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〈Regular Article〉

A Novel "Anti-Pollution" Cosmetic Ingredient, *Phellodendron amurense* Bark Extract, Attenuates Air Pollution-Induced Oxidative Stress and Inflammatory Reactions of Human Keratinocytes (HaCaT) *via* the AhR-Nrf2 Pathway

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Abstract

Recent epidemiological studies have demonstrated that air pollution is one of the risk factors for developing skin aging, which is characterized by pigmented spots such as solar lentigos, wrinkles and sagging. Therefore, daily skin care is an important treatment to alleviate the adverse effects of air pollutants on the skin. In this study, we investigated the effects of *Phellodendron amurense* Bark Extract (PABE) on oxidative stress and the secretion of an inflammatory cytokine by HaCaT keratinocytes treated with diesel exhaust particles (DEP), SRM1975, a model of air pollutants. In general, air pollutants induce a detoxifying enzyme, *CYP1A1*, and increase oxidative stress through the activation of aryl hydrocarbon receptor (AhR). Treatment with PABE significantly suppressed levels of reactive oxygen species (ROS) and the secretion of IL-8 by HaCaT keratinocytes treated with DEP without affecting the mRNA expression level of *CYP1A1*. Furthermore, treatment with PABE significantly suppressed the matrix metalloproteinase-1 (MMP-1) activity of normal human dermal fibroblasts (NHDFs) cultured with the conditioned medium of DEP-treated HaCaT keratinocytes. Treatment with PABE increased the mRNA expression levels of *γ-GCS* and *NQO1* due to increased levels of Nrf2. Based on these results, we conclude that PABE alleviates the progression of skin aging due to the removal of oxidative stress without affecting the metabolism of polycyclic aromatic hydrocarbons (PAHs). In conclusion, PABE is expected to be an effective cosmetic ingredient that prevents the acceleration of skin aging by air pollutants.

Key words: *Phellodendron amurense*, air pollution, skin aging, oxidative stress, AhR-Nrf2.

1. Introduction

Air pollution has been gaining increased attention as one of the risk factors for developing skin aging because some epidemiological studies have reported that subjects living in areas where levels of air pollution are higher, have increased symptoms of skin aging characterized by wrinkles and pigmented spots. For example, Vierkötter *et al.* reported that soot and particles generated by traffic are responsible for the appearance of pigmented spots on the foreheads and cheeks of subjects in Germany at a frequency of more than 20%[1)]. Li *et al.* reported that cooking with solid fuels is associated with the appearance of wrinkles on the faces of subjects in China at a frequency of 5–8%[2)]. It was reported by the WHO in 2018 that 91% of the world's population (billions of people) live in places that exceed the WHO air quality guideline levels[3)]. These circumstances emphasize the importance of dealing with air pollution in order to prevent the risk of developing skin aging. Generally thinking, there are two approaches to deal with air pollutants; one is to prevent air pollutants from adhering to the skin by shielding it with films formed by polymer or cosmetic formulation technology, while another is to reduce the adverse influence of air pollutants on the skin. In this study, we investigated the preventive effects of several plant extracts on skin aging initiated by air pollutants, in order to identify effective solutions in daily skin care against the adverse effects of air pollutants.

Although the mechanism of action of air pollutants to accelerate skin aging is not yet fully understood, the involvement of the aryl hydrocarbon receptor (AhR), which is activated by polycyclic aromatic hydrocarbons (PAHs) as ligands, has been considered as a major candidate mechanism. Benzo(*a*)pyrene (B*a*P) is one PAH that is contained in cigarette smoke and in diesel exhaust particles (DEP). In order to metabolize B*a*P, the binding of B*a*P to AhR strongly induces the expression of cytochrome P450 1A1 (CYP1A1) and concomitantly stimulates the generation of reactive oxygen species (ROS) and the synthesis of interleukin-1 (IL-1) and in-

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