

The skin equivalent was cultured for fourteen days under the following three different conditions: (i) no addition; (ii) AMA added; and (iii) nano-AMA added. Subsequently, melanins were extracted from the skin equivalent to determine the quantities. As a result, the inhibitory effect of nano-AMA on melanin production in the skin equivalent was found to be about double that of normal AMA (Fig. 9).

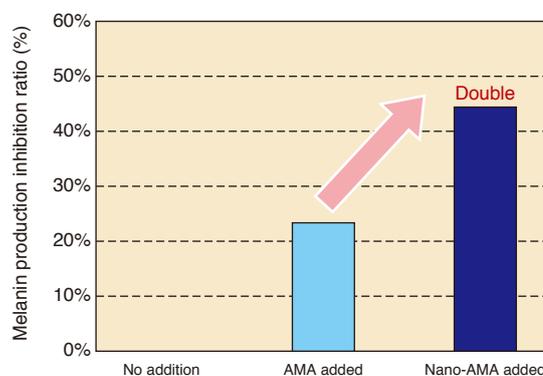


Fig. 9 Nano-sized AMA dispersion has twice the skin brightening effect of AMA.

#### Inhibitory effect of nano-AMA on the elongation of melanocyte dendrites

The morphological characteristics of melanocytes were also observed in the test. In the skin equivalent nano-AMA added, it was confirmed that dendrite elongation was greatly suppressed in dormancy (contraction) and thus the production of melanin was inhibited (Fig. 10). It can be considered to have happened because the permeability of AMA into the skin increased via nanoization, enhancing the effect on melanocytes.

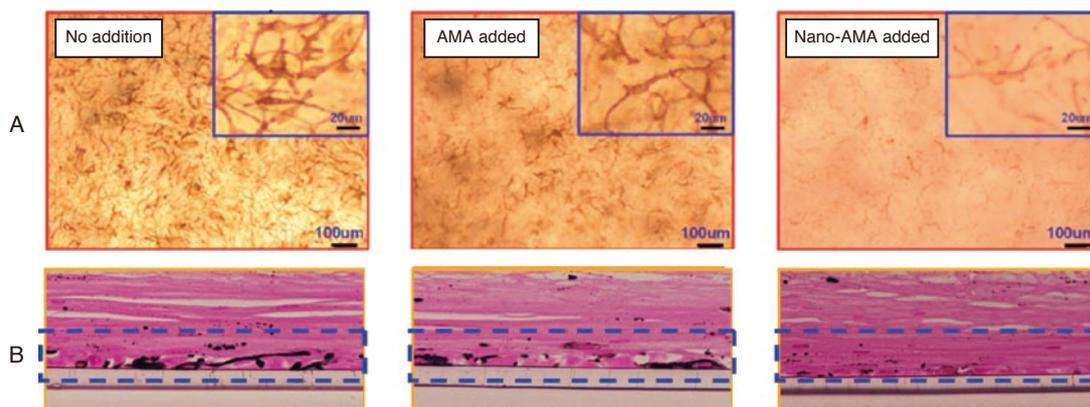


Fig. 10 (A) Nano-sized AMA dispersion suppressed dendrite elongation of melanocytes. (B) Nano-sized AMA dispersion suppressed melanin synthesis.

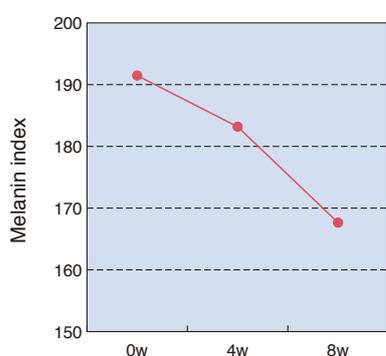


Fig. 11 Decrease of melanin index after eight weeks of continuous use.

#### 4. Confirmation of the effects of ASTALIFT WHITE ESSENCE INFILT in vivo by a clinical test

We show the results of the clinical test to confirm the brightening effects of ASTALIFT WHITE ESSENCE INFILT which is formulated with nano-AMA below.

We recruited 26 women, aged 32-59, who had dark spots on their faces, and determined one spot to be observed for each subject. All the subjects have applied ASTALIFT WHITE ESSENCE INFILT to their entire faces twice a day for eight weeks. We measured the darkness of the spots as melanin index and took images before first application, after four weeks and eight weeks applications.

The average of melanin index of the spots was significantly decreased from 191 to 183 ( $p < 0.01$ ) after four weeks of application, and from 183 to 168 ( $p < 0.0001$ ) after another four weeks (Fig. 11). As the average of melanin index of normal region was 140, those results meant the spots moved to closer normalcy by ASTALIFT WHITE ESSENCE INFILT application. Fig. 12 shows improvement of the spot as a typical case. Large spot with a well-defined border on the cheek was brightened, with indistinct border. It was obvious that the spot were brightened and not only by measured value but also by visual observation.

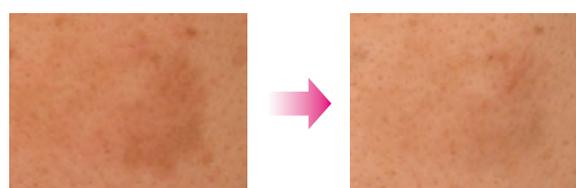


Fig. 12 A typical case of the spot improvement after four weeks application.

In addition, 77% (20/26) and 85% (22/26) subjects found their spots were improved by themselves, after four weeks and eight weeks application, respectively. Thus, we have achieved our goal of developing skin care products with high brightening effects enough to satisfy women who had not realize before.

#### 5. Conclusion

ASTALIFT WHITE described in this paper is a functional cosmetic using original dispersions created based on the emulsification and dispersion technology we have acquired via conventional development activities in the field of photography. The effect was proved with a model close to actual human skin.

Leveraging our own expertise, we are going to keep striving for the development of functional cosmetics that create new customer value.

#### References

- 1) Lin, C. B. et al. Journal of Dermatological science. **59** (2), p.91-97 (2010)

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