Shiseido Discovers New Mechanism that Gives Rise to Nasolabial Folds — Prevention and Improvement Using Rubus suavissimus Shugan Lee. Extract Derived from the Leaves —

Shiseido has newly clarified the formation mechanism of nasolabial folds (Figure 1), which become deeper and longer as a person becomes older, as well as discovered that *Rubus suavissimus* Shugan Lee. Extract derived from its leaves is effective for the prevention and improvement of these folds.

**New Breakthrough regarding Formation Mechanism of Nasolabial Folds and Treatment Ingredient [Agent]**

1. Shiseido has made a new breakthrough regarding the formation mechanism of nasolabial folds. Specifically, research has revealed that when subcutaneous fat in the cheek increases, adipocytes become enlarged and “bad” [negative] factors (free fatty acids) are secreted excessively, thereby causing dermal damage. Consequently, the damaged dermis loses its resilience and elasticity and its ability to support the cheeks, which in turn causes nasolabial folds to become deeper and longer. (Figures 2 and 3)

2. Shiseido has identified a new measure for “preventing and improving nasolabial folds by helping enlarged adipocytes return to a healthy size and recovering the skin’s resilience and elasticity by reducing the secretion of “bad” [negative] factors that cause dermal damage.” In this regard, researchers found that *Rubus suavissimus* Shugan Lee Extract is effective for the prevention and improvement of these folds as a treatment ingredient [agent]. (Figure 4)

Patents have been applied for regarding the current research results not only in Japan but also overseas. Further, Shiseido will apply these findings to new anti-aging skincare and cosmetics products set to be launched in autumn 2012.

Figure 1: Formation of nasolabial fold as a result of sagging cheek
Background regarding the Start of Research on Nasolabial Folds

Nasolabial folds were generally considered to be “deep wrinkles” caused by a decline in the skin’s resilience, elasticity and other relevant factors due to aging, and the dermatological causes of the development of nasolabial folds have remained unclear up until now.

Shiseido has previously promoted various research that differed in terms of dermatology, including wrinkles. At this time, however, Shiseido began conducting research as a means of clearly explaining the fundamental formation mechanism of nasolabial folds, which have been noted as a more difficult problem than wrinkles, and developing new technologies that will fully address the issue of the prevention and improvement of these folds.

Clarification of Formation Mechanism of Nasolabial Folds from a Dermatological Standpoint

First of all, the facial shape of the same person while in a sitting position and lying position. As a result, nasolabial folds were prominent in a sitting position and less prominent in a lying position. This revealed that nasolabial folds are “boundary lines” that develop as a result of sagging cheeks due to gravity rather than a fixed configuration [pattern] like wrinkles. Additionally, Shiseido was the first at this time to verify that nasolabial folds have a high correlation with age and become deeper and longer as a person becomes older. (Figure 5)

Second, Shiseido conducted research regarding the cause of sagging cheeks. Since there is more subcutaneous fat within the cheek compared with other parts of the face, research was carried out with a focus on the amount of subcutaneous fat and sagging cheeks. As a result, the following relationships were clarified.

- Adipocytes, which constitute the cheek’s subcutaneous fat, not only get heavier as they become enlarged but also excessively secrete “bad” [negative] factors (free fatty acids).
- These “bad” [negative] factors inhibit the proliferation of fibroblasts, which produce dermal components (collagen and elastin), also reducing the amount of dermal components.
- The dermis is damaged as a result and loses its resilience and elasticity. Also, nasolabial folds become deeper and longer due to a decline in the dermis’ ability to support the cheeks.

Through such means, Shiseido has clarified the formation mechanism of nasolabial folds from a dermatological standpoint, whereby dermal damage caused by the enlargement of adipocytes in the cheeks and a decline in the skin’s resilience and elasticity due to aging are closely related to the formation of longer and deeper nasolabial folds.
**Discovery of the Effects of *Rubus suavissimus* Shugan Lee. Extract to Prevent and Improve Nasolabial Folds**

It is important for adipocytes to be in a good condition (reduce the size of enlarged adipocyte and return to a healthy condition)” in order to prevent and improve nasolabial folds. As a result of screening various plant-derived extracts, Shiseido found that *Rubus suavissimus* Shugan Lee. Extract derived from its leaves has excellent effects as a treatment ingredient (agent).

*Rubus suavissimus* Shugan Lee. Extract reduces the size of enlarged adipocytes, decreases the secretion of “bad” [negative] factors and increases the secretion of “good” positive factors. As a result, the condition of the dermis gets better, thereby leading to the expected prevention and improvement of nasolabial folds.

---

**A person with thinner subcutaneous fat**

**A person with thicker subcutaneous fat**

![Small adipocyte](image1)

![Enlarged adipocyte](image2)

**Figure 2: Enlargement of adipocytes in line with an increase in subcutaneous fat**

---

**Figure 3: “Bad” [Negative] factors that damage the dermis (in vitro data, relative value)**

![Graph 1](image3)

![Graph 2](image4)

![Graph 3](image5)
Figure 4: *Rubus suavissimus* Shugan Lee. Extract restores enlarged adipocytes to a healthy size (in vitro data, relative value)
Figure 5: Nasolabial folds that become deeper and longer due to aging
(Figures on vertical axis: Visual evaluation)