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Novel Supplement with Phenolic Compounds for Treatment of Melasma: Double Blind Placebo Controlled Trial Safety and Efficacy Evaluation

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Abstract

Background: Melasma is a chronic skin problem that causes dark, discolored patches on the skin and therefore can have adverse effects on quality of life. Recently, a novel complex was shown to decrease melasma. Specifically, the goal of the study was to prove that the formula can reduce melasma, overall hyperpigmentation and non-transient erythema.

Objectives: The primary efficacy outcome measure was a minimum of 50% improvement of the modified melasma area and severity index (mMASI) score from the baseline at the 90 day follow-up visit. Secondary outcomes were overall hyperpigmentation score collection and analyses, patient's self-assessment regarding their non-transient erythema score when evaluated across the whole patient population at the baseline and at 90 days and the analyses of adverse events.

Methods: Forty subjects with Fitzpatrick skin types III-V were enrolled in the double-blinded, randomized, placebo controlled trial: 20 were treated over 90 days with the oral supplement and 20 received a placebo over 90 days. Subjects were assessed at onset and re-assessed at 60 and 90 days by the Modified Melasma Area and Severity Index (mMASI), photographic documentation, hyperpigmentation tool, erythema index and client satisfaction. Subjects used the product or a placebo (in tablet form) orally once a day.

Results: At 90 days, the modified melasma area and severity index score (mMASI) improved by more than 50% in 75% of cases ($p < 0.001$), thus indicating treatment efficacy. There was a greater decrease in mMASI for the supplement group vs placebo (-3.28 for the active arm vs. -0.73 for the placebo arm, $p < 0.001$). Furthermore, at the 90-day follow-up visit, the overall hyperpigmentation and non-transient erythema scores ($p < 0.001$) improved significantly: by 55% and 38%, respectively. Results obtained from patients showed overall satisfaction with the therapy course and results. The product was well tolerated, with no reports of adverse events or side effects.

Conclusion: Consistent, statistically significant reductions in melasma, as measured by mMASI scores, overall hyperpigmentation and non-transient erythema scores were achieved while meeting patient expectations at the 90 day follow-up evaluation point when compared to placebo. Results from this clinical trial suggest that this oral supplement is an effective treatment for melasma and may provide an alternative treatment for overall hyperpigmentation and non-transient erythema, while meeting expectations of patients. The product was well tolerated, with no reports of adverse events or side effects.

Keywords: Melasma; Hyperpigmentation; Erythema; Pine; Bark; Carotenoids; NanoMD

Introduction

Melasma (or chloasma) is a chronic acquired dyschromia that is distributed mostly on sun-exposed areas of the face and neck. While melasma is seen in both sexes, women are most commonly affected. The word originates from the Greek root "melas," which means black and refers to its dark clinical presentation. The pathogenesis of melasma is not fully understood. It includes genetic factors, exposure to UV radiation, hormonal contraceptives, photosensitizing drugs, inflammatory processes of the skin and stressful events [1,2].

Melasma has a profound impact on appearance; patients commonly report feelings of shame and low self-esteem and a lack of motivation

to go out. Population incidence of melasma is not precisely known; however, higher prevalence is reported among East Asians, Indian, Pakistani, Middle Eastern and Mediterranean-African populations. In the Americas, it is common in intertropical areas with greater exposure to ultraviolet radiation [3]. Sunscreen with a high protective factor may reduce the intensity of the disease in up to 50% of cases; oxidative stress plays a major role in the biological effects produced by UVA and UVB radiation [4]. The disease is triggered by pregnancy or oral contraceptives in approximately 40%-50% of female patients [5].

Current treatments involve elimination of potential causative factors and diligent use of broad-spectrum sunscreen products that regulate the pigmentation pathway. They also include external application of hypopigmenting agents (tretinoin/hydroquinones), chemical peels and laser therapy and administration of vitamin C and/or vitamin E and —

in some countries — intravenous injection of vitamin C and/or glutathiones.

Furthermore, clinical studies have documented protective effects of carotenoid phytonutrients against UVR related skin damage [6].

Recently, a product with enhanced bioavailability of monomeric phenolic compounds was clinically evaluated. Its complex addresses multiple pathways in pigmentation and UV exposure management and was shown to be safe and effective. The goal of this study was to investigate NanoMD Bright™ (Boston Sante, Inc., Boston, MA), a unique complex of monomeric phenolic compounds (pine bark extract) and specific carotenoids with bioavailability enhanced by utilizing nanotechnology for the control of melasma.

Methods

Forty subjects with Fitzpatrick skin types III-V in good general health between the ages of 22 and 59 are presented in these pages. 20 subjects used the supplement (in tablet form) orally once a day over a 12 week period, with evaluations at the baseline period, at 60 days and 90 days and 20 subjects used the placebo (in tablet form) orally once a day over a 12 week period, with evaluations at the baseline period, at 60 days and 90 days. The modified melasma area and severity index (mMASI) tool was used for evaluating melasma. Melasma was assessed by a blinded evaluator in four sections of the face (forehead, right malar, left malar and chin). The overall hyperpigmentation scale tool was used by a blinded evaluator for evaluating hyperpigmentation. Additionally, all subjects completed a questionnaire using the 5-point Likert Scale evaluating their satisfaction with the product at 90 days.

Results

Progressive improvement in melasma (clinical trial primary objective) was observed. At 60 days, the mMASI score improved by 49%, and at 90 days it improved by 57%. In the placebo group, the mMASI score improved by 10% at 60 days and 11% at 90 days. In the non-placebo treatment group, the plateau effect for these efficacy parameters was not seen at 90 days; subjects showed an 8% increase in mMASI reduction. There was a greater decrease in mMASI for the supplement group vs. placebo (-3.28 for the active arm vs. -0.73 for the placebo arm, $p < 0.001$). 38 patients completed all 3 visits, 2 subjects withdrew after the first visit. The primary efficacy outcome measure was met, with subjects showing a 57% average decrease in mMASI after 90 of treatment (Table 1) (Figures 1,2).

Arm		Change in mMASI (60 Days - Baseline) $p < 0.001$	Change in mMASI (90 Days - Baseline) $p < 0.001$
Active	N	20	20
	Mean	-2.81	-3.28
	Std. Deviation	2.1	2.5
	Minimum	-6.4	-6.9
	Maximum	0.9	1.8
	Median	-3	-3.6
Placebo	N	18	18

Mean	-0.65	-0.73
Std. Deviation	3.12	2.96
Minimum	-4.2	-4.2
Maximum	1.5	1.2
Median	0	-0.6

Table 1: Comparison of mMASI score between active and placebo group.

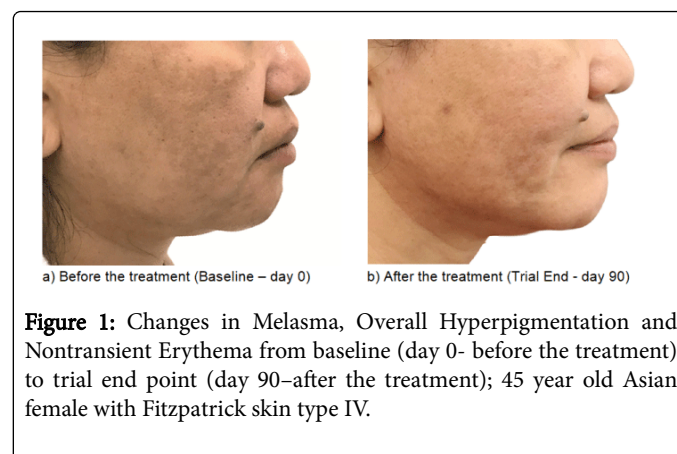


Figure 1: Changes in Melasma, Overall Hyperpigmentation and Nontransient Erythema from baseline (day 0- before the treatment) to trial end point (day 90-after the treatment); 45 year old Asian female with Fitzpatrick skin type IV.

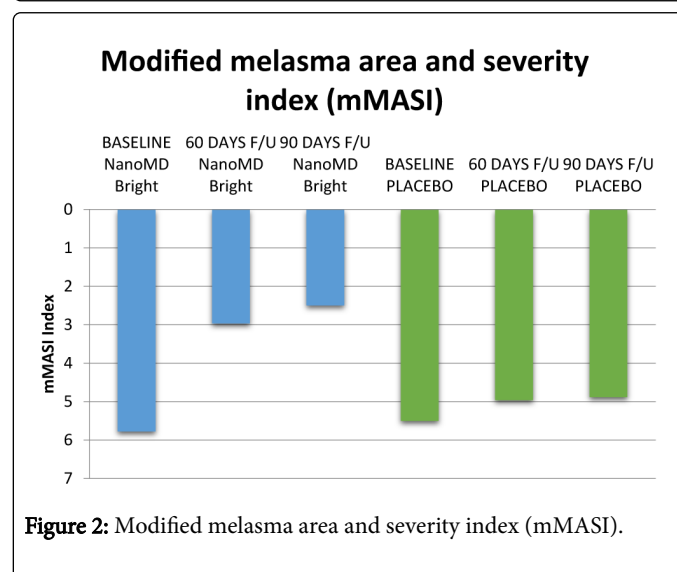
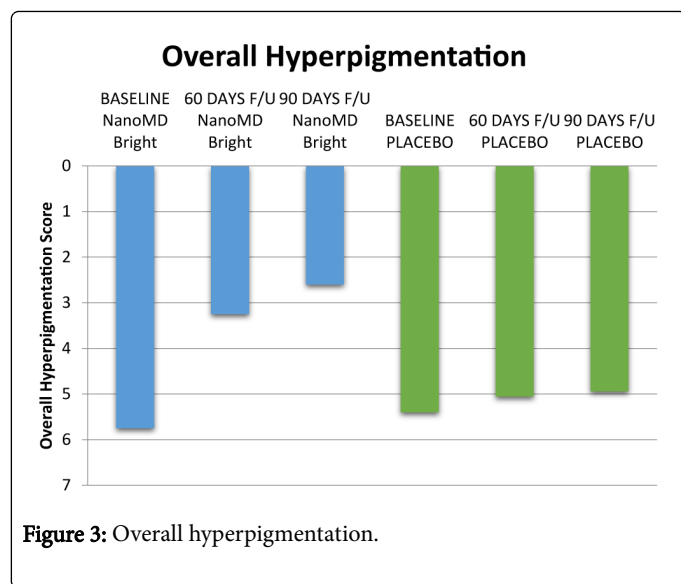


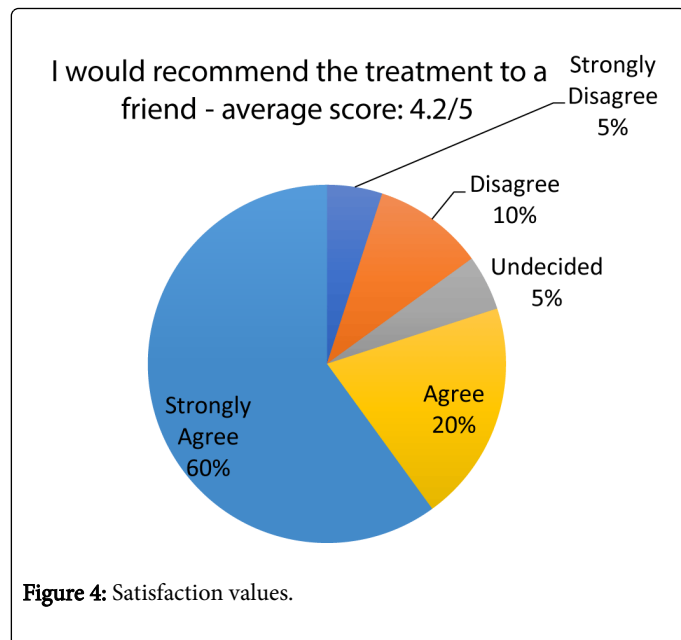
Figure 2: Modified melasma area and severity index (mMASI).

Regarding trial secondary objectives, progressive improvement in hyperpigmentation was observed. At 60 days, the overall hyperpigmentation score improved by 43% and at 90 days it improved significantly ($p < 0.001$) — by 55%. In the placebo group, the overall hyperpigmentation score improved by 6% at 60 days and 8% at 90 days. In the non-placebo treatment group, the plateau effect for these efficacy parameters was not seen at 90 days; subjects showed a 12% increase in overall hyperpigmentation score reduction (Figure 3).



Improvement in the non-transient erythema score was observed. At 90 days, the non-transient erythema score significantly ($p < 0.001$) improved — by 38%. In the placebo group, the non-transient erythema score improved by 9%. Furthermore, 90% of subjects self-reported overall satisfaction, with 80% of subjects reporting they would recommend the treatment to a friend.

The product was well-tolerated, with no reports of adverse effects (Figure 4).



Discussion

There are several treatments available to control melasma. Results from this study suggest that this oral supplement is effective in treatment and management of melasma. An optimal supply of antioxidant micronutrients ensures an increased basal dermal defence against UV irradiation and contributes towards long-term protection and maintenance of skin health [6,7]. The study provides a strong rationale for the use of product that use a complex of monomeric phenolic compounds and selected carotenoids enhanced by nanotechnology for the control of melasma and suggest such products may provide an alternative treatment for overall hyperpigmentation and non-transient erythema.

Conclusion

Consistent, statistically significant reductions in melasma, as measured by mMASI scores, overall hyperpigmentation and nontransient erythema scores were achieved while meeting patient expectations at the 90 day follow-up evaluation point when compared to placebo. The product was well-tolerated, with no reports of adverse events or side effects.

References

1. Elling SV, Powell FC (1997) Physiological changes in the skin during pregnancy. *Clin Dermatol* 15: 35-43.
2. Wolf R, Wolf D, Tamir A, Politi Y (1991) Melasma: A mask of stress. *Br J Dermatol* 125: 192-192.
3. Taylor SC (2003) Epidemiology of skin diseases in ethnic populations. *Dermatol Clin* 21: 601-607.
4. Miot HA, Miot LDB (2009) Topical 10% Zinc sulfate solution for treatment of melasma. *Dermatol Surg* 35: 2050-2051.
5. Handel AC, Miot LDB, Miot HA (2014) Melasma: A clinical and epidemiological review. *An Bras Dermatol* 89: 771-782.
6. Sies H, Stahl W (2004) Nutritional protection against skin damage from sunlight. *Annu Rev Nutr* 24: 173-200.
7. Aust O, Stahl W, Sies H, Tronnier H, Heinrich U (2005) Supplementation with tomato-based products increases lycopene, phytofluene, and phytoene levels in human serum and protects against UV-light-induced erythema. *Int J Vitam Nutr Res* 75: 54-60.