日本香粧品学会誌　Vol. 46, No. 2, pp. 129–136（2022）

〈一般論文〉

線維芽細胞由来肝細胞増殖因子（Hepatocyte Growth Factor）のメラノサイトへの影響とシソ葉エキスの美白効果

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Effects of HGF (Hepatocyte Growth Factor) Secreted from Fibroblasts on Melanocytes and of a Perilla Leaf Extract on Pigmentation

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(Accepted: November 8, 2021)

Abstract

Melanogenesis in melanocytes is regulated by various factors from nearby cells. In particular, inflammatory factors derived from epidermal cells have an influence on melanogenesis. Recent studies have shown that melanocytes are not only activated by mediators from epidermal cells but also mediators from dermal cells. Recent research reports show that the expression of HGF (hepatocyte growth factor) secreted from fibroblasts is increased in areas of solar lentigo and aging tissues. Therefore, HGF is thought to have an influence on excessive melanization. Thus, we investigated the influence of HGF secreted from fibroblasts on melanocytes and the inhibitory effect of a perilla extract on excessive melanogenesis caused by HGF in melanocytes. We chose the perilla leaf because it is known to contain polyphenols that show antioxidant activity and anti-inflammatory effects that contribute to a suppressive effect on inflammation. This suggested that a perilla leaf extract might well suppress melanogenesis.

We confirmed that UV-B irradiation increased HGF gene expression in cultured fibroblasts (NB1RGB) and that the perilla leaf extract had an inhibitory effect on HGF gene expression in cultured fibroblasts irradiated with UV-B light.

Furthermore, we investigated the influence on the proliferation of melanocytes and the transcription activity of STAT-3 in cultured human melanocytes (NHEMs) with and without the addition of HGF and perilla leaf extract. We confirmed that the proliferation of melanocytes and transcription activity of STAT-3 were increased when HGF was added to melanocytes. On the other hand, perilla leaf extract inhibited the increase in proliferation of melanocytes and transcription activity of STAT-3 induced by HGF. We also investigated other effects of perilla leaf extract, and we found that it had an inhibitory effect on tyrosinase activity.

In the *in vivo* study, we prepared a cream containing the perilla leaf extract, and application of the cream inhibited the pigmentation induced by UV-B in human skin.

In addition, we aimed to confirm the safety of perilla leaf extract by checking for toxicity to melanocytes. We applied the cream containing the perilla leaf extract to human skin twice per day for 2 weeks, and then irradiated the site with UV-B to induce pigmentation equivalent to that in the control area. The results showed that the perilla leaf extract did not exhibit toxicity in melanocytes. In conclusion, we developed an original perilla leaf extract as a functional natural material that inhibits the stimulation of melanocytes *via* fibroblasts.

Key words: fibroblast, HGF, melanocyte, STAT3, Perilla leaf.