HYDROQUINONE FREE BRIGHTENING COMPLEX - A MULTI-CENTER STUDY FOR SKIN AGING

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INTRODUCTION

Melanogenesis is the result of a cascade of processes involving (1) transport of melanin precursors phenylalanine and tyrosine into melanoocyte and melanosome, (2) enzymatic transformation of tyrosine to dopamine, dopaquinone and later melanin by tyrosinase, which is enhanced after sun exposure via α-MSH, (3) melanosome maturation, and (4) melanosome transfer from melanoocyte to keratinocyte (Fig.1). Currently, hydroquinone at prescription strength is considered the gold standard for effective skin whitening. Safe and effective alternatives to hydroquinone are being researched. This study describes a skin brightening complex comprising four actives interfering with several key processes of melanogenesis. The actives of the complex are L-leucine, sodium glycerophosphate, phenylethyl resorcinol and undecylenoyl phenylalanine.

METHODS & MATERIAL

Study design: In a four center study approved by the Independent IRB (Plantation FL), eighty female subjects between 35 to 65 years of age (53 ± 7 years) of skin type I to III (I: 9%, II: 67%, III: 24%) were included. Subjects with dermal or mixed epidermal and dermal melasma (as assessed with the Wood’s lamp) and with post-inflammatory hyperpigmentation (due to acne or other causes) were excluded. Included were only subjects not using topical products with skin lightening actives, alpha-hydroxy and beta-hydroxy acids, concentrated vitamin C products, steroids, retinoids, or undergoing light to medium peels or microdermabrasion for two weeks.

Treatment regimen: After a washout period of 4 weeks with gentle cleanser and a processed skin cell proteins containing day cream with SPF30+ in morning, the subjects applied the skin brightening cream twice daily to entire face after cleansing with gentle cleanser (all test products provided by Nestecite, Inc., San Francisco, CA). The application of the sunscreen was continued in morning at least 15 minutes after application of the skin brightening cream.

Evaluations: The facial skin of the subjects was evaluated by the clinical investigators before the washout period, after the washout period (week 0), and at 4, 8 and 12 week treatment with the skin brightening cream. The evaluations included: Clinical photography under standardized position and lighting conditions of the cleansed face. Assessment of the primary efficacy outcome measure mottled hyperpigmentation on a 5-point visual scale (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe), irregular depigmentation (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe), lentigines (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe), skin tone (0 = even over entire face, 1 = even over almost entire face, 2 = uneven in some areas but in less than about ¼ of face, 3 = uneven in between about ½ to ¾ of face, 4 = uneven in more than ¾ of face), skin brightness and radiance (0 = bright/brilliant over eye, 1 = bright/brilliant over entire face, 2 = bright/brilliant over majority of face, 3 = bright/brilliant areas and dull areas about equal, 4 = more dull than bright/brilliant areas, 5 = mostly dull areas, 6 = very dull) and count of small (diameter smaller than about 1/8 inch) and large (larger than about 1/8 inch) solar lentigines. Global response assessment from baseline using a 7-point scale (0 = complete response (complete resolution of photodamage), 1 = almost complete response (approximately 50% improvement), 2 = marked response (approximately 75% improvement), 3 = moderate response (approximately 50% improvement), 4 = slight response (approximately 25% improvement), 5 = no response, 6 = condition worsened). Assessment of local tolerability including erythema, burning/stinging, pruritus, dryness, peeling, itching and telangiectasia using the 4-point scale: 0 = none, 1 = mild, 2 = moderate, and 4 = severe.

RESULTS

The study was completed by 75 subjects. Two subjects were lost during the wash-out period and three subjects were lost to follow-up after starting the skin brightening cream. No subject was lost or missed a visit due to adverse events. Of the five subjects who did not complete the study, one was lost due to follow-up, two were excluded due to protocol violations, and two subjects could not meet the scheduled visits. Figure 2 illustrates the averaged results obtained by the clinical investigators. Figure 3 shows the global response assessment from baseline by the clinical investigator and Figure 3 provides clinical photography of a representative subjects before and after the 12 week treatment period.

CONCLUSIONS

The clinical study with eighty female subjects with photodamage revealed that a skin brightening cream with a complex comprising of L-leucine, sodium glycerophosphate, phenylethyl resorcinol and undecylenoyl phenylalanine was effective in improving the signs of facial skin discolorations including mottled hyperpigmentation, skin tone and appearance of solar lentigines when used together with daily sun protection. The cream was well tolerated; particularly when comparing to hydroquinone or skin brightening products with exfoliating agents. The trial included a one month wash-out period with the study sunscreen where no significant changes were observed. In a previous study in twenty females with epi- dermal melasma, the same complex was shown to reduce melasma area and severity by 43% after 12 weeks twice daily use with a sunscreen (J Cosmet Derm. 2011;10:189-196). For comparison, a 0.1% tazarotene cream resulted in improvement of mottled hyperpigmentation (by at least 1 unit) in about 70% of the subjects after 12 weeks (J Am Acad Dermatol. 2009;62:268-274) as assessed with the identical 5-point visual scoring system as used in the present study. Whilst the study was placebo-controlled, the subjects also used a sunscreen. Numerous skin brightening products contain ingredients with exfoliating properties such as glycolic acid. While exfoliation is an accepted method to help lighten skin, leave-on products with exfoliating ingredients can cause significant burning and stinging, skin irritation, peeling and dryness. In addition, repeated use of glycolic acid products makes skin more sensitive to sun, which may enhance sun induced photodamage and lead to an increase in pigmentation even in the absence of noticeable irritation.