INFLUENCING THE EXPRESSION OF GENES ASSOCIATED WITH SKIN INFLAMMATION BY COMBINING NARCISSUS TAZETTA BULB EXTRACT AND SCHIZANDRA CHINENSIS FRUIT EXTRACT - AN IN VITRO ANALYSIS

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BACKGROUND

Skin inflammation is regulated by multiple pathways and inflammatory mediators. The activation and/or deactivation of certain mediators can influence how the skin responds to certain irritants. Research has shown that topical application of certain plant extracts may be able to regulate the expression of inflammatory mediators. Narcissus Tazetta Bulb Extract, a bulb extract from the daffodil plant family has been used topically to delay cellular proliferation. Schizandra Chinensis Fruit Extract, a red berry fruit extract belonging to the magnolia plant family, has been used for decades in Chinese medicine to promote general well-being and vitality when taken orally.

Research on these two extracts individually has shown that they have effective anti-inflammatory benefits when taken orally. However there is limited research on the anti-inflammatory benefits for topical applications on either of these extracts. Recent in–house unpublished clinical studies involving these extracts in finished topical formulations have led to the hypothesis that when combined, Narcissus Tazetta Bulb Extract and Schizandra Chinensis Fruit Extract may be able to reduce skin inflammation. This research investigates the in vitro effect of a proprietary blend of these extracts on genes related to skin inflammation when applied topically.

METHODS AND MATERIALS

A combination of Narcissus Tazetta Bulb Extract (0.2%) and Schizandra Chinensis Fruit Extract (0.5%) was applied to human full-thickness 3D epidermal equivalents (FTEE, MatTek, Ashland, MA). One hundred microliters of the test article was applied to each culture and incubated for 24 hours. Following incubation, the cultures were thoroughly washed with sterile phosphate buffered saline to remove test materials and consequently placed in RNAlater solution for gene expression analysis. qPCR analysis was carried out using Custom Taqman Low Density Arrays (TLDA's) created by Life Technologies (Foster City, CA). An Applied Biosystems 7900HT instrument was used for amplification and fluorescence detection. Data analysis was carried out according to RQ analysis using RQ Manager and StatMiner (v3.1) software.

RESULTS

Gene Name	Gene Symbol	Role in Skin Inflammation
leukotriene B4 receptor	LTBR4	enhances allergic contact dermatitis[4]
platelet-activating factor receptor	PTAFR	involved in the synthesis of pro-inflammatory mediators[5,6]
histamine receptor 1	HRH1	mediates itch response on the skin[7]
v-erb-b2 erythroblastic leukemia viral oncogene homolog 2	ERBB2	activator of UV induced pro-inflammatory mediators[1]
interleukin 1 receptor antagonist	IL1RN	mediates IL-1 inflammatory response[2]
metallothionein 1H	MT1H	helps with immune response and wound healing[3]
metallothionein 2A	MT2A	helps with immune response and wound healing[3]
intercellular adhesion molecule 2	ICAM2	helps suppress inflammation[8]

TABLE I. Summary of key inflammatory mediators investigated in this study.

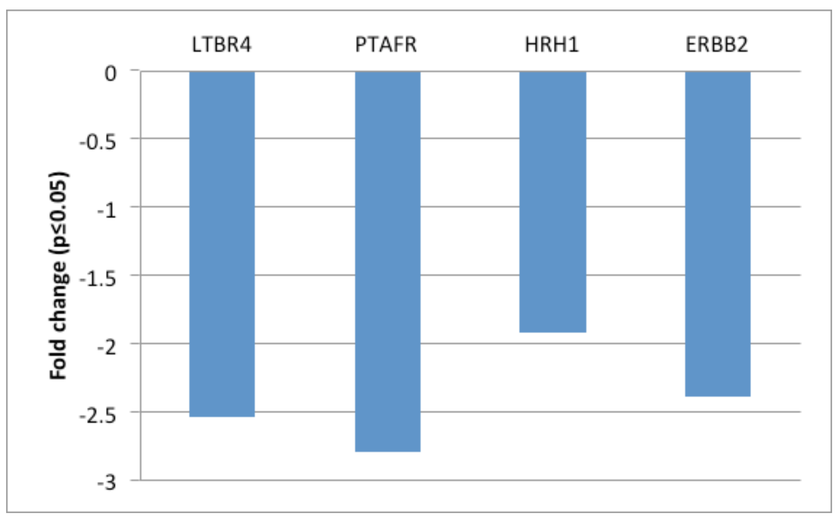

FIGURE 1: qPCR data illustrating a decrease in expression of key pro-inflammatory genes after 24 hours of incubation with test material (see Table 1 for full description of genes and functions).

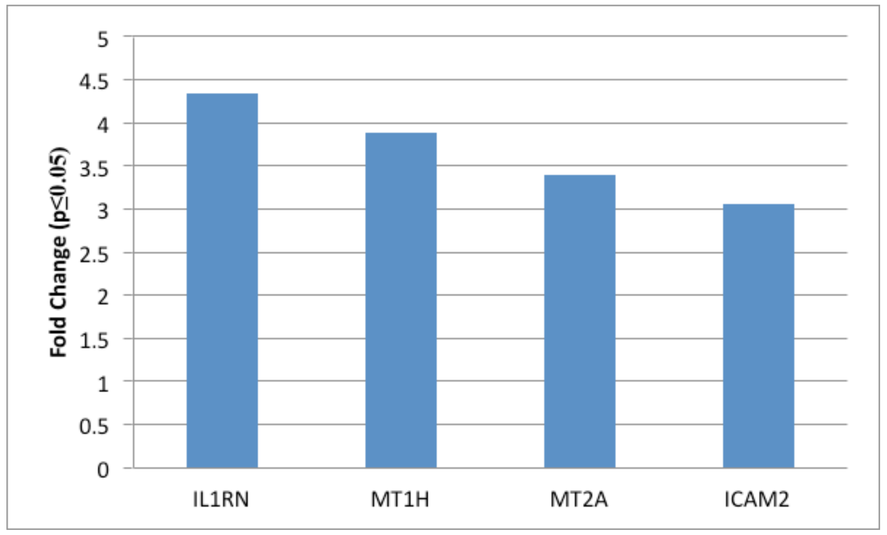

FIGURE 2: qPCR data illustrating an increase in expression of key anti-inflammatory genes after 24 hours of incubation with test material (see Table 1 for full description of genes and functions).

DISCUSSION

Results showed that a combination of Narcissus Tazetta Bulb Extract (0.2%) and Schizandra Chinensis Fruit Extract (0.5%) reduced the expression of four key genes associated with skin inflammation while increasing the expression of four key genes related to anti-inflammation. The expression of genes such as PTAFR and LTBR4 were lowered, indicating a possible role of these two extracts in addressing inflammation via the arachidonic acid pathway. The expression of histamine receptor 1 gene (HRH1) was also lowered, showing potential in itch mediation of these two extracts. ERBB2, a gene known to stimulate the expression of various UV-induced pro-inflammatory mediators was also downregulated[1]. Along with decreasing the expression of pro- inflammatory mediators, Narcissus Tazetta Bulb Extract and Schizandra Chinensis Fruit Extract also increased the expression of genes related to anti-inflammation. IL1RN, interleukin 1 receptor antagonist was increased. Research has shown that IL1RN may play a role in the regulation of IL-1-induced inflammatory responses, and an appropriate balance between IL-1 and IL1RN may help to maintain homeostasis of the skin2. Metallothioneins, which helps in wound healing and also help regulate immune response from irritants were also increased[3]. See Table 1 for a summary of genes and their role in inflammation.

CONCLUSION

The findings from this study suggest a possible role of a combination of Narcissus Tazetta Bulb Extract and Schizandra Chinensis Fruit Extract on skin inflammation when applied topically.

REFERENCES

1. Madson JG, Lynch DT, Tinkum KL, Putta SK, Hansen LA. Erbb2 regulates inflammation and proliferation in the skin after ultraviolet irradiation. Am J Pathol. 2006 Oct;169(4):1402-14.
2. Hiraco T, Aoki H, Yoshida T, Sato Y, Kamoda H. Elevation of interleukin 1 receptor antagonist in the stratum corneum of sun-exposed and ultraviolet B-irradiated human skin. J Invest Dermatol. 1996 May; 106(5):1102-7.
3. Lansdown AB, Sampson B. Trace metals in keratinizing epithelia in beagle dogs. Veterinary Record. 1997 Nov; 141(22):571-2.
4. Aked DM, Foster SJ. Leukotriene B4 and prostaglandin E2 mediate the inflammatory response of rabbit skin to intradermal arachidonic acid. Br J Pharmacol. 1987 Nov; 92(3):545-552.
5. Morley J, Page CP, Paul W. Inflammatory actions of platelet activating factor (Pafacether) in guinea-pig skin. Br J Pharmacol. 1983 Nov; 80(3):503-9.
6. Pei Y, Barber LA, Murphy RC, Johnson CA, Kelley SW, Dy LC, Fertel RH, Nguyen TM, Williams DA, Travers JB. Activation of the epidermal platelet-activating factor receptor results in cytokine and cyclooxygenase-2 biosynthesis. J Immunol. 1998 Aug; 161(4):1954-61.
7. Harvima IT. Induction of Matrix Metalloproteinase-9 in keratinocytes by Histamine. J Invest Dermatol. 2008 Dec; 128(12):2748-50.
8. Huang MT, Larbi KY, Scheiermann C, Woodfin A, Gerwin N, Haskard DO, Nourshargh S. ICAM-2 mediates neutrophil transmigration in vivo: evidence for stimulus specificity and a role in PECAM-1-independent transmigration. Blood. 2006 Jun: 107(12):4721-7.