POLA ORBIS HOLDINGS
NEWS RELEASE

July 14, 2016

A world first! POLA CHEMICAL INDUSTRIES, INC. receives marketing approval for a quasi-drug that improves wrinkles

Development of an active ingredient that inhibits the activity of neutrophil elastase, an enzyme that causes wrinkles

POLA CHEMICAL INDUSTRIES, INC. (Headquarters: Yokohama, Kanagawa, JAPAN; President: Takao Miura) of the POLA ORBIS Group has received marketing approval for "POLA Wrinkle Shot Medical Serum" (the serum), which effectively improves the appearance of wrinkles.

After spending 15 long years exploring the mechanisms of wrinkle formation and developing substances to improve wrinkles, POLA CHEMICAL INDUSTRIES, INC. has received the world's first approval for a wrinkle-improving quasi-drug※ that contains our newly developed active ingredient, Sodium [[[trifluoro-isopropyl-oxopropyl]aminocarbonyl]pyrrolidinyl]carbonyl]-methylpropyl]amino carbonyl]benzoylamino]acetate (the active ingredient).

This product is scheduled for release by POLA INC. (POLA ORBIS Group) onto the market in early 2017. ※See the reference material.

Verifying the wrinkle-improving effects of the active ingredient

Based on the Guidelines for Evaluation of Anti-Wrinkle Products from the Japanese Cosmetic Science Society, POLA CHEMICAL INDUSTRIES, INC. conducted a double-masked, randomized trial comparing a preparation containing the active ingredient (the serum) with a preparation without the active ingredient (placebo). The serum and placebo were applied twice a day for 12 weeks to the corner of one eye each, in 68 healthy Japanese women with wrinkles at the corners of the eyes. Visual evaluation (wrinkle grade evaluation; Fig. 1) and instrumental evaluation (maximum depth of the largest wrinkle*; Fig. 2), performed in the 12th week of use, showed a significant improvement of wrinkles with the serum compared to placebo use.

*Maximum depth of the largest wrinkle: depth of the deepest part of the largest wrinkle at the corner of the subject's eye

Fig. 1. Wrinkle-improving effect of the serum (wrinkle grade evaluation)

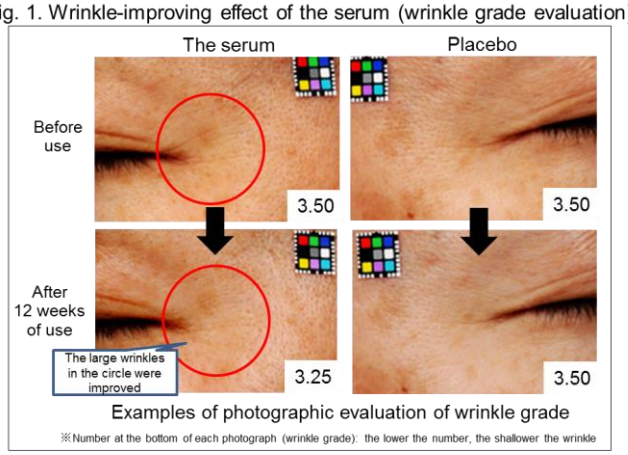
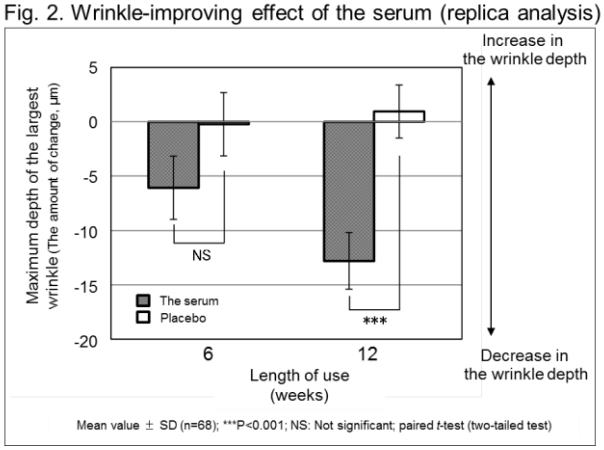


Fig. 2. Wrinkle-improving effect of the serum (replica analysis)



Safety

The following trials were conducted under dermatologist supervision to confirm the safety of the serum.

1) 12-month continuous-use trial in 122 healthy Japanese women
2) 48-h occlusive patch test after 6 months of continuous use in 102 healthy Japanese women to more carefully evaluate cutaneous allergenic potential

In both tests, continuous use comprised twice-daily application of a moderate amount of the serum to an area with wrinkles. In the 12-month continuous-use trial, no adverse effects were observed, and the serum was determined to be safe in all cases. In the 48-h occlusive patch test after 6 months of continuous use, no positive reactions or adverse effects were observed. These findings indicate that the serum containing the active ingredient is safe for use as a quasi-drug.

In addition, as the serum contains a novel quasi-drug as the active ingredient, the Ministry of Health, Labour and Welfare has mandated that POLA CHEMICAL INDUSTRIES, INC. conduct post-marketing surveillance. We will continue to confirm the safety of the serum for consumers for at least two years after its release.

For related inquiries, contact: rm-webmaster@pola.co.jp (POLA CHEMICAL INDUSTRIES, INC.)

“Reference material”

What is a quasi-drug?

Quasi-drugs exist in an intermediate category between drugs and cosmetics, and are defined as articles used only for certain purposes that are specifically designated by the Ministry of Health, Labour and Welfare in Japan. They are required to contain active ingredient(s) that exert the depicted efficacy. The approval system for quasi-drugs requires submission of the formulation used, testing methods utilized for the identification and quantification of active ingredients, and safety data on the formulation and the active ingredients. The legal definition of quasi-drugs is described in “The Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices” (November 25, 2014).

The process of wrinkle formation

Wrinkles are creases of skin that appear on the skin surface, particularly on the forehead, neck, and around the eyes and mouth. Mild inflammation normally occurs within the skin in response to exposure to stimuli such as ultraviolet rays and dryness from the external environment. However, this mild, chronic inflammation causes deterioration of extracellular matrix components* such as collagen and elastin, particularly in the dermis. Over the long term this process, together with creasing of the skin due to facial expressions, simultaneously exacerbate wrinkles.

*Material that fills the extracellular space and forms the framework that supports the internal structure of the skin

Fig. 3. Staining of neutrophil elastase in the skin

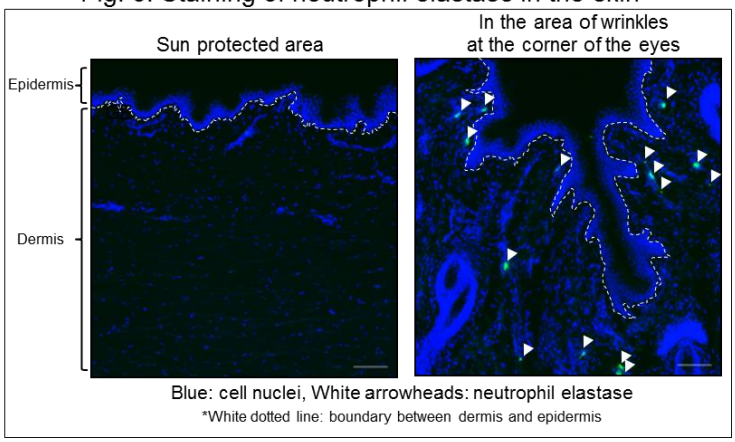
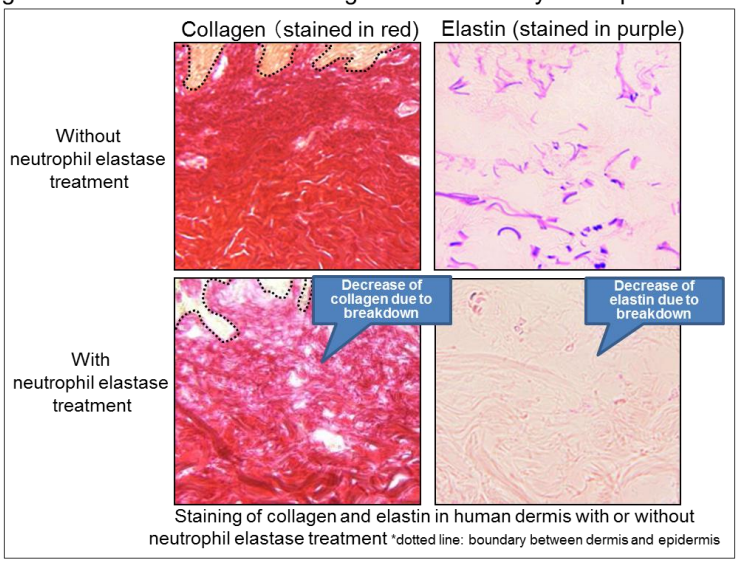


Fig. 4. Breakdown of dermal collagen and elastin by neutrophil elastase



Our approach to improving wrinkles

Inflammation in the dermis causes neutrophil (a type of lymphocyte) infiltration, leading to excessive secretion of neutrophil elastase (Fig. 3). This enzyme breaks down and reduces the amount of extracellular matrix components such as collagen and elastin in the dermis (Fig. 4). In order to adjust the balance of reduction and production of extracellular matrix and thus improve wrinkles, we aimed to prevent the breakdown of the extracellular matrix; in other words, to inhibit the activity of the neutrophil elastase causing this breakdown.

The search for an ingredient to inhibit neutrophil elastase

Over 5,000 substances were investigated to identify the neutrophil elastase inhibitor that has strong inhibitory activity and safety characteristics.