ANTIAGING AND WOUND HEALING PROPERTIES OF *POUTERIA LUCUMA SEED* EXTRACT

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INTRODUCTION

Wound healing and skin aging share common biochemical cascades, such as the accumulation of free radicals, the formation of extra cellular gaps, accelerated cell senescence, inflammation, extracellular matrix remodeling and re-epithelialization.

Lucuma seed extract (LSE): A unique and proprietary extract of lucuma (*Pouteria lucuma O Kezte*) seed extract (LSE), rich in bioactive fatty acids (FAs) was evaluated for its effects on elastin expression, fibroblasts migration, angiogenesis, inflammation and tissue regeneration. *P. lucuma* is a subtropical fruit of Andean origin that grows mostly in Peru and Chile. In South America lucuma pulp is popular for flavoring of ice creams and other confectioneries.

MATERIALS & METHODS

GC-MS and HPLC/MS analyses of fatty acids were used for the identification bioactive compounds of LSE. *In vitro* studies were done with LSE investigating the induction of cell migration, elastin mRNA expression by RT-PCR, and immunocytochemical detection of elastin in cultured human fibroblasts. The anti-inflammatory effect of LSE was studied in LPS-stimulated macrophages. Tail fin regeneration and blood vessel sprouting was studied in transgenic zebrafish larvae expressing enhanced green fluorescent protein (EGFP) in vascular endothelial cells. The effect of topical LSE-based formulations was evaluated on dermal wounds of CD-1 mice.

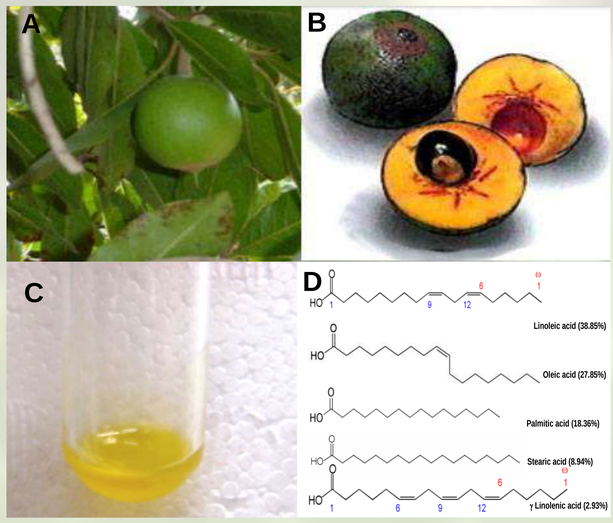

Figure 1. (A, B) *P lucuma* fruit. (C) Lucuma seed extract. (D) Major fatty acids in lucuma seed extract (LSE)

RESULTS

Bioactives in lucuma seed extract: LSE contains a unique combination of natural free fatty acids (FAs), 99.7% of which correspond to linoleic acid (38.9%), oleic acid (27.9%), palmitic acid (18.6%), stearic acid (8.9%), γ-linolenic acid (2.9%) and other 16 minor FAs. We observed that LSE induced cell migration and cytoskeleton remodeling in human fibroblasts and inhibited LPS-induced nitric oxide production in macrophages.

Anti aging: LSE also significantly increased elastin at protein (Fig. 2 C,D) and mRNA levels (Fig.2 G). LSE also prevented aberrant nuclei phenotype in our model of cellular senescence (Fig. 3)

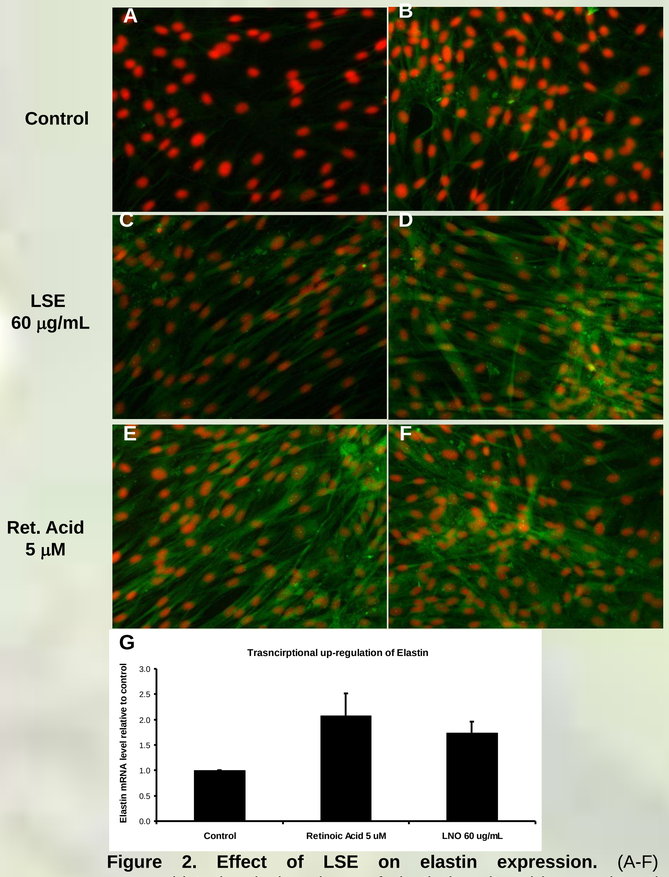

Figure 2. Effect of LSE on elastin expression. (A-F) Immunohistochemical analyzes of elastin in cultured human dermal fibroblasts showed that LSE induced the formation of elastic fibers. (D) mRNA expression levels of elastin

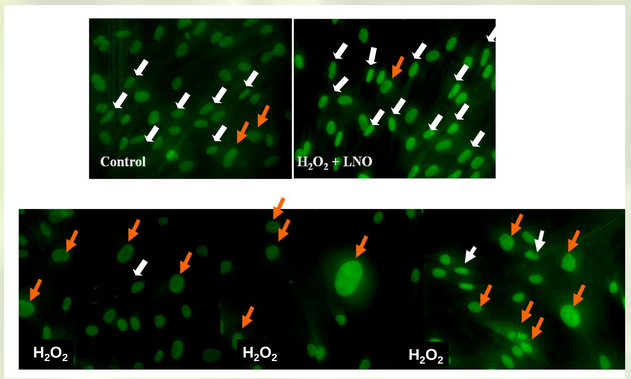

Figure 3. Effect of LSE on H_2O_2–induced senescence: LSE prevent aberrant nuclear morphology. Nuclear shape of non-senescent dermal fibroblast is elongated (white arrows). Abnormal morphology (globular, folded or oversized) was observed in senescent fibroblasts (orange arrows)

Wound Healing: LSE significantly accelerated wound healing in two animal models. In addition, LSE promoted tissue regeneration and re-vascularization in Tg(fli1a:EGFP)y1/+ transgenic zebrafish (Fig. 3), which expresses enhanced green fluorescent protein (EGFP) in vascular endothelial cells. Skin wounds of CD-1 mice treated with topical LSE-containing formulations showed significant increased in wound closure compared to 2-p-(2-Carboxyethyl) phenethylamino-5′-N-ethylcarboxamidoadenosine (CGS)-treated animals (Fig. 4).

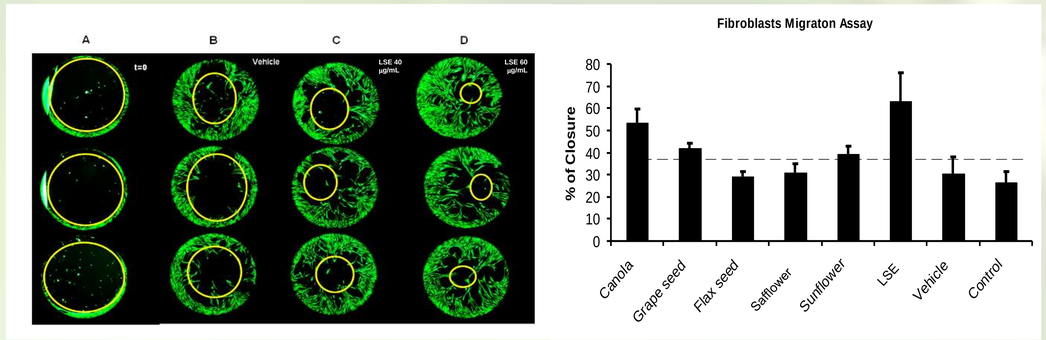

Figure 4. Effect of LSE on human fibroblasts migration: (A-D) LSE increased migration capacity of green fluorescently labeled human fibroblasts. (D) LSE was superior to other common edible extracts in increasing migratory capacity of human fibroblasts

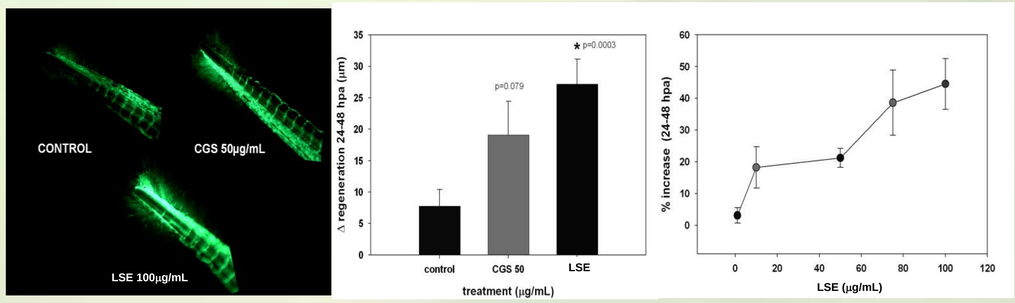

***Figure 5. Effect of LSE on vessel sprouting in transgenic zebrafish :** (A) LSE increased formation of new blood vessels after amputation of tail fin in Tg(fli1a:EGFP)y1/+ zebrafish larvae. (B, C) The effect of LSE was comparable to a potent wound healing adenosine agonist CGS and dose dependent.

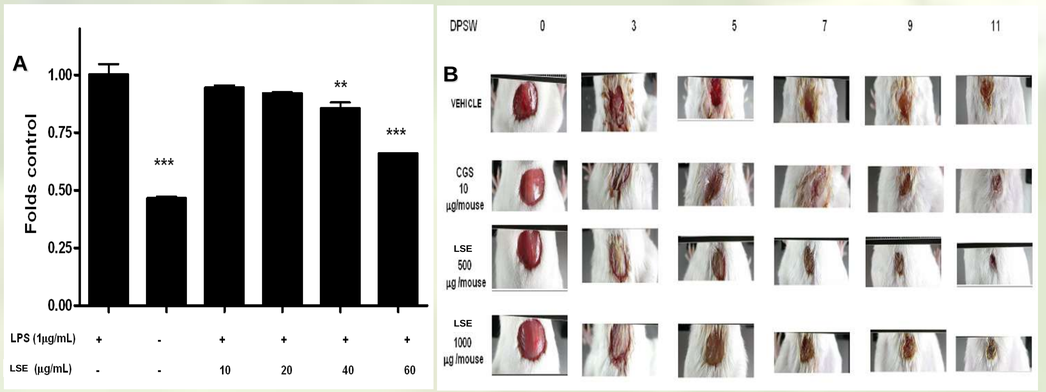

***Figure 6. Anti-inflammatory and wound healing effect of LSE:** (A) Decreased LPS-induced Nitric oxide production in macrophages. (B) Skin wounds of CD-1 mice treated with topical LSE-containing formulations showed significant increased in wound closure compared to 2-p-(2-Carboxyethyl) phenethylamino-5′-N-ethylcarboxamidoadenosine (CGS)-treated animals. DPSW=days post skin wound

CONCLUSION

This data suggest that LSE can be developed as a novel and efficacious cosmetic ingredient capable of anti-inflammatory, anti-aging and skin-repair effects on human skin. On going studies will provide more evidence on the potential applications of LSE as a cosmetic and ingredient.
*Note: Animal studies by Rutgers University (Figs. 5 and 6B) were performed for medical applications.