TARGETING GENES RELATED TO SKIN FIRMNESS—AN IN-VITRO APPROACH

Remona Gopaul, Helen E. Knaggs, Dale G. Kern and Jan F. Lephart

Nu Skin Center for Anti-Aging Research, Nu Skin Enterprises, Provo, UT, USA

INTRODUCTION

Gene expression in the skin is regulated by thousands of genes. Genes related to skin aging may fall into the following categories: cellular proliferation, protection, structure, hydration, and pigmentation[1]. The loss of skin structure or elasticity is usually one of the first and most noticeable signs of skin aging. Firm skin is physically taut, having few visible wrinkles and high elasticity. Research has shown that Echinacea Purpurea Extract, Centella Asiatica Extract, and Commiphora Mukul Resin Extract have significant anti-aging skin benefits.[2, 3, 4] A recent combination of Echinacea Purpurea Extract and Centella Asiatica Extract was shown to have clinical benefits on skin firmness, in an internal study. Clinical studies of Commiphora Mukul Resin Extract from India's Mukul Myrrh tree also show benefits on skin firmness when applied topically. In this investigation, genes were selected based on their relevance in influencing skin firmness as referenced in published literature. The effects of a blend of Echinacea Purpurea Extract, Centella Asiatica Extract, and Commiphora Mukul Resin Extract on these genes alone were measured on these genes to further substantiate the potential benefits of these materials on skin firmness.

Echinacea plant

Centella Asiatica plant

Commiphora Mukul Resin Extract from Mukul Myrrh tree

MATERIALS AND METHODS

Epidermal full-thickness skin cultures were obtained from MatTek (Ashland, MA, USA). These cultures were comprised of normal human-derived epidermal keratinocytes and normal human-derived dermal fibroblasts. A combination of Echinacea Purpurea Extract and Centella Asiatica Extract (1%), and Commiphora Mukul Resin Extract (1%) were separately applied to the cultures for 24 hours. Cultures incubated without the extracts were used as control. RNA was extracted from the cultures and converted to cDNA using the High Capacity Transcription Kit from Life Technologies (Foster City, CA USA). Reactions were performed according to manufacturer instructions. Custom Taqman Low Density Arrays (TLDAs) were created using Life Technologies validated gene expression assays. Each TLDA card contained 379 target genes and five common endogenous control genes. An Applied Biosystems 7900HT (Applied Biosystems, Foster City, CA USA) was used for amplification and fluorescence detection. Data analysis for qPCR was carried out according to the RQ analysis method using RQ Manager and STATMINER (v3.1) software programs.

RESULTS

Gene	Gene Symbol	Role in Skin Structure
AR	Androgen Receptor	Collagen Breakdown[5]
FOS	v-fos FBJ murine osteosarcoma viral oncogene homolog	Promotes MMP's[6]
IL1α	Interleukin 1 Alpha	Induced Collagenase[7]
JUN	JUN	Promotes MMP's[8]
NFKβ	Nuclear Factor Kappa Beta	Diverse effects[9]
PDGFA	Platelet-derived growth factor subunit A	UV induced collagenase[10]
TP53	Tumor protein p53	Suppressor of collagen gene [11]
MMP9	Metalloproteinase 9	Degrades collagen gene[12]

Table I. Summary of key skin structure genes investigated in this study

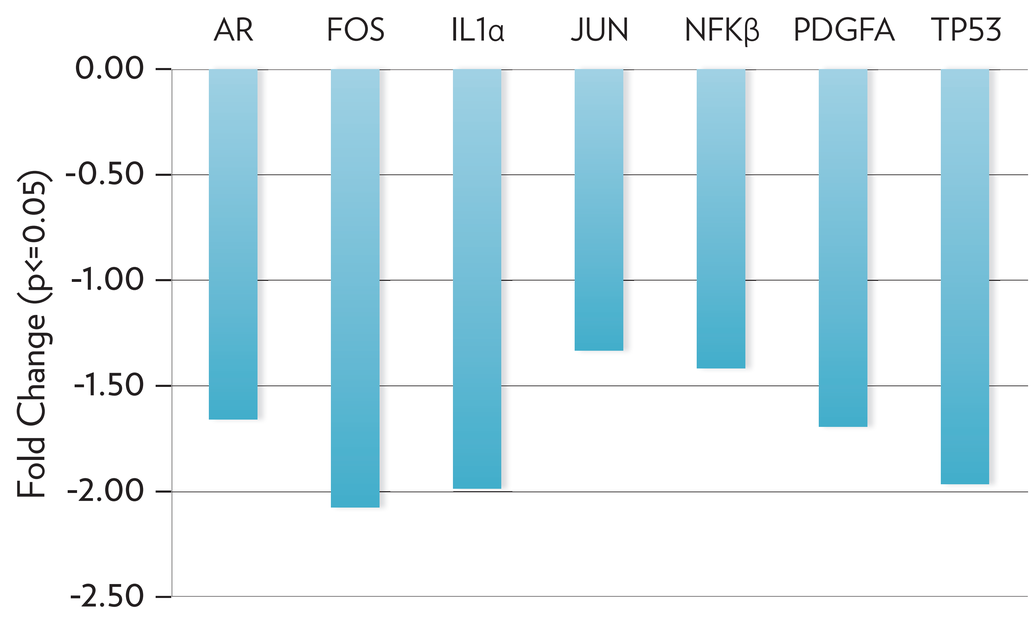

Figure 1. qPCR data illustrating a decrease in expression of genes associated with skin structure deterioration after 24 hours of incubation with Commiphora Mukul Resin Extract (see Table 1 for full description of genes and functions).

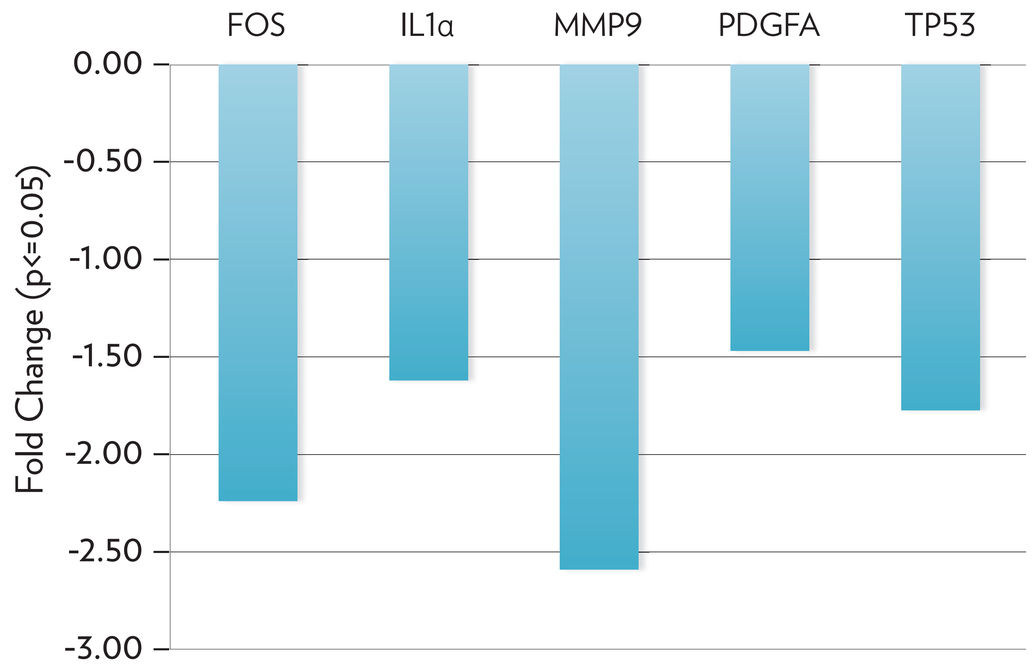

Figure 2. qPCR data illustrating a decrease in expression of genes associated with skin structure deterioration after 24 hours of incubation with a combination of Echinacea Purpurea Extract and Centella Asiatica Extract (see Table 1 for full description of genes and functions).

DISCUSSION

Results showed that a combination of Echinacea Purpurea Extract and Centella Asiatica Extract (1%) and Commiphora Mukul Resin Extract (1%) reduced the expression of key genes associated with the deterioration of skin structure proteins. The combination of Echinacea Purpurea Extract and Centella Asiatica Extract downregulated some of the same genes related to skin structure degradation as Commiphora Mukul Resin Extract. These included JUN, FOS, IL1α, AR, PDGFA and TP53. However, the expression of MMP9 was also lowered by the combination of Echinacea Purpurea Extract and Centella Asiatica Extract. MMP9 is a collagenase responsible for the breakdown of the key skin structure protein, collagen.[1,2] By decreasing the regulation of this gene, the combination of Echinacea Purpurea Extract and Centella Asiatica Extract may have the ability to decrease the production of collagenase when used topically. While Commiphora Mukul Resin Extract did not regulate MMP9, this active material downregulated another important skin structure related gene—namely, NFKβ. NFKβ is a key gene that is activated during oxidative stress that is responsible for the degradation of key skin structure proteins relevant for the maintenance of firm looking skin.[9] By downregulating this gene, Commiphora Mukul Resin Extract may be acting as an inhibitor of NFKβ. It is proposed that a combination of Echinacea Purpurea Extract, Centella Asiatica Extract, and Commiphora Mukul Resin Extract in a topical cosmetic formulation may be able to increase skin firmness by decreasing key genes responsible for the degradation of skin structure proteins. Recent unpublished clinical studies involving the combination of all three of these materials in a finished topical formulation seemed to support the hypothesis that skin firmness is improved when these extracts are combined in this manner. Additional work is needed to measure the upregulation of genes related to skin firmness by this combination of active materials to further validate this hypothesis.

CONCLUSION

The findings from this study suggest a possible role of a combination of Echinacea Purpurea Extract, Centella Asiatica Extract, and Commiphora Mukul Resin Extract on enhancing skin firmness when applied topically.

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