Synopsis of Original Research Paper

Screening of natural products to find cosmetic agents that modulate PPAR function

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The permeability barrier is required for terrestrial life and it is localized at the outermost layer of the epidermis, the stratum corneum, where extracellular lipid membranes inhibit water movement. The stratum corneum is the end product of keratinocyte differentiation and comprises a layer of cross-linked proteins and lipids. Epidermal homeostasis and the barrier function integrity depend on the tight coordination of keratinocyte proliferation, differentiation, and programmed death.

Peroxisome proliferator-activated receptor α (PPARα) is a ligand-activated transcription factor belonging to the nuclear hormone receptor superfamily. PPARα is mainly expressed in the liver, and is also present in the epidermis. PPARα binds to peroxisome proliferator responsive element (PPRE) and activates several target genes, which leads to fatty acid catabolism. PPARα ligands have been used to treat dyslipidemia by reducing plasma triglycerides and increasing high-density lipoprotein cholesterol. On the other hand, various cell culture and in vivo approaches suggest that PPARα contributes to fetal skin development, epidermal barrier maturation, and sebocyte activity. Thus, PPARα represents a research target for understanding and improving the recovery of skin barrier function.

Previously, we established a tightly tetracycline-regulated human hepatoblastoma cell line that can be induced to express human PPARα (HepG2-tet-off-hPPARα). We subsequently engineered reporter cell line expressing the luciferase gene that can be used to quantify the PPARα activity by modulators using HepG2-tet-off-hPPARα.

In this study, we evaluated extracts of approximately 200 natural products and found an extract that enhanced reporter gene activity. Furthermore, this extract up-regulated the expression of adipose differentiation-related protein (ADRP), which is a known PPARα target gene. These findings suggest that the extract is a candidate agent for improving epidermal permeability barrier function.