SHISEIDO
NEWS RELEASE

**Shiseido Elucidates that the Functional Decline of Skin Capillaries Is Involved in Skin Aging**

# Development of Cassia Extract as an Ingredient to Restore Impaired Skin Capillary Function

Shiseido has discovered through joint research with Professor Jin Ho Chung of the Department of Dermatology of Seoul National University that the function of skin capillaries declines when people reach their late 40s, also making it more difficult to provide nutrients throughout the skin to the extremities. Based on these findings, Shiseido promoted joint research with Professor Nobuyuki Takakura of the Research Institute for Microbial Diseases at Osaka University and discovered for the first time in the world that Cassia Extract, which is derived from the stem bark of *Cinnamomum cassia* Blume (Lauraceae), is effective for improving the functional decline of these skin capillaries.

Shiseido will apply the current research results to supplements and promote the development of an anti-aging skincare system as a new concept that incorporates internal and external beauty care. This novel approach is directed toward realizing skincare from inside (within the body) and out by adding supplements to conventional topical skincare products.

## Skin Capillaries Play an Important Role as a Nutrient Supply Route

Skin capillaries are responsible for supplying sufficient nutrients throughout the skin to the extremities and are made up of a double-layer structure incorporating vascular endothelial cells surrounded by pericytes. When the structure is normal, the required amounts of nutrients are delivered to the skin as if they are seeping from a fine mesh. It has been previously recognized that in such cases where skin irritation occurs and the skin becomes red due to UV rays and other factors, the bonds of vascular endothelial cells and pericytes peel off, which in turn causes nutrients to easily leak excessively from skin capillaries (Figure 1).

Although it has been previously said that there is a certain relationship between skin conditions such as aging and the supply of nutrients via skin capillaries, Shiseido has made a new breakthrough at this time.

## Tendency for Nutrients to Easily Leak Excessively from Skin Capillaries in Late 40s

Shiseido conducted joint research with the MGH/Harvard Cutaneous Biology Research Center (CBRC)[*1] by focusing on blood vessels, which deliver nutrients to the skin, and the circulatory system, which is made up of lymphatic vessels that recover waste products. Additionally, in order to accelerate research regarding the relationship between skin capillaries and aging, structural analysis of skin capillaries of people in their 20s to 80s was conducted jointly with Professor Chung from the Department of Dermatology of Seoul National University.

As a result, young skin capillaries of persons up until their 30s had a double-layer structure with normal vascular endothelial cells and pericytes, while pericytes started to peel off and skin capillaries with a tendency to leak excessively were occasionally found in people in their late 40s. Consequently, in-depth analysis was conducted using image analysis software, in which it was clarified that skin capillaries with a tendency to leak excessively significantly increase from the late 40s (Figure 2).

*1 MGH/Harvard Cutaneous Biology Research Center (CBRC):
A comprehensive center for cutaneous research jointly set up in 1989 by Shiseido, Massachusetts General Hospital (MGH) and Harvard Medical School of Medicine of Boston, USA. Shiseido sends its researchers to the CBRC team to collaborate with the world's top scientists.

## Quantity of Activated Tie2 in Skin Capillaries Declines Due to Aging

In order to thoroughly investigate the cause of excessive leakage from skin capillaries due to aging, joint research was promoted with Professor Nobuyuki Takakura of the Research Institute for Microbial Diseases at Osaka University regarding the function (activity) of Tie2, which is a receptor of vascular endothelial cells and is important for bonding

vascular endothelial cells and pericytes. It has been previously identified that the activation of Tie2 adhesively bonded vascular endothelial cells and pericytes, thereby properly delivering nutrients throughout the skin. As a result of carrying out research at this time on changes in the activity of Tie2 by using a vascular endothelial cell aging model (a method in which cells are repeatedly and repeated cultured so that they are aged), Shiseido discovered that the quantity of activated Tie2 declines in conjunction with aging.

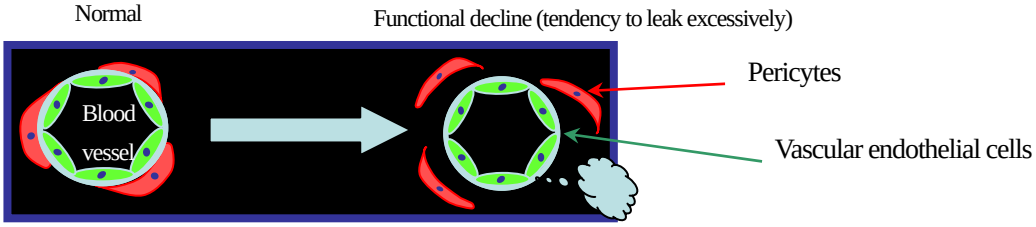
**Development of Ingredient that Restores Impaired Capillaries Due to Aging**

As a result of investigating more than 200 types of naturally occurring ingredients with the aim of increasing the quantity of activated Tie2, which is reduced due to aging, and developing an ingredient that will normalize the function of skin capillaries, Cassia Extract[*2] was identified for the first time in the world as possessing such effects (Figure 3). Additionally, it has been confirmed that Tie2 activation by the addition of Cassia Extract to skin capillaries resulted in the inhibition of excessive leakage.

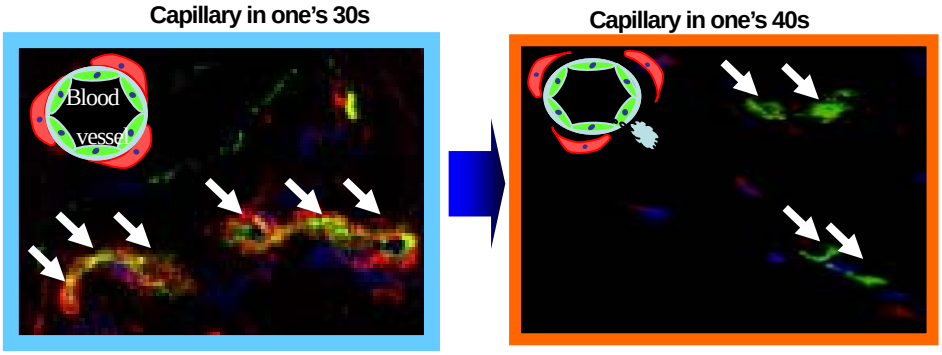
Shiseido plans to apply the current research results to supplements that will restore the supply route of nutrients to the skin (skin capillary function) for "healthy and beautiful skin" by targeting women who are starting to experience rapid aging of the skin or weaker effects of cosmetics. Additionally, Shiseido will promote the development of a new anti-aging skincare system in conjunction with cosmetics while continuously conducting research on blood vessels and lymphatic vessels in the skin.

*2 Cassia Extract was prepared from the stem bark of *Cinnamomum cassia* Blume (Lauraceae), which is mainly found in China and northern Vietnam. It is generally noted for its effects on perspiration, pain relief, sedation and peripheral vasodilatation.

[Figure 1] Capillary structure and condition in which function declined with a tendency to leak excessively




[Figure 2] Difference of capillary condition by age group




Normal blood vessel surrounded by pericytes

Pericytes peel off resulting in a tendency to leak excessively (arrows)

[Figure 3] Effects of Cassia Extract that restores the function of impaired capillaries