TRIPHALA WITH BROAD SPECTRUM SUNSCREEN IMPROVES MELANIN INDEX AND MELASMA SEVERITY INDEX IN FACIAL MELASMA

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ABSTRACT
Though sunscreens have been an indispensable part in treating melasma, there is, however, a paucity of data in the literature evaluating the effect of broad-spectrum sunscreen with antioxidant in its treatment. The aim of this study was to evaluate the synergistic antioxidant effect of triphala and UV protecting effect of sunscreen in facial melasma. A total of 42 patients with melasma who have routinely used sunscreen without triphala were included. The sun protection and antioxidant level of the sunscreen with triphala was evaluated. Melanin index, erythema index, Melasma Area Severity Score (MASI) and skin moisture were evaluated following the application of sunscreen once daily in the morning for 4 weeks. Mean SPF value of the sunscreen was 11.85. Mean UVAPF value was 6.89. Mean critical wavelength was 383.89 nm. DPPH (2,2-Diphenyl-1-picrylhydrazyl), ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) and FRAP (Ferric Reducing Antioxidant Power) assays of the triphala extract were 219.30, 170.40, 364.43 mg of Trolox equivalent antioxidant capacity/ml, respectively. At the highest point of cheekbone, melanin index decreased from 217 before to 190 after the treatment ($p<0.05$). The average MASI score of patients decreased by 2.2 points, falling from 5.2 at the baseline to 3.0 ($p<0.05$). However, Erythema index was not different when compared between 310 before and 317 ($p>0.05$). Skin moisture was also not different, with the level of hydration 39.7 before and 36.4 after ($p>0.05$). The triphala sunscreen can lighten skin reducing the melanin index and MASI. The triphala sunscreen could thus be considered an effective anti-melasma component.
Keywords: Triphala, Antioxidant, Sunscreen, Melasma, MASI, Melanin Index

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INTRODUCTION

Melasma is a common pigmentary disorder affecting patients with Fitzpatrick skin type III or higher. Many factors have been implicated in the etiology of this disorder, sunlight being the most important. This condition has significant psychological and emotional effects on the patients, adversely affecting the quality of life. No definitive treatment has been developed yet for its recurrence, despite new drugs being continuously being added to the armamentarium. Many treatments options such as skin lightening agents, chemical peels, and lasers have been extensively studied in the treatment of melasma. These treatment options carry their own side effects [1].

Sunscreens have been recommended in combination therapies for melasma and found to be effective. As broad-spectrum sunscreens minimize melanocyte reactivation from sun exposure, UV protection is important along with other forms of treatment. A double-blinded study comparing a broad-spectrum sunscreen agent, used concomitantly with hydroquinone in the treatment of melasma, confirmed the positive role of sun protection in the treatment of melasma overuse of hydroquinone alone. The previous study further showed that there was the improvement of MASI after 12 weeks of using sunscreen alone without hydroquinone [2].

Additional benefits against sun damage can be gained by adding antioxidants to sunscreens. Sunscreen alone decreased the level of MMP1 per area by 43%, whereas sunscreen with antioxidants diminished MMP1 production by 60% in vivo. Y. Wu et al. provide clear evidence for the potential for antioxidant to add value to a broad-spectrum sunscreen in terms of protecting against UVR-induced damage markers such as hyperpigmentation, epidermal thickening, overexpression of CKs, MMPs and CD1a, and depletion of LCs [3].

Triphala is a combination of three medicinal plants, Amalaki (Emblica officinalis), Haritaki (Terminalia chebula), and Bahera (Terminalia bellirica), and has been extensively used in Ayurveda since ancient times. Triphala extract exhibited significant free radical scavenging activity on hydrogen peroxide-induced cell damage and senescence. Triphala and its individual constituents were found to be effective in inhibiting γ-radiation induced damage in microsomal lipids and plasmid pBR322 DNA. One of the factors responsible for the biological activity of triphala is its ability to scavenge free radicals. The experiments with 2,2′-diphenyl-1-picrylhydrazyl and superoxide radicals suggest that all the extracts show ability to scavenge free radicals but Haritaki shows maximum free radical neutralizing ability both in terms of 2,2-diphenyl-1-picrylhydrazyl and superoxide radicals. Thus, the mixture is expected to possess greater activity compared with any individual components [4].

Triphala extract also exerted highly protective antiaging effects on human skin cells in vitro. Triphala extract affects gene expression of human skin cells, stimulating collagen-1 and elastin-synthesizing genes and antioxidant genes responsible for the cellular antioxidant, SOD-2. Triphala extract was found to inhibit melanin production and hyperpigmentation due to the presence of protective phytochemicals. Furthermore, the developed topical Triphala serum at the concentration of 1.0 and 5.0%w/w successfully decreased melanin content and showed no skin irritation after using topically for 30 days in healthy volunteers. These results demonstrate potential dermal antiaging effects of Triphala, such as increasing collagen and elastin, increasing cellular antioxidants, and decreasing hyperpigmentation [5].

Though sunscreens have been an indispensable part in treating melasma, there is, however, a paucity of data in the literature evaluating the effect of broad-spectrum sunscreen with antioxidant in its treatment or prevention. The aim of this study was to evaluate the synergistic antioxidant effect of topical triphala and UV protecting effect of topical sunscreen in vivo. Since melasma affects the patient's quality of life (QOL) as well, both objective and subjective tools were used for assessment. There have been no previous published studies that have assessed the synergistic effect of these two compounds in facial melasma.

RESEARCH METHODOLOGY

Single-arm, open-label, rater-blinded prospective study was conducted. Thai volunteers aged 30 o 70 both male and female with melasma on both sides of face. Forty-two volunteers, who were qualified with inclusion criteria and without the exclusion criteria, were recruited from the patients with melasma in Mae Fah Luang University hospital, Asok, Bangkok, Thailand.

Each of the 42 subjects will be asked to stop any prior sunscreen. The subjects will be treated with sunscreen plus Triphala. The proper method of measuring and application of sunscreen was demonstrated to the patients. The subjects were instructed to apply sunscreen evenly to the face using the 2-finger tips unit once a day in the morning. The subjects continued their routine gentle cleansers and moisturizers for the duration of the study, and continued to avoid brightening agents such as retinols, retinoids, hydroquinone, and non-hydroquinone lightening agents such as kojic acid and arbutin.

Objective and subjective evaluations on the degree of pigment clearance and adverse effects were obtained at baseline and 4 weeks. Skin parameters were measured at baseline and after 4 weeks of test product use by the dermatologist in a single-blinded fashion. Subjects were required to rinse their face thoroughly with a neutral lotion and acclimatized to the ambient environment for at least 15 minutes before measurements. Patient skin will be evaluated the color using melanin index parameter (Mexameter MX18®) and the moisture (Corneometer CM825®) on both upper cheeks in well-defined measurement locations. Blinded observers evaluated the degree of pigment clearance by comparing baseline photographs with post-treatment photographs. Standardized photographs were taken from the front and sides of both cheeks using a clinical imaging system (VISIA®-CR; Canfield Scientific, Parsippany, NJ). Patient satisfaction was done at 4 weeks. The same investigator did MASI and the satisfaction every time for each patient.

The SPF of the sunscreen was measured. The sunscreen was spread on an adequate substrate (PMMA) and spectrophotometric method was used to analyze the UV protection level. Sample was loaded and spread evenly onto the PMMA plate to let the sample on the plate of 1.3 mg/cm2. Then, sample loaded PMMA plate was allowed to be dried for 30 min in dark condition at 25±2 ºC before the measurement. The sample loaded PMMA plate was measured for SPF and UVAPF value by UV-2000s. The sample was prepared in triplicate and the obtained results are averaged. Standard sunscreen was used to be a reference standard in the measurement. SPF of P8 reference standard had to be in a range of 43.9-82.3.

Data analysis

All results were expressed as mean ± standard deviation. The results were compared between baseline 4 weeks using paired t test with two-tailed significance level of 5% using GraphPad Prism.

RESEARCH RESULTS

Demographic data

A total of 42 melasma patients were included in the study. Among these 25 were females and 15 were males. The female to male ratio was 5:3. The mean age of the patients was 52.6 years with standard deviation (SD) of ± 14.1 years. The minimum age in the study was 30 years, and maximum was 70 years. The demographic data are presented in Table 1. Forty-two subjects completed the study, and 1 subject withdrew for personal reasons.

Most of the patients had Fitzpatrick skin type III-IV. Among the study population, melasma affected the face only; extra- facial involvement was not noted among any study subject. The first onset of pigmentation was most reported over the cheeks in 90% followed by forehead in 10%. The color of the pigmentation noted on clinical examination was dark brown in 70%, light brown in 30%. The median duration of the disease in the studied patients was 4.0 years, ranging from 1 to 12 years.

Effect of sunscreen with triphala on facial melasma measured by Mexameter

At the highest point of cheekbone, Melanin index decreased from 217 before the treatment to 190 after one month, (p value < 0.05) using sunscreen plus triphala. However, Erythema index was not different when compared between 310 before and 317 after the 4-week treatment, (p value > 0.05) Table 2 and Figure 1-2.

Effect of sunscreen with triphala on facial melasma measured by Corneometer

Following the application of sunscreen plus triphala, skin moisture was not different, with the level of hydration 39.7 before and 36.4 after (p>0.05) 4 weeks of application. No significant differences in hydration index were observed between measurement locations (Table 2 and Figure 3).

Overall treatment efficacy of the sunscreen plus triphala in facial melasma based on MASI

A comparison of the effectiveness of treatment according to the MASI score is shown in Table 2. During the study intervals, the MASI score significantly decreased (p < 0.001) from the 4 week onwards. In general, the average MASI score of patients decreased by 2.2 points, falling from 5.2 at the baseline to 3.0 in 4 weeks (Table 2 and Figure 4). Figures 5-7 show both sides of the face of two patients before treatment and 4 weeks later.

Adverse Effects

No significant adverse effects were noted.

In vitro SPF study

In vitro SPF test is an evaluation of the sun protection factor (SPF) that expresses the sun protection level of cosmetic product to the full UV spectrum (290-400 nm). Mean SPF value of Standard P8 (Lot No: 2302G): 65.22±0.63 (43.9-82.3). Mean SPF value of sample: 11.85±1.54. Mean UVAPF value of sample: 6.89±0.85. Mean Critical wavelength (nm): 383.89±0.19.

Antioxidant activity

The antioxidant capacity of the sunscreen was measured using DPPH (2,2-Diphenyl-1-picrylhydrazyl), ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) and FRAP (Ferric Reducing Antioxidant Power) assays. DPPH 219.30 ±2.98 mg TEAC/ml, ABTS 170.40 ±0.41 mg TEAC/ml and FRAP 364.43 ±5.9 mg TEAC/ml.

Table 1 Demographic data of the study population

Age	52.6 ±14.1
Gender (n)	
Female	28
Male	14
Flitzpatrick (n)	
Type I	
Type II	
Type III	30
Type IV	12
Type V	
Duration (year)	
Median	4
Min, Max	1, 12
Distribution (N)	
Centrofacial	6
Malar	46

Table 2 Statistical analysis of effect of sunscreen plus triphala on facial melasma at 0th and 4th week

	Week 0	Week 4	Mean difference	P-value
Melanin index	217 ±55	190 ±51	-27	<0.001
Erythema index	310 ±89	317 ±85	6.8	0.28
Hydration index	39 ±13	37 ±12	-2.8	0.09
MASI	5.2 ±2.4	3.0 ±1.3	-2.1	<0.001

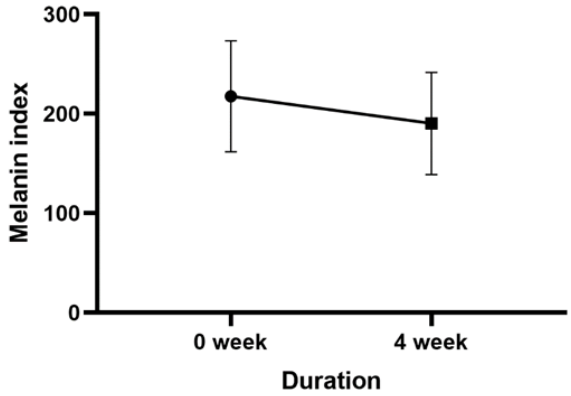

Figure 1 Linear graph showing melanin index at each visit (p<0.001)

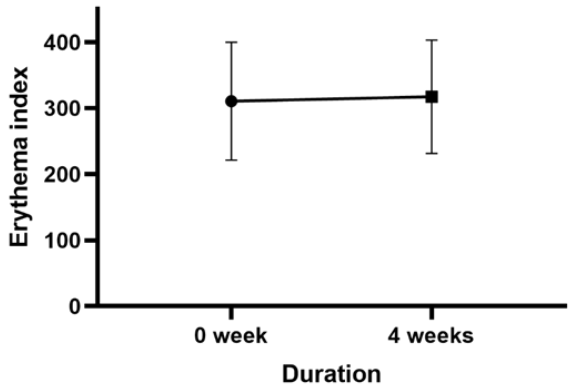

Figure 2 Linear graph showing erythema index at each visit (p = 0.28)

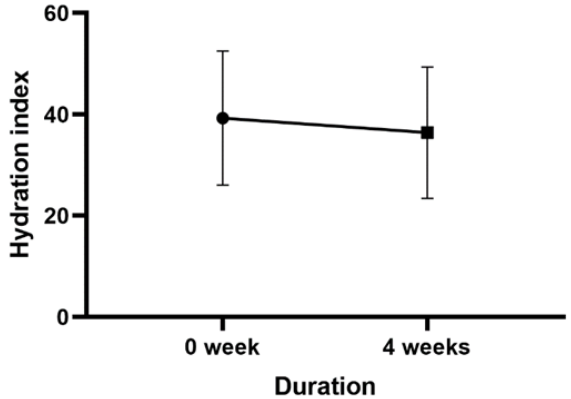

Figure 3 Linear graph showing hydration index at each visit (p = 0.09)

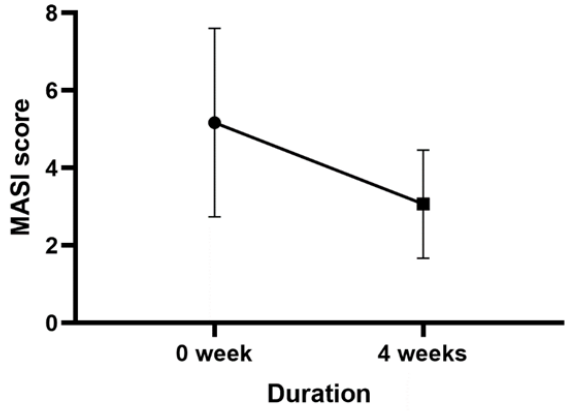

Figure 4 Linear graph showing MASI score at each visit (p<0.001)

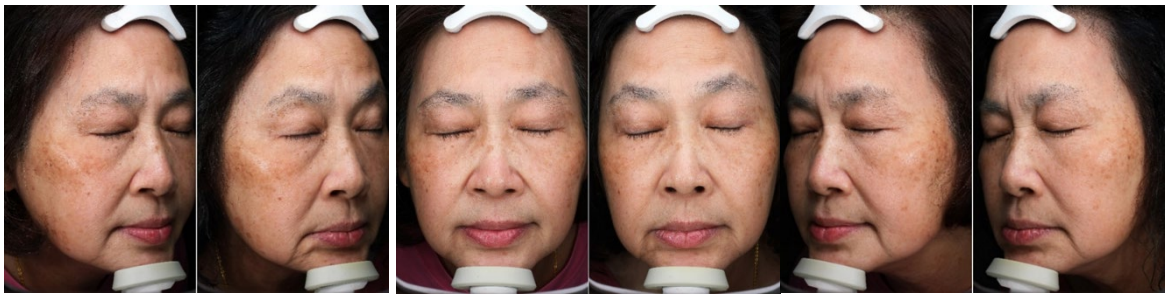

Figure 5 Diffuse pigmentation over cheek at the beginning of the study (MASI-3.6, MI = 181) and decrease in pigmentation at end of 4 weeks (MASI-2.4, MI = 136)

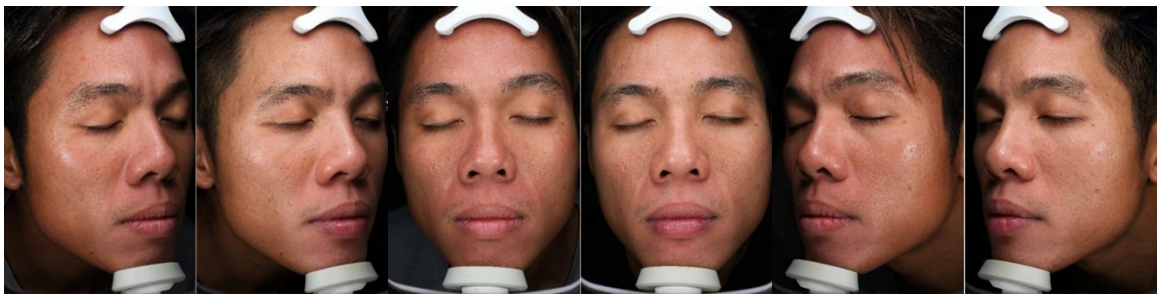

Figure 6 Diffuse pigmentation over cheek and temporal area at the beginning of the study (MASI-8.1, MI = 293) and decrease in pigmentation at end of 4 weeks (MASI-3.9, MI = 256)

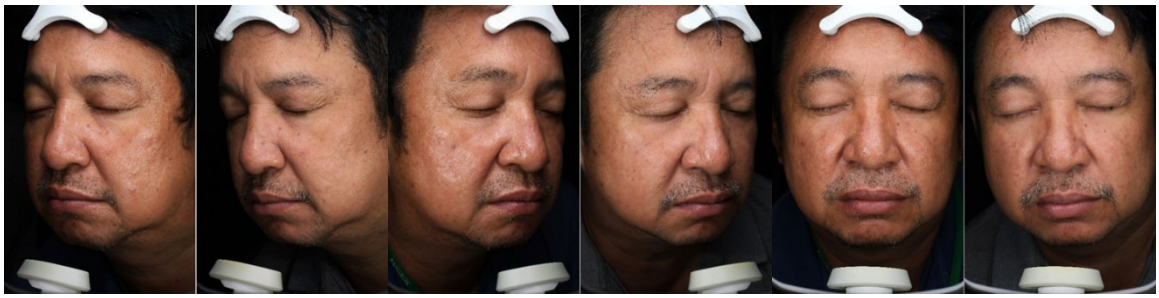

Figure 7 Diffuse pigmentation over cheek and temporal area at the beginning of the study (MASI-8.1, MI = 256) and decrease in pigmentation at end of 4 weeks (MASI-3.9, MI = 224)

DISCUSSION & CONCLUSION

Melasma is an acquired condition of the facial skin. Clinically, it commonly affects the face in a centrofacial pattern. The course of the disease is resistant to treatment and has a high recurrence rate. Darkened skin color in melasma is a result of increased and redistributed epidermal melanin. It is a familiar and well-studied response of normal skin to ultraviolet (UV) irradiation in humans. Immediate pigment darkening is caused by redistribution and oxidation of pre-existing melanin which occurs after low-dose ultraviolet A (UVA) exposure and usually fades after 2 hours. Persistent pigment darkening lasts up to 24 hours and it occurs after higher doses of UVA exposure [6].

We carried out a clinical study over a 4-weeks period on 42 participants of different ages, gender and phototypes, having applied a broad-spectrum sunscreen with triphala preparation (SPF 12, UVA-PF 7) to their face. This study demonstrated the effectiveness of this well-tolerated sunscreen preparation. These results were confirmed by the colorimetric evaluations using Mexameter, since the melanin index measuring the melanin content of the skin decreased in 74% of participants. Approximately four of five of the volunteers presented an identical or lighter complexion compared to that noted at the inclusion visit.

We used MASI scores to evaluate efficacy of a broad-spectrum sunscreen plus triphala with UVA and UVB protection for treatment of melasma. Photography was also used to assess changes in lightening before and after treatment. Studies which have substantiated the role of visible light in melasma have also used MASI as a successful tool. Another study evaluated the effectiveness of a broad-spectrum sunscreen in the prevention of melasma in Asian pregnant women and concluded that they are well tolerated and effective in the prevention of melasma. Two previous studies have also been shown that broad-spectrum sunscreen alone could improve MASI in melasma patient [7]. In our study, there was a decrease in the mean MASI in the study group at the end. This difference was statistically significant. Hence, there was an objective improvement of melasma after using sunscreens plus triphala. Hardly any of the previous studies have evaluated the role of sunscreens with antioxidant in treatment of melasma.

The treatment measures for melasma should not just aim at improving objective scores but also improve the patient's feeling of well-being and quality of life. Few studies have evaluated therapeutic efficacy of a modality in terms of improvement in quality of life and found this tool effective. Thirty-six patients rated themselves to have significant or moderate improvements after 4-week of using the sunscreen.

Excessive solar radiation on the skin induces the production of large amounts of reactive oxygen species causing direct skin tissue damage exacerbating facial melasma. We chose triphala as an antioxidant and combined it with sunscreens. We showed that the triphala sunscreen was a nonirritating product that lightened skin reducing the melanin index significantly. Therefore, triphala sunscreen could thus be considered an effective anti-melasma component.

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Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Conflicts of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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