

**Shiseido Discovers New Mechanism of the Generation of Stress-related Acne
through Research at a Gene Expression Level
Successful Development of New Inhibitory Ingredient Neem Leaf Extract**

Shiseido has discovered a new mechanism of the generation of stress-related acne through research at a gene expression level in which stress hormones, which are largely produced in the body due to psychological stress, have been found to worsen the inflammatory reaction of acne. Additionally, in conjunction with this research, Neem Leaf Extract has been successfully developed through studying ingredients that will alleviate the inflammatory reaction and inhibit the worsening of acne caused by stress hormones.

Based on these current research results, Shiseido plans to promote the development of skincare products that will prevent stress-related acne and maintain good skin condition for healthy, beautiful skin.

Cause of occurrence and worsening of acne

Various factors are related to the occurrence and worsening of acne. There are a considerable number of sebaceous glands, which are made up of groups of cells that secrete sebum in human facial skin, and sebum secreted from sebaceous glands is pushed to the skin surface via pores. Acne occurs during this process when the openings of pores are clogged due to various reasons such as the impeded secretion of sebum, whereby sebum builds up within pores, which swell and can lead to acne. Additionally, *Propionibacterium acnes* (*P. acnes*), the bacteria responsible for acne, are constantly present on skin. These bacteria produce substances that decompose sebum and cause irritation, acting on skin cells to cause an inflammatory reaction often associated with acne.

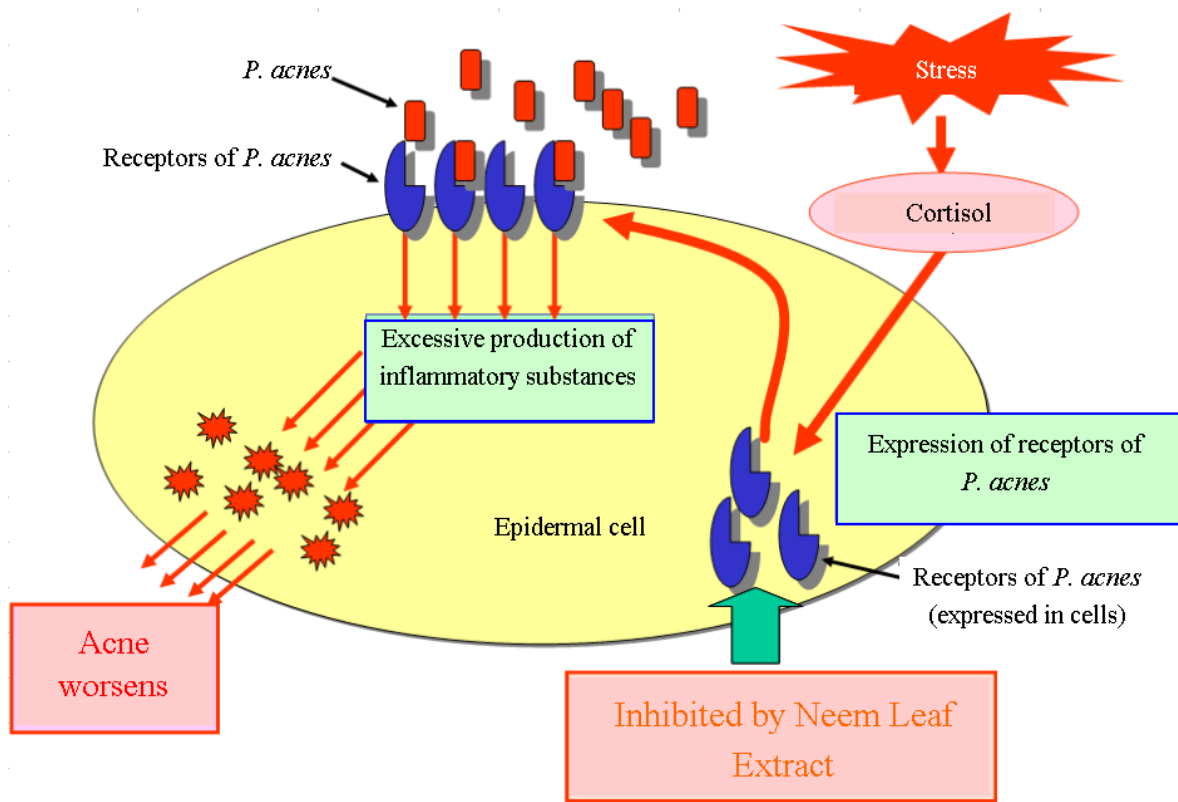
Furthermore, the environment of today's stress-filled society and greater psychological stress in line with career demands are said to be related to the occurrence and worsening of acne. "Stress-related acne" caused by these factors was previously purported to "worsen as a result of an increase of facial sebum induced by changes in hormone balance within the body due to stress."

Amid such an environment, there are many women who are concerned about acne in their daily life and have a need for skincare products that will prevent stress-related acne and lead to healthy, beautiful skin.

Discovering new mechanism of the generation of acne caused by stress and development of inhibitory ingredient

Shiseido has promoted research at a gene expression level using human epidermal cells, in which a number of results were attained confirming that "cortisol," a primary stress hormone, increases (promotes) the expression of the receptor of *P. acnes* [Toll-like receptor 2 (TLR2)] present in epidermal cells. The results indicated that the "expression of the receptor of *P. acnes* in the skin is increased by the stress hormone cortisol, and thus, skin becomes more sensitive to *P. acnes* and worsens the inflammatory reaction of acne." This represents a new mechanism of the generation of stress-related acne not recognized until now. (see diagram)

Consequently, research into agents that have an inhibitory effect on the expression of the receptor of *P. acnes* was conducted, whereby Neem Leaf Extract was identified from among more than 100 candidate ingredients to possess such an inhibitory effect. Neem Leaf Extract is a liquid extracted from leaves of the Neem tree, an evergreen tree of the Meliaceae family (scientific name: *Melia Azadirachta*; see image) that contains many active ingredients to achieve various effects, including anti-inflammatory and anti-oxidative effects. The Neem tree is widely grown in India, Southeast Asia, South America and Africa and is commonly used for various treatments of diseases, including malaria and tuberculosis, as well as for other purposes such as insect repellent, toothpaste and soap.



[Diagram] New mechanism of generation and worsening of acne caused by stress



[Image] Neem (Scientific name: *Melia Azadirachta*)