

The efficacy of skin care products containing glutathione in delivering skin lightening in Indonesian women

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Abstract

Glutathione is a potent antioxidant, which is widely used in skin care products for skin lightening especially in the Asian market. Presently, there was only one study of topical 2% oxidized glutathione (GSSG) in Philipino women, further study is needed to evaluate the efficacy and safety of cosmetic products containing glutathione. A double blind randomized clinical trial study was conducted in Yogyakarta, Indonesia, in 74 healthy Indonesian women, with average age 33.3 ± 5.9 years when subjects participated in the study. Each subject received supervised applications of Facial Wash twice a day, Day Cream with sunscreen and Night Cream. The subjects were divided into 3 groups based on the active ingredients of the tested products, which included glutathione reduced (GSH) 0.1%, GSH 0.5%, and without GSH. The effects of the tested products in lightening skin color and pigmentation were measured colorimetry with Chromameter Minolta for L*. Compared to a baseline, there were significant increases of L* (lightness) or ΔL^* detected as early as week 2 in which group of GSH 0.1% were significantly higher compared to group of GSH 0.5% and group without GSH. Hyperpigmented lesions also improved, where GSH 0.5% group showed its superiority compared to others groups in week 8. The undesired effect were few minutes mild tingling sensation after night cream, and worsening of acne in all tested products. Conclusion skin care products containing GSH 0.1% and 0.5% were effective in facial skin lightening.

Introduction

Fair and flawless skin is a concept of beauty care especially in colored ethnic

groups. Consequently, the dream of having light colored skin becomes an exploited arena by the cosmetic industry. There are many reports of adverse events of misuse of bleaching agents for skin lightening of normal skin such as mercury, corticosteroid and hydroquinone. Moreover some countries have banned the use of hydroquinone for cosmetic purposes.^{1,2} Nevertheless, the need of gaining light colored skin apparently cannot be prevented or prohibited. One study showed despite label warnings, 2.6% of pregnant women in Sweden still recklessly using bleaching agents.³ Consequently it appears that there is a need for a lightening agent, which is safe and effective. An interesting agent is glutathione, a cysteine-glycine-glutamate tripeptide, which exerts several effects on melanogenesis through different mechanisms involving the function and cellular transport of tyrosinase.⁴ Its skin-lightening effect results from direct as well as indirect inhibition of tyrosinase enzyme and switching from eumelanin to pheomelanin production.^{5,6}

The efficacy of systemic glutathione in skin lightening had been studied currently in Thailand, Philippines and Indonesia which showed decreased of melanin indices within 2- 4 weeks,⁷⁻⁹ however there are no established long-term safety studies and the risk of potentially adverse events led to serious questioning on the use of the systemic glutathione just for temporary skin lightening.¹⁰ Topical glutathione could be used as one alternative if skin lightening is still needed. While currently products with topical GSH are abundant in the commercial cosmetic market, only one randomized clinical study of had been conducted to evaluate the efficacy and safety in Phillipino women.¹¹ Currently, according to Indonesia National Agency of Food and Drug Control, there are 68 registered cosmetics containing glutathione (GSH).¹² However there is no evidence of clinical efficacy and safety of topical GSH in Indonesia. More studies are needed to evaluate the efficacy of the developed glutathione products, especially in Indonesian women, who are currently the prevalent users of lightening skin care products. This *in vivo* study evaluated active and supportive ingredients comprehensively and simultaneously. Furthermore it provides accurate information on the product safety to the manufacturing companies, community, customers and regulatory board.

Materials and Methods

This research is a double-blind randomized controlled study. We enrolled 81

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healthy women, which have Fitzpatrick skin phototype IV, V, were aged 33.3 ± 5.9 years, with Body Mass Index 25.4 ± 5.6 .

Reasons for exclusion from the study were use of skin lightening or anti-aging products in the previous four weeks, current pregnancy, lactation, using hormonal contraceptive, intake of any medications, including supplements.

Each participant received day cream, night cream and facial wash which was applied under supervision of study officer to certify compliance. The participants were divided randomly into three groups depending on the concentration of the GSH in the skin care products, which were 0.1%, 0.5% and without GSH. All of the day cream contains octocrylene, Butyl Methoxydibenzoylmethane, Bis-ethylhexyloxyphenol Methoxyphenyl Triazine, and Titanium Dioxide with SPF 15.

Biophysical evaluations were performed at baseline data and every two weeks for a total period of 8 weeks, while safety evaluation were conducted by a trained consultant and certified Dermatologist, and confirmed with standardized digital photography. Safety assess-

ment was determined based on signs of dermatitis and acne of the face at baseline, every 2 weeks of treatment until week 8. While skin color measurements were obtained from the middle of the forehead and cheek, also from one pigmented area on the face. Reading of skin color or L^* were conducted with a Chromameter Minolta CR 200. Three readings were taken from each distinct location of normal skin from the forehead and left and right cheeks, and the averages of readings were recorded. The colorimetry was also used to measure readings from one spot of hyperpigmentation lesions.

Informed consent was obtained prior to the subjects inclusion, and the study was conducted in accordance with Declaration of Helsinki. Ethical Clearance Approval was obtained before the commencement of the study from the Medical and Health Research Ethics Committee (MREC) of the Universitas Gadjah Mada.

Results

Seventy four participants completed the 8 weeks study, since 7 subjects could not comply with the daily product application due to the distance from the study place and were considered to be drop outs from the study.

Skin lightening effects of normal facial skin

Compared to baseline there are significant percentage increases of L^* or ΔL^* of the normal non-lesional skin of the face detected at week 8 in the 2 groups who received the GSH products ($p < 0.05$), although the increase was highest with products containing GSH 0.1%, however statistically there were no significant differences of the ΔL^* between the tested groups (Figure 1).

Skin lightening effect on hyperpigmented lesions

Additionally from hyperpigmented lesions of the face (lentiginos and melasma), there was also significant increases of percentage of L^* or whitening of the lesions compared to baseline which was highest in GSH 0.5 % group ($p < 0.05$) (Figure 2).

Side effects

Mild side effects were some tingling sensation after night cream application which disappeared after a few minutes, which were 7.4% in night cream contain GSH 0.1%, 12.5% night cream contain 0.5% GSH, and 8.7% in placebo with ave-

rage 9.5% of total subjects. The development and worsening of acne were also detected in 18.5% subjects from GSH 0.1% group, 8.3% from GSH 0.5% group, and 8.7% from placebo group or average of 11.8% of the total subjects.

Discussion

All tested skin care product groups showed significant skin lightening compared to baseline, including skin care products without GSH or placebo. While the placebo using in this study was skin care product without GSH, however it contained sunscreen which was applied once a day in the morning. This result points to the importance of sun avoidance or sunscreen in any

skin lightening products to obtain the best results. However the GSH groups (0.1% and 0.05%) still showed superiority over the placebo in skin lightening, especially in hyperpigmented lesions.

The skin care products which were tested in this study were comprised of facial wash which was used twice a day before application of day cream and night cream, in which the tested combination of skin care products was intended to increase the absorption of active ingredients especially GSH.

The mechanism of GSH in skin lightening occurs through tyrosinase inhibition and also activation of the pheomelanin pathway. The effect of skin lightening is more clearly pronounced in hyperpigmented lesions, which fits with the finding that

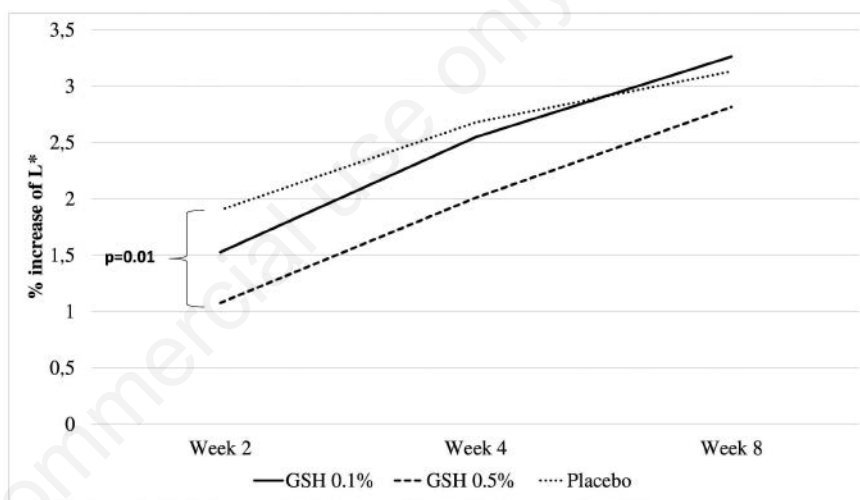


Figure 1. The increase of lightness in normal facial skin which is best after treatment at week 8 with skin care products containing GSH 0.1%.

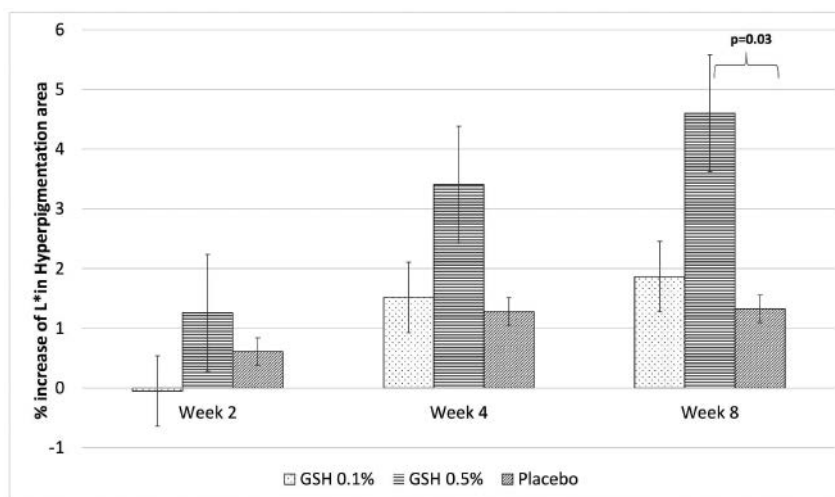


Figure 2. The increase of lightness in hyperpigmented lesion of the face which is best after treatment at week 8 with skin care products containing GSH 0.5%.

GSH affects new melanogenesis. The antioxidant properties of glutathione were shown in other study of the linolenic glutathione conjugate (lin-GSH) 2% cream. In which the application of lin-GSH before UVB irradiation showed the significant decrease of Minimal Erythematous Dose (MED), while application of the lin-GSH 2% cream after irradiation did not show any change in MED.¹³ This study showed the antioxidant properties of glutathione which its pharmacokinetic modified via acetylation with long chain polyunsaturated fatty to improve its passage through phospholipidic membranes.

One clinical study in Filipino women with topical 2% oxidized glutathione (GSSG) showed a decrease of melanin index, an increase in moisture content of the stratum corneum, suppression of wrinkle formation, and improvement in skin smoothness.¹¹ This study also showed not only skin lightening in Indonesian women, but also the reduction of, melasma, and lentiginos as signs of photoaging which is especially due to long term expose to Ultraviolet B (UVB).

Conclusions

In conclusion, the present study demonstrates the lightening effect of daily applications of a combination of day cream SPF 15, night cream and facial wash containing GSH 0.1% and GSH 0.5% in healthy Indonesian female subjects for an 8 week period, based on colorimetric assessment. Products containing GSH 0.1% were found to be significantly superior compared to products containing GSH 0.5% and products without GSH in skin lightening of normal sun exposed skin, while products con-

taining GSH 0.5% work better on hyperpigmented lesions. The worsening of acne found in all groups during the study needs further consideration in reformulating the products, especially the sunscreen used in hot humid areas of the world, since the use of sunscreen is important to achieve the best result of any lightening or anti-aging products. Nine and a half percent of subjects experienced a tolerable, mild tingling sensation during the night cream application. No other significant side effects due to the tested products were found during the study.

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