



## Effects of Lavender Oil on Hair Growth-Relevant Enzyme Activity and Cytokine Expression in C57BL/6 Mice

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### C57BL/6 마우스에서 라벤더 오일이 모발성장 관련 효소활성과 사이토카인 발현에 미치는 효과

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The purpose of this study was to determine the effects of lavender oil (LO) on hair growth-relevant enzyme activity and cytokine expression in C57BL/6 mice. The experimental animals were divided into the following groups: i) normal (N: saline), ii) vehicle control (VC: jojoba oil), iii) positive control (PC: 3% minoxidil), iv) experimental 1 (E1: 3% LO), and v) experimental 2 (E2: 5% LO). Test compound solutions were topically applied to the backs of the mice (100  $\mu$ L per application), once per day, 5 times a week, for 4 weeks. At week 4, the activities of  $\gamma$ -glutamyl transpeptidase (GT) in the E1 and E2 groups were 11% and 15% higher than the N group ( $p < 0.05$ ), respectively. The expression levels of keratinocyte growth factor (KGF) mRNA were significantly greater [10%; ( $p < 0.05$ )] in the E1 and E2 groups, compared to the N group. The expression of insulin-like growth factor (IGF)-1 mRNA also significantly increased by 21% and 22% ( $p < 0.05$ ) in the E1 and E2 groups, compared to the N group, respectively. Hepatocyte growth factor (HGF) mRNA expression levels were significantly higher in the E1 and E2 groups than the N group [14% and 17%; ( $p < 0.05$ )], respectively. The expression of vascular endothelial growth factor (VEGF) mRNA increased by 22% ( $p < 0.05$ ) in both the E1 and E2 groups, when compared to the N group. The correlation coefficients among hair growth-relevant factors were significantly high each other ( $p < 0.001$ ). The correlation coefficient between hair growth area and KGF mRNA expression was 0.940. These results confirm that LO has hair growth-promoting effects as identified by hair growth-relevant enzyme activity and cytokine expression in C57BL/6 mice.

**Keywords :** C57BL/6 mice, IGF-1, Lavender oil,  $\gamma$ -GT, VEGF

## INTRODUCTION

Given the role of hair in psychosocial communication (as a symbol of youth, health, fertility, and sexual potency), hair loss often has an underestimated psychosocial impact on an

individual's self-esteem, interpersonal relationships, and positioning within a society (Hendrix et al., 2005). Telogen effluvium, androgenetic alopecia, and alopecia areata, the 3 most frequent hair loss disorders encountered in clinical practice, exemplify how a range of negative psychological and social experiences translate into significant stressors that possibly conspire to further aggravate hair loss (Arck et al., 2005).

At present, finasteride (oral treatment) and minoxidil (MXD,

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transdermal ointment) are the products approved as hair restorers by the U.S. Food and Drug Administration (US-FDA). However, it was reported that these products can cause adverse effects such as pruritis, scaling, sexual dysfunction, and birth of deformed children (McClellan & Markham, 1999). Accordingly, research on hair loss and hair growth stimulators is being vigorously pursued with new drugs and cosmetics being developed following cytological, biochemical and molecular biological advances.

In the hair cycle, hair growth and hair loss are caused by a variety of factors. When hair is induced into the anagen phase, there is an increase in the activity of the enzymes,  $\gamma$ -glutamyl transpeptidase ( $\gamma$ -GT) and alkaline phosphatase (ALP), which are indicators of hair growth (Hattori & Ogawa, 1983).

The hair follicle (HF) is an important functional unit for hair shaft elongation where various kinds of cytokines and growth factors are involved in the regulation of hair morphogenesis and hair growth (Stenn & Paus, 2001; Park et al., 2013; Lee BS, 2014; Oh et al., 2014). Such factors include epidermal growth factor (EGF), transforming growth factor (TGF)- $\alpha$ , TGF- $\beta$ , keratinocyte growth factor (KGF), insulin-like growth factor (IGF-1)-1, interleukin (IL)-1, basic fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), and vascular endothelial growth factor (VEGF) (Shimaoka et al., 1995; Jindo et al., 1998; Lee et al., 2015).

IGF-1 is critically involved in promoting hair growth by regulating cellular proliferation and migration during the development of HFs. IGF-1 has been shown to be produced by dermal papilla cells (DPCs) in HFs (Itami & Inui, 2005). Since IGF-1 receptor mRNA was detected in keratinocytes (Tavakkol et al., 1992), it is possible that IGF-1 produced by DPCs might act on keratinocytes, thereby promoting hair growth by stimulating the proliferation of these keratinocytes in HFs (Sadagurski et al., 2006). KGF and HGF stimulate the subsequent steps of anagen development (Danilenko et al., 1995; Sato et al., 1999). KGF signaling pathways are conventionally seen as promoters of cell growth and proliferation in the inter-follicular epidermis (Schneider et al., 2008). HGF is produced from DPCs and stimulates outer root sheath cells and eventually promotes the elongation of hair shafts (Fujie et al., 2001). In the anagen phase, VEGF mRNA is strongly expressed in the dermal papillae, whereas VEGF transcripts are decreased in the catagen and telogen phases, suggesting that VEGF is an autocrine growth factor for DPCs (Yano et al., 2001). The transgenic over-expression of VEGF in the outer root sheath increases perifollicular vascularization and leads to accelerated hair growth following depilation and the growth of larger hairs (Elliott et al., 1999).

Lavender is genus *Lavandula* and family Laviatae (Asiatic self-heal), and its scientific name is *Lavandula* species that is medicinal stuff widely applied in aroma therapy because of its good effects on acne, eczema and sunburn by functions of anti-inflammation, sterilization, cell growth promotion, and

**Table 1.** Composition of lavender oil and jojoba oil

Peppermint oil	%	Jojoba oil	%
Linalyl acetate	38.8	Docosenyl elcosenoate	41.5
Linalool	31.7	Elcosenyl elcosenoate	27.7
Trans- $\beta$ -3-ocimene	4.9	Elcosenyl docosenoate	10.3
Cis- $\beta$ -ocimene	3.0	Tetracosanyl elcosanate	6.3
Lavandulyl acetate	2.3	Elcosenyl oleate	5.4
Terpinene-4-ol	1.3	Docosenyl stearate	3.2
$\alpha$ -Terpineol	0.6	Other esters	5.6
Camphre	0.6		
1,8-Cineole	0.6		
Lavandulol	0.4		
$\beta$ -Phellandrene	0.2		
Octanone 3	0.2		
Limonene	0.2		
The others	15.2		
Total	100.0	Total	100.0

sebum secretion regulation (Cavanagh & Wilkinson, 2002). The main ingredients of lavender are linalool and linalyl acetate and it is known that if it is put on skin and massaged, it is properly absorbed through skin and the plasma concentration reaches the highest after approximately 19 minutes (Jäger et al., 1992) and acts to inhibit central nervous system. Among various effects of lavender oil (LO), especially, inhibition of oxidization and skin reconstruction promoting effect make us expect hair growth effect and therefore, we examined hair growth promoting effect of LO by using experimental animals.

In our recent study (Lee et al., 2016), we found that LO promoted hair growth in C57BL/6 mouse model. In this study, we investigated the effects of LO on hair growth-relevant enzyme activity and cytokine expression in C57BL/6 mice.

## MATERIALS AND METHODS

**Reagents and apparatus.**  $\gamma$ -GT was purchased from Thermo (Finland). cDNA synthesis and *real-Time* RT-PCR kits, and primers for KGF, HGF, VEGF, HGF and GAPDH were purchased from Roche (Germany) and for other general reagents, special grade goods were used. LO was purchased from Sanoflore company (France) and jojoba oil was purchased from Bio & Bio (Korea). The chemical composition of LO and jojoba oil is listed in Table 1. The 3% MXD was obtained from Hyundai Pharmacia (Korea). In order to prepare the 3% and 5% solutions, LO was mixed with jojoba oil.

PCR machine (Roche, Panplex™ thermal cycler, Germany), mini centrifuge (Hitachi, MIKRO 200R, Japan), and automated biochemical analyzer (Beckman Coulter, UniCel™ DxI 800, USA) were used.

**Experimental animal.** Five-week-old female C57BL/6 mice were purchased from Dae Han Biolink Co (Korea). The animals were housed and allowed to adapt to the laboratory