Press Release

# Recognition of effect and efficacy in improving skin wrinkles with retinol acting ingredient acquired for the first time in Japan

## "Deep" wrinkles improved in nine weeks

Caution: The contents herein concern approval based on Japan's Pharmaceutical Affairs Act.

Shiseido Company, Limited ("Shiseido") has received recognition from the Japanese Ministry of Health, Labour and Welfare for effect and efficacy of a retinol formulation in improving wrinkles. The new product with retinol as the acting ingredient was found to be effective in improving the wrinkle classification grade (see bottom) by four levels with use for nine weeks.

Shiseido is the only company in Japan that can manufacture and sell quasi-drug products formulated with retinol as an active ingredient, based on core technology from retinol research spanning nearly 30 years, and will continue research in the anti-aging field for application to skin care products.

#### Efficacy of retinol in improving wrinkles

A clinical trial was conducted with healthy Japanese women (age 37–54 years, mean age 46 years) who had shallow to deep wrinkles at the corners of the eyes, in accordance with the "Guidelines for Evaluation of Anti-Wrinkle Products" developed by the Japanese Cosmetic Science Society. The women used the new product containing retinol as the active ingredient and a product without retinol for nine weeks. The effect on wrinkles was then judged by dermatologists and analyzed with a measuring instrument.

After nine weeks of use, marked improvement was seen in deep lines from the corners of the eyes and fine wrinkles around the eyes (the so-called "crow's feet") (Figure 1). The instrument analysis also showed decreases in wrinkles with the new product compared with the non-retinol product (Figure 2). Marked improvements were also acknowledged from three-dimensional images of wrinkle areas (green) (Figure 3).

The results were also verified through a questionnaire on subjective efficacy, in which the women recognized an improvement in wrinkles with use of the new product.

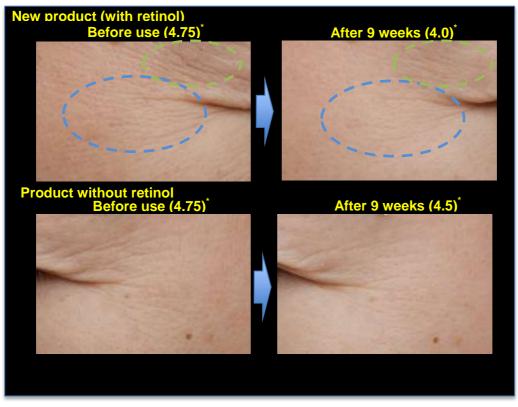
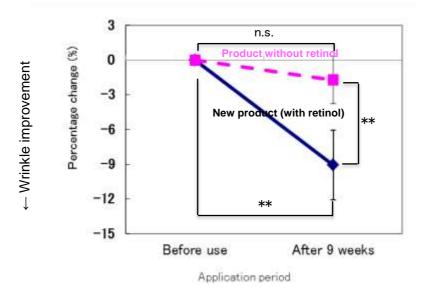


Figure 1. Representative case of wrinkle improvement with the new product \*Numbers in parentheses are wrinkle grade judgments



Mean  $\pm$  standard error, N=77, paired t-test (2-sided) n.s.: Not significant, \*\*; p<0.01 Figure 2. Change in wrinkle area ratio with measuring instrument

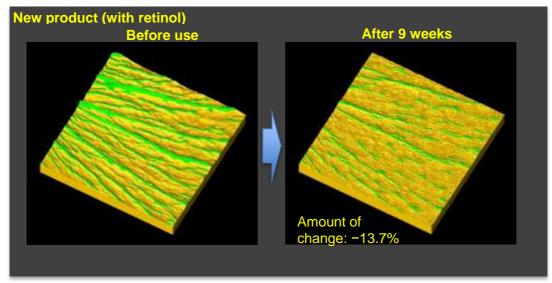


Figure 3. Representative example of wrinkle improvement with 3D image analysis

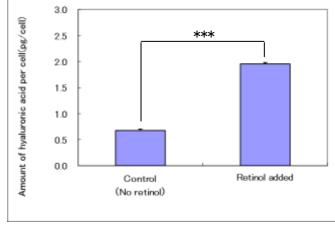
Wrinkles are shown with green

## Retinol stabilization technology

Retinol has been previously used in quasi-drugs as an active ingredient for rough dry skin, but it is a very unstable component that does not stand up well to heat, sunlight, and oxygen. With the application of formulation technology cultivated through many years of research, Shiseido successfully produced and launched in 1993 a stable formulation in which retinol does not degrade. A unique container for use with retinol formulations has also been developed. Stability is ensured with this formulation technology and container development, making Shiseido the only company in Japan for which retinol as an active ingredient in quasi-drugs has been recognized.

### Mechanism of action

Retinol significantly promotes the production of hyaluronic acid in cultured human epidermal keratinocytes (Figure 4). Hyaluronic acid is an important component of skin that contributes to moisture retention and the maintenance of skin elasticity. It is also known to decrease with age. Retinol increases the production of hyaluronic acid and imparts pliability to the skin, reducing wrinkles.



Mean ± standard error 2-sample t-test (2-sided) \*\*\*: p<0.001

Figure 4. Action of retinol in facilitating the generation of hyaluronic acid

Wrinkle grades (standard): Based on the guidelines developed by the Japanese Cosmetic Science Society